Grant RUS-304-G02T
The Tomsk Oblast Comprehensive Strategy to Reduce the Burden of DR-TB

Final narrative report
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**Abbreviations**

TB – Tuberculosis
NP – New patient
MDR-TB – Multidrug-resistant tuberculosis
XDR-TB – Extensively drug-resistant tuberculosis
DR – Drug-resistant tuberculosis
PDR-TB – Polidrug-resistant tuberculosis
PT – Preventive therapy
TO – Tomsk oblast
Materials and methods

The project was evaluated by specialists who participated in the project implementation (Appendix 1) based on the design of the project (Appendix 2). Since most activities were implemented under strict organizational and financial monitoring by the principal recipient (“Partners In Health,” a non-governmental organization), some input and output variables were not analysed in this report. Instead, significant attention was paid to the results of major clinical and programmatic activities that influenced treatment results (clinical outcomes and treatment adherence).

Results were reported to the GF by region with both civilian and prison sectors combined. However, most activities and achievements pertain primarily to the civilian sector. Many graphs in this report focus on yearly results from the initial phase of civilian sector program (2004-2009) or prior to the GF grant.

The bulk of data used in the evaluation were collected routinely by the local TB program (national TB system indicators) and under general reporting to GF using standard monitoring forms. We used data from existing databases in civilian and prison sectors. The Tomsk TB program’s main electronic database was established in 1998, and every year it is improved to comply with new government reporting regulations as well as donor reporting standards. Implementation of an MDR-TB treatment program by Partners In Health in partnership with the Oblast Department of Health and the Federal Ministry of Justice in 2000 was the starting point for a special system of monitoring DR-TB cases and MDR-TB treatment.

Main data sources are forms from the state statistics reporting body, approved by RF MoH edicts №№ 109 and 50, including Forms №№: 8 and 33; registration forms №№ 01-TB/u and 03-TB/u, reporting forms №№ 2-TB, 7-TB, 8-TB and 10-TB.

As of 2013, the Russian Federation has not yet adopted a national strategy for the treatment of DR-TB, including MDR-TB and XDR-TB. Currently, the Chief TB Physician of Russia has organized a high-level working group that is developing recommendations to supplement Prikaz 109, including reporting and recording systems for DR-TB cases.

The Tomsk TB program has already developed forms for MDR-TB and poly-drug resistant TB cases, which serve as a basis for the new national forms. All program indicators for patients with susceptible TB align with national indicators and national methodology.

The HIV/AIDS Services reporting and recording systems do not include detailed information about TB and PPD testing, and they lack precise information about patients who are co-infected with TB and HIV and are taking or have completed Isoniazid prophylaxis. The Tomsk TB-HIV sub-program developed most forms in 2004 for the R3 grant and new forms have been developed for prophylaxis in 2009 for the RCC grant.

Additional information about implementation of sub-programs was submitted by each sub-recipient on a quarterly basis in specially developed forms and the quality of the data was monitored closely.

Finally, key implementers were interviewed by an independent specialist based on the key activities of the project and results (Appendix 3).
Summary

In 1994-1995, the WHO-recommended DOTS strategy was introduced in Tomsk Oblast. The DOTS strategy uses short-course chemotherapy to treat TB. It was first introduced in the civilian sector and then subsequently in the penitentiary system with technical and financial support of MERLIN (a UK-based non-governmental organization). However, due to the high rates of drug resistance among TB patients in the civilian and penitentiary sectors, the DOTS strategy resulted in high rates of treatment failure and death. Drug-resistant (DR) tuberculosis continued to spread in congregate settings (prisons and hospitals) and in the communities where undiagnosed and untreated patients lived.

In 2000 Tomsk Oblast became the first MDR-TB treatment project in Russia approved by what was then a new World Health Organization/Stop TB Partnership mechanism to expand high-quality treatment of drug-resistant TB, the Green Light Committee (GLC). For 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.

In 2004 Tomsk Oblast applied for a grant from the Global Fund to Fight AIDS, TB and Malaria in Round 3 and received an approval to start the only regional project in Russia focusing on the expansion of 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, including improved social and psychological supports during the entire treatment. It also allowed the program to strengthen DR-TB laboratory diagnosis and improve infection control mechanisms for inpatients in the civilian and penitentiary sectors, as well as develop sub-programs focused on reduction of alcohol use, treatment adherence and early case detection.

In 2009, the projects success resulted in continued funding from the Global Fund through the Rolling Continuation Channel. This enabled Tomsk TB Services to expand activities and improve their efficiency. The Global Fund funding ended on November 30, 2013.
Introduction.

General profile of the setting (Map 1)

Located in western Siberia, Tomsk Oblast covers an area of 316,900 km² (about the size of Poland) and has a population of more than 1 million people. A unique landscape, including vast swamp areas and rivers that are passable only in winter, makes it difficult to provide proper medical care to the population. The climate is severe, with temperatures that drop below minus -40 degrees Celsius.

More than a half of the population lives in the regional center, the city of Tomsk, and the rest reside in rural areas. Tomsk, the administrative center of Tomsk Oblast, is located on the Tom River and is one of the oldest towns in Siberia, having recently celebrated its 400th anniversary. The population of the city is steadily albeit slowly increasing, from 500,000 in 1998 to 525,000 in 2010, according to census data.

Tomsk Oblast is rich in natural resources, particularly oil, natural gas, ferrous and non-ferrous metals, peat, and underground waters. Forests are also among the most significant assets of the oblast: about 20% of the West Siberian forest resources are located in Tomsk Oblast. Industry makes up about half of the regional GDP, while agriculture contributes 19% and construction 13%. Chemical and oil industries are the most developed in the region, followed by machine construction. The oblast's major export items are: oil (62.1%), methanol (30.2%), and machines and equipment (4.8%). Oil extraction and lumbering are the major business of the region's joint ventures.

The annual per capita income in 2001 was US$1,998, with an estimated 26% of the population living below the official poverty line.

TB and DR-TB in Tomsk Oblast 1991-2000¹

Although Russia is not a poor country by global standards, the political, social and economic shifts of the 1990s resulted in profound income disparities and more severe poverty among already marginalized populations. The abrupt economic and political transformation of the 1990s was associated with increases in alcohol consumption, a breakdown of health and social services, and socioeconomic instability. The effect of these forces on public health was profound, including a sharp rise in mortality, particularly from deaths due to cardiovascular diseases, infectious diseases, and injuries. Differences in mortality by socioeconomic status (e.g., income, educational level, and type of employment) widened, especially among alcohol-related deaths and those due to infectious causes. As social cohesion disintegrated, individuals living in relative poverty became increasingly isolated and unable to access formal and informal resources, including health services and social support.

It is in this context that the Russian Federation witnessed the reversal of 30 years of successful TB control (Fig. 1). Between 1991 and 2000, TB incidence in Russia increased from 34 to 91 per 100,000 people, while TB mortality climbed from 8.1 to 19.9 per 100,000 people. TB incidence and prevalence rates were even higher in the Siberian oblasts. Several regions reported that homelessness and unemployment were the leading risk factors for TB mortality, highlighting the role poverty played in the epidemic. A drastic rise in incarceration rates, mostly for petty crimes, helped fuel the TB epidemic in overcrowded prisons and pretrial detention centers. Unsurprisingly, these penitentiary institutions were filled with individuals from the poorest stratum of society, including alcoholics, homeless men, and individuals struggling with mental illness. TB incidence rates in Russian prisons were as high as 7,000 per 100,000. In the 1990s, prisoners made up approximately 25% of all newly diagnosed TB cases in Russia, and approximately 30% of newly diagnosed civilian cases had been imprisoned at some point. Although the prison system may have functioned as an "epidemiological pump," releasing tens of thousands of active TB cases into the civilian population, the same forces driving the prison epidemic were independently contributing to a TB crisis in the civilian population.

During this same period, Russia began reporting some of the highest MDR-TB rates in the world. Two processes were at play in the expansion of MDR-TB. First, breakdowns in the supply chain, medication stock outs, insufficient monitoring and follow up, and similar challenges that interrupted TB treatment spurred and amplified drug resistance among patients. Second, primary cases of MDR-TB transmitted in institutions like hospitals and prisons—but also in communities—increased.

Social and programmatic factors play an overwhelming role in treatment adherence and therefore in the acquisition of MDR-TB. In Russia, a typical patient—homeless, addicted, drifting in and out of the penal system—was unlikely to overcome barriers to successfully complete months of daily treatment. The quality of TB services declined as public health expenditures decreased. The hospitals—underfunded and overcrowded—began to function as additional "epidemiological pumps," becoming a focus for primary transmission of MDR-TB.

In 1994, MERLIN (Medical Emergency Relief International, a UK-based non-governmental organization) became the first foreign organization in Russia to tackle the sharp growth of tuberculosis after the breakup of the Soviet Union. A collaborative project was established in Tomsk Oblast, marking the first attempt to shape TB control practices along the lines recommended by the WHO. A primary goal of the project was to determine the effectiveness of WHO’s DOTS strategy in Russia.

After six years of DOTS program implementation, Tomsk failed to reach the WHO target cure rate of 85% for new patients. In fact, even before the DOTS program started, there were warning signs that the strategy might not succeed. Data from the early to mid-1990s showed that 29% of new civilian cases had some level of resistance to at least one of four first-line drugs; rates of MDR-TB were 6.5% during the same period. A study conducted in 1999 found that of 244 patients newly diagnosed with TB between January and December of that year, 49.6% were infected with a strain of M. tuberculosis that was resistant to at least one of the prescribed TB medications and 13.1% had MDR-TB.

By 2000, Tomsk’s civilian and prison TB programs were clearly in trouble. 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. 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 was 2,357 per 100,000 people, with a mortality 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. The DOTS program cure rates for smear-positive patients in Tomsk were between 50% and 60% for new and retreatment patients in both sectors.

**TABLE 1. TB incidence, prevalence, and mortality in Tomsk Oblast Civilian Sector, 1998–2003**

<table>
<thead>
<tr>
<th>Variable</th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB case notification/100,000</td>
<td>76.2</td>
<td>87.9</td>
<td>90.3</td>
<td>88.2</td>
<td>93.7</td>
<td>93.4</td>
</tr>
<tr>
<td>TB Prevalence/100,000</td>
<td>244.7</td>
<td>247.7</td>
<td>251.5</td>
<td>247.5</td>
<td>252.6</td>
<td>239.5</td>
</tr>
<tr>
<td>TB Mortality/100,000</td>
<td>16.9</td>
<td>20.7</td>
<td>21.2</td>
<td>18.6</td>
<td>18.3</td>
<td>17.6</td>
</tr>
<tr>
<td>% MDR-TB among new cases</td>
<td>6.9</td>
<td>12.3</td>
<td>8.5</td>
<td>10.2</td>
<td>13.5</td>
<td>11.2</td>
</tr>
<tr>
<td>% MDR-TB among retreatment cases</td>
<td>24.1</td>
<td>43.3</td>
<td>32.2</td>
<td>42.4</td>
<td>42.9</td>
<td>42.2</td>
</tr>
</tbody>
</table>

*Source: Tomsk Oblast Tuberculosis Services, Tomsk, Russian Federation, July 2005.*
MDR-TB treatment program in Tomsk Oblast, 2000-2004

In 2000, the Green Light Committee (GLC) approved an application from Tomsk Oblast to gain access to quality-assured second-line TB drugs to treat 630 MDR-TB patients. The project was one of five projects approved by the GLC to treat MDR-TB patients. MDR-TB was recognized as laboratory confirmed resistance to a minimum of two potent first-line TB drugs together, Isoniazid and Rifampicin. After approval, 630 MDR-TB patients were enrolled in the MDR-TB treatment program in civilian and penitentiary sectors in 2000-2004. MDR-TB treatment started in early September 2000 at a specialized treatment and correction facility within the penitentiary sector. Within a year and a half of implementation of a comprehensive TB treatment program that included both patients with drug-susceptible and drug-resistant disease, the mortality rate in the Tomsk penitentiary sector dropped from 129.9 per 100,000 people to zero. Later, the program was expanded to the civilian sector.

The majority of patients enrolled into new treatment had laboratory confirmed MDR-TB and started treatment at specialized facilities of civilian and prison TB services. However, around 26% of patients started treatment with empiric MDR-TB regimens as close contacts of known MDR-TB patients. Regimens used for MDR-TB were based on drug-susceptibility testing performed at the Regional TB Reference Laboratory and included an average six anti-TB medicines that were known to be effective. During the first years it was identified that the average duration of the intensive phase should be no less than 8 months, while the whole duration of therapy should average 21 months and more. Treatment results of the first patient cohort (244) showed a high effectiveness (78.3%) of MDR-TB treatment with individualized regimens, which contributed to defining a policy of drug-resistant TB management in Russia and bolstered subsequent WHO recommendations. However, a closer examination of this first cohort revealed that the fundamental association between TB and poverty remained a persistent challenge to successful TB control. Most of this cohort was unemployed; approximately half were either incarcerated or had spent time in prison and had a history of substance dependence/abuse.

During the first years of the MDR-TB treatment program’s implementation, PIH played a significant role in developing and introducing approaches for the medical management of MDR-TB, including regimen design, diagnosis and management of adverse reactions, and developing the system of pharmacovigilance. PIH provided significant input into the development of recording and reporting forms used for registration of case, as well as treatment monitoring and follow-up. Significant efforts had been placed on developing the regional electronic medical records system for TB and DR-TB in Tomsk to cumulate collected information and use as a source for generating evidence.

As a partner of the Tomsk MDR-TB Program, PIH contributed to the work of the DR-TB Committee and DR-TB Working Group, which became an interagency medical collegial body responsible for protocol development, treatment regimen design, recording of treatment outcomes, and complicated case counseling. PIH representatives worked closely with medical workers of the civilian and prison sectors. PIH specialists took an active part in the meetings of DR-TB Committee; they provided technical and methodological support to develop and implement MDR-TB program activities, collected evidence-based data, and analyzed and published articles in international medical journals. Due to the technical and financial support of PIH, a training center started to function in Tomsk Oblast, which hosted the first training programs on clinical and programmatic management of MDR-TB in the region.

During the initial implementation of the MDR-TB program in Tomsk, PIH and the Tomsk TB Services identified the key pillars of a successful MDR-TB program: political commitment, quality diagnosis, an effective treatment delivery mechanism (we use directly observed therapy as much as possible), uninterrupted treatment, guaranteed supply of TB drugs, and regular and rigorous monitoring and evaluation. Although TOTBS and the UIN had basic infrastructure in place, the initiation of the MDR-TB program required substantial enhancements. Major developments were as follows.
**Political Commitment**

Introducing MDR-TB management in Tomsk fostered both local and national political commitment. Because MDR-TB management relies on a properly functioning tuberculosis program, the urgent need for MDR-TB therapy motivated the local TB Service in Tomsk to evaluate its existing program and to request more resources from the Oblast Health Administration. Once several MDR-TB treatment pilot projects in Russia reported favorable outcomes, national TB policymakers responded. Drawing from the experiences of Russia’s longstanding TB control programs and the MDR-TB treatment pilot programs, the Ministry of Health took steps to enshrine these ideas into general practice, culminating in Edict 109 in March 2003, which integrated MDR-TB management into a comprehensive TB control strategy for Russia.

**Quality Diagnosis**

MDR-TB management required improvement in diagnostics, including radiography and laboratory capacity in both the penal and civilian sectors. The pilot program brought in resources and technical support to revive these services, including mycobacterial culture and smear microscopy. With technical assistance and quality assurance from the Massachusetts State Laboratory Institute (MSLI), the local laboratories validated their DST methods and currently perform DST on all patients starting TB treatment.

**Effective treatment delivery mechanism**

Treatment of TB in Russia has traditionally been hospital-based; yet completing 18–24 months of MDR-TB therapy under current inpatient conditions was not feasible for many patients. Although patients started MDR-TB treatment as inpatients, most were released to ambulatory services after smear conversion. The Tomsk program responded by changing the structure of the ambulatory treatment program to provide direct observation of therapy for all MDR-TB patients by offering several options for treatment delivery, like the TB polyclinic, the TB day hospital, and rural TB facilities or village clinics. Patients too sick to travel (e.g., patients with disabilities, comorbidities, and substance abuse problems) received treatment at home. Where possible, patients were given public transportation vouchers and hot meals or food supplements. Working with PIH, the district government provided fuel subsidies for defaulter searches and the provision of treatment. Eventually, these improvements were expanded to all TB patients and have become the standard of care in Tomsk.
Uninterrupted Treatment

In the late 1990s, Tomsk, as in most of Russia, lacked a well-coordinated system to monitor patient transfers between services (urban and rural; general facilities and specialized facilities) and sectors (prison and civilian), which contributed to treatment interruptions. In 1999 and 2000 in Tomsk, only 53.9% and 58.8%, respectively, of patients released from prison with active TB reported to civilian health authorities to continue treatment. As part of the MDR-TB treatment program in Tomsk, civilian and prison TB services, with assistance from MERLIN, PHRI and later PIH, formed a shared mechanism to ensure uniformity of treatment regimens and uninterrupted treatment between penal and civilian facilities. For civilian and prison TB services, a system was implemented to share important information from medical records to ensure that all patients—those with drug-susceptible or drug-resistant disease—continue treatment no matter where they resided.

Guaranteed Quality Drug Supply

Procurement of anti-TB medications to treat MDR-TB in the early 2000s was not regulated by the MOH, and the majority of Russian regions, including Tomsk, were experiencing shortages of second-line drugs. Further complicating this issue was the lack of a national protocol regulating DR-TB regimens and the medicines required for therapy. In Tomsk, the MDR-TB program had access to quality-assured second-line medications procured through the GLC mechanism and backed by a centralized drug storage facility created for both the civilian and prison TB services. This helped ensure sufficient drug stock to treat all patients on therapy and a steady supply for patients transferring between systems.

Monitoring and Evaluation

In 2000, TOTBS faced problems with monitoring and evaluation of DR treatment. Through the MDR-TB treatment program, the monitoring of patients with drug-resistant TB improved substantially. Standardized reporting forms and effective data management have achieved timely and accurate data on patients with drug-susceptible and drug-resistant disease. In addition to data collection, on-site monitoring was also improved through the training of supervisors on monitoring and evaluation practices and increased resources to fund raion visits. Regular visits from the GLC—part of the mechanism’s program monitoring and technical assistance provision—further enhanced activities for all tuberculosis patients. Because continued GLC approval was contingent upon adequate performance, feedback from these site visits provided external pressure to maintain and/or improve services.
**GFATM Project, stage 1: 2004-2009**

In 2003 participants of the Tomsk Oblast DOTS-Plus program applied for funding from Round 3 of the Global Fund to fight AIDS, Tuberculosis and Malaria (http://portfolio.theglobalfund.org/en/Grant/Index/RUS-304-G02-T).

In 2004 the application was approved and Partners In Health and Tomsk TB Services received an approval to launch the only sub-national project in Russia with an emphasis on expanding universal access to treatment for MDR-TB patients by strengthening comprehensive and integrated management of TB and MDR-TB. The Round 3 grant allowed the program to provide wide-ranging care for TB and MDR-TB patients, including enhanced social and psychological support for the entire duration of treatment, strengthened laboratory diagnosis of DR-TB, and improved infection control mechanisms for inpatients in both the civilian and penitentiary sectors. A number of sub-programs were introduced during the project implementation focusing on reducing alcohol abuse, improving patients’ adherence to treatment, and improving methods for early detection of TB.

The key objectives and activities, and indicators of the program are given in Table 3. “Objectives, activities and indicators of GFATM project I, GFATM project II (RCC)”.

**GFATM Project, stage 2: 2009-2013**

In 2009, the positive results of the program allowed for continued GFATM funding under the Rolling Continuation Channel. It also allowed Tomsk TB Services to build on their success by expanding program activities and enhancing the effectiveness of their interventions. The GFATM funding ended on November 30, 2013.

The key objectives, activities and indicators of the program are given in Table 3. “Objectives, activities and indicators of GFATM project I, GFATM project II (RCC)”.
## Table 3. Objectives, activities and indicators of GFATM project I, GFATM project II (RCC).

<table>
<thead>
<tr>
<th>Goals</th>
<th>GFATM I, 2004 – 2009 activities</th>
<th>Funding</th>
<th>Indicators - title</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1</td>
<td>Improvement of the TB diagnostics system in the civilian and penitentiary sectors of Tomsk Oblast</td>
<td>$ 881 019</td>
<td></td>
</tr>
<tr>
<td>1.1</td>
<td>Improvement of the laboratory services. Equipment. External quality control.</td>
<td>$ 731 218</td>
<td>1.1.1. Number and % of new smear+ TB cases (out of total number of detected TB patients) in civilian sector</td>
</tr>
<tr>
<td>1.2</td>
<td>Improvement of X-ray monitoring of TB patients.</td>
<td>$ 149 801</td>
<td>1.1.2. Number and % of new smear+ TB cases (out of total number of detected TB patients) in prison sector</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.1.3. Number and % of healthcare facilities provided with laboratory equipment in civilian and prison sectors</td>
</tr>
<tr>
<td># 2</td>
<td>Improvement of TB treatment system in the civilian and penitentiary sectors of Tomsk Oblast</td>
<td>$ 3 621 631</td>
<td></td>
</tr>
<tr>
<td>2.1</td>
<td>Procurement of second-line TB drugs to treat MDR-TB patients. Procurement of side effect medications.</td>
<td>$ 2 671 031</td>
<td>2.1.1. Number of MDR-TB patients enrolled in DOTS+ program in civilian sector</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.1.2. Number of MDR-TB patients enrolled in DOTS+ program in prison sector</td>
</tr>
<tr>
<td>2.2</td>
<td>Clinical monitoring. Biochemical tests, consultations of healthcare specialists.</td>
<td>$ 142 767</td>
<td>2.2.1. % of cured patients with susceptible TB in civilian sector</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.2.2. % of cured patients with susceptible TB in prison sector</td>
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<td>2.3</td>
<td>Information monitoring.</td>
<td>$ 290 762</td>
<td>No specific indicators for reporting to GFATM available</td>
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<tr>
<td>2.4</td>
<td>Human resources for GFATM project implementation.</td>
<td>$ 517 073</td>
<td>No specific indicators for reporting to GFATM available</td>
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<td># 3</td>
<td>Improvement of TB patient’s adherence to treatment including MDR-TB patients in the civilian and penitentiary sectors of Tomsk Oblast</td>
<td>$ 3 472 939</td>
<td></td>
</tr>
<tr>
<td>3.1</td>
<td>Improvement of observed treatment. In-home therapy. Russian Red Cross.</td>
<td>$ 1 420 396</td>
<td>3.1.1. % of “failure” among patients with susceptible TB in civilian sector</td>
</tr>
<tr>
<td>3.2</td>
<td>A sub-program of alcohol and substance addiction treatment for TB patients.</td>
<td>$ 160 575</td>
<td>3.1.2. % of “failure” among patients with susceptible TB in prison sector</td>
</tr>
<tr>
<td>3.3</td>
<td>Provision of rural healthcare facilities and TB services with transport resources to monitor treatment. Vehicles. Gasoline. Inspector’s visits.</td>
<td>$ 194 334</td>
<td>3.2.1. % of “default” among patients with susceptible TB in civilian sector</td>
</tr>
<tr>
<td>3.4</td>
<td>Provision of TB patients with food and social support.</td>
<td>$ 1 697 634</td>
<td>3.2.2. % of “default” among patients with susceptible TB in prison sector</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>3.3.1. Number of patients receiving food support in civilian sector</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.3.2. Number of patients receiving food support in prison sector</td>
</tr>
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<td># 4</td>
<td>Reduction of TB transmission to HIV patients in the civilian and penitentiary sectors of Tomsk Oblast.</td>
<td>$ 202 236</td>
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<tr>
<td>4.1</td>
<td>TB/HIV sub-program.</td>
<td>$ 202 236</td>
<td>4.1.1. Number of HIV patients with PPD skin test provided in civilian sector</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>4.1.2. Number of HIV patients with PPD skin test provided in prison sector</td>
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<td></td>
<td></td>
<td>4.2.1. Number and percent of TB-HIV patients with Isonizid preventive therapy received in civilian sector</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4.2.2 Number and percent of TB-HIV patients with Isonizid preventive therapy received in prison sector</td>
</tr>
<tr>
<td># 5</td>
<td>Improvement of infection control in TB hospitals and clinics in the civilian and penitentiary sectors of Tomsk Oblast.</td>
<td>$ 1 238 907</td>
<td></td>
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<tr>
<td>5.1</td>
<td>Ventilation and UV lamps in TB Hospital, TB Dispensary and Central laboratory.</td>
<td>$ 1 003 859</td>
<td>5.1. Number and % of TB facilities installed with ventilation equipment</td>
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<tr>
<td>5.2</td>
<td>Improvement of infection control among healthcare workers.</td>
<td>$ 235 049</td>
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</tr>
<tr>
<td># 6</td>
<td>Improvement of health education among risk groups in the civilian and penitentiary sectors; training of healthcare staff of the civilian and penitentiary sectors of Tomsk Oblast; attracting risk groups to early TB detection.</td>
<td>$ 942 996</td>
<td></td>
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<td>6.1</td>
<td>Improvement of health education among general population and patients in the civilian and penitentiary sectors.</td>
<td>$ 99 488</td>
<td>6.1.1. Number of trained healthcare staff on TB treatment and monitoring</td>
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<td></td>
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<td>6.1.2. Number of TB patients educated on TB in civilian sector</td>
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<tr>
<td>6.2</td>
<td>Training of healthcare workers of the civilian and penitentiary sectors. Training of General Healthcare Services staff.</td>
<td>$ 286 890</td>
<td>6.2.1. Number of TB patients educated on TB in civilian sector</td>
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<td></td>
<td></td>
<td>6.2.2. Number of inmates educated on TB in prison sector</td>
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<tr>
<td>6.3</td>
<td>A sub-program to improve early TB detection among general population and risk groups.</td>
<td>$ 555 718</td>
<td>No specific indicators for reporting to GFATM available</td>
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<td>$10 358 830</td>
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Grant RUS-304-G02T | The Tomsk Oblast Comprehensive Strategy to Reduce the Burden of DR-TB
**Goals** | **GFATM II (RCC), 2009 – 2013 activities** | **Funding** | **Indicators - title**
--- | --- | --- | ---
# 1 | Drug-resistant TB treatment (DR-TB) | $ 5 863 138 | 1. % of MDR-TB patients cured 2. % of susceptible TB patient treated effectively
1.1 | Improvement of TB diagnostics and detection of polyresistant TB, MDR-TB and XDR-TB. | $ 485 378 | 1.1. Number of DST to first-line TB drugs. 1.2. Number of DST to second-line TB drugs.
1.2 | Second-line TB drugs for DR-TB treatment. | $1 961 703 | 1.3. Number of MDR-TB and XDR-TB patients enrolled in DOTS+ program. 1.4. Number of polyresistant TB patients enrolled in DOTS+ program. 1.5. Interim results of MDR-TB and XDR-TB treatment. 1.6. Number and percentage of MDR-TB and XDR-TB patients registered under DOTS Plus who are successfully treated in Tomsk oblast.
1.3 | Side effect medications for DR-TB patients. | $ 239 814 |
1.4 | Clinical observation of DR-TB treatment. | $614 945 |
1.5 | Strengthening of compliance with regimen among susceptible and DR-TB patients. | $ 1 644 917 | 1.7. Default rate of MDR-TB and XDR-TB patients enrolled in DOTS+ program. 1.8. Default rate in DOTS (among smear+, NP registered 12-15 months ago). 1.9. Number of new susceptible, PR-TB and MDR/XDR-TB patients provided with food support at the outpatient phase
1.6 | Improvement of treatment programs for high risk patients. | $ 279 172 |
1.7 | Improvement of infection control in Tomsk Oblast hospitals and clinics. | $ 241 314 |
1.8 | Monitoring of TB and DR-TB control program implementation. | $ 395 895 |
# 2 | Reduction of TB spread among HIV patients in the civilian and penitentiary sectors of Tomsk Oblast | $ 286 718 |
2.1. | TB/HIV sub-program. | $ 286 718 | 2.1.1. Number of HIV patients with PPD skin test, civilian sector. 2.1.1. Number of HIV patients with PPD skin test, prison sector 2.2.1. Number and % of TB-HIV patients offered and completed Isoniazid preventive therapy in civilian sector. 2.2.1. Number and % of TB-HIV patients offered and completed Isoniazid preventive therapy in prison sector.
# 3 | Operational research and dissemination of Tomsk MDR-TB control program in Russia | $ 111 602 |
3.1 | Operational research on GFATM grant-related activities. | $ 27 237 | 3.1. 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)
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 |
--- | --- | --- |
**TOTAL** | **$6 261 458** |
Improving the TB treatment system.

