

SUSTAINABLE IMPLEMENTATION OF NEW TESTS AND DRUGS

Beating back drug-resistant tuberculosis in Central Asia

After the collapse of the Soviet Union in the 1990s, the health systems of the Central Asian Republics were in disarray. Following decades of poorly managed TB treatment and inadequate regulation and supply of TB drugs, many Central Asian countries now struggle with very high rates of drug-resistant TB. New drugs bring new hope but also new challenges, because if patients also grow resistant to these, there will be no cure for them at all. That is why the operational testing and management of these new drugs and accompanying regimens is of the utmost importance.

Our impact in short

Together with the Central Asian Republics, KNCV is striving to stop the spread of drug-resistant TB by supporting and facilitating the introduction and management of new diagnostic tools and drugs. A safe and sustainable use of new drugs and treatment regimens is crucial to save the lives of people with drug-resistant TB now and in the future.

What is KNCV's approach in the Central Asian Republics?

Through our regional office in Kazakhstan and country offices in Kyrgyzstan and Tajikistan, KNCV provides support in early diagnosis and treatment of patients with TB, MDR-TB and extensively drug-resistant TB. Thanks to improved diagnostics such as GeneXpert, which determines not only whether patients have TB but also which type of TB, more patients are being accurately diagnosed. To be able to give them the right treatment for the type of TB they have, we help to organize drug management and treatment evaluation. The immediate and appropriate treatment of patients diagnosed with drug-resistant TB will save many lives that are now at risk, as well as avert the emergence of further drug resistance.

Why is it so important to try to prevent drug resistance?

The newest drugs, such as bedaquiline and delamanid, will be of great importance for reducing MDR-TB. Combined with improved treatment regimens, these drugs will not only potentially save many lives; they are also the last known chance to successfully treat patients with drug-resistant TB. We cannot afford to let any new resistance to TB drugs emerge.

What are the challenges that KNCV faces in this area?

Proper drug management is highly dependent on the quality and accuracy of the available data on the number of patients diagnosed, which drugs they need, and the current drug stock situations. KNCV has an extensive track record in supporting countries around the world in the programmatic management of drug-resistant TB. This includes being able to



The added value of QuanTB in Kazakhstan

KNCV has supported TB control in Kazakhstan for many years and has achieved significant impact. The annual estimated incidence of TB (all new cases occurring in one year) declined by over fifty percent in the past ten years: from 147 TB cases per 100,000 people in 2005 to 58,5 cases per 100,000 people in 2015.

Year by year, the Kazakhstan Government has been significantly raising its national budget for TB control, with a focus on the rapid scale-up of treatment for people with MDR-TB. However, now that new drugs are available, it is important to further improve on drug management and quantification. That is why in 2015, we helped to introduce the use of QuanTB to Kazakhstan's NTP.

The QuanTB tool helps to predict and estimate the needed volume of TB drugs. The tool that was formerly being used to manage this, was not designed for shortened treatment regimens and new or non-standard drug combinations. Therefore it could not be used for country-wide management and control of drug stocks for drug-resistant TB. With QuanTB this is now possible.

An additional reason to introduce QuanTB in Kazakhstan is that the use of the tool requires accurate and complete data on TB patients. So by introducing QuanTB, the quality of patient data will also be improved.

forecast and manage the necessary drug supplies. Internationally, the supply of second-line drugs for the treatment of drug-resistant TB is coordinated by the Global Drug Facility (GDF). For countries to be able to place timely orders they need to have their national TB drug supplies management in order. To help countries manage their local second-line drug supplies, KNCV's partner MSH has developed a software tool called QuanTB.

Why this tool? What does it do?

