

Joint tuberculosis control programme review mission to the Republic of Moldova



Consolidated report by
Dr. Maya Kavtaradze and Dr. Silviu Ciobanu

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ABSTRACT

The WHO Regional Office for Europe organized a comprehensive national tuberculosis programme (NTP) review mission in the Republic of Moldova on 7–11 September and 22–29 November 2009. The review focused on achievements and issues in the treatment of tuberculosis (TB) based on the WHO Stop TB Strategy components, including political commitment, case detection and diagnosis, directly observed treatment, drug supply, monitoring and evaluation. A separate review focused on the management of HIV-TB coinfection in the context of multidrug resistance, health system strengthening, empowerment of TB patients, civil society engagement and cross-sector cooperation between various health care providers, including the prison system and the Transnistria region. The structure of TB services in the health system was investigated in detail, alongside a thorough analysis of the epidemiological situation. For each component, strengths and remaining gaps were identified, and relevant and specific areas for action suggested. The review's conclusions and recommendations pave the way for the development of the new NTP of 2011–2015.

KEYWORDS

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EXECUTIVE SUMMARY

TB control in the Republic of Moldova has benefited from national political support and attention. Collaboration and considerable financial and technical support have been provided by international agencies. In general, since the adoption of the DOTS (directly observed treatment, short-course) strategy in 2001, the NTP team has managed the programme commendably and skilfully, developing strategies and guidelines for TB management, securing procurement and a distribution system for first-line and now also second-line TB drugs, training staff, and establishing a system for case detection and case management as a basis for further expansion. The challenges ahead – predominantly related to multidrug-resistant TB (MDR-TB) control – are great indeed, because of the high prevalence of MDR-TB among both new and retreatment cases. Nevertheless, considerable achievements and valuable experience have been gained, indicating that the NTP team is very capable and well prepared to meet the future challenges.

The Republic of Moldova ranks 19th among the 27 countries with the highest levels of MDR-TB in the world.¹ A national drug resistance survey in 2006 found MDR-TB in 19% of new cases and 51% of previously treated cases. An estimated 2200 MDR-TB cases arise in the country each year, of which 1700 are sputum smear-positive. In addition to these incident cases, the country probably has thousands of patients with MDR-TB from earlier years. Until their MDR-TB is diagnosed and appropriately treated, these 2200 incident (and the additional prevalent) cases continue to spread MDR-TB. In 2008, the country also detected 25 cases of extensively drug-resistant TB (XDR-TB).

The NTP has made major progress in enhancing the detection of MDR-TB. Primary health care (PHC) doctors have been trained to identify TB suspects and to refer them to one of the country's 57 microscopy laboratories to obtain sputum. Current policy recommends that culture and drug susceptibility testing (DST) be performed in addition to smear microscopy. In 2008, the Republic of Moldova's well-functioning laboratory network detected 1048 cases of MDR-TB, which represents 48% of the estimated number of MDR-TB cases arising that year.

The NTP has also made progress in treating MDR-TB, successfully securing three TB awards from the Global Fund to Fight AIDS, TB and Malaria (TGF) that have helped to finance the Green Light Committee-approved project in the country. The Republic of

¹ Global tuberculosis control: epidemiology, strategy, financing: WHO report 2009 (WHO global TB control report 2009). Geneva, World Health Organization, 2009 (http://www.who.int/tb/publications/global_report/2009/en/, accessed 16 November 2011).

Moldova's programmatic management of drug-resistant TB (PMDT) initiative enrolled 522 patients in 2008, which represents 50% of the 1048 MDR-TB cases detected (see Table 6). With the aim of offering universal access to MDR-TB diagnosis and treatment, the NTP plans to use TGF Round 8 funds to enrol in the region of 700 patients per year (approximately one-third of the estimated annual incident cases). The PMDT initiative is functioning as an integral part of the NTP.

Today, the Republic of Moldova faces both serious challenges and important opportunities. Detecting 48% of the estimated incident cases and enrolling 50% of those that were detected means that the PMDT initiative effectively treated only one-quarter of the national burden of 2200 MDR-TB cases that arose in 2008. The country's challenge is to detect and treat the other three-quarters of patients (1678 MDR-TB cases arising each year), so that they do not spread these deadly strains or die of MDR-TB. The detection of TB cases in general is difficult; WHO estimates that one-third of the most infectious cases go undetected each year. In addition, among those who begin treatment, high levels of default and failure prevent the NTP from achieving treatment success.

Nevertheless, with robust leadership and vision, the Republic of Moldova has built a strong foundation to be able to take advantage of some key opportunities in TB control. One such opportunity is the implementation of a new laboratory technology (rapid molecular-based testing) that shortens the time taken to detect MDR-TB from months to days. Another is a powerful, case-based TB information system to guide and evaluate programme improvements, and to monitor trends in the MDR-TB epidemic. The following recommendations are intended to support the NTP in maximizing opportunities to strengthen its ability to protect the public from the threat of MDR-TB.

KEY RECOMMENDATIONS BY STOP TB STRATEGY COMPONENT

1. Pursue high-quality DOTS expansion and enhancement

1a. Political commitment with increased and sustained funding should be secured in order to:

- strengthen high-level coordination and governance mechanisms to oversee TB control in the Republic of Moldova;
- review the financing, oversight and accountability mandates of key actors in TB control, with a view to reducing fragmentation and dealing more successfully with the multifaceted nature of TB;
- safeguard all TB-related services from cuts related to the economic crisis;
- review options for a higher level of influencing and prioritization of TB in the health care system, including engagement of civil society organizations.

1b. Case detection needs to be enhanced through quality-assured bacteriology by:

- improving the country's detection of smear-positive cases, identifying and addressing system barriers to TB diagnosis and notification;
- implementing rapid laboratory methods to detect drug resistance rapidly and confirm *Mycobacterium tuberculosis* countrywide.

1c. Treatment should be standardized with supervision and patient support to:

- diminish defaulting through the development of patient-centred approaches;
- ensure treatment supervision for all doses of TB medicines.

1d. An effective drug supply and management system needs to be established and maintained, including the introduction of child-friendly TB drug formulations.

1e. Monitoring and evaluation systems and impact measurement should be improved by:

- fully utilizing individual case-based TB surveillance information system (SIME-TB) data;
- employing a supervision tool to assess and improve NTP performance at the national and district levels.

2. Address MDR-TB, TB/HIV coinfection and other challenges

2a. MDR-TB prevention and control need to be enhanced by:

- developing a national MDR-TB plan to ensure rapid, successful and sustainable expansion to universal access to MDR-TB diagnosis, treatment and care;
- increasing MDR-TB case detection, and monitoring and increasing the proportion of new and previously treated patients who have culture and DST performed at the start of treatment;
- creating ambulatory options for MDR-TB treatment, with patient-centred support – this is likely to improve enrolment and treatment success, as well as diminishing the risk of MDR-TB spreading in TB hospitals.

2b. Action on TB/HIV coinfection should be improved by:

- ensuring that TB and HIV programme databases are consistent;
- considering the infection control situation and the high risks of nosocomial transmission for HIV-positive patients;
- enlisting nongovernmental organizations (NGOs) working on HIV and TB among vulnerable groups to conduct intensified case detection and follow-up of TB/HIV treatment.

3. Contribute to health system strengthening

- Policies need to be developed and implemented to move TB treatment from hospitals to ambulatory settings, and redirect the resources accordingly.
- Re-introduction of financial incentives for early detection/successful treatment at the PHC level could be reconsidered, as well as a review of options for complementing the above with additional direct incentives to patients to improve compliance with treatment, coupled with “social protection status” of TB patients and their families.
- The newly released TB infection control guidelines should be used to assess and strengthen measures to prevent TB transmission within the Republic of Moldova’s highest risk facilities.
- Optimal coordination between the NTP, PHC providers and insurance services needs to be assured so that high-quality follow-up care, including directly observed treatment, is available from trained, motivated staff wherever the TB patient will be seen, through to the completion of her/his TB treatment.

4. Engage all care providers

- Further technical assistance should be provided to penitentiary services (especially Transnistria) in collaboration with Caritas Luxembourg NGO (Carlux), the Ministry of Justice and the NTP.

5. Empower people with TB, and communities

- Partners should be engaged to expand ambulatory directly observed treatment and treatment support;

- A system needs to be established to enable timely diagnosis and treatment compliance among the migrant population.

6. Enable and promote research

- Where surveillance data routinely collected via SIME-TB are insufficient to understand gaps in programme performance, selected operational research should be undertaken to guide programme improvements.

ORGANIZATION OF TB SERVICES IN THE REPUBLIC OF MOLDOVA

The Republic of Moldova is a country in transition in eastern Europe, which gained independence after the collapse of the Soviet Union in 1991 and became a parliamentary republic in 2001. The total population is 3.8 million, including approximately 0.6 million in the breakaway region of Transnistria. The gross national income is US\$ 1500 per capita (Atlas method).²

The residents of the Republic of Moldova are served by a well-organized NTP. The Ministry of Health has overall responsibility for TB control in the country. It undertakes this function through the NTP Central Unit at the Institute of Phthisiopneumology, and involves the Ministry of Justice and other governmental entities, in collaboration with NGOs and international partners, in the planning, implementation, monitoring and evaluation of activities. TB control interventions are delivered through a network of specialized TB service institutions and PHC services. Organized via the family medicine model, PHC providers have been involved in TB control from the early stages of DOTS implementation.

Passive case detection is the main method of TB detection. PHC providers are responsible for the identification of TB suspects and their referral to the TB service. The diagnosis of TB is established by sputum smear microscopy (supported by X-ray when necessary) and confirmed by culture. The network of TB laboratories includes 57 microscopy laboratories, 3 regional reference laboratories and the National TB Reference Laboratory.

The majority of infectious TB patients are hospitalized during the intensive phase of treatment. During outpatient treatment, patient follow-up and drug dispensing are carried out at PHC facilities under the supervision of TB specialists. Directly observed treatment is in place for all inpatients and for about 60% of outpatients. Because of the low directly observed treatment performance at the PHC level, community-based directly observed treatment activities have been developed with the support of a TGF Round 9-supported project.

TB treatment delivery sites include thirteen inpatient institutions with a total

² Moldova at a glance. Washington DC, World Bank, 2009 (http://devdata.worldbank.org/AAG/mda_aag.pdf, accessed 16 November 2011).

capacity of 1630 beds (of which there are three facilities with 310 beds in Transnistria and two facilities with 220 beds in the penitentiary sector). In recent years, 490 beds in seven facilities have been re-profiled for MDR-TB treatment. In outpatient settings, there are 57 TB cabinets located in general health service institutions.

The TB service has a total of 965 staff, including 371 TB doctors, 275 nurses, 12 laboratory doctors (bacteriologists) and 117 laboratory technicians (of these, about 140 people are assigned to MDR-TB inpatient treatment delivery sites). The NTP Central Unit is responsible for the continuing education of TB service staff. The DOTS training programme has been extended and now covers PHC providers as well as specific topics such as TB/HIV coinfection and MDR-TB.

The mission team was told of reported difficulties in recruiting PHC staff and of a relatively high average age of PHC staff. Workloads were further reported to be high and salary scales of PHC staff comparatively low. Within the penitentiary system up to one-third of posts were reported to be vacant, with difficulties in filling posts threatening the quality of services delivered.

