



**CENTER FOR GLOBAL  
HEALTH DELIVERY-DUBAI**  
HARVARD MEDICAL SCHOOL

# Stemming the Tide of Drug-Resistant Tuberculosis

Handbook on Best Practices for Clinical  
and Program Management of Drug-resistant  
Tuberculosis: Lessons Learned from the Global  
Fund to Fight Aids, Tuberculosis, and Malaria TB  
Grants in Eastern Europe and Central Asia



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HEALTH DELIVERY-DUBAI  
HARVARD MEDICAL SCHOOL

Partners  Партнеры  
In Health во имя Здоровья



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# Handbook on Best Practices for Clinical and Program Management of Drug-Resistant Tuberculosis: Lessons Learned from Global Fund to Fight AIDS, Tuberculosis, and Malaria TB Grants in Eastern Europe and Central Asia

## STEMMING THE TIDE OF DRUG-RESISTANT TUBERCULOSIS

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## **ABOUT PARTNERS IN HEALTH:**

Partners In Health (PIH) is a non-profit corporation focused on delivering quality healthcare to poor people in eleven countries worldwide.

Since 2000, the Tomsk Oblast TB Services has worked in close collaboration with PIH to implement a comprehensive, multicomponent program to combat multi/extensively drug-resistant TB (M/XDR-TB) in the region's civilian and prison sectors. The program began receiving funding from the GFATM in 2004, when the Tomsk Region was successfully approved as the only sub-national project in Russia with total funding of \$10.8 million.

The application to receive funding from GFATM was highly supported by the Administration of Tomsk Region and the Russian Ministry of Justice. Later in 2009, the Tomsk R3 GFATM grant received an extension for another four years through the rolling-continuation channel (RCC) mechanism, which resulted in the overall enrollment of 2,500 patients with M/XDR-TB and introduction of various patient-centered strategies aimed at improving program performance. This project builds upon the experience that PIH and Russia's Tomsk Oblast TB Program gained during the implementation of the R3 GFATM grant.

## **ABOUT THE HARVARD MEDICAL SCHOOL CENTER FOR GLOBAL HEALTH DELIVERY-- DUBAI**

The Harvard Medical School Center for Global Health Delivery-- Dubai is addressing some of the most pressing health challenges in the region by focusing on research, medical education, and training that promise to improve health care delivery systems and patient outcomes for diseases prevalent in the United Arab Emirates, Middle East, North Africa, and neighboring regions in Africa, Asia, and Europe.

The Center was established by the Harvard Medical School in Boston and Dubai in 2014. It is a hub for policy formulation and analysis that is optimizing the last phase of health care delivery, ensuring that care providers have the systems and tools necessary to alleviate human suffering caused by disease. The Center does not provide patient care but focuses exclusively on research and training.

## **ABOUT THE "STEMMING THE TIDE OF DR-TB" SYMPOSIUM AND THE HANDBOOK:**

Partners In Health is pleased to introduce this handbook based on the collection of best practices presented at an international symposium "Stemming the Tide of DR-TB" held on December 4-6, 2014. The symposium was organized in partnership with the Harvard Center for Global Health Delivery-Dubai, and took place on its premises in Dubai, U.A.E.

This publication serves as a summary of the achievements of the Tomsk Regional TB Program (Tomsk Oblast, Russia) and other Eastern European and Central Asian countries implementing GFATM (The Global Fund to Fight AIDS, Tuberculosis and Malaria) grants. The handbook aims to provide a framework for ensuring the replication of best practices at both the national and global levels.

The primary goal of the international symposium was to outline and disseminate effective approaches for improving care delivery for TB and MDR-TB.

Treating MDR-TB is a gruelling and complicated process that can take up to two years and thousands of doses of medication, some of which can cause painful and adverse reactions. It is also a programmatic challenge that requires stellar management and deeply committed staff. The symposium drew largely upon the experience of Russia's Tomsk Oblast TB Program, an internationally recognized GFATM success story and pioneer in combatting the global M/XDR-TB pandemic, as well as from the best practices that have emerged from other GFATM projects. Examples from Tomsk's TB Program are highly relevant to and replicable in countries of the former Soviet Union and Eastern Europe, given the similarities in the structure of health service delivery systems and disease profiles.

The symposium was organized with generous support from the GIZ (Deutsche Gesellschaft für Internationale Zusammenarbeit) BACK-UP initiative. The printing and design of this publication was supported by the Eli Lilly MDR-TB Partnership, and the Harvard Medical School Center for Global Health Delivery-- Dubai.



## WELCOME LETTER FROM DR. PAUL FARMER TO THE SYMPOSIUM ATTENDEES



*Dear Colleagues:*

I extend my warmest welcome to you, and my deepest gratitude for sharing your time, talent, and expertise with all those gathered here in Dubai.

As those of us working in global health know too well, multidrug-resistant tuberculosis remains one of the most pressing health issues of our time. It is an airborne disease that we, as a global community, cannot afford to ignore or declare “incurable.” It is long past time for swift, comprehensive action in addressing and treating MDRTB. Unfortunately, in addition to being in too-short in supply globally, the current treatment regimen for extensively drug-resistant tuberculosis can only be described as grueling. We need new and better therapies: safer, more effective, more tolerable, cheaper, and faster-acting.

But projects like Sputnik in Tomsk, Russia show us that, even though our treatments are imperfect, when patients are the center of all of our efforts—when our attentions and resources revolve, like satellites, around them—we succeed. The Sputnik project has made clear that, if patients receive appropriate medical care and the social and psychological support required to complete therapy, rates of recovery—even among those so often and so cruelly deemed “untreatable”—are high.

The Sputnik project serves as a model for ways in which the notion of accompaniment can be applied to improve clinical outcomes and strengthen our response to new public health challenges. As we discuss and learn from its successes, we must ask ourselves: how might we link lessons from projects like Sputnik in Tomsk (or accompaniment in Belarus, or social support in Moldova) to the challenges still before us? A few things are clear: we need to adopt more widely an integrated approach to health care delivery, to set aside resources to respond to new problems, and to deploy new tools for old problems. Most of all, we need long-term commitments to health equity.

Thank you for your partnership and commitment as we work together to stem the tide of drug-resistant tuberculosis worldwide. All of us at Harvard Medical School and at Partners In Health sites around the world are eager to continue collaborating with you on research and training efforts in the months and years ahead.

With every best wish for a successful conference, and with great admiration for your work,

A handwritten signature in black ink, which appears to read "Paul Farmer". The signature is fluid and cursive.

Paul Farmer



## Session 1.

### 1.1 Best Practice: Clinical trial and compassionate use of Bedaquiline, an example from Russia.

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#### INTRODUCTION

After decades of using first and second line TB drugs, like all bacteria, *Mycobacterium tuberculosis* has acquired genetically determined resistance to essential chemotherapy drugs. This resistance has an impact on the efficacy of TB patient treatment. Extensively drug-resistant tuberculosis (XDR-TB) is the most complicated type of drug resistance in *Mycobacterium tuberculosis*. Currently, the extent of the XDR-TB problem in the Russian Federation (RF) has yet to be clearly estimated. However, based on WHO data suggesting that the proportion of XDR-TB patients is 9.6%, it is assumed that in 2013 there were 3,339 patients with XDR-TB living in Russia. According to data from the Central TB Research Institute (CTRI), in thirteen territories of Russia, XDR-TB was reported in 2.7% of new MDR-TB patients, in 6.7% of patients with TB relapse, and in 7.8% of patients with retreatment.

Due to the increase in M/XDR-TB, the Russian Society of TB Doctors (RSTBD) made the decision to revise approaches to TB diagnosis and treatment. In 2014, the Federal Clinical Recommendations for Pulmonary TB Diagnosis and Treatment were developed for the diagnosis and treatment of MDR and XDR-TB. These provisions included an algorithm for TB screening that integrated molecular genetic methods that detect drug-resistant TB.

#### BACKGROUND

The RSTBD treatment regimens were based on individualized drug sensitivity testing (DST) results in TB patients. Special treatment regimens were developed for susceptible, poly-resistant, MDR, and XDR-TB strains. When DST results were unavailable, decisions about

treatment regimens were based upon the patient's risk of acquiring MDR-TB. Treatment regimens for MDR-TB patients also depend on additional drug resistance and may include aminoglycosides or polypeptides, third or fourth generation fluoroquinolones, first-line drugs (such as pyrazinamide and ethambutol), thioamides, and other bacteriostatic drugs (including cycloserine/terizidone and amino-salicylic acid). The high-dose isoniazid is not recommended for MDR-TB treatment in Russia, since in 95% of cases isoniazid resistance is associated with mutations in the *katG* gene. However, for MDR-TB patients with ofloxacin-resistant TB, bedaquiline is the recommended treatment, though it should only be administered when the patient's isolate has been shown to be susceptible to three or more drugs, and when administering levofloxacin as a 1.0 g dose. Bedaquiline should not be added to an ineffective regimen. For XDR-TB patients, some studies have shown that linezolid, oxazolidinone antibiotic should be a required component of the regimen, as it can have a positive impact on this difficult category of patients.

#### METHODS AND RESOURCES

To increase the treatment effectiveness for XDR-TB patients, we studied the efficacy of a drug combination treatment on XDR-TB patients. In the study, 174 patients were treated at the CTRI between 2006 and 2012. *Mycobacterium tuberculosis* drug susceptibility testing to first-line TB drugs (including isoniazid, rifampicin, ethambutol, streptomycin, and pyrazinamide) and second-line TB drugs (amikacin/kanamycin, capreomycin, ofloxacin, prothionamide, para-aminosalicylate sodium (PAS), and cycloserine) was performed using culture methods (absolute

Table 1.1.1. Impact of adding bedaquiline to the regimen on therapy efficacy.

TB drug prescribed	Number of patients	Effective treatment	Ineffective treatment	OR	CI95%	p
Moxifloxacin	140	111	29	7.02	2.90-17.21	<0.05
Linezolid	76	69	7	8.03	3.16-21.30	<0.05
Bedaquiline	20	19	1	9.13	1.23-188.23	<0.05

concentration and BACTEC MGIT 960). The efficacy of the therapy was evaluated on the second, fourth, sixth, eighth, and twelfth months of the study, and was based upon frequency and time to sputum culture conversion. The moment of sputum culture conversion was considered to be the month when the first negative sputum culture results were received, provided that all consecutive sputum tests had no growth of *Mycobacterium tuberculosis*. The patients in the study were divided into four subgroups: subgroup 1, XDR-TB patients treated with ofloxacin (34 patients); subgroup 2, patients treated with moxifloxacin and amoxicillin clavulanate, or clarithromycin (64 patients); subgroup 3, patients treated with moxifloxacin and linezolid (56 patients); and subgroup 4, patients treated with moxifloxacin, linezolid, and bedaquiline (20 patients). The regimens for all patient subgroups also included kanamycin, amikacin, or capreomycin; and pyrazinamide, prothionamide, PAS, cycloserine (or terizidone). In all cases, TB therapy was comprised of two phases: an intensive (initial) phase, and a continuation phase. The intensive phase of treatment lasted until four consecutive negative culture results were available for at least six months. The injectable drug was stopped for the continuation phase of treatment.

## RESULTS

Based on culture conversion by the end of the first year of treatment, the efficacy of therapy in XDR-TB patients varied and depended upon the prescribed treatment regimen. The highest indicators were reported in subgroups 4 and 3, with 95% (19 of 20) and 89.3% (50 of 56) of patients reporting, respectively. This indicator was lower in subgroup 2, with 65.9% (42 of 64) of patients reporting. The lowest therapy effectiveness was reported in subgroup 1, with 35.3% (12 of 34) of the patients reporting ( $p < 0.05$ ). The sputum

culture conversion rate was highest in patients of subgroup 4 – after 2 months of treatment, 35% (7 of 20) of the patients had a negative culture ( $p < 0.05$ ). A similar trend was observed for the entire treatment.

To study the impact of prescribing moxifloxacin, linezolid, and bedaquiline on XDR-TB patient therapy effectiveness, we calculated an odds ratio for effective treatment (based on sputum culture conversion) when administering the drugs (Table 1.1.1).

## CONCLUSIONS

According to the data, the odds for effective therapy in XDR-TB patients increase with therapy considered by sputum culture conversion at month twelve with addition of moxifloxacin, linezolid, and bedaquiline to the regimen (OR=7.02, 8.03 and 9.13, respectively).

Thus, using moxifloxacin, linezolid, and bedaquiline in XDR-TB patients results in effective treatment of MDR-TB patients who have no additional drug resistance to fluoroquinolones, aminoglycoside, or polypeptide. These results give hope for curing those patients who have been considered incurable, which has important implications for those suffering from TB, and society at large.

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## 1.2 Best Practice: Compassionate use of Bedaquiline, an example from Armenia.

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### INTRODUCTION

The emergence and spread of MDR-TB and XDR-TB is a major medical concern threatening global public health. Treatment for MDR-TB is cost-intensive and time-consuming, with the minimum treatment regimen lasting approximately twenty months. Both MDR-TB and (especially) XDR-TB are associated with a high mortality rate and lower quality treatment outcomes than drug-susceptible TB. Thus, new treatments are needed.

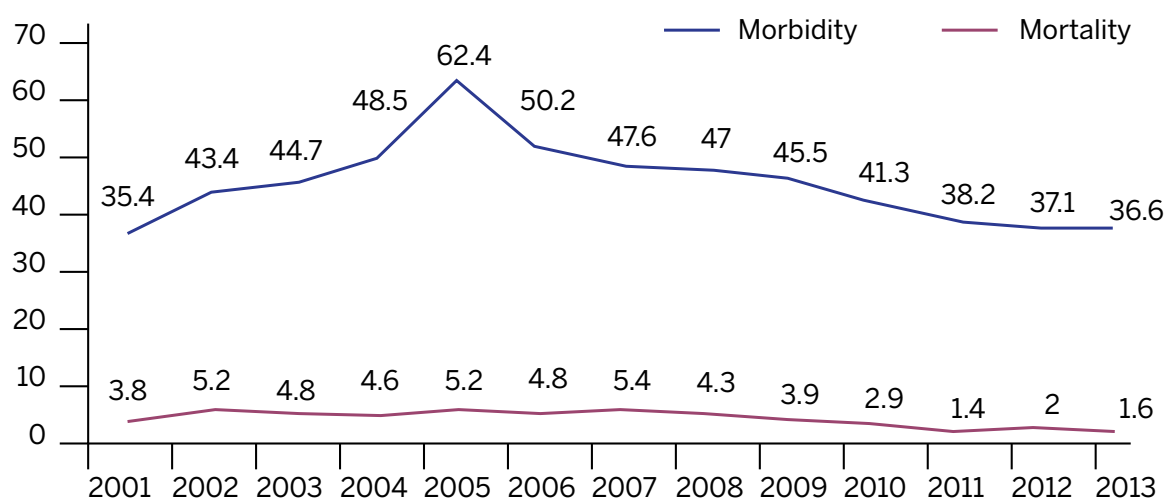
Between 2001 and 2013, the incidence and mortality of TB and MDR-TB in Armenia decreased, while the treatment effectiveness increased (Figures 1.2.1.-1.2.5).

TB treatment and care in Armenia are based on the National TB Control Strategy, National Response Plan to Combat M/XDR-TB for 2012-2015, National Treatment Guidelines on

Drug-Resistant TB (DR-TB), and National TB Guidelines. Patients with DR-TB are eligible to start treatment under a compassionate use program (CU) in the case of MDR-TB treatment failure. Management of all DR-TB patients, including those under the CU program, is performed in both inpatient and outpatient settings, including home-based care in the city of Yerevan.

Criteria for inclusion to a CU treatment program include life-threatening conditions (XDR-TB or pre-XDR-TB) in patients either eighteen years or older, or cases in which TB treatment options are severely limited. Women receiving treatment must be on adequate contraception methods, taking into account the following criteria for caution: laboratory abnormalities (such as renal and liver function); long QT interval or other ECG abnormalities; or a family history of long QT syndrome.

Figure 1.2.1. TB morbidity and mortality in Armenia (2001-2013)



Submission and approval for CU treatment assumes the following:

1. Selection has been based on eligibility criteria (set forth by the Ministry of Health (MOH)/National TB Program (NTP), or Médecins Sans Frontières (MSF))
2. Cases have been presented to the Armenian DR-TB Committee for endorsement
3. Cases have been submitted to the MSF/Partners in Health (PIH) Medical Committee for endorsement and clinical advice. (Members: three from MSF, two from PIH, one expert from Argentina, and one from the Union)
4. Two external experts have been consulted in the case of disagreement amongst the committee
5. Written consent from the patient
6. The patient's clinical dossier has been submitted to Janssen for the final approval
7. Final approval by Janssen, (J&J)
8. Importation procedure (4-6 weeks)

Figure 1.2.2. Treatment success rates among new smear (+) patients.

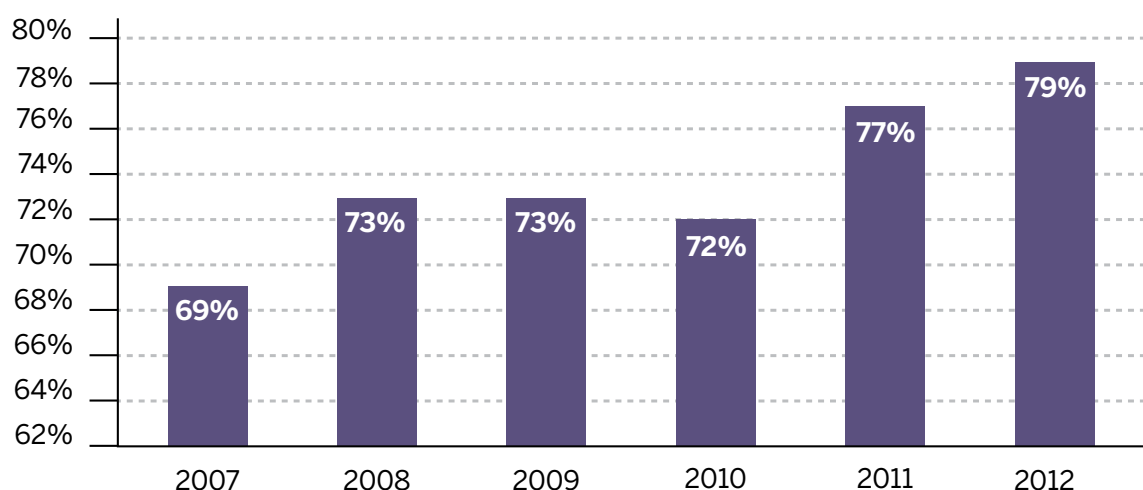
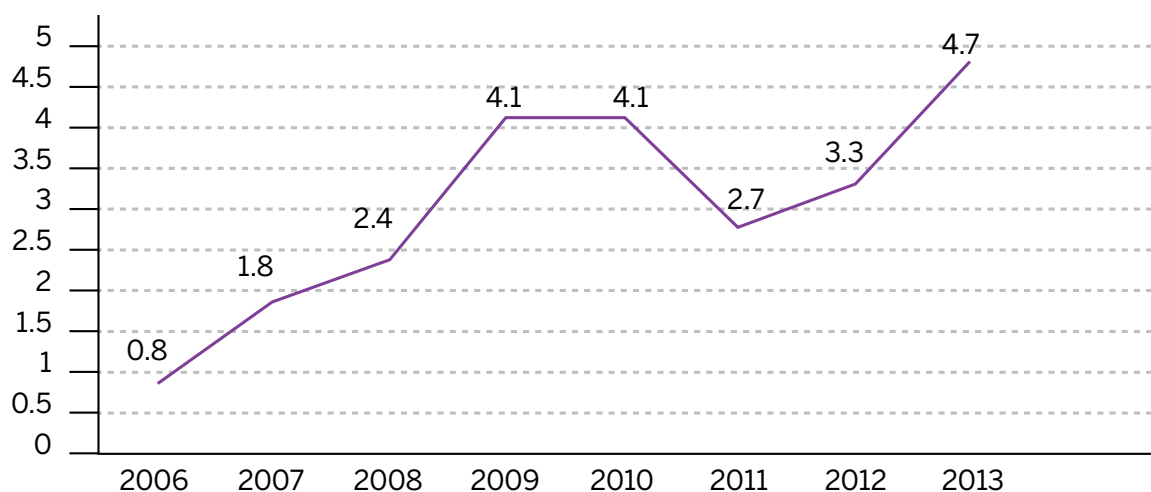


Figure 1.2.3 MDR-TB among new cases (2006-2013)





The treatment of XDR-TB is extremely difficult; only a few drugs are available, they are less efficient in comparison to first-line drugs, and they have strong side effects. Consequently, the treatment of XDR-TB is complex and must be undertaken by a highly experienced physician.

The use of new and repurposed drugs in the treatment regimen, such as linezolid (Lzd), bedaquiline (Bdq), and imipenem (Imp), is associated with the following

concerns: the lack of knowledge regarding the safety of these drugs over long-term usage; the cost of Lzd; and the method of administration for imipenem/cilastatin (Imp/CIs), particularly in ambulatory settings.

The inclusion of patients in the CU treatment program is based on: compliance to the Clinical Protocol developed by the MOH and MSF; the presence of trained medical personnel; intensive follow-up procedures; and the introduction of a pharmacovigilance system.

Figure 1.2.4. Absolute number of MDR-TB cases (2007-2013)

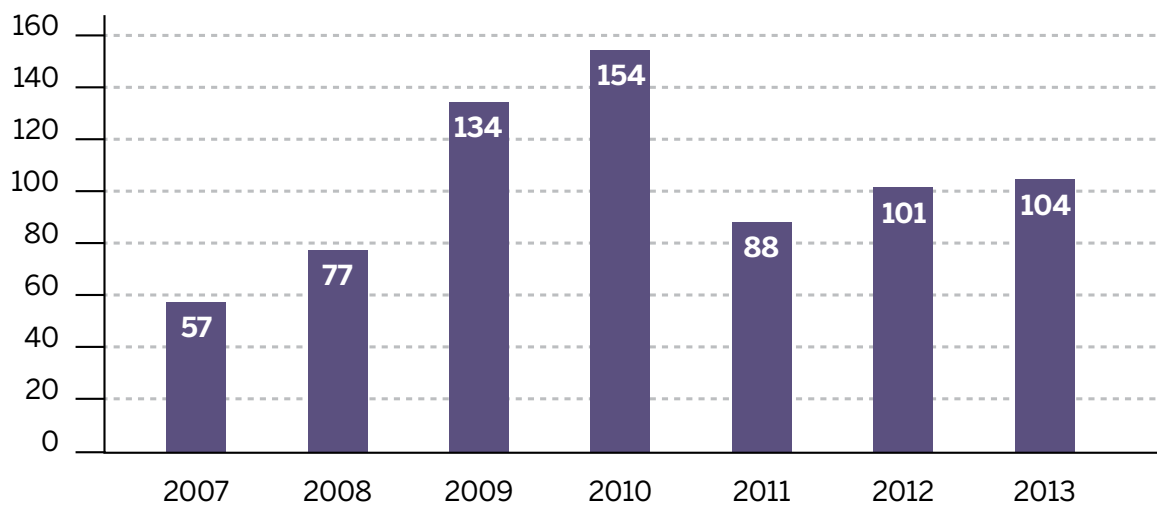


Figure 1.2.5. Treatment success rates of MDR-TB cases (2007-2010)

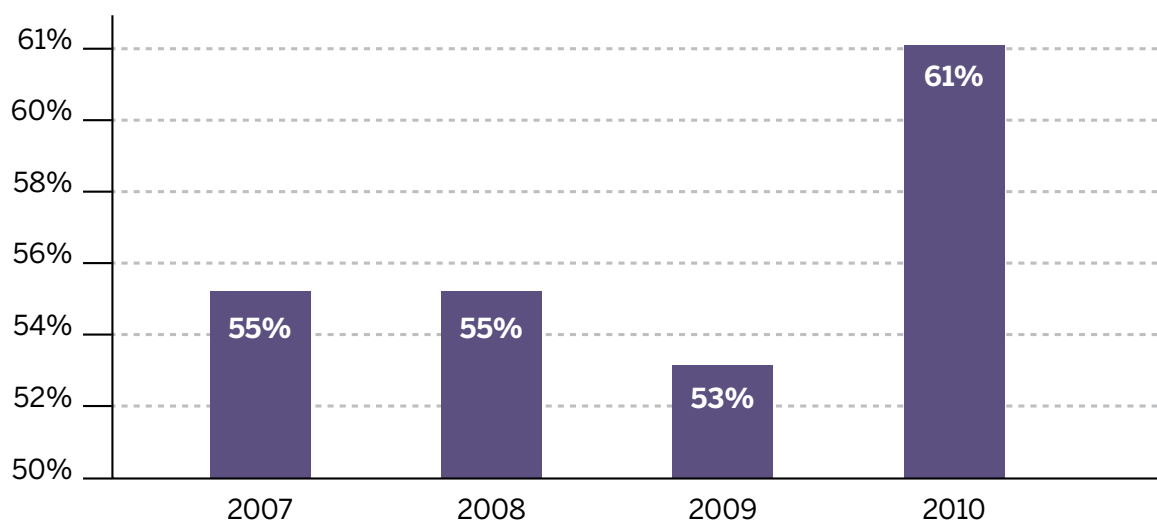


Table 1.2.6. Treatment regimens with Bedaquiline

Bdq, Lzd, Ipm, Cm, Lfx AmxCl/Cfz	Bdq, Lzd, Km, AmxCl/Cfz, Pas, Z
Bdq, Lzd, Lfx, Pto, AmxCl/Cfz	Bdq, Lzd, Cm, Cs, Pto, Cfz
Bdq, Lzd, Km, Lfx, Cfz, Cs, Z	Bdq, Lzd, Cm, AmxCl/Cfz
Bdq, Lzd, Imp, Cm, Lfx, Z, E	Bdq, Lzd, Imp, Cs, Pas, XCfz, H
Bdq, Lzd, Imp, Km, Lfx, Pto	Bdq, Lzd, Cm, Cs, Pto, Cfz
Bdq, Lzd, Lfx, Cs, Pto, Pas, AmxCl/Cfz, Z	Bdq, Lzd, Imp, Km, Lfx, Pto
Bdq, Lzd, Cm, Lfx, Cs, Pas, AmxCl/Cfz	

Figure 1.2.7. Social composition of TB patients (%)

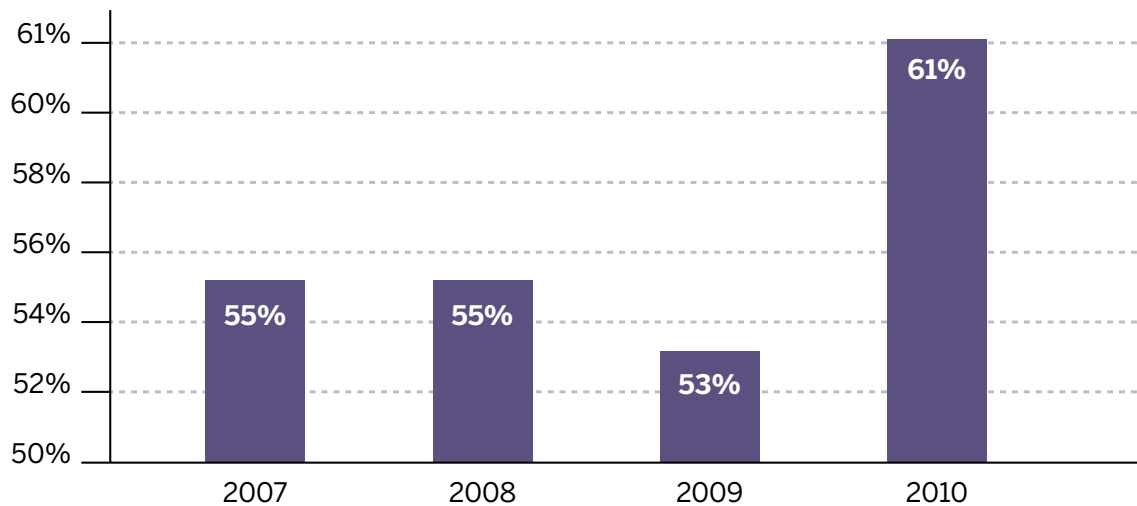


Figure 1.2.8. Clinical structure of XDR-TB patients (%)

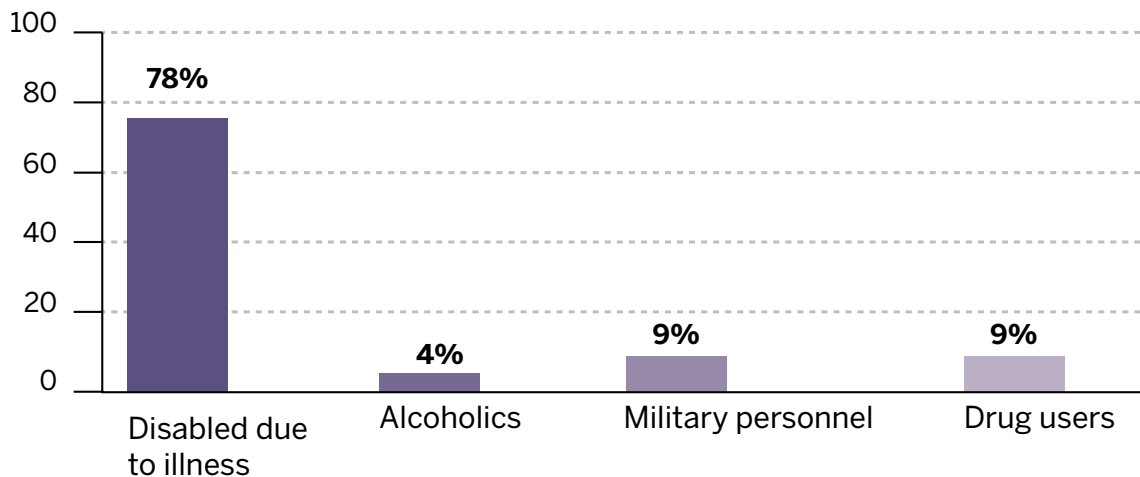


Table 1.2.9 . Bacteriological status after completion of 6-month course of Bdq, April 2013 – December 2014.

