Original research

LINKAGE BETWEEN DIAGNOSIS AND TREATMENT OF SMEAR-POSITIVE PULMONARY TUBERCULOSIS IN URBAN AND RURAL AREAS IN KYRGYZSTAN

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ABSTRACT

The performance of the tuberculosis (TB) programme should be judged on the basis of detected TB cases recorded in the laboratory register and not just those placed on treatment and recorded in the TB treatment register. We examined the performance of the TB programme in this regard in Kyrgyzstan in 2012.

This retrospective cohort study included all sputum smear-positive pulmonary TB cases registered in the TB laboratory register (584 persons). Data variables on geographical region, TB diagnosis, TB treatment and outcomes were sourced from various registers. We analysed (1) initial lost to follow-up (LTFU) between urban and rural areas; (2) time of starting treatment after diagnosis; (3) treatment outcomes of laboratory-registered and treatment-registered patients.

Of 584 patients diagnosed with new smear-positive pulmonary TB in two cities and eight rural districts, 59 (10%) were not traced in the patient TB treatment register and considered as initial LTFU. Rural areas had significantly higher initial LTFU (13%) compared with urban areas (8%). The mean time to initiating treatment among those who were entered in the TB register was 14 days (range 8–28 days). When all TB cases included in the laboratory register were used as the denominator, the overall treatment success rate reduced from 75% to 67% (a drop of 8%).

Reporting on TB programme outcomes without including initial LTFU tends to exaggerate TB programme performance. Concerted efforts are needed to limit initial LTFU and accelerate progress towards ending TB as a public health problem.

Keywords: PERFORMANCE, LABORATORY REGISTER, TREATMENT REGISTER, INITIAL LTFU, TREATMENT OUTCOMES, OPERATIONAL RESEARCH, SORT IT

INTRODUCTION

Of the estimated 9 million incident cases of tuberculosis (TB) that occurred worldwide in 2013, only 6.1 million were detected and notified within national TB notification systems. *(1)* This left a gap of about 3 million people with TB who were "missed", either because they were not diagnosed or because they were diagnosed in the laboratory but never started on treatment. Finding these "missed cases" is one of the priority actions needed to accelerate progress towards meeting the Sustainable Development Goal of ending TB by 2030 *(2)*.

Kyrgyzstan is one of the countries in the world with a high burden of multidrug-resistant TB (MDR-TB; resistance to isoniazid and rifampicin). TB case

detection is estimated to be 80% *(1)*. One of the possible reasons for the lower-than-desired case detection rate could be that individuals who are diagnosed with smear-positive pulmonary TB (PTB) in the laboratory are not entered in the patient TB treatment register, and thus not started on treatment. Such individuals are referred to as "initial losses to follow-up" (initial LTFU) *(3)* – formerly termed "initial defaulters" *(4,5)*.

All detected TB cases must be placed on treatment and the World Health Organization (WHO) thus recommends that TB programme performance for smear-positive infectious cases should be assessed using the laboratory register as the denominator *(3,6)*.

Previous studies have shown initial LTFU of 5% in India *(6)*, 8% in Viet Nam *(7)*, 15% in Malawi *(4)* and 38% in Ghana *(8)*. A recent systematic review with studies from Africa, Asia and the Pacific revealed an initial LTFU of 4–38% *(9)*. Assessing the extent of initial LTFU is an important first step towards identifying shortcomings in linkages between diagnostic and treatment centres. There are currently no published studies from eastern Europe and central Asia on initial LTFU. In Kyrgyzstan, laboratory diagnosis of TB is centralized while treatment for TB is offered at decentralized facilities. This may be associated with initial LTFU, but the scope of this problem has never been assessed. We thus aimed to assess the linkage of TB diagnostic services to TB treatment in urban and rural areas of Kyrgyzstan.

Specific objectives were to determine (a) the proportion of sputum smear-positive PTB cases diagnosed in the laboratory who never started TB treatment (initial LFTU), (b) time to treatment initiation after diagnosis, and (c) standardized TB treatment outcomes based on the laboratory register versus the TB treatment register.

METHODS

STUDY DESIGN

This was a retrospective cohort study that used routine programme data.

SETTING

General setting: The Republic of Kyrgyzstan is a country that borders Kazakhstan, Tajikistan, Uzbekistan and China. The population is about 5.8 million with 40% of the inhabitants living in cities.

