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Review of tuberculosis prevention and care services in Kyrgyzstan 30 June – 5 July 2014 Mission report

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Abstract

Kyrgyzstan is one of 27 countries in the world with a high burden of multidrug-resistant tuberculosis and is among the 18 high-priority countries for tuberculosis (TB) in the WHO European Region. At the request of the Minister of Health of Kyrgyzstan, received in April 2014, the tuberculosis and multidrug- and extensively drug-resistant tuberculosis programme of the WHO Regional Office for Europe, working with the WHO country office in Kyrgyzstan and in collaboration with the national TB control programme, conducted a midterm programme review of TB prevention, control and care activities. The review was conducted between 30 June and 5 July 2014 by a team of 10 international experts from bodies including the Green Light Committee and the Global Drug Facility and observers from the Global Fund to Fight AIDS, Tuberculosis and Malaria. The review provides valuable information and recommendations for planning the programmatic management of TB and multidrug- and extensively drug-resistant TB in the country.

Keywords

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Executive summary

Kyrgyzstan is one of 27 countries in the world with a high burden of multidrug-resistant tuberculosis (MDR-TB) and among the 18 high-priority countries for tuberculosis (TB) in the World Health Organization (WHO) European Region. At the request of the Minister of Health of Kyrgyzstan, the Tuberculosis and Multidrug- and Extensively Drug Resistant Tuberculosis programme of the WHO Regional Office for Europe, with the WHO Country Office in Kyrgyzstan and in collaboration with the national TB control programme (NTP) conducted a midterm programme review of TB prevention, control and care activities. The review was conducted on 30 June–5 July 2014. The last extensive TB programme review was conducted in 2010: in the meantime, the country has hosted several technical assistance missions by the WHO Regional Office for Europe and its partners, including the Green Light Committee (GLC) for the WHO European Region.

The WHO Country Office in Kyrgyzstan led the preparation and coordination of the review process in collaboration with WHO Regional Office for Europe, with the support of the Global Fund to Fight AIDS, TB and Malaria (Global Fund) and the United Nations Development Programme (UNDP). Before the programme review, an epidemiological review was conducted to assess the burden of TB in the country and evaluate the functionality of the TB recording and reporting system. The review team comprised 10 international experts including GLC, the Global Drug Facility (GDF) and observers from the Global Fund. All relevant technical reports, clinical protocols and guidelines, regulatory and national strategic documents, surveillance and epidemiological data were reviewed. The team visited inpatient and outpatient treatment facilities, laboratories, family medicine centres and paediatric hospitals in Bishkek City and Chui, Jalal-Abad and Osh oblasts. The team interviewed oblast (regional) TB coordinators, TB physicians, health-care staff and directors of medical facilities. They also met the staff of the Republican Centre for Medical Information, Sanitary Epidemiological Service (SES), Health Policy Analysis Centre, Mandatory Health Insurance Fund (MHIF) and Department of Strategic Planning and Department of Drug Procurement and Supply of the Ministry of Health. The review team members also met representatives of civil society organizations, international partners, and Country Coordination Mechanism members and Secretariat. In addition, the team visited a penitentiary system TB treatment facility.

TB prevention, control and care interventions were assessed based on the following relevant key areas of the terms of reference:

- strategic guidance and political commitment;
- drug-susceptible and drug-resistant TB;
- TB in prisons;
- TB monitoring and evaluation and surveillance;
- laboratory services;
- infection control;
- civil society engagement and advocacy, communication and social mobilization (ACSM);
- HIV-related TB;
- TB among children;
- health system strengthening, focusing on TB governance and funding;
- drug management.

Key findings

- Kyrgyzstan is among the countries with the highest TB burden (all forms) in the WHO European Region, with an estimated incidence of 141 (124–157) per 100 000 population, prevalence 217 (101–376) per 100 000 population and a death rate of 9.5

(9.3–9.8) per 100 000 population.[1] According to the latest available official WHO data, the prevalence of MDR-TB is 26% among new TB cases and 68% among previously treated TB cases.

- The latest treatment success rates reported by the NTP for new sputum-smear-positive patients and people with pulmonary TB undergoing retreatment are 78% and 56% respectively (2011 cohort).
- Since the previous programme review conducted in 2010, Kyrgyzstan has made significant progress in following and addressing the main recommendations, including those on MDR-TB, infection control and childhood TB.
- Political commitment is shown by recent and updated national policy documents such as the Den Sooluk National Health Reform Programme, which stress the importance of TB prevention and control in the country context.
- The national strategic plan for TB prevention and control is in the final stage of development.
- Diagnosis and treatment of TB and MDR-TB are conducted according to WHO recommendations, including restructuring of TB services and the priority given to ambulatory treatment and care.
- A full and comprehensive set of data recording and reporting forms was developed in accordance with international standards.
- An uninterrupted supply of quality-assured anti-TB medicines and drugs for management of adverse reactions has been maintained for the past two years, with funding from the Global Fund and other external donors.
- The Kyrgyz State Institute for Continuing Education and Kyrgyz State Medical Academy have introduced standard courses on TB infection control and risk assessment.
- The governance and management of the NTP have been further developed. There is intensive collaboration and coordination among stakeholders at all levels of the NTP. Recently the Ministry of Health assigned the coordination of the TB programme to the directors of the family medicine centres at oblast level.
- TB hospital rationalization is ongoing in accordance with Den Sooluk. According to information from NTP and the Ministry of Health, the number of TB beds was reduced by 312 in the past year and will be reduced by 400 in the near future.
- TB, MDR-TB and TB/HIV management have been successfully implemented in the penitentiary system.
- Collaborative TB and HIV activities have been established and nearly everyone with TB is tested for HIV in inpatient and outpatient treatment facilities; people living with HIV are screened for TB according to the protocol, and people suspected of having TB are examined according to the existing algorithm.
- There is a national ACSM strategy and 12 patient support groups established and functioning in four oblasts.
- The TB laboratory network and the structure for management of drug-resistant TB are being systematically strengthened (using all diagnostic tests).

Challenges

- The TB control programme is highly dependent on international donors, including the Global Fund. The share of the national budgetary contribution to TB prevention and control was approximately 60% in 2013.

[1] Global tuberculosis report 2013. Geneva: World Health Organization; 2013.

- The current funding level for the TB programme is not sufficient to scale up MDR-TB prevention and control activities fully or to achieve and sustainably maintain full MDR-TB control in the country.
- Despite comprehensive collection of data on health funding, managed by the MHIF, there is no comprehensive and public reporting on the funding of TB control to allow more efficient use and allocation of resources.
- High levels of drug-resistant TB: the overall number of diagnosed MDR-TB cases has increased from 806 in 2011 to 1160 in 2013.
- Ambulatory treatment in primary health care services is not functioning to its full potential. Not all primary health care institutions are equally prepared for providing outpatient treatment and care. There is room for better planning and creation of acceptable motivation packages to increase cooperation with TB services.
- According to NTP estimates, 1200–1400 people with M/XDR-TB need treatment in 2015, and a considerable gap in funding for second-line drugs is expected.
- Laboratory transport is available on a (bi-)weekly basis only in some oblasts and rayons (districts), jeopardizing the timely diagnosis of rifampicin-resistant TB and MDR-TB and maintenance of key equipment.
- Because the TB hospital infrastructure has a large capacity, current treatment practices are highly inefficient in terms of resource use and pose a serious threat in terms of nosocomial (hospital-acquired) transmission of TB.
- Social support for people with TB depends largely on donor support. The availability of funds from oblasts requires negotiations between the NTP and local authorities.
- TB among external migrants is not being adequately addressed. No cross-border TB control and care mechanism is in place.
- Despite some progress, children are still hospitalized for at least six months, with all the known implications. i.e. disruption of family life and schooling and exposure to transmission if infection control is inadequate.
- A patient-centred approach and social support services for people with TB and MDR-TB exist on only a very limited scale and lack standardization.

Key recommendations

- Further revise and update the national strategic plan for TB prevention and control by December 2014.
    - Include costing to reflect the incremental increase in (national) public expenditure on TB, the monitoring and evaluation plan and human resource development plan.
- Boost the application planning process for the Global Fund New Funding Model and start preparations for development of the concept note (submission date either 15 October 2014 or 15 January 2015).
- At the Government level, create a road map for the sustainability of TB services in Kyrgyzstan; use existing resources more efficiently and gradually increase the national budget for TB control.
- The master plan for optimizing TB hospital treatment and ambulatory treatment and care is a key element for the national TB strategy; WHO should assess this plan, particularly with regard to costing and budget (re)allocation and smooth transfer of human resources. If the plan does not ensure an uninterrupted supply of quality-assured anti-TB medicines after the end of the current donor-supported programmes, explore possibilities for gradual procurement of first-line and second-line TB drugs through the national budget; a transition plan should be developed for this.

- Accelerate the expansion of ambulatory treatment for people with TB, home-based care and day-care treatment, including all eligible people with TB, particularly those who are sputum smear-negative (as well as people with sputum smear-negative MDR-TB).
- Develop a budgeted implementation plan for patient-centred approaches, including social support for adherence to TB treatment based on the pilot results and involving community and civil society to the maximum possible extent.
- Expand the coverage of the electronic TB registry to the primary health care level (including the penitentiary system), developing and introducing further "laboratory" and "pharmacy" modules and also incorporating WHO-recommended TB surveillance standards and benchmarks into the existing monitoring and evaluation TB supervision and mentorship system.
- TB among migrants should be addressed more systematically, and sanatorium treatment practices for children should be further optimized (the latter measure aimed at further reducing the average duration of hospitalization).

Overview of key recommendations

Area	Action	Timeline	Responsible agency
1. Cross-cutting: strategic guidance and political commitment	Finalize revision of the national strategic plan for TB prevention and control.	At the latest one month before the submission date of the TB concept note (in 2014)	NTP
	Initiate an application planning process for the Global Fund New Funding Model and finalize preparations for developing the concept note.	In parallel with updating the national strategic plan and in accordance with the request of the Country Coordinating Mechanism on submission date of the concept note (see above)	NTP
2. Drug-susceptible TB	Maintain achievements in directly observed therapy (DOT) and ensure more active involvement of nurses at the primary health care level; expand patient support groups.	From November 2014	NTP, primary health care
	Expand further ambulatory care of people with sputum smear-negative results, including people with sputum smear-negative MDR-TB, expanding ambulatory treatment from pilot sites to all regions.	From November 2014	NTP, primary health care
	Increase the motivation of primary health care staff to deal with people with TB by improving training and feedback from TB coordinators.	From November 2014	NTP, primary health care
3. MDR-TB prevention and control	Continue mobilizing resources to ensure the sustainability of activities related to DR-TB, especially providing second-line drugs and covering an estimated gap in treatment for 527 people with MDR-TB, 24 people with XDR-TB and 266 people with pandrug-resistant TB per regimen (enrolment foreseen for 2015, to be chiefly covered by the Global Fund concept note).	From September 2014	NTP, Ministry of Health and partners

	Scale up second-line treatment for everyone diagnosed with MDR-TB in the civilian and prison sectors. Conduct training in management of MDR-TB: revise guidelines for PDR and XDR-TB management.	Beginning of 2015	Ministry of Health, NTP and SSEP under the Government of the Kyrgyz Republic
	Ensure that drug susceptibility testing to second-line drugs will be performed for everyone with any resistance to first-line drugs (including when rifampicin (R) resistance is discovered by Xpert MTB/RIF).	By end 2015	NTP, Ministry of Health
	Agree on and develop a treatment strategy for XDR-TB.	By June 2015	NTP, Ministry of Health
4. Migration and TB	Ensure the completion of intensive phase of treatment for external migrants before any potential deportation and continue health promotion activities targeting TB among migrant workers (and e.g. returnees from foreign countries).	From December 2014	Ministry of Health in collaboration with Ministry of Interior
5. TB and HIV collaborative activities	Develop joint work plan for TB and HIV activities; define indicators and develop a monitoring and evaluation plan.	By March 2015	NTP in collaboration with National AIDS Centre
	Establish regular meetings between responsible staff in both programmes; develop data exchange and a cross-checking mechanism.	From September 2014	NTP in collaboration with National AIDS Centre
	Engage nongovernmental and civil society organizations to ensure treatment adherence for people with TB in risk groups and develop a mechanism to ensure that further HIV treatment and care is maintained among people with both TB and HIV after hospital discharge.	From October 2014	NTP in collaboration with National AIDS Centre and partners
	Develop a plan for expanding integrated TB and HIV services with further integration into harm-reduction services.	By June 2015	Ministry of Health, NTP and National AIDS Centre
	Provide training sessions for practitioners, particularly at the primary health care level, to improve joint TB/HIV care further.	From January 2015	NTP in collaboration with National AIDS Centre
6. TB infection control	Clarify the roles of the central NTP, SES, primary health care and international nongovernmental organizations to allow implementation of TB infection control activities in a coordinated way at the national, oblast and local levels. For example, the SES carries out monitoring and evaluation, the central NTP carries out supportive supervision and international nongovernmental organizations continue building the capacity of SES and NTP.	From September 2014	NTP and Ministry of Health
	Establish a national-level Thematic Working Group on TB infection control as a part of the existing Coordination Committee on TB at the Ministry of Health.	From January 2015	Ministry of Health and partners

	Conduct a comprehensive review of infection control at the ambulatory care level (primary health care). As part of the review, develop a form to collect and systematize information about TB infection control at all facilities where people with TB are treated and use it for setting priorities.	From January 2015	NTP in collaboration with partners, USAID Quality Health Care Project and UNDP
7. Civil society engagement and ACSM for TB	Strengthen the ACSM Thematic Working Group in order to improve partner alignment and standardization and to support national strategic planning and monitoring of ACSM. Include (more) local nongovernmental organizations in the working group.	From September 2014	NTP, international nongovernmental organizations
	Consider giving local civil society organizations access to domestic funding to participate in the TB response through social procurement.	From September 2014	Ministry of Health
	Join forces to continue to address the main barriers to treatment access: stigma and discrimination and informal payments for TB treatment.	In accordance with the ACSM plan	Local and international civil society organizations, NTP, Ministry of Health
	Cost the ACSM operational plan and use impact indicators that are mentioned in the ACSM strategy document in addition to output or process indicators.	From October 2014	NTP
8. Contact investigation	Update skills and knowledge of primary health care physicians and nurses (especially through on-the-job training) to include TB contact tracing and adequate active case-finding strategies (including the roles and responsibilities of the TB and primary health care systems). Develop indicators to monitor and evaluate contact-tracing activities.	By July 2015	Ministry of Health, NTP, primary health care
9. TB laboratory	Further develop the national TB laboratory strategy and use it as a road map for reorganization of TB diagnostic services and for implementation of new diagnostic algorithms, new diagnostic tools, functional logistics, human resources capacity-building, maintenance, quality management, and reporting.	2016	Ministry of Health, NTP, National TB Reference Laboratory (NRL), supranational TB reference laboratory partner (SRL)
	Further strengthen the administrative management of the laboratory network by appointing a TB laboratory network commissioner under the the NTP, with a separate budget for TB laboratory services. Further develop the quality management system of the laboratory network, working towards ISO 15189:2013 accreditation.	By April 2016	NTP, NRL

	Increase capacities and availability of molecular tests in the country. Equip TB hospitals with GeneXpert machines. Perform Xpert MTB/Rif RIF tests on all newly hospitalized patients upon admission and immediately separate patients with rifampicin-resistant forms of TB.	From January 2016	NTP, NRL
	Reduce access time to rapid tests for all TB suspects to less than 72 hours by implementing a universal and countrywide logistical system for the transportation of specimens and reports which will operate daily.	From April 2016	NTP, NRL
10. Childhood TB	Critically review criteria for hospitalization to reduce hospital stays in accordance with WHO recommendations (i.e. discontinue practice of admission to sanatoriums for children with latent TB infection and non-infectious TB).	By June 2015	Ministry of Health, NTP
	Give priority to children who are contacts, as a high-risk group, in active case-finding (including at least quarterly symptomatic assessment and follow-up of children who are contacts of people with MDR-TB).	From December 2014	Ministry of Health, NTP
11. Monitoring and evaluation; surveillance	Discontinue the further application of outdated recording and reporting standards; endorse the set of recording and reporting forms aligned with international standards instead.	By end of 2015	NTP, oblast TB centres, National Centre for Medical Statistics, partners
	Incorporate new WHO-recommended TB surveillance standards and benchmarks into the existing supervision and mentorship system for monitoring and evaluation of TB.	By May 2015	As above
	Ensure that the national strategic plan contains realistic and measurable goal, outcome and output indicators and regularly report and measure progress against the targets. Disseminate the results of progress analysis among all stakeholders and use them for further informed planning and action.	By October 2014	Ministry of Health, NTP with partners
	Expand coverage of the electronic TB registry developed or adapted in the country to the primary health care level (including the penitentiary system), developing and introducing further “laboratory” and “pharmacy” modules.	By July 2015	Ministry of Health, National Centre for Medical Statistics, NTP with partners
12. Penitentiary sector	Improve inmate motivation and psychological care to decrease the rate of default and dropout from treatment.	By July 2015	Ministry of Health in collaboration with SSEP
	Review staffing and prepare plan for sustainability of services (including human resource aspects) after partners’ support comes to an end.	By June 2015	Ministry of Health in collaboration with SSEP

	Consider sharing the findings and recommendations of this review with SSEP via the Country Coordination Mechanism.	By March 2015	NTP through Country Coordination Mechanism Secretariat
13. Drug and supply chain management	Revise MDR-TB treatment regimens in line with drug susceptibility testing (DST) results for the injectable anti-TB drugs.	Immediately	Ministry of Health, NTP
	Place an order for procurement of second-line drugs.	By end August 2014	Ministry of Health, NTP, with UNDP
	Develop a brief plan for procurement of first-line drugs for adults and children.	By end 2014	Ministry of Health, NTP
	Develop a transition plan ensuring uninterrupted supply of quality-assured anti-TB medicines beyond 2015. Ensure that the plan is incorporated into the national TB control strategy and adequately costed.	By March 2015	Ministry of Health, NTP with partners
	Work with the Global Drug Facility and manufacturers to facilitate the registration of quality-assured anti-TB medicines and ensure the availability of international sources of these medicines when the country switches to Government-funded procurement.	By March 2015	NTP in collaboration with UNDP and partner(s)
	The drug management unit of the NTP should take full responsibility for implementation of endorsed standard operating procedures at all levels: it should unify and standardize the distribution system, recording and reporting forms, storage practices and supervision.	By end 2014	Ministry of Health, NTP and partners
14. TB governance and funding	Establish a merit-based organizational process for appointing and evaluating NTP managers. Use performance-based contracts and incentives, especially for the people involved in managing the NTP. This contract should be different from those relating to the other work performed for the National Centre of Phthisiatry and those of any other service provider.	By end 2015	Ministry of Health
	Strengthen NTP governance by applying results-based management methods.	By end 2015	NTP
	Establish a payment mechanism in primary care for TB services, enabling the savings from the reduced number of hospital beds to be used for incentives for the use of ambulatory services for TB control. Develop a transition plan for funding TB services and link to the master plan on the changes in the service delivery model (see also under point 1 above).	By end 2015	Ministry of Health
	Compile and consider regular publishing of a comprehensive TB-specific national account of expenditure on TB services.	By May 2015	Ministry of Health
	Regularly publish a comprehensive performance assessment of TB services.	By April 2015	Ministry of Health

Abbreviations and acronyms

ACSM	advocacy, communication and social mobilization
AMX/CL	amoxicillin/clavulanic acid
Cm	capreomycin
Cs	cycloserine
DOT	directly observed therapy
DOTS	directly observed therapy, short course – the basic package that underpins the WHO Stop TB Strategy
DR-TB	drug-resistant TB
DST	drug susceptibility testing
E	ethambutol
GDF	Global Drug Facility
GDP	gross domestic product
GIZ	Deutsche Gesellschaft für Internationale Zusammenarbeit (German international cooperation agency)
GLC	Green Light Committee
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
GMP	good manufacturing practices
H	isoniazid
IC	infection control
ICRC	International Committee of the Red Cross
ISO	International Organization for Standardization
KNCV	Netherlands TB Foundation
Lfx	levofloxacin
LJ	Lowenstein-Jensen medium
MDR-TB	multidrug-resistant TB (resistant to isoniazid and rifampicin)
MGIT	Mycobacteria Growth Indicator Tube
MHIF	Mandatory Health Insurance Fund
MSF	Médecins Sans Frontières
MTB	*Mycobacterium tuberculosis*
NCPh	National Centre of Phthisiatry
NRL	National Reference Laboratory
NTP	national tuberculosis control programme
PAS	*p*-salicylic acid
PDR-TB	polydrug-resistant tuberculosis
Pto	protionamide
R	rifampicin
S	streptomycin
SES	Sanitary Epidemiological Service
SIZO	pretrial detention centre
SRL	Supranational Reference Laboratory
SSEP	State Service for Execution of Punishments
TB	tuberculosis
TB-IC	TB infection control
UNDP	United Nations Development Programme
US$	United States dollar
USAID	United States Agency for International Development
UVGI	ultraviolet germicidal irradiation
WHO	World Health Organization
XDR-TB	extensively drug-resistant TB
Xpert MTB/RIF	cartridge-based automated diagnostic test to identify *Mycobacterium tuberculosis* DNA and resistance to rifampicin by nucleic acid amplification technique
Z	pyrazinamide

1. TB burden: mortality, incidence and prevalence

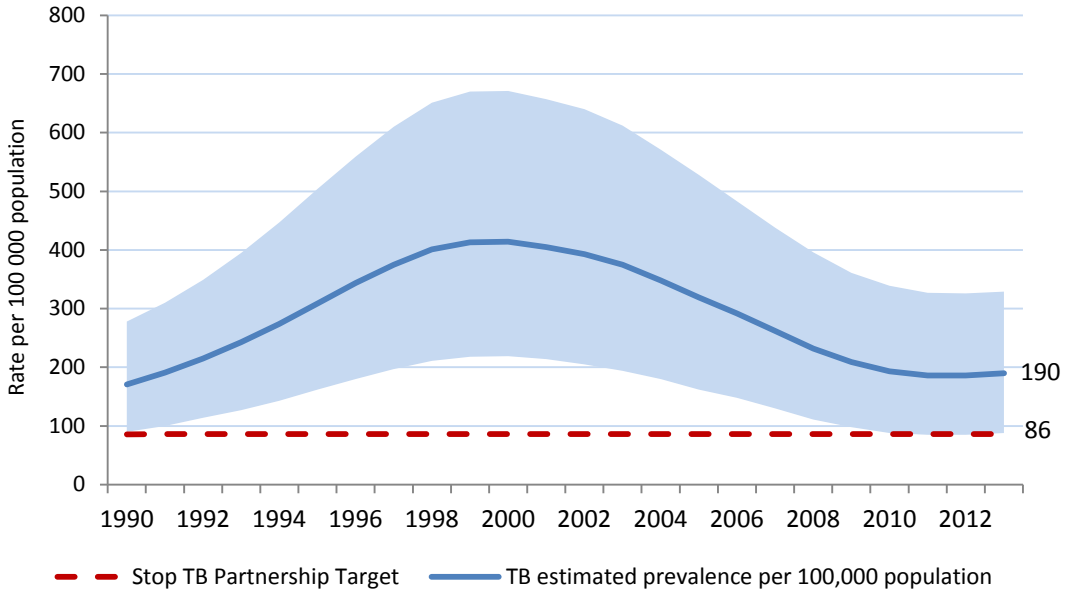
The estimated tuberculosis mortality for Kyrgyzstan is derived from National Statistical Committee data. Estimated TB mortality increased rapidly from 9.1 per 100 000 population in 1990, and peaked at 29 per 100 000 population in 2001. From 2002, the TB mortality rate gradually declined. By the end of 2013, estimated TB mortality was reported at 11 per 100 000, which is more than twice the Stop TB Partnership goal of halving TB mortality by 2015 compared with 1990 levels, which for Kyrgyzstan would be 4.5 per 100 000 (Fig. 1).

Fig. 1. Estimated TB mortality (excluding TB/HIV mortality) per 100 000 population, Kyrgyzstan, 1990–2013

Note: Shaded areas represent uncertainty band of WHO estimate of TB mortality. Horizontal dashed line represents Millennium Development Goal 6 target 8 of 50% reduction in prevalence by 2015 compared with 1990.
VRS = Vital Registration System.
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

In 2013, the estimated number of tuberculosis patients in Kyrgyzstan was 11 000 (range: 4900–18 000), equivalent to 190 (88–329) per 100 000 population. TB prevalence increased sharply between 1990 and 2000 and then gradually declined by an average of 6.4% annually. Nevertheless, the target of halving TB prevalence by 2015 compared with 1990 is probably not feasible (Fig. 2).

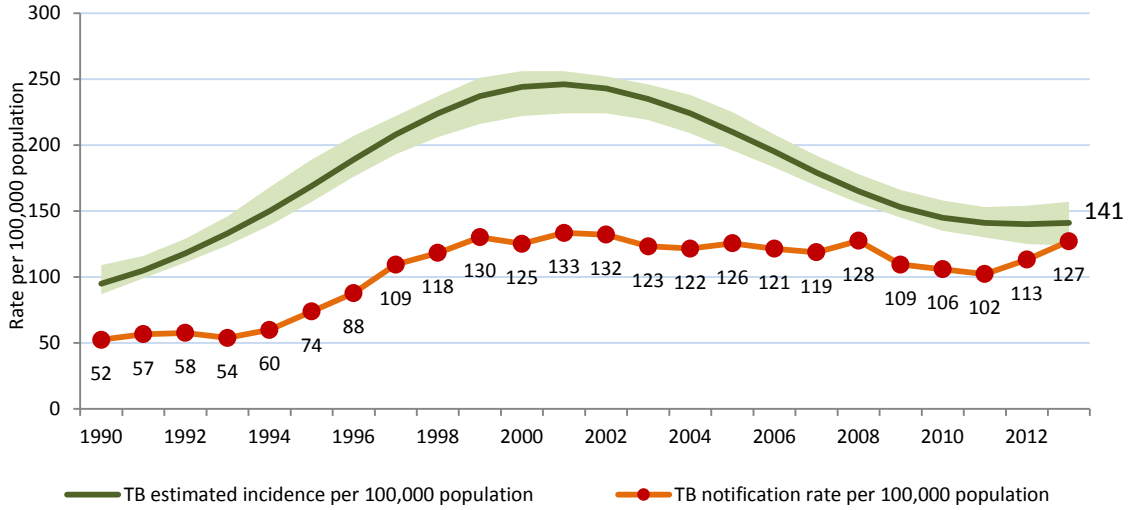
Fig. 2. Estimated TB prevalence per 100 000 population, Kyrgyzstan, 1990–2013



Note: Shaded areas represent uncertainty band. Horizontal dashed line represents Stop TB Partnership target of 50% reduction in prevalence by 2015 compared with 1990.
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

In 2013, there were an estimated 7800 incident cases of TB (uncertainty range 6900–8700), equivalent to a rate of 141 (124–157) per 100 000 population. TB incidence, following the same trend as TB mortality and prevalence, increased from 95 per 100 000 in 1990 to 246 in 2001. Then the trend was reversed and incidence since then has decreased by an average of 4.9% annually (Fig. 3).

Fig. 3. Estimated TB incidence and notification rates of incident TB cases (new and relapsed), Kyrgyzstan, 1990–2013



Note: Shaded areas represent uncertainty band.
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

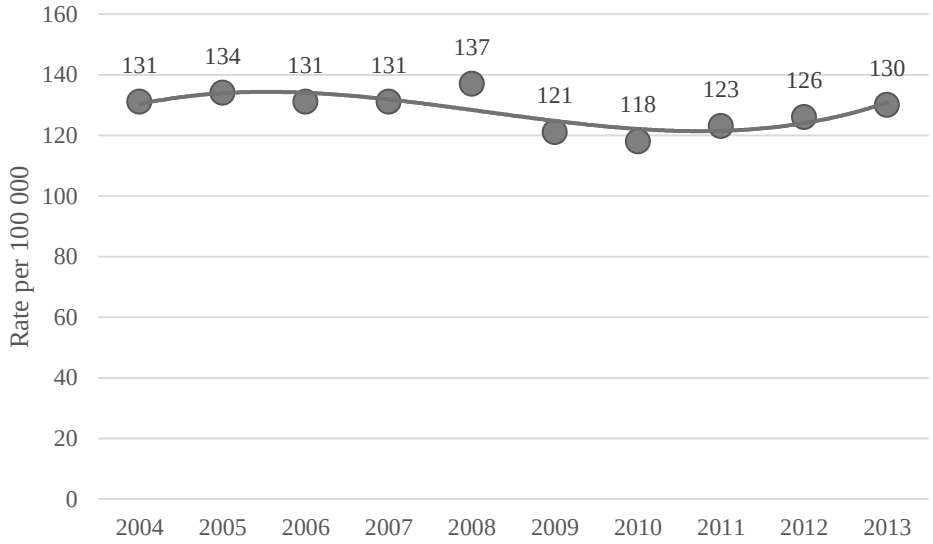
With the decreasing TB burden, the gap between TB notifications and estimated incidence rates has progressively reduced, indicating an improvement in the case-detection rate. In 2013, it was estimated that about 91% of TB cases are detected by the health-care system. The TB notification rate in 2013 was 127 per 100 000 population. The sharp increase in notifications of incident TB cases between 2012 and 2013 is related to the changeover to the revised recording and reporting framework

(classification of returned clinically diagnosed patients as “relapsed” who previously were “successfully treated”).

Trends in TB case notification

Over the last 10 years at the national level, the TB notification rate (all forms of TB) varied between 118 and 137 per 100 000 population, without any clear trend over time. In 2013, a total of 7209 tuberculosis cases were notified, equivalent to a notification rate of 130 per 100 000 (Fig. 4).

Fig. 4. TB notifications (all forms) per 100 000 population, with polynomial trend lines, Kyrgyzstan, 2004−2013



Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

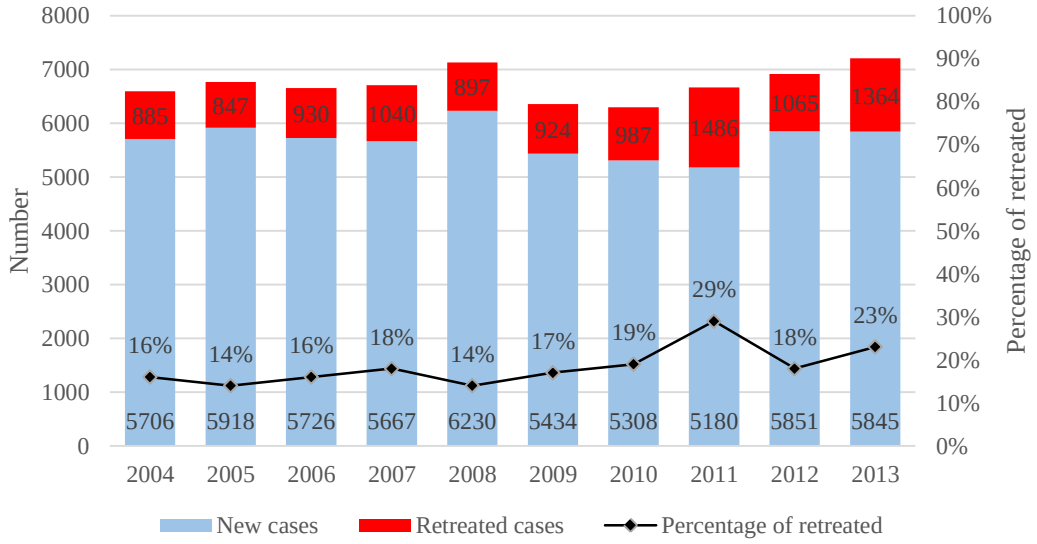
TB notifications by geographical distribution

At the province level, TB notification rates vary notably. The highest level of TB incident cases in 2013 was reported in Chui Province (144 per 100 000) followed by Bishkek City (131 per 100 000), while in Issyk-Kul and Jalal-Abad the TB notification rate was 79 and 89 per 100 000 population, respectively

TB notifications by previous history of disease

The proportion of retreated TB cases among notified all-TB cases varied over the last 10 years (14–29%), with sharp year-to-year fluctuations, especially over the last three years, indicating weaknesses in surveillance. In 2013, of the notified 7209 tuberculosis patients, 1364 (23%) had been previously treated (Fig. 5).

Fig. 5. Number of notified new and retreated TB cases and proportion of previously treated TB cases, Kyrgyzstan, 2004–2013

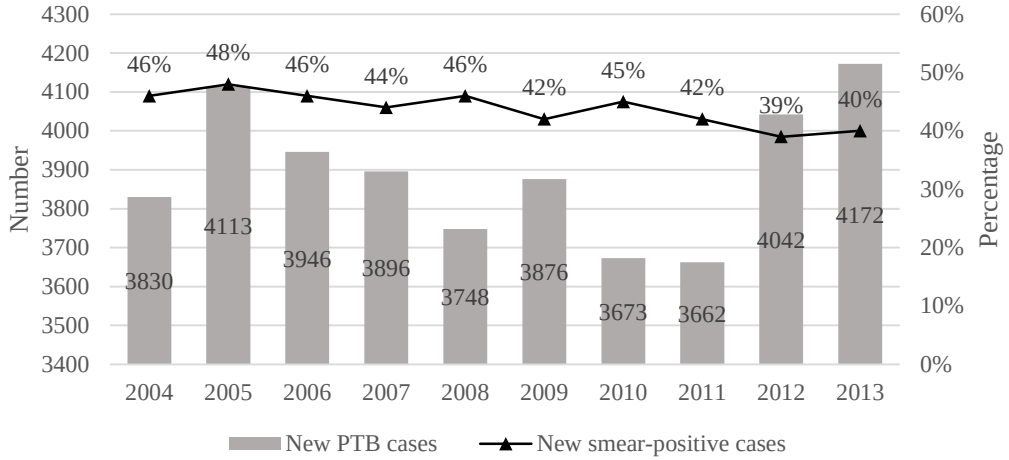


Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

Trends in TB notification by laboratory confirmation

The proportion of smear-positive pulmonary TB cases gradually decreased over the last 10 years, from 46% in 2004 to 40% in 2013; this is quite low compared with the regional average and indicates limited access to high-quality laboratory diagnostics. The proportion of bacteriologically confirmed cases among new pulmonary TB in 2013 (smear- or culture-positive or positive by WHO-recommended rapid diagnostics such as Xpert MTB/RIF) was only 41.1% (Fig. 6).

