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Study on the prevalence and incidence of pulmonary tuberculosis in high-risk populations in China

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Abstract: Objective: To obtain the prevalence, incidence of tuberculosis (TB) and influencing factors among elderly people aged 65 years and older, diabetic patients, people with TB history, close contacts of active TB patients, and HIV/AIDS patients (referred as "five key populations" hereafter) in China through continuous screening, and to provide basic evidence for developing screening strategies in key populations. Methods: In 27 townships/communities of 10 counties (districts) selected from 10 provincial-level regions located in eastern, central and western regions of China, face-to-face questionnaire surveys and chest X-ray examination were performed on all participants every year for three consecutive years. TB prevalence and incidence density of the five key populations were calculated, and univariate and multivariate analyses of different demographic characteristics were also conducted. Results: From 2013 to 2015, 38,193, 35,305 and 30,295 participants were screened respectively. After three years of continuous screening, the prevalence of bacteriologically confirmed TB in all key populations dropped by 28.9% [(246.1 – 174.9)/246.1 × 100%], and the annual decline rate was $15.7\%[(\sqrt{\frac{246.1}{174.9}}-1)\times 100\%]$; the prevalence of active TB dropped by 32.3% [(746.2 – 505.0)/746.2 × 100%], and the annual decline rate was $17.7\%[(\sqrt{\frac{746.2}{505.0}}-1)\times 100\%]$. Taking survey of 2013 as the baseline, the incidence density of bacteriologically confirmed TB and active TB with 1-year follow-up (2014) in all key populations were 132.3 per 100,000 person-years (36/27,202.4) and 143.7 per 100,000 person-years (71/49,393.8), while with 2-years follow-up (2015), they were 488.9 per 100,000 person-years (133/27,202.4) and 475.8 per 100,000 person-years (235/49,393.8). Multivariate analysis found: male, advanced age (group aged 75–84 and group aged 85 and older), living in rural areas, ethnic minorities, unmarried/divorced/widowed, low annual family income per capita (CNY 2300–9999) and malnutrition (body mass index BMI <18.5) were risk factors for TB (*OR* (95%*CI*) were 3.4 (2.6–4.5), 1.6 (1.22.2) and 2.2 (1.3–3. 5), 2.0 (1.5–2.8), 2.2 (1.6–3.0), 1.4 (1.1–1.9), 1.8 (1.3–2.4) and 1.9 (1.4–2.6), respectively), and overweight (body mass index ≧24) was a protective factor for TB (*OR* (95%*CI*) = 0.3 (0.2–0.5)). Male, ethnic minorities and low annual family income per capita (CNY 2300–9999) were risk factors for the onset of TB (*aHR* (95%*CI*) were 2.5 (1.9–3.5), 6.8 (4.8–9.6), 1.4 (1.0–1.9)), and overweight (BMI ≧ 24) was a protective factor for the onset of TB (*aHR* (95%*CI*) was 0.5 (0.4–0.7)). Conclusion: The five key populations are high-risk populations of TB in China. Continuous active screening should be carried out in those key populations to quickly reduce the tuberculosis epidemic. Through identifying people with different combinations of risk factors, we can set high-risk populations to target at them, thereby to increase the screening benefits.

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Systematic screening of close contacts of tuberculosis (TB) patients and other high-risk groups to achieve early detection and diagnosis of TB is an important part of the World Health Organization (WHO)'s End TB Strategy [1]. In 2013, the WHO issued systematic screening guidelines, systematic screening for TB in close contacts of tuberculosis patients, HIV/AIDS patients and those exposed to silica dust, is strongly recommended. And systematic screening for TB in other specific high-risk groups, such as people with TB history and diabetic patients, is conditionally recommended. It is to consider commending systematic screening to the population of different characteristics with a prevalence above 1% [2].

China is a country with high TB burden. In recent years, the number of newly registered pulmonary tuberculosis (PTB) patients has been around 800,000 per year, and there are a huge number of people with TB history, close contacts and people with latent TB infection. Moreover, the risk of morbidity increases with age [3–5], and the proportion of confirmed elderly TB patients reached 48.8% in the 2010 national TB epidemic sampling survey [6]. Therefore, in order to obtain the prevalence and incidence of PTB among former TB patients, close contacts of active TB patients, patients with diabetes mellitus, patients with HIV/AIDS, and the elderly aged 65 years and over (referred to as the "five key populations"), this study carried out active TB detection in the above five key populations for three consecutive years, so as to explore the impact of continuous screening on the prevalence of TB in these populations and provide basic data for the development of related screening strategies.

