Treating Multidrug-Resistant Tuberculosis in Tomsk, Russia

Developing Programs That Address the Linkage between Poverty and Disease

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Tuberculosis (TB) and multidrug-resistant TB (MDR-TB) are diseases of poverty. Because *Mycobacterium tuberculosis* exists predominantly in a social space often defined by poverty and its comorbidities—overcrowded or congregate living conditions, substance dependence or abuse, and lack of access to proper health services, to name a few—the biology of this organism and of TB drug resistance is intimately linked to the social world in which patients live. This association is demonstrated in Russia, where political changes in the 1990s resulted in increased socioeconomic inequality and a breakdown in health services. The effect on TB and MDR-TB is reflected both in terms of a rise in TB and MDR-TB incidence and increased morbidity and mortality associated with the disease. We present the case example of Tomsk Oblast to delineate how poverty contributed to a growing MDR-TB epidemic and increasing socioeconomic barriers to successful care, even when available. The MDR-TB pilot project implemented in Tomsk addressed both programmatic and socioeconomic factors associated with unfavorable outcomes. The result has been a strengthening of the overall TB control program in the region and improved case-holding for the most vulnerable patients. The model of MDR-TB care in Tomsk is applicable for other resource-poor settings facing challenges to TB and MDR-TB control.

Key words: **drug-resistant tuberculosis; MDR-TB; DOTS-Plus; DOTS; poverty; Tomsk; inequality; Russia; Partners In Health; scaleup of MDR-TB treatment**

Introduction

Tuberculosis (TB) is one of the leading infectious killers of adults in the world today. It is estimated that one-third of the world's population, roughly 2 billion people, is infected with *Mycobacterium tuberculosis*. Estimates of mortality range from 2 million to 3 million deaths per year.[1,2] Poor countries bear most of the global TB burden, with 54% of cases occurring in Africa and Asia.[3] In rich countries, TB is predominantly a disease of the poor and marginalized, affecting in particular the homeless and institutionalized, the foreign-born, and those living with human immunodeficiency virus (HIV).[4–7]

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Since the introduction of the first antituberculous drug in the 1950s, physicians and patients have been challenged by the complexities of TB therapy. Early strategies of monotherapy with streptomycin soon proved inadequate because of the mycobacterium's ability to mutate and produce drug-resistant strains. Other antituberculous agents soon followed, allowing for combination therapies, with improved clinical outcomes when administered for prolonged durations. However, high pill burdens and medication toxic effects posed formidable difficulties for patients. Not surprisingly, completion of therapy was the exception rather than the rule. Even worse, irregular therapy allowed selection of drug-resistant strains, further diminishing the chance of cure.

Currently, drug-resistant strains of *M. tuberculosis* have been found in more than 100 countries.[1] A growing body of data confirms that multidrug-resistant TB (MDR-TB) is emerging as an increasingly important cause of TB morbidity and death.[8–16] In the United States, Europe, and Latin America, highly resistant strains of TB have caused explosive institutional outbreaks in hospitals, prisons, and homeless shelters, with high case fatality rates among immunosuppressed people as well as high rates of transmission to other patients, caregivers, and family members.[17–25] A recent nosocomial outbreak of highly drug-resistant TB among HIV-positive patients demonstrated the devastating effect of drug-resistant disease and its predilection for vulnerable populations.[26] In a rural area in KwaZulu Natal, South Africa, 53 HIV-positive patients were infected with MDR-TB that was resistant to almost all effective drugs; this condition is now termed extensively drug-resistant tuberculosis (XDR TB).[27] All but one of these patients died, with a median survival time of merely 16 days from the time of diagnosis. Outbreak investigation confirmed that patients were infected by the XDR-TB strains while hospitalized.

