A systematic review of the investigation and management of close contacts of tuberculosis in China

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ABSTRACT

Background Contact investigation is a logical approach to intensified case finding in China. However, currently there are no written national guidelines. The aim of this study is to review the published literature that describes the procedures followed by local level and report the yield for active tuberculosis (TB) cases.

Methods Studies conducted in China and published between 1997 and 2007 on contact investigation were searched.

Results Twelve studies were included in the review. There was no standard definition of contact and no study provided details on how to prioritize contacts. Investigation methods vary between each study. The number of contacts investigated per index case ranged from 22.7 to 658 in congregate settings and from 1.5 to 5.8 in household. The yields for active TB ranged from 0 to 11.765% in congregate settings and from 0 to 6.897% in household. The weighted yields for smear-positive index and smear-negative index were 1 and 0.2% respectively in household and 0.5% for pulmonary case index in congregate settings.

Conclusion There is considerable heterogeneity amongst the methods used and the cases yielded in these studies, and in general the quality of contact investigation is low; therefore, there is a need for China to develop national guidelines on contact investigation.

Keywords contact investigation, contact tracing, household contact, Mycobacterium tuberculosis, screening, tuberculosis

Introduction

China has the world’s second largest tuberculosis (TB) burden (after India) with more than 1.3 million new cases of TB every year.1 However, tremendous progress has been reached over the last decade: the global TB targets of 70% case detection rate and 85% cure rate set by the World Health Assembly2 were achieved by 2005 and have been maintained since that time.

In China, TB is principally diagnosed through evaluation of persons who present at TB institutions with symptoms and signs suggestive of TB. TB institutions fall under the responsibility of the Center for Disease Control and Prevention (CDC) that is responsible for all TB services including TB diagnosis, treatment and management in a defined area. Each province, prefecture and county has a TB institution. Passive identification of symptomatic cases and their effective treatment remains the pillar of the TB control strategy for China. In some settings where resources permit contact tracing and screening is conducted through interviews with local TB doctors. However, this is not common practice and is poorly documented.
In recent years, with more funding devoted to TB control, the threat of multi-drug resistant TB (MDR-TB) and growing prevalence of co-infection with TB and HIV, the current control strategy that stresses passive case finding alone may not be enough to have an impact on the transmission and incidence of TB. Consequently, contact investigation could be utilized both as an efficient and effective targeted approach to intensify TB case finding in a country that has already reached 70% of case detection rate. At the same time, contact investigation could identify high-priority candidates for treatment of latent TB infection (LTBI), which has been identified by public health officials as a priority area in China.

The World Health Organization has not issued clear guidance on how to conduct contact investigation or how to prioritize contacts except to say in children <5 years of age and persons with HIV infection who should be considered high-priority groups for tracing. However, guidance for contact investigation is provided in selected policy documents such as British Thoracic Society\(^3\) and National Institute for Health and Clinical Excellence\(^4\) but these are generally for use in low TB incidence and high resource settings. In China there are no detailed guidelines for contact investigation and the procedures for contact investigation have not been standardized at a national level; contact investigations are largely dependent on local understanding and practice. Up until now there have been no systematic reviews of the published literature on contact investigation in China. Therefore, a systematic review is needed to better understand the current practice and yield of active TB cases of contact investigations and to provide evidence base for formulation of appropriate policies in China.

### Methods

All published articles that reported contact investigation efforts were included in the review. The language of publications was restricted to English and Chinese and the location of contact investigations is limited to China. Pubmed, Ovid, CDSR, CINAHL and EMBASE and the most comprehensive Chinese electronic database Wanfang Data were searched up until October 2007. The search terms included: ‘tuberculosis’, ‘Mycobacterium tuberculosis’, ‘contact tracing’, ‘contact investigation’, ‘screening’ and ‘household contact’. Several additional search strategies were used to supplement this search to identify relevant articles not found in these databases. This included hand searching The Journal of the Chinese Antituberculosis Association for articles published between January 1997 and October 2007 and searching the reference lists of primary studies, reviews and editorials for additional relevant studies. Studies that reported the result of contact investigation in either congregate settings or households were included. No existing systematic reviews were found, nor was any literature found that specifically assessed studies of contact investigation. Ethics approval was not required for this review.

