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SORT IT TB Key Population

Who is doing worse? Retrospective cross-sectional study of TB key population treatment outcomes in Kyrgyzstan (2015-2017)

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Abstract

Introduction: Tuberculosis (TB) is a global public health problem. The incidence of TB is especially high among TB key populations, such as the homeless, people who use drugs, prisoners, and migrants. The study aimed to assess the associations between affiliation to TB key populations and treatment outcome.

Methodology: This retrospective cross-sectional study used data extracted from the National TB Registry of Kyrgyzstan for the region of Chuy (including the city of Bishkek) for 2015–2017. Descriptive statistics was used to summarize the data. Logistic regression was used to assess the associations.

Results: The study included 1,526 patients among whom more than half (52.5%) fell into the youngest group (18-35 years old). Migrants were the most highly represented group comprising 67.8% of all TB key populations. Men (63.0%) and patients with pulmonary TB (83.0%) prevailed in the cohort. The proportions of patients who had completed the treatment were high among all the key populations. Logistic regression was used to assess the association between affiliation to a certain TB key population and the TB treatment outcome. Patients who belonged to more than one TB key population were found to have the highest risk of unsuccessful TB treatment outcomes, both in the region of Chuy (OR = 9.9, 95% CI 2.0–48.1, p = 0.04) and the city of Bishkek (OR = 24.9, 95% CI 7.2–86.4, p < 0.001).

Conclusion: The homeless, people who use drugs, ex-prisoners, and TB patients who belonged to more than one TB key population were found to have higher risks of unsuccessful TB treatment outcome in comparison to migrants.

Key words: Tuberculosis key populations; treatment outcomes, Kyrgyzstan, operational research; SORT IT.

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Introduction

Tuberculosis (TB) remains an important public health problem in both high-income and low- and middle-income countries [1]. The majority of TB cases occur in groups which are referred to as TB key populations, such as the homeless, people who use drugs (PWUD), prisoners, and migrants. TB management in TB key populations remains one of the major obstacles for TB control worldwide. There is a high risk of exposure to TB in these populations and, subsequently, a higher risk of the infection. The high risk arises due to a variety of factors – biological, behavioral, social and limited access to healthcare [2].

In the process towards elimination of TB, it is very important to diagnose and completely treat all patients who are part of the TB key populations. The standardized models of healthcare used for prevention and control of TB are not usually found to be efficient enough for these groups, as they are designed for the general population, so specific interventions need to be implemented [3].

Another obstacle towards elimination of TB is the alarmingly high rate of multidrug resistant TB (MDR-TB), particularly in many countries in eastern Europe and Central Asia (e.g. Kazakhstan, Kyrgyzstan and Uzbekistan) [4]. The increase of prevalence of TB in these countries is shown to be associated with a high rate of incarceration [5]. Studies done in Kazakhstan revealed that diabetes, HIV, tobacco and alcohol use, being unmarried, and having history of incarceration were associated with having TB [6,7].

Kyrgyzstan is one of the countries with high burden of TB and MDR-TB. Since 2017, it has had the highest incidence of TB in the region. Over the past 10 years (2007-2017), the morbidity of TB in Kyrgyzstan has decreased slightly, from 165 to 144 cases per 100,000 population. Over the same period, the detection rate of TB cases increased from 78% to 82% due to the

improvement of TB diagnostics, the introduction of new algorithms, and new laboratory methods. The success rate of TB treatment among the new and relapsed cases registered in 2017 was 82% and this number has remained relatively stable during the last several years [8]. Kyrgyzstan also has a high proportion of TB key populations, including a large number of internal migrants [9]. These conditions contribute to high exposure to TB, increased risk of recurrence, delay in treatment-seeking, and increased severity of the disease. A recent study in Kyrgyzstan showed that 45% of revealed TB cases were among migrants [10]. Kyrgyzstan offers treatment to TB key populations but there is no published information on the proportions of these populations among TB patients and their treatment outcomes. According to the literature, a range of factors, such as age, HIV status, body mass index (BMI), alcohol use, and gender can affect the treatment outcomes [11-14].

