# Prevalence of tuberculosis skin test positivity among healthcare workers: results of an observational study

## *Prevalenza della positività al test cutaneo per la tubercolosi tra gli operatori sanitari: risultati di uno studio osservazionale*

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**ABSTRACT**

*Background*. Tuberculosis is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. Healthcare workers (HCWs) are at risk of becoming infected and, in turn, becoming contagious. The aim of our study was to assess the prevalence of latent tuberculosis infection (LTBI) among HCWs and to identify associated factors, with the goal of defining the specific residual risk within work environments.

*Methods*. The data from the health surveillance of HCWs between January 2017 and January 2020 were collected at the Policlinico Umberto I Hospital in Rome and used to assess the prevalence of LTBI through purified protein derivative (PPD) and interferon-gamma release assay (IGRA) tests (QuantiFERON®-TB Gold).

*Results*. Out of 3,102 HCWs, the PPD was positive in 431 subjects (13.9%); however, out of 479 operators undergoing TB Gold, 42.8% were positive. The risk of testing positive for LTBI increased with age, particularly in the nursing profession and, in subjects over 50, among technicians.

*Conclusions*. Our study identified a relatively high prevalence of LTBI, confirming that the risk among HCWs is higher than in the general population. Furthermore, the PPD test, despite having low specificity, can be considered a first-level screening tool in Italian hospitals, with positive results requiring confirmation by IGRA tests.

**Key words:** screening, Mantoux, QuantiFERON®-TB Gold, latent infection..

**RIASSUNTO**

*Contesto*. La tubercolosi è una malattia infettiva causata dal bacillo *Mycobacterium tuberculosis*. Gli operatori sanitari (OS) sono a rischio di contrarre l'infezione e, a loro volta, di diventare contagiosi. L'obiettivo del nostro studio è stato quello di valutare la prevalenza dell'infezione tubercolare latente (ITBL) tra gli OS e i fattori ad essa associati, al fine di determinare il rischio residuo specifico negli ambienti di lavoro.

*Metodi*. I dati della sorveglianza sanitaria degli OS sono stati raccolti presso il Policlinico Umberto I di Roma, nel periodo compreso tra gennaio 2017 e gennaio 2020, e utilizzati per valutare la prevalenza dell'ITBL attraverso i test PPD (derivato proteico purificato) e IGRA (*interferon-gamma release assay*, QuantiFERON®-TB Gold).

*Risultati*. Su 3,102 OS, il test PPD è risultato positivo in 431 soggetti (13.9%); tuttavia, tra i 479 operatori sottoposti al test TB Gold, la positività è salita al 42.8%. Il rischio di positività all'ITBL è risultato aumentare con l'età, in particolare nella professione infermieristica e, nei soggetti sopra i 50 anni, tra i tecnici.

*Conclusioni*. Il nostro studio ha evidenziato una prevalenza relativamente alta di ITBL, confermando che il rischio di positività tra gli OS è superiore rispetto a quello riscontrato nella popolazione generale. Inoltre, il test PPD, nonostante la bassa specificità, può essere considerato uno strumento di screening di primo livello negli ospedali italiani, i cui risultati positivi dovrebbero essere confermati tramite test IGRA.

**Parole chiave:** screening, Mantoux, QuantiFERON®-TB Gold, infezione latente.

## Introduction

Tuberculosis (TB) is an airborne disease caused by the bacillus *Mycobacterium tuberculosis*. It typically affects the lungs but can also affect other sites, and it has three phases: primary infection, latent infection, and active infection.