EPIDEMIOLOGICAL ANALYSIS OF TB IN THE REPUBLIC OF MOLDOVA

TB emerged as an important public health problem after independence in 1991 and its burden remains high. WHO estimates that the TB case rate (all forms) in the Republic of Moldova was 62 per 100 000 population in 1991. This rose rapidly to 140 per 100 000 in 2001 and has remained level through 2007. DOTS implementation was begun in late 2001, and was expanded to cover the entire country by the beginning of 2004, including the penitentiary sector and Transnistria region. In 2007, 4857 new and relapse cases were reported, which corresponds to a case notification rate of 128 per 100 000.

According to the WHO estimates for 2007 outlined in the global TB control report of 2009, the Republic of Moldova had the second highest TB case rate and the second highest TB mortality rate among the 53 countries of the WHO European Region (after Tajikistan). The Republic of Moldova experienced a 9% decline in TB notification in 2008 (see Fig. 1).

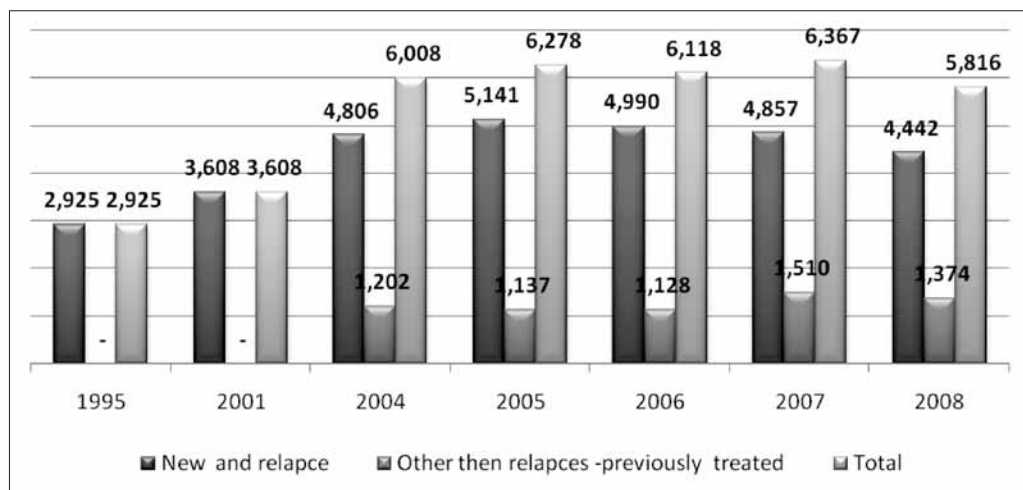


Fig. 1. TB case notifications 1995–2008 by category (absolute numbers)

Source: WHO global TB control report 2010³

³ Global tuberculosis control: WHO report 2010 (WHO global TB control report 2010). Geneva, World Health Organization, 2010 (http://whqlibdoc.who.int/publications/2010/9789241564069_eng.pdf, accessed 16 November 2011).

The proportion of smear-positive cases among new pulmonary cases detected rose from 38% in 2001 to 46% in 2004, but has not shown further improvement since then, remaining stable at 44% from 2005 to 2008 (see Fig. 2).

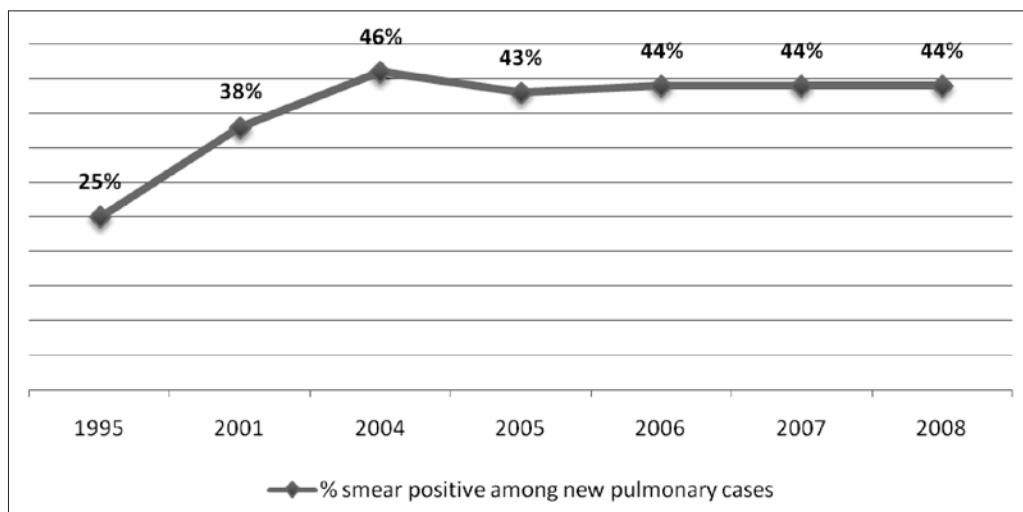


Fig. 2. Percentage of smear-positive cases among new pulmonary cases 1995–2008
 Source: WHO global TB control report 2010

The 2007 new smear-positive case detection rate of 67% also falls short of the global target of 70% (see Fig. 3), although that level was achieved in 2005 and 2006.

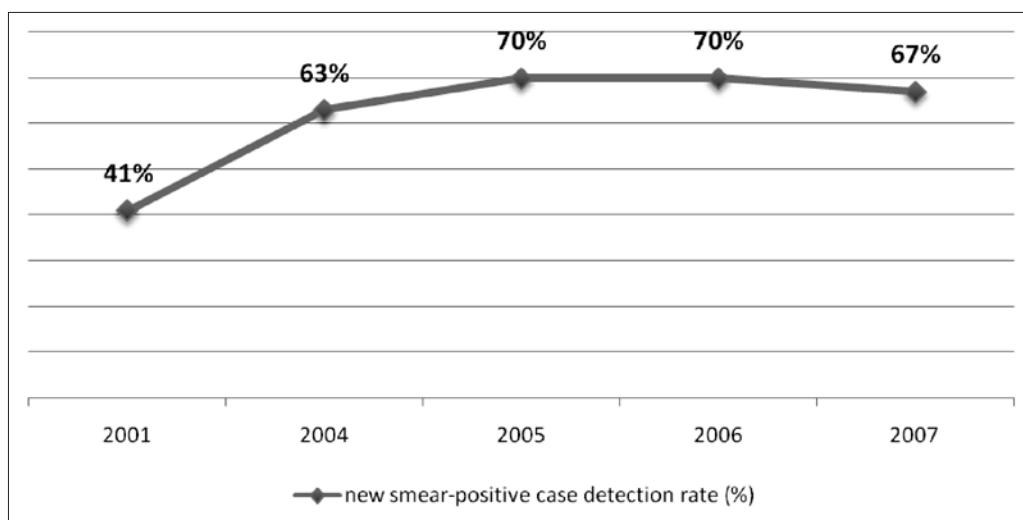


Fig. 3. New smear-positive case detection rate 2001–2007
 Source: WHO global TB control report 2009

Among the new smear-positive patients who were treated successfully, all but 2–4% received bacteriological confirmation of cure. However, the proportion of successfully treated smear-positive TB cases has not significantly improved since 2004. Treatment success for the 2004–2006 cohorts, outlined in the WHO global TB control reports of 2007, 2008 and 2009, remained at 62%, far short of the global target of 85%.⁴ In these cohorts, 11–12% of all cases failed, 10–12% defaulted, and 9–11% died (see Fig. 4).

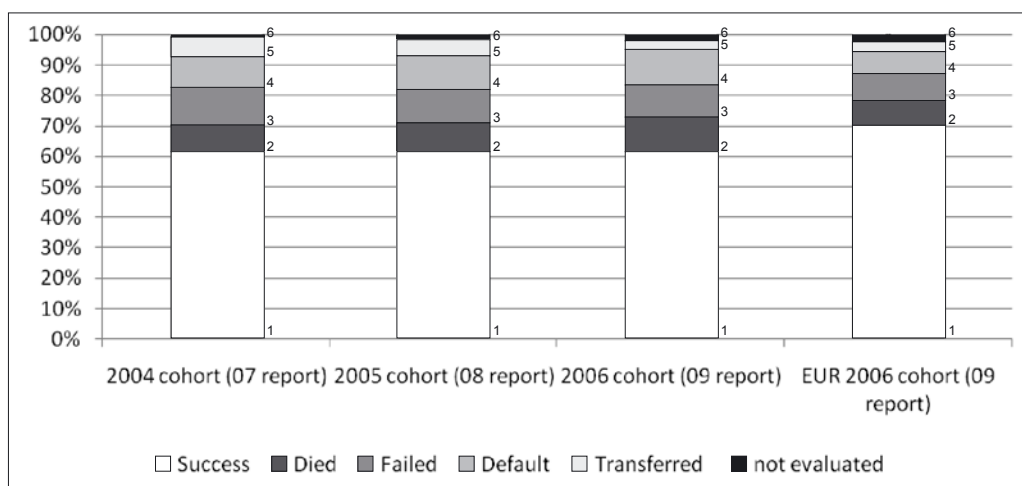


Fig. 4. Treatment outcomes of new smear-positive cases for 2004–2006 cohorts, the Republic of Moldova compared to the WHO European Region in 2006

Source: WHO global TB control reports 2007, 2008 and 2009

The proportion of retreatment smear-positive patients with poor outcomes is high: the death rate is around 16%, the failure rate 20%, and the default rate 17%. The success rate is very low, remaining stable at 35% (see Fig. 5).

The Stop TB Partnership has set TB impact measurement targets of halving the per capita TB prevalence and death rate from the 1990 baseline by 2015.⁵ The Republic of Moldova’s TB prevalence rate was 105 cases per 100 000 population in 1990, but it rose to 215 cases per 100 000 by 2000. The rate remained level at 151 cases per 100 000 from 2004 to 2008, but this is still three times higher than the 2015 target of 52 cases per 100 000.

⁴ Global tuberculosis control: surveillance, planning, financing: WHO report 2007 (WHO global TB control report 2007). Geneva, World Health Organization, 2007 (http://www.who.int/tb/publications/global_report/2007/pdf/full.pdf, accessed 16 November 2011); Global tuberculosis control: surveillance, planning, financing: WHO report 2008 (WHO global TB control report 2008). Geneva, World Health Organization, 2008 (http://www.who.int/tb/publications/global_report/2008/pdf/fullreport.pdf, accessed 16 November 2011).

⁵ The Stop TB Strategy. Geneva, World Health Organization, 2006 (http://www.stoptb.org/assets/documents/resources/publications/plan_strategy/The_Stop_TB_Strategy_Final.pdf, accessed 17 November 2011).

The Republic of Moldova's TB mortality rate was only 9 TB deaths per 100 000 population in 1990, but rose to 20 TB deaths per 100 000 by 2000. From 2004 to 2007, the rate stagnated at 18 TB deaths per 100 000, a long way from the 2015 target of 4.5 TB deaths per 100 000.