The aim of the current study is to investigate the risk factors and treatment outcomes among different TB key populations (internal migrants, homeless, PWUD, ex-prisoners) for the period 2015 to 2017 in the region of Chuy (which includes the capital city of Bishkek) of Kyrgyzstan.

Specific objectives were to assess:

a) the proportions of TB key populations among all registered TB cases;

b) the distribution of treatment outcomes;

c) the associations between the affiliation to a certain TB key population and the treatment outcome.

Methodology

Operational definitions of treatment outcomes used

Cured

A pulmonary TB patient with bacteriologically confirmed TB at the beginning of the treatment who was smear- or culture-negative in the last month of the treatment and on at least one previous occasion.

Treatment completed

A TB patient who the completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results were negative in the last month of treatment and on at least one previous occasion, either because tests were not done or because results are unavailable.

Treatment failed

A TB patient whose sputum smear or culture is positive at month 5 or later during the treatment.

Died

A TB patient who dies because of any reason before starting or during the course of the treatment.

Lost to follow-up

A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.

TB treatment success rate

The TB treatment success rate is calculated by dividing the number of new, registered TB cases that were cured or completed a full course of treatment by the total number of new registered cases and multiplying by 100.

Study Design

This was a retrospective cross-sectional study, using 2015-2017 data from the National TB Registry (TB-02) of Kyrgyzstan (region of Chuy, including the city of Bishkek).

Study Setting

Kyrgyzstan is a country in the Central Asian region which borders with Kazakhstan, Tajikistan, Uzbekistan and China. The population is about 6.3 million. More than half of the people live in urban areas and have a below average income level.

National Tuberculosis Program

Since 1995, the Directly Observed Treatment Short (DOTS) strategy recommended by WHO has been implemented in Kyrgyzstan. On the basis of this strategy, the first National TB Control Program was established. This Program is funded by the state budget and international donors. The tuberculosis treatment regimen in Kyrgyzstan corresponds to the DOTS program. A patient with newly diagnosed drug-sensitive pulmonary tuberculosis receives treatment according to a 6-month regimen of chemotherapy with inclusion of rifampicin (2HREZ / 4HR). The optimal frequency of taking drugs is daily throughout the course of the treatment. In case the patient has previously received treatment, maintaining sensitivity to the first-line anti-TB drugs, treatment is changed to correspond to a 3HRZE / 5-6HR scheme. If the result of the test done by Xpert MBT / RIF shows rifampicin resistance, MDR TB treatment (2nd-line drugs) is prescribed immediately after discussion at the consultation.

Study Site and Study Population

The study site was the National TB Control Center of Kyrgyzstan. The study included TB cases from TB key populations (homeless, PWUD, ex-prisoners, internal migrants) who initiated and completed TB treatment during the 2015-2017 period in the region of Chuy. Exclusion criterion for participants was the age of 18 years or younger.

Data collection

Data on TB cases were collected and extracted to a Microsoft Excel spreadsheet from the National TB Control Center of Kyrgyzstan database for the years 2015-2017.

Data management and analysis

The data were entered into an MS Excel spreadsheet. Data analysis was done using Easystat (a web-based statistical application (https://easystat.app/) and Stata 14 statistical software [15]. All the errors identified via running frequencies were corrected in the MS Excel spreadsheet. Levels of significance were set at 5%. Data were summarized by proportions for categorical variables, and means with standard deviations for continuous variables. To compare the treatment outcomes among the TB key populations, "cured" and "completed" were merged into "successful", while "failed", "lost-to-follow-up" and "died" were merged into "unsuccessful". The patients who could be classified into more than one TB key

Table 1. Demographic and clinical characteristics of TB key populations registered with TB in the region of Chuy (including the city of Bishkek), 2015-2017.

