

## Improving Surveillance on Tuberculosis and HIV Co-Infection in Kazakhstan

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**Abstract:** In Kazakhstan, tuberculosis (TB) patients are screened for human immunodeficiency virus (HIV), and HIV-infected individuals are screened for active TB. However, there is no exchange of case-based information between the TB and HIV/AIDS programs.

To assess the proportion of co-infected patients registered as such in both registers and to assess reasons for patients missing in either register, we compared 2009 data from the TB and HIV/AIDS registers from two areas in Kazakhstan. Almaty city and the adjacent Almaty oblast, represent 22% of the country's population. Also, co-infected patients as well as a number of HIV-infected individuals were interviewed.

In total, 85 patients diagnosed with TB and HIV were registered, of whom 73 were registered in the TB register, 79 in the HIV/AIDS register, and 67 in both registers. In the TB register, twelve patients were wrongly recorded as HIV negative. Only 9 (11%) out of the 82 patients who started treatment (three died shortly after diagnosis) had been prescribed antiretroviral treatment.

In conclusion, gaps and mistakes with regard to TB/HIV patients were identified in both registers. Collaboration between the TB and HIV/AIDS centers was strengthened, which includes routine monitoring of TB/HIV diagnoses and treatment. This should lead to improved quality of care for TB/HIV patients and an improved insight in TB/HIV epidemiology.

**Keywords:** AIDS, HIV, Kazakhstan, surveillance, tuberculosis, KNCV.

### INTRODUCTION

#### Background

Close collaboration between HIV/AIDS programs and tuberculosis (TB) programs is needed to improve diagnostics, care and preventive services for people living with HIV and TB [1]. TB is a major cause of mortality among people living with HIV/AIDS (PLWHA), even if TB treatment is started [2, 3]. According to international guidelines [4], PLWHA are to be screened routinely for

active TB disease and latent TB infection. PLWHA with active TB should be provided with anti-TB treatment and anti-retroviral therapy (ART) and cotrimoxazol preventive therapy (CPT). PLWHA without active TB, and with or without proof of latent TB infection, should be offered preventive therapy to prevent progression to active disease. Exchange of information on co-infected patients between the TB and HIV/AIDS programs should be part of the collaboration between these two vertical programs, as to be able to provide optimal care to these co-infected patients.

Kazakhstan is a country with a low prevalence of HIV, but the proportion of notified TB cases registered as HIV-positive is increasing. According to national regulations, HIV testing is offered to all TB patients, with high actual

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uptake (97%). PLWHA should be regularly screened for TB. In 2009 1.1% of all active TB cases screened for HIV were tested positive in comparison with 0.4% in 2005. In the same period, the estimated TB incidence rate decreased from 215 to 163 per 100,000 [5].

In Kazakhstan, exchange of information on TB/HIV patients between the two vertical programs has not been implemented yet. To assess the proportion of co-infected patients registered as such in both registers and to assess reasons for patients missing in either register, we compared the 2009 data on TB/HIV from both the TB and HIV/AIDS registers from Almaty city and Almaty oblast, in Kazakhstan. Almaty city and Almaty oblast are two adjacent areas and represent approximately 22% of the total population of Kazakhstan [6].

By means of comparing both registers, we assessed the total number of HIV-positive active TB patients in this region in 2009, and the proportion of those that got prescribed ART (and CPT and IPT). In addition, we interviewed HIV-positive individuals who were prescribed IPT to assess adherence, and we interviewed recent HIV-positive patients with active TB to establish practices in CPT, IPT and ART use. The results led to the joint development of practical recommendations on strengthening the collaboration between the TB and HIV/AIDS programs, including regarding surveillance.

#### Technical Assistance

Prior to this project, the regional office of KNCV Tuberculosis Foundation (KNCV) was already involved in TB/HIV activities in Kazakhstan, with a focus on strengthening collaboration between the TB and HIV/AIDS programs. As one of the partners in the national technical working group on TB/HIV, KNCV helped to develop national policy documents on TB/HIV: ministerial orders (prikaz), program indicators, recording and reporting forms, and monitoring tools. KNCV assisted also in the development of training modules on TB/HIV, including on clinical management and monitoring of activities. KNCV also co-organized and facilitated national and regional workshops on development of work plans regarding TB/HIV.