1 Objects and methods

1.1 Study sites and objects

1.1.1 Study sites

This study was conducted as part of the project of Study on Tuberculosis Epidemic and intervention Model, a National Science and Technology Major Project during the 12th Five-Year Plan period. The principles and methods of the study site selection were the same as those of research literature of this project [7]. A total of 27 townships (10) and communities (17) were selected from 10 counties/districts in Shanghai, Jiangsu, Zhejiang, Guangdong, Heilongjiang, Henan, Hubei, Sichuan, Yunnan, and Guangxi Zhuang Autonomous Region.

1.1.2 Objects

Face-to-face questionnaire surveys and chest X-ray examination were performed for three consecutive years from July to September during 2013–2015 among five key populations who had been living, working or studying at each study site for six months or more, including both registered and non-registered residents, as well as those who had been living at the research site but were away for short periods (< 6 months). From 2013 to 2015, 38,193, 35,305 and 30,295 were respectively screened, with a total of 103,793.

Definition of five key populations: (1) People with TB history: TB patients registered in the TB Management Information System during 2005–2012; (2) Close contacts of active TB patients: during the baseline survey, all close contacts of treated or newly diagnosed active PTB patients were defined as family members who lived in the same residence (including using the same bedroom or living room) with active pulmonary tuberculosis patients for at least 7 days or other people who were in direct contact with smear-positive patients for at least 8 hours or smear-negative patients for 40 hours within 3 months before diagnosis; (3) Diabetic patients: those who were registered in the personal health records of community health service centers/stations (village clinics), or who were asked to have a previous diagnosis of diabetes during the field investigation; (4) HIV/AIDS patients: HIV/AIDS persons registered in the county/district's Center for Disease Control and Prevention; and (5) People aged 65 years and older: people aged 65 years and older by September 30, 2013.

1.2 Survey content and methods

The national research group determined the project implementation plan and provided unified and standardized training for on-site researchers. An investigation team composed of staff from provincial, prefectural and county-level centers for disease control and prevention and doctors from township hospitals, village clinics and community health service centers (stations) was responsible for field investigation. The specific procedures were as follows。

1.2.1 Questionnaire survey and chest X-ray examination

Face-to-face questionnaire survey and chest X-ray examination were conducted among the five key populations. The questionnaire included basic demographic information, occurrence and duration of suspicious symptoms of PTB, contact history, past medical history, personal life style, and so on.

1.2.2 Sputum specimen examination

Three sputum samples of morning, night and immediate from patients with suspicious symptoms of PTB or abnormal chest X-ray examination were collected for smear, culture and strain identification. TB was defined as any one of the following three symptoms: (1) cough or expectoration for more than 2 weeks; (2) hemoptysis; and (3) cough and expectoration for 1-2 weeks, accompanied by any of the symptoms of fever, chest pain, night sweats, loss of appetite, fatigue and weight loss (> 3 kg).

1.3 Ethics review and quality control

This study was approved by the Ethics Review Board of Chinese Center for Disease Control and Prevention (approval number: 201322). The investigators were required to explain the purpose, significance, content, benefits and possible harms of the study to each subject in detail. All subjects signed an informed consent form, and if the subject was less than 15 years old (born after October 1, 1998), it was signed by their statutory guardian.

After preliminary verification of the questionnaire information, the site investigators used the online data collection system Information Management System for Study on the Incidence and Intervention Model of Tuberculosis to conduct double data entry. The data were exported and saved in the form of Excel (Microsoft office 2016). Westat company, a third-party organization, was invited to supervise and control the on-site implementation. At the same time, members of the national research group regularly went to the site for data verification, and spot checked the on-site data according to the proportion of 5% of patients.

A diagnostic team composed of clinicians, imaging doctors and laboratory experts from medical institutions at or above the county level was established in each study site to diagnose TB patients according to the WS 288-2008 Diagnostic Criteria for Tuberculosis [8], and all suspected and confirmed patients were reexamined by a national diagnostic expert group.