Although nosocomial and institutional outbreaks provide dramatic examples of MDR-TB transmission and resulting morbidity, MDR-TB (including XDR TB) is increasingly a community-acquired disease. Population surveys from many countries have revealed MDR-TB to be present at every site studied.[28,29] In fact, the total global burden of MDR-TB in 2004 was estimated at almost 425,000 new cases per year, or 4.3% of all TB cases, with a yearly incidence of 181,400 cases among previously treated TB patients alone.[30] As can be expected, in settings with substantial MDR-TB, standardized short-course chemotherapy will not result in adequate cure rates.[31–35] Indeed, many drug-resistant patients will fail such regimens and acquire more resistance in the process.[36]

In recent years, there has been a sea change in the international TB community's position on the treatment of MDR-TB in resource-poor settings.[37] In response to the global danger posed by drug-resistant strains of TB, in 1998 the World Health Organization (WHO) and a consortium of international governmental and nongovernmental partners began a series of pilot MDR-TB treatment programs, including one in Tomsk, Russia.[38,39] Termed "DOTS-Plus", these initiatives used a case-management strategy based on the five components of WHO's DOTS (directly observed therapy short-course) strategy, adding laboratory diagnosis of drug resistance and using second-line antituberculosis medications.[40–43] The projects operated under the aegis of a WHO-based Green Light Committee (GLC), which facilitated both technical assistance for projects and the purchase of antibiotics at concessionary prices.[28,44] This expanded strategy fostered a mechanism to identify individual drug-resistant TB strains and treat patients with appropriate second-line TB drugs.[43,45,46] Through these initiatives, the cost of MDR-TB treatment has dropped from an estimated US$130,000 per patient for hospital-based treatment in the United States to less than US$2,500 for community-based approaches in low-income countries.[47–49] Early intervention with appropriate and aggressive second-line drug regimens—requiring 18–24 months of therapy with four to eight medications, including daily injections for at least 6 months—can result in cure rates of more than 75%.[50–54]

As the TB community embarks on global scaleup of MDR-TB treatment,[55] some important questions remain about how programs can adequately address factors that generate MDR-TB in resource-poor settings. Because *M. tuberculosis* exists predominantly in a social space defined by poverty and its comorbidities—for example, overcrowded or congregate living conditions, malnutrition, substance use, and lack of access to proper health services including disease diagnostics and treatment—the biology of this organism and of TB drug resistance is intimately linked to the social world in which patients live. One example of this is the issue of nonadherence to TB treatment and the amplification of drug resistance. Although mainstream literature had attributed nonadherence largely to patient attitudes and beliefs,[56,57] empiric literature has identified important contributory environmental, structural, and operational factors that place adherence to treatment beyond a patient's control.[58] Thus, the existence of selective environmental pressures on *M. tuberculosis*

that cause it to acquire drug resistance—thought to be the result of patients taking anti-TB medications irregularly—are directly linked to broader social, economic, and political determinants that affect a patient's access to appropriate medications and appropriate care.

Perhaps nowhere is this phenomenon more evident than in Russia and the countries of the former Soviet Union, which saw an upsurge of MDR-TB during the post-Soviet period.[32,34–36,59–61] Using the case study of MDR-TB in Tomsk, Russia, we describe how poverty and social instability have shaped the epidemic through contributing to the generation of drug-resistant strains and by weakening health services. We will then discuss a model MDR-TB treatment project that addresses programmatic and socioeconomic factors for poor MDR-TB outcomes and has thus strengthened overall TB control in the region. Finally, we will argue that such models are relevant for other resource-poor settings where both absolute and relative poverty contribute to growing rates of MDR-TB.

TB in Russia

Although Russia is not a poor country by global standards, the social and economic upheaval after the collapse of the Soviet Union resulted in profound wealth disparity and greater poverty among already marginalized populations.[62] The abrupt economic and political transformation in 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 population health was profound, including a sharp rise in mortality, particularly among deaths from cardiovascular diseases, infectious diseases, and injuries.[63–65] Differences in mortality by socioeconomic status (e.g., income, educational level, and type of employment) widened in the 1990s, especially among alcohol-related deaths and those due to infectious causes.[66–70] As social cohesion became increasingly fragmented in Russian society, individuals living in relative poverty became increasingly isolated and unable to access formal and informal resources, including health services and social support.[71–74]

