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SORT IT TB Key Population

New approach for tuberculosis contact tracing implemented in the two regions of Kyrgyz Republic during 2017-2018

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Abstract
Introduction: Tuberculosis (TB) contact investigation as a proved approach for finding new TB cases, is not fully performed in Kyrgyzstan. In 2018, the country started aligning the National Guidelines for tracking contacts with the WHO recommendations by expanding the definition for TB index cases to all close contacts, regardless of their TB risk status.
Methodology: This cross-sectional census aimed to determine the active case detection changes among TB contacts after implementation of a new TB tracing strategy using the National Surveillance data. We compared populations in Chui and Issyk-Kul regions of Kyrgyzstan who had contacts with TB index cases before (2017) and after (2018) strategic changes for the rates of indexes, contacts, screened contacts, and detected TB among screened contacts.
Results: New TB tracing strategy resulted in increased numbers of indexes (21%) and contacts (36%). Though the smaller number of contacts (1730 *vs*. 1590) have been screened in 2018, the proportion of TB diagnosed was substantially higher (95% CI: 0.024-0.005; p = 0.002) in 2018 *vs*. 2017. The mean numbers of TB contacts per-one-index-case also has increased dramatically by 117% (1.8 *vs*. 3.9) in Chui and by 43% (3.0 *vs*. 4.3) in Issyk-Kul regions (95% CI: 3.20-3.37; p < 0.001 and 95% CI: 2.97-3.09; p < 0.001, respectively) between 2018 and 2017.
Conclusion: Extending new tracing approach to other regions of Kyrgyzstan will increase the number of identified contacts, leading to better TB control in the country and prevention of more severe TB development among the unidentified contacts.

Key words: tuberculosis; contact; Kyrgyzstan; SORT IT.

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Introduction
The importance of tuberculosis (TB) control has been widely acknowledged for decades, and in this context, the World Health Organization (WHO) STOP TB Partnership has set ambitious targets for eliminating TB as a public health problem by 2050 [1]. The essential role to achieve these targets belongs to the identification of more TB cases at an earlier stage of the illness [2]. Contact tracing helps to identify new cases at an earlier stage and to start treatment earlier, since the contacts have a higher risk of developing TB than the general population. Moreover, late diagnosis and treatment initiation might become a cause for more severe forms of TB development among unidentified contacts [3]. It increases TB case detection and prevents further disease transmission [3-5]. Tuberculosis contact tracing, or contact investigation, is proved to be an efficient, targeted approach to TB case finding [2,4,5]. Systematic reviews of published studies from low- and middle-income countries show that from 3.5% to 5.5% of active TB could be found among previously undiagnosed contact persons [2,4,6].

In 2012, the WHO introduced “Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries”. It highlights the importance of contact tracing as a supporting strategy for national and local TB control programs in low- and middle-income countries [7]. WHO ranks the Kyrgyz Republic as a high TB burden country with incidence rate of 144 per 100,000 population [1].

Until June 2018, in Kyrgyzstan, the contact investigation was applied only to persons exposed to new smear-positive pulmonary TB cases and only household contacts were traced. Despite the potential benefit, the contact tracing is still not fully performed in Kyrgyzstan. Hence, the approach to tracing contact persons was changed and the National Guidelines for Tracking contact cases were aligned with WHO recommendations [7].

The absence of published research on contact tracing programs in Central Asia and advanced approach for contact tracing introduced in Kyrgyzstan created a need for understanding the changes that happened after the implementation of the new system. This study aimed to explore the active case detection rate changes (if any), occurred among TB patients' contacts after implementation of a TB Contact Tracing Program in Chui and Issyk-Kul Regions of Kyrgyzstan.