Globally, in 2018, 10 million people (132 cases per 100,000 inhabitants) fell ill with TB. Most of the estimated cases occurred in the World Health Organization (WHO) Southeast Asia region (44%), the African region (24%), and the Western Pacific region (18%); lower rates of cases occurred in the Eastern Mediterranean (8.1%), the Americas (2.9%), and the WHO European regions.[1]

Transmission occurs in the case of active pulmonary TB with a high bacterial load, particularly in the absence of specific therapy and adequate air exchange. Most primary infections (approximately 95%) are asymptomatic and are followed by a latent infection.[2] Nevertheless, timely diagnosis is crucial for initiating targeted antibiotic therapy, especially as extensively drug-resistant strains of TB (XDR-TB) pose a serious threat to public health, in particular in settings that lack adequate infection control measures.[3]

In 2022, 41 experts active in the field of TB participated in a clinical standard aimed at guiding the assessment and management of TB infection and the implementation of TB preventive therapy. After rounds of revision, eight clinical standards were defined. This document guides clinicians, program managers, and public health officers in planning and implementing adequate measures to assess and manage tuberculosis infections.[4]

Transmission of TB in healthcare settings is a major clinical and public health problem.[5,6] Healthcare workers (HCWs) at the highest risk engage directly with individuals with active infections. The introduction of TB transmission control measures can reduce the annual incidence of TB up to 49%, 27%, and

81% in countries with low, intermediate, and high TB incidence, respectively.[7]

The activities necessary to achieve the control of TB, in order of importance, are i) pharmacological treatment; ii) management of patients with active TB; iii) identification, surveillance, and preventive treatment of high-risk groups (contacts of TB cases, people with HIV); iv) vaccination with Bacillus Calmette-Guérin (BCG); v) epidemiological surveillance; and vi) evaluation of control programs.[8]

In low-incidence epidemiological contexts such as Italy, the control of TB disease occurs through the prevention of transmission by contagious subjects and the prevention of the progression of latent TB infection (LTBI) to active TB.[9] Several studies have reported various incidence and prevalence rates of LTBI and TB in HCWs over the years. Frequent exposure to patients with contagious tuberculosis, as well as the performance of certain high-risk procedures in healthcare settings, places HCWs at a significantly higher risk of contracting LTBI compared to the general population.[10]

In this study, we assessed the prevalence of LTBI in HCWs and associated factors, such as age, gender, job, and department, using purified protein derivative (PPD) and interferon-gamma release assay (IGRA) tests (QuantiFERON®-TB Gold).

## Methods

### Setting

The health surveillance data of HCWs were collected from January 2017 to January 2020 at the Policlinico Umberto I hospital in Rome. During the health surveillance visit, socio-demographic, clinical, and occupational data were collected. At the same time, the staff of the Infectious Diseases Prevention Service assessed susceptibility to TB using the PPD test, employing the standard Mantoux technique, which involves an intradermal injection of 0.1 mL (5 IU) of purified *Mycobacterium tuberculosis* proteins. The reading was taken 72 hours after injection, and a test in the presence of skin erythema associated with dermal induration with a diameter greater than 10 mm was evaluated as positive.

The TB-Gold test was used as a screening tool in individuals returning to work post-pregnancy while breastfeeding, those who had received the BCG vaccine, and those with a previous positive Mantoux test result.

A second-level diagnostic test was also used in individuals with positive skin reactions and a previous negative Mantoux test, as indicated by Health Ministry guidelines.

All collected data were stored in a password-protected database, which was queried anonymously.

### Study population

The data relating to 3,102 HCWs undergoing health surveillance visits or following contact with TB cases were selected; of these, 479 underwent second-level diagnostic tests with IGRA.

### Statistical analysis

The statistical analysis was conducted by creating frequency and contingency tables.

The differences in susceptibility to exanthematous diseases and positivity to the TST (tuberculin skin test) were assessed using univariate analysis. The chi-squared test was used for the qualitative variables, while the Student's *t*-test was used for the quantitative variables.

Subsequently, a multivariate analysis was performed using multiple logistic regression models with a backward stepwise selection method. The explanatory variables included gender, age, department type, professional qualification, and type of affiliation. Susceptibility to infection was used as the dependent variable. The results of the logistic regression models are presented as odds ratios (OR) with corresponding 95% confidence intervals (CI). The explanatory variables considered in the univariate analysis were age, gender, Integrated Welfare Departments (*Dipartimenti Assistenziali Integrati* [DAI]), professional qualification, and organizational affiliation. Healthcare professionals considered in the study worked in the 15 DAI, as reported in Table 1.