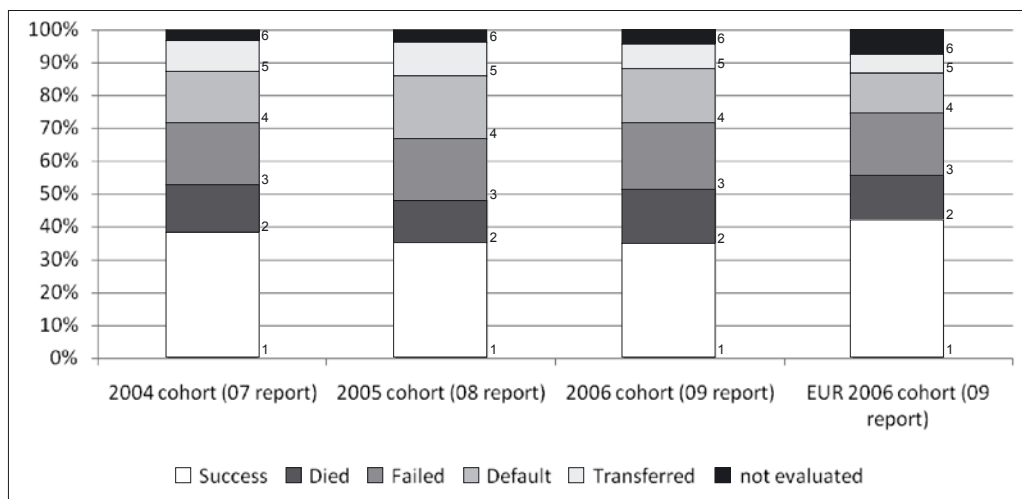


Fig. 5. Treatment outcomes of previously treated smear-positive cases for 2004–2006 cohorts, the Republic of Moldova compared to the WHO European Region in 2006

Source: WHO global TB control reports 2007, 2008 and 2009

Drug resistance is a major contributor to the country's failure to meet global TB targets. The Republic of Moldova ranks 19th among the 27 countries with the highest levels of MDR-TB in the world.⁶ An estimated 2200 MDR-TB cases arise in the country each year, of which 1700 are sputum smear-positive. In addition to these incident cases, the country probably has thousands of TB patients with MDR-TB from earlier years. Until their MDR-TB is diagnosed and appropriately treated, these 2200 incident (and the additional prevalent) cases continue to spread MDR-TB and generate even more cases.

A national drug resistance survey in 2006 found MDR-TB in 19% of new cases and 51% of previously treated cases, and the level appears to be rising; in 2008, 25% of new cases and 61% of retreatment cases tested were MDR. However, about 20–30% of cases did not have DST performed, so those tested may not be representative of all cases. The apparent rise could be a result of clinicians being more likely to obtain culture and DST on those patients they suspect may have MDR-TB. In 2008, the country also detected 25 cases of XDR-TB.

Drug resistance other than MDR is also a significant challenge. At the start of treatment, an estimated 12% of new patients and 11% of previously treated patients (a total of 660 cases per year) have isoniazid (H) resistance patterns other than MDR.

⁶ WHO global TB control report 2009

Rifampicin (R) resistance is estimated to be present in 12% of new and and 54% of retreatment cases at the start of treatment (see Table 1). These cases are just one drug away from developing into MDR-TB cases.

Table 1.
Estimated cases of drug resistance (other than MDR) arising each year (rounded)

	A	B	C	D	E	F	G	H
	% any H resistance	% MDR	% H resistance without MDR	Number of notifications in 2007	Expected number of H-resistant cases per year	% any resistance	% resistance without MDR	Expected number of R-resistant cases per year
New pulmonary cases	31	19	12	3653	431	21	1	47
Previously treated cases	61	51	11	2201	231	54	3	68
Total					662			116
Calculation			A-B		C×D		F-B	G×D

Source: NTP data, 2008.

The Ministry of Health has committed to providing the second-line drugs needed to treat drug-resistant patients who do not have MDR-TB. Green Light Committee advisers have recommended that WHO guidelines for regimens be followed. Treatment protocols and practices for this group of patients were not reviewed during the site visits.

SUMMARY OF PROGRAMME BY STOP TB STRATEGY COMPONENT

1. PURSUE HIGH-QUALITY DOTS EXPANSION AND ENHANCEMENT

1a. Political commitment with increased and sustained financing

Strengths and remaining gaps

DOTS is the official strategy for TB control in the Republic of Moldova. Implementation was begun in late 2001, and was expanded to cover the entire country by the beginning of 2004, including the penitentiary sector and Transnistria region. The level of government support to the TB budget increased from 2004 to 2008.

TB control interventions are guided by the *National Programme for Control and Prevention of Tuberculosis for 2006–2010*, endorsed by the government on 30 December 2005 and regulated by a number of laws, sublaws and regulatory acts, including a 2007 Ministry of Health order spelling out the programme's guidelines. The Ministry of Health has overall responsibility for TB control in the country, undertaking this function through the NTP Central Unit at the Institute of Phthisiopneumology. The NTP Central Unit is responsible for practical aspects of planning, implementation, monitoring and evaluation of interventions within the programme.

A technical working group on TB has been established and functions within the Country Coordinating Mechanism, which acts as a single national authority coordinating national responses to HIV/AIDS, sexually transmitted infections and TB epidemics. The Country Coordination Mechanism, although well organized, with multisector presence and several technical working groups, is by mandate focused on the management of TGF resources and is less well suited for engaging actors involved in other key areas such as PHC or financing policy. As part of the USAID Millennium Challenge Corporation project, a revised TB treatment protocol is under development.

The global economic crisis threatens government and TGF support to the NTP. There are few civil society organization partners and no Stop TB Partnership committee members to advocate from outside the NTP. The NTP is trying hard to influence other players outside the system but has limited leverage to influence other non-health players and lacks means to protect itself from budget cuts. There is strong collaboration between the NTP and Transnistria, but poor political dialogue weakens TB control in the region, which results in limited supplies and poorer treatment outcomes.

Effective coordination of the various actors needed for strong TB control is a central challenge; there is poor clarification of the roles and relationships of the Institute

of Phthisiopneumology, the Institute for Public Health Management, the National Centre for Preventive Medicine, the hospital system and PHC providers. The same problem exists with organizations outside the Ministry of Health – the TGF project coordinating unit and the other principle recipient, the Centre for Health Policies and Studies.

A regulation recently passed on coercive TB treatment does not ensure that detaining a patient against his/her will be used only as a last resort once all other appropriate options have been tried and failed (such as ambulatory treatment rather than hospitalization, adequate food and income support, alcohol and substance abuse treatment, and so on). This new regulation has several points that will need to be clarified: there is no clear explanation of what this coercive treatment means, the procedural rights, types of order and conditions required to gain release from detention, the services provided during detention or patients' rights for legal representation. In addition, no planning is in place for the regulation's implementation or funding.

Suggested areas for action

- Options for a high-level coordination or governance mechanism overseeing TB control should be reviewed. Such a coordination mechanism needs to be built around a common understanding and to include plans for all relevant government ministries and other actors, along with a systematic approach needed to get to grips with the epidemic in the Republic of Moldova.
- Options for a higher level of influencing and prioritization of TB in the health care system, including engagement of civil society organizations, should be reviewed.
- Mandates governing financing, oversight and accountability lines of key actors in TB control should be reviewed, with a view to reducing fragmentation and dealing more effectively with the multifaceted nature of TB.
- All TB-related services should be protected from cuts resulting from the economic crisis.
- Plans for development of a sector-wide approach in health, including options for optimal linkage of the TB coordination mechanism into the approach, should be continued. Options to ensure synergy between planned strengthening of systems – supported by the European Commission and WHO – for evidence-informed policy and operational research for TB control should be reviewed.
- The TB order from the Ministry of Health should be revised in light of the recommendations from the programme review.
- International technical assistance is needed to revise the TB and MDR-TB management guidelines developed under the USAID Millennium Challenge Corporation project.
- The Ministry of Health with partners (WHO, United Nations, patient advocates) should review the 7 August 2009 regulation on coercive TB treatment, and use this opportunity to leverage an increase in support provided to patients.

1b. Case detection through quality-assured bacteriology

Strengths and remaining gaps

Case detection in the Republic of Moldova involves good coordination between family practitioners, epidemiologists, hospitals and dispensaries. Following international recommendations, TB case detection starts with symptomatic patients seeking care in the PHC network. Since the inception of DOTS, family doctors have been identifying TB suspects and referring them to dispensaries for diagnosis. For rural patients who cannot travel to a laboratory, a specimen transport system is in place. Only TB doctors (based in dispensaries) are authorized to diagnose (and treat) TB. There is a strong focus on active case detection (contact tracing) with provision of prophylaxis as a programmatic intervention. However, overreliance on the importance of active case detection in the general population using mobile fluorography was observed. There is evidence that distances between PHC providers and diagnosing dispensaries, combined with transport costs, contribute to low case detection.

The laboratory network is well organized, with the National TB Reference Laboratory overseeing three regional laboratories that perform culture and DST. The regional laboratories in turn oversee the country's 57 microscopy laboratories. Staff in the laboratories visited are very competent and well trained and the facilities themselves mostly well organized. However, external quality assurance checking for smear microscopy is not blinded. The WHO-recommended Lot Quality Assurance System is not fully in place, but the quality control programme of the Supranational Reference Laboratory in Borstel, Germany for DST performed at the National TB Reference Laboratory is implemented. Laboratory guidelines are in place, although not all laboratories have adequate biosafety conditions.

The case detection rate is below the global target and has not improved since 2005. From 2003 to 2005 the number of patients submitting sputum for smear microscopy increased from 11 000 per year to 52 000 per year. However, from 2005 to 2008 this number did not increase.

Culture and DST are widely in use for the diagnosis of new and previously treated patients. DST is performed routinely on practically all new and previously treated pulmonary TB patients, allowing identification within a couple of months of incident MDR-TB patients. However, late results for traditional solid cultures contribute to low detection rates, programme drop-out and delays in diagnosis of MDR-TB (see also section 2a). In addition, when MDR-TB is identified, second-line DST is not routinely performed on the same isolated strain by the same laboratory that identified the MDR-TB.

One of the three regional laboratories (Bender) has not been able to participate in quality assurance testing of DST because test strains of *Mycobacterium tuberculosis* cannot be transported into Transnistria.

Suggested areas for action

- The practice of active case detection with mobile fluorography in the general population should be discontinued.
- Existing TB and HIV NGOs could be used to assist with intensified case detection among vulnerable groups (provided the members are trained and equipped with the proper tools).
- Interventions should be designed to improve the detection of smear-positive cases.
- If a patient has been transferred to another hospital, DST should be performed for second-line drugs from the first strain isolated.
- To improve culture sensitivity, the N-acetyl-l-cysteine–sodium hydroxide (NALC–NaOH) decontamination procedure should be used for all specimens.
- Rapid methods need to be implemented to detect drug resistance and confirm *Mycobacterium tuberculosis*.⁷
- DST for first-line drugs should be performed in Mycobacteria Growth Indicator Tubes, and with line probe assays from positive cultures. Ideally, line probe assays should be performed from smear-positive sputum specimens.
- Staff need to be trained on the implementation of new diagnostic tools by the Supranational Reference Laboratory.⁸
- Good records should be maintained in each laboratory for quality assurance and maintenance.
- All laboratories should routinely use an internal and external (blinded) quality control programme.
- Steps should be taken to ensure that enough technicians are trained and available.
- Problems with the transportation of strains to Bender need to be solved so that this regional laboratory can participate in external quality assessment for DST.

1c. Standardized treatment with supervision and patient support

Strengths and remaining gaps

There is consistent and correct use of standardized treatment for all TB patients; treatment results and tests are properly recorded. NTP policy is to hospitalize TB patients during the intensive phase. Current hospital financing by the health insurance fund is linked to the standard prescribed hospital time (six months), even if culture results become negative earlier; thus the duration of hospitalization seems longer than needed. This arrangement contributes to higher rates of cross-infection within facilities, overcrowding and higher costs to the system in general. Directly observed treatment was correctly delivered to the patients in the inpatient units visited. Psychiatric support

⁷ The National TB Reference Laboratory began to use rapid methods in 2009.

