Original Article

In a Hospital Setting, is There any Benefit in Prioritizing Risk following Exposure to Tuberculosis? - A Preliminary Report

Panthong J, MD[1], Chaiear N, MD, MMedSc, PhD[1], Jongkumchok W, MD[1], Janpho P, BNS[2]

[1] Division of Occupational Medicine, Department of Community Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
[2] Occupational Health and Safety Office, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Objective: To study a program of post-exposure management for pulmonary tuberculosis (TB) in the hospital setting.

Materials and Methods: A study was conducted among hospital personnel (HP) from March 2016 to June 2017. A program of post-exposure management for pulmonary TB in the hospital setting was instituted which followed the "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis: Recommendations from the National Tuberculosis Controllers Association and CDC" using the QuantiFERON®-TB Gold In-Tube assay (QFT-GIT), an Interferon-Gamma Release Assay (IGRA), as a screening test.

Results: Three hundreds and twelve HP were classified as the contact persons and 15 TB patients were confirmed as the index cases. Among 312 HP, 134 (42.9%) was classified as high or medium priority contacts, and 30 of them (22.4%) were investigated by QFT-GIT after being exposed. Two HP (6.7%) revealed positive result and were confirmed as having latent tuberculosis infection, but only one HP accepted INH preventive treatment. Twenty six (8.3%) HP could not be prioritized due to their incomplete information.

Conclusion: This program was unable to statistically identify the post-exposed HP with infectious tuberculosis due to limited numbers. The appropriate guidelines need to be developed more clearly with definition of a 'close contact'. This will be more useful for Thailand hospital settings.

Keywords: Latent tuberculosis infection, Hospital personnel, Post-exposure, Interferon-Gamma Release Assay

J Med Assoc Thai 2019;102(Suppl.1): S27-S32
Website: http://www.jmatonline.com

Tuberculosis (TB) is caused by *Mycobacterium tuberculosis* (MTB) that most often affect the lungs. Tuberculosis is curable and preventable[1].About one-third of the world's population has latent TB infection (LTBI), which means state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB[2,3]. The lifetime risk of reactivation TB for a person with documented LTBI is estimated to be 5 to 10%, with the majority developing TB disease within the first two years after initial infection[4,5].

Thailand, 1 of 14 high burden countries for TB, TB/HIV and MDR-TB[6], adopted the World Health Organization (WHO)'s "Global Plan to End TB, 2016 to 2020": to ensure 90% of all people with TB have been diagnosed and receive treatment; ensure 90% of the most vulnerable populations in all countries are diagnosed and treated; and ensure 90% of those diagnosed successfully complete therapy and have access to adherence and social support[7].

Health personnel (HP) are at risk of infection with TB in view of their exposure to infected patients. Occupational TB can lead to loss of skilled HP and may lead to the avoidance of working in high risk clinical areas[8]. Post-exposure surveillance and treatment of LTBI should be considered for HP, and high TB burden countries. Either Interferon-Gamma Releasing Assays (IGRAs) or Tuberculin Skin Test (TST) should be used to test for LTBI[9]. Isoniazid (INH) was demonstrated to be effective in preventing TB among household contacts of persons with TB disease[10]. Investigations of contacts and treatment of contacts with LTBI became a strategy in the control and elimination of TB[10,11].

IGRA is highly MTB-specific and based on the measurement of gamma-interferon (IFN-γ) production from peripheral blood mononuclear cells in response to MTB antigenic, which are absent in the vaccine strain BCG. Thus unspecific reactions in populations containing a high proportion of BCG-vaccinated individuals are avoided[12,13].

Correspondence to:

Chaiear N.

Division of Occupational Medicine, Department of Community Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

Phone: +66-43-363588

E-mail: naesinee@kku.ac.th

How to cite this article: Panthong J, Chaiear N, Jongkumchok W, Janpho P. In a hospital setting, is there any benefit in prioritizing risk following exposure to tuberculosis? - A preliminary report. J Med Assoc Thai 2019;102;Suppl.1: S27-S32.

The advantages of IGRA are its specificity, the need for only a single visit, can be completed in less than 24 hours, and the lack of a booster effect. However, it requires complex laboratory steps and is expensive to perform.