Improving TB diagnostics in Tomsk Oblast and detection of drug-resistant TB

In order to improve TB diagnostics, 15 laboratories in Tomsk Oblast were supplied with necessary equipment and commodities, exceeding the target of strengthening 14 laboratories. Microscopy stations were set up in almost all of the rural health facilities and in Tomsk City to augment the central (reference) laboratory.

During the 5-year grant period, the Central Bacteriological Laboratory of the Regional TB Dispensary continued its efforts to improve operations and quality control for TB diagnosis by sputum smear microscopy and mycobacterial cell culture through:

- Trainings of laboratory specialists and microbiologists of primary care and rural laboratories,
- Regular inspector visits in rural laboratories at least twice a year,
- Regular checks of the standard forms that are filled out by all laboratories,
- Preparation and provision of culture media for rural laboratories,
- Re-checks of all positive and all questionable slides, as well as 10% of negative slides from all diagnostic laboratories.

The Central Bacteriological Laboratory of the Regional TB Dispensary is the major laboratory in the civilian sector where drug susceptibility testing (DST) is performed. Quality assurance of DST was performed twice a year by the Novosibirsk TB Research Institute laboratory and showed high concordance (see results in Table 4).

### Table 4: Concordance of the results for sensitivity testing to anti-TB drugs by Tomsk Oblast TB laboratory

<table>
<thead>
<tr>
<th>Drug</th>
<th>Novosibirsk TB Research Institute laboratory</th>
<th>Moscow laboratories (Federal system of external quality control)</th>
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<tr>
<td>Isoniazid</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>Prothionamide / Ethionamide</td>
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<td>95%</td>
</tr>
<tr>
<td>Cycloserine</td>
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<td>100%</td>
</tr>
<tr>
<td>PAS</td>
<td>100%</td>
<td>90%</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>95%</td>
<td>100%</td>
</tr>
</tbody>
</table>

In 2008, the Ministry of Health and the Federal Customs Service issued an order forbidding any biological materials to be exported outside of Russia, thus continuation of quality control activities by the supranational laboratory (MSLI) in Boston, USA, became impossible. (However, according to the MSLI, performance characteristics for all drugs ranged from “good” to “excellent” for both sectors in 2002-2003). After 2008, quality control was performed by the Federal system at the national level via the Moscow National Laboratory.

MSLI quality control results from the prison system were on 98% level in 2001. External quality control activities for prison laboratory services were also performed by the Federal system of quality control since 2007 and presented a 100% concordance for many years.

### Table 4a: Concordance of the results for sensitivity testing to anti-TB drugs by Tomsk Prison TB laboratory

<table>
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<td>Isoniazid</td>
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<td>100%</td>
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<tr>
<td>Rifampicin</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>94.7%</td>
<td>100%</td>
<td>100%</td>
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<td>Streptomycin</td>
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<td>100%</td>
<td>84.2%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>94.7%</td>
<td>58%</td>
<td>100%</td>
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<tr>
<td>Kanamycin</td>
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<td>94.7%</td>
<td></td>
<td></td>
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<tr>
<td>Ofloxacin</td>
<td></td>
<td>100%</td>
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<tr>
<td>Capreomycin</td>
<td></td>
<td>100%</td>
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</table>

In Tomsk Oblast, culture tests and DST to first-line TB drugs are performed at the central bacteriological laboratory for all new TB patients. Culture tests are performed traditionally on Lowenstein-Jensen solid media. Drug susceptibility testing (DST) to second-line TB drugs is performed in all patients who have laboratory confirmed resistance to Isoniazid and Rifampicin or Rifampicin-resistance confirmed by molecular genetic testing (Xpert MTB/RIF). Additionally, DST to first- and second-line TB drugs is performed in all patients suspected of TB who are close contacts of a patient with MDR/XDR-TB.
Patients in the prison were transferred from other regions. Detection of TB by mass was not associated with previous years. Most patients with available DST results among patients with available DST results. From year to year, bacteria excretion and, correspondingly, DST results were less available among new patients, relapse cases and all TB cases in general. Detection of TB by mass fluorography is still a national priority and has resulted in a high prevalence of sputum-negative forms of TB (and hence no DST results for these patients).

Prison sector.

Most patients in the prison were transferred from other regions. Their pattern of resistance changed every year and was not associated with previous years.

Civilian sector.

Between 2000-2013, on average 64.6% of new TB patients had positive sputum culture; at least 99% of them had DST to first-line drugs performed. The percentage of mono-resistant and poly-resistant TB patients has not changed dramatically over 14 years, with rates between 5-12% and 11-17%, respectively. Between 2009 and 2013, the percent of new MDR-TB patients as a proportion of all TB cases increased to 26%, whereas the proportion of susceptible TB patients decreased to 52% (out of all patients with available DST results). Since MDR-TB patients are first registered as ‘failure” under regimen 1 and then re-registered under regimen IV, achieving an overall treatment effectiveness of greater than 80% is difficult to achieve.

Among relapse cases, a percent of MDR-TB increased every year and it reached 63.5% in 2013. Between 2000-2013, the average percent of MDR-TB among all TB patients in the civilian sector of Tomsk Oblast (new patients, relapse cases and cases of TB retreatment) was 26.7%, and it exceeded 30% in 2012 and 2013.

From 2007, an absolute number of new MDR-TB cases did not exceed 80, after a slight increase in 2004-2006. In 2009, 8 new cases of XDR-TB were reported; the same number was registered in 2011.

Modifying factors.

It should be noted that MDR-TB prevalence was calculated among patients with available DST results. From year to year, bacteria excretion and, correspondingly, DST results were less available among new patients, relapse cases and all TB cases in general. Detection of TB by mass fluorography is still a national priority and has resulted in a high prevalence of sputum-negative forms of TB (and hence no DST results for these patients).
Enrollment in the GLC treatment program using second-line TB drugs.

How many patients were enrolled in the GFATM project?

The grant program started in December, 1 and most of the reporting periods in 2004-2013 were based on the “program year,” or December to November of the following year. However, all official statistics of TB services is based on a calendar year. In other words, most data are provided in a calendar version, except Figure 7, where numbers correspond to the reports’ data submitted to the GF.

From 2000-2013, a total of 2,475 DR-TB patients, including MDR-TB and PR-TB, received treatment with second-line TB drugs provided by the GLC in Tomsk Oblast (Figure 7). Under the Global Fund project, 1,845 DR-TB patients were enrolled in the treatment program (1,427 in the civilian sector and 418 in the penitentiary system).

In the fall of 2009, under the GFATM RCC project, some changes in enrollment occurred. The aim of the project was to provide universal access to treatment of all forms of TB, including polyresistant TB (PR-TB), MDR and XDR-TB. Thus,

- Measures were taken to increase treatment coverage with TB drugs provided by the GLC.
- Official enrollment of PR-TB patients started. (In rare cases in the past, PR-TB patients had been enrolled in the program if resistance to a larger number of TB drugs was reported, including Rifampicin, or if their clinical condition was severe).

The principal recipient and sub-recipients made the following attempts to provide DR-TB treatment to the maximum number of patients:

1. Enrollment of all new patients into the program.
   a. When a patient was diagnosed with DR-TB (PR/MDR/XDR), a TB doctor prepared documentation to present the case at the Unified Clinical Expert Committee (Clinical Committee) which convened 1-2 times a week.
   b. A decision to enroll a patient into the treatment program was made by the Clinical Committee at the presence of the patient. The Committee designed treatment regimens and developed treatment approaches (possible treatment sites, consultations by specialized doctors if required, activities to enhance adherence to treatment). The patient was informed about the need to receive treatment, the treatment details, the treatment stages, and the importance of complying with the treatment regimen. During the conversation with the patient, potential problems were detected.
   c. Immediately before starting treatment, each patient admitted to TB Hospital was consulted by a psychologist and psychiatrist, in addition to standard consultations by specialized doctors. Each patient signed an informed consent form.
   d. At the beginning of the MDR-TB treatment project (2000-2004), there were some restrictions in treatment enrollment, such as poor motivation to treatment and severe concomitant conditions. However, these restrictions were eliminated after the program was expanded, and patient-centered approaches (social support, daily food sets, consultations by specialized doctors, substance abuse aid, in-home therapy service, the Sputnik project) were funded and implemented. All patients who agreed to receive treatment were enrolled in the program.

2. Analysis of DR-TB reservoir.
   a. Patients with chronic TB, who had failed previous treatment, were re-enrolled in the program.
Regardless of the efforts of TB Services to encourage and motivate patients to start treatment, some patients refused treatment with second-line TB drugs. Such patients were specifically controlled by heads of departments in the TB Dispensary. District TB doctors continued to invite patients who had been detected earlier to initiate treatment.

As a result of efforts to increase and maximize treatment coverage during the four years of the RCC project, 757 DR-TB patients were enrolled in the civilian sector and 138 patients were enrolled in the penitentiary system, totaling 895 patients.

**Were all MDR-TB patients enrolled in the GFATM project? Was the enrollment goal reached?**

**Indicator**
- “Number of MDR-TB and XDR-TB patients provided with DOTS Plus treatment in Tomsk oblast” (in 2004-2009 was reported separately for civilian and prison sector)
- Set from: 2004
- Target for 2004-2013: 1991 patients to be enrolled
- Enrolled in 2004-2013 actually: 1795

Prior to 2005, an average of 49.8% of MDR-TB patients detected in civilian sector received treatment using TB drugs provided by the GLC (the rest received medicines provided locally by the Russian Ministry of Health). Under the GFATM project, from 2005 to 2013, an average of 81.4% of patients detected with MDR-TB among all categories in civilian sector were enrolled on treatment with TB drugs provided by the GLC. The coverage increased from 76.3% in 2005-2009 to 87.7% in 2010-2013. Thus, from 2010 onward, the RCC goal to provide universal coverage of MDR-TB patients with treatment was almost reached.

In 2009, due to completion of the GFATM Round 3 Grant (April) and delayed start of the GFATM Rolling Continuation Channel Grant (December), enrollment of patients with drug-resistant TB was suspended; therefore, new MDR-TB patients started treatment with second-line TB drugs provided by the Russian Ministry of Health (MoH). However, due to insufficient amount of second-line drugs, it was impossible to design adequate treatment regimens. Funding of social support for TB patients was cut off, which resulted in increased patient defaults, specifically in rural settings of Tomsk Oblast. All the above had a negative impact on treatment effectiveness of patients in that period. In order to ameliorate damage caused to the patients by the cessation of activities, an agreement with the Global Fund was reached to start enrolling patients on treatment two months earlier – from 1 October 2009. A “waiting list” was prepared, which included MDR-TB patients who had not received treatment before or were treated with TB drugs provided by the Russian Ministry of Health. Additionally, a protocol to transfer patients from the Ministry of Health program to the GFATM program was developed. According to the transfer protocol, patients who had not been treated or treated with MoH TB drugs for no longer than three months were transferred to the GFATM project. Duration of previous treatment before enrollment in the GFATM project was considered if the previous regimen included minimum 4-5 effective TB drugs (with retained susceptibility), and clinical and bacteriological results showed improvements. Otherwise, a “failure” outcome was registered according to the MoH reporting system, and a new treatment course was started using TB drugs provided by the GLC.
It should be noted that enrollment was not limited by new MDR-TB patients only, as demonstrated on graphs 9 and 9a. According to the decision of the Unified Clinical Expert Committee, all patients were considered to be enrolled in the project, including those with multiple re-treatment courses. The number of patients enrolled in the program annually included those who had been detected with MDR-TB two years before and earlier.

**Table 5. Enrollment of MDR-TB patients in the GLC program on category IV, detected during different years in civilian sector of Tomsk Oblast.**

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</table>

*** based on GeneXpert test results

In prison all cases with MDR-TB were considered to be enrolled, but they were then screened according to organizational criteria:

1. The patient was considered for enrollment in the program if he/she had a long-term sentence to serve after MDR-TB was diagnosed.
2. If the patient was to be released on parole, a place of his residence before imprisonment or potential location after release was considered. Many TB inmates arrived at Tomsk prison from other Russian regions, Siberia and the Far East, and later they were sent back. Thus, they were unlikely to continue treatment in the civilian sector of Tomsk.
3. The patient was assessed in terms of TB treatment adherence while waiting for DST results and confirmation of MDR-TB. TB drug tolerance and refusal of treatment were considered as well.
4. The patient was informed on treatment with second-line TB drugs. If the patient refused treatment because of the myth that it was an “American” treatment or the conspiracy theory that treatment was a form of experimentation, and so on, the patient was not enrolled in the program. However, motivational talks were conducted on a regular basis.

As a result, enrollment in DOTS-Plus in prison did not reach 100% of all patients detected with MDR-TB.

It is clear from Figures 9 and 9a that enrollment goals were over-estimated for 2010 and 2011, at least for the civilian sector; in fact, even with universal access it was not possible to find that many patients (new or re-treatment) in the Tomsk Oblast civilian sector.
Were all XDR-TB patients enrolled in the GFATM project? Was the enrollment goal reached?

Under the GFATM RCC project, enrollment of PR-TB patients started in 2010.

The enrollment process was halted at the start of the RCC project because second-line drugs were not delivered to Russia because the Humanitarian Aid Committee, which is responsible for granting approval for drug shipments, did not meet to make such a decision for six months. The Humanitarian Aid Committee approved a shipment in July 2010, and in August, enrollment of patients in treatment was restarted. While the delay allowed PIH and Tomsk TB Services to develop treatment protocols for PDR-TB cases—which was then approved by the GLC—it resulted in a delay in patient enrollment in the program in 2010.

Despite the difficulties in 2010, more than 90% of PR-TB new and relapse cases in the civilian sector were enrolled in 2010-2013. The lower enrollment rate of 49% in the prison sector is explained by the same reasons as for the MDR-TB cases (outside Tomsk region, short sentence in Tomsk prison, and refusal of treatment). In general, 68.3% of all detected cases in Tomsk Oblast, including new, relapse and other/re-treated cases in both sectors, were enrolled in the GLC program.

The Figures above show that the estimates of the number of patients with PR-TB made at the time of the GFATM RCC application, were over-estimates. In general, the estimates were unachievable even in 2013 after the rationale for new estimates was provided to the Global Fund Secretariat. This may suggest that the reservoir of such patients had gone down or that we needed an alternative case-finding strategy.
Activities in clinical management in Tomsk Oblast

In 2000, Tomsk Oblast started treatment of MDR-TB patients using second-line TB drugs using individual regimens based on a patient’s drug-susceptibility testing. All patients are provided with medical care according to the approved protocols that have been constantly improved and revised in accordance with international standards and orders of the RF Ministry of Health. It should be noted that many WHO recommendations were based on the Tomsk program experience.

In Tomsk Oblast, treatment of MDR-TB patients XDR-TB patients is based on the following guidelines:

1. The Unified Clinical Expert Committee (UCEC) is responsible for making decisions about administering treatment regimens, changes in regimens, completion of the intensive phase, and treatment per se. Prescription of any second-line TB drugs is considered by the UCEC;
2. Access to quality-assured second-line TB drugs is provided to all MDR-TB patients regardless of patient’s history of treatment type, residence, social status, citizenship, and concomitant conditions;
3. A patient with MDR-TB is a case with documented drug resistance to at least Isoniazid (H) and Rifampicin (R), simultaneously;
4. A patient with XDR-TB is a case with documented drug resistance to at least Isoniazid (H), Rifampicin (R), any second-line injectable agent [Amikacin (Am), Kanamycin (Km), Capreomycin (Cm)] and one of the fluoroquinolones [Ofloxacin (Ofx), Levofloxacin (Lfx), Moxifloxacin (Mfx)] simultaneously.
5. MDR-TB treatment is provided in two phases, intensive and continuation phases. TB drugs are given at least six days a week under direct observation by a trained health care worker or volunteer. Family members as volunteers are strongly discouraged;
6. An MDR-TB regimen should include at least four effective second-line anti-TB drugs and pyrazinamide (as a fifth drug) during the intensive phase:
   - Injectable (Kanamycin, Amikacin, Capreomycin)
   - Fluoroquinolone
   - Ethionamide or Prothionamide
   - Cycloserine and/or PAS (if no Cycloserine available)
   - Pyrazinamide
7. DST to first and second-line drugs is guiding the regimen;
8. The intensive phase of MDR-TB treatment is at least 8 months and should be based on sustained cessation of bacillary excretion confirmed by culture with clinical and X-ray improvements. Duration of the use of injectable agent for XDR-TB is usually 12 months and more, and is based on strong evidence of culture conversion and response to therapy;
9. Total MDR-TB treatment is at least 20 months and should be based on sustained cessation of bacillary excretion confirmed by culture with clinical and X-ray improvements. Duration of XDR-TB treatment is no less than 24 months and more, and is based on strong evidence of culture conversion and response to therapy;
10. TB drugs are taken once a day, if possible:
    - In the continuation phase, when a health worker or volunteer cannot observe the second dose, TB drugs are taken once a day;
    - Fluoroquinolones (Levofloxacin, Moxifloxacin) are taken once a day during the entire treatment;
    - Note: As a rule, Ethionamide/Prothionamide, Cycloserine, and PAS are split into 2-3 doses during the intensive phase in order to prevent side effects;
11. All taken and missed doses of TB drugs are calculated at the end of each month:
    - The intensive phase and total treatment period can be prolonged according to the UCEC decision for a period that accounts for the total number of missed doses;
    - For patients on Category IV treatment who interrupt treatment for 2 months and longer, the patient is considered to be in “treatment default” and treatment is resumed starting from the beginning to fulfill all program requirements.
12. Intensive clinical, bacteriological, and X-ray monitoring is performed during the entire MDR-TB treatment:
    - Prior to treatment, sputum smear and three sputum samples are examined by culture in all MDR-TB patients. During treatment, two sputum samples are collected for culture test every month;
    - Drug susceptibility testing (DST) to first- and second-line drugs is performed in all bacillary TB patients prior the start of therapy;
    - DST to second-line TB drugs is repeated if patient remain smear/culture positive after 3-4 months of treatment under strict observation and there is no respond to treatment found during routine chest radiography examination;
• DST to second-line TB drugs is performed in patients with persistent bacillary excretion who interrupt treatment for multiple times for any reason for longer than one month;

• Careful clinical monitoring is performed during the entire treatment and include complete blood count, urine analysis, and biochemical blood tests are performed prior to treatment and every month during the treatment. If required, these tests are performed more frequent as requested by a TB doctor;

• It is required to test electrolyte level (K, Na), serum creatinine, BUN, bilirubin, and liver enzymes, on a monthly basis especially during the intensive phase;

• Chest radiography examinations are performed at the start of treatment and further on a quarterly basis until the end of therapy;

• If necessary, specialized doctors (eye doctor, ENT specialist, neurologist, psychiatry and substance addiction specialist, endocrinologist, and others) examine patients prior to and during treatment.

13. Intensive monitoring and management of side effects are performed during the whole course of treatment:

• Detection and management of side effects shall be performed in a timely fashion. For this purpose, health care staff providing observed therapy are regularly trained;

• Questionnaires and information pamphlets were developed to help nurses and volunteers to detect side effects;

• During treatment, a TB doctor fills out a side effects form to record any adverse reaction associated with TB therapy. All data are entered into the electronic data base at both civilian and prison sector and lately analyzed for pharmacovigilance purposes;

• Diagnosis and elimination of side effects and treatment of concomitant conditions are performed during the entire treatment in accordance with the clinical algorithm approved by the MDR-TB treatment program of Tomsk Oblast;

• All patients should receive pyridoxine (Vitamin B6) while receiving cycloserine (it is based on the calculation: pyridoxine 50mg per cycloserine 250 mg, maximum daily dose of pyridoxine is 300 mg)

• Vitamin and mineral complex is advisable to all patients during the entire treatment;

• A list of medications for symptomatic and pathogenic treatment has been approved which is annually revised and adjusted depending on requirements of the committee, which consists of deputy head doctors, a pharmacy head, and a PIH clinical specialist;

• All ancillary medication for the management of side effects are provided free of charge to all patients in all treatment locations.

14. Outcome definitions match the WHO definitions with “Cured” identified as completed as a case without evidence of failure and three or more consecutive negative cultures taken at least 30 days apart are negative after intensive phase. “Treatment completed” is identified as successfully treated case but with no record of three or more consecutive negative cultures taken at least 30 days apart are negative after intensive phase. “Treatment failure” outcome is approved by a joint decision at the UCEC meeting when a patient remained smear/culture positive after 12 months of directly observed therapy and when there is an evidence of additional acquired resistance to fluoroquinolones and/or second-line drugs, or severe and life threatening adverse reactions;

15. A patient-centered approach is applied to all patients without exceptions regardless of the source of TB drugs supply;

• Social and psychological support of patients who receive regimen IV treatment helps improve adherence to treatment;

• Types and methods of social support are different and patients can receive social support during the entire treatment (food sets, assistance in document renewal, housing assistance, clothes, etc.);

16. Surgery is one of the important stages in MDR-TB treatment and significantly improves treatment effectiveness with appropriate indications and timing:

• Regardless of specificity, surgery should be done timely, preferably early in treatment;

• When cavity or tuberculoma occurs, a surgeon should consult the patient no sooner than 3-4 months after treatment start;

• Before surgery, the patient should be treated with TB drugs for no less than 3 months;

• If the patient has positive smear and/or culture at the time of surgery, and in case of thoracoplasty, a general duration of treatment should be at least 18 months after culture conversion;

• After surgery, the patient is proscribed with an injectable drug for 3 months; the case is presented and discussed at the UCEC meeting to make a decision to prolong or cancel the injectable drug;
If at the time of surgery the patient was smear and culture negative and:

i. *M. tuberculosis* was detected in resection material by culture, a general duration of treatment after surgery should be at least 12 months;

ii. *M. tuberculosis* was not detected in resection material by culture, a general duration of treatment should be at least 9 months;

In case of limited localized TB, the duration of MDR-TB treatment after surgery is at least 9 months and an injectable drug should be used for at least 3 months;

i. In case of generalized TB when there is no chance to remove all changes in lung parenchyma, a general duration of MDR-TB treatment after surgery should be at least 12 months, and an injectable drug should be used for at least 3-6 months.

Since 1999, the UCEC has been the central body of clinical monitoring. Prior to 2002, it was a joint committee for both civilian and prison sectors. Then, for convenience in operation, the UCEC was divided into two separate committees for each sector.

The UCEC meetings are convened every week or more frequently if required at different clinical sites. More than 650 meetings, including clinical discussions of MDR-TB patients, were conducted during the entire period of the UCEC functioning. The Chair of the Committee had two deputies; one represented polyclinic (outpatient) services, the other represented the inpatient departments of TB service of Tomsk Oblast. The secretary was responsible for taking minutes of the UCEC meetings and bringing UCEC decisions into medical documents. UCEC members were specialists from different departments dealing with diagnostics and treatment of MDR-TB patients.