Cases completed Bdq course (C+, C- at treatment initiation)	32	
<b>1. Culture positive at the treatment initiation</b>	<b>26</b>	<b>%</b>
Culture converted by 6 months (2 cons Neg culture)	22	84%
Culture not converted by 6 months	3	12%
Culture results pending	1	4%
Reverted back to culture positive after conversion (n=22)	4	18%
<b>2. Culture negative at the treatment initiation</b>	<b>6</b>	<b>%</b>
Remained culture negative by end of Bdq course	6	100%

Table 1.2.10. Bacteriological status, culture conversion by months, April 2013 – December 2014.

Culture Conversion by Completion of 6-Month Course of Bdq (for 26 C+ cases)						
	1 <sup>st</sup> month	2 <sup>nd</sup> month	3 <sup>rd</sup> month	4 <sup>th</sup> month	5 <sup>th</sup> month	6 <sup>th</sup> month
Number of patients, cumulative	6	14	15	20	21	22
Proportion, cumulative	23%	54%	58%	77%	81%	85%
3 cases remained culture positive after 6-moths course of Bdq						
4 culture converted cases reverted back to positive later on						

Figure 1.2.11. Timeline of sputum conversion of XDR-TB patients (%/month)

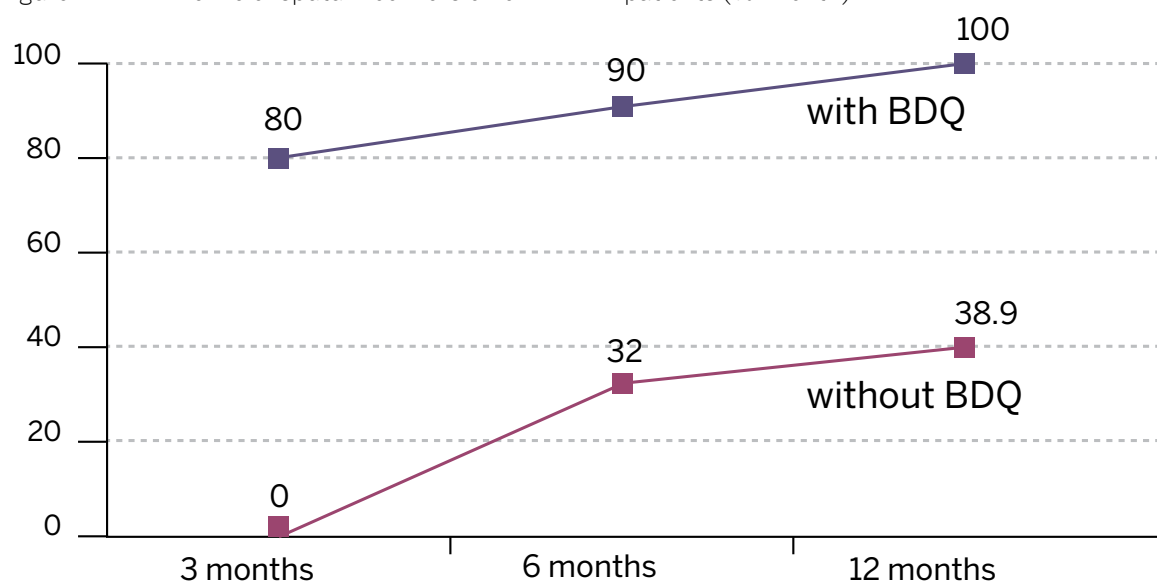
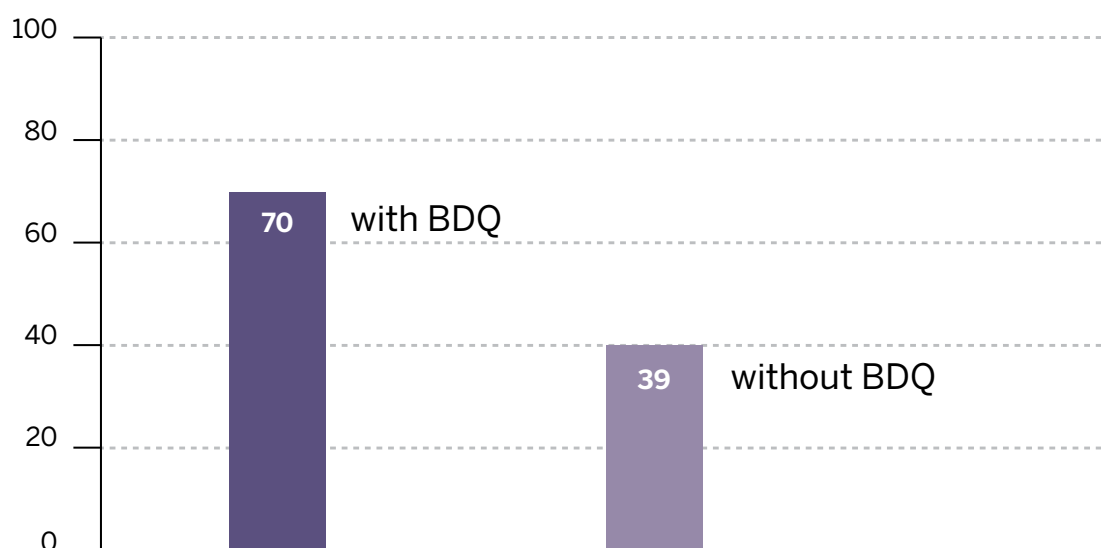


Figure 1.2.12. Healing of destructive changes in patients with XDR-TB (%)



## METHODS AND RESOURCES

Between April 2013 and December 2014, the MSF-PIH Expert Committee evaluated 73 total cases for a new treatment. The MSF-PIH Expert Committee approved of 69 patients (96%), and rejected 4 patients (4%). Three of the approved patients died before submission to J&J. Of the 66 cases that were submitted to J&J, 63 were approved (95%) and 3 were rejected (5%).

From the 63 patients approved by J&J for treatment with Bdq, 53 patients started treatment (83%), 6 patients refused (9%), 2 cases were lost to follow-up before starting treatment with Bdq (4%), and 1 patient died before starting treatment with Bdq (2%). One patient was approved but had not yet started the treatment at the time the study was undertaken (2%).

The demographics and clinical structure of the XDR-TB patients are presented below (Figure 1.2.6, 1.1.7).

Among the 53 patients who started Bdq treatment, 46 were male (87%), and 7 were female (13%).

The DST pattern (started on Bdq) finished with the following results: XDR-TB patients (n=24; 45%); pre-XDR-TB patients with fluoroquinolone resistance (n=26; 49%); and pre-XDR-TB patients with resistance to injectable drugs (n=3; 6%). DOT points included: 15 inpatient department (IPD) (36%); 19 ambulatory or TB clinic locations (45%); and 8 home-based care teams (19%).

Forty patients (75%) started their treatment on Imp/CIs either with a Port-a-Cath installed (n=13; 33%), or without one (n=27; 68%).

The schemes administered to pre-XDR/XDR-TB patients in accordance with DST results are depicted in Table 1.2.1.

## RESULTS

An analysis of monitoring data showed that sputum conversion was much higher in patients with new treatment regimens, including Bdq (n=32; 86.5%), compared to patients without Bdq administration (Table 1.2.2, 1.2.3; Figure 1.2.8). Positive clinical and radiological dynamics of TB process after twelve-month treatment in the first group was also higher in the group receiving Bdq (Figure 1.2.9).

## CONCLUSIONS

The combination of new drugs (bedaquiline) and repurposed companion drugs (linezolid, and imipenem) notably improves treatment efficacy for patients with pre-XDR-TB and XDR-TB and can be recommended for use according to the latest WHO Policy Guidance. However, adherence to therapy still remains a major challenge. Thus, there is a need for developing newer regimens which will shorten duration of therapy and will be more effective, less toxic, and easier to administer.

## 1.3 Best Practice: Addressing adverse reactions, example from Tomsk.

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### INTRODUCTION

The treatment of MDR-TB presents an enormous challenge globally, and is especially problematic in the Russian Federation. Given the need for long-term treatment and the number of TB drugs used, adverse drug reactions have a great impact on treatment effectiveness in the category of patients with MDR-TB. When providing TB therapy that includes first-line TB drugs, the number of adverse reactions range from 8% to 20%, and when using second-line TB drugs, these adverse reactions range from 85% to 100%. Late diagnosis and inadequate management of side effects increases the chances of treatment default, which then can lead to the development of treatment interruption and treatment failure.

### METHODS AND RESOURCES

1. Adverse effect management protocol and a list of ancillary medicines.
2. Ongoing training (seminars) of doctors, nurses, and volunteers on the diagnosis and management of adverse effects.
3. Availability of regulatory mechanisms to allocate funding for procuring ancillary medicines in accordance with the list of adverse effect medications; and regulatory documentation that allow distributing the ancillary medicines to treatment facilities.
4. Recording forms for the detection and registration of side effects that can be generated from a database.

5. Availability of clinical monitoring (logistics for biological specimen delivery), and counseling by medical specialists.
6. Availability of free transportation for patients (including rural patients), regardless of treatment site.
7. Ability to provide directly observed treatment two times a day in outpatient situations.

### RESULTS

Between 2000 and 2013, the epidemiological situation of TB in Tomsk Oblast significantly improved. The number of MDR-TB patients on treatment decreased 2.5 times from 823 patients to 324 patients, and basic epidemiological TB measures (per 100,000 population) declined by the following rates:

1. TB mortality – 3.9 times (from 21.9 to 5.6);
2. TB prevalence – 2.5 times (from 224.7 to 86.8);
3. TB incidence – 1.7 times (from 116.7 to 67.2).

### CONCLUSIONS

This is the first time a complex approach to adverse effect management of MDR-TB treatment has been implemented in a region of the Russian Federation. This approach to addressing adverse reactions in patients has produced favorable outcomes.

Figure 1.3.1. Impact of patient centered approaches on treatment default patients in MDR-TB treatment; outcomes in the civilian sector (%)

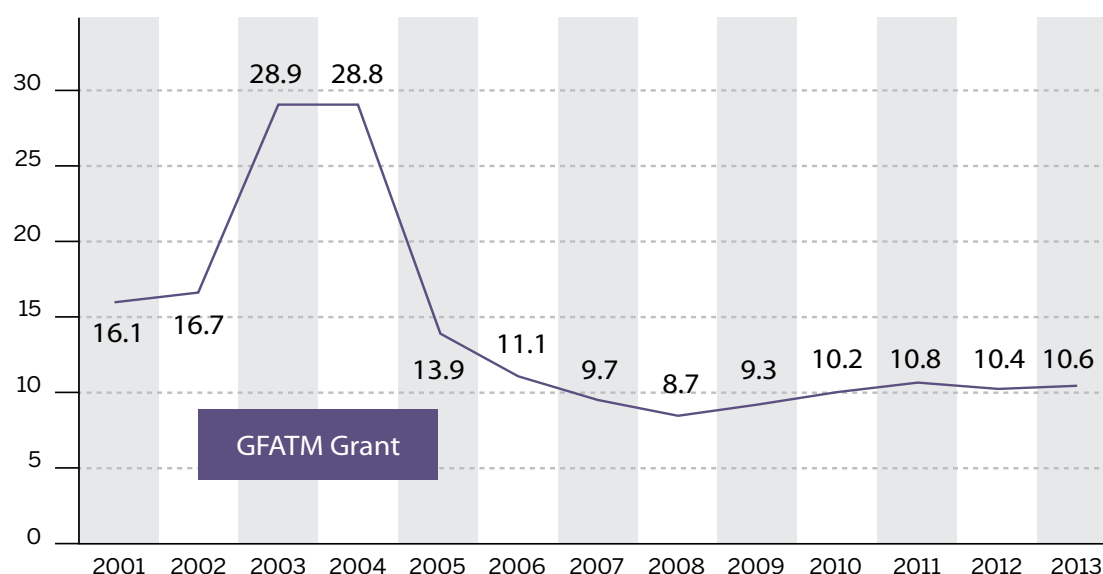
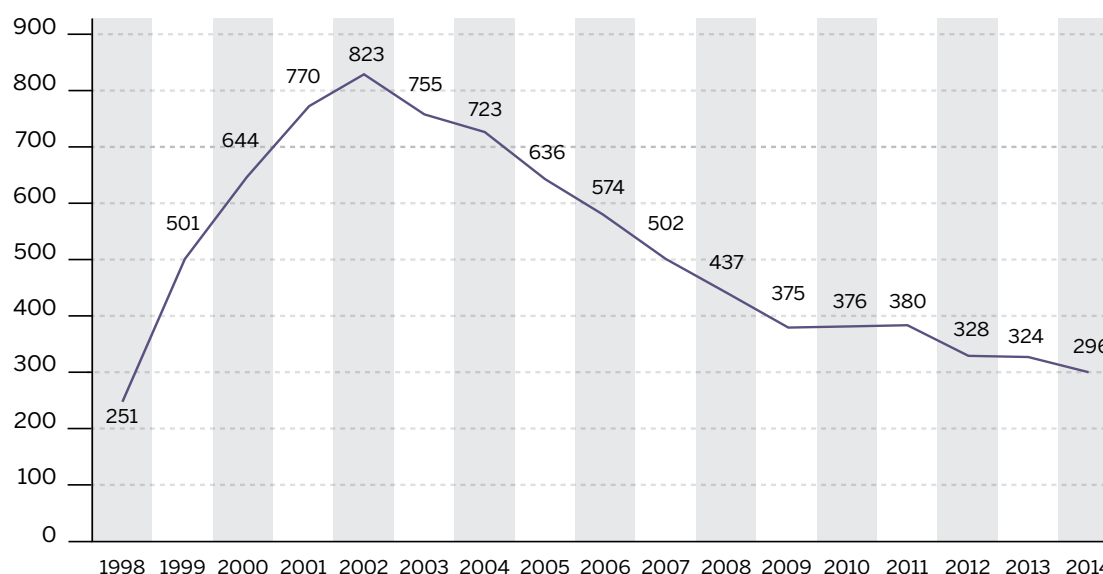


Figure 1.3.2. Number of MDR-TB patients in Tomsk Oblast, civilian sector (absolute number)



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## 1.4 Best Practice: Treatment of HIV and drug-resistant TB patients, an example from Ukraine.

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### INTRODUCTION

The prevalence rates of TB and HIV in Ukraine have an impact not only on the incidence of TB in Eastern Europe, but throughout all of Europe as well.

Historically, the healthcare provided to patients with TB in Ukraine has been characterized by extensive hospitalization in inpatient clinics that lack infection control, a shortage of anti-TB drugs, and the lack of social support for TB patients during the ambulatory phase of treatment. These conditions have perpetuated the rapid spread of MDR-TB in Ukraine. Between 2011 and 2014, the number of MDR-TB patients in the country increased by 41%. Additionally, the progression of the HIV epidemic in Ukraine, characterized by the sustained and increasing impact of sexual transmission in the general population, set the stage for the growing problem of TB/HIV co-infection.

Thus, at a time of economic instability and the need for healthcare reforms that would foster the development of a public health system, Ukraine's most effective response to the challenge of TB/HIV co-infection involves developing a multidisciplinary approach that integrates patient-centered health services.

### BACKGROUND

According to WHO European Bureau estimates, the incidence of TB in Ukraine is 96 per a population of 100,000, and the incidence of TB/HIV coinfection is 16 per 100,000. Most of the TB/HIV burden is in the southeastern regions of Ukraine (Figure 1.4.1). The HIV-associated TB rate is 51.9% among new HIV cases, and

62.7% among those who died (2013). TB is the main cause of death associated with AIDS.

In the WHO European Region, Ukraine ranks second in MDR-TB prevalence (following the Russian Federation). According to preliminary data, in 2014 Ukraine registered 8,854 MDR-TB patients and 93% of them started treatment with second line anti-TB drugs. The proportion of XDR-TB patients among MDR-TB patients is 14.7%.

Given the growing problem of TB/HIV and the spread of MDR-TB, healthcare expenditures that were not directed towards systemic improvement of the healthcare system for TB patients (but instead focused on TB-related healthcare activities, like the maintenance of TB beds), may be considered an irrational use of funding. The resulting lack of a quality training system for healthcare staff proved to be problematic at addressing issues pertaining to TB healthcare. Moreover, this use of limited funding was ineffective at supporting a large number of TB hospitals and laboratories, further worsening the problem.

### METHODS AND RESOURCES

Since 2012, the Ukrainian Ministry of Health has implemented a strategy to optimize approaches to health care for TB, TB/HIV, and MDR-TB. The strategy is based on the effective coordination of activities between national programs, Global Fund grants, and technical support projects funded by USAID.

The first step in reorganizing program management to combat social diseases involved founding the Ukrainian Center for Social Disease Control in 2012, within the

Ukrainian Ministry of Health. The development strategy of the Center is based on the functions of public health as defined by the WHO Health's 2020 strategy.

To ensure the effectiveness of program activities, the following tools were created in accordance with WHO recommendations, including evidence-based data, and international standards and protocols:

1. A regulatory basis for health care provided to TB and MDR-TB patients;
2. A quality control system for TB laboratory testing; and;
3. A monitoring and control system, including the development and introduction of a unified electronic register of TB patients at the regional and national levels.

## RESULTS

All regions of Ukraine have access to modern TB diagnostic methods (mycobacterial sputum culture using liquid media) and DST for first- and second-line anti-TB drugs. In addition, molecular genetic methods for rapid TB diagnosis have recently been introduced, reducing the amount of time required to detect rifampicin-resistant TB from about one and a half to two months, to between three and five days.

The time between diagnosis and treatment initiation for MDR-TB patients was reduced from 2-3 weeks, to 5-7 days. Due to the reorganization of the TB laboratory network and implementation of a quality control system for laboratory testing,

the detection rate for confirmed TB cases increased from 48% in 2010, to 53.7% in 2014.

In 2014, among 690 Level 1 TB laboratories, 657 (95.2%) successfully completed external quality control. In addition, all Level 3 TB laboratories successfully completed quality control of bacteriological testing. Introducing the electronic register for TB patients as part of a larger monitoring and control system also improved the data management system for TB control overall (98% concordance between the printed version and electronic reporting data for all TB cases from 2014 has been provided). According to a WHO expert assessment, this serves as the best implementation of a complex electronic information system in the WHO European Region.

Treatment efficacy was reported at 67.6% among the new smear-positive cases registered in 2013, and 53% among the TB/HIV patient cohort (Figure 1.4.2). The primary challenges to achieving the WHO-recommended indicators for treatment effectiveness included a high TB/HIV prevalence, and low patient treatment adherence during the ambulatory stage.

The reported treatment efficacy among the MDR-TB patient cohort in 2011 was only 34%, which was associated with both low adherence and a shortage in the second-line TB drug supply that was funded by the federal budget. Later, however, the implementation of the GFATM grant provided for quality, uninterrupted treatment of MDR-TB patients,

Figure 1.4.1. Epidemiological TB and HIV situation in Ukraine

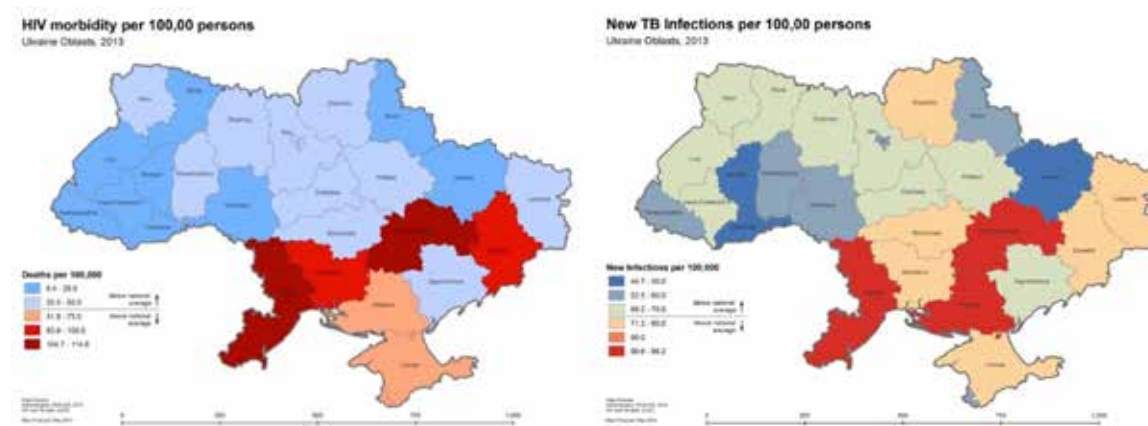
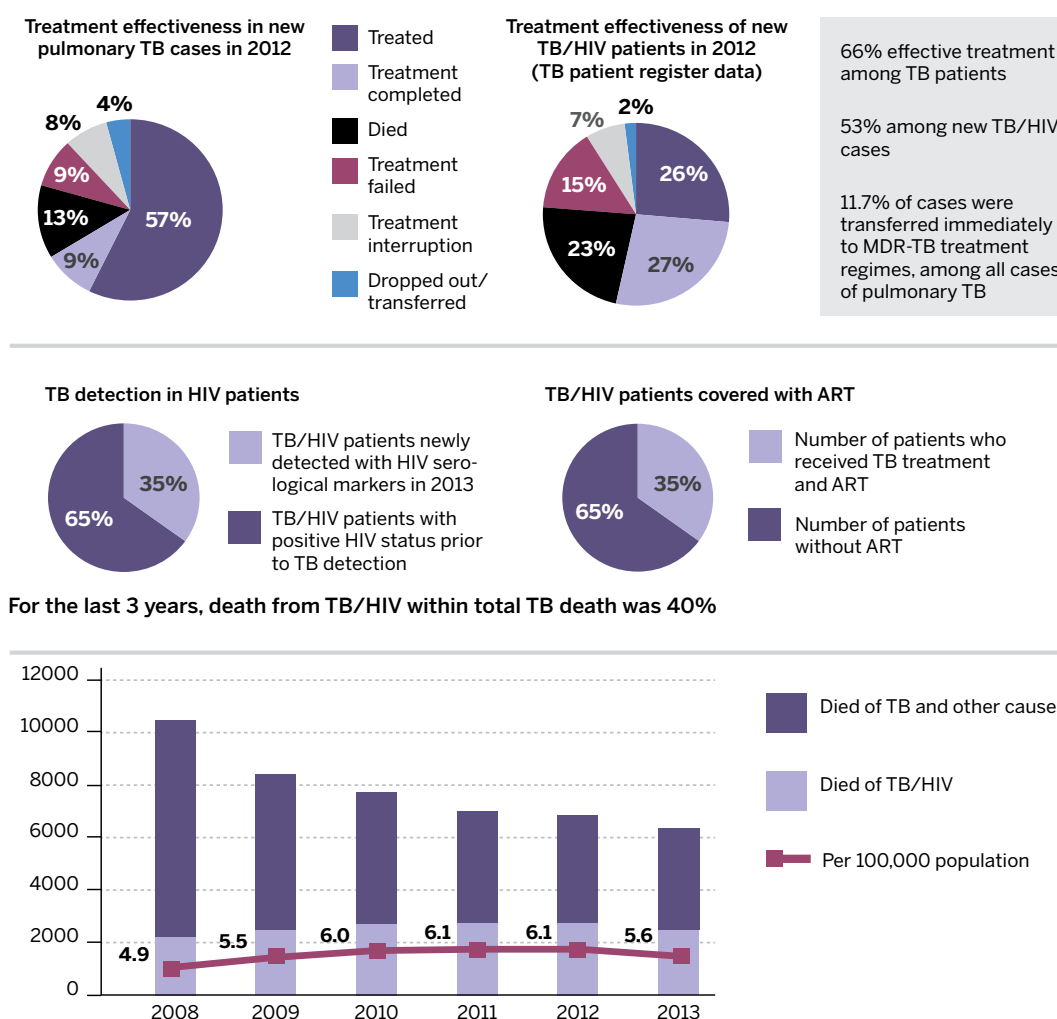




Figure 1.4.2. Treatment effectiveness of TB and HIV in Ukraine



as well as social support during all stages of their treatment. According to preliminary outcomes, the treatment efficacy in the first cohort of those MDR-TB patients treated under the GFATM grant in 2012 was 65%.

Due to the implementation of a comprehensive policy to combat TB/HIV in Ukraine, voluntary HIV counseling and testing was also performed in 95% of TB patients. ART coverage of co-infected patients has increased annually; in 2013, 65% of all patients were on treatment. Currently, infectious disease physicians are employed in 80% of the regional TB dispensaries, and substitution therapy websites are available at about 84% of the regional TB dispensaries. Moreover, 83% of the Regional Centers for AIDS Prevention and Control have implemented active TB screening by using questionnaires

for patients during each visit. Of these AIDS Centers, 63% perform regular smear examination of HIV patients suspected for TB, and 42% provide outpatient treatment of non-infectious TB/HIV patients (Figures on p.15).

## CONCLUSIONS

Coordinating a multidisciplinary approach that focuses on patient care, and utilizes data gathered through effective monitoring and evaluation, plays a crucial role in improving organizational models for patient treatment, and permits for the effective usage of resources. Implementing these practices has important implications, and improves the system of healthcare for patients with TB, MDR-TB, and TB/HIV co-infection.

## Session 2.

# The Global Fund to Fight AIDS, Tuberculosis and Malaria: Plans to support the expansion of new drugs.

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### INTRODUCTION

Bedaquiline, the first new anti-tuberculosis medicine to be introduced into the market in almost 50 years, is an important new tool in the fight against drug-resistant TB. With the growing M/XDR-TB epidemic in the Eastern Europe and Central Asia (EECA) region, countries are strongly encouraged to begin planning how and when to introduce bedaquiline/delamanid, and to work with the existing in-country and regional partners.

The Global Fund supports the rational introduction and use of bedaquiline/delamanid and emphasizes the need for countries to adhere to WHO's interim policy guidance regarding their usage. WHO has made a framework to help countries reflect on various aspects of implementation, and to ensure that a robust implementation plan is developed to facilitate access to new TB medicines.

Unfortunately, the Global Fund does not have a specifically dedicated pool of funds available for the introduction of new TB medicines. Countries wishing to introduce new medicines through their Global Fund grants will need to do so from their existing funding allocations and, given the limited resources available for TB, countries will need to make difficult decisions about how to allocate the resources.

We acknowledge that there is a delicate balance between ensuring that new medicines are quickly made available and ensuring that these medicines remain effective for as long as possible; this balance is critical at safeguarding the investment in research and development, and ensuring maximum benefit to patients.

Challenges identified in the EECA Region include:

- Weak/un-reformed TB healthcare systems, hospital-based treatment, and delay to ambulatory care;
- Lack of prescriber adherence to the WHO-recommended standardized treatment regimens-- this is reinforced by the lack of availability of standardized fixed-dose combination medicines;
- The use of second-line anti-TB medicines for first-line treatment, and vice versa;
- Lack of available medicines to adequately manage the side effects of TB medicines (contributing to high default rates);
- Weak or non-existent pharmacovigilance systems which, in most countries, are not linked to existing TB programs;
- Low treatment success, high default rates;
- Self-treatment, and the sale of anti-TB drugs without prescription;

- Multiple implementers interested in rolling out of new drugs, leading to multiple pilot projects;
- Multiple recording and reporting systems;
- Multiple streams for drug supply (donor and domestic); and
- Insufficient domestic funding to take over after the end of the Global Fund support (end of 2017 for most EECA countries).

In order for the new medicines not to become a “magic bullet shot in the jungle,” the Global Fund encourages the following health system strengthening measures to accompany the introduction of new medicines, as well as for which funding is available under the Global Fund grants:

- Strengthening of the laboratory system to ensure timely access to DST results;
- Establishing and/or reinforcing the country’s pharmacovigilance system;
- Access to the more expensive “Group 5” medicines to ensure that a robust treatment regimen is available;
- Access to medicines for the management of adverse reactions;
- Access to clinical monitoring;
- Support for treatment adherence; and
- Sustainability arrangements after the Global Fund funding ends.

Therefore, in the first stage of the rollout of new medicines, the Global Fund favors ring-fencing the introduction of new drugs through pilot projects, or specific sites where a dedicated team of professionals is available for mobile hands-on supportive supervision.

## 2.1 Best Practice: Impact of the GFATM project on TB burden, Tomsk Project, Russia.

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Tomsk Pthisiopulmonological Medical Center, Tomsk, Russian Federation.