Methodology

Study design and settings

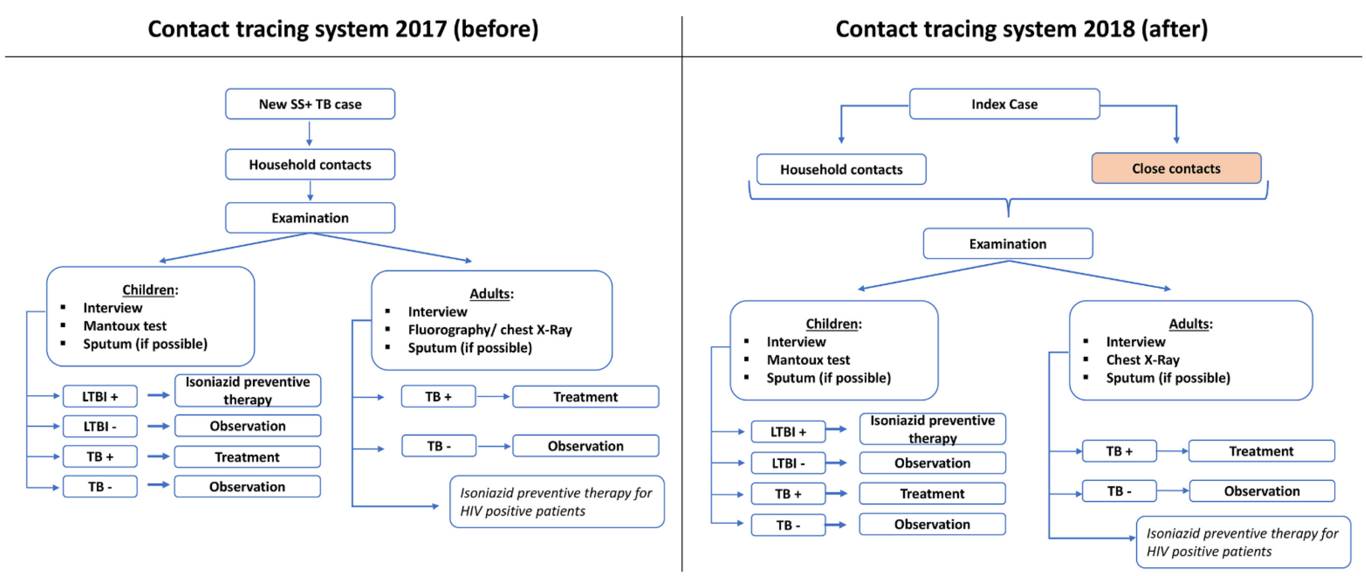
This was a cross-sectional census to determine the changes in active case detection among TB patients' contacts based on data from the National Department for Disease Prevention and State Sanitary Epidemiological Surveillance.

The Kyrgyz Republic has an area of 198,500 km^2, which borders Kazakhstan, Tajikistan, Uzbekistan and China. The population is more than 6.2 million; there are seven regions and two big cities. The Republic of Kyrgyzstan is classified as a middle-income country. Health coverage is provided to all areas of Kyrgyzstan. Pulmonary services are free for all TB patients nationwide, however, screening of TB contacts relies on the population's out of pocket payment [8]. The Department of Disease Prevention and State Sanitary and Epidemiological Surveillance has overall coordination and responsibility for tracing and investigating TB contact persons by conducting an epidemiological investigation after receiving emergency case notifications [9].

Changes in TB contact tracing system in Kyrgyzstan:

Before 2018, the limited contact tracing was applied. It included: 1) only persons who were exposed to any new smear-positive TB patient (adult or child); 2) only household contacts; and 3) no clear distinction between the roles and responsibilities of the primary healthcare (PHC) provider and epidemiologists was defined (Figure 1) [10]. The algorithm for further monitoring of TB contacts for index cases with drug-susceptible TB included the following three steps: a) Interview of contact persons for the presence of TB symptoms after 3 months; b) X-rays are taken to contact persons at the end of the treatment of the index case; c) Observation of contact persons cases when the index case of TB is favorable. The algorithm for further monitoring of TB contacts for index cases with drug-resistant TB included the following three steps: a) Interview of contact persons for the presence of TB symptoms after 3 months from the start of the treatment of index case and then every 6 months; b) X-rays of TB contact persons every 6 months; c) General observation of TB contacts for 2 years. Starting in 2018, the expanded contact tracing strategy has been applied. It

Figure 1. TB contact tracing system before (2017) and after (2018) new approach in Kyrgyzstan.