It is in this context that the Russian Federation witnessed the reversal of 30 years of successful TB control.[75–77] Between 1991 and 2001, TB incidence in Russia increased from 34 to 88 per 100,000 population, whereas TB mortality climbed from 8.1 to 19.9.[78,79] TB incidence and prevalence were even higher in the Siberian oblasts of the Russian Federation.[80] In the region of Orel, near Moscow, risk factors for mortality were unemployment and homelessness, highlighting the role of poverty in poor TB outcomes.[81] A drastic rise in petty crimes created ideal conditions for generating a TB epidemic: Overcrowded prisons and pretrial detention centers were crammed with individuals from the poorest stratum of society: the alcoholic, homeless, and mentally ill.[82] TB incidence rates in Russian prisons were as high as 7,000 per 100,000.[83,84] In the 1990s, prisoners made up approximately 25% of all newly diagnosed TB cases in Russia,[61,85] and approximately 30% of newly diagnosed civilian cases had a history of prior imprisonment.[86] Although the prison system may have functioned as an "epidemiological pump," releasing tens of thousands of active TB cases into the civilian population,[32,61,87] the same forces driving the prison epidemic were independently contributing to rising rates of TB in the civilian population.[88,89]

The Specter of MDR-TB

In many ways, poverty and growing inequality—generating a growing pool of vulnerable individuals and contributing to a public health crisis—were at the root of the TB epidemic in Russia.[90] In this setting, Russia not only experienced a dramatic rise in TB incidence but also reported among the highest rates of MDR-TB in the world.[28,32–35,61] Two processes were at play in the expansion of MDR-TB: (1) patients with resistance amplified because of substandard treatment due to insufficient medications, treatment for insufficient periods, and/or treatment with frequent interruptions and poor treatment adherence and (2) primary cases of MDR-TB transmitted from previously infected individuals.

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 6 months of daily treatment. TB services deteriorated because of decreases in public health expenditures. Depletions of first- and second-line TB drugs became increasingly common. Because of costs of inpatient care, resources for TB hospitals diminished, lowering the quality of inpatient care. Sometimes greater emphasis was placed on ambulatory treatment, but without funds to build an appropriate system to deliver it. Adherence enablers, such as nutritional support and transportation vouchers, were curtailed.[91] The poor, unemployed, and disabled patients, who relied on the hospital system for shelter and food especially during the winter months, became more vulnerable to disease and death.[92]

Because of underfunding and overcrowding, the hospitals themselves began to function as additional epidemiological pumps, becoming a locus for primary transmission of MDR-TB. Among patients entering TB treatment in Tomsk in 2000, the primary risk factor for acquiring drug resistance was not nonadherence; rather, it was hospitalization during TB treatment.[93] Because these facilities were more likely to be populated with poor and disadvantaged patients, this population became an easy target for infection with drug-resistant strains. As individuals with active MDR-TB drifted in and out of these congregate settings, drug-resistant strains were subsequently carried into the community.

Faced with medication shortages, breakdown in case detection systems, and a substantial deterioration in social services, the local Russian health care systems were hard pressed in the immediate post-Soviet period to deal with the burgeoning MDR-TB epidemic. They were strongly advised by the WHO, other multilateral organizations, and some international nongovernmental organizations, to adopt the standardized DOTS approach. Although there were some similarities between the Soviet and WHO-recommended approaches to TB treatment, there were also important differences. Similar to practices in the United States and other developed countries,[94] Russian physicians relied on multiple diagnostic strategies instead of solely smear microscopy; they tailored therapy to each individual on the basis of drug susceptibility testing and early indicators of clinical response.[79,95] Also, DOTS promoted purely ambulatory care—an anathema to a system based primarily on inpatient care.[96] Although initially met with resistance among Russian TB physicians and policy makers,[79] DOTS was eventually adopted in some areas, as international pressure and the influx of resources associated with DOTS expansion prevailed. Given high rates of MDR-TB, the DOTS approach alone in Russia contributed to poor outcomes and high mortality, making the need for an integrated program of MDR-TB treatment unquestionable.[32–36,60,61,97,98]