Fourteen publications that related to contact investigations in China were initially identified. Seven used household contact investigation and the other seven employed congregate settings (schools and one hotel) contact investigation methods. Two publications were excluded as they only reported the purified protein derivative (PPD) results of close contacts of TB patients. Thus, this study reviewed 5 published studies, with six in household and six in congregate settings (see Table 1).

The yield data are simple proportions for each study. Yield and prevalence of each study are weighted by the number of contacts investigated to summarize the weighted yield and prevalence. For the weighted calculation, in congregate settings, studies in Baoding\(^6\) and Hangzhou\(^7\) are excluded due to the inconsistency of characteristics of index case from the other studies. In household settings, studies in Changle\(^8\) and Hongkong\(^9\) are excluded due to lack of specific data on different types of pulmonary TB (PTB) patients.

### Findings

#### Contact investigation procedures used in China

##### Decision to initiate contact investigation

Of the 12 studies, 6 of them do not specify the bacteriology of index cases. Two studies initiate contact investigations from smear-positive index cases only, and three studies start from both smear- and smear-negative TB index cases and one remaining research in Hong Kong starts from clinical PTB cases (See Table 1).

##### Definition and nature of contacts in selected studies

There is no uniform definition of contact and close contact across the publications. The definition is largely dependent on local understanding and practices. Only two household investigations reported definition of contact\(^9,10\). One study in Hong Kong reported the definition of contact as family members living in the same room with the index cases for more than 30 days.\(^9\) The other research study in Yichang, Hubei\(^10\) reported the definition of contact as family members or other people who lived with smear-positive pulmonary TB cases for more than half a year. All six congregate setting investigations reported the definition of contact. They generally defined contacts as classmates or grade mates, close friends, coworkers and dormitory mates living in the same level of the building with the initial case detected.
### Table 1  Yield of contact investigations for studies reviewed

<table>
<thead>
<tr>
<th>Place</th>
<th>Year of study</th>
<th>Setting</th>
<th>Nature of index cases</th>
<th>Index cases</th>
<th>Nature of contacts</th>
<th>Contacts investigated</th>
<th>Contacts investigated per index case</th>
<th>Contacts with active TB (yield %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congregate settings</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baoding, Hebei</td>
<td>2003</td>
<td>College</td>
<td>All kinds</td>
<td>5</td>
<td>Same class and dormitory</td>
<td>1210</td>
<td>242</td>
<td>13 (1.1)</td>
</tr>
<tr>
<td>Benxi (1), Liaoning</td>
<td>1997/2000</td>
<td>School</td>
<td>PTB</td>
<td>1</td>
<td>Same class and same year</td>
<td>49</td>
<td>49</td>
<td>1 (2.0)</td>
</tr>
<tr>
<td>Benxi (2), Liaoning</td>
<td></td>
<td></td>
<td>PTB</td>
<td>1</td>
<td>Same class and family members</td>
<td>658</td>
<td>658</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dezhou, Shandong</td>
<td>2002/2003</td>
<td>School</td>
<td>PTB</td>
<td>3</td>
<td>Same class and same year and same dormitory</td>
<td>68</td>
<td>22.7</td>
<td>8 (11.8)</td>
</tr>
<tr>
<td>Dongshan, Guangzhou</td>
<td>2004</td>
<td>School</td>
<td>PTB</td>
<td>13</td>
<td>Same class</td>
<td>1095</td>
<td>84.2</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Hangzhou, Zhejiang</td>
<td>2003–2005</td>
<td>College</td>
<td>PTB (smear positive + smear negative)</td>
<td>1</td>
<td>Same workplace</td>
<td>35</td>
<td>35</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Qingdao, Shandong</td>
<td>2004</td>
<td>Hotel</td>
<td>PTB</td>
<td>1</td>
<td></td>
<td>2381</td>
<td>903</td>
<td></td>
</tr>
<tr>
<td>Household</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wuhan (1), Hubei</td>
<td>Not specified</td>
<td>Family</td>
<td>Smear-positive PTB</td>
<td>16</td>
<td>Family members</td>
<td>29</td>
<td>1.8</td>
<td>2 (6.9)</td>
</tr>
<tr>
<td>Wuhan (2), Hubei</td>
<td>Not specified</td>
<td>Family</td>
<td>Smear-negative PTB</td>
<td>26</td>
<td></td>
<td>38</td>
<td>1.5</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Changle, Fujian</td>
<td>Not specified</td>
<td>Family</td>
<td>PTB</td>
<td>49</td>
<td>Family members</td>
<td>174</td>
<td>3.6</td>
<td>7 (4.0)</td>
</tr>
<tr>
<td>Fengxian (1), Jiangsu</td>
<td>2005</td>
<td>Family</td>
<td>Smear-positive PTB</td>
<td>386</td>
<td>Family members and neighbors</td>
<td>2258</td>
<td>5.8</td>
<td>5 (0.2)</td>
</tr>
<tr>
<td>Fengxian (2), Jiangsu</td>
<td></td>
<td></td>
<td>Smear-negative PTB</td>
<td>278</td>
<td></td>
<td>1426</td>
<td>5.1</td>
<td>3 (0.2)</td>
</tr>
<tr>
<td>Henan</td>
<td>1993–1999</td>
<td>Family</td>
<td>Smear-positive PTB</td>
<td>4499</td>
<td>Family members</td>
<td>38423</td>
<td>4.4</td>
<td>357 (0.9)</td>
</tr>
<tr>
<td>Yichang, Hubei</td>
<td>1992–2001</td>
<td>Family</td>
<td>Smear-positive PTB</td>
<td>8672</td>
<td>Family members</td>
<td>2381</td>
<td>2.6</td>
<td>41 (1.7)</td>
</tr>
<tr>
<td>Hongkong</td>
<td>1996</td>
<td>Family</td>
<td>All kinds (clinical PTB)</td>
<td>903</td>
<td>Family members and colleagues</td>
<td>2381</td>
<td>2.6</td>
<td>41 (1.7)</td>
</tr>
</tbody>
</table>
Decision about how to prioritize contacts