Variable	Total (N = 1,526) n (%)	Ex-prisoners n = 77	Homeless n = 237	Migrants n = 1034	PWUD n = 147	Multi [a] n = 31
Age Group (n, %)						
18-35	801 (52.5%)	28 (36.4%)	63 (26.6%)	660 (63.8%)	46 (31.3%)	4 (12.9%)
36-56	570 (37.4%)	41 (53.2%)	148 (62.4%)	281 (27.2%)	76 (51.7%)	24 (77.4%)
> 56	155 (10.2%)	8 (10.4%)	26 (11.0%)	93 (9.0%)	25 (17.0%)	3 (9.7%)
Sex (n, %)						
Males	962 (63.0%)	72 (93.5%)	205 (86.5%)	541 (52.3%)	117 (79.6%)	27 (87.1%)
Females	564 (37.0%)	5 (6.5%)	32 (13.5%)	493 (47.7%)	30 (20.4%)	4 (12.9%)
TB form (n, %)						
EPTB	259 (17.0%)	6 (7.8%)	16 (6.8%)	231 (22.3%)	4 (2.7%)	2 (6.5%)
PTB	1267 (83.0%)	71 (92.2%)	221 (93.2%)	803 (77.7%)	143 (97.3%)	29 (93.5%)
Residence (n, %)						
City of Bishkek	620 (40.6%)	29 (37.7%)	185 (78.1%)	375 (36.3%)	9 (6.1%)	22 (71.0%)
Region of Chuy	906 (59.4%)	48 (62.3%)	52 (21.9%)	659 (63.7%)	138 (93.9%)	9 (29.0%)
Category of TB (n, %)						
New cases	1050 (68.8%)	45 (58.4%)	113 (47.7%)	808 (78.1%)	73 (49.7%)	11 (35.5%)
Retreatment cases	476 (31.2%)	32 (41.6%)	124 (52.3%)	226 (21.9%)	74 (50.3%)	20 (64.5%)
Sputum microscopy test (n, %)						
Smear-negative PTB	445 (29.2%)	22 (28.6%)	69 (29.1%)	309 (29.9%)	38 (25.9%)	7 (22.6%)
Smear-positive PTB	822 (53.9%)	49 (63.6%)	152 (64.1%)	494 (47.8%)	105 (71.4%)	22 (70.9%)
Not done (EPTB)	259 (16.9%)	6 (7.8%)	16 (6.8%)	231 (22.3%)	4 (2.7%)	2 (6.5%)
Drug resistance (n, %)						
MDR	281 (18.4%)	19 (24.7%)	58 (24.5%)	164 (15.9%)	34 (23.1%)	6 (19.4%)
MonoDR	16 (1.1%)	0 (0%)	3 (1.3%)	12 (1.2%)	1 (0.7%)	0 (0%)
PDR	150 (9.8%)	10 (13.0%)	28 (11.8%)	85 (8.2%)	21 (14.3%)	6 (19.4%)
Pan-susceptible	1057 (69.3%)	46 (59.7%)	142 (59.9%)	767 (74.2%)	87 (59.2%)	15 (48.4%)
XDR	22 (1.4%)	2 (2.6%)	6 (2.5%)	6 (0.6%)	4 (2.7%)	4 (12.9%)
Outcome Types (n, %)						
Completed	622 (40.8%)	23 (29.9%)	41 (17.3%)	514 (49.7%)	39 (26.5%)	5 (16.1%)
Cured	344 (22.5%)	18 (23.4%)	28 (11.8%)	272 (26.3%)	26 (17.7%)	0 (0%)
Died	136 (8.9%)	6 (7.8%)	52 (21.9%)	40 (3.9%)	27 (18.4%)	11 (35.5%)
Failed	56 (3.7%)	3 (3.9%)	9 (3.8%)	36 (3.5%)	5 (3.4%)	3 (9.7%)
LFU	368 (24.1%)	27 (35.1%)	107 (45.1%)	172 (16.6%)	50 (34.0%)	12 (38.7%)
HIV test results (n, %)						
HIV negative	1,243 (91.7%)	48 (78.7%)	142 (71.0%)	932 (98.3%)	108 (87.1%)	13 (56.5%)
HIV positive	113 (8.3%)	13 (21.3%)	58 (29.0%)	16 (1.7%)	16 (12.9%)	10 (43.5%)

EPTB: extrapulmonary TB; LFU: lost-to-follow-up; MDR: multi-drug resistant; MonoDR: mono-drug resistant; PDR: poly-drug resistant; PTB: pulmonary TB; PWUD: People who use drugs; XDR: extensively drug-resistant. [a] The patients from group called "Multi" were simultaneously relating to ≥ 2 risk groups.