The following professional figures were taken into consideration: doctors, nurses, laboratory technicians, and other health professionals. The workers were divided into two groups: those affiliated with Policlinico Umberto I Hospital and those affiliated with Sapienza University of Rome. All the analyses were performed using SPSS, release 26.0. The significance level was set at $p<0.05$.

## Results

### Purified protein derivative

A total of 3,102 HCWs were examined, comprising 1,235 males (39.8%) and 1,867 females (60.2%). The professional distribution was as follows: 1,228 nurses (39.9%), 1,014 physicians (32.7%), 378 laboratory technicians (12.2%), 463 other healthcare professionals (14.9%), and 17 administrative staff members (0.5%) (Table 1). Age ranged from 20.6 to 71.9 years (standard deviation [SD]=54.1±8.8). In total, 431 HCWs tested positive for the PPD, representing 13.9% of the cohort, with 245 (56.8%) being female and 186 (43.2%) male.

#### *Univariate analysis*

Table 1 presents the results related to PPD positivity, using a 10 mm diameter as the cut-off. Age was significantly associated with positivity: the positive cases had an average age of 57.1 years, whereas the negative cases had an average age of 53.5 years ($p<0.001$).

As regards professional qualification, 10.1% of doctors, 18.3% of nurses, 10.9% of technicians, and 12.3% of other HCWs tested positive ($p<0.001$), while for the institution of origin, university students had a positivity of 15.6% and companies of 13.7% ($p<0.001$). Gender and DAI were not significantly associated with skin test positivity.

#### *Multivariate analysis*

Table 2 shows the results of the multivariate analysis relating to PPD positivity. The study showed that the probability of being positive for the PPD test increases with age (OR 1.06, CI 95%: 1.04-1.07). Nursing is associated with a higher probability of developing a positive PPD test (OR 2.51, 95% CI: 1.99-3.15) compared to other study professions, confirming the occupational risk. Additionally, the female gender is associated with a lower probability of being positive on the PPD test (OR 0.81, 95% CI: 0.65-1.2).

#### *Stratified analysis*

The stratified analysis by gender revealed that, in females, the probability of having a positive PPD test increases with age (OR 1.05, 95% CI: 1.03-1.06) and is significantly higher among

individuals in the nursing profession (OR 2.29, 95% CI: 1.71-3.09). Similarly, in males, the probability of having a positive PPD test rises with age (OR 1.08, 95% CI: 1.06-1.11) (Table 3).

The stratified analysis by age showed that women ≥50 years have a lower risk of testing positive (OR 0.71, 95% CI: 0.55-0.91), nurses have a higher risk (OR 2.20, 95% CI: 1.69-2.87), and the risk increases with age (OR 1.04, 95% CI: 1.02-1.07).

Among subjects <50 years, the probability of having a positive

**Table 1.** PPD: univariate analysis.

| Variable | Positive n (%) or median (range) | Negative n (%) or median (range) | p-value |
|---|---|---|---|
| Age | 57.1 (26.4-70.3) | 53.5 (20.6-71.9) | **<0.001** |
| Gender | | | 0.127 |
| Female | 245 (13.1%) | 1622 (86.9%) | |
| Male | 186 (15.1%) | 1049 (84.9%) | |
| DAI (22 missing) | | | |
| Health Professions Area | 6 (6.3%) | 89 (93.7%) | 0.083 |
| Cardio-Thoraco-Vascular Surgery and Organ Transplants | 40 (15.2%) | 224 (84.8%) | |
| General Surgery and Day Surgery | 18 (16.5%) | 91 (83.5%) | |
| General surgery. Plastic surgery | 12 (13.8%) | 75 (86.2%) | |
| Directions | 14 (14.9%) | 80 (85.1%) | |
| Hematology. Oncology and Dermatology | 31 (13.2%) | 203 (86.8%) | |
| Emergency Acc. Anesthesia and Critical Areas | 56 (11.2%) | 442 (88.8%) | |
| Maternal Infantile and Urological Sci. Hospital of Gender | 68 (16.8%) | 336 (83.2%) | |
| Int Medicine and Infectious Diseases | 31 (17.1%) | 150 (82.9%) | |
| Internal Medicine and Geriatric Medical Specialties | 21 (13.5%) | 135 (86.5%) | |
| Forensic Medicine | 0 (0.0%) | 3 (100.0%) | |
| Neuroscience/Mental Health | 38 (18.6%) | 166 (81.4%) | |
| Diagnostic Services | 45 (10.9%) | 366 (89.1%) | |
| Head-Neck | 50 (14.7%) | 290 (85.3%) | |
| Qualification | | | |
| Doctors | 102 (10.1%) | 912 (89.9%) | **<0.001** |
| Nurses | 225 (18.3%) | 1003 (81.7%) | |
| Technicians | 41(10.9%) | 335 (89.1%) | |
| Other healthcare professionals | 57 (12.3%) | 406 (87.7%) | |
| Affiliation | | | |
| Hospital | 230 (13.7%) | 1452 (86.3%) | **<0.001** |
| University | 196 (15.6%) | 1064 (84.4%) | |
| Residents | 3 (2.1%) | 143 (97.9%) | |
| Other | 2 (14.3%) | 12 (85.7%) | |