UCEC tasks included:

- Development of an individual plan for clinical and program management of a patient: prescription and completion of treatment, therapy adjustments, elimination of side effects and concomitant conditions, completion of the intensive phase of treatment, decision on surgery and treatment site, and determination of treatment outcomes;

- Patients with bacillary excretion at month 4 were presented at UCEC meetings by TB doctors in order to determine reasons and make adjustments to the medical and program management;

- The committee members interviewed the patient before treatment, during treatment (if there were issues related to management, and treatment adherence), and upon completion of therapy.

Due to UCEC:

- A unified clinical and programmatic approach to design an individual plan for each patient was developed;

- Decisions were made collectively, which was particularly important in complicated cases;

- Patients felt a positive impact from the individualized focus;

- Continuity of treatment between inpatient and outpatient stages was achieved;

- Professional qualification of specialists improved, understanding of MDR-TB specifics extended, and analysis and generalization of principles resulted in the development of recommendations.

Most of patients in the civilian sector (65%) treated under the GFATM project started TB treatment in the TB Hospital. The average duration of inpatient treatment was 7.4 months. Then patients were transferred to outpatient treatment under direct observation provided by the TB Dispensary, General Healthcare Services and Russian Red Cross. An average duration of the outpatient treatment was 20.3 months.

About one third of patients (27%) started outpatient treatment in Tomsk city and rural settings of Tomsk Oblast. In most cases, there were patients with limited TB disease (focal TB, tuberculoma) with no sputum smear and severe comorbid conditions. In rare cases, there were patients who refused inpatient treatment. The general guidelines of managing those patients were not different from those who started intensive phase treatment in the inpatient department. In Tomsk city, the most complicated clinical cases (poor TB drug tolerance, concomitant conditions) were transferred to the Day Care Hospital, where TB patients were treated under observation during the daytime hours.

The Principle Recipient’s employees – PIH – performed requirements calculation, procurement, and supply of second-line TB drugs during the project period. A central warehouse of TB drugs was set up at the premises of TB Dispensary to supply TB drugs to all treatment sites of Tomsk Oblast, both in civilian and prison sectors. This approach allowed for an uninterrupted and centralized supply of equally effective TB drugs regardless of treatment site. The information on supply, usage, remaining medications, and expiry dates for each drug was entered into the pharmacy’s electronic data base to keep records and plan further procurement of TB drugs.

To receive second-line TB drugs, an application form was filled out for each patient with the name, date of treatment start, resistance pattern, treatment regimen (TB drugs, doses), and date of regimen change. Data on the regimen of each patient (TB drugs, doses, date of regimen change) were entered by a physician in charge of the electronic data base.
Management of side effects in patients with polyresistant TB, MDR-TB, and XDR-TB.

Given the duration of treatment, number of TB drugs taken and their effects, adverse reactions to TB drugs have a significant impact on the effectiveness of MDR-TB treatment. The frequency of adverse reactions to first-line TB drug treatment ranges from 8% to 20%; for second-line drugs it ranges from 85% to 100%. Delayed and inadequate elimination of side effects often results in patients’ refusing some TB drugs, inadequate regimens, failures in treatment, and treatment interruptions.

In order to diagnose and treat side effects in MDR/XDR/PR-TB patients, TB doctors used the protocols given in “The PIH Guide to the Medical Management of Multidrug-resistant Tuberculosis”.

Due to clinical training and practice (participation in UCEC meetings and other medical committees), TB doctors constantly improved their clinical qualification in detecting and managing side effects.

The analysis of side effects in patients treated with regimen IV and enrolled between 17 January, 2000 and 20 January, 2006 in civilian sector of Tomsk Oblast (452 MDR-TB patients) showed that 86.3% of patients had side effects to TB therapy. At the same time, side effects in one-third of patients were managed without suspending TB drugs. In 27% of patients one or several TB drugs were suspended, and in 27.4% of patients side effects happened to be intractable, and as a result, one or several TB drugs were discontinued (Fig. 11). However, treatment was not completely stopped in any patient.

Most frequently (42.7%), patients complained of gastro-intestinal side effects (nausea, vomiting, heartburn, diarrhea, etc.). Almost one-third of patients had joint pain (32.5%), hearing disorder (37.4%), and urinary tract side effects (36.5%). Every fifth patient had hepatobiliary disorders (21.2%), as well as psychiatric disorders (24.8%) and high levels of thyroid-stimulating hormone (27.2%). Electrolyte disorders were less frequent (12.4%) as well as allergic reactions (15.3%).

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Seventy-seven of all side effects were registered in the first 8 months of treatment. (Fig. 12). Nevertheless, a small proportion of patients had side effects until the end of therapy. It should be noted that the analysis included patients who were on treatment and reported side effects; it did not include side effects of patients who defaulted from treatment after the moment of default (especially because of side effects).

### Table 7. Side effects in patients using alcohol during MDR-TB patient compared to non-drinking (407 patients).

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Alcohol drinkers, n=253 (%)</th>
<th>Non-drinkers, n=154, %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any side effects</td>
<td>230 (90.9)</td>
<td>137 (88.9)</td>
<td>0.52</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>246 (97)</td>
<td>145 (94)</td>
<td>0.1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>163 (65)</td>
<td>88 (57)</td>
<td>0.005</td>
</tr>
<tr>
<td>Depression</td>
<td>33 (13)</td>
<td>26 (17)</td>
<td>0.04</td>
</tr>
<tr>
<td>Psychosis</td>
<td>13 (5)</td>
<td>23 (15)</td>
<td>1.00</td>
</tr>
<tr>
<td>Seizure</td>
<td>45 (18)</td>
<td>31 (20)</td>
<td>0.32</td>
</tr>
<tr>
<td>Ototoxicity</td>
<td>60 (24)</td>
<td>42 (27)</td>
<td>0.81</td>
</tr>
<tr>
<td>Joint pain</td>
<td>180 (71)</td>
<td>119 (77)</td>
<td>0.14</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>44 (17)</td>
<td>31 (20)</td>
<td>0.23</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>27 (11)</td>
<td>20 (13)</td>
<td>0.19</td>
</tr>
<tr>
<td>Nephrotoxicity</td>
<td>36 (14)</td>
<td>17 (11)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>55 (22)</td>
<td>32 (21)</td>
<td>0.51</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>156 (62)</td>
<td>96 (62)</td>
<td>0.83</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>28 (11)</td>
<td>14 (9)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

Due to high prevalence of alcoholism, treatment outcomes and side effect frequency were analyzed among patients with alcohol abuse compared to those who did not use alcohol during MDR-TB therapy [3]. No significant difference was identified in the frequency of side effects among alcohol users and non-users, except diarrhea, which occurred more often among those who did not use alcohol (Table 7). Nevertheless, 74.6% of patients who did not use alcohol during treatment completed therapy as “cured” compared to 46.6% of alcohol users (p < 0.001). Interestingly, favorable treatment outcomes among alcohol users happened to be related to treatment adherence (taking 80% and more doses of TB drugs)7.

### Some changes in clinical management of patients:

1. Starting in December 2009, a list of medications for symptomatic and pathogenic treatment, procured for DR-TB patients in the GFATM program, was expanded. From 2012, based on the needs analysis, the cost of symptomatic medications in the civilian sector increased from US$13 to US$24 for one patient per month

2. In 2010, the first successful experience of using Linezolid was reported. Due to the request of the PIH medical director, Pfizer, the pharmaceutical corporation, donated Zyvox (Linezolid) for 12 months to be used in the treatment of a 22-year-old XDR-TB patient. Using Linezolid in the regimen of the patient stabilized the disease, allowing for surgery to be performed and helping complete treatment successfully. In 2014, based on the international experience, PIH developed a protocol for using Linezolid in XDR-TB treatment, procured the drug, and enrolled 22 XDR-TB

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patients who are currently on treatment.

3. In 2011, Levofloxacin was identified as fluoroquinolone of first choice and replaced Ofloxacin in MDR-TB and PDR-TB regimens. Additionally, Moxifloxacin started to be used more aggressively (it was used in the regimen for all patients with Ofloxacin resistance).

4. Improving surgery:
   - Due to the procurement of surgical equipment and extended indications for surgery, the number of MDR-TB patients who were operated on increased from 20 in 2011 to 43 in 2012.
   - A team of surgeons from Novosibirsk TB Research Institute had visited Tomsk in June 2012 with the purpose to review patients require surgery and conduct a series of operations for training purposes. Some patients were operated by Tomsk surgeons under the observation by Novosibirsk TBRI team.
   - In 2010, according to the UCEC surgery indications, valvular bronchial blocking started to be used in DR-TB patients. However, in 2013 a trained bronchologist left TB hospital and the surgery was stopped. A training of the new specialists will be conducted this year.

**Improving infection control in TB service of Tomsk Oblast**

Improvement of infection control included the installation of modern ventilation equipment in 8 TB facilities of Tomsk Oblast, across both civilian and penitentiary sectors.

In addition to ventilation equipment, the GFATM funding was used to procure gowns and respirators (3-M) for medical staff to protect them from drug-resistant strains. Due to the GFATM funding, a well-organized individual infection control program helped to significantly decrease TB incidence among medical staff in TB services.

In March-April 2011, an “Anti-tuberculosis infection control: Organization and practical aspects” training was conducted for healthcare workers of Tomsk Oblast TB Services and was attended by infection control experts. Following the training, a fit-test to accurately fit and wear respirators was introduced into practice. Furthermore, shielded UV-lamps were procured and administrative measures of infection control were revised (separation of patient flow).
MDR-TB treatment results

What was the frequency of risk factors associated with negative outcomes?

The negative outcomes are more common in patients with the following characteristics:

1. At treatment start:
   a. Alcohol/drug dependence (or during treatment), unemployed, homeless, history of imprisonment, defaulted treatment in the past6.
   b. *M. tuberculosis* confirmed by smear microscopy at the beginning of the current treatment; bilateral abnormality; pulmonary cavities; BMI less than 18.5; previous use of fluoroquinolones or resistance to fluoroquinolones; resistance to any thionamides6,8,9,10,11.

2. During treatment:
   a. A lack of culture conversion by month three; three or more days of missing doses in the intensive phase12; or less than 80% doses taken8,10.

Clinical and social characteristics associated with negative treatment outcomes of patients enrolled in the GLC project are given in Table 8. Clinical risk factors occurred most often in patients enrolled in the program in 2002, 2005, and 2009-2013. From the point of view of social characteristics, the most difficult were patient cohorts of 2004-2008.

The most complex cohorts in prison, based on the same clinical and social features, were cohorts of patients enrolled in 2004, 2005, 2008, and 2010-2011 years (in 2013 only 3 MDR-TB patients were enrolled).

How soon was regimen IV prescribed to the patients in need in the GLC project?

At the beginning patients with chronic TB were enrolled in the project. A thorough study of the TB patient reservoir in Tomsk was carried out. As a result, a period between MDR-TB detection and the start of regimen IV was quite long.

Beginning in 2005, half of the patients started to receive regimen IV using TB drugs provided by the GLC in two months. From 2010 onward, the duration dropped to one month. In 2012-2013, introduction of the molecular genetic testing (MGT) allowed the team to reduce this period up to one week. Delay of treatment in the 2009 cohort is also clear.

In the fall of 2011 a GeneXpert machine was procured for Tomsk TB Services. According to the developed protocol, the following patients were subject to testing:

1. Any patient with TB treatment in the past (relapse, failure or default case).
2. Patients with no TB treatment in the past (or there is no information about previous treatment), but with high risk of MDR-TB:
   - Patients who had contact with an MDR-TB patient;
   - Patients released from prison;
   - Patients suspected in receiving TB treatment in the past.
3. HIV patients with suspected TB.

The proportion of patients enrolled in the GLC program using GeneXpert results increased to 30.5% (Fig. 13a.).

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3. Gelmanova IV, Keshavjee S, Gelmanova IV, Atwood S, Franke MF, Mishustin SP, Sterlis AK, Andreew YG, Pasechnikov AD, Barnashov A, Tomsk 2013. Introduction of the molecular genetic testing (MGT) allowed the team to reduce this period up to one week. Delay of treatment in the 2009 cohort is also clear.

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*Grant RUS-304-G02T | The Tomsk Oblast Comprehensive Strategy to Reduce the Burden of DR-TB*
Table 8. Selective clinical and social characteristics associated with negative outcomes among patients with MDR-TB enrolled in the GLC project, civilian sector

<table>
<thead>
<tr>
<th>Clinical risk factors, %</th>
<th>C*</th>
<th>Social risk factors, %</th>
<th>S*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort, years</strong></td>
<td><strong>DR to FQ</strong></td>
<td><strong>DR to all injec.</strong></td>
<td><strong>DR to Eth</strong></td>
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<tr>
<td>2001</td>
<td>8.5</td>
<td>13.4</td>
<td>50.0</td>
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<tr>
<td>2002</td>
<td>11.9</td>
<td>25.8</td>
<td>79.8</td>
</tr>
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<td>2003</td>
<td>5.0</td>
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<td>2004</td>
<td>3.9</td>
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<td>2005</td>
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</tr>
<tr>
<td>2007</td>
<td>9.2</td>
<td>9.9</td>
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<tr>
<td>2008</td>
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<td>2012</td>
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<td>2013</td>
<td>23.2</td>
<td>16.2</td>
<td>51.5</td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td>9.2</td>
<td>14.7</td>
<td>40.3</td>
</tr>
</tbody>
</table>

Table 8a. Selective clinical and social characteristics associated with negative outcomes among patients with MDR-TB enrolled in the GLC project, prison sector

<table>
<thead>
<tr>
<th>Clinical risk factors, %</th>
<th>C*</th>
<th>Social risk factors, %</th>
<th>S*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort, years</strong></td>
<td><strong>DR to FQ</strong></td>
<td><strong>DR to all injec.</strong></td>
<td><strong>DR to Eth</strong></td>
</tr>
<tr>
<td>2000</td>
<td>0.0</td>
<td>0.0</td>
<td>55.3</td>
</tr>
<tr>
<td>2001</td>
<td>0.0</td>
<td>0.0</td>
<td>25.0</td>
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<tr>
<td>2002</td>
<td>5.6</td>
<td>0.0</td>
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</tr>
<tr>
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<td>6.5</td>
<td>2.2</td>
<td>23.9</td>
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<tr>
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<tr>
<td>2010</td>
<td>16.0</td>
<td>8.0</td>
<td>48.0</td>
</tr>
<tr>
<td>2011</td>
<td>22.6</td>
<td>17.0</td>
<td>35.8</td>
</tr>
<tr>
<td>2012</td>
<td>9.5</td>
<td>9.5</td>
<td>38.1</td>
</tr>
<tr>
<td>2013</td>
<td>0.0</td>
<td>33.3</td>
<td>100.0</td>
</tr>
</tbody>
</table>

«*» - the sum of the marked cells. The cell is marked if the number is above median.

FCTB - pulmonary cavities
Interim treatment results

Indicator

- Name “Number and percentage of MDR-TB and XDR-TB patients registered under DOTS Plus who are culture negative at six month of treatment in Tomsk oblast”
- Set from: 2009

Since 2009, “The interim results of MDR-TB treatment” has become one of the accepted indicators for international programs. This indicator was introduced into the GFATM project in 2010. The indicator shows cohorts history at month 6 after the start of regimen IV (percent of outcomes: “died”, “treatment interruption”, “transferred out”), as well as culture results. A positive achievement is considered to be a high percent of patients with “negative” culture.

In 2009 – 2010 cohorts, this indicator was lower than the target indicator due to several reasons:

- There was a half-year delay in the indicator period (from May 2009) and the start of the grant (December 2009). Therefore monitoring of the new indicator and increased efforts to reach the targets in a timely manner were late.
- In 2009 the PR and SRs made incorrect estimates. In late 2010 the WHO released guidelines on how to calculate (MDR-TB INDICATORS (A minimum set of indicators for the programmatic management of MDR-TB in national tuberculosis control programs)). Targets were based on the negative sputum at either 5 or 6 months of treatment, but it emerged later that only sputum at month 6 should be taken into account. As a result, PIH discussed with sub-recipients the new methodology – the sputum should be collected strictly between 153 and 184 days of the treatment.
- High proportion of patients without test result within the frames of 153-184 days in civilian sector (Fig.15).
- Worse clinical features of patients enrolled into the RCC cohorts from late 2009 compared with previous cohorts of patients.

PR and SRs increased their efforts to improve this indicator, in particular:

- Increased monitoring of SRs organizational efforts to take sputum from TB patients exactly in the sixth-month frame (especially in the civilian sector) by PIH monitoring unit.
- Development and monitoring of monthly clinical requests of GF patients’ datasets with several clinical features, including smear/sputum status, for early failure detection and prevention.
- And clinical discussions of the complex patients on committees twice a week with presence of PIH representative to provide better clinical management of complex cases.

As a result, in 2011 and 2012 results slightly improved.
An average period of treatment of the GLC patients enrolled under the GFATM project lasted the same time as in the past. On average, the duration of treatment was 20.3 months (19.9 months in 2000-2004), and half of the patients were treated for 18.8 (18.1 in 2000-2004).

Among failures, the average period was 18.6 (median 17.6), and patients died of TB on average after 9.3 months of regimen IV treatment (median 8.3).

Are treatment outcomes high in MDR-TB cohort?

Effective treatment rate (patients who finished their course as “cured” plus “treatment completed”) among patients enrolled in GFATM grant treatment was higher 60% in almost all cohorts. In 4 out of 7 cohorts of patients with known results, the result was higher than the target.

The effective treatment rate dipped in 2008 due to a high default rate among patients enrolled in prison and lost to follow up after their release. Generally, since 2005, 4% to 9% were reported to have died from reasons other than TB (alcohol poisoning, accident, other).

Severe pulmonary damage with cavities and fibrosis, co-morbid conditions like diabetes, along with a history of previous treatment served as predominant factors for treatment failure among all cohorts of patients enrolled since 2005. Of the patients reported as treatment failure in 2004–2006 cohorts, 82% had history of previous treatment, and 27% of them had been already exposed to second-line TB drugs prior the start of MDR-TB regimen; they had wide drug resistance patterns to up to 6 drugs, including fluoroquinolones. However, percentage of patients who failed therapy during 2006-2008 decreased to 9-15%, which is considered low, especially with patients with complex clinical and socio-economic profile.
The following rise in the rates of treatment failures in 2009 cohort was closely related to the 9-month gap in patient enrollment and delays with initiation of the RCC grant. The cohort of patients enrolled in the transitional period in 2009 was one of the most complex in terms of clinical characteristics; 20% of patients had XDR-TB at the start of regimen IV. Waiting for treatment in 2009 resulted in deterioration of TB processes in the lungs of many patients enrolled in the fall of 2009, which led to lower efficiency of clinical management of the cases. The proportion of patients who enrolled and finished their treatment as “cured” was 48% in the civilian sector, which is lower than estimated and the lowest results of the Tomsk program. More recently, in the 2010-2012 cohorts, the percentage of unfavorable outcomes significantly decreased and returned to its lowest levels due to improvements in several program areas, including a sufficient drug supply, adequate treatment, and implementation of complex social support and adherence-strengthening interventions.

It should be mentioned that average rate of effective treatment is higher among the average MDR-TB projects results. According to the published reviews13,14, an average cure rate for MDR-TB world projects is 62% (95% CI 58-67%), and 62.8% in GLC projects (WHO’ STOP-TB partnership data).

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**Are treatment outcomes high in MDR-TB cohorts without XDR-TB?**

According to the WHO guidelines15, if the proportion of XDR-TB in the MDR-TB cohort exceeds 5%, the results should be reported separately. Tomsk TB program doesn’t have separate indicators for XDR-TB cohorts in the Performance Framework and PU/DR. The proportion of MDR-TB patients effectively treated excluding XDR-TB is quite high. In the civilian sector, starting 2005, on average 66% of patients finished their treatment effectively, and in three massive cohorts of patients the rate was well above 70% (2006, 2007 and 2010). In prison, where traditionally the rate of effective treatment is higher than in the civilian sector, the rate for cohorts from 2005-2011 was more than 83% on average.

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15 “MDR-TB INDICATORS (A minimum set of indicators for the programmatic management of MDR-TB in national tuberculosis control programs)”
What are treatment outcomes in XDR-TB cohorts?

XDR-TB cohorts have lower cure rate than MDR-TB cohorts. The proportion of patients with XDR-TB grew between 2010-2013. The proportion of patients treated effectively has also grown since 2009.

Out of 608 MDR-TB patients who had treatment in civilian and prison services in Tomsk between September 2000 and September 2004, 4.8% of patients had baseline XDR-TB (29) and treatment failure was most common among them. Those patients did not receive linezolid or clofazimine, or any other third-line drug. Treatment failure was more common in patients with XDR than in those with non-XDR (31% vs 8.5%, p=0.0008). Still, 48.3% of patients with XDR-TB tuberculosis and 66.7% of patients with non-XDR TB had treatment cure or completion (p=0.04), which were the highest rates ever reported without the use of new drugs and other group 5 agents.

In average treatment outcomes of XDR-TB in Tomsk hardly exceed 50% of favorable outcome (vary from 13.3% (2005) to 52.4% (2011)), with most of the patients remained culture positive and considered as treatment failure. Treatment failure was mostly associated with massive pulmonary damage, wide spectrum of drug resistance and further amplification to other second-line drugs (Ethionamide and PAS), which limited therapeutic capabilities of regimens. Generally, the development of treatment failure of XDR-TB cohorts was closely associated with the absence of effective drugs in the XDR-TB regimen and not treatment interruptions. Default rate of XDR-TB cohort is lower than in MDR-TB and frequency of adverse reactions is the same. Treatment of XDR-TB showed better outcomes with some of Group 5 drugs added to the regimen besides the longer use of Capreomycin or later generation fluoroquinolones (Moxifloxacin).

What are treatment outcomes of patients with polydrug-resistant tuberculosis?

Management of patients with PDR-TB was performed according to the clinical protocol developed with technical assistance from PIH. Design of PDR-TB regimens are driven by results of the DST and include all first-line drugs, which remain susceptible. Second-line drugs, such as injectable agents, fluoroquinolone and ethionamide, are added in regimens for patients with certain drug-resistance patterns when there is no chance to assure availability of 4 effective anti-TB agents. Patients diagnosed with any resistance to Rifampicin, even with mono or polydrug-resistance, are considered for treatment with MDR-TB regimens.

In prison, the overall number of patients enrolled into GLC treatment is too low to show outcomes by years; 26 patients in 2010-2013. The overall cure rate of enrolled PDR-TB patients was 82%, and 13.6% were transferred out.
**Challenges and lessons**

**Challenges:**
- Old regulatory base (Prikaz 109), which allowed the use of weak regimens, including an incomplete spectrum of second-line drugs for patients at high risk of MDR-TB. This eventually resulted in amplification of drug resistance.
- Availability and uninterrupted supply of second-line drugs. Shortages of drugs due to organizational constrains (late start of the RCC grant, sporadic shortages of some certain drugs) are the leading causes of unfavorable outcomes.
- Lack of availability of new regimens and Group 5 agents to address the burden of patients with XDR-TB and resistance to fluoroquinolone.
- Late diagnosis of TB and drug-resistant TB in early years of grant implementation. Lack of rapid diagnostic tools to identify patients and initiate appropriate regimens in a timely fashion. As a result, patients are diagnosed at late stages of disease and have suffered massive pulmonary destruction.
- Socio-economic profile of patients directly influence on treatment outcomes. Those patients with lack of access to adequate nutrition had higher chances of either slowly respond to therapy or fail/die. Poverty, malnutrition and alcoholism are directly associated with poor outcomes.
- Co-morbid conditions, including diabetes mellitus, HIV, hepatitis C and B; a lack of knowledge for treating patients with HIV co-infection; and a lack of strategies to address dual infection.
- Risk of nosocomial transmission of infection at inpatient facility. Patients, including those with XDR-TB and pre-XDR with resistance to fluoroquinolone including those with massive pulmonary damage, are still sharing wards with other DR-TB patients on treatment.
- Lack of availability of ancillary medicines in rural areas for those patients on continuation phase treatment.
- Adherence to treatment.

**The lessons learned during the implementation of the program are:**

1. Strict clinical and organizational monitoring and implementation of program activities led to effective program management:
   a. Central clinical committees consisting of TB experts should be the main body responsible for issuing guidelines and decision-making for difficult projects like treatment of MDR TB patients. The members of the committees should further provide education and monitoring at the workplace. The regular monitoring visits from regional TB services to remote rural areas should be organized.
   b. Great management efforts were made by the PR staff to allocate funds to evidence-based programs and to implement activities proven to work in the context of the vertical TB system in Russia.
   c. Motivation of personnel: Performance-based funding and management based on results was implemented, including motivational payments for the personnel. Tomsk project implementation required additional work that was not provided for by current Ministry of Health regulations, and organizational skills that are not required by Russian TB services, thus incentives payments served as a great motivation for many staff members. Unfortunately, the expansion of effective sub-programs requires additional funds and personnel, but these programs are not recognized by the current health care system financing. The limitation of funds for Russian TB projects will likely have a negative impact on the effectiveness of programs overall.
   d. Effective enrollment and drug procurement: The enrollment rate was accelerated to cover most patients with MDR-TB during the 5 years of the program. At the end of Phase 2, all necessary second-line drugs were procured for all patients still on treatment from the R 3 project budget.

2. Implementation of the evidence-based adherence activities adjusted to the local conditions led to improved adherence for TB patients on all regimens of treatment and resulted in higher treatment success rates:
   The availability of drugs to mitigate side effects increased treatment adherence. These medications should always be available alongside second-line drugs because side effects contribute greatly to the interruption of treatment for many patients.