Y. Andreev  
Tomsk Oblast Department of Corrections, Tomsk, Russian Federation.

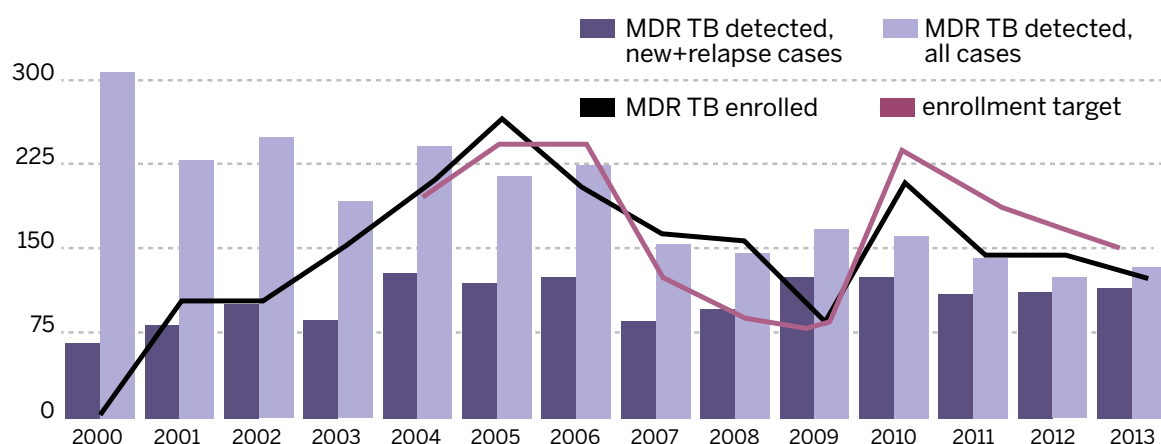
### INTRODUCTION

The Tomsk DR-TB project was one of the first projects in the world aiming to treat MDR-TB patients within their communities using second-line drugs since 2000. Since 2004, the GFATM project has supported activities that were clearly effective and necessary in the field-work. With a cohort larger than 100 patients, the treatment results of patients with DR-TB between 2001 and 2013 was among the highest in the world. As such, the average overall epidemiological picture in the Russian Federation has improved relatively well in comparison to its neighboring regions.

### BACKGROUND

Between 1994-1995, the WHO-recommended DOTS strategy was first introduced in the civilian sector of Tomsk Oblast, and subsequently introduced in the penitentiary system. However, by the year 2000, Tomsk's civilian and prison TB programs had significant problems. The TB case notification rate in Tomsk was 90.3 per 100,000 people in the civilian sector, with a mortality rate of 21.2 per 100,000 people. The percentage of MDR-TB among new cases and retreatment cases was 8.5% and 32.2%, respectively. In the penal sector, the TB case notification rate was 3,357 people per 100,000, with a mortality

Figure 2.1.1. MDR-TB: number of patients detected, courses within the GLC project and enrollment target, civilian sector, absolute numbers.



rate of 129.9 per 100,000. The percentage of MDR-TB among new cases and retreatment cases was 13.1% and 34.9%, respectively. In both the civilian and penal sectors, the DOTS program cure rates for smear-positive patients in Tomsk were between 50% and 60% for new and retreatment patients, respectively.

In 2000, Tomsk Oblast became the first MDR-TB treatment project in Russia approved by what was then a new WHO/Stop TB Partnership mechanism; this mechanism, known as the Green Light Committee (GLC), was aimed at expanding the high-quality treatment of drug-resistant TB. In the case of Tomsk, this provided an opportunity to treat MDR-TB (and, once it was defined, extensively drug-resistant TB (XDR-TB)) with high quality second-line anti-TB

drugs under good programmatic conditions. After approval, 630 MDR-TB patients were enrolled in the MDR-TB treatment program in both the civilian and penitentiary sectors between 2000-2004. MDR-TB treatment first started in early September of 2000 at a specialized treatment and correction facility within the penitentiary sector. The program was later expanded to the civilian sector.

Treatment results of the first patient cohort (244 patients) displayed a high efficacy (78.3%) of MDR-TB treatment with individualized regimens, which contributed to both defining a policy of drug-resistant TB management in Russia, and bolstering subsequent WHO recommendations. However, a closer examination of this first cohort revealed that the

Figure 2.1.2. MDR-TB: number of patients detected, enrolled in the GLC project and enrollment target, prison sector, absolute numbers.

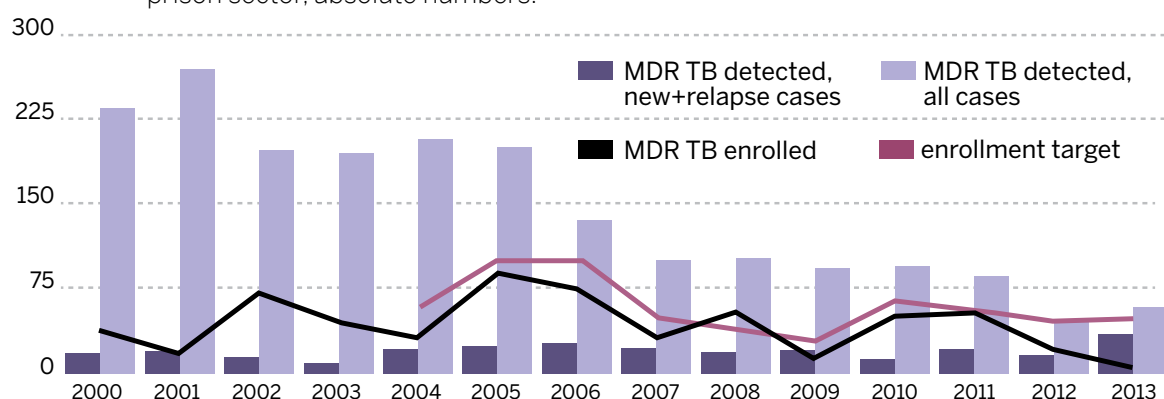


Figure 2.1.3. Final MDR-TB treatment goals and results, TO, both sectors.

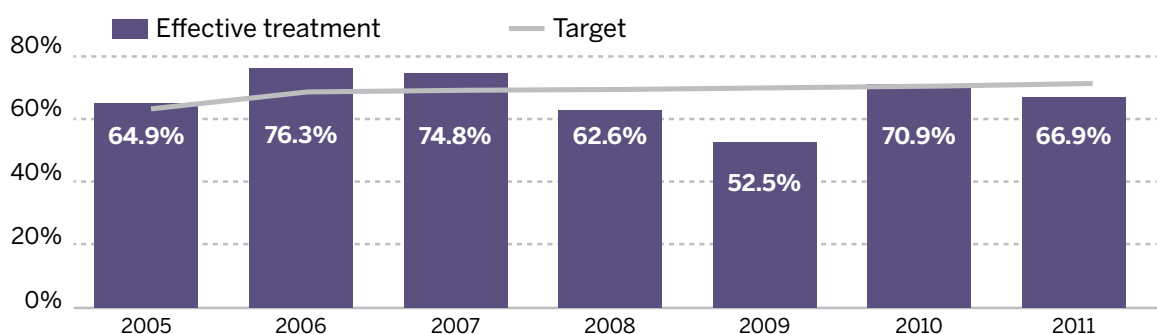


Table 2.1.1. Objectives, activities, and indicators of GFATM project I, GFATM project II (RCC).

Goals	GFATM I. 2004 – 2009 activities	Funding	Indicators
<b>#1</b>	<b>Improvement of the TB diagnostics system in the civilian and penitentiary sections of Tomsk Oblast</b>	<b>\$881,019</b>	
1.1	Improvement of laboratory services, equipment, external quality control	\$731,218	1.1.1. Number and % of new smear+ TB cases (out of total number of detected TB patients) in civilian sector 1.1.2. Number and % of new smear+ TB cases (out of total number of detected TB patients) in prison sector
1.2	Improvement of X-ray monitoring of TB patients	\$149,801	1.1.3. Number and % of healthcare facilities provided with laboratory equipment in civilian and prison sectors
<b>#2</b>	<b>Improvement of the TB treatment system in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$3,621,633</b>	
2.1	Procurement of second-line TB drugs to treat MDR-TB patients Procurement of side effect medications	\$2,671,031	2.1.1. Number of MDR-TB patients enrolled in DOTS+ program in civilian sector 2.1.2. Number of MDR-TB patients enrolled in DOTS+ program in prison sector
2.2	Clinical monitoring. Biochemical tests, consultations with healthcare specialists	\$142,767	2.2.1. % of cured patients with susceptible TB in civilian sector 2.2.2. % of cured patients with susceptible TB in prison sector 2.3.1. Number of cured patients with susceptible TB in prison sector (except new patients) 2.4.1. % of MDR-TB patients treated effectively
2.3	Information monitoring	\$142,767	No specific indicators for reporting to GFATM available
2.4	Human resources for GFATM project implementation	\$517,073	No specific indicators for reporting to GFATM available
<b>#3</b>	<b>Improvement of TB patient adherence to treatment, including MDR-TB patients in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$3,472,939</b>	

Continued on page 23

fundamental association between TB and poverty remained a persistent challenge to successful TB control. Adverse social conditions also played a large factor in treatment, as most of this cohort was reportedly unemployed and/or had a history of substance dependence/abuse, and approximately half were either incarcerated or had spent time in prison.

PIH support could not cover 100% of DR-TB patients in need of appropriate second-line drugs, and further cohorts showed a higher default rate due to a higher enrollment of patients with low socio-economic status. In addition, appropriately organized TB health-care services and social services were not always available in outpatient settings.

## METHODS AND RESOURCES

In 2004, Tomsk Oblast applied for a grant from the Global Fund to Fight AIDS, TB, and Malaria

in Round 3, and received approval to start the only regional project in Russia. This project focused on expanding MDR-TB treatment through the introduction of a comprehensive and integrated program for TB and MDR-TB. The GFATM Round 3 Grant allowed Tomsk to provide optimal care to TB and MDR-TB patients via improved social and psychological supports that were available during the entire treatment.

In addition, this grant allowed the program to address many healthcare-related issues pertaining to the treatment of TB, by way of: providing mechanisms that strengthened the DR-TB laboratory diagnosis; improving infection control mechanisms for inpatients in the civilian and penitentiary sectors; and developing sub-programs focused on social issues relating to treatment, including the reduction of alcohol use, treatment adherence, and early case detection.

Figure 2.1.4. Treatment outcomes of MDR-TB patients enrolled in the GLC project, civilian sector, %.

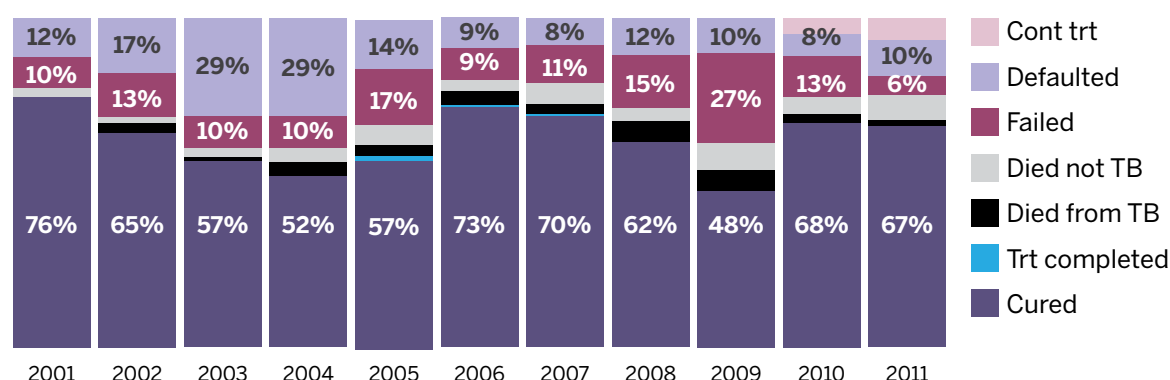


Figure 2.1.5. Treatment outcomes, new smear+ patients, excluding MDR-TB cases, civilian sector, %.

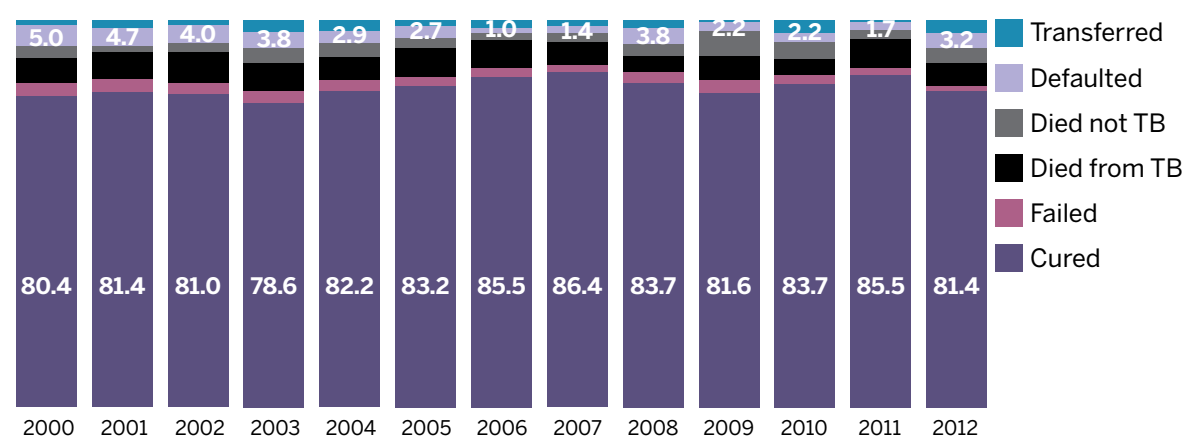


Table 2.1.1. Objectives, activities, and indicators of GFATM project I, GFATM project II (RCC). (cont)

Goals	GFATM I. 2004 – 2009 activities	Funding	Indicators
<b>#1</b>	<b>Improvement of the TB diagnostics system in the civilian and penitentiary sections of Tomsk Oblast</b>	<b>\$881,019</b>	
1.1	Improvement of laboratory services, equipment, external quality control	\$731,218	1.1.1. Number and % of new smear+ TB cases (out of total number of detected TB patients) in civilian sector
1.2	Improvement of X-ray monitoring of TB patients	\$149,801	1.1.2. Number and % of new smear+ TB cases (out of total number of detected TB patients) in prison sector 1.1.3. Number and % of healthcare facilities provided with laboratory equipment in civilian and prison sectors
<b>#2</b>	<b>Improvement of the TB treatment system in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$3,621,633</b>	
2.1	Procurement of second-line TB drugs to treat MDR-TB patients Procurement of side effect medications	\$2,671,031	2.1.1. Number of MDR-TB patients enrolled in DOTS+ program in civilian sector 2.1.2. Number of MDR-TB patients enrolled in DOTS+ program in prison sector
2.2	Clinical monitoring. Biochemical tests, consultations with healthcare specialists	\$142,767	2.2.1. % of cured patients with susceptible TB in civilian sector 2.2.2. % of cured patients with susceptible TB in prison sector 2.3.1. Number of cured patients with susceptible TB in prison sector (except new patients) 2.4.1. % of MDR-TB patients treated effectively
2.3	Information monitoring	\$142,767	No specific indicators for reporting to GFATM available
2.4	Human resources for GFATM project implementation	\$517,073	No specific indicators for reporting to GFATM available
<b>#3</b>	<b>Improvement of TB patient adherence to treatment, including MDR-TB patients in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$3,472,939</b>	

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In 2009, the project's success resulted in continued funding from the Global Fund through the Rolling Continuation Channel until the funding ended on November 30, 2013. This enabled Tomsk TB Services to expand its healthcare activities and improve their efficiency. The key objectives, activities, and indicators of GFATM project I, and GFATM project II (RCC) are given in Table 2.1.1.

## RESULTS

The activities supported by GFATM between 2004-2013 in Tomsk Oblast resulted in the following key achievements:

1. DST was performed in 99-100% of new patients in the region. The Central Bacteriological Laboratory of the Regional TB Dispensary had 95-100% concordance of DST results for most first- and second-line drugs with regional and federal laboratories.
2. The coverage of detected MDR-TB patients by treatment using GLC TB drugs increased during GFATM project. In the civilian sector, coverage of detected MDR-TB patients increased from an average of 49.8% prior to 2005, to 76.3% in 2005-2009, and to 87.7% in 2010-2013.
3. Between 2010-2013, more than 90% of new and relapse MDR-TB cases in the civilian sector were enrolled in the GLC treatment. In general, more than 68.3% of all cases detected in Tomsk Oblast, including new, relapse, and other/re-treated cases in both sectors, were enrolled in the GLC program.
4. Altogether, the effective treatment rate among patients enrolled in the GFATM grant treatment was 67% in the 2005-2011 civilian and prison cohorts. Without

Figure 2.1.6. Default rate among smear+, civilian sector, Tomsk city/rural area.

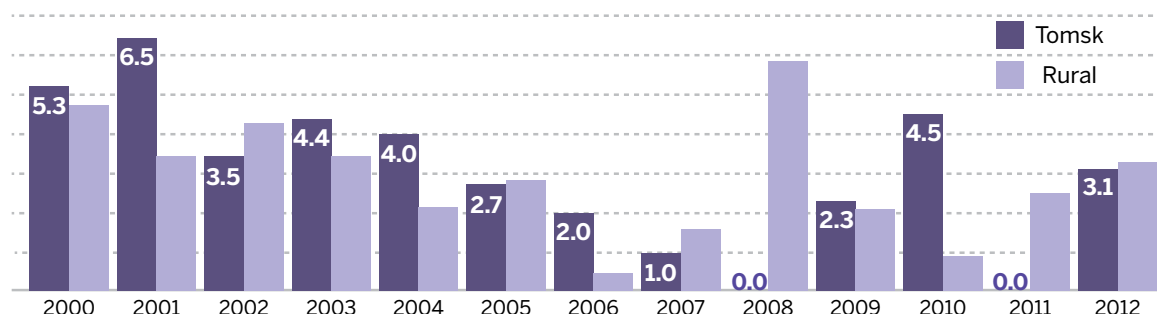


Figure 2.1.7. Chemoprophylaxis results, civilian sector.

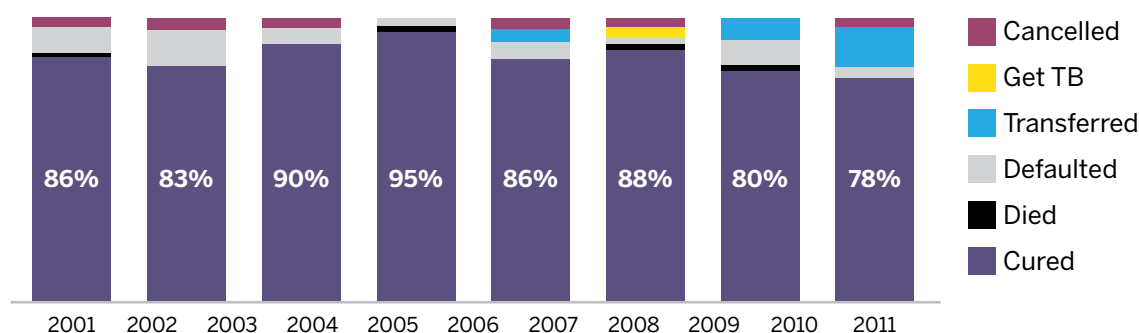


Table 2.1.1. Objectives, activities, and indicators of GFATM project I, GFATM project II (RCC). **(cont)**

Goals	GFATM I. 2004 – 2009 activities	Funding	Indicators
3.1	Improvement of observed treatment; in-home therapy; Russian Red Cross	\$1,420,396	3.1.1. % of “failure” among patients with susceptible TB in civilian sector
3.2	A sub-program of alcohol and substance addiction treatment for TB patients	\$160,575	3.1.2. % of “failure” among patients with susceptible TB in prison sector
3.3	Provision of rural healthcare facilities and TB services with transport resources to monitor treatment (e.g. vehicles and gasoline for inspector’s visits)	\$194,334	3.2.1. % of “default” among patients with susceptible TB in civilian sector
3.4	Provision of TB patients with food and social support	\$1,697,634	3.2.2. % of “default” among patients with susceptible TB in prison sector
<b>#4</b>	<b>Reduction of TB transmission to HIV patients in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$202,236</b>	3.3.1. Number of patients receiving food support in civilian sector
4.1	TB/HIV sub-program.	\$202,236	3.3.2. Number of patients receiving food support in prison sector
			4.1.1. Number of HIV patients with PPD skin test provided in civilian sector
			4.1.2. Number of HIV patients with PPD skin test provided in prison sector
			4.2.1. Number and percent of TB-HIV patients with Isoniazid Preventive Therapy received in civilian sector
			4.2.2. Number and percent of TB-HIV patients with Isoniazid Preventive Therapy received in prison sector
<b>#5</b>	<b>Improvement of infection control in TB hospitals and clinics in the Tomsk Oblast civilian and penitentiary sectors</b>	<b>\$1,238,907</b>	
5.1	Ventilation and UV lamps in TB Hospital, TB Dispensary and Central laboratory	\$1,003,859	5.1.1. Number and % of TB facilities installed with ventilation equipment
5.2	Improvement of infection control among healthcare workers	\$235,049	
<b>#6</b>	<b>Improvement of health education among risk groups in the civilian and penitentiary sectors; training of healthcare staff of the Tomsk Oblast civilian and penitentiary sectors; attracting risk groups to early TB detection</b>	<b>\$942,096</b>	

Continued on page 27

XDR-TB cases, effective treatment was registered among 66% and 82% cases of the 2005-2011 cohorts in the civilian and prison sectors, respectively.

5. All patients with all forms of TB and on any category of treatment were covered by intensive clinical management and numerous effective adherence activities. The default rate in the civilian sector was one of the lowest among cases with susceptible TB in Russia (1-2%), and among MDR-TB cases in the world (8-9%).
6. Patients from high-risk groups with TB and TB-HIV were covered by specially targeted activities that were also effective (including the "Sputnik" project, TB-HIV detection, and treatment). The civilian sector was one of the lowest among cases with susceptible TB in Russia (1-2%) and among MDR-TB cases in the world (8-9%).

The great outcomes of the treatment had a positive effect on the epidemiological picture in the region.

The overall TB epidemiological picture in Tomsk Oblast improved compared to the 1999-2000 levels; the incidence decreased to 67.6 per 100,000 people, and mortality dropped to 6.3 per 100,000 people in the region (both sectors) in 2013. The prevalence rate in 2013 was 87.3. Dye's prognosis was met.

Not only is it evident that the incidence of TB in the Russian Federation is decreasing when compared to the Siberian regions and Russian epidemiological data at large, but also the incidence of TB and its associated mortality rates are decreasing more quickly in Tomsk.

In 2013, the incidence dropped to 57.5% of the 1999 incidence rate and mortality dropped to 27.9% of the 1999 mortality rate, while the wider Russian averages were 73.9% and 56.5%, respectively (Figures 9,10). Siberian levels were even higher than the Russian averages. The mortality drop after 2004 and overall decrease of incidence three years after the grant started (in 2008-2009) could be due to the implementation of intensive activities under the GFATM grant.

## CONCLUSIONS

Since 2001, the Tomsk TB project has implemented many activities along with a few other projects that later became a standard for DR-TB care. The complex program showed significant treatment results and influence on TB incidence and mortality. Under GFATM support, many adherence strategies were used and standard practices were developed after considering the project's achievements and weaknesses. These recommendations and practices are widely used in Russian and international TB settings.

Figure 2.1.8. TB incidence, prevalence and mortality, per 100 000 population, Tomsk Oblast.

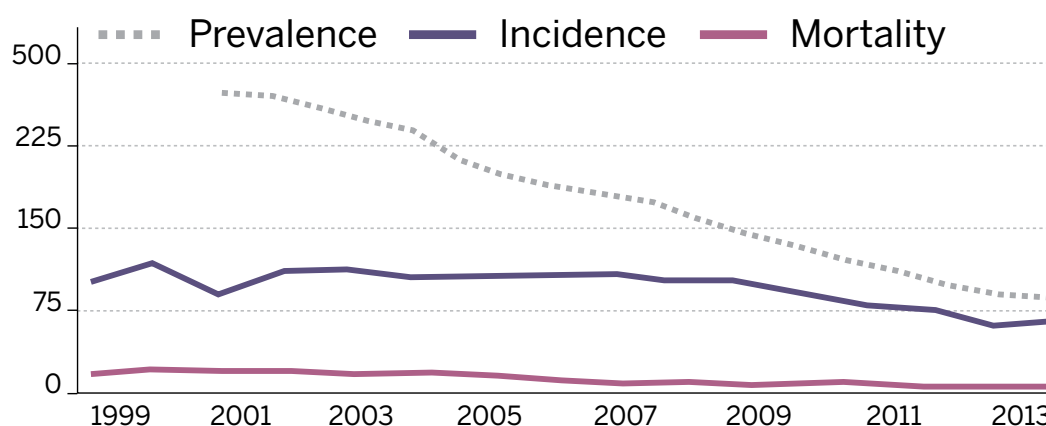


Table 2.1.1. Objectives, activities, and indicators of GFATM project I, GFATM project II (RCC). **(cont)**

Goals	GFATM I. 2004 – 2009 activities	Funding	Indicators
6.1	Improvement of health education among general population and patients in the civilian and penitentiary sectors	\$99,488	6.1.1. Number of trained healthcare staff on TB treatment and monitoring
6.2	Training of civilian and penitentiary sector healthcare workers; training of General Healthcare Services staff	\$555,718	6.2.1. Number of TB patients educated on TB in civilian sector 6.2.2. Number of inmates educated on TB in prison sector
6.3	A sub-program to improve early TB detection among general population and risk groups	\$555,718	No specific indicators for reporting to GFATM available
<b>TOTAL</b>		<b>\$10,358,830</b>	

Goals	GFATM II (RCC). 2009 – 2013 activities	Funding	Indicators
<b>#1</b>	<b>Drug-resistant TB treatment (DR-TB)</b>	<b>\$5,863,138</b>	<b>% of MDR-TB patients cured % of susceptible TB patient treated effectively</b>
1.1	Improvement of TB diagnostics and detection of polyresistant TB, MDR-TB and XDR-TB	\$485,378	1.1.1. Number of DST to first-line TB drugs 1.1.2. Number of DST to second-line TB drugs
1.2	Second-line TB drugs for DR-TB treatment	\$1,961,703	1.2.1. Number of MDR-TB and XDR-TB patients enrolled in DOTS+ program 1.2.2. Number of polyresistant TB patients enrolled in DOTS+ program
1.3	Side effect medications for DR-TB patients	\$239,814	1.2.3. Interim results of MDR-TB and XDR-TB treatment
1.4	Clinical observation of DR-TB treatment	\$614,945	1.2.4. Number and percentage of MDR-TB and XDR-TB patients registered under DOTS Plus who are successfully treated in Tomsk oblast
1.5	Strengthening of compliance with regimen among drug-susceptible and DR-TB patients	\$1,644,917	1.5.1. Default rate of MDR-TB and XDR-TB patients enrolled in DOTS+ program
1.6	Improvement of treatment programs for high-risk patients	\$279,172	1.6.1. Default rate in DOTS (among smear+, NP registered 12-15 months ago) 1.6.2. Number of new drug-susceptible, PR-TB and MDR/XDR-TB patients provided with food support at the outpatient phase

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Figure 2.1.9. TB incidence changes, percentage compared to 1999 data.

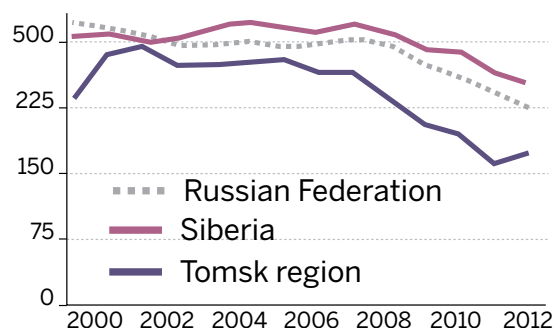
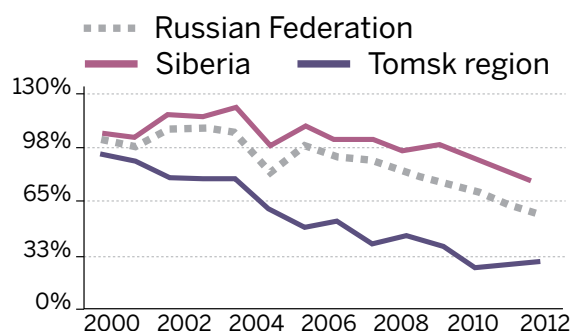


Figure 2.1.10. TB mortality changes, percentage compared to 1999 data.