Fig. 6. Number of notified new pulmonary TB cases and proportion of smear-positive TB cases, Kyrgyzstan, 2004–2013

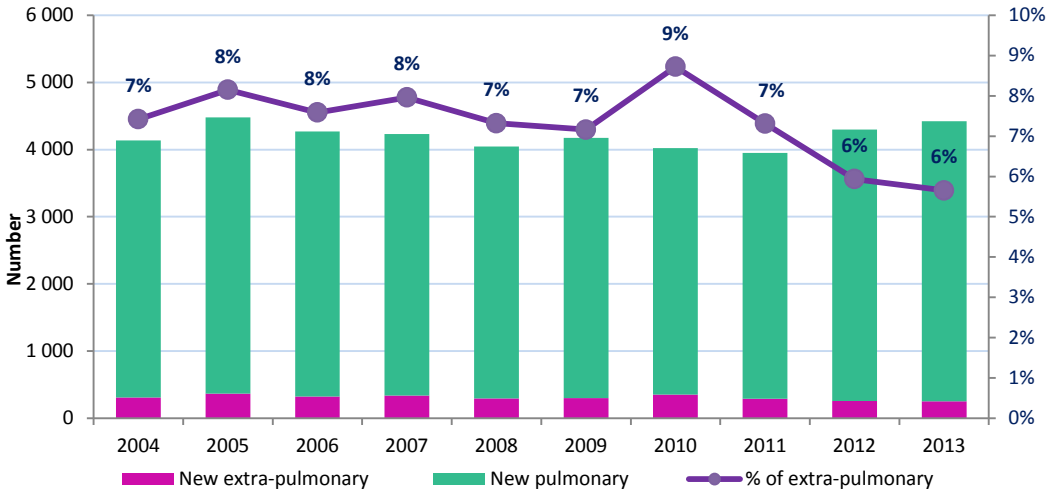


PTB = pulmonary TB
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

Trends in TB notification by site of disease

The proportion of extrapulmonary TB cases remained more or less constant over the last 10 years, varying between 6% and 9%, with a declining trend over the last three years. In 2013, the proportion of extrapulmonary TB cases among new cases was only 6%, which is one of the lowest rates in the region (Fig. 7).

Fig. 7. Number of notified new pulmonary and extrapulmonary TB cases and proportion of smear-positive TB cases, Kyrgyzstan, 2004–2013



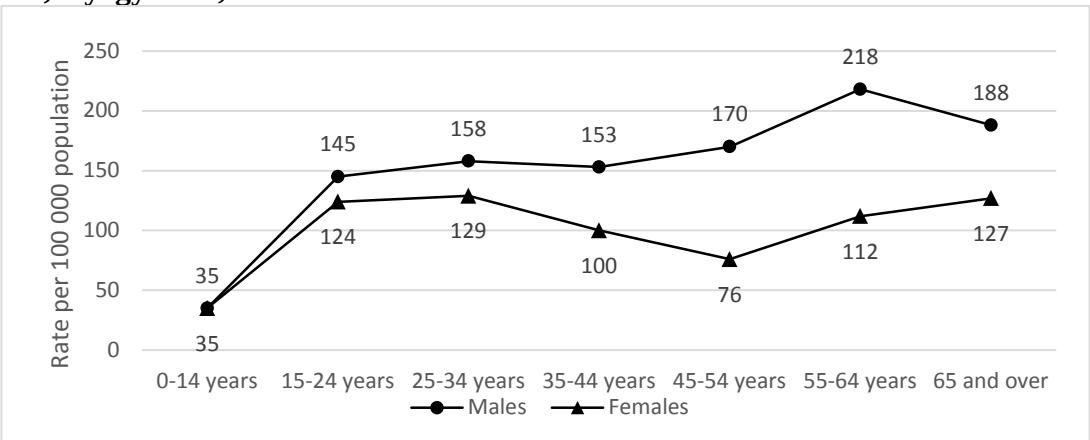
PTB = pulmonary TB
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

TB notifications by age and sex

The ratio of males to females among new and relapsed cases in 2013 was 1.3. The proportion of males over the last 10 years was constant, without notable variations over time. However, the risk of TB among male and female patients varies notably by age group. As expected, at a young age (up to 24 years), TB is almost evenly distributed between males and females. With increasing age, the male-to-female ratio increases, with a ratio of over 2.0 in the age group 45–54.

The age-specific notification rate among males increased with age. The highest age-specific TB notification rate is observed among the group aged 55-64, at 218 cases per 100 000 population. Among the female population, the highest risk of TB is clustered around two age groups: 15–34 (around 125 cases per 100 000) and 65 and over (Fig. 8).

Fig. 8. Pattern of age-specific notification rate of new and relapsed TB cases disaggregated by sex, Kyrgyzstan, 2013

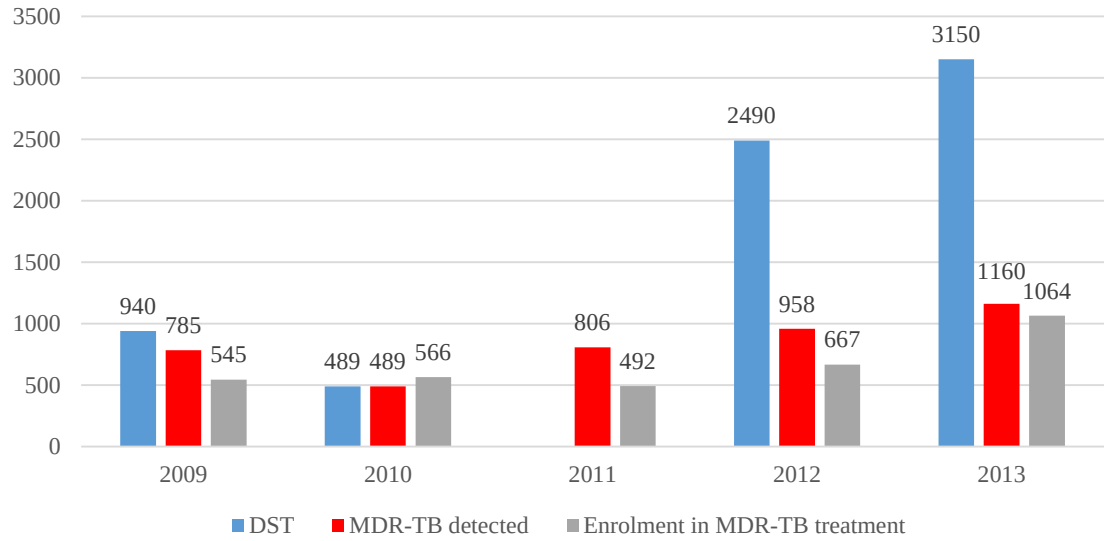


Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

Drug resistance surveillance

According to WHO estimates,[1] about 1800 (range: 1600–1900) multidrug-resistant TB (MDR-TB) cases are detected annually in Kyrgyzstan among all notified pulmonary TB cases. About one in four new pulmonary TB cases has MDR-TB. Among previously treated cases, the percentage of MDR-TB is 55%, which poses a substantial burden of TB control. Laboratory capacity to perform DST has substantially increased in recent years – in 2013 it was reported that a total of 3150 TB cases had DST results, which is over four times higher than the number of tests performed in 2009. In 2013, a total of 1160 MDR-TB cases were detected, which represents 73% of the estimated number of MDR-TB cases. See Fig. 9 and Fig. 10.

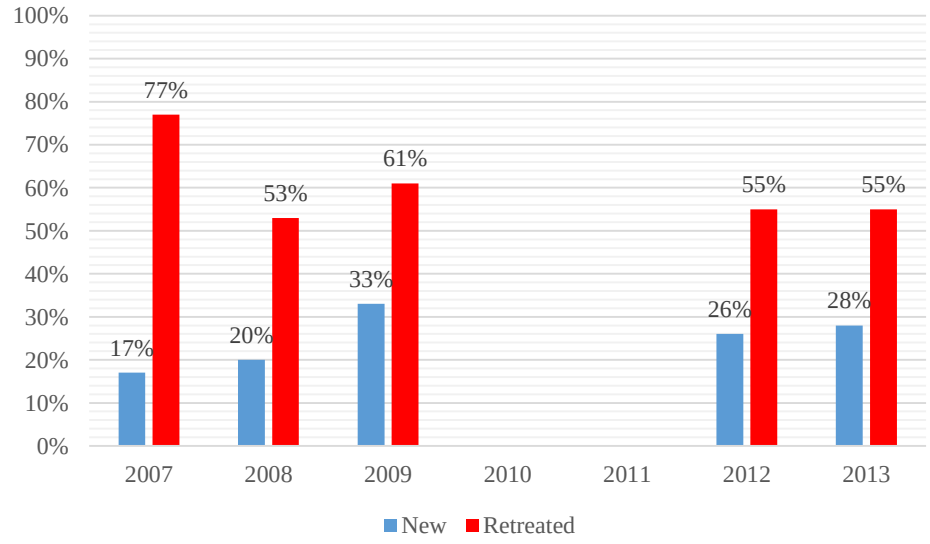
Fig. 9. Trend over time of total number of TB cases with DST results, MDR-TB cases detected and MDR-TB cases enrolled into second-line treatment programme, Kyrgyzstan, 2009–2013



DST = drug susceptibility testing
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

[1] Global Tuberculosis Report 2014: Key indicators for the WHO European Region. Copenhagen: WHO Regional Office for Europe; 2014 (http://www.who.int/tb/publications/global_report/indicators_european_region.pdf?ua=1, accessed 12 July 2015).

Fig. 10. Percentage of MDR-TB patients among new and previously treated pulmonary TB patients with DST results, Kyrgyzstan, 2007–2013

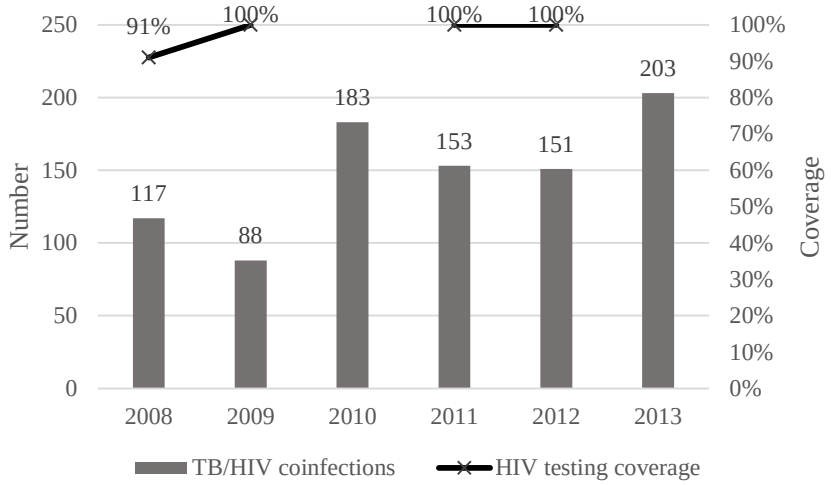


MDR-TB = multidrug-resistant TB DST = drug susceptibility testing
PTB = pulmonary TB
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

HIV surveillance among TB cases

Coverage of HIV testing is high, close to 100%. However, in 2013, Kyrgyzstan failed to report to the WHO Global TB Database the total number of TB cases with documented HIV test results, although it did report the total number of cases with HIV-positive test results. The estimated percentage of HIV cases among incident TB cases in 2013 was 3% (range 2.5–3.7). Among the notified cases, a total of 203 TB/HIV cases were detected. The number of TB/HIV coinfected cases fluctuates sharply from year to year: nevertheless, the percentage of TB/HIV coinfection over time is tending to increase (Fig. 11).

Fig. 11. Number of notified TB/HIV coinfections and HIV test coverage among notified TB patients, Kyrgyzstan, 2008–2013

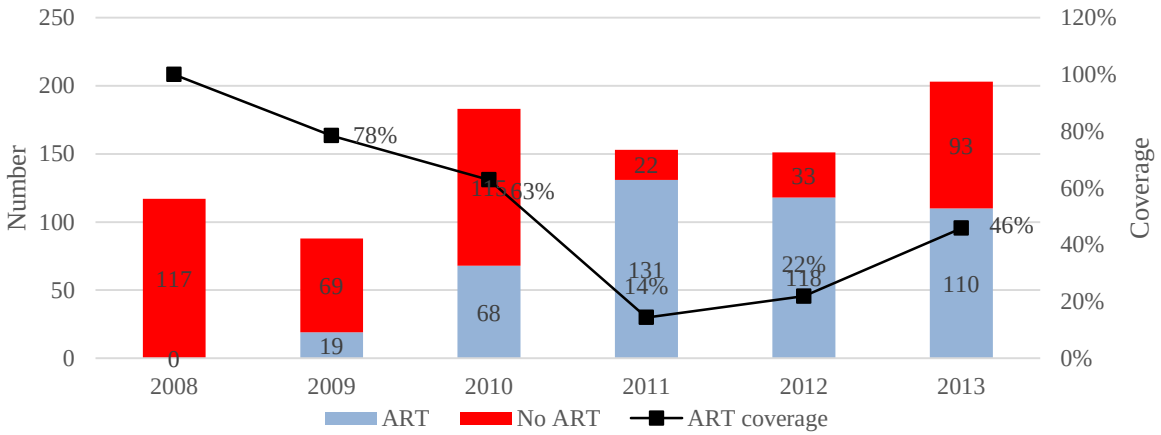


Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

Of 203 HIV-positive TB patients notified in 2013, only 110 patients (54%) were enrolled on antiretroviral therapy, which is much lower than the 86% antiretroviral therapy coverage reported in 2011 (Fig. 12). Cotrimoxazole preventive therapy coverage in Kyrgyzstan is even lower, suggesting

that there is ample scope to improve HIV/TB collaborative activities to reach the 100% antiretroviral therapy and cotrimoxazole preventive therapy coverage recommended by WHO.

Fig. 12. Number and percentage of HIV-positive TB patients enrolled in antiretroviral therapy, Kyrgyzstan, 2008–2013

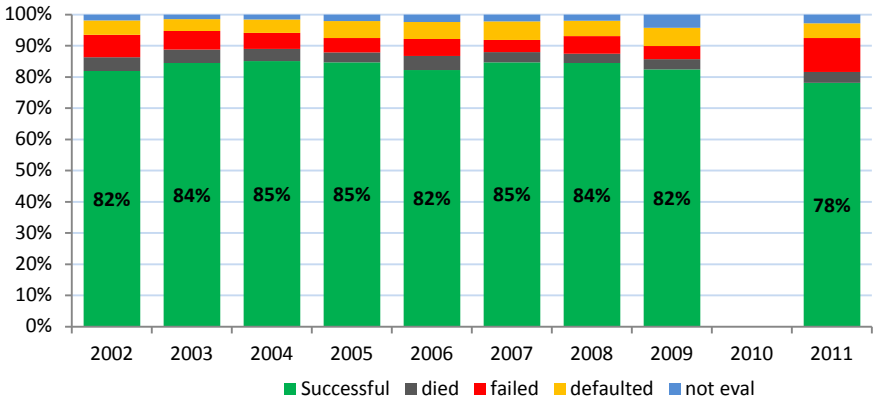


HIV+ = HIV-positive ART = antiretroviral therapy
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

TB treatment outcomes

According to NTP records, the treatment success rate among new smear-positive pulmonary TB patients over the last decade has been consistently high – above 80%. Some decrease in the treatment success rate was observed in 2011. However, in view of the recorded 26% of MDR-TB among new TB cases in 2011, even the reported 78% treatment success rate (as per 2006 reporting and recording framework) seems unreliable, suggesting weakness in the capacity to perform cohort analysis (Fig. 13).

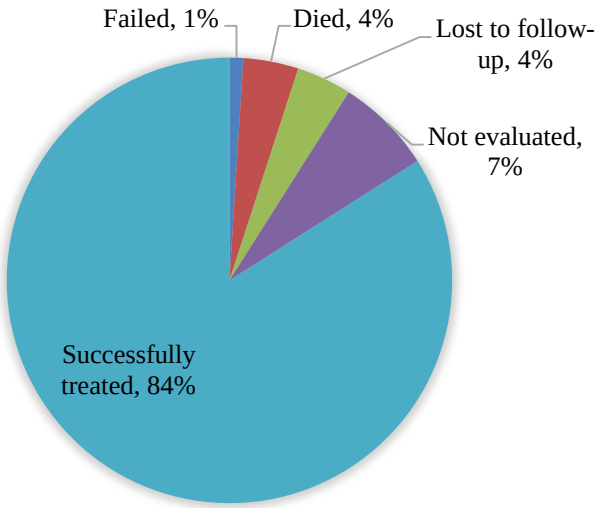
Fig. 13. Treatment outcomes of new sputum smear-positive TB cases, Kyrgyzstan, 2002–2011



Note: data for 2010 not available.
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

Fig. 14 below illustrates treatment outcomes of all new and relapsed cases (bacteriologically confirmed or clinically diagnosed, pulmonary or extrapulmonary) of TB patients notified in 2012 according to the WHO revised recording and reporting framework and case definitions. According to the revised case definitions, the treatment success rate in new and relapsed TB cases is 84% and the failure rate is only 1%.

Fig. 14. Treatment outcomes of notified new and relapsed TB cases (all forms), Kyrgyzstan, 2012 (n=6390)

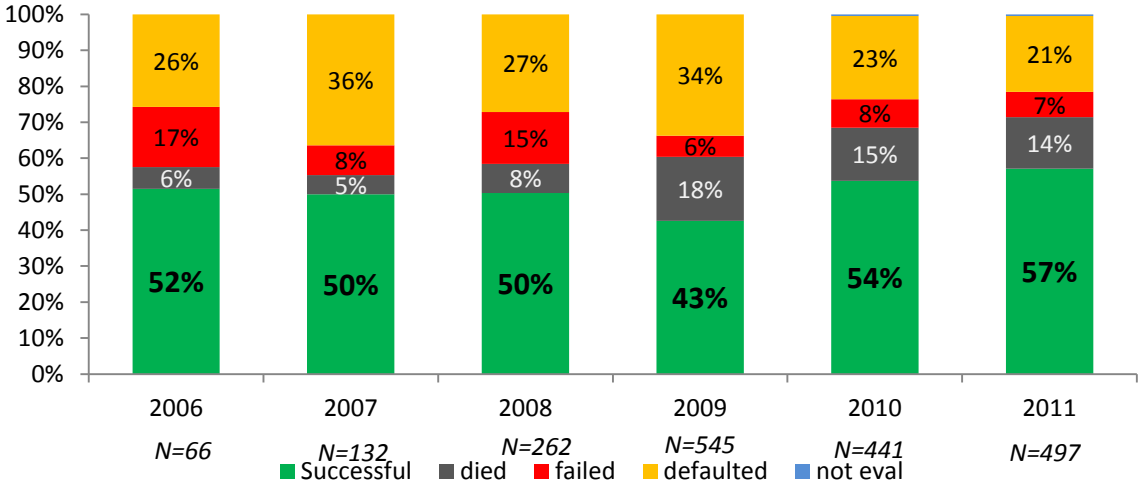


Source: NTP.

MDR-TB treatment outcomes

MDR-TB treatment in Kyrgyzstan has been available since 2006. In the first three cohorts, the MDR-TB treatment success rate was around 50%. In 2009, there was a sharp decline in the treatment success rate. In 2010 and 2011, there were notable improvements in the treatment outcomes. Thus, in the 2011 MDR-TB cohort, the treatment success rate was 57% which, while far below the target rate of 75%, is notably higher than the regional average. The main reason for an unfavourable treatment outcome is loss to follow-up (Fig. 15).

Fig. 15. Treatment outcomes of MDR-TB patients, Kyrgyzstan, 2006–2011



MDR-TB = multidrug-resistant TB
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

2. Health system

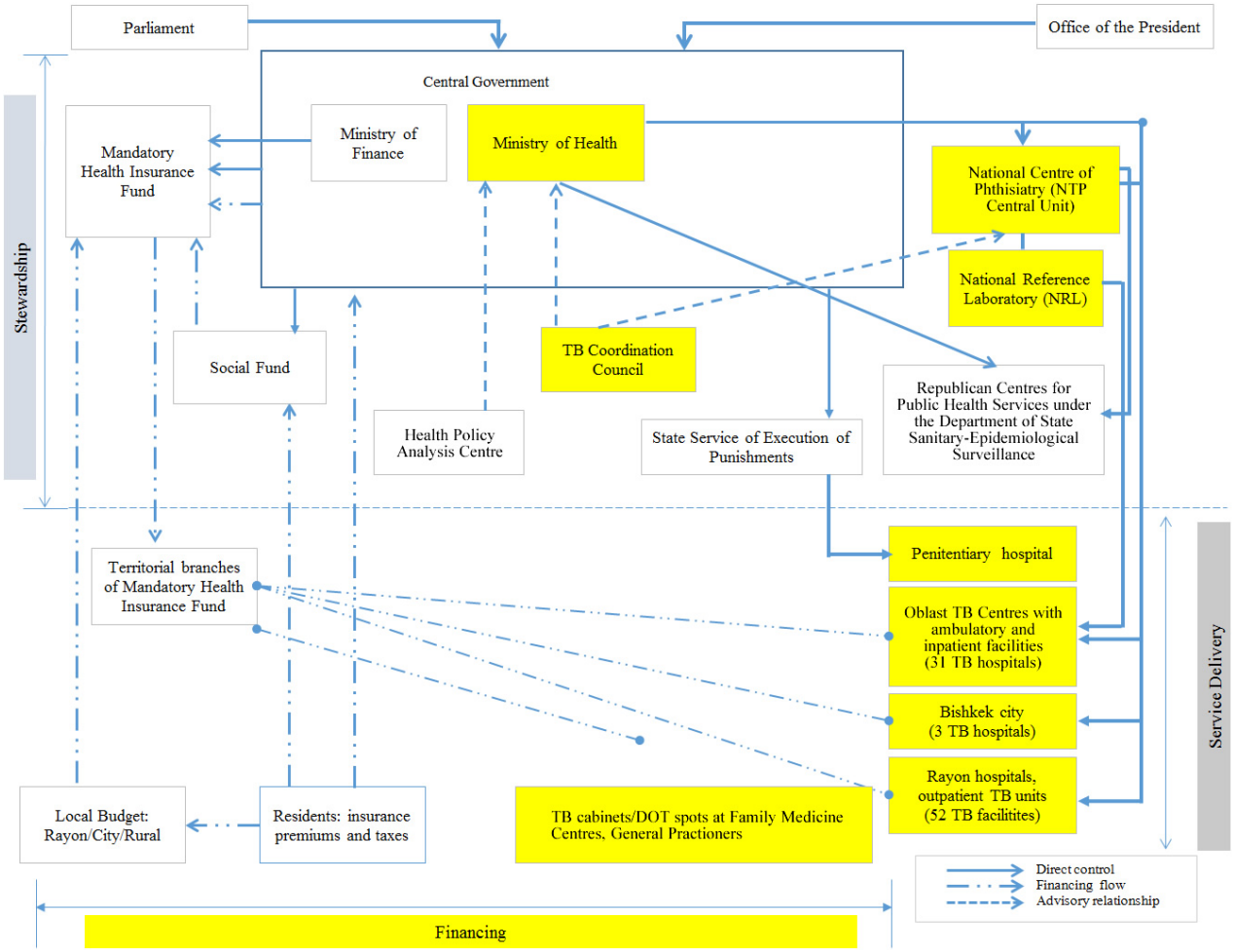
The health sector of Kyrgyzstan has been gradually and steadily improved via the Kyrgyz Government's Manas and Manas Talimi programmes and will be further strengthened through the implementation of the recently adopted Den Sooluk health reform programme.[1] Despite some shortcomings in the system, there have been notable improvements. The small-sized and understaffed Ministry of Health and MHIF have played an important role in the remarkable achievements and maintenance of the health system. Residents have good access to basic health services. The reforms implemented by the Government have supported and will further support the health system in general and its TB control programme in particular. Major challenges are physical access to facilities (i.e. tertiary-level/specialized facilities are not evenly distributed throughout the country), financial access and other reasons, such as the stigma attached to HIV/AIDS and TB, which may prevent patients from seeking care. For the structure of the health system, see Fig. 16.

The national health system of Kyrgyzstan has been based on a purchaser-provider split since 1997, when the mandatory health insurance system was introduced. In 2009, MHIF was separated from the Ministry of Health and made directly accountable to the Kyrgyz Government. MHIF pools the funds for health services from local and central resources, acts as a single public payer for health services and administers the State Guaranteed Benefit Package and Additional Drug Package. The Ministry of Health coordinates and ensures hierarchical top-down control through coordination commissions on health management and owns the facilities of the territorial hospitals. Purchasing is based on a contractual relationship between MHIF and providers of health services. The contracts are updated annually, and MHIF pays for services using output-based payment mechanisms. Priority health programmes such as TB are not fully integrated into the general health system, although MHIF has started integrating the financing of TB services.[2]

[1] Den Sooluk National Health Reform Programme in the Kyrgyz Republic for 2012-2016. Bishkek: Ministry of Health; 2012 (http://densooluk.med.kg/en/home-en/2-uncategorised/2-den-sooluk-national-health-reform-program-of-the-kyrgyz-republic.html, accessed 20 June 2015).

[2] Ibraimova A, Akkazieva B, Ibraimov A, Manzhieva E, Rechel B. Kyrgyzstan: Health system review. Health Systems in Transition, 2011; 13(3):1-152.

Fig. 16. Health system structure, Kyrgyzstan



TB control in the Kyrgyz Republic was originally organized as a vertical system offering a broad range of services to TB patients, some of which could also be offered by the mainstream system of primary, secondary and tertiary health care. This vertical approach to socially significant diseases was common in all parts of the former Soviet Union and is still common in many of its former members, now independent States. Attempts have been made to integrate TB services into the mainstream system, starting with the involvement of primary health care services and more recently by incorporating hospital-based TB services into the State Guaranteed Benefit Package. However, the process has not been easy and barriers to cost-effective TB care are still being reported, e.g. the limited capacity of primary health care, the tedious reporting requirements and the absence of additional finance or incentives for primary health care for TB. In the area of hospital-based TB care, the planned integration into mainstream care together with reduction of hospitals and beds has started recently and had been partially implemented at the time of review. The financing system for hospital TB care needs further reforms in line with the integration of TB care into the State Guaranteed Benefit Package.

In July 2012, hospital-based TB care was included in the State Guaranteed Benefit Package, paid by MHIF. This means that the service is no longer paid through the Ministry of Health from general revenue, but through the MHIF single-payer system which is used to pay for primary health care services, including those for TB. The inclusion of all TB care in the State Guaranteed Benefit Package and payment by MHIF increases the potential for integration of primary and hospital care services. It also enables MHIF to act as a purchaser and review the appropriateness of the care provided. However, this purchasing function can only be fully exercised after the adoption and implementation of new MHIF clinical practice guidelines as a reference for evaluating the performance of TB services. At the time of the review, these clinical practice guidelines were in development. MHIF,

implementing its purchasing role and using these guidelines, could help to reduce unnecessary hospitalization and shorten patients' stay in hospital. A reduction in hospitalization will help to reduce the likelihood of nosocomial infections (including TB). It will also contribute to improved TB care and optimize resources. In order to use its purchasing potential to the full, MHIF should have the opportunity to contract the volume of care selectively, according to actual needs. Its purchasing role should be complemented by autonomy for health service providers to optimize their use of resources.

The Ministry of Health is in charge of civilian TB and general health services in the country, especially primary health care. Specialized TB services operate from the National TB Control Centre downwards to TB units in the family medicine centres, but not to family group practices or feldscher-midwife units, which come under the family medicine centres. However, TB units in the family medicine centres are supposed to support and supervise the TB services of family group practices and feldscher-midwife units, albeit without formal authority. The health promotion units under the National Health Promotion Centre support the family medicine centres, family group practices and feldscher-midwife units in health promotion activities related to TB awareness-raising and adherence to treatment.

Obviously, the Minister of Health is ultimately responsible for TB services coming under the Ministry of Health. One of the Deputy Ministers deals with the curative sector and oversees the Ministry of Health Curative Care Department.

The National TB Control Centre represents the highest point of TB care and TB-related professional education, research and innovation. According to its mandate, the Centre is tasked with the coordination of the "entire set of TB activities". It is also currently in charge of the NTP, and its General Director is in charge of implementation, although the NTP is supposed to be implemented by many stakeholders. The Republican Epidemiology and Information Centre under the National TB Control Centre is in charge of evaluation, as well as collection and analysis of TB-related data.

Other actors in TB control

The TB services controlled by the Ministry of Health, depicted in Fig. 16 above, represents only some of the actors in the health sector and their mandates and relationships related to TB control. Other important actors and bodies are described below.

- The independent ***MHIF***, which has an advisory relationship with the Ministry of Health in respect of health services, including TB. The Ministry of Health does not intervene in health insurance operations and can only provide advice about some of the activities of MHIF via the Government of Kyrgyzstan, on policies related to the State Guaranteed Benefit Package, readjusting payments for primary health care with TB hospitals, etc. In return, MHIF can only request the Ministry of Health to develop clinical guidelines which it can use as a yardstick in performance reviews of health services providers. Current collaboration, or the lack of it, is dependent on the willingness of the Minister of Health. The Den Sooluk implementation plan includes an activity aiming to improve the structural relationship between the Ministry of Health and MHIF.
- The Ministry of Health ***Collegium***, composed of representatives of health-sector institutions. It provides an advisory role for the Ministry of Health, reviewing reports and proposals. Although it has no formal position related to the Ministry of Health, it is perceived as powerful and influential.
- The Ministry of Health ***Public Health Unit*** which deals with public health and other issues.
- The Ministry of Health ***Sanitary Epidemiological Service*** (SES or SANEPID) which deals with infectious diseases, but only partially with TB. It aims to provide full TB

surveillance and be involved in the evaluation of the national TB programme. However, its current capacity to fulfil this mandate seems limited.

- ***Republican Epidemiology and Information Centre,*** which is involved in TB surveillance and monitoring and evaluation of the NTP. It functions under the General Director of the National TB Control Centre, who is also in charge of NTP implementation. The positioning of the Republican Epidemiology and Information Centre, and in particular its mandate to evaluate the NTP, may cast doubt on the validity of the evaluation. The mandates of SES and the Republican Epidemiology and Information Centre relating to TB surveillance and monitoring and evaluation of the NTP deserve further scrutiny.
- The Ministry of Health coordinates via a dedicated ***Ministry of Health-SSEP Coordination Council*** with the health services responsible for the care of people in pre-detention centres and penitentiary institutions. The Chairman of SSEP and the Minister of Health have agreed on this coordination and on specific TB activities, particularly related to continuity of care for discharged prisoners. TB services in the civilian sector and in the penitentiary institutions report to different ministers.
- The ***TB Coordination Council,*** which has an advisory and consultative role with the Ministry of Health and other actors in TB control. Its main objective is the "improvement of implementation of the National TB Programme by strengthening DOTS (Directly Observed Therapy Short Course) and DOTS+ Strategies in the Kyrgyz Republic". Prevention of TB is not mentioned as an objective.

Governance

At the time of the review, the last strategic plan, covering the period 2006–2010, had been extended while the new draft for the national plan (2013–2016) was finalized. In the meantime, the Ministry of Health and the Central Unit of the NTP prepared a new plan, the National Plan for Prevention and Control of Drug-Resistant Tuberculosis in the Kyrgyz Republic for 2013, which was approved by the Ministry in February 2013. There are specific and time-bound targets in these documents.[1] The Ministry of Health informed the mission that the draft strategy would be approved in the near future and that it would scale up the prevention and management of TB and MDR-TB in the context of health system strengthening as a whole, and use improved health governance tools for intersectoral cooperation and enhanced programme coordination.

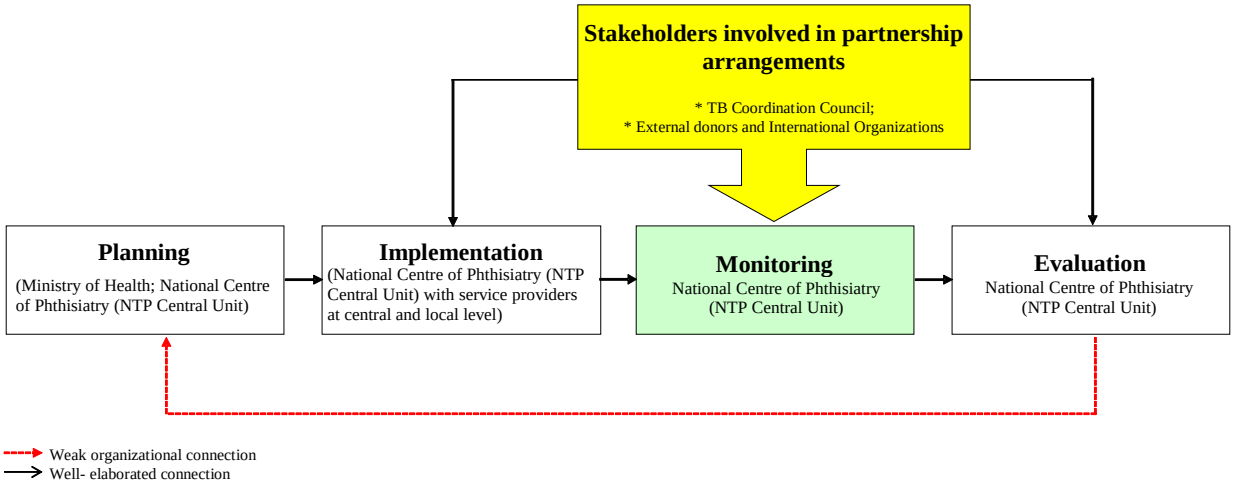
There is no doubt that the current governance approach of the NTP in Kyrgyzstan places great emphasis on coordination through partnership arrangements involving most of the actors in coordination councils. This can be explained by the fact that the Ministry of Health has to rely on the voluntary collaboration of many actors in the area of TB prevention and control and that most of the actors represent one of the coordination councils. Governance and management of the NTP have recently been elaborated further by assigning the coordination role of the TB programme to the directors of the family medicine centres at oblast level.

In general, there is an emphasis on an innovative and evidence-based approach to health policy-making, such as the practice of joint annual review that includes a partial evaluation of the performance of the TB control services.

Fig. 17 shows the policy cycle.

[1] Mosneaga A. GLC/EUROPE mission for monitoring of the implementation of the national M/XDR response plan, 2013. Available on request from tuberculosis@euro.who.int.

Fig. 17. Main elements of the NTP policy cycle in Kyrgyzstan



Challenges

Although there is an agreement between the Ministry of Health and MHIF that the funds saved by reducing the number of hospital beds should be used for TB control, no governance mechanism has been established to set priorities for expenditure or determine how the funds should be transferred to ambulatory care.

The Ministry of Health cannot enforce follow-up of agreements reached by the coordination councils, except in the area of its own jurisdiction. Furthermore, there is no consistent line of accountability for the overall performance of the NTP in the organizational framework of TB control. This is because the directors of the family medicine centres, who act as NTP coordinators, are also charged with the coordination of several other health programmes at the oblast level. From the accountability point of view, it is not clear how the family medicine centres can be held accountable for performance or how they can be incentivized. The National TB Control Centre, which is currently in charge of coordinating the NTP at the central level, has to focus primarily on providing hospital services at tertiary level. It can contribute to assessing the performance of the providers, but it has a limited role in the management and coordination of the programme at regional and local level. There are no performance incentives for the coordinators of the NTP.

The overall performance assessment of the NTP relies mainly on self-assessment by the NTP coordinators at oblast and national level. Without external appraisal, a conflict of interest can be seen in this practice, as the NTP coordinators, including the National TB Control Centre, are supposed to coordinate and implement the TB control activities that they are also evaluating. At the same time, no comprehensive annual report is published at national level to provide an assessment of all the important criteria of performance, such as efficiency and unmet needs.

Recommendations

- Set up a commission of representatives of the Ministry of Health, MHIF and the NTP within the framework of the TB Coordination Council to follow up the financing of the NTP, and especially to draw up proposals for transferring the savings from the planned downsizing of hospital care to the ambulatory care system. The recommendations of this commission should be approved by the Ministry of Health, and MHIF should deal with the technical aspects of reallocating the resources.
- Regularly publish a comprehensive performance assessment of TB services and have it appraised by independent local agencies.

