INTRODUCTION

Tuberculosis (TB) has re-emerged as a major threat to public health, as the spread of multidrug-resistant TB and extensively drug-resistant TB has complicated eradication attempts in recent years [1,2]. Significant geographic variation in TB infection rates persists across the world, which means that health care workers (HCWs) in different areas face different risks of TB [3]. TB is an occupational disease among HCWs, and physicians, nurses, and other HCWs—particularly TB laboratory staff—are at higher risk [4,5]. The relative risk of TB infection in HCWs has been reported to be higher than that of other community groups in all parts of the world [6,7].

TB remains a major public health problem in Iran [1]. The prevalence of latent TB infections (LTBI) among HCWs in Iran has been reported to range from 2 to 49% [8-12].

The aim of this nationwide study was to determine the prevalence of LTBI among TB laboratory employees in all mycobacteriology laboratories in Iran.
MATERIALS AND METHODS

This was a national cross-sectional study performed from October to December 2013 in 50 universities of medical sciences in 31 provinces throughout Iran. All staff members (689 individuals) employed in the TB laboratories of Iranian universities of medical sciences were included as HCWs in this study. Additionally, we included another randomly chosen group of individuals with similar characteristics in terms of sex, age, and length of employment. This group consisted of 317 participants, corresponding to almost half of the TB laboratory staff population from each university of medical sciences. These participants were drawn from the administrative, finance, and service personnel, and were considered to be low-risk HCWs.

A previously designed checklist was used to gather the necessary information regarding the baseline variables. Potential risk factors included work history, length of employment, contact with TB patients, history of smoking, history of purified protein derivative (PPD) testing, Bacillus Calmette-Guérin (BCG) vaccination, and history of TB and other chronic diseases. In addition, we recorded the results of PPD tests.

Chronic disease was defined as morbidity due to hypertension, diabetes mellitus, cancer, or other chronic diseases. Data regarding chronic diseases were obtained based on self-reporting by the participants.

The Ethics Committee of the Pasteur Institute of Iran approved the protocol of this study. All participants enrolled in the study voluntarily and provided written informed consent.

The PPD-S containing 5 tuberculin units (Razi Institute, Tehran, Iran) was injected between the upper one-third and lower two-thirds of the forearm using the Mantoux technique for all participants, and the results were read by an experienced nurse who underwent training regarding the implementation of the Mantoux test in this study. Results were read 72 hours after the injection using the palpation method and a millimeter ruler, and indurations of ≥ 10 mm were considered positive [13]. For low-risk HCWs who had a positive tuberculin skin test (TST) or clinical signs of active TB, and for all TB laboratory staff, chest X-rays (CXRs) were taken and read by an experienced radiologist at each medical university. Individuals with a positive TST (> 10 mm) and any CXR abnormality were examined by a physician specializing in infectious diseases. Active TB was diagnosed based on clinical findings, including general symptoms (such as fatigue, malaise, fever, weight loss, and/or anorexia) and a chronic, productive cough with purulent sputum, in combination with a CXR demonstrating radiological features consistent with TB disease or the detection of acid-fast bacilli in the sputum (smear or culture).

The prevalence of LTBI and the mean diameter of the indurations of the TST test were estimated and reported with 95% confidence intervals (CIs). Analysis of variance was used to compare the mean diameter of the TST indurations across subgroups. Logistic regression was used to identify risk factors associated with positive TST results. Unadjusted and adjusted prevalence odds ratios (PORs) were reported to assess the effects of the covariates on LTBI. All statistical analyses were conducted using Stata 11 (Stata-Corp, College Station, TX, USA) and reported with 95% CIs.

RESULTS

During the study period, 689 TB laboratory staff and 317 low-risk HCWs were screened for LTBI in 50 medical universities. Males were more common among the study subjects, comprising 68.7% and 71.61% of subjects among the TB laboratory staff and low-risk HCWs, respectively. The mean (standard deviation) age of participants was 38.06 years (7.76 years) and 37.31 years (7.32 years) among the TB laboratory staff and low-risk HCWs, respectively (Table 1). The most common chronic diseases among all participants were hypertension (38.95%) and diabetes (12.63%).