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Table 2.1.1. Objectives, activities, and indicators of GFATM project I, GFATM project II (RCC). **(cont)**

Goals	GFATM II (RCC). 2009 – 2013 activities	Funding	Indicators
1.7	Improvement of infection control in Tomsk Oblast hospitals and clinics	\$241,314	No specific indicators for reporting to GFATM available
1.8	Monitoring of TB and DR-TB control program implementation	\$395,895	No specific indicators for reporting to GFATM available
#2	Reduction of TB spread among HIV patients in the Tomsk Oblast civilian and penitentiary sectors	\$286,718	
2.1	TB/HIV sub-program	\$286,718	<p>2.1.1. Number of HIV patients with PPD skin test, civilian sector</p> <p>2.1.1. Number of HIV patients with PPD skin test, prison sector</p> <p>2.2.1. Number and % of TB-HIV patients offered and completed Isoniazid preventive therapy in civilian sector</p> <p>2.2.1. Number and % of TB-HIV patients offered and completed Isoniazid preventive therapy in prison sector</p>
#3	Optimal research and dissemination of Tomsk MDR-TB control program in Russia	\$111,602	
3.1	Operational research on GFATM grant-related activities	\$27,237	<p>3.1.1. Number of staff trained in the Siberian Federal Territory and Far East Federal Territory (healthcare workers and bacteriologists trained on DR-TB diagnosis and management)</p> <p>3.2.1. Number of staff trained in Tomsk Oblast (healthcare workers and volunteers trained on directly observed treatment and DR-TB)</p>
3.2	Building capacity of the Novosibirsk TB Research Institute to train doctors from Siberian and Far East regions on MDR-TB management	\$26,435	
3.3	Strengthening the Novosibirsk TB Research Institute in scaling up the MDR-TB programs in 25 Russian regions; inspection	\$57,931	
<b>TOTAL</b>		<b>\$6,261,458</b>	

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## Session 3.

# Introduction: What are the major gaps in the countries of Eastern Europe and Central Asia to decrease the TB transmission in community and congregate settings?

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### INTRODUCTION

The transmission of tuberculosis and its drug-resistant forms is prevalent in Eastern Europe and Central Asia. The incidence of tuberculosis is especially a concern for the most vulnerable populations of these regions, including social groups such as the homeless, unemployed, alcohol and substance abusers, the penitentiary population, and the Roma communities. These groups are not mutually exclusive, allowing the confluence of these adverse social conditions to multiply the risk of transmission. Another factor that is exacerbating the spread of tuberculosis is the growing HIV epidemic which, when coupled with weak HAART coverage and suboptimal PLWHIV treatment, increases the likelihood of comorbidity. Unfortunately, a substantial portion of these high-risk population groups are not covered by primary health care services due to the lack of incentive, low educational level, and low income of the groups.

Existing TB screening programs are based on regular chest x-rays for the whole adult population. This form of expensive yet unfocused active TB case-finding is funded in states throughout much of the region, but its coverage of the population groups often deemed most vulnerable remains insufficient.

The high degree of nosocomial TB transmission is perpetuated by the lack of effective tuberculosis infection control interventions in the existing

healthcare system. These poor infection control practices employed in specialized TB control institutions foster the transmission of drug-resistant TB due to factors such as over-hospitalization, the lack of effective patient separation and isolation for contagious cases, the lack of rapid molecular testing, and delayed initiation of effective treatment.

Another major obstacle for environmental TB control involves sustainability due to unrealistic planning and poor maintenance. Outpatient healthcare services intended to provide DOT for TB patients are weak in many cases, and there is no community involvement in most Eastern European and Central Asian countries. Due to these factors, treatment default rates are high and treatment effectiveness remains suboptimal in the majority of these countries.

To reduce TB transmission in the community and congregate settings, the practice of active TB case-finding should be more focused on the high-risk groups listed above. But achieving a high level of coverage of such specific population groups is challenging and requires the following: creative, informal, group-specific approaches; motivation; and the involvement of community leaders.

Unfortunately, effective examples of such practices are extremely rare. For this reason, one of the priorities for TB control programs in the region may involve concentrating resources and focusing on

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high-risk groups when implementing national active TB screening programs.

It is critical to implement the FAST strategy to reduce TB transmission in the health care and community settings. Rapid molecular testing of TB suspects should also be an essential part of the TB diagnostic algorithm. The rapid identification of *M. tuberculosis* and its drug resistance would permit for effective patient separation or isolation (if required), as well as immediate and effective treatment initiation according to the drug-resistance pattern.

Further results of quality assured liquid media DST should be used to tailor individualized treatment regimens for every patient. Smear-positive TB patients, especially those with drug resistance, should be isolated in environmentally controlled conditions to reduce airborne TB transmission. The choice of environmental controls for such high-risk settings depends on factors such as climate, resources, architectural conditions, professional maintenance availability, among others. Natural or mechanical

ventilation providing controlled airflow and/or professionally installed and maintained upper room ultraviolet irradiation are recommended for high TB transmission areas. The isolation term depends on treatment effectiveness, which may vary for extensively drug-resistant cases. In addition, easy and inexpensive interventions, such as cough hygiene for all respiratory patients and surgical mask use for TB suspects and contagious TB patients, reduces the risk of TB transmission by half.

Patient-centered incentive programs to support and improve treatment adherence are able to substantially increase the effectiveness of TB treatment. The “Sputnik” program in Tomsk, Russia is one example of how effective interventions are able to increase the overall efficiency of TB control programs. Strengthened outpatient services providing DOT reduces the duration of hospital treatment, which is also important in terms of reducing TB transmission in the community setting.

### 3.1 Best Practice: Active case finding of TB and DR-TB, an example from Tomsk, Russia.

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#### INTRODUCTION

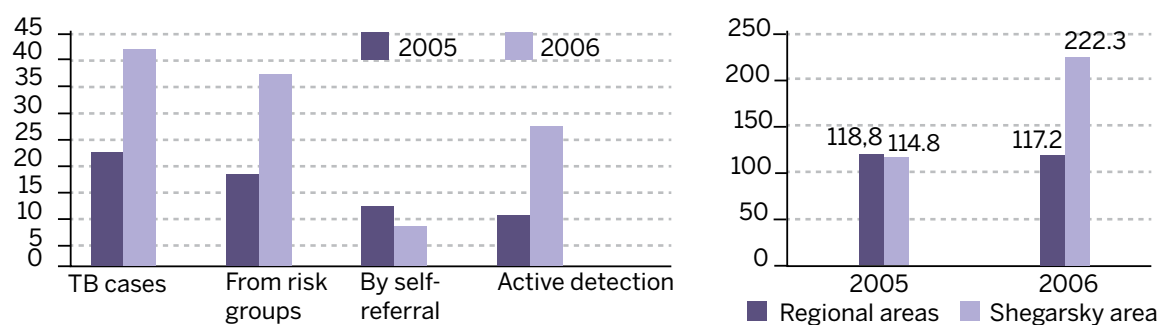
Late referral for medical care and the delay in TB diagnosis by medical specialists contribute to the high number of the patients with extensive pulmonary tissue involvement and significant destructive changes when coming to TB services.

Timely and proper diagnosis of active TB is the biggest challenge. Since 2000, the DOTS-PLUS program for MDR-TB treatment has operated in the territory of Tomsk Region. As work progressed, it became apparent that though patients could successfully be treated, it was impossible to stop the spread of the disease without effective TB detection tools. Among new cases registered in 2004 in the region, 52% had smear positive microscopy and 72.7% of cases were diagnosed with destructive

forms of tuberculosis, whereas only 16.2% of patients were diagnosed with minor forms of tuberculosis. This indicates the late detection of TB and underactive population screening in high-risk groups (69% of new patients belonged to groups at risk of developing TB).

Since 2006, the Tomsk Region has implemented an early tuberculosis detection program among its general medical services (GMS). The purpose of the program involves the timely detection of all diagnosed tuberculosis cases among the population of high-risk groups. The program objectives are as follows: improvement of working efficiency of the GMS medical staff on early diagnosis of respiratory tuberculosis; raising public awareness about prevention, detection, and treatment of tuberculosis; and regular maintenance of the active detection of all cases of tuberculosis.

Figure 3.1.1. TB cases and TB incidence in Shegarsky district.



More tuberculosis can be found in certain population categories compared to others, and it is sensible to look for tuberculosis among those communities where it is more likely to develop. However, if the issue is about targeted screening, it generally covers the healthy, concerned population, that gives rise to the cost thereof. In consideration of economic savings, it is necessary to give priority to the examination of the risk groups, that is, to seek tuberculosis where its detection probability is higher. Thus, screening becomes more cost-effective and brings better results. One can do a great job, but there will be no ultimate outcome, and one can do less, however the strategic minimum will be done and the result achieved. It is necessary to prioritize gradually when working with organizational and financial capacity.

## METHODS AND RESOURCES

All activities held within the program can be divided into three groups.

The first group is comprised of the activities aimed at improving the GMS operation, which includes training of the district and rural TB doctors in basic mechanisms and measures of early detection of tuberculosis, regular visits of the TB doctors to the supervised area/clinic to advise on issues of TB diagnosis, and holding training workshops for specialists in the general medical services on aspects of early detection of tuberculosis.

The second group comprises activities aimed at raising public awareness through the media. We designed and circulated a series of posters, booklets and leaflets to inform the public

about methods of TB transmission, prevention, and treatment. Mass media coverage of the issue of timely TB detection was presented on TV and radio, and by video distribution in public places (i.e. clinics, banks, etc).

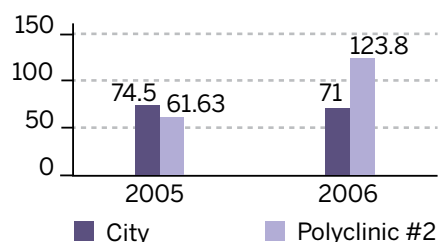
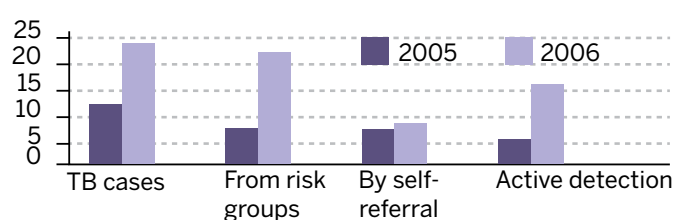
The third group includes activities directly aimed at active case detection of tuberculosis, including: outreach work performed by specialists from general medical services; and keeping personal records for the population living in the supervised area, including resident questionnaire surveys for the purpose of TB detection. If the symptoms of pulmonary tuberculosis had been detected or the resident had been referred to a risk group, then sputum was collected for microscopy and appointment for a chest x-ray was issued to the patient. An information booklet about the symptoms of pulmonary tuberculosis and its treatment was handed out in every yard/house by medical professionals.

The key focus in the active detection of tuberculosis should be predicated off of those from social risk groups, including: the unemployed; the homeless; migrants; refugees; forced migrants; ex-prisoners; those living in orphanages; overnight shelters and retirement homes; and persons exposed to TB infection.

## RESULTS

For the duration of the program operation in Tomsk Region, the participants were comprised of six central district hospitals with a total supervised area population of 128,000 and four municipal polyclinics which provide medical services to 105,000 people.

Figure 3.1.2. TB cases and TB incidence in Polyclinic #2.



The program compensated training in the issues of TB detection for general medical professionals, as well as providing the health care facilities with microscopes, containers for sputum collection, and health educational materials in all areas participating areas. Outreach activities included the obligatory questionnaire surveys of residents for the purpose of TB detection. As a result of this work, an increase in TB incidence was observed within the areas among participants of the program as compared to the other districts, as well as a significant increase in the rate of early detected cases of tuberculosis among new patients. Thus, as a result of the project, the recorded incidence of pulmonary tuberculosis increased in the adult population within the pilot areas, and more people were

covered by preventive screening. The incidence of tuberculosis within the pilot areas increased almost twofold (in 2006), as active detection of tuberculosis increased up to 95% in rural areas and up to 78% in urban settings.

This work is the basis for any program of TB control. In any region, it is impossible to control tuberculosis without active case finding strategies.

## **CONCLUSIONS**

Introduction of high-quality treatment programs and improvement of TB system without appropriately searching for TB patients in the community will not lead to a significant reduction in TB incidence.

## 3.2 Best Practice: Improving hospital tuberculosis infection/transmission control in Russian regions: the F-A-S-T strategy.

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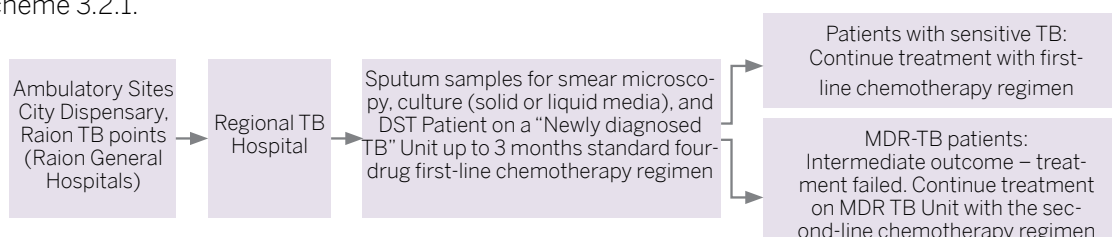
### INTRODUCTION

Tuberculosis treatment in Russia is heavily hospital dependent, and renovating thousands of hospitals to improve the infrastructure, is a daunting challenge. Currently, patients with newly diagnosed tuberculosis are admitted to general hospitals or tuberculosis hospitals based on sputum smear microscopy or clinical findings, and are usually started on the standard four-drug first-line short-course chemotherapy regimen while awaiting culture confirmation and drug susceptibility testing (DST). It can take as long as two to four months to obtain results, delaying bacteriological diagnosis of MDR-TB and XDR-TB (Scheme 3.2.1). This results in prolonged infectiousness from undiagnosed tuberculosis cases or undiagnosed drug resistance. Because patients being treated for tuberculosis in the Russian Federation are usually hospitalized for a prolonged period, the result is that patients with undiagnosed drug-resistant disease often share the same wards and rooms with patients with

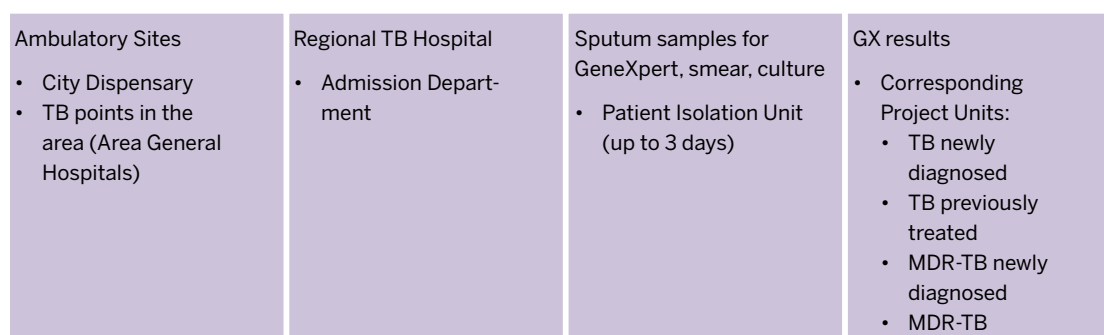
drug-sensitive disease. Through this mechanism, nosocomial transmission of drug-resistant disease can occur.

The most important aspect of stopping transmission of tuberculosis at hospital settings is to control the time from presentation with cough and diagnosis of TB (including DST) to the initiation of appropriate treatment. The advent of rapid DNA-based diagnostic methods, such as Gene Xpert, allows for the rapid diagnosis of Rifampicin resistance in *M. tuberculosis*. In many settings, this is believed to be a good surrogate for MDR-TB. As part of a core package of tuberculosis transmission control / infection control (TC/IC) interventions, in January 2013 we started the implementation process of the F-A-S-T strategy at two oblasts' tuberculosis services – Voronezh and Petrozavodsk (Republic of Karelia). They have been employing rapid DNA-based diagnostics (the GeneXpert system) to Find cases Actively (identifying MDR-TB patients), Separate patients safely to reduce exposure to drug-resistant strains (stopping nosocomial

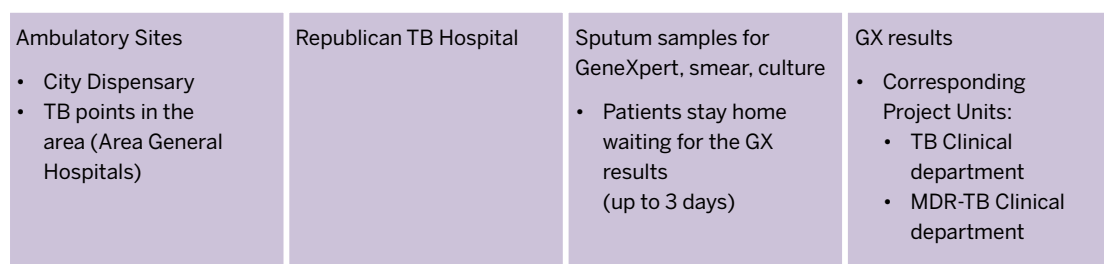
Scheme 3.2.1.



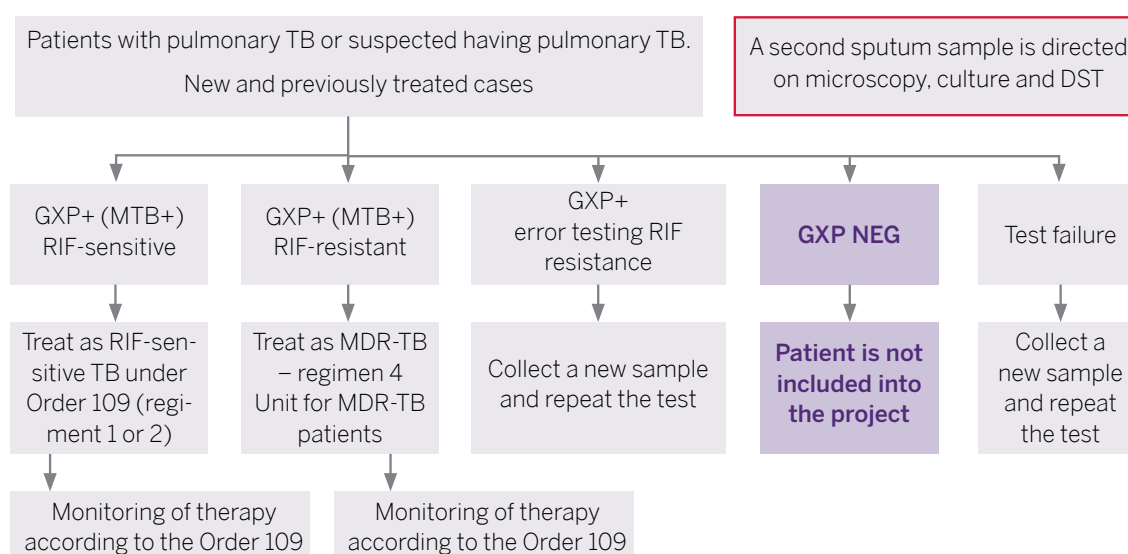
Patient flow, Voronezh.



Patient flow, Petrozavodsk.



Scheme 3.2.2.



transmission), and Treat effectively with second-line drugs where appropriate (F-A-S-T.)

With the F-A-S-T approach, we expect to reduce the time for diagnosing MDR/XDR TB from months to days. Thus, we hope to rapidly reduce or stop transmission in hospitals, and with sufficient empirical data from the training/implementation cycles, we can provide a basis for major policy change in the Russian Federation and elsewhere.

## METHODS AND RESOURCES

To begin the Project, the TB hospital administration had to make important modifications in patient-flow protocols.

One of the issues we have come across concerns group of patients with uncertain TB diagnoses. They are typically placed in a special Diagnostic Unit before their diagnosis conformation. The length of hospitalization without treatment for some of those patients could be up to 30 days. Our project raised the question of the feasibility of rapid testing for these patients from both a clinical and financial point of view. We are still waiting for more data and working on the optimal solution.

First critical point: TB doctors have made the decision at the Admission Department. An "Inclusion/Exclusion Criteria Form" has been developed and filled out for 100% of the hospitalized patients. By answering questions on the form, a doctor determines if a patient has to be tested by GeneXpert. All patients with pulmonary TB or suspected of having pulmonary TB admitted at a TB inpatient facility have been immediately tested for MDR-TB with Xpert MTB/RIF. Medical personnel have followed the below algorithm:

Using Xpert MTB/RIF, results for Rifampicin resistance are usually back from the laboratory the same or the next day. While doctors are waiting for the results, patients are placed into a specially designated Isolation Unit. This Unit is considered a high-risk infectious area for patients with unknown TB status and no treatment. We have participated in the construction of the Unit: this area has been separated with closed gates and well equipped with UVGI open light systems operating 24 hours per day. In addition, patients as well as medical personnel wear respirators.

Scheme 3.2.3.

Number of patients who were hospitalized during the quarter	Number of patients who meet the criteria for the Project and have to be tested (persons with suspected pulmonary TB)	Number of patients with performed GX before or after hospitalization	Number of patients for whom GX was done in the first 2 days after admission (from column 3)	Test results GeneXpert-MTB (from column 3)		Test results GeneXpert RIF - resistance (from column 5)		# patients enrolled into the Project	The number of patients who were assigned MDR-TB-treatment within 3 working days after the test
1	2	3	4	5	6	7	8	9	10
3524	1603	1592	1479 (93%)	POS	712	Resistant	249	285	283 (99%)
						Sensitive	418	403	
				NEG	880	x	x	x	x



Patients diagnosed with Rifampicin resistance are placed on effective treatment (regimen 4, according to national MDR-TB guidelines) and transferred to MDR Units (for newly diagnosed or previously treated patients).

Patients who are shown to be Rifampicin (RIF) sensitive by the Xpert MTB/RIF test are placed on standard TB treatment according to national guidelines – regimen 1 or 2.

What we want to achieve:

#### *RIF-sensitive patients*

- Do not get super-infection with RIF-resistant strains from TB-resistant patients
- Better outcomes with fewer failures in treatment
- No need for long-term hospitalization and treatment with second-line TB drugs

#### *RIF-resistant patients*

- No resistance amplification to Ethambutol and/or Pyrazinamide
- Receive proper treatment on day 3, not month 3; better treatment outcomes and fewer unfavorable outcomes
- Financial savings by using a smaller amount of second-line drugs and shorter length of hospitalization.

We have several indicator levels to measure and analyze whether rapidly provided data helps in the early separation of patients with drug-resistant from those with drug-sensitive disease. Patient enrollment has been completed in both regions.

We think that this practice is innovative for the following reasons:

- Measurable results.
- Feasible: Successfully fits within existing TB service structure.
- Replicable: Can be used, or adapted for use, in different inpatient environments.
- Cost-effective.

The F-A-S-T strategy is a well-defined subset of the WHO recommended set of hospital administrative infection controls: Finding cases Actively, Separating them safely and Treating them effectively.

Moving treatment from hospitals and clinics to communities, with appropriate infrastructure development is another promising strategy to reduce hospital transmission. Risk in the community is minimized if effective treatment is assured by trained workers.

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## Session 4.

# Introduction: Major DR-TB diagnostic gaps in the countries of Eastern Europe and Central

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### INTRODUCTION

Panel 4, entitled, “What is needed to improve early diagnosis of TB and DR-TB?” focused on laboratory diagnostics for DR-TB. The presentations from Dr. Michael Rich, Dr. Stela Bivol (Moldova), Dr. Giorgi Kuchukhidze (Georgia) and Dr. Bekzat Toksanbayeva (Kazakhstan) highlighted their respective countries’ achievements for developing culture and DSTs for detection of drug resistance and implementation of quick methods of RIF resistance (via GeneXpert).

In particular, countries presented information about the rollout of GeneXpert and LPA (via the Hain test) for rapid detection of RIF-resistance among suspected cases. New tools helped NTPs to diagnose up to 30% more DR-TB patients and rapidly enroll them in treatment. The scaleup of GX also allowed countries to improve coverage and access to TB and DR-TB testing in hard-to-reach areas where sample transportation is a challenge. Bringing lab techniques closer to patients reduces these delays in lab testing and treatment initiation, and improves overall turnaround time. As a result, patients are enrolled more quickly in treatment and results are improved.

The presenters also emphasized the importance of updating current diagnostic algorithms when new tools and techniques are adopted by NTPs in order to use the lab network more efficiently and avoid the cost and time involved in the duplication of services (i.e. when one patient may get numerous and sometimes similar tests for TB and DR-TB).

The major gaps that prevent rapid and efficient implementation of TB and DR-TB programs in E&E and CA are the following:

- Even with the rapid scaleup of GeneXpert technology, access to rapid TB and DR-TB is still below the minimal. Many patients still either do not have access to a reliable TB lab network or to rapid TB and DR-TB detection. In most countries the sample transportation system is not developed enough yet to handle quick turnaround of sample results from the rapid (one to two days) detection system. Because a short turnaround time is best, the transportation system should also be able to pick up the sample within one day and return the result (in paper form) within one day as well. However, the current transportation systems in many counties are far from achieving these targets, with the exception of Georgia, where the National Post service was involved in sample delivery with very quick response times.
- For the appropriate and comprehensive development of DR-TB programs, both covering MDR and XDR-TB, DST to first- and second- line drugs is needed. At this moment, many counties in the region do have good access to first-line DST; however, the second-line is mostly underdeveloped. Usually only one national lab in the country will have access to second-line DST, and a very limited number of tests are being done. With the

introduction of new anti-TB medicines and new regimens for DR-TB, comprehensive coverage for second-line DST is urgently needed.

- The panel discussed the issue that with the introduction of new lab tests and techniques, the lab network becomes more cumbersome and duplicative. Clear and effective lab testing algorithms are needed to direct tests for each group of patients (such as suspects, high- and low-risk, contacts, HIV-positive, children, etc.) appropriately, so the tests are done quickly, results are obtained immediately, and no repetitive tests are done. This will both improve efficiency and save program funds.
- Absent or underdeveloped lab information systems that would link all labs, GX machines, and other techniques was also discussed by the panel. TB suspects and patients receive many TB tests before and during the treatment, but for most cases those results are not consolidated in one database under the auspices of the National Lab Network or the Reference Laboratory.
- Lastly, many countries in the EECA region are moving to higher economic levels according to World Bank classification, and so will have less chances to qualify for GFATM grants. Therefore, more emphasis should be on country ownership and sustainability through government resources. The question of whether or not national health insurance and other government resources can help should be urgently discussed by NTPs.
- There is no magical solution that can help countries to solve all issues at once, but a number of actions, activities and steps must be implemented on the country level in order to solve/improve the situation. The following steps recommendations should be examined:
  - Countries should pay more attention to their ownership of the tuberculosis activities, and should plan a way to keep program activities sustainable over time after donor funds come to an end. Developing sustainability plans, increasing program budgets from government funds, and implementing national health insurance schemes may be a good start for these countries. Also, NTPs should look for efficiency gains during the programming and implementing phase of TB programs. Implementating the best practices and international recommendations could help save resources and reallocate them towards programmatic gaps.
  - When the TB lab network is developed or strengthened, updating SOPs, guidelines and algorithms will help systems run more smoothly and efficiently. Keeping the patient abreast of all program activities will ensure that program is patient-centered, easily accessible, and available. NTPs should aim for good program utilization while keeping the highest quality standards.
  - Lastly, implementation and scaleup of rapid tools for TB and DR-TB detection is the way forward. However, NTPs should also aim for comprehensive diagnostic tests for first- and second-line medications. New TB regimens and medications should only be applied when proper DSTs are done, and as quickly as possible. Initiating patients on appropriate treatment will reduce transmission of TB and stop the epidemic.

## 4.1 Best Practice: Scaleup of access to Xpert MTB/RIF in Moldova.

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### BACKGROUND

Tuberculosis (TB) is a significant public health challenge in the Republic of Moldova. The burden of multi drug-resistant TB (MDR-TB) in the country is one of the highest in the world. In recent years, the MDR-TB prevalence has been between 24-26% in new cases and over 60% in previously treated cases. Almost all cases with resistance to Rifampicin are MDR. Currently, Moldova implements TB control interventions in line with international recommendations and provides universal access to diagnosis and treatment of all forms of TB, including MDR-TB and extensively drug-resistance strains (XDR). Moldova also has an extensive diagnostic network of TB laboratories. At the same time, the National Tuberculosis Program (NTP) was concerned with frequent cases of service delays along the patient pathway, leading to late and incomplete diagnosis, incorrect treatment and, as a result, further spread and amplification of drug resistance. In order to improve early detection of TB and MDR-TB, the country applied to TB-REACH and received funding for the years 2012-2014. The Center for Health Policies and Studies (PAS Center) continues to implement the project as part of Wave 4 funding.

### RESULTS

The key inputs were delivery of MTB/RIF Xpert machines and cartridges, and collaboration with the project sites to introduce and expand the testing through relevant training, monitoring, and supervision. In total, 30 Xpert machines were supplied and placed at peripheral TB units in the civilian sector, reference TB laboratories, and clinical departments responsible for clinical follow-up of people living with HIV

and TB units in the penitentiary sector (in 19 out of 35 administrative territories, including the autonomous region of Transnistria). The overall evaluation population was 2.61 million, or 64% of the country's total population.

The last progress report showed that the workload has reached the planned full functionality levels. While positive Xpert MTB/RIF positive test rates were high at the initial stage of the project (23.8%-37.2%) due to under-utilization of the new technology and selective testing, the results of last quarter's positive test rate approached the planned screening targets (10-12%). The rate of errors ('test invalid,' 'test error,' and 'test no result') was 4.0% in the last reporting quarter, which is lower than the levels documented in the majority of Xpert projects supported by TB-REACH.

