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Cross-sectional study of preventive treatment for students with latent tuberculosis infection in Shanghai, China

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ABSTRACT

Introduction Tuberculosis preventive treatment (TPT) has been initiated systematically in Shanghai supported by a public health project. This study aimed to evaluate the acceptance of TPT, identify the factors related to its refusal, and find an optimal way to promote TPT among student tuberculosis (TB) contacts.

Methods We screened contacts of the TB index case from a TB outbreak on campus. A two-step approach of first conducting a lecture of TB health literacy, followed by one-on-one TPT consultations was used to mobilise TPT among students with latent TB infection (LTBI). A semistructured questionnaire was designed between the lecture and the one-on-one TPT consultations, covering general demographic information, awareness of core TB knowledge and willingness to accept TPT, along with the reasons for refusal. Logistic regression analysis was used to identify the risk factors for refusing TPT.

Results A total of 52 contacts were identified with LTBI. After the lecture on TB health literacy, their scores on the core TB knowledge was 14.0±2.3. Students had a poor awareness rate of TB knowledge in the part of TB treatment and policy (70.2%) and *Mycobacterium tuberculosis* infection preventive measures and LTBI (67.3%) compared with the average rate (84.3%). The acceptance rate of TPT reached 42.3% at the end of the two-step promotion. The main reasons for refusing TPT included: (1) the duration for TPT was too long and follow-up management was too cumbersome; (2) the confidence in their own immunity and belief in their low risk of TB and (3) the fear of side effects of TPT.

Conclusions The two-step approach of first conducting a lecture of TB health literacy, followed by one-on-one TPT consultations, is effective for mobilising TPT. To further implement TPT, we recommend making the scientific popularisation for LTBI in a more easy-to-understand way and optimising the management of TPT.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ It is estimated that about one-quarter of the global population is infected with *Mycobacterium tuberculosis*, which serves as an enormous reservoir for future tuberculosis (TB) cases. However, the implementation of tuberculosis preventive treatment (TPT) has not yet been widely adopted on a global scale.

WHAT THIS STUDY ADDS

⇒ The two-step approach of first conducting a lecture of TB health literacy, followed by one-on-one TPT consultations, is effective for mobilising TPT. Physicians play a crucial role in promoting TPT. Focusing on the scientific popularisation for latent TB infection in a more easy-to-understand way and optimising the management of TPT can both contribute to this effort.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study provides practical insights and valuable recommendations for the implementation of TPT.

INTRODUCTION

Tuberculosis (TB) is a major threat to global health and economic development, and China is 1 of the 30 high-burden countries for TB, with the third highest number of cases globally.[1] Meanwhile, China has the highest burden of latent TB infection (LTBI), with nearly 350 million people infected with *Mycobacterium tuberculosis* (MTB). The lifetime risk of developing TB for individuals with LTBI is estimated to be 5%–10%, especially in the first 2 years after initial infection.[2] Therefore, identifying and controlling LTBI is key to reducing the incidence of TB.[3]

More than 40% of new TB cases globally in 2023 were under 25 years old.[4] Students are a key group in TB control in China, who are in close contact with each other for a long time, providing conditions for the spread of MTB. Once there is a contagious TB patient, it can easily lead to new infections and a TB outbreak.[5 6] To prevent the spread of MTB on campus, screening for contacts of student TB patients should be actively carried out.[7 8] Timely detection of all TB patients interrupts

transmission, and early intervention with LTBI reduces subsequent cases.

Shanghai is a high-income city located in eastern China with a low TB incidence. The registration rate of TB cases was 19.8 per 100 000 population, and 8.3 per 100 000 students in 2023. Tuberculosis preventive treatment (TPT) for LTBI is crucial for diminishing the burden of TB in Shanghai. While there have been notable barriers towards TPT among students with LTBI in school TB outbreaks over the years. Among 37 student TB contacts with LTBI identified through screening in 19 outbreaks in Shanghai in 2019, none of them received TPT.[9] The author's previous qualitative research on this issue and related research reports in Shanghai suggested that the reasons for the poor acceptance can be summarised into four main aspects: (1) Lack of relevant documents and financial support at the government level; (2) Physicians are reluctant to promote TPT due to concerns about the risk of drug resistance from irregular medication use, the side effects and the substantial follow-up workload associated with TPT; (3) Insufficient understanding of TPT among students and their parents and (4) Inconveniences in seeking TPT services for individuals with LTBI for the lack of TPT clinics nearby.[10 11]