The distribution of TST indurations in TB laboratory staff and low-risk HCWs is shown in Figure 1. The mean diameter of TST indurations in TB laboratory staff (6.47 mm) was greater than was observed among low-risk HCWs (4.36 mm) (p = 0.001). The mean TST induration among TB laboratory staff who had been employed for ≥ 25 years was significantly larger than was observed staff who had been employed for < 1 year (p < 0.001). The mean TST induration diameter significantly increased with age (p < 0.001). The TST induration diameter among low-risk HCWs was significantly associated with sex (p = 0.05), age (p < 0.05), and length of employment (p = 0.017).

In TB laboratory staff, the mean TST indurations among males (p = 0.003) and females (p = 0.012) were higher than among low-risk HCWs. In participants 22-31 years of age (p = 0.049) and 32-45 years (p = 0.003) and females (p = 0.012) were higher than among low-risk HCWs.

Table 1. Demographic characteristics of TB laboratory staff and low-risk HCWs

| Variable                     | TB laboratory staff | Low-risk HCWs | p-value |
|------------------------------|---------------------|---------------|---------|
| Sex                          | 294 (43.2)          | 165 (52.2)    | 0.25    |
| Female                       | 220 (31.9)          | 90 (28.4)     |         |
| Male                         | 469 (68.7)          | 277 (71.6)    |         |
| Age (yr)                     | 38.06±7.76          | 37.31±7.32    | 0.14    |
| Marriage status              | 158 (22.9)          | 59 (18.6)     | 0.44    |
| Single                       | 90 (13.1)           | 36 (11.4)     |         |
| Married                      | 599 (86.9)          | 281 (88.6)    |         |
| Education (yr)               | 13.35±7.76          | 13.14±7.32    | 0.36    |
| Length of employment (yr)    | 9.45±7.21           | 12.73±7.94    | 0.001   |
| Job                          |                     |               |         |
| Expert (laboratory)          | 221 (32.1)          | n/a           |         |
| Associate technician (laboratory) | 268 (38.9)      | n/a           |         |
| Technician (laboratory)      | 29 (4.2)            | n/a           |         |
| Service personnel (laboratory) | 158 (22.9)      | n/a           |         |
| Administrative laboratory staff | 13 (1.9)           | n/a           |         |
| Administrative staff         | n/a                 | 212 (66.9)    |         |
| Financial staff              | n/a                 | 49 (15.5)     |         |
| Service personnel            | n/a                 | 56 (17.7)     |         |

Values are presented as number (%) or mean±standard deviation. TB, tuberculosis; HCW, health care worker; n/a, not applicable.
41 years of age (p = 0.006), the mean diameter of indurations among TB laboratory staff was much higher than among low-risk HCWs (Table 2).

The prevalence of LTBI among TB laboratory staff was 24.38% (95% CI, 21.31 to 27.74%), which was higher than was observed among low-risk HCWs (14.82%; 95% CI, 11.31 to 19.20%) (p < 0.001). Among TB laboratory staff, the prevalence of LTBI increased with age, from 23.91% in subjects 22-31 years of age group to 50% in the oldest age group (Table 3). Inconsistent results were found in the age group of 32-41 years, as the prevalence of LTBI in that group was lower than was observed in the age group of 22-31 years. The prevalence tended to be higher among subjects with low levels of education. The prevalence of LTBI was 51.85% (95% CI, 33.26 to 69.95%) among TB laboratory staff who had been employed for ≥ 25 years. The prevalence of LTBI among laboratory technicians who had only received a high school diploma (37.93%; 95% CI, 22.15 to 56.76%) was greater than was observed in other job groups. The prevalence of LTBI among TB laboratory staff and low-risk HCWs did not significantly vary according to BCG vaccination status. However, the prevalence of LTBI among vaccinated TB laboratory staff was significantly greater than was observed among vaccinated low-risk HCWs (p = 0.001) (Table 3).

Among low-risk HCWs, the prevalence of LTBI increased with age (p = 0.006), and was greater in males than in female (p = 0.026). The prevalence was higher among subjects with a low level of education. The prevalence of LTBI among low-risk HCWs significantly varied according to length of employment (p = 0.009), and the prevalence among individuals who had been employed for ≥ 25 years (36.00%; 95% CI, 19.59 to 56.50%) was greater than the prevalence among those who had been employed for < 25 years (Table 3).