1.4 Statistical analysis

SAS 9.3 software was used to analyze the data. The prevalence was described by the number of cases (constituent ratio, %) or cases [prevalence (95%*CI*), 1/100,000]. The continuous screening was described by the decline of prevalence (%) and annual decline rate (%). Incidence density (1/100,000 person-years) was used as a surrogate index for incidence rate, considering that the cohort follow-up data may be irregular. Fixed cohort was used to calculate the incidence density, that is, taking the five key populations identified in 2013 as the baseline survey, the follow-up person-years of each subject (case) were calculated, and the incidence density (95%*CI*) was used as “1/100,000 person-years”, and Cox proportional hazard model was used for univariate analysis and multivariate analysis of data. Among them, the prevalence decline rate $= \frac{\text{prevalence in 2015} - \text{prevalence in 2013}}{\text{prevalence in 2013}} \times 100\%$, prevalence annual decline rate $= \left(\sqrt{\frac{\text{prevalence in 2015}}{\text{prevalence in 2013}}} - 1\right) \times 100\%$; the incidence density (/100,000 person-years) = $\frac{\text{number of cases in the follow-up years}}{\text{sum of person-years for all participants in the follow-up years}} \times 100{,}000 / 100{,}000 \text{ person-years}$.

2 Results

2.1 TB prevalence of the five key populations

Of the 103,793 participants screened from 2013–2015, 90.38% (93,804/103,793) were aged 65 years and above, and 13.30% (13,802/103,793) were diabetic patients. In 2013, the screening found that the prevalence of bacterial-positive PTB and active PTB in all key populations was 246.1 per 100,000 and 746.2 per 100,000, respectively, with the highest in people with TB history, as shown in Table 1. After 3 years of continuous screening, the prevalence of bacteriological PTB in all key populations decreased by 28.9%, and the annual decline rate was 15.7%. The prevalence of active PTB decreased by 32.3%, and the annual decline rate was 17.7%.

2.2 Prevalence of TB in the five key populations with different demographic characteristics

Because the prevalence of different characteristics of the surveyed population was basically similar in the three years, only the baseline survey data in 2013 was used as an example. The results of the univariate analysis of the logistics regression model showed that there were significant differences in all characteristics except marital status, and the prevalence of male, ≥ 75 years old, minority ethnic group, low family income per capita, malnutrition (BMI < 18.5), smoking history and drinking history were more than 1%. Multivariate analysis found that male, advanced age (≧ 75 years old), unmarried/divorced/widowed, living in rural areas, ethnic minorities, low annual family income per capita (CNY 2300–9999) and malnutrition (BMI < 18.5) were risk factors for TB and overweight (body mass index ≧ 24) was a protective factor for TB. Due to the obvious skewed distribution of age samples, although people with the age of below 65 also have a high prevalence rate, it is not considered to be of analytical significance. The details are shown in Table 2.

2.3 The incidence of TB in the five key populations

Taking 2013 as the baseline survey, the incidence of bacteria-positive PTB and active PTB detected in 1 year (2014) and 2 years (2015) of follow-up of all key populations was expressed as the incidence density. The incidence rates were 132.3/100,000 person-years and 143.7/100,000 person-years, 488.9/100,000 person-years and 475.8/100,000 person-years, respectively, with the highest incidence density among patients with previous TB. Due to the small number of observation person-years and incident cases in patients with active TB and HIV/AIDS, no valid incidence density was obtained. The details are shown in Table 3.

Table 1 Prevalence of TB of the five key populations in 2013–2015

Key populations	No.	Composition ratio (%)	Smear-positive TB		Active TB	
			No.	Prevalence rate(95%*CI*, /100000)	No.	Prevalence rate(95%*CI*, /100000)
In 2013						
People aged 65 years and older	34269	89.7	62	180.9(135.9–226.0)	193	563.2(483.7–642.6)
Diabetic patients	5150	13.5	15	291.3(143.9–438.7)	28	543.7(342.3–745.1)
People with TB history	1518	4.0	35	2305.7(1541.8–3069.5)	108	7114.6(5772.8–8456.5)
Close contacts of active TB patients	378	1.0	3	793.7(163.8–2320.1)	11	2910.1(1190.3–4629.8)
HIV/AIDS patients	59	0.2	1	1694.9(42.9–9440.7)	3	5084.7(1049.2–14864.4)
All key populations	38193	100.0	94	246.1(196.4–295.9)	285	746.2(659.6–832.8)
In 2014						
People aged 65 years and older	31999	90.6	42	131.3(91.6–170.9)	186	581.3(497.7–664.8)
Diabetic patients	4889	13.8	2	40.9(4.9–147.7)	18	368.2(198.1–538.3)
People with TB history	1275	3.6	23	1803.9(1066.7–2541.2)	90	7058.8(5600.5–8517.2)
Close contacts of active TB patients	493	1.4	1	202.8(5.1–1129.8)	2	405.7(49.1–1464.5)
HIV/AIDS patients	61	0.2	0	0.0(0.0–6049.2)	1	1639,3(41.5–9131.3)
All key populations	35305	100.0	58	164.3(122.0–206.6)	247	699.6(612.4–786.9)
In 2015						
People aged 65 years and older	27536	90.9	39	141.6(97.2–186.1)	122	443.2(364.4–521.7)
Diabetic patients	3763	12.4	5	132.9(43.1–310.1)	11	292.3(119.6–465.1)
People with TB history	1034	3.4	7	677.0(271.8–1394.6)	20	1934.2(1086.5–2782)
Close contacts of active TB patients	620	2.0	1	161.3(4.1–898.4)	6	967.8(354.8–2106.5)
HIV/AIDS patients	63	0.2	1	1587.3(40.2–8841.3)	1	1587.3(40.2–8841.3)
All key populations	30295	100.0	53	174.9(127.8–222.0)	153	505.0(425.0–585.1)