⁸ The Supranational Reference Laboratory began training staff of the National TB Reference Laboratory in 2010.

is not available in the hospitals. Doctors in inpatient departments are under pressure from the regulation of the health insurance fund, which pays only for “validated” cases. Payment received or not received from the health insurance fund for uninsured patients is unclear and fluctuating.

After discharge, dispensaries provide clinic-based directly observed treatment; however, in one dispensary visited, one-third of patients were picking up a weekly supply of medication. For patients who live at a distance from dispensaries, PHC facilities in rural areas provide clinic-based directly observed treatment.

The high proportion of failing new and retreatment cases is probably related to at least two problems: there is incomplete detection of MDR-TB, and in 2008 only half the notified MDR-TB cases were registered for treatment.

Well-established rapport exists between TB doctors and family doctors, who have been trained in DOTS; however, different levels of collaboration and involvement of PHC providers in case detection and treatment follow-up, and different grades of directly observed treatment implemented after discharge from hospital were observed. Health care providers at all levels have a clear interest in obtaining a high treatment success rate and in decreasing defaulting rates. At some facilities a multisectoral approach in case management (involving HIV, TB, psychosocial and narcology workers) was observed.

Social support for TB patients, especially for those without insurance, is insufficient. Involvement of community-based and voluntary organizations in delivering treatment is limited. Lack of patient support and migration both contribute to high defaulting rates. Numerous cases of treatment defaulters and re-appearances were reported, resulting from poverty and alcoholism. Dispensary staff described using their own money to help TB patients with transportation or food costs. Treatment for alcoholism is not accessible. Overall, there is limited patient health education, with few educational materials used during the hospitalization phase.

As mentioned in section 1a, the new regulation on coercive treatment has several points that will need to be clarified: there is no clear explanation of what this treatment involves, the procedural rights, types of order and conditions required to gain release from detention, the services provided during detention, patients’ rights for legal representation or how it will be implemented and funded.

In Transnistria, the diagnostic committee clears TB patients to return to work once they are smear-negative, except teachers or students, who are not permitted to return to schools until they complete the entire course of treatment. It is unclear whether sick leave benefits are sufficient during this time.

Suggested areas for action

- Movement towards a patient-centred approach for TB patients involving medical and psychosocial management should be considered.
- Proper involvement of PHC providers – doctors and nurses – in TB case management, especially during directly observed treatment after discharge from hospital, needs to be ensured.
- The weight of TB patient management should gradually be moved from the

inpatient/hospital system to the community, particularly for extrapulmonary TB and bacteriological negative cases, and earlier discharge for inpatients with converted cases facilitated.

- A countrywide patient education system with proper materials and training sessions should be developed.
- Existing TB and HIV NGOs could be used to follow up on treatment (provided the members are trained and equipped with the proper tools).
- A formal revision of the regulation on coercive treatment needs to be organized, and this opportunity used to increase the support provided to patients.
- TB and MDR-TB management guidelines developed under the USAID Millennium Challenge Corporation project with international technical assistance need to be revised.
- New and refresher staff training courses in MDR-TB management at the national level should be considered.
- The existing database should be used to map places of origin and destination of TB cases among former migrants. Epidemiological studies need to be conducted to evaluate the contribution of migrants to the transmission of TB in the Republic of Moldova.
- Social support should be provided to labour migrants with TB, regardless of their health insurance status.

1d. An effective drug supply and management system

Strengths and remaining gaps

The mission team observed availability of all first-line drugs provided free of charge for all TB patients and contacts countrywide. No stockouts have occurred. There is a drug management system with buffer stocks and a new warehouse for all TB drugs (first- and second-line) is rehabilitated, refurbished and ready for use. The Ministry of Health has increased its commitment to funding first-line drugs.

One gap identified is the lack of child-friendly formulations. The mission team also learned of a 2–3 week stockout of syringes for injectable drugs for MDR-TB patients in Bender in 2009, as well as hearing accounts of patients having to purchase medication for side-effects.

Suggested areas for action

- Procurement of child-friendly formulations should be prioritized.
- Stockouts of syringes needed for injectable TB drugs should be avoided.
- Full funding for TB drug side-effect management needs to be ensured.
- Once the NTP stops its current policy of discontinuing treatment for 2–3 days before each sputum collection, drug needs should be recalculated for MDR-TB and all other patients.

1e. Monitoring and evaluation system, and impact measurement

Strengths and remaining gaps

The TB monitoring and evaluation mechanism in the Republic of Moldova is delegated to the Monitoring and Evaluation Unit of the National Centre for Health Management, where SIME-TB has been in use countrywide since 2007. This is a relational database management system, a mixed tool allowing either online or offline patient data management from 35 reporting units, including:

- epidemiological data for case notification, management and treatment of TB;
- laboratory data for diagnosis (smear, culture and first-line DST) and treatment monitoring;
- pharmaceutical data for first-line TB drug management.

Aggregated data access and interpretation are available in the public domain as standardized reports with additional options for non-standardized operative analysis; the individualized database is password protected and access is secure for case data viewing and data-based synchronization. The software can be accessed by interested counterparts in the NTP, the National Centre for Preventive Medicine (communicable disease surveillance and the National AIDS Centre).

SIME-TB includes a first-line TB drug management module, and a PHC module from web-based tool e-TB Manager is also integrated. There are no data available on TB/HIV collaborative activities, although development of SIME-HIV is underway, which is planned to link with SIME-TB.

All the standard indicators for evaluating impacts and outcomes are in place in separate tables, but the potential for integrating data operations is not fully utilized: TB data are not integrated into communicable disease surveillance. Case definitions for treatment outcomes are not in line with WHO recommendations and are confusing to interpret (using terms such as failure, default, still on treatment). The vital registration system does not cover eastern districts, where TB mortality data and denominators of impact and process indicators are not managed according to SIME-TB. Limited availability of sex- and age-stratified data makes it difficult to target responses effectively.

The NTP has established well-functioning field supervision, for which teams and a full structure are in place. However, including the National Centre for Health Management representative in the supervisory team would assist with data analysis. Field supervision reports are available, but this information is insufficiently used to strengthen TB services at the district level. Roles and responsibilities for monitoring and evaluation activities between the NTP and the National Centre for Health Management monitoring and evaluation teams are very well defined.

Suggested areas for action

- Notification and treatment evaluation data should be integrated into a dedicated spreadsheet, using standard layouts.

- The National Centre for Preventive Medicine (including the National AIDS Centre) should communicate with the National Centre for Health Management to integrate TB into communicable disease surveillance.
- Case definitions need to be harmonized in national guidelines according to the latest WHO recommendations.
- The mechanism for delivering data to the field should be strengthened.
- The experience and advantages of web-based data reading, analysis and interpretation should be rolled out in the field and to the NTP monitoring and evaluation team, the National Centre for Preventive Medicine and the National AIDS Centre.
- The National Centre for Health Management representative should be included in monitoring and evaluation teams for field supervision.
- A data operation and analysis tool should be established to follow recommendations made by monitoring and evaluation teams.
- Effective communication with local health authorities on findings and follow-up of recommendations are needed.
- Collaboration between surveillance officers and the NTP monitoring and evaluation unit on medical case management should be strengthened, following WHO recommendations.
- A mechanism for collecting data on TB mortality should be established in eastern districts, as well as denominators for impact and process indicators (such as population, human resources or laboratory).
- Comprehensive analysis and operational research should be performed on unsuccessful patient treatments.
- Options for strengthening the health management information system to provide disaggregated data on population sex and age for better targeted interventions should be considered.

2. ADDRESS MDR-TB, TB/HIV COINFECTION AND OTHER CHALLENGES

2a. Prevent and control MDR-TB

Strengths and remaining gaps

The DOTS strategy was introduced in the Republic of Moldova in 2001 and national coverage was achieved by 2004. It was clear that resistant TB had become a major problem, as in many former Soviet Union countries, as a result of years of inadequate TB control. Eventually establishing that DOTS default and failure rates were over 10% each was a clear warning of the growing MDR-TB problem.

The first representative national drug resistance survey in 2006 corroborated this assumption. The figures for MDR-TB showed that 19.4% of TB patients who had never before been treated had MDR-TB. Among previously treated TB patients the rate was 50.8%. Applying these rates to the 2007 figures would mean that of the 4132 new smear-positive and smear-negative pulmonary and extrapulmonary cases that year, the number of newly diagnosed primary MDR-TB cases would amount to approximately 800; the group of 1885 candidates for retreatment (relapses, treatment after failure and default) would add a further 960 MDR-TB cases. To this total of 1760 MDR-TB patients calculated for 2007, the NTP estimates that a backlog of another 1600 MDR-TB patients who have received no adequate treatment must be added, bringing the figure to 3360. Putting this in perspective, from 2006 to 2008 during the initial scale-up of MDR expansion the NTP started 522 MDR-TB patients on PMDT treatment.

The NTP has made major progress in addressing its MDR-TB epidemic through enhanced detection. In 2008 the Republic of Moldova's laboratory network detected 1048 cases of MDR-TB, which represents about half of the MDR-TB cases estimated to have arisen that year (see Table 2). In order to design interventions to detect the other half, it is necessary to examine the coverage of culture and DST among TB cases at the start of treatment ("diagnostic" DST).

The NTP states that its policy is to obtain sputum for culture from all patients at the start of therapy, and to perform DST for first-line drugs for all culture-positive patients. The highest yield for detection of MDR-TB cases is among previously treated patients, since the drug resistance survey found that at 51% the level of MDR-TB in this group was more than double the level (19%) in new cases.

Provisional data from the WHO Regional Office for Europe show that of the 603 smear- and/or culture-positive relapse cases notified in 2008, 455 had results from DST for at least isoniazid and rifampicin. Assuming that all would be culture-positive if tested, this suggests that about 75% (455/603) of the relapse cases underwent culture. (Of the tested relapse cases, 58% were found to have MDR-TB.)

The proportion of new cases with DST performed at the start of treatment has increased from 32% to 79% between 2005 and 2007 (see Table 2). However, at least 20% of new pulmonary smear-positive TB cases have not had DST performed.

Table 2.

DST performed at start of treatment in new cases, yield of MDR-TB, 2005–2008

	A	B	C	D	E	F
Year	Number of lab-confirmed MDR-TB cases	Number of notified new pulmonary smear+ cases	Number of new cases with DST	Estimated percentage of new pulmonary smear+ cases with DST	Number of new cases with MDR-TB	Percentage of MDR-TB in new cases with DST
2008	1048	1533	1212	79%	300	25%
2007	896	1610	1311	81%	311	24%
2006	1040	1679	1051	63%	242	23%
2005	338	1696	536	32%	68	13%
Calculation				C/B		E/C

Source: WHO global TB control reports 2007, 2008 and 2009

Note: Column D is based on the denominator of notified new pulmonary smear-positive cases (column B), but some of the DSTs performed in new cases may have been in smear-negative patients.

In 2006 (the year of the drug resistance survey), over 95% of the notified retreatment cases underwent DST (see Table 3). In the subsequent two years, however, only 42% and 66% of retreatment cases had DST performed, so there is ample scope for improved MDR-TB case detection among previously treated patients. Testing these patients at the start of retreatment is urgent, given that 50–60% will be found to have MDR-TB. If this is not detected, they will receive inappropriate treatment, which puts them at risk of dying or spreading MDR-TB.

Table 3.

