International Journal of Infectious Diseases 88 (2019) 34–40

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Assessment of active tuberculosis findings in the eastern area of China: A 3-year sequential screening study

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ARTICLE INFO

Article history:
Received 9 May 2019
Received in revised form 23 July 2019
Accepted 24 July 2019
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Tuberculosis
Active screening
High prevalence
Target population

ABSTRACT

Background: Tuberculosis (TB) is a critical global public threat, and limited epidemiology studies have been performed to explore the efficacy of active TB screening.
Methods: Three sites located in eastern China were chosen in 2013, and three rounds of systematic screenings were performed in permanent residents aged older than 15 years.
Results: The TB incidence showed a downtrend after several rounds of active screening at the three sites, and a significant change was observed at site A in the overall population. In the target population at sites A and B, both the elderly and people with a history of TB had a remarkable decline through the first or second round of screening. The implementation of active case-finding identified 2.36 [1.47,3.81] (2013 vs. 2012) and 1.49 [1.1,2.03] (2013–2015 vs. 2010–2012) more potential cases than the passive case-finding by the surveillance system at site A.
Conclusions: Active case-finding of tuberculosis might be effective in high prevalence area with a low economic level, particularly among the elderly and people with a history of TB. Additionally, new rapid diagnosis technology should be considered to decrease the prevalence among people with a history of TB. Ultimately, active screening identified more active TB cases than passive case-finding, particularly in high prevalence area with underdeveloped economics.

Introduction

As the ninth leading cause of death in 2016, tuberculosis (TB) is a major public health issue worldwide, particularly in low- and middle-income developing countries, and nearly one-third of the global population is believed to be infected with TB (Sánchez et al., 2018; Floyd et al., 2018; Karki et al., 2017). According to the Global Tuberculosis Report in 2018, 10.0 million people, including 5.8 million men, 3.2 million women, and 1.0 million children, developed TB in 2017; two-thirds of these cases occurred in eight countries, and China, which has a high disease burden, was the second highest country, accounting for 9% (World Health Organization Geneva, 2018). As a rapidly developing country, China also has 13% of all drug-resistant TB cases worldwide, including multidrug resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB) cases (World Health Organization Geneva, 2018). Thus, controlling the threat from TB remains a vital public health concern in China.

The established targets of the End TB Strategy suggest that compared with 2015, a 90% reduction in TB deaths along with an 80% reduction in TB incidence should be achieved by 2030 (World Health Organization Geneva, 2018). To accomplish this goal, a

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https://doi.org/10.1016/j.ijid.2019.07.029

series of procedures, including the early diagnosis of TB, sufficient resources from political commitments and new tools and vaccination for TB, should be urgently carried out. Active case-finding (ACF) screening was deemed an appropriate method to identify more active cases, and relevant recommendations were released by the World Health Organization (WHO), which included strong recommendations for screening household contacts and other close contacts, people living with HIV and current and former workers in workplaces with silica exposure (World Health Organization Geneva, 2013). Additionally, the WHO provided guidelines regarding the diagnosis and management of TB in people with diabetes, refugees and prisoners. However, previous studies had demonstrated that the high morbidity of TB in China was found in some specific groups, such as the elderly, without a superior recommendation level by the WHO (Wang and Chen, 2012; World Health Organization Geneva, 2011; Chen et al., 2017). Thus, simply following the WHO recommendations might not result in a sharp reduction in TB prevalence, and the suitable target population for the implementation of ACF screening in China is still unclear (Gao et al., 2017).

Thus, the aims of this study were to investigate the efficacy and efficiency of ACF screening in the eastern regions of China, covering three unique research sites with different baselines of TB incidences and economic statuses. Simultaneously, the feasibility of ACF development in specific groups was explored in this study.

Methods

Study design and participants

We designed and carried out a prospective screening study using ACF among the overall populations at three sites (A, B and C) at the community level in eastern China. According to the general principles, including the well construction of health service system and low population mobility, three sites with diversity in TB epidemics and economic statuses were ultimately chosen. At each site, people aged older than 15 years who continuously lived at the site for six months or longer were eligible for our prospective study and viewed as the overall population. The overall population comprised the target population and nontarget population. The target population for TB included the elderly population ($\geq$65 years), the diabetic population, people with a history of TB, contacts from historical index cases and the HIV/AIDS population; all other individuals constituted the nontarget population. The collection of related baseline data included information regarding the permanent population, and the preliminary identification of the target population was performed based on electronic resident health records and door-to-door interviews during the first half of 2013.