Table 2 The prevalence and influencing factors of TB in the five key populations with different demographic characteristics in 2013

Demographic characteristics	No.	Smear-positive TB		Active TB					
		No.	Prevalence rate (95%CI, /100000)	No.	Prevalence rate (95%CI, /100000)	χ^2	P	OR (95%CI)	aOR (95%CI)
Gender						80.637	<0.001	3.1(2.4–4.1)	3.4(2.6–4.5)
male	17908	70	390.9(299.3–482.5)	209	1167.1(1008.8–1325.3)				
female	20285	24	118.3(71.0–165.6)	76	374.7(290.4–458.9)				
Agegroup (years)						167.918	<0.001		
<65	3924	32	815.5(532.9–1098.0)	92	2344.5(1865.5–2823.6)			5.5(4.1–7.4)	7.6(5.6–10.3)
65–74	21685	22	101.5(59.1–143.8)	93	428.9(341.7–516.0)				
75–84	10658	30	281.5(180.8–382.2)	79	741.2(577.8–904.7)			1.7(1.3–2.3)	1.6(1.2–2.2)
>85	1926	10	519.2(197.4–841.0)	21	1090.3(624.0–1556.7)			2.6(1.6–4.2)	2.2(1.3–3.5)
Degree of education [a]						13.199	0.001		
illiterate or semi-illiterate	12538	31	247.2(160.2–334.3)	83	662.0(519.6–804.4)			1.4(0.9–2.3)	-
primary school or junior high school	19780	54	273.0(200.2–345.8)	181	915.1(781.8–1048.4)			2.0(1.3–3.2)	-
Senior high school and above	4592	9	196.0(89.7–372.0)	21	457.3(261.7–652.9)				
Urbanorrural area						48.607	<0.001		
urban area	14456	22	152.2(88.6–215.8)	51	352.8(256.0–449.6)				
rural area	23737	72	303.3(233.3–373.4)	234	985.8(859.5–1112.1)			2.9(2.2–4.0)	2.0(1.5–2.8)
Ethnic group[a]						26.488	<0.001		
Han	33430	81	242.3(189.5–295.1)	221	661.1(573.9–748.2)				
ethic minorities	4747	13	273.9(125.0–422.7)	64	1348.2(1017.9–1678.5)			2.6(2.0–3.4)	2.2(1.6–3.0)
Marital status[a]						0.011	0.917		
married	28439	67	235.6(179.2–292.0)	213	749.0(648.4–849.6)				
unmarried / divorced / widowed	9750	27	276.9(172.5–381.4)	72	738.5(567.9–909.0)			1.1(0.8–1.5)	1.4(1.1–1.9)
Annual family income per capita(CNY)						48.073	<0.001		
<2300	6084	18	295.9(159.2–432.5)	54	887.6(650.8–1124.3)			2.4(1.7–3.4)	1.3(0.9–1.9)
2300–9999	13394	51	380.8(276.3–485.3)	148	1105.0(926.9–1283.0)			2.5(1.9–3.3)	1.8(1.3–2.4)
≥10000	18715	25	133.6(81.2–185.9)	83	443.5(348.1–538.9)				
Body mass index(BMI)						74.528	<0.001		
<18.5	3916	21	536.3(306.9–765.6)	63	1608.8(1211.5–2006.1)			2.0(1.5–2.7)	1.9(1.4–2.6)
18.5–	22921	60	261.8(195.5–328.0)	190	828.9(711.1–946.8)				
≥24	11356	13	114.5(52.2–176.7)	32	281.8(184.2–379.4)			0.3(0.2–0.5)	0.3(0.2–0.5)
History of smoking[a]						34.938	<0.001		
yes	7758	32	412.5(269.6–555.4)	98	1263.2(1013.1–1513.3)			2.0(1.6–2.6)	-
no	30376	62	204.1(153.3–254.9)	187	615.6(527.4–703.9)				
History of alcohol consumption[a]						9.413	0.002		
Yes	7424	26	350.2(215.6–484.8)	76	1023.7(793.5–1253.9)			1.5(1.1–1.9)	-
No	30659	68	221.8(169.1–274.5)	209	681.7(589.3–774.1)				