To use time and resources wisely and efficiently, contact investigation should be focused on close contacts and contacts that are at high risk of developing disease if infected. None of the 12 published studies reviewed described the detailed procedures for identifying contacts and how they prioritized contacts. Only three\(^5,9,10\) stratified their contacts by age but the classification of children was inconsistent with children classified as under 14 in the Henan study,\(^1\) but under 15 in the Hubei study.\(^1\)

Investigation methods of contacts and medical treatment for contacts with LTBI

Investigation methods for TB contact varied across the studies assessed. Of the 12 published studies, \(^10\)\(^5\)–\(^8\),\(^11\)–\(^16\) investigated the contact by administering PPD skin test at the first step. Among these, five used PPD skin test as an independent screening strategy followed by chest radiograph for those with strong positive PPD results.\(^6\),\(^8\),\(^11\)–\(^14\),\(^16\) The other five administered chest radiograph and PPD simultaneously to contacts, followed by medical evaluation or sputum examination.\(^5\),\(^7\),\(^12\),\(^13\),\(^15\)

In the five studies with PPD as a first screening step, there were three different ways of classification of tuberculin reaction as criteria for further examination based on the different skin test reaction induration's diameter size.\(^8\) The remaining two studies report that patients with PPD positive result should undergo further test without defining what constitute a positive result.\(^8\),\(^11\)

Only three of the 12 published studies mentioned administering preventive treatment to people with LTBI.\(^5\),\(^11\)–\(^14\) Among these three, two\(^11\)–\(^14\) used isoniazid (INH) for 3 and 6 months, respectively. The other one,\(^16\) conducted in Henan, randomly allocates the people who need preventive therapy into three groups: the first group uses INH for 6 months; the second uses the combination of INH and rifampicin (RMP) for 3 months and the third uses the combination of RMP and pyrazinamide (PZA) for 2 months. This research shows that the first two groups using combination methods are both better than using INH alone in terms of acceptance and compliance by people.

Contact investigation among children or HIV-positive contacts

Only the study in Hong Kong\(^9\) focused on children under 5 years old who were exposed to infectious cases and differentiated the investigation methods between people who were over and under 5 years old. None of the published research reported HIV or other immunosuppressed status among contacts. No study reported offering HIV counseling and testing to contacts whose HIV-infection status was unknown. Only one publication\(^9\) in Hong Kong mentioned the concept of a window period for contacts of children under 5 years old, but did not give a follow-up test at the end of the window period.

Yield of contact investigations for active TB

In the six published studies in congregate settings, the number of contacts investigated per index case ranged from 22.7 to 658. The yield for active TB ranged from 0 to 11.8%. The highest yield of 11.8% was initiated from three active TB cases of school students, and a total of 68 contacts were investigated including 60 classmates, six teachers and two family contacts. Eight active TB were found among these 68 contacts. The number of contacts investigated per index case is 22.7 in this investigation. The weighted yield for PTB index case was 0.5%.