Study procedures

The overall population in this study was required to complete a questionnaire survey and a simple physical examination by a door-to-door interview. During the course of performing the survey, the respondents who had difficulty in communicating were interviewed by their family members. In this survey, the uniform questionnaire was used to collect demographic data, such as age, gender, occupation, educational level, and smoking and drinking history, and the information regarding the target population was reconfirmed. The physical examination was employed to acquire some check-up data, such as height, weight and waist data, from the screened population. Combined with the previous baseline survey and on-site confirmation, all respondents were divided into the nontarget population and target population with different dispositions. The respondents in the nontarget population underwent a symptom screening, which was used to collect information regarding the presence and duration of symptoms implying a possibility of TB, including the possible symptoms of cough, hemoptysis, fever, chest pain, night sweat, decreased appetite, weakness and weight loss (>3 kg), over the past one month (Corbett et al., 2010a; Golub et al., 2005). Based on the common symptoms of active TB and available studies, people with one of the following options during the symptom screening were denoted as TB suspects: (1) continuous cough for more than 2 weeks; (2) onset of hemoptysis; and (3) cough between 1 and 2 weeks along with any of the remaining symptoms mentioned above (Corbett et al., 2010a; Golub et al., 2005). If abnormalities were identified in the symptom screening, the suspect respondents further underwent chest radiography, sputum tests covering sputum smear and sputum culture to identify active TB cases. The chest radiography was performed using a Mobile X-ray light car or arranging for an immediate radiation examination at community hospitals; three sputum specimens (one on the spot, one in the early morning and one at night) were collected for a series of laboratory diagnostic tests. The target population was directly screened by chest radiography (X-ray); In the case of an abnormal chest radiograph, the sputum tests were performed. Based on the combination of a clinical diagnosis and/or etiological outcomes from the laboratory, the number of active TB cases was determined. The detailed implementation of this study is shown in Figure 1.

Study outcome definitions

In this study, three rounds of ACF screening were carried out each year between 2013 and 2015, and the study outcomes were categorized as an incident of TB, death, transfer from the study sites, or rejection of a yearly chest radiography during the screening process. We observed and recorded the first outcome above as the ending point of this study. For those diagnosed with TB, medical treatment was arranged at a local designated hospital, and health education for the prevention and treatment of TB was provided to the family members. Four categories of the target population, including the elderly population, the diabetic population, people with a history of TB and the HIV/AIDS population, were identified by available surveillance systems, monitoring reports and local community health records. Additionally, contacts from historical index cases, who were defined as close contacts with smear-positive TB cases for more than 8 h or smear-negative TB cases for more than 40 h in the previous three months, were confirmed by consulting the active TB cases identified by ACF screening.

The diagnostic criteria for TB refer to WS288-2008 in China. A bacteriologically positive TB patient was defined as an individual with at least one positive sputum smear or culture. A positive smear was defined as a sputum specimen that had at least one acid-fast bacillus identified within 100 fields under microscopy. A positive culture was defined as a specimen with at least one positive isolated colony of *Mycobacterium tuberculosis* using Löwenstein-Jensen medium. The results of etiologic diagnosis or clinical diagnosis were gained within three months from local designated hospitals. In the designated hospital, for those diagnosed with bacteriologically negative TB or without pathogenic results, the final results of the clinical diagnosis were discussed, and consensus was reached by a group of experts, who were recruited from provincial/municipal TB designated hospitals. The final diagnosis of TB was confirmed after obtaining any of the following results: positive bacteriological test, diagnostic treatment failure, changes observed in chest radiography film before and after anti-TB treatment, or other consistent agreements regarding related tests by the expert group.