Table 2. Distribution of treatment outcomes among the TB key populations for the period, 2015-2017.

Treatment outcomes	Total (N = 1,526,) n (%)	2015 (N = 437) n (%)	2016 (N = 581) n (%)	2017 (N = 506) n (%)
Completed	622 (40.8%)	196 (44.6%)	229 (39.4%)	197 (38.9%)
Cured	344 (22.5%)	66 (15.0%)	129 (22.2%)	149 (29.4%)
Died	136 (8.9%)	41 (9.3%)	55 (9.5%)	40 (7.9%)
Failed	56 (3.7%)	14 (3.2%)	24 (4.1%)	18 (3.6%)
LFU	368 (24.1%)	122 (27.8%)	144 (24.8%)	102 (20.2%)

LFU: Lost-to-follow-up.

population were marked as "multi". In order to assess the strength of association between selected variables and favorable TB treatment outcome, bivariate logistic regression was performed. Results of regression analysis were presented with odds ratios (OR) and 95% confidence intervals (CI).

Ethical Approval

Permission for the study was received from National Ethics Committee of Kyrgyzstan.

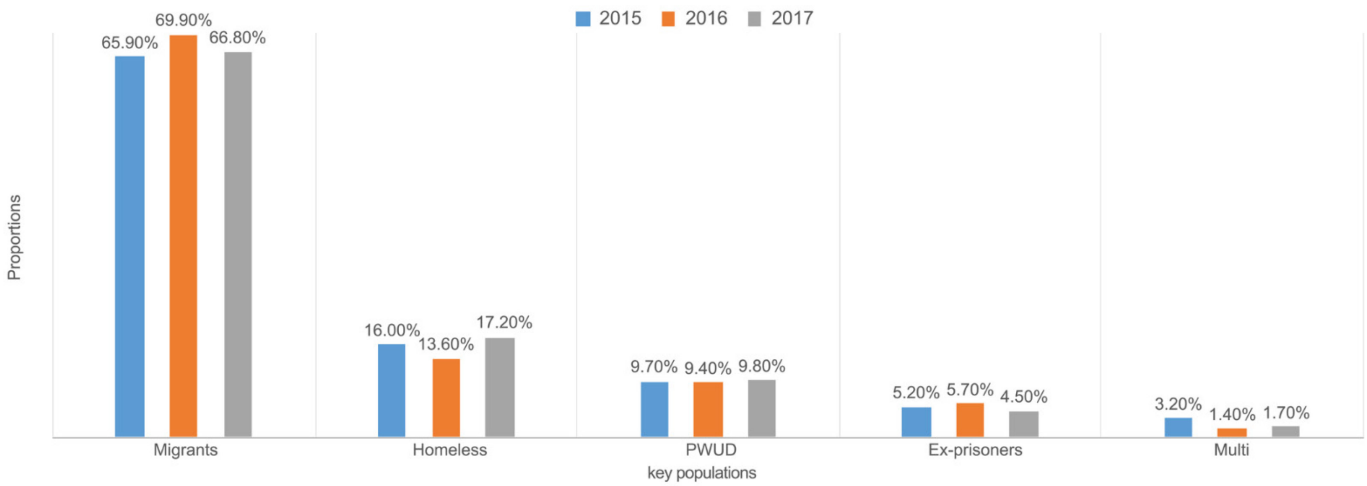
Results

The study included 1,526 patients with TB from the registry for the region of Chuy (including the city of Bishkek) in 2015-2017. Demographic and clinical characteristics for the cohort are presented in Table 1. The youngest age group (18-35 years) were the most predominant (52.5%) among all groups of participants. There was a greater proportion of males (63.0%) and migrants (67.8%) among the TB key populations. Among all the TB key populations, patients with pulmonary tuberculosis (PTB) were most common. The test for drug sensitivity revealed a high proportion (69.3%) of people with pan-susceptible TB among all the groups. Sputum microscopy showed that the majority of the participants had smear-positive PTB. The characteristics 'residence'revealed differences in terms of patients' affiliation to a particular TB key population. The share of 'homeless' was found to be more than 3.5 times higher in the city of Bishkek compared to the Chuy region (78.1% *vs* 21.9%), whereas PWUD were represented by more than 15 times in the region of Chuy compared to Bishkek (93.9% *vs* 6.1%).

The distribution of proportions of TB key populations over time (2015-2017) is presented in Figure 1, which shows that it remained relatively constant for the time period covered. Most of the patients among the TB key populations were migrants (66.1%, 69.9%, and 66.8%, for the years 2015, 2016 and 2017, respectively), followed by the homeless (16.2%, 13.8% and 17.0% in 2015, 2016 and 2017, respectively).

Table 2 shows the proportions of treatment outcomes over time. The proportions of patients who were cured and had completed the treatment were higher among all the key populations. The proportion of those who completed the treatment decreased (from 44.6% in 2015 to 38.9% in 2017) and the proportion of those who were cured increased (from 15.0% in 2015 to 29.4% in 2017) over time. The treatment success rate was found to be 70.1% and 71.2% in the city of Bishkek and the region of Chuy, respectively.