PPD, purified protein derivative; DAI, *Dipartimenti Assistenziali Integrati* (Integrated Welfare Departments).

**Table 2.** PPD and TB Gold tests: multivariate analysis.

| Variable | PPD Test | | TB Gold | |
|---|---|---|---|---|
| | Model 1 Full model OR (95% CI) | Model 2 Backward elimination OR (95% CI) | Model 1 Full model OR (95% CI) | Model 2 Backward elimination OR (95% CI) |
| Age | 1.06 (1.05-1.08) | 1.06 (1.04-1.07) | 1.05 (1.02-1.09) | 1.05 (1.02-1.08) |
| Gender | | | | |
| Female | 0.78 (0.62-0.98) | 0.81 (0.65-1.2) | 1.21 (0.76-1.93) | |
| Male (ref.) | 1 | | 1 | |
| Department | | | | |
| Surgery | 0.91 (0.73-1.14) | | 1.03 (0.67-1.60) | |
| Clinic (ref.) | 1 | | 1 | |
| Qualification | | | | |
| Doctors | 0.73 (0.51-1.04) | | 0.93 (0.46-1.86) | |
| Nurses | 2.05 (1.48-2.83) | 2.51 (1.99-3.15) | 0.53 (0.28-0.99) | 0.56 (0.35-0.89) |
| Technicians | 0.82 (0.53-1.27) | | 2.07 (0.83-5.16) | 2.10 (0.95-4.67) |
| Other healthcare professionals (ref.) | 1 | | 1 | |
| Typology of affiliation | | | | |
| Hospital | 1.1 (0.87-1.4) | | 0.93 (0.60-1.46) | |
| University (ref.) | 1 | | 1 | |

PPD, purified protein derivative; TB Gold, QuantiFERON®-TB Gold; OR, odds ratio; CI, confidence interval.

PPD test is significantly higher in nurses (OR 3.51, 95% CI: 2.12-5.80) and grows with age (OR 1.08, 95% CI: 1.04-1.12) (Table 4).

## QuantiFERON®-TB Gold

A total of 479 HCWs were examined, comprising 205 males (42.8%) and 279 females (58.2%), categorized as follows: 243 nurses (50.7%), 122 doctors (25.5%), 46 laboratory technicians (9.6%), 62 other healthcare professionals (12.9%), and 6 administrative staff (1.3%). Age ranged from 20.6 to 70.3 years. TB Gold was positive in 205 HCWs, of which 108 were female (52.7%) and 97 were male (47.3%) (Table 5).

### *Univariate analysis*

As regards professional qualification, 48.4% of doctors, 32.5% of nurses, 63% of technicians, 56.5% of other HCWs, and 50% of administrators tested positive (p<0.001). Gender, DAI, and the institution to which they belong were not significantly associated with the positivity of the skin test (Table 5).