An increasing number of studies have targeted the willingness to accept TPT. Previous research has shown that willingness to accept TPT was associated with TB knowledge.[12 13] In this context, the authors conducted a survey to assess the level of TB knowledge among students after a lecture of TB health literacy, identify potential challenges related to TPT apart from TB awareness and find an optimal way to promote TPT.

METHODS

This was a cross-sectional study. On 20 June 2024, a 19-year-old student was diagnosed with TB based on bacteriological diagnosis. Epidemiological and contact investigations were conducted on the campus. All investigation processes were conducted in accordance with the guidelines of the Chinese School Tuberculosis Control and Prevention Technical Work Regulations. The procedure for the close contact investigation was as follows: First, staff from the Shanghai Municipal Center for Disease Control and Prevention (SCDC) conducted symptom screening, ESAT6–CFP10 (EC) skin tests and chest X-ray (CXR) for all close contacts of the index case. Second, individuals with suspicious symptoms, positive EC results or abnormal CXR scans were referred to a local designated TB hospital for further evaluation, including sputum smear, sputum culture, GeneXpert MTB/RIF testing and CT imaging. Third, students with positive microbiological results or abnormal CT findings underwent further diagnostic evaluation. Those who were excluded active TB but with positive EC results were identified as LTBI and received a lecture of TB health literacy, a questionnaire survey and TPT consultations (figure 1).

A two-step approach of first conducting a lecture on TB health literacy, followed by one-on-one TPT consultations, was used to mobilise TPT. First, students with LTBI were engaged in a lecture of TB health literacy conducted by physicians from the designated TB hospital, which covered the following topics: (1) Basic knowledge of TB, including its symptoms, transmissibility, prevention

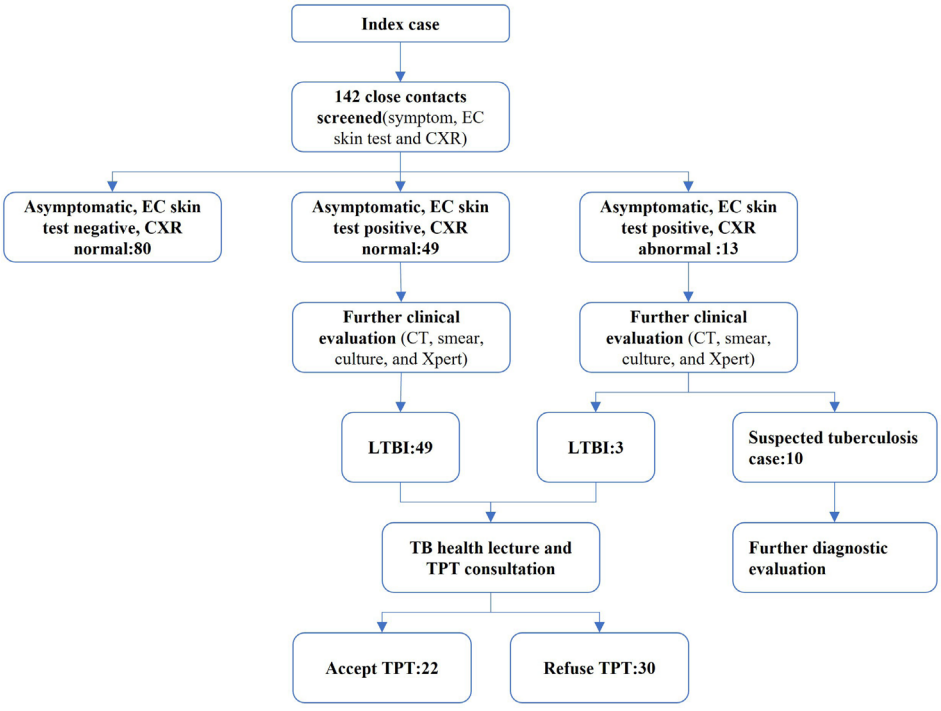

Figure 1 Flow chart for the screening and management of close contacts during the on-campus TB outbreak. CXR, chest X-ray; LTBI, latent TB infection; TB, tuberculosis; TPT, tuberculosis preventive treatment.