Based on an unadjusted logistic regression analysis, the POR of having an LTBI among TB laboratory staff was 1.85 (95% CI, 1.30 to 2.64) in comparison to low-risk HCWs. The age groups of ≥ 52 and 42-51 years had PORs of 4.05 and 1.60 in comparison to subjects who were 22-31 years old. The POR of having an LTBI decreased with increasing levels of education. The POR of having an LTBI among TB laboratory staff who had been employed for ≥ 25 years was 3.70 (95% CI, 1.50 to 9.14) (Table 4).

The adjusted logistic regression analysis revealed that employment as TB laboratory staff (POR, 2.06; 95% CI, 1.35 to 3.17), ≥ 25 years of employment as TB laboratory staff (POR, 3.15; 95% CI, 1.11 to 8.98), and morbidity due to chronic disease (POR, 1.82; 95% CI, 1.13 to 2.95) were risk factors for having an LTBI (Table 4).

Radiological abnormalities compatible with TB were found in 60 subjects (46 cases among TB laboratory staff and 14 cases among low-risk HCWs). Additionally, 180 sputum samples (3 sputum samples per case) collected from these 60 individuals were subjected to further examination by acid-fast staining, and all samples had negative results. Based on CXRs, physical examination, and acid-fast staining, all these cases were considered to be LTBI.

**DISCUSSION**

The results of this cross-sectional study showed that the prevalence of LTBI among TB laboratory staff was significantly greater than among low-risk HCWs. LTBI were two times more prevalent among TB laboratory staff than among low-risk HCWs, and
the prevalence increased with length of employment. These results indicate that LTBI may be considered an occupational infection. Age, length of employment, morbidity due to chronic disease, and low levels of education were associated with a greater risk of LTBI.

The risk of transmission of *Mycobacterium tuberculosis* from TB patients to other patients in the hospital and to HCWs has been recognized for many years [14,15]. This risk is greater in areas where TB is endemic, because HCWs must manage larger numbers of TB patients at health care facilities and in TB laboratories [16]. Due to the high global burden of TB and the limited resources of countries in which TB is endemic, health systems must focus mainly on passive case identification and treatment strategies [17,18]. In this situation, even low-cost strategies to reduce TB transmission among HCWs are rarely implemented [16, 19]. Countries where TB is endemic constitute more than 90% of the global TB burden, despite having limited resources [17,18].

This study was the first to survey the prevalence of LTBI among TB laboratory staff, a group of HCWs with a high risk of encountering TB in the workplace in countries where TB is endemic. According to a report of the World Health Organization, the incidence rate of TB in 2015 was 16 (95% CI, 12 to 20) per 100,000 population in Iran [20]. TB laboratory staffs are exposed to sputum samples from active TB patients, and if they do not comply with biosafety regulations, the probability of exposure is increased.

A limited number of the participants of the current study (177 HCWs and 67 non-TB staffs participated in a comparison of TST and interferon-gamma release assay (IGRA) testing. In this study, the prevalence of LTBI identified by TST and IGRA testing was

