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Extensive review of tuberculosis prevention, control and care in Georgia
6–14 November 2014

ABSTRACT

The tuberculosis (TB) epidemiological situation remains a public health issue in Georgia and a matter of concern for the Ministry of Labour, Health and Social Affairs, the community and other stakeholders. Georgia is one of 18 countries giving priority to the fight against TB in the WHO European Region. A review of the TB epidemiological situation, including interventions to prevent and control TB and MDR-TB, was carried out by a team of international experts facilitated by the WHO Regional Office for Europe, with the participation of national experts and the support and observation of the Global Fund and other international stakeholders. This report: (i) documents the progress and shortcomings in TB prevention, control and care; (ii) assesses the health care network, including laboratories, and reports on the quality of TB services delivery; (iii) assesses the links, synergies and opportunities for TB control in relation to health financing, health system strengthening and other disease-specific interventions; and (iv) assesses partnerships in TB care and coordination and collaboration with the national TB programme.

CONTENTS

Acknowledgements

Abbreviations

Amx/Clv	amoxicillin-clavulanate
ART	antiretroviral therapy
Bdq	bedaquiline
CDC	Centers for Disease Control and Prevention
Cfz	clofazimine
Clr	clarithromycin
Cm	capreomycin
CPT	cotrimoxazole preventive therapy
Cs	cycloserine
DOT	directly observed therapy
DSM	direct smear microscopy
DST	drug-susceptibility testing
E	ethambutol
GDF	Global Drug Facility
GLC	Green Light Committee
GMP	good manufacturing practice
H	isoniazid
Imi/Cln	imipenem/cilastatin
IPT	isoniazid preventive therapy
Km	kanamycin
Lfx	levoflaxicin
LSS	laboratory surveillance station
Lzd	linezolid
MDR	multidrug-resistant
MGIT	mycobacteria growth indicator tube
MoLHSA	Ministry of Labour, Health and Social Affairs
NCDC	National Centre for Disease Control
NCTLD	National Centre of Tuberculosis and Lung Diseases
NRL	National Reference Laboratory
NSP	National TB Strategy and Operational Plan for 2013–2015
Ofx	ofloxacin
PAL	practical approach to lung health
PAS	p-aminosalicylic acid
Pto	prothionamide
RRL	regional reference laboratory
R	rifampicin
S	streptomycin
SSM	sputum smear microscopy
SARMA	State Agency for Regulation of Medical Activities
TB	tuberculosis
URC	University Research Co.
USAID	United States Agency for International Development
XDR	extensively drug-resistant
Z	pyrazinamide
ZDL	zonal diagnostic laboratory

Executive summary

Tuberculosis (TB) has re-emerged as an important public health concern in Georgia since 1991, and its burden remains high in the country. At the beginning of 2015, the population was 3.73 million of Abkhazia and South Ossetia), of whom 57.4% lived in urban areas *(1)*. In 2013, the estimated gross national income was US$ 3560 per capita, while about 15% of the population lived below the national poverty line *(2)*.

In 2013, there were an estimated 5000 incident cases of TB (uncertainty range 4700–5500), equivalent to a rate of 116/100 000 population. TB incidence steadily decreased after 1990, with an annual rate of decline from 2001 to 2013 averaging -5.8%. Despite such an impressive decrease in the TB burden, it was estimated that only 68% of TB cases in 2013 were detected by the health care system *(3)*.

Given the need to ensure an effective national response to the situation regarding TB through addressing the emerging challenges and strengthening evidence-based TB control interventions, the Ministry of Labour, Health and Social Affairs (MoLHSA) asked the WHO Regional Office for Europe to carry out a comprehensive assessment of the national TB programme (NTP). In cooperation with the Ministry, WHO conducted a review of the NTP from 6 to 14 November 2014 with the participation of the Global Drug Facility (GDF), Green Light Committee, Centers for Disease Control and Prevention (CDC), TB Europe Coalition and national experts.

The burden of multidrug-resistant (MDR) TB is the key challenge for the NTP and the main obstacle to effective TB control in the country. WHO estimated that 710 patients with MDR-TB needed treatment in 2013 *(4)*. In 2013, drug susceptibility testing (DST) by the National Reference Laboratory found MDR-TB in 11.2% of new cases and in 38.1% of previously treated cases. Findings show that this may have also occurred as a result of mismanagement of patients in their initial and following treatment episodes, poor treatment adherence outcomes and adverse reactions. Adherence counsellors' posts have been abolished and there is a need to ensure that the available health care staff are properly trained, enabled and motivated to make further efforts to bring down the default rates.

Privatization has had a negative impact on TB control services, with an unusually sharp (25%) decrease in notifications from 104 TB cases per 100 000 population in 2011to 79 in 2013 and an increase in treatment lost to follow-up. The quality of services requires meticulous field monitoring and staff mentorship, including finding out patients' perspectives on the health care services provided.

