Programmatic management of multidrug-resistant tuberculosis: models from three countries


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with referral to district hospitals for complicated care. Community health workers (CHWs), known as *promotores*, were recognized by the Ministry of Health, but were neither organized nor paid. TB care was provided at the health centre level using DOTS. Smear microscopy was available at health centers, cultures were performed at district laboratories and first-line drug susceptibility testing (DST) could be performed at the central National Reference Laboratory. First-line anti-tuberculosis drugs were available free of charge and second-line medications were available on the free market. Although political will for DOTS was high, there was little recognition of MDR-TB or interest in treating such cases.10

**INITIAL IMPLEMENTATION.** In 1995, 12 cases of MDR-TB were identified in a slum in northern Lima after an American priest working there died of the disease. In 1996, PIH and its partners began to treat 10 of these patients using ambulatory (i.e., in health centers) and community-based care (i.e., directly observed treatment [DOT] in patients’ homes by trained and paid CHWs). Individualized regimens were tailored to drug resistance data and treatment history.11 The treatment team consisted of Ministry of Health (MOH) providers, US-based technical advisors (two of whom lived in Lima during the initial implementation), and a community-based team employed by the NGO’s sister organization, Socios En Salud (SES). The Massachusetts State Laboratory Institute (MSLI) provided laboratory services. Drugs were procured privately through a US hospital. Initial political support in Peru was limited, but local MOH providers were directly involved in patient care. All patients received free medication and nutritional and transportation support. The program scaled up to 75 patients from early morning until evening, including meals for patients. Social support and incentives were an inherent component of Russian TB services.16 The prison health care system functioned largely apart from the civilian health sector.17 For both systems, smear microscopy, culture and first-line DST were widely available throughout the oblast, and both cultures and first-line DST could be performed at central facilities. First-line TB drugs were available free of charge, while second-line medications were available on the free market. At the national level, political will was strongest within the prison system (Ministry of Justice [MOJ]), while collaboration was strong at the oblast level in both civilian and prison sectors.

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**Initial implementation.** In the late 1990s, high rates of MDR-TB were described in the former Soviet
Union, particularly among prisoners. Tomsk houses a large TB prison, and an alarming number of MDR-TB cases were noted. The Russian MOJ requested assistance from PIH, and in 1998, the Open Society Institute (OSI), PIH, Tomsk Oblast Tuberculosis Services (TOTBS), the MOJ, and the Public Health Research Institute (PHRI) initiated a program in Tomsk Oblast to treat prisoners with MDR-TB. Starting with 38 patients, individualized regimens tailored to drug resistance data and treatment history were administered under strict DOT. The treatment team consisted of MOJ providers at the prison and four US-based physician advisors. In addition to receiving medications free of charge, all patients received additional protein rations throughout treatment. MDR-TB patients were housed separately from those with pan-susceptible disease. The MSLI assisted the Russian laboratory system in instituting external quality assurance for DST. Drugs were procured in the United States, registered in Russia and donated to the TOTBS. Political will remained strong in the oblast.

PROGRAM EVOLUTION. Four months after initiation of the prison-based program, treatment was quickly expanded to the civilian sector. The civilian team of TOTBS physicians collaborated closely with MOJ physicians and US collaborators. Civilian patients were initially treated as in-patients. However, as the TB hospital filled, stable patients were transitioned to ambulatory treatment sites, with provision of nutritional and socio-economic support by the Red Cross. In more remote regions, treatment was given at TB dispensaries or at home by fieldshers. In the first year of the program, 244 patients were enrolled for MDR-TB treatment.

By 2004, the project had achieved coverage throughout Tomsk Oblast. To date, more than 1700 patients have received MDR-TB treatment, and MDR-TB and TB incidence have declined in the oblast. Care is provided by Russian providers in prisons, hospitals, ambulatory sites and at home. The Tomsk laboratory system is used for DST. Drugs are obtained through the GLC and managed at a central pharmacy in Tomsk. Intensive social support for patients is provided through a program called ‘Sputnik’, which identifies patients at greatest risk for default and provides them with home-based DOT and nutritional and transportation support. The Tomsk TB Alcoholic Working Group was also established to employ evidence-based strategies to reduce the impact of alcohol consumption on TB control. Political support has deepened locally and at the national level; TOTBS and PIH have worked with the Russian Medical Academies to develop national norms for management of MDR-TB (Prikaz 109). Funding for the first 12 months of the program (US$2.2 million) was provided by the OSI. Ongoing funds have come from the Bill & Melinda Gates Foundation, the World Bank, the Eli Lilly Foundation and the Global Fund.