| Variable                              | TB laboratory staff | p-value | Low-risk HCW      | p-value | p-value |
|---------------------------------------|---------------------|---------|-------------------|---------|---------|
| Size of TST test result (mm)           | 6.47 (5.79, 7.14)   | -       | 4.36 (3.60, 5.12) | -       | <0.001  |
| Age (yr)                              |                     |         |                   |         |         |
| 22-31                                 | 6.08 (4.81, 7.34)   | <0.001  | 4.12 (2.85, 5.39) | 0.01    | 0.05    |
| 32-41                                 | 5.35 (4.42, 6.28)   |         | 3.16 (2.18, 4.13) | 0.006   |         |
| 42-51                                 | 7.50 (6.11, 8.90)   |         | 6.10 (4.44, 7.76) | 0.22    |         |
| ≥52                                   | 12.18 (6.67, 15.69) |         | 5.57 (0.00, 16.81)| 0.33    |         |
| Marital status                        |                     |         |                   |         |         |
| Married                               | 6.42 (5.69, 7.15)   | 0.70    | 4.23 (3.41, 5.05) | 0.34    | <0.001  |
| Single                                | 6.81 (5.03, 8.59)   |         | 5.39 (3.37, 7.41) |         | 0.37    |
| Education                             |                     |         |                   |         |         |
| Elementary                            | 7.95 (5.64, 10.25)  | 0.15    | 6.07 (3.40, 8.73) | 0.25    | 0.36    |
| Intermediate                          | 8.48 (4.72, 14.24)  |         | 6.00 (1.90, 10.10)| 0.42    |         |
| Diploma                               | 7.45 (5.61, 9.30)   |         | 4.67 (2.38, 6.07) | 0.02    |         |
| Associate’s degree                    | 6.56 (5.43, 6.55)   |         | 3.93 (1.92, 5.94) | 0.07    |         |
| License                               | 5.41 (4.31, 6.51)   |         | 3.34 (2.34, 5.95) | 0.02    |         |
| Master’s or higher                    | 4.80 (1.07, 7.90)   |         | 6.43 (0.30, 12.57)| 0.61    |         |
| Length of employment (yr)             |                     |         |                   |         |         |
| <1                                    | 4.61 (2.75, 6.47)   | <0.001  | 4.17 (1.51, 6.83) | 0.02    | 0.87    |
| 1-4                                   | 6.88 (5.56, 8.21)   |         | 3.88 (2.38, 5.40) | 0.01    |         |
| 5-9                                   | 5.35 (4.23, 6.47)   |         | 3.79 (2.10, 5.48) | 0.15    |         |
| 10-14                                 | 5.09 (3.57, 6.58)   |         | 3.00 (1.80, 4.81) | 0.10    |         |
| 15-19                                 | 7.32 (5.32, 9.33)   |         | 3.42 (2.02, 4.81) | 0.004   |         |
| 20-24                                 | 9.50 (6.07, 12.91)  |         | 6.72 (4.05, 9.39) | 0.21    |         |
| ≥25                                   | 12.42 (8.24, 16.61) |         | 7.68 (4.03, 11.32)| 0.10    |         |
| Job                                   |                     |         |                   |         |         |
| Expert (laboratory)                   | 5.18 (4.11, 6.26)   | 0.11    | n/a               |         |         |
| Associate technician (laboratory)     | 6.80 (5.68, 7.91)   |         | n/a               |         |         |
| Technician (laboratory)               | 8.11 (4.53, 11.69)  |         | n/a               |         |         |
| Service personnel laboratory          | 7.39 (5.95, 8.82)   |         | n/a               |         |         |
| Administrative staff (laboratory)     | 7.00 (2.08, 11.92)  |         | n/a               |         |         |
| Administrative staff                  | n/a                 |         | 4.61 (3.63, 5.59) | 0.52    |         |
| Financial staff                       | n/a                 |         | 3.37 (1.68, 5.05) |         |         |
| Service personnel                     | n/a                 |         | 4.28 (2.66, 5.89) |         |         |

Values are presented as mean (95% confidence interval).

TST, tuberculin skin test; TB, tuberculosis; HCW, health care worker; PPD, purified protein derivative; n/a, not applicable.

1Comparison of the mean size of the PPD test result between laboratory workers and low-risk HCWs.
Table 3. Prevalence of LTBI in TB laboratory staff and low-risk HCWs based on TST results