- Establish a merit-based organizational process for appointment and evaluation of NTP managers. Use performance-based contracts and incentives, especially for those involved in NTP management. The contract should be separate from those relating to other work done for the National Centre of Phthisiatry (NCPh) or work for any other service providers.
- Continue, and where necessary strengthen, the current participatory approach for horizontal governance, especially in respect of TB financing and cooperation with other health and non-health programmes addressing the social determinants of health.
- Strengthen assessment of the performance of the NTP by contracting external consultants or a more independent agency, such as the Health Policy Analysis Centre, to appraise the NTP self-assessment reports and develop a rigorous methodological framework for performance assessment including all important performance criteria, e.g. efficiency and equity.
- Create a consistent accountability line for coordination and management of the NTP. Nomination of NTP managers on performance-based contracts can be considered. Financial incentives should be based on performance targets. Following the implementation of performance-based contracts, performance assessment should be conducted by external consultants. If the performance of the programme cannot be improved in the current organizational context, in which the NTP and National TB Control Centre operate under the same management, the NTP can be separated off from the National TB Control Centre, with its management and staff organized as an independent legal entity reporting directly to the Ministry of Health. The new unit would integrate all central managerial functions of the NTP and have the authority to nominate the local and regional NTP coordinators. If it is decided to follow up this recommendation, the details need to be elaborated and regulations amended. Compile a detailed feasibility study on the possible new organizational framework of this management unit before the final decision on the new structure is made.

Financing

Public expenditure on health has been increasing since 2000. In 2012, it accounted for 4.3% of gross domestic product (GDP) and a significant level of private spending, amounting to up to 39.9% of total health expenditure (Table 1). The spending on health in the general Government budget was 12.2% in 2012. These indicators show that, in comparison with other countries of central Asia, there is a relatively strong Government commitment to distributing a fair share of the Government budget to the health system. It is important to note, however, that the official GDP per capita is very low, which makes public expenditure on health per capita very low as well.

Table 1. Trends in health expenditure, Kyrgyzstan, 1995–2012

Indicators	1995	2000	2005	2010	2011	2012
Total health expenditure (% GDP)	6.0	4.7	5.8	6.7	6.2	7.1
GGHE (% GDP)	3.1	2.1	2.4	3.7	3.7	4.3
GGHE (% GGE)	10.7	12.0	11.9	11.9	11.6	12.2
External resources on health (% THE)	1.1	6.0	12.7	11.4	10.8	12.2
GGHE (% THE)	51.2	44.3	40.9	55.7	59.9	60.1
PvHE (% THE)	48.8	55.7	59.1	44.3	40.1	39.9
Out of pocket expenditure (% PvHE)	92.6	89.3	94.7	87.3	86.0	87.2
Out of pocket expenditure (% THE)	45.2	49.8	56.0	38.7	34.5	34.8
GGEH (current US$ per capita)	9.9	5.7	11.6	33.3	42.5	50.6
PvHE (current US$ per capita)	9.5	7.2	16.8	26.5	28.4	33.7
GDP (current US$ per capita)	324.9	276.5	487.9	898.8	1 147.0	1 182.8

GDP = gross domestic product
GGE = general Government expenditure
GGHE = general Government health expenditure
PvHE = private health expenditure
THE = total health expenditure
US$ = United States dollar
Source: WHO National Health Accounts 2013, http://www.who.int/health-accounts/en/.

At first glance, the expenditure on TB, reported in the 2013 WHO data collection form as a share of public expenditure on health, was 4.1% of public expenditure on health excluding donations from international donors and other grants in 2012 (Table 2). If we add the donation from international donors, especially the Global Fund, then public expenditure on TB was in fact 6.9% of public expenditure on health in that year.

Table 2. Expenditure in US$ on TB programme, Kyrgyzstan, 2013

Budget items	Government	Global Fund	Other grants	Total	%
First-line TB drugs	0	282 591	488 744	771 335	4.06
TB staff wages	5 725 991	189 665	125 160	6 040 816	31.80
NTP management and supervision	14 404	0	24 261	38 665	0.20
Laboratory supplies and equipment	0	166 051	342 071	508 122	2.68
PAL	0	0	0	0	0
PPM (public-public, public-private mix – DOTS)			13 840	13 840	0.07
Collaborative TB/HIV activities	0	0	236 197	236 197	1.24
Second-line drugs for MDR-TB	0	2 939 931	0	2 939 931	15.48
Management of MDT-TB (excluding second-line drugs)	0	0	36 837	36 837	0.19
Community involvement	0	0	51 846	51 846	0.27
ACSM	0	21 809	33 712	55 521	0.29
Operational research	0	0	0	0	0.00
Surveys to measure TB burden and impact on control	0	0	4 678	4 678	0.02
All other budget lines for TB	5 660 235	2 520 456	115 437	8 296 128	43.68
Total	***11 400 630***	***6 120 503***	***1 472 783***	***18 993 916***	***100***
Percentage	***60.02***	***32.22***	***7.75***	***100***	

ACSM = advocacy, communication and social mobilization
DOTS = directly observed therapy, short course
MDR = multidrug-resistant
PAL = Practical Approach to Lung Health
PPM = private-public mix
US$ = United States dollar
Source: WHO data collection form, 2013.

In 2012, the expenditure reported through the WHO data collection form included first-line and second-line drugs (19.5%) as well as the salaries of medical professionals and staff (32%). The share

for programme management and supervision activities was reported as 0.2% of the total expenditure on TB, which seems very low. Of the total expenditure on TB, 60% was funded by the Government, which mainly pays salaries, management and supervision costs and other budget lines for the providers. The remaining 40% of expenditure was funded by external donors and grants. The Global Fund alone covered the cost of second-line drugs for MDR-TB. There was no Government contribution for laboratory supplies or equipment. Food costs are covered by the hospitals, although the sum allocated for meals, which was reported as 76 Kyrgyz som/day (US$ 1.4), appears low. It was reported that TB services are available free of charge to patients, but that suspect cases have to pay for services if they are not diagnosed with TB (100 som/X-ray). This practice seems unfair to people tested as part of contact tracing and case-finding.

In the annual national report of the NTP, the distribution of expenditure on TB and health-care functions and the cost per patient are not calculated, even though Kyrgyzstan was one of the first countries in the WHO European Region to compile a TB-specific health account, in 2007. National TB Control Centre experts have therefore estimated the distribution of expenditure between the different health-care functions within the NTP. The estimated amount is almost completely consistent with the amount reported in the 2013 WHO TB data collection form (Table 2) which indicates that it is possible to achieve reliable, coherent and effective data collection relating to health financing in the NTP.

According to the National TB Control Centre estimates presented in Table 3, expenditure on outpatient services, apart from case-finding, represents only 5.2% of total expenditure on TB, which appears low compared with spending on inpatient services (52.3%). The Ministry of Health and the National TB Control Centre informed the mission that a planned TB hospital rationalization is under way as part of health sector reforms. According to the NTP and the Ministry of Health, the number of TB beds was reduced by 312 in the last year and will be reduced by a further 400 in the near future. The representative of the National Health Insurance Fund Administration confirmed that there is an agreement between the Ministry of Health and the Administration that the funds saved by rationalizing TB beds are expected to remain in the TB system and be allocated for TB control. The Administration introduced a case-based payment method for TB care in 2013, which is still being implemented. Since 2014, the strict line-item budget system has been relaxed and the providers have been given more flexibility in financial management. Outpatient services, including primary health care, are financed on a per capita basis that includes financing for TB services. In a pilot region, Issyk-Ata, incentives are offered to increase performance in active case-finding (100 som per detected case). At the time of the mission, no information was available on the impact of these incentives.

Table 3. Estimated expenditure on TB services, Kyrgyzstan, 2012

Services	Payment mechanisms	Som (thousands)	US$ (thousands)	Percentage
Outpatient				
Case-finding	P4P pilot	149 442 500	2 988 850	15.6
Pharmaceuticals	Procurement	190 406 800	3 808 136	19.9
Outpatient services	Per-capita	50 000 000	1 000 000	5.2
BCG vaccination	Per-case	1 600 000	32 000	
Laboratory, diagnostics	Procurement	62 800 000	1 256 000	0.2
Inpatient				
Hospital services	Per-case	500 000 000	10 000 000	52.3
Total expenditure		***954 249 300***	***19 084 986***	***100.00***

BCG = bacillus Calmette–Guérin P4P = pay-for-performance US$ = United States dollar

Source: NTP estimates (requested by the review mission).

Challenges

- Intensive use of hospital care, that diverts financial resources away from ambulatory care, can still be observed. However, there is a strong political commitment to changing the service delivery model. Even though the Ministry of Health and the National Health Insurance Fund Administration have reportedly agreed that the funds saved by cutting bed numbers should be used for TB control, no governance or financing mechanism have been established in order to prioritize the saved funds and channel them into ambulatory care.
- It should be stressed that the case-based payment which has been introduced will not create incentives to reduce the use of hospital care. Empirical evidence indicates that case-based payment can reduce the length of hospital stays and the cost per admission and make the performance reports of the providers more transparent but, at the same time, it increases the number of admissions and readmissions. In this regard, the National TB Control Centre reported to the mission that, although clinical guidelines have been drawn up and discussed, they had still not been approved by the Ministry of Health at the time of the mission. In practice, these would be very important for enabling the National Health Insurance Fund Administration to control unnecessary hospital admissions. Furthermore, per capita financing of ambulatory care in combination with case-payment at hospital level actually encourages treatment of patients in hospital rather than in the ambulatory setting.
- Despite the collection of comprehensive data on health finance, managed by MHIF, and the pioneering role of Kyrgyzstan in the implementation of a TB-specific health account in 2007, no comprehensive or regularly published public assessment of the distribution of resources and efficiency of the financing of TB control has been undertaken. The various stakeholders involved in TB control may have limited information about the total amount spent on TB control and its allocation to different health-care functions.
- The TB control programme is still heavily dependent on international donors, including the Global Fund. The national contribution to TB prevention and control was approximately 60% in 2012, while the remainder was funded by international donors. The current domestic funding level for the TB programme is not sufficient to scale up MDR-TB prevention and control activities and achieve full MDR-TB coverage throughout the country as well as replacing funding from external donors for first-line and second-line drugs.
- Spending on management, supervision and incentives for better performance seems to be limited.
- The incentive offered to encourage active case-finding seems fairly low (100 som per detected case).

Recommendations

- Establish an ambulatory, rather than per capita, case-payment system for TB services in primary care. This could help to incentivize the use of ambulatory services for TB control and would make use of savings gained by reducing the number of hospital beds. Develop a transition plan for TB health financing and link to the master plan of changes in the service delivery model. At the same time, it will be necessary to establish a subcommittee of the TB Coordination Council, with the involvement of leading stakeholders from the Ministry of Health, NTP management and the National Health Insurance Fund Administration. This subcommittee will assess and guide the allocation and use of funds for TB control, including setting priorities for the allocation of the saved funds or extra funding between the various health-care functions of the NTP.

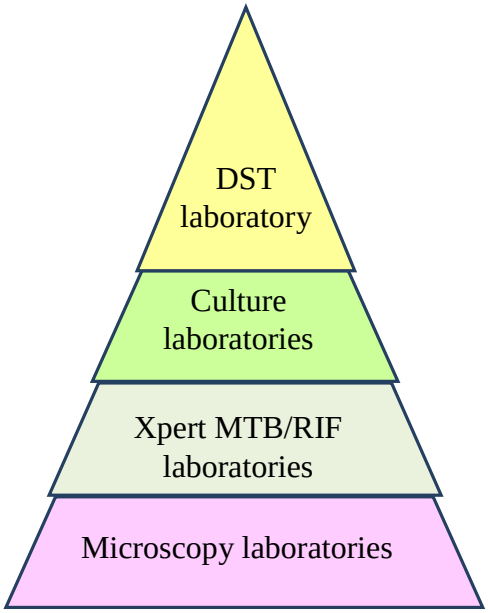
- Compile and publish regularly a comprehensive financial report, including an assessment of efficiency, as part of the annual report that should be circulated to all stakeholders involved in TB control. The WHO Health Accounts Production Tool should be applied, using the methods recommended in the System of Health Accounts 2011 accounting framework, with technical support from WHO. When this tool has been implemented, the overall distribution of expenditure on TB, with health-care functions and providers and sources of funds, can be analysed and planned in the interests of better decision making.
- Implement performance-based contracts and incentives, especially for those persons involved in the management and coordination of the NTP. This contract should be separate from those relating to other work done for NCPh or any other service providers. Increase funding for supervision and monitoring of the NTP.

3. Service delivery

Laboratory and diagnostic services

Laboratory network

Fig. 18. Levels of TB laboratory



The 125 laboratories of the Kyrgyz TB laboratory network are hierarchically organized (Fig. 18). One hundred and eleven microscopy laboratories perform the basic diagnostics. They are supposed to refer their specimens to a laboratory which is equipped with GeneXpert machines. In the event of a positive Xpert MTB/RIF result, the specimens are referred on to TB culture laboratories. Positive cultures are eventually sent to the laboratory in Osh or to the NRL for DST.

TB laboratories (Table 4) are located in various administrative units (oblasts and rayons) and assigned to various medical sectors – the TB sector (located at TB centres), primary health care sector (located at the family medicine centres) and prison sector (located in prisons, colonies or pretrial detention centres (SIZO)). In the primary health care sector, TB laboratories are integrated into larger laboratory units which also offer analyses in clinical chemistry, haematology, etc. They are financially and organizationally independent of the NTP but are supposed to follow technical orders from the NRL regarding the use of diagnostic tests and procedures, quality management, etc. Laboratories in the penitentiary system are subordinate to SSEP. All TB laboratories report their statistics quarterly to the NRL.

Table 4. Kyrgyzstan laboratory network

Sector	No.	EQA	Regular training/supervision
Microscopy	**111**	Monitoring < 50%	Sporadically by Project HOPE and KNCV
TB sector	20		
PHC sector	87		
Prison sector	4		Regularly by ICRC and MSF
Xpert MTB/RIF and microscopy	**5**		
TB sector	3		
PHC sector	1		
Prison sector (SIZO No. 1)	1		
Culture	**7**	Monitoring by NRL	Sporadically by NRL
TB sector	6		
Xpert MTB/RIF	1		
DST	**2**		
Osh	1	Panel tests from SRL	Regularly by SRL, ICRC, MSF
NRL and Xpert MTB/RIF	1	Panel tests from SRL	Regularly by SRL, ICRC, MSF

DST = drug susceptibility testing
EQA = external quality assurance
ICRC = International Committee of the Red Cross
KNCV = KNCV Tuberculosis Foundation, Netherlands
MSF = Médecins sans Frontières
NRL = National Reference Laboratory
PHC = primary health care
SRL = Supranational Reference Laboratory
Source: Registers of NRL, Osh TB laboratory

The two laboratories performing DST are the NRL at the National Tuberculosis Centre and the laboratory of the Osh Oblast TB Hospital. They receive positive cultures from culture laboratories and

perform first- and second-line DST and molecular line probe assay GenoType MTBDR*plus* (HAIN Lifescience, Germany) testing.

The seven culture laboratories are located in:

1. Chui Oblast TB Centre
2. Kara-Balta TB Rehabilitation Centre
3. Talas Oblast TB Hospital
4. Naryn Oblast TB Hospital
5. Issyk-Kul Oblast TB Hospital
6. Jeti Oguz Republican TB Rehabilitation Centre
7. Jalal-Abad Oblast TB Hospital.

The Chui Oblast TB Centre is additionally equipped with a GeneXpert machine. Theoretically, culture laboratories receive specimens from all lower-level laboratories. However, because of the unreliable transport system, they mostly analyse specimens from their affiliated medical centres only.

The vast majority (80%) of the 111 microscopy laboratories are affiliated to institutions of the primary health care sector. One of them is equipped with a GeneXpert machine, as are three (15%) of the 20 microscopy laboratories of the TB sector and one (25% – SIZO No. 1) of the four laboratories of the prison sector.

The total number of laboratories was reduced substantially from 442 in 2000 to 125 in 2014.

The management structure of the network is quite loose. The head of the NRL serves as the director of the network. The NRL develops guidelines and shares standard operating procedures with other laboratories. It collects the data for the NTP quarterly statistics and coordinates and supervises quality control activities.

The external quality control and monitoring system seems to function quite well. Every laboratory visited during this review mission was regularly monitored by higher-level laboratory experts. Monitoring results were documented in the relevant checklists and feedback was provided. Sputum smears were rechecked in compliance with WHO rules. The results of the rechecking were centrally analysed and reported.

Challenges

- A strategic plan for further development and strengthening of the TB laboratory network is lacking.
- The network is too large and diversified. Active networking between the laboratories could only be observed locally, e.g. between two neighbouring laboratories sharing one GeneXpert machine. Collaboration and communication is underdeveloped. Much stronger synergies could result from more effective networking.
- The NRL neither has the capacity nor receives sufficient support from the NTP to serve as a central network management unit. The tasks and responsibilities of network management are not defined. Therefore, management activities of the NRL can only focus on technical issues, and organizational and logistical aspects are neglected.
- The tasks and responsibilities of the different types and levels of laboratory are not yet well defined.

Recommendations

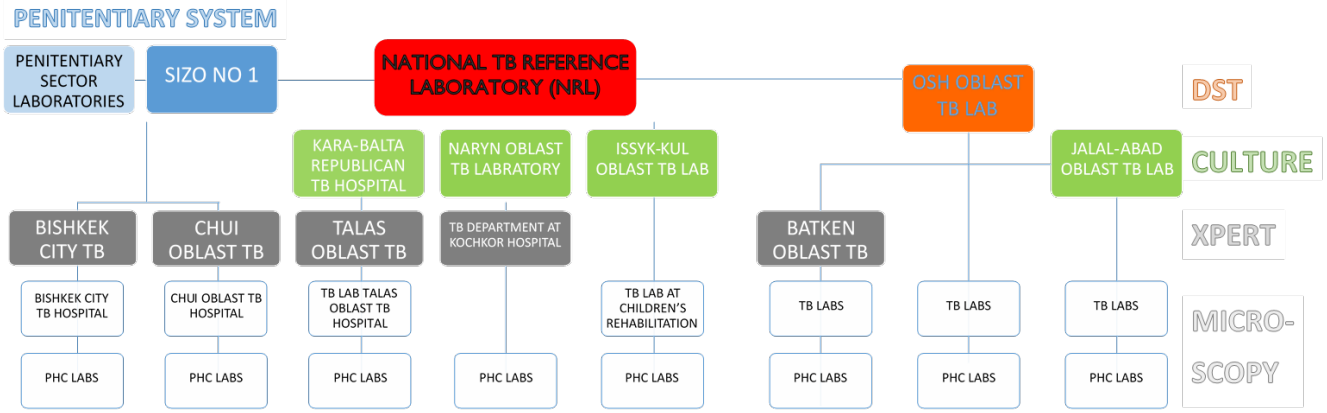
High priority

- Develop a national strategy for further development of the TB laboratory network and share it with all stakeholders. Use this plan as a road map for implementation. Implement all components within the following three years, with technical assistance from the SRL partner and other stakeholders in the field. Consider all aspects of network management, including the most urgent topics of human resources capacity-building, logistics, procurement, equipment, maintenance, quality management, reporting and the interaction between clinical and diagnostic services.
- Further strengthen the administrative management of the laboratory network. Assign a separate TB laboratory network commissioner under the NTP, with sufficient competencies and financial resources to realize the plans of the TB laboratory strategy. The network management should assure appropriate organizational conditions for the implementation of reliable diagnostic services and include, among others, human resources capacity-building, development of adequate infrastructure, provision of equipment, regular maintenance of infrastructure and equipment, implementation of a functional logistics system for transportation of laboratory materials and specimens, communication of reports, realization of an optimal flow of data and coordination of donor activities within the TB laboratory strategic plan of the Ministry of Health/NTP.

Medium priority

- Increase the efficiency of laboratory diagnostics by consolidating the laboratory network. Restrict the number of culture laboratories to four, and the number of TB microscopy laboratories to 50–75 throughout the country. Increase sustainability of diagnostic services by enlarging the laboratory teams to a minimum of two to three specialists. The resulting TB laboratory network should be organized as displayed in Fig. 19.
- Officially define the responsibilities of the NRL, including all technical competencies of laboratory diagnostic services. These should include the development of guidelines and standards for laboratory diagnostics, the specification of standard operating procedures, the predefinition of requirements for the pre- and post-analysis phases, the definition of internal and external quality controls, and the provision of external quality control materials.
- Strengthen and guide collaboration and communication between the laboratories of the network and exploit synergies arising from closer collaboration between the TB laboratories. Provide communication tools (telephone, fax, Internet, etc.). Organize regular meetings of representatives of all laboratories for staff development, facilitate network transformation projects, exchange ideas and experiences.
- Define tasks and responsibilities for each type and level of laboratory. Issue documents informing each laboratory about its tasks and responsibilities within the network and advising it how to fulfil them.

Fig. 19. Organigram of the recommended laboratory network structure



DST = drug susceptibility testing
PHC = primary health care
* DST laboratories are marked in red; culture laboratories in green, Xpert MTB/RIFmicroscopy laboratories in grey, microscopy laboratories in white and the laboratories of the penitentiary sector in blue.

DST laboratories

Two laboratories test the susceptibility of TB isolates: the NRL and the laboratory of the Osh Oblast TB Hospital. Their basic characteristics are shown in Table 5 and are discussed further in the next sections.

Table 5. Basic characteristics of DST laboratories

	National Reference Laboratory	Osh Oblast TB Reference Laboratory
Location	National TB Control Centre, National Centre of Phthisiatry	Oblast TB Hospital
Culture	Solid (LJ), fluid (MGIT)	Solid (LJ), fluid (MGIT)
DST	FLD (LJ and MGIT) SLD (LJ and MGIT) For diagnostic patients: MGIT + LJ	FLD (LJ) SLD (LJ)
EQA 2013	Passed	Failed
Molecular diagnostics	GenoType MTBDR*plus* (HAIN) Xpert MTB/RIF	GenoType MTBDR*plus* (HAIN)
Infrastructure	Newly renovated, very good condition	Fair
Equipment	BSC: 3x Autoclave: 3x functioning regular maintenance	BSC: 2x Autoclave: 2x no effective maintenance
Biosafety	Meets highest international biosafety level 3 standards	Ventilation missing, severe breach of maintenance standards
Training	Regular supervision and training by SRL, MSF, ICRC	Regular supervision by ICRC and MSF Recent training by SRL
Quality management	SOPs available for all procedures and equipment, procurement, HR	Some SOPs available for procedures/equipment

BSC = biosafety cabinet
EQA = external quality assurance
FLD = first-line drugs
HR = human resources
ICRC = International Committee of the Red Cross
LJ = Lowenstein-Jensen medium
MGIT = Mycobacteria Growth Indicator Tube
MSF = Médecins Sans Frontières
SLD = second-line drugs
SOP = standard operating procedure
Source: Personal laboratory inspection in Osh and NRL.

National Reference Laboratory

The National Reference Laboratory was built in 2013 with technical assistance from GITEC Consult and SRL Gauting, Germany, and financed by the German development bank (KfW Development Bank). The premises are modern and well adjusted to local needs and meet the highest biosafety standards. The laboratory is equipped with three class-II biosafety cabinets (BSC) and three autoclaves which are fully functional and technically controlled. The electricity supply is assured by a combination of uninterruptible power supply and emergency generator. Maintenance costs are to be covered by KfW for the first three years after commissioning (until summer 2016).

The NRL performs the reference diagnostics for the northern part of the country. It is linked with SRL Gauting by an NRL-SRL partnership registered by WHO in 2008 and reconfirmed by the Ministry of Health in 2012. The NRL performs Ziehl-Neelsen and fluorescence microscopy, culture using Lowenstein-Jensen medium (LJ) and Mycobacteria Growth Indicator Tubes (MGIT), DST for first-line drugs in MGIT, DST for first-line and second-line drugs using the proportional method on LJ medium, molecular resistance testing with GenoType MTBDR*plus* (HAIN Lifescience, Germany) as well as Xpert MTB/RIF. It successfully passed the 2013 external quality assessment, resulting in certification of microscopy and DST for first-line and second-line drugs.

Osh Oblast TB Hospital Laboratory

The infrastructure of the Osh DST laboratory was partially renovated approximately four years ago with financial and technical support from the ICRC. The laboratory is equipped with one MGIT machine and modern fridges and freezers, as well as two class-II BSC, autoclaves and centrifuges. All critical equipment is connected to an uninterruptible power supply and emergency generator. Financial support for the instalment of an active ventilation system with adequate air exchange, filtering and directed air flow will be considered by the ICRC as soon as funds are available. The windows of the laboratory can be opened, and technicians make use of this option on hot days.

The laboratory receives clinical specimens from Osh oblast. Additionally, all culture laboratories from the south-west of Kyrgyzstan are supposed to send their positive cultures there.

Recommendations

High priority

- Send all positive TB cultures from Chui, Talas, Issyk-Kul and Naryn to the NRL and those from Osh, Batken and Jalal-Abad to the Osh Oblast TB laboratory for DST.
- Implement front-line and second-line DST in MGIT, the NRL and the Osh laboratory. Stop DST in LJ in Osh. Restrict highly specialized DST (e.g. for new drugs) to the NRL.
- Give high priority to the installation of a ventilation system in the biosafety level 3 area of the Osh laboratory.

Medium priority

- Standardize and equalize equipment, workflow, tests, procedures, pre-analytical, analytical and post-analytical standards in both laboratories.
- After the installation of the ventilation system in Osh, block the windows of the high-risk containment area and seal them hermetically.

Culture laboratories

The seven culture laboratories perform bright-field microscopy after Ziehl-Neelsen stain and solid culture on LJ medium. The laboratory at the Chui Oblast TB centre also performs Xpert MTB/RIF

testing. The laboratory of Jalal-Abad was undergoing refurbishment at the time of the visit. The room and construction plans presented to the team seemed reasonable and well thought-out. Other culture laboratories were not visited during this mission, but were inspected during a laboratory assessment by UNDP and the SRL in 2012.[1] According to the report, the laboratories of Kara-Balta and Issyk-Kul showed a reasonably good infrastructure, while none of the other culture laboratories fulfilled basic WHO biosafety requirements.

Recommendations

High priority

- Refurbish all culture laboratories and bring them to a reasonable biosafety level consistent with the most recent (2012) WHO recommendations.[2]
- Reduce the number of culture laboratories to four: Kara-Balta Republican TB Hospital, Naryn Oblast TB Hospital, Issyk-Kul Oblast TB Hospital and Jalal-Abad Oblast TB Hospital. Implement Xpert MTB/RIF (Cepheid, USA) and/or GenoType MTBDR*plus* (HAIN Lifescience, Germany) at each culture laboratory.
- Make sure that both the Chui Oblast TB Centre and the Talas Oblast TB Hospital are equipped with fluorescence microscopes and GeneXpert machines. Transfer specimens from peripheral laboratories to these centres for polymerase chain reaction diagnostics, including screening for rifampicin resistance.

Xpert MTB/RIF and microscopy laboratories

Seven GeneXpert machines have so far been supplied from project funds given by MSF, the USAID Quality Health Care Project and TB REACH (Table 6). Five of the projects ended in the years 2012 and 2013. Since then, consumables have been procured by different donors, including the Global Fund and the UNITAID EXPAND-TB project which will finish by the end of 2015. The procurement of five additional GeneXpert machines and 24 000 cartridges is planned in the near future under the new Global Fund financing mechanism.

[1] Review of the TB laboratory network of the Republic of Kyrgyzstan 2012. Bishkek: Ministry of Health of Kyrgyzstan; 2012 (available upon request from the Ministry of Health).
[2] Tuberculosis laboratory biosafety manual (document WHO/HTM/TB/2012.11). Geneva: World Health Organization; 2012.

Table 6. Xpert MTB/RIF laboratories and funding projects

Project	No. of Gene Xpert machines	Institution	Project start	Project end	Target group
MSF – Switzerland	2	SIZO No. 1	Oct 2011	2015	Persons under investigation, prisoners
		Kara-Suu TB Hospital, Osh oblast	May 2012	2015	TB patients of Kara-Suu rayon
USAID Quality Health Care Project	1	Issyk-Ata FMC, Chui Oblast	Oct 2012	Apr 2013	Outpatient TB patients (ambulatory treatment)
TB Reach Wave 2 project of NTP	4	Chui Oblast TB Centre Bishkek City TB Centre Osh Children's Interoblast TB Centre NRL, Bishkek city	Apr 2012	2012	Internal migrants
Total	***7***				

FMC = family medicine centre
MSF = Médicins Sans Frontières
NRL = National Reference Laboratory
SIZO = pretrial detention centre
USAID = United States Agency for International Development
Source: NRL/NTP registers, stakeholder meeting.

The infrastructure of the Xpert MTB/RIF laboratories is generally identical to that of the microscopy laboratories. During the current mission, only one microscopy laboratory was inspected, at a family medicine centre. The findings corresponded to those of previous reports, including the SRL/UNDP laboratory assessment of 2012. Kyrgyz microscopy laboratories usually consist of two simple rooms, one for documentation and the other for analysis. Some of the laboratories are equipped with simple class-I biosafety cabinets. The others handle clinical specimens on the open benches, although a natural air flow is rarely assured throughout the year. Surfaces are mostly wooden and difficult to disinfect. All in all, the infrastructure of most microscopy laboratories breaks important biosafety rules, although the requirements are quite basic.

Recommendations

High priority

- Equip the laboratories of all TB hospitals with GeneXpert machines. The only exception should be the MDR-TB hospital of Kara Balta, where all patients are already pre-diagnosed before hospitalization.

Medium priority

- Equip all microscopy laboratories with class-I biosafety cabinets (air extraction cabinet).
- Install new workbenches with synthetic surfaces which can be easily disinfected to protect the staff from any type of infectious diseases transmitted via clinical specimens, including viral diseases such as influenza or enteroviruses, acute bacterial infections such as pneumococci or meningococci, or moulds and parasites.

- Merge small microscopy laboratories to create larger laboratory units wherever two or more TB laboratories are located less than 50 km apart.

Low priority

- Change conventional bright-field microscopy to LED fluorescence microscopy in all laboratories where the workload might exceed 20 smears per staff member and per day.

Equipment and maintenance

All TB laboratories in the network are equipped with bright-field microscopes, some with modern iLED (Zeiss MicroImaging) fluorescence microscopes. Eight out of 10 bright-field microscopes were clean and protected from dust. The remaining two were extremely dirty. Almost all condensors, i.e. the optical units centralizing and bundling the light from the lower light source underneath the objects, were set in the wrong position, leading to underexposed and blurred vision fields.

Crucial high-tech laboratory equipment available in culture and DST laboratories is listed in Table 7. It demonstrates that the network is rather well equipped. The equipment of the NRL is new and still maintained by the manufacturer. Yearly maintenance is assured by the contractor AJZ under the TB III/IV project of KfW Development Bank until 2016.

According to verbal information from Osh, biosafety cabinets in culture and DST laboratories were maintained in 2012. However, protocols and certificates prove that the functionality of the HEPA filters has not been checked by the use of particle counters. The biosafety cabinets have obviously never been calibrated. The function of the autoclaves has never been controlled by the use of bioindicators. Centrifuges have been neither calibrated nor lubricated. Thus, most of the expensive and important laboratory equipment has basically not been professionally maintained for years.

Table 7. Main equipment in Xpert MTB/RIF, culture and DST laboratories, Kyrgyzstan, 2014

Laboratory	**BSC** (f/m)	**Autoclave** (f/m)	**Centrifuges** (f/m)	**Xpert MTB/RIF** (f/m)	**Microscopes** (fl/BF)
NRL	3 (3/3)	3 (3/2)	2 (2/2)	HAIN + 1(1/1)	7 (7/7)
Bishkek City TB Centre	None	None	None	1 (1/1)	2 (0/2)
Osh DST	2 (2/0)	2 (2/0)	2 (2/0)	HAIN	4 (2/2)
Chui Oblast culture	None	None	None	1 (1/1)	3 (2/1)
Kara-Balta culture	1 (1/0)	2 (2/0)	1 (1/0)	None	3 (2/1)
Talas Oblast culture	1 (1/0)	2 (2/0)	1 (1/0)	None	3 (2/1)
Naryn Oblast culture	1 (1/0)	2 (2/0)	1 (0/0)	None	3 (3/1)
Issyk-Kul culture	1 (0/0)	2 (2/0)	1 (1/0)	None	3 (3/1)
Jeti Oguz culture*	1 (1/0)	2 (2/0)	1 (1/0)	None	3 (3/1)
Jalal-Abad culture	1 (1/0)	2 (2/0)	1 (1/0)	None	4 (2/2)
SIZO	BSC-1 (1/0)	None	None	1 (1/1)	3 (0/3)
Kara-Suu	None	None	None	1 (1/1)	3 (1/3)
Osh City TB Dispensary	None	None	None	1 (1/1)	2 (0/2)
Issi Ata District FMC	None	None	None	1 (1/1)	1 (0/1)

* may be closed soon f = functioning m = maintained
BF = bright field fl = fluorescence SIZO = pretrial detention centre
BSC = biosafety cabinet
Source: communication with laboratory staff in person and by phone with assistance from NRL staff.

Recommendations

High priority

- Maintain all equipment listed in Table 7 and the ventilation systems (if available) and other crucial installations on a yearly basis. Make sure that maintenance is performed

only by engineers who have verifiable knowledge and skills and who are officially certified by the manufacturing companies to perform the maintenance. Build capacity in the country to perform maintenance adequately by training local engineers (see sections on human resources and infection control below). Also impart basic maintenance knowledge and skills to the laboratory staff so that they can supervise and judge the quality of the maintenance work done by the engineers.

Medium priority

- Prepare a central register of all available equipment in all TB laboratories. Develop a strategy to keep this register up to date. Include data on maintenance (usually yearly or every second year) and replacement of equipment (usually after 10 years) in the register. Implement a central plan of maintenance for all equipment. Entrust the management of maintenance procedures to the laboratory network commissioner.
- Establish local maintenance services with staff who are well educated and certified in function control and maintaining crucial laboratory equipment (biosafety cabinets, autoclaves, centrifuges) as well as installations (ventilation, water purification, etc.).
- Prevent damage to equipment by providing culture and DST laboratories with an uninterruptible power supply for each priority laboratory device, with electronic control panels.

Low priority

- Equip larger microscopy laboratory centres with fluorescence microscopes and start moving diagnostic policies over to Auramine O staining and fluorescence microscopy. Train microscopy staff in centralizing and focusing the condensers (Koehler procedure).

Diagnostic services, tests and procedures

The national TB laboratory network offers all types of procedures needed for TB diagnostics in the country. Table 8 gives an overview of the types and number of tests performed in 2013.

Table 8. Types and number of diagnostic tests performed, Kyrgyzstan, 2013

Test	Total number of tests performed
Smear microscopy	120 606
Culture	13 686
Xpert MTB/RIF	6 129
GenoType MTBDR*plus*	2 000
GenoType MTBDR*sl*	158
FLD – DST	3 157
SLD – DST	1 966

DST = drug susceptibility testing
FLD = first-line drugs
SDL = second-line drugs
Source: NTP/NRL registers.

