# Prevalence of positive TST among Healthcare workers in high-burden TB setting in Peru

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# Abstract

**Background:** Tuberculosis (TB) transmission has long been recognized as an important occupational hazard for healthcare workers (HCWs). HCWs possess a 5.8% annual risk of exposure and three times greater risk of developing active TB than the general population.

**Methods:** We conducted an observational cross-sectional study between September 2014 and March 2015 among HCWs in a high-burden TB setting in Lima to estimate the prevalence of positive Tuberculin Skin Test (TST) and to investigate factors associated with a positive TST.

**Results:** 240 participants were included in the analysis; TST was administered to 190 (79.2%) while the rest were exempt due to a previous positive TST result, history of TB or refused the test. A positive TST result was found among 56.2% of participants who were applied the TST (95% CI: 49.22% - 63.55%). When considering those who had a previous positive TST result and those with a history of TB, the prevalence was 64.3% (95% CI: 57.8% - 70.3%). No significant differences were observed between clinical/paramedical and administrative staff in the health center. The use of N95 mask during work hours was reported by 142 (69.9%) participants. Prevalence ratios (PR) show that workers with more than 120 months as a HCW were 1.44 times more likely to be TST positive. The multivariate analysis found that HCWs with over 10 years of service were 1.52 times more likely to be TST positive.

**Conclusion:** This study supports previous reports that TB infection is an occupational hazard for HCWs. Prevention of TB transmission through control measures, as well as timely diagnosis of LTBI in this selected risk group, is critical for the individual and for public health.


# Background

According to the World Health Organization (WHO), approximately one-quarter of the world's population is estimated to have latent tuberculosis infection (LTBI) [1]. This constitutes a major challenge for tuberculosis (TB) control due to the lifetime risk of developing active TB disease, which is estimated to be 5–10%, most of which occur within the first five years after the initial infection [2]. LTBI can be effectively treated to reduce the risk of progression to active TB by 60 to 90% [3].

TB transmission has long been recognized as an important occupation hazard for healthcare workers (HCWs), with a 5.8% median annual risk attributable to TB exposure [4, 5]. WHO guidelines recommend systematic screening for TB in at-risk populations including HCWs, prisoners and immigrants from high-burden countries [3]. Traditionally, tuberculin skin testing (TST) has been used as a cheap and widely-used diagnostic test for LTBI, but recently, interferon-gamma release assays (IGRA) have emerged as an alternative providing higher specificity though at a higher cost [6]. A recent systematic review estimates that the prevalence of LTBI in HCWs measured by TST is 51% [7], while another concluded that, when compared to the general population, the risk of LTBI was 2.27 times greater for HCWs [8].

In 2015, around 31,000 new cases of TB were registered in Peru; Lima and Callao notified 59.3% of these cases [9], therefore, HCWs working in these areas are exposed to more than half of the country's TB burden. LTBI prevalence in HCWs has been previously explored in Callao, showing 56% of IGRA-positive results [10]. Such studies have not been performed in San Juan de Lurigancho (SJL), a district of Lima which possesses one of the highest numbers of TB cases reported among other districts [11]**.** The main objective of this study is to determine the prevalence of LTBI based on TST positive result in HCWs at SJL health centers and identify factors associated with a positive TST result.

# Methods

### Study design

We conducted a cross-sectional observational study between September 2014 and March 2015 in health centers in SJL; these provide primary care for almost a million people in the district.

### Setting and participants

At present, no studies have addressed community LTBI prevalence in Peru despite its high rate of TB cases compared to other Latin American countries; in the last years, approximately 120 new cases per 100,000 inhabitants have been reported [1]. During this period, the incidence rate of TB among HCWs decreased from 215 cases in 2011 to 126 cases in 2015 [9]. There are approximately 660 HCWs distributed throughout 34 health centers in SJL; the study population included workers from 13 of these health centers. HCWs were defined as a paid worker employed by an institution whose primary intent is to improve health [12]; they were required to be 18 years of age or older and be employed by the health center for the past 3 months. Participants were enrolled through convenience sampling.

Tuberculin for TST administration were provided by the Peruvian Center for Disease Control and Prevention for surveillance of SJL and study conduction. All participants were interviewed before TST administration; TST was not applied to workers who reported a history of TB, a previous positive TST or declined the procedure. A case report form included information on demographic and occupational characteristics,

history of TB, previous TST results, risk factors for TB, comorbidities including HIV, and previous screening procedures for active and latent TB infection.