QuanTB is a management tool which was designed to help predict and estimate the need for TB drugs. It is very helpful for both planning and procurement and can be used for any type of treatment, including the quantification of companion drugs. This is very important, now that new drugs and regimens are being implemented to fight MDR-TB. An additional advantage of the use of the tool is that it also enhances the quality of patient data, which is needed to evaluate and further improve treatment regimens.>>

Saving lives with new treatment regimens in Kyrgyzstan

Each year, around 100 patients are diagnosed with XDR-TB in Kyrgyzstan, for which there has been little to no effective treatment. Patients have been dying as a result. The introduction of the treatment regimens containing new drugs for these patients is a matter of life and death. In recent years, more patients with drug-resistant TB in Kyrgyzstan have been diagnosed thanks to the introduction of new diagnostics. Within five years, the detection of drug-resistant TB increased by a factor of 1.5: from 835 MDR-TB cases in 2009 to 1,223 cases in 2013. This makes the need for specific drug-resistant treatment regimens more urgent than ever before.

In September 2015, the Global Fund approved the Kyrgyzstan Concept Note for a grant application. This will enable the procurement of second-line TB drugs for the next two years, with technical assistance from KNCV for the introduction of the new TB drugs and shortened regimens in Kyrgyzstan.

All stakeholders including civil society need to be involved in the Country Coordinating Mechanism for the implementation of the country-wide Global Fund-financed program. For our approach on this, see the question 'How does KNCV involve the local community in fighting drug-resistant TB?' page 28.

Pharmacovigilance

Pharmacovigilance is a system for the safe use of TB drugs. It consists of two parts:

1. The clinical monitoring of treatment with TB drugs. It is important that doctors who are treating TB patients report adverse treatment effects in patients, in a nationwide system.
2. The collection of data on the use of the drugs and the subsequent analysis and monitoring of the adverse effects of TB drugs.

A pharmacovigilance center has specific expertise and the authority to collect and analyze adverse effects. It is authorized to give permission to import equipment and drugs. Effective pharmacovigilance relies on the close collaboration between the pharmacovigilance center and the National TB Program (NTP). Clinicians can report the adverse events of TB treatment regimens to a center of excellence on pharmacovigilance or to the NTP. In either case, the information is shared between both organizations.

>> How is KNCV involved in the implementation of QuanTB, and how is it funded?

In April 2015, KNCV and the Lilly MDR-TB Partnership signed an agreement for a project of two years with the purpose of strengthening MDR-TB drug management and quantification in several countries. Within this project funded by Lilly, KNCV is supporting the introduction of QuanTB and supply chain management in the Central Asian countries Kazakhstan and Kyrgyzstan, with the objective to improve

KNCV stimulates pharmacovigilance by giving technical support to the NTP and health service, and training to relevant health providers.

the uninterrupted supply and availability of first- and second-line TB drugs.

In 2015, KNCV organized several meetings to prepare for the introduction of QuanTB, as well as a workshop on drug management and the use of QuanTB in Kazakhstan and Kyrgyzstan. We also organized trainings on the use of the tool.

Is this new tool enough to ensure effective drug management?

QuanTB is a very helpful tool to ensure TB drug supplies are managed and coordinated effectively, but it is also important that clinicians who administer the new drugs and treatment regimens are using and sharing the latest knowledge and expertise, especially on the effects of the treatment. This is where pharmacovigilance comes in: it is a system for the safe use of the both existing TB drugs and new drugs coming onto the market. This system consists of gathering and analyzing treatment experiences and creating protocols for administering the new drugs.

It is also important that there is a legal foundation for the procurement of the drugs and that information about both the use and effect of the drugs is collected and reported. Lastly, reporting forms, and if possible an electronic recording and reporting system should be in place. >>





The Director of the TB Patients Coalition

Indira Kaziyeva is the Director of the Kyrgyzstan TB Patients Coalition. She used to work as a TB doctor in a hospital for patients with MDR-TB and was trained as a lawyer. She became sick with TB herself, and while she was undergoing treatment, her four children developed TB. Although Dr. Kaziyeva also has an education as a lawyer, she was not able to protect her own rights.