Note: [a]: There are missing data. "-": This is the no-adjusted value.

Table 3 Incidence density of PTB in five key populations at 1 and 2 years of follow-up

Five key populations	Person-years of follow-up	Smear-positive TB		Active TB	
		No.	incidence density(95%*CI*, /100000 person-years)	No.	incidence density(95%*CI*, /100000 person-years)
All key populations					
1-year follow-up	27202.4	36	132.3(89.1–175.6)	133	488.9(405.8–572.0)
2-years follow-up	49393.8	71	143.7(110.3–177.2)	235	475.8(414.9–536.6)
Elderly people aged 65years and older					
1-year follow-up	24446.0	30	122.7(78.8–166.6)	123	503.1(414.2–592.1)
2-years follow-up	44622.2	62	138.9(104.4–173.5)	215	481.8(417.4–546.2)
Diabetic patients					
1-year follow-up	3650.9	1	27.4(0.7–152.6)	10	273.9(104.1–443.7)
2-years follow-up	6383.5	3	47.0(9.7–137.4)	16	250.6(127.8–373.5)
People with TB history					
1-year follow-up	1020.8	8	783.7(338.0–1543.9)	22	2155.2(1254.6–3055.8)
2-years follow-up	1773.7	9	507.4(232.3–963.0)	28	1578.6(993.9–2163.4)
CLOSE contacts of active TB patients					
1-year follow-up	265.8	0	0.0(0.0–1388.3)	0	0.0(0.0–1388.3)
2-years follow-up	494.4	0	0.0(0.0–746.4)	1	202.3(5.1–1126.6)
HIV/AIDS patients					
1-year follow-up	40.7	0	0.0(0.0–9066.3)	0	0.0(0.0–9066.3)
2-years follow-up	77.1	0	0.0(0.0–4786.0)	0	0.0(0.0–4786.0)

Note: $\text{The incidence density (person-years)} = \frac{\text{The number of cases in the follow-up years}}{\text{Total number of person-years for all subjects in the follow-up years}} \times 100\%$

2.4 Analysis of influencing factors of the incidence density of TB in the five key populations with different demographic characteristics

Due to the large size of follow-up data, considering that the 2-year follow-up data are more stable than the 1-year follow-up data, this study only analyzed the incidence of patients with different characteristics during the 2-year follow-up. The results of the univariate analysis of the Cox proportional hazard model showed that except for the differences between degree of education, living areas and marital status, the differences between all other characteristics were statistically significant; and the incidence density of people who had these characteristics, such as male, advanced age (group aged 75–84), ethnic minorities, low annual family income per capita, malnutrition (BMI < 18.5), history of smoking or alcohol consumption all reached 0.5%–1.0%, as shown in Table 3. Multivariate analysis found that male, ethnic minorities and low annual family income per capita (CNY 2300–9999) were risk factors for the onset of TB, and overweight (BMI ≧ 24) was a protective factor for the onset of TB. Due to the apparently skewed distribution of the age data, which made the reliability of the results unclear, they were not analyzed in this study. The details are shown in Table 4.

3 Discussions

The results of this study are consistent with previous studies that the five key populations are known to be at high risk of TB disease due to factors such as weakened immunity or injury, prolonged close contact exposure, relapse and re-infection [3, 9–14]. The survey showed that the prevalence of TB in the five key populations from 2013 to 2015 was 0.5%–7%, which was at a relatively high level and several to more than ten times that of the population aged 15 years and above in the fifth national TB epidemiological survey in 2010 [6], which was considered to be related to the screening of the five key high-risk populations. This also suggests that active case-finding should be considered in these high-risk populations in China.