3. Try everything possible to find programmatic solutions to clinical or organizational challenges. Often, different approaches need to be tested in order to find the right solution. For many doctors, the GFATM was the only tool to use or to reinvent effective approaches to improve outcomes for patients. Therefore, implementers should devise potential solutions to clinical and/or programmatic challenges as they see fit, so long as such programs are monitored and modified as needed.

4. Monitoring and evaluation should be carried out by specialists not working in the TB system. Several ideas that could have helped program implementation based on timely monitoring and evaluation were not effective simply because the TB personnel were not motivated or had another point of view about the program implementation.
Improving adherence

In 1994, Tomsk Oblast became one of the first territories in Russia to implement pilot projects in observed treatment of TB patients with the assistance of international partners. In 1995, TB treatment under direct observation by healthcare workers was implemented within the entire territory of Tomsk Oblast. Since 1997, treatment of each patient has been monitored using a computerized database and continuity between civilian and prison sectors has been established. In 1999, in collaboration with the Tomsk Branch of the Russian Red Cross, patients who were adherent to treatment started to receive social support in the form of hot meals and monthly food sets, and transportation costs, which were paid from the local budget. In addition to a medical procedure office, a day care hospital opened in Tomsk city, and services from visiting nurse services were delivered; up to 50 patients were visited a day by the visiting nurse services. Some homeless patients were referred to the Center of Social Adaptation for accommodation and treatment.

Initially, in 2000-2002, patients considered socially stable were given preference to be enrolled on treatment due to the limited number of second-line TB drugs. The MDR-TB project showed the highest effectiveness during this period. However, later in 2003-2004, all patients in need were enrolled in the program, which impaired treatment results due to an increased proportion of patients who interrupted treatment. Thus, in the 2001 cohort, the proportion of defaulters was 11.8%, and in 2004 it reached 28.6% in the civilian sector.

Starting in 2005, activities to prevent treatment interruption in Tomsk Oblast were expanded due to the funding of the GFATM Regional Grant.

- All patients treated in outpatient facilities started to receive daily food sets and monthly hygiene packages;
- Psychological and substance abuse assistance was expanded;
- Control of out-of-schedule TB hospital discharges was strengthened;
- A system of monitoring and attracting patients to treatment who missed TB drugs for 2-3 days was established, which allowed staff to further consider each case at the weekly Administrative Board responsible for treatment interruption;
- A monthly assessment of health care worker activity to attract patients to treatment was implemented;
- Social workers of the “Harm Reduction: Tomsk” project at “Tomsk-AntiAIDS” Foundation provided DOT to some patients with drug addiction.

As a result, the proportion of MDR-TB patients who discontinued treatment ahead of time in the 2005 civilian sector cohort decreased to 14.3%. However, this level seemed to be overstated and further efforts were made to expand those activities.

Adherence activities, with emphasis on Tomsk city, civilian sector

**Training of healthcare workers.**

The main goal of training healthcare providers and nurses was to improve their communication skills. In order to motivate a patient at risk of defaulting from treatment, it was important to involve a multi-faceted team. The team consisted of a TB doctor, nurses, psychologists, social workers, and employees of non-profit organizations. They all participated in collective training. This approach is effective in that it promotes and strengthens knowledge sharing across a wide array of disciplines—healthcare workers, psychologists and social workers, among others. For the last 7 years, training sessions were conducted both for physicians and nurses. During workshops and training sessions, trainees had an opportunity to master counseling skills in the workplace, consider complicated case reports, and receive tools to work with patients unmotivated to treatment.

Motivational counseling, short intervention method and many other approaches to counseling are universal and equally useful for medical and non-medical workers. As a result of mastering those methods, the staff showed tolerance to patients with psychoactive substance addiction in the past and referred them to visit a psychologist and substance addiction specialist instead of accusing and criticizing the patient.

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16 It means daily treatment under observation by specifically assigned nurses using 1-2 vehicles daily. They are not district nurses who visit patients according to the district of residence on a prophylaxis day, who count TB drugs given to a patient for 7-10 days.
Observed treatment - 100% of coverage.

According to multiple research findings, there are no patients that would be “once and for all” motivated for treatment. The way patients take TB drugs depends on ever-changing life conditions. Giving TB drugs directly to the patient for self-administration or under observation by the patient’s relatives and volunteers who are not trained in administration of directly observed treatment and who are not properly supervised by healthcare workers, often results in persistent smear positive sputum or bacillary recurrence and early TB relapse. Observed TB treatment includes not only administration of TB drugs, but also monitoring for side effects monitoring, and communicating across parties to identify problems and provide support.

A network of DOT points included

- TB Hospital (370 beds) and Psychiatric Hospital (up to 60 patients),
- Tomsk city (297.2 km²/ 524 669 pop):
  - Day care hospital (170 patients),
  - Medical procedures office at the TB outpatient clinic (80 patients),
  - Red Cross (2 stations for up to 50 patients),
  - Center for Social Adaptation for homeless people (10 patients),
  - “Tomsk-AntiAIDS” Foundation (5 patients),
  - In-Home Therapy Services (55 patients),
  - “Sputnik” (15 patients)

The overall number of patients treated in the civilian sector was decreasing in the last years when compared with the start of GFATM activities (2005). However, number of MDR-TB patients on treatment was growing. At any moment in the Tomsk city, fewer than 400 patients received treatment; 115-130 of them had MDR-TB (Fig. 24). The proportion of patients who received their daily TB medicines by treatment-in-home teams, Sputnik team and searching evening team was growing (Fig. 25).
One important element is building awareness among nurses of the need to observe TB treatment and how the patient is tolerating treatment. From the beginning of the program, TB nurses responsible for TB treatment administration took part in regular annual trainings on clinical and organizational management of TB cases. In addition, senior nurses conducted on-the-job training in TB departments, and supervised the administration of observed treatment. In addition to supervision provided by TB doctors, heads of TB departments submitted monthly the data on patients who missed 25% of TB doses. Additionally, senior nurses together with a coordinator of Partners In Health checked treatment cards (LU – 01, LU – 01/y), and considered each case when unobserved treatment cases were found. For instance, a patient, treated in the medical procedures office or Day Care Hospital, found a temporary job and he/she could not come to the treatment site to receive TB drugs due to a lack of time. Under these circumstances, the patient’s case was submitted for consideration for the Treatment Interruption Board, which convened weekly and made a decision on the treatment site for the patient to continue therapy. As a rule, such patients were transferred to receive treatment provided by the In-Home Therapy Services.

Monitoring of the In-Home Therapy Services and Sputnik was provided at different levels: physical examination of patients was conducted at least once every 10 days; the head of the city TB department or senior nurse of the city TB department visited patients once a month; and a PIH program coordinator visited patients once a month. During collaborative visits, close attention was paid to the way nurses communicated with the patients; how the nurses provided observed treatment; how they searched for the patient in case he/she was absent; whether TB drugs were given to the patient’s self-control intake, as well as other aspects of the work. If any issues were noted, for instance, inappropriate attitude of healthcare staff to the patient, then that issue was discussed in the vehicle of the In-Home Therapy Services. The main goal of collaborative visits was counseling. The task of the coordinator is to find mutual remedies to problems in a friendly environment. For some patients, a chance to communicate with a physician or representative of healthcare authorities has a “magical” effect. Therefore, a conversation with “troubled” patients is a regular practice used during the visits, when it is explained why it is necessary to continue taking TB drugs without missing doses. During a conversation, patients can discuss side effects and non-medical issues, which they do not mention to nurses for various reasons.

**Treatment start and additional specialists**

After detection of a TB case, a primary assessment of risk factors related to negative TB treatment outcomes was made. This includes the following:

1. The first health care provider to contact a patient – a district TB doctor or a nurse of the outpatient department and a psychologist or social worker of the inpatient department (in case a patient is admitted to TB hospital, not an outpatient facility) – fills out a social card for the patient.

All new patients undergo “AUDIT” test, which has demonstrated high confidence in alcohol use detection based on international practices7. If ‘alcohol or drug addiction’ is diagnosed, or if “AUDIT” results are higher than a score of 15, the patient is referred for a consultation by a psychologist and addiction psychiatrist.

a. According to “AUDIT” test results, patients could be divided into 3 groups: 1-7 low risk drinkers, 8-19 high risk drinkers, 20 and more probable alcohol dependence

2. Patients with drug-resistant TB should be assessed by a psychologist and addiction specialist before the patient is presented at a medical board meeting on MDR-TB (MB-MDR). A physician referring the patient for a consultation will contact the specialist; if the patient does not come for a consultation, he/she should make another referral and oversee the process until completion.

3. All patients with drug-resistant TB are considered by the MDR-TB Medical Board, which develops an individual plan for clinical and programmatic management of the patient, including: treatment regimen design; regimen adjustments, analysis of concomitant conditions and approaches to elimination of the conditions; needs for surgical treatment;

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determination of treatment sites; and determination of treatment outcome. The patients should be presented at the MDR-TB Medical Board meeting.

**Reassessment during TB treatment.** If healthcare workers or relatives report alcohol/drug use by the patient and/or the patient takes less than 75% of TB drug doses, the treating doctor refers the patient for another consultation by a psychologist, addiction psychiatrist and social worker. The lists of patients who have taken less than 75% of TB drugs are submitted daily by heads of TB departments of TB Services to psychologists, addiction psychiatrists, and social workers.

Appointments to visit any other specialists can be made individually by patients, or according to the decision of the “treatment interruption” medical board.

A multi-professional team works with patients at all stations of directly observed treatment and at the TB hospital during the entire period of treatment.

**TB doctor and the nurse:** Primary activities conducted with the patient by the district healthcare service start as soon as TB is detected. During each visit the treating doctor and the nurse talk to the patient (using TB pamphlets and leaflets) about the importance of adhering to the treatment regimen, the state of the disease, terms of treatment, active TB detection and timely elimination of side effects.

A district TB doctor informs the patient about the duration of TB therapy and agrees with the patient on the place and time of treatment start (depending on clinical conditions and patient’s circumstances). The patient signs a treatment contract. The doctor or district nurse collects and records the information about the patient, his/her relatives and immediate surroundings; they tell the patient about available treatment sites and social support; they also fill out a social card, which is submitted to a social worker to make a service plan and decision about patient’s problems.

**Training of patients.** All new patients are trained on tuberculosis and treatment adherence: they receive training materials. Classes for patients are conducted at the outpatient and inpatient stages of treatment. Classes are used to both improve patient’s awareness of disease and treatment adherence, and help to train volunteers among TB inpatients to perform preventive activities among those who confront the disease. The practice includes surveys, videos, lectures, open discussions.

The topics of classes correspond to the training modules. In TB hospital, the course includes 11 topic-related classes. One class lasts for 45 minutes. Pre- and post-tests are used to check the knowledge attained from the class. The training is conducted by psychologists in each TB department. At the outpatient stage, training is conducted by a social worker at the Day Care Hospital once a month. Depending on the topic, a social worker and psychologists involve other specialists. Compared to the inpatient facility, group members in the outpatient facility change/rotate each class due to different circumstances.

**The psychologist.** Currently, the psychologist does not provide her service any longer at the outpatient stage of treatment since patients have not made appointments to visit the specialist and receive care. Methods used in the TB Hospital do not crossover because outpatient treatment occurs in the patient’s usual environment and they try to leave the treatment facility after taking their medications. Home visits from a psychologist are not all that effective because psychological counseling requires a combination of appropriate environment and sufficient time, which is often difficult to arrange for the team of in-home treatment services.

The main goal of the psychologist in the TB hospital is to prevent missing doses of TB drugs. During her work, the psychologist focuses on dealing with psychological issues of patients that occurred while being in TB Hospital (they are not “echoes” from the past).

As a rule, simple tests are used for primary diagnostics, and if the patient is open and interested in advanced activities, special tests are applied.

In-person or group meetings are conducted both in physicians’ offices and patient wards. Counseling can be provided in hallways of the TB hospital (for example, inviting patients to come for a consultation), and outside while going for a walk (in summer time, at patient’s choice).
The addiction doctor/ psychiatrist

The first and most important task of treating patients with alcohol disorders is to provide a complete course of tuberculosis treatment in the inpatient facility, get smear and culture conversion, and then discharge him/her from the hospital to outpatient treatment. Treatment of alcohol addiction among TB patients, provided in a combination with TB therapy, consists of three stages.

Stage 1: Psychological and therapeutic intervention; detoxification therapy in order to eliminate excessive drinking; general therapy; elimination of psychopathy-like disorders using medical interventions and behavioral interventions. Vitamin B1, B6, C are important in treatment of withdrawal syndrome.

Stage 2: Intensive anti-alcohol therapy to stop cravings for alcohol and develop an aversion and intolerance to. This therapy should be administered to all patients in inpatient departments and, if possible, in outpatient facilities as well. Alcohol sensitizing drugs are used for treatment, as well as opioid receptor antagonists.

Stage 3: Providing therapy to make the patient stay sober. This includes constant psychological and therapeutic interventions, supportive therapy, and various rehabilitation activities.

All required medications are procured through the Program and are free for patients

Treatment of patients with opioid addiction

Treatment of TB patients suffering from drug addiction is comprehensive and combined with intensive psychotherapy. All healthcare workers involved in TB therapy of drug addicts are required to constantly instill confidence in patients for treatment success.

Treatment of drug withdrawal syndrome is administered in the intensive therapy ward of inpatient department, according to the accepted standards (pain relievers, sleeping pills, tranquilizers, neuroleptics, and other medications). TB therapy is not administered while providing withdrawal syndrome treatment. After withdrawal treatment, the patient is transferred to TB department for TB treatment. At this stage, supportive therapy is provided (with the use of antidepressants, sleeping pills, tranquilizers and other medications) and different rehabilitation activities are used. Once the patient is transferred from the intensive therapy ward, all medications are listed in the treatment administration record and are given to the patient under direct observation of the nurse.

Overall, the number of consultations provided was adequate to number of patients treated and increased as implementation efforts increased (Table 9).

Continuity of care

Every patient is closely monitored from the beginning of treatment in the hospital. When the patient is planned to be discharged from hospital, the hospital physician or deputy makes a call to the outpatient care facility to TB physician responsible for particular patient at his/her place of residence or living. The outpatient TB physician checks the validity of information provided by patient – that he is registered at this place, he is known here, and a close social network is informed that the patient is on treatment. The TB physician prepares TB medications and performs all necessary steps, and after that, the patient could be discharged from hospital.

Unfortunately, many patients do not inform physicians about their plans. The proportion of patients who left the hospital was high and all organizational efforts to overcome this challenge and to make discharge had a minimal effect. The proportion of defaults that happened after discharge decreased.
From the early 2000s information about patients to be released was appropriately transferred to civilian TB services (usually 2 weeks before release) and the proportion of patients successfully transferred to civilian TB services improved from year to year. A social worker providing assistance at the outpatient treatment stage makes monthly visits to the School of Release Preparedness at the prison facilities. She provides patients with the information on TB treatment sites and social support options in the civilian sector, thus, a social worker performs prevention of treatment interruption among TB prisoners to be released from the prison. Also, a social worker collects additional information about prisoners to be released and submits it to the district TB doctors to ensure continuity between prison and civilian sectors.

**Responding to missing treatments, treatment interruption board.**

In cases when a patient misses three days of treatment, senior nurses from all stations of observed treatment call the TB Dispensary’s information center.

Daily responsibilities of the nurse at the information center:

- Ask district TB doctors for the information about TB patients (address, telephone number, relatives) to give it to the visiting nurse services;
- Provide information to the visiting nurse services of appropriate city districts to search for the patients; collect search results from all visiting nurse services (teams); share information with the teams (information received from the morning shift team is shared with the night shift team);
- Provide information on patients missing treatment from TB Hospital to the rural department of TB Dispensary;
- Provide information to district TB doctors about the need to eliminate side effects and other urgent information received from visiting nurses;
- Make reports at the weekly meetings of the Treatment Interruption Board, a collective body based at TB polyclinic that consists of the head of organizational and methodical department, heads/representatives of observed treatment stations, a TB doctor, psychologist and addiction psychiatrist, social worker and PIH representative. The Board fulfills the following tasks on a weekly basis:
  - Maintains and oversees activities to attract patients to TB treatment;
  - Selects patients who need to be transferred to the visiting nurse services or “Sputnik” due to disabilities and poor treatment adherence.

Decisions are made collectively, which are recorded in a treatment interruption register (Appendix 8-3) and on the medical treatment card of the patient.
Social support, food sets.
To monitor the needs and requirements of patients, a TB doctor fills out a social card for each patient who has started outpatient TB treatment. A social worker associated with the TB Dispensary analyzes the cards and works with patients who need assistance and support (a social worker accompanies patients at all stages of treatment).

Social workers at the TB Dispensary and TB Hospital assist patients in obtaining pertinent documents, including those needed to apply for disability and pension benefits.

During inpatient and outpatient treatment, social workers provide a variety of assistance. This includes receiving technical rehabilitation devices, orthotic and prosthetic devices. It also includes helping with document renewal; receiving benefit payments: assistance in obtaining a health insurance certificate, passport, Individual Taxpayer Identification Number certificate, Insurance Number of Individual Account certificate, as well as preparing documents for medical and social expertise, applying for disability pension, applying for subsidies, receiving financial assistance, obtaining reimbursement of travel expenses to TB treatment sites, and various other tasks.

A TB doctor or a nurse of the district TB service performs a needs and requirements assessment of all patients who proceed to outpatient treatment. At the inpatient facility the healthcare worker who first makes contact with the patient fulfills this assessment. To improve motivation and prevent voluntary discontinuation of treatment among homeless patients and those with psychoactive substance addiction, consultations are given by a social worker. When patients face difficult circumstances, a social worker, in cooperation with the patient, makes a service plan to solve social problems. The plan includes priority activities and people/facilities responsible for implementation. If the patient receiving outpatient care is transferred to the inpatient department, then the service plan is attached to the referral. In the inpatient department, the service plan is given to a specialist in social work to provide further service to the patient. When the patient is discharged from the inpatient department, the service plan is attached to hospital discharge papers as well. When discharge papers reach TB dispensary, the service plan is passed to the social worker of the outpatient TB facility.

Patients are given daily food sets, which serve as a reliable source of motivation to visit treatment sites. Starting in 2008, daily food sets were provided to patients on outpatient treatment. All patients enrolled in the Global Fund program were provided with motivational sets. Additionally, patients with adherence difficulties and those in need of motivation received food sets, in most cases they were treated through In-Home Therapy Services or Sputnik.

Food sets for susceptible TB patients were distributed according to the results of the completed social cards.

The cost of one food set for susceptible TB patients was 55 rubles; the maximum permissible number of patients who received food sets at one time was 40. The cost of one food set for polypresistant TB patients was 65 rubles; the maximum permissible number of patients (enrolled in the GF program only) who received food sets at one time was 32. The cost of one food set for MDR-TB patients was 65 rubles; the maximum permissible number of patients (enrolled in the GF program only) who received food sets at one time was 58 patients.

Patients in desperate need of food sets treated with regiment IV (Ministry of Health) could receive food sets under the Global Fund program based on a decision of the Board (consisting of: a social worker at the TB Dispensary, a PIH representative and a TB doctor).

From the end of 2010 to the beginning of 2011, as incentive, additional food and hygiene sets were provided to patients who were in need of greater support. Criteria for distributing additional social support were developed:

1. Social cards of all patients who need additional social support should be filled out.
2. Additional food sets are provided to:
   a. Specific categories of patients (homeless, poor patients) treated in the medical procedures office, Day Care Hospital – on a weekly bases;
   b. All patients treated by Sputnik team – every two weeks;
   c. Poor patients treated by In-Home Therapy Services – once a month.
3. Hygiene packages and/or clothes (T-shirts, socks, linens, and towels) were provided to homeless and poor patients once a month at all treatment stages.
4. Beginning from 2011, all TB patients who were released from prison received one-time sets during the first visit to the district TB doctor.

In 2011, 4 focus groups were conducted to discuss menus and the significance of the food set on patient motivation. The menu was changed to be more attractive to patients and include items they specifically requested. The price of food sets also increased as a result: 70 rubles for patients with susceptible TB and 100 rubles for PDR-TB and MDR-TB patients.

A new nutritional monitoring system was implemented in December 2009 in the civilian sector to monitor the number of patients in need (specifically patients with susceptible TB) on a weekly basis. All patients who started treatment at outpatient settings are registered in the database, as well as those who started to receive food sets. The Red Cross’ nutritional databases for patients with susceptible TB, PDR-TB, MDR-TB and XDR-TB continue to be used in a renewed format, and most patients in rural settings receive food sets.
As of 2011, patients in Day Care Hospital receive nutritional support through co-financing from MOHSD budget – food sets with similar amount and quality of items, and all recording forms with patients’ signatures are collected, too. They did not receive food sets from the grant and were not counted. Given the co-financing, coverage of food support in the Tomsk civilian sector was 95%-99%.

In 2005-2013, 5,639 patients with all forms of TB were enrolled in Red Cross social support program.

The work of the Russian Red Cross on patient’s adherence to treatment included the following:

- Distribution of daily food sets;
- Distribution of monthly hygiene packages;
- Providing clothes to patients in need;
- Making it easier to access observed treatment units;
- Creating comfortable environment in observed treatment stations

Assistance was provided by:

- The team of Tomsk Branch of the Russian Red Cross (medical and financial coordinators, logistics specialist, 2 social work managers and a driver);
- Raion coordinators - volunteers (Russian Red Cross workers, healthcare workers of Central Raion Hospitals) - 21 people;
- Volunteers who provide directly observed treatment – 145 (feldshers, patients’ relatives, patients’ neighbors)
As a result of very intensive and highly successful work, only 28 patients enrolled on social support out of 5639 defaulted from their treatment course (0.5%) in 2005-2013.

In-home treatment.
Starting in 1998, in-home treatment of patients was provided by the city TB department of TB Dispensary. At that time the entire city was served by one team, which consisted of a nurse and driver who worked one shift five days a week. On average, the team provided observed treatment to 40 patients who waited for the team at a certain place (agreed to in advance), most often at home. Most of the patients had susceptible TB, therefore, only one meeting was needed to provide one dose of TB. Patients selected for in-home treatment could not visit observed treatment stations every day due to different reasons. The basic selection criteria were: older people or patients with other medical conditions; TB concomitant conditions that resulted in walking disability; living in remote districts of the city that lack public transportation. In 2006, when the Global Fund program started, additional vehicles were procured, staff was selected and trained, and a monitoring system was developed.

Job responsibilities of the personnel were identified. A nurse and driver provided observed treatment in a unified approach; they also detected clinical, psychological, and social problems of a patient, called the information center of TB Dispensary, and helped solve these problems with assistance from a TB doctor/head of TB department and specialists involved (bringing patients to examination, hospitalization, providing side effect medications, counseling and social support).

Healthcare employees responsible for treatment adherence in the city (head of TB department and senior nurse) started to supervise the personnel’s work during joint visits (once a week). Complicated TB cases were considered and discussed at weekly meetings.

In order to provide visiting nurse services, the city was divided into two parts. Two teams served each part of the city, one taking a morning shift and the other taking an evening shift.

Each team served regular patients and those who interrupted treatment in the district under the service:

- Patients who were not provided adequate treatment during the morning shift;
- Or patients from TB Hospital/ Day Care Hospital/ Red Cross station/ Center for Social Adaptation for homeless people/ Anti-AIDS Foundation, the information on them was received from a nurse of the information center of TB Dispensary.

Each team consists of one nurse (1.5 salary for work complexity), one driver (1 salary). A district TB doctor continues to follow up with the patient and visits him/her once every 10-14 days (or a doctor from the Day Care Hospital if case history was recorded in the Day Care Hospital).

Each team served 20-25 patients (addresses) for 6 hours and spent an average of approximately 15 minutes on each patient (4 addresses an hour). Upwards of 40 patients—approximately 10 with MDR and 5 who had interrupted treatment—were to be served in one part of the city by 2 teams. When a team member was sick or on vacation, another team member or healthcare worker filled in and covered the shift.

In 2010, an idea started to be discussed to expand the visiting nurse services to three teams to work morning hours, which would increase the time allotted to serve one patient and improve service quality. In 2011, the structure of the visiting nurse services/in-home therapy services was slightly modified. The city was divided into 3 routes during the daytime shift (from 9.00 to 16.00) with each district served by a designated team.

The main focus of the evening shift team (from 16.00 to 19.00) was to search for and locate patients who did not show up for treatment due to different reasons (alcoholism, inconvenient work time, family circumstances, etc.) and those who dropped out of the sight of TB Services’ specialists for more than three days. In the evening the city was virtually divided into two parts again, each part served by a designated team. On average, 60% of patients who missed their doses were found and served by evening teams (Fig. 32).

“Sputnik” program
In 2006, it became obvious that the cure rate of MDR-TB treatment was low primarily due to the high rate of default cases (28-30%). The analysis and discussion of the key issues at hand led to the creation of the “Sputnik” program. The program was developed to work with patients who were “just about to interrupt treatment” despite the above-mentioned activities. In this case, a standard procedure would be used for such patients, i.e. documents would be prepared for compulsory hospitalization followed by execution of the procedure. The main goal of the program is to help patients complete TB treatment using any available resources and action mechanisms, encompassing the patient with care and attention like a companion would. The Tomsk program enrolls patients refusing treatment and those who missed more than 25% of TB drugs for the last 1-2 months. Before enrollment, other approaches (e.g. hospital at home) should have been explored.
The prevalence of alcohol or drug abuse, a history of incarceration or therapy default rates in program patients is 1.5–3 times higher than in other TB patients in the region (see Table 10).