### Sample size

For the sample size calculation, an error margin of 0.05 and a prevalence of LTBI of 54% among HCWs were considered [13]. A sample size of 243 participants (95%CI, 49 - 59) was established in a population of 660 HCWs in SJL.

### TSTprocedure

We performed a single-step TST using 0.1 ml [5 international units (IU)] tuberculin (Tubersol®), administered using the Mantoux method [14]. Skin reactions were read 48 to 72 hours after TST placement by research staff. Self-reporting of results was not allowed. We considered a TST induration size of ≥ 10mm as positive and a TST reaction of ≥ 5mm in HIV-infected persons [15]. All TST-positive HCWs were advised to have close follow-up for the development of any active TB symptoms.

### Statistical analyses

Obtained data was entered into an electronic database on Excel XP (Microsoft, US). Descriptive analysis with frequencies and percentages was obtained. Participants were divided into two groups: TST-positive and TST-negative. TST-positive included participants with a history of TB, previous positive TST result, or participants with a positive TST applied during this study; TST-negative included participants with a negative TST result. The bivariate analysis was performed using Poisson regression with robust variance to calculate prevalence ratio (PR); the multivariate analysis was performed using variables from the bivariate analysis that were significant ($p<0.05$) or known factors such as having a household TB contact, being overweight and not using N95 mask. Stata SE 15.1 (StataCorp, US) was used for data analysis.

## Results

We enrolled 240 participants in the study and all completed the interview. Among the 190 (79.2%) participants who were applied the TST, six did not return for the TST-result reading appointment (Response rate: 96.8%). The remaining 50 (20.8%) participants were exempt from TST application because 26 (10.8%) had a previous positive TST result, 14 (5.8%) had a history of TB and 10 (4.2%) refused TST application **(Figure 1).**

Most of the participants were female (80.8%) and the average age was 41.9 years (Min: 21, Max: 68). The median time working as a HCW was 120 months (IQR: 48-240) and working on the health center was 48 months (IQR: 17-168). Most participants were employed as clinical staff (47.1%), followed by administrative (20.4%) and paramedical staff (13.7%) **(Table 1).**

Regarding biosafety, 205 (85.4%) HCWs provided treatment and care to TB patients. The use of N95 masks during work hours was reported by 142 (69.9%) participants, however, only 48 (31.4%) use it always **(Table 2).** Concerning active tuberculosis screening, we found that routine sputum sample and chest radiograph was done in 99 (41.3%) and 128 (53.3%) participants, respectively. Over the last year, 59 participants (24.6%) presented cough for more than 2 weeks, and the actions taken are described in **Table 3.** As part of the latent TB screening workup, half of our participants (124) had a TST during the last year. Most participants (85.2%) who were applied the TST agreed to take Isoniazid preventive therapy (IPT) if the result was positive.

We found a positive TST result in 56.5% of participants (95% CI: 49.2% - 63.5%). The mean size of the induration was 17.2 mm (SD = 5.1) and 1.6 mm (SD = 2.8) when the TST results were positive and negative, respectively. The prevalence of a positive TST result among HCWs was 64.3% (95% CI: 57.8% - 70.3%) which included participants with previous positive TST results or a history of TB. **Table 4** shows that time working as a HCW (95%CI 146.10 - 186.86) and time working on the health center (95%CI 97.28 - 139.88) were associated with a positive TST result. Age was also associated with a positive TST result (95% CI 41.55 - 44.88). No significant differences were observed between clinical/paramedical and administrative staff in the health center.

In the bivariate analysis, the PRs show that workers with more than 120 months as a HCW were 1.44 times more likely to be TST positive. Being overweight, having reported a household TB contact and not using N95 masks were not significantly associated with a positive TST result. In the multivariate analysis, HCWs with over 10 years of service were 1.52 times more likely to be TST positive when compared to the factors used in the bivariate analysis that albeit non-significant we consider to be important determinant factors for a TST positive result (**Table 5).** Age and time working on the health center were not included in the univariate or multivariate analysis since they are closely related to time working as a HCWs, which is more specific for TB exposure.

## Discussion

Our study documented that 56.5% of the 184 health workers had a positive TST result reading; the prevalence rises to 64.3% when we include workers with previous positive TST results and a history of active TB disease. Both estimates are within the range expected for HCWs in low-income countries (33%) and middle-income countries (79%) [13]. Recent systematic reviews have found a prevalence of 49% and 37% with a mean incidence rate of active TB of 97 new cases per 100,000 HCWs [7, 8]. Our result is also slightly over the prevalence of 56% reported in a study among HCWs in Callao using IGRA [10]. These rates depict HCWs as a population at risk of developing active TB, since more than half of them are diagnosed with LTBI.