For this project, KNCV Tuberculosis Foundation regional office together with the National Center for Tuberculosis Problems prepared data collection as described in the methods section, and a workshop to discuss the results, discuss practices, and to formulate practical recommendations on strengthening collaboration, including surveillance, between the TB and HIV/AIDS programs.

## METHODS

### HIV/AIDS Program and Register

Kazakhstan is divided into 16 administrative areas: 14 oblasts and the cities Almaty and Astana.

The HIV/AIDS program is coordinated by the republican HIV/AIDS center and 16 HIV/AIDS centers in the 14 oblasts and 2 cities. The oblast level HIV/AIDS centers also provide services to the prison system.

In Kazakhstan, defined groups are to be tested for HIV infection: prisoners, drug users, sex workers, men having sex with men, medical staff, school staff, military staff, blood

donors, pregnant women. PLWHA should be regularly screened for active TB. For diagnosis, TB suspects are referred to TB dispensaries. According to the national guidelines, all newly diagnosed HIV positive individuals without active TB should receive isoniazid preventive therapy, independently of TB history and tuberculin skin test results. CPT is recommended for use in PLWHA in case of a CD4-count below 200. For HIV-infected TB patients, CPT is recommended for use during the whole TB treatment course independent from CD4 cell count.

In accordance with the 2004 international guidelines [7], the main criteria for PLWHA to start ART are clinical stage of HIV infection (3 or 4) and/or a low number of CD4 cells. Patients with a CD4-count below 200 should receive ART, for those with a CD4-count 200-350, ART should be considered.

### Tuberculosis Program and Register

The TB program is coordinated by the national TB center and 16 oblast and city TB dispensaries. All TB patients are systematically offered HIV testing since 2002. Blood samples are sent to the AIDS center for testing, by ELISA and confirmatory Western Blot. HIV test results are registered in the TB patient file and register. The national electronic TB register includes TB patients reported in the public sector. Patients in the military and currently incarcerated are captured in separate registers. The number of patients treated there or in the private sector is estimated to be less than 5% of all TB cases.

### Comparison of TB Register and HIV/AIDS Register

Data on TB/HIV patients registered as diagnosed with TB in 2009 was extracted from both the TB register and the AIDS program registers in Almaty city and Almaty oblast (Almatinskaya). Identification of individuals in both registers was based on the following patient identifiers: name, date of birth, gender, identification card number, address. Data extraction was done by staff members from the regional centers with support from staff of the national TB center, and entered into Excel. Individuals registered in the HIV/AIDS register from the penitentiary and military sector as well as individuals who were not official residents in these two regions, were excluded from the comparison to make the denominators comparable.

The data were compared during a workshop attended by staff from the national and regional TB and AIDS centers, and individuals identified in only the TB or HIV/AIDS register, were actively searched for in the other register. Data were collected on diagnosis of TB and HIV/AIDS, and on ART, IPT and CPT use.

### Patient Interviews

All 23 TB patients registered as HIV-positive in the TB register in 2010 in either of the regions were interviewed on previous preventive therapy, and ART and CPT prescription after they were diagnosed with TB. In addition, a convenience sample of 32 HIV-positive individuals who had been prescribed IPT in 2009, at least six months before the time of interview, was interviewed on screening for active TB, TB treatment history, and adherence to IPT. The number

of interviews was limited to 32 due to limited resources and availability of interviewers.

### Ethical Considerations

Official permission was granted by the national and regional HIV/AIDS and TB centers to collect and link data from individual patients. As routine data were used to link the data from both programs, no informed consent from the patients was deemed necessary.

For patient interviews, the treating physician was provided with information on the aims of the interviews and was requested to ask the patient for permission to be approached, and informed consent was obtained from the patients.

## RESULTS

### Number of Diagnoses of HIV/AIDS and TB

Out of the total population of 3.4 million in the two regions, 251 023 (about 8%) individuals were screened for HIV-infection in 2009 of whom 550 (0.2%) registered as HIV positive (Table 1). Among those, 179 (33%) had been prescribed CPT, and 324 (59%) had been prescribed IPT after they had been diagnosed with HIV. Regarding IPT prescription there was a difference between the two regions: 37% (124/342) in Almaty city and 96% (200/208) in Almaty oblast. The total number of PLWHA by 25-12-2009 was 1931; of whom 1408 (73%) were screened for TB during that year. In 2009, 85 persons were registered as a TB-HIV patient (4.2% of total number of PLWHA).