| Variable                  | TB laboratory staff | Low-risk HCW (%) | p-value | p-value* |
|---------------------------|---------------------|------------------|---------|----------|
|                           | Prevalence (%)      | 95% CI           |         |          |
| Sex                       | 25.59               | 21.83, 29.74     | 0.29    |          |
|                           | 21.82               | 16.83, 27.79     |         |          |
| Age (yr)                  |                     |                  |         |          |
| 22-31                     | 23.91               | 17.45, 31.77     | <0.001  |          |
| 32-41                     | 18.77               | 14.87, 23.40     |         | 0.006    |
| 42-51                     | 29.03               | 22.93, 35.99     |         | 0.41     |
| ≥52                       | 50.00               | 34.77, 65.22     |         | 0.58     |
| Marital status            |                     |                  |         |          |
| Married                   | 23.87               | 20.62, 27.46     | 0.42    | 0.01     |
| Single                    | 27.78               | 19.46, 37.97     |         | 0.33     |
| Education                 |                     |                  |         |          |
| Elementary                | 38.36               | 27.88, 50.04     | 0.006   | 0.63     |
| Intermediate              | 34.78               | 18.13, 56.22     |         | 0.55     |
| Diploma                   | 30.53               | 22.06, 40.55     |         | 0.005    |
| Associate's degree        | 23.05               | 18.28, 28.62     |         | 0.07     |
| License                   | 18.43               | 13.80, 24.18     |         | 0.07     |
| Master's or higher        | 16.00               | 6.00, 36.24      |         | 0.89     |
| Length of employment (yr) |                     |                  |         |          |
| <1                        | 17.78               | 9.06, 31.92      | 0.001   | 0.95     |
| 1-4                       | 27.68               | 21.57, 34.76     |         | 0.003    |
| 5-9                       | 18.29               | 13.21, 24.74     |         | 0.19     |
| 10-14                     | 17.74               | 11.95, 25.53     |         | 0.12     |
| 15-19                     | 29.03               | 20.67, 39.11     |         | 0.01     |
| 20-24                     | 33.33               | 21.41, 47.86     |         | 0.40     |
| ≥25                       | 51.85               | 33.26, 69.95     |         | 0.25     |
| BCG vaccination status    |                     |                  |         |          |
| Yes                       | 25.04               | 21.50, 28.58     | 0.49    | 0.001    |
| No                        | 22.78               | 13.46, 32.11     |         | 0.16     |
| Unknown                   | 16.12               | 2.94, 29.31      |         | 0.79     |
| Job                       |                     |                  |         |          |
| Expert (laboratory)       | 17.65               | 13.15, 23.26     | 0.007   | n/a      |
| Associate technician (laboratory) | 23.51 | 18.80, 28.98   | n/a     | n/a      |
| Technician (laboratory)   | 37.93               | 22.15, 56.76     |         | n/a      |
| Service personnel (laboratory) | 32.27  | 25.42, 39.99  | n/a     | n/a      |
| Administrative staff (laboratory) | 30.77 | 11.52, 60.28 | n/a     | n/a      |
| Administrative staff      | n/a                 | n/a              | 15.57   | 0.61     |
| Financial staff           | n/a                 | n/a              | 10.20   | 0.25     |
| Service personnel         | n/a                 | n/a              | 16.07   | 0.12     |
| Total                     | 24.38               | 21.31, 27.74     |         | <0.001   |

TB, tuberculosis; LTBI, latent tuberculosis infection; HCW, health care worker; TST, tuberculin skin test; CI, confidence interval; BCG, Bacillus Calmette-Guérin; n/a, not applicable.

*Comparison of the prevalence of LTBI between TB laboratory staff and low-risk HCWs.

17% (95% CI, 12 to 21%) and 16% (95% CI, 11 to 21%), respectively [21]. However, we did not have sufficient financial resources to use the IGRA test for all subjects.

The prevalence of LTBI among HCWs has been reported to range from 1.8 to 47.0% in Iran [8,9,19,22]. A low prevalence of LTBI (1.8%) was reported among medical and nursing students in Iran [22]. In contrast, a high prevalence of LTBI (38 to 49%) has been previously reported among HCWs in Iran [8,9,11,12]. These studies were conducted in general hospitals and evaluated LTBI among nurses, ward sisters, physicians, and service workers, most of whom have close contact with patients. The prevalence of LTBI found in the current study among TB laboratory staff is lower than has been reported among other HCWs in Iran [8-12]. A reason for this difference may be attributed to the selection of TB laboratory staff as HCWs in the current study. These HCWs have a risk of TB infection, but have less frequent close contact with
Table 4. Potential risk factors for LTBI based on TST results