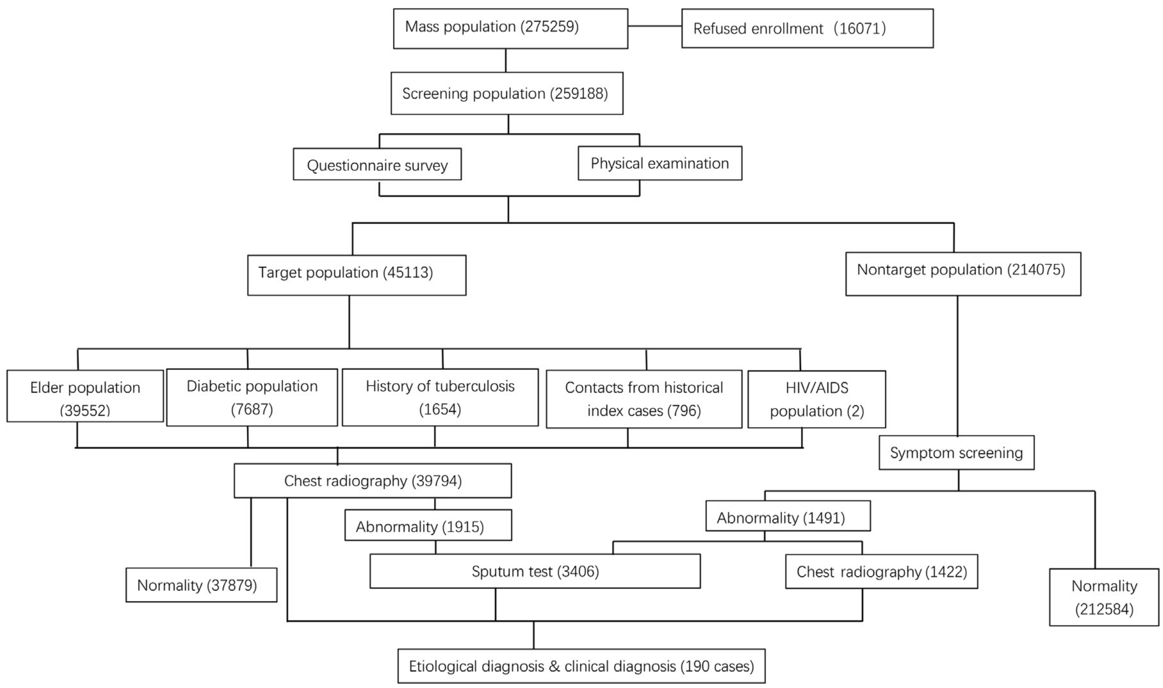

Figure 1. Flow chart of the active TB screening performed in this study. The number without unit in each level was viewed as the screening of man-time.

Table 1
General information of the included sites in three areas.

Province		Zhejiang Province	Jiangsu Province	Shanghai City
Region		Site A in Jiangshan City	Site B in Danyang County	Site C in Minhang District
Screening location		Mobile X-ray light car	Mobile X-ray light car	Mobile X-ray light car/radiological department at community hospitals
GDP per capita		38,888 RMB	67,478 RMB	68,664 RMB
X-ray equipment		Digital radiography	Digital radiography	Digital radiography
Current standard		500 (mA)	500 (mA)	500 (mA)
2013	Screened population	29,834	31,403	31,585
2014	Screened population	30,195	32,110	30,333
2015	Screened population	30,266	31,746	27,787

Ethics statement

This study was approved by the Ethics Committee of the Chinese Center for Disease Control and Prevention. Informed consent forms were signed by all responders. All personal information was kept confidential as required. The active TB and suspect cases were given information regarding additional consultation and referrals to designated local hospitals.

Statistical analysis

The information from all valid questionnaires was double-entered by using EpiData software (EpiData 3.01 for Windows; The EpiData Association, Odense, Denmark). All results were determined using SAS 9.2 (SAS Institute Inc., Cary, NC), R (R version 3.5.2) and SPSS Statistics 20.0 (SPSS Inc., Chicago, USA). All results were considered statistically significant at a two-sided $P < 0.05$.

Results

General details of the active TB screening at the three sites

In this study, the selected sites carried out this survey with the same design proposal. The GDP per capita at site A was lower than that at the other two sites. The information of the three sites is shown in Table 1, and the details of the screening rate and examination rate by X-ray over the three years are presented (Supplement Table).

Active case-finding screening for TB at the three sites

The active screening for TB at the three locations identified a total of 103 active TB cases at site A, 56 cases at site B and 31 cases at site C. Over three years, the absolute number of findings declined at the three locations, particularly at site A. In addition, the details of diagnostic results in three sites over three years are presented in Table 2.

Table 2
The details of TB diagnostic results in three sites over three years.

Region	Year	Etiological diagnosis of TB	Clinical diagnosis of TB	Total
Site A	2013	21	36	57
	2014	10	18	28
	2015	9	9	18
Site B	2013	8	14	22
	2014	7	15	22
	2015	4	8	12
Site C	2013	6	6	12
	2014	8	5	13
	2015	2	4	6

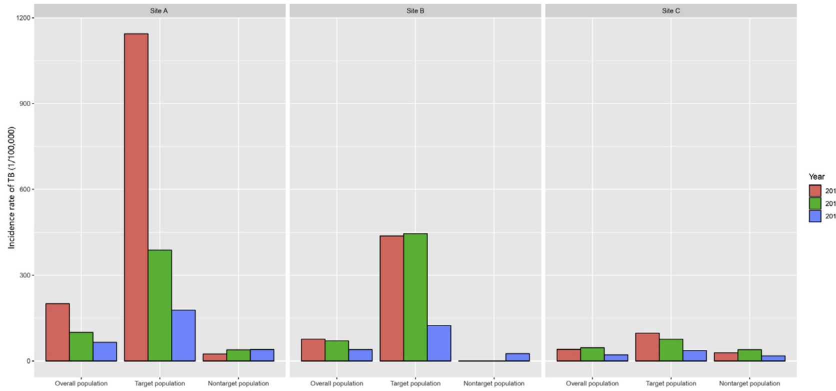

Figure 2. Fluctuation in the active TB incidence at three sites during the active screening.