and control measures, and treatment management; (2) Screening and management of close contacts of TB patients; (3) The concept of LTBI and the risk of progression to TB in individuals with LTBI; (4) The benefits of TPT and the potential side effects during the course of treatment and (5) The regimen and duration of TPT and other precautions during TPT. Second, each student participated in a one-on-one TPT consultation conducted by physicians from the designated TB hospital, which covered the following topics: (1) Re-educate students on the basic knowledge of LTBI; (2) Re-emphasise the risk of progression to TB and its potential impact on academic performance; (3) Introduction to the support measures provided by the designated TB hospital, such as the medical green channel, continuous professional medical services and management of potential side effects during TPT; (4) Introduction to the free-of-charge strategy, that is, the entire process of TPT, including screenings and medication, is provided free of charge. After the TPT consultation, students decided whether to receive TPT and explained the reasons.

Individual face-to-face questionnaire surveys were conducted by researchers from the SCDC among students with LTBI between the lecture and the one-on-one TPT consultations. A semistructured questionnaire (online supplemental file 1) was designed for the interviews, covering general demographic information, awareness of core TB knowledge and willingness to accept TPT, along with the reasons for refusal. Interviewers were trained on each question. Core TB knowledge was evaluated through four categories of questions, totalling 16 items. These questions aimed to assess participants' comprehension across four crucial aspects: (1) TB symptoms and communicability; (2) TB treatment and policy; (3) MTB infection preventive measures and LTBI; (4) TPT for LTBI. Each correct answer was awarded 1 point, and the total score ranged from 0 to 16. The awareness rate for each category of TB knowledge was calculated by dividing the total number of items correctly answered by all participants by the total number of all items. Average awareness rates served as threshold values that were used to judge awareness levels as good or poor, with rates above the average awareness level for all parts combined indicating good awareness and rates below the average awareness level for all parts combined indicating poor awareness.

All the data were input into the database using Microsoft Excel 2019 (Microsoft, Redmond, Washington, USA) and R Statistical Software V.3.6.0 (R Foundation for Statistical Computing, Vienna, Austria) was used in the analysis. Frequency, per cent, means and SDs were used for the analysis. One-way analysis of variance was used for continuous variables, while the χ^2 test was applied for categorical variables. Logistic regression analysis was used to identify the risk factors for refusing TPT. The significance level (α) was set at 0.05.

Definition

Index case: The earliest case identified in a TB outbreak.

Close contact: Person in close contact with the infectious index case during a likely period of infectiousness (online supplemental file 2).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

RESULTS

During this on-campus TB outbreak, a total of 142 students were identified as close contacts of the index case, and all of them underwent an inquiry about suspicious TB symptoms, an EC skin test, and a CXR. After the screening process, 80 students had normal results in all tests and 62 students had abnormal results. Of the 62 students with abnormal results, 13 had both abnormal CXR and positive EC results, while 49 had only positive EC results. These 62 students with abnormal results were referred to the local designated TB hospital for further evaluation. Of these, 10 were diagnosed as suspected TB and 52 were identified with LTBI (figure 1). Among the 52 students with LTBI, 51 (98.1%) were male, 43 (82.7%) were domestic migrants, 24 (46.2%) had normal body mass index, 4 (7.7%) were underweight, 14 (26.9%) were overweight and 10 (19.2%) were obese. The mean age was 19 years old. The demographic and sociological information of the students with LTBI is detailed in table 1.

The 52 students with LTBI scored 13.48±1.35 in the core TB knowledge survey. No significant difference in the knowledge level was observed (p>0.05). Students had a poor awareness rate of TB knowledge in the second (70.2%) and third (67.3%) parts compared with the average rate for all parts combined (84.3%) (table 2).