DST performed at start of treatment in previously treated cases, yield of MDR-TB, 2005–2008

	A	B	C	D	E	F
Year	Number of lab-confirmed MDR-TB cases	Number of notified previously treated cases	Number of previously treated cases with DST	Estimated percentage of previously treated cases with DST	Number of previously treated cases with MDR-TB	Percentage of MDR-TB in previously treated cases with DST
2008	1048	1865	1227	66%	748	61%
2007	896	2201	934	42%	585	63%
2006	1040	1730	1655	96%	798	48%
2005	338	1777	652	37%	270	41%
Calculation				C/B		E/C

Source: WHO global TB control reports 2007, 2008 and 2009

Routine ongoing surveillance of drug resistance will be possible as the country implements culture and DST at the start of treatment for all cases.

Another major problem with MDR-TB case detection is timeliness. Solid culture typically has a two-month turnaround time from specimen collection to date of DST results. This means that patients receive inappropriate regimens for two months

before their MDR-TB is detected. Financial reimbursement to laboratories (tied to patient hospitalization) may also promote unnecessary delays in obtaining second-line DST. In addition, when MDR-TB is identified, second-line DST is not currently routinely performed on the same isolated strain by the same laboratory that identified the MDR-TB.

The TGF Round 8 project will scale up the use of liquid culture as well as of rapid molecular-based methods, which will greatly aid the speed of MDR-TB case detection. These methods will also definitively identify *Mycobacterium tuberculosis*, whereas the current methods using colonial morphology and microscopy may incorrectly be including some non-TB mycobacteria (which are often drug-resistant).

Guidelines for MDR-TB management have been produced and disseminated; TB doctors have been trained, and they in turn have trained family doctors. The Republic of Moldova follows the strategy of a standardized treatment regimen for MDR-TB patients: this includes an intensive phase of capreomycin (Cm), ofloxacin (Of), ethionamide (Et), cycloserine (Cs) and pyrazinamide (Z) for at least six months and a continuation phase with Of, Et, Cs and Z for at least 18 months, where para-aminosalicylic acid (PAS) may be substituted for Cs or Et in case of intolerance to one of these latter drugs. So far the intensive phase entails hospitalization for usually six months or more; re-training and a change of attitude among doctors will be required to allow more patients to be discharged early from hospital and treated as outpatients.

The national protocol includes treatment interruptions preceding the date of each sputum specimen collection of two days for MDR-TB patients and three days for all other TB patients. Sputum continues to be collected every month. This unnecessary drug interruption reduces effective MDR-TB treatment by 24–36 days per patient treatment, as these missed doses are not added to lengthen the course of therapy.

In previous years, both during the Soviet period and in the turmoil after the collapse of the old system, relatively few patients had access to second-line TB drugs. The former irrational practice of prescribing inadequate regimens and even today the treatment of chronic cases that already have MDR-TB with regimens such as Z, Et and Of are bound to produce further drug resistance. XDR-TB patients have already been identified and in one convenience sample of sputum cultures on which second-line DST was performed 16% of samples were found to have fluoroquinolone-resistant TB bacteria.

In the Republic of Moldova, during the typical two-month delay in MDR-TB case detection, those patients who are most infectious (the smear-positive ones) are generally hospitalized with other TB patients. This poses the risk of cross-infection of MDR-TB strains to the other patients. Nearly one in three hospitalized TB patients would be found to have MDR-TB if all underwent culture and DST (see Table 4).

Table 4.

Estimates for undetected MDR-TB cases in a hypothetical 100-bed TB ward

	Number of patients	2006 drug resistance survey MDR-TB rates	Estimated number identified as MDR-TB cases once lab results available
Previously treated patients	35	51%	18
New patients	65	19%	12
Total	100	31%	30

MDR-TB patients are treated in special wards in five hospitals (the Republican and Municipal Hospitals in Chisinau; outside the capital in Vorniceni, Bender and Balti) with limited bed capacity. They are routinely hospitalized for at least six months, even if their results become smear-negative. Wards are generally crowded with no privacy, segregation of infectious patients from newly smear-negative patients is inadequate and there are insufficient infection control measures. Patients at different stages of treatment, with XDR-TB, HIV infection or unrecognized MDR-TB share wards with new TB patients with fully drug-sensitive TB. Poor hygiene facilities for patients (such as bathrooms and toilets) were observed to be shared by men and women.

The Republic of Moldova has successfully secured three TB grants from TGF Rounds 1, 6, and 8 that have helped to finance a Green Light Committee-approved project. TGF support has enabled renovation of hospital facilities for MDR-TB patients and training of physicians and nurses involved in TB control activities, as well as making it possible to purchase second-line drugs. This last arrangement has been completed with the approval of the Green Light Committee: after a pre-approval visit in 2004 and a revised project proposal in 2005 second-line drugs were finally delivered in the latter half of 2005. From then until the end of 2008, 522 MDR-TB patients were recruited, surpassing the targets by 25%. The number of MDR-TB patients to be enrolled under the expansion plan is outlined below (see Table 5).

Table 5.

Number of patients with MDR-TB enrolled in the Green Light Committee-approved project and in a future planned project expansion (with funding sources)

Year	First cohort	Second cohort	Expansion plan
2006	100 (TGF Round 1)		
2007		200 (TGF Round 1)	
2008		200 (TGF Round 6)	
2009		200 (TGF Round 6)	150 (TGF Round 6 phase I) + 500 (TGF Round 6 phase II)
2010			250 (TGF Round 6) + 500 (TGF Round 8)
2011			730 (TGF Round 8)
2012			700 (TGF Round 8)
2013			670 (TGF Round 8)
2014			650 (TGF Round 8)
TOTAL	100	600	4150 (of which 3250 from TGF Round 8)

The Republic of Moldova's PMDT initiative⁹ enrolled 522 patients in 2008, which represents 50% of the 1048 MDR-TB cases detected. Progress was made towards universal access to MDR-TB treatment in the Republic of Moldova during 2005–2008 (see Table 6).

Table 6.
Progress towards universal access to MDR-TB treatment, 2005–2008

	2005	2006	2007	2008	cumulative
Estimated number of incident MDR-TB cases	2200	2200	2200	2200	
Number diagnosed and notified	338	1040	896	1048	3322
Percentage of estimated MDR-TB cases	15%	47%	41%	48%	
Number registered for treatment	17	88	254	522	881
Percentage of notified MDR-TB cases	5%	8%	28%	50%	
Percentage of estimated incident MDR-TB cases	1%	4%	12%	24%	

Source: NTP data, 2008.

For various personal or family reasons, a number of patients cannot submit to hospitalization and are thus excluded from PMDT treatment. For patients unable to remain in hospital, after the intensive phase of daily injections of Cm a TB dispensary or family doctor is chosen close to the patient's home, where ambulatory supervised treatment can be given six days a week for the remaining time – normally 18 months.

The mission team observed non-standard second-line drug regimens provided by dispensaries for MDR-TB patients who do not enter the MDR-TB treatment cohort. Another approach observed in the Bender dispensary was continued use of first-line drugs. TB coordinators described ongoing follow-up of such patients in the TB clinics without any special infection control precautions. Staff did not have guidance to provide about preventing the spread of MDR-TB from ineffectively or untreated MDR-TB patients.

The PMDT initiative is functioning as an integral part of the NTP, but an operational plan to secure resources and coordinate a successful scale-up – including laboratory strengthening, patient support, human resource development and advocacy – is lacking. Significant bottlenecks remain in accessing MDR-TB treatment, particularly surrounding the number of available treatment slots. The NTP has plans to enrol approximately 700 patients per year (around one-third of the estimated annual incident cases) with TGF Round 8 funds, but this will still leave a high proportion of MDR-TB cases without treatment. Strict exclusion criteria currently bar many patients from accessing treatment.

The selection committee (“consilium”) meets in Chisinau twice weekly, and in alternative regional sites twice monthly. During these meetings the TB doctor responsible for a PMDT candidate will present on the case; based on the patient's history,

⁹ PMDT was formerly known as “DOTS-plus”, an extended DOTS programme for the detection and treatment of MDR-TB.

confirmation of MDR-TB, previous clinical development and treatment, a decision is taken whether or not to treat, according to Green Light Committee guidelines. The consilium is also an excellent forum for mutual and continual learning and teaching, as all major aspects of individual case management of MDR-TB patients are discussed and decided on by the NTP team and the TB doctors involved in MDR-TB treatment.

Systematically collected data were not available on the number of patients never presented to the consilium or those excluded by it. However, visits to dispensaries revealed that some patients were disqualified because they had defaulted from treatment in the past and others were not presented because they were alcoholic. Some of the so-called “refusals” of patients to sign the consent form to begin MDR-TB treatment are not refusals of treatment per se; instead, they reflect the patient’s inability to submit to six months of hospitalization – the only currently available option for MDR-TB treatment in the Republic of Moldova. The TB coordinator presented to the mission team an MDR-TB case who was unable to forgo his usual livelihood: economic reasons prevented him from signing the consent form, so his case was never presented to the consilium. As a consequence, the children of this patient (in whom active TB had been excluded) were removed from their home and placed in a distant rehabilitation centre.

Procurement of second-line drugs of quality-assured standards from the International Dispensary Association through the Green Light Committee has been successful and central distribution of MDR-TB drugs to the periphery has occurred without stockouts. Drugs are packed for individual patients and sent on a monthly basis from the medical warehouse to hospitals and TB dispensaries. The consilium is convened frequently, reducing the time lapse between diagnosis and treatment of an MDR-TB patient and securing rational case management according to guidelines. The Ministry of Health has shifted its focus from a parallel MDR-TB treatment programme to treating non-MDR poly-resistant TB cases with predefined treatment regimens based on type of resistance.

Recording and reporting of MDR-TB patient treatment is manual, and forms are not consistent with WHO recommendations. Drug administration to individual patients is meticulously registered on Ministry of Health forms, but the (WHO) PMDT patient treatment cards that allow a quick overview of all relevant information concerning treatment, microbiological results and clinical development are rarely found filled in.

The NTP has achieved 65–67% treatment success in the first (carefully selected) 105 PMDT patients (the 2005 and 2006 cohort). However, there is concern for the 2007 cohort: even though more than half are still on treatment, 22% have already defaulted, and the number of defaults will rise as the cohort follow-up is completed.

TB coordinators in several hospitals and dispensaries pointed to the lack of support of MDR-TB patients as contributing to the high default rates: although MDR-TB patients receive modest (US\$ 30/month) social support from Carlux, there is inadequate support to assess and address the social, economic and psychological needs of individual patients, and many patients are too weak to work or are already jobless. Among the 151 MDR-TB patients who began treatment in Vorniceni TB Hospital in 2008, 13% abandoned treatment or were expelled due to behavioural problems or

alcoholism. In principle, the family doctor is responsible for the retrieval of a defaulting patient, but a lack of patient-friendly treatment, migration to look for work outside the Republic of Moldova, and unwillingness on the part of the patient to continue treatment are all important determinants of defaulting.

A number of the issues mentioned above – including making services more patient-friendly, expanding outpatient case holding, offering economical and psychological support to patients and improving infection control – will need to be revisited when designing TB control strategies for the coming years. The number of MDR-TB patients will grow considerably, so increased involvement of and collaboration with the PHC sector and further training of family doctors and primary care nurses will be essential. In addition, there must also be a focus on DOTS performance: default rates above 10% underscore the need for insisting on directly observed therapy and on strong systems for retrieving defaulters as much as possible.