Table 10. Social and demographic profile of the patients included in the program (N = 138), as compared to non-program patients on treatment (N = 3265) in the program region within the period from December 17, 2006 through December 31, 2012.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Program patients</th>
<th>Other patients in the program region</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>%</td>
<td>n/N</td>
</tr>
<tr>
<td>Males</td>
<td>101/138</td>
<td>73.2</td>
<td>2179/3265</td>
</tr>
<tr>
<td>Young / under 40 years old</td>
<td>105/138</td>
<td>76.1</td>
<td>1887/3265</td>
</tr>
<tr>
<td>Married / lives with a partner</td>
<td>59/136</td>
<td>43.4</td>
<td>1315/3151</td>
</tr>
<tr>
<td>Nonworkers</td>
<td>114/138</td>
<td>82.6</td>
<td>1740/3265</td>
</tr>
<tr>
<td>A history of incarceration</td>
<td>53/138</td>
<td>38.4</td>
<td>636/3265</td>
</tr>
<tr>
<td>A history of chemotherapy interruptions</td>
<td>9/138</td>
<td>6.5</td>
<td>32/3265</td>
</tr>
<tr>
<td>Homeless persons</td>
<td>14/138</td>
<td>10.1</td>
<td>269/3265</td>
</tr>
<tr>
<td>Chronic alcohol-related issues</td>
<td>111/138</td>
<td>80.4</td>
<td>981/3265</td>
</tr>
<tr>
<td>Drug abuse prior to or in the course of this treatment</td>
<td>49/138</td>
<td>35.5</td>
<td>237/3265</td>
</tr>
<tr>
<td>Mental disorders</td>
<td>7/138</td>
<td>5.1</td>
<td>134/3265</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>63/138</td>
<td>45.6</td>
<td>584/3265</td>
</tr>
<tr>
<td>HIV</td>
<td>6/138</td>
<td>4.3</td>
<td>83/3265</td>
</tr>
<tr>
<td>Newly diagnosed</td>
<td>42/138</td>
<td>30.4</td>
<td>2270/3265</td>
</tr>
<tr>
<td>MBT+ confirmed with smear and/or culture before therapy</td>
<td>133/138</td>
<td>96.4</td>
<td>2097/3265</td>
</tr>
<tr>
<td># of MDR-TB among all drug susceptibility tested cases</td>
<td>104/138</td>
<td>75.4</td>
<td>890/3265</td>
</tr>
<tr>
<td>Therapy regimen:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category I/II/III</td>
<td>16/138</td>
<td>11.6</td>
<td>2274/3265</td>
</tr>
<tr>
<td>Category IV (MDR treatment)</td>
<td>104/138</td>
<td>75.4</td>
<td>619/3265</td>
</tr>
<tr>
<td>Mono-resistant and poly-resistant tuberculosis; other therapy regimens</td>
<td>18/138</td>
<td>13.0</td>
<td>372/3265</td>
</tr>
</tbody>
</table>

*Fisher’s exact test

The difference of the “Sputnik” program from in-home treatment observed by the authors in other regions are given in Table 11 below. A detailed description of the program is given in the program leaflet (www.pih.ru).
The driver is involved in patient visits: he safeguards the nurse, communicates with the patient, and participates in search activities.

Vehicle, mobile phones, work clothes, 3M respirators, medicine to address adverse effects, sputum containers

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Home-based with visiting nurse (a typical mode)</th>
<th>Sputnik program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work hours</td>
<td>• 8 a.m. through 3 p.m.</td>
<td>• 8 a.m. through 8 p.m.</td>
</tr>
<tr>
<td>Visits per day</td>
<td>• About 50</td>
<td>• No more than 25 patients (an average of 15, most of them receive medications twice a day)</td>
</tr>
<tr>
<td>Time per each patient</td>
<td>• Less than 10 minutes (including travel time to the patient)</td>
<td>• 30–60 minutes (including travel time to the patient)</td>
</tr>
<tr>
<td>Staff</td>
<td>• Driver, nurse</td>
<td>• Driver (a volunteer), nurses, a TB clinician. The driver is involved in patient visits: he safeguards the nurse, communicates with the patient, and participates in search activities.</td>
</tr>
<tr>
<td>Equipment and supplies</td>
<td>• Vehicle, mobile phones, work clothes, 3M respirators</td>
<td>• Vehicle, mobile phones, work clothes, 3M respirators, medications to address adverse effects, sputum containers</td>
</tr>
<tr>
<td>Patient selection</td>
<td>If not attending the health facility, the local GP arranges for patient transfer pending approval of the chief physician (Medical Board)</td>
<td>Each case is reviewed by the Board (including an NGO coordinator, psychologist, drug addiction specialist, and social worker), all available information is evaluated to make a shared decision.</td>
</tr>
<tr>
<td>Patient assessment</td>
<td>No therapy adherence and other factor assessments</td>
<td>All adherence-related factors are assessed by the entire team to develop a shared case-management system/approach</td>
</tr>
<tr>
<td>Personnel attitude to the patient</td>
<td>• Each patient is visited as scheduled solely by the team (the route charted by the driver)</td>
<td>• Therapy delivered at the time and place chosen by the patient</td>
</tr>
<tr>
<td></td>
<td>• The staff is not aware of each patient’s personal details, sometimes they do not know the patient’s name and his/her Mtb+ status</td>
<td>• Friendly staff, well informed on the patient's life, his/her character, diagnosis and clinical manifestations of the disease</td>
</tr>
<tr>
<td></td>
<td>• The staff tends to criticize patients for unhealthy habits, insist on changing lifestyle</td>
<td>• Unhealthy habits and lifestyle issues can be touched only when trustworthy relations are established, and the patient is willing to discuss.</td>
</tr>
<tr>
<td></td>
<td>• Confidentiality maintained if possible</td>
<td>• Confidentiality maintained. Nurses dress casually. If necessary to communicate with neighbors and friends, Sputnik staff often introduce themselves as social service.</td>
</tr>
<tr>
<td>Search activities</td>
<td>Very limited. If patient is not at home, the team will not visit again at this day, nor would it search for him in other possible locations.</td>
<td>Patient is contacted on the phone before visiting. If patient is absent from a scheduled meeting, the team would search for him in all other possible locations, as well as visit him repeatedly at this day.</td>
</tr>
<tr>
<td>Clinical case management</td>
<td>All local TB practitioners are supposed to see patients they are in charge of. In the case of serious issues with a patient, nurses communicate information to the supervising TB clinician.</td>
<td>The team involves a dedicated TB clinician who is selected based on a set of program-tailored interpersonal and professional competencies. Nurses communicate recently updated patient information to the supervising TB clinician on a daily basis. The TB doctor visits patients jointly with the team every 10–14 days.</td>
</tr>
<tr>
<td>Adverse effects and concomitant diseases treatment</td>
<td>• Nurses are duly trained to identify side effects but are not proactive/motivated to do it because of a high workload or personal attitudes</td>
<td>• Nurses are duly trained to identify therapy-related side effects actively</td>
</tr>
<tr>
<td></td>
<td>• Medications to manage side effects are at the patient’s expense, often not procured.</td>
<td>• Side-effect medicines are provided to patients for free (at the program’s expense) within 1–2 days, including medicines to address alcohol-related effects</td>
</tr>
<tr>
<td></td>
<td>• Additional specialists can visit patients at home</td>
<td>• Additional specialists can visit patients at home</td>
</tr>
<tr>
<td>Social support</td>
<td>• All patients receive food packages</td>
<td>• Blood specimens can be collected at home</td>
</tr>
<tr>
<td>Administrative support/ team coordination</td>
<td>• Supervisory visits to monitor team performance are hardly ever conducted</td>
<td>• Hospital admission for a detox course for patients with chronic alcoholic issues</td>
</tr>
<tr>
<td></td>
<td>• Team does not have meetings to review the progress and discuss complicated cases</td>
<td>• The team is involved in the management of concomitant diseases in program patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 11. Therapy management in nonadherent patients: patient-centered vs. standard approaches
Since December 2006, the “Sputnik” program has functioned at the outpatient department of the Tomsk Phtisiopulmonary Medical Center (district services) in Tomsk and surrounding rural settlements with population of 521,635 (50.2% of the entire Tomsk Oblast) and area of 297,2 km².

Sputnik follows these overarching guidelines:

- The patient chooses the time and place for daily use of TB drugs;
- The team is responsible for a patient’s treatment result from the time a patient is enrolled through the end of the therapy. This responsibility includes:
  - Carrying out intensive searches for patients,
  - Completely observing daily treatment (i.e. all TB drugs are taken in the presence of staff),
  - Active detection of clinical, psychological and social problems of the patient and, if possible, making prompt decisions,
  - Respecting the patients and their confidentiality.
- The team’s work will be monitored by the program head (inspector) during joint visits. Weekly meetings to consider each case will be conducted, and complete and immediate administrative support of the team will be provided.

The project started in 2006 and continues in 2014. On average, 13 out of 250 TB outpatients (5%) received program treatment at one time (on any day of the year) in Tomsk. From December 2006 to December 2012, 3,403 TB patients received treatment within the program area; of them 138 were enrolled in Sputnik. Among program patients, chronic alcoholism, drug addiction, imprisonment history and treatment interruption in the past were reported 1.5 - 3 times more often than among those who were not enrolled. Most of the patients (75.4%) were treated with regimen IV due to MDR-TB.

In 122 patients who continued treatment that was initiated before the program, adherence to therapy increased to 78.3% compared with 59.8% before the program. In 7 patients who started a new course of treatment after referral to the program, adherence to treatment reached 74.2%. An average level of treatment adherence among MDR-TB patients was 77.1%. As a result of the program, an “effective therapy” outcome was reached in 70.5% of TB patients and 68% of MDR-TB patients.
TB care for homeless patients

When a homeless patient is admitted to TB hospital, members of the Social and Psychological Aid Office (SPAO) fill out a form along with a picture of the patient. Before that, the patient signs an informed consent form.

SPAO members enter data on such patients to a general card catalog and create a service plan. Each SPAO member has a certain inpatient department assigned to him/her.

Information on registered patients goes to the Information Center on a weekly basis. The function of this center is fulfilled by SPAO of the therapy department. A psychologist is in charge of collecting information, registering patients at SPAO and updating a unified list of patients registered at SPAO.

If a designated doctor is absent due to illness or vacation, another psychologist performs the functions of the designated specialist.

A unified list of patients registered at SPAO is updated weekly and distributed to all inpatient departments. This unified list can help avoid secondary registration of the same patient.

When the patient is discharged from hospital or he/she leaves voluntarily; a member of SPAO passes this information to a TB treating physician of the outpatient facility.

To solve different issues, social workers cooperate with numerous players, including the Tomsk Regional Welfare Department, the Center for Social Adaptation, the Comprehensive Center for Social Services of Population, Pension Fund, Migration Services, the Crisis Center for Women, the Anti-AIDS Center, “Tomsk-AntiAIDS” Foundation, rehabilitation centers for substance addiction and harm-reduction programs, and city centers of social support, among others. Clergymen are also involved, working with certain inpatients. In order to improve treatment adherence among patients using injecting drugs, workers of the Tomsk-AntiAIDS Foundation who specialize in activities with vulnerable groups take part in the treatment, providing motivational talks, assisting with observed treatment, and delivering other support as needed.

Monitoring the performance of program activities in the city:

- Check all treatment cards at all stations of observed treatment every two weeks. Discuss instances of low treatment adherence with heads of TB departments to identify further management approaches and discussions at regular meetings of the Treatment Interruption Board.

- Conduct monthly visits with the Sputnik and In-Home Therapy Services/visiting nurse service teams to identify organizational problems; assess skills of healthcare workers for providing observed treatment and active detection of side effects; if required, conduct on-the-job training.

- Participate in weekly meetings of medical boards, conduct UCEC meetings at the inpatients and outpatient treatment stages, keep track of patient enrollment on treatment, and comply with clinical protocol.

- Participate in meetings of the Treatment Interruption Board; keep track of compliance with criteria and timely enrollment of patients on treatment provided by In-Home Therapy Services and Sputnik.
Challenges and lessons

1. Shortage of human resources: 70% of healthcare staff has reached retirement age. It complicates training processes because they are reluctant to adapt to innovation. It is hard to change ideology. While it is easier to hire new people, their responsibilities must be clearly delineated and they need to cooperate closely with health care staff. They should not play second fiddle or be ignored.

2. Challenges within the alcohol-treatment program at the outpatient stage:
   - Limited recruitment of addiction specialists due to both their fear of contracting TB and the reduced financial compensation compared to that in private practice. It is uncommon for TB services to regularly employ or budget for addiction specialists, psychologist, psychotherapists, or social workers, and they do not provide special licenses for drug and alcohol abuse support specialists. This limitation often led to staff turnover.
   - TB patients were reluctant to receive treatment. Some refused to acknowledge their alcoholism; others raised concerns with the stigma associated with addiction treatment. There was also the misconception that acknowledging alcoholism during TB treatment will negatively impact care, which resulted in lower rates of referral to the subprogram for patients struggling with alcohol abuse. Even after the introduction of a program that included specialists who deliver treatment at home and the operations of the Sputnik program, the problem remained. Patients refused to receive alcohol abuse counseling even at home. In addition, a translated evidence-based manual for self-help was tested with a focus group and then issued to patients. However, use of the manual by patients was considerably lower than staff expected.

Fig. 33. Referral to addictions specialists and/or psychologist, by year N=3406

- Limited communication between AUD specialists, physicians, and patients. Strong supervision is needed to support referring patients to specialists and to set up interdisciplinary teams operating under a patient-oriented approach to treatment. Several trainings for TB doctors were conducted to improve communication skills and provide professional support in hopes of reducing fatigue and burnout. However, impact was seen only in the prison sector. Alcoholic Anonymous groups were difficult to establish within official in-patient TB services (even for smear-converted patients).

3. In-home treatment and Sputnik yield good results if staff time is well managed, tasks are distributed, and conditions to work effectively are put in place. When calculating workload, it should be realized that treatment of one adherent patient at home requires at least 15 minutes. For patients struggling with alcohol or drug addiction, more time will likely be needed.

4. Regardless of multiple trainings and workshops, healthcare staff does not always actively detect side effects at the outpatient stage of treatment. The above-mentioned approach of having supervisors make monthly home visits with nurses and care-delivery teams helped improve active detection of side effects.

5. Food sets should be provided daily, and the cost and products should be valuable for the patient.

6. A patient-centered approach should be used for non-adherent and homeless patients at the outpatient stage of treatment on the following conditions: there is an available network of stations for directly observed treatment and there is a stable system of interagency collaboration (with shelters for homeless people, social services, penitentiary system, AIDS centers and non-profit organizations).

7. Monitoring: External quality control of activities is required to provide continuity, support enrollment performance and improve quality of services. No internal quality control is provided.
The rural initiative subprogram

The Russian Federation inherited from the Soviet Union a strong “vertical” system of TB control that had been in place for decades, as well as specialized TB facilities and trained TB personnel. TB hospitals were the centers of TB treatment. After the Soviet system collapsed, some Russian regions decided to keep MDR-TB patients in TB hospitals for 2 years due to complicated treatments. Unfortunately, many patients left the hospitals ahead of time and stopped taking their treatment because no systems were in place to accompany them and link them to the proper outpatient facilities. Treatment default in some programs reached 40%. In cases when patients received TB drugs for self-administration without being observed, the outpatient phase of treatment often resulted in high rates of treatment failure and drug resistance.

Results from TB treatment systems were always poor in the Russian regions that used outpatient treatment in both cities and rural settings. These systems could not provide any activities for patients to comply with treatment regimens because those activities were not listed in the responsibilities of TB facilities and they were not funded by the TB Dispensaries.

The Russian Red Cross was invited to join and provide anti-TB activities in Tomsk Oblast after DOTS and MDR-TB program had shown poor results. Initially, beginning from 1998, Red Cross provided patients with monthly food sets, but after a short time it turned out that daily food incentives were more effective for patients to adhere to treatment.

In 2002 PIH followed the successful example and in collaboration with Red Cross launched the food sets provision to MDR-TB patients. Due to limited funds, food sets were distributed on a monthly bases until GF grant funding (December, 2004) allowed daily food set provision/distribution to to 300 TB patients and to all MDR-TB patients who received treatment in outpatient facilities. In the first 4.5 years of the grant implementation, 300 TB patients on Category 1-3 treatment in rural settings were provided with daily social support, which improved their adherence to TB treatment and overall treatment success rates. However, due to reduced funding in the last 6 months of the grant, only 50 drug-sensitive TB patients were provided with such support in rural settings. By the end of November 2009, all TB patients in rural settings finished treatment and were excluded from the social support program.

In 2010, PIH specialists in observed treatment and TB services physicians discussed difficulties and capacities to expand efforts under the RCC project. It was much more difficult to provide observed TB treatment in rural settings than in the city where TB service could be delivered through various means. Outside town centers in rural settings, TB treatment was provided by specialists of the general healthcare services (feldshers, nurses), for whom TB treatment was not a principle responsibility. The long distances that patients had to cover to get from their houses to a treatment site with no public transportation often resulted in missed treatment. It was not uncommon that a village had neither a healthcare worker nor a healthcare unit. The lack of infrastructure and resources resulted in poor observed treatment, frequent missed doses, and early treatment discontinuation. In order to increase effectiveness of TB treatment in rural settings of Tomsk Oblast, a “Rural Initiative” program started in 2010.

The program goal was to increase effectiveness of TB treatment in rural settings of Tomsk Oblast. Objectives included:

1. Improve observation and quality of outpatient TB treatment;
2. Increase patient’s adherence to treatment by means of:
   - bringing TB care closer to the patient (creating in-home therapy services, Sputnik services);
   - enhancing social support of patients treated in outpatient facilities using workforce and resources of the local administrations;
3. Improve clinical monitoring (clinical, laboratory examination);
4. Improve effectiveness of rural TB inspectors, raion specialist, feldshers (through training, updating job descriptions, and salary adjustments).

The following activities were performed under the program:

**Objective 1: Improve observation and quality of outpatient TB treatment**

1. Organization of observed outpatient TB treatment in rural settings.

Direct observed treatment (DOT) became a standard for TB treatment in Tomsk region during implementation of collaborative TB project between TOTBS and British humanitarian organization MERLIN in 1994-2000. Medical providers both in TB services and primary health facilities were trained to provide DOT. This work continued during all following years with expansion to MDR-TB patients. Since 1996, the Tomsk Red Cross has been working together with TOTBS by strengthening DOT through food sets provision to adherent patients.

Members of the Russian Red Cross who provided treatment observation and social support of patients in 16 raions of Tomsk Oblast by means of local coordinators and volunteers played an important role in organizing directly observed TB treatment. A raion coordinator was responsible for organizing this activity in each raion, which included the delivery of treatment and food sets from Tomsk city to patients’ residence, supervising the work of volunteers, collecting documents and producing reports. In rural settings, feldshers at feldsher’s stations (medical nurses at rural outpatient clinics) became volunteers who supervised treatment and handed out food sets. In challenging situations, such as when there was no healthcare professional...
available in a village or the patient’s house was located far from the healthcare station, volunteers were recruited from local, socially responsible residents (non-medical workers). Each volunteer had to be trained to discuss TB and TB treatment, explain why it was mandatory to take all TB drugs regularly, and explain what side effects could occur (a patient questionnaire was developed specifically to help volunteers). Volunteers were paid an allowance for their work. When treatment is observed by a volunteer, a feldsher should supervise the treatment once a week, raion TB specialist – at least once every two weeks in early treatment, and later – at least once a month.

2. Regular inspection visits by raion TB specialists.
Visits were made at least once a month to the feldsher’s station or rural outpatient clinic where patients received treatment, and reports were provided. In rare cases, as agreed between curators, visits could be made less frequently—if it was a remote rural village with limited accessibility or if there were months of successful patient treatments with no complications, for instance. However, a visit still had to be made at least once every three months. During the visit TB, inspectors monitored treatment administration, checked medical documents, calculated remaining medications, and visited patients at the place of residence.

3. Regular raion visits by rural TB inspectors (at least once in three months) confirmed by reports.

As agreed with the head of TB department and head of organizational and methodical department, the frequency of visits can be changed and “trouble” raions may be visited more often. During the visits a rural TB inspector supervises the way the observed treatment is organized and provides administrative support of TB activities in the raion. More than 600 visits to Tomsk Oblast raions were made during the program period (taking into account weekly visits to Tomsky raion).

Objective 2: Increase patient adherence to treatment
In order to improve patient adherence to treatment,

- In-Home Therapy Services were set up in raion central towns. This service was delivered by a raion TB specialist and a nurse in the homes of patients who resided far away from a TB specialist’s office, as well as in the homes of socially marginalized patients. A vehicle was provided daily to deliver the service (1-2 hours a day). The so-called “Sputniks” were set up in Asino, Kolpashevo, and Tomsk raions, as well as Strezevoy city and Seversk city. Timely elimination of side effects via detection of side effects by a volunteer (training, questionnaires) was central to this work. An uninterrupted supply of all essential medications for symptomatic treatment and elimination of side effects to TB drugs was provided.

- To improve motivation of patients to visit healthcare stations and receive observed therapy, daily food sets were provided to patients, which would be received after taking daily TB drug dose. Employees of the Russian Red Cross and TB Services conducted surveys and questionnaires on a regular basis, which could help reveal patients’ needs and find additional motivation to treatment. Social support was provided through local administrations and included previously mentioned social welfare services (restoring documents, transportation to the raion central town for regular medical examination, assistance in job search, provision of warm clothes and firewood, etc.). Since 2014, TB drug supply has been provided by TB Services.

- Conducting meetings with representatives of local authorities in order to get support in providing anti-TB activities (social support of patients, assistance in recruiting volunteers, encouraging patients to have medical examinations and treatment, developing local anti-TB programs);

Objective 3: Improve clinical monitoring
Raion TB specialists supervise the work of feldshers and volunteers on a regular basis, helping them solve any issues and conducting trainings. Raion TB specialists should make a visit to the treatment site at least once a month.

A rural TB inspector supervises the work of raion TB specialists via inspection visits and regular review of submitted reports

Rural TB inspectors observe treatment of rural patients and help raion TB specialists organize and provide TB care. Rural TB inspectors consult on complicated cases, arrange medical and social assessment of patients, and convene meetings of the medical panel. During inspection visits, a rural TB inspector examines how observed treatment is provided, paying specific attention to accurate administration of treatment regimen, and terms and completeness of medical examinations. Additionally, rural TB inspectors provide administrative support of anti-TB activities in raions, thus contributing to the meaningful work performed by raion TB specialists.

Objective 4: Improve effectiveness of the work of TB rural inspectors, raion TB specialist, feldshers

- Training of feldshers and nurses on conducting observed TB therapy, diagnostics skills, and elimination of side effects;

- Train raion TB specialists on conducting inspection visits; host refresher courses in elimination of side effects; foster knowledge sharing among leading territories.
Lessons learned

1. Creating a department of rural TB inspectors proved to be successful and justified in cases of extreme raion remoteness or when there were no raion TB specialists available.

2. It is quite difficult to provide clinical monitoring in raions; therefore, it requires careful attention and thorough planning. To improve performance and provide timely examinations of patients in raions, it is helpful to develop a list of patient data on side effects and have a system for tracking and easily accessing laboratory, X-ray, and bacteriological results, which are submitted by the raion TB specialist to the rural TB inspector on a monthly basis. This allows the rural TB inspector to better supervise and assist with treating the patient. All patients treated in raions have to be reported by the rural TB inspector at the UCEC meeting.

3. Inspector’s visits should be regular and complete (including visits to villages, feldsher’s stations and patients). One of the main tasks of a TB inspector is to help raion TB specialists receive administrative support. Authorities at the raion’s hospital can support efforts by: Organizing in-home treatments using hospital vehicles and arranging regular visits with the raion TB specialist to villages where TB patients receive treatment, examinations and consultations by specialized doctors. In the raions where all activities mentioned above were implemented, the percent of cured patients was higher.

4. A centralized supply of both TB drugs and symptomatic medications from the Head TB Dispensary ensures uninterrupted and proper treatment of patients in the raion.

5. The significance of the daily food set in the treatment of rural patients cannot be overestimated. It is powerful motivation for patients to continue treatment.

6. Timely delivery of medications, proper medication storage, and distribution of food sets are complicated tasks that were completed successfully by the Russian Red Cross.

7. Under conditions of medical staff turnover in raions, it is particularly important to conduct regular training (minimum once a year) of raion healthcare workers on TB detection, observed TB treatment, diagnosis and treatment of side effects, and filling out medical documents.
**Results of adherence activities**

As a result of directly observed treatment activities, early relapse rate among patients with successful treatment outcomes decreased to 1.5 per 100 people in observation group, and it approached the same level as the rate in other regions that participated in international projects (it should be noted that the regions taken for comparison are much smaller in size and number of patients compared to Tomsk Oblast).

A proportion of patients who interrupted treatment do not depend on organizational efforts only, but on the cohort of patients – their number and proportion of patients to medical staff (given a decreasing number of TB service staff in Russia and Tomsk Oblast). After initiation of the GFATM project, a proportion of those who interrupted therapy to the total number of patients on treatment in specific year (regardless of cohort – the current year or previous) was relatively stable: among susceptible TB patients it was gradually decreasing to 1% and lower, and among patients who received second line TB drugs it was less than 5% (GLC) and a bit higher (Ministry of Health).

As was shown in the interim results of MDR-TB treatment through the GLC, up to half of patients who interrupt therapy do so in the first 4 to 6 months of treatment. Since it is difficult to find out reasons for interruption and related errors in the study, we can only speculate: we can assume that inadequate detection and management of side effects have an impact on treatment interruption or it may be the influence of other patients in the hospital (who have negative attitude to treatment). We also can see that treatment interruption at the ambulatory stage did not become prevalent after 2004 when a strategy of treatment coverage expansion was used and patients with severe clinical and social characteristics were enrolled.
In general, the rate of treatment interruption among new patients with positive smear microscopy who received treatment of susceptible TB slightly decreased after 2005 and it did not exceed 1% in the best years.