MDR-TB Treatment in Tomsk Oblast: Addressing the Problem

Located in western Siberia, Tomsk Oblast covers an area of 316,900 km^2 (about the size of Poland). Just over 1 million people reside in Tomsk, approximately half of whom live in the capital, Tomsk City; the rest live in rural communities. The annual per capita income in 2001 was US$1,998, with an estimated 26% of the population living below the official poverty line (data were presented in Russian Rubles and converted to U.S. dollars at the average exchange rate for 2001 of 30.14 Rubles/USD).[99] Like other parts of Russia, Tomsk had a predominantly inpatient program of treatment, which suffered after the collapse of the Soviet Union.[100] The British humanitarian organization MERLIN (Medical Emergency Relief International) worked with the Tomsk Oblast TB Services (TOTBS) to implement DOTS starting in 1994. In 1999, the Public Health Research Institute of New York formed a similar DOTS partnership with the Tomsk Penitentiary System (UIN).

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 DOTS might not succeed. Data from the early to mid-1990s showed resistance among new civilian cases to any of the four first-line drugs to be 29%; rates of MDR-TB were 6.5% during the same period.[28,88] 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 anti-TB medications and 13.1% had MDR-TB.[88]

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.[101] 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 3,357 per 100,000, with a mortality rate of 129.9 per 100,000.[102] The percentage of MDR-TB among new cases and retreatment cases was 13.1% and 34.9%, respectively (see TABLES 1 and 2). The DOTS program cure rates for smear-positive patients in Tomsk were between 50% and 60% for new and retreatment patients in both sectors.[101,102]

Because of the strong association between pretreatment drug resistance and treatment failure,[36] a pilot MDR-TB treatment program was initiated in Tomsk as a coordinated civilian–prison effort. The project was started in collaboration between TOTBS, UIN, the Siberian State Medical University, the Open Society Institute, Public Health Research Institute, MERLIN, the Russian Red Cross, Partners In Health (PIH), and the Massachusetts State Laboratory Institute. The project ultimately received funding from the Open Society Institute; the Bill and Melinda Gates Foundation; the Eli Lilly Foundation; and the Global Fund to Fight AIDS, TB, and Malaria, becoming a model global public–private initiative for TB control. The project

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

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

Source: Tomsk Oblast Tuberculosis Services, Tomsk, Russian Federation, July 2005.

TABLE 2. TB incidence, prevalence, and mortality in Tomsk Oblast Penal Sector, 1998–2003

Variable	1998	1999	2000	2001	2002	2003
Holding Section TB case notification/100,000	3, 565	3, 081	3, 388	3, 416	2, 720.2	1, 983.1
Holding Section TB Prevalence/100,000	3, 743.5	2, 830.8	2, 753.5	2, 012.9	2, 550.1	2, 784.8
Prison TB case notification/100,000	4, 042	4, 523	3, 357	3, 008.9	2, 809.8	2, 192.9
Prison TB Prevalence/100,000	21, 581.7	18, 995.3	18, 320.2	16, 469.2	16, 101.0	15, 366.8
TB Mortality/100,000	353.1	383.9	129.9	107.7	0	11.85
% MDR-TB among new cases	28.0	18.6	13.1	15.9	12.2	14.9
% MDR-TB among retreatment cases	54.4	25.0	34.9	77.4	63.6	85.7

Source: Tomsk Oblast Penitentiary Tuberculosis Services, Tomsk, Russian Federation, July 2005.

began in September 2000 and over the past 7 years has built on the existing TB system's infrastructure to improve TB and MDR-TB care.

Enhancement of Program Organization and Function through Treatment of MDR-TB

MDR-TB programs require intensive management, clinical oversight, social support, and data management. Although TOTBS and the UIN had basic infrastructure in place, the arrival of DOTS-Plus required substantial enhancement of the TB Program. 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 DOTS 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. A stakeholders' meeting and subsequent meetings with district administrators solidified commitment at multiple government levels for a comprehensive program, including increased project staffing and funding for vehicles and fuel. Once several DOTS-Plus pilot projects in Russia reported favorable outcomes, national TB policy makers responded. The Russian Ministry of Health and the WHO convened TB working groups, including representatives from government, academe, and multinational and nongovernmental organizations. Drawing from the experiences of Russia's longstanding TB control programs and the DOTS-Plus pilot programs, Ministry of Health efforts culminated in Edict 109 in March 2003, which integrated MDR-TB management into a comprehensive TB control strategy for Russia.[103]

Quality Diagnosis

During the Soviet era, diagnosis of symptomatic TB patients was made using chest radiography, sputum microscopy and culture, and drug sensitivity testing (DST).[95] Much of this process deteriorated in the immediate post-Soviet period. 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, the local laboratories validated their DST

methods and currently perform DST on all patients starting TB treatment.