Suggested areas for action

- A national MDR- and XDR-TB plan should be developed to ensure gradual expansion from individual projects to countrywide coverage and access to proper diagnosis, treatment and care.
- The national guidelines for MDR-TB management should be adjusted according to the latest WHO recommendations and should take into account the need to introduce patient-friendly solutions.
- Further expansion of availability of PMDT through access to funds from TGF should be pursued and supported.
- Until rapid molecular-based tests are available for the diagnosis of all MDR-TB cases, patients with the highest risk of MDR-TB should be placed on a standard empirical MDR-TB regimen while awaiting the results of conventional DST.¹⁰
- Criteria should be developed to identify those MDR-TB patients most likely to adhere to the regimen during outpatient treatment. These patients can then be discharged as outpatients as soon as their infectiousness is effectively reduced (when sputum smear-negative) provided they tolerate and understand their treatment well.
- Use of hospitals for all smear-positive patients should be reduced by expanding ambulatory treatment with patient support to diminish the risk of undetected MDR-TB spreading.
- “Individualized regimens” containing second-line drugs in combinations that will not cure chronic TB patients should be abolished to prevent further spread of second-line drug resistance; all patients on second-line drug treatments should be included in the Green Light Committee cohorts.
- Drug interruptions preceding sputum collection should be abolished.
- Treatment monitoring of MDR-TB patients should be simplified: during the

¹⁰ Rapid molecular-based tests have been available for the diagnosis of all MDR cases since 2010.

continuation phase, sputum for culture and microscopy should be obtained every three months unless the patient's progress is unsatisfactory.

- DST for second-line drugs should only be performed once before the start of MDR-TB treatment, provided the patient does not receive second-line drugs before enrolment into the PMDT programme.
- Infection control must be enhanced and improved in all facilities dealing with MDR-TB patients and staff should be trained accordingly.¹¹
- MDR-TB forms in use for patient management should be reviewed and the SIME-TB module on MDR-TB implemented.
- The number and proportion of MDR-TB cases detected at the start of therapy should be analysed every year, as well as the number and proportion of non-MDR-TB cases that acquire (or are re-infected to become) MDR-TB during treatment.
- Qualitative studies interviewing TB service staff and MDR-TB patients that have defaulted from PMDT should be undertaken to identify ways of preventing and reducing defaulting.
- A representative sample of second-line DST for MDR-TB patients should be performed annually to monitor the need for future modification of the standard regimen and any possible need for individualized treatments.

2b. Implement collaborative TB/HIV activities

Strengths and remaining gaps

WHO estimates that 3.7% of the Republic of Moldova's TB cases in 2007 were HIV-positive. The proportion of TB patients for whom HIV test results are known increased from about 40% in 2006 to 68% in 2007. Of the 161 HIV-positive TB patients detected, only 5 (3%) started or continued co-trimoxazole preventive therapy, and 34 (21%) started or continued antiretroviral therapy.¹²

The mission team observed good collaboration between the NTP and the HIV/AIDS Programme, formalized by an order of the Health Minister with a clear description of the flow of patients between the two programmes. Voluntary testing and counselling is offered to all TB patients at TB facilities, but a discrepancy was observed in the data presented by the TB and HIV/AIDS Programmes on the number of TB patients tested for HIV each year.

Educational materials on TB and TB/HIV coinfection are available in the National AIDS Centre and HIV and TB NGOs are working among vulnerable groups for potentially intensified case detection and follow-up of treatment.

Suggested areas for action

¹¹ See also section 3.

¹² WHO global TB control report 2009.

- Regular meetings should be organized to cross-check the data available in the two national databases, especially on TB patients tested for HIV.
- In view of the infection control situation and high risks of nosocomial transmission, consideration should be given to enabling HIV patients to consult TB specialists in HIV departments.
- Proper isolation of all people living with HIV and with active TB during treatment should be ensured.
- Training and materials on implementation of TB/HIV coinfection collaborative activities should be provided to NGOs working with vulnerable populations.
- Existing HIV and TB NGOs could be enlisted to conduct intensified case detection among vulnerable groups and to follow up on TB/HIV treatment.
- Proper training on HIV pre- and post-test, TB, hepatitis and sexually transmitted infections should be given to staff providing voluntary counselling and testing at TB dispensaries.
- Availability of materials for health education in Romanian and Russian and condoms for distribution should be ensured.

2c. Address prisoners, migrants, refugees and other high-risk groups and special situations

(See sections 4 and 5)

3. CONTRIBUTE TO HEALTH SYSTEM STRENGTHENING

As this report is organized into sections based on Stop TB components, health system function information has also been distributed among the different sections as appropriate. This section covers the mission's key findings on financing, resource generation and service delivery – three of the four functions of health systems. The fourth function, governance, is covered above in section 1a.

Strengths and remaining gaps

The Republic of Moldova recognizes that how services related to TB control are financed has a major bearing on how they are executed and received; during the review the mission team found that several initiatives had been undertaken to reflect this.

The specialized, vertically-organized TB service consists of 965 staff (371 doctors, 275 nurses, 12 laboratory doctors, and 117 laboratory technicians). Staff are routinely screened for TB, at the beginning of employment and periodically (once a year) or if symptoms are identified. Staff screening is widely based on X-ray and TB case rates by occupation are available. Closures or mergers of several excessive TB facilities over the past decade have led to savings and improved efficiency.

The NTP relies on the primary care system of family doctors to investigate TB in patients presenting with chronic respiratory symptoms, but one-third of the Republic of Moldova's most infectious TB cases are not detected. Potential barriers to accessing primary care, providers failing to suspect TB, or problems with obtaining sputum smear microscopy have not been fully explored. The NTP director expressed concern that family doctors are understaffed and may give low priority to TB, yet they are critical to case detection and directly observed treatment during the ambulatory phase of TB treatment.¹³

The mission team heard reported difficulties in recruiting family doctors and a relatively high average age of PHC staff. Workloads were further reported to be high and salary scales of PHC staff comparatively low. Within the penitentiary system up to one-third of posts were reported to be vacant, with difficulties in filling posts threatening the quality of services delivered.

Salaries within the NTP, on the other hand, have been increased to an average of US\$500 a month (but can be as high as US\$900 a month in certain regions), compared with the average health worker's salary of US\$270 a month – an important factor to attract and maintain a competent workforce. The mission team also found that some measures are in place to ensure staff maintenance and motivation including trainings and re-training programmes.

Financial incentives for PHC workers to encourage stronger TB management based on the number of cases detected and treated were piloted during 2007–2009 (US\$40 for early detection and US\$70 for successful treatment of TB cases). Revenue is shared across the team. However, the mission team found anecdotal evidence that financial incentives were not always received.¹⁴

TB services in the Republic of Moldova are heavily skewed towards inpatient treatment, which is expensive, poses the risk of nosocomial spread, and requires patients to leave their homes, families and sources of income. The country has 1630 TB-designated hospital beds; vested interests and reimbursement structures may pose difficulties in reorienting towards ambulatory services. Even if TB policy changes to emphasize patient-centred approaches, the NTP may not be able to redirect the country's major inpatient investments to an ambulatory model.

Current hospital financing is linked to standard prescribed hospital time (six months) even if culture results become negative earlier. This arrangement can contribute to higher rates of cross-infection within facilities, overcrowding and higher costs to the system in general. Reimbursement by the health insurance fund covers only insured and "validated" cases (if a patient defaults, the hospital is not reimbursed). While there is a mandatory health insurance system, a high proportion of TB patients are uninsured (figures up to 65% were mentioned). The NTP budget is transferred to the National Health Insurance Company for uninsured patients. This is important as it ensures coherence in health financing policy.

¹³ In 2010 new legislation was enacted making PHC access universal: this improves access to the health system for the uninsured, and a large percentage of TB patients are uninsured.

¹⁴ In 2010 these incentives were discontinued altogether (this was partly related to budget cuts).

A specific budget has been allocated for cash benefits and food stamps for the continuation phase, strengthening compliance and treatment. The mission team also found evidence of effective partnerships with civil society and NGOs (Carlux, for example) in critical areas such as outreach and social support, but also in ensuring continuity of care – for example, between the penitentiary system and the general health system.

There is anecdotal evidence that a very large migrant population, poverty and weak incentive systems (social assistance programmes) for patients, as well as long distances between PHC providers and diagnosing dispensaries – combined with transport costs – contribute to low case detection and adherence. Furthermore, late results for traditional cultures contribute to low detection rates and programme drop-out. There is a need for an overall strategy for management of MDR-TB and chronic cases returning to the community. The mission team heard of several hundred failed treatment cases that had been released back to the community.

As a follow-up to the September review mission, another review focused on infection control was conducted in November 2009. During the visit the mission assessed five MDR-TB inpatient facilities, two outpatient facilities, three of the TB reference laboratories and two regional laboratories for microscopy. The mission team noted a serious lack of managerial, administrative, environmental and personal protection measures in many facilities visited. National TB infection control guidelines have recently been released – once implemented, these will help protect patients as well as staff.

Hospitals are a major cause for concern, given that the national policy is for inpatient treatment of the most infectious TB cases and that current laboratory techniques take months to identify MDR-TB. As shown in Table 4 above, at any point one in three hospitalized TB patients may have undetected MDR-TB. With weak infection control and delayed detection of MDR-TB, TB hospitals are likely to be important sites of MDR-TB transmission.

Two coordinating mechanisms for infection control function at the national level: an NTP working group for TB infection control coordinated by the Ministry of Health and a national working group for nosocomial infections coordinated by the Centre for Preventive Medicine. Both working groups have developed relevant materials (national guidelines for infection control) that have been disseminated via the epidemiology service of the Ministry of Health and are beginning to be implemented.

These guidelines are also the basis for development of an infection control plan in TB units. Most units visited have an infection control plan approved by internal regulation and an infection control committee. Some have a staff member dedicated to infection control activities, but this position is not remunerated and in some cases the responsible person is not involved in the practical aspects of infection control. For units with more than 300 beds the law states that an epidemiologist should be employed, but for smaller units someone on the staff has to be identified and empowered to implement infection control activities. Staff training in infection control is routinely provided for doctors, but it needs to be extended to nurses and technical staff. In 2008 the Ministry of Health adopted an order authorizing 2% of the epidemiology service budget to be designated for infection control activities.

TGF particularly supports engagement of civil society, advocacy and communication activities in TB infection control: educational materials have been developed, media materials are being created and some communitarian centres offering counselling to TB patients will begin work in 2010. Patients are offered information through educational materials (most of them developed by Centre for Health Policies and Studies with TGF grant financing) and educational support from doctors, psychologists and nurses.

Several operational research activities have been organized in the field of TB (including a laboratory analysis focused on the transmission of MDR-TB germs inside hospitals). According to the study results, cases of re-infection of TB patients with MDR-TB strains (nosocomial infection phenomenon) were found in some hospitals. The NTP has proposed different research activities focused on the epidemiological survey of nosocomial transmission of TB.

Extensive identification of TB suspects is undertaken by family doctors trained in TB management. Microscopy is widely used to identify TB cases and an algorithm of identification is in place. The NTP intends to intensify activities based on the examination of risk categories and to revise the diagnostic algorithm by extended use of rapid culture tests.

TB suspects identified during triage in ambulatory settings are not routinely isolated, unlike smear-positive patients, who are hospitalized. However, smear-positive and smear-negative patients are not sufficiently separated in most hospitals and inpatient settings. No isolation rooms are available for patients with unknown bacteriological status until results are available. Identified MDR-TB cases are separated, those patients included in the PMDT initiative being hospitalized in special departments. However, there is no clear policy for MDR-TB patients not included in the PMDT initiative, as they can be hospitalized in regular TB departments.