The TB control programme is still heavily dependent on international donors, including the Global Fund to Fight AIDS, Tuberculosis and Malaria. In 2012, 62 % of the total funding for the national TB programme came from international donors. The pulmonology and phthisiology services should be merged and posts established for phthisiopulmonogists.

In order to curb the epidemics, especially in view of the gradual phasing out of the Global Fund in a couple of years, it is important for the country to increase its domestic resources for TB control. A TB sub-account under the national health account is recommended.

There is an excellent surveillance system with electronic and case-based data.

The newly recommended treatment regimen with new medicines for eligible patients should be introduced. The team recommends that the MoLHSA facilitate the registration of new medicines. Active pharmacovigilance should be improved with meticulous recording and reporting of adverse events. Medicines for adverse events should be made available free. The current management of medicines does not allow for easy redistribution of medicines from centres where they may expire to other health care units. This needs to be addressed by setting up a central drug management system with warnings on the shelf life of medicines and measures to allow the movement of medicines between the health care centres, including those in the private sector.

The infrastructure of the TB children's hospital is in urgent need of attention. The team recommends that the health authorities look into alternative premises or fully renovate the current facility.

The review team notes good progress as regards decreasing overcrowding and improving the quality of services in correctional facilities. The team strongly recommends that released prisoners with TB are followed up in the civilian sector; to this end, a comprehensive continuum of care mechanism should be in place, including for those who are released through an amnesty. Progress should be measured.

The team acknowledges the recently established coordinating body for the national TB programme, and recommends further development of its roles and responsibilities and the appointment of a national TB programme manager. It would be highly beneficial for a document to be drawn up laying down the governance structure of the NTP and describing the terms, responsibilities and accountabilities for all the main stakeholders involved in TB control. This should be endorsed by the ministerial decree on the new coordinating committee for TB control.

Cross-border TB control and care is to be strengthened and consideration should be given to using WHO for the facilitation of the necessary links between health authorities and nongovernmental organizations providing care in other countries.

References

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Introduction

Georgia is a country in transition in the South Caucasus. At the beginning of 2015, the population was 3.73 million, of whom 57.4% lived in urban areas *(1)*. According to the World Bank, the economy registered an average 5.5% annual growth during the last five years. In 2013, the estimated gross national income was US$ 3560 per capita, while about 15% of the population lived below the national poverty line *(2)*.

Tuberculosis (TB) re-emerged as an important public health problem after 1991 and its burden remains high. Given the need to ensure an effective national response to the situation regarding TB through addressing the emerging challenges and strengthening evidence-based TB control interventions, the Ministry of Labour, Health and Social Affairs (MoLHSA) asked the WHO Regional Office for Europe to carry out a comprehensive assessment of the national TB programme (NTP). In cooperation with the Ministry, WHO conducted a review of the NTP from 6 to 14 November 2014 with the participation of the Global Drug Facility (GDF), Green Light Committee, Centers for Disease Control and Prevention (CDC), TB Europe Coalition and national experts.

The objectives of the review were:
- to visit TB service institutions and other relevant health care facilities, including laboratories, and report on the quality of services;
- to analyse epidemiological data and assess the accuracy of TB recording/reporting and the monitoring system;
- to assess the links, synergies and opportunities for TB control in relation to strengthening the health system and other disease-specific interventions;
- to assess partnership, coordination and collaboration in TB control between relevant national stakeholders and international partners;
- to develop a comprehensive set of recommendations and a prioritized action plan for improving TB prevention, control and care.

The team assessed components of the NTP, including:
- government commitment and policy (including TB control as part of the overall health system, financing, organizational structure and guidelines);
- development of human resources for TB control;
- epidemiological assessment, recording and reporting, monitoring and evaluation;
- TB case detection and diagnosis, laboratory services;
- infection control and biosafety;
- intersectoral collaboration and TB care services for vulnerable populations, such as HIV/TB collaborative activities, TB in prisons;
- treatment (in- and outpatient phases), multidrug-resistant (MDR) TB case management and childhood TB;
- management of anti-TB drugs, supply management systems for equipment and consumables;

- involvement of civil society, ethics and human rights, public-private partnerships and advocacy, communication and social mobilization;
- operational research.

The review teams visited five regions: Tbilisi, Imereti (Kutaisi, Zestaponi), Kvemo Kartli (Rustavi, Gardabani, Marneuli), Samegrelo (Zugdidi) and Shida Kartli (Gori, Kvakhvreli, Kaspi), and evaluated national, regional, district and commune levels of health care service delivery. They met the leading agencies developing public health strategy and health financing: MoLHSA (National Centre for Disease Control (NCDC), National Centre of Tuberculosis and Lung Diseases (NCTLD) and the Social Service Agency); State Agency for Regulation of Medical Activities; Tbilisi State Medical University; the Infectious Disease, AIDS and Clinical Immunology Research Centre; Ministry of Corrections (Ksani Prison); and partners such as the Tuberculosis Prevention Project of the the University Research Co. (URC) and Médecins Sans Frontières. They were given full access to information throughout the country and were able to observe the structure for delivery of TB care, resources and practices, note the main strengths and weaknesses and propose key recommendations to improve the effectiveness of the NTP.