Although contact investigations are important component of strategies for TB elimination, they involve complicated decisions for priority to investigation or treatment of LTBI. However, Thailand did not issue any specific or detailed guidelines for dealing with LTBI in HP after exposure to TB in workplace[14]. Only a few hospitals consider using CDC guideline but not in such a full program. However, in a university hospital of northeastern, Thailand, the program for post exposure surveillance among contacts was implemented using CDC 2005 guideline. Therefore, the aim was to study the usefulness of the CDC's program when implemented in a hospital in Thailand.

Materials and Methods

Study design

The retrospective descriptive study was conducted using existing data.

Study population

The target population was the hospital personnel (HP) who were exposed to TB patients (index cases) and had no previous TB infection. The data were recorded by Occupational Health and Safety (OH&S) office, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand from March 2016 to June 2017. A total of 312 cases met the inclusion criteria. The required sample size was estimated to be 260 cases by the finite population proportion formula.

Questionnaire

HP who were part of a contact investigation were selected on a case-by-case basis by questionnaire in order to be prioritized for close contact HP according to the risk of infection[14,15], as follows: (1) infectiousness of the index case, (2) overlap with the infectious period of the index case, (3) characteristics of individual contacts, (4) procedures that could increase the risk for transmission during contact (e.g. sputum induction, bronchoscopy, and airway suction), (5) the use of respiratory protective equipment, (6) duration of exposure, (7) built environment (size of the rooms, ventilation and overcrowding).

Index case classification and contacts prioritizations

An index case was defined to initiate a contact investigation. This study defined an index case based on clinical factors: pulmonary, laryngeal or pleural TB disease with acid-fast bacilli (AFB) sputum smear positive or positive sputum culture for TB or cavitary chest radiograph have priority for investigation[14].

Priorities for contact investigation are determined on the basis of the characteristics of the index case, susceptibility and vulnerability of contacts, and circumstances of the exposures. The algorithms for assigning priorities to individual contacts for evaluation presents (Figure 1 to 3). In summary, the prioritizing of contacts exposed to TB patients was classified as high priority if the contacts

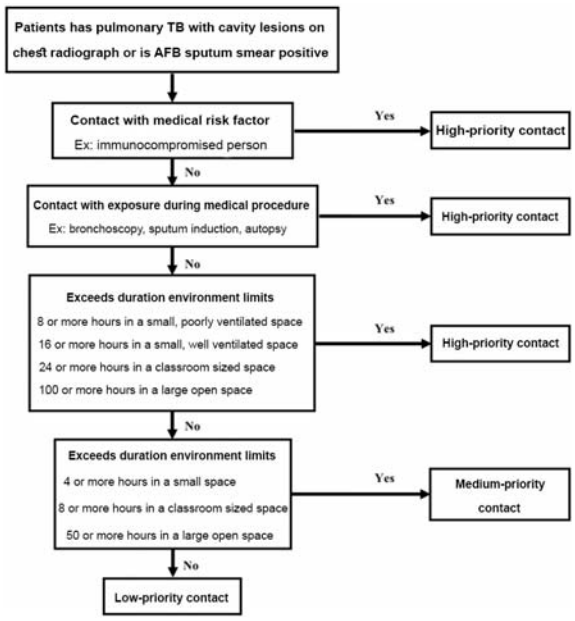

Figure 1. Prioritization of contacts exposed to persons with acid-fast bacilli (AFB) sputum smear-positive or cavity tuberculosis (TB) cases

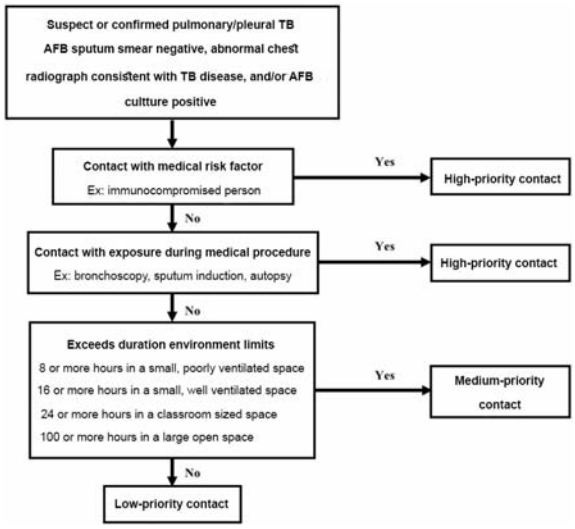

Figure 2. Priority assignments for contacts exposed to persons with acid-fast bacilli (AFB) sputum smear-negative tuberculosis (TB) cases.