In high-risk areas such as bronchology departments and MDR-TB surgery areas, guidelines for procedures need to be revised, since these procedures are only performed on selected cases.

Natural ventilation is widely used in most ambulatory settings and in some inpatient settings. Mechanical ventilation is available in most inpatient settings for MDR-TB patients (four of the five facilities) and in the three reference laboratories, but in most cases the systems are not functioning adequately and maintenance is not performed on a regular basis. There is great need for refurbishment of the ventilation systems (especially in the Municipal TB Hospitals in Chisinau and Balti, the Institute of Phthisiopneumology and the laboratories) to prevent problems such as positive pressure in patients' rooms, negative pressure in the staff area and noisy systems that cannot be used continuously. A new building for MDR-TB cases being constructed in Bender must be equipped with an adequate ventilation system.

Ultraviolet light is widely used in the Republic of Moldova, but only with unshielded flexures, which are not as convenient as shielded ultraviolet lights; these have many advantages as they can be used with several people in the room, and their efficacy is proved.

Respirators are available in all TB units and are used during contact with patients and high-risk procedures, but are not always adequate models; masks are not tested

to ensure that they fit correctly. The policy on visitors to MDR-TB departments does not allow them access to the patients' area. In selected cases where patients cannot be moved to meeting areas (usually placed outside), visitors must be allowed inside the MDR-TB department, but only with respirators.

Surgical masks are available and are used by patients when leaving rooms and by staff members entering patients' rooms.

Suggested areas for action

- Policies should be developed and implemented to move TB treatment from hospitals to ambulatory settings, and to redirect resources accordingly.
- The Ministry of Health should urgently consider options for changing the payment mechanism for hospitals to minimize unnecessary inpatient stay and improve efficiency. This could be addressed by shifting to “per day” financing of hospitals. An alternative could include adjusted case payment based on DOTS categories.
- All TB-related services (including all departments, social services, PHC, penitentiaries) should be protected from cuts resulting from the economic crisis.
- The Ministry of Health should consider re-introducing financial incentives for early detection/successful treatment at the PHC level. Similarly, the relevant ministries should consider revising benefit packages for penitentiary staff.
- Options to complement such incentives with additional direct incentives to patients to improve compliance with treatment should be reviewed, coupled with “social status protection” of TB patients and their families.
- Smear-positive patients, when requiring admission to hospital or prison, should be regarded as potential MDR-TB patients and be kept isolated in separate rooms until either DST or the result of a rapid molecular-based test has proven otherwise.
- In the interim before rapid molecular-based tests are universally available, patients with DST pending should be segregated from those already documented as having susceptible disease and responding to therapy. HIV status and prior treatment history should also be considered when developing policies for segregation within TB hospital wards.
- A policy on placing all MDR-TB patients within MDR-TB units (with single rooms for HIV-positive MDR-TB and XDR-TB patients) should be developed.
- The Ministry of Health should review options to develop a hospice service for failed treatment cases with a focus on patient-centred care.
- Using the new national infection control guidelines, the status of infection control in the most important TB facilities, including MDR-TB wards, should be assessed and improved.
- A national infection control plan should be developed and the TB units supported to develop specific infection control plans.

- Triage of TB suspects must be performed routinely. Protective materials (such as tissues and surgical masks) must be given to coughers in crowded areas of medical units.
- Educational materials should be used frequently and visibly (hung on the walls) in all units.
- Measures should be taken to rehabilitate the infrastructure for TB inpatient care with a view to improving infection control.
- Maintenance of the existing ventilation systems in hospitals should be considered.
- Additional infection control measures (such as ventilation and respirators) should be added to the administrative guidelines in high-risk areas (including bronchology departments and MDR-TB surgery areas).
- Respiratory protection programmes for high-risk staff should be sustained, including training, fitness testing, and procurement of respirators.
- The recommendation to use shielded ultraviolet light in medium- and high-risk TB transmission areas should be considered.
- Staff training in infection control measures should be continued and expanded.
- WHO should continue to provide technical assistance for infection control to the NTP in the Republic of Moldova.

4. ENGAGE ALL CARE PROVIDERS

This section covers prisons, a key provider of TB services in the Republic of Moldova outside the NTP.

Strengths and remaining gaps

The penitentiary system of the Republic of Moldova was established by decree 1036-XIII on 17 December 1996. The system consists of five isolation wards in pretrial detention facilities, two penitentiary hospitals and eleven prisons. The total capacity of the penitentiaries is 10 570 detainees; as of 1 January 2007 they contained 9042 detainees (85.5%). Through penal reform and the introduction of alternative forms of punishment the number of detainees decreased to 6830 (65%) in January 2009.

Provision of medical and TB care to detainees is regulated by a number of laws, bylaws and regulatory acts, including agreements between the Ministries of Health and Justice, and between the health division of the Ministry of Justice and Carlux. Outside Transnistria, DOTS and the PMDT initiative are well implemented in penitentiary services, and there is close collaboration between prisons, pretrial detention facilities and civilian health services on continuity of care (involving patient transfer).

The health division of the Ministry of Justice is responsible for health care in the penitentiary system, including staff health care. The health division comprises two

units: the health unit/military medical commission and the organizational and preventive medicine unit, which comprises nine staff representing different health fields including phthysiology, psychiatry, surgery, epidemiology and pharmacy.

A pilot project to implement DOTS in prisons was started in 2001, supported by international partners. The project was first launched in prison hospitals and expanded across the penitentiary system nationwide from the end of 2004. The NTP has a supporting role in TB control in the prison system, providing TB drugs and supplies under a Global Drug Facility grant, external quality assurance for sputum smear examination, microscopy, culture and DST services for prisoners and clinical guidance in complicated cases. The number of patients with active TB registered in penitentiary institutions fell during 2005–2008 (see Table 7).

Table 7.

Number of TB cases registered in the penitentiary system in 2005–2008

Category	2005	2006	2007	2008
New smear-positive	129	108	71	38
New smear-negative	187	195	153	110
New extrapulmonary	17	13	6	3
TB other			3	2
Relapse smear-positive	103	82	82	44
Relapse smear-negative	88	99	91	48
Readmitted extrapulmonary	0		1	0
After default smear-positive	7	14	28	15
After default smear-negative	4	4	10	18
Transferred in smear-positive	77	75		8
Transferred in smear-negative	52	69		1
After failure	89	37	61	59
Chronic	110	95	76	17
Total	863	789	582	363

Source: NTP data, 2008.

The number of TB patients in prisons reached a peak in 2003–2004 before DOTS coverage was extended; thereafter a decreasing trend is observed, and by 2009 the number had fallen to 307 prisoners with active TB among a prison population of 6523. The prevalence of all TB cases in prison in 2005 was 2777/100 000 population (while in the country as a whole the prevalence was 149/100 000) and in 2008 it decreased to 1754/100 000 (while in the country as a whole prevalence remained almost the same at 148/100 000).

Case detection policy in the penitentiary system is based mainly on radiographic investigation. Everyone entering the system undergoes a chest X-ray examination as entry screening, as well as a general medical examination. TB suspects are isolated

in quarantine for further investigation. Remarkably, well-established entry screening allowed identification of 20% of TB cases in 2006 and 2007.

All prisoners are also checked by fluorography for mass population screening every six months. In May 2009, of 4051 prisoners, (99.2% of the prison population) were screened by X-ray during mass screening, and only 33 (0.8%) detainees refused. 49 new TB cases were identified, which is 1.2% of the population screened. Screening for TB takes place regularly in the penitentiary system but there is no register to monitor the procedure; this should be introduced to avoid duplication or loss of cases. At the time of the mission there was only one mobile microradiography unit in the penitentiary system, which was produced in 1962, but a new digital unit was planned to be purchased with TGF funds by the end of 2009.

Treatment regimens in the penitentiary system of the Republic of Moldova correspond to WHO recommendations, with no deviations found. Treatment success increased from 58% in 2006 to 62% in 2007, but is still below the WHO target rate. Treatment success rates in the penitentiary system are similar to those in the civilian sector, notably with a high failure rate (14.1% failure among new sputum smear pulmonary patients) and a high default rate (7% default: mostly patients who refuse treatment) in the 2007 cohort. The full course of treatment is carried out under the supervision of a phthisiologist and nurses; they also conduct initial and final evaluations. Psychologists are not available to support patients and improve their adherence.

There are three laboratories in the penitentiary system for sputum microscopy. Culture examinations and DST are carried out by the Ministry of Health at Vorniceni laboratory. The penitentiary system does not purchase drugs; detainees are provided with high-quality anti-TB drugs according to the general distribution plan of the NTP, and depend on TGF sources. During the review no stockouts or shortages of drugs were found.

The recording and reporting system is adapted from WHO recommendations with minor modifications. The phthisiologist from the penitentiary system presents reports to the Institute of Phthisiopneumology and the NTP, in compliance with the general requirements. SIME-TB has been used since 2006 to enable rapid verification of declared cases and maximum transparency within the penitentiary system. In view of the specific nature of penitentiary institutions, only the health division is connected to the Internet.

Since 2006, the PMDT pilot project has been implemented for MDR-TB treatment. Written consent from the patient is an obligatory condition for inclusion in second-line treatment. In total, 95 patients have been enrolled in the treatment. It is worth noting that Carlux provides monthly food packages (of around US\$ 30) to all MDR-TB patients.

Information concerning released detainees with TB is transferred to the civilian sector via different channels including SIME-TB, presentation of medical documents to the Institute of Phthisiopneumology and rechecking detainees' domiciles. In 2006, 170 of the 2001 released prisoners had TB; in 2008, 95 of the 2709 released prisoners were TB patients. Unfortunately, not all prisoners complete their treatment once released: Carlux and KNCV Tuberculosis Foundation have worked closely with the Ministries of Justice and Health to improve the continuum of care, but 60% of those released still

abandon treatment or fail to visit the doctor. From 2009 a Carlux project, financed by TGF, has reinitiated provision of social support and incentives for TB patients released from prisons to increase treatment adherence, and preliminary results are positive.

Since 2004 all patients tested for TB have also been tested for HIV, and since 2007 TB tests have been performed every six months. Examination coverage was 98% in 2007 and 97.6% in 2008. Thanks to the regular checks, 19 new HIV cases were identified in the penitentiary system in 2007, and 15 new HIV cases were diagnosed in 2008. Nearly 50% of primary cases of HIV+ have been identified in connection with TB. Despite the falling number of TB cases overall, the proportion of TB/HIV coinfection is on the rise – 6.3% in 2007 vs. 10.2% in 2008.