According to the TB register, 2571 active TB patients were diagnosed in 2009 (incidence 76/100,000), of whom 74 (2.9%) HIV-positive: 5.1% in Almaty city compared to 1.4% in Almaty oblast (Table 1).

### Comparison of HIV/AIDS and TB Register

When comparing the patients among official residents diagnosed outside of the penitentiary sector in the two

registers (Table 2), a total of 85 TB/HIV patients were registered as HIV-positive individuals diagnosed with active TB in 2009. Of the 85, 79 (93%) patients were registered in the HIV/AIDS register, 73 (86%) in the TB register, and 67 (79%) in both registers.

Three (4%) patients who died after TB diagnosis but before having started TB treatment were registered in the HIV/AIDS register but not recorded as having TB, and three (4%) TB/HIV patients could not be retrieved from the HIV/AIDS register at all. All 85 could be retrieved from the TB register, but twelve (14%) were wrongly registered as HIV-negative. Nine of the 82 (11%) TB/HIV patients who did not die shortly after diagnosis were prescribed ART. In Almaty city, 44 (69%) were prescribed CPT after TB diagnosis, and 43 (68%) had been prescribed IPT before TB diagnosis. These data were not available for Almaty oblast.

### Interviews with TB/HIV Patients

23 TB/HIV patients were identified from the 2010 TB register, 11 from Almaty city and 12 from Almaty oblast. Ten out of the 11 (91%) TB/HIV patients from Almaty city and three out of 12 (25%) from Almaty oblast were already known to be HIV-positive before TB was diagnosed and thus would have been eligible for IPT. In reality only three (23%) individuals out of these thirteen had been prescribed IPT prior to TB diagnosis. None of the cases were detected through routine screening for TB, and one had been diagnosed following a contact investigation. Five of the 23 cases (22%) had been prescribed ART, and seven (30%) had been prescribed CPT at the time of interview (Table 3).

### Interviews with PLWHA who had been Prescribed Preventive Therapy

Thirty-two HIV+ individuals who were prescribed preventive therapy at least 6 months ago (and thus could have finished the standard 6 month course) were interviewed, 14 from Almaty city and 18 from Almaty oblast. This includes the three patients from Almaty city who

**Table 1. Summary of 2009 TB/HIV Data from the HIV/AIDS Register and TB Register in Almaty City and Almaty Oblast, in the Republic of Kazakhstan**

	Almaty City (1.4 Million Population)		Almaty Oblast (2.0 Million Population)		Total	
	n	(%)	n	(%)	n	(%)
<b>HIV/AIDS Register</b>						
Number of individuals tested for HIV in 2009	119,944	(9%)	131,079	(7%)	251,023	(8%)
Number of individuals with positive test result	342	(0.3%)	208	(0.2%)	550	(0.2%)
– CPT provision	67	(19.6%)	112	(53.8%)	179	(32.5%)
– IPT provision	124	(36.3%)	200	(96.2%)	324	(58.9%)
Total number of HIV-positive individuals registered on 25-12-2009 (prevalence)	1,666		765		2,431	
Number of HIV-positive individuals screened for TB in 2009	834	(50.1%)	574	(75.0%)	1,408	(72.9%)
Number of HIV-positive TB patients registered	61	(5.7%)	21	(3.7%)	85	(4.2%)
<b>TB Register</b>						
TB patients	1,044		1,527		2,571	
Registered as HIV-positive	53	(5.1%)	21	(1.4%)	74	(2.9%)

**Table 2. Comparison of Number of HIV-Positive Individuals with Active TB in the Registers from the TB and HIV/AIDS Registers in Almaty City and Almaty Oblast, Kazakhstan, in 2009**

	HIV/AIDS Register		Not Included in HIV/AIDS Register	Total
	Registered as HIV-Positive TB Patient	Registered as HIV-Positive, Non-TB Patient		
<b>TB register</b>				
Registered as HIV-positive	67 <sup>1</sup>	3 <sup>2</sup>	3	73
Falsely registered as HIV-negative	12			12
<b>Total</b>	<b>79</b>	<b>3</b>	<b>3</b>	<b>85</b>

<sup>1</sup>Excluding three patients mistakenly registered as HIV-positive in the TB register.