Figure 1. Proportions of TB key populations, region of Chuy (including the city of Bishkek), 2015-2017.



Logistic regression was run to determine the risk of unsuccessful outcome for different TB key populations. As the proportions of TB key populations were found to be very different in the region of Chuy and in the city of Bishkek, the risks were calculated separately for these two subgroups. The group of migrants, being the largest in the database and the most important group as it has the potential to include other risks, was chosen as a reference group. The results of the analysis are presented in Table 3 (for the region of Chuy) and Table 4 (for the city of Bishkek). The data show that the risks of unsuccessful outcomes were higher in all the TB key populations compared to migrants, in both places of residence. However, the risk of unsuccessful outcomes for the patients living in the city of Bishkek was much higher in all the risk groups compared to those from Chuy.

Discussion

In this study, we assessed the associations between the affiliation to a certain TB key population and the treatment outcome. The migrants were found to have the best treatment outcomes and those with multiple risk factors, the worst. This finding can be explained by the fact that the migrants are in a better situation, than the other key populations. The addition of each of the risk factors – being homeless, using drugs, or being incarcerated - increases the possibility of health impairment and thus decreases the chances of a successful treatment outcome [16-19]. Very few studies have reported an association between unsuccessful TB treatment outcome and factors related to the social characteristics of patients. Several studies showed results similar to ours, pointing out that being homeless or a PWUD can lead to worse TB treatment outcomes than being a migrant [20]. A study from the Netherlands showed that being a migrant was not included in a multivariate model of risk factors for unsuccessful treatment outcomes, while being homeless or a PWUD were shown to increase the risk by 9.1 and 6.7 times, respectively [21]. In Italy, the treatment success rate was found to be the same for the migrants and the general population [22] , while in Switzerland, the risk of potentially unsatisfactory outcome was associated with being an asylum seeker (OR = 1.9), while there was almost no association with being a migrant (OR = 1.1) [23]. Unsuccessful treatment outcome (particularly, treatment interruption) was shown to be associated with homelessness and injecting drugs in Germany and Spain [24,25].

The treatment success rates were 70.1% and 71.2% in the city of Bishkek and the region of Chuy, respectively. This is lower than the national average in 2017 (82%) [8], but the rate for our study participants was calculated for the period 2015-2017, and only for the city of Bishkek and the region of Chuy, which could be the reason for the difference.