DST and genetic resistance tests

The DST laboratories of Osh and the NRL together performed 3157 drug susceptibility tests using phenotypic methods (NRL 2049 (65%), Osh 1108 (35%), Table 9). A total of 1242 isolates (39%) showed resistance to rifampicin. The rates of rifampicin were 42% at the NRL and 35% in Osh, and the rates for isoniazid resistance 59% and 49%, respectively.

Two different types of genotypic resistance tests are performed in Kyrgyzstan: the real-time polymerase chain reaction assay Xpert MTB/RIF on the GeneXpert platform (Cepheid, USA) which detects rifampicin resistance, and the reverse hybridization assays GenoType MTBDR*plus* and MTBDR*sl* (HAIN Lifescience, Germany) which additionally detect isoniazid and second-line-drug resistance.

Table 9. Phenotypic drug susceptibility tests, NRL and the Osh Oblast TB laboratory, 2013

	National Reference Laboratory			Osh Oblast TB laboratory		
	Never treated	Prev. treated	Total	Never treated	Prev. treated	Total
	n (%)	*n (%)*	*n (%)*	*n (%)*	*n (%)*	*n (%)*
Sensitive	548 (40.0)	128 (19.0)	676 (33.1)	383 (48.7)	97 (30.2)	480 (43.3)
Res. to H only	44 (3.2)	16 (2.4)	60 (2.9)	63 (8.0)	20 (6.2)	83 (7.5)
Res. to R only	11 (0.8)	3 (0.4)	14 (0.7)	13 (1.7)	4 (1.2)	17 (1.5)
Res. to E only	25 (1.8)	8 (1.2)	33 (1.6)	18 (2.3)	3 (0.9)	21 (1.9)
Res. to S only	53 (3.9)	12 (1.8)	65 (3.2)	26 (3.3)	1 (0.3)	27 (2.4)
Total mono-resistance	***133 (9.7)***	***39 (5.8)***	***172 (8.4)***	***120 (15.2)***	***28 (8.7)***	***148 (13.4)***
H + R	11 (0.8)	9 (1.3)	20 (1.0)	14 (1.8)	8 (2.5)	22 (2.0)
H + R + E	9 (0.7)	4 (0.6)	13 (0.6)	22 (2.8)	8 (2.5)	30 (2.7)
H + R + S	105 (7.7)	57 (8.5)	162 (7.9)	36 (4.6)	25 (7.8)	61 (5.5)
H + R + E + S	291 (21.2)	315 (46.9)	606 (29.7)	125 (15.9)	121 (37.7)	246 (22.2)
Total MDR	***416 (30.4)***	***385 (57.3)***	***801 (39.2)***	***197 (25.0)***	***162 (50.5)***	***359 (32.4)***
H + E	9 (0.7)	3 (0.4)	12 (0.6)	18 (2.3)	5 (1.6)	23 (2.1)
H + S	154 (11.2)	59 (8.8)	213 (10.4)	30 (3.8)	13 (4.0)	43 (3.9)
H + E + S	89 (6.5)	37 (5.5)	126 (6.2)	20 (2.5)	11 (3.4)	31 (2.8)
R + E	11 (0.8)	3 (0.4)	14 (0.7)	3 (0.4)	0 (0)	3 (0.3)
R + S	1 (0.1)	4 (0.6)	5 (0.2)	0 (0)	0 (0)	0 (0)
R + E + S	10 (0.7)	11 (1.6)	21 (1.0)	7 (0.9)	1 (0.3)	8 (0.7)
E + S	6 (0.4)	3 (0.4)	9 (0.4)	9 (1.1)	5 (1.6)	14 (1.3)
Total PDR	280 (20.4)	120 (19.7)	400 (19.6)	87 (11.1)	35 (10.9)	122 (11.0)
Total patients with DST	1 370	672	2 042	787	321	1 108

E = ethambutol MDR = multidrug-resistant R = rifampicin S = streptomycin
H = isoniazid PDR = polydrug-resistant Res. = resistance

Source: NTP registers.

In total, 2000 GenoType MTBDR*plus* assays were performed in 2013 (Table 10). Of these, 999 yielded valid results at the NRL and 963 in Osh. The NRL and Osh detected rifampicin resistance in 566 (57%) and 373 (39%) cases, respectively, and isoniazid resistance in 546 (55%) and 506 (53%) cases, respectively. While the rates corresponded quite well to the phenotypic resistance rates in Osh, the molecular rifampicin resistance rate of the NRL was surprisingly higher than the phenotypic one (41.8% rifampicin resistance). Additionally, the genotypic resistance rate for rifampicin was higher than the one for isoniazid, which is not plausible, as usually the rate of isoniazid resistance exceeds that of rifampicin resistance by at least 10%.

Table 10. Results of GenoType MTBDR*plus* (HAIN Lifescience, Germany), 2013

Laboratory	Rs-Hs	Rs-Hr	Rr-Hs	MDR	Indeter-minate	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n
NRL	315 (31.2)	118 (11.7)	139 (13.7)	427 (42.2)	12 (1.2)	1 011
Osh Oblast TB laboratory	433 (43.8)	157 (15.9)	24 (2.4)	349 (35.3)	26 (2.6)	989
Total	***748 (37.4)***	***275 (13.8)***	***163 (8.2)***	***776 (38.8)***	***38 (1.8)***	***2 000***

H = isoniazid R = rifampicin
NRL = National Reference Laboratory s = susceptibility
r = resistance
Source: Laboratory registers of NRL and Osh TB laboratory.

Of the 6129 Xpert MTB/RIF tests performed in 2013, 5595 (91%) yielded valid results (Table 11). A total of 1686 (28%) detected *Mycobacterium tuberculosis* (MTB) complex in the clinical specimens: this is considered an excellent positivity rate, proving a good preselection of patients as well as skilful analytics in the laboratory.

Table 11. Results of Xpert MTB/RIF at various sites, Kyrgyzstan, 2013

Laboratory	MTB/RIF resistant			MTB/RIF susceptible		MTB negative		MTB/RIF indeterminate		Error		To
	n	% of all	% of MTB positives	n	%	n	%	n	%	n	%	n
NRL	27	11%	35%	51	22%	148	63%	5	2%	5	2%	236
Bishkek City TB dispensary	94	11%	32%	197	23%	514	59%	0	0%	65	7%	870
Chui Oblast TB hospital	171	14%	33%	352	30%	628	53%	1	0%	32	3%	1184
Osh Oblast children's TB hospital	81	6%	32%	172	13%	867	64%	6	0%	236	17%	1362
Kara-Suu (MDR-TB hospital in Osh Oblast)	86	6%	27%	232	17%	948	70%	8	1%	73	5%	1347
Issyk Ata (PHC centre Chui Oblast)	69	6%	31%	154	14%	804	71%	0	0%	103	9%	1130
SIZO #1	90	7%	58%	64	5%	771	59%	13	1%	134	10%	1314
Total	***618***	***8%***	***34%***	***1222***	***16%***	***4680***	***63%***	***33***	***0%***	***648***	***9%***	***7443***

MDR-TB = multi-drug resistant tuberculosis NRL = National Reference Laboratory SIZO = pretrial detention centre
n/a = data not available PHC = primary health care
Source: NTP/NRL register.

About 35% (618 tests) of all MTB-positive tests indicated rifampicin resistance, ranging from 27% in Kara-Suu through 35% in the NRL to 58% in SIZO #1; these results corresponded well with phenotypic DST results and data from the National Drug Resistance Surveys (DRS) in 2006 and 2011. Error and indeterminate rates were significantly higher than the average in the laboratories of Issyk-Ata and the Osh Oblast Children TB Hospital.

Culture

In 2013, a total of 13 686 LJ solid media cultures were inoculated by the regional culture laboratories. Approximately one quarter (3242) were positive and 97% were subjected to phenotypic DST, which is considered an ideal rate. The rates of positive and negative cultures corresponded well to positivity

and negativity rates of Xpert MTB/RIF, proving the analytical accuracy of both methods. The average contamination rate was 5%, which is a little high (default 1-3%). The highest contamination rates, 7% and 15%, were observed in the laboratories of Jalal-Abad and Chui Oblast, respectively (Table 12).

Table 12. Results of TB culture diagnostics at different sites, Kyrgyzstan, 2013

Laboratory	Cx+ n (%)	Cx- n (%)	Contamination n (%)	Total
Chui Oblast	206 (35)	295 (50)	87 (15)	***588***
Bishkek City TB Centre	994 (19)	3 852 (75)	278 (5)	***5 124***
Naryn Oblast	196 (21)	702 (76)	26 (3)	***924***
Talas Oblast	120 (10)	1 072 (89)	12 (1)	***1 204***
Isikul	280 (29)	678 (71)	0 (0)	***958***
Jalal-Abad	1 250 (32)	2 413 (62)	259 (7)	***3 922***
Kara-Balta	196 (20)	730 (76)	40 (4)	***966***
Total	***3 242 (24)***	***9 742 (71)***	***702 (5)***	***13 686***

Cx - = culture-negative
Cx + = culture-positive
Source: NTP/NRL register.

Microscopy diagnostics

Despite the introduction of Xpert MTB/RIF and GenoType MTBDR*plus* (HAIN Lifescience, Germany) at several sites, microbiological TB diagnostics still relies greatly on smear microscopy. Overall 120 605 smears were read in 2013, of which 7% were positive, which is a reasonably high rate. Approximately three quarters of the smear microscopies were requested for diagnostic purposes, one fifth for treatment follow-up and 5% for screening of the contingent of so called chronic cases for potentially infectious patients (Table 13).

Table 13. Percentage of sputum-smear-positive test results by administrative region, Kyrgyzstan, 2013

City and regions	Diagnostic		Samples	Follow-up		Samples	Chronic		Total	
	Spc.	Pt.	(average)	Spc.	Pt.	(average)	Spc.	Pt.	Spc.	Pt.
Bishkek	9.0	10.5	2.9	7.5	9.3	2.0	7.7	8.8	8.3	9.5
Chui Oblast	10.2	10.5	3	12.8	13.3	2.0	17.9	17.7	12.0	12.6
Tallas Oblast	11.9	11.9	3	4.6	4.6	2.0	6.5	6.5	9.0	7.9
Naryn Oblast	5.3	5.8	3	6.4	15.0	2.0	7.6	7.4	5.9	10.0
Issyk-Kul Oblast	12.4	12.4	3	7.1	7.1	2.0	30.9	28.0	11.2	10.8
Batken Oblast	12.5	12.4	3	5.6	5.7	2.0	6.2	6.2	9.0	8.3
Osh Oblast	16.3	17.4	3	8.4	8.3	2.0	21.5	22.3	15.9	16.6
Osh City	9.3	9.3	3	1.6	1.6	2.0	4.6	4.4	6.5	5.9
Jalal-Abad Oblast	19.9	20.3	2.9	2.6	2.6	2.0	11.7	10.4	12.6	11.1
Prison system	8.8	11.7	2.3	14.5	17.5	1.8	0	0	11.7	14.9
Total	***11.6***	***12.4***	***2.9***	***8.6***	***9.8***	***2.0***	***11.8***	***11.6***	***10.9***	***11.4***

Sp. = specimen Pt. = patients
Source: NTP/NRL register.

Health providers in Kyrgyzstan continue to request three smears for each diagnostic case. The mean yield of positive results from all diagnostic smears is 11.6% for diagnostic cases and 8.6% for follow-up cases. Annex 3 shows all microscopy laboratories, the number of tests performed by each and their results by patient groups. Twenty-eight laboratories reported a rate for positive results of below 3%, while 39 laboratories reported a rate over 10%. All but four of the former group belonged to the primary health care system and were all staffed by a single expert each. Fifteen (38%) of the latter

group belonged to the TB system and were staffed by more than one person. Eighty laboratories read on average less than three smears per day, while only 12 laboratories read more than 10 smears.

Challenges

- The expected number of notifications of MDR-TB cases is approximately 1330 per year. Approximately 10 times more rapid tests are needed in order to ensure that all MDR-cases are rapidly diagnosed. Thus, fewer than half of the required number of Xpert MTB/RIF or GenoType MTBDR*plus* tests were performed in 2013.
- Only a few TB hospitals have GeneXpert machines available. Upon hospitalization, patients are admitted to a kind of reception ward which serves as a holding area for all patients until the results of rapid resistance tests arrive. When rifampicin resistance status has been determined, patients are sent either to the MDR-TB wards or to the areas for drug-susceptible TB. During this waiting period, rifampicin-resistant TB is spread between patients who are accommodated together in the six-bed rooms of the reception ward.
- The runtimes of most projects supporting Xpert MTB/RIF implementation have already expired, or will expire very soon. Financing of consumables and maintenance is neither planned nor assured after expiry of the grants.
- The clinical indications for culture diagnostics are not well defined in national guidelines. Doctors do not seem to be well informed about the medical indications for TB culture. Consequently, cultures are ordered for cases which do not need them, making the service unavailable to other cases who would need it.
- Culture diagnostics suffers from high contamination rates in some laboratories.
- There are unexplained discrepancies in resistance rates between genetic and phenotypic tests at the NRL.
- The workload (the daily number of smears) is too low in the majority of microscopy laboratories.

Recommendations

High priority

- Equip every TB hospital with a GeneXpert machine. Perform an Xpert MTB/RIF test for every newly hospitalized patient. Immediately separate patients with rifampicin-resistant forms of TB from those with drug-susceptible pathogens.
- Increase the capacity for molecular tests in the country to supplement microscopy. The majority of MDR-TB cases should be rapidly diagnosed with the use of molecular tests in order to prevent the further spread of MDR-TB.
- Plan and allocate a budget for the rapid tests. Apply for external grants (from e.g. TB REACH) for financial support for rapid TB diagnostics.

Medium priority

- Enlist the assistance of experienced experts (e.g. the SRL partner) to analyse the cause of the high contamination rates in some laboratories. Provide focused staff training to prevent similar contamination rates in future.
- Clearly define clinical indications for culture diagnostics. Enable laboratory doctors to train clinicians to request and interpret culture and DST diagnostics correctly. Support the laboratory experts by officially authorizing them to reject requests which are not in line with the mutually defined indications.
- Analyse the causes of the discrepancies in resistance rates between genetic and phenotypic tests at the NRL, resolve them and prevent them in future by focused staff training.

- Increase the number of smears per laboratory by merging laboratories in close proximity or transferring the specimens to larger laboratory centres using a suitable transport system (see following section, “Logistics and transportation”).

Logistics and transportation

A functional logistic system of laboratory networks is intended to ensure that:

- specimens are transported daily from all medical institutions (hospitals, polyclinics, etc.) to the nearest TB laboratory;
- specimens or cultures are transported promptly from lower-level to higher-level laboratories;
- reagents, consumables and equipment are delivered rapidly and safely without interruption of cool-chains if needed;
- laboratory reports reach the clinician the day after completion of the analyses, at the latest;
- accumulated laboratory results reach the NRL and the NTP in time.

The following modes of transportation/communications could be used, depending on availability:

- institutional bicycles and cars
- public transport
- email and Internet connection
- institutional mobile phones, telephones or fax machines.

In facilities where the laboratory and the medical institution are in the same compound, the patient is usually referred to the laboratory with a laboratory request form (TB 05 or TB 06) for sputum collection. If the patient cannot reach the laboratory, nurses or doctors sometimes deliver the specimens to the laboratory themselves.

When the laboratory is part of another institution, specimens reach it via:

- institutional transportation, which is provided once every one or two weeks;
- nurses or doctors, who occasionally transport specimens from their clinic (which can be a long distance away) using institutional cars or public transport;
- patients, who are sent via public transport.

Laboratory results are mainly reported back via the institutional telephone line and/or private mobile prepaid cell phones. Written reports are entered on request forms TB 05 or TB 06 and sent to the attending doctor with the next person bringing specimens to the laboratory or with an institutional car which visits the institution concerned every one or two weeks. Rarely, laboratory results are reported by email. Fax is not yet used for the transmission of laboratory results, mostly because of the lack of fax machines or landlines.

Reagents and consumables are delivered either by institutional cars or by the laboratory doctors or technicians themselves visiting the oblast TB laboratory, mostly using public transport and paying out of their own pocket.

Challenges

The unreliable transportation system leads to delays in the delivery of laboratory results to health-care facilities. In several TB hospitals visited, clinicians waited up to six weeks for results of Xpert MTB/RIF tests. The reason for the delay is the following: the institutional cars usually transport the specimens every other week to the nearest Xpert MTB/RIF laboratory, and large numbers of samples arrive at a laboratory from several regions at the same time. This delays the analysis. The reports of

the Xpert MTB/RIF results are also transported back by institutional car, which again delays delivery by up to two weeks.

A reliable and universal transportation system is lacking throughout the laboratory network. Transportation is too dependent on unpredictable external factors, such as nurses or doctors who are supposed to collect the specimens from a neighbouring laboratory when they occasionally travel there. The current modes of transportation lead to the perception of laboratory diagnostics as a hurdle and a burden for all concerned, patients, nurses and doctors, for three reasons:

- the transportation of specimens from the health facilities needs to be organized for each batch of specimens individually;
- transportation is time-consuming;
- costs of transportation are only partly reimbursed from the case-management budget.

Sending TB suspects or patients to the nearest laboratory via public transport means potentially exposing other passengers to TB.

Recommendations

High priority

- Implement a universal and countrywide logistical system for transportation of specimens, laboratory materials, and reports which is reliable and free of charge. Make it possible to collect sputum specimens in each hospital, polyclinic or TB dispensary in the country on a daily basis and transport them on the same day to the nearest laboratory, using an intelligent combination of institutional bicycles inside cities and small districts, institutional cars for longer distances (above 10 km) and/or public transport for long journeys, remote areas or in cases when other options are not available. The implementation of a reliable logistics system is a challenging process. It will most likely require technical assistance from external experts. Once established, the system can also be used by other services within the system (such as primary health care, HIV control, etc.).
- Calculate and allocate the budget for the transportation system in the health budget and refinance it as far as possible by reducing the numbers of laboratories as recommended in previous chapters.

Medium priority

- Install fax machines or other telecommunication devices in every TB laboratory and medical institution. Establish a system of transmitting the reports via the telecommunications network.

Human resources

About 45% of laboratories (55 laboratories) are staffed by one specialist only, 33% (40 laboratories) by two specialists, and 21% (26 laboratories) by more than two specialists. Of the 228 specialists working in TB laboratories, 23% (53) had less than three years of experience, indicating high staff turnover, with almost one quarter of specialists quitting the service within three years. Since almost half the laboratories are staffed by one specialist, one in 10 of them is left without staff within two to three years.

The situation in the laboratory of Osh was particularly challenging. The International Committee of the Red Cross regularly trained staff over several years. In the summer of 2012, the SRL provided special training for the staff in Osh. By 2013, all trained specialists had left the service, with the only exception being the laboratory head.

Recommendations

High priority

Set up a human resource capacity development plan which considers the following issues.

- Stronger integration of practical TB diagnostics training in the educational curriculum of laboratory experts at universities (e.g. for laboratory doctors) and basic medical colleges (e.g. for technicians).
- Prevention of the loss of experienced personnel from the system by continuous motivation of the laboratory staff. According to the results of the interviews conducted during the review mission, the strongest motivators would be to ensure adequate salaries and to improve biosafety precautions in the laboratories.
- Reorganization of the staffing system so that laboratory specialists working on their own are put together with the staff of other laboratories, resulting in teams of at least two or three specialists. This will prevent the complete loss of knowledge from a laboratory if a specialist resigns. The daily number of TB specimens for testing should be more than 10 per specialist.
- Strengthening of logistics and transportation between the laboratories of the network and the clinical partners.
- A team of at least three engineers should be duly qualified in function control, maintenance and certification of crucial laboratory equipment and ventilation systems. The engineers shall be acknowledged and certified by the relevant equipment manufacturers and documentation of their certification should be available.

Low priority

- Develop a training policy and annual training plans for every laboratory staff member based on regular training needs assessments, and ensure that training is provided according to the plans.
- Update and/or develop job descriptions for TB laboratory network staff. Include the main responsibilities and tasks of personnel, reporting lines, organizational position, scope of authority, required qualifications, etc. The SRL partner has drafted relevant documents for the NRL which can be used as a blueprint for the other laboratories of the network.

Biosafety

Biosafety rules were available in all visited TB laboratories. They are partly taken over from WHO recommendations and partly introduced by SES. These two sets of standards are contradictory in some respects, leading to suboptimal hybrid solutions (e.g. use of disinfectants). Less than 10% of all specimens sent to TB laboratories yield MTB; others are likely to contain other pathogens which have caused the patient's symptoms. Thus, laboratory staff are exposed not only to MTB, but to many other highly infectious pathogens, including influenza, Coxsackie or Epstein-Barr viruses (e.g. through sputum), hepatitis (e.g. through stool samples or blood), HIV (e.g. through genital specimens or blood), as well as to the full range of bacterial and fungal pathogens. However, the standards of disinfection only consider TB bacteria and disregard all other pathogens. Laboratories mainly use hypochlorite or 70% ethanol, which are either slow-acting or small in their spectrum of action. Only the NRL and the Osh laboratory use wider-acting and more potent disinfectants supplied by international donors (KfW, MSF, ICRC).

The SRL partner has assisted with the implementation of standards for the prevention of and appropriate reaction to biohazards in high-risk containment areas. Similar standards are lacking in

medium-risk culture laboratories, although the potential for dropping and breaking culture tubes puts staff at a similar risk of exposure.

FFP-3 respirators were available in all laboratories visited: however, when staff were asked to demonstrate their use, they either did not know how to put them on or the models did not fit tightly.

Recommendations

High priority

- Review the models of respirator in use in TB laboratories. They must fulfil at least FFP-2 standards, must not be reused too frequently and must fit tightly to the face. Train the staff regularly in the use of respirators. Introduce regular respirator fit testing, using special kits.

Medium priority

- Update national biosafety standards for laboratories in collaboration with international microbiology laboratory experts. Update the disinfection guidelines considering the full range of potent pathogens in TB laboratories.
- Implement up-to-date biosafety plans in all TB laboratories. The biosafety plan must be available to all authorized workers and should form part of their health and safety training under the biosafety permit. The biosafety plan should be reviewed annually and updated to reflect changes, including changes to the biosafety permit. The plan should include the safety measures in place to protect workers from exposure to biological or other identified hazards. Safety measures should be commensurate with the identified hazards and may include:
    - engineering controls (e.g. facility design, biosafety cabinets, chemical storage)
    - work procedures and rules
    - personal protective equipment.
- Medical surveillance (implement annual controls for possible TB infection in all laboratory staff working with TB by Mantoux or chest X-ray, as applicable, depending on the serum conversion status of the personnel concerned, and also a registration system).

Quality management

The NRL has implemented standard operating procedures for all analytical tests and procedures, equipment and the main managerial processes, such as procurement, stock-keeping and staff management. The head of the NRL is highly motivated to develop the quality management system further and to bring it to accreditation according to the International Organization for Standardization standard ISO 15189:2013. For this purpose, a quality management commissioner has been identified to work closely with the SRL partner to develop the quality management system further and close the existing gaps. During the review mission, an international consultant from the American Society for Microbiology audited the existing quality management system, using the WHO Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) checklists, and will provide recommendations for following Strengthening Laboratory Management Toward Accreditation (SLMTA) processes.

The NRL has shared the most important standard operating procedures with culture and DST laboratories, so that some documents are already identical throughout the network. This is considered an important starting point for the development of a common quality management system for the whole laboratory network.

The current quality management team has the potential to fulfil ISO 15189:2013 requirements for accreditation within the next two to three years. It closely collaborates with the SRL partner, which has long-standing experience in laboratory accreditation and quality management system structuring.

Challenges

- A large number of superordinated managerial standard operating procedures are still lacking.
- Except for the head of the NRL and the quality management commissioner, knowledge and understanding of quality management is weak, particularly outside the NRL.

Recommendations

High priority

- Continue the development of the quality management system, aiming to achieve ISO 15189:2013 accreditation. Closely collaborate with the SRL partner and profit from its broad experience in organizing and structuring quality management systems for laboratories. Raise funds for further development and implementation of quality management.

Medium priority

- Make use of the documents drafted by the SRL as much as possible. This will ensure that similar documents are used in all central Asian TB laboratories which are partners of SRL Gauting. This will later facilitate the cross-border exchange of documents, experiences and auditors with laboratories from neighbouring countries.
- Share quality management tools (quality management handbook, standard operating procedures, standard forms for e.g. laboratory requests, reports, procurement orders, documentation of analytical results, etc.) with all laboratories of the network.

Budgeting and procurement

TB diagnostic services are provided by two medical sectors: primary health care and the national TB programme. The budget of the NTP comes directly from the Ministry of Health. All laboratories in the TB sector are under the direct organizational and financial control of the NTP management. TB diagnostic services at the primary health care level belong to fully integrated laboratories located at general medicine facilities providing clinical chemistry, haematology and microbiology analysis, including TB. They are fully financed by the facility to which they belong, which may be a polyclinic or a general hospital. The regional health administration sets the annual budget of the facility. The NTP delivers equipment, reagents and consumables for smear microscopy.

Challenges

- The costs of TB laboratory services are for the most part unknown. The following cost components add to the full costs of laboratory services: running costs (infrastructure, water, electricity), consumables and reagents, maintenance and replacement of equipment, staff, quality assurance, logistics and communication. None of these costs ever seems to have been subjected to robust analysis or budget forecasts.
- The laboratory network is considered the backbone of TB diagnostics, providing the most important tools of TB notification, i.e. microscopy, molecular tests, culture and DST. Despite its high importance, no separate budget line has been defined for the TB laboratory network. Laboratory budgets seem to be allocated arbitrarily according to the financial resources available at the institution concerned rather than according to financial need.

Recommendations

High priority

- Define and allocate a separate budget line for the TB laboratory network, which should be managed by a TB laboratory network manager (see earlier section). To this end, analyse costs of laboratory services using an independent and professional consulting service having experience in public health economics.

Medium priority

- Develop a formula used to establish the annual allocation for each single laboratory of the network according to the spectrum of tests and procedures it performs, the number of specimens analysed and quality of service and analysis determined annually in a standardized way.
- Allocate annual budgets to each laboratory according to this formula.

Case-finding

Suspected TB cases are defined as people who present with symptoms, are contacts of a TB case or belong to a high-risk group. Diagnosis is based on a physical examination, laboratory results, chest X-ray, previous treatment and/or previous history of TB. Often, patients with TB-like symptoms are first put on empirical treatment for about two weeks (using a wide-spectrum antibiotic); if the treatment does not work, then the patient is considered a TB suspect. In addition, one or two sputum samples are investigated (WHO recommends two specimens per patient for a reliable diagnosis). Only TB doctors can diagnose TB; however, after a consultation with a TB doctor at primary health care level or at local dispensary the majority of TB suspects are referred to specialized TB hospitals and/or departments. Since 2012, according to new regulations, 10-15% of patients have been able to start treatment in the outpatient setting. This also applies to bacteriologically confirmed cases, if they can provide the necessary conditions for directly observed therapy (DOT) not far from their homes. From the family medicine centres, smear microscopy laboratories or feldscher points, sputum samples are sent to the regional culture laboratories or NRL for culture and rapid molecular tests (Hain, Xpert MTB/RIF). In some facilities, samples of patients are never sent or do not reach the higher-level laboratories (Osh/NRL) for culture or DST. This results in underdiagnosis or misdiagnosis of TB patients. The detection rate using smear microscopy and culture is still too low. Often, delays are due to transportation problems and other logistical issues (described in detail in the section “Laboratory and diagnostic services”).

Existing national TB diagnostics guidelines cover smear microscopy. These are in line with WHO recommendations and specify the process from sputum collection, through smear preparation, staining and reading smears, to reporting the results to the responsible clinician. They define indications for smear microscopy and the conclusions to be drawn from positive as well as negative results. Aspects of monitoring and external quality assurance are included. The national guidelines are available countrywide and could be seen in every laboratory visited during this review.

Challenges

- Except for microscopy, no diagnostic tools are given sufficient consideration in the national guidelines. Written standards are not yet fully developed for, among others:
    - molecular tests for TB detection in primary specimens, MTB/RIF or GenoType MTBDR*plus* second generation (HAIN Lifescience);
    - culture on LJ medium and/or in MGIT;
    - molecular and/or phenotypic DST for first- and second-line drugs. The national guidelines do not consider risk factors for complicated TB (such as people who

have undergone previous treatment, children, contacts of MDR-TB, migrants, (ex-)prisoners, HIV-positive people, etc.).

- The national guidelines do not take advantage of synergies resulting from the hierarchical order of the laboratory network, i.e. potential benefits of transferring specimens or cultures from lower- to higher-level laboratories for further processing with more complex test systems (e.g. molecular tests, culture or DST).
- The system of revision and implementation of national guidelines via orders from the Ministry of Health is too bureaucratic and tedious. Given the rapid changes and developments in TB diagnostics, existing orders are too rigid to adjust smoothly to new diagnostic options or knowledge.

Recommendations

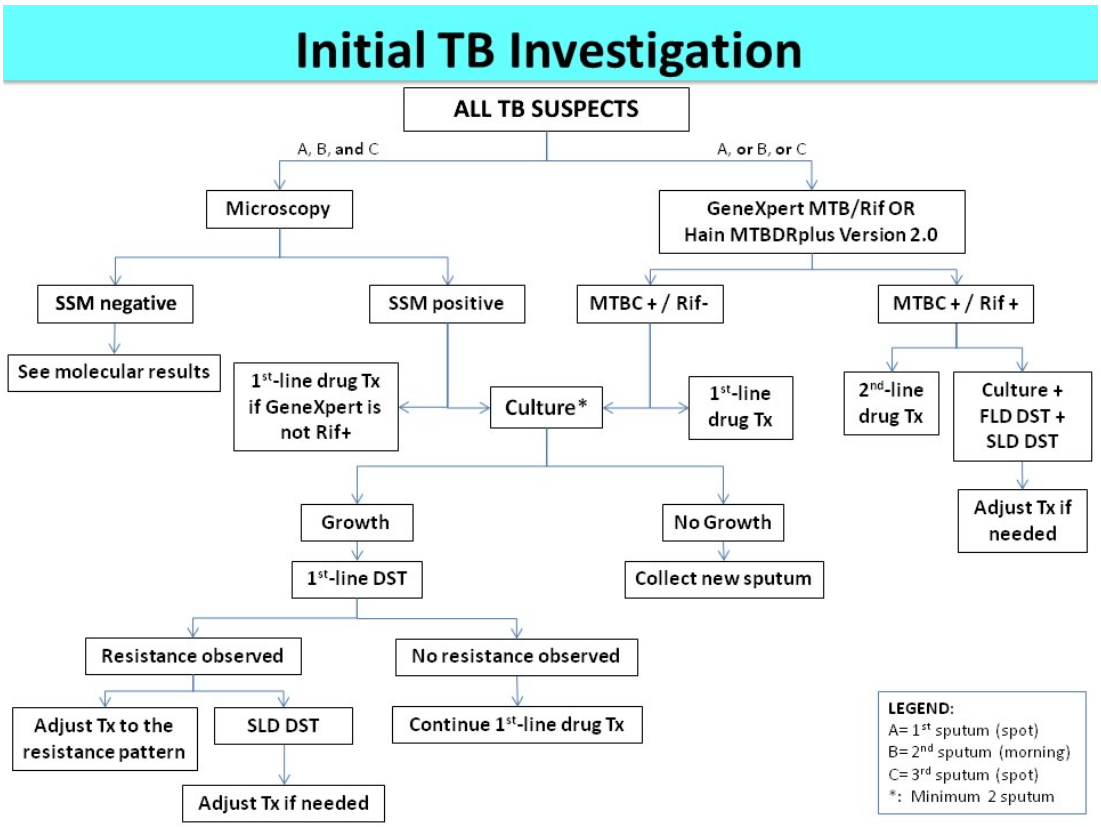
High priority

- Set up an expert board for regular development and revision of national TB diagnostic guidelines. The board should consist of no more than eight experts meeting at least twice per year. It should be chaired by the head of the NRL and a clinician. The experts should represent the DST laboratories, the SRL partner, national and international stakeholders and leading clinicians. The board should be given the responsibility and competence to issue binding national standards for TB laboratory diagnostics, annually revise guidelines and agree on additional guidelines according to new developments and diagnostic options.
- Within the next two years, issue and implement new national guidelines for TB diagnostics. The guidelines should consider all diagnostic tools, the options and synergies resulting from the diversified network with different levels of laboratories and risk assessments for complicated TB. An example for a potential flow-chart of TB diagnostics in the national system is given in Fig. 20.
- Consider the following recommendations for a new diagnostic algorithm:
    - In view of more than 30% of MDR-TB among all cases, Xpert MTB/RIF or GenoType MTBDR*plus* should be performed for every TB suspect;
    - TB culture should be performed:
        - for every case which shows rifampicin resistance in molecular rapid tests;
        - for treatment follow-up examinations;
        - for extrapulmonary TB suspects (e.g. from urine, ascites, semen, operation tissue, pleural or cerebrospinal fluid);
        - for patients with risk factors for complicated TB (TB/HIV coinfection, children, etc.) for whom molecular test results are available;
    - Discontinue using Xpert MTB/RIF or any other molecular test for treatment monitoring.

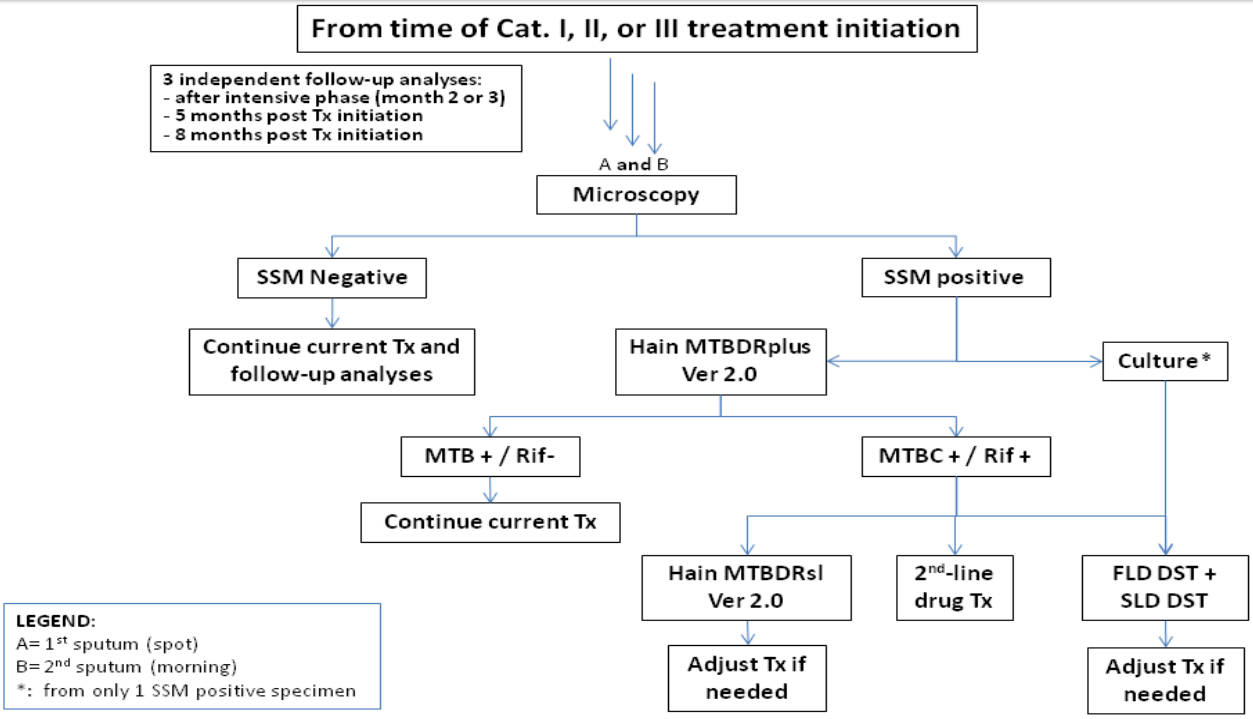
Medium priority

- From worldwide experience, the compliance of laboratory experts in following standards is far higher than that of clinicians. Therefore, give more responsibility to the experts of the laboratory network to decide which diagnostic test should be performed for which patient and with which specimen. Develop new laboratory request forms, including information needed for this kind of decision (e.g. type of TB suspect, type of case following the WHO classification, type of material, number of materials).
- Strengthen the understanding and knowledge of clinicians with regards to laboratory procedures and tests and their significance. Strengthen the communication and interaction between clinicians and laboratory experts.