Similar to our study, *Soto-Cabezas et al.* in Peru, found a significant association between age and time working as a HCW with LTBI [10]. Likewise, *Rafiza et al.* in Malaysia found an increased prevalence of LTBI in employees with more than 11 years of work (OR: 3.48) and *Pai et al.* in India found an association with 10 or more years on the job, presenting a three-fold increase prevalence to those employed less than a year [16, 17]. An active TB patient with smear-positive sputum will infect on average between 10 to 15 people every year [18]; since most people will go to health care centers as their first point of contact regarding diagnosis, treatment, and monitoring of TB, it should come as no surprise that the longer time of employment on this health care setting could reflect repetitive exposure to *M. tuberculosis*. A study found a 10% probability of progression to active disease within a year for single exposure; furthermore, they established a greater probability of progression among individuals with 18 or more exposures [19].

We compared clinical and laboratory staff, whom we considered being a group of high-risk for transmission, against administrative workers and, although time spent with TB patients has been shown to be a risk factor [7, 13, 20, 21], our analysis did not find an association with LTBI. Additionally, health centers are bound to limited space with common waiting areas and most rooms are in near proximity to the area assigned for daily TB treatment, thus, TB exposure may be comparable between staff unlike in other settings such as large hospitals. Occupational differences in TST results prove difficult under these circumstances, in contrast to what has been found elsewhere [7]. Regardless of their occupation, the lack of association may be due to the staff's exposure to the high prevalence of TB outside the health center or due to a household contact; moreover, TB infection may have occurred as children or TST positivity may be due to BCG universal vaccination at birth provided in Peru. Most of our participants were women, which is often the case in the healthcare setting as women constitute more than half of the healthcare workforce [12]. We found no association between gender and TST results.

The implementation of TB transmission control measures such as natural ventilation, a supply of N95 masks and routine screening, is essential to protect HCWs and may decrease annual TB incidence by as much as 49%, 27%, and 81% in countries with low, intermediate, and high TB incidence, respectively [22]. A risk assessment of obstacles in using N95 masks among HCWs ranked heat around the face and inaccessibility to masks as the main reasons for not wearing protective gear [23]. Our study found that 60.3% of HCWs did not wear N95 masks because the health center failed to provide them with the masks; this is a flaw in TB control which must be avoided in all settings, especially in a country with high TB incidence. Nonetheless, HCWs usually only wear masks when dealing with known TB cases, however, it is not common practice to continuously wear masks, therefore, transmission in healthcare facilities may be due to undiagnosed cases [24].

Only half of our participants had previous active TB screening during the last year; although these were standardized screening procedures by their place of work, we can see how the health center is unable to ensure TB screening for all its workers and some of them may have to access these tests out of pocket. Furthermore, considering the high LTBI prevalence found in our study, it seems unlikely that only 26 participants were exempt from TST application due to a previous positive TST result. It is likely that HCWs overreported having been tested in the last year, instead of underreporting a positive TST. In Portugal, from a sample size of 2015 registered physicians and nurses, a survey reported that 784 (39.5%) were never screened and, of these, 741 (94.5%) were never offered screening [25]. Moreover, in China, where no policy on medical TB surveillance among HCWs has been implemented, a large study identified 124 HCWs with presumptive active TB while noting that the screening methods and framework used is not yet optimal for the high-burden of TB in the country [26]. Establishing screening procedures for this high-risk population should be ensured either as routine or post-exposure to contribute to occupational health.

Even though 85.2% of participants agreed to take IPT if their result was positive, some refused the prophylaxis due to lack of knowledge including possible adverse events and immunological reactions or a belief of long-lasting immunity against TB. Although standards of TB care in Peru dictate that IPT must be administered to health workers and people attending prisoners, with a recent TST conversion after ruling out active TB [27], studies found acceptance rates for chemoprophylaxis amongst HCWs between 65-84% in low-prevalence settings [28, 29]. However, the use of IPT is debatable in settings of high rates of MDR-TB cases, as in Peru [1], which could explain why HCWs refuse the prophylaxis and prefer close monitoring of TB symptoms for at least two years, as per WHO recommendations [3]. Education and close monitoring of active TB symptoms must be provided for all HCWs, not only those who are TST positive.