In addition, after three years of continuous active screening, it was found that continuous active screening could significantly reduce the prevalence of bacteria positive and active PTB in the five key populations, and the annual decline rates were 15.7% and 17.7%, respectively. It suggested that continuous active screening could detect patients early and reduce the number of patients year by year, which played an important role in shortening the infectious period of PTB patients. However, the prevalence was still at a high level, and this result was only detected by traditional diagnostic techniques, suggesting that with the support of new diagnostic techniques, higher detection rates will be obtained, which highlights the importance of continuous screening of key populations.

The *Technical Specification for Tuberculosis Prevention and Control in China (2020 Edition)*[15] issued by the National Health Commission of the People's Republic of China has made new regulations on the screening of close contacts of etiologically positive TB patients and people with HIV/AIDS, requiring that people with HIV/AIDS should receive TB examination at least once a year after the first screening. However, close contacts of etiologically positive PTB patients were required to be screened for suspicious symptoms of TB after the index case was diagnosed, 6 months and 1 year after the first screening. Considering that the patients with bacteriologically positive PTB in this study accounted for nearly one third of all patients with active PTB, we believe that it is necessary to expand the index case from patients with positive pathogens to all patients with active PTB. In addition, the fifth epidemiological survey of tuberculosis in China found that about 50% of patients had no cough symptoms, and about 50% of patients with cough had cough for less than 2 weeks. Therefore, it is considered that only symptom screening as a primary screening method is obviously insufficient [6]. A study in Tanzania also found that only one third of people with suspicious symptoms of PTB took the initiative to seek medical treatment, and simultaneous screening of symptoms and chest X-ray had the highest sensitivity [16]. Therefore, in the active screening of close contacts of active PTB patients, symptom screening and chest X-ray examination should be used as a combined primary screening method. In addition, results of this survey show that the prevalence of close contacts of active PTB patients is

Table 4 The incidence of TB in the five key populations with different demographic characteristics in 2-years follow-up

Demographic characteristics	Person-year of follow-up	Smear-positive TB		Active TB					
		No.	Incidence density(95%*CI*, /100000 person-years)	No.	Incidence density(95%*CI*, /100000 person-years)	χ^2	*P*	*HR* (95%*CI*)	*aHR* (95%*CI*)
Gender						37.032	<0.001	2.3(1.8–3.1)	2.5(1.9–3.5)
male	22776.2	47	206.4(147.4–265.4)	156	684.9(577.4–792.4)				
female	26617.6	24	90.2(54.1–126.2)	79	296.8(231.3–362.2)				
Age group (years)						7.953	0.047		
<65	4771.5	9	188.6(86.3–358.0)	20	419.2(235.5–602.9)			1.0(0.6–1.5)	1.3(0.8–2.1)
65–74	28910.3	33	114.1(75.2–153.1)	121	418.5(344.0–493.1)				
75–84	13645.8	26	190.5(117.3–263.8)	85	622.9(490.5–755.3)			1.5(1.1–1.9)	1.3(0.98–1.8)
>85	2066.1	3	145.2(30.0–424.5)	9	435.6(199.4–826.7			1.3(0.6–2.5)	1.1(0.5–2.1