TB epidemiology

Georgia is one of the 18 high-priority countries in the WHO European Region's Plan to Stop TB *(3)*, one of the top five countries in the Region with the highest incidence rate of TB and one of the 27 countries in the world with the highest burden of MDR-TB. TB re-emerged as an important public health threat after 1991, and its burden remains high in Georgia. According to WHO *(4)*, the latest (2013) estimated TB incidence was 116 per 100 000 population, the fourth highest level among the 53 countries of the WHO European Region. The estimated 2013 mortality rate was 7.0 per 100 000 population (excluding HIV/TB cases).

TB incidence

In 2013, there were an estimated 5000 incident cases of TB (uncertainty range 4700–5500), equivalent to a rate of 116 (109–126)/100 000 population (Fig. 1). TB incidence steadily decreased after 1990; the annual rate of decline from 2001 to 2013 averaged -5.8%.

Despite such an impressive decrease in the TB burden, it was estimated that only 68% of TB cases (63–73) in 2013 were detected by the health care system *(4)*.

TB prevalence

There are no data from direct measurements of TB prevalence in Georgia. The only available information on TB prevalence comes from indirect estimates by WHO. In 2013, the estimated number of prevalent TB patients was 7100 (3400–12 000), equivalent to a rate of 163 (79–277)/ 100 000 population. From 1990, TB prevalence fell steadily to the point where by 2005 the Stop TB Partnership target to halve TB prevalence by 2015 compared to the 1990 prevalence estimate had been achieved *(5)* (Fig. 2).

Fig. 1. Estimated TB incidence rate and notification of incident TB cases (new and relapsed per 100 000 population), Georgia, 1990–2013
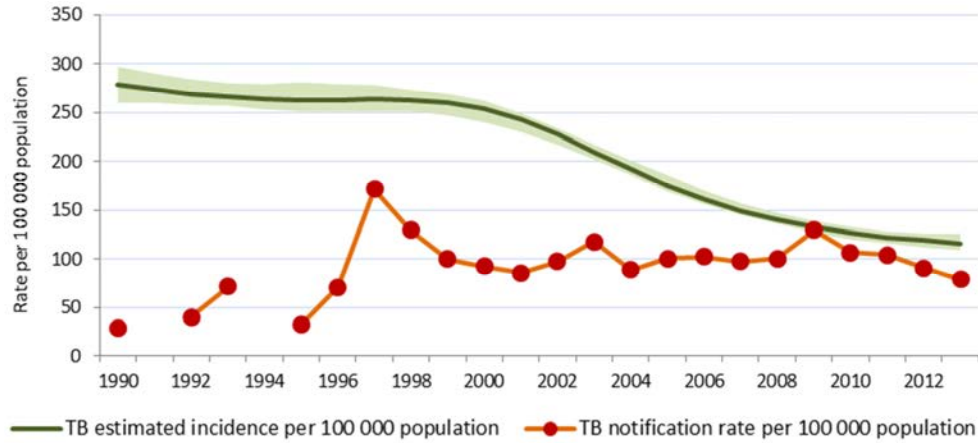
Shaded areas represent uncertainty band.
Source: WHO *(6).*

Fig. 2. Estimated TB prevalence rate per 100 000 population, Georgia, 1990–2013
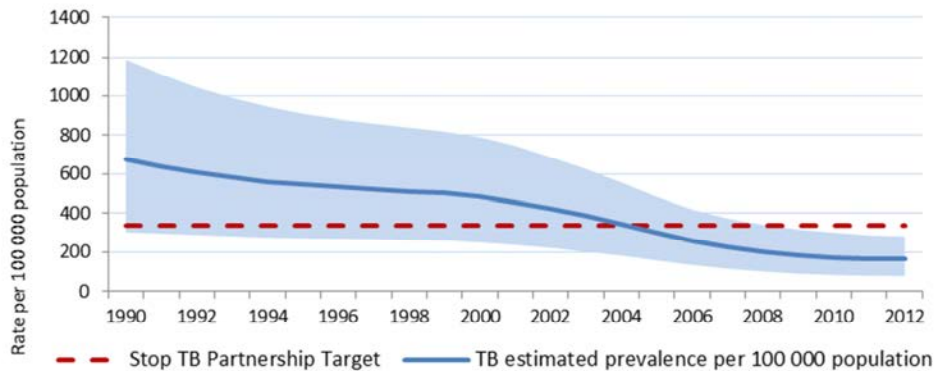
Shaded areas represent uncertainty band. Horizontal dashed line represents Stop TB Partnership target of 50% reduction in prevalence rate by 2015 compared to 1990.
Source: WHO *(6).*