Finally, some limitations must be recognized. Recall bias may have affected the participant's responses to previous indentation or results for TST or whether or not they presented with a confirmed case of active TB. An important confounding factor is that we were not able to obtain a full picture of the participants before entering the health system for work: exposure to TB could have occurred before working as a HCW, especially if they lived in SJL or another high-burden area in Lima. This also includes reliable information on BCG vaccination. Self-reported use

of N95 masks is not reliable as HCWs may feel compelled to overreport its use; additionally, the reported frequency of use is not quantitatively stated and, therefore, is open to interpretation by the HCWs completing the questionnaire. Other important variables were not significant in the multivariable analysis; this may be because the power of the study is less than needed to detect association due to the sample size.

## Conclusion

This study supports previous reports that TB infection is an occupational hazard for HCWs. Although we were not able to identify specific areas in the health center where workers are more likely to be exposed, it is prudent to say that measures of TB control should be instituted throughout the health center, especially considering the potential reduction of TB incidence. The high prevalence of LTBI and the risk for active disease emphasize the need for these measures and regular screening. Prevention of active TB, as well as timely diagnosis of LTBI in this selected risk group, is critical for the individual and for public health.

## Declarations

### Ethics approval and consent to participate

The study was approved by the Institutional Ethics Committee of *Universidad Peruana Cayetano Heredia* (SIDISI: 60644) and the project implementation was authorized by local authorities. All participants signed an informed consent form before the interview and the TST procedure. Participant's records/information was anonymized and entered into a secure database prior to analysis.

### Consent for publication

Not applicable

### Availability of data and materials

All data generated or analyzed during this study is available upon reasonable demand to the corresponding author.

### Competing interests

The authors declare no conflict of interest.

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### Author's contributions

All authors made substantial contributions to the manuscript. All have read and approved the final version.

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## Tables

**Table 1.** Demographic characteristics of HCWs.

| Characteristic (n = 240) | |
|---|---|
| **Age, years, mean (SD)** | 41.9 (11.2) |
| **Female gender** | 194 (80.8) |
| **BMI, kg/m$^2$, median (IQR)** | 25.9 (5) |
| **District of residence** | |
| SJL | 135 (56.3) |
| Others | 105 (43.8) |
| **Time of residency on SJL, years, median (IQR)** | 25 (21.7) |
| **Time working as HCW, months, median (IQR)** | 120 (192) |
| **Time working on Health Center, months, median (IQR)** | 48 (151.5) |
| **Occupation** | |
| **Clinical staff** | |
| Physician | 22 (9.2) |
| Nurse | 31 (12.9) |
| Nursing technician | 48 (20) |
| Obstetrician | 12 (5) |
| **Paramedical staff** | |
| Laboratory technician | 17 (7.1) |
| Psychologist | 11 (4.6) |
| Nutritionist | 5 (2.1) |
| **Support staff** | |
| Social worker | 6 (2.5) |
| **Administrative staff** | 49 (20.4) |
| **Other staff** | 39 (16.2) |
| **Underlying disease** | |
| HIV | 1 (0.4) |
| DM | 9 (3.8) |
| HTN | 14 (5.8) |
| Asthma | 9 (3.7) |
| Gastritis | 8 (3.3) |
| Cancer | 3 (1.2) |
| Other | 25 (10.4) |

*Values are n (%) unless noted otherwise. HCW: Healthcare worker. SD: Standard deviation. BMI: Body mass index. IQR: Interquartile range. SJL: San Juan de Lurigancho. HIV: Human immunodeficiency virus. DM: Diabetes mellitus. HTN: Hypertension.*

**Table 2.** Tuberculosis exposure and workplace biosafety.

| Characteristic (n = 240) | |
|---|---|
| **Directly attend patients** | |
| Yes | 205 (85.4) |
| **Use of N95 mask (n = 203)** | |
| Always | 44 (21.7) |
| Almost always | 49 (24.1) |
| Sometimes | 47 (23.2) |
| Never | 63 (31.0) |
| **Reason for not using N95 mask (n = 63)** | |
| They are uncomfortable | 11 (17.4) |
| Masks not provided by health center | 38 (60.3) |
| Does not want to use it | 1 (1.6) |
| Other | 15 (23.8) |
| **TB household contact (n = 72)** | |
| Yes | 22 (30.5) |
| **Received IPT because of TB household contact (n = 22)** | |
| Yes | 5 (22.7) |

*Values are n (%). TB: Tuberculosis. IPT: Isoniazid preventive therapy.*

**Table 3.** Active and latent tuberculosis screening among HCWs.

| Characteristic (n = 240) | |
|---|---|
| **Routine sputum sample during the last year** | |
| Yes | 99 (41.3) |
| **Chest radiography during the last year** | |
| Yes | 128 (53.3) |
| **Routine TST during the last year** | |
| Yes | 124 (51.7) |
| **Cough for more than 2 weeks during the last year** | |
| Yes | 59 (24.6) |
| **Action taken (n = 59)** | |
| Consult with physician | 18 (30.5) |
| Sputum smear | 9 (15.3) |
| Sputum smear + Chest X-Ray | 10 (16.9) |
| Attributed to underlying disease | 10 (16.9) |
| Self-medicated | 7 (11.9) |
| None | 5 (8.5) |

Values are *n* (%). TST: Tuberculin skin test. IPT: Isoniazid preventive therapy.