During the transition period (2009), strengthened activities in treatment adherence provided in the city allowed us to decrease the percent of patients with treatment interruption to 0% (mainly due to searching activities, treatment at home, and sputnik). At the same time, in rural settings it was obvious that food sets played a key role in treatment adherence – treatment interruption rate increased up to 6% and then it declined when food support was renewed through the Red Cross.

After 2005-2006, a proportion of interruption among MDR-TB patients who received treatment through GLC in civilian sector started to fluctuate in the range of 8-10%, and we consider it to be appropriate for a field project where all patients are covered with treatment.

Treatment interruption rate among MDR-TB patients in rural areas is typically lower than among MDR-TB patients in the city, except in the 2007 and 2008 cohorts, when new initiatives in Tomsk city were at the peak of enthusiasm.
TB-HIV Program

<table>
<thead>
<tr>
<th>Indicators</th>
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<tbody>
<tr>
<td>• Number of HIV-positive patients screened for TB PPD test in civilian sector</td>
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<tr>
<td>• Number of HIV-positive patients screened for TB PPD test in penitentiary sector</td>
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<tr>
<td>• Number and percentage of patients dually infected with TB and HIV offered Isoniazid prophylaxis in civilian sector</td>
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<tr>
<td>a. Since 2010 - Number and percentage of patients dually infected with TB and HIV offered and completed Isoniazid prophylaxis in civilian sector</td>
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In 1993 Tomsk Oblast started to register HIV-patients; the number of new patients diagnosed with HIV has since increased each year. HIV-positive patients refer to the risk groups of TB due to immunodeficiency. It is known that an HIV-positive patient has a 10% chance of developing active TB each year while a patient without HIV has a 10% chance of progressing to active TB over her/his entire lifetime. According to the epidemiological data of the Tomsk Regional Anti-AIDS Center (a MoH Center for HIV treatment and epidemic control), HIV patients die of TB more often than any other reason. Additionally, an increase in the number of patients co-infected with TB and HIV has been reported.

In 2005, a comprehensive collaboration between TB Services and the Anti-AIDS Center was implemented under the GFATM Round 3 Grant. The goal of the program was to decrease TB incidence among people living with HIV/AIDS (PLWH) in Tomsk Oblast (Tomsk city and Strezhevoy city).

**All participants of the program from 2005 to 2013:**

- Tomsk Regional Center for AIDS and infectious diseases prevention and control (Anti-AIDS Center).
- Tomsk Oblast TB Dispensary (TB Dispensary).
- Municipal healthcare facility Strezhevoy city hospital (Strezhevoy city hospital),
- “Partners In Health” Representative office (PIH); and Tomsk regional nonprofit charitable foundation “Tomsk-AntiAIDS”.

The following activities were performed under the program:

1. Organizing TB screening and latent TB infection diagnostics among PLWH.
2. TB screening among vulnerable population groups.
3. TB preventive therapy with TB drugs among PLWH.
4. Training of healthcare workers on drug-resistant TB in HIV patients (since 2010).
5. TB education among population groups.

**Organizing TB screening and latent TB infection diagnostics among PLWH.**

TB services are provided by a TB doctor at the facility of the Anti-AIDS Center in order to reduce the number of visits a HIV-infected patient would have to make to TB outpatient facilities. For this purpose, half the salary of a TB doctor was budgeted for, the TB doctor’s office was equipped, and the Anti-AIDS Center was licensed to perform TB services. A TB doctor from TB Services who receives patients also provides aid to HIV-positive patients. In addition, this doctor coordinates efforts between TB and Anti-AIDS Services.

In cases where a patient resides in a rural area of the Tomsk Region and he is not able to visit the Anti-AIDS Center in Tomsk city, he can visit an office for infectious disease prevention at the nearest hospitals. In the city of Strezhevoy, due to its remoteness from the Regional center and high HIV incidence, an office for counseling and diagnostics was set up at the city hospital to follow up with HIV-positive patients. The specialists of the counseling and diagnostics office work in close collaboration with the TB doctor.

All HIV patients, including new cases and registered patients, undergo photofluorography examination when HIV is detected; if they were previously examined more than 6 months ago, then it is conducted twice a year. A planned fluorography examination of HIV-positive patients is conducted free of charge at TB outpatient facilities. The doctor at the Anti-AIDS Center provides patients with a referral for fluorography examination issued by the TB doctor. It is important that an HIV-positive patient does not need to come back to pick up the examination result. Rather, the TB doctor of the Anti-AIDS Center collects the results and immediately reviews them. It is important to note that the TB doctor at the Anti-AIDS Center work only 3 days a week; when changes on photofluorogram are detected, the doctor calls a visiting nurse of the Anti-AIDS Center as soon as possible, informs the nurse about the results, and asks the nurse to make the patient come to the outpatient TB clinic.
for a follow-up examination. The TB doctor who consults HIV patients at the Anti-AIDS Center is responsible for keeping photofluorography records at the TB facility. In addition, photofluorography results are backed up at the Anti-AIDS Center using computer software for registering HIV patients; the results are also duplicated in reporting form # 30 “A control card of follow-up monitoring.”

Beginning in 2005, Mantoux TB skin test with 2 TU was provided at the Anti-AIDS Center to PLWH at the time of registration and to those who had been registered before and had negative skin test results in the past.

In 2010, an algorithm to select patients subject to TB screening was changed. PPD skin test was provided at the time of registering a patient at the treatment facility, then once a year, excluding those with large reactions in the past. Due to these changes, a twofold increase of those subject to PPD test was reported from 2010 to 2013, whereas the coverage rate decreased by 6% regardless of higher number of PPD tests provided, which increased two times compared to the previous years. Most of PLWH not covered with PPD skin test from 2010 – 2013 were citizens of Strezhbov city, located in the north of Tomsk Oblast. They were considered a hard-to-reach population group by healthcare workers due to their rotating shift work.

Diagram: Number of registered PLWH subject to Mantoux skin test, and those who received skin test, civilian sector, Tomsk Oblast).

Before 2010, all new HIV patients, registered as PLWH with negative skin test results in the past, were subject to PPD test (after the first positive skin test result received, the patient was excluded from the group of those subject to PPD test).

Definition used from 2010: Patients subject to Mantoux skin test include all new HIV patients, and registered HIV patients with no Mantoux skin test received during the last year, and patients with suspected TB. Mantoux skin test is given no more than every 6 months (except those with large PPD reaction in the past).

When a positive Mantoux reaction is detected (5mm and larger), or reaction is less than 5 mm and CD4 count <200 cell/ml, a patient is referred to the TB doctor of the Anti-AIDS Center for a follow-up examination to rule out active TB. A patient is examined to detect possible TB symptoms: cough, fever, night sweats, weight loss, chest pain; percussion and auscultation examinations are performed. When needed, a follow-up examination is performed at the outpatient TB clinic: chest X-ray; CT scan, when possible; Diaskin-test; sputum examination when sputum is available (sputum smear microscopy, culture, PCR using Gene Xpert since 2012). Additionally, a patient might be hospitalized to the diagnostic TB hospital department to verify the diagnosis. A detailed algorithm of examination and assessment was developed and used.

In order to increase patient’s adherence to TB screening, distribution of food sets was set up from the start of the GFATM Grant (2005): one food set was given at the time of Mantoux skin test administration, the second one was given 3 days later when Mantoux reaction was interpreted. The cost of two food sets was 75 rubles.

TB screening among vulnerable population groups.
Due to the charitable foundation Tomsk-AntiAIDS, which joined the program in 2010, it became possible to cover at-risk groups (injection drug users, migrants, commercial sex workers) with TB screening, including PLWH. The main task was to increase the coverage of preventive TB screening among vulnerable groups, provide early TB detection, and enroll patients in the national treatment programs.

Effective TB monitoring in those groups provides a basic understanding of risks to revise TB control activities. Also, if performed with local community involvement, such as the charitable foundation Tomsk-AntiAIDS, the program helps overcome resistance and distrust often encountered in these groups. Tomsk-AntiAIDS is based in a low threshold center, “Our Clinic,” which provides medical, social and psychological services. This is a client-centered program.

Outreach workers make efforts to motivate a client for TB screening and, if necessary, keep him/her on treatment in the future. During 2010 – 2012, a cohort of 2,039 people was identified as a risk group for TB. Screening was conducted twice a year and included basic evaluation of symptoms (chronic cough, weight loss, night sweats and hemoptysis), PPD, and chest fluorography and sputum microscopy.
Outreach workers of Tomsk-AntiAIDS provide field counseling, TB and HIV education, phlebotomy, PPD with further referral to TB Services for medical evaluation. Nutritional support, hygiene packages and accompaniment are used as incentives to complete screening process. The main principles for effective work with vulnerable groups are:

- Anonymity;
- Involvement of TB prevention and TB screening provided by outreach workers and peer consultants involved in a harm reduction project;
- Mobility of outreach workers of Tomsk-AntiAIDS by using a designated vehicle to provide personal field counseling and other activities;
- Provision of every client with motivation sets after completing TB screening;
- Establishments with multiple services on-site: for example, syringe exchange, consultation, sputum collection and provision of IDUs with appointment cards for fluorography;
- A coordinated approach to each client through strong relations between TB and HIV Services, social departments and rehabilitation programs, and drug addiction specialists;
- Compliance with the principles of low-threshold service; a client will be provided care even when he/she does not have an ID, for instance.

All clients of Tomsk-AntiAIDS requiring services were initially screened for TB using a questionnaire regarding overall health, risk factors, and complaints consistent with TB (fever, cough, fatigue, sweats, date of previous TB examination, TB contacts). Based on this questionnaire, a patient may be referred to TB Services for photofluorography examination.

Additionally, all clients who had chest photofluorography examination more than one-year prior were referred for a photofluorography examination. If clients had a cough, sputum was collected at “Our Clinic” Center or during outreach activities. After sputum was collected, a consultant filled out a referral form provided by TB Services for sputum smear microscopy and a Tomsk-AntiAIDS vehicle delivered sputum samples to the laboratory. For commercial sex workers (CSW), Diaskin-test was the first screening method apart from a survey. Most activities among this group of clients were conducted when they were visited by a mobile service station. A positive Diaskin-test result was a powerful motivation factor for them to be examined at the TB Dispensary.

The following activities were widely practiced as motivational factors to attract risk groups to TB examination:

1) Outreach work. Employees from Tomsk-AntiAIDS made 5 visits a week to locations where target-group representatives gathered (apartments, known hangs), conducted TB/HIV awareness activities, and detected clients who had complaints consistent with TB. Clients who had complaints consistent with TB were referred for fluorography examination; among those with long-term cough, sputum was collected on the spot. During outreach work, target group representatives received pamphlets and leaflets about HIV/TB and personal protection measures (condoms, syringes, needles). Treatment adherence activities were conducted with each TB or HIV client, and when needed, these clients were accompanied to a doctor for a regular examination.

2) Free and anonymous fluorography examination (without ID and healthcare insurance) by referral, and microscopic examination of sputum smear samples collected from clients during outreach visits and at the “Our Clinic” low-threshold center.

3) Provision of food sets (250 rubles) and hygiene packages (150 rubles) to the clients who completed examination;

4) Outreach workers of Tomsk-AntiAIDS were mobile and responsive, using an available vehicle to help specialists visit the field, provide counseling on the spot, perform blood collection and Diaskin-test administration, and conduct TB and HIV health education among clients;

5) Accompanying clients to TB examination. If a client agrees, an outreach worker can be present at the meeting with a TB doctor and other specialists.

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<table>
<thead>
<tr>
<th>Results of TB examination among vulnerable groups:</th>
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<tr>
<td>In 2010, 619 people were examined for TB using all available methods (fluorography, Mantoux skin test, Diaskin-test, sputum smear microscopy). Six of them were detected with TB, including 3 MDR-TB cases. TB detection rate was 14 patients per 1,000 examined vs. 0.7 in general population.</td>
</tr>
<tr>
<td>In 2011, 576 people were examined for TB. Seven of them were detected with active TB, including 2 MDR-TB cases. TB detection rate was 15 patients per 1,000 examined vs. 0.6 in general population.</td>
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<tr>
<td>In 2012, 844 people were examined for TB. Six of them were detected with active TB. TB detection rate was 7.6 patients per 1,000 examined vs. 0.5 in general population.</td>
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<tr>
<td>In 2013, 687 people were examined for TB. Eight of them were diagnosed with active TB, including 3 MDR-TB cases. TB detection rate was 11.6 patients per 1,000 examined vs. 0.6 in general population.</td>
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**Fig. 44. TB-HIV epidemiological data, civilian sector (per 100,000)**

- Incidence TB-HIV
- Prevalence TB-HIV
- Mortality TB-HIV
TB preventive therapy with TB drugs among PLWH.

When latent TB infection is detected in HIV patients, the TB doctor at the Anti-AIDS Center prescribes TB preventive therapy. To optimize preventive therapy procedures, specialists of TB Services and at the Anti-AIDS Center developed an algorithm to assess examination results of registered HIV patients. While prescribing preventive therapy, it is important to consider Mantoux skin test result, as well as CD4+ lymphocytes, contacts with TB patients, and risk group relations.

TB preventive therapy is performed at the Anti-AIDS Center under observation by the TB doctor, HIV doctor and nurses from the follow-up and treatment department. Preventive therapy regimen: Isoniazid 600.0mg + Rifampicin 600.0mg, 3 times a week for 4 months. TB drugs for preventive therapy were supplied by TB Services.

This regimen was introduced into practice in 2004 before the start of the “Risk reduction of TB infection in HIV patients in Tomsk Oblast” project, which was based on research and recommendations developed by professor Edward Nardell of Harvard Medical School (Partners In Health). The regimen was agreed on by Olga P. Frolova, Director of the Russian MOH TB Health Care Delivery Center for HIV-Infected Patients. The main reason why using Isoniazid alone was not recommended was high Isoniazid-resistance rates among new TB patients (32%). Additionally, if using Isoniazid alone, a course of chemoprophylaxis in HIV patients should be 9 months—it makes it more complex in terms of adherence. Due to this reason, Rifampicin was added to the regimen of preventive therapy. Findings of a randomized, placebo-controlled clinical trial on preventive therapy for tuberculosis in Ugandan HIV-infected adults showed an efficient use of Isoniazid and Rifampicin for 3 months in 59% cases. In order to follow up side effects to preventive therapy, a survey and examination of patients are conducted during each visit; complete blood cell count and biochemical blood assay are performed every two weeks in the first month, then every 3-4 weeks.

As motivation, the following activities were used at the start and the end of preventive therapy:

1) Early detection and timely elimination of side effects to TB drugs. Procurement of medications for symptomatic treatment under the GFATM project.

2) Prevention of interruptions in preventive therapy. In case a patient does not show up to receive preventive therapy with TB drugs, a visiting nurse calls the patient by phone and finds out the reasons he/she has not come. If the patient cannot be reached by phone, the nurse goes to visit the patient at home to find out the reasons of missed treatment and gives a dose of TB drugs to the patient’s house is considered.

3) Involvement of a psychologist and social worker to the work with patients who interrupt treatment.

4) Food sets are given to patients after they take a dose of TB drugs. The cost of a food set increased from 50 rubles on average in 2006 to 75 rubles in 2010, and then in 2012 it was about 160 rubles.

5) Provision of travel passes for municipal transport made it easier for patients to travel to Anti-AIDS Center and helped reduce travel expenses.

6) Public organizations (Tomsk-AntiAIDS Foundation) experienced in working with injection drug users, commercial sex workers and other vulnerable groups help search for patients who defaulted from treatment and accompany them during the treatment period (delivery of TB drugs and food, accompanying patients to follow up examinations and specialist’s counseling).

7) When a patient refused preventive therapy, a chemoprophylaxis default form was filled out. Approaches to treatment management of patients missing preventive therapy drugs were discussed at the weekly meetings of the AIDS-Center medical board, which was attended by the HIV specialist and TB doctor. Also, reasons for treatment interruption were determined, and a plan of further steps to prevent interruption was outlined.

During the weekly meetings of the AIDS-Center medical board, close attention was paid to monitoring the number of HIV patients examined for TB, the number of new patients detected with TB/HIV co-infection, as well as patients subject to preventive therapy (monitoring results were recorded in the minutes of the meetings). Monthly monitoring was provided when
a reporting form “Information on HIV, Hepatitis B and C prevention, HIV detection and treatment” was filled in. Quarterly monitoring was conducted at the meetings of head physicians of the AIDS-Center when minutes of the meetings were recorded and quarterly reporting forms on detection and treatment of TB patients were filled out. A statistics form #61, “Data on HIV-infected populations” was filled out annually.

A decrease of preventive therapy coverage from 2011 was related to different factors. Beginning in 2005, sexual route of HIV transmission was dominant. Due to this fact, a population of new HIV patients changed: they were socially safe and employed patients. In 2009, an increase of HIV incidence was reported related to drug use: The percent of HIV transmission via injection drug use increased from 26.1% in 2008 to 81.3% in 2013. Among HIV patients, most of them used heroin 1-3 times a week. Most drug users were socially safe and employed people; they were adherent to follow up and therapy. At the end of 2012, synthetic drugs, so-called “bath salts,” started to become prevalent in Tomsk Oblast. These drugs had severe toxic effects, which quickly destroyed the physical and mental health of patients. HIV-positive patient’s behavior was more aggressive; when they showed up at the AIDS Center they had a feeling of euphoria or, conversely, they felt depressed. Furthermore, they displayed impaired memory and mental status, and confusion. In this regard, patients who required TB preventive therapy could not comprehend the information about treatment and respond adequately; most of them gave an outright refusal to receive therapy. Oftentimes, the patient could not be found since his/her location was unknown.

Obviously, the economic recession had an effect on the work. In 2008, the percent of unemployed HIV-positive patients was 29.2%. In 2013 it had increased to 45.3%.

Drug addicted patients face specific behavioral and social issues that result in the need for consistent follow-up monitoring. Their addiction often leads them to a criminal lifestyle. Drug addicted patients are often fired from their jobs or expelled from college. The fact that a person has HIV may result in fallouts with families and relatives. Oftentimes, HIV patients have little motivation to seek care and follow a treatment regimen; they are characterized by self-destructive behavior. Due to their unwillingness, most of the patients refuse to take “chemistry;” some patients do not want to visit AIDS Center to take TB drugs. A food set, in most cases, is not a significant incentive to regularly visit AIDS Center. Drug addicted patients have their own priorities.

Most of the patients have financial and social problems. The Anti-AIDS Center is located far from downtown. Additionally, transport fares, including municipal transport, have increased.

Up to 70% of HIV patients have chronic viral hepatitis B and C. Due to this fact, they often refuse preventive therapy with TB drugs because they are afraid of negative effects of TB drugs on the liver.

A significant increase of HIV patients subject to preventive therapy and low coverage with chemoprophylaxis and Mantoux skin test occurred mainly due to the registered patients who do not come for the follow-up visit.

Strezhevoy city has a particular impact on HIV situation in general, since most of PLWH patients registered in the clinical and diagnostic office work on rotating shift schedule. PLWH in this city rely on erratic shift work, which makes it difficult to arrange steady access to treatment.

One persistent challenge is that patients begin chemoprophylaxis and are optimistic and feel good. Then, however, the side effects of TB drugs occur. It is often the case that patients do not want to continue taking TB drugs even after side effect medications have been prescribed. They stop taking preventive therapy drugs immediately and they do not yield to persuasion.

Effectiveness of latent TB chemoprophylaxis was assessed based on regular and timely intake of TB drugs and lack of TB signs within one year after therapy start among those enrolled in the program.

In total, from 2006 to 2012, 513 people were subject to preventive therapy of latent TB infection. 426 patients (83%) were enrolled in preventive therapy, of them 334 (78.4%) completed therapy. Only 4 persons who received a complete course of preventive therapy developed TB within a year after therapy completion. An average annual percent of people who developed TB within a year after preventive therapy completion was 1.1±0.3%. A long-term annual average percent of those who developed TB without preventive therapy was 2.2±0.2%. Thus, it is statistically significant that patients who had received preventive therapy of latent TB infection developed TB 2 times less than HIV patients who had not received preventive therapy.
Training of healthcare worker on drug-resistant TB in HIV patients (since 2010).
Due to increasing trends of HIV incidence in Tomsk Oblast by the end of 2009, the issues of diagnostics, clinical progress and management of patients with HIV/TB co-infection became relevant. During a period of significant decrease of CD4-lymphosites (less than 200 cells/mcl), TB is characterized by atypical clinical and X-ray syndromocomplex and polyorganic lesions [4, 5]. It is particularly difficult to suspect and identify TB when no changes occur on X-ray. TB Services staff responsible for TB diagnosis in HIV patients should be trained on TB progression in HIV based on immunosuppression level. For this purpose, training of TB doctors, HIV doctors, doctors of general healthcare service on clinical progression, diagnosis and treatment of tuberculosis in HIV patients was conducted. From 2010 to 2013, 4 two-day training workshops were conducted, which were attended by Russian and foreign TB/HIV specialists.

The percent of TB doctors and HIV doctors trained on HIV/TB co-infection was 90% of all physicians employed in Tomsk Region.

In order to improve collaboration between TB Services and HIV Services to provide care to HIV/TB patients, including injection drug users, regular two-day training-workshops were organized for healthcare workers, social workers, and workers of Tomsk-AntiAIDS. The titles of workshops included: “Need and requirements of vulnerable groups. Barriers to comprehensive care, ways to overcome”; “Preventive work with vulnerable groups”; “TB/HIV counseling of vulnerable groups”; and “Effective work strategies for vulnerable groups.” From 2010 to 2013, a total of 18 training workshops were conducted.

All workshops under the GFATM project were conducted at the AIDS Center and TB Services, non-profit AIDS-service organizations, treatment and preventive therapy facilities.

TB education among population groups.
Materials designed to increase TB awareness was provided among target populations, addressing topics such as routes of transmission, prevention and treatment. This included printing and distribution of leaflets, pamphlets, and posters.

Challenges and lessons of the TB/HIV program implementation
1. Because it is challenging to induce sputum in injection drug users (IDUs), fluorography is the main screening method used in this group. To provide effective TB screening among vulnerable groups, use of all available methods of TB detection in HIV patients is required: fluorography examination, Mantoux skin test, chest X-ray, CT scan, when possible; Diaskin-test; sputum examination when sputum is available (sputum smear microscopy, culture, PCR using Gene Xpert);
2. What works - a flexible algorithm of TB screening, collaboration with non-profit organizations (charitable foundations), involvement of outreach workers, low threshold to “enter” the program (no health insurance or ID are required for TB screening), motivation sets that provide high coverage of target group representatives, effective TB detection performed by health care workers in hard-to-reach groups of population, and bringing the patient to treatment in the national TB facility.
3. Close collaboration of TB Services and AIDS-Center to provide TB screening and preventive therapy among PLWH helps reduce the number of visits to TB outpatient facilities and contacts between HIV patients with TB patients.
4. Challenges in attracting and keeping patients on preventive TB therapy. If the patient is an injection drug user, motivation cannot be achieved through food sets, monthly travel passes for public transport, counseling provided by psychologists, or assistant from social workers. It is difficult to find motivational factors that have a significant impact on adherence to preventive therapy among this group of patients.
5. Challenges in monitoring the program in remote areas (city of Strezhevoy). It is required to visit the areas to assess activities on site. Since 2011, declining enrollment of patients subject to preventive therapy has been reported due to reduced monitoring visits related to funding shortages from the Global Fund.
6. Since most of Strezhevoy population works on a rotating shift schedule, it is likely that patients interrupt therapy early in the course of treatment or self-administered therapy is provided.
Operational research

The promotion of research is one of the main components of the GF strategy, which includes program-based operational research (OR) and research on introducing new tools into practice. The importance of OR in improving tuberculosis (TB) control was recognized, and historical OR studies have been instrumental in the development of major strategies for TB control.

Promotion of the operational research (OR) activities is one of the important components of the Tomsk (RF) program funded by the RCC GF grant. The GF, as the funding organization, has recognized the need for OR and has accepted our proposed framework to conduct research, which covers a spectrum of local setting-oriented projects in TB control.

Its aims include:

1) Estimating the cost of inpatient TB treatment, outpatient treatment, and treatment at home;
2) Analysis of TB/HIV collaboration program;
3) Screening for tuberculosis and tuberculosis infection among vulnerable populations in Tomsk, Russia, particularly, Injecting Drug Users (IDU) and People Living with HIV and AIDS.

Suggestions are made for potential steps for improved purpose-driven OR, which may help to improve TB control locally and inform policy recommendations internationally. The program “2” and “3” descriptions and main results have been fully described at the corresponding chapters of the manuscript.

Estimating the cost of inpatient treatment, outpatient treatment, and treatment at home

The goal of the study was to estimate the cost of treating susceptible and drug-resistant TB in different facilities of Tomsk city: TB hospital, Day care hospital, TB office and through treatment at home options (“Home Hospital” and Sputnik program) to advise policy-makers on more efficient budget allocation.

Methods: The data about annual expenditures (detailed with personnel salaries, building, equipment, transportation, food and other budget lines) and the list of personnel in each department was requested from Tomsk Oblast Tuberculosis Services (dispensary) and Tomsk Oblast Tuberculosis hospital. All sources of financing (governmental and grants) were included. Interviews were performed to assess working time allocation of the staff serving several treatment departments. The data about patient-time in each researched department, the frequency of bacteriological testing was retrieved from Tomsk TB dispensary database. Random patients' charts reviews were performed to assess the volume of biochemical examinations in different treatment categories. Data about monthly TB medications’ consumption was obtained from the pharmacy.