TB mortality

Between 1990 and 2005, the mortality rate gradually decreased (with some fluctuations) from 8.9 to 7.0, followed by a sudden sharp decrease to 3.8 per 100 000 population in 2005 and, from 2007, a marked increase until 2012 (Fig. 3). Such sharp swings are probably artefacts related to a weakness in the ability of the vital registration system to capture and report causes of death. By the end of 2013, estimated TB mortality was reported as 7.0, higher than the Stop TB Partnership Goal to halve TB mortality by 2015 compared to 1990. The country will not, therefore, reduce TB mortality to the Stop TB Partnership target of 4.5/100 000.

Fig. 3. Estimated TB mortality rate (excluding HIV/TB mortality) per 100 000 population, Georgia, 1990–2013

Shaded areas represent uncertainty band of WHO estimated TB mortality. Horizontal dashed line represents Stop TB Partnership target of 50%
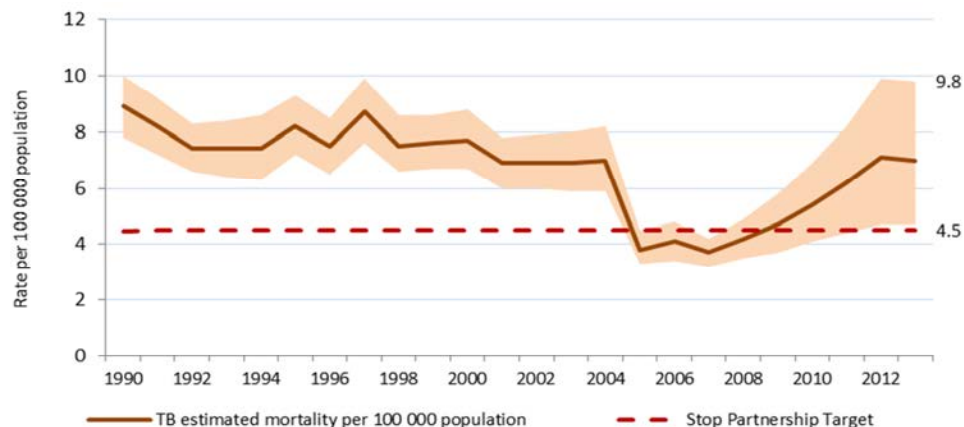
reduction in TB mortality rate by 2015 compared to 1990.
Source: WHO *(6).*

TB notifications

At national level, the number of notified TB cases (all forms) increased from 5993 cases (equivalent to 131 per 100 000) in 2003 to a peak of 6448 (144 per 100 000) cases in 2005 and then fell again (Fig. 4). In 2013, a total of 4319 TB cases (99 per 100 000) were notified by the health system, the lowest number and level of TB cases recorded since 2003. The average annual rate of decrease in the notifications rate of all TB cases from 2005 to 2013 was 5.4%.

Fig. 4. Notification of TB (all forms), absolute number (left) and rate per 100 000 population (right) (fitted with polynomial trendlines), Georgia, 2003–2013
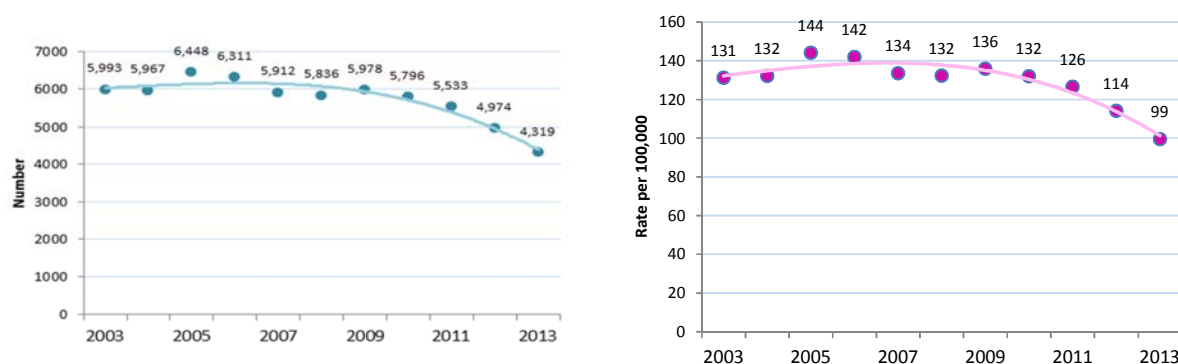
Source: WHO *(6).*

According to the NTP notifications data, a total of 3850 TB cases (103.3 per 100 000 population) all forms, were registered in 2014, including in the penitentiary sector, of which 2807 were new cases (75.3 per 100 000). Between 2012 and 2014, a substantially decreasing trend in the absolute number of TB cases was documented, with the total number of TB notifications falling by 22.6% and the number of new cases by 25.7%. On the other hand, an alarming feature is

that the proportion of previously treated cases among all those notified increased from 24.0% in 2012 to 27.1% in 2014 (Table 1).