Lesotho

BASELINE HEALTH SYSTEM. In 2006, primary health care in Lesotho was provided by nurses and nursing assistants at health centers. Due to extreme health worker shortages and a national human immunodeficiency virus (HIV) seroprevalence of 24%, most health centers were non-functional. Despite the NTP policy of universal TB treatment at health centers, very few patients were diagnosed or treated for TB. TB care was largely provided at district hospitals using facility-based DOTS, and complicated patients were referred to the national hospital in Maseru. CHWs worked with health centers, but most were not providing care and none were paid. Smear microscopy was only available at the central laboratory and cultures and DST were not available in the country. First-line drugs were provided free of charge, and both aminoglycosides and fluoroquinolones were available on the open market. Political will was strong, but the MOH lacked the staff and funding to manage TB adequately. Further complicating TB care were the high rates of HIV co-infection in TB patients, estimated to be 70–90%.

INITIAL IMPLEMENTATION. PIH began working in Lesotho in February 2006, assisting in HIV prevention and treatment scale-up. In 2007, following an outbreak of extensively drug-resistant TB (XDR-TB) in neighboring KwaZulu-Natal, a small survey conducted with the support of the MSLI documented several cases of MDR-TB in Lesotho. In 2007, a centralized MDR-TB treatment program was established by PIH and the NTP. Ten patients were enrolled in a hospital-based treatment program after a local health facility was equipped with proper infection control. Patients were treated with individualized regimens and rapidly initiated on antiretroviral treatment (ART) if they were HIV-positive. The program was staffed by a local physician, two US physicians, and a team of MOH nurses and paid CHWs from both the HIV and the TB programs. Patients were given nutritional support. Culture and DST were performed in South Africa, while the Foundation for Innovative and New Diagnostics (FIND) started improving the laboratory at the central hospital in Maseru. Drugs were procured from the GLC and stored in a central pharmacy in Maseru. Political will remained high, with the MOH actively engaged on all levels. In the first year of implementation, 76 patients were enrolled for treatment.

PROGRAM EVOLUTION. The program was formally assumed by the MOH in 2009. By 2010, the program was decentralized into all 10 health districts in Lesotho; the project has enrolled 300 patients to date. Individualized regimens and rapid initiation of ART...
remain the common treating principles. Default is less than 5%, but given the late diagnoses and concomitant HIV, treatment success is about 60%. Patients are initially stabilized in the TB hospital and rapidly discharged home for ongoing care from paid CHWs. For patients from remote areas, temporary housing is provided in Maseru. Patients receive nutritional, housing and transportation support. Care is still provided by PIH and MOH physicians and nurses from both the TB and the HIV programs, including seven local physicians. Additional MOH CHWs have been recruited, and it is now the norm for all CHWs in Lesotho to be paid. The improved laboratory was completed and functioning within 8 months, and now provides on-site culture, Mycobacterial Growth Indicator Tube-based DST and rapid rifampin testing. Drugs are procured through the GLC and stored in the central Maseru pharmacy. Political will remains strong. Initial funding for the project was provided by the OSI for a total of US$3 million for the first 3 years, including the costs of building the laboratory and the in-patient facility. Ongoing funding comes through the Global Fund.

Theme analysis

The following six overarching themes emerged in all three settings and are compared across the sites in this section: 1) importance of baseline assessments, 2) early identification of key collaborators, 3) identification of initial locus of care, 4) minimization of patient-incurred costs, 5) targeted interventions for vulnerable populations and 6) importance of technical assistance and funding.