Direct Observation of Therapy

Treatment of TB in Russia has traditionally been hospital based,[79,96] yet completing 18–24 months of MDR-TB therapy under current inpatient conditions was infeasible 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 DOT for all MDR-TB patients. DOT options had to be flexible: Whereas most presented daily to ambulatory centers (e.g., TB polyclinic, TB day hospital, and rural TB facilities or village clinics), some too sick to travel (e.g., patients with disabilities, comorbidities, and substance abuse problems) received DOT at home. For those living in rural areas, the Russian Red Cross or local non–family members provided DOT. 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 DOT. Eventually, these improvements were expanded to all TB patients and have become standard of care in Tomsk.

Uninterrupted Treatment

In Russia, TB treatment is divided among several ministries. Correctional facilities operate under the aegis of the federal Ministry of Justice, whereas the civilian TB services fall under the local health administration in each of the Russian Federation's 89 administrative units. Lack of coordination of patient transfer between ministries contributes to treatment interruption. In 1999 and 2000 in Tomsk, only 53.9% and 58.8%, respectively, of patients released from prison with active TB reported to the civilian health authorities to continue treatment.[101,102] As part of the MDR-TB treatment program, a centralized physician committee was formed to ensure uniformity of treatment regimens and uninterrupted treatment between penal and civilian facilities. For both DOTS and DOTS-Plus patients, civilian and prison TB services implemented a system to share important information from medical records; sometimes released prisoners are transported directly to civilian TB services.

Guaranteed Quality Drug Supply

In many parts of Russia, first- and second-line medications are procured without federal and oblast-level coordination. When DOTS-Plus began in Tomsk, a combined central pharmacy, created when DOTS began, was strengthened to manage second-line and side-effect medications for both the civilian and penal systems. Quality-assured second-line medications were procured through the GLC mechanism, and a data base was established in the central pharmacy to manage their use, further uniting the civilian and penal TB treatment programs and ensuring sufficient drug stock upon transfer of patients between systems.

Monitoring and Evaluation

In 2000, TOTBS faced problems with monitoring and evaluation. Through DOTS-Plus, the monitoring of patients with drug-resistant TB improved substantially. Standardized reporting forms and effective data management have achieved timely and accurate data on both DOT and DOTS-Plus patients. In addition to data collection, on-site monitoring was also improved through training of supervisors on monitoring and evaluation practices and increased resources to fund rayon visits. Regular visits from the GLC—part of program monitoring and technical assistance promotion—have further assessed both DOTS and DOTS-Plus activities. Because continued GLC approval is contingent upon adequate performance, feedback from these site visits has provided external pressure to maintain and/or improve services.

Toward a More Patient-Centered Approach to Care: MDR-TB Further Exposes the Fault Lines

The MDR-TB pilot project has had a positive effect on TB control (see TABLES 1 and 2). DOTS treatment success rates have gone up from 50%–60% in 2000 to 80.6% in 2006.[101,102,104] Patients with MDR-TB receive individualized treatment; among the first 244 patients enrolled in the DOTS-Plus program, 77.0% were cured, 11.5% defaulted, 6.6% failed, and 4.9% died.[105] These outcomes are similar to those documented in other recent MDR-TB cohorts.[46,49,106–108]

However, closer examination of this first cohort of MDR-TB patients reveals that the fundamental association between TB and poverty remains a persistent challenge to successful TB control.[31,34,109] 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. Bilateral cavitary disease—a proxy for both severity and chronicity of illness—and alcohol use during treatment were found to be statistically significantly associated with poor treatment outcome.