LTBI: Latent Tuberculosis Infection; TB: Tuberculosis.

includes: 1) persons exposed to any drug-susceptible (DS) smear-positive and smear-negative TB patients (adults and children) with cavity findings in X-Ray, multidrug-resistant (MDR) or extensively drug-resistant (XDR) TB patients regardless of their smear status, TB/HIV coinfected patients regardless of their TB type; 2) household contacts plus other close contacts; 3) clear distinction between the roles and responsibilities of the PHC workers and epidemiologists: epidemiologists interview the index case, visit and survey contact persons, make a list of prioritized contact persons depending on the type of contact, and notify the PHC provider for case investigation. Further control and follow-up are carried out by family doctors and nurses (Table 1, Figure 1) [9].

Study population and timing

The study included all persons who had contacts with TB cases/index cases in Chui and Issyk-Kul regions of Kyrgyzstan during two different timepoints: 2017 and 2018. These two regions represent the areas with high (Chui) and low (Issyk-Kul) TB burden in Kyrgyzstan and were among the limited number of places where the pilot of a new tracing strategy was implemented in the country. We compared two groups of population during one calendar year (January-December) each. One group, named 'study group', included people traced in 2018 to assess the active case detection rate after the new tracing program implementation. Another group named 'comparison group' included people traced in 2017 to assess the active case detection rate before the new program implementation.

Data source and variables

We extracted the data from the reports of Centers for Disease Prevention and State Sanitary Epidemiological Surveillance and the National TB Program. Study included the number of TB cases/indexes, number of contacts with TB cases/indexes, number of screened contacts, and the number of TB cases detected among screened contacts.

Data logistic and analysis

Data was analyzed using OpenEpi software (Open Source Epidemiologic Statistics for Public Health. Available at www.OpenEpi.com.). Firstly, a cascade of contact tracing outcomes was presented with frequencies of the contacts named by TB cases/index cases. Contacts tested for TB and identified TB-positives were compared between the study groups. Then, descriptive statistics and distributions for the

Table 1. Definitions for TB contacts tracing system new approach.

Index case	**The initially identified TB in a person who has:**
	Sputum smear-positive DS-TB
	Sputum smear-negative TB with cavity findings in X-Ray
	MDR- or XDR-TB regardless of bacterial excretion
	TB/HIV regardless of type of TB
	TB in children under 5 years of age regardless of type of TB
Household contact	A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.
Close contact	A person who is not in the household but shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods (more than 6 hours) during the day with the index case during the 3 months before commencement of the current treatment episode.
High risk groups	The high-risk groups for developing TB include contact persons: with MDR-TB, children under 5 years of age, and under treatment affecting immune system (HIV, diabetes, kidney disease, cancer, steroid therapy).
	Risk for infection: Persons having at least one of the following:
	Frequent change of place of residence (migrant)
	Uses drugs
	Homeless for 2 years or longer
	Previous contact with TB
	Was in prison
	Risk for progression Persons who have at least one of the listed health conditions:
	HIV
	Diabetes
	Chronic renal failure
	Oncological disease
	Immunosuppressive therapy
	COPD

COPD: chronic obstructive pulmonary disease; DS: drug-susceptible; MDR: multidrug-resistant; XDR: extensively drug-resistant.

number of tested contacts per one identified TB case was compared between the study groups. Finally, we described sociodemographic and clinical characteristics of contacts tested for TB and estimate factors associated with TB diagnosis by binary logistic regressions. Associations were presented with odds ratios (OR). For all statistical analyses the 95% confidence interval (CI) was set and calculated.

Ethics approval

The study protocol was waived from submission to the Committee of Ethics because this study was based on the aggregated retrospective data from the national registers only and did not include personal contact information of the study population.

Results

The distribution of contact persons by gender (male/female) and by groups (study 2018/comparison 2017) was equal, with average 51.2% males. Similarly, almost equivalent number of adults (> 18) and children were among contact persons across the groups, comprising 59.5% of adults. In both groups, the majority (> 70%) of the identified people were in contacts with the DS-TB patients. However, statistically significantly more cases who were in contacts with the DS-TB patients were identified in the study group than in the comparison group, 95% CI: 0.71-0.90; p = 0.0001 (Table 2).