Table 1 Background characteristics of students with LTBI

	Classification	N (%)
Gender	Female	1 (1.9)
	Male	51 (98.1)
Age	18	13 (25.0)
	19	27 (51.9)
	20	11 (21.2)
	23	1 (1.9)
Domestic migrant	No	9 (17.3)
	Yes	43 (82.7)
BMI	Underweight	4 (7.7)
	Normal	24 (46.2)
	Overweight	14 (26.9)
	Obese	10 (19.2)

BMI, body mass index; LTBI, latent tuberculosis infection.

Table 2 Core TB knowledge scores in students with LTBI

	Score	The awareness rate (%)
Knowledge 1 : TB symptoms and communicability (0–5)	4.67±0.58	93.5
Knowledge 2 : TB treatment and policy (0–4)	2.81±0.72	70.2
Knowledge 3 : MTB infection preventive measures and LTBI (0–3)	1.23±0.67	67.3
Knowledge 4 : Preventive treatment for LTBI (0–4)	3.98±0.14	99.5
Total (0–16)	13.48±1.35	84.3

LTBI, latent TB infection; MTB, Mycobacterium tuberculosis; TB, tuberculosis.

After the consultation, 22 students with LTBI accepted and initiated TPT, with an acceptance rate of 42.3%. Both univariate and multivariate logistic regression analyses did not identify any variables significantly associated with the acceptance of TPT (p>0.05).

The main reason for receiving TPT was fearing that they might get TB in the future, which they believed would affect their academic performance. The main reasons for refusing TPT included: (1) the belief that TPT was too long in duration and follow-up management was too cumbersome; (2) the confidence in their own immunity and belief in their low risk of TB and (3) the fear of side effects of TPT (table 3).

DISCUSSION

Individuals with LTBI have a high risk of developing TB, especially in the first few years of infection.[14 15] It is generally assumed that students with LTBI identified through screening during school TB outbreaks are newly infected, and they have a higher risk of developing TB than other groups due to factors such as heavy study loads, immature immune systems and declining protective efficacy of the BCG vaccine.[16] It is an important public health strategy to actively identify and treat students with LTBI to prevent the progression to TB and transmission of MTB on campus.[17 18] With the efforts of the Shanghai government this year, TPT has been systematically initiated in Shanghai, supported by policy and funding through a public health project. TPT clinics have been established in every district, and there has been a significant shift in the attitude of physicians towards TPT.

The author's previous study reported that the prevalence of LTBI was 4.8% among student TB contacts in Shanghai universities.[9] The infection rate in this outbreak was nearly 10 times higher than the baseline level, suggesting that MTB had already transmitted among close contacts, with a high risk of subsequent cases. To prevent further spread of this epidemic, physicians strongly recommended TPT. In this context, the reasons why students with LTBI refuse TPT warrant further investigation.

Li *et al* found that the level of knowledge of TB affected the acceptance of TPT.[8] In response to this outbreak, a lecture on TB health literacy was first delivered to students with LTBI, followed by a questionnaire survey and one-on-one TPT consultation. After the lecture, the students' knowledge overall scores on TB were generally high. However, the awareness rate of 'MTB infection preventive measures and LTBI' was the lowest, indicating that their understanding of LTBI was still relatively poor

Table 3 Reasons for acceptance and refusal of TPT

Variable	N (%)
Reasons for accepting TPT	
Fear of getting TB in the future	16 (72.7)
Worried about the impact of TB on their academic performance	9 (40.9)
Worried about spreading MTB to others in the future	5 (22.7)
Endorsed the concept of TPT and believed that they would benefit from TPT	4 (18.2)
Reasons for refusing TPT	
Treatment was too long and follow-up management was too cumbersome	16 (53.3)
The confidencein their own immunity and belief in their low risk of TB	15 (50.0)
The fear of side effects of TPT	13 (43.3)
Low protective rate of TPT	2 (6.7)
Risk of drug resistance	1 (3.3)
Stated clearly that he would only acquire TPT at hometown	1 (3.3)

MTB, Mycobacterium tuberculosis; TB, tuberculosis; TPT, tuberculosis preventive treatment.

after the lecture on TB health literacy. The awareness of LTBI is directly related to whether they accept TPT,[19] which suggests that more emphasis should be placed on LTBI education in a more straightforward and easy-to-understand way.