1 Importance of baseline qualitative assessments

All sites carried out baseline and ongoing qualitative assessments to determine needs and adaptations required for program improvements. In each site, the baseline and ongoing assessments were performed by medical anthropologists with expertise in MDR-TB management. Initial assessments included a rapid health systems survey performed in parallel with participant observation, key informant interviewing and focus group discussions. Once the baseline assessments were complete, ongoing participant observation, interviews and focus groups were done in patient, policy and program settings. Explanatory models of care and cultural factors related to care were also explored.

2 Early identification of key collaborators and personnel

All three sites identified the MOH and public sector programs under the NTP as necessary collaborators. The nature of these MOH collaborations varied by site. Early collaboration was complicated in Peru, largely because MDR-TB treatment was not accepted internationally. Once the program had gained international recognition, national MOH leadership assumed responsibility for programmatic scale-up. In Tomsk, strong collaborators were involved at the oblast level, but national sanction by the Russian MOH and MOJ was also required. Once the project had demonstrated success, PIH actively fostered collaboration around training and policy development with leaders in the Russian Medical Academies. In Lesotho, the MOH was involved in the program planning from the beginning. MOH support came largely in an advisory role, given the limited human and financial resources. As each program evolved, the MOH assumed primary programmatic and responsibility.

Each program also identified other key collaborators, including laboratory networks and drug procurement groups. Each site had different challenges. In Peru, expanded culture capacity and DST using rapid methods were introduced. Russia had a strong laboratory infrastructure at the start of the program, and external support confirmed the validity of DST methods being used by local laboratories. Lesotho had a central laboratory that was only capable of performing smear microscopy. With the collaboration of FIND, smear microscopy resources were expanded, and culture capacity and rapid DST were introduced. In all three sites, technical assistance included help to implement quality assurance and quality control procedures. Drug procurement also varied in the three settings: in Peru, drugs were originally obtained from a US hospital; the program then transitioned to GLC procurement with a central Lima pharmacy. Tomsk followed the same model, but also required central registration of medications. Lesotho was able to benefit from the GLC at program initiation.

In all sites, links with other NGOs (e.g., community health organizations, the Red Cross, the Clinton Foundation) were crucial in maximizing resources and avoiding duplication of efforts. Other key collaborators depended on the setting. In Peru, laboratory and NTP directors needed to work together to develop a rational policy for DST testing. In Russia, collaboration between civilian and prison sector providers ensured standardized medical management and coordination of care for patients moving between sectors. In Lesotho, given the high rates of HIV, close coordination was needed between the HIV and TB programs.

3 Identification of initial locus of care

PIH has advocated for the use of an ‘accompaniment’ model, i.e., medical, social, and economic support delivered by paid CHWs. While this model was used in each site, the primary locus of care varied greatly. In Peru, the program started with a strong community-based component. All patients initiated and received most of their treatment in their homes. Local youth working in a community health program were readily trained to accompany MDR-TB patients.
through the end of their treatment. This remains the case in Peru currently. In Tomsk, patients routinely received treatment as in-patients until injectable treatment was discontinued. Community-based care with CHWs is reserved for the most at-risk individuals via the Sputnik program. Lesotho developed a combined community and hospital program. Most patients are so critically ill they require hospitalization for treatment initiation. Most are rapidly discharged and receive ongoing treatment supported by CHWs in their homes or in the community housing supported by the project.

4 Minimization of patient-incurred costs

Multiple potential patient-incurred costs were identified in each site. These included costs related to diagnosis, medications for MDR-TB treatment and side effect management, transportation, work disruption, nutritional needs and housing. Programs worked to minimize these costs in different ways. In all three sites, patients received their medications for TB and side effects free of charge. Patients were also given access to improved diagnostic modalities free of charge in each site. Other potential patient-incurred costs were managed differently at each site. In Peru, nutritional support was provided via popular kitchens (comedores), where patients could have two meals a day free of charge. For patients needing to travel to referral centers, money was given during the first year of treatment on a trip-by-trip basis. In Peru, housing was improved for families where ongoing household transmission was suspected due to overcrowded living conditions. In Tomsk, patients received nutritional support and daily transport costs to ambulatory sites. In Lesotho, patients were given monthly food packages for the family during the first 6 months of treatment, which were continued if the patients began to lose weight. Program vehicles were used for patient transportation throughout treatment. In both Peru and Lesotho, community housing was provided for patients from remote regions. All three sites had flexible DOT hours to allow patients to continue to work.