The demographic and clinical characteristics of the contact persons who were diagnosed with TB after screening differ dramatically between the study and the comparison groups. Though in majority of cases in both groups, the contact persons diagnosed with TB were males (over 70%), statistically significantly more male TB cases were detected among the study group than in the comparison group: 44 (97.8%) *vs*. 16 (69.6%), respectively (95% CI: 0.01-0.42; p = 0.006). After implementation of the new tracing strategy, among the screened contact persons statistically significantly more adults were diagnosed with TB: 27 (60.0%) in 2018 *vs*. 5 (21.7%) in 2017, showing that odds of TB detection among adult contact persons compared to children under five, is 13 times higher if the country follows the new tracing strategy (95% CI: 2.02-90.02; p = 0.007) (Table 2). Also, after the new strategy implementation, statistically significantly more people were identified with TB among those who had contacts with drug-resistant patients compared to 2017 (37% *vs*. 8.7%). In addition, the odds of identifying TB among those who had contacts with DS-TB patients when the country

Table 2. Sociodemographic and clinical characteristics of identified and diagnosed with TB contacts stratified by 2017 (before) and 2018 (after) a new tracing system implementation.

Variable	Comparison group 2017 N (%)	Study group 2018 N (%)	Total	OR	95% CI	p-value
Contact persons						
Gender						
Female	1190 (48.5)	1632 (49.1)	2822 (48.8)	1	-	-
Male	1263 (51.5)	1693 (50.9)	2956 (51.2)	0.98	0.88-1.08	0.668
Age group (years)						
< 5	261 (10.6)	336 (10.1)	597 (10.3)	1	-	-
5-17	757 (30.9)	986 (29.7)	1743 (30.2)	1.01	0.84-1.22	0.903
Adults (>18)	1435 (58.5)	2003 (60.2)	3438 (59.5)	1.08	0.91-1.29	0.366
Index Case Category						
DR TB	730 (29.8)	840 (25.3)	1570 (27.2)	1	-	-
DS TB	1723 (70.2)	2485 (74.7)	4208 (72.8)	0.80	0.71-0.90	0,0001*
Contact persons with detected TB						
Gender:						
Female	7 (30.4)	1 (2.2)	8 (11.8)	1	-	-
Male	16 (69.6)	44 (97.8)	60 (88.2)	0.05	0.01-0.42	0.006*
Age group (years)						
< 5	5 (21.7)	2 (4.4)	7 (10.3)	1	-	-
5-17	13 (56.5)	16 (35.6)	29 (42.6)	3.08	0.51-18.54	0.213
Adults (> 18)	5 (21.7)	27 (60.0)	32 (47.1)	13.5	2.02-90.02	0.007*
Index Case Category						
DR TB	2 (8.7)	17 (37.8)	19 (27.9)	1	-	-
DS TB	21 (91.3)	28 (62.2)	49 (72.1)	6.38	1.33-30.66	0.021*

* Statistically significant finding. CI: confidence interval; OR: odds ratio; DR: drug-resistant; DS: drug-susceptible.

follows the new tracing strategy, is six times higher (95% CI: 1.33-30.66; p = 0.021) (Table 2).

Figure 2 illustrates that with a change of the TB contact tracing approach in 2018, the number of index cases increased by 21% and the number of contact cases increased by 36%. It also shows that though after the new approach implementation a smaller number of cases (8%) have been screened among contacts, the percent of screened contacts that were diagnosed with TB statistically significantly increased from 1.3% to 2.8% (95% CI: 0.024-0.005; p = 0.002). The mean numbers of TB contacts per one index case has increased by 117% (1.8 *vs*. 3.9) in Chui region and has increased by 43% (3.0 *vs*. 4.3) in Issyk-Kul regions, showing statistically significant difference between the years 2018 and 2017 (95% CI: 3.20-3.37; p < 0.001 and 2.97-3.09; p < 0.001, respectively) (Figure 3).