One of the interesting findings of the study was the difference of proportions of TB key populations in the region of Chuy and the city of Bishkek. The distribution of participants by their place of residence was almost the same for the study population as a whole (40.6% and 59.4%), for migrants (36.3% and 63.7%) and ex-prisoners (37.7% and 62.3%), showing that there were 1.5–2 times more participants from the region of Chuy compared to the city of Bishkek. However, the proportion of the homeless was found to be about four times higher in the Region than in the City. The literature shows, though, that homeless people often tend to live in urban areas. A landmark study done in

Table 3. Risk of unsuccessful outcome in different TB key populations compared to the group of migrants, region of Chuy, 2015-2017.

Key populations	OR	95% CI	p-value
Migrants	1	–	–
Homeless	4.2	2.3 – 7.5	<0.001
PWUD	3.5	2.4 – 5.1	<0.001
Ex-prisoners	2.4	1.3 – 4.3	0.004
Multi	9.9	2.0 – 48.1	0.004

CI: confidence interval; OR: odds ratio; PWUD – People who use drugs.

Table 4. Risk of unsuccessful outcome in different TB key populations compared to the group of migrants, city of Bishkek, 2015-2017.

Key populations	OR	95% CI	p-value
Migrants	1	–	–
Homeless	11.2	7.4 – 17.0	< 0.001
PWUD	7.9	1.9 – 32.2	0.004
Ex-prisoners	3.7	1.7 – 7.9	0.001
Multi	24.9	7.2 – 86.4	< 0.001

CI: confidence interval; OR: odds ratio; PWUD – People who use drugs.

the USA showed that only 30% of the homeless were in suburban and rural areas. Another study done by National Health Care for the Homeless Council looked at the differences between the homeless in urban and rural areas [19,26]. Studies claim that homeless people in urban areas are usually poorer and have problems finding food, while the homeless from rural areas are usually less educated but are more likely to be employed, which may be the reason why we have such a pattern in our results. The results of our study could be explained by the fact that living costs in the capital/city are usually higher than in the region, which increases the likelihood of loss of property. Besides, there can be differences in statistics related to the issue in developed and developing countries.

Another interesting finding was the proportion of PWUD, that was about 15 times higher in the region of Chuy than in the city of Bishkek. Historically, drug use has been conceptualized as an urban problem [27]. Data from the US National Household Survey on Drug Abuse (2005) showed that people living in metropolitan areas were more likely to have used illicit drugs than those who did not [28]. However, in October 2017, the Centers for Disease Control and Prevention announced that the rates of overdose fatalities in rural areas surpassed those of the urban areas [29]. We assumed that maybe the high prevalence of PWUD in the Region is related to stricter compliance to the laws/rules in the City than in the Region, or possibly to higher availability of illicit drugs in the Region.

Considering all of this information,we suggest that further research is needed to identify the main causes of the differences between urban and rural areas in the proportions of key populations among TB patients.

As a recommendation, we would like to suggest that healthcare providers should be more cautious in treating those TB key populations who can be expected to have the worst outcomes.

Strengths and Limitations

One of the strengths of our study is the large dataset (1,526 cases) and the very small number of missing values, which improves the interpretation of results.

Another strength is that the migrants included in the study are only internal migrants. Our study did not include cross-border migrants, who are from different countries and may have characteristics which make them different from the internal migrants. So, the results of our study can only be generalized to internal migrants in Kyrgyzstan.

The limitations of the study are mainly related to the data collection and data entry phases. The initial raw data from which the Excel database was created was a paper-based registry; in the process of data transmission errors could happen. Besides, the data was not double entered and though it was cleaned by running the frequencies and correcting the issues which arose, we cannot be sure that there were no mistakes left.

Conclusions

The associations measured between the affiliation to TB key population and the outcome of TB treatment showed that internal migrants had the highest rate of successful outcomes among all the TB key populations. Further research can shed light on the causes of differences in proportions of different TB key populations in the cities and more rural regions in Kyrgyzstan.

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Data confidentiality

Data was entered based on the information recorded in the registry. No personal identifiers (such as name, phone number, address) about participants are present in the database. Electronic data file will be kept in a password protected computer. The collected electronic data will remain secure and can be accessed only by the corresponding author and will be retained for at least 3 years from the publication of study findings.

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