Efficacy of active TB screening among different populations

According to the ACF screening, we further analyzed the incidence of TB in the overall population, target population and nontarget population. Regarding the overall population, the ACF screening for TB showed an obvious decline in the TB incidence during the following two years compared with the baseline incidence based on the screening performed in 2013, particularly at site A with a nearly 67% reduction. Regarding the target population, a sizable decrease in the active TB incidence was demonstrated, but this phenomenon was not found in the nontarget population. These details are presented in Figure 2.

Subgroup analysis of active TB screening in the target population

Considering the screening effectiveness in different subgroups of the target population, the changes in the active TB incidence are described in Table 3. The results revealed that performing ACF screening in the elderly population could contribute to a consecutive decrease in the TB incidence at the three sites. In the group of people with a history of TB, the TB incidences at the three sites were all higher than those in the other subgroups based on the result from the first year of screening. Additionally, the TB incidence among people with a history of TB showed a decreasing trend after several rounds of screening.

Effectiveness and efficacy of active TB screening in the study population

In this study, the rate difference (RD) and its 95% CI (confidence interval) were used to evaluate the effectiveness and efficacy of ACF. Using consecutive active TB screening from 2013 to 2015, only the incidence at site A after the first round of screening showed a reduction with statistical significance in the overall population. Furthermore, in the target population, site A presented a successive decline ($P < 0.05$) during the study period, and the results obtained at site B displayed a significant decrease after two rounds of ACF screening. In addition, our limited results suggest that some specific subgroups, such as the elderly population and people with a history of TB, could benefit from ACF screening at site A and site B. In the diabetic population, ACF screening could generate a rapid reduction during the first round of screening at site A. No statistically significant difference was identified at site C. The details are shown in Table 3.

Comparison of active case identification between ACF screening and the TB surveillance system

Given that the screening efficacy of ACF was only found in the overall population at site A, we further collected the number of reported TB cases through a surveillance system (also called passive case-finding, PCF) during the 2010–2012 period. Our available results showed that ACF was 2.36 [1.47,3.81] (2013 vs. 2012) and 1.49 [1.10,2.03] (2013–2015 vs. 2010-2012) times than PCF.

Discussion

Although the UN Sustainable Development Goals and the WHO's End TB Strategy were issued over the past few years, the downtrend in the estimated TB incidence was slow worldwide, especially in high-burden countries. Recently, a renewed focus on the ACF screening has emerged to control epidemics (Dobler, 2016). Growing studies have explored whether ACF could improve the early finding of active cases, lower TB transmission at the community level, and shorten the diagnostic delay (Kranzer et al., 2013). Although the intervention methods, study objects, and assessment methods vary and controversies exist, some studies have proven the potential effect of active TB screening on the control of TB epidemics (Kranzer et al., 2013). One study conducted in the United States assessed a project involving mandatory screening along with phylaxis and treatment for homeless people, and the results showed that the TB incidence had decreased by nearly 90% over ten years with a more dramatic decrease than that observed in other districts (Rendleman, 1999). Other scholars have also documented that the decreasing TB incidence might be caused to some extent by the implementation of ACF (Ayles et al., 2013; Corbett et al., 2010b).

In China, the existing strategy used to control and prevent active TB is based on PCF, denoting that symptomatic patients actively seek assistance from medical services. The influence of sociodemographic characteristics, such as unemployment, low income, limited medical conditions, patient delay and health system delay, might be inescapable, consequentially inducing TB transmission and infection in the overall population or some specific groups (Cai et al., 2015; Li et al., 2018). Thus, using the ACF strategy to identify active TB cases and shorten the various delays has potential merit. However, to the best of our knowledge, long-term research investigating different sites based on a baseline of various TB incidences and distinct economic levels is still a paucity in China, and the assessment of active TB screening in diverse subgroups has not been performed.