Table 1. TB notifications by case category, Georgia, 2012–2014

Category	2012	2013	2014
New cases:	3779	3133	2807
pulmonary smear-positive	1649	1334	1142
pulmonary smear-negative/unknown	1186	1078	1004
extrapulmonary	944	721	661
Retreatment cases:	1196	1187	1043
pulmonary smear-positive	631	579	474
pulmonary smear-negative/unknown	441	513	474
extrapulmonary	124	95	95
All TB cases	4975	4320	3850

Source: NCTLD *(7).*

Among new TB cases registered, almost 70% were in males (ratio of males to females 2 : 24). The disease affects the mainly young and most economically productive part of the population: almost two thirds of all new TB cases are in the group aged 15–44 years.

TB notifications by geographic distribution

The TB notifications rate varies widely across regions and settings. The reasons could be true differences in the TB burden as well as different levels of access to quality health care and capacity to detect TB. The national TB policy dictates that cases are notified from the site of diagnosis, which is probably why so many TB cases are notified in Tbilisi, as a large proportion of TB patients from all regions are referred or refer themselves to the NCTLD for diagnosis and initial treatment.

According to national statistics, in 2013 the lowest rate of TB (all cases) was recorded in Samckhe-Javakheti (44/100 000) and the highest – over four times higher than in Samckhe-Javakheti – in Adjara (Table 2). The TB rate in prisons was 25.5 times higher than in the civilian population.

Table 2. TB notification rate per 100 000 population by regions and prison and mean year-on-year change in notification rate of all TB cases, Georgia, 2009–2013

Region	2008	2009	2010	2011	2012	2013	Mean annual change in rate (%)
Tbilisi	154.4	138.5	122.9	126.4	118.6	116.3	-5.4
Mtskheta-Mtianeti	103.8	98.8	117.3	101.4	103.4	82.6	-3.5
Kakheti	73.7	77.2	71.3	71.1	74.6	60.7	-3.4
Shida Kartli	99.4	95.8	88.8	83.5	83.1	72.4	-6.1
Kvemo Kartli	107.9	107.1	88.3	85.9	73.0	73.4	-7.1
Imereti	82.3	84.1	71.5	66.3	74.8	66.1	-3.8
Guria	105.7	105.5	100.6	73.4	77.3	91.4	-1.7
Samegrelo	132.1	142.5	116.3	111.2	106.4	103.7	-4.4
Samckhe-Javakheti	72.9	70.6	53.8	47.8	44.4	44.0	-9.2
Adjara	183.6	163.3	162.3	141.3	153.3	147.4	-4.0
Racha-Lechkhumi	No data	54.5	35.8	63.6	36.4	54.2	12.4
Prisons	3296.0	4484.0	5400.3	4860.2	3483.4	2326.5	-3.0

Source: NCTLD *(7).*

The TB notification rate fell between 2008 and 2013 across all regions except Racha-Lechkhumi. The average annual decrease varied between -1.7 in Guria) and -9.2% in Samckhe-Javakheti. In Racha-Lechkumi the rate increased by an average of 12.4%, but given the low number of patients in that region, large stochastic variations are possible.

Trend in TB notifications by smear microscopy result

Between 2003 and 2013, the proportion of new sputum smear-positive pulmonary TB patients varied markedly. From 2003 to 2007 the proportion increased from 35% to 66%, suggesting improvements in laboratory diagnostics. This level was sustained until 2010, and then it decreased by 10% to 55% in 2013 (Fig. 5).

Trend in TB by site of disease

The percentage of new extrapulmonary cases was stable between 2003 and 2009. The proportion of new extrapulmonary cases among new TB cases decreased gradually from 30% in 2007 to 23% in 2013 (Fig. 6).

**Fig. 5. Trend in proportion of new smear-positive and smear-negative
pulmonary TB cases among new pulmonary TB cases, Georgia, 2003–2013**
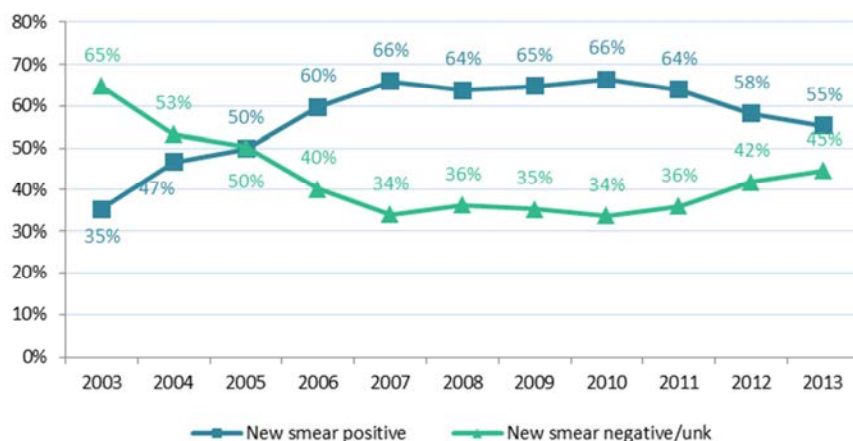
Source: WHO *(6).*