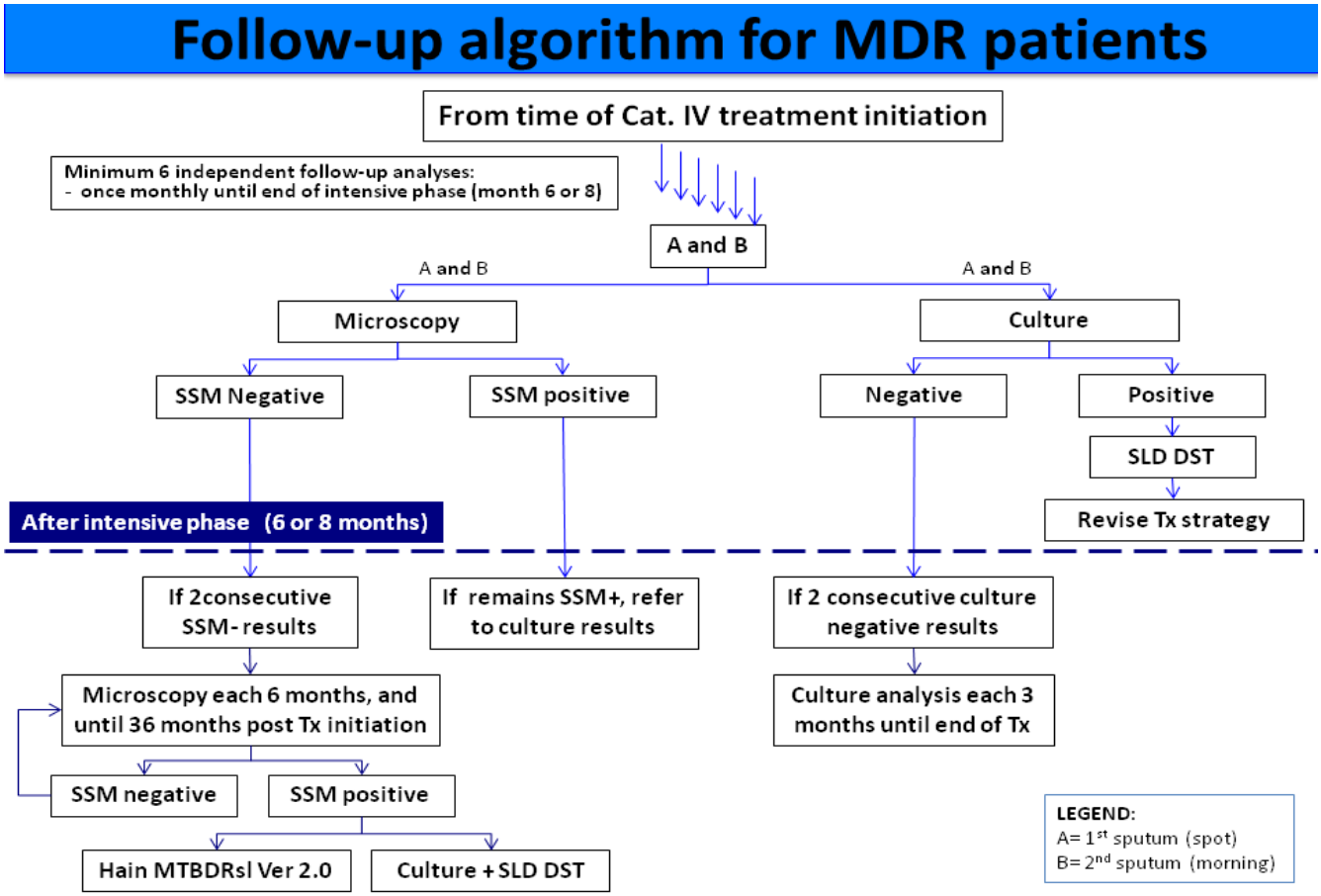
Fig. 20. Sample flow-chart for the recommended diagnostic algorithm



Follow-up algorithm for patients on Category I, II, or III Regimen



Note: if after five and eight months there is no smear conversion, this should be considered as treatment failure and treatment scheme should be changed.
Tx =treatment.



Tx =treatment.

Patient management

The Ministry of Health has the overall responsibility for TB control in the country. TB control interventions are delivered through a network of specialized TB service institutions and primary health care services. The Central Unit of the NTP, represented by NCPh and SSEP, coordinate all TB control activities in the civilian and prison system. TB is regarded as a socially significant disease with a substantial negative impact on society.

For many years, representatives of the Global Fund and other donor organizations have been concerned about the serious epidemiological situation in the country. A high proportion of MDR-TB cases, low treatment success rates and problems of adherence to treatment showed the need for rapid changes in TB care models, e.g. increasing the involvement of primary health care, improving patient follow-up, upgrading the existing TB surveillance system, scaling up rapid diagnostic methods and treating drug-resistant TB cases according to internationally accepted, evidence-based guidelines. Since the last mission to the country, there have been several reports by different international experts with recommendations on ways to improve TB control. However, many of these have been delayed or not implemented.

Service delivery network

The specialized TB services are organized on three levels: national level (NCPh and the NRL), regional level (oblast TB centres with ambulatory and inpatient facilities) and rayon level (hospitals, outpatient TB units and TB cabinets/DOT spots at the family medicine centre). The NCPh is the leading national TB institution, providing supervisory, educational, treatment and diagnostics, counselling and highly specialized TB services.

TB facilities include 34 inpatient departments with 3172 beds, 560 of which are for MDR-TB patients. The Ministry of Health and NTP are aware of the fact that the current TB hospital network is too large; 312 TB hospital beds were closed during 2013 and there is a plan to continue reducing the number (e.g. 400 beds in 2014). Reducing bed numbers and shortening the duration of hospital treatment will potentially free up additional resources that NCPh can use to strengthen outpatient care. According to information from the director of NCPh and the Ministry of Health, there is a preliminary agreement on this issue.

As for the financial aspects, the single-payer system under MHIF creates good opportunities for optimization of the TB service delivery network and more efficient use of resources. For this purpose, the NTP should work intensively with MHIF on payment mechanisms and quality-of-care criteria.

Since the last country review, one of the key achievements has been the revision of the inpatient treatment concept and a new emphasis on ambulatory treatment. In November 2012, with the support of partners, two pilot projects were launched in two regions, focusing on initiation of treatment at ambulatory level. After two years, excellent results have been documented in the sites visited – Alamedin and Issyk-Ata family medicine centres.

At the same time, it was documented that not all family medicine centres and other outpatient treatment institutions provide an appropriate level of TB care. Overall, the primary health care system is not fully ready for large-scale ambulatory treatment. The shift to ambulatory treatment should be planned step by step. The review team was informed that 80% of family medicine centres are understaffed and only a few have a TB specialist or specialists in place. Lack of training and understanding of management of MDR-TB cases in outpatient settings, in relation to both follow-up and side-effects, has been one of the key obstacles countrywide. On the other hand, based on current laws, hospital and outpatient care are not supported equally – either politically or financially. There are serious challenges for NTP and the Ministry of Health if they are to improve the situation.

Good progress can be seen in the main aspects of case-finding, diagnosis, treatment and social support for TB patients. The majority of positive changes were observed over the last two years. Improvements in diagnostic methods due to new rapid-detection tools such as Xpert MTB/RIF and HAIN testing have changed the treatment strategy for both susceptible and drug-resistant cases.

Treatment

Several national guidelines and clinical protocols were prepared by NTP and approved by the Ministry of Health in 2013–2014 in respect of different management issues: MDR-TB treatment, TB in children, infection control, TB at the primary health care level, new case-registration forms and protocols to increase patient adherence to treatment and manage TB contacts. These documents are in line with international standards and outline a number of key interventions for improved TB control. Some of these documents were only recently approved, and it takes time to introduce them to staff.

Treatment regimens for drug-susceptible TB cases are standardized according to the DOTS guidelines. The treatment of patients in Categories I and II has been reorganized: patients with smear-positive TB are hospitalized at least until smear conversion, or for the intensive phase for patients in high-risk groups (depending on social background, comorbidities, drug/alcohol dependence, etc.). The shorter period of inpatient treatment and prioritization of outpatient care is strictly observed. In some pilot areas, 20-50% of patients start treatment in an outpatient setting (Table 14). The NCPh team needs more active supervisory programmes for all regions. Regular visits should be planned with clear recommendations for how to reduce the inpatient period (no regular monitoring visits to regions were conducted at all in 2009–2014!).

Table 14. Start of TB treatment in the ambulatory setting, Kyrgyzstan, 2014 (six-month period)

Oblast	All cases (new and retreated)	Started ambulatory n (%)	New cases	Started ambulatory n (%)	Retreated cases	Started ambulatory n (%)
Bishkek	676	168 (24.9)	591	125 (21.2)	85	22 (25.9)
Chui	846	154 (18.2)	624	120 (19.2)	222	34 (15.3)
Issyk-Kul	179	3 (1.7)	144	3 (2.1)	35	0 (0)
Naryn	178	8 (4.5)	137	5 (3.6)	41	3 (7.3)
Talas	173	12 (6.9)	122	11 (9)	51	1 (2.0)
Jalal-Abad	288	22 (7.6)	232	17 (7.3)	56	5 (8.9)
Osh City	154	9 (5.8)	132	9 (6.8)	22	0 (0)
Osh Oblast	771	50 (6.5)	597	50 (8.4)	174	0 (0)
Batken	243	8 (3.3)	205	8 (3.9)	38	0 (0)
Total	***3 508***	***434 (12.4)***	***2 784***	***348 (12.5)***	***724***	***65 (9.0)***

Source: NTP, 2014.

Primary health care providers work on family medicine principles (family medicine centres and rural family doctors' offices) and are responsible for detection of TB patients (examination of TB suspects as a priority, use of sputum collection guidelines in their routine practice, sputum storage and transfer to the TB laboratory under special conditions), referral of TB patients to specialized TB services for diagnosis and treatment and management of cases in the ambulatory phase of treatment (treatment six times a week). Incentives (food packages, money) for TB patients during ambulatory treatment are provided by UNDP (funded by the Global Fund) in some facilities and by local authorities in others. Treatment for side-effects is provided by UNDP (since 2013) and in some regions from the local oblast budget (it mostly consists of a first aid kit/anti-shock medicines).

In smear-negative and extrapulmonary cases, treatment is ambulatory from day one and is provided at the primary health care level or by a rayon or oblast TB specialist. The length of stay in hospital has been reduced substantially. In some inpatient facilities, the average length of stay is two weeks, until a negative microscopy result is reported; however, in some inpatient facilities (e.g. in Chui Oblast hospital, with only drug-susceptible cases) the average length of stay is 56 days.

The NTP has adopted international standards for TB diagnosis and treatment in line with WHO recommendations. Hospitals for treatment of drug-susceptible TB mostly use fixed-dose drug combinations with standard dosages. All TB patients, including retreatment patients, are treated with first-line drugs pending culture and DST. To shorten the duration of hospitalization, the first control sample from all smear-positive patients will be sent to the laboratory after two weeks of treatment. If there is smear conversion, the patient can start ambulatory treatment. Table 15 shows treatment outcomes by case category for the 2011 cohort.

Table 15. Treatment outcomes by case category, 2011 cohort

Category	Civilian sector			Penitentiary sector		
	Total	Treatment success		Total	Treatment success	
	n	n	%	n	n	%
New cases	**5 184**	**4 514**	**87.1**	**280**	**180**	**64.3**
New pulmonary smear-positive	1 537	1 201	78.1	109	61	56.0
New pulmonary smear-negative	2 125	1 889	88.9	149	106	71.1
New extrapulmonary	1 522	1 424	93.6	22	13	59.1
Previously treated cases	**1 081**	**755**	**69.8**	**157**	**69**	**43.9**
Relapses pulmonary smear-positive	348	213	61.2	53	16	30.2
Other retreatment smear-positive	172	75	43.6	25	8	32.0
Other retreatment cases	561	467	83.2	79	45	57.0
All TB cases	**6 265**	**5 269**	**84.1**	**437**	**249**	**57.0**

Source: NTP, 2014.

Treatment of MDR-TB

Drug-resistant TB represents an acute challenge to the national TB control programme. The country did not have systematic data on the drug resistance burden until the completion of the first nationwide representative drug resistance survey, which was carried out in January–December 2011. The survey results showed very high prevalence of resistance: MDR-TB was found in 26.4% of new cases and in 51.6% of previously treated cases. In addition, polydrug-resistant TB (PDR-TB) was detected in 18.7% and 16.9% of cases, respectively. In the entire sample, MTB strains sensitive to all first-line drugs accounted only for 33.1% of the total of 783 cases tested. MDR-TB treatment started in 2005, with approval of the first application to the GLC.

According to NTP and NCPh, since 2005 a total of 4359 MDR-TB cases have been enrolled for treatment with second-line drugs. Between 2011 and 2013, there was an increase in the number of diagnosed MDR-TB patients, as well as an increase in enrolment in treatment (Table 16). The absolute number of MDR-TB cases detected increased by more than 40% between 2011 and 2013 and is expected to increase further in the future. This is attributable to a further increase in culture and DST coverage, with wider use of new diagnostic tools. These new tests will further increase the number of MDR-TB cases detected, with important implications for the provision of second-line drugs in the country. Table 17 shows treatment outcomes among MDR-TB cases in the period 2009-2011.

Table 16. Number of diagnosed MDR-TB cases and enrolment for treatment, Kyrgyzstan, 2011–2013

	2011	2012	2013	Total
Number of diagnosed MDR-TB cases	806	958	1 163	2 927
MDR-TB patients enrolled for SLD treatment	492	775	1 064	2 331
Percentage of enrolment for treatment	61.0	80.9	91.5	79.5
Number of XDR-TB patients	15	34	60	109

MDR-TB = multidrug-resistant TB SLD = second-line drugs
XDR-TB = extensively drug-resistant TB
Source: NTP.

Table 17. Treatment outcomes among patients with MDR-TB, Bishkek, 2009–2011

	2009	2010	2011
Number of patients undergoing MDR-TB treatment	118	77	100
Treatment default (%)	36.4	20.8	32.0
Treatment failure (%)	11.9	13.0	6.0
Treatment success (%)	45.8	59.7	57.0

MDR = multidrug-resistant TB

Source: Annual report on the implementation of grants provided by the Global Fund in Kyrgyzstan, 2013, p. 38.[1]

Currently, 1198 patients are undergoing MDR-TB treatment with drugs provided with Global Fund support. A total of 1389 patients have been treated through the programme since 2011. According to NCPh data, 881 patients started treatment in 2013, of whom 846 were multidrug-resistant and 35 extensively drug-resistant. In addition to the Global Fund support, the country has other sources of second- and third-line drugs. Table 18 shows patients with MDR/XDR-TB by all sources of drugs.

Table 18. Number of patients with M/XDR-TB admitted to treatment by all sources of drugs in 2013

	UNDP		Previous PR		ICRC		MSF		Total	
	MDR	XDR	MDR	XDR	MDR	XDR	MDR	XDR	MDR	XDR
Civilian	818	25	53	0	0	0	121	8	992	33
Penal	28	10	0	0	30	0	14	0	72	10

ICRC = International Committee of the Red Cross
MDR = multidrug-resistant TB
MSF = Médecins Sans Frontières
PR = Principal Recipient
UNDP = United Nations Development Programme
XDR = extensively drug-resistant TB

Source: Annual report on the implementation of grants provided by the Global Fund in Kyrgyzstan, 2013, p. 39.[1]

During 2011 and 2012, there was a serious gap between the number of diagnosed cases and those enrolled in treatment. The increasing number of cases was related to the introduction of Xpert MTB/RIF techniques and the overall improvement in laboratory services: coverage with DST increased from 26% in 2011 to 56% in 2012 and 72% in 2013. Misdiagnoses and delays in the procurement process resulted in a shortage of second-line drugs. In 2012, around 300 patients were on the waiting list for five months. About 360 patients did not have access to second-line drugs from spring until September 2013. By the end of January 2014 this number dropped to 30 cases and at the time of mission there were no patients waiting for treatment.

The mission was informed that, according to NTP calculations, there will be an increase of 20-30% in the number of M/XDR-TB cases in 2015–2016. Current financial support from donors is not enough to cover all treatment. There will be a treatment gap equivalent to about 800 DR-TB patients.

DST coverage for second-line drugs is low, thus preventing the use of optimal treatment regimens in MDR-TB patients. The final treatment results for the 2009–2011 cohorts showed a treatment success rate of 42.6%, 53.5% and 56.9% respectively, while the default rate was between 33.8% and 21.5%. In prisons, the MDR-TB treatment success rate is as low as 36%, and the default rate is around 45%. The treatment outcomes for MDR-TB patients are still poor, although a clear positive trend has been observed for the last two years.

According to very preliminary data, the treatment success rate for 174 MDR-TB patients who started treatment during the first quarter of 2012 is 70.7% and the default rate is only 13.2% (Annex 3/Table A3.6.).

[1] Global Fund/UNDP Kyrgyzstan. Annual report on the implementation of grants provided by the Global Fund in Kyrgyzstan, 2013. Bishkek: UNDP Kyrgyzstan; 2013 (http://www.kg.undp.org/content/dam/kyrgyzstan/Publications/hiv-tb-malaria/kgz_UNDP-GFATM-Annual_report_2013_ENG.pdf, accessed 2 August 2015).

The current diagnosis and treatment protocols for management of DR-TB have been developed in line with WHO recommendations. The main case definitions are consistent with the WHO recommendations and are based on the status of the disease, the prior treatment history and the type of drug resistance. Some changes in definitions and registration of case categories were planned for 2014. New intervention methods remain the key requirement for preventing resistance. It has become clear that timely diagnosis and proper treatment of DR-TB cases are necessary for overall success in combating the TB epidemic, given the very high DR-TB burden. As soon as the patient is diagnosed with MDR-TB or tests positive with Xpert MTB/RIF, he/she is referred to a specialized department for MDR-TB treatment. All diagnosed MDR-TB cases are notified to the NCPh. The decision to enrol the patient on treatment with second-line drugs is made by the NCPh Consilium or regional MDR-TB committee headed by the local MDR-TB coordinator. Since the beginning of 2014, there have been eight regional consiliums to decentralize the decision-making process. The DR-TB consilium is responsible for coordinating the medical management of DR-TB patients and covers both civilian and prison services. Patients are presented to the committee for decisions on diagnosis, treatment initiation, change of regimen and mode of treatment delivery (inpatient vs. outpatient, transfers from/to prison, etc.). The majority of MDR-TB cases still start treatment as inpatients, although the average length of stay in hospital has steadily shortened. After the intensive phase of treatment, MDR-TB patients can continue the treatment in the ambulatory setting. The approved clinical protocol for MDR-TB treatment includes a separate chapter on management of side-effects. UNDP ensures availability of ancillary medicines for outpatient care, and adherence support for MDR-TB patients is available through the Global Fund project (US$ 18 per month). However, delays in the start of treatment lasting up to several months have been reported in some cases, including the prison sector.

To provide access to free treatment for side-effects during the outpatient treatment phase, ancillary drugs were procured in blister packs, not hospital packs. This allows their distribution not only to TB hospitals but also to primary health care facilities responsible for outpatient treatment of TB, including feldscher-midwife units and family group practices.

Patients' travelling expenses to places of treatment and examination are covered by the programme in all regions of the country. Until 2013, they were available in Bishkek only.

In all departments visited, the basic package of ancillary medicines and knowledge of the importance of adverse event management were in place. As mentioned earlier, some primary health care providers are still insufficiently involved in MDR-TB case management.

The performance-based model of incentive payments to medical workers was first introduced in 2013. Oblast TB coordinators started to be paid based on the performance of programme indicators and doctors for achieving sputum conversion and treatment success and making available the results of all tests required for detection of side-effects.

According to the local management strategy (agreed with GLC), the treatment of MDR-TB patients is standardized. The main treatment regimen during the intensive phase consists of six drugs capreomycin (Cm) (70%) (other injectable Km-30%), levofloxacin (Lfx), protionamide (Pto), cycloserine (Cs), p-salicylic acid (PAS), pyrazinamide (Z). During the continuation phase, 4-5 drugs are administered. The duration of the intensive phase is eight months and until the patient has at least two culture-negative results; the total treatment duration is up to 24 months. Injectables are used on a daily basis; however, it has been suggested that six times per week is sufficient. Intermittent use of injectables after culture conversion can be considered to avoid toxicity (3-5 times per week) and can be confined to patients with high risk of renal failure. XDR-TB patients are treated with moxifloxacin instead of levofloxacin, adding drugs from group 5 to the standardized treatment regimen. However, the only group 5 drugs available to the NTP are high-dose isoniazid, amoxicillin/clavulanic acid

(AMX/CL) and clarithromycin. Linezolid is not available in the country at present but it may be purchased in future through GDF, if additional funding becomes available. For these patients, the treatment regimen can omit AMX-CL and clarithromycin. The possibility of strengthening the treatment regimen for some XDR-TB patients using more powerful new drugs was discussed during the visit. Although this regimen is more costly, some patients will definitely benefit from it. For the laboratory, it means introducing an additional DST method in future.

All MDR-TB patients should be considered for second-line drug testing (HAIN GenoType MTBDR*sl*) to diagnose XDR-TB prior to the start of Category IV treatment.

For patients with advanced disease and extensive resistance (XDR-TB), who have been failed by the available treatment options, facilities and beds for palliative care are allocated by the NTP. Two institutions have been reprofiled to provide palliative care in Kemin (Chui Oblast) and Shekaftar (Jalal-Abad Oblast), each with 60 beds.

For better follow-up of treatment efficacy, the recommendation is to conduct monthly sputum smear and culture during the intensive phase and monthly sputum smear and quarterly culture during the continuation phase of treatment. The management of side-effects needs to be improved: audiometry should be provided for all patients who receive injectables, and special training is needed for interpreting results.

Treatment cards were reviewed at inpatient and outpatient sites. Regimens are designed in line with local clinical protocols and documentation is correctly marked. An important problem is the lack of proper treatment for PDR-TB patients (use of second-line drugs). Regimens for PDR-TB should be determined by the DR-TB consilium as well.

The clinical monitoring of patients is performed adequately. There is a need to discuss the requirements for clinical and bacteriological monitoring during treatment and to adapt to the new laboratory methods. It was noticed that, in some cases, Xpert-MTB/RIF was used for monitoring of the treatment response and in several cases no liquid culture was performed.

Key findings

- Good progress has been observed in the main aspects of case-finding, diagnosis, treatment and social support for TB patients. The majority of positive changes were observed during the last two years.
- Several orders and clinical guidelines have been approved to support programmatic and clinical management of different categories of patients.
- The diagnosis and treatment of TB and MDR-TB are carried out according to WHO recommendations.
- An ongoing restructuring of TB services is under way, giving priority to ambulatory treatment.
- The treatment success rate has increased for patients with drug-susceptible TB and DR-TB.
- Rapid molecular diagnosis of DR-TB is available.
- Since August 2013, there has been no waiting list for MDR-TB treatment.
- A programme of palliative care has been introduced.
- TB control activities have been gradually integrated into primary health care services.
- There are good examples from pilot oblasts for outpatient treatment of MDR-TB from the beginning.

Challenges

- In order to ensure uninterrupted treatment with second-line drugs in 2015/2016, the NTP team and international partners should identify additional financial resources to cover treatment of 800 MDR-TB and 80 XDR-TB patients.
- Because of the large capacity of the TB hospital infrastructure, current treatment practices are highly inefficient in terms of resource use and pose a serious threat of nosocomial transmission of TB.
- Ambulatory treatment in primary health care services is not functioning to its full potential. Not all primary health care facilities are equally prepared to provide outpatient treatment and care. There is still some scope for better planning and the identification of acceptable motivation packages to increase cooperation with TB services.
- Social support for patients largely depends on donor support. The availability of funds from oblasts requires negotiation between the NTP and local authorities.
- TB among external migrants is not adequately addressed. No cross-border TB control and care mechanism is in place.

Recommendations

- Continue support for restructuring of TB services and optimization of hospital beds in TB sector.
- Identify additional sources of funding to cover needs in second-line drugs.
- Strengthen the training and monitoring of treatment sites at regional and local (primary health care) levels (feedback from TB coordinators is crucial).
- Carry out MDR/XDR-TB management training for oblast MDR-TB coordinators (January 2015).
- Revise current guidelines for PDR-TB and XDR-TB, with possible use of new drugs in a future
- Find additional financial and other support from local authorities to increase the adherence to treatment.
- Expand ambulatory treatment of patients with more flexible and patient-friendly options; countrywide implementation of existing good experiences of outpatient care from pilot oblasts should be done gradually, with careful planning and training of primary health care staff.
- Increase motivation of primary health care staff to deal with TB patients.

Infection control

Monitoring of TB infection control

An ad hoc Ministry of Health commission on TB infection control (TB-IC) conducted an evaluation in June 2014 and identified some progress at TB facilities. At the republican level, SES carries out control of TB-IC at primary health care and TB facilities. At oblast and district levels, the local SES departments are responsible. SES visits are supposed to be conducted at least once a year with funding from the State. Stakeholders, however, reported that SES has no funds to conduct regular monitoring visits. There is also no routine monitoring and supervision of TB-IC at the level of the central NTP.

Fifteen SES epidemiologists at the republic and oblast level have been trained in TB infection control. Specialists from oblast, city and district levels still have to be trained (also to compensate for staff turnover). According to SES representatives, training is planned.

TB infection control guidelines and plan

In 2012, the Ministry of Health approved guidelines on "Infection Control of Tuberculosis in Healthcare Institutions of the Kyrgyz Republic". The guidelines and protocols for ambulatory care, including TB-IC in households, are about to be endorsed. There is a detailed TB-IC activity plan for 2012–2016. This plan still lacks indicators and a budget, but it is reportedly used by IC stakeholders: NTP, Republican Centre for Infection Control, international nongovernmental organizations and WHO.

KNCV (Netherlands TB Foundation) and the USAID-funded Quality Health Care Project have funds for TB-IC and implement TB-IC activities. KNCV provides support for the republican TB facility and Bishkek City and Oblast TB dispensaries, while the Quality Health Care Project focuses on ambulatories.

TB in health-care workers

The TB risk for employees of medical facilities is higher than in the general population because of the occupational risk of exposure to (undiagnosed) TB patients. This risk remains high for health-care workers, even if TB-IC practices are adhered to. TB disease in staff of medical facilities should be treated without any discrimination or implication that the staff are not good at their job.

TB disease among health-care workers is an important indicator of nosocomial TB transmission. In Kyrgyzstan the Ministry of Health Order "On protection of the population from tuberculosis", Chapter VII, article 23, states that "health and other workers of TB facilities … have obligatory State insurance in case of occurrence of occupational disease damaging their health or causing death when fulfilling their official duties, in the amount of up to 120 monthly salaries". However, if one of their employees contracts TB, it is the responsibility of the facility concerned (not the Social Fund). Facilities do not have any additional sources of funds to pay compensation. An investigation is conducted in order to assess whether a health-care worker has contracted TB in the course of his/her work. An investigation is then carried out by the TB physician, a trusted doctor and an SES epidemiologist, who identifies the index case and traces the contacts. The combination of the large amount of compensation payable to health-care workers with occupational TB, the need for an investigation and the potential fear of discrimination may be a reason for potential underreporting of TB among the staff of health-care facilities.

It is important to address potential underreporting by either revising Chapter VII, article 23 of the Order "On protection of population from tuberculosis" to establish schemes for reasonable compensation, including paid leave for all health-care workers with TB, without the need to prove that their disease is occupational in origin. It is important to acknowledge that transmission occupationally or elsewhere can rarely be proven (unless applying DNA fingerprinting techniques), so compensation should never be dependent on this proof. Changes in legislation can be long-term and complex; therefore, a pilot initiative to address this problem at several facilities would be desirable.

Availability of equipment

There were mixed messages regarding the availability of respirators and surgical masks at the TB and primary health care facilities. On the basis of TB-IC plans developed by the facilities, UNDP procured ultraviolet (UV) meters, anemometers, fit-tests for oblast-level TB facilities, respirators, 650 ultraviolet germicidal irradiation (UVGI) units (but 300 additional were not bought), surgical masks and HEPA filters. Repairs were carried out to separate "clean" and "dirty" zones at Bishkek City TB Dispensary. The plan was to allocate funds for engineering interventions to separate the zones in TB facilities, but later money was channelled to buy anti-TB drugs instead. IC measurement equipment has been procured and distributed in TB facilities, with follow-up on-the-job training. SES

epidemiologists (at oblast, city and district levels) have to be trained to use the measuring equipment. Such training is planned but the equipment is not currently available.

Previously, and at the time of the review mission, SH2930V premium valved respirators (San Huei United) were available (type FFP-3, with a plastic nose clip). UNDP informed the mission that they have procured two other models: Aura by 3M and VWR N95 by VWR (one size). UNDP drew up a distribution plan for the oblast level, and distribution started in June 2014.

Primary health care

In primary health care (family doctors) there is low awareness of and skills in TB-IC. Primary health care providers do not know about the TB-IC guidelines. They still need to implement cough etiquette, organize sputum collection points and promptly identify patients with TB symptoms.

At the level of primary health care, TB-IC and overall management (using the USAID FAST strategy[1]) is subcontracted by the Quality Health Care Project to family doctor groups, which are supposed to assist with timely triage, cough surveillance and improved diagnostic practices in primary health care. The San Huei type of respirator is available in primary health care, but there is no fit testing.

Some observations from visited facilities

Because of a shortage of time, only two TB-IC responsible persons from two facilities could be interviewed. One facility was visited; however, owing to the unavailability of an appropriately fitting respirator, the review team member could not visit the high-risk areas. At the two visited facilities, there was an IC plan which was updated annually. Ward attendants, nurses and doctors are trained in TB-IC. SH2930V-type respirators are available, but it cannot be determined what percentage of staff they fit, since fit testing is not conducted for all staff.

The facilities visited have started implementing TB-IC plans, but do not have the budget to move equipment in order to ensure proper zoning, or do not have the space needed to separate patients appropriately. There are shortages of replacement UV lamps. Visited facilities do not have an engineer (visiting or staff) for the maintenance of the UVGI units; knowledge of the UV measurement procedure among medical staff who were in charge of this task varied from very good to very poor.

Key findings

- The Ministry of Health is paying increased attention to TB-IC: TB-IC is reported quarterly by the central NTP to the Ministry of Health, and the indicator used is TB disease in health-care workers.
- The TB infection control guideline has been developed and approved. There is a TB-IC plan for 2012–2016.
- The Kyrgyz State Institute for Continuing Education and Kyrgyz State Medical Academy faculty have introduced standard courses on TB-IC and risk assessment.
- TB facilities have started implementing facility-level TB-IC plans and have increased availability of respirators, UV lamps, surgical masks for patients, equipment including fit tests at oblast-level facilities, and HEPA filters.
- Local SES epidemiologists are trained but may need further training, especially for those involved in environmental TB-IC.

[1] FAST: Finding TB cases Actively, Separating safely, and Treating effectively. See: FAST: A tuberculosis infection control strategy [e-book]. Washington, D.C.: United States Agency for International Development; 2013 (https://drtbnetwork.org/fast-tuberculosis-infection-control-strategy_eBook, accessed 20 June 2015).

Challenges

Managerial TB-IC measures at the national level

- At the central NTP level, aggregated or quantitative information on the results of monitoring and reporting on TB-IC was not available.
- The TB IC plan 2012–2016 has been developed but the indicators are not finalized. The budget has not been calculated.
- TB-IC stakeholders mention that the situation of TB-IC at the primary health care level needs urgent improvement and that there are still many facilities with poor TB-IC, for instance the hospital of mental diseases in Chym Korgon, where at the time of the review nine MDR-TB and 16-18 drug-susceptible TB patients were being treated.
- SES is currently not fully involved in monitoring or implementation of TB-IC measures, possibly due to its reform and its limited funds. Training of SES epidemiologists at oblast, district and city levels is necessary.

Environmental TB-IC

- The local company providing maintenance services for laboratories is not coping with the task. KNCV drew up maintenance guidelines for laboratory equipment but there are no biomedical engineers available to check the autoclaves, centrifuges or biosafety cabinets.
- Understanding of the benefits and limitations of natural ventilation on the part of staff of the visited facilities is limited. It should be understood that opening windows whenever possible is a good practice. However, natural ventilation is unpredictable, and a room that at one point in time has 20 air changes per hour may have less than six air changes per hour when the wind direction changes.
- Coverage by UVGI is not sufficient; there are no replacement UV lamps.

Personal respiratory protection

- The San Huei respirators procured previously do not appear to fit all the staff and/or fit tests were not adequately carried out. Fit testing was not done because there was no alternative size or model of respirator.

Recommendations

To the Ministry of Health and SES

- The roles of the central NTP, SES, primary health care and international nongovernmental organizations implementing TB-IC should be clear and fine-tuned in order to allow implementation of TB-IC activities, including training, supervision and monitoring, in a coordinated way at the national, oblast and local levels.
    - Since TB-IC control/monitoring function is the responsibility of SES, the NTP could be made responsible for supportive supervision of facilities to separate supportive supervision from monitoring/control. Supportive supervision is a possibility for on-the-job learning from the supervisor, and ideally it follows a plan which enables any arising issue to be addressed on the spot.
    - It is important to align the TB-IC messages given by international nongovernmental organizations, SES and the NTP with modern TB-IC principles. Since TB is not transmitted via surfaces or objects, make sure that there is no message that e.g. homes of TB patients have to be disinfected.
- Establish a national-level TB-IC Thematic Working Group as part of the existing Coordination Committee on TB at the Ministry of Health. This group should make sure

that the national TB-IC plan 2012–2016 is approved, budgeted and implemented, including updating of sanitary rules and norms.

- Revise Chapter VII, article 23 of the "Order on protection of the population from tuberculosis" to establish schemes for reasonable compensation, including paid leave, for all health-care workers with TB, without the need to prove that their disease is occupational. Transmission occupationally or elsewhere can rarely be proven (unless applying DNA fingerprinting techniques) so compensation should never be dependent on this proof.
- Allocate a budget for TB-IC in primary health care facilities, assess risks, develop facility TB-IC plans and train staff.
- Identify training needs of SES staff (including engineers) and their need for equipment to monitor TB-IC at facilities where TB patients are treated.