5 Targeted interventions for vulnerable populations

Each site identified vulnerable populations at increased risk of contracting MDR-TB or doing poorly once infected. All three sites identified populations living in poverty as vulnerable to MDR-TB. In Peru, strong family clustering of the disease was noted and contact monitoring was crucial. In Tomsk, prisoners and patients with substance abuse issues were found to be vulnerable and were actively supported. In Lesotho, HIV patients and mine workers were identified as vulnerable populations. Universal screening and male outreach initiatives were established to address the needs of these groups.

6 Importance of technical assistance and funding

Each program required initial financial support and long-term technical assistance. In Peru, MDR-TB treatment was not available, and global recommendations on MDR-TB management did not exist. Intensive technical assistance was thus provided, and experts remained heavily engaged in the first 6 years of the program. The initial US$1.7 million were provided by private donations. In Russia, technical assistance was intense during the first year of the program, but as more Russian providers became trained, assistance was provided on a quarterly basis. The initial US$2.2 million were provided by the OSI. In Lesotho, ongoing technical assistance was provided over a 2-year period, then reduced to an every-other-month basis. The initial US$3 million were provided by the OSI. All programs now have local leadership, and PIH provides ongoing technical assistance as needed. All three now receive the bulk of their funding from the Global Fund and their own NTPs (Table 2).

DISCUSSION

This article is a qualitative, operational analysis of three programs providing programmatic MDR-TB treatment. Rigorous qualitative methods were employed to provide setting/program analyses and a thematic analysis of overarching themes. The programs operate in vastly different geographic, cultural, economic, epidemiologic and health care settings, and all managed to implement successful MDR-TB programs. Six thematic areas emphasize 1) the importance of baselines assessments; 2) identification of key collaborators, including the MOH, laboratory and procurement networks, while allowing for collaboration with organizations relevant to the affected populations in each area; 3) identification of a primary locus of care, a component of which is community based; 4) minimization of patient-incurred costs by providing medications and diagnostics free of charge, as well as support for housing, transport and food; 5) identification of and focused interventions with vulnerable populations such as family clusters, prisoners, substance users, HIV-positive persons and mine workers; and 6) provision of initial external technical and financial assistance (in the US$2–3 million range) while transitioning to local leadership and funding from the Global Fund and MOH.

Ongoing costs and technical assistance for each of these projects are important areas of analysis. A cost-effectiveness analysis of these projects is forthcoming and beyond the scope of this article. It is believed that a substantial proportion of initial costs went into set-up and infrastructure building. Anecdotally, costs for medications have decreased significantly from Peru to Lesotho. Only Peru and Tomsk receive funding from their NTPs, and all three sites rely heavily on funding from the Global Fund. How
Table 2  Summary of key program components