Fig. 6. Trend in notification numbers of new pulmonary and extrapulmonary TB cases, and proportion of extrapulmonary cases among new TB cases, Georgia, 2003–2013
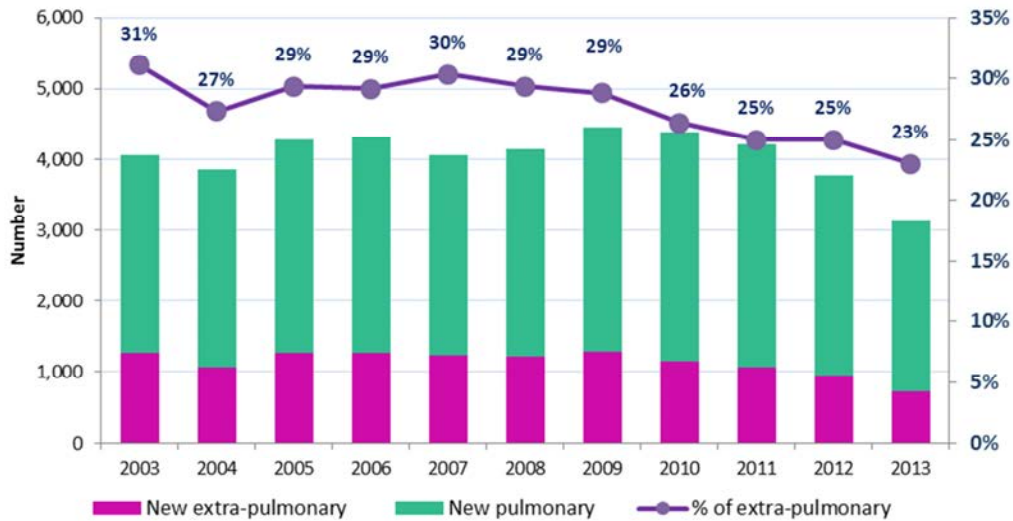
Source: WHO *(6).*

Trend in childhood TB

The absolute number of child TB cases almost halved from 347 in 2006 to 182 in 2013 (Fig. 7). The relative number of child TB cases also fell from 8.0% in 2006 to 5.8% in 2013. In 2014, 129 TB cases, all forms, were registered in children aged 0–14 years (26 pulmonary TB cases and 103 extrapulmonary cases), constituting 19.9 TB cases per 100 000 of the child population. Five paediatric TB meningitis cases occurred in 2014, while no such cases were registered during 2013.

Fig. 7. Trend in notified number of TB cases in children disaggregated by age group, and proportion of child TB among all new TB cases, Georgia, 2006–2013
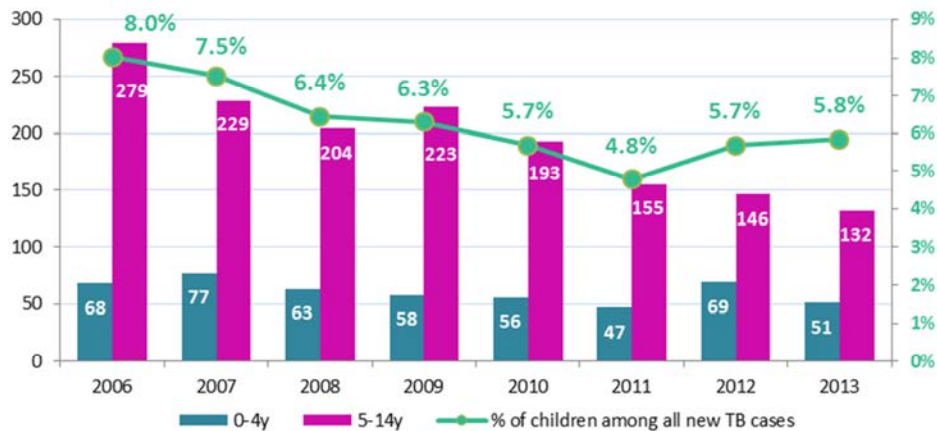
Source: WHO *(6).*

Trend in TB notifications by sex

Between 2006 and 2013, the proportion of males among TB cases was more or less stable, ranging from 68% to 73% among new TB cases (the 2013 data included relapsed cases) (Fig. 8). The proportion of males was highest in 2010 and then fell to 69% in 2013.