To NTP, KNCV, Quality Health Care Project and UNDP

- Conduct a review of airborne IC in all TB facilities and at hospitals and ambulatories where TB patients are treated. Collect and organize information about TB-IC and use it for prioritization and monitoring (e.g. first improve TB-IC at facilities where MDR-TB and XDR-TB patients are (or are planned to be) treated, where there have been TB cases among staff members and where larger numbers of TB patients are served).
- Together with the national TB-IC Thematic Working Group, make sure that the national TB-IC plan 2012–2016 is approved, budgeted and implemented.

To NTP

- Central NTP to employ staff (if necessary), train them and provide supportive supervision for facilities (TB and primary health care) on TB-IC.
- Where available, have specialists in charge of environmental TB-IC.
    - Use caution with cascade training in TB-IC, because of the possible distortion of information, especially regarding environmental TB-IC (ventilation, filtration and use of UVGI).
    - Use caution when making non-engineering staff members responsible for environmental TB-IC (e.g. maintenance of UVGI units) as they may not always have sufficient skills and may need additional on-the-job support to be able to perform well.
    - Medical staff who are in charge of engineering for TB-IC may require additional training on the procedure of UV measurement.
    - Staff should be trained only in the skills they will require. Information given during training should avoid confusing them as far as possible. The quality of "cascade" training should always be controlled so that the TB-IC messages it gives are consistent and correct. For instance, currently staff are calculating air changes per hour but, in contrast to mechanical ventilation conditions, in natural ventilation conditions the number of air changes per hour is not a stable TB-IC indicator, and this should be well understood.
- Strengthen the knowledge of **all** employees (including attendants, guards, drivers, etc., especially in TB facilities) about modes of TB transmission and personal respiratory protection.

To NTP and UNDP

- Make Aura by 3M and VWR N95 by VWR available to facilities, even if they still have San Huei respirators. Facilities should conduct fit testing for staff according to the TB-IC guidelines and protocol. The staff whom San Huei respirators fit well should use

them. The other staff should use Aura by 3M or VWR N95 by VWR, depending on the fit-test results. Do not wait until all San Huei respirators have been used up.

TB/HIV collaborative activities

HIV is a concentrated epidemic in Kyrgyzstan, with low prevalence, estimated at 0.2% in the general adult population.[1] Country authorities reported a cumulative total of 5115 HIV cases and 600 AIDS cases by the end of 2013 (data: National AIDS Centre) which is 64% of the UNAIDS estimate of 8000.

According to the National AIDS Centre, the cumulative number of TB/HIV coinfected cases registered by end of 2013 was 2027; 203 cases were reported in 2013. The National AIDS Centre reports that at the beginning of 2014 out of 877 cumulative deaths among HIV-infected cases 330 were due to TB (38%).

TB/HIV activities

The Ministry of Health and the Government of Kyrgyzstan acknowledge the significance of the TB and HIV/AIDS epidemics in the country. The ongoing health reform programme, Den Sooluk, has four priority areas, including both TB and HIV/AIDS. TB and HIV service provision is the responsibility of two vertical programmes managed by NCPh and the Republican AIDS Centre, with a certain level of integration into primary health care services – the family medicine centres.

Management of TB/HIV coinfection is an objective in both the main documents relating to TB and HIV, with a separate chapter in the Tuberculosis 4 National Programme for 2012–2016 and in the section on diagnosis and treatment of opportunistic infections in the National Plan on Stabilization of the HIV Epidemic. Clinical protocols on management of TB/HIV coinfection were recently elaborated by both programmes, with support from WHO and partners.

Representatives of programmes at the central level meet irregularly, mainly to discuss specific clinical cases. There is no coordination body or permanent responsible staff in the programmes to coordinate TB/HIV activities, there is no plan for joint HIV/TB activities and, therefore, there is no plan for monitoring of activities.

The data on TB/HIV coinfection are scarce and mostly not reliable, owing to inconsistencies in the information systems, especially in the TB programme. There is a lack of data-sharing and cross-checking between TB and HIV/AIDS services. The National AIDS Centre collects and publishes countrywide HIV/AIDS data on a regular monthly basis, including TB/HIV statistics. Data presented on TB/HIV contain information on clinical classification of TB cases, which is less important and does not provide information on resistance. Information in the TB programme on coinfected cases is very limited and mainly provided by the HIV programme. There is no information on TB treatment outcomes among TB/HIV cases. However, an electronic system of TB recording/reporting and monitoring of activities is in development at the NTP, and information on TB/HIV cases will be available once it is implemented.

Reducing the burden of TB in people living with HIV

HIV-infected patients are screened for TB once per year under the existing protocol. Generally it is a problem to keep people living with HIV in the health system for regular visits, and special efforts are needed to improve patient adherence to the system. There is no information about the number of

[1] The gap report. Geneva: Joint United Nations Programme on HIV/AIDS; 2014.

registered TB/HIV cases which have developed TB after being diagnosed as HIV-infected, or how many have a new HIV-positive test after getting a diagnosis of TB.

Patients complete a questionnaire on TB symptoms and are then referred to TB services for testing. The regular procedure for testing of patients in TB services is X-ray and smear microscopy; 1125 X-rays were performed in 2013 as a TB diagnostic procedure on people living with HIV, according to information from the National AIDS Centre. Although seven Xpert MTB/RIF platforms are available in the country, the Xpert MTB/RIF test is not commonly used to test people living with HIV because of the inadequate specimen transportation system and the lack of commitment to this method of testing among staff. There is no information on exactly how many HIV-positive cases have been tested using MTB/RIF or on the results.

The referral system does not function adequately. HIV services often do not get information back on TB testing. A better system of testing HIV patients for TB is observed in family medicine centres, where both services can be obtained in the same facility and patients can be monitored closely by medical staff.

Information on isoniazid preventive therapy among people living with HIV is limited. The TB facility is responsible for provision of the service; isoniazid preventive therapy is not monitored adequately and the impact of the therapy is not measured.

TB-IC measures need to be improved in TB facilities, especially considering the high MDR-TB rates in the country. The admission of patients to the TB hospitals is conducted in accordance with the sensitivity of the strains, and drug-resistant cases are separated from other TB patients. However, diagnosis often takes a long time, and there are no special measures for people with HIV, so the chance of nosocomial infection is high. There is a national TB-IC guideline and national plan, developed and approved by the Ministry of Health, although it is not yet fully implemented in TB and primary health care facilities.

Reducing the burden of HIV in patients with presumptive and diagnosed TB

There has been a drastic improvement in the number of TB patients tested for HIV; almost 100% of TB cases are screened for HIV. However, the screening (blood testing) is done as a compulsory, routine procedure and the majority of patients receive no counselling. TB-suspect cases are not tested for HIV. The first test for HIV (enzyme-linked immunosorbent assay – ELISA) is normally performed within one week of the patient's admission to the TB hospital, and negative results should be available in about one week. The sample for testing is sent to one of 40 laboratories in the country which perform HIV tests. Negative results are available at the TB facility in about one week. If the first test is positive, a request comes to the TB facility to collect a sample for the second test, which should be performed at the central (Bishkek) or regional (Osh) laboratory.

After confirmation of a positive result, the laboratory specialist sends information to the central level – the National AIDS Centre. The information from the central level is then transmitted to the peripheral-level health authorities. As a result, an epidemiologist visits the patient in the TB facility and initiates care related to HIV. The time period from the first (initial) positive result to the visit of the epidemiologist varies from 2-3 to 5-6 weeks, or even longer in some cases.

Despite the availability of antiretroviral therapy in the country, only 54% (110 out of 203 cases registered) of TB/HIV patients were receiving HIV treatment in 2013; this is fewer than in 2012 (78%) or in 2011 (86%) (Table 19). The data are collected and communicated by the National AIDS Centre; there is no information at the NTP on antiretroviral therapy among TB patients.

Usually there are no entries in the medical file by the HIV specialist; the medical file does not contain information on antiretroviral therapy or side-effects of the treatment, and it is thus unclear when the antiretroviral therapy started. Usually antiretroviral drugs are delivered from the HIV/AIDS regional centre to the TB hospital by family members of the patient on a monthly basis. In the majority of cases, antiretroviral therapy is given to the patient and is self-administered; drug intake is not monitored by medical staff. At facility level, awareness of antiretroviral therapy among TB staff differs from facility to facility. In some TB hospitals, the medical staff do not know whether patients have been prescribed and are receiving antiretroviral therapy; in other cases, there is communication between TB and HIV specialists.

Table 19. TB/HIV collaborative activities, Kyrgyzstan, 2008–2013

Year	Registered TB cases	TB cases tested on HIV	TB/HIV cases	TB/HIV among TB %	TB/HIV cases on ART n (%)	TB/HIV cases on CPT n (%)
2008	7 127	6 508	117	1.8	0	n/a
2009	6 358	6 358	88	1.4	19 (22)	88 (100%)
2010	6 295	n/a	183	n/a	68 (37)	125 (68%)
2011	6 666	6 666	153	2.3	131 (86)	92 (60%)
2012	6 916	6 916	151	2.2	118 (78)	101 (66%)
2013	7 209	n/a	203	n/a	110 (54)	92 (45%)

ART = antiretroviral therapy
CPT = cotrimoxazole preventive therapy
n/a = data not available
Source: Global TB database (http://www.who.int/tb/country/data/download/en/, accessed 20 June 2015).

The existing situation is explained by the supposed confidentiality of the patient's HIV status, even though, in reality, that confidentiality does not exist. The medical staff are aware of the patient's HIV-positive status because of the request for a second HIV test and the visit by the HIV specialist. However, in the penitentiary TB treatment facility, Prison No. 31, which is supported by ICRC, Karasy TB Hospital and an MSF pilot project, it was observed that antiretroviral drugs were stored by medical staff and that treatment was observed and monitored. Generally, the knowledge of TB staff about HIV treatment and possible side-effects by interaction with TB treatment needs to be improved.

Cotrimoxazole preventive therapy was provided for 92 TB/HIV patients, of a total of 203 registered cases (45%) in 2013, which is fewer than in previous years (Table 19). There are no entries in the medical files relating to cotrimoxazole preventive therapy; therefore, at the level of the TB services, it is unclear how long patients are on this therapy.

Information regarding the regular administration of antiretroviral therapy among TB/HIV patients under ambulatory treatment is also not clear. Medical records are not kept and communication between TB and HIV specialists is inadequate and irregular.

Integrated TB and HIV services, along with opioid replacement therapy, are provided at two sites in the country, in Bishkek and Osh. Integrated services can be provided at family medicine centres where both TB and HIV specialists operate under one roof; Issyk-Ata family medicine centre is a good example of collaboration between the two services.

The network of civil society organizations engaged in provision of HIV services is well developed in Kyrgyzstan; however, their participation in TB control activities is very limited. Civil society organizations could play a significant role in helping TB/HIV coinfected patients to access TB and HIV services and in the introduction of HIV prevention interventions for patients with presumptive and diagnosed TB, in collaboration with harm reduction services and reduction of stigma and discrimination related to TB and HIV.

Recommendations

The NTP and HIV/AIDS programmes should work together on the following tasks.

- Draw up a work plan for joint activities and begin on its implementation.
- Set up a monitoring and evaluation system with defined indicators.
- Ensure necessary funding for activities and monitoring.
- Organize regular meetings between appointed staff for data cross-checking and follow-up of planned activities.
- Develop a training module based on updated clinical guidelines; provide training sessions for staff working in TB and HIV, including communication skills. Increase the number of patients with TB/HIV on antiretroviral therapy.
- Provide Xpert MTB/RIF testing for people living with HIV, where necessary, by improving the specimen transportation system and linking with TB specimen transportation.
- Improve the referral system between TB and HIV services.
- Improve provision and monitoring of isoniazid preventive therapy for people living with HIV.
- Ensure availability of medical information for medical personnel responsible for TB/HIV patient care by extending the range of staff who have access to confidential information.
- Ensure antiretroviral therapy for all cases with TB/HIV.
- Ensure provision of routine cotrimoxazole preventive therapy for all TB/HIV cases.
- Promote TB and HIV treatment adherence via introduction of a multidisciplinary approach involving local nongovernmental organizations.
- Support collaboration between TB and HIV practitioners and improve monitoring of the treatment process from both sides.
- Promote integration of TB and HIV services and consider further integration with harm reduction services and hepatitis care.
- Use existing evidence to address barriers in patient-centred service provision and adopt an ambulatory model of treatment for TB/HIV patients, where possible.

TB in children

The NTP TB treatment and management guide and associated materials, reflecting WHO recommendations concerning dosages and composition of treatment regimens, include the diagnosis and management of TB in children. The national policy on TB in children and guidelines on prevention and treatment are also consistent with WHO guidelines and the *Roadmap for childhood tuberculosis*;[1] they are currently being revised to include the most up-to-date treatment and care guidelines for childhood MDR-TB. Treatment outcomes for children with TB are shown in Table 20.

[1] Roadmap for childhood tuberculosis: towards zero deaths. Geneva: World Health Organization; 2013.

Table 20. Treatment outcomes for children (0-14 years) with TB, Kyrgyzstan, 2013

Cases	Number	%
Total number of cases registered	594	100.0
Cured and treatment completed (success rate)	553	93.1
Died	5	0.8
Failed	1	0.2
Defaulted	4	0.7
Transferred out	7	1.2
Not evaluated (moved to MDR cohort)	21	3.5
Diagnosis not confirmed	3	0.5

Source: NTP.

In 2013, 594 paediatric TB cases (aged 0–14 years) were notified (8.2% of the adult caseload). This figure is lower than that expected for overall population size (which would be around 10–15%) and suggests that TB case-finding among children and/or reporting of notified paediatric cases needs improvement. There were 107 TB cases among 0-4-year-olds in 2013 (18% of all paediatric cases) and 487 in the 5-14-year age group (82%). This age distribution does not correspond with the estimate that two thirds of paediatric cases will be in the 0–4 group and one third in the 5-14-year-old group, suggesting a relative underdiagnosis and/or underreporting of TB in the vulnerable and difficult-to-diagnose 0–4 group.

Intersectoral collaboration involving, for example, TB services, primary health care, paediatrics and maternity and vaccination-related services exists and features in policy and programme documents, but paediatric health workers' collaboration with TB services (and vice versa) is neither systematic nor comprehensive (patient files, for instance, are not systematically shared or exchanged). The same applies to collaboration between TB services and antenatal care.

Policy and guidance exist at national level for prophylactic treatment of children who have been in contact with smear-positive TB cases. It is of concern, however, that the practice continues of sending children (contacts and paediatric TB cases in the continuation phase of their treatment) to a sanatorium although, and positively so, the duration of hospitalization has been significantly shortened from an average of two years to 6-9 months. However, this practice should be further revised and gradually discontinued on social and infection control grounds. Intensive follow-up of children in contact with people with MDR-TB is neither fully implemented nor systematized and institutionalized yet.

Recommendations

- The practice of admitting children with TB to a sanatorium should ideally and ultimately be discontinued by the end of 2015. Sanatorium and related staff should benefit from a rational and feasible reallocation and transformation strategy, thus allowing efficient use of resources, both human and material, and also in an effort to pre-empt resistance to implementation of this recommendation.
- Children who are TB contacts, and particularly contacts of MDR-TB cases, should be prioritized as a high-risk group for active case-finding.
- A robust, comprehensive and systematic follow-up approach (quarterly symptomatic assessment) should be introduced for children who are contacts of MDR–TB cases.
- Knowledge and capacity in relation to TB diagnosis and treatment in children should be further developed and sustained, particularly among primary health care workers (including nurses) and community workers, to enable children with currently underdiagnosed TB to receive a quick and accurate diagnosis and commence treatment without delay (and increase detection of currently undetected children).
- The maternal and child care department of the Ministry of Health and the NTP should develop a plan to improve collaboration and achieve full integration of services, in line

with the principles of Integrated Management of Childhood Illness (IMCI), fully covering TB prevention, treatment and care in children and clearly detailing the terms of reference of all involved players in TB and paediatric services, including epidemiological recording and reporting, data-processing and file-processing activities and referral activities and pathways.

BCG vaccination

National vaccination guidelines are generally consistent with the WHO guidelines[1] for TB vaccination using bacillus Calmette–Guérin (BCG), i.e. vaccination is recommended once, at birth, with isoniazid preventive therapy at nine months for non-HIV-infected and HIV-infected infants exposed to TB. However, revaccination is reported to be sporadically continued at different ages.

According to the NTP, over 95% of children are vaccinated at birth. However, BCG vaccination delivery takes place in the home in rural areas, and the completeness and quality of the vaccination of children in these areas depends on the parents' compliance and knowledge of the vaccination programme and on the accessibility of health-care services. The information on BCG vaccination is recorded in the neonate's personal file.

Recommendations

- The WHO-recommended BCG vaccination approach should continue to be included in all national document-updating processes, including not only those relating primarily to TB but also those relating to childhood TB and vaccination policies, treatment and care guidelines and protocols.
- BCG vaccination should be part of outreach activities and be included in training for community workers, including religious leaders and parents.

TB control in prisons

There are a total of 13 penitentiary facilities in Kyrgyzstan including four SIZOs. The average annual prison population (excluding settlement colonies) has substantially decreased over the last decade and currently stands at about 8000 persons. The Medical Department of the SSEP of the Kyrgyz Republic is responsible for provision of medical services for detainees, including those for TB. Taking into account international recommendations, the SSEP decided to merge the two TB treatment sites (Colonies No. 27 and 31) into one institution. For this purpose, an agreement was reached with MSF that it will gradually hand over all support in Colony No. 31 to ICRC. With the support of ICRC, major reorganizations of prison TB services are under way. The process of restructuring the two colonies will be finalized by the end of 2014. This will allow an integrated approach to management of TB, HIV/AIDS, drug abuse (e.g. harm reduction and methadone programme) and mental health of the detainees – with all required services provided at one site ("one-stop-shopping" principle).

The SSEP signed a direct agreement with UNDP in 2013 and started implementing a multilateral approach to solving the problems faced by the programmes for prevention of HIV among inmates. These activities are very relevant to TB patients as well. The number of TB patients diagnosed in the prison sector has been steadily decreasing (Table 21).

[1] Guidance for national tuberculosis programmes on the management of tuberculosis in children, 2nd ed. Geneva: World Health Organization; 2014.

Table 21. Main epidemiological data for prison sector

Year	Average prison population	New TB cases		New pulmonary ss+		Mortality	
		n	Rate*	n	Rate*	n	Rate*
2006	16 210	1 047	6 459.0	221	1 363.4	135	832.8
2010	9 119	290	3 180.2	87	954.1	32	350.9
2011	8 296	366	4 412.0	109	1 314.0	19	229.0
2012	7 697	257	3 339.0	66	857.5	31	402.8
2013	7 744	149	1 924.1	51	658.6	25	322.8

* rate per 100 000
ss+ = sputum-smear-positive
Source: NTP, prison report.

TB case detection in prisons is carried out by a combination of passive and active case-finding methods. The penitentiary service has one mobile mass miniature radiography unit (which had not been operative for the last six months) and one stationary mass miniature radiography unit (located in SIZO Bishkek). Five microscopy laboratories in the system are located in Colonies No. 27, No. 31, No. 3 and No. 8 (all in Chui oblast) and in Bishkek SIZO. There is also a GeneXpert machine at Bishkek SIZO (provided by MSF). For culturing and DST, sputum specimens are sent to the NRL at NCPh; ICRC sends specimens to Borstel laboratory in Germany to double-check the results, which means a 3-4-month delay before medical treatment starts. Table 22 shows the number of drug-susceptible and DR-TB cases detected in the prison sector in 2013.

Table 22. Absolute number of all TB cases detected in prison sector, 2013

Drug-susceptible TB cases	PDR-TB cases	MDR-TB cases	XDR-TB cases	Total
151	25	70	7	253
59.7%	9.9%	27.7%	2.8%	100%

MDR-TB = multidrug-resistant TB XDR-TB = extensively drug-resistant TB
PDR-TB = polydrug-resistant TB
Source: NTP, prison report.

TB treatment in prisons is carried out at two institutions; both facilities are located in Moldovanovka village, Chui Oblast. Colony No. 27 has 100 beds (60 beds for palliative treatment for MDR-TB patients and 40 beds for active MDR-TB patients). Colony No. 31 has 150 beds for drug-sensitive and PDR-TB cases and is supported by ICRC. In November 2013, in the territory of the colony, an ambulatory TB treatment department was opened for 164 patients, setting a good example to all neighbouring countries.

New buildings with good IC measures allow different categories of patients to be separated by smear/culture and DST results. The building for treatment of MDR-TB patients with sputum-smear-positive results will be opened in September 2014. The treatment conditions observed in Colony No. 31 were good and the personnel were motivated and very knowledgeable. However, the prison facility has a lack of staff (four out of the nine medical doctor positions are vacant).

Regarding MDR-TB treatment, currently there is no waiting list and all diagnosed MDR patients are enrolled in treatment. About 100 MDR-TB patients are diagnosed annually in the penitentiary system. Since February 2014, the NCPh has assigned a coordinator responsible for the prison system, who leads the activities of the Council of Physicians, participates in drafting of documents and coordinates the transfer of patients from the penitentiary to the civilian sector. The NCPh provides counselling and methodological assistance to the SSEP on a regular basis.

First-line drugs for sensitive TB cases and second-line drugs for MDR cases are supplied by the Global Fund grant and medicines for treatment of PDR-TB patients were previously provided by MSF. Currently, the drugs are supplied by the NCPh. Drugs for management of the side-effects of TB drugs are financed from the State budget. National protocols are available and there is a unified approach to programmatic management of DR-TB with the civilian sector. Training for prison medical staff is provided by international partners (ICRC).

The prison TB recording and reporting system is based on the Epi-Info platform and is integrated with that of the civilian sector: all data from prisons are submitted to the NCPh on paper on a quarterly basis and are incorporated into the overall country reporting. However, there is a plan to introduce the same platform as in the civilian sector to harmonize data entry and create a link with the central TB registry.

Incentives (food packages) for TB patients in prisons are provided by ICRC once per week. ICRC also implements various activities (a "social support package") for following up released ex-detainees who need to complete their TB treatment in the civilian sector.

The TB treatment success rate in the drug-susceptible TB cohort for the last three years (2011–2013) has been around 85% and the default rate 4.5%. In the same period, the overall treatment success rate for DR-TB cases has been very poor – below 40%. In addition to the high default rate, the success rate is affected by TB/HIV coinfection. Despite the intensive adherence support provided, the default rates for both detainees and ex-detainees following their release are very high, and this remains the key concern for the TB programme in prisons. Among MDR-TB cases, the rate of default after discharge is as high as 40% (Table 23).

The system of pre-release and post-release care for TB patients is well organized, with the support of ICRC and coordination by the civilian sector. It was explained to the mission that the reason behind the high default rates for detainees is the side-effects of TB medicines.

Table 23. Treatment outcomes, MDR-TB cohort, 2007–2012 (Q1 and Q2)

Year	Cases notified	Put on treatment	Treatment success	Failure	Defaulted	Died	Still on treatment
2007	116	69	34.8	14.5	**50.7**	n/a	n/a
2008	203	113	37.2	18.6	**40.7**	3.5	n/a
2009	121	110	29.1	13.6	**49.1**	8.2	n/a
2010	87	78	34.6	12.8	**47.4**	5.1	n/a
2011	107	64	42.2	6.3	**46.9**	4.7	n/a
2012 (1st, 2nd Q)	64	44	45.5	9.1	**34.1**	6.8	4.5
Total	*698*	*478*	*36.0*	*13.4*	***45.4***	*4.8*	*n/a*

n/a = data not available
Q = quarter
Source: NTP database.

Four years ago, SSEP introduced social worker posts into the staffing schedule of all penitentiaries. The social workers are responsible for preparing detainees for release (e.g. where they need continuing TB treatment). However, the effectiveness of their work in such cases is limited, as they cannot act "outside the prison walls" and follow up the ex-prisoners with TB.

There are about 300 people living with HIV in the penitentiary system, of whom 60-70 persons are diagnosed with TB/HIV annually. At the time of the mission, 40 detainees were receiving antiretroviral therapy. Methadone substitution treatment is provided in Colony No. 31. The average dosage of methadone is 150 ml.

Key findings

- Major reorganizations of prison TB services are under way with the support of the ICRC. The merging of Colonies No. 27 and No. 31 will be finalized by the end of 2014.
- New buildings with excellent IC measures allow the separation of different categories of patients by smear/culture and DST results.
- The ambulatory department was opened in November 2013, setting a good example to all neighbouring countries.
- The number of TB patients diagnosed in the prison sector has steadily decreased.
- National protocols are available and there is a unified approach to programmatic management of MDR-TB with the civilian sector.
- The post-release system for TB patients is well organized with the support of ICRC and coordination by the civilian sector.
- The penitentiary system has its own well functioning electronic surveillance system; however, there is a plan to introduce the same platform as used in the civilian sector to unify data entry and create a link with the central TB registry.
- The penitentiary system has all second-line drugs and antiretroviral therapy required for all MDR/XDR-TB patients.
- There is a shortage of physicians in the penitentiary sector (four out of nine assigned physician positions are vacant).

Recommendations

- Finalize reorganization of the TB control network and prepare a plan for sustainability (including human resources aspects) of services after partner support ends.
- Improve inmate motivation and psychological care to decrease the default rate and dropout from treatment.
- Address the problem of understaffing and personnel motivation by development of a sustainable human resources plan after donor support ends.
- Manage the system of pre- and post-release of TB and DR-TB patients from prison to civilian TB services to ensure continuation and follow-up of the treatment.
- Set up a sustainability programme to avoid interruption of treatment during patient movements within the penitentiary system (pretrial/court/colonies).
- Update the current electronic surveillance system to bring it into line with the central TB registry database.
- Provide proper treatment for patients with PDR- and XDR-TB. Calculate needs for reserve drugs in prisons, colonies and pretrial institutions.

4. Medical products, vaccines and technologies

Management of anti-TB medicines and supplies

The Ministry of Health has the overall responsibility for TB control in the country. It undertakes this function through the Central Unit of the NTP. TB control interventions are delivered through a network of specialized TB service institutions and primary health care services. The TB control programme is organized as a three-level network: national level – NCPh; regional level – oblast TB dispensaries and hospitals; rayon level – district TB dispensaries and hospitals, TB cabinets/DOT rooms in family medicine centres.

The drug management unit of the national TB control programme was strengthened following the recommendations of the previous technical missions and currently consists of four pharmacists, two being based at the central store and two at the NTP central office. The unit is responsible for planning, forecasting the programme needs for anti-TB drugs and medicines for management of adverse drug reactions, preparation of requests; partial placement of orders and receipt of shipments after customs clearance, storage, inventory and further distribution of these medicines to TB facilities, including the penitentiary sector, in coordination with UNDP – the Principal Recipient of the Global Fund grants in the country. TB drug management is performed at all levels of the distribution chain by an appointed or assigned drug coordinator and responsibilities will vary from level to level. It may include analysis and control of consumption of the drugs and supplies, as well as development and implementation of relevant training programmes, monitoring of the drug supply chain and facilitation of the drug management information system. The drug management unit is also coordinating all activities related to process safety management with other partners. The laboratory equipment, reagents and supplies for TB diagnosis are quantified, procured and managed through the laboratory unit, led by the NRL coordinator.

Selection

Medicines for treatment of TB are selected by the NTP in coordination with technical partners and in accordance with national treatment guidelines which are in line with WHO recommendations. Since 2007, the programme has rapidly increased the use of fixed-dose combinations, and almost 90% of patients with drug-susceptible forms of TB are currently treated with fixed-dose combinations at all levels. The limited use of single-dose formulations (10%) is mostly attributable to adjustments in drug regimens when a monodrug/polydrug resistance pattern is identified. A few fixed-dose combinations have been withdrawn over the last 24 months because of side-effects, as reported and/or observed by the visited health facilities.

The treatment of TB is very much standardized, and the list of medicines that are currently recommended in the national TB guidelines are as follows (Table 24; see also Annex 5).

Table 24. Recommended first-line and second-line drugs, Kyrgyzstan

First-line drugs	Second-line drugs
RHZ (60/30/150 mg tab)	Kanamycin 1g vial
RH (60/30 mg tab), dispersible	Capreomycin 1g vial
RH (60/60 mg tab) dispersible	PASER (acid/sodium) 4g sachet
RHZE (150/75/400/ 275 mg tab)	Protionamide 250 mg tab
RH (150/75 mg tab)	Cycloserine 250 mg cap
RH (150/150 mg tab)	Levofloxacin 250 mg tab
Ethambutol 100 mg tab	Moxifloxacin 400 mg tab
Ethambutol 400 mg tab	Clarithromycin 500 mg tab
Isoniazid 100ml tab	Amoxicillin + clavulanic acid 875/125 mg tab
Isoniazid 400mg tab	
Pyrazinamide 400 mg tab	
Streptomycin 1.0 g vial	
Rifampicin 150 mg tab	
Rifampicin 300 mg tab	

R = rifampicin H = isoniazid
Z = pyrazinamide E = ethambutol

Since the last review mission in 2010, the NTP has shifted from an intermittent to a daily regimen. Despite this shift, 10% of patients are still to be treated in an intermittent regimen in 2015. Due to the substantial burden of DR-TB in the country and as per the latest WHO recommendations (2011),[1] the mission recommended that the programme should stop the intermittent regimen at once. As per the repeated recommendations of the technical partners, the Drug Regulatory Authority, represented by the Department of Medicine Supply and Equipment, included most of the anti-TB drugs in the National Essential Medicines List in 2012; this is revised every two years. The National Essential Medicines List follows the pharmacological principle of classification, and therefore some of the front-line drugs (R, S) and second-line drugs (amoxicillin, capreomycin, kanamycin) are not in the group of anti-TB medicines. As for group 5 drugs, it is hoped that, with the revision of the TB treatment guidelines, the inclusion of these lifesaving medicines in the National Essential Medicines List will pose no problem. The products on the National Essential Medicines List are prioritized for registration and procurement with Government funding.

The key problems observed with selection of anti-TB medicines in Kyrgyz Republic were the following.

- Selection of capreomycin, a more costly injectable for treatment of DR-TB, over alternative drugs (over 80% of cases were prescribed this drug). This practice was discussed with technical experts and partners in detail in an open meeting, and changes will be reflected in revised calculations. It was agreed that changes will be based on the estimates derived from DST and financial savings will be used for procurement of additional second-line drugs.
- Inclusion of non-standard, non-required strengths and formulations of anti-TB drugs, not recommended by the national TB treatment guidelines, in the National Essential Medicines List. This, in turn, permits in-country registration and further dispensing of such products on an over-the-counter basis through the pharmacy network. The matter was extensively discussed in a meeting with representatives of the Quality and Medicines Policy and Medicines and Supplies Procurement departments of the Ministry of Health. It is expected that such medicines and formulations will no longer be registered in the country. The mission report will be shared with both departments of

[1] Guidelines for the programmatic management of drug-resistant tuberculosis – 2011 update. Geneva: World Health Organization; 2011.

the Ministry of Health for their information and further action, in addition to the comments that were provided during and after the meeting.

Procurement

The Procurement Law regulates all aspects of public procurement in the Kyrgyz Republic. The procurement of essential medicines is fully decentralized and organized by each hospital on a quarterly basis, using the central/State allocated budget and according to the domestic tender requirements. Procurement from the local budget (health facility budget) is organized as follows: the health facility places an announcement on the procurement website of the Ministry of Finance;[1] the tenders are evaluated by the working group of the health facility; orders are placed monthly; the successful tenderer delivers the medicines to the final destination, i.e. the hospital(s). Despite the bidding process, the medicines purchased are expensive, because of the fragmentation and small size of the market, and of poor or unknown quality. This makes the decentralized public procurement practices unreliable and unsustainable. As per the current procurement regulations, compliance with the Good Manufacturing Practices (GMP) standard is not yet a requirement for medicines. The main selection criteria are still the lowest price and the longest shelf life. It is expected that, with the approval of the revised National Drug Policy (NDP), the preference and requirement for GMP compliance, coupled with approved statuses of medicines issued by the WHO Prequalification of Medicines Programme and stringent regulatory authorities, will be enforced through the Drug Regulatory Authority as the main eligibility criterion for procurement and registration of anti-TB medicines and, it is hoped, all antimicrobial agents.

An uninterrupted supply of quality-assured anti-TB drugs and medicines for management of adverse reactions has been maintained for the last two years, and there was no waiting list for treatment in any of the visited health facilities. This is a key achievement for the programme, since in 2012 the waiting list numbered over 300 DR-TB patients. The procurement of anti-TB medicines and medicines for management of adverse drug reactions has been fully donor-dependent for over a decade, and requires coordination among multiple players such as the NTP, UNITAID, the Global Fund project (Principal Recipients Project Hope and UNDP), MSF, ICRC and GDF (see Annex 4). Procurement through donor funding and grants takes place once a year, based on needs estimated by the drug management team in coordination with other NTP experts and technical partners. The current procedure for procurement of anti-TB drugs and medicines for management of adverse drug reactions is as follows: the NTP selects the drugs, provides the specification which includes dosage, formulation and packaging, quantifies the needs per year using all available tools and prepares the draft order. Project Hope and UNDP Kyrgyzstan finalize the drug orders, sign technical agreements with GDF and coordinate the disbursement of funds to the GDF procurement agent. Countrywide drug orders are usually placed once a year, with deliveries planned every six months to ensure timely arrival of medicines and replenishment of all stocks at central warehouses. Programme needs for medicines are quantified by the drug management team with the support of Project Hope, UNDP and the USAID Quality Health Care Project, using the GDF drug calculation sheet and other self-developed Excel workbooks. The recording and reporting system for second-line drugs relies in practice on the information system developed for first-line medicines. Based on the information and funding available, the programme has quantified its needs for first-line drugs effectively, without shortages or large losses/expiries, while second-line drug quantification has proved to be less straightforward, owing to the lack of relevant and timely data and an electronic drug management module.

Adult first-line drugs were supplied to the programme through a GDF grant from 2007–2010 and were then switched to the GDF direct procurement mechanism, using Global Fund grants and organized by

[1] http://www.goszakupki.gov.kg/, accessed 20 June 2015 (in Russian).

Project Hope from 2011 up to the present. An additional one-year emergency grant for first-line drugs was provided by GDF to fill treatment gaps in 2013. The planned treatments through the Global Fund grant for 6500 patient treatments in 2013–2014 were partially delivered before the mission took place, and almost 7000 treatments are to be procured in 2015. A follow-up discussion will have to take place during the next GDF/GLC mission to ensure that necessary arrangements for order placements are made to avoid drug shortage and treatment interruption. As for the paediatric formulations, the programme received two-term grants, each for three years, from GDF to access treatment for children. Medicines from the second-term year 2 grants were delivered to the programme in 2014. The next and previous year's grant medicines are due in early 2015. The Government of the Kyrgyz Republic will take over the procurement of quality-assured first line drugs through GDF direct procurement mechanism from 2016 onwards.