were exposed to patient who was definitely diagnosis by positive in chest x-ray (CXR) or sputum acid fast bacilli (AFB) or suspected (by positive in CXR) and the contacts whose immune systems were weak or manipulated procedure, e.g., bronchoscopy, sputum induction, and autopsy. If not those mentioned, duration of exposure and ventilation system

of the room were further taking into account. For medium priority, they should not be in the invasive, there for only account duration of exposure and ventilation system of the room. Any contacts that were not classified as high or medium priority are assigned a low priority.

Interferon Gamma Release Assay (IGRA)

This study used QuantiFERON®-TB Gold In-Tube assay (QFT-GIT), an interferon-Gamma release assay (IGRA), to diagnose LTBI. The IGRA measured IFN-γ released from memory immune cells induced by specific MTB antigens that not found in BCG vaccine[12,13]. In addition, this test is easy to perform and to interpret. If IGRA is positive, the cases were referred for chest radiography and carefully examined by specialist. A diagnosis of LTBI was given to test-positive participants not presenting with clinical or radiographic signs of active TB[2,3,13,14]. All HP with newly positive results on follow-up testing (converters) would be considered for treatment for LTBI, as shown in Figure 4.

Statistical analysis

All analyses were performed using SPSS (version 19.0) and the results were presented as frequency and percentage.

Ethical consideration

The ethical concern was primarily with respect to confidentiality of personal data. The present study was reviewed and approved by Khon Kaen University Ethics Committee in Human Research (HE601475).

Results

In this study, the prioritizing was performed and the high, medium and low priority contacts were as follow the patients who had sputum AFB or cultural confirmed pulmonary TB (Figure 1 to 3). One hundred and six HP (34.0%) were high, 28 HP (9.0%) were medium and 152 HP (48.7%) were low priority contacts. Twenty six (8.3%) HP could not be classified for priorities due to incomplete data to fulfill in the guidelines. No HP was investigated by IGRAs in 3 to 5 days after being exposed as indicated in the guideline (Figure 4) because the index cases were delayed in diagnosis. Thirty of high and medium priority contacts (22.4%) were investigated by IGRAs 8 weeks after being exposed and the rest rejected to investigate. Two HP (6.7%) had positive result and were confirmed LTBI. Finally, 1 HP accepted INH prophylaxis, respectively, as shown in Figure 5.

Discussion

TB infection of contacted HP is an occupational disease that should to be managed and coordinated between occupational health staff, public health/TB control staff and hospital infection control. Hospital TB contact follow-up benefits from close coordination and collaboration.

The recent conversion among the contacted HP were not identified due to no HP was investigated by IGRAs in 3 to 5 days after being the exposed; the index cases were delayed in diagnosis and contacted HPs had no baseline IGRA. The response rate of this study was quite low. The reasons

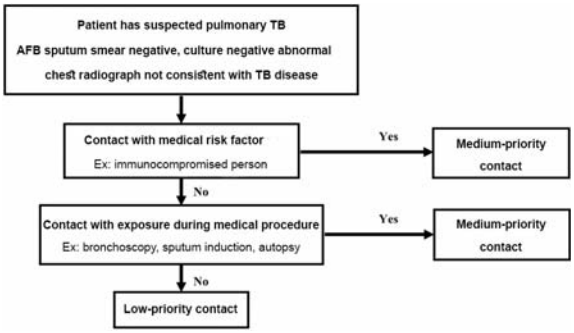

Figure 3. Prioritization of contacts exposed to persons with suspected tuberculosis (TB) cases with abnormal chest radiographs not consistent with TB disease