Continued

Demographic characteristics	Person-year of follow-up	Smear-positive TB		Active TB					
		No.	Incidence density(95%*CI*, /100000 person-years)	No.	Incidence density(95%*CI*, /100000 person-years)	χ^2	*P*	*HR* (95%*CI*)	*aHR* (95%*CI*)
Degree of education [a]						5.047	0.080		
illiterate or semi-illiterate	17174.0	29	168.9(107.4–230.3)	97	564.8(452.4–677.2)			1.4(0.8–2.4)	-
primary school or junior high school	26255.5	123	137.1(92.3–181.9)	123	468.5(385.7–551.3)			1.0(0.6–1.8)	-
senior high school and above	4496.4	6	133.4(48.9–290.5	15	333.6(164.8–502.4)				
Urban or rural area						0.130	0.719		
urban area	15482.5	22	142.1(82.7–201.5)	65	419.8(317.8–521.9)				
rural area	33911.3	49	144.5(104.0–185.0)	170	501.3(425.9–576.7)			1.0(0.7–1.3)	-
Ethnic group[a]						135.290	<0.001		
Han	43483.4	70	161.0(123.3–198.7)	176	404.8(345.0–464.6)				
ethic minorities	5900.6	1	16.9(0.4–94.4)	59	999.9(744.8–1255.0)			6.9(5.0–9.6)	6.8(4.8–9.6)
Marital status [a]						1.065	0.302		
married	36798.6	58	157.6(117.1–198.2)	188	510.9(437.9–583.9)				
unmarried / divorced / widowed	12590.3	13	103.3(47.1–159.4)	47	373.3(266.6–480.0)			0.8(0.6–1.2)	-
Annual family income per capita [a](CNY)						16.762	0.002		
<2300	6136.1	19	309.6(170.4–448.9)	42	684.5(477.5–891.5)			2.0(1.4–2.9)	-
2300–9999	19085.1	46	241.0(171.4–310.7)	119	623.5(511.5–735.6)			1.7(1.3–2.2)	1.4(1.0–1.9)
≥10000	22037.8	6	27.2(10.0–59.3)	74	335.8(259.3–412.3)				
Body mass index [a]						27.184	<0.001		
<18.5	5047.6	19	376.4(207.2–545.7)	39	772.6(530.1–1015.1)			1.4(0.97–2.0)	1.3(0.9–1.8)
18.5–	29840.8	46	154.2(109.6–198.7)	161	539.5(456.2–622.9)				
≥24	14434.4	6	41.6(15.2–90.5)	35	242.5(162.1–322.8)			0.4(0.3–0.6)	0.5(0.4–0.7)
History of smoking [a]						13.169	0.000		
Yes	13.169	27	266.8(166.2–367.4)	74	731.2(564.6–897.9)			1.7(1.3–2.2)	-
No	39203.6	44	112.2(79.1–145.4)	161	410.7(347.2–474.1)				
History of alcohol consumption [a]						7.109	0.008		
Yes	9851.6	19	192.9(106.1–279.6)	68	690.2(526.2–854.3)			1.5(1.1–2.0)	-
No	39432.1	52	131.9(96.0–167.7)	167	423.5(359.3–487.7)				

Notes: [a]: There are missing data. $\text{Incidence density (person-years)} = \frac{\text{Number of cases in the follow-up years}}{\text{Total number of person-years for all subjects in the follow-up years}} \times 100\%$. *aHR*: Adjust risk ratio."-": This is the no-adjusted value.

still high after 1 or 2 years of follow-up. Therefore, it is recommended to further extend the 1-year follow-up time of close contacts of active PTB patients, but further research of screening interval is needed.

It is worth noting that the proportion of elderly people aged 65 years and above in this screening reached about 90%, and the proportion of diabetic patients also reached 13%. This is extremely instructive for case finding in older populations and patients with diabetes. Although the prevalence of these two groups were lower than that of the five key populations, they have reached the WHO's standard for TB screening in the general population [17], that is, screening is conditionally recommended for people with prevalence ≥ 0.5%. At present, as one of the most important supporting evidences, the active screening of the elderly and diabetic patients has been included in the *Technical Specification for Tuberculosis Prevention and Control in China (2020 Edition)* [15]. However, there is no specific strategy, and the actual work is still mainly based on symptom screening. Therefore, based on the results of this study, the authors believe that under the condition of comprehensive consideration of the local epidemic situation, economic development level, medical and health resources and other conditions, each region can conduct regular screening of these two groups of people as an option and formulate specific screening strategies. For example, for these two groups of people, suspicious symptoms of PTB and chest X-ray screening at the same time can be carried out; or it may be more cost-effective to screen for suspicious symptoms of TB and chest X-ray in people with the higher-risk factors of the two groups, while screening only for suspicious symptoms of TB in the rest of the two groups.

Further improvement of screening efficiency and reduction of screening cost should be the goals of screening. In the multivariate analysis of the prevalence and incidence density of tuberculosis in different subgroups, it was found that male, minority ethnic group and low family income per capita were risk factors for the prevalence and incidence of TB, and overweight (BMI ≥ 24) was a protective factor. Older age, rural residence, unmarried/divorced/widowed, and malnutrition (BMI < 18.5) are risk factors for TB, which can help us to identify a variety of high-risk factors and screening target population with higher risk, so as to obtain higher screening cost-effectiveness [18].

This study also had the following limitations. First, although people living with HIV/AIDS and their close contacts were clearly at high risk of TB, due to the small number of people in this study, it could not reflect the real incidence level of TB in this population in China. Second, factors such as diabetes, history of smoking and alcohol consumption were self-reported, which may lead to study bias. Third, in the screening population, age and education level may be affected by biases and confounding factors, and there is obvious statistical bias, the results of which were not analyzed in this study.