"A lot of patients do not know their rights, and feel under pressure. They do not have access to services because they don't know their rights and don't know how to protect themselves. They are very afraid. Patients need legal protection as well as medical support."

With the Coalition Indira Kaziyeva wants to work more broadly, and more globally. "It is like building a big ship for patients. The ship will protect TB patients through their treatment journey by helping them to understand their rights. For a safe trip we need special laws and regulations, and the involvement of civil society organizations."

She stresses the importance of case management for TB patients, as some patients have no family support or have a lack of money for food. Referring these patients – migrants, ex-prisoners or the homeless – to outpatients care can be a problem, as they run a risk of stopping before they complete their treatment. "Case management of TB patients helps reduce TB and the number of treatment failures. This is good, not only for the patients themselves, but also for the entire country", says Dr. Kaziyeva.

The Kyrgyzstan TB Patients Coalition, with in the middle director Indira Kaziyeva

> Why does a country need pharmacovigilance?

Pharmacovigilance plays an important role in collecting the information that is needed for the successful registration of new drugs. In Kyrgyzstan the Ministry of Health decided not to seek registration until all necessary information about effectiveness of treatment and drugs safety has been gathered, including developing a protocol to decide which patients are eligible for the new drugs and under which conditions they should be administered. This protocol also includes the criteria for excluding the use of new drugs or shortened regimens. The very strict rules of the protocol are necessary for the responsible introduction of the drugs with a minimum of risk to patients. KNCV stimulates pharmacovigilance by giving technical support to the NTP and health services, and training to relevant health providers.

How does KNCV involve the local community in fighting drug-resistant TB?

Local non-governmental organizations (NGOs) play an important part in the implementation of TB control in a country. That is why involving these organizations is an essential part of our mission. For



The former TB-patient giving support

Sultan first developed TB ten years ago. He does not speak Russian, he speaks the Kyrgyz language. Sultan was sick with TB in another region, where his disease was detected but not treated. Eventually he came from to the city of Bishkek for treatment. "I was a migrant worker, working in construction and also as a taxi driver. I was travelling a lot and I met a lot of people. I was under a lot of stress and did not always have enough food, or a good space to live. This caused me from time to time to stop my TB treatment, which I know was not good." Sultan developed MDR-TB. He is now cured and joined the TB Patient Coalition. "I know what it is like, so I now use my experiences to help other MDR-TB patients through the treatment process."

example, as patients are enrolled on new drugs and shortened drug regimes, we anticipate that many will also be put on ambulatory (outpatient) treatment. Therefore we need to develop a system for supporting these patients. NGOs will be engaged to provide patient support and medical staff will be needed to make sure the patients finish their treatment.

Local TB Civil Society Organizations (CSOs) are also involved, for instance in the Country Coordinating Mechanism (CCM), which oversees the implementation of a country's national TB control activities financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria.

In 2015 KNCV supported two civil society organizations in Kyrgyzstan. One is Socium, a local NGO which fights against HIV, TB and drug abuse, for which we successfully helped to secure funding from the Stop TB Partnership for a proposal to improve the capacity of TB CSOs in representing TB patients' interests. The other is a new CSO established by former TB patients to represent their interests in the CCM: the Kyrgyzstan national TB Patients Coalition (see inset). It was accepted as a CCM member, meaning that now there is a TB patients' civil society representation in the implementation of the Global Fund grant.

The TB Patient Coalition will also be involved in the implementation of new drugs and regimens. There are now fifty members of the Coalition, including TB doctors and former patients from all across Kyrgyzstan, who are active as outreach workers. They provide essential support to patients, because they know the situation these patients find themselves in, and understand the support and help which they need to adhere to their treatment. To prepare for the new TB drugs to be introduced in 2016, KNCV experts will provide technical assistance to the Coalition and organize trainings for the representatives, as well as meetings about patient enrolment and eligibility. ■