Our study performed a 3-year screening in the eastern area of China at three sites with various levels of economic status; the GDP per capita at site A was half of that at sites B and C. After three rounds of ACF screening between 2013 and 2015, in total, 103, 56, and 31 active cases were identified at site A, site B and site C, respectively. According to the incidence rate based on ACF screening in the overall population in 2013, we classified the three sites as high epidemic (>100/100,000), medium epidemic (50/100,000–100/100,000) and low epidemic

Table 3
Incidence rate (1/100,000) and rate difference (RD) among different groups at three sites during the 2013–2015 period.

Region	Indicators	Year	Overall population	Target population						Nontarget population
				Elderly population	Diabetic population	History of tuberculosis	Contacts from historical index cases	HIV/AIDS population	Total	
Site A	Incidence rate	2013	200.3	1136.7	1912.6	5610.6	0	–	1144	24.9
		2014	99.9	394.5	0	664.5	790.5	–	387.8	38.9
		2015	65.4	175.1	0	655.7	0	–	178	40.1
	RD[a] and 95% CI, P	2013 vs.2014	100.4[36.3,164.3], $P=0.002$	742.1[367.3, 1116.9], $P<0.001$	1912.6[533.0,3292.0], $P=0.007$	4946.1[2117.0,7775.0], $P<0.001$	−790.5[-1939.6,358.5], $P=0.175$	–	756.2[405.4,1107.1], $P<0.001$	$P>0.05$
		2013 vs.2015	134.9[74.2,195.5], $P<0.001$	961.6[625.6, 1297.6], $P=0.001$	1912.6[592.0,3234.0], $P=0.005$	4954.9[2145.0, 7765.0], $P<0.001$	–		966.0[646.2,1285.8], $P<0.001$	
		2014 vs.2015	34.5[-13.4,82.4], $P=0.158$	219.4[-1.4,440.3], $P=0.051$	-	8.8[-1285.0, 1302.4], $P=0.980$	−790.5[-591.5,2172.5], $P=0.262$		209.8[1.4,418.1], $P=0.049$	
Site B	Incidence rate	2013	76.4	409.5	120.2	11029.4	0	–	437.6	0
		2014	70.5	331.0	365.9	9523.8	0	–	445.4	0
		2015	39.8	123.5	0	2739.7	0	–	124.1	23.7
	RD and 95% CI, P	2013 vs.2014	5.9[-37.4, 49.3], $P=0.789$	78.5[-178.6, 335.6], $P=0.550$	−245.7 [-720.2, 228.9], $P=0.310$	1505.6[−7289.0,10300], $P=0.737$		–	−7.8[-268.7, 253.1], $P=0.953$	–
		2013 vs.2015	36.6[-2.2, 75.4], $P=0.064$	286.0[63.2, 508.8], $P=0.012$	120.2[-117.0,357.3], $P=0.320$	8289.7[179.0,16400.0], $P=0.045$			313.5[103.2, 523.9], $P=0.004$	−23.7[-43.3, -4.13], $P=0.018$
		2014 vs.2015	30.7[-6.6, 67.9], $P=0.107$	207.5[1.0,413.9], $P=0.049$	365.9[-47.9,779.6], $P=0.083$	6784.1 [-1131.0,14699.0], $P=0.093$			321.4[109.2, 533.6], $P=0.003$	−23.7[-42.31, -5.1], $P=0.013$
Site C	Incidence rate	2013	40.9	66.7	0	1183.4	0	–	97.5	28.9
		2014	46.3	42.9	0	641	0	100000	76	39.4
		2015	21.8	40.2	0	787.4	0	0	36.4	18.1
	RD and 95% CI, P	2013 vs.2014	−5.4[-39.5, 28.7], $P=0.757$	23.8[-71.92,119.6], $P=0.626$	–	542.4[-1548.3, 2633.2], $P=0.611$	–	–	21.5[-91.7, 134.6], $P=0.710$	−10.5[-43.8,22.8], $P=0.536$
		2013 vs.2015	19.1[-10.1, 48.3], $P=0.200$	26.5[-66.2,119.2], $P=0.575$		396.0[-1921.2, 2713.2], $P=0.738$		–	61.1[-36.5, 158.7], $P=0.220$	10.8[-17.4,38.9], $P=0.453$
		2014 vs.2015	24.5[-6.2, 55.2], $P=0.118$	2.7[-78.8, 84.1], $P=0.949$		−146.4[-2115.6,1822.9], $P=0.884$		1.0 [96000.0,296000.0], $P=0.317$	39.6[-49.6, 128.8], $P=0.380$	21.3[-10.2,52.3], $P=0.185$

[a] RD: rate difference; CI: confidence interval. –: beyond computation.