Specific setting – National Tuberculosis Programme: The National TB Programme is funded through the federal budget and international donors. TB management in Kyrgyzstan is in line with WHO guidelines *(10)*. TB control interventions are delivered through a network of dedicated TB diagnostic and care facilities. These include TB hospitals/centres and family medicine centres (primary polyclinic services). In 2012, there were 123 facilities in Kyrgyzstan that offered sputum smear microscopy services and 28 facilities where patients could receive in-patient TB treatment. TB treatment is offered free of charge. There is as yet no clear and established mechanism to follow-up/trace patients diagnosed with smear-positive TB at the laboratory level. Patients with presumptive TB (formerly called TB suspects) have their sputum specimens examined in the same facility they present to or have their specimens sent to centralized sites, and results are sent back to the referring facility. According to the Ministry of Health Order, patients should visit the health facility at least twice for sputum collection. Once a patient is confirmed to have sputum smear-positive TB, he/she is referred to a TB physician and then entered in the TB treatment register.

STUDY SITES

These included 43 laboratories and seven treatment sites in Bishkek city, Tokmok City and the rural Chui province (with eight rural districts).

STUDY POPULATION

All sputum smear-positive PTB cases registered in the TB laboratory registers in 2012 were included in the study.

DATA AND STATISTICAL ANALYSIS

To date, there is no time cut-off in terms of the number of days allowed after being recorded in the laboratory register to start TB treatment in the Kyrgyz Republic. Ideally, it is expected that TB treatment will be initiated on the same day as the diagnosis. Thus, all diagnosed TB patients, irrespective of delay, who never made it to the TB treatment register were considered as initial LTFU.

Data variables on geographical region, TB diagnosis, TB treatment and outcomes were sourced from various

registers, including the TB laboratory registers (TB 04), client cards (TB 01), institutional TB registers (TB 03) and TB referral/transfer registers.

Data in the TB laboratory register was cross-verified with the TB treatment register using names, addresses and dates of birth.

Standardized TB treatment outcomes included cured, treatment completed, died, lost to follow-up, transferred out, stopped, failure and unrecorded, and were in line with WHO guidelines *(3)*. Differences between groups were assessed using the chi-square test and a *P* value of ≤0.05 was considered significant. Data were entered and analysed using Epi Info (CDC, Atlanta, GA 30333). The following groups of variables were analysed: (1) LTFU between urban and rural areas; (2) time of starting treatment after diagnosis; (3) treatment outcomes of laboratory-registered and treatment-registered patients.

ETHICS

The study protocol was approved by the Ministry of Health of Kyrgyzstan and the National Committee for Bioethics. Ethical approval was received from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Diseases, Paris, France.

RESULTS

The proportion of sputum smear-positive PTB cases diagnosed in the laboratory who never started anti-TB treatment (initial LFTU)

Table 1 shows the initial LTFU in rural and urban areas of Kyrgyzstan. Of 584 patients diagnosed with smear-positive PTB in the laboratory register, 59 (10%) were not traced in the patient treatment register and considered initial LTFU, which ranged between 8% and 20% by geographical region. Rural areas of Kyrgyzstan had significantly higher initial LTFU individuals (13%) compared with urban areas (8%, *P*=0.05).

Time to treatment initiation

The mean time to initiate treatment after TB diagnosis was 14 days (range 8–28 days). Of 525 patients who started treatment, 443 (84%) started within 7 days of diagnosis (Table 2).

TABLE 1. NUMBERS OF NEW SPUTUM SMEAR-POSITIVE PULMONARY TUBERCULOSIS PATIENTS DIAGNOSED IN THE LABORATORY REGISTER AND LOST TO FOLLOW-UPIN URBAN AND RURAL AREAS OF KYRGYZSTAN, 2012

Region	Number in laboratory register	Initial LTFU	
		n	(%)
Rural	**247**	**32**	**(13)**
Moskow district	20	4	(20)
Panfilov district	10	2	(20)
Jaiyl district	57	10	(18)
Ysyk Ata district	28	4	(14)
Sokuluk district	57	6	(10)
Chui district	23	2	(9)
Kemin district	12	1	(8)
Alamedin district	40	3	(8)
Urban	**337**	**27**	**(8)**
Tokmok city	13	1	(8)
Bishkek city	324	26	(8)
Total	**584**	**59**	**(10)**

Initial LTFU: Initial loss to follow-up (number of diagnosed TB cases in the laboratory - number started on TB treatment)

TABLE 2. TIME TO TREATMENT INITIATION AFTER TUBERCULOSIS DIAGNOSIS IN PATIENTS WITH NEW SPUTUM SMEAR-POSITIVE PULMONARY TUBERCULOSIS, KYRGYZSTAN, 2012

Time in days	Initiated treatment	
	n	(%)
< 3	320	(61)
4-7	123	(23)
8-14	50	(10)
> 14	32	(6)
Total	**525**	

National TB Programme outcomes based on the laboratory register versus the treatment register

Table 3 compares TB treatment outcomes from the cohort of smear-positive patients entered in the laboratory register with those in the TB treatment register.