The acceptance rate of TPT among students with LTBI in this on-campus TB outbreak reached 42.3%, which is significantly higher than the rates in previous TB outbreaks in Shanghai schools,[9] yet still far behind when compared with other countries.[20–22] The gap in acceptance rates highlights the need to explore more effective strategies for promoting TPT among student TB contacts. A study has shown that policy support, financial assistance, health education and emotional support from family and peers all contribute to increasing the acceptance of TPT for individuals with LTBI.[23]

Over 50% of the students refused TPT. The most frequently reported reason for refusing TPT was the long duration of treatment and the cumbersome follow-up management. According to China's national TB control guidelines, individuals initiating TPT are required to visit the hospital regularly for liver and kidney function monitoring through blood tests. A 3-month regimen of isoniazid plus rifapentine was recommended in this TB outbreak. Due to the upcoming summer vacation, students were expected to undergo at least four blood tests at their hometown hospitals. Many students felt this would disrupt their summer plans and thought the follow-up process was too troublesome. If TPT was administered during the semester and convenient follow-up services were offered at school, some students who had previously refused TPT indicated that they would reconsider their decision and opt for TPT. However, this also highlights the need for continuous improvement in our approach. WHO recommends several TPT regimens,[24] including shorter courses such as 1-month regimen of isoniazid plus rifapentine, which is non-inferior to the traditional regimen and has a higher completion rate.[25 26] As more evidence becomes available, shorter courses may become more common. Meanwhile, optimising TPT management is essential. Digital tools have been increasingly used in TB treatment, significantly improving patient adherence.[27 28] These tools can be fully used in TPT programmes, with features such as medication reminders, clock games to encourage regular medication intake and rewards for completing games. Furthermore, we can establish a community for TPT among students with LTBI, which will provide peer education and emotional support.[29]

Another barrier to TPT acceptance was students' confidence in their own immunity and their belief in a low risk of TB. The college where the outbreak occurred is a semimilitary management school, and the students involved in this outbreak are required to engage in frequent physical exercise as part of their daily academic life, which differs from other college students. Previous studies have shown that students who engage in more physical activity tend to perceive their health status as better and believe they have no health issues.[30 31] This may be a specific factor affecting the acceptance rate of TPT in this outbreak.

Moreover, concerns regarding side effects were another reason for refusing TPT, which was the same as other studies.[19] Physicians play a crucial role in promoting TPT. In the past, during consultations on TPT, physicians would overemphasise potential side effects of TPT, which could discourage TPT engagement. In contrast, in this consultation, physicians first informed students about the risks of LTBI and the benefits of TPT, then told the potential side effects. They also emphasised that comprehensive services would be provided, assuring students that any side effects during TPT would be promptly addressed, with timely and free medical support available. This balanced approach—providing both information on risks and assurances of support—significantly bolstered students' confidence in receiving TPT. Furthermore, current data on side effects associated with TPT are predominantly reported in international literature. Domestic data from China are urgently needed to provide robust local evidence during TPT consultations.

This cross-sectional study was conducted among students with LTBI in a college TB outbreak. The results are more convincing than those of other studies that investigated their willingness to receive TPT on the premise of not being infected. While there are limitations to this study. First, the sample size is relatively small. Second, the findings may be unique to the student group, especially among first-year college students. Our future research will include a larger sample size and broaden our demographic scope.

CONCLUSIONS

TPT in Shanghai has shown incremental progress. The two-step approach of first conducting a lecture on TB health literacy on TB, followed by one-on-one TPT consultations, is effective for mobilising TPT. Physicians play a crucial role in promoting TPT. In order to further improve this work, we recommend: (1) focusing on the scientific popularisation for LTBI in a more easy-to-understand way to enhance the knowledge on LTBI and TPT among students and (2) optimising the management of TPT, including provision of convenient medical services, intelligent tool applications and peer emotional support.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants. The ethical approval of this study was obtained from the Ethics Committee of the Shanghai Municipal Center for Disease Control and Prevention (ID: 2019-16). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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