Fig. 8. Number of notified new TB cases by sex (2013 data include new and relapsed cases) and proportion of cases who are male, Georgia, 2006–2013

Source: WHO *(6).*

Trend in TB notifications by category

The proportion of retreated TB cases among all notified TB cases fell markedly between 2003 and 2013 (Fig. 9). In 2013, a marked increase in the proportion of retreated cases was due to a sharp decline in the notification of new TB cases.

Fig. 9. Number of notified new and retreated TB cases and proportion of retreated TB cases, Georgia 2003–2013
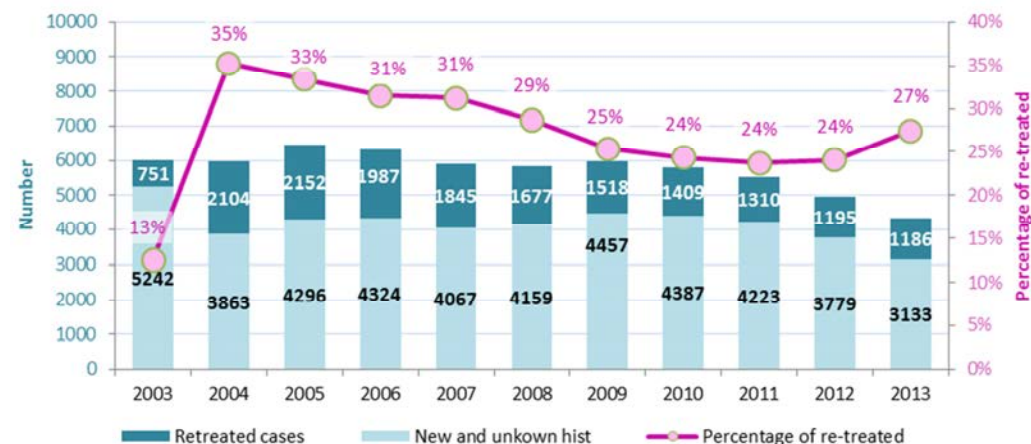
Source: WHO *(6).*

Drug-resistant TB

Georgia is one of the 15 countries with a high burden of MDR-TB among the 53 regional Member States. This burden is the key challenge for the NTP and the main obstacle for effective TB control in the country. WHO estimated that 710 patients with MDR-TB needed treatment in 2013 *(4)*. The first nationwide representative drug resistance survey, which was conducted in 2005–2006, revealed an MDR-TB prevalence of 6.8% among new smear-positive cases and 27.4% among previously treated cases *(8)*. In 2013, drug susceptibility testing (DST) by the National Reference Laboratory found MDR-TB in 11.2% of new cases and in 38.1% of previously treated cases.

Access to isoniazid and rifampicin has increased markedly in recent decades. As a result, from 2011 to 2013 about 70% of new pulmonary TB cases had documented DST results (Fig. 10).

Fig. 10. Number of notified pulmonary TB cases, number of pulmonary TB cases with first-line DST results and percentage of pulmonary TB cases with DST results, Georgia, 2005–2013
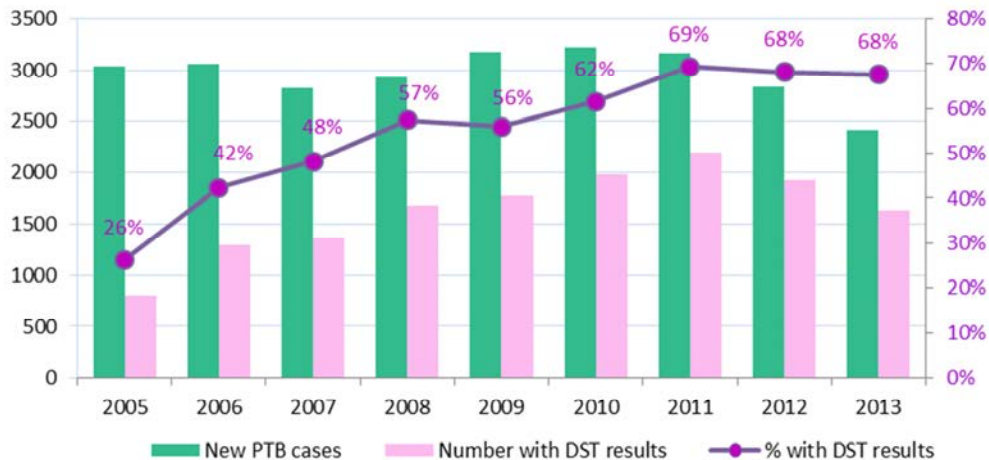
Source: WHO *(6)*.