All costs involved in treatment were included: personnel salaries, capital expenditures (buildings, ventilation system installation, equipment, and vehicles), operational expenditures (utilities, fuel, buildings/cars maintenance, equipment repair, and disposables), food, TB and ancillary medications, bacteriological, biochemical and instrumental examinations, specialists’ consultations, pharmacy, administrative expenditures. The costs were assessed per 1 month of treatment in each department. The summary of the results is presented below:

Table 12. Average monthly expenditures associated with 1 category treatment (per 1 patient).

<table>
<thead>
<tr>
<th>Costs</th>
<th>TB hospital</th>
<th>Day care hospital</th>
<th>TB office</th>
<th>”Hospital at home” team</th>
<th>Sputnik</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment provision in the department</td>
<td>$90.90</td>
<td>$202.18</td>
<td>$150.02</td>
<td>$185.73</td>
<td>$268.37</td>
</tr>
<tr>
<td>Medications to treat TB and side effects</td>
<td>$15.87</td>
<td>$15.87</td>
<td>$15.87</td>
<td>$15.84</td>
<td>$15.87</td>
</tr>
<tr>
<td>Food and social support</td>
<td>$228.43</td>
<td>$125.94</td>
<td>$53.22</td>
<td>$53.22</td>
<td>$59.52</td>
</tr>
<tr>
<td>Treatment and side effects monitoring</td>
<td>$62.06</td>
<td>$77.44</td>
<td>$77.44</td>
<td>$77.44</td>
<td>$104.27</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>$797.26</strong></td>
<td><strong>$421.43</strong></td>
<td><strong>$296.55</strong></td>
<td><strong>$332.23</strong></td>
<td><strong>$448.03</strong></td>
</tr>
</tbody>
</table>

This includes: Personnel salaries, capital expenditures (buildings, ventilation system installation, equipment, and vehicles), operational expenditures (utilities, fuel, buildings/cars maintenance, equipment repair, disposables), and administrative costs

1 An average cost of medications per 1 month of treatment (based on reports from the pharmacy)

2 Hospital and Day care hospital also include kitchen costs (personnel, capital, operational, and administrative costs).

3 Treatment and side effects monitoring includes regular bacteriological, biochemical, radiological examination; specialist consultations.
Table 12a. Average monthly expenditures associated with IV category of treatment (per 1 patient).

<table>
<thead>
<tr>
<th>Costs</th>
<th>TB hospital</th>
<th>Day care hospital</th>
<th>TB office</th>
<th>“Hospital at home” team**</th>
<th>Sputnik††</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment provision in the department</td>
<td>$574.32</td>
<td>$279.73</td>
<td>$203.68</td>
<td>$307.96</td>
<td>$460.84</td>
</tr>
<tr>
<td>Medications to treat TB and side effects†</td>
<td>$177.06</td>
<td>$177.06</td>
<td>$177.06</td>
<td>$177.06</td>
<td>$177.06</td>
</tr>
<tr>
<td>Food and social support†</td>
<td>$239.42</td>
<td>$193.56††</td>
<td>$67.35</td>
<td>$67.35</td>
<td>$72.90</td>
</tr>
<tr>
<td>Treatment and side effects monitoring†</td>
<td>$66.79</td>
<td>$82.17</td>
<td>$82.17</td>
<td>$82.17</td>
<td>$109.00</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$1057.59</td>
<td>$732.52</td>
<td>$530.26</td>
<td>$634.54</td>
<td>$819.80</td>
</tr>
</tbody>
</table>

This includes: Personnel salaries, capital expenditures (buildings, ventilation system installation, equipment, and vehicles), operational expenditures (utilities, fuel, buildings/cars maintenance, equipment repair, disposables), and administrative costs
† An average cost of medications per 1 month of treatment (based on reports from the pharmacy)
†† Hospital and Day care hospital also include kitchen costs (personnel, capital, operational, and administrative costs).
§ Treatment and side effects monitoring includes regular bacteriological, biochemical, radiological examination; specialist consultations.
** Treatment was provided twice a day for 90% of patients on IV category
†† Patients on IV category were receiving packaged food sets in addition to hot dishes cooked by Day Care hospital kitchen personnel.

The total cost of treatment was the highest in the hospital as a result of high personnel costs, utilities bills, building maintenance, kitchen and administrative costs.

“Hospital at home” treatment was slightly higher than treating patients at the TB office (12% higher for I category and 20 % higher for IV category) but lower than treatment at the Day Care hospital (21% less for I category and 13 % less for IV category) and inpatient care (58 % less for I category and 40 % less for IV category). Usually “hospital at home” was reserved for immobile patients who couldn’t attend the Dispensary and patients with low adherence, which put them on the brink of defaulting or failing treatment. Published research shows patients’ preferences for home treatment and higher treatment results of those treated at home. Based on our economic analyses we recommend wider “hospital at home” implementation with an option for patients to choose themselves where to be treated.

The patient-centered approach of the Sputnik program provides treatment at the patient’s preferred location and timing, organizes specialists’ consultations at clients’ homes and has a limited number of patients to give Sputnik personnel enough time to interact with them. Sputnik had the highest costs among all ambulatory options, however, it is usually the last treatment option considered after all other departments failed to keep the patients on adequate medications intake. A number of Sputnik patients were about to be declared defaulters after missing several weeks of treatment consequently. Troubled by alcohol and drug addiction these patients were not able to set up and follow strict treatment schedule and put them on the brink of defaulting or failing treatment. Published research shows patients’ preferences for home treatment and higher treatment results of those treated at home. Based on our economic analyses we recommend wider home treatment and should be considered for all patients in need to prevent default and treatment failure.

Dissemination of the findings: An article is currently being written for publication in a peer-reviewed Russian scientific journal.

Treatment outcomes and two-year follow up among MDR-TB patients enrolled on treatment between December 2, 2004 and April 6, 2009.

Specific aims:
1) Examination of failures and deaths among MDR-TB patients enrolled on MDR-TB treatment.
   a. What are the reasons for growing failure rates in 2008-2009 cohorts as compared to 2006-2007 cohorts? Is it the result of increased number of patients with known risk factors for failure or inadequate regimens and poor adherence?
   b. What is happening to failures after treatment discontinuation? How long are they living after failure?
2) Long-term treatment results for patients who defaulted from MDR-TB treatment. Factors contributing to sustainable 2-year culture negative status after default.
3) Comparison of treatment outcomes and frequency of side effects among MDR-TB patients with and without diabetes.
4) Comparison of treatment outcomes and frequency of side effects among MDR-TB patients with and without hepatitis B/hepatitis C.
5) Comparison of treatment outcomes and frequency of side effects among MDR-TB patients with and without psychiatric diseases.
6) To assess treatment outcomes and frequency of side effects among MDR-TB patients depending on AUDIT (Alcohol Use Disorders Identification Test) rating.
7) To assess treatment outcomes for TDR-TB (totally drug resistance TB).
Research design and methods:

This is a retrospective study of 1,174 subjects enrolled to receive individualized MDR-TB treatment under the Tomsk TB Control Programs between December 2, 2004 and April 6, 2009. All patients who received IV category of treatment with GF or MOH medications were included in this study.

By this date the following tasks were accomplished: (1) All important information from existing routine MDR-TB paper forms, which was routinely collected but not entered into Tomsk TB civilian and penitentiary electronic databases, was entered. (2) Missing bacteriological data were requested from laboratories all over the oblast and subsequently entered into existing Tomsk TB civilian electronic database. (3) For each subject, treatment outcomes, demographic information, exposure variables, adverse events and other covariates were abstracted from Tomsk TB civilian and penitentiary electronic databases. (4) All variables were confirmed and missing variables added through retrospective medical record review, using the data collection form. Trained reviewers extracted required data from patients’ charts in Tomsk city, Seversk, rural places and penitentiary sector. (5) The data were double entered into newly developed electronic database.

The following tasks are currently performed: (1) Discrepancies in data entries are being reviewed. (2) Data are being “cleaned” through identification of non-logical statements and numbers with the following re-check of this information with primary sources of data (patients’ charts).

The next steps, data analyses for presentations and publications, are planned in the coming months as soon as the data are clean.
Impact on epidemiological picture

As was described in previous chapters, grant activities 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 has 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. For example, in civilian sector on average from 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 PDR-TB cases in 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. Effective treatment rate among patients enrolled in the GFATM grant treatment was 67% in 2005-2011 civilian and prison cohorts altogether. Without XDR-TB cases, effective treatment was registered among 66% and 82% cases of 2005-2011 cohorts in civilian and prison sector, 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 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 special targeted activities that were also effective (“Sputnik” project, TB-HIV detection and treatment).

Great outcomes of the treatment had positive effect on the epidemiological picture in the region.

Development of the impact indicators was based on the Stop TB Partnership targets, according to which prevalence and mortality rates should be lowered in 2015 to 50% when compared with 1990s average\textsuperscript{15}. These targets are in line with Target 8 of Goal 6 (“Combat HIV/AIDS, Malaria and other diseases”) of the Millennium Development Goals. However, since the bulk of the burden of TB in 2001-2003 was in Eastern Europe and countries from FSU, the leading experts in TB estimate that targets could not be reached by 2015\textsuperscript{19}.

The WHO experts suggested targets that are more feasible\textsuperscript{20}:

- To decrease the prevalence rate to 130-140 per 100,000
- To decrease mortality rate to 8-10 per 100,000
- Incidence rate could be decreased by 4% per year, according to Chris Dye’s calculations\textsuperscript{2}. Since the 1999 incidence rate in Tomsk region was higher than in 2001-2003 and was 117.6/100,000, the possible prognosis for 2015 was around 76 per 100,000.

The overall TB epidemiological picture in Tomsk oblast really improved compared to 1999-2000 level. Incidence decreased to 67.6 per 100,000 and mortality dropped to 6.3 per 100,000 in the region (both sectors) in 2013. The prevalence rate in 2013 was 87.3. Dye’s prognosis was met.

It is obvious that the TB epidemic in all Russian settings goes down. However, compared to the Siberian regions and all-Russian data, Tomsk TB incidence and mortality rates are decreasing faster.

Incidence dropped to the 57.5% level of 1999’s and mortality to the 27.9% of the 1999’s rate, whereas the wider Russian average was 73.9% and 56.5%, respectively.

Siberian levels are even higher than the Russian average. The mortality drop after 2004 and overall decrease of incidence after 3 years of the grant start (in 2008-2009) could be due to the implementation of intensive activities under the GFATM grant.

\textsuperscript{15}Stop TB Partnership and World Health Organization. Global Plan to Stop TB 2006-2015
The rate of change was higher after GFATM grant start, compared to the 2000-2004 rate, when the MDR-TB program was implemented by PIH with limited resources and lower enrollment rate.

Table 13. The rate of incidence change (next year - previous year/ previous year data)

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomsk region</td>
<td>117,6</td>
<td>-1,0%</td>
<td>-5,2%</td>
<td>-2,7%</td>
<td>-13,6%</td>
<td>-6,8%</td>
<td>-27,4%</td>
</tr>
<tr>
<td>Siberia</td>
<td>126,4</td>
<td>0,8%</td>
<td>4,0%</td>
<td>-0,3%</td>
<td>-1,7%</td>
<td>-3,7%</td>
<td>-19,9%</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>85,2</td>
<td>-0,4%</td>
<td>-2,2%</td>
<td>-0,1%</td>
<td>-0,5%</td>
<td>-4,5%</td>
<td>-26,2%</td>
</tr>
</tbody>
</table>

However, comparing with Russian and Siberian changes in incidence and mortality, rates were the highest in 2000-2004 period.

Table 13a. The rate of mortality change (next year - previous year/ previous year data)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tomsk region</td>
<td>22,6</td>
<td>-4,6%</td>
<td>-22,9%</td>
<td>-10,1%</td>
<td>-50,6%</td>
<td>-8,4%</td>
<td>-33,4%</td>
</tr>
<tr>
<td>Siberia</td>
<td>28,6</td>
<td>4,3%</td>
<td>21,3%</td>
<td>-4,2%</td>
<td>-21,2%</td>
<td>-8,0%</td>
<td>-22,4%</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>20</td>
<td>1,4%</td>
<td>6,9%</td>
<td>-4,0%</td>
<td>-20,0%</td>
<td>-10,0%</td>
<td>-36,0%</td>
</tr>
</tbody>
</table>

Overall number of patients that are infectious at the end of the year decreased more than 2 times compared to 2000 data. Most cases are on treatment.

The incidence rate of MDR-TB cases in the civilian sector dropped after 2004 and is around 6 per 100,000 in Tomsk. The rate in the prison sector depends on the amount of new inmates transferred from other regions; however, it has been stable for many years.
Program participants’ view on the project effectiveness, implementation challenges and lessons learned.
We have surveyed 33 participants of the project. Healthcare workers who participated in the survey included: nurses, TB doctors from TB hospital and outpatient TB treatment facilities and rural TB inspectors, heads and representatives of administration, and PR personnel (PIH-Russia).

According to opinion of the key project participants in the civilian and penitentiary sectors, the main objectives of the GFATM project in 2005-2013 were:

1. Organization of observed treatment;
2. Treatment of MDR-TB patients;
3. Improvement of treatment adherence, social support, patient-centered approaches
4. Recording-reporting documentation

Compared to that period, participants remember that prior to 2005, the main objective was treatment of MDR-TB patients and adjustment of uninterrupted supply of second-line TB drugs (employees of TB services and PIH), as well as organization of observed treatment (as per TB services employees).

Main expectations from the project were related to program enrollment and provision of patients with TB drugs, improvement of treatment results, and the overall epidemiological situation in the region. “I did my work in a routine manner and any innovation was not accepted happily. It was difficult to comply exactly with the requirements. But with the start of the grant we hoped that we could treat chronic patients.” Many employees hoped that adherence and treatment programs would be expanded. These expectations are different from those in 2001, when most of employees were either unhappy because they were expecting “extra responsibilities and no result” or they associated the project with an improved supply of TB drugs for MDR-TB treatment.

From the beginning of the project it was difficult for TB services employees to accept and follow new treatment regimens for MDR-TB patients – “a lot of drugs at once.” New and additional recording-reporting documentation resulted in irritability. They could not believe at all in such organizational innovations like the administrative committee on treatment interruption and the Sputnik project.

Employees’ attitudes have changed upon the results from new activity: “the attitude has changed when we saw the results: more cured patients, less defaults in the city, observation of treatment has improved treatment outcomes. Now everyone is matching Sputnik in their work.” Some of them put up with it and got used to it.

Regardless of general distrust of new activities, some administration personnel believed from the beginning in the necessity and usefulness of observed treatment, adherence programs, and their attitude to those activities was improving.

According to TB services employees, the 2005-2013 project was given 3.4 points on a 5-point grading scale – that is, “more likely that it achieved the goals.” PIH employees give 3.6 points to the project achievements; at the same time, they emphasize the first phase of the project (2005-2009) as the one that absolutely achieved the stated goals.

In their answers to the question “what did you expect and it happened,” the respondents indicated improved resources and knowledge; improvement in treatment results, including among so-called chronic cases and for the overall epidemiological situation; and a decline in the number of patients in the region. One response should be noticed: “with appropriate organization of care, any patient can complete treatment successfully.”

Interesting responses were given to the question “what did not you expect but it happened” – they were both positive and negative

<table>
<thead>
<tr>
<th>Significant improvement in knowledge level of each doctor</th>
<th>Decrease in doctor’s role image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doctors have become more tolerant to the patients</td>
<td>Many doctors feel burnout syndrome</td>
</tr>
<tr>
<td>Observed treatment has become a reality</td>
<td>Increase in percent of MDR-TB patients among all those on treatment which means high workload</td>
</tr>
<tr>
<td>Effectiveness of the Sputnik program</td>
<td>Motivation sets have become a responsibility, patients are not motivated by food sets any longer, they demand the support</td>
</tr>
<tr>
<td>Significant decline in epidemiological rates</td>
<td>Negative attitude of employees to the activities under implementation.</td>
</tr>
</tbody>
</table>

Among missed activities and opportunities, the respondents emphasized those that were not direct activities within the grant program or in most cases they depended on the actions from TB service itself, for instance – early detection of limited TB forms, pathogenic treatment of MDR-TB (using immune modulators), insufficient use of side effect medications, surgery practice development, strengthening activities to work with alcohol dependent patients, and development of “Sputnik” in rural settings. The reason for it, as per one representative of the administration, was “a lack of unified vision of goals and objectives, poor management inside TB services.”
According to PIH employees, not all potentials of laboratory diagnostics of drug-resistant TB cases were implemented, the collaboration between hospital and ambulatory treatment stages was not perfect, and treatment adherence activities were not implemented to the extent and effectiveness as expected.

According to the respondents, the best results were achieved in the following activities:

<table>
<thead>
<tr>
<th>Table 14. Activities</th>
<th>Achievement Average score***</th>
<th>Number of respondents who marked the activity as important</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quality improvement of laboratory service</td>
<td>4.3</td>
<td>9</td>
</tr>
<tr>
<td>2. Early TB detection in primary healthcare service (sub-program)</td>
<td>2.8</td>
<td>4</td>
</tr>
<tr>
<td>3. Drugs supply and management /turnover</td>
<td>4.7</td>
<td>13</td>
</tr>
<tr>
<td>4. Enrollment of all DR-TB patients on treatment regardless of their social characteristics</td>
<td>4.2</td>
<td>4</td>
</tr>
<tr>
<td>5. Quality improvement of clinical management of DR patients (number of drugs, duration of treatment, etc.)</td>
<td>4.3</td>
<td>10</td>
</tr>
<tr>
<td>6. Active detection and management of side effects</td>
<td>4.5</td>
<td>10</td>
</tr>
<tr>
<td>7. Improvement of clinical management of DR patients with concomitant conditions</td>
<td>4.3</td>
<td>7</td>
</tr>
<tr>
<td>8. Surgery in DR patients</td>
<td>2.9</td>
<td>1</td>
</tr>
<tr>
<td>9. Infection control. Separation of patients’ flows.</td>
<td>3.3</td>
<td>5</td>
</tr>
<tr>
<td>10. DOT for all patients.</td>
<td>4.5</td>
<td>12</td>
</tr>
<tr>
<td>11. Inspector visits to rural facilities, management of rural patients</td>
<td>4.6</td>
<td>6</td>
</tr>
<tr>
<td>12. Collaboration between prison-civilian sector, hospital- outpatient facilities</td>
<td>4.4</td>
<td>6</td>
</tr>
<tr>
<td>13. Personnel activities in response to non-adherence (searching of patients who missed doses, monitoring of non-adherent patients, adherence committee)</td>
<td>4.7</td>
<td>11</td>
</tr>
<tr>
<td>14. Expansion of treatment at home service</td>
<td>4.8</td>
<td>8</td>
</tr>
<tr>
<td>15. Sputnik project</td>
<td>5.0</td>
<td>10</td>
</tr>
<tr>
<td>16. Food sets, hygiene packages, transportation passes, other kinds of support</td>
<td>4.8</td>
<td>14</td>
</tr>
<tr>
<td>17. Social workers activities</td>
<td>4.3</td>
<td>7</td>
</tr>
<tr>
<td>18. Activities /sub-programs to improve adherence among drug/alcohol addicted patients</td>
<td>3.9</td>
<td>6</td>
</tr>
<tr>
<td>19. Monitoring, recording and reporting / database</td>
<td>4.8</td>
<td>3</td>
</tr>
<tr>
<td>20. Detection and treatment of TB-HIV</td>
<td>4.0</td>
<td>4</td>
</tr>
</tbody>
</table>

***1-absolutely NOT achieved, 2-more likely not achieved, 3 – more likely achieved, 4 – absolutely achieved, 5 – significantly exceeded

According to the respondents, the main reasons for success are:

1. Proper personnel and training, motivating personnel, interested personnel.
2. Ongoing monitoring and control of activities
3. Proper organization of work, management
4. Coordinated work of TB services and PIH. Assistance from PIH as a principle recipient of the grant and the program implementers
5. Uninterrupted supply of second-line drugs including creation of TB drug warehouse. Funding.

The next section of questions was related to improvement of knowledge and skills in employees as possible reasons for the project success. In general, most respondents think their knowledge and skills have improved, and in some areas they have become experts.

<table>
<thead>
<tr>
<th>Table 14a. Activities</th>
<th>Knowledge</th>
<th>Skills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical management of MDR-TB patients</td>
<td>4.5</td>
<td>4.6</td>
</tr>
<tr>
<td>Clinical management of susceptible TB patients</td>
<td>4.2</td>
<td>4.3</td>
</tr>
<tr>
<td>Organization of observed treatment in your facility/in the area of the region</td>
<td>4.9</td>
<td>4.8</td>
</tr>
<tr>
<td>Organization of social support</td>
<td>4.6</td>
<td>4.6</td>
</tr>
<tr>
<td>Organization of “treatment at home”/ “Sputnik” program</td>
<td>4.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Detection and treatment of TB-HIV</td>
<td>4.3</td>
<td>4.3</td>
</tr>
</tbody>
</table>

***1 - no gain in knowledge/skills; 2 – minimal gain; 3 – knowledge is similar to other areas; 4 – knowledge has improved compared to other areas; 5 – knowledge has significantly improved, I can be an instructor; 6-I don't know

Did you use the same skills and approaches at the beginning of the project as well as you are using them now? “No” was the response of all respondents, except heads of TB services in the civilian and penitentiary sectors. A lack of knowledge and skills was improved through intensive training, implementation and monitoring, and through assistance from PIH.
Again, most of the respondents emphasized that if they had all the resource available in the 2000s, they would not have reached the same results on their own than those achieved in collaboration with partner-organizations (except senior managers of TB services).

Since the project implementation, according to the respondents, was given 3.4 points on a 5-point grading scale, it was interesting to know the answers to the questions about the reasons for failure and barriers to the project implementation.

One of the possible reasons for failure to reach a result can be overstated goals and expectations. One half of the TB services representatives think, “everything was justified.” Another half thinks that the requirements were too high in: “organizing observed treatment and effectiveness of treatment, social support, patient-centered approach and a leading role of patients, prevention of voluntary leave from hospital, and activities for alcohol dependent patients.” Nobody mentioned the indicators.

In general, TB Services employees in their response to the question about a potential for more effective implementation of the project, gave “2” points – probably yes, it was possible. Regardless of shared opinion of doctors and administration, all nurses consider that “absolutely, better results could be reached.” Out of the list of activities that could strengthen the project, the respondents indicated recruitment of new personnel and increased salary; stronger and strict management of the project and accurate supervision of indicator implementation; and use of third-line drugs and pathogenic treatment, as well as surgery. PIH employees answered this question equally – probably yes, and yes, absolutely.

TB Services employees consider the main reasons for decline of treatment effectiveness in patients’ cohorts was related to extended enrollment of patients and increases in percent of chronic cases, deterioration of social characteristics – increase in percent of patients with substance abuse, and failure to work with them. One-third of the respondents put blame on second-line TB drug stock-outs in 2009. Two employees think that low-quality management and less control from the head doctor and heads of departments are the main reasons.

Interestingly, did the respondents link the previous two questions with each other thinking that, on the one hand, better results could be reached and on the other hand blaming patients in failures? For a complete decline of TB reservoir in the region, it is required to treat all patients, including chronic cases. A large number of chronic cases in the 2000s were related by the respondents to a lack of second-line TB drugs and inadequate organization of treatment (no observed treatment and patient-centered activities available). The attitude of the respondents to the fact that chronic cases had to be taken for treatment from the beginning of the project, divided equally: one half was negative about this decision (“internal protest”, “hopeless”), and the other half thought that the patients needed treatment. A half of the respondents with negative attitude to a potential to treat chronic cases changed their attitude during the project when they saw the results. According to almost all respondents, the project helped to decrease TB reservoir in the region.

The question “What was your view at the beginning of the project about delivering care to non-adherent patients?” was answered by most of civilian sector respondents that “there were some concerns, it was a controversial issue, but it was our work”. Again the attitude changed from negative to positive. One response of a senior manager of the civilian TB services employees should be mentioned: “Initially, I thought I did not want to treat them, let them die. Now – it is opposite. There is an approach for every patient. For everyone. It requires: 1) Careful attention of healthcare workers; 2) Finding out the reasons for poor adherence; 3) Team work; 4) Proper management of side effects”. Many respondents share this opinion. Nevertheless, below you can find a complete list of what is needed for successful treatment for non-adherent patients:

1. Careful attention of healthcare workers
2. Team work
3. Uninterrupted supply and availability of all TB drugs. Access to new TB drugs.
4. Find out the reasons for poor adherence to treatment. Look for motivation in each case
5. Work of psychologist
6. Active participation of addiction specialist
7. Proper management of side effects
8. Organizing free time activities for TB patients in TB hospital
9. Social support.
10. Patient-centered approaches. Just one Sputnik is not enough – more teams are required.
11. Successful experience of other patients - peer consultants
12. Monetary support at the end of treatment. Improvement of material wellbeing
13. Make patients more responsible
14. A locked hospital – to lock in patients during the time of hard drinking. In a locked facility the patient cannot drink alcohol every day. It is the law of involuntary hospitalization in practice. Involuntary treatment to those who could not be managed by Sputnik.
15. Hospice care
16. Improve treatment continuity between all parties and AIDS-Center

It should be noted that PIH has made efforts to introduce or strengthen most of the above-mentioned activities in different years of the program implementation except involuntary hospitalization.
‘Should we fight for non-adherent patients”, we asked and received 100% of “yes” response.

In the final section of questions about implementation of the project we asked respondents about their personal contribution to the project and the sub-programs they worked in.

Half of TB Services respondents think that they managed to implement all the ideas and activities they planned and only 17% of PIH employees.