**Table 3.** PPD and TB Gold tests: stratified analysis by gender.

| | PPD | | | | TB Gold | | | |
|---|---|---|---|---|---|---|---|---|
| | Female | | Male | | Female | | Male | |
| Variable | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination |
| | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Age | 1.05 (1.03-1.07) | 1.05 (1.03-1.06) | 1.08 (1.06-1.11) | 1.08 (1.06-1.11) | 1.04 (1.01-1.08) | 1.04 (1.01-1.08) | 1.07 (1.02-1.13) | 1.07 (1.02-1.12) |
| Department | | | | | | | | |
| Surgery | 0.9 (0.67-1.21) | | 0.92 (0.66-1.29) | | 0.55 (0.32-0.95) | 0.52 (0.30-0.89) | 1.42 (0.77-2.61) | |
| Clinic (ref.) | 1 | | 1 | | 1 | | 1 | |
| Qualification | | | | | | | | |
| Doctors | 0.96 (0.59-1.56) | | 0.53 (0.31-0.91) | 0.6 (0.39-0.91) | 0.81 (0.331-1.975) | | 0.55 (0.20-1.48) | |
| Nurses | 2.17 (1.43-3.28) | 2.29 (1.71-3.09) | 1.76 (1.03-2.99) | 2.00 (1.33-3.04) | 0.43 (0.20-0.94) | 0.45 (0.26-0.78) | 0.64 (0.23-1.67) | |
| Technicians | 0.67 (0.33-1.38) | | 0.78 (0.42-1.43) | | 1.77 (0.44- 7.04) | | 1.34 (0.44-4.04) | |
| Other healthcare professionals (ref.) | 1 | | 1 | | 1 | | 1 | |
| Affiliation | | | | | | | | |
| Hospital | 0.92 (0.68-1.26) | | 1.38 (0.96-1.99) | 1.38 (0.96-1.98) | 1.08 (0.61-1.92) | | 0.84 (0.44-1.60) | |
| University (ref.) | 1 | | 1 | | 1 | | 1 | |

PPD, purified protein derivative; TB Gold, QuantiFERON®-TB Gold; OR, odds ratio; CI, confidence interval.

**Table 4.** PPD and TB Gold tests: stratified analysis by age.

| | PPD | | | | TB Gold | | | |
|---|---|---|---|---|---|---|---|---|
| | Female | | Male | | Female | | Male | |
| Variable | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination | Model 1 Full model | Model 2 Backward elimination |
| | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Age | 1.04 (1.02-1.07) | 1.04 (1.01-1.07) | 1.08 (1.04-1.12) | 1.08 (1.04-1.12) | 1.13 (1.07-1.19) | 1.14 (1.08-1.19) | 1.06 (0.98-1.15) | 1.06 (0.98-1.14) |
| Gender | | | | | | | | |
| Female | 0.67 (0.52-0.87) | 0.71 (0.55-0.91) | 1.27 (0.72-2.26) | | 1.01 (0.62-1.62) | | 0.62 (0.16-2.37) | |
| Male (ref.) | 1 | | 1 | | 1 | | 1 | |
| Department | | | | | | | | |
| Surgery | 0.924 (0.72-1.19) | | 0.80 (0.51-1.27) | | 0.97 (0.62-1.54) | | 0.50 (0.19-1.30) | |
| Clinic (ref.) | 1 | | 1 | | 1 | | 1 | |
| Qualification | | | | | | | | |
| Doctors | 0.72 (0.48-1.06) | | 0.98 (0.36-2.703) | | 0.65 (0.33-1.31) | | 2.06 (0.23-18.72) | |
| Nurses | 1.75 (1.23-2.50) | 2.20 (1.69-2.87) | 3.41 (1.41-8.24) | 3.51 (2.12-5.80) | 0.58 (0.30-1.11) | | 0.69 (0.11-4.22) | |
| Technicians | 0.76 (0.48-1.21) | | 1.15 (0.27-4.87) | | 2.86 (1.12-7.31) | 4.27 (1.97-9.26) | - | - |
| Other healthcare professionals (ref.) | 1 | | 1 | | 1 | | 1 | |
| Affiliation | | | | | | | | |
| Hospital | 1.14 (0.88-1.47) | | 1.13 (0.59-2.16) | | 1.07 (0.67-1.70) | | 0.41 (0.10-1.65) | |
| University (ref.) | 1 | | 1 | | 1 | | 1 | |

PPD, purified protein derivative; TB Gold, QuantiFERON®-TB Gold; OR, odds ratio; CI, confidence interval.