<sup>2</sup>Deceased before TB treatment was started.

were also interviewed because they were diagnosed with active TB in 2010. All had been screened for active TB disease before prescription of IPT. One of the patients had been treated already for TB before, in 1996. Out of the 32 patients, 27 (84%) had completed the six months of treatment. The five patients who had not completed treatment could not recall why IPT had been prescribed (Table 4).

## DISCUSSION

By means of a comparison of the TB and HIV/AIDS registers, we showed that both registers were incomplete with regard to recording of co-infected patients. Out of the total of 85 TB/HIV patients included in either register, twelve (14%) and six (7%) were missed in the TB and HIV/AIDS register, respectively. It is worrying that twelve out of 85 (14%) TB/HIV patients with a positive HIV test result reported back by the HIV/AIDS center, were not registered as such in the TB register. This is probably due to the fact that the HIV test result comes back after other baseline data of the patient have already been entered into the electronic TB register. This implies that there is underreporting of co-infected patients from the TB surveillance system. Vice versa, three TB patients identified as HIV-positive at TB diagnosis, were not known at the HIV/AIDS center and thus not included in their register.

Collaborative TB/HIV activities have the objective of creating mechanisms of collaboration between TB and HIV/AIDS programs, with the aim to reduce the burden of TB among people living with HIV and to reduce the burden of HIV among TB patients [2]. Mechanisms of communication include surveillance of TB/HIV. Registration of HIV prevalence among TB patients was introduced already in 2002. However, exchange of registration data on an individual level between the two vertical programs had not been set up yet. This exercise shows the added value of such data exchange. It displays flaws in the data, and enables to improve insight in the true number of (diagnosed) co-infected patients, which in turn enables optimization of care for those patients.

Reducing the burden of TB among PLWHA can be reached through the 'three I's': intensified TB case finding, IPT, and TB infection control [2]. In Kazakhstan, PLWHA are to be screened for active TB at least yearly, and IPT should be provided. The data from these two regions show that IPT is not provided to all HIV-positive individuals.

During the workshop, it was stated that persons not trusted to finish preventive therapy are not prescribed IPT. The staff of the AIDS centers estimated that about a third of all individuals diagnosed with HIV are not prescribed IPT. The HIV epidemic in Kazakhstan is driven by injecting drug-using networks [8]. Drug users often are from marginalized groups, and are expected to be less adherent to therapy. Although not mentioned as an argument not to prescribe IPT, it was noted that IPT may not prevent development of TB infection to disease in a considerable proportion of individuals in this region, with a high prevalence of drug resistance to both isoniazid and other drugs.

Reducing the burden of HIV in TB patients is achieved by providing HIV testing and counseling, HIV prevention and care, and by provision of CPT and ART [1]. The data from the Almaty region in Kazakhstan show that CPT and ART are not provided to all patients: 69% and 11%, respectively, received CPT and ART at the time of the interview. This is in accordance with the national data from 2009: 11% of TB/HIV patients were provided CPT and 7% ART [3]. There is a need to update clinical guidelines in suit with international guidelines, to optimize care for co-infected patients. Three recent clinical trials have shown that optimal timing of starting ART is at the beginning of the continuation phase of TB treatment, except when the CD4-count is <50 cells/mm [3, 9-12]. This also is true for multi-drug resistant (MDR) TB cases [13-15], important for a high MDR-TB prevalent setting like Kazakhstan [16]. As shown in the recent clinical trials, starting within two weeks after the initiation of TB therapy seems most beneficial in reducing mortality and the incidence of new AIDS-defining illnesses. These benefits strongly outweigh the increased risks for immune reconstitution inflammatory syndrome and other adverse events, although clinicians do need to be vigilant in monitoring for such events. According to the ministerial order on TB/HIV in Kazakhstan, ART should be started after 4-8 weeks in patients with CD4-counts below 200. In practice however, most of the HIV positive TB patients who receive ART, start only after they complete TB treatment. The same is true for CPT. Thus it is possible that more of the TB/HIV patients interviewed would be prescribed ART and CPT later on. However, similar to IPT, ART and CPT are prescribed only when patients are expected to be adherent. Setting up patient-friendly support mechanisms enabling adherence, including patient education, might be beneficial.