As for second-line drugs, they have been supplied to the programme through the UNITAID and Global Fund grants and the ICRC and MSF projects. Over 1050 DR-TB cases were enrolled for treatment in 2013, including patients from the penitentiary sector. It was planned that over 810 patients in 2014 and over 1000 DR-TB patients in 2015 would potentially be enrolled for treatment through funding from various donor grants. However, based on the WHO DR-TB estimated incidence rates and the follow-up discussion with partners and experts, a treatment gap of 700-900 DR-TB patient treatments is anticipated in 2015–2016. There is an urgent need to identify the required financial resources and to fill the financial gap to avoid further amplification and transmission of resistant forms of TB. The mission team flagged up the gap at the debriefing meetings with partners and the Ministry of Health.

The concept note to support further diagnosis and treatment of DR-TB in Kyrgyzstan for the period until 2017 was extensively discussed during the mission and will be developed and submitted to the Global Fund for funding by the end of 2014. The key points, including access to treatment of all DR-TB cases anticipated in 2015–2017 coupled with plans for the gradual takeover of financing by the Government, will be addressed in the concept note.

Ancillary drugs for management of side-effects of DR-TB treatment are procured internationally through the Global Fund grants for the approved cohort and by MSF for the supported project. For the remaining DR-TB cases that are enrolled annually for treatment, ancillary drugs are either made available through leftover stock or are partially procured from the local market using the State budget or self-purchased by patients. The chapter on management of adverse reactions in the endorsed DR-TB treatment guidelines supports the development of list of such medicines, which are then approved by the NTP management team. All ancillary drugs are supplied free of charge to hospitalized patients, while access to these drugs at the ambulatory level was reported in only some of the visited facilities. Out-of-pocket payments were therefore also made.

Since the procurement of these medicines is usually combined with other goods required for the hospitals, it was impossible to identify medicine costs separately during the planned health facility visits. Due to the limited size (facility-based) and fragmentation of the market, domestic procurement has not gone so smoothly. Delays in signing contracts and disbursing funds, joined with poor product quality, were mentioned by a few of the visited facilities. With the plans to decentralize DR-TB treatment further and the shift to more rapid initiation of treatment at ambulatory level, access to and availability of ancillary drugs must be substantially increased in order to encourage adherence by patients and better treatment outcomes.

Table 25 shows the list of ancillary drugs approved and procured over the last 12 months.

Table 25. Ancillary drugs approved and procured, Kyrgyzstan 2013-2014

Medicine name	Dosage/form	Medicine name	Dosage/form
Metoclopramide	10mg tab., and sol. inj. 10mg/2 ml	Betahistine	Tab. 16 mg
Promethazine	Tab. 12.5 or 25 mg	Fluoxetine	Tab. 20 mg
Chlorpromazine	Tab. 25 or 50 mg	Haloperidol	Tab. 5 mg and sol.
Diphenhydramine	Tab. 25 mg	Risperidone	Tab. 5 mg
Diazepam	Tab. 5 mg	Chlorpromazine	Sol. 5%
Ondansetron	Tab. 8 g	Zolpidem	Tab. 5 or 10 mg
Rehydron	Pwd. 18.9	Levothyroxine	Tab. 50 or 100 mcg
Ranitidine	Tab. 150 mg	Asparcam	Tab.
Famotidine	Tab. 20 mg	Spironoloctone	Tab. 50 mg
Omeprazole	Tab. 20 mg	Panangin	Tab.
Loperamide	Tab. 2 mg	Magnesium sulfate	Sol. Inj. 50 or 100 ml
Pyridoxine hydrocloride	Sol. Inj	Loratadine	Tab. 10 mg
Ibuprofen	Tab. 200 or 400 mg	Hydrocortisone	0.5% or 1% topic
Paracetamol	Tab. 500 mg	Prednisolone	Tab. 1 or 2.5 mg
Diclofenac	Sol. Inj 75 mg/3 ml	Dexamethazone	Sol. Inj. 0,5 ml/5ml
Carbamazepine	Tab. 10 mg	Medicines with iron	Tab.
Amitriptyline	Tab. 25 mg	Folic acid	Tab.
Phenobarbital	Sol. inj.		

inj. = injectable
pwd. = powder
sol. = solution
tab. = tablet
Source: NTP.

Registration

According to the Drug Law of Kyrgyzstan of 13 March 2003, all medicines can be produced, sold and used in the country if they are registered by the Drug Regulatory Authority/Department of Medicine Supply and Equipment of the Ministry of Health. The marketing authorization is then issued by the Department of Medicine Supply and Equipment based on which the product is registered in the State Register. The list of all medicines registered is available on the Department website.[1] See Annex 5 for the list of anti-TB medicines registered in the Kyrgyz Republic.

To date, many of the anti-TB drugs provided through the GDF have been exempted from registration. Such waivers are issued for each shipment under the humanitarian aid legislation. In accordance with this Drug Law, all drugs imported into the country must be registered and authorized for use in medical practice throughout the Kyrgyz Republic. The process of registration takes six months. The fee for registration is US$ 1500 for a new medicine registration and US$ 750 for a reregistration (Ministry of Health order No. 117 of 14 April 2010).[2] The registration is valid for five years, after which the marketing authorization holder has to apply for reregistration. The Drug Regulatory Authority signed an agreement on a fast-track registration procedure with the WHO prequalification programme in 2012. The procedure can be exercised at any time, and can also be applied to medicines authorized for use by the stringent regulatory authorities. Thus, WHO-prequalified medicines and those authorized by the stringent regulatory authorities can be registered within 30-45 working days in Kyrgyzstan. It is important for the programme to initiate registration, jointly with GDF, of all anti-TB medicines, including those supplied through UNDP, as soon as possible.

[1] www.pharm.med.kg, accessed 20 June 2015 (in Russian).
[2] http://www.pharm.kg/ru/legislation, accessed 20 June 2015 (in Russian).

The previous joint review mission commented on double standards in the registration of medicines, with those manufactured in the former Soviet states achieving registration more easily while those produced in the rest of the world were restricted, and on delays in customs clearances linked to inadequate funding to cover the fees levied on imported medicines. These comments were taken into consideration by the Drug Regulatory Authority and, with technical support from partners, relevant provisions were included in the revised National Drug Policy. The National Drug Policy is, however, still awaiting Government endorsement and, thus, the present mission made it a key recommendation to the Ministry of Health to expedite approval and facilitate implementation of its provisions. Under the revised National Drug Policy, the country should be committed to procuring anti-TB medicines with domestic funding, following the currently established quality requirements (WHO Prequalification of Medicines Programme or stringent regulatory authorities) and the specifications for international bidding. There will thus be no threat to the availability, accessibility or affordability of quality-assured anti-TB medicines for patients in Kyrgyzstan. Since legal provisions supporting these requirements are included in the National Drug Policy, its endorsement by the Government will certainly facilitate rapid implementation of these provisions.

Distribution and storage

Receipt, recording and reporting, distributing and storing of anti-TB drugs within the NTP are carried out in accordance with the manual approved by Ministry of Health Order No. 458 of 26 December 2007, which defines procedures for the above functions and for management of drugs at all levels of distribution.

The distribution system for TB medicines is not integrated with the national supply system for essential medicines. The NTP drug management unit is responsible for storage and distribution of medicines to all TB facilities in the country. The first-line and second-line TB medicines arrive in the Kyrgyz Republic by air and are stored at the customs service warehouse. For all unregistered medicines, a special waiver is required for each shipment: it takes between seven and 45 days on average to clear the medicines through customs, which is very long for these life-saving medicines.

Anti-TB drugs are distributed according to the distribution plan approved by the Ministry of Health/NTP and the standard operating procedures in place. After customs clearance, first-line drugs and some second-line drugs are delivered to the NTP central warehouses. The NTP has two warehouses: one in Bishkek and the other in Vorontsovka village, which was not visited during this mission. Space at the NTP main stores is limited for storage of the full stock of medicines required for the whole country and, therefore, twice-yearly distribution is the most favourable option. However, it is crucial to maintain good storage practices at the peripheral level, where most medicines need to be stored, to avoid a negative impact on quality. These include provision of adequate space for storage of medicines, a separate staff room, functional racks/shelves, pallets and ladders, window blinds/curtains, fire extinguishers, thermometers and of course relevant forms and functional desktop computers in these facilities. Despite the fact that many oblast-level warehouses were rehabilitated through Global Fund grants by the implementing partners, many of the visited facilities were still lacking these basic requirements, and the heads of facilities were informed so that they could take the necessary action.

Distribution from central to oblast level and further down the supply chain is done through a push system. This is based on an analysis of the quarterly TB case-notification reports, the consumption of drugs v. level of stock on hand and anticipated number of new cases to be enrolled for treatment. First-line drugs are distributed twice a year from the central NTP store to the oblast level (oblast TB centres). In turn, the oblast TB centres distribute drugs quarterly to the district level. The family medicine centres at district level then distribute them to the primary health care level for continuation of treatment. The intensive phase of treatment mostly takes place in hospitals. According to the

standard operating procedures, each level of distribution should have a buffer stock for first-line drugs which for the central level is at least six months and for oblast and district levels at least three months; there is no buffer stock envisaged for the primary health care level. There is also no buffer stock for second-line drugs because of funding constraints. The programme may not require a 50% buffer stock because of the short distances between most of the referral facilities.

The second-line drugs stocked at the NTP main stores are distributed on a quarterly basis to the oblast level, and further distribution down the supply chain becomes the responsibility of the health facilities (pull system). The larger stock of second-line drugs purchased by the Global Fund Principal Recipient, UNDP, is stored in a separate warehouse, contracted to and managed by UNDP. UNDP keeps its own recording and reporting forms which are then required to be used by all TB health facilities along the supply chain, despite the availability of relevant forms through the NTP. UNDP provides quarterly stock reports to the drug management unit of the NTP. The allocation of second-line drugs to the various levels is again based on quarterly TB reports and takes into consideration the stock consumed and on hand and the number of DR-TB patients already on or planned for treatment. The request for second-line drugs and the required quantities for distribution are validated by the MDR-TB coordinator.

The current distribution system requires pickup and delivery of medicines and laboratory reagents between central and oblast levels; further down the supply chain, the medicines and reagents come under the responsibility of the regional and oblast authorities and district health facilities. Several visited health facilities reported delays in the delivery of their medicines. Most of the visited facilities reported this as a challenging aspect because of the limited availability of fuel and/or transportation, since there are no relevant expenditure lines in the existing budgets. This requires the NTP's urgent attention and it should be discussed and addressed jointly with the Ministry of Health.

Fig. 21. Reporting and recording registers

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The medicines delivered to all warehouses and health facilities are stored, recorded, distributed, dispensed and reported upon separately by sources of supply or budget, e.g. GDF, NTP, UNDP, Project HOPE, UNITAID, MSF or ICRC. This is a time-consuming and burdensome task for all levels. During visits to the health facilities, it was observed that it is impossible to gain a general overview of stock on hand because of the segregated recording and reporting requirements imposed by funding agencies (nine registers maintained, as shown in Fig. 21). In the absence of an electronic system, this practice requires substantial management efforts from staff in charge and supervisors to verify the stock and organize the inventory. In one of the oblast stores, it was observed that cycloserine capsules must be stored in seven different locations and recorded in seven different books, and eight reports must be provided on a monthly or quarterly basis for the same product. This practice must be abandoned as soon as possible, and instead the use of the form and standard operating procedures developed by the NTP should be encouraged. This will also facilitate more holistic supervisory approaches across the country.

In the visited rayon and primary health care facilities, the stock records were up to date and the records tallied with the quantities of medicines on the shelves. In the oblast and central warehouse, data on the quantities distributed are not recorded in the register at the time of distribution/dispensing, but only once per week, which makes spot checks difficult and time-consuming. However, once all checks had

been done in the visited facilities, no discrepancies were found between the latest registered data v. stock on hand, minus the issued quantities. Despite the shortage of space, the first-expiry/first-out (FEFO) principle has been fully adhered to at these levels. Although standard operating procedures for handling importation, storage, inventory and distribution of TB medicines have been developed and in place since 2012, their implementation requires training and enforcement with the support of all partners.

Use of TB medicines

The treatment of drug-susceptible TB follows WHO recommendations and includes treatment of new and retreatment cases. The Category III regimen was phased out in 2012 and replaced by a treatment-of-new-cases regimen. The daily regimen was introduced in 2013 and the programme aims at directly observed treatment for all TB cases throughout the course of treatment. The treatment of TB in children has been improved since the last review mission, and the visited health facilities confirmed that full access to paediatric formulations has been available for the last 24 months. The *WHO Rapid advice*[1] recommendations on the use of higher dosages of anti-TB medicines in children with TB were implemented in the visited facilities.

The clinical management of DR-TB follows WHO recommendations. All treatment regimens for DR-TB cases are designed by the NTP Consilium; changes to the regimens are possible and can be made by doctors at treatment sites. Currently, four treatment regimens are used for M/XDR-TB treatment. The treatment of other PDR cases is based on DST. The treatment is performed under strict DOT conditions at all the visited treatment sites, with defaulter tracing and some patient support programmes in place. The patient support programme includes reimbursement of transport costs and monthly packages of food and hygiene products for patients to ensure treatment adherence and for medical providers as an incentive. Wherever necessary, bank accounts were created for patients to promote smooth transactions and avoid facility-based corruption. This social support is funded through the Global Fund grant, and there are no plans as yet for the Government to take it over.

Kyrgyzstan has been a full member of the WHO Programme for International Drug Monitoring since 2003, and reports to the Uppsala Monitoring Centre, Sweden. The Ministry of Health of the Kyrgyz Republic issued Order No. 535 of December 25, 2002 “On the improvement of health facilities’ activity in control and registration of drug adverse reactions”. In accordance with this Order, all medical workers must define and register adverse reactions to drugs used in the country. The Order also approved the “yellow card” that must be filled in by medical workers and submitted to the Drug Information Centre of the Department of Medicine Supply and Equipment. The Drug Information Centre/Pharmacovigilance Centre collects and analyses information on adverse drug reactions. This project was supported by Project HOPE and funded by USAID, and has conducted a survey on serious adverse reactions among new smear-positive patients. According to the project data, over 80% of adverse reactions occurred during the first month of treatment. Pyrazinamide was the most common causative agent, followed by rifampicin.

The approved treatment guidelines on TB include a separate chapter on management of adverse drug reactions. The chapter is in line with WHO recommendations. According to NTP data, 98% of all M/XDR-TB cases on treatment reported some side-effects. The most frequently reported side-effects were: nausea (76.5%), arthralgia (31.8%), hepatitis (27.8%) and headaches (25.3%). On average, fewer than 200 adverse drug reaction reports are sent to Uppsala every year, and less than 10% are related to first-line or second-line anti-TB drugs (rifampicin, kanamycin, pyrazinamide, PASER formulation of PAS, protionamide and cycloserine). Temporary or permanent withdrawal of second-line drugs from the regimen is possible only if there are severe side-effects; remarks to this effect are

[1] Rapid advice: treatment of tuberculosis in children. Geneva: World Health Organization; 2010.

usually included on the reporting form and patient treatment card, but may not necessarily be reported to the Pharmacovigilance Centre immediately. The Pharmacovigilance Centre has two trained staff and has published at least one report with analysis. It is, therefore, crucial that all observed adverse drug reactions are reported regularly and in detail to the Pharmacovigilance Centre and forwarded to the Uppsala Monitoring Centre for full review and analysis. In TB hospitals, the basic package of ancillary medicines is either provided through UNDP/MSF or purchased from the budget of the health facility. Availability of ancillary medicines is a major problem in treatment at the ambulatory level, and could be an additional reason why adverse drug reactions are not reported to the Pharmacovigilance Centre as soon as they occur. During the meeting with the Department of Medicine Supply and Equipment, it was stressed that collaboration between the NTP and the Pharmacovigilance Centre will be further strengthened in light of the introduction of new innovative medicines (bedaquiline to be provided through the UNITAID grant via MSF for treatment of pre-/XDR treatments from 2015 to 2019) and training of doctors in use of the "yellow cards" will be intensified, with support from all implementing partners.

Fig. 22. Anti-TB drugs on sale in pharmacy

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Anti-TB drugs are available for sale in pharmacies without restriction, despite the Ministry of Health Order that bans over-the-counter sales of anti-TB medicines and other antimicrobials (Fig. 22). Eight pharmacies were visited during the mission, and all of them had at least two or three anti-TB medicines available for dispensing without a prescription. Of the first-line drugs, rifampicin is most often requested, and of the second-line drugs, kanamycin, amikacin injections and fluoroquinolone tablets are in high demand. These medicines are mostly used and misused for non-TB indications and/or veterinary treatment, leading to further amplification of drug resistance. It is, therefore, imperative that the Ministry of Health/Department of Medicine Supply and Equipment, with other ministries and departments, should ban registration of non-WHO-recommended formulations and combinations of anti-TB medicines and the use of rifampicin for non-TB indications. Further, the issuance of rifampicin and other antimicrobials in pharmacies on an over-the-counter basis must be banned and strict penalties imposed. The revised National Drug Policy makes the required provision for this.

Quality assurance

Good manufacturing practices are currently not a legal requirement for registration of medicines. Local and foreign manufacturers have not been inspected for GMP compliance up to now, although a request for a GMP-type certificate may be requested when an application is submitted. The Department of Medicine Supply and Equipment has signed an agreement on fast-track registration with the WHO Prequalification of Medicines Programme, and plans to make use of these provisions soon. It was also agreed that GDF suppliers could be approached to initiate the process. The legal requirement for GMP and Good Distribution Practices are included in the revised National Drug Policy document. The Department of Medicine Supply and Equipment confirmed that it will encourage and continue to use the requirements for WHO prequalification or stringent regulatory authority authorization for anti-TB products in its domestic procurement. According to information from the Department of Medicine Supply and Equipment, there is a medical quality control testing laboratory in place, but it has not been ISO-certified and there are no plans for the laboratory to consider WHO prequalification as yet. The laboratory takes responsibility for post-marketing surveillance. For most medicines, samples are collected by Government inspectors (pharmaceutical inspectorate) at the stage of registration for post-marketing quality monitoring and in case of

complaints. The samples are supposed to be taken from the pharmacy or warehouse stocks after prior notice has been given (inspectors have no authority to perform unannounced inspections or post-marketing sampling). Based on the test results, the product is authorized for or banned from further use in the country. According to the Department of Medicine Supply and Equipment, no anti-TB drugs failed quality control testing in 2013 or 2014. Due to its limited financial resources and the inadequate and irrelevant legal provisions, the Department of Medicine Supply and Equipment and the pharmaceutical inspectorate are unable to assume their responsibilities fully. With the approval of the National Drug Policy, substantive changes for the better are expected.

TB drug information management

The information system for management of anti-TB drugs is mostly paper-based, as presented for each level of the supply chain in Table 26 below, and appears not to be consolidated throughout the country: registers for medicine supply and dispensing are kept at all levels; stock cards at central and oblast stores are maintained only in some stores; electronic Excel forms for recording medicines are used at the central level only. No consolidated reports can be obtained from such a system to show stock-outs, consumption v. number of patients on treatment, anticipated and pending deliveries, etc. Monitoring the use of medicines therefore remains a challenge. Development of an electronic drug management system and laboratory modules under the e-TB Manager has been pending since 2011, and the final phase of testing is now planned before the end of the year. It is anticipated that these modules will be ready for countrywide use from January 2015. They will allow the programme to link the drug and laboratory management components with the treatment of TB for each patient within one comprehensive database.

Table 26. Reporting and recording forms by level of distribution

Level	Recording documents	Reporting documents
National	• Stock card • Anti-TB drug register • Anti-TB drug register in hospital • Anti-TB drug order sheet in hospital • Invoice for issuing of anti-TB drugs • Inventory report • Needs quantification form for anti-TB drugs	• Annual consolidated national report, includes “Balance for beginning of quarter”, “Received”, “Issued”, “Balance for the end of quarter” (paper and electronic format)
Oblast	• Stock card • Anti-TB drug register • Anti-TB drug register in hospital • Anti-TB drug order sheet, needs quantification form for anti-TB drugs at oblast level • Anti-TB drug order sheet • Invoice for issuing of anti-TB drugs • Inventory report	• Quarterly report TB-10, Part B, oblast level (approved by Ministry of Health Order No. 436 dated 7 December 2001) • Quarterly rayon consolidated report
Rayon	• Anti-TB drug register • Anti-TB drug order sheet in hospital • Invoice for issuing of anti-TB drugs	• Quarterly report, TB-07, Part A, rayon level (approved by Ministry of Health No. 436 dated 7 December 2001)

Level	Recording documents	Reporting documents
PHC: FMC, family doctors	• TB patient medical card TB-01 • Anti-TB drug dispensing card at PHC level • Outpatient card	

MoH = Ministry of Health PHC = primary health care FMC = family medicine centre
Source: NTP.

The reporting forms are prepared at district, oblast and national levels. Each district enters the stock balance at the beginning and end of each quarter and the quantities of drugs received and dispensed quarterly on form TB-07 "Consolidated District Quarterly Report". Form TB-07, together with the anti-TB drug indent, is submitted to the oblast level every quarter. In turn, each oblast records the stock balance at the beginning and the end of each quarter and the quantities of drugs received and dispensed quarterly on form TB-10 "Consolidated Oblast Quarterly Report". Form TB-10 is submitted to the national level (Information/Epidemiology Department of National TB Centre) each quarter. On the basis of reports received from oblasts, the national level prepares the annual national report using data from consolidated quarterly reports from all oblasts. This includes the following information: stock at the beginning of quarter, received, dispensed and stock at the end of quarter. This report is prepared in hard-copy and electronic formats. The reports are developed on a quarterly basis. The form does not stipulate mandatory reporting of shelf life for stocked medicines. There is a lack of practice in assessing the consumption rate compared with the number of patients on treatment and the number of days of stock-out. Monitoring practices in place are not efficient at either central or regional levels. As for primary health care facilities, there is no reporting to the rayon level. The rayon dispenses anti-TB drugs to primary health care facilities for specific patients for the entire course of treatment (mostly the continuation phase) without any buffer stock, expecting that all the dispensed drugs will be consumed by patients. In case of death or default, the drugs are returned to rayon-level facilities (family medicine centre, TB room).

Recommendations

Strategic: Ministry of Health jointly with other ministries

- Expedite submission of the revised National Drug Policy document for Cabinet/Government approval.
- Secure funding for procurement of adequate treatment courses for the anticipated P/M/XDR cases through mutual agreements with partners for 2015, and ensure availability of financial resources for timely procurement of first-line anti-TB medicines, including paediatric formulations, for the period from 2015 onwards.
- Jointly with external partners, plan for gradual domestic financing of second-line drugs for P/M/XDR treatment for the period beyond 2016.
- Urgently develop mechanisms and ban over-the-counter sales of all antibiotics/anti-TB medicines to reduce amplification of drug resistance across the country.
- Restrict registration and procurement of anti-TB medicines to quality-assured products (WHO prequalified and authorized for use by stringent regulatory authorities).

Technical: NTP and implementing partners

- Revise MDR treatment regimens in consideration of DST results for injectable anti-TB drugs. Place an order for procurement of second-line drugs as soon as possible.
- Within the next four months, develop a stepwise transition plan for procurement of quality-assured first-line anti-TB medicines for 2015 through GDF, using Government funds. The budget should cover programme needs for first-line drugs, including paediatric formulations, with at least 50% buffer stock and all related costs (shipment,

pre-shipment inspection, quality control, fees and insurance). Ensure that the plan is incorporated into the National TB Control Strategy and adequately budgeted.

- Work with GDF and manufacturers to facilitate registration of quality-assured anti-TB medicines to ensure availability of international sources of these medicines (for when the country switches to the Government-funded procurement).
- The drug management unit of the NTP should take full responsibility for implementation of approved standard operating procedures at all levels and unify and standardize the distribution system, recording and reporting forms, storage practices and supervision.
- Promote rational use of antibiotics through awareness-raising in and collaboration with the private pharmacy network and the Ministry of Health/pharmaceutical inspectorate/ Department of Medicine Supply and Equipment.
- Support and facilitate collection and reporting of adverse reactions to all second-line anti-TB medicines from TB treatment facilities and the central NTP and ensure prompt reporting to the Pharmacovigilance Centre.

WHO Kyrgyzstan country office and other partners

- Jointly with the NTP, GDF and the WHO Regional Office for Europe, initiate and facilitate fast-track registration of all anti-TB medicines as per the standard treatment guidelines (waive registration fee if small quantities are required).
- Assist in the development of action plans for implementation of new and revised polices, as defined in the National Drug Policy.

GDF

- Assist the Ministry of Health and NTP with planning and execution of procurement of first-line drugs with Government funding for 2015.
- Provide timely updates to the NTP/Global Fund Principal Recipient for placed orders.
- Assist with registration of all medicines procured through GDF.

5. Partnership, ACSM and community involvement

Social procurement possibilities

International nongovernmental organizations are active in the TB response in Kyrgyzstan, using their own funds (MSF), implementing projects of other donors such as USAID (KNCV, Quality Health Care Project) or acting as Global Fund Principal Recipient(s) (Project HOPE). One good example is Population Services International and seven local nongovernmental organizations, mostly targeting high-risk groups (people living with HIV, people who use drugs, migrants) which are involved in the USAID Dialogue on TB and HIV project. From September 2009 to March 2014, they referred 4605 persons for TB testing, 201 of whom were diagnosed with TB, and 400 TB patients (including the 201 detected by the project) received treatment adherence support. The project will run until the end of March 2015. It appears that there are no regulations either to prevent or to promote participation by nongovernmental organizations in the TB response: there are no institutional barriers. There is a law on social procurement; this facility has not yet been used by the Ministry of Health. A few local nongovernmental organizations, including one implementing HIV/TB activities, had previously received social procurement grants from the Ministry of Social Protection.

Advocacy, communication and social mobilization strategy, plan and Thematic Working Group

There is a national advocacy, communication and social mobilization (ACSM) strategy, although it is not officially endorsed. It is annexed to the Tuberculosis 4 National Programme. Every year, an operational plan is developed, but the cost of its implementation is not estimated. The minutes of the ACSM Thematic Working Group note an attempt to add a budget section to the plan, but at the time of the review there was still no budget. Various international organizations carry out ACSM activities from their own working plans. The ACSM Technical Working Group meets bimonthly and is currently led by the Quality Health Care Project. At present, the goal and the three objectives of the ACSM Thematic Working Group are mainly aimed at formal education activities. This seems to be something that should be addressed by the human resource development focal point and not necessarily by the ACSM Thematic Working Group. It is advised to separate education from ACSM in order to give the Thematic Working Group a clearer focus and to revise the membership accordingly. Please revisit the definition of ACSM for a better understanding of advocacy and social mobilization concepts and their difference from (formal) educational activities. It is also advisable for the Thematic Working Group to inform itself about issues of community systems strengthening, human rights and gender (as per Global Fund definitions).

Strengthening the ACSM Thematic Working Group will help to increase collaboration and coordination between international and the local civil society and the NTP/Ministry of Health. The critical underlying factor for national planning is the fact that very few organizations besides the Ministry of Health deal with national-level coverage. Many organizations work in smaller geographical areas or with specific population groups. For instance, in the area of stigma reduction, there is a need to campaign together and to develop activities that complement one another rather than competing for the same market and audience. The NTP has limited funds in general and does not appear to have any budget for ACSM.

The ACSM Thematic Working Group can continue to receive support from the Quality Health Care Project and can use advisory support from e.g. MSF in capacity-building, including the capacity of the ACSM focal point within the central NTP. However, while the ACSM Thematic Working Group is dependent on donor financing via different international nongovernmental organizations, it will remain difficult to integrate efforts under one strategy and ensure central monitoring of its implementation. Often, the donor’s mandate has a stronger influence, and the ACSM Thematic Working Group does not yet have its own funding under the leadership of the NTP/Ministry of Health.

MSF has established an advocacy group chaired by MSF. Currently, only international nongovernmental organizations are members (WHO, KNCV, Quality Health Care Project, United Nations, GIZ), represented mainly by the heads of their medical programmes. The main approach of the advocacy group is to facilitate information exchange with a small group in order to align programme methodologies where possible and build common approaches to lobbying the Ministry of Health. Under the advocacy group there is a communications working group, which aims to use materials and resources more effectively by means of standardization of materials and joint campaigning. The communications group includes local nongovernmental organizations. Both groups are informal and have operated since 2012.

Access to services and patient support

Social support from the Global Fund is provided via Project HOPE for drug-susceptible TB patients and via UNDP for DR-TB patients. Social support for ex-prisoners is provided by MSF and ICRC. The local authorities can engage in the provision of social support after the Global Fund activities are phased out, but their changed mandate needs to be confirmed by legislation in order to allow and create a mechanism for such support to the key affected population. This population – people affected by TB – has to be defined more clearly, based on the epidemiological information.

The Quality Health Care Project has helped to update a database of the enrolled population together with MHIF. The database allows funding for patients even if they are not registered at an official domicile. Unregistered Kyrgyz citizens, including homeless people, can go to the health facility, obtain a temporary registration (*pripiska*) on the database and receive medical assistance in accordance with the joint order of the Ministry of Health (No. 358) and MHIF (Order No. 126) of 26 June 2013. The database is based at the Republican Epidemiology and Information Centre, and public outreach activities informing the public about this new opportunity are planned for 2015.

There are still legislation issues that prevent people from accessing services, e.g. work restrictions resulting in a loss of income. Together with stigma, these could be an important reason why some people self-medicate in order to avoid being known as TB patients. Some of those on official treatment may default once they feel some improvement, because they have to resume work to support themselves and their families. Sometimes they go abroad in search of work. There are currently no laws to facilitate cross-border service provision. Mandatory hospitalization is coupled with insufficient resources at the implementation level, i.e. there are not enough resources going to primary health care for it to improve its services and infrastructure and develop TB care skills.

Article 12 of the TB law (Ministry of Health Order No. 670 of 27 November 2013) stipulates that TB testing is free of charge or has to be covered by the organization or institution which refers the TB suspect for testing. One local nongovernmental organization referring homeless persons was repeatedly asked by TB dispensary staff to pay an amount which steadily increased. Even though there is a yearly programme of State guarantees, the Ministry of Health /MHIF order of 26 June 2013, article 12, can potentially lead to delays in diagnosis for vulnerable populations.

Patient support groups established initially at the pilot site by the Quality Health Care Project have been operating for 18 months; currently there are 12 patient support groups. The objective of the groups is to support TB patients psychologically and reinforce treatment adherence. They are made up of current and former TB patients, family members and some friends of TB patients. At group meetings, they discuss problems, share their experiences, have focus group discussions and watch TV shows on special topics selected by the group. The group members raise many questions, usually regarding nutrition and side-effects of TB treatment. A representative of the TB service attends the group meetings. The staff of the Quality Health Care Project facilitate the groups. The group meetings

are held in a special room at a health-care facility or TB cabinet. The groups also talk about the rights and responsibilities of patients and staff, including some elements of the Patients' Charter for Tuberculosis Care.[1]

It is important to involve patient support groups in the work of the Country Coordinating Mechanism so that they can participate in the constituency feedback/input mechanism to provide input and receive information from people living with the disease. This is required under eligibility requirement 5 of the *Guidelines and requirements for Country Coordinating Mechanisms* (ensuring an inclusive and meaningful representation in Country Coordination Mechanism composition), Minimum Standard i): "CCM has clearly defined processes of soliciting inputs from and providing feedback to their constituencies that selected them to represent their interests in the CCM".[2]

Stigma and discrimination

In Kyrgyzstan, the Quality Health Care Project engaged in an anti-stigma campaign between 2011 and 2013, starting in Chui Oblast and then expanding nationwide. This demonstrated an improvement in knowledge about TB transmission and an increase in potential supportive behaviour towards TB patients. Nonetheless, there are still acute levels of stigma, reported by many stakeholders, and a lack of informed choice by patients, reported by at least one organization.

It is important to recognize that continuing with lengthy mandatory hospitalization for adults and children, including children hospitalized for latent TB infection, contributes to the stigma attached to TB patients.

Challenges

- The ACSM operational plan does not have a budget or impact indicators. It is not clear who owns the plan or who should monitor its implementation.
- The ACSM Thematic Working Group has informal reporting; however, it has no actual power, since it does not have any funds and the ACSM plan mainly consists of activities by international nongovernmental organizations/Global Fund Principal Representative. International nongovernmental organizations/Principal Representative are accountable to their respective donors rather than to the Thematic Working Group.
- Social support for TB patients is entirely dependent on the Global Fund grants.
- The Ministry of Health currently does not offer social procurement funding to civil society organizations working with people affected by TB.
- Psychological support for TB patients is available only in prison (organized by ICRC).
- Stigma and discrimination may still be leading to late TB diagnosis, self-treatment and treatment default.

Recommendations

To the Ministry of Health

- Provide funding for HIV service organizations and other nongovernmental organizations representing the key affected population through social procurement, since they have the knowledge of the target group and the capacity to implement outreach anti-TB activities. Make use of HIV civil society organizations while they are funded by the Global Fund and are able to do some additional work on case-finding and adherence support in their target groups.

[1] Patients' charter for tuberculosis care. Viols en Laval: World Care Council; 2006.
[2] Guidelines and requirements for Country Coordinating Mechanisms. Geneva: Global Fund to Fight AIDS, Tuberculosis and Malaria (http://www.theglobalfund.org/en/ccm/guidelines/, accessed 20 June 2015).

- In collaboration with civil society, define the roles, functions and authority of nongovernmental organizations and reflect them in the law on TB.

To NTP, Ministry of Health

- Cost and provide budget for the ACSM operational plan and use impact indicators that are mentioned in the ACSM strategy document in order to measure more than just output or process indicators. Organize all stakeholders in a planning session, where they make clear commitments and develop a mechanism to work on ACSM activities in an efficient, coordinated and monitored way. The NTP/Ministry of Health should take the lead rather than being merely observers.

To ACSM Thematic Working Group

- The functioning of the Thematic Working Group needs to be improved in terms of partner alignment, standardization, national strategic planning and monitoring of activities.
- Monitor the implementation of the ACSM operational plan and the ACSM strategy and produce a report at the end of the year. Use the results of monitoring for decision-making.
  - Improve coordination among civil society organizations; the key international organizations should find a common language and follow a joint plan.
  - Include (more) local nongovernmental organizations in the Thematic Working Group.
- Separate the "education" part of the terms of reference of the Thematic Working Group from the ACSM part and adjust the membership accordingly.

To international nongovernmental organizations

- Always provide assistance in capacity-building (training, mentoring, etc.) for local specialists as part of transferring knowledge, increasing institutionalization and ensuring sustainability of services. Sustainability should be the main foundation of activities, and the international nongovernmental organizations should not, in the medium and long term, fulfil the functions of the local structures.

To international and local nongovernmental organizations

- Continue to address barriers to access to treatment: stigma and discrimination, informal payments for TB treatment.
  - Make vulnerable groups aware of the Ministry of Health/MHIF Order of 26 June 2013 (State guarantees) and use it to improve access by the key affected population to TB services.
  - In collaboration with the Ministry of Health, define the roles, functions and authority of nongovernmental organizations and reflect them in the law on TB.
  - Continue to provide information materials, with the emphasis on MDR-TB, for communities, patients and treatment supporters.
  - Draw up a clear definition of the key affected populations for TB.
  - Continue the practice of multidisciplinary teams accessing and assisting the key affected population.
  - Strengthen the partnerships with primary health care and the TB programme.
- Advocate for social procurement by the Ministry of Health.
- Continue the work of the informal advocacy group (run by MSF). MSF is recommended gradually to involve local nongovernmental organizations in advocacy.