<table>
<thead>
<tr>
<th>Variable</th>
<th>Peru</th>
<th>Tomsk</th>
<th>Lesotho</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial phase patients</td>
<td>75</td>
<td>244</td>
<td>76</td>
</tr>
<tr>
<td>Initial phase funding source</td>
<td>Private donors</td>
<td>OSI</td>
<td>OSI</td>
</tr>
<tr>
<td>Initial phase costs</td>
<td>US$1.7 million</td>
<td>US$2.2 million</td>
<td>US$3 million</td>
</tr>
<tr>
<td>Scale-up phase patients</td>
<td>15 000</td>
<td>1708</td>
<td>300</td>
</tr>
<tr>
<td>Year responsibility assumed by MOH</td>
<td>2000</td>
<td>2004</td>
<td>2009</td>
</tr>
<tr>
<td>Scale-up phase funding sources</td>
<td>Bill &amp; Melinda Gates Foundation, NTP</td>
<td>Bill &amp; Melinda Gates Foundation, Eli Lilly Foundation, World Bank, the Global Fund, NTP</td>
<td>The Global Fund</td>
</tr>
<tr>
<td>Laboratory evolution</td>
<td>Increased culture capacity, established second-line DST, established molecular methods</td>
<td>Quality assurance, improvements in molecular methods</td>
<td>Increased smear capacity, established culture capacity, established first-line DST, established molecular methods</td>
</tr>
<tr>
<td>Procurement evolution</td>
<td>Private sources to full GLC</td>
<td>Private sources to full GLC</td>
<td>GLC</td>
</tr>
<tr>
<td>Baseline evaluation staff</td>
<td>3 anthropologists</td>
<td>1 anthropologist</td>
<td>1 anthropologist</td>
</tr>
<tr>
<td>Initial locus of care</td>
<td>Community</td>
<td>Prison/hospital</td>
<td>Combined hospital/community</td>
</tr>
<tr>
<td>Vulnerable populations</td>
<td>Poor, family clusters</td>
<td>Poor, prisoners, substance users</td>
<td>Poor, HIV-positive patients, mine workers</td>
</tr>
<tr>
<td>Methods to reduce patient-incurred costs</td>
<td>Free TB medications, free adverse effects medications, nutritional assistance, housing assistance, transportation support</td>
<td>Free TB medications, free adverse effects medications, nutritional assistance, transportation support</td>
<td>Free TB medications, free adverse effects medications, nutritional assistance, housing assistance, transportation support</td>
</tr>
<tr>
<td>Key collaborators</td>
<td>MOH, community-based organizations, NTP</td>
<td>MOH, MOJ, NTP, TOTBS, prison advocacy groups, alcohol treatment and support groups</td>
<td>MOH, NTP, HIV program, mine workers groups</td>
</tr>
<tr>
<td>On-going funding sources</td>
<td>The Global Fund</td>
<td>Eli Lilly Foundation, the Global Fund</td>
<td>The Global Fund</td>
</tr>
</tbody>
</table>

OSI = Open Society Institute; MOH = Ministry of Health; Global Fund = Global Fund to Fight AIDS, Tuberculosis and Malaria; NTP = National TB Control Program; DST = drug susceptibility testing; GLC = Green Light Committee; HIV = human immunodeficiency virus; TB = tuberculosis; MOJ = Ministry of Justice; TOTBS = Tomsk Oblast Tuberculosis Services.

costs will be controlled and assumed by NTPs is an important and unanswered question in programmatic management of MDR-TB.

The study has some notable limitations. Data were collected at different periods of time by different observers. Although the data were verified by several members of the team, historical as well as inter-observer bias may have occurred. The three program sites represent a wide array of experiences but these may not be generalizable to all global settings.

Many countries face enormous challenges in the implementation and scale-up of MDR-TB treatment programs, including high burdens of MDR-TB—such as China, India and the former Soviet Union—or a relative lack of existing infrastructure and convergence of HIV and TB epidemics, as is the case with many countries in sub-Saharan Africa. Our analysis suggests that efforts to understand the local context and to design site-specific strategies related to the six themes will aid in the implementation and expansion of national MDR-TB treatment programs.

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References

6 Herce M E, Chapman J A, Castro A, Garcia-Salyano G, Khoshnood K. Role for community health promoters in tuber-
CONTEXTE : La tuberculose multirésistante (TB-MDR) constitue un problème majeur de santé dans le monde ; toutefois, la mise en œuvre du traitement dans les programmes est parfois défi ciente.

MÉTHODES : Cet article décrit les modèles de traitement de la TB-MDR dans trois pays, le Pérou, la Russie et le Lesotho, en utilisant des données qualitatives recueillies au cours d’une période de 13 ans.

RÉSULTATS : Une analyse du programme est développée pour chaque pays en se focalisant sur les soins médicaux de base, la mise en œuvre initiale et l’évolution du programme. Une analyse des modèles a révélé six thèmes dominants communs aux trois programmes : 1) l’importance des évaluations de base ; 2) l’identification précoce des collaborateurs-clé ; 3) l’identification du lieu de soins initial ; 4) la minimisation des coûts encourus par le patient ; 5) le ciblage des interventions sur les populations vulnérables ; et 6) l’importance de l’assistance technique et du financement. Les caractères communs et les différences par site ont été analysés dans chacun de ces secteurs.

CONCLUSIONS : Nous recommandons que tous les programmes garantissant le traitement de la TB-MDR impliquent ces six thèmes au cours de l’élaboration et de la mise en œuvre du programme.