Preliminary analysis of the second cohort of 391 patients, treated from September 2002 through October 2004, highlights challenges to scaling up MDR-TB treatment in vulnerable populations. This group had higher levels of substance dependence/abuse, and outcomes had higher default rates and lower cure rates.[110] Defaulters were predominantly young, unemployed men. They often presented with advanced disease, largely because of marginalization from health services and severe substance abuse/dependence. Frequent institutionalization—through previous incarceration and prior inpatient TB treatments—tended to interrupt routine life and prevent these patients from establishing stable socioeconomic roles. Upon returning to their home environments after release from hospitals and prisons, these group members found that their intimate social networks, ability to find work, and aspirations for the future were profoundly limited.

Recently, TOTBS joined forces with PIH to pioneer a program for patients who have not been able to adhere to TB therapy. Based on PIH's experience with ambulatory care treatment *accompanateurs* in Boston and Haiti,[111,112] this program—named "Sputnik"—is aimed at overcoming some of the social and economic factors that undermine the ability to adhere to DOTS or DOTS-Plus. Daily, supervised treatment is provided at the time and place of the patient's choosing. Nurses are responsible for only five to seven patients, with the aim of creating a sense of community with patients and their close family and associates. In the 8 months since the program started, 15 MDR-TB patients have enrolled in Sputnik. Preliminary outcomes show that although one patient dropped out of the program, 14 (93%) previously defaulting patients remained in treatment. The overall adherence to therapy for this group has increased from 56% to 88%.[113]

Discussion

The MDR-TB epidemic in Russia illustrates the fundamental link between poverty, lack of access to appropriate care, and the emergence of MDR-TB among those most at risk for infection and disease. The epidemic has demonstrated that even well-developed TB control programs are vulnerable at times of social dissonance and dislocation. More importantly, it has clearly shown the danger of leaving unfettered the specter of MDR-TB.

Given that MDR-TB represents one of the most extreme products of poorly controlled TB epidemics in settings of inequality and relative poverty, the Tomsk DOTS-Plus program—which addressed programmatic and socioeconomic barriers to effective MDR-TB care—improved not only MDR-TB management but also overall TB care. Although the model for MDR-TB treatment in Tomsk is not perfect, it provides some important lessons. First, it demonstrates the false dichotomy inherent in the programmatic separation of drug-resistant and drug-susceptible TB in high-burden areas. Although treating drug-resistant disease is more expensive than treating drug-susceptible TB, ignoring the former can profoundly affect TB epidemiology. Both approaches are equally important parts of an integrated TB program aimed at reducing the burden of TB and preventing unnecessary mortality.

Second, MDR-TB treatment does not divert money from overall TB control, as some suggest.[114,115] On the contrary, integrating MDR-TB treatment brought more resources to bear on the problem of TB in Tomsk and encouraged a renewed political commitment to TB treatment overall. In fact, the complexity of MDR-TB management forced the TB services to strengthen the capacity of diagnostic services, clinical management, and case management. It also necessitated forming interministry partnerships and partnership with global civil society. In areas of high-burden drug-resistant TB, this capacity building is now a necessity for effective global TB control.

Third, integrating effective MDR-TB treatment into the DOTS program is a relevant model for sites with fewer resources than Russia. In most resource-poor settings, steep gradients of inequality have created ideal environments for generating MDR-TB and XDR TB: partial or intermittent access to first- and second-line TB drugs; weak TB infrastructure; unstable populations characterized by migration; overcrowded congregate settings such as mines, prisons, and hospitals; and high rates of comorbid conditions, such as HIV, substance use, and mental health disorders. Effective TB control in such settings requires a fundamental restructuring of TB services. TB programs must innovate beyond current models of care and specifically address the effect of poverty on TB and MDR-TB at both programmatic and individual levels. Studies in the United States have shown that financial incentives can have a huge bearing on patients' adherence to TB treatment.[116,117] The Tomsk program addresses specific barriers, such as poor nutrition, lack of transportation, adverse effects, and social isolation, to facilitate TB case holding. In so doing, this program can serve as a model in an important paradigm shift that must take place for TB control to succeed: providers and program planners—not patients—must assume primary responsibility for ensuring treatment

adherence and successful delivery of care to vulnerable sectors of the population.

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