**Table 5.** TB Gold: univariate analysis.

| Variable | Positive n (%) or median (range) 205 (42.8%) | Negative n (%) or median (range) 274 (57.2%) | p-value |
|---|---|---|---|
| Age | 59.2 (31.8-70.3) | 55.2 (20.6-69.00) | <0.001 |
| Gender | | | 0.33 |
| Female | 108 (38.7%) | 171 (61.3%) | |
| Male | 97 (48.5%) | 103 (51.5%) | |
| DAI (22 missing) | | | |
| Health Professions Area | 2 (25%) | 6 (75%) | 0.71 |
| Cardiothoracic and Vascular Surgery and Organ Transplants | 17 (39.5%) | 26 (60.5%) | |
| General Surgery and Day Surgery | 9 (39.1%) | 14 (60.09%) | |
| General surgery and Plastic surgery | 6 46.2%) | 7 (53.8%) | |
| Directions | 7 46.7%) | 8 (53.3) | |
| Hematology, Oncology and Dermatology | 11 (40.7%) | 16 (59.3%) | |
| Emergency, Anesthesia and Critical Areas | 22 (32.8%) | 45 (67.2%) | |
| Maternal, Infantile and Urological Sciences Hospital of Gender | 29 (42%) | 40 (58%) | |
| Internal Medicine and Infectious Diseases | 16 (50%) | 16 (50%) | |
| Internal Medicine and Geriatric Medical Specialties | 9 (39.1%) | 14 (60.9%) | |
| Forensic Medicine | | | |
| Neuroscience/Mental Health | 19 (42.2%) | 26 (57.8%) | |
| Diagnostic Services | 28 (56%) | 22 (44%) | |
| Head-Neck | 29 (46%) | 34 (54%) | |
| Qualification | | | |
| Doctors | 59 (48.4%) | 63 (51.6%) | <0.001 |
| Nurses | 79 (32.5%) | 164 (67.5%) | |
| Technicians | 29 (63%) | 17 (37%) | |
| Other healthcare professionals | 38 (55.9%) | 30 (44.1%) | |
| Affiliation | | | |
| Hospital | 96 (38.1%) | 156 (61.9%) | 0.167 |
| University | 107 (48.2%) | 115 (51.8%) | |
| Residents | 1 (33.3%) | 2 (66.7%) | |
| Other | 1 (50%) | 1 (50%) | |

TB Gold, QuantiFERON®-TB Gold; DAI, *Dipartimenti Assistenziali Integrati* (Integrated Welfare Departments).

### *Multivariate analysis*

Multivariate analysis showed that the probability of being positive for TB Gold increases with age (OR 1.05, 95% CI: 1.02-1.09) (Table 2). Nursing is associated with a lower probability of developing a positive test (OR 0.56, 95% CI: 0.35-0.89), while the profession of technician is associated with a higher risk (OR 2.10, 95% CI: 0.95-4.67).

### *Stratified analysis*

The stratified analysis by gender revealed that in women, the probability of having a positive TB Gold test increases with age (OR 1.04, 95% CI: 1.01-1.08), while it is significantly lower in the nursing profession (OR 0.45, 95% CI: 0.26-0.78) and in surgical departments (OR 0.52, 95% CI: 0.30-0.89). In men, the probability of having a positive TB Gold also rises with age (OR 1.07, 95% CI: 1.02-1.12) (Table 3).

The stratified analysis by age indicated that technicians ≥50 years have a higher risk of a positive result (OR 4.27, 95% CI: 1.97-9.26), with the risk increasing with age (OR 1.14, 95% CI: 1.08-1.19). Among subjects <50 years, the probability of having a positive TB Gold rises with age (OR 1.06, 95% CI: 0.98-1.14) (Table 4).

