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#### Review

# Tuberculosis, drug use and HIV infection in Central Asia: An urgent need for attention



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#### ABSTRACT

Introduction: Rates of tuberculosis in Central Asia are extremely high, and even more alarming are the very high rates of multidrug-resistant tuberculosis (MDR-TB) in Kazakhstan, Uzbekistan, Tajikistan and Kyrgyzstan. In addition, rates of HIV infection related to injection drug use seems to be rising as well, thus creating conditions for a potentially devastating co-epidemic of TB/HIV and MDR-TB/HIV which would have terrible consequences for public health in these countries.

Current status: In many countries of Central Asia, diagnosis of tuberculosis still rests on clinical grounds or simple technologies such as chest radiograph and sputum smear examination. Modern molecular techniques such as GenExpert are being introduced in Kazakhstan and Uzbekistan, and perhaps soon in Kyrgyzstan. Treatment of TB is still often centered around prolonged inpatient stay at TB hospitals. Only a minority of patients with HIV infection are receiving ART, and TB and HIV services are not well integrated. Needle exchange programs are becoming increasingly available, but opioid substitution therapy is rarely used in Central Asia. TB, drug treatment and HIV services are generally not well-integrated.

Conclusions: To combat this developing storm, integration of TB services, HIV care, and substance abuse treatment programs is needed urgently to allow efficient and effective diagnosis and treatment of these conditions in a coordinated manner.

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#### 1. Introduction

Tuberculosis is one of the world's leading public health problems. Twenty years after the World Health Organization classified tuberculosis as a global public health emergency, it remains the 10th leading cause of death in the world, and cases seems to be declining globally only at a rate of about 1% per year, according to WHO estimates. In the last twenty years, two features of global tuberculosis epidemiology have posed great challenges to worldwide control efforts: HIV infection and the emergence of multidrug-resistant tuberculosis (MDR-TB, defined as a case of tuberculosis resistant to at least isoniazid and rifampin). Both of these threaten to erase any and all gains that have been made in controlling tuberculosis globally in the past several decades, and both are of particular importance for the overall situation of tuberculosis in Central Asia.

#### 1.1. Tuberculosis in Central Asia

Incidence rates for TB overall in Kazakhstan, Uzbekistan, Tajikistan and Kyrgyzstan are extremely high (see Table 1). More worrisome, all of these countries of Central Asia are among the 27 high-burden countries for MDR-TB in the world. The percentages both of new cases and previously treated cases of tuberculosis that demonstrate multidrug-resistance in Kazakhstan, Uzbekistan, Tajikistan and Kyrgyzstan are among the highest in the world (see Table 1). The burden of HIV-associated tuberculosis, an enormous problem in sub-Saharan Africa, seems to be much lower in Central Asia at present, although HIV infection rates in Central Asia seem to be rising quite rapidly, and in some estimates are the fasting rising rates in the world (Thorne et al., 2010).

According to WHO, the percentage of TB cases in which there is HIV co-infection in Kazakhstan, Uzbekistan, and Tajikistan is 2%, 3%, and 2%, respectively, and in all these countries 82–100% of TB patients have been tested for HIV. (Data from Kyrgyzstan are sparse and unreliable in regards to HIV-testing of TB patients.) Given the rapidly rising HIV infection rates in Central Asia and the already very high rates of tuberculosis and MDR-TB, it seems likely that in the very near future, the incidence of HIV infection among persons with tuberculosis will begin to rise quickly, and this will pose enormous challenges to the tuberculosis control programs in these countries. This will require substantial efforts and improvements in diagnosis and treatment to control the staggering epidemics of tuberculosis and especially drug-resistant tuberculosis in Central Asia.

In many ways, the situation in Central Asia is reminiscent of, though certainly worse than, the tuberculosis epidemic in New York in the late 1980s and early 1990s. At its peak in 1992, there was an overall incidence rate of 50.4/100,000 and 13% of new cases were MDR. At that time, there were very high rates of substance abuse among TB patients in New York, and this similarly posed great challenges for the TB control program there (Selwyn et al., 1989). Currently, the brewing storm of TB and HIV among IDUs in Central Asia is under-recognized, almost unknown, and without prompt recognition, it threatens to grow quickly.

This paper will focus on the following issues related to diagnosis and treatment of TB in HIV-infected IDUs: the need for more

intensive diagnostic approaches, the complex problems of simultaneous treatment of TB and HIV, adherence to treatment, and the need to integrate programs of care for TB, HIV and substance abuse.

#### 1.2. Drug use and HIV infection in Central Asia

The total number of drug users in the four Central Asian countries is estimated to be between 340,000 and 417,000 (Renton et al., 2006). One of the well-studied countries in Central Asia in terms of drug use is Kazakhstan. Overall, it is estimated that 1% of the population of Kazakhstan are injection drug users, although as many as 10% of the population along major drug trafficking routes inject drugs. The government estimates that there are a total of 122,850 injection drug users in the country, of whom 17,000 reside in Almaty, the country's largest city (Yusopov et al., 2012).

In a recent study from Uzbekistan, nearly 30% of a sample of injection drug users was HIV positive (Sanchez et al., 2006). A study carried out in Almaty, the largest city in Kazakhstan, similarly found that 28% of injection drug users were HIV infected (El-Bassel et al., 2013). Contributing to the problem is the relatively limited availability of harm reduction programs such as substitution therapy in this region (Thorne et al., 2010). HIV infections increased by 20% in Eastern Europe and Central Asia from 2005 to 2011, and most of the increase was seen in young injection drug users. UNAIDS estimates that only about 25% of HIV-infected persons in the region are receiving antiviral therapy, and as a result AIDS-related mortality increased by 21% in Eastern Europe and Central Asia from 2005 to 2011 (UNAIDS, 2012)

Extant data therefore suggests the potential for rapid escalation of an already serious problem regarding tuberculosis in Central Asia: very high rates of tuberculosis and MDR-TB in a region with a high-prevalence of injection drug use, an increasing incidence of HIV infection among drug users, and few services related to harm reduction for drug use. Injection drug use, independent of HIV infection, has repeatedly been shown to be a risk for tuberculosis, owing to a combination of behavioral and biological factors related to TB knowledge, shared living quarters, and immune dysregulation (Casal et al., 2005; Nyamathi et al., 2004).

#### 2. Tuberculosis, drug use and HIV infection in Central Asia

Few studies have examined the convergence of tuberculosis and HIV infection in Central Asia especially among people who use drugs, but experience in other regions around the world points to several areas of great challenges, mostly related to diagnosis of tuberculosis in HIV positive patients, difficulties of drug treatment in persons co-infected with HIV and TB, and problems of adherence to therapy for tuberculosis patients, particularly those with ongoing substance abuse problems. We will comment briefly on each of these challenges.

 Table 1

 Incidence and prevalence of tuberculosis and multidrug-resistant tuberculosis in Central Asia.

	Kazakhstan	Uzbekistan	Tajikistan	Kyrgyzstan
TB incidence (per 100,000 population)	129	101	193	128
Percentage of new cases of TB that are MDR	30%	23%	13%	26%
Percentage of previously treated cases that are MDR	51%	62%	54%	52%

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