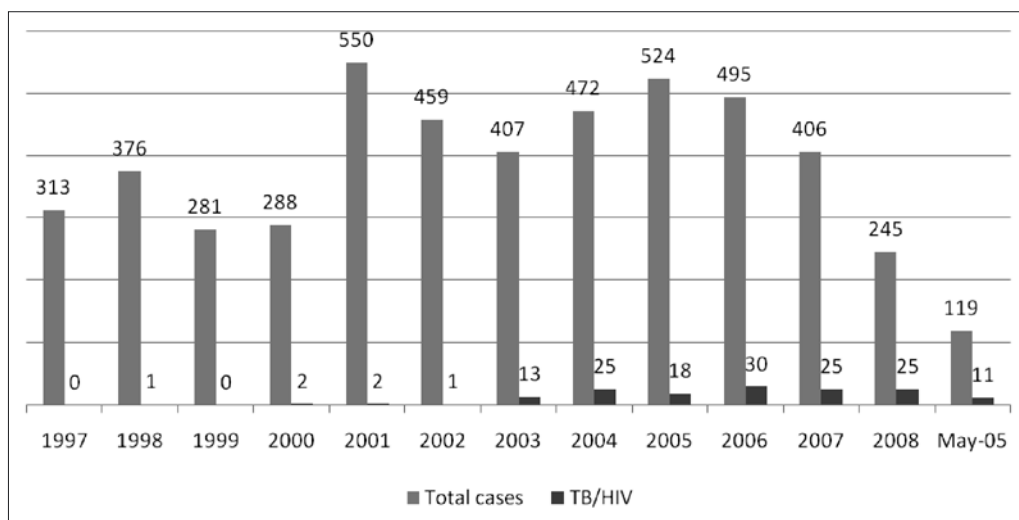


Fig. 6. TB and TB/HIV (all) coinfection in detainees
Source: Health Unit, Department for Prison Facilities, Ministry of Justice, 2009

Penitentiary services in Transnistria are not accessible to the prison health authorities of the Republic of Moldova; the link between civilian and penitentiary services is also weak in Transnistria. The mission team visited prisons in both the Republic of Moldova and Transnistria and found TB services in Transnistria greatly inferior and in need of significant improvement.

The prison population in Transnistria is around 3500, housed in six penitentiary institutions: two pretrial detention facilities and four prisons. Medical personnel include 24 doctors (19 female and 5 male doctors) and 44 nurses. The prison medical staff are unmotivated and overloaded and their salaries are low, which is the main reason for the shortage of professional staff.

Entry screening and mass screening are established, but not performed regularly; intermittent screening of inmates has not been not introduced. Mass screening takes five to six months and no documentation exists to register the results. Screening is based on radiography/fluorography, but X-ray equipment is 50 years old and of very low quality.

The Transnistria penitentiary system reports a 70% treatment success rate but this figure is not reliable. Second-line TB treatment is not available.

The recording and reporting system is not well organized: old TB recording and reporting forms are still in use, while the civilian sector introduced new forms some years earlier. One person is assigned to entering data in SIME-TB, but it is not done adequately. There are many discrepancies between the manual TB forms and the data entered, which cause many problems, including misinterpretation of correct data.

TB infection control measures are not in place. No respirators or masks are used by either medical personnel or patients; no ultraviolet lamps or mechanical ventilation systems are functioning.

Early diagnosis and treatment of MDR-TB is not available in prisons in Transnistria. HIV testing does not take place regularly; only 64% of TB patients were tested for HIV.

Drug management is poor. During the mission visit a shortage of first-line drugs was observed and no action had been taken. After mission members became involved the prison doctor managed to borrow a certain amount of drugs from another institution while awaiting a drug delivery from Chisinau.

Suggested areas for action

- Further technical assistance should be provided to penitentiary services (especially in Transnistria) in collaboration with Carlux, KNCV Tuberculosis Foundation, the Ministry of Justice and the NTP.
- A special screening register should be introduced to monitor case detection procedures in order to avoid the duplication or loss of cases.
- TB infection control needs to be improved in penitentiary services (including assessment and improvement of administrative, environmental and personal protection measures).
- The health authorities in Transnistria should urgently address the irregular supply of anti-TB drugs from civilian health services to prisons.
- The prison health authorities in Transnistria should ensure timely diagnosis and treatment of MDR-TB patients in prisons.
- Carlux and KNCV Tuberculosis Foundation should proceed with improving continuity of care across civilian and penitentiary services, involving laboratory services in prisons in the countrywide external quality assurance system.
- The Ministry of Justice should introduce rapid molecular-based diagnosis of MDR-TB in penitentiary services.
- The Ministry of Justice should ensure that treatment outcomes of released TB patients are recorded in the first centre where the patient is registered.

5. EMPOWER PEOPLE WITH TB AND COMMUNITIES

Strengths and remaining gaps

The Republic of Moldova is a country experiencing a massive emigration phenomenon among its citizens: an estimated 25% of the adult population is working in other countries, and in 2008 as many as 335 600 Moldovan citizens had moved abroad for work or to seek work. The existing SIME-TB database captures data on migration, but information is not recorded regarding destination countries, time spent abroad, labour sector, and so on. Migration is perceived as a significant problem related to TB treatment defaulting.

Approximately one-third of Moldovan migrants reside illegally in their host countries. Illegal residence status seems to have become more widespread among Moldovan migrants in the Commonwealth of Independent States, while the situation has improved in the European Union and other host countries.

High levels of migration (legal and illegal), underlying vulnerabilities, poor access to services by migrants and marginalized populations, as well as limited coordination with other countries on TB control services, are likely to be significant drivers of the TB epidemic. There is significant stigma around TB in the Roma community, and difficulty ensuring continuity of care when the community migrates.

While there is an urgent need for treatment support to prevent defaulting, the mission team observed no community care models. However, the country's Round 9 application to the TGF includes involvement of NGOs in TB care, which will positively contribute to empowering people with TB and communities.

Suggested areas for action

- The existing database should be used to map places of origin and destinations of TB cases among former migrants.
- Social support should be provided to labour migrants with TB, regardless of their health insurance status.
- Qualitative and quantitative studies should be conducted to identify causes of TB treatment default among labour migrants.
- An Immigration Resources Centres should be established to provide health promotion information on TB/HIV coinfection and on the risks of irregular migration, especially in certain destination countries, involving affected communities (such as migrants and Roma communities).
- The role of pre-departure or post-arrival health assessments for migrants should be evaluated.
- Epidemiological studies should be conducted to evaluate the contribution of migrants to transmission of TB in the Republic of Moldova.
- The Ministry of Health should commission a study to inform and review policy options for increasing incentives for patients to stay in the Republic of Moldova and complete treatment.
- The Ministry of Health should consider options to make health services more

flexible for TB patients, particularly in migrant populations.

- The Republic of Moldova should review options for promoting bilateral agreements with destination countries for migrants.

6. ENABLE AND PROMOTE RESEARCH

Areas of the NTP that could be informed and improved by operational research are described in the individual sections above.

CONCLUSIONS

The Republic of Moldova faces both serious challenges and important opportunities. Detecting 48% of the estimated incident cases and enrolling 50% of those detected means that the PMDT initiative is effectively treating one-quarter of the national burden of 2200 MDR-TB cases arising each year. The Republic of Moldova's challenge is to detect and treat the other three-quarters (1678 MDR-TB cases per year), so that they do not spread these deadly strains or die of MDR-TB. Other challenges include strengthening basic DOTS and infection control to prevent the development and spread of MDR-TB.

With strong leadership and vision, the Republic of Moldova has built the foundation to be able to take advantage of some key opportunities, such as new rapid molecular-based laboratory tests to detect MDR-TB. The Republic of Moldova should take the opportunity to develop and implement a plan for rapid scale-up to universal access to MDR-TB detection and treatment. This will help to mobilize the necessary resources for an effective response to its MDR/XDR-TB epidemic.

Investing today will protect future generations, and will be more cost-effective than waiting until its MDR-TB epidemic is even larger, and the strains even more resistant. Effectively addressing the MDR-TB epidemic will keep TB curable. Given the major emigration phenomenon from the Republic of Moldova to other countries, the WHO European Region also stands to benefit from the country's success, and will be able to learn from the Republic of Moldova's experiences and innovations.

ANNEX 1

DETAILS OF THE JOINT TB INFECTION CONTROL MISSION,
7–11 SEPTEMBER AND 22–28 NOVEMBER 2009

Mission team members

International experts

- Nicolas Cantau, Portfolio Manager for the Republic of Moldova, TGF
- Dato Chorgoliani, KNCV Tuberculosis Foundation
- Andrei Dadu, WHO Regional Office for Europe, Copenhagen
- Masoud Dara, KNCV Tuberculosis Foundation
- Dr Lucica Ditiu, WHO Regional Office for Europe, Copenhagen: Team Leader
- Christopher Gilpin, International Organization for Migration
- Cristian Popa, Infection Control Consultant
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- Maria Skarphedinsdottir, WHO Regional Office for Europe, Copenhagen
- Soren Thybo, Green Light Committee Consultant

Local experts

- Valeriu Crudu, Head of the TB Microbiology and Morphology Department, National TB Institute
- Vasile Degtariov, TB specialist, National TB Institute
- Svetlana Doltu, TB specialist, Health Unit of the Department for Prison Facilities, Ministry of Justice
- Liliana Domete, Head of Outpatient Consultations Department, National TB Institute
- Stefan Gheorghita, Deputy Director of the National Centre for Public Health, Director of the National AIDS Centre
- Constantin Iavorschi, Acting Director of the National TB Institute
- Nicolae Moraru, Head of the National TB Reference Laboratory, Chisinau
- Nicolae Nalivaico, Deputy Director, National TB Institute
- Dumitru Sain, NTP Manager, National TB Institute
- Otilia Scutelnicuic, Head of the Monitoring and Evaluation Unit for National Programmes, National Centre for Health Management

- Rita Seicas, Drug Management Consultant, TGF Project Coordination Unit
- Aliona Serbulenco, Head of the Public Health Policy Division, Ministry of Health

Objectives

The objectives of the mission were:

- to carry out a comprehensive analysis of the components and technical areas of the NTP at the national and peripheral/facility levels;
- to identify – in cooperation with national counterparts – challenges and recommend possible interventions for progress towards reaching the TB control targets for the Republic of Moldova;
- to identify possible areas of future collaboration between the NTP, the WHO Regional Office for Europe and all partners in the area of control and prevention of TB.

Technical areas

Technical areas analysed by the mission included:

- management of the NTP and links with the national health system;
- TB surveillance, including drug resistance surveillance;
- TB diagnosis;
- TB and MDR-TB case management;
- TB control in high-risk groups such as prisoners, children, the Roma population and people living with HIV/AIDS;
- infection control.

Sites visited

The mission conducted visits to the following locations:

- Buiucani Territorial Medical Association Outpatient Department, district of Buiucani, municipality of Chisinau;
- Ocnita district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;
- Centru Territorial Medical Association Outpatient Department, district of Centru, municipality of Chisinau;
- Pretrial Detention Facility, Municipal TB Hospital, municipality of Balti;
- Regional TB Reference Laboratory, Bender;
- Cahul district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;
- Comrat district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;

- Nisporeni district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;
- Pruncul Prison Hospital no. 16;
- Rezina district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;
- Soldanesti district, meeting local public authorities representing the TB department, PHC providers, the National Centre for Preventive Medicine, the health centre;
- National TB Institute, Chisinau;
- Penitentiary Facility no. 1, Transnistria;
- Vorniceni TB Hospital (MDR-TB department, regional reference laboratory), district of Straseni.

ANNEX 2

ABBREVIATIONS AND ACRONYMS

Carlux	Caritas Luxembourg NGO
DOTS	Directly observed treatment, short-course: the internationally recommended strategy for TB control
DST	Drug susceptibility testing
MDR-TB	Multidrug-resistant TB
NGO	Nongovernmental organization
NTP	National TB Programme
PHC	Primary health care
PMDT	Programmatic management of drug-resistant TB
SIME-TB	A case-based TB surveillance information system
TB	Tuberculosis
TGF	The Global Fund to Fight AIDS, TB and Malaria
XDR-TB	Extensively drug-resistant TB