In conclusion, continuous active TB screening in key populations is one of the key measures to rapidly reduce the TB epidemic. Based on the results of this study, the author puts forward the following policy recommendations. First, the current policy and strategy for people living with HIV/AIDS can be maintained. Second, regular screening of all close contacts of patients with active PTB is recommended, and screening for symptoms and chest X-ray should be carried out at the same time. Third, it is necessary to include people with TB history in the active screening population, and annual TB screening is recommended. Fourth, based on the TB epidemic, economic development level, and access to health care resources in each region, we should consider regular TB chest X-ray screening for the elderly, people with diabetes, or those with higher risk characteristics in both groups to improve screening efficiency.

References

[1] World Health Organization. The End TB Strategy. Geneva: World Health Organization, 2015.
[2] World Health Organization. Systematic screening for active tuberculosis: principles and recommendations. Geneva: World Health Organization, 2013.
[3] Hoa NB, Sy DN, Nhung NV, et al. National survey of tuberculosis prevalence in Viet Nam. Bull World Health Organ, 2010, 88(4): 273–280. doi: 10.2471/BLT.09.067801.
[4] Law I, Sylavanh P, Bounmala S, et al. The first national tuberculosis prevalence survey of Lao PDR (2010–2011). Trop Med Int Health, 2015, 20(9): 1146–1154. doi: 10.1111/tmi.12536.
[5] Wang L, Zhang H, Ruan Y, et al. Tuberculosis prevalence in China, 1990–2010; a longitudinal analysis of national survey data. Lancet, 2014, 383(9934): 2057–2064. doi: 10.1016/S0140-6736(13)62639-2.
[6] Wang Y. Compilation of data from the fifth national sampling survey of tuberculosis epidemiology. Beijing: Military Medical Science Press, 2011: 31 (in Chinese).
[7] Zhang H, Cheng J, Yu Y, et al. Evaluation of the effectiveness of community-based pulmonary tuberculosis active case-finding among key populations: a multicenter prospective cohort study. Chinese Journal of Antituberculosis, 2021, 43(12): 1248–1259. doi: 10.3969/j.issn.1000-6621.2021.12.005 (in Chinese).
[8] National Health and Family Planning Commission of the People's Republic of China. WS 288-2008 Diagnostic criteria for pulmonary tuberculosis. 2008-01–16 (in Chinese).
[9] World Health Organization. National tuberculosis prevalence surveys 2007–2016. Geneva: World Health Organization, 2021.
[10] Lönnroth K, Castro KG, Chakaya JM, et al. Tuberculosis control and elimination 2010–50: cure, care, and social development. Lancet, 2010, 375(9728): 1814–1829. doi: 10.1016/S0140-6736(10)60483-7.
[11] Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med, 2008, 5(7): e152. doi: 10.1371/journal.pmed.0050152.
[12] Morrison J, Pai M, Hopewell PC. Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Infect Dis, 2008, 8(6): 359–368. doi: 10.1016/S1473-3099(08)70071-9.
[13] Verver S, Warren RM, Beyers N, et al. Rate of reinfection tuberculosis after successful treatment is higher than rate of new tuberculosis. Am J Respir Crit Care Med, 2005, 171(12): 1430–1535. doi: 10.1164/rccm.200409-1200OC.
[14] Crampin AC, Mwaungulu JN, Mwaungulu FD, et al. Recurrent TB: relapse or reinfection? The effect of HIV in a general population cohort in Malawi. AIDS, 2010, 24(3): 417–426. doi: 10.1097/QAD.0b013e32832f51cf.
[15] National Health Commission of the People's Republic of China. Technical specification for tuberculosis prevention and control in China (2020 edition). 2020-04-02 (in Chinese).
[16] Senkoro M, Hinderaker SG, Mfinanga SG, et al. Health care-seeking

behaviour among people with cough in Tanzania: Findings from a tuberculosis prevalence survey. Int J Tuberc Lung Dis, 2015, 19(6): 640–646. doi: 10.5588/ijtld.14.0499.
[17] World Health Organization. WHO consolidated guidelines on tuberculosis. Module 2: screening-systematic screening for tuberculosis disease. Geneva: World Health Organization, 2021.
[18] Nishikiori N, Van Weezenbeek C. Target prioritization and strategy selection for active case-finding of pulmonary tuberculosis: a tool to support country-level project planning. BMC Public Health, 2013, 13: 97. doi: 10.1186/1471-2458-13-97.