**Table 3. Description of HIV-Positive Individuals Diagnosed with Active Tuberculosis (TB) in Almaty City and Almaty Oblast, Kazakhstan, in January-April 2010**

	Almaty City (n=11)	Almaty Oblast (n=12)	Total (n=23)
Male gender	7	10	17 (74%)
Age (years)			
<20	0	0	0 (0%)
20-29	0	2	2 (9%)
30-39	6	9	15 (65%)
≥40	5	1	6 (26%)
Pulmonary TB	10	10	20 (87%)
<i>Smear positive</i>	6	7	13 (56%)
<i>Smear negative</i>	4	3	7 (44%)
HIV-positive status known before TB diagnosis	10	3	13 (56%)
Prescription of IPT before TB diagnosis	3	0	3 (13%)
Assessment of CD4-count at TB diagnosis	9	7	16 (70%)
>300	4	3	7 (44%)
250-300	5	4	9 (56%)
<250	0	0	0 (0%)
Prescription of ART after TB diagnosis, at the time of the interview	2	3	5 (22%)
Prescription of CPT after TB diagnosis, at the time of the interview	7	1	8 (35%)

IPT=isoniazid preventive therapy, ART=antiretroviral therapy, CPT=cotrimoxazol preventive therapy.

It seems likely that not many patients are missed through combining data from both registers, considering that all patients could be retrieved from the TB register and the small number of patients not retrieved from the HIV/AIDS register. This may be explained by the fact that both vertical systems are the only sections of the health care system where treatment for these infectious diseases is possible in Kazakhstan. Still, there may be patients without or with limited access to health care, like the homeless and migrants. These patients would be underrepresented in both registers.

Based on the results, practical recommendations on strengthening collaboration, and improving surveillance and patient care were formulated together by the staff from the TB and HIV/AIDS programs. Firstly, the recently updated WHO guidelines on IPT and ICF [4] were taken as a starting point for an update of the ministerial orders and protocols on TB/HIV, especially regarding criteria for ART. The updated order describes the responsibilities of the different public health services. Implementation is overseen by the national working group. Secondly, it was decided by staff from the regional TB and AIDS centers that data on newly diagnosed TB/HIV cases will be collected monthly per region, by means of standardized forms by the TB/HIV coordinators from both centers. Coordinators were appointed both in the regional TB center and regional AIDS center. The TB/HIV coordinator at the AIDS center fills it in first and sends it on to the TB/HIV coordinator at the TB center. The TB/HIV coordinator at the TB center compiles the final list and, if necessary, traces missing data from the TB and AIDS centers at the oblast and/or rayon level. If HIV-positive TB patients

do not get timely and adequate treatment according to the orders, the TB/HIV coordinator ensures that the physician from the AIDS center joins a meeting of the central committee at the TB center to discuss the reasons, and to rectify this. The central committee confirms TB diagnoses and decides on which treatment regimen is given. Thirdly, TB treatment outcomes for co-infected patients should be reported to the AIDS center so they will be registered there as well.

## CONCLUSIONS AND RECOMMENDATIONS

In conclusion, gaps and mistakes with regard to TB/HIV patients were identified in both the TB register and HIV/AIDS register. Collaboration between the TB and HIV/AIDS centers was strengthened, which includes routine monitoring of TB/HIV diagnoses and treatment from both sides. This should lead to an improved insight in TB/HIV epidemiology, improved monitoring and evaluation of TB/HIV activities, and hereby improved quality of care for TB/HIV patients. In this small-scale regional operational research study we were not able to include staff and data from all regions in Kazakhstan in this exercise. The national and regional TB/HIV coordinators have recommended implementing this mechanism in all regions in Kazakhstan, and this has been taken up. Based on the experiences of this regional study, national roll out is facilitated.

## CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

**Table 4. Description of HIV-Positive Individuals Who had been Prescribed Isoniazid Preventive Therapy (IPT) in Almaty City and Almaty Oblast, Kazakhstan, in 2009**

	Almaty City (n=14)	Almaty Oblast (n=18)	Total (n=32)
Male gender	9	4	13 (41%)
Age (years)			
<20	0	1	1 (3%)
20-29	3	5	8 (25%)
30-39	10	12	22 (69%)
≥40	1	0	1 (3%)
Assessment of CD4-count at HIV diagnosis	14	1	15 (47%)
>300	8	0	8 (25%)
250-300	4	1	5 (16%)
<250	2	0	2 (6%)
Previous TB diagnosis	1	0	1 (3%)
Screening for active TB disease before prescription of IPT	14	18	32 (100%)
Completion of full 6 month course of IPT	9	18	27 (84%)

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