| Variables            | TST outcome | Unadjusted logistic regression | Adjusted logistic regression |
|----------------------|-------------|--------------------------------|-----------------------------|
|                      |             | OR                              | 95% CI                      | p-value | OR                              | 95% CI                      | p-value |
|                      | PPD+        | PPD-                            |                            |         | PPD+                            | PPD-                            |         |
| Group                |             |                                 |                            |         |                                 |                                |         |
| Low-risk HCWs        | 270         | 47                              | 1.00                        | Reference | 1.00                            | Reference                       |         |
| TB laboratory staff  | 521         | 168                             | 1.85                        | 1.30, 2.64 | 0.001                           | 2.06                            | 1.35, 3.17 | 0.001 |
| Sex                  |             |                                 |                            |         |                                 |                                |         |
| Female               | 255         | 55                              | 1.00                        | Reference | 1.00                            | Reference                       |         |
| Male                 | 536         | 160                             | 1.38                        | 0.98, 1.94 | 0.06                            | 1.14                            | 0.78, 1.65 | 0.50  |
| Age (yr)             |             |                                 |                            |         |                                 |                                |         |
| 22-31                | 174         | 41                              | 1.00                        | Reference | 1.00                            | Reference                       |         |
| 32-41                | 386         | 74                              | 0.81                        | 0.53, 1.24 | 0.34                            | 0.81                            | 0.49, 1.32 | 0.39  |
| 42-51                | 209         | 79                              | 1.60                        | 1.05, 2.46 | 0.03                            | 0.97                            | 0.53, 1.74 | 0.91  |
| ≥52                  | 22          | 21                              | 4.05                        | 2.04, 8.06 | <0.001                          | 1.31                            | 0.54, 3.17 | 0.55  |
| Education            |             |                                 |                            |         |                                 |                                |         |
| Elementary           | 65          | 38                              | 1.00                        | Reference | 1.00                            | Reference                       |         |
| Intermediate         | 24          | 11                              | 0.78                        | 0.35, 1.78 | 0.56                            | 0.86                            | 0.36, 2.02 | 0.73  |
| Diploma              | 156         | 44                              | 0.48                        | 0.29, 0.81 | 0.006                           | 0.58                            | 0.34, 1.02 | 0.06  |
| Associate’s degree    | 237         | 64                              | 0.46                        | 0.28, 0.75 | 0.002                           | 0.50                            | 0.28, 0.80 | 0.005 |
| License              | 276         | 52                              | 0.32                        | 0.20, 0.53 | <0.001                          | 0.40                            | 0.23, 0.69 | 0.001 |
| Master’s or higher   | 33          | 6                               | 0.31                        | 0.12, 0.81 | 0.02                            | 0.37                            | 0.13, 1.01 | 0.05  |
| Length of employment (yr) |     |                                 |                            |         |                                 |                                |         |
| <1                   | 42          | 9                               | 1.00                        | Reference | 1.00                            | Reference                       |         |
| 1-4                  | 185         | 55                              | 1.39                        | 0.64, 3.03 | 0.41                            | 1.45                            | 0.65, 3.23 | 0.36  |
| 5-9                  | 199         | 39                              | 0.91                        | 0.41, 2.03 | 0.83                            | 1.01                            | 0.44, 2.32 | 0.97  |
| 10-14                | 146         | 26                              | 0.83                        | 0.36, 1.90 | 0.66                            | 0.90                            | 0.37, 2.19 | 0.82  |
| 15-19                | 123         | 35                              | 1.33                        | 0.60, 3.00 | 0.49                            | 1.53                            | 0.63, 3.67 | 0.35  |
| 20-24                | 67          | 28                              | 1.95                        | 0.84, 4.54 | 0.12                            | 2.04                            | 0.77, 5.35 | 0.15  |
| ≥25                  | 29          | 23                              | 3.70                        | 1.50, 9.14 | 0.005                           | 3.15                            | 1.11, 8.98 | 0.03  |
| Contact with TB patients |     |                                 |                            |         |                                 |                                |         |
| No                   | 451         | 99                              | 1.00                        | Reference | 1.00                            | Reference                       |         |
| Yes                  | 340         | 116                             | 1.55                        | 1.45, 2.10 | 0.004                           | 1.32                            | 0.99, 1.58 | 0.11  |
| History of smoking   |             |                                 |                            |         |                                 |                                |         |
| No                   | 690         | 175                             | 1.00                        | Reference | 1.00                            | Reference                       |         |
| Yes                  | 101         | 40                              | 1.56                        | 1.04, 2.33 | 0.03                            | 1.18                            | 0.75, 1.86 | 0.473 |
| Chronic diseases     |             |                                 |                            |         |                                 |                                |         |
| No                   | 730         | 181                             | 1.00                        | Reference | 1.00                            | Reference                       |         |
| Yes                  | 61          | 34                              | 2.24                        | 1.43, 3.53 | <0.001                          | 1.82                            | 1.13, 2.95 | 0.01  |

TB, tuberculosis; LBTI, latent tuberculosis infection; TST, tuberculin skin test; PPD, purified protein derivative; HCW, health care worker; OR, odds ratio; CI, confidence interval.
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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare for this
study.

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