## Discussion

This study was conducted to evaluate the prevalence of tuberculosis infection among HCWs and its associated factors. The population considered accounted for 3,102 employees of the Umberto I General Hospital, including both healthcare and administrative workers. The study indicated a 13.9% positivity rate for the PPD test and a 42.80% positivity rate for the TB Gold test, consistent with existing literature evidence.[11,12]

On the contrary, in a study conducted in 2017 at another hospital in Rome,[13] out of 2,290 HCWs enrolled, 141 (6.1%) were positive for PPD; of these, 99 (70.2%) underwent IGRA, and 16 (16.1%) resulted positive. To explain the increase in positivity, we utilize a result from our study, namely that the probability of being positive in the tuberculin test increases with age. In particular, the average age of workers who underwent PPD testing ranged from 26.4 to 71.9 years (mean: 54.1±8.8 years), whereas the study by Napoli *et al.* [13] reported a mean age of 44 ± 13 years. The percentage of positivity to TB Gold in our study is also higher; however, it should be noted that we considered, in addition to the PPD positives, individuals who returned to work post-pregnancy while breastfeeding, as well as those vaccinated with BCG. Furthermore, our study has shown that the DAI and the affiliation

are not significantly associated with positivity to the skin test, a result also present in the research by Napoli and colleagues.

Although not statistically significant, the association of work seniority and the higher age class (>40 years old) with an increased risk of latent TB was also identified in a study conducted by another Italian university hospital. In this study, the presence of LTBI was assessed using only TB Gold. Among 852 HCWs, 35 (4.2%) tested positive, and the association with the male gender was statistically significant. This study also confirms the low prevalence of LTBI in the Italian HCWs.[14]

Supporting the evidence that the likelihood of testing positive for TB increases with age, a study conducted in Italy on 881 healthcare students (mean age: 23.6 years, SD=3.1) found that only 0.5% tested positive with the TB Gold test. The only significant association between positivity and potential risk factors was being born in high TB incidence areas.[15]

Another survey carried out in Italy aimed to assess how many of the subjects who tested positive for the cutiversion were then confirmed by TB Gold.[16] Both positive and negative results to the PPD followed the TB Gold, which confirmed the negativity in all the negatives and the positivity in only 25% of the operators who tested positive at cutiversion. This indicates that the correspondence between PPD and TB Gold is low, a finding confirmed by our study.

Our research has shown that the nursing profession is associated with a higher probability of a positive PPD test, confirming the occupational risk. Similar results are observed in a Saudi Arabian study, where the risk of testing positive for PPD was particularly higher among those over 50 and in the nursing profession. We found that with increasing age, the likelihood of TB Gold positivity increases, another finding in common with the Saudi Arabia study.[17]

Finally, the stratified analysis by age shows that, in operators over 50, women have a lower risk of testing positive for PPD.

Regarding the TB Gold, the profession of nursing is associated with a lower probability of developing a positive test; in this case, it is the profession of technician that is associated with a higher risk, for which there is no evidence in the literature.

The importance of periodic TB screening is also linked to economic factors. This is confirmed by an Italian study conducted after a pediatrician infected with TB worked in an outpatient vaccination service, which resulted in the infection of 15 adults and 9 children. The total outbreak costed €1,017,903. The study proposed a series of screening strategies, each of which proved to be cost-effective when compared to the real-life outbreak investigation. A cut-off of 474 outpatient HCWs tested was identified as the threshold beyond which the screening strategy would result in cost savings.[18]

The literature presents numerous studies related to hospital TB surveillance;[19] however, one of the strengths of our study is the large number of people enrolled, which allows for statistically significant results. Furthermore, all participants were hospital employees, resulting in a homogeneous population.

We need to acknowledge some limitations of this study. Firstly, the TST was conducted only for those HCWs considered at risk for TB during the three-year period; therefore, since not all personnel were tested, a selection bias cannot be excluded. Moreover, a precise identification of possible exposure outside work was not possible.

## Conclusions

Our study identified a relatively high prevalence of latent tuberculosis infection, confirming that this risk among healthcare professionals is higher than that observed in the general population and that it must be carefully monitored over time by health surveillance. The PPD test used for screening has several limitations, such as low specificity. However, in low-incidence countries like Italy, it can be considered a good first-level screening test, and positive results should be further confirmed by IGRA testing.

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