In the six household studies, the number of contacts ranges from 1.5 to 5.8 per index case and the yield for active TB ranged from 0 to 6.9% (see Table 1). The highest yield of 6.9% is initiated from 16 smear-positive PTB cases and a total of 29 contacts were investigated. Two active TB cases were found among these 29 contacts. The number of contacts investigated per index case is 1.8 in this investigation. The weighted yield for smear-positive and smear-negative index case was 1 and 0.2%, respectively.

Discussion

Main findings of this study

The systematic review seems to show that despite a great variation in the reported rates of yields for active TB in studies from congregate (range 0–11.8%) and household (range 0–6.9%) settings, investigation of contacts of TB cases is an effective mean for intensified case finding for TB in China. The weighted yield for smear-positive and smear-negative index case is 1 and 0.2%, respectively, in household. In congregate settings, the weighted yield for pulmonary TB index case is 0.5%. This means that the prevalence of active TB is particularly high in risk groups such as household contacts and congregate settings that are easily identifiable. In fact, our systematic review shows that in household the weighted prevalence of contacts of smear-positive and smear-negative index cases is 995/100 000 and 205/100 000, respectively while in congregate setting the weighted prevalence of contacts is 552/100 000.

What is already known on this topic?
The World Health Organization has not issued clear recommendations on contact investigation except for children
<5 years of age and persons with HIV who are exposed to infectious TB. For this reason, countries have not been urged to develop written guidelines for the use and approaches to contact investigation that is only conducted in countries with high resources and low TB burden. Lack of guidance resulted in lack of consistency around the definition of index case, contacts and methodology on how to conduct contact investigation and on how to prioritize contact groups. Two recent studies by US CDC also indicated that a lack of consistency about contact definitions is common throughout USA. The American authors observed that the variations in definitions limited the ability to analyse data on contact investigations. This is the same type of problem we encountered in our systematic review.

What this study adds and limitation of this study
A systematic review on household contact investigations in low- and middle-income countries showed that the pooled yield among household contacts was 4.5% for all active TB (bacteriologically confirmed and clinically diagnosed), 2.3% for bacteriological confirmed TB and 51.4% for LTBI. These are remarkably high yields for a TB control intervention. For the six household studies in China, which reported eight investigations (two of the publications reported two different investigations), we reported much lower weighted yield with great variance in the reported rates of yields of active TB (range 0–6.9%). Possible explanations for the widely varying yields may include different nature of index cases in which contact investigation initiated, great variability in diagnostic criteria among studies, a lack of standard criteria for expanding investigations beyond the most frequent contacts to include those with less frequent exposure and no standard procedures for identifying, screening and tracking contacts, etc. Furthermore, most of the studies had a small sample size and number of papers that met the criteria for this review was also small. All of the above justifications are also part of the limitations of our systematic review.

Another area that requires further investigation is a relatively high yield for active TB in congregate settings. This high yield highlights importance and urgent need to consider contact investigation as a key strategy in TB control work in schools.

If contact investigation is a mean of intensified case finding in high TB burden area, it also can help identify a group at risk of developing active TB (because of presumed recent infection) in the following 1–2 years who may be candidates for treatment of LTBI. Although the primary aim of the systematic review was not to assess the LTBI preventive therapy, three studies did provide LTBI preventive therapy and five studies did use PPD as a screening method for contact investigation. Although we acknowledge the importance of exclusion of active TB and treatment of latent infection we believe that the interpretation of the results of the PPD readings should not be part of this paper. Instead, we call for more research and for the use of gamma-immunoassay to assess infection in a Bacillus Calmette–Guérin immunized population like in China if treatment of latent TB infection is going to be a strategy to be adopted.

In conclusion, the weighted prevalence of contacts of index cases in both households and congregate settings is high enough to merit attention as a target group for intensified case finding. At the same time, the great variation in the reported rates from the studies shows the poor quality of data and calls for caution in their interpretation. However, with more funding devoted to TB control, priority should be given to development of clear national guidance on contact investigations and implementation of further research to help evaluate the effectiveness of such interventions. China will greatly benefit from interventions that will improve its TB control strategy to reach a 100% case detection rate. Based on our systematic review, contact investigation is well placed to contribute to reach such target.

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