(<50/100,000) areas. Generally, through the 3-year screening, the active TB incidence at the three sites had decreased by half compared to the prior incidence, especially in the target population. This decrease might be attributed to ACF screening along with a series of daily prevention and control measures and relevant policy-making related to TB. Interestingly, the downtrends of TB incidence at the three sites were identified, while a significant decrease in the overall population was observed only at site A, which had a lower economic level and a higher TB incidence than the other two sites. The following reasons might explain this phenomenon. First, regions with a high prevalence have a sizable number of active TB cases, and active identification with reasonable treatment could further reduce chronic transmission in the ambient environment. Second, given the low economic level, some people living in this region might not have initially been willing to visit a doctor due to transportation inconvenience or costly medical expenses. Nonetheless, the active TB screening available for free in this study and propaganda regarding the potential risk and available relief measures during the process of screening might not only offer the potential convenience of primary diagnosis to respondents but also improve the zeal of TB treatment in the community population. Meanwhile, in developed areas with a low TB prevalence, such as site C, the comfortable and humanistic local medical environment might contribute to advancement in seeking treatment for symptomatic patients, promoting the maintenance of a lower TB incidence. In this study, further results showed that the ACF strategy in the target population presented a downtrend in the TB incidence at sites A and B with a high or medium TB incidence, while this decrease was not demonstrated in the low TB incidence area, i.e., site C. Additionally, the ACF screening in the nontarget population did not show an effect on incidence decline at site A and C, and even a reversal was observed at site B. Combined with the above evidence, this finding implied that the implementation of ACF might be more suitable in high prevalence areas and that its critical role was to identify more active TB cases in the target population. Furthermore, the reversal in the nontarget population at site B might be attributable to the close contact of active TB cases in the migrant population and TB occurrence from previous latent tuberculous infection (LTBI). Even so, by using several rounds of active screening, the TB incidence in the nontarget population was under the low prevalence observed at site B.

In this survey, combined with the WHO recommendations and actual situation in China, five subgroups comprising the elderly population, the diabetic population, people with a history of TB, contacts from historical index cases and the HIV/AIDS population were considered as the target population. The rate difference (RD) and its 95% confidence interval (CI) were utilized to explore the efficacy of TB screening. In various target populations, increasing evidence has demonstrated that the elderly represented a high-risk group, especially in rural western China (Chen et al., 2017). Our results showed that ACF screening might decrease the TB epidemic in the senior group after several rounds at high and medium epidemic sites, but this decrease was not observed in the economically developed low-epidemic region, i.e., site C. This might be largely attributable to the convenient accessibility to physical examinations of this specific group by ACF screening. Thus, more active TB cases among the elderly population could be identified, which prompted timely treatment in this group. However, in developed area with a low incidence of TB, the high-quality medical environment could attract more suspected cases seeking medical services, which might play the same role as ACF screening, causing the indistinctive difference consequently. Regarding people with a history of TB, we found that the active TB incidence at the three sites was higher than that in the other subgroups from the result of the first year of screening. This extraordinary phenomenon might be caused by the diagnosis and treatment quality of TB and reinfection of TB in external environments. That is to say, the imperfection in the TB cure criteria in the clinic and previous lack of diagnostic tools with a high sensitivity might inevitably lead to the misdiagnosis of cure at the end of the routine course. Meanwhile, a circle of friends in this specific group might have active TB unidentifiably, possibly causing TB reinfection after becoming cured, particularly in areas with a high prevalence of TB. Although these hypotheses were not proven in this study, testing for pathogens using new rapid diagnosis technology should be popularized and applied as soon as possible in designated hospitals at the county level. Such testing could enhance the identification of etiology after the achievement of treatment and increase the active TB findings in close contacts. Among the diabetic population, ACF screening presented a rapid reduction at site A, but no statistical significance was observed at site B. Available studies had demonstrated a positive association between diabetes and TB (Cheng et al., 2017). At site A, some factors such as the nutritional status, risk of TB infection and levels of blood glucose control might influence the baseline level of comorbidity of the two diseases. Additionally, the lower economic level at this site might cause a lower intention of undergoing PCF whereas ACF screening might evade the issues, consequently resulting in a decline of TB incidence in the following years. In total, although potential mechanisms and other influencing factors in target populations were not further explored, the available clues suggest that areas with a high TB incidence and low financial situation, such as site A, might benefit from ACF screening in this study. Furthermore, due to the paucity of sufficient data, the findings of contacts from historical index cases and the HIV/AIDS population were not identified and should be investigated in the future. Interestingly, at site C, although the implementation of ACF did not show a statistical advantage in decreasing the TB epidemic, it still presented a downtrend and maintained a low prevalence level. Given the possibility of population mobility from high prevalence areas, we suggest that more attention should be focused on migrant populations and LTBI in the local population to fulfil the Stop TB strategy in developed regions of China.