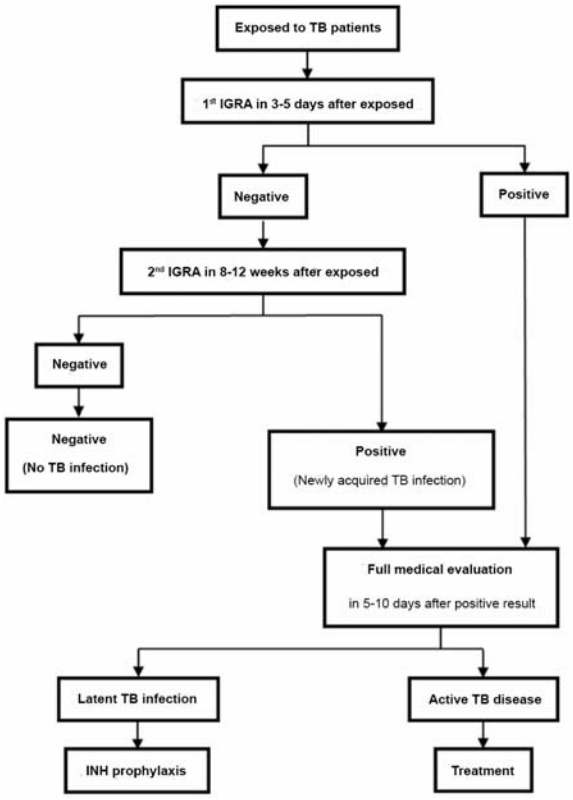

Figure 4. Post-exposure management for high and moderate priority of TB contacts

for reject of high and medium priority contacts that most of them did not accept INH preventive treatment although LTBI was confirm. Because they had to take 9 month courses of INH for completely treatment that longer than standard tuberculosis treatment regimens and did not accept side-effects of INH[1,2,7].

The two IGRA positive HP had different point

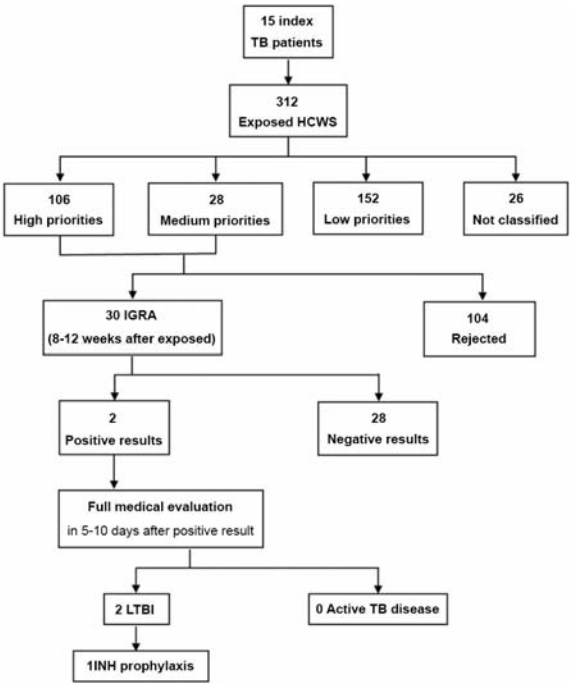

Figure 5. Results of post-exposure management for TB contacted HCWs.

from the 28 IGRA negative HP. The index cases were AFB sputum smear positive with cavitary chest radiograph and 2 IGRA positive HP exposed to them with no use of respirator. On the other hand, some IGRA negative HP were high priority contacts from transmission procedures. Those HP may be well protected because they knew that procedures could increase the risk for transmission during contact.

Although Thailand was considered a country with a high burden for TB[6], this study identified a relatively low proportion (6.7%) of LTBI in contacts in contrast to other studies where approximately 30 to 50% of all contacted HP were LTBI[14-16]. There are two possible reasons. (1) HP completed a screening questionnaire by themselves and that they might have overestimated for a contact time. (2) Over inclusion due to unclear definition of a 'close contact'; HP who were part of a contact investigation need to be selected on a case-by-case basis according to the risk of infection.

The likelihood of infection depends on the intensity, frequency, and duration of exposure[17-21]. However, making successful decisions during a contact investigation required a number of data sources and information. The majority of which were made on incomplete data, and dozens of time-consuming interventions. One problem of this study was the definition of the first date of contacted HP being exposed to the index cases. It might have been started at the first day of TB diagnosed or the first day of index cases' admission. Therefore the mentioned definition affected diagnosis the recent conversion in IGRA positive HP.