When initial LTFU was included in the analysis by using all TB cases in the laboratory register as the denominator, the overall treatment success rate declined by 8%.

DISCUSSION

This is the first study to assess initial LTFU in rural and urban areas of Kyrgyzstan. It shows that about two in 10 individuals diagnosed with TB do not get

TABLE 3. TB PROGRAMME OUTCOMES BASED ON THE LABORATORY REGISTER VERSUS THE PATIENT'S TB TREATMENT REGISTER AMONG NEW SPUTUM SMEAR-POSITIVE PULMONARY TB PATIENTS, KYRGYZSTAN, 2012

Treatment outcomes	Number in laboratory register		Number in TB treatment register	
	n	(%)	n	(%)
Successful outcomes	**392**	**(67)**	**392**	**(75)**
Cured	388		388	
Completed	4		4	
Unsuccessful outcomes	**190**	**(33)**	**131**	**(25)**
Died	4		4	
Lost to follow-up	59		0	
Transferred out	39		39	
Failure	19		19	
Stopped	69		69	
Unknown	2	(< 1)	2	(< 1)
Total	**584**		**525**	

TB: tuberculosis

treatment. Reporting on TB programme outcomes without including this group tends to exaggerate TB programme performance.

Effective TB control depends on ensuring that every diagnosed TB patient is promptly placed on treatment so that TB transmission is curtailed. Knowing that there is initial LTFU is important from both the public health and patient perspective. From the public health perspective, the proportion of initial LTFU is an indicator of the strength of the linkage between TB diagnosis and treatment. In addition, infectious TB patients not placed on TB treatment become a source of community TB transmission. From a patient perspective, initial LTFU negatively impacts patient survival and programme outcomes, as reported in previous studies *(7,8,11,12)*. This thus seems to be a universal problem facing TB control and will need to be addressed.

The strengths of our study are that we included all laboratories and treatment centres in a wide geographical area of the country, and the findings are thus likely to reflect the ground reality. Furthermore, laboratory data and treatment registers were rigorously cross-checked, and we thus feel that the data are robust. We also adhered to STROBE guidelines for reporting of operational research *(13)*.

An important limitation of our study is that some patients declared as being initial LTFU may have actually started TB treatment outside the study area. We might thus have exaggerated the proportion of initial LTFU. We also do not know the reasons for initial LTFU, which merits specific research.

The findings from this study raise questions around how the current initial LTFU can be curtailed in Kyrgyzstan. This is possible in a number of ways. First, patient information contained in the TB laboratory register needs to include unique laboratory codes, names, addresses and, in particular, telephone numbers. Laboratory results should be written out in duplicate, one copy to be given to the patient, and the other to be sent to the referring facility. Such information will facilitate tracing of patients who, despite being referred, do not arrive at any given health facility. Short message service (SMS) reminders could also be used and may be a practical way of contacting patients.

Currently, staff working in the TB laboratory and treatment centres does not consider "tracing" initial LTFU as being a part of their mandate. This lack of designated responsibility is a practical problem but it seems logical that district TB coordinators include this activity within their mandate. If there are workload issues, additional human resources may be considered.

Second, Kyrgyzstan is planning to introduce an online electronic TB registration and reporting system. This system should ensure that data on all diagnosed TB patients and those placed on treatment are captured. Ensuring that unique patient identity codes are entered in both the TB laboratory and treatment registers would permit rapid identification of initial LTFU and help to trace those who are lost.

Third, quarterly reporting of TB activity is now restricted to those who appear on the TB treatment register. This would need to be broadened to include – as the denominator – all TB patients diagnosed in the laboratory, as this is ideal for assessing the actual performance of the TB programme.

Fourth, efforts should be strengthened to enhance patient and provider empowerment to ensure that all diagnosed TB patients seek care.

Finally, there was higher initial LTFU in rural areas compared with urban areas. We believe this may be

related to TB treatment centres being centralized in rural areas, because affected people live mainly in poor rural areas and they do not have the means to travel to central facilities. Improving decentralized access through ambulatory approaches may be the way forward *(11)*.

In conclusion, initial LTFU is an adverse programme outcome and TB programmes need to make concerted efforts towards limiting it. This would be vital to achieve the "end TB" strategy *(2)*.

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