Resistance to Rifampicin is a very close proxy for the diagnosis of MDR in Moldova, as MDR is confirmed in up to 94% of strains resistant to Rifampicin. Xpert MTB/RIF testing supported by the TB-REACH project thus confirms very high rates of MDR in the country. A high sensitivity of Xpert MTB/RIF as the initial diagnostic test for TB was observed, as 45.2% MTB-positive Xpert cases (2,957 out of 6,545 MTB-positive Xpert cases) were negative by microscopy. This rate has been generally stable over time, as shown in Figure 4.1.1.

Given the overall trend of the Moldova TB epidemic (i.e. stabilization and decrease in notifications of all TB cases, as well as in the number of new cases over the last decade), the project aims primarily at improving bacteriological confirmation of TB by Xpert MTB/RIF, rather than at increasing the absolute number

and rate notified. Additionality was calculated for bacteriologically confirmed cases by direct sputum microscopy (DSM) and Xpert for the evaluation population, where data for the actual period of implementation was compared with the previous year for the same areas (Actual: sputum smear positive (SS+) cases plus Xpert MTB+ cases with negative DSM results or DSM not done; Control: SS+ cases). Results have shown a 28.4% increase in bacteriological confirmation in Year 1 compared to baseline 2011 and 35.9% more in Year 3 compared to Year 2 (Figure 4.1.2). The above data indicate the high effectiveness of the new technology in terms of bacteriological confirmation of pulmonary TB.

## CONCLUSIONS

The best practice in Moldova for implementation of MTB/RIF Xpert technology followed WHO recommendations and was based on the provisions of the National TB Control Program for 2011-2015. Moldova implemented Xpert as an initial diagnostic test for TB and was among the first countries in the world to roll out this novel technology to the peripheral service level. Instruments were placed at the level where the diagnosis of TB is established. With no previous mechanism for specimen transportation for Xpert testing (which is crucial for this particular context), the rollout of this novel

Figure 4.1.1. Xpert added value (yield) to smear microscopy by quarter (SS- results as % of MTB+ GX results with valid microscopy results)

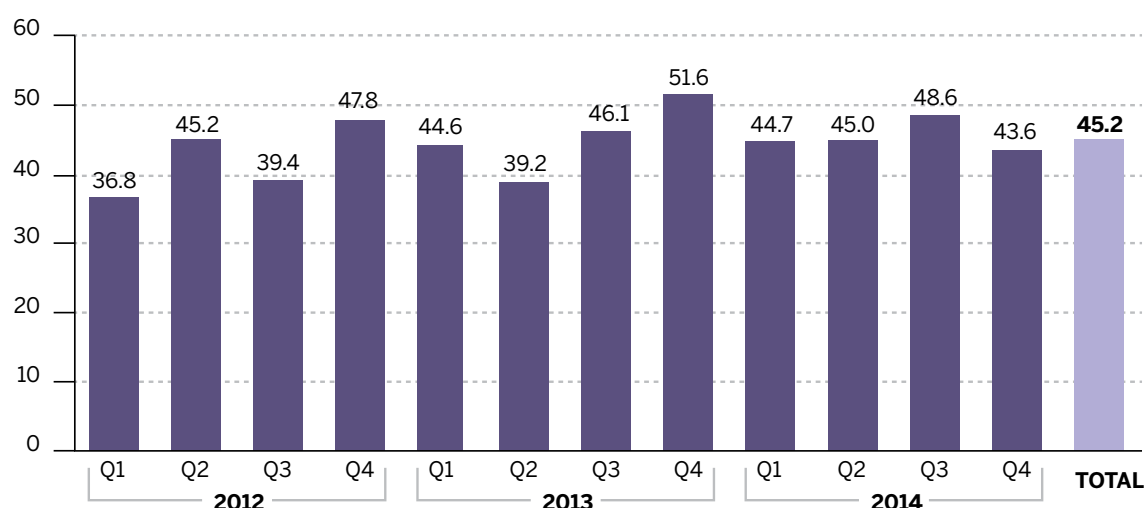
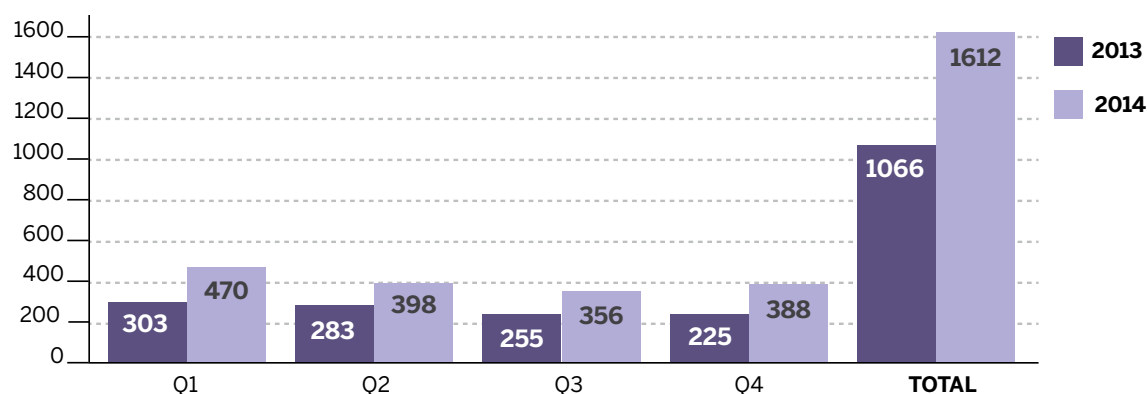


Figure 4.1.2. Additionality by Xpert MTB/RIF, bacteriologically confirmed cases (SS+ and Xpert MTB+), 2013-2014 (compared by quarter)



technology has many implications for the future institutionalization of the new technology, and will allow for increasing use and replacement of conventional microscopy in the future as a method for screening and primary diagnosis of TB and DR-TB at peripheral TB units.

### **KEY SUCCESS FACTORS**

1. The openness and commitment of the NTP to innovations aimed at improving access and quality of TB care, which has catalyzed the rapid scale-up process;
2. Intensive training and retraining of TB specialists and lab staff, along with close and regular supportive supervision of project implementation at all project sites, which has helped to ensure a smooth rollout of this new technology;
3. Professional technical support for Xpert installation, on-site training, servicing, maintenance, and repairs; and

4. The fact that the implementation of Xpert MTB/RIF is seen as a trigger for changes in the TB care delivery system based on decentralization and implementation of patient-centered approaches.

### **LESSONS LEARNED AND CHALLENGES**

Delays in accepting the new technology and incorrect methods used by some TB service staff at the peripheral level has been observed. There is a need to close the gap between rapid, reliable diagnosis by Xpert and the outdated approaches to treatment and case management still used by some providers. Finally, the Xpert database and the national TB database are not linked to each other, which makes it difficult to trace patients along the diagnosis and treatment pathway in order to identify service delays and quality of care bottlenecks.

## 4.2 Best Practice: Strengthening Laboratory Networks, example from Georgia.

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### BACKGROUND

Georgia is a country in transition with a population of 4.4 million, which gained its independence from the Soviet Union in 1991. Since then, tuberculosis (TB) has re-emerged as a significant public health issue in Georgia, and the disease burden has remained high. In 2013, there were 4,320 reported cases of TB in Georgia, resulting in an incidence rate of 76 cases per 100,000 population with an overall notification rate (prevalence) of 96 cases per 100,000 population.

The National TB Program (NTP) has achieved significant progress by fully implementing the Directly Observed Treatment, Short Course (DOTS) program since 1995. The WHO case detection target (at least 70% by 2015) was achieved and even exceeded (78% in 2012); substantial improvements were attained with regard to treatment results (TB treatment success rate in new cases was 84%, in 2012), establishing routine drug resistance surveillance in 2005, and providing universal access to drug resistant TB (DR-TB) treatment since 2009. However, serious challenges remain and much needs to be done in order to sustain these fragile achievements and move forward. Indeed, as in the other former Soviet republics,

resistance to anti-TB drugs represents a serious obstacle to effective control of the TB epidemic. In 2013, multidrug-resistant TB (MDR-TB) in Georgia was found in 11% of new cases and 38% of previously treated cases. The treatment success rate among confirmed MDR-TB cases is 50% (2011 cohort).<sup>2</sup>

Since 2012, the vertical setup of the Georgian NTP has been reformed to a horizontal one, with integration of TB service delivery into primary health care (PHC). The Ministry of Labour, Health and Social Affairs (MoL-HSA) decided to reorganize the laboratory network as well. Currently, the network is divided into three levels, and consists of the National Reference Laboratory (NRL) in Tbilisi; the Regional Reference Laboratory (RRL) in Kutaisi; and nine laboratories for sputum smear microscopy in the civilian sector, and two in the penitentiary system. This amounts to eleven microscopy labs in total, resulting in 0.3 laboratories per 100,000 population.

The transportation of sputum samples from TB service providers to the smear microscopy laboratories is fully subsidized by the state. One vehicle is assigned to every region and it goes to each service delivery point at the district level two to three times per week to

Table 4.2.1.

Georgian Post	Transportation with the NTP vehicle
Daily pickup*	2-3 times per week
Patient receives test results in 3 days	Patient receives test results in 5-7 days
20-25 sputum samples enter the lab every day	50-60 sputum samples enter the lab simultaneously

\* Three to four times per week in some mountainous districts



deliver collected sputum samples to the diagnostic laboratories. Consequently, patients receive test results in five to seven days.

## METHODS AND RESOURCES

Starting in July 2013, the Georgian NTP started sputum sample transportation through the Georgian Post in three regions: Samegrelo-Zemo Svaneti, Racha-Lechkhumi, and Imereti. The program was initiated as a pilot with a possible extension depending on the outcomes of the pilot.

The Georgian Post provides universal postal service in the country and holds the leading position in the market. The company has been a member of the Universal Postal Union since 1993 and, in recent years, has undergone major reforms with consequent, noticeable improvements in service delivery.

Delivery service using the Georgian Post was funded by the National Center for Disease Control and Public Health and, in line with the contract terms, the NCDC is paying a special reduced price per parcel (approximately \$1.50 USD for transportation of one cold box).

Each region in Georgia consists of several districts. One TB service delivery point that collects sputum from presumptive TB cases is located in each district. Transportation is carried out with cold boxes. Sputum is placed in a triple pack that includes the sputum container, a special closed box that can hold six sputum containers, and a cold box that can hold two of the special closed boxes. Thus, a single cold box may contain up to twelve samples of sputum. The NTP purchased three cold boxes for each TB service delivery point. Each cold box has a specific location in the vehicle and is fastened to the wall. The Georgian Post and TB service delivery personnel (postal delivery carriers, physicians, and nurses) were all trained in biosafety issues.

For most service delivery points, the Georgian Post provides daily sputum pickup. For

other districts pickup occurs three or four times per week. Each service delivery point is aware of the approximate time that the delivery carrier stops by the facility. If there is no need for sputum to be collected that day, a nurse or doctor informs the postman so that he can skip that particular facility.

## RESULTS

Table 4.2.1 summarizes a comparison of the old system to the new Georgian Post pilot sputum transportation system.

The Georgian NTP plans to expand the Georgian Post service. Recently, the Adjara region was also included in the contract and sputum sample transportation in the region is now being performed through the Georgian Post. Currently, ongoing negotiations are being held with the Georgian Post to agree on routes for the eastern part of Georgia.

## CONCLUSIONS

To our knowledge, this is the first attempt by the NTP to use the postal service for transportation of sputum samples. The service is cost-effective, decreases transportation time, and reduces the time for patients to receive test results from five to seven days, to three days. This successful Georgian practice may trigger the involvement of the postal service in sputum sample logistics within the National TB Programs of other countries as well.

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## 4.3 Best Practice: Scaleup of access to DST for first- and second-line drugs, an example from Kazakhstan.

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### INTRODUCTION

In the modern era, drug resistant tuberculosis is a global challenge. Despite a decreasing trend in TB incidence in the Republic of Kazakhstan, the prevalence of multi-drug resistant TB remains high. (Figure 4.3.1).

The country is reportedly as one of eighteen countries with high MDR-TB burden in the WHO European Region. In 2013, primary drug resistance in Kazakhstan was 25.2%, and secondary drug resistance was 48.6%. The increasing trend of MDR-TB can be conditioned by rapid diagnostic methods for TB and MDR-TB introduced in all TB service facilities. The methods include BACTEC MGIT and rapid molecular genetic tests, such as MTBDR plus and Gen Xpert MBT/RIF.

### METHODS

A great deal of preliminary work was accomplished prior to the implementation of the rapid diagnostic methods, and was performed in collaboration with the National TB Center of Kazakhstan and several international organizations, including: the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM); USAID (KNCV, Project HOPE, QHCP); FIND; WHO; and the Supranational Reference Laboratory (Borstel, Germany).

In order to achieve our objectives, sustained efforts were made to improve bacteriological services available in the country and to reorganize laboratory resources to conform to the requirements of infection control

Map of Kazakhstan



and biosafety. Simultaneously, the National Reference Laboratory was reconstructed according to international standards and obtained ISO: 9001 certification. The status of the National Reference Laboratory was confirmed by the Supranational Reference Laboratory in Borstel, Germany.

The TB laboratory network has a specific structure due to the vast territory it covers combined with low population density and geographical conditions.

The first level (the district level) includes 466 microscopy laboratories. The second level (the regional level) has twenty-one bacteriological laboratories that perform all microbiological tests, including DST to first and second line anti-TB drugs. The third level (the national level) is represented by the National Reference Laboratory and, thus, utilizes all microbiological and molecular genetic methods for TB, MDR-TB, and XDR-TB diagnosis, and coordinates TB Service.

With support of the Global Fund, health care workers at the National Reference Laboratory in Kazakhstan were trained to use the new technologies. Cascade training was then provided for all other laboratory physicians at TB outpatient clinics.

A precise coordination plan played a significant role in providing all regional bacteriological laboratories (including the penitentiary system in Karaganda) with up-to-date equipment for

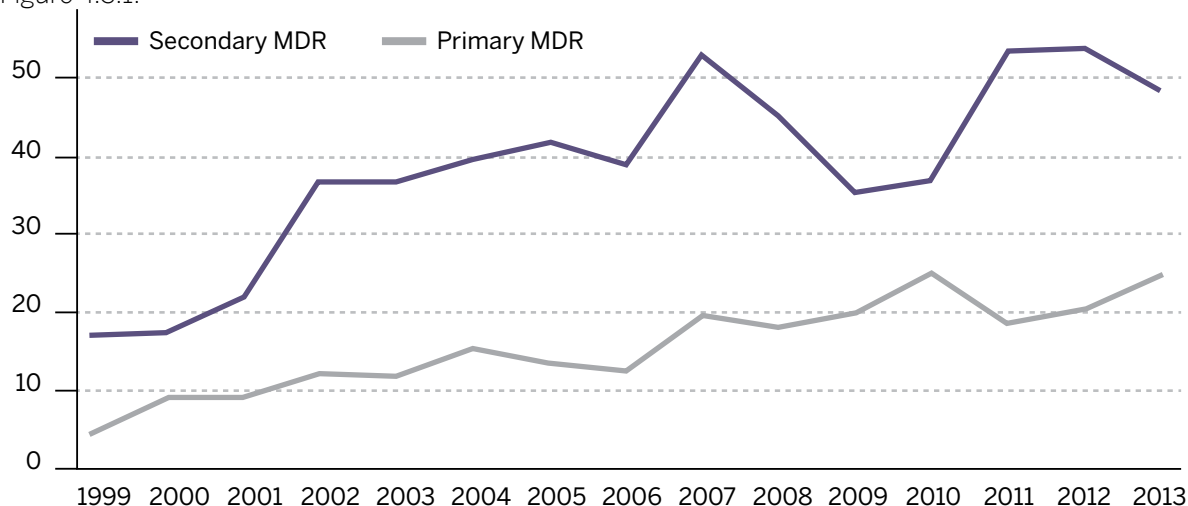
utilizing new technologies. All these efforts constituted sections of the National TB Program, which has ongoing political support from the national government. Provision of equipment and commodity supply for all peripheral bacteriological laboratories was financially supported by the national budget as well as the Global Fund and international organizations.

It should be emphasized that all new implemented methods, including BACTEC MGIT, MTBDR plus and GenXpert MBT/RIF, along with test results, are monitored and verified on a regular basis against classical diagnostic methods both at the National Reference Laboratory and Supranational TB laboratory in Borstel, Germany.

Given the wide range of diagnostic tests available in TB facilities around the country and the significant capacities of the new diagnostic methods (i.e. high specificity and sensitivity), the National TB Center has developed a diagnostic algorithm for bacteriological examination of patients suspected of TB and MDR-TB in collaboration with a FIND consultant and the Supranational TB Laboratory. It should be noted that due to this algorithm, each patient can be examined using almost all methods for differential diagnosis.

Finally, a special ongoing “monitoring and evaluation” group was created at all levels to improve the quality of bacteriological service within the entire country.

Figure 4.3.1.








## RESULTS AND CONCLUSION

Due to the quality changes brought to all bacteriological service facilities of Kazakhstan in 2014, the coverage of TB patients with drug susceptibility testing to anti-TB drugs was higher than 95%. These efforts have made it possible to administer timely and adequate therapy, achieve high efficacy in MDR-TB treatment, decrease treatment duration, improve infection control, and decrease cross-contamination among TB patients.

Thus, it is believed that, this demonstrated the best practice, leadership, and innovation to detect drug resistant TB based on the following:

- The most advanced technologies recommended by WHO with high specificity and sensitivity are utilized throughout the country;
- Up-to-date diagnostic methods are implemented at the central, national, and regional levels, which provide for better access to DST for first- and second-line anti-TB drugs and timely detection of drug resistant tuberculosis; and
- Ongoing political support by the national government, as well as close coordination and integration with international organizations, provided for prompt, quality detection of drug resistant tuberculosis.

Table 4.3.2. Distribution of TB testing equipment

<b>Microscopy</b> 	All laboratories - 466
<b>Culture and DST</b>  	National Reference Laboratory 21 regional laboratories
<b>HAIN-test</b> 	National Reference Laboratory 11 regional laboratories
<b>GeneXpert</b> 	National Reference Laboratory 18 regional laboratories

## Session 5.

# Introduction: Solving TB treatment adherence problems in the region.

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### INTRODUCTION

Panel 5 was dedicated to solving TB treatment adherence problems, which are very common in the region (especially amongst MDR-TB patients). In the presentations, Uzbekistan reported 22.2% default among MDR-TB patients (2011); Moldova, 21.4% (2009); and Tomsk, 10.3% (2011) as compared to 28.6% seven years earlier (2004). Kazakhstan had the lowest rate of treatment interruption at 7.6% (2011) but also mentioned the challenges of keeping patients on treatment. Besides those unable to complete treatment, there are many patients who stay on treatment but do not take their medications regularly and, as a result, end up with treatment failure or TB-related death.

Current MDR-TB treatment requires patients to take highly toxic medications for 18 to 24 months. This can become unbearable, especially for those with co-morbid conditions such as HIV, diabetes, and alcohol/drug addictions, as well as for those with social challenges such as homelessness and unemployment. Some patients might try to take breaks from treatment to diminish side effects, while others are simply not capable of making regular visits to a medical facility for timely medication intake. In a recent meta-analysis of 75 studies, it was shown that directly observed therapy (DOT) throughout MDR-TB treatment has been associated with lower default rates.<sup>5</sup> Patient-centered interventions, such as home-based treatment, patient education, utilization of community health workers (CHW) in the community (as compared to a CHW in a facility or a nurse), and the use of a package of combined financial/nutritional support and transportation reimbursement, were all associated with lower default.<sup>1</sup> Thus, directly

observed therapy combined with a complex of patient-centered interventions should be the way forward in MDR-TB treatment.

It was great to see that all of the presented projects employed DOT and a number of patient-centered interventions to strengthen the treatment organization, and facilitates patient adherence. The social support was universally provided, as DOT centers were organized closer to patients, home-based options were introduced, volunteers were trained to support patients, and SMS messages were used to remind patients about regular medication intake. There are a few things that should be noted for future planning:

- Patient-centered interventions should be considered as an essential “medicine” for TB treatment, and their financing should not be cut in favor of other important budgeted items. If a patient defaults, the resources spent on his/her treatment, including months of hospitalization and highly priced medications, are wasted; he/she continues spreading TB infection to other people who will also require expensive treatment. Thus, the added costs of patient-centered interventions to the program might be less than the costs associated with defaulting patients.
- Sound management of side effects with timely detection and provision of free ancillary medications should be provided to all patients in all locations.
- Patient-centered interventions should be expanded to cover all TB patients in the country, not only those in the pilot projects. Other than Kazakhstan and

Moldova, all other projects were local and did not cover the whole country.

- All of the projects were partially financed by grants (GFATM). While it is difficult to expect all interventions in low-income countries to be completely covered through local funding, it is advisable to look for ways to increase the financing share from governmental and local NGOs and ensure some sustainability. For example, Kazakhstan's reforms, which involved a substantial cut in hospital beds, can help fund ambulatory care. The shift in financing mechanism from the funds per beds to funds per case treated, as it is planned in Kazakhstan, can create incentives towards stronger ambulatory care.
- As an alternative to hospital-based treatment, it is advisable to expand home-based treatment to more patients. For example, mobile "home-treatment" and Sputnik teams treat about 40-50% of ambulatory MDR-TB patients in the city of Tomsk. Home-based treatment is the most convenient way for patients to take medications under DOT. Since nutrition is an important part of TB treatment, daily food packages in home-based treatment can replace hospital-provided hot meals. Daily food packages will also serve as incentives for patients.
- Monitoring and supervision are important to ensure that all elements of the system are working properly. Monitoring

of patient transfers helps to prevent treatment interruptions, and well-performed supervisory visits to treatment facilities achieve several goals: improving DOT and treatment organization, and motivating and training personnel.

- DOT is a standard of care for MDR-TB but it can be labor intensive. Modern technology has the potential to provide some relief; besides the usage of SMS in Tajikistan, other electronic innovations can be used to provide DOT (e.g., DOT through video on patient cell phones or personal computers) or to ensure that DOT is indeed provided (e.g., patient fingerprinting at the time of DOT).
- Hopefully, when new TB medications become available and shorter treatments designed, the effective treatment structure we build now will allow us to bring TB to extinction in our region.

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2. 49% of all MDR-TB patients in ambulatory sector in Tomsk-city in 2011 were treated by "home-based" and Sputnik teams at home. (Unpublished data)

## 5.1 Best Practice: Strengthening the ambulatory care model, an example from Tomsk, Russia.

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### BACKGROUND

In 2000, the DOTS-PLUS program for treatment of multidrug-resistant tuberculosis (MDR-TB) was launched in the Tomsk Region. With the expansion of patients' enrollment into the program, the number of patients unable to complete treatment has also been steadily growing. By 2004, the rate of those defaulting from MDR-TB treatment had reached 28.8%. However, the introduction of medical and social support measures reduced the default rate down to 13.9% in 2005, and further to 9.7% in 2007. "The Pyramid of Compliance" (Figure 5.1.1) presents a system of measures that enhanced outpatient treatment in the Tomsk Region.

At the top of the pyramid are more resource-intensive types of treatment aimed at retention of the "difficult" patients who are most likely to interrupt treatment. At the bottom of the pyramid are the services for the majority of patients who are more self-sufficient and able to visit the DOT unit on a daily basis.

Outpatient treatment of TB in Tomsk can be organized in the day hospital or in the clinic, as well as at home. In rural areas of the Tomsk Region, patients are treated in the TB offices of district hospitals, in health units, or at home.

### "THE PYRAMID OF COMPLIANCE" LEVELS 1-3: GENERAL MEASURES OF OUTPATIENT TREATMENT

Continuity between the services is ensured by close interaction and timely provision of documentation. Before a patient is released from the medical correctional facility of the penitentiary system, medical records are passed to the civil medical outpatient treatment facility. Once a month, a social worker from the TB Dispensary participates in the Release School to inform those in prison about the organizations where they can receive medical and social care after their release. The patients who are referred for registration to the TB Dispensary after their release from detention facilities will get the food package as an incentive. (Note: A description of measures for interaction of the penitentiary and civil sectors is presented in Section 7.2 Inter-agency collaboration between penitentiary and civilian TB control services: Experience from Tomsk, Russia by S. P. Mishustin.)

Information about patients soon to be discharged from the TB hospital is passed to the local outpatient physician or district TB doctor two weeks before the discharge. This allows staff



to prepare a site for outpatient treatment of the patient, particularly in rural areas, for which they supply the TB drugs, food packages, and clarification on the possibility of outpatient treatment.

After consultation with the patient, the local TB doctor makes a decision on which DOT unit to refer the patient to.

In addition to their regular consulting during working hours, psychologists and substance abuse doctors may also provide emergency counseling services to patients at home with the health team. When detoxification is required, the patient is taken to the hospital.

Supervisory visits became an effective tool to monitor and improve the efficiency of TB patient treatment in rural areas. Supervisory visits are held by the district TB doctor once every two weeks at the beginning of treatment, then on a monthly basis, and by the doctor-supervisor of the TB dispensary depending on accessibility and remoteness of the area - once every three to six months, more often if necessary. The supervisory visit is performed in accordance

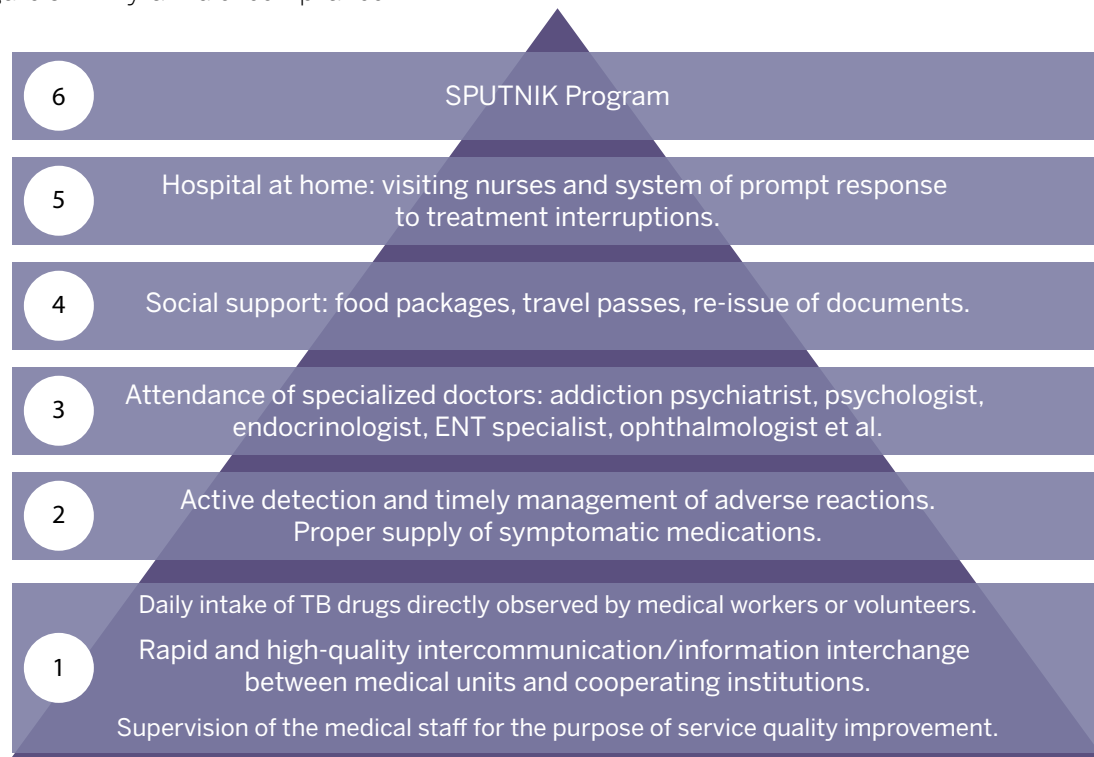
with special DOT unit protocol, with an obligatory visit to the patient's home.

#### **"THE PYRAMID OF COMPLIANCE" LEVEL 4: SOCIAL SUPPORT**

To identify the problems and needs of patients in medical and social care, the managing TB doctor fills in a social card for every patient. The social worker analyzes these cards and identifies the patients who are in need of help and support. After that, the plan for the patient's support at all stages of treatment is worked out jointly by the social worker and the patient. The social workers advise on re-issuing documents, registration of disability, and setting and payment of any retirement benefits.

On a daily basis, the patients are provided with food packages as an incentive to visit the DOT unit. An analysis made by the Russian Red Cross showed that providing daily food packages is a more effective method to motivate patients to visit the DOT unit than providing a complete food package once a week.

Figure 5.1.1. Pyramid of compliance



A particularly important role is played by food packages in terms of TB treatment compliance with patients from rural areas, which reduced defaults from treatment to almost zero in this cohort. Between 2005-2013, only 28 (0.5%) of 5639 patients treated in the region districts who were included in the social support program by the Russian Red Cross interrupted their treatment.