The CDC guidelines did not clearly define what a 'close contact' was. They suggests that a close contact was a person who shared the same air space in a household or other enclosed environment for a prolonged duration (days or weeks, rather than minutes or a few hours) with someone suspected of, or confirmed TB[14] as well as the UK guideline, there is no clear definition of a close contact and it is therefore difficult to give guidance about who to trace. However, it also notes that people should be regarded as at risk of infection if they have spent more than 8 hours in the same hospital bay with an inpatient with sputum smear-positive TB who had a cough[22]. The Tuberculosis Network European Trials Group recommends that close non-household contacts are those who are exposed for a cumulative time of 8 hours, if the index is sputum smear-positive, or 40 hours, if only sputum culture-positive[23]. On the other hand, Maryland recommended that close contacts were those who were exposed for a cumulative time of 8 hours in a small poorly ventilated space or 16 hours in a small well ventilated space or 24 hours in a classroom sized space or 100 hours in a large open space, if the index is sputum smear-positive[15].

In Thailand, HP was not tested for LTBI as part of contact investigations or periodic follow-up. Thailand guidelines for systematic screening for active TB and drug-resistant TB in HP recommended that a contact investigation should be initiated immediately if HP contacted to the diagnosed or suspected TB patient. All contacts should receive symptom screening and chest radiograph every 6 months for first 2 years but LTBI screening and treatment were not implemented in this guideline[24]. On the other hand, NICE guideline and CDC offered TST or IGRA to new HP who had contact with patients in settings where TB was highly prevalent. If this assessment was positive, assessed for active TB and if negative, offered them treatment for LTBI[2,11,25]. For Thailand, newborns have been given the BCG vaccine for the past 40 years and nontuberculous mycobacteria (NTM) infections are common in Thailand. Then, TST may lead to false positive result and IGRA in Thailand is still high cost and is not routinely available[26].

Conclusion

The program for TB contact investigation is a valuable public health tool although this program might not appropriately identify post-exposed HP with infectious tuberculosis. However, our results showed that program should be developed to assist TB field workers in prioritizing contacts for investigation. The appropriate guideline is needed to be developed clearer definition of a 'close contact' for further screening and risk communication to prevent LTBI. Enlarged samples will be benefit for an assessment of a screening tool (questionnaire) of TB contact prioritizing.

What is already known on this topic?

Thailand had systematic screening guidelines for active TB but no guidelines for LTBI as part of contact investigations or periodic follow-up.

What this study adds?

Our results showed that program should be developed to assist TB field workers in prioritizing contacts for investigation.