Of those who did not manage to implement all scheduled activities, most of them emphasized insufficient funding as a principle barrier. The challenges included: rejection of recording-reporting documentation and low motivation among doctors and TB patients, as well as organizational challenges. What helped to overcome those difficulties were personal collaboration, humble submission and acceptance as well as training programs and discussions with colleagues and PIH employees. What could not you implement? Surprisingly, most of respondents who answered this question regret they could not expand Sputnik program to the regional districts (not all respondents dealt with treatment in rural settings). Additionally, respondents highlighted difficulties related to infection control and surgery as well as addiction care for patients.

Sixteen of 17 TB services respondents think that the sub-program they worked in was effective. Given previous responses about evaluation of the entire project and effectiveness of certain activities, respondents are likely to give low evaluation points to those activities that were implemented by their colleagues.

What additional resources were required to overcome all those difficulties: “stable economy in the country,” “building new standard facilities,” “assistance from Health department, finance.” It should be stated that the Global Fund could not help on this matter.

The next section of questions was related to the lessons from the outcomes of the project implemented in Tomsk Oblast.

All respondents think that activities implemented in Tomsk Oblast can be implemented in any Russian region. However, the following requirements need to be complied with:

1. Desire to work, not only among senior managers but among providers as well.
2. Political will supported by budget funding.
3. A trained team. Special qualification of the participants, experience in the implementation of grant programs is preferred.
4. Involvement of international NGOs.

According to Tomsk TB Services employees, there are no specific approaches required for implementation of this project in Russian settings.

In their answer to the question what must be implemented from the above mentioned activities, most of the respondents chose the following (in descending order):

1. Drugs supply and management /turnover
2. Food sets, hygiene packages, transportation passes, other kinds of support
3. Quality improvement of laboratory service
4. Directly observed treatment for all patients
5. Collaboration between prison-civilian sector, hospital-outpatient facilities
6. Quality improvement of clinical management of DR patients (number of drugs, duration of treatment, etc.)
7. Active detection and management of side effects
8. Activities /sub-programs to improve adherence among drug/ alcohol addicted patients
9. Expansion of treatment at home service
10. Other activities

Regardless of new regulation documents and expansion of Tomsk experience in Russia, some of the project components are still controversial and not accepted by Russian TB Services, including the following:

- Hospital substitution technologies, “This is expensive, the cost. If a senior executive is a TB doctor, he understands how important the components are.”
- Social support, food sets
- “Patient-centered programs are very expensive”

According to TB Services respondents, the most effective managerial decisions within the project are:

- Creation of a centralized TB drug fund
- Creation of UCEC and treatment interruption committee
- Expansion of treatment at home service
Increasing TB inspector’s visits
- Monitoring of activities by PIH
- Creation of ‘Sputnik’ program
- Activity agreements with all program participants
- Implementation of specific recording-reporting forms on TB activities

The final section of the survey included questions on the role of the principle recipient in the project implementation. Regardless of routine attitude to PIH employees as inspectors, TB services employees highlighted other sides of collaboration:

- “A very big role. First of all, it is their knowledge and experience. Any initiative needs a master. You cannot always find time to read literature and they give it on training, clinical protocols and algorithms for what to do have been developed. PIH’s word was substantial”
- Methodological accompaniment, connection to the world scientific community
- Management – overall leadership and coordination.

Below is evaluation provided by the respondents from TB services of PIH participation in different components of the project.

<table>
<thead>
<tr>
<th>Table 15. Activities</th>
<th>Average score***</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Quality improvement of laboratory service</td>
<td>4.0</td>
</tr>
<tr>
<td>2. Early TB detection in primary health care service (sub-program)</td>
<td>4.2</td>
</tr>
<tr>
<td>3. Drugs supply and management /turnover</td>
<td>4.6</td>
</tr>
<tr>
<td>4. Enrollment of all DR-TB patients on treatment regardless of their social characteristics</td>
<td>4.6</td>
</tr>
<tr>
<td>5. Quality improvement of clinical management of DR patients (number of drugs, duration of treatment, etc.)</td>
<td>4.5</td>
</tr>
<tr>
<td>6. Active detection and management of side effects</td>
<td>4.7</td>
</tr>
<tr>
<td>7. Improvement of clinical management of DR patients with concomitant conditions</td>
<td>4.6</td>
</tr>
<tr>
<td>8. Surgery in DR patients</td>
<td>3.0</td>
</tr>
<tr>
<td>9. Infection control. Separation of patients’ flows.</td>
<td>4.1</td>
</tr>
<tr>
<td>10. DOT for all patients.</td>
<td>4.9</td>
</tr>
<tr>
<td>11. Inspector visits to rural facilities, management of rural patients</td>
<td>4.8</td>
</tr>
<tr>
<td>12. Collaboration between prison-civilian sector, hospital- outpatient facilities</td>
<td>4.3</td>
</tr>
<tr>
<td>13. Personnel activities in response to non-adherence (searching of patients who missed doses, monitoring of non-adherent patients, adherence committee).</td>
<td>4.8</td>
</tr>
<tr>
<td>14. Expansion of treatment at home service</td>
<td>5.0</td>
</tr>
<tr>
<td>15. Sputnik project</td>
<td>5.0</td>
</tr>
<tr>
<td>16. Food sets, hygiene packages, transportation passes, other kinds of support</td>
<td>4.9</td>
</tr>
<tr>
<td>17. Social workers activities</td>
<td>4.4</td>
</tr>
<tr>
<td>18. Activities /sub-programs to improve adherence among drug/ alcohol addicted patients</td>
<td>4.6</td>
</tr>
<tr>
<td>19. Monitoring, recording and reporting , database</td>
<td>4.6</td>
</tr>
</tbody>
</table>

*** 1–not important at all; 2–low; 3–50/50; 4 good; 5–very good; 6–I don’t know

In conclusion, we provide responses to the question - Has PIH brought something more to the Tomsk project than just monitoring of the grant implementation?

- Work of PIH employees including accurate planning of activities, new approaches to work, organizational and methodological assistance. Organization of the entire process.
- Close cooperation with TB Services employees – organization of social support and continuity, Sputnik, expansion of treatment at home service. Nurses emphasized specifically – “practical assistance in the work with patients.”
- “Team work, outside point of view is very important. Most of PIH employees have TB medical background.”
- Due to PIH, the project was promoted in the world scientific community, recognition of the project and all its participants in the world.
- “If it were not PIH, there would not be a project,” and “PIH is a locomotive engine of the project.”
Successful implementation of the MDR-TB program in Tomsk was acknowledged by the Russian authorities and local TB Research Institutions, which are the focal points for TB control in Russia. Novosibirsk TB Research Institute (NTBRI) is one of the five federal TB research institutions that supervise the implementation of TB program activities in 26 Russian territories in Siberia and the Far East Federal regions of Russia. Tomsk Oblast is one of the Siberian territories, which is supervised by the Novosibirsk TBRI.

As part of RCC grant, the Novosibirsk TBRI organized clinical trainings on management of drug-resistant TB for TB doctors and program managers.

In 2011 training was provided only. A total of 10 workshops in five regions provided training to 766 specialists on M/XDR-TB program and clinical management using the training materials developed on experience from Tomsk TB Program. As a supervisory body for Siberia and Far East of Russia, the Novosibirsk TBRI combined supervisory monitoring visits to all Siberian and Far-Eastern oblasts and conducted trainings on various aspects of PMDT to address challenges of TB control. Visits to the regions were conducted as a part of the grant aiming on replicating the the expertise from Tomsk TB Program, where Novosibirsk TBRI acted as sub-recipient of the grant.

During two years, 67% of the Siberian Federal Territory and 56% of the Far East Federal Territory were covered by visits. This allowed the quality of TB and MDR-TB care to be evaluated, detecting major problems and identifying solutions.

Main problems identified during visits included:

- Facility conditions that cannot provide for MDR-TB departments to be organized according to the requirements.
- Infection control measures are not fully complied with by all territories (ventilation, separation of flows, personal protection equipment).
- Inadequate attention is paid to TB case finding by simple sputum smear microscopy in primary health care facilities.
- Limited budget does not allow all the territories to introduce rapid MDR-TB diagnosis methods.
- Patients are not always accurately and timely reregistered on treatment regimen IV.
- Most territories do not keep special registers for MDR-TB patients enrolled on treatment regimen IV.
- Second-line TB drug management has not been developed appropriately in all territories.
- Observed treatment at ambulatory stage has not been organized properly.
- Medical treatment charts 01-TB/r for MDR-TB patients have been introduced mainly in those territories that participated in international projects.
• Side effect monitoring charts for MDR-TB patients have not been kept.
• Analysis of MDR-TB treatment outcomes has not been performed.

A total 26 training activities were organized and conducted during the three years, and they were attended totally by 1,431 specialists in laboratory diagnosis, TB treatment, and general practitioners.

<table>
<thead>
<tr>
<th></th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of training</td>
<td>10</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Number of those trained</td>
<td>766</td>
<td>377</td>
<td>288</td>
</tr>
</tbody>
</table>
Appendix 1. A project evaluation team

A project evaluation team consists of specialists who collect and interpret data, provide general assessment of received data and data relationships; they also circulate project evaluation at different levels. Table 1 shows employees and their functions in the evaluation process.

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
<th>Evaluation functions</th>
</tr>
</thead>
</table>
| Dmitry V. Taran              | PIH- Russia                | • Responsible for project evaluation  
• Develop a general strategy of data collection  
• Involve evaluation staff  
• Take part in data analysis  
• Take part in final general evaluation of the project  
• Make graphic data presentation  
• Write a final evaluation report to GFATM |
| Askar B. Yedilbayev          | PIH – Boston               | • Develop a general strategy of data collection  
• Take part in data analysis  
• Take part in final general evaluation of the project  
• Make graphic data presentation  
• Circulate evaluation results at a high level |
| Sergey P. Mishustin          | TB Services                | • Coordinate data collection within TB Services of Tomsk Oblast  
• Take part in final general evaluation of the project  
• Circulate evaluation results at a high level |
| Evgeny G. Andreev            | Penitentiary system        | • Coordinate data collection within the penitentiary system of Tomsk Oblast  
• Take part in final general evaluation of the project  
• Circulate evaluation results at a high level |
| Alexander S. Chernov         | AIDS-Center                | • Coordinate HIV/AIDS, TB/HIV data collection  
• Take part in final general evaluation of the project  
• Circulate evaluation results at a high level |
| Olga B. Sirotkina            | TB Services                | • Make adjustment to data collection approaches  
• Provide data collection  
• Take part in data analysis |
| Natalia Y. Sidorenko         | Interviewer                | • Provide staff interviewing  
• Write transcripts of interview records |
| Olga V. Revyakina            | Novosibirsk TB Research Institute | • Make adjustment to data collection approaches  
• Take part in data verification  
• Take part in data analysis  
• Take part in final general evaluation of the project  
• Provide data collection on control regions for comparison  
• Circulate evaluation results at a high level |
| Oksana I. Ponomarenko        | PIH – Russia               | • Take part in final general evaluation of the project  
• Circulate evaluation results at a high level |
| Olga S. Kobyakova            | Health Department of Tomsk Oblast | • Coordinate data collection beyond Tomsk Oblast TB services competence  
• Take part in final general evaluation of the project  
• Circulate evaluation results at a high level |
Appendix 2. A Project Evaluation Model

<table>
<thead>
<tr>
<th>Resources</th>
<th>Activities</th>
<th>Activity results (changes in TB services)</th>
<th>Project results (changes in patients)</th>
<th>Effect (reservoir)</th>
</tr>
</thead>
</table>
| • Equipment, drugs, food sets, vehicles  
  • Staff are trained  
  • Protocols, programs, decrees are developed and communicated to providers  
  • Resources are regularly replenished | • Improvement of TB and MDR-TB diagnosis in General Healthcare Services  
  • Improvement of TB and MDR-TB among contacts  
  • Improvement of DST coverage and quality  
  • Monitoring system setup  
  • Data analysis and adjustment of clinical and organizational actions  
  • Improvement of clinical management  
  • Clinical monitoring according to protocols  
  • Improvement of detection and elimination of side effects  
  • Strengthening surgery  
  • Observed treatment administration  
  • Improvement of continuity between services and sectors  
  • Improvement of treatment adherence among all patients  
  • Improvement of treatment adherence among risk groups  
  • In case of failure or refusal of treatment, a smear positive patient is isolated  
  • Latent TB detection among HIV patients  
  • Preventive therapy  
  • TB/HIV treatment | • Clinical and organizational services are set up, supervised, and collaborate  
  • DR-TB patients are timely diagnosed and promptly prescribed with regimen 4 treatment.  
  • Patient flows are divided.  
  • GFATM DR-TB patients receive adequate treatment regimen.  
  • Surgery is timely performed for all GFATM DR-TB patients, if required.  
  • GFATM DR-TB patients are covered with treatment adherence activities.  
  • (in-home therapy, motivation sets, patient search, contracts with patients, consultations by specialists, continuity between services and facilities, etc.) | • Prompt effect of therapy (interim results).  
  • Early cessation of bacillary excretion.  
  • DR-TB is not spread and does not occur in susceptible TB patients.  
  • Increase of successful therapy results in GFATM DR-TB patients | • Decrease of smear positive DR-TB reservoir.  
  • Decrease of DR-TB prevalence.  
  • Decrease of DR-TB incidence.  
  • Decrease of smear positive TB reservoir.  
  • Decrease of TB prevalence.  
  • Decrease of TB incidence  
  • Decrease of TB mortality  
  • HIV patients do not develop TB after preventive therapy  
  • TB/HIV prevalence is stable. |
## Appendix 3. Questionnaire for interview of key persons involved in the program implementation

### Introduction to the respondent

Dear ____________________________

We are conducting a survey among specialists who participated in the implementation of TB and MDR-TB treatment program in Tomsk Oblast. Your participation contributed a lot to the program results. We would like to know your opinion about the project, your attitude to some specific achievements and your recommendations to your colleagues from other regions and countries that increase their efforts to control MDR-TB.

MDR-TB treatment project started in Tomsk Oblast in 2001. However, in 2004-2005, when the Global Fund project started, it resulted in increased resources and activities. Therefore, we request you to keep in mind that the period of 2001-2013 includes 2001-2004 and 2005-2013.

### Let’s start from general questions and background

<table>
<thead>
<tr>
<th>x</th>
<th>Name, position in TB service</th>
</tr>
</thead>
<tbody>
<tr>
<td>x1</td>
<td>Since what time have you been involved in the MDR-TB treatment project? Starting from 2001.</td>
</tr>
<tr>
<td>x2</td>
<td>What were your responsibilities?</td>
</tr>
</tbody>
</table>

### I would like to ask you some questions about your attitude towards the project results

#### 1.1 In your opinion, what were the objectives and key elements of the project in 2001-2004 and 2005-2013?

| 1.15 | Do you remember what you expected from the project in 2001? When the GF arrived, what did you expect from the project? |

#### 1.2 Speaking about the GF project 2005-2013, did the project achieve its goals and objectives? Did it surpass them?

| Please use the following scale to grade overall project from 1-5 |
|---|---|
| 1 – absolutely NOT; 2 – probably yes; 3 – exceeded a lot; 4 – probably no achievements; 5 – definitely achieved; 6 - don’t know |

#### 1.3 How would you grade the project achievements by components on a 5-grade scale?

| go to Annex 1 |

#### 1.4 In your opinion, what components of the project were the most important?

| go to Annex 1 |

#### 1.5 Were there any components that you initially rejected/did not accept/did not believe in/did not want to perform?

| go to Annex 2 |

#### 1.6 Did your attitude change somehow over time? Why?

| go to Annex 2 |

#### 1.7 Was there something in the project that you initially believed in and supported?

| go to Annex 2 |

#### 1.8 Did your attitude change somehow over time? Why?

| go to Annex 2 |

#### 1.9 What did you expect from the project and it happened?

#### 1.10 What was the project outcome that you didn’t expect?

#### 1.11 What did you expect from the project and it didn’t happen? What components were neglected during the project?

### Let’s talk about you

#### 2.1 What are the main reasons of success of the components of the project that you mentioned as successful?

#### 2.2 Do the reasons you’ve mentioned interact? What are the main interactions?

#### 2.3 In what components of the project were you involved?

#### 2.4 Were your tasks clear to you at the beginning?

#### During the project you took part in trainings, gained experience, performed your duties

| Please use the following scale to assess the change: 1 - no gain; 2 – minimal knowledge; 3 – mediate knowledge; 4 – knowledge is above average in other areas; 5 - became a master in the area; 6-don’t know |

#### 2.5 In your opinion, did you obtain knowledge due to the project? In what areas?

| go to Annex 1 |

#### 2.6 In your opinion, did you obtain skills due to the project? In what areas?

| go to Annex 2 |

### Let’s start from general questions and background

#### 2.7 What did you expect from the project and it didn’t happen? What components were neglected during the project?

#### 2.8 What were your responsibilities?

#### 2.9 What were your responsibilities?

#### 2.10 What was the project important?

#### 2.11 In your opinion, what were the achievements and your recommendations to your colleagues from other regions and countries that increase their efforts to control MDR-TB?

#### 2.12 What components were neglected during the project?

#### 2.13 What did you expect from the project and it didn’t happen? What components were neglected during the project?

#### 2.14 What was the project important?

#### 2.15 What did you expect from the project?

#### 2.16 What were your responsibilities?

#### 2.17 What were your responsibilities?

#### 2.18 What were your responsibilities?

#### 2.19 What were your responsibilities?

#### 2.20 What were your responsibilities?

### Let’s talk about you

#### 2.21 What are the main reasons of success of the components of the project that you mentioned as successful?

#### 2.22 Do the reasons you’ve mentioned interact? What are the main interactions?

#### 2.23 In what components of the project were you involved?

#### 2.24 Were your tasks clear to you at the beginning?

#### During the project you took part in trainings, gained experience, performed your duties

| Please use the following scale to assess the change: 1 - no gain; 2 – minimal knowledge; 3 – mediate knowledge; 4 – knowledge is above average in other areas; 5 - became a master in the area; 6-don’t know |

#### 2.25 In your opinion, did you obtain knowledge due to the project? In what areas?

| go to Annex 1 |

#### 2.26 In your opinion, did you obtain skills due to the project? In what areas?

| go to Annex 2 |
| 2.7 | Did you use the same skills and approaches at the beginning of the project as well as you are using them now? |
| 2.8 | If "NO" – Why didn’t you? Was it due to a lack of resources or knowledge or skill or TB service management, etc.? |
| 2.9 | If "YES" – could you describe what changed during the implementation of the project? Was it associated with the project or with Russian TB services orders and change in practice in Russia? |
| 2.10 | Would you have achieved the same if you had sufficient resources? |

3.1 Let’s talk about challenges in the project implementation

| 3.1 | In your opinion and based on your conversations with colleagues, director, PIH members, were you required to achieve targets that were too high for you? |
| 3.2 | Could the overall project be implemented in more effective way? |
| 3.3 | How would you strengthen the project in general (implementation methods, decision making, strengthening or distribution of resources, etc.) and particularly? |
| 3.4 | During 2001-2012 the project experienced decrease of cure rate, high default rate and failure. What were the main reasons, in your opinion? |
| 3.5 | What was your view at the beginning of the project about delivering care to non-adherent patients? |
| 3.6 | Has the project changed your view about what is required to deliver care to non-adherent patients? What is required for non-adherent patients to complete treatment? Should we advocate for them? |
| 3.7 | What was your view initially about DOTS+ treatment for chronic cases and fibrocavernous TB patients? |
| 3.8 | Why were there so many chronic cases in the early 2000s? Did the project help to reduce this number? |
| 3.9 | Has the project changed your view about treatment of chronic cases? Did you personally implement all ideas/activities that you planned? |
| 3.10 | What challenges did you face during the project? |
| 3.11 | How did you overcome the challenges? |
| 3.12 | What was the result of your efforts? Was it effective? What did you manage to do? |
| 3.13 | What did you try to implement and it failed? |
| 3.14 | What additional resources or support would you have required to overcome any challenges? |
| 3.15 | Do you think your sub-program was successful? |
| 3.16 | Why or why not? What barriers did you have that differ from those mentioned above? |

4.1 What would you advise or recommend to your colleagues from different regions

| 4.1 | Do you think it is possible to implement such project in any Russian setting? |
| 4.2 | What could be the basic requirements at the setting? |
| 4.3 | Do you think Russian settings require special approach in implementation of such projects? |
| 4.4 | What exactly do you think is necessary to implement and will give results and impact? |
| 4.5 | What should be implemented on 1st step? |
| 4.6 | What do you think could be implemented later (it is costly, difficult, but will have positive additional result)? |
| 4.7 | What components or approaches do you think are still new and/or controversial for Russian TB doctors? |
| 4.8 | What management decisions/approaches do you think were more effective? |
| 4.9 | What management tools/decisions could be implemented in a different way? |
| 4.10 | What components of Tomsk TB program should be continued and couldn’t be stopped |
| 4.11 | If there was a chance to receive more funding (including MoH funding), what new activities do you think could affect TB epidemic and MDR-TB treatment results? |

5.1 PIH

<p>| 5.1 | What was PIH’s role in the project? |
| 5.2 | How would you rate their participation? |
| 5.3 | What management tools/decisions of PIH as principal recipient could be made in different way? |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5.4</td>
<td>What management tools/decisions of PIH as program consultants or implementers could be made in different way?</td>
</tr>
<tr>
<td>5.5</td>
<td>What did PIH bring to the project and was it really effective?</td>
</tr>
<tr>
<td>5.6</td>
<td>Do you think PIH needs to stay in Tomsk or not?</td>
</tr>
<tr>
<td>5.7</td>
<td>In what activities do you think PIH could be useful for you?</td>
</tr>
</tbody>
</table>
Annex 1.

<table>
<thead>
<tr>
<th>main issues</th>
<th>1.3</th>
<th>1.4</th>
<th>4.4</th>
<th>4.5/4.6</th>
<th>5.1/5.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 – very low; 2 – low; 3 – so so; 4 – good; 5 – very good; 6 – don’t know</td>
<td>1 – not important at all; 2 – not important; 3 – so so; 4 – important; 5 – very important; 6 – don’t know</td>
<td>mark “V”</td>
<td>mark “1”</td>
<td>mark “2”</td>
</tr>
<tr>
<td>1. Improving quality of laboratory control</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2. Early detection of TB in primary care (sub-program)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>3. Drugs supply and management for DR patients</td>
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<tr>
<td>4. Enrollment of all DR-TB patients regardless of patients characteristics</td>
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<tr>
<td>5. Improving quality of clinical management of DR patients (number of drugs, length of treatment, etc.)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>6. Active detection of side effects and management</td>
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<td></td>
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<td>21. OTHER NOT MENTIONED</td>
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### Annex 2.

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<tr>
<td>1. Improving quality of laboratory control</td>
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<td>2. Early detection of TB in primary care (sub-program)</td>
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<td>3. Drugs supply and management for DR patients</td>
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<td>4. Enrollment of all DR-TB patients regardless of patients characteristics</td>
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<tr>
<td>Name</td>
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<tr>
<td>Sergey Mishustin</td>
<td>TB services, head doctor until 2012, head TB specialist</td>
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<tr>
<td>Petr Golubchikov</td>
<td>TB services, deputy head doctor, responsible for treatment activity since 2008</td>
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<td>Irina Prvdina</td>
<td>TB services, Day care hospital, head</td>
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<td>Vera Golubchikova</td>
<td>TB services, head of M&amp;E UNIT, before that – responsible for ambulatory treatment stage, all adherence subprograms</td>
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<td>Alexander Barnashov</td>
<td>TB services, early TB detection subprogram</td>
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<tr>
<td>Lyudmila Maslyanko</td>
<td>TB services, head of ambulatory polyclinic department #2, rural TB program</td>
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<td>Valentina Berezina</td>
<td>TB services, head of ambulatory polyclinic department, treatment at home subprogram, searching patients subprogram</td>
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<tr>
<td>Tatiana Fedotkina</td>
<td>TB services, senior nurse of ambulatory service since 2002</td>
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<tr>
<td>Sergey Yanov</td>
<td>TB services, TB hospital, substance addiction specialist</td>
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<td>Focus group 1 (5 doctors)</td>
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<td>Focus group 2 (8 nurses)</td>
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<td>Tamara Tonkel</td>
<td>Deputy head doctor, responsible for treatment activity until 2008</td>
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<tr>
<td>Yevgeny Andreev</td>
<td>Head of Medical Department, Russian Federal Service of Corrections in Tomsk Oblast</td>
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<tr>
<td>Alexander Isakov</td>
<td>Deputy head of TB hospital, responsible for treatment activities, Russian Federal Service of Corrections in Tomsk Oblast</td>
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<td>Vera Bayerlen</td>
<td>Chair of Tomsk Division of the Russian Red Cross</td>
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<td>Andrey Sasarov</td>
<td>&quot;Tomsk-AntiAIDS&quot; Foundation</td>
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<tr>
<td>Askar Yedilbayev</td>
<td>PIH program director</td>
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<td>Oksana Ponomarenko</td>
<td>Director of PIH Representative Office in Russia</td>
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<tr>
<td>Natalia Zemlyanaya</td>
<td>Coordinator of rural TB programs until 2008, since 2008 – GF project manager in Tomsk</td>
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<td>Alexandra Solovyova</td>
<td>Treatment adherence in the city, TB-HIV program</td>
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<tr>
<td>Nina Polyakova</td>
<td>Coordinator of rural TB program, coordinator of MDR and XDR-TB treatment</td>
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<tr>
<td>Dmitry Taran</td>
<td>Treatment adherence in the city and in rural settings until 2010, monitoring and evaluation of the GF grant</td>
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