- Build capacity and leadership in the community through ongoing work with patient support groups and link them to the TB representative on the Country Coordinating Mechanism.

To the Country Coordinating Mechanism

- Include patient support groups in the constituency feedback/input mechanism as per eligibility requirement 5 of the *Guidelines and requirements for Country Coordinating Mechanisms* (ensuring an inclusive and meaningful representation in CCM composition), Minimum Standard i): "CCM has clearly defined processes of soliciting inputs from and providing feedback to their constituencies that selected them to represent their interests in the CCM".
- Include community systems strengthening, human rights and gender in the concept note in line with the national TB strategic plan and with the national "Den Sooluk" health programme.

Annex 1. Agenda of the review

Kyrgyzstan NTP review
30 June – 5 July 2014

Review team

1. Martin van den Boom – Cross-cutting issues, TB in children
2. Manfred Danilovits – TB, DR-TB, TB in prisons
3. Veronica Iljina – TB, DR-TB (with Manfred Danilovits)
4. Szabolcs Szigeti – TB governance, health system strengthening, TB financing
5. Nonna Turusbekova – civil society, political commitment, infection control
6. Harald Hoffman – Laboratory
7. Hasmik Margaryan– Laboratory (with Harold Hoffman)
8. Nigorsulton Muzafarova – Drug management
9. Nikoloz Nasidze – TB/HIV
10. Andrei Dadu – Epidemiological review, TB burden, mortality, incidence and prevalence, TB surveillance systems (23 – 30 June)
11. Saliya Karymbaeva – overall support
12. Kamilla Nurbaeva – Observer (June 30 – July 3)
13. Sandra Irbe – Observer (July 4 – 5)
14. Michel Kazatchkine – Observer (July 4-5)

Programme
of visits and activities

Date	*Time*	*Activity*	*Participants*	*Venue*	*Accom-panying person/car*
29 June 2014	16:00	Arrival at Bishkek Meeting at Lobby		Park Hotel	
30 June 2014	08:40	Departure from Hotel	All experts		Bus
	09:00 10:30	Meeting with Head of WHO CO, Security Issues	All experts	UN House	
	10:30 11:30	NTP presentation/ follow-up of the 2010 NTP Review and last GLC recommendations	All experts	UN House	
	11:30 11:45	Coffee/Tea		UN House	
	11:45 13:00	NTP presentation/ follow-up of the 2010 mission recommendations (continued)	All experts	UN House	
	13:00 13:30	Coffee with snacks		UN House	

Date	*Time*	*Activity*	*Participants*	*Venue*	*Accom-panying person/car*
	13:30 15:30	Meeting with Partners; Presentation of electronic database	All experts	UN House	
	16:00 18:00	Visit to the TB Centre units; working with National TB Centre staff	M. van den Boom M. Danilovits V. Iljina H. Hoffman H. Margaryan N. Muzafarova N. Nasidze	TB Centre Hospital, NTP Information centre, M&E unit, NRL	
	16:00 18:00	Health Policy Analysis Centre	S. Szigeti N. Turusbekova	UN House	Translator Nurgul
	Time TBD	Flight to Osh, trip to Jalal-Abad by car	H. Hoffman H. Margaryan		Gulmira Kalmambetova
01 July 2014	09:55 (Flight)	Flight to Osh	All experts except H. Hoffman H. Margaryan		N. Nasidze
	09:00 13:00	Osh TB Centre (Oblast level)	All experts except H. Hoffman H. Margaryan		
	09:00 13:00	Visit to Jalal-Abad lab, trip to Osh, join the team	H. Hoffman H. Margaryan		Gulmira Kalmambetova
	13:00 14:00	Lunch			
	14:00 17:00	1. Osh City TB Dispensary 2. Family Medicine Centre 3. Children's Rehabilitation Centre	All experts		
	14:00 17:00	Meeting with civil society in Osh	N. Turusbekova		
	18:45 (Flight)	Flight to Bishkek	All experts		

Date	*Time*	*Activity*	*Participants*	*Venue*	*Accom-panying person/car*
02 July 2014	09:00 09:30	Trip to Moldovanovka (Prison)	M. van den Boom M. Danilovits V. Iljina H. Margaryan N. Nasidze		Bus
	09:30 12:00	Visit to Prison TB Treatment facility No. 31	M. van den Boom M. Danilovits V. Iljina H. Margaryan N. Nasidze		
	09:00 10:00	Ministry of Health Department of Strategic Planning	S. Szigeti N. Turusbekova	MOH	S. Karymbaeva Translator Nurgul Car
	10:30 12:00	Mandatory Health Insurance Fund	S. Szigeti	MHIF building, 122 Chui str;	S. Karymbaeva translator Nurgul Car
	10:30 12:00	Meetings with civil society in Bishkek – national partners	N. Turusbekova	TB Centre	Car
	09:00 10:00	MOH Unit of Quality and Medicines Policy	N. Muzafarova	MOH	Car
	10:30 12:00	Department of Drug Procurement and Supply	N. Muzafarova		S. Karymbaeva Aelita Car

Date	*Time*	*Activity*	*Participants*	*Venue*	*Accom-panying person/car*
	12:00 12:30	Trip to Issyk-Ata: Group 1 – from Moldovanovka, Group 2 – from Bishkek	Group 1: M. van den Boom M. Danilovits V. Iljina H. Margaryan N. Nasidze Group 2: S. Szigeti H. Hoffman N. Muzafarova S. Karymbaeva K. Nurbaeva N. Turusbekova		Bus
	12:30 13:00	Lunch			
	13:30 16:30	Issyk-Ata Family Health Practitioners Centre – pilot site of ambulatory model of treatment	All experts		
	16:30 17:30	Trip back to Bishkek	All experts		
03 July 2014	09:00 09:30	Trip from Bishkek to Alamedin	All experts except N. Turusbekova		Bus
	09:30 12:00	Visit to Alamedin Family Health Practitioners Centre	All experts except N. Turusbekova		
	12:00 13:30	Lunch, Trip to Chui Oblast			
	13:30 16:30	Visit to Chui oblast TB hospital	All experts except N. Turusbekova		
	16:30 17:30	Trip back to Bishkek			Bus
	09:00 13:00	Meetings with civil society in Bishkek – international: Project HOPE, MSF, ICRC, KNCV	N. Turusbekova	In the offices of named organizations	Car
	15:00 17:00	Joint meeting with civil society to propose actions to improve collaboration	N. Turusbekova	TB Centre	Car

Date	*Time*	*Activity*	*Participants*	*Venue*	*Accom-panying person/car*
04 July 2014	09:00 12:00	Preparation of presentations for MOH	All experts	Park Hotel	
	12:00 13:00	Debriefing with NTP	All experts	Park Hotel	
	13:00 15:00	Coffee break/meeting with M. Kazatchkine	All experts	Park Hotel	
	16:00 17:00	MoH debriefing	All experts M. Kazatchkine	MOH	
	18:00	Dinner			
05 July 2014	10:00 12:00	Debriefing with partners	All experts M. Kazatchkine	Park Hotel	
	12.00 14.00	Visit of M. Kazatchkine to HIV/AIDS and TB centres			S. Karymbaeva N. Nasidze Car
	13:00 14:00	Lunch			
	14:00 15:00				
	15:00 16:00				

Annex 2. List of documents reviewed

1. Tuberculosis surveillance and monitoring in Europe, 2014
2. WHO global tuberculosis report, 2014
3. Review of the TB laboratory network of the Kyrgyz Republic, 2012
4. UNDP annual report on the implementation of grants provided by the Global Fund to fight AIDS, Tuberculosis and Malaria in Kyrgyzstan – 2013
5. WHO review of tuberculosis control in Kyrgyzstan, 2010
6. Отчет о миссии по оценке мер инфекционного контроля в противотуберкулезных учреждениях Республики Кыргызстан [Report on the mission to evaluate infection control measures in TB facilities in the Kyrgyz Republic], 2012; KNCV
7. GLC/Europe mission for monitoring of the implementation of the national M/XDR response plan in Kyrgyzstan, 2013
8. Global Drug Facility procurement and supply chain management mission, 2013

Annex 3. Detailed tables

Table A3.1. Smear microscopy by administrative region, Kyrgyzstan

(a) Smear microscopy by administrative region (diagnostic)

City and regions	Specimens		Patients		Average no of samples
	Total	ss+ n (%)	Total	ss+ n (%)	
Bishkek	13 451	1 206 (9.0)	4 570	478 (10.5)	2.9
Chui Oblast	13 952	1 417 (10.2)	4 656	488 (10.5)	3
Tallas Oblast	2 169	258 (11.9)	723	86 (11.9)	3
Naryn Oblast	2 617	138 (5.3)	879	51 (5.8)	3
Issyk-Kul Oblast	1 956	243 (12.4)	651	81 (12.4)	3
Batken Oblast	3 501	439 (12.5)	1 181	147 (12.4)	3
Osh Oblast	7 918	1 289 (16.3)	2 622	455 (17.4)	3
Osh City	3 669	340 (9.3)	1 237	115 (9.3)	3
Jalal-Abad Oblast	6 066	1 205 (19.9)	2 098	421 (20.3)	2.9
Prison system	3 495	309 (8.8)	1 551	181 (11.7)	2.3
Total	***58 794***	***6 844 (11.6)***	***20 168***	***2 503 (12.4)***	***2.9***

(b) Smear microscopy by administrative region (follow-up)

City and regions	Specimens		Patients		Average no of samples
	Total	ss+ n (%)	Total	ss+ n (%)	
Bishkek	5414	407 (7.5)	2 704	251 (9.3)	2.0
Chui Oblast	8 321	1 068 (12.8)	4 158	544 (13.3)	2.0
Tallas Oblast	950	44 (4.6)	475	22 (4.6)	2.0
Naryn Oblast	1 738	112 (6.4)	868	130 (15.0)	2.0
Issyk-Kul Oblast	1 416	100 (7.1)	708	50 (7.1)	2.0
Batken Oblast	2 005	112 (5.6)	986	56 (5.7)	2.0
Osh Oblast	3 617	305 (8.4)	1 841	153 (8.3)	2.0
Osh City	1 601	25 (1.6)	805	13(1.6)	2.0
Jalal-Abad Oblast	3 573	94 (2.6)	1 802	47 (2.6)	2.0
Prison system	3 463	503 (14.5)	1 881	329 (17.5)	1.8
Total	***32 098***	***2 770 (8.6)***	***16 228***	***1 595 (9.8)***	***2.0***

(c) Smear microscopy by administrative region (chronic)

City and regions	Specimens		Patients	
	Total	ss+ n (%)	Total	ss+ n (%)
Bishkek	8 972	692 (7.7)	5 893	521 (8.8)
Chui Oblast	3 032	544 (17.9)	1 607	285 (17.7)
Tallas Oblast	891	58 (6.5)	891	58 (6.5)
Naryn Oblast	458	35 (7.6)	243	18 (7.4)
Issyk-Kul Oblast	178	55 (30.9)	93	26 (28.0)
Batken Oblast	1 922	120 (6.2)	1 098	68 (6.2)
Osh Oblast	4 310	928 (21.5)	2 360	527 (22.3)
Osh City	1 169	54 (4.6)	476	21 (4.4)
Jalal-Abad Oblast	8 782	1 026 (11.7)	4 928	513 (10.4)
Prison system	0	0 (0)	0	0 (0)
Total	***29 714***	***3 512 (11.8)***	***17 589***	***2 037 (11.6)***

(d) Smear microscopy by administrative region (all patients)

City and regions	Specimens		Patients	
	Total	ss+ n (%)	Total	ss+ n (%)
Bishkek	27 837	2 305 (8.3)	13 167	1 250 (9.5)
Chui Oblast	25 305	3 029 (12.0)	10 421	1 317 (12.6)
Tallas Oblast	4 010	360 (9.0)	2 089	166 (7.9)
Naryn Oblast	4 813	285 (5.9)	1 990	199 (10.0)
Issyk-Kul Oblast	3 550	398 (11.2)	1 452	157 (10.8)
Batken Oblast	7 428	671 (9.0)	3 265	271 (8.3)
Osh Oblast	15 845	2 522 (15.9)	6 823	1 135 (16.6)
Osh City	6 439	419 (6.5)	2 518	149 (5.9)
Jalal-Abad Oblast	18 421	2 325 (12.6)	8 828	981 (11.1)
Prison system	6 958	812 (11.7)	3 432	510 (14.9)
Total	***120 606***	***13 126 (10.9)***	***53 985***	***6 135 (11.4)***

Table A3.2. Estimated gap in treatments with second-line drugs for 2015, Kyrgyzstan

RR/MDR-TB cases		XDR-TB cases		PDR-TB (notified)	
Total number of MDR-TB cases expected to be notified	1 242	Total number of MDR-TB cases expected to be notified	1 242	Total number of PDR-TB cases notified in 2013	522
Number of MDR-TB cases expected to be enrolled in treatment (90% out of total expected + 1.5% R-resistant cases starting treatment as MDR-TB)	1 136	Expected number of XDR (6% of MDR)	75	Notified resistant to HE, HS	291
		Number of XDR-TB cases expected to be enrolled in treatment (80% out of total expected)	60	Number of resistant to HE, HS to be treated with SLD (20%)	58
Number of cases covered by GF UNDP	516	Number of cases covered by GF UNDP	24	Notified resistant to HES	**157**
Number of cases covered by MSF	75	Number of cases covered MSF	10	Number resistant to HES to be treated with SLD (100%)	**157**
Number of full courses combined from leftover medications (3% of cases covered by GF UNDP)	18	Number of full courses combined from leftover medications (5% of cases in treatment)	2	Notified resistant to RE, RS, RES	51
Number of MDR cases covered with treatment by donors	609	Number of XDR cases covered with treatment by donors	36	Number of resistant to RE, RS, RES to be enrolled in treatment with SLD	**51**
Gap	**527**	**Gap**	**24**	**Gap**	**266**
Total gap for SLD 817					

E = ethambutol
H = isoniazid
MDR-TB = multidrug-resistant TB
PDR-TB = polydrug-resistant TB
R = rifampicin
RR = rifampicin-resistant
S = streptomycin
SLD = second-line drugs
UNDP = United Nations Development Programme
XDR-TB = extensively drug-resistant TB

Source: NTP (estimate done with the support of NTP review mission experts and international partners)

Table A3.3. DST coverage by category of patients, Kyrgyzstan, 2013

Category of patients	N of patients	Culture not done	Culture done	DST done	% DST coverage
New cases ss +	1 514	170	1 299	1 073	70.9
New cases ss -	2 698	689	1 892	673	24.9
Total for new cases	**4 212**	**859**	**3 191**	**1 746**	**41.5**
Previously treated ss+	456	48	385	369	80.9
Previously treated ss-	641	145	458	221	34.5
Total for retreated cases	**1 097**	**193**	**843**	**590**	**53.8**
Total	***5 309***	***1 052***	***4 034***	***2 336***	***44.0***

ss+ = sputum smear-positive
ss- = sputum smear-negative
DST = drug susceptibility testing
N = number
Source: NTP

Table A3.4. Number of patients starting treatment with second-line drugs and other reserve drugs, Kyrgyzstan, January–June 2014

Regions	2014/Q1			2014/Q2			2014 (January-June)		
	On treatment	UNDP	MSF	On treat-ment	UNDP	MSF	On treat-ment	UNDP	MSF
Chui									
MDR-TB	80	80	0	86	86	0	166	166	0
PDR-TB	6	6	0	4	4	0	10	10	0
XDR-TB	4	4	0	1	1	0	5	5	0
Bishkek									
MDR-TB	45	45	0	54	54	0	99	99	0
PDR-TB	5	5	0	8	8	0	13	13	0
XDR-TB	1	1	0	1	1	0	2	2	0
Issyk-Kul									
MDR-TB	8	8	0	8	8	0	16	16	0
PDR-TB	0	0	0	0	0	0	0	0	0
XDR-TB	1	1	0	0	0	0	1	1	0
Naryn									
MDR-TB	6	6	0	12	12	0	18	18	0
PDR-TB	1	1	0	2	2	0	3	3	0
XDR-TB	1	1	0	0	0	0	1	1	0
Talas									
MDR-TB	11	11	0	18	18	0	29	29	0
PDR-TB	0	0	0	1	1		1	1	0
XDR-TB	0	0	0	2	2	0	2	2	0
Osh									
MDR-TB	58	39	19	56	41	15	114	80	34
PDR-TB	6	1	5	5	3	2	11	4	7
XDR-TB	1	0	1	4	3	1	5	3	2
Jalal-Abad									
MDR-TB	58	58	0	63	63	0	121	121	0
PDR-TB	3	3	0	6	6	0	9	9	0
XDR-TB	2	2	0	2	2	0	4	4	0
Batken									
MDR-TB	7	7	0	9	9	0	16	16	0
PDR-TB	2	2	0	0	0	0	2	2	0
XDR-TB	0	0	0	0	0	0	0	0	0
Prison									
MDR-TB	9	9	0	15	15	0	24	24	0
PDR-TB	0	0	0	0	0	0	0	0	0
XDR-TB	0	0	0	0	0	0	0	0	0
Total									
MDR-TB	282	263	19	321	306	15	603	569	34
PDR-TB	23	18	5	26	24	2	49	42	7
XDR-TB	10	9	1	10	9	1	20	18	2

Q = quarter
MDR-TB = multidrug-resistant TB
MSF = Médecins Sans Frontières
PDR-TB = polydrug-resistant TB
Source: NTP
SLD = second-line drugs
UNDP = United Nations Development Programme
XDR-TB = extensively drug-resistant TB

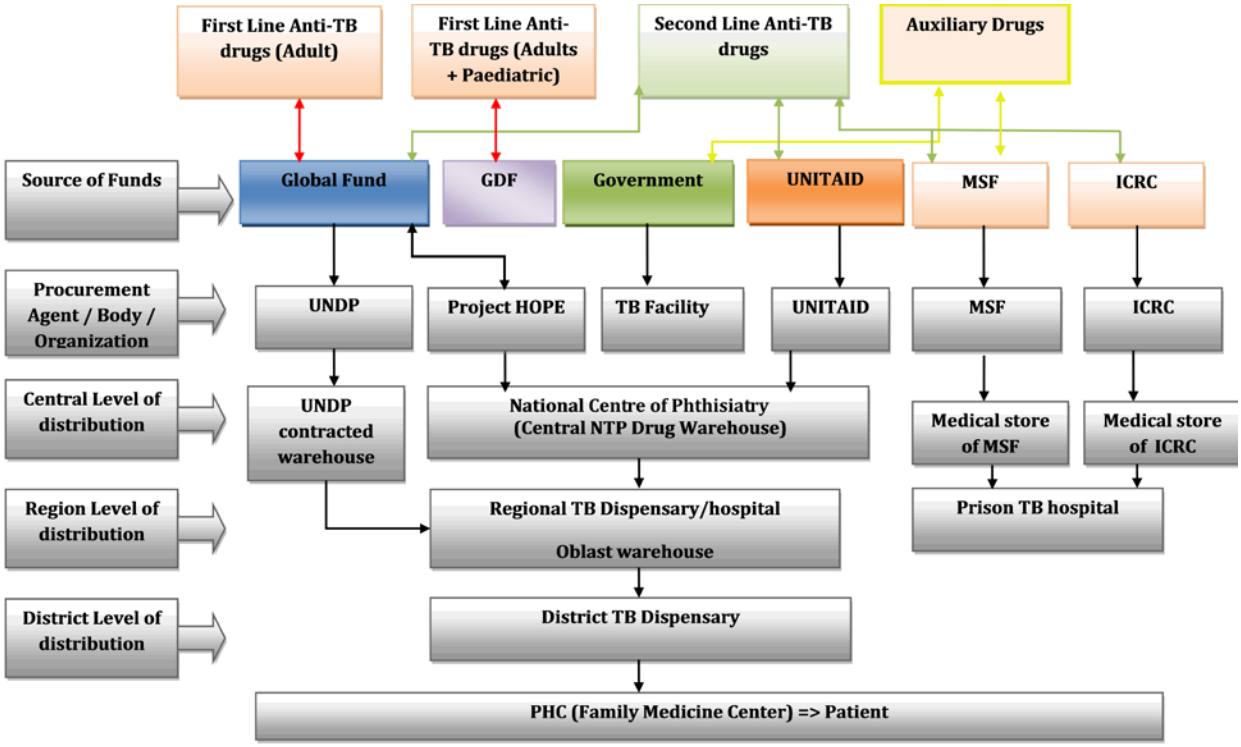
Table A3.5. Total DST results and resistant cases, by previous anti-TB treatment status, Kyrgyzstan, 2013

										V
								TB history		2013
[In countries where information on anti-TB treatment history is not available or incomplete, data can be provided according to TB history]										
1- Please complete only the white cells (yellow cells are calculated).										
2- If data by previous anti-TB treatment status are not available, complete the "Unknown" column.								*[This should correspond to Q11.3]*		
3- Don't forget to fill in the first line with the total numbers of patients with DST results [A]										
				Previous anti-TB treatment status						
				Never treated		**Previously treated [B]**		**Unknown**		**Total**
				N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Total patients with DST results (H+R) [A]				2 157	100%	993	100%	0	*(0%)*	3150	100%
I [C]	Any resistance to isoniazid (H)			1 040	48.2%	711	71.6%	0	0	1751	55.6%
	Any resistance to rifampicin (R)			669	31.0%	573	57.7%	0	0	1242	39.4%
	Any resistance to ethambutol (E)			672	31.2%	538	54.2%	0	0	1210	38.4%
	Any resistance to streptomycin (S)			962	44.6%	675	68.0%	0	0	1637	52.0%
II	Resistance to H only			107	5.0%	36	3.6%	0	0	143	4.5%
	Resistance to R only			24	1.1%	7	0.7%	0	0	31	1.0%
	Resistance to E only			43	2.0%	11	1.1%	0	0	54	1.7%
	Resistance to S only			79	3.7%	13	1.3%	0	0	92	2.9%
	Total mono-resistance			253	11.7%	67	6.7%	0	0	320	10.2%
III	H + R			25	1.2%	17	1.7%	0	0	42	1.3%
	H + R + E			31	1.4%	12	1.2%	0	0	43	1.4%
	H + R + S			141	6.5%	82	8.3%	0	0	223	7.1%
	H + R + E + S			416	19.3%	436	43.9%	0	0	852	27.0%
	Total Multidrug Resistance (MDR) [D]			**613**	**28.4%**	**547**	**55.1%**	**0**	**0**	**1160**	**36.8%**
IV	H + E			27	1.3%	8	0.8%	0	0	35	1.1%
	H + S			184	8.5%	72	7.3%	0	0	256	8.1%
	H + E + S			109	5.1%	48	4.8%	0	0	157	5.0%
	R + E			14	0.6%	3	0.3%	0	0	17	0.5%
	R + S			1	0.0%	4	0.4%	0	0	5	0.2%
	R + E + S			17	0.8%	12	1.2%	0	0	29	0.9%
	E + S			15	0.7%	8	0.8%	0	0	23	0.7%
	Total poly-resistance other than MDR [E]			367	17.0%	155	15.6%	0	0	522	16.6%
Sensitive				**931**	43.2%	**225**	22.7%			**1 156**	**36.7%**
Total Mono (H+R+E)				374	17.3%	138	13.9%	0	0	512	16.3%
Total MDR				613	28.4%	547	55.1%	0	0	1160	36.8%
Total Other poly R				167	7.7%	71	7.2%	0	0	238	7.6%
sensitive H+R+E (# of tested for all 3)				1 003	46.5%	237	23.9%	0	0	1240	39.4%
	[A] Total number of cases with DST result for at least Isoniazid and Rifampicin										
	[D] Concomitant resistance to Isoniazid and Rifampicin, with or without resistance to other anti-TB drugs.										
	[E] Resistance to two or more drugs other than MDR.										
	Validity check: numbers below in yellow cells are calculated for each drug from sections II, III, and IV and should equal numbers in section I. If Cells in blue differ from zero please check the data entry										
	Any resistance to:										
	Isoniazid (H)			1040	0	711	0	0	0	1751	0
	Rifampicin (R)			669	0	573	0	0	0	1242	0
	Ethambutol (E)			672	0	538	0	0	0	1210	0
	Streptomycin (S)			962	0	675	0	0	0	1637	0

Table A3.6. Treatment outcomes of MDR-TB patients, 2012 cohort, Kyrgyzstan

		Chui	Bish-kek	Issyk-Kul	Jalal-Abad	Osh	Naryn	Tallas	Batken	Prison	Total
Cured	Q1	23	21	4	28	11	4	5	0	0	96
	Q2	20	33	4	12	31	1	1	0	18	120
	Q3	18	31	1	14	14	4	4	0	0	86
	Q4	7	8	2	4	15	0	0	0	0	36
	Total	**68**	**93**	**11**	**58**	**71**	**9**	**10**	**0**	**18**	**338**
Completed treatment	Q1	2	2	8	7	3	2	3	0	0	27
	Q2	5	3	0	6	7	2	0	0	5	28
	Q3	2	2	0	5	2	2	2	0	0	15
	Q4	2	0	0	1	1	0	0	0	1	5
	Total	**11**	**7**	**8**	**19**	**13**	**6**	**5**	**0**	**6**	**75**
Failure	Q1	4	3	2	2	1	0	0	0	0	12
	Q2	5	4	2	2	8	1	1	0	3	26
	Q3	8	2	2	2	0	1	1	0	1	17
	Q4	1	2	1	0	2	0	0	0	1	7
	Total	**18**	**11**	**7**	**6**	**11**	**2**	**2**	**0**	**5**	**62**
Defaulted	Q1	5	8	1	4	1	3	0	0	1	23
	Q2	8	11	1	5	2	1	0	0	13	41
	Q3	9	16	1	1	1	2	5	0	3	38
	Q4	3	4	0	0	13	0	0	0	1	21
	Total	**25**	**39**	**3**	**10**	**17**	**6**	**5**	**0**	**18**	**123**
Died	Q1	6	3	1	3	0	0	2	0	1	16
	Q2	10	6	1	3	6	3	3	0	3	35
	Q3	9	5	0	4	3	2	2	0	0	25
	Q4	1	2	0	2	7	0	0	0	0	12
	Total	**26**	**16**	**2**	**12**	**16**	**5**	**7**	**0**	**4**	**88**
Still on treatment	Q1	0	0	0	0	0	0	0	0	0	0
	Q2	0	0	2	0	1	0	0	0	0	3
	Q3	2	2	0	3	22	0	0	0	2	31
	Q4	5	0	2	7	35	1	1	0	4	55
	Total	**7**	**2**	**4**	**10**	**58**	**1**	**1**	**0**	**6**	**89**
Total		**155**	**168**	**35**	**115**	**186**	**29**	**30**	**0**	**57**	**775**

Annex 4. Medicine procurement and supply chain system, NTP Kyrgyzstan



Annex 5. List of anti-TB drugs registered in Kyrgyzstan, 2014

First-line TB medicines								Marketing authorization in Kyrgyz Republic		
#	Name	Formulation and strength	Applicant	Manufacturing site	Packaging	Date of PQP	Manufacturing site status	Application status	Ref. standard required	Decision by DRA
1	Pyrazinamide B.P.	400 mg	Cadila Pharmaceuticals Limited	1389, Dholka – 387810, District: Ahmedabad, Gujarat State, India	28 blister	11/13/2003	WHO GMP-compliant	Submitted 14/01/09	No	MA # 5938 10.07.2009
2	Ethambutol B.P.	400 mg	Cadila Pharmaceuticals Limited	1389, Dholka – 387810, District: Ahmedabad, Gujarat State, India	28 blister	11/13/2003	WHO GMP-compliant	Submitted 14/01/09	No	MA # 5939 10.07.2009
3	Ethambutol + Isoniazid + Pyrazinamide + Rifampicin	275 mg + 75 mg + 400 mg + 150 mg	Svizerta Europe B. V. Manufactured: Svizera Labs Private ltd.	Plot No. D – 16/6, TTC Industrial Area, MIDC, Turbhe, Navi-Mumbai – 400703, India	28 blister		WHO GMP-compliant	Submitted 15/01/09	No	MA # 5943 10.07.2009
4	Streptomycin	1.0	Svizerta Europe B. V. Manufactured: Shijiazhung Pharma Group Zhongnuo Pharmaceutical (Shijiazhung) Co., Ltd.	No. 188 Gongnong Road, Shijiazhung, China	50 vial		WHO GMP-compliant	Submitted 02/08/08	No	MA # 5380 05.12.2008
5	Ethambutol	400 mg	Svizerta Europe B. V. Manufactured: Svizera Labs Pvt. Ltd.	Plot D16/6, TTC Ind. Area, MIDC, Turbhe, Navi Mumbai 400703, India	28 blister		WHO GMP-compliant	Submitted 02/08/08	No	MA # 5379 12.05.2008
6	Isoniazid + Rifampicin	75 mg + 150 mg	Lupin Limited	Aurangabad Works: A-28/1, M.I.D. C. Industrial Area, Chikalthana, Aurangabad 431 210, India. Tel. (91240) 2485871-4, Fax: (91240) 2484121. Corporate Office: 159, C.S.T. Road, Kalina, Santakruz (East), Mumbai 400 098. India. Tel.: (9122) 26931001–10, 2652 6391.	28 blister	11/13/2003	WHO GMP-compliant	Submitted 10/03/2009	No	MA # 5940 10.07.2009
7	Isoniazid + Rifampicin	150 mg + 150 mg	Lupin Limited	Aurangabad Works: A-28/1, M.I.D. C. Industrial Area, Chikalthana, Aurangabad 431210, India. Tel. (91240) 2485871-4, Fax: (91240) 2484121. Corporate Office: 159, C.S.T. Road, Kalina, Santakruz (East), Mumbai 400 098. India. Tel.: (9122) 26931001 – 10, 26526391.	28 blister		WHO GMP-compliant	Submitted 03/06/2009	No	MA # 5942 10.07.2009
8	Sterilized water for injection	5 ml	Svizerta Europe B. V. Antennestraat 43, 1322 AH Almere, P.O. Box 603000, 1320 AJ Almere, The Netherlands Tel: 31 36 539 7340; Fax. 31 36 539 7349	Nirma Limited, Village-Sachana, Taluka-Viramgam District-Ahmedabad 382150 Gujarat, India, Tel: + 91-02715-248001 to 248010; Fax: + 91-02715-248007	5 ampoule		WHO GMP-compliant	Submitted 27/05/2009	No	MA # 5947 10.07.2009

Paediatric anti-TB drugs								Marketing authorization in Kyrgyz Republic		
#	Name	Formulation and strength	Applicant	Manufacturing site	Packaging	Date of PQP	Manufacturing site status	Application status	Ref. standard required	Decision by DRA
9	Rifampicin + Isoniazid + Pyrazinamide	60 mg + 30 mg + 150 mg	Macleods Pharmaceuticals LTD. Kachigam, Daman - 396 210 (U.T), Mumbai - 400 059	Macleods Pharmaceuticals Limited Plot No. 25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman - 396210. India	3 x 28	March 2009		Submitted 15/10/09	No	MA # 6797 22.02.2010
10	Rifampicin + Isoniazid	60 mg + 30 mg	Macleods Pharmaceuticals LTD. Kachigam, Daman - 396 210 (U.T), Mumbai - 400 059	Macleods Pharmaceuticals Limited Plot No.25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman - 396210. India	3 x 28	March 2009		Submitted 15/10/09	No	MA # 6796 22.02.2010
11	Rifampicin + Isoniazid	60 mg + 60 mg	Macleods Pharmaceuticals LTD. Kachigam, Daman - 396 210 (U.T), Mumbai - 400 059	Macleods Pharmaceuticals Limited Plot No.25-27, Survey No. 366, Premier Industrial Estate, Kachigam, Daman - 396210. India	1000 jar; blister 3 x 28			Submitted 15/10/09	No	MA # 6798 22.02.2010
12	Ethambutol-100 B (500) (EMB-Fatol 100 #500)	100 mg	RIEMSER Arzneimittel AG, Fatol, Germany	RIEMSER Arzneimittel AG An der Wiek 7 17493 Greifswald – Insel Riems, Germany				Submitted 22/10/09	No	MA # 6799 22.02.2010
13	Isoniazid	100 mg	LUPIN LTD.	159, C.S.T. Road, Kalina, Santacruz (E), Mumbai – 400 098, India	10 blister		WHO GMP-compliant	Submitted 19/01/09	No	MA # 5941 10.07.2009

	Second-line TB medicines						Marketing authorization in Kyrgyz Republic			
#	Name	Formulation and strength	Applicant	Manufacturing site	Packaging	Manufacturing site status	Application status	Ref. standard required	Decision by DRA	
1	Capreomycin	1 g powder for inj vial	Eli Lilly - USA		vial	FDA-GMP-compliant	Under consideration 20/08/09	No	Under registration process	
2	Cycloserine	250 mg capsules	Macleods Pharmaceuticals Ltd. Kachigam, Daman - 396 210 (U.T), Mumbai - 400 059	Macleods Pharmaceuticals Limited Plot №. 24-27, Survey № 366, Premier Industrial Estate, Kachigam, Daman – 396210, India	Al strip	WHO GMP-compliant	Submitted 15/06/09	No	MA # 5944 10.07.2009	
3	Kanamycin	1 g powder for inj vial	Panpharma-France		vial	EU-GMP-compliant	Under consideration 20/07/09	No	**CANCELLED**	
4	Ofloxacin	200, 400 mg tablets	Macleods Pharmaceuticals Ltd. Kachigam, Daman - 396	Macleods Pharmaceuticals Limited 304-310, Atlanta Arcade,	100 jar /blister	WHO GMP-compliant	Submitted 15/06/09	No	MA # 5945 10.07.2009	

			210 (U.T), Mumbai - 400 059	Marol Church Road, Andheri (East), Mumbai – 400 059, India.						
5	PAS acid	4 g	PASER - USA	Jacobus Pharmaceutical Company Inc., USA 37 Cleveland Lane P.O BOX 5290 Princeton, New Jersey 08540	sachet	FDA GMP-compliant	Submitted 17/06/09	No	MA # 5946 10.07.2009	
6	Peteha (Protionamide)	250 mg tablets	Fatol – Germany	RIEMSER Arzneimittel AG An der Wiek 7 17493 Greifswald – Insel Riems, Germany	100 jar /blister	EU – GMP-compliant	Submitted 12/11/09	No	MA # 6503 20.11.2009	
7	Levofloxacin	250 mg tablets	Macleods Pharmaceuticals Ltd. Kachigam, Daman - 396 210 (U.T), Mumbai - 400 059	Macleods Pharmaceuticals Limited 304-310, Atlanta Arcade, Marol Church Road, Andheri (East), Mumbai – 400 059, India.	blister	WHO – GMP-compliant	Submitted 12/09/10	No	MA # 7691 15.11.2010	
8	Amikacin sulphate	500 mg powder for inj vial	MEDOCHEMIE LTD., LIMASSOL-CYPRUS			EU – GMP-compliant	Submitted 12/09/11	No	MA # 8693 22.09.2011	
9	Pyrazinamide	500mg	Micro Labs Limited Hosur (IN)						**CANCELLED**	

DRA = drug regulatory authority Ref. = reference
MA = marketing authorization PQP = WHO Prequalification of Medicines Programme