Acknowledgements

The authors would like to thank (a) Occupational Health and Safety (OH&S) office, Faculty of Medicine, Khon Kaen University, Khon Kaen (b) and the Faculty of Medicine, Khon Kaen University for their support and allowing use of their data and (c) Mr. Bryan Roderick Hamman for assistance with the English-language presentation of the manuscript.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. World Health Organization. Tuberculosis [Internet]. 2017 [cited 2017 Dec 17]. Available from: http://www.who.int/mediacentre/factsheets/fs104/en/
2. Centers for Disease Control and Prevention. Latent tuberculosis infection: a guide for primary health care providers - Treatment of latent TB infection [Internet]. 2013 [cited 2017 Dec 14]. Available from: https://www.cdc.gov/tb/publications/ltbi/treatment.htm.
3. Mack U, Migliori GB, Sester M, Rieder HL, Ehlers S, Goletti D, et al. LTBI: latent tuberculosis infection or lasting immune responses to M. tuberculosis? A TBNET consensus statement. Eur Respir J 2009;33:956-73.
4. Dye C, Scheele S, Dolin P, Pathania V, Raviglione MC. Consensus statement. Global burden of tuberculosis: estimated incidence, prevalence, and mortality by country. WHO Global surveillance and monitoring project. JAMA 1999;282:677-86.
5. Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol 1974;99:131-8.
6. World Health Organization. Global tuberculosis report 2017 [Internet]. 2017 [cited 2017 Dec 11]. Available from: https://www.who.int/tb/publications/global_report/en/.
7. Centers for Disease Control and Prevention. Global plan to end TB, 2016-2020 [Internet]. 2015 [cited 2017 Dec 11]. Available from: https://www.cdc.gov/globalaids/in-the-news/paradigmshift.html.
8. He GX, van denHof S, van der Werf MJ, Wang GJ, Ma SW, Zhao DY, et al. Infection control and the burden of tuberculosis infection and disease in health care workers in china: a cross-sectional study. BMC Infect Dis 2010;10:313.
9. Centers for Disease Control and Prevention. Core curriculum on tuberculosis: What the clinician should know [Internet]. 2013 [cited 2017 Dec 14]. Available from: https://www.cdc.gov/tb/education/corecurr/pdf/corecurr_all.pdf.
10. Centers for Disease Control and Prevention. Latent tuberculosis infection: A guide for primary health care providers [Internet]. 2013 [cited 2017 Dec 14]. Available from: https://www.cdc.gov/tb/publications/ltbi/pdf/targetedltbi.pdf.
11. Centers for Disease Control and Prevention. Essential components of a tuberculosis prevention and control program. Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR Recomm Rep 1995;44:1-16.
12. Pai M, Kalantri S, Dheda K. New tools and emerging technologies for the diagnosis of tuberculosis: part II. Active tuberculosis and drug resistance. Expert Rev Mol Diagn 2006;6:423-32.
13. Ringshausen FC, Nienhaus A, Schablon A, Schlosser S, Schultze-Werninghaus G, Rohde G. Predictors of persistently positive Mycobacterium-tuberculosis-specific interferon-gamma responses in the serial testing of health care workers. BMC Infect Dis 2010;10:220.
14. Centers for Disease Control and Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recomm Rep 2005;54:1-47.
15. Maryland Department of Health and Mental Hygiene. Maryland TB guidelines for prevention and treatment of tuberculosis [Internet]. 2007 [cited 2018 Jan 9]. Available from: https://phpa.health.maryland.gov/OIDPCS/CTBCP/CTBCPDocuments/tbguidelines.pdf.
16. Yanai H, Limpakarnjanarat K, Uthaivoravit W, Mastro TD, Mori T, Tappero JW. Risk of Mycobacterium tuberculosis infection and disease among health care workers, Chiang Rai, Thailand. Int J Tuberc Lung Dis 2003;7:36-45.
17. Lamberti M, Muoio MR, Westermann C, Nienhaus A, Arnese A, Ribeiro Sobrinho AP, et al. Prevalence and associated risk factors of latent tuberculosis infection among undergraduate and postgraduate dental students: A retrospective study. Arch Environ Occup Health 2017;72:99-105.
18. Bailey WC, Gerald LB, Kimerling ME, Redden D, Brook N, Bruce F, et al. Predictive model to identify positive tuberculosis skin test results during contact investigations. JAMA 2002;287:996-1002.
19. Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. Am J Respir Crit Care Med 2000;162:2033-8.
20. Reichler MR, Reves R, Bur S, Thompson V, Mangura BT, Ford J, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. JAMA 2002;287:991-5.
21. Gerald LB, Tang S, Bruce F, Redden D, Kimerling ME, Brook N, et al. A decision tree for tuberculosis contact investigation. Am J Respir Crit Care Med 2002;166:1122-7.
22. National Institute for Health and Care Excellence. Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control [Internet]. 2011 [cited 2018 Jan 9]. Available from: https://www.nice.org.uk/guidance/cg117.
23. Erkens CG, Kamphorst M, Abubakar I, Bothamley GH, Chemtob D, Haas W, et al. Tuberculosis contact investigation in low prevalence countries: a European consensus. Eur Respir J 2010;36:925-49.
24. Bureau of Tuberculosis Department of Disease Control Ministry of Public Health, Thailand. Systematic screening for active TB and drug-resistant TB [Internet].

2017 [cited 2018 Jan 9]. Available from: https://goo.gl/oTSFnj.
25. National Institute for Health and Care Excellence. Tuberculosis: Guidance and guidelines [Internet]. 2016 [cited 2018 Mar 11]. Available from: https://www.nice.org.uk/guidance/ng33.
26. Nonghanphithak D, Reechaipichitkul W, Chaiyasung T, Faksri K. Risk factors for latent tuberculosis infection among health-care workers in Northeastern Thailand. Southeast Asian J Trop Med Public Health 2016;47: 1198-208.