Along with the positive changes that new strategy brought to the TB tracing system in Kirgizstan, some data remained unchangeable between the study group 2018 and the comparison group 2017. Though the number of identified cases per one index case went up from 0.033 in 2017 to 0.053 in 2018, it did not show the statistically significant improvement.

Discussion

We conducted this study to determine the extent to which the implementation of a new strategy on active case detection rates for TB patients has changed after implementation of the TB Contact Tracing Program in two regions of Kyrgyzstan: Chui and Issyk-Kul. Although tracing was part of the national TB program in 2017 and earlier, the three main differences implemented in the tracing approach in Kyrgyzstan

Figure 3. Comparison of average number of TB contacts per one index case before (2017) and after (2018) new tracing system implementation by Chui and Issyk-Kul regions.

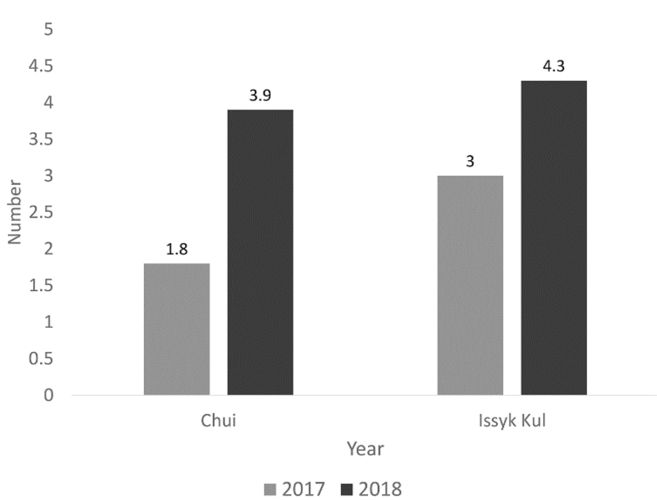
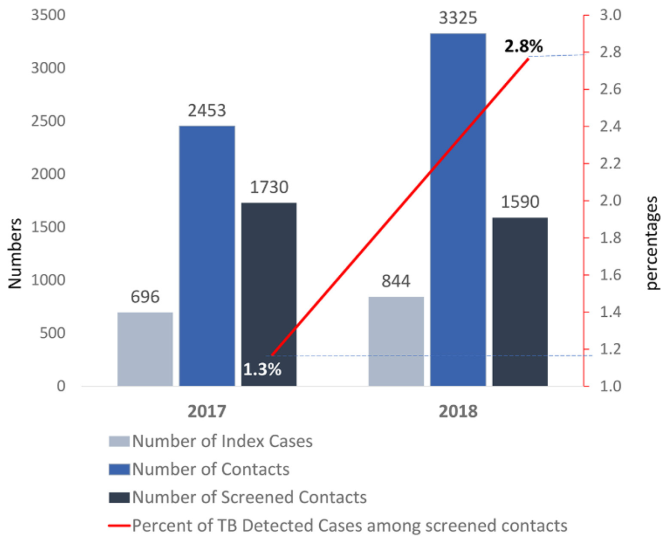


Figure 2. Cascade of TB contact tracing outcomes before (2017) and after (2018) new tracing system implementation in Kyrgyzstan.



since 2018 to follow the WHO recommendations [7], have dramatically influenced the rates of identification, screening, and detection of new TB cases among active contacts (Figure 4). No clear distinction between the roles and responsibilities for the PHC providers and the epidemiologists defined up to 2018 most probably caused improper follow-up of patients and their families and lack of communication between the professionals. It also might cause inconsistency in detection of new contact cases and completion of the screenings for previously identified cases, resulting in relatively lower rates of identified contacts. Considering that the contacts are at higher risk of TB development, their late identification might lead to the development of more severe TB cases [3].