Additionally, we compared the TB identification by ACF screening with the results of PCF from the surveillance system. The results demonstrated that the number of TB identification at site A by ACF during the first year and throughout the study period was significantly more than in 2012 and the 2010-2012 period. This finding is consistent with previous studies (Chen et al., 2017; Eang et al., 2012). Thus, this consequence further proved the superiority of ACF screening in areas with high epidemics and underdeveloped economies by enhancing the identification of active TB cases.

Ultimately, after three rounds of TB screening, the target population still presented a higher TB incidence than the nontarget population at our study sites. This phenomenon suggests that the implementation of ACF should be carried out long-term rather than via a singular action. Therefore, the persistent interval of ACF screening for TB and the influencing factors in relation to the period of ACF screening should be explored in the future.

Limitations

Some limitations in this study should be mentioned. First, the cost-effectiveness of TB screening was of substantial importance for TB control and intervention by influencing the popularization and application of the screening strategy, while it was not considered and analyzed in this study. Second, although the common routine of TB screening was utilized in this study, new diagnostic tools, such as Xpert MTB/RIF, were not used in the screening, which might reduce the sensitivity and speed of active TB identification. In addition, given the high TB prevalence in China, research investigating LTBI in the overall population was not a priority in this study; thus, the distribution of LTBI in subgroups coupled with further intervention was not explored, which might cause the continuous onset of TB in some target populations with a higher prevalence than that in the non-target population despite performing several rounds of screening. Additionally, given only the final results of etiological diagnosis or clinical diagnosis required from the local designated hospital, some details such as valid results of both smear and culture were not collected in our previous design, which caused a deficiency and might influence the assessment of denominators in the lab sessions. Ultimately, no parallel control groups were established, which could affect the evaluation of ACF screening at the study sites.

Conclusion

In conclusion, this study identified some important aspects after the implementation of TB screening at three different sites in eastern China. The eligible evidence showed that ACF screening might be effective and efficient in high prevalence area with a low economic level by playing a vital role in accelerating the identification of more cases, reducing the TB incidence and controlling the epidemic, particularly in elderly individuals and people with a history of TB. Additionally, new rapid diagnosis technology should be considered to decrease the TB prevalence in people with a history of TB. Ultimately, ACF screening could identify more active TB cases than PCF by a TB surveillance system in high prevalence area with underdeveloped economics.

Author contributions

L.K. drafted the manuscript. P.Y. collected and screened the data. Z.Q. implemented the study. C.J. revised the manuscript. Y.H. implemented the study. T.L. implemented the study. C.B. revised the manuscript. W.W. revised the manuscript. W.F. revised the manuscript. H.T. analyzed the data, Z.Y. drafted the manuscript. Z.L. revised the manuscript. C.S. analyzed the data. C.C. collected and screened the data. B.H. interpreted the results. W.X. wrote and revised the manuscript. J.J. wrote and revised the manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

This work was supported by the Project of Key Project of Chinese National Programs, China [2013ZX10003004-001], Zhejiang Provincial Science and Public Welfare (LGF19H260004), Key Laboratory of Public Health Safety (Fudan University), Ministry of Education, China (GW2019-3), Philosophy and Social Science Project of Zhejiang Province (19NDJC243YB), and Project of Zhejiang Provincial Medical and Health (2015KYB428, 2016KYB055 and 2019RC135). We would like to thank the National Center for Tuberculosis Control and Prevention, Chinese Centers for Disease Control and Prevention (CDC) for their support and assistance. We also appreciate the local Center for Disease Control and Prevention (CDCs), community healthcare center and TB-designed hospitals for their help in the operation of the survey in Zhejiang Province, Jiangsu Province, and Shanghai Municipality.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ijid.2019.07.029.

References

Ayles H, Muyoyeta M, Du Toit E, Schaap A, Floyd S, Simwinga M, et al. Effect of household and community interventions on the burden of tuberculosis in southern Africa: the ZAMSTAR community-randomised trial. Lancet 2013;382:1183–94.

Cai J, Wang X, Ma A, Wang Q, Han X, Li Y. Factors associated with patient and provider delays for tuberculosis diagnosis and treatment in Asia: a systematic review and meta-analysis. PLoS One 2015;10:e0120088, doi:http://dx.doi.org/10.1016/S0140-6736(10)61425-0.