To ensure transportation to places of treatment, monthly travel passes are issued for the patients. The patients from rural areas have the right for free travel to the city for examination, consultation service and medical treatment (at the expense of the regional budget).

The regional public agency of The Center of Social Adaptation provides its services for the homeless people in the city. Two wards, five beds in each, are opened based on the homeless patients undergoing TB treatment. Through this center, the homeless have the opportunity to complete the course of treatment.

**“THE PYRAMID OF COMPLIANCE”  
LEVEL 5: HOSPITAL AT HOME,  
VISITING NURSES, AND SYSTEM OF PROMPT RESPONSE TO  
TREATMENT INTERRUPTIONS**

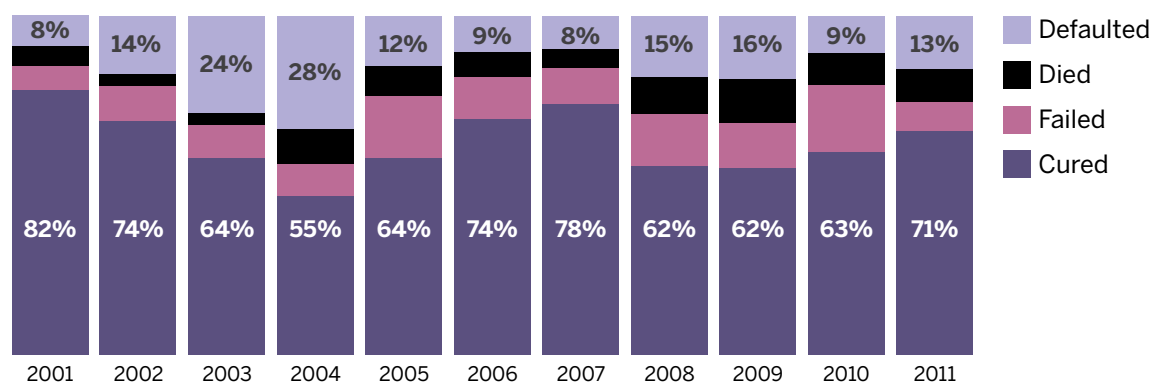
The head nurses of all DOT units report on any cases of three-day patient absence to the TB Dispensary attention center for the attention of the head visiting nurse.

The head visiting nurse's daily duties include:

- Checking the patient data with the district TB doctor (addresses, phone numbers, and contact information of relatives) for transfer to the visiting nurses;
- Sending information to the visiting nurses regarding the patients' search and collecting information about the search results from the visiting team;
- Sending information about the patients who interrupted hospital treatment to the rural office of the Regional TB Dispensary; and
- Transferring requests to district TB doctors for management of adverse events and other urgent information received from visiting nurses.

In addition, the head visiting nurse reports to the meeting of the Compliance Enhancement Commission on a weekly basis. The Compliance Enhancement Commission is a collegial body, based in the polyclinic of the TB Dispensary, and includes the chairman, representatives of DOT units, managing TB doctors, psychologists, social workers, and representatives of nonprofit organizations. The commission reviews the cases of the patients who intake less than 75% of TB drug doses, and a plan is developed to improve the treatment compliance. In particular, the decision is made on the most suitable place for treatment of a particular patient, while in complicated cases the patients are transferred to the Sputnik program. The decisions are made

Figure 5.1.2. Treatment outcomes of MDR-TB program, 2001-2011, Tomsk oblast, %.





collectively and recorded in a special register and in the patients' charts.

The patients who are not able to visit the DOT units for various reasons (difficulties in moving, small children, work, etc.) are treated at home. Depending on the number of patients who are in need of treatment at their residence, during the day shift (9:00 to 16:00), the city is divided into three routes and each is served by a separate "hospital at home" team (i.e., a driver and a nurse). Each team visits between twenty and twenty-five patients over six hours, and an average of fifteen minutes is scheduled for every patient.

In the evening (16:00 to 19:00), the visiting health team looks for the patients who, for whatever reason (e.g., alcohol dependence, inconvenient work schedule, family problems, and so on) missed their treatment or were absent from TB services for longer than three days.

The monitoring of treatment compliance is the responsibility of the coordinators in the city. Together with the head nurse, they monitor the work of the visiting teams during joint monthly visits. In addition, weekly meetings are held for the lessons learned in terms of the most difficult cases.

"The pyramid of compliance," level 6: SPUTNIK program is described in the chapter "Addressing treatment defaults: Sputnik Initiative. Example from Tomsk, Russia".

## CONCLUSIONS

The model of outpatient treatment in the Tomsk Region proves its success through beneficial results of treatment and a low default rate (Figure 5.1.2). Its good performance is demonstrated by the following set of measures:

1. Regular monitoring of all patients and well-adjusted continuity between all segments, wherever the patient is treated.
2. Directly observed treatment.
3. Bringing the therapy to the patients through the provision of directly observed treatment in such places and at such times that are the most comfortable for patients.
4. Appropriate chemotherapy regimen and effective management of adverse reactions and treatment of concurrent diseases.
5. Patient support in the course of the treatment, and use of incentives and motivation in the form of food packages.
6. Rapid response of the TB service staff in case of missing anti-TB drugs intake by patients.
7. Individual approach to every patient with respect from the medical staff.

## 5.2 Best Practice: mHealth solutions for TB Control in Tajikistan.

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A. Habib

*Interactive Health Solutions, Karachi, Pakistan.*

### BACKGROUND

Tajikistan has one of the highest TB prevalence rates, at 382 per 100,000 population, and an incidence rate of 206 per 100,000 population. The drug-resistant TB rates among new TB patients is 12.5%, but rates are up to 54% in previously treated TB patients. WHO estimates that there are as many as 14,000 TB cases per year. The healthcare system in Tajikistan has a strong emphasis on hospitalization, especially for TB care. The National Guidelines on TB Management in Tajikistan recommends that all TB cases are hospitalized during the intensive phase of treatment, after which they may be shifted to ambulatory care through Primary Health Care (PHC) facilities. However, due to the unavailability of beds and the inability of people to endure long hospital stays, only approximately 50% of patients receive the full course of treatment through the ambulatory care system. Studies have shown that hospitalization of TB patients leads to increased risk of disease transmission and a greater socioeconomic burden on patients and their households. The American College of Chest Physicians recommends ambulatory care, stating “infectiousness alone is not an indication for hospitalization.” Moreover, the WHO DOTS strategy also favors ambulatory care. Due to these recommendations, new guidelines were formulated by the National TB Control Program for 2010-2015 and the country started to implement a community-based TB and MDR-TB project with the collaboration of local civil society organizations. Community MDR-TB initiatives were implemented in two pilots, Kulyab City and Kulyab District.

In addition, managing MDR-TB patient data requires careful recording and reporting over up to two years for each patient. Doing this using paper-based forms and reports leads to gaps in data and difficulties in centralizing data from different parts of the country.

### INTERVENTION AND RESULTS

Multiple strategies were initiated to address the challenges faced by the TB program.

First, operational research was conducted in collaboration with the Republican TB Centre, Tajikistan, and the Country Office of the World Health Organization Tajikistan with the financial support of the UNDP/Global Fund. This research was conducted to compare treatment outcomes for hospital and ambulatory based care of TB, as well as to assess the economic burden for both models of care in Tajikistan. The operational results clearly demonstrated that the patients treated through the ambulatory model have similar treatment outcomes to hospital-based patients. In addition, the ambulatory/community-based model is cheaper than the hospital-based model of care for both the patients and the health system.

Secondly, for the scale-up of community based DOTS for TB and DR-TB, a strategy was written and a manual to train community health workers was developed along with a monitoring framework. Overall, seven trainings were conducted for a total of five pilot sites: five trainings for 103 volunteers in Khatlon oblast covering Kulyab, Vose and Hamadoni, and two trainings for 33 volunteers in Sugd oblast covering Khujand and Bobojon-Ghafoorov districts. Topics



included: DR-TB transmission, diagnosis, management; the role of health workers as DOT providers; and adverse event monitoring, amongst others. Following the classroom training, volunteers were assigned patients to follow up, and hands-on practical work was undertaken.

Simultaneously, a specialized electronic medical record system was set up at the National TB Programme headquarters in Dushanbe as a pilot so that all data could be centralized in a single standardized database. The system, OpenMRS (<http://www.openmrs.org>), is a highly customizable database that was easy to tailor to Tajikistan's needs. The system was also translated into Russian for use in Tajikistan. The system was set up in Dushanbe and piloted in Dushanbe and Kulob, with further expansion to several other parts of the country. The MDR-TB database setup cost a total of about \$40,000 USD over one year. The initial assessment was funded by UNDP with the development and deployment funding by the WHO Country Office in Tajikistan. It was later extended to incorporate drug-susceptible TB data as well. Technology implementation and trainings were performed by a consultant visiting Tajikistan and the following expansion was led by a local informatics manager with NTP staff.

Lastly, an initiative aimed at early detection of drug-susceptible TB was undertaken with funding support from TB REACH. Community-based screeners used special software on a mobile phone to perform verbal symptom screens in order to identify presumptive TB patients using an automatic algorithm. Presumptive patients were diagnosed using smear microscopy or GeneXpert before starting treatment. Of the 849,215 people screened at 17 polyclinics, 9,742



were identified as suspects and of these, 1,776 patients tested positive and were started on TB treatment. This reflected a 220% increase in sputum smear positive cases and 60% of all forms of TB cases notified from the previous year in the intervention area. As part of the same project, SMS reminders were sent out to a subset of patients to assess the feasibility of using phone reminders as DOT providers.

## CONCLUSIONS

The National TB Program and Ministry of Health in Tajikistan should advocate treating TB patients in the ambulatory/community model, as it is cost effective. In addition, engagement of active case finding strategies at the polyclinics using mobile phone-based technology and the help of volunteers in the community have shown to yield significant gains in the diagnosing and management of TB patients, thus reducing morbidity and transmission.

Electronic recording and reporting of tuberculosis data minimizes errors and allows for more efficient and rapid reporting at all levels of the health system. If implementation is done well, expansion can be done by local staff in-country without requiring constant on-the-ground support from external consultants.

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## 5.3 Best Practice: Expanding access to care through primary health care, example from Uzbekistan.

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### BACKGROUND

With a population of more than 30 million people, Uzbekistan reported a TB incidence of 50.8 per 100,000 people and a TB mortality rate of 3.6 per 100,000 people in 2013. Uzbekistan is considered to be one of twenty-seven countries with a high burden of MDR-TB. The rate of primary MDR-TB is 12% and is extremely high among previously treated patients (62%), while the rate of DR-TB treatment success is much lower: 53% (2011 cohort, 855 patients).

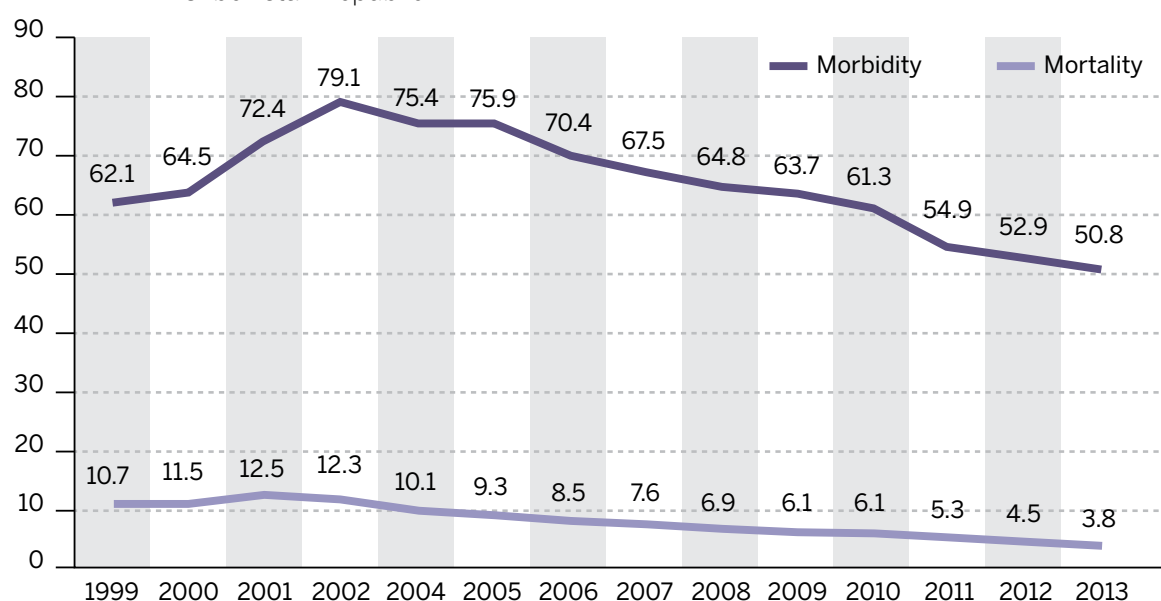
Since 2001, international standards for providing anti-TB care to the population have been introduced. In 2005, the Country Coordination Committee received approval for the Global Fund grant on TB (Round 4). In 2010, the implementation of Round 8 began. In total,

about \$84,726,078 USD in funds were received between 2005 and 2015.

The implementation of a program to provide help to patients with drug-resistant TB in Uzbekistan began in 2003 with small pilot projects in Karakalpakstan. By 2013, the program had been expanded throughout the country.

The Ministry of Health coordinates the national program to fight TB through a network of anti-TB institutions: the Republican Specialized Scientific Practical Medical Centre of Phthisiology and Pulmonology; the Republican DOTS Centre; regional anti-tuberculosis dispensaries within hospitals; and district anti-tuberculosis dispensaries. In 2001, a vertical program to fight TB was decentralized, and anti-TB drugs were provided under direct supervision

Figure 5.3.1. Changes in TB Incidence and Mortality (1999-2013) (per 100,000 population) in Uzbekistan Republic



within patients' households through the ramified network of rural medical points and polyclinics (there are DOTS services available in every one of these institutions).

The success of this approach is demonstrated through the changes in the epidemiology of TB in Uzbekistan, including:

The success of this approach is indicated by the development of the epidemiological situation on tuberculosis in the country, including:

- A decrease in TB morbidity and mortality rates since 2003;
- High treatment effectiveness among patients (79-80% among drug-sensitive patients); and
- High treatment initiation among patients (up to 90% of diagnosed MDR-TB patients begin treatment).

It is peculiar that Uzbekistan's decentralized outpatient anti-TB treatment program did not plan to provide monetary incentives to primary medical care workers to ensure the stability of the program. However, great attention was given to training the large number of specialists, including general practice physicians, nurses, and laboratory assistants. Additionally, the system of constant regular monitoring and program assessment was regulated by a well-educated centralized team from the Republican DOTS Centre. For the pilot regions (including the Republic of Karakalpakstan, Tashkent, and Tashkent region), vehicles were procured for the district anti-TB dispensaries, which render direct controlled treatment of DR-TB eliminators of bacilli under domestic conditions on daily basis.

The guarantee of the program's success is its effective, modern, well-elaborated national program management system to fight TB.

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## 5.4 Best Practice: Social support of TB patients, an example from Moldova.

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### INTRODUCTION

This article describes the Moldovan experience with distributing cash incentives for better treatment adherence in TB outpatients. The conclusions are based on results of the study entitled, “Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova?” and the experience of the Act For Involvement NGO since 2009. We consider cash incentive distribution an efficient tool, as it gives better results than in-kind incentives (food parcels, food vouchers, etc.) in terms of treatment adherence and outcomes. In addition, cash incentives also have a number of advantages compared to traditional approaches, such as:

- Reduced costs and time of distribution;
- With cash, patients can cover a wider spectrum of needs other than food
- Cash distribution can be monitored easily as long as it is implemented through modern transfer systems (bank transfers, by post)
- Less effort is required than in with in-kind support

### BACKGROUND

The Republic of Moldova is among the WHO European Region's eighteen high-priority countries for TB control and is one of the world's twenty-seven multidrug-resistant TB (MDR-TB) high burden countries. During 2007–2011, the loss to follow-up rates among patients on first-line anti-TB drug regimens were high, between 10–12%. Among MDR-TB patients, the loss to follow-up was even higher, at around

25%. To improve treatment adherence, a system of incentives for patients, all provided after hospital care, was introduced in 2009, and had reached countrywide coverage (with the exclusion of the region of Transnistria) only by the end of 2010. Different types of incentives ('small' cash, 'bigger' cash, vouchers for food/hygiene products, reimbursement for transport costs, other support) were provided in four different combinations. The incentive was stopped if treatment was interrupted for a maximum of five days during one month.

Since non-cash incentives are the most common form of patient support during the treatment, we intend to describe the advantages of cash incentives distribution in Moldova as we find it more convenient for the patients and less costly for the implementer/donor compared with traditional forms of support (food parcels, food vouchers, transportation tickets, etc.).

### METHODS AND RESOURCES

For a successful implementation of cash incentives distribution, the following conditions must be present with regard to implementation:

1. Rapid communication network (internet, fax) linking the implementing unit and the outpatient treatment facilities: in Moldova, the implementing unit is situated in the capital and links through internet to 50 TB cabinets all over the country.
2. Availability of a nationwide service allowing bank transfers to individuals: AFI is distributing remittances to TB patients through a commercial bank with national coverage. Currently in Moldova, the cost

of one transfer to a patient is \$0.16 USD. Postal services (money orders) can also be used for the same purpose.

3. A legal framework allowing the distribution of cash to TB patients without taxes.

The distribution process includes the following activities:

4. Setting up the implementation unit with standard office equipment, communication equipment, and necessary staff.
5. Establishment of a communication mechanism with outpatient TB

treatment facilities for permanent information exchange. The information includes lists of patients adherent to treatment who are supposed to receive incentives.

6. Selection of the money transfer operator (bank or post service) with a correspondent coverage in the area.
7. Distribution of cash incentives based on information received from the TB case managers.

Table 5.4.1. Type of incentives provided to tuberculosis patients registered for treatment, Republic of Moldova, 2011

Type of incentive	Patients n (%)
Total patients with incentives	1895 (100)
“Small cash”	888 (47)
Small and large sums of cash	319 (17)
Non-cash food vouchers	104 (5)
Combination of cash and non-cash	584 (31)
Total patients without incentives	483

Table 5.4.2. Treatment outcomes among new drug-susceptible tuberculosis patients, classified by incentives received, Republic of Moldova, 2011

Combination of incentives	Successful treatment n(%)	Treatment failure n(%)	Lost to follow-up n(%)	Death n(%)
Total with incentives	1801 (95)	40 (2)	38 (2)	16 (1)
“Small cash”	836 (94)	17 (2)	23 (3)	12 (1)
Small and large sums of cash	308 (97)	7 (2)	3 (0,7)	1 (0,3)
Non-cash (food vouchers)	96 (92)	4 (4)	4 (4)	0 (0)
Cash and non-cash	561 (96)	12 (2)	8 (1)	3 (1)
No incentives	280 (58)	11 (2)	87 (18)	105 (22)



## RESULTS

Our study, “Do incentives improve tuberculosis treatment outcomes in the Republic of Moldova?” suggests that cash incentives are more effective than other incentives in terms of treatment adherence and outcomes.

Using the cash distribution mechanism, a team of three members has the capacity to provide up to 3000 patients per year with monthly incentive distribution.

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## 5.5 Best Practice: Transition to outpatient treatment. Healthcare reform in Kazakhstan.

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### INTRODUCTION

The Republic of Kazakhstan (KR) is an independent republic located in Central Asia which occupies a region of 2.7 million km<sup>2</sup>. It is the largest republic of the former Soviet Union after the Russian Federation, and is ranked ninth in terms of size globally. The population of the country is over 17 million. The area includes 16 administrative units, 14 regions, and the cities of Astana and Almaty. The healthcare system is mainly public (80%).

Kazakhstan has a wide network of TB facilities. Currently, there are only 290 specialized TB medical units with 11,848 hospital beds, including the NTSPT (the National Center of Tuberculosis). In addition to the TB units, treatment of TB patients is also provided at primary care facilities.

While Kazakhstan has managed to improve the TB epidemiological situation in the last decade by reducing the incidence twofold and the mortality rate by four times, the prevalence of drug-resistant TB remains high. Multidrug-resistance is diagnosed in a quarter of new cases of TB, and half of patients have repeated treatment. In many ways, such high rates are explained by the widespread provision of TB services with express diagnostic techniques such as BACTEC and Hain-test, and in recent years, Xpert MTB/RIF.

Annually, countrywide coverage with drug susceptibility tests for TB patients exceeds 95%. This allows timely prescription of adequate therapy. For example, in 2012 at the domestic level, the WHO minimum standard for second-line drug coverage of MDR-TB patients was reached (86.9%) and, in 2013, the coverage was 99.6%.

The efficiency of MDR TB treatment remains fairly high. For example, with the 2011 cohort the rate was 74.2%. However, the analysis of all treatment outcomes of 2008-2011 cohorts showed a growing number of patients incompliant with treatment, from 4.4% to 7.6%. Despite positive changes in epidemiological rates as a whole, the incidence, including that of drug-resistant TB, remains high after all.

In this regard, in 2014, a Comprehensive Plan for Tuberculosis Control for 2014-2020 was launched on the country level. This plan was approved by a Decree of the Government and aimed to reduce the incidence of TB and TB mortality.

The comprehensive plan includes four strategic areas:

1. Enhancing inter-agency and cross-sectorial cooperation in tuberculosis control.
2. Modernizing TB services in Kazakhstan, including transformation of the financing system and expansion of outpatient care for TB patients.
3. Improving access to the modern, highly effective technologies for tuberculosis prevention, diagnosis, and treatment.
4. Enhancing the systems for infection control, monitoring, and evaluation of TB control activities.

The implementation of the TB service reform mission implies cutting 35% of current hospital beds (4 147) over three years. The greatest reduction (18%) is planned for 2016.

As part of the task for enhancement of the systems for infection control, monitoring, and evaluation of TB control activities, arrangements

are planned to provide 100% access to express tools of TB diagnosis, and to introduce special programs to improve patients' compliance (e.g., SPUTNIK program, "hospital at home," day center), including psychosocial support. It is also planned to ensure a complete supply of the second- and third-line drugs of guaranteed quality with introduction of individual treatment regimens and new drugs, including for patients from the penitentiary sector. Special attention will be paid to infection control at inpatient facilities for M/XDR-TB, and symptomatic and compulsory treatment. It is planned to ensure complete manpower support of the free experts for monitoring and evaluation in all respects of TB services and support of the bacteriological laboratories staffing.

Development of TB outpatient care will include the following areas:

- Developing financial flows, based on the treated case;
- Providing consistent and regular social support and psychosocial consultations; and
- Introducing technologies that substitute for hospital treatment (e.g., day center, "hospital at home," the SPUTNIK program).

Incentives for outpatient treatment will include the following:

- Every month about \$100 will be added to a patient's current bank card account as long as patient has a full intake of anti-tuberculosis drugs;
- Patients poorly tolerating anti-tuberculosis drugs will be treated at the day center with a once-daily meal in the amount of \$4;
- Mobile teams similar to the ones in the SPUTNIK program will be used for the most vulnerable groups of patients (5% of the total number of patients in outpatient treatment); and
- Food packages in the amount of \$50 will be given to patients treated under conditions substituting for hospital treat-

ment. The average number of packages per patient is 15 (9 months x 2 packages per month x 85%). The packages will be given every other week when there is full treatment compliance.

To date, the social support of TB patients is provided mainly in the form of a monthly funds transfer in the amount of \$100 to the bank account, in the form of free hot meals at the day center, or monthly travel tickets to DOT locations.

As part of the comprehensive plan implementation, a number of actions have already been taken:

- A road map for the KP implementation has been developed.
- A plan has been developed for transition of all domestic TB organizations to the right of economic jurisdiction.
- A plan of optimization and reorientation of the TB hospital beds has been developed.
- The financial flow of TB services is being improved.
- Regulations for hospital substituting technology are being developed.
- The "personal agreement of TB patient" form has been revised.
- A draft order to render medical care to the patients with TB/HIV co-infection has been developed.

The following results are expected by 2020 with development of outpatient treatment:

1. Cutting back hospital beds by 40%.
2. Cutting back TB beds by 20%.
3. Hospital stay duration decreased by 60% (down to 37 hospital bed-days).
4. Number of patients who start treatment on outpatient basis increased by up to 50%.
5. Provision of monthly social support for up to 90% patients on treatment.

## Session 6.

### 6.1 Best Practice: Successfully addressing treatment defaults with the Sputnik Initiative.

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*“MDR-TB is one of the most pressing health problems of our times. By some estimates, there are half a million new (‘incident’) cases of MDR-TB each year. It is an airborne disease and cannot be hidden away or ignored or declared ‘incurable.’ Curing extensively drug-resistant TB requires what can only be described as grueling treatment. We need new and better therapies: safe, effective, tolerable, and faster-acting. But the Sputnik experience shows us that when patients are the center of all of our efforts — when our attentions and resources revolve, like satellites, around them — we succeed, even though our treatments are imperfect. Cure rates are high if patients receive, each day, the medicines and the social support required to complete therapy”.*

— Paul Farmer

#### BACKGROUND/PROBLEM STATEMENT

PIH started its collaborative work in Russia with Tomsk TB services in 1998 in both prison and civilian sectors. Using funding from the George Soros Open Society Institute (and later from the late philanthropist Tom White), the first MDR-TB patient was enrolled in treatment in 2000. Starting with the most disadvantaged cohort — prisoners suffering from MDR-TB — the program was eventually expanded with support from the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) to all MDR-TB patients in the whole oblast, including those living in remote villages. At that time in Tomsk, the TB system was organized around the prolonged hospitalization of

patients, viewed as the only way of ensuring adherence to treatment. Ironically, the overcrowded and underfunded hospitals became a primary source for transmission of MDR-TB.

PIH suggested an alternative approach to improve adherence and stem transmission: by strengthening ambulatory treatment and providing comprehensive accompaniment, including social support, throughout the whole course of therapy, patients would be able to receive care in the communities where they and their families lived. The home treatment program in Tomsk City was expanded and a number of small “home visit” teams were organized in rural centers. Patients were offered monthly, and then daily, food packages to support their treatment.

However, in 2006, the number of patients unable to adhere to treatment was increasing. The situation was the worst in rural areas. Local physicians expressed concern that this group of patients had “social problems,” were “irresponsible,” and difficult to treat. Most were ex-prisoners, patients who had been discharged from hospitals because of behavioral issues, and patients with addictions to alcohol and drugs. Many patients were also unemployed, isolated, and without sufficient family and social support. The general view was that treating them successfully would be near impossible. Without a comprehensive support system to ensure the proper delivery and intake of medications, these patients remained uncured and thus not only stayed sick themselves but were a source of MDR-TB transmission that imperiled their communities.

## METHODS AND RESOURCES

In 2006, PIH and Tomsk Oblast Tuberculosis Services launched the “Sputnik” Initiative, a model of intense patient-centered accompaniment (PCA). Sputnik aimed to provide missing

social support by creating a network of care for patients that would not only increase their rates of adherence to treatment but also reduce transmission of TB infection in their communities and improve quality of life for everyone.

Program nurses were trained to become “sputniks” themselves — satellites that revolved around their patients throughout their long and difficult recovery.

At the beginning, comfortable working conditions were created for the Sputnik team and were supplied with everything needed for their work (Table 6.1.1). Sputnik is a relatively inexpensive operation in terms of supplies. The costliest item is a four-wheel-drive vehicle, necessary to help staff to track down and locate patients throughout Tomsk year-round, including when the roads are snowy, muddy, and flooded. A mobile phone is also essential for locating patients and arranging rendezvous points. Nurses are also equipped with some form of personal safety device, such as a can of pepper spray. The staff also has respirators.

Table 6.1.1. Social and clinical characteristics of Sputnik program patients (N = 138) compared to other Tomsk city patients (N = 3265) receiving TB treatment between December 17, 2006 and December 31, 2012.

Patient's characteristics	Sputnik, %	Others, 100%	p
Unemployed	82.6	53.3	<0.001
Previously incarcerated	38.4	19.5	<0.001
Previous default	6.5	1.0	<0.001
Homeless	10.1	8.2	0.427
Chronic alcoholism	80.4	30.0	<0.001
Drug abuse, before or during the treatment	35.5	7.9	<0.001
Hepatitis	45.6	17.9	<0.001
HIV – infection	4.3	2.5	0.193
Newly diagnosed (first treatment course)	30.4	69.5	<0.001
Smear/culture positive at the treatment start	96.4	64.2	<0.001
MDR-TB	75.4	27.2	<0.001

a flashlight, a medical bag with basic supplies, containers for sputum collection, and a cold pouch for transporting the samples.

At the beginning of the program in 2006, all staff members were trained on the basis of the “Harm Reduction – Tomsk” initiative with a focus on making contact with IDUs, motivational counseling, prevention of opiate overdoses, etc.

The Tomsk City TB Clinical Committee referred the most challenging and “difficult to treat” patients to Sputnik.

The following details the Sputnik enrollment criteria:

- Patients are taking less than 75% of their prescribed doses, per month
- Patients who refuse to start or continue treatment
- Previously treated patients with a history of a default
- Household members of the Sputnik patients

Patients were referred to the Sputnik program after all standard options were exhausted and could be enrolled in the program at any point during their treatment if they were deemed to be at a high risk for default.