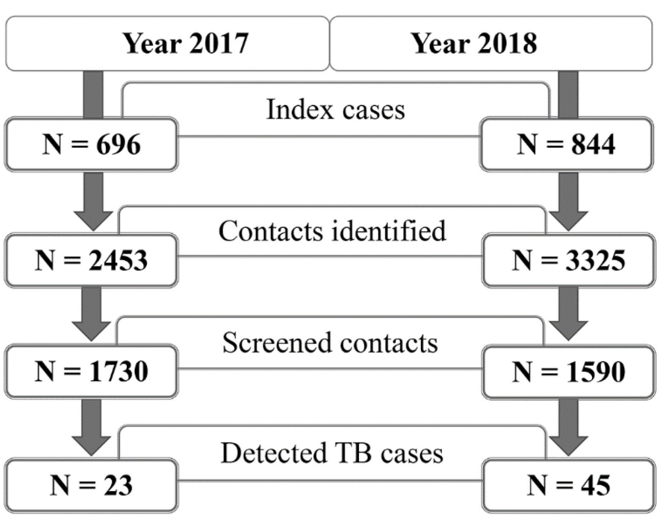
With implementation of a new tracing approach in the Chui and Issyk-Kul regions of Kyrgyzstan, not surprisingly, substantially more index cases started to be identified (over one-fifth increase), since the coverage for index cases was extended and began to comprise the TB patients (adults and children) irrespective of the smear diagnosis, high-risk groups including all DR-TB patients, and TB/HIV coinfected patients, like in other countries [11].

In addition, the mean number of identified contact persons per one index case for 2018 has substantially increased in both studied regions. Moreover, in the Chui region, where the TB burden is among the highest in the country, the mean number of identified contact persons per one index case has more than doubled reaching four persons per one index. This directs the country toward reaching the international recommendations and standards for the high TB burden countries [1]. Inclusion in the TB tracking system not only household contacts of the index cases, as was done in 2017 and earlier, but also their close contacts, including those sharing with them the same social gathering place, workplace or facility, has dramatically (by more than one-third) positively changed the number of contacts identified. The international experience confirms the effectiveness of the selection criteria extension [1].

The new tracing strategy did not impact the screening rates of the identified contacts. This might happen due to inconsistency in the routine processes of health facilities, responsible for patients screening, reluctant attitude of the primary healthcare providers toward changes, or insufficiency of the population knowledge on screening importance. Low screening rates among identified contacts before and after the new strategy implementation, resulted in low rates of TB detection per one index case (identification of one TB case by screening contacts of 30 indexes in 2017 *vs*. 19 indexes in 2018). Even though a new strategy helped to increase efficiency of TB detection among contacts a little, the difference was not statistically significant. To reach better detection rates, the screening should be done among all identified contacts under routine program conditions with the continuous follow-up as it was implemented in South Africa [11]. This will require additional financial and human resources.

However, despite the smaller number of screened contacts, TB detection rate among screened has more than doubled since the new strategy implementation (Figure 4). Like others [12], our study showed an increase in TB cases detection among adult population, which is explained by higher prevalence rates of TB among adults in general. This new strategy enhanced the prevalence of active TB detection among screened contacts to 2.8%, making the rates comparable to other countries with similar socio-economic and health profile: 3.3% in Georgia, 3.8% in China, 1.6% in Nepal [13-15] and advance TB contacts detection system: 2-3.1% in US urban population [6].

Figure 4. Flowchart for TB tracing before (2017) and after (2018) new approach in Kyrgyzstan.



The main weakness of this study is the limited number of regions included in the TB tracing system assessment and analysis. Although the representatives of the regions with both: high and low TB burden in Kyrgyzstan, were involved in the study, having data from only two regions of the entire country may not be enough for the data generalizability. However, considering that we were assessing a pilot project of a new TB tracing strategy implementation, that by the time of the study included very limited regions of Kyrgyzstan with ability to report one-year data to the National Department for Disease Prevention and State Sanitary Epidemiological Surveillance, we believe that this study might become a starting tool for the further national scale-up assessment programs.

Conclusion

The national TB control program in Kyrgyzstan made substantial improvement toward identification of TB index cases, new contacts, and the rates of active TB detection among contacts with implementation of the new tracing strategy in Chui and Issyk-Kul regions. Improvement of screening practices among identified contacts and extension of the program to the entire territory of Kyrgyzstan will benefit the whole population, prevent development of more severe TB cases among late screened or unscreened contacts, and will facilitate the TB control in the country in general.

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