Chen C, Yang CG, Gao X, Lu ZZ, Tang FX, Cheng J, et al. Community-based active case finding for tuberculosis in rural western China: a cross-sectional study. Int J Tuberc Lung Dis 2017;21:1134–9, doi:http://dx.doi.org/10.5588/ijtld.17.0123.

Cheng J, Zhang H, Zhao YL, Wang LX, Chen MT. Mutual Impact of diabetes mellitus and tuberculosis in China. Biomed Environ Sci 2017;30(5)384–9, doi:http://dx.doi.org/10.3967/bes2017.051 Epub 2017/05/28.

Corbett EL, Zezai A, Cheung YB, Bandason T, Dauya E, Munyati SS, et al. Provider-initiated symptom screening for tuberculosis in Zimbabwe: diagnostic value and the effect of HIV status. Bull World Health Organ 2010a;88:13–21, doi:http://dx.doi.org/10.2471/blt.08.055467.

Corbett EL, Bandason T, Duong T, Dauya E, Makamure B, Churchyard GJ, et al. Comparison of two active case-finding strategies for community-based diagnosis of symptomatic smear-positive tuberculosis and control of infectious tuberculosis in Harare, Zimbabwe (DETECTB): a cluster-randomised trial. Lancet 2010b;376:1244–53, doi:http://dx.doi.org/10.1016/S0140-6736(13)61131-9.

Dobler CC. Screening strategies for active tuberculosis: focus on cost-effectiveness. Clinicoecon Outcomes Res 2016;8:335–47, doi:http://dx.doi.org/10.2147/ceor.s92244.

Eang MT, Satha P, Yadav RP, Morishita F, Nishikiori N, van-Maaren P, et al. Early detection of tuberculosis through community-based active case finding in Cambodia. BMC Public Health 2012;12:469, doi:http://dx.doi.org/10.1186/1471-2458-12-469.

Floyd K, Glaziou P, Zumla A, Raviglione M. The global tuberculosis epidemic and progress in care, prevention, and research: an overview in year 3 of the End TB era. Lancet Respir Med 2018;6:299–314, doi:http://dx.doi.org/10.1016/s2213-2600(18)30057-2.

Gao L, Li X, Liu J, Wang X, Lu W, Bai L, et al. Incidence of active tuberculosis in individuals with latent tuberculosis infection in rural China: follow-up results of a population-based, multicentre, prospective cohort study. Lancet Infect Dis 2017;17:1053–61, doi:http://dx.doi.org/10.1016/S1473-3099(17)30402-4.

Golub JE, Mohan CI, Comstock GW, Chaisson RE. Active case finding of tuberculosis: historical perspective and future prospects. Int J Tuberc Lung Dis 2005;9:1183–203.

Karki B, Kittel G, Bolokon Jr. I, Duke T. Active community-based case finding for tuberculosis with limited resources. Asia Pac J Public Health 2017;29:17–27, doi:http://dx.doi.org/10.1177/1010539516683497.

Kranzer K, Afnan-Holmes H, Tomlin K, Golub JE, Shapiro AE, Schaap A, et al. The benefits to communities and individuals of screening for active tuberculosis disease: a systematic review. Int J Tuberc Lung Dis 2013;17:432–46, doi:http://dx.doi.org/10.5588/ijtld.12.0743.

Li T, Zhang H, Shewade HD, Soe KT, Wang L, Du X. Patient and health system delays before registration among migrant patients with tuberculosis who were transferred out in China. BMC Health Serv Res 2018;18:786, doi:http://dx.doi.org/10.1186/s12913-018-3583-y.

Rendleman NJ. Mandated tuberculosis screening in a community of homeless people. Am J Prev Med 1999;17:108–13.

Sánchez MA, Pino J, Pacheco R, García JF. [Lethality analysis in patients with tuberculosis diagnosis in a high complexity hospital in Cali, Colombia]. Rev Chilena Infectol 2018;35:133–9, doi:http://dx.doi.org/10.4067/s0716-10182018000200133.

Wang LCS, Chen M. The fifth national tuberculosis epidemiological survey in 2010. Chin J Antituberc 2012;34:485–508.

World Health Organization Geneva. Collaborative framework for care and control of tuberculosis and diabetes. 2011. . [Accessed 7 July 2019] https://www.ncbi.nlm.nih.gov/books/NBK310833/.

World Health Organization Geneva. Systematic screening for active tuberculosis: principles and recommendations. 2013. . [Accessed 7 July 2019] https://apps.who.int/iris/handle/10665/84971.

World Health Organization Geneva. Global W. tuberculosis report 2018. 2018. . [Accessed 7 July 2019] https://www.who.int/tb/publications/global_report/en/.