Through this approach, Sputnik shifted the onus of responsibility for adherence from the patient to the program team. This shift marked an important change in moral orientation: rather than being seen as “defaulters” or “treatment failures,” patients who were unable to take their medicines became programmatic challenges for which a programmatic solution could be found.

## **BASIC PRINCIPLES OF THE SPUTNIK INITIATIVE**

### **Deliver directly observed TB therapy at the patient’s home or any other location.**

All medications are taken under direct supervision of the Sputnik team. Care is offered to every patient, at any place and at any time, wherever it is most convenient for the patient.

### **Search for patient if he/she is absent from scheduled meeting location.**

The team — nurses and driver — communicate with the patient to agree on a location and time to meet for medication. If a patient refuses to meet, the Sputnik team asks why and attempts to convince the patient to take his/her medicines at any point during the day. If no agreement is achieved, other project staff — social workers, psychologists, alcohol/drug addiction specialists, or supervisors — are contacted for support and help.

If the patient still has not been located, the team visits the next patient but keeps trying to locate the missing patient by calling relatives and friends. If they are unsuccessful, the team returns to the initial meeting place and starts looking for the patient at all known locations within his/her social network.

### **Provide nutritional support in order to motivate patients to continue treatment.**

In order to identify and address patient’s social needs and increase patients’ motivation and adherence to treatment, the Sputnik team conducts a survey to learn of the patients’ social and nutritional needs. Using the findings, a daily menu for nutritional support is developed. Each day patients receive food and support after taking the complete dose of the treatment regimen. Some common food items include canned meat or chicken, canned vegetables, pasta, and condensed milk, among others. For a majority of patients, the nutritional support provided might be the only meal they have other than bread and alcohol.

### **Establish trustworthy, open relationships with patients and their families, friends, and neighbors.**

PIH’s main selection criteria for the Sputnik team are the ability to listen, the presence of compassion, and the desire to help. Patients acknowledge the importance of strong relationships with the Sputnik team and say that their attitude toward treatment and life hinges on this relationship. Project staff are trained to understand the principle that “there are

no bad or dysfunctional patients — there are patients with specific psychological and social needs which we cannot always understand.”

### **Deliver additional medical, psychological, and social support by connecting patients with local resources.**

The Sputnik team is trained to identify and assist with any unique non-medical needs that might pose as a barrier to treatment. This could include providing goods such as hygienic sets, cold weather clothing, or hot plates, or helping patients renew passports or get a state disability allowance. Timely diagnosis and management of adverse reactions is also important in order to minimize the risk of treatment default. Some drugs used in treating MDR-TB carry the potential for severe adverse effects, including psychiatric disorders, kidney failure, liver toxicity, hearing loss, and others, which might result in patient refusing treatment. The Sputnik team is trained to closely monitor and detect such effects, and they work closely with physicians to tailor treatment regimens to mitigate such risks.

### **Create real-time action plans.**

To promote information sharing and ensure everyone is abreast of emerging challenges, a mandatory weekly meeting is held for all

Sputnik staff. Patient problems are discussed and further plans of action are developed to properly address them. From time to time, psychologists, substance abuse specialists, and social workers who collaborate on Sputnik are invited to attend these meetings.

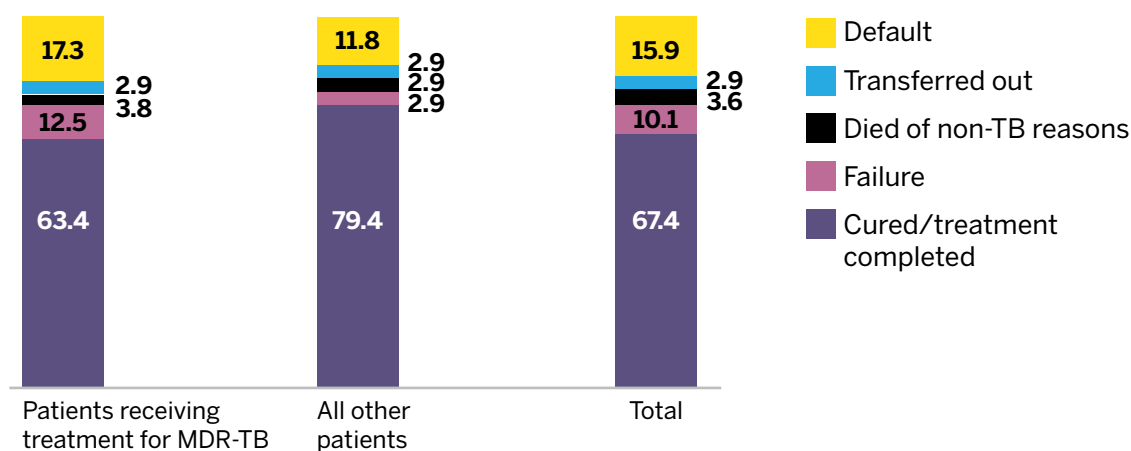
## **RESULTS**

During the first five years of the project (November 18, 2006 – December 31, 2012), 138 patients were included in the Sputnik program. 82% of them were unemployed and 38% were previously incarcerated. Among the patients referred to Sputnik, chronic alcoholism and drug addiction were 2.68 and 4.5 times more likely, respectively, as compared to the rest of the patient population. The majority of the Sputnik patients were smear/culture positive at the treatment start (96.4%) and had MDR-TB (75.4%) (Table 6.1.1). Treatment outcome for all Sputnik patients and depending on the DR is seen in Graph 6.1.1.

## **INNOVATION**

The Sputnik Initiative is a highly innovative program because it demonstrates that treating vulnerable patients with social and behavioral challenges is possible through comprehensive social and psychological support. Successfully

Figure 6.1.2. Patient adherence to treatment, calculated as the proportion of doses taken over the total number of doses prescribed, increased from 59.8% prior to enrolment to 78.5%.



Outcomes of the patients enrolled in Sputnik program between December 17, 2006 and December 31, 2012.

treating patients at high risk of default is exceptionally difficult. It requires strong programmatic commitment and innovative approaches. In many public health circles, people suffering from substance abuse, former prisoners, and the homeless are considered “impossible” to treat for TB and its drug-resistant forms. Sputnik, however, has demonstrated that treatment in this patient population is feasible so long as a well-established referral system is in place and daily, comprehensive accompaniment is provided throughout the entire duration of treatment. Sputnik further demonstrates that by treating these at-risk patients, it is possible to improve treatment outcomes, and lessen the prevalence of drug-resistant strains in particular geographic regions.

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## 6.2 Best Practice: Piloting patient-centered accompaniment (PCA), an example from Mogilev Oblast, Belarus.

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### BACKGROUND

Positive changes in TB epidemiological rates were observed for the past five years (between 2009-2014), in accordance with the data of the national registration system. The TB incidence in the Belarus Republic has decreased by 26.5% – from 45.9 to 33.8 per 100,000 population. However, there are two main implications from reducing the number of TB unit beds for the sake of cost-effectiveness:

- The risk of potential decrease of TB services funding, as at present TB services are funded in accordance with the number of beds; and
- The absence of developed mechanisms to provide continued funding for primary care medical staff, and the provision of social supports needed for patients at the outpatient stage of treatment.

Following a scientific practical conference held in November 2014 (supported by the WHO Regional Office), the decision was made to pilot a project that would change the TB financing model to follow an example from Estonia. The pilot TB financing model would use funds saved through the reduction of TB

hospital beds to encourage medical staff to perform outpatient DOT in remote rural areas.

The Project for Piloting Outpatient Directly Observed Treatment was implemented in April 2014 in accordance with MOH regulations. The session of the Mogilev Regional Parliament passed the decision On Using Regional Budget Funds in 2014 for Payment of Medical Worker Incentives Involved in the Implementation of the Pilot Project, "Directly Observed Treatment of TB Patients on an Outpatient Basis." The project was funded by monies saved through cutting 5 beds from the Mogilev Regional TB Dispensary.

### METHODS

A Ministry of Health working group, with consulting support from the WHO Regional Office for Europe, developed guidelines for the referral of patients discharged from TB hospitals. The group also developed standard agreement and reporting forms for incentive payments made to medical staff in the primary health care system who were performing DOT. Incentive payments were USD \$1 for each TB patient who visited the clinic and received DOT, and approximately USD \$4 for each visit to a TB patient's home, considering the additional time and

transportation costs involved. These payments are much lower compared to the costs of a patient's hospital stay, which was about USD \$27 per day in the Mogilev TB Dispensary.

Additionally, to improve the financing model for outpatient treatment, the pilot project helped to strengthen the health care system, since the additional funds were re-allocated for the targeted support of peripheral units of the primary medical services. The pilot project also contributed to the satisfaction of the medical staff of the primary medical services due to the compensation for their extra efforts in the organization of directly observed treatment. In addition, patients react positively to early transfer to outpatient controlled treatment.

## RESULTS

Outcomes of the pilot project in Mogilev Region for 2014 are as follows: 13 patients were included in the pilot project. Of these, four had drug-susceptible tuberculosis (received six months of treatment), and nine had drug-resistant tuberculosis (receiving 18-24 months of treatment). As of December 2014, three patients had completed treatment for new cases with no defaults. Treatment efficiency for pulmonary TB patients improved in the Mogilev Region where the pilot project was implemented. Thus, successful treatment outcomes for new pulmonary TB patients, as per the data of cohort analysis for nine months of 2012, were achieved in 62%

of patients and for nine months of 2013 in 70% of patients. The motivation of medical staff to provide directly observed outpatient treatment also increased: extra payments increased from US \$40 to US \$120 per month. The budget savings from April-December 2014 was US \$11,000.

Information about the progress of the pilot project was presented at a meeting in the Ministry of Health. The decision of the Ministry of Health board recommended dissemination of the pilot program experience to all regions of the Republic and to at least one district in each region. In 2015, the Health Department of Mogilev Regional Executive Committee plans to implement the pilot program measures in two additional districts, Bobruysky and Osipovichsky. The support for dissemination of this project in 2016-2018 is also planned within the application submitted to the Global Fund.

## CONCLUSION

The increase in satisfaction both of primary care medical staff, due to additional financial incentives, and patients, due to earlier discharge from the hospital, was noted. In addition, during the project implementation there were no defaulters among the most vulnerable and difficult category of patients, those with alcohol addiction living in remote rural areas.

## 6.3 Best Practice: Targeting patients from risk groups. Migrants and Roma population, example from Bulgaria.

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### INTRODUCTION

The experience of the Bulgarian Ministry of Health gained under the Global Fund (GF) funded grant BUL-809-G03-T, “Strengthening the National Tuberculosis Programme in Bulgaria,” is a best practice to be shared with other countries that shows an innovative way of engaging resources among risk group populations to reduce TB transmission.

Over the past several years, the investments were targeted towards engaging local NGOs, extending the ability of the National Tuberculosis Program to undertake active screening, and case finding within risk group populations. There is an exceptionally close relationship between health services and NGOs, resulting in a significant increase in screening and contact tracing.

Bulgaria is situated in southeast Europe on the eastern part of the Balkan Peninsula. The country has borders with Romania to the north, Serbia and the Former Yugoslav Republic of Macedonia to the west, and Greece and Turkey to the south. The Black Sea is a natural border to the east. Bulgaria covers an area of approximately 111,000 square kilometers, and has a population of over seven million inhabitants. It is among the twenty-seven countries designated by the WHO as having a high burden of multidrug-resistant tuberculosis (MDR-TB).

With the support provided by the GF in Rounds 6 and 8, since 2013 Bulgaria has increased the detection rate of new TB cases to 91%. In 2013, the total number of TB cases notified in Bulgaria was 1,932 (26.5 per 100,000 population). In the last five years, the TB notification rate has steadily declined by ten points.

The program funded by the GF, “Strengthening the National Tuberculosis Programme in Bulgaria,” has been implemented with effective collaboration between the Ministry of Health and a large network of NGOs, especially through outreach services to support access to health care and the provision of quality services for key populations (i.e., TB and MDR-TB contacts, prisoners, Roma people, migrants, refugees and asylum seekers, street children, and others). The efforts to unite medical experts, social workers from the NGO sector, and community representatives in the prevention, diagnosis, treatment and control contributed to decreasing the incidence TB. The main goals of the GF funded TB Programme are as follows:

- To reduce the burden of tuberculosis in Bulgaria by reducing the national TB incidence rate, and increasing the national TB treatment success rate; and
- To sustain implementation of the NTP through the high-quality TB diagnosis, treatment, and improved control of MDR-TB.

Under the GF Round 8 TB Programme, more than 20 NGOs implemented activities among refugees, asylum seekers, migrants, and the Roma population. Best practices for TB prevention and control activities, implemented by NGOs and financed by the Global Fund, are as follows:

1. Mapping the regions and the TB endemic areas
2. Outreach work among risk groups: screening, consulting, referral to TB

facilities; accompaniment to TB facilities; distribution of informational-educational materials

3. Support for the TB facilities: motivation for sputum collection; tracing of diagnosed patients who have left the TB facility; support in the continuation phase of treatment; contact tracing; and support in follow up of chemoprophylaxis
4. Organization and conduct of informational-educational campaigns in the communities

## METHODS AND RESOURCES

Refugees and migrants are at increased risk of developing TB and having poor access to TB care and control services. Factors such as malnutrition and overcrowding in camp settings further increase the vulnerability of these populations. Health care is provided mainly by humanitarian agencies, including nongovernmental organizations (NGOs). As a result, NGOs are crucial implementing partners for TB care and control in Bulgaria. In 2014, there were seven refugee reception centers and two detention centers for illegal migrants. In 2014, more than 6,000 Syrians and more than 2,900 refugees from Afghanistan applied for refugee status. The collaboration activities

between NGOs, health facilities, and staff is a key strategy for providing regular outreach work: screening, counselling, motivation, medical examination, supporting the patients during the active and continuation phase, etc.

The primary strategies to address migrants, refugees, and asylum seekers regarding TB prevention and control involve:

1. Early detection of TB through a specifically designed questionnaire. The NGO outreach work teams include key community workers from the target groups to overcome the language barrier. The TB prevention activities supported by the NGO teams are performed through protection and promotion of their human rights.
2. Establishment and functioning of a network between the NGO outreach team, the patronage nurses from the TB facilities, and staff from the reception centers for refugees. Within all regions with refugee centers, TB activities are assigned to the NGO staff. The NGO staff is supported by the local TB facility through inclusion of the nurse during outreach visits.
3. Health promotion and TB awareness – distribution of specially designed

Table 6.3.1. Collaboration between TB Health Facilities and NGOs in Bulgaria within “Open Doors” Campaign, 2009-2013

Year	Number of people screened for the risk of TB	Number of people examined and consulted	Number of people diagnosed with active TB	Number of people with LTBI
2009	11,557	7,920	120	339
2010	20,217	13,149	181	820
2011	19,048	12,528	215	705
2012	11,994	7,578	176	335
2013	5,197	3,814	62	267
Total	68,013	44,989	754	2,466

informational and educational materials in Arabic and English.

4. Selection and training of medical specialists, outreach workers, and people from the community who participate in TB control among the risk groups.
5. Assistance and support for adherence to treatment of patients from these communities, especially in the continuous phase, as well as referral of TB contacts.

## THE ROMA COMMUNITY

Roma community members (about 10 % of the Bulgarian population, according to civil society estimation) are overrepresented among the TB patients in Bulgaria. Hiring outreach workers from their own community is recognized to facilitate contact with this population, as well as increase detection of suspect cases, timely diagnosis in TB treatment facilities, and the rates of successful treatment during the ambulatory phase. TB activities are implemented within 15 municipalities throughout the country. Community-based service delivery is performed in partnership with the local TB health facilities. Outreach workers provide a wide range of community-based services, such as: mapping of subgroups at high risk of tuberculosis; administration of questionnaires for identification of risk of TB infection; referral and accompaniment to local/regional health facilities; provision of information for TB and health services; motivation for early treatment; TB patient contacts tracing; motivation for medical check-ups of TB symptoms; support for TB patients and their families during the treatment; and stigma reduction towards TB within the community. The main approaches involve:

- Establishing and operating eight centers for health and social support within the Roma community;
- Referring the TB suspects from the community for testing, with the help of trained outreach workers from the Roma community;
- Engaging of local health facilities in TB activities through “open doors”

campaigns ensuring access to all patients for check-up and screening for TB;

- Strengthening health care provider capacity through regular trainings;
- Distributing information, education, and communication to increase public awareness about TB prevention and control;
- Reaching out to representatives of the community to bring positive change in public attitude to the provided services for prevention, treatment and care, related to the distribution of specially designed informational and educational materials about TB. The existing stigma toward patients with TB is one of the biggest obstacles against open conversations, help, and health care seeking behavior in the Roma community. Therefore, reducing the stigma and discrimination against people living with tuberculosis is a priority in the mass campaign, in community work, and in patients' consultations in health services.

## RESULTS

Results are summarized in Table 6.3.1.

## CONCLUSIONS

This collaboration with the NGO sector and with representatives from vulnerable communities shows how to increase the number of people reached through active TB screening, and is an example of an effective way to change the behavior of TB patients towards successful treatment. The Global Fund's support allowed Bulgarian NGOs to raise their profile and become respected members of the national programme working to combat TB. NGOs are involved in ensuring that affected communities receive adequate TB care and support. Travelling by nurses and outreach workers to remote and isolated communities has allowed TB rates to be reduced in those problem areas particularly. Nationally, the result has been the halving of TB incidence rates in the country.

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## Session 7.

### 7.1 Best Practice: Treating patients with MDR-TB in prisons, example from Azerbaijan.

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#### INTRODUCTION

High rates of drug resistance are common in penitentiary facilities, specifically in the Former Soviet republics. Regardless of penitentiary conditions considered to be perfect for the implementation of TB control activities, the rates of successful treatment of drug-resistant tuberculosis in prisons are typically extremely low.

#### METHODS

The Azerbaijan Penitentiary System (APS) is comprised of twenty-five facilities, including two hospitals. The rate of imprisonment equals 180 per 100,000 population. Since 2007, all patients with drug-resistant tuberculosis (DR-TB) detected in the penitentiary system have been enrolled in individualized treatment with second line anti-TB drugs. Prior to December 1, 2014, 736 DR-TB patients were enrolled in treatment, and 482 of them completed treatment.

By the time treatment begins, each patient has results available from smear microscopy, culture, and drug susceptibility testing to first and second line anti-TB drugs. All laboratory tests are performed at the Specialized Treatment Facility (STF) Laboratory certified by the Supranational Reference Laboratory in Borstel, Germany.

Since January 2013, Xpert MTB/RIF has been a part of the diagnostic algorithm to enroll

DR-TB patients in treatment within a few days after TB detection. Individualized regimens are designed based on DST results and World Health Organization (WHO) DR-TB management guidelines. Treatment monitoring and evaluation are also performed in compliance with WHO guidelines. Patients take anti-TB drugs under direct observation, six times a week, during the entire treatment. All patients are hospitalized to the Specialized Treatment Facility for the entire treatment, where they are provided with high-calorie meals and additional incentives such as food and hygiene packages. The Specialized Treatment Facility utilizes strict infection control measures, including assigning patients to different departments based on the results of smear microscopy, culture, DST, treatment phase, and detention regime determined by the court. All patient rooms are equipped with UV light lamps and hospital departments are equipped with a negative pressure ventilation system. Patients and physicians are provided with personal protective equipment such as masks and respirators.

All TB control activities are performed in compliance with TB Control Program Guidelines in the Azerbaijan Penitentiary System, which have been developed and revised according to current WHO requirements. Particular attention has been given to the training and education of medical and



non-medical staff of the penitentiary facilities, and a Training Center for TB Control in Prisons has functioned since 2012 for this purpose. In 2014, the Training Center was designated as a WHO Collaborating Center on TB prevention and treatment in prisons.

The TB control program is funded primarily from the budget of the Azerbaijan MoJ. Since 2007, the program has also been supported through the Global Fund to Fight AIDS, TB and Malaria for investment in diagnostic innovations, infection control strengthening, and DR-TB treatment with an emphasis on continuing treatment of patients after they are released from prison. Since 2011, a nonprofit organization has supervised continued treatment of patients released from prison, which has contributed to the high rates of successful treatment.

## RESULTS

As a result of proper implementation of the WHO recommendations for TB control, DR-TB incidence and TB burden have significantly decreased among patients in the penitentiary system.

The rate of successful treatment in the 2011 patient cohort was 80% (Figure 7.1.1).

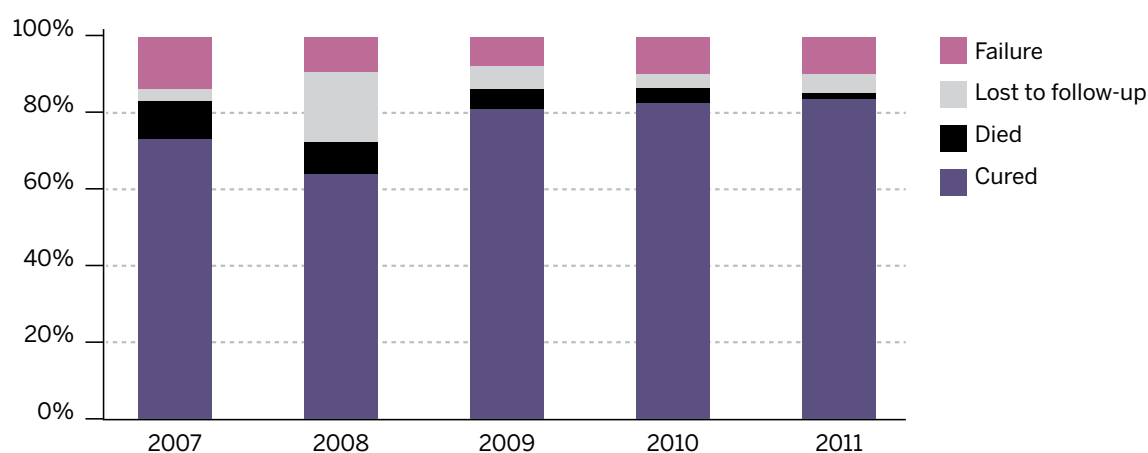
Successful implementation of the TB control program in the penitentiary system has

also been reflected in the Green Light Committee monitoring mission reports and NTP Review mission report with an emphasis on the decreased number of TB cases, an exceptionally high rate of successful treatment in DR-TB and non-DR-TB patients, and infection control measures. The program's success was published in "The Consolidated Action Plan to Prevent and Combat MDR- and XDR-TB in the WHO European Region" and "Best Practices in Prevention, Control and Care for Drug-resistant TB." Additionally, the Program was given an award in 2013 by the International Corrections and Prisons Association for health care in prisons. For the last several years, about 100 representatives from 10 countries, including all countries of Central Asia as well as China, the Philippines, Iraq, Belarus, and Moldova, have visited Azerbaijan to learn from its experience with the TB control program in the penitentiary system.

## CONCLUSIONS

The experience of the Head Medical Department of the Azerbaijan MoJ suggests that early and rapid diagnosis, initiation of the correct therapy, and support during treatment leads to higher cure rates and a reduced TB burden within the penitentiary facilities.

Figure 7.1.1. Treatment results for drug-resistant TB patients enrolled in treatment with second line anti-TB drugs in the Azerbaijan penitentiary system between 2007-2014, %.





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## 7.2 Best Practice: Interagency collaboration between penitentiary and civilian TB control services, example from Tomsk, Russia.

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### INTRODUCTION

The problem of widespread disease spread by social contact, including tuberculosis (TB), requires innovative approaches to prevention and treatment. In Tomsk Oblast, Russia, up to 65% of all TB patients are from poor and socially marginalized populations, and 10% have a history of previous imprisonment. In Russia, about 25% of TB patients released from prisons require continuation of TB treatment; they are referred to the civilian sector as “transferred out.” Uncontrolled migration of TB patients to and from the penitentiary system and civilian sector provides conditions for transmission of infection, poor treatment outcomes, and further development of drug-resistant TB.

Integration of the civilian and penitentiary TB services is an essential component of the Unified TB and MDR-TB Control Program in Tomsk Oblast, Russia. The WHO-recommended strategies to combat TB and MDR-TB (DOTS and DOTS-Plus programs) were launched in Tomsk in 1994 and 2000, respectively, with support and in close collaboration and support from international nonprofit organizations: MERLIN (UK), Partners In Health (Boston, MA, USA), and PHRI (New York, NY, USA). In 2000, the MDR-TB Treatment Program in Tomsk Oblast was approved by the WHO Green Light Committee

to access quality-assured second-line anti-TB medicines for MDR-TB for 630 patients. In 2004-2013, the Tomsk TB and MDR-TB Program was financially supported by the Global Fund to Fight AIDS, TB and Malaria (GFATM) grant.

### METHODS

Integration is based on a series of principles: TB services administration provided by the Coordination Interagency Committee, centralized distribution of TB drugs, ongoing information exchange, continuity in patient treatment, extensive psychological and social support, and a unified TB reporting system. A coordination protocol between civilian and penitentiary TB Services on patient management was developed and applied, and included the following stages:

#### Stage 1. Public health education of the patient prior to release

The TB prison colony of the Tomsk Oblast Department of the Federal Service of Corrections has created an infrastructure where medical staff, along with psychologists, administrative and operations staff, contribute to improving the TB epidemiological situation. Two months prior to release, the patient starts to be involved in mandatory individual activities called “school for inmates to be released,” where correctional facility TB

doctors explain to patients that they need to get registered at the TB dispensary and continue treatment after being released.

One month prior to release: Counseling is provided by a penitentiary system psychologist and civilian social worker from TB Services to discover any issues the patient may face after release and to assess if the patient is willing to continue treatment. A civilian sector TB doctor evaluates the epidemiological risk of the patient being released. If the patient is willing, he is asked to continue treatment in one of the treatment facilities (TB hospital, day care hospital, treatment at home services, and outpatient treatment). A social worker informs the patient about assistance the patient can be provided with upon release after being registered to continue treatment, including ID renewal, social support (food packages, clothing, a public transportation pass, employment, and residence registration assistance), legal support, and psychological support. The patient is given the opportunity to sign an agreement stating that he has to visit TB Services within 10 days.

### Stage 2. Organizational planning

One month before release, a list of patients to be released is transferred from the penitentiary system to civilian TB Services, including information on possible places of residence and relative contacts. Civilian TB Services district nurses verify this information within 3 days. If they fail to verify, the Department of Correctional Services is contacted in order to update the information.

### Stage 3. Activities during patient's release from prison

If immediate hospitalization is needed upon release, patients are transported to a TB hospital by a civilian TB Services medical vehicle. Within 3 days after release, the Department of Correctional Services provides a hospital discharge summary, TB-01 Form, and x-ray results to civilian TB Services. Hospital discharge summary data are entered to the register of TB patients transferred from the Department of Correctional Services, and immediately sent to TB facilities of Tomsk city or rural areas in

the place of the patient's residence. A plan for continued observed treatment is made, including treatment site and post-treatment follow up.

### Stage 4. After release from prison

During the first visit to TB Services, the patient receives food package incentives (worth USD \$10.00). The patient continues his treatment regimen designed in prison or, based on the patient's status, the treatment regimen is adjusted. In ambulatory facilities, daily food packages worth \$2.50 are provided to patients as incentives for taking all daily TB drugs. Data on patient's treatment progress are entered into an electronic database monthly. Released patient treatment outcomes are sent on a quarterly basis to the Department of Correctional Services.

## RESULTS

Treatment outcomes in 467 MDR-TB patients who started treatment in 2000-2009: 305 (65.3%) cured; 28 (6.0%) treatment failure; 13 (2.8%) treatment default; 40 (8.6%) died; and 117 (25.1%) patients were released from prison prior to treatment completion. Out of 117 MDR-TB patients, 105 were released to reside in Tomsk Oblast. Of them, 90 (85.7%) continued treatment and 15 (14.3%) failed to continue treatment. Treatment outcomes among all 105 released patients: 20 (19.0%) treatment default; 61 (58.1%) cured, including 5 new patients admitted to the correctional facility; 4 (3.8%) treatment failure; 4 (3.8%) died, including 3 patients who died of non-TB causes (injury, poisoning). Of 12 patients who were released and transferred out of Tomsk Oblast: 7 (58.3%) failed to continue treatment; 5 (41.7%) continued treatment; 3 (25.0%) treatment default; and 2 (16.7%) cured. Final treatment outcomes of 467 MDR-TB inmate patients, including those released: 368 (78.8%) cured.

Out of 1,081 MDR-TB patients who started treatment in the civilian sector in 2000-2009, 22 (2.0%) were arrested prior to treatment completion. Of these, 19 (86.7%) continued treatment and 3 (13.3%) failed to continue treatment. Treatment outcomes: 14 cured, 4 treatment failure, and 1 treatment

default in prison. In total, of 22 MDR-TB patients transferred from the civilian sector to prison, 14 (63.6%) were cured.