**Table 4.** Comparison between TST positive and negative groups.

| Variables | TST negative (n = 80) | TST positive (n = 144) | PR | P value |
|---|---|---|---|---|
| **Gender** | | | | |
| Female | 68 (85) | 117 (81.2) | 1.09 | 0.45 |
| **District of residency** | | | | |
| SJL | 45 (56.2) | 81 (56.2) | 1.00 | 1.0 |
| **Use of N95 mask** | | | | |
| Yes | 44 (55) | 85 (59) | 0.88 | 0.3 |
| **TB household contact** | | | | |
| Yes | 17 (21.2) | 32 (22.2) | 1.18 | 0.22 |
| **Cough > 15 days during the last year** | | | | |
| Yes | 18 (22.5) | 36 (25) | 1.05 | 0.43 |
| **BMI** | | | | |
| < 25 | 32 (40) | 58 (40.3) | 0.99 | 0.97 |
| ≥ 25 | 48 (60) | 86 (59.7) | Ref. | |
| **Occupation** | | | | |
| Clinical/paramedical staff | 48 (60) | 88 (61.1) | 0.86 | 0.25 |
| Administrative | 17 (21.2) | 32 (22.2) | Ref. | |
| **Age, years, median (SD)** | 38.3 (12.47) | 43.2 (10.11) | 1.01 | 0.004 |
| **Time working as health worker, months, mean (SD)** | 118.2 (122.2) | 166.5 (123.7) | 1.00 | 0.005 |
| **Time working on health center, months, mean (SD)** | 73.7 (99.9) | 118.6 (129.4) | 1.00 | 0.001 |

*Values are n (%) unless noted otherwise. TST: Tuberculin skin test. PR: Prevalence ratios. SJL: San Juan de Lurigancho. TB: Tuberculosis. BMI: Body mass index.*
*TST negative: Participants with negative TST result. TST positive: Participants with positive TST, previous positive TST and history of TB.*
*Chi-squared test used for categorical variables. Student's t-test used when means are displayed.*

**Table 5.** Factors associated with TST positive result.

| Variables | PR (Bivariate analysis) | 95% CI | PR (Multivariate analysis) | 95% CI | P value |
|---|---|---|---|---|---|
| Overweight (BMI > 25) | 0.99 | 0.81 – 1.21 | 0.99 | 0.80 – 1.23 | 0.94 |
| Household TB contacts | 1.18 | 0.90 – 1.56 | 1.02 | 0.73 – 1.42 | 0.90 |
| Not using N95 mask | 1.13 | 0.89 – 1.45 | 1.08 | 0.85 – 1.38 | 0.54 |
| Time working as HCW (> 120 months) | 1.44 | 1.16 – 1.77 | 1.52 | 1.19 – 1.95 | 0.001 |

*PR: Prevalence ratio. BMI: Body Mass Index. TB: Tuberculosis. HCW: Healthcare worker.*

## Figures

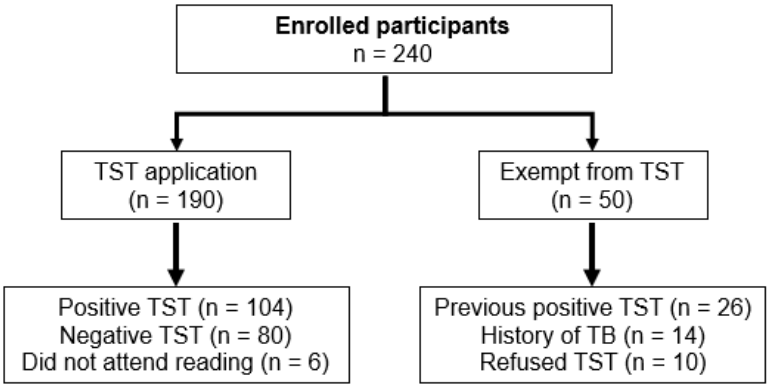


**Figure 1**

Flow diagram of participants in the study.