## CONCLUSIONS

Tomsk Oblast has implemented an effective system of collaboration between civilian and penitentiary TB Services for TB detection, treatment, and prevention. Through well-developed integration, the rate of patients released from prison and registered in civilian TB facilities has increased from 53.9% (in 1999) to 83.1% (in 2012). The number of treatment default cases has significantly declined and treatment effectiveness has increased. The Tomsk Oblast correctional system is no longer a source of TB infection for the civilian population, which has been proven for the last 10 years. Psychological and social support, along with food packages provided to patients every day once their daily TB dose has been taken, is a foundation to ensure patient adherence to continued ambulatory treatment. Between 2000 and 2014, the TB epidemiological situation improved. For example, TB rates decreased (per 100,000): TB mortality – 4.7 times (from 21.9 to 5.0), TB prevalence – 2.6 times (from 224.7 to 86.3), and TB incidence – 1.7 times (from 116.7 to 66.1).

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## 7.3 Best Practice: Follow-up on TB patient treatment after release from prisons, example from Azerbaijan.

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### INTRODUCTION

In 2011, Saglamliga Khidmat (SK), a public union (translated as “Support to Health”) and a national non-governmental organization (NGO), was selected as a subrecipient on a Global Fund Round 9 TB grant to implement the “Treatment Follow-Up after Release from Prison” project as one of the components of the program entitled “Strengthening TB Control in the Penitentiary System.” The project contributes to progress towards ensuring that ex-prisoners with drug-sensitive TB and drug-resistant TB have full access to continuation of treatment after their discharge from penitentiary facilities.

The objective of this patient support project is to ensure that all TB patients released from prison without completing their TB treatment are provided with continuation of treatment with appropriate follow-up until end of treatment at civilian anti-TB facilities (NTP, TB dispensaries, DOTS Centers), and thus reduce the burden of tuberculosis in Azerbaijan.

Tuberculosis (TB) is a current public health problem and remains the most common cause of mortality from infectious disease worldwide and in Eastern Europe. Azerbaijan is among 27 countries with the highest rates of multidrug-resistant tuberculosis (MDR-TB) in the world.

The treatment adherence rate was very low in the years before the project started. Each year between 1998 and 2010, about 100-120

people were released from prison facilities while still sick with TB, joining the civilian population and spreading TB all over the country by discontinuing their TB treatment after discharge from prison. Twenty percent of these former prisoners had MDR-TB.

The released TB patients belong to a very specific and vulnerable population. The majority are drug users and alcohol consumers, illiterate, and often very aggressive in nature. Therefore, they need social and psychosocial support, guidance, control, and care after release from prison. TB treatment in this group needs to be followed up until the completion of their chemotherapy course.

### METHODS AND RESULTS

The implementation of the post-prison treatment follow-up project started in March 2011 by SK with the support of the main medical department at the Ministry of Justice (MoJ) of the Republic of Azerbaijan. In order to tackle treatment interruption problems, needs were assessed and motivational tools were identified and designed through effective involvement of the NGO.

This active involvement in the follow-up of MDR-TB patients has dramatically improved treatment adherence and success rates among released prisoners in Azerbaijan. NGOs play a valuable role in providing psycho-social care, working closely with



patients and their family members, and providing incentives and enablers.

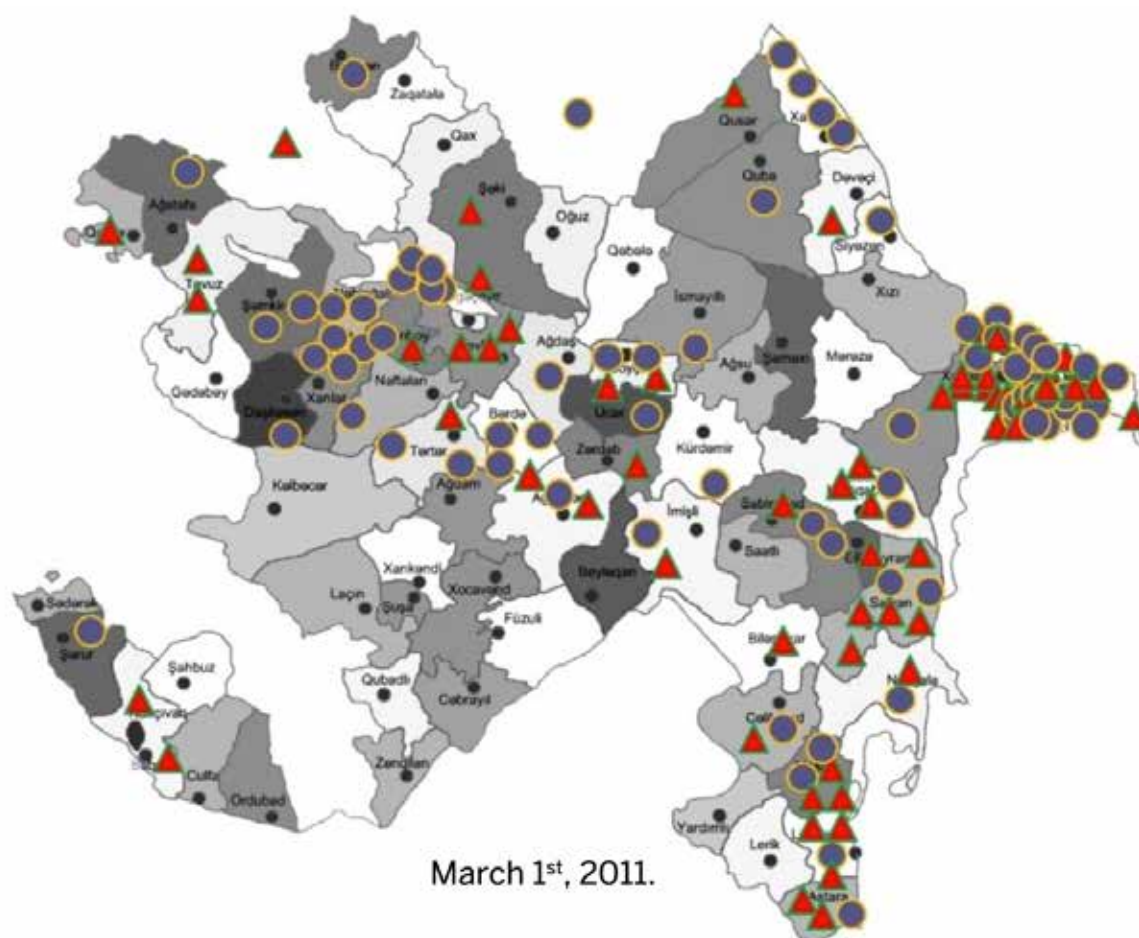
Since the project started (2011-2014), 428 TB patients (276 DS-TB and 152 DR-TB) were enrolled in the project. All were transferred out to civilian TB facilities and followed up by SK personnel and assisted in completing their treatment.

The patient support project was innovatively designed by taking into account all barriers that influence treatment adherence. The project places a special emphasis on strengthening adherence to TB treatment by identifying the factors that lead to treatment interruption among ex-prisoners. For instance, patients

were in need of social and consultation support by adherence counselors during the three months prior to release from prison. Once released, monthly food packages and daily transport fees motivate patients to arrive at DOT centers to take their medication. Incentives should be given to DOT supporters, in recognition that these patients need more attention from medical personnel.

The project activities were divided into two phases: activities that need to be carried out in the prison TB facility before the patient leaves prison, and activities in civilian TB facilities after release from prison.

Figures 7.3.1 Phase 1 (Before release) of Enhancing Treatment Adherence through involvement of community based organizations in the follow up of ex-prisoners project



### Phase 1 activities:

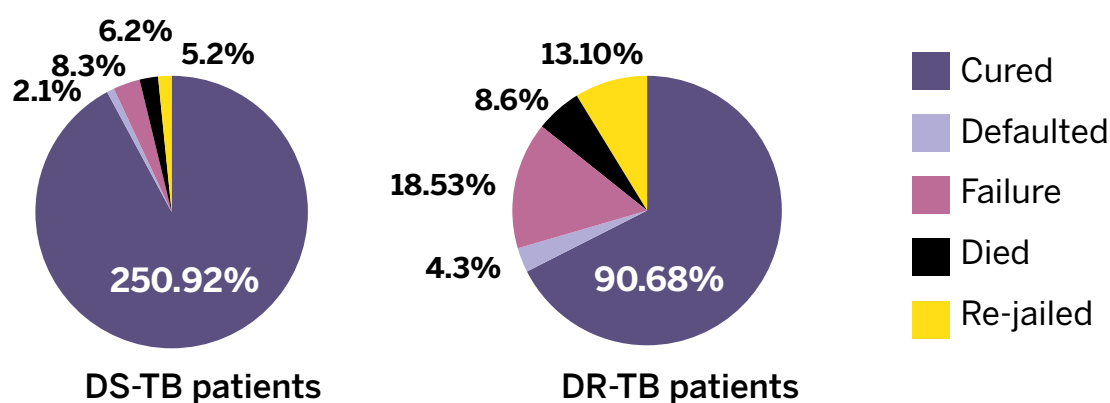
- The adherence counselor prepares a list of to-be-released patients three months prior to release
- Education and counseling sessions are conducted twice a week until the patient is released
- Collection of all information, both medical and non-medical, including all available telephone numbers of family members, relatives, and friends in order to trace the patient when needed
- All information is shared with the SK coordinator responsible for organizing and followup of treatment follow-up after the patient is discharged from prison
- Preparation of an envelope that contains the addresses of all TB facilities in the country, with the names of responsible DOT supporters, contact phone numbers, a health education brochure, copy

of epicresis, TB9 transfer form, and SK contact information.

### Phase 2 activities

- Upon receiving all information from the prison adherence counsellor, the SK coordinator contacts the NTP and defines the DOT center where each patient will continue his treatment after release
- Each patient's TB drugs are delivered to the DOT center so that he continues his treatment as soon as he is transferred from prison to the civilian TB facility
- Patients receive a monthly food parcel and a daily transport fee to motivate them to arrive at DOT centers every day for drug intake with the goal of improving treatment adherence
- DOT supporters are provided monthly incentives to help them to take good care of ex-prisoners who are usually difficult to cope with

Figures 7.3.2. and 7.3.3. "Treatment Follow-Up after Release from Prison" project outcomes.



Released TB patient data.

Released	2008	2009	2010	2011	2012	2013	2014	Total
1st LD				70	84	73	49	276
2nd LD	1	17	24	28	39	38	31	178
Total	1	17	24	98	123	111	80	454

All necessary information on ex-prisoner TB patients is entered into a special geographical electronic database jointly created by SK and the main medical department of MoJ. This electronic software enables TB program managers to store and spatially analyze treatment-related and DOT-related information, including a list of all TB patients, DOT caregivers, addresses, DOT facilities locations, and social support (i.e., incentives, transport fees), from one source. Being internet-based, the database is easily accessible everywhere and serves DOT supporters in any patient contact or medical data search.

The impact of the project has been periodically evaluated by the GFATM Round 9 Project Implementation Unit of the MoJ, by the oversight committee of the Country Coordination Mechanism, and at the international level by WHO and the GFATM Office of the Inspector General (October 2012).

This project demonstrates that patient support programs can significantly improve TB treatment adherence and success rates among released prisoners through the involvement of local NGOs.

## CONCLUSION

In Azerbaijan, the problems linked with treatment adherence among ex-prisoners were successfully tackled through the involvement of a local NGO. The SK NGO managed to follow up 98% of released patients, compared to a treatment continuation rate of only 10% in previous years.

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Dr. Berikova is the country coordinator for MDR-TB management and the author of various publications and medical guides on various topics, including the management and treatment of M/XDR-TB. She led the working group for the development of the "Strategic Plan for the Treatment of TB in the Republic of Kazakhstan for 2014-2020," which was approved in May 2014.

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She has been involved in all aspects of MDR-TB clinical management, but her focus has been in setting up treatment delivery outreach in rural areas and developing programs aimed at improving adherence and final treatment outcomes.

Starting from social support provision and expansion of home-based treatment between 2001 and 2004, Dr. Gelmanova and her colleagues designed and launched Sputnik, the first patient-centered program in Russia, in 2006. The aim of Sputnik is to reach and cure TB and MDR-TB in the most challenging patients. The success of the Sputnik program has inspired several regions in Russia and the former Soviet Union to start similar projects. Beginning in 2004, Dr. Gelmanova complemented her operational work with research projects on MDR-TB treatment and prevention, which resulted in a number of publications in peer-reviewed journals.

Dr. Gelmanova has also assisted the Thailand Ministry of Health in developing a 5-year MDR-TB plan, and she has provided programmatic support and consulting services to different projects in Kazakhstan and Uzbekistan.

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## The Global Fund



The Global Fund is a 21st-century partnership organization designed to accelerate the end of AIDS, tuberculosis and malaria as epidemics.

Founded in 2002, the Global Fund is a partnership between governments, civil society, the private sector and people affected by the diseases. The Global Fund raises and invests nearly US \$4 billion a year to support programs run by local experts in countries and communities most in need.

The Global Fund is a financing institution, providing support to countries in the response to the three diseases; the Global Fund does not implement programs on the ground. Global Fund staff, based in Geneva, Switzerland, come from all professional backgrounds and from more than 100 different countries.

By challenging barriers and embracing innovative approaches, the Global Fund partnership strives for maximum impact. Working together, we have saved millions of lives and provided prevention, treatment and care services to hundreds of millions of people, helping to revitalize entire communities, strengthen local health systems and improve economies.

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Dr. Hurevich is the author of more than 462 scientific works, including 48 methodological recommendation and guidelines, six clinical guides, and four education and training materials. Dr. Hurevich is a highly qualified specialist in the field of phthisiatry and pulmonology, the leader of the National Pulmonology Center, the curator of the pulmonology ward for adult patients in clinic center No. 1 and the curator for TB issues for the Gomel Oblast.

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As of July 2015, Dr. Hussain led existing Interactive Research and Development (IRD) programs in Bangladesh, including the introduction of new TB drugs and drug regimens through endTB, a multi-country consortium initiative led by Partners In Health (PIH), Médecins Sans Frontières (MSF) and IRD.

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Previously, Dr. Kuchukhidze worked as an epidemiologist at the HIV/AIDS, Hepatitis, STI and TB Surveillance Department of the National Center for Disease Control and Public Health. He has also been a principle investigator and a co-investigator in several research projects. His primary research interests include multi-drug resistant tuberculosis (MDR-TB) and tuberculosis in children.

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The project covers several areas, including improving tuberculosis infection and transmission control in the Russian Federation (RF), building a sustainable model for high-quality M/XDR-TB care delivery with a focus on ambulatory strategies, establishing academic relations among PIH and TB Research Institutes in RF, and developing education programs for TB specialists.

Dr. Livchits started her work for PIH as a research project coordinator for the NIAAA-funded clinical trial to assess the effectiveness of alcohol interventions when integrated into TB care (IMPACT study, RO1 AA016318-01; PI: Sonya Shin, MD, MPH). Prior to her participation in the trial, she had more than ten years of laboratory and public health experience.

A native Russian, Dr. Livchits trained in medicine in Russia and, after naturalization in the United States, subsequently obtained an MPH at the State University of New York in Albany School of Public Health. Her familiarity with Russian medical culture and her public health experience have contributed greatly to the success of the randomized controlled trial.

She has been instrumental in developing and implementing study interventions in a culturally-appropriate manner and effectively transmitting the importance of the study and nuances of the interventions to the Tomsk physicians. Dr. Livchits has effectively directed the further modification of study training materials, study instruments, and data collection and management procedures.

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In his current position, Dr. Mehtiyev has managed to strengthen the funding for the medical facilities in the penitentiary sector, mobilize additional personnel, and re-organize the leadership structure. He has improved the relationship with various international organizations. The Global Fund project for treatment of MDR-TB amongst incarcerated persons in Azerbaijan has received high reviews from many international experts.

Under the leadership of Dr. Mehtiyev, the WHO has recognized the TB control program in the penitentiary sector multiple times as an example of best practices in the anti-tuberculosis management field in the European Region. In 2013, the International Association of Prisons based in the United States recognized the program with an award "Public Health in Prisons." In 2014, the Training Center, operating under the TB control program in Azerbaijan's penitentiary sector, became a collaborating WHO center for TB control and prevention in prisons. Over the past years, hundreds of representatives from more than ten countries have visited the Training Center.

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Dr. Mishustin helped organize the implementation of the pilot TB programs based on the WHO strategies within the penitentiary system of Tomsk Oblast. This included organizing the DOTS implementation beginning in 1995 and DOTS Plus beginning in 2000, where he was involved in project implementation for international non-profit organizations, including MERLIN (UK), Public Health Research Institute (Newark, New Jersey, U.S.A.), and Partners In Health (Boston, MA, U.S.A.). Dr. Mishustin participated in writing grant proposals for the Tomsk TB Services to The Global Fund to Fight AIDS, TB, and Malaria that were awarded to Tomsk Oblast for 2004-2009 and 2010-2015. In 1998-2000, a pilot project was conducted in collaboration with the Public Health Research Institute to study TB strain prevalence in Tomsk Oblast using molecular genetic methods. Dr. Mishustin initiated development of the interagency integration between penitentiary and civilian TB Services of Tomsk Oblast. He advocates for a strict separation of patients with different drug resistance patterns, and pilots patient-centered approaches to improve patient adherence to ambulatory treatment.

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In 1997, Mr. Mukhtarli started his career in the field of public health by working as a Health Educator in the Department of Tuberculosis of the International Committee of the Red Cross (ICRC). His genuine desire to become a health promoter and wish to help vulnerable people led him to the position of Team Leader in health education and TB case finding programs. Later, he was promoted to Acting Head of Department and Head of the “Health in Prison” program.

Mr. Mukhtarli has occupied many managerial positions in TB Control programs and has acted as an initiator in the implementation of TB and TB/HIV related projects. Since 2011, he is the head of a “patient support program to follow up TB treatment for ex-prisoners after discharge.”

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## D. Taran



Dr. Dmitry Taran graduated from the Medical Faculty of Moscow Sechenov Medical Academy in 2001. In 2003, he completed his specialization in Public Health Management at the Public

Health Management Faculty of Moscow Sechenov Medical Academy. In 2006, Dr. Taran completed his Master of Public Health at the Braun School of Public Health and Community Medicine, Hebrew University-Hadassah, Jerusalem, Israel. He started his career working at as the Coordinator of Public Health Programs for the NGO Open Health Institute in Moscow. In 2006, he continued his practical work with Partners In Health Russia as a Project Coordinator, and then as a Project Manager and M&E Specialist.

Dr. Taran has successfully implemented patient-centered and adherence projects in Tomsk Oblast, as well in six other Russian regions. He has supported and improved the M&E system for the Global Fund reporting as part of the PIH Russia Tomsk Project as well as other activities. Dr. Taran recently finished "Best practices in TB and TB-HIV control in the Russian Federation," a project supported by the World Bank. He has several publications in international and Russian TB journals and has presented at various Russian and international conferences.

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## B. Toksanbayeva



Dr. Bekzat Toksanbayeva is a medical doctor working as the Director of the National Reference Laboratory at the National Center for Tuberculosis of the Republic of Kazakh-

stan. From 1992 to 2002, Dr. Toksanbayeva was the Associate Director of the Clinical Laboratory for the Tuberculosis Dispensary for Zambylsky Oblast. From 2002 to 2009, she was the Laboratory Coordinator for the Project HOPE/USAID program. She continued as the Laboratory Consultant for an additional year working for the same project. From 2010 to 2011, she worked for the representative office of Technology Management Company, Inc., as the USA/Kazakhstan Medical Coordinator. From 2011 to 2014, Dr. Toksanbayeva acted as the Laboratory Regional Specialist for Quality Health Care Project/USAID. She was a member of the WHO European Laboratory Group from 2012 to 2014.

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## G. Uzakova



Dr. Gulnoz Tulkunovna Uzakova is the manager of PIU GFATM (TB) in Uzbekistan, with a fund portfolio of \$82 million. She is closely involved in the StopTB strategy im-

plementation and PMDT expansion, and has trained medical personnel among the national, regional, and district levels.

In 1988, Dr. Uzakova began her labor activity as a doctor for the Pulmonological Center within the Department of Pulmonology at the Scientific Research Institute of Phthysiology and Pulmonology. In 1995, she defended her dissertation within the pulmonology specialty. In 1999, she became a doctoral candidate within the Department of Pulmonology at the Scientific Research Institute of Phthysiology and Pulmonology. Finally, in 2001, she became the Director of the Republican DOTS Center, as a National TB Coordinator, where she served until 2012.

Dr. Uzakova has actively participated in international and national TB trainings and conferences, and she has published articles, theses, and manuscripts. She has also successfully collaborated with national and international organizations involved in TB control such as the Ministry of Health, Ministry of Internal Affairs, WHO, USAID, Germany Development Bank, World Bank, Makhalla Fund, and others. She is a member of a working group for National TB Programs' elaboration and implementation in Uzbekistan and is the author of TB-related orders and recommendations.

Dr. Uzakova was born in Tashkent and is of Uzbek heritage. She graduated from the Central Asian Medical Pediatric Institute in 1988 with a specialty in pediatrics and she speaks Russian, English, and Uzbek.

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## T. Varleva



Dr. Tonka Varleva acquired two specializations from the Medical Academy in Sofia, Bulgaria: Epidemiology and Virology.

Since 1995, Dr. Varleva has been working at the Ministry of Health; in 2004 she became the Director of the Programs Financed by the Global Fund to Fight AIDS, Tuberculosis and Malaria.

In 2008, in recognition of Dr. Varleva's successful work, she was elected member of the Board of the Global Fund to Fight AIDS, Tuberculosis and Malaria, representing the countries of Eastern Europe and Central Asia. She served as a board member until 2010.

From 2009 to 2011, Dr. Varleva was an elected member of the StopTB Partnership Coordination Board.

Dr. Varleva has been coordinating the Bulgaria's participation in all major European networks and initiatives related to epidemiological surveillance, prevention and control of HIV/AIDS and European HIV testing policies.

Dr. Varleva has over 35 publications in the field of planning, coordination, implementation and evaluation of programs for health promotion and prevention of HIV/AIDS.

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## I. Vasilyeva



Dr. Irina Anatolievna Vasilyeva is a senior TB physician at the Russian Ministry of Health, and Director of the Phthisiology Division at the Central TB Research Institute in

Russia. After graduating from the 1st Moscow Medical Institute named after Sechenov, Dr. Vasilyeva had a clinical internship in phthisiopulmonology at the Central TB Research Institute of the Russian Academy of Medical Science (CTRI RAMS).

Since 2008, she has worked as the head of the leading scientific and clinical division of CTRI where an advance center for multidrug-resistant TB (MDR-TB) was created. Since 2013, Dr. Vasilyeva has combined her work at CTRI with the responsibilities of the senior non-staff TB specialist of the Russian Ministry of Health.

Dr. Vasilyeva's research expertise includes various aspects of M/XDR-TB treatment, comorbidity (TB/HIV, TB, and diabetes mellitus), development of TB chemotherapy regimens based on molecular genetic methods for diagnosis of mycobacteria drug resistance, and the development of measures for the prevention of tuberculosis in patients with HIV and diabetes.

As a senior TB physician in Russia, Dr. Vasilyeva contributes significantly to solving issues with TB care management in the Russian Federation. Under her leadership, the following documents have been developed: a strategy for the development of TB care in the Russian Federation until 2020, a national plan for the prevention of M/XDR-TB and TB/HIV spread, modern approaches to drug supply and TB treatment management, and an update of legal TB documents. She has been instrumental in guiding efforts to introduce modern medical and organizational technologies to TB practice.

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## G. Volchenkov



Dr. Grigory Volchenkov is a TB Infection Control (IC) expert and the Chief Doctor at the Vladimir Regional Tuberculosis Control Center in Russia. Since 2002, he has been

the head of the Vladimir Regional Tuberculosis Control Center and director of the regional TB control program. During 2002 and 2003, he moved the TB dispensary to a new building and implemented an intensive TB IC program supported by the Center for Disease Control (CDC) and World Health Organization (WHO) TB control program in the Russian Federation. This resulted in a substantial reduction of occupational TB among healthcare workers.

Since 2008, the Vladimir Oblast TB Dispensary became a Center of Excellence for TB IC for the Russian Federation, supported by the CDC, USAID, the TB control program within the WHO in the Russian Federation, and the Central TB Research Institute in Moscow. Dr. Volchenkov is a co-author of the national TB IC guidelines created within several Eastern European, South-East Asian, and Central Asian countries. He has coordinated and chaired TB IC related postgraduate courses, symposia and sessions at IUATLD World and European Conferences between 2005 and 2012.

Dr. Volchenkov is dedicated to TB infection prevention and control, TB case finding, DRS, and MDR and XDR TB epidemiology. He has served as a faculty member at the Harvard School of Public Health, and taught a course titled Building Design and Engineering Approaches to Airborne Infection Control from 2008 to 2013.

Dr. Volchenkov was born in Murom, Russia and graduated from the Ivanovo State Medical Institute in Russia in 1985.

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## N. Zemlyanaya



Nataliya Alexandrovna Zemlyanaya, MD, PhD, is a TB physician currently conducting research on treatment efficacy of drug-resistant TB patients. She has worked at

Partners In Health since 2008. Since 2002, she has been a physician in the MDR-TB Department within the Tomsk TB Hospital. Dr. Zemlyanaya has managed projects to improve TB detection and treatment in rural settings of the Tomsk Region, and coordinated the Global Fund project in Tomsk City.

Dr. Zemlyanaya is a faculty member of the Phthisiology and Pulmonology Department at the Siberian State Medical University. Her research areas of interest include drug-resistant TB treatment, management of patients co-infected with TB and HIV, TB treatment management, and TB treatment adherence.

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## Salmaan Keshavjee



Salmaan Keshavjee, MD, PhD, ScM, is the Director of Harvard Medical School's Center for Global Health Delivery—Dubai. He is also an Associate Professor of Global Health and Social Medicine at the

Department of Global Health and Social Medicine (DGHSM) at Harvard Medical School and an Associate Professor of Medicine in the Division of Global Health Equity at Brigham and Women's Hospital.

Dr. Keshavjee has been leading the Harvard Medical School Center for Global Health Delivery—Dubai since 2014. Under his direction, the Center addresses some of the most pressing health challenges in the region by focusing on research, medical education and training that promises to improve healthcare delivery systems and patient outcomes for diseases prevalent in the United Arab Emirates, Middle East, North Africa and neighboring regions.

With advanced training in both medicine and anthropology, Dr. Keshavjee is a leading expert in drug-resistant tuberculosis treatment and the anthropology of health policy. He is the author of *Blind Spot: How neoliberalism infiltrated global health*, which is based on his doctoral research in Central Asia (Tajikistan). He has worked extensively with the Boston-based non-profit Partners In Health (PIH) on the treatment of drug-resistant tuberculosis. Dr. Keshavjee has been very involved in global policy discussions around the treatment of drug-resistant tuberculosis. He has spent considerable time working on alternate mechanisms for drug procurement, technical assistance delivery, and program implementation. Dr. Keshavjee is leading an initiative at Harvard Medical School on how to achieve zero deaths from tuberculosis.

## Oksana Ponomorenko



For dozens of years, Oksana Ponomarenko has been researching tuberculosis and implementing evidence-based strategies to treat patients and curb trans-

mission of this global scourge. As country director for Partners In Health Russia, much of Mrs. Ponomarenko's work is focused on hard-to-treat, drug-resistant strains of tuberculosis among vulnerable patients, including prisoners and those in the throes of chronic alcoholism and drug addiction.

Over the years, Mrs. Ponomarenko and her team have forged critically important partnerships with the Russian Ministry of Health, the World Health Organization, and the Global Fund Global Fund to Fight AIDS, Tuberculosis and Malaria, among many others. The findings gleaned from PIH/Russia's work have helped shape global policy on treating multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) in community-based settings.

## Askar Yedilbayev



Askar Yedilbayev is a Medical Doctor from Kazakhstan with the Master's Degree in Public Health from Boston University, and works as Program Director for Russia and Kazakhstan/

Medical Officer at Partners In Health (PIH), a non-profit international corporation based in Boston, MA. He has worked extensively with PIH's drug-resistant tuberculosis in Tomsk, Russia since 2002 and was one of the authors of the R3 GFATM application from Tomsk Oblast.

Dr. Yedilbayev had led the new initiative of replicating the experience from Tomsk TB program to four territories of Russia and provided extensive technical assistance on program and medical management of drug-resistant tuberculosis. This work resulted in scaling up the enrollment of 2000 M/XDR-TB patients to treatment in civilian and prison sectors in four regions of Russia, intensive capacity building of TB doctors and nurses and technical assistance on clinical aspects of MDR-TB and strengthening the adherence to treatment. In 2008 Dr. Yedilbayev was also involved as DR-TB physician at MDR-TB Hospital at PIH-Lesotho treating patients with DR-TB and HIV. Between 2010-2013, Dr. Yedilbayev was responsible for the PIH program in Kazakhstan, a Central Asian country with alarming rates of drug-resistant tuberculosis in the World, with the major focus on prison sector, building best practices of clinical care and ambulatory treatment.

Starting 2015 he is acting as Program Director for the endTB Project in Kazakhstan, which is focusing on expanding access to new TB drugs – Bedaquiline and Delamanid – for management of 600 patients with M/XDR-TB. Dr. Yedilbayev is acting as the member of the regional GLC for the WHO European Region and is an Associate Physician at the Division of Global Health Equity, Department of Medicine of Brigham and Women's Hospital, Boston, MA.





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