According to routine drug resistance surveillance among the patients notified in 2013, three quarters of new pulmonary TB cases were susceptible to any of isoniazid, rifampicin or ethambutol, while 8% were polyresistant (Fig. 11). The proportions of TB cases that were isoniazid-resistant without rifampicin resistance were 11.8% among new cases and 11.2% among retreated cases.

Fig. 11. Pattern of drug-resistance among pulmonary TB patients, Georgia, 2013
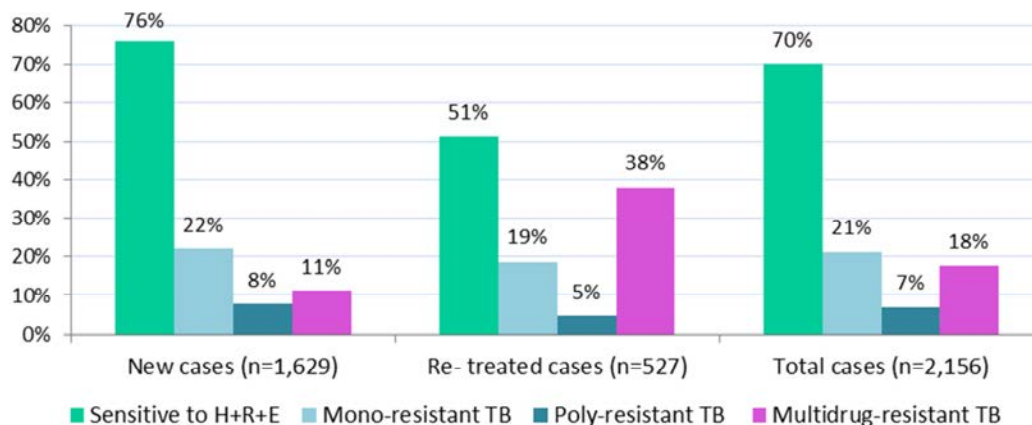
Source: NCTLD *(7).*

The trend in MDR-TB stabilized between 2007 and 2013. After 2008 the proportion of MDR-TB among new TB cases varied between 9% and 11% and among previously treated cases between 31% and 40% (Fig. 12).

Fig. 12. Percentage of MDR-TB patients among new and previously treated pulmonary TB patients with DST results based on routine surveillance, Georgia, 2007–2013

Data source: Global TB database
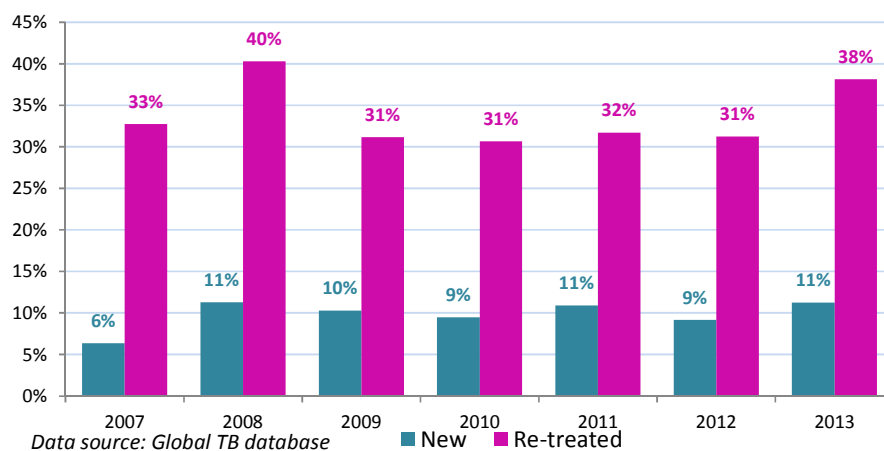
Source: WHO *(6).*

In 2013, Georgia notified 400 MDR-TB cases to the global TB database, in contrast to the 720 cases estimated by WHO. The actual number of MDR-TB cases detected is, however, much higher than reported. There are several reasons for the underreporting of MDR-TB cases: patients who were detected and notified in the previous year but confirmed with MDR-TB in the following year are not notified as MDR-TB cases in the following year notification cohort. In addition, Georgian practice is not to notify as new cases patients that are diagnosed with MDR-TB while being treated (acquired MDR). Thus MDR-TB detection is underestimated if it is based on routine surveillance data.

Data from the National Reference Laboratory (NRL) for DST to first-line drugs for 2014 show an MDR prevalence of 11.6% and 39.2% in new and previously treated cases, respectively (among all cases with DST results, MDR-TB was found in 18.6%). Table 3 shows the first-line resistance profile for 2010–2014.

Table 3. Pattern of resistance to first-line anti-TB drugs in new and previously treated culture-positive cases, Georgia, 2010–2014

Pattern of resistance	2010	2011	2012	2013	2014
New cases:					
Cases with DST results	1988	2197	1931	1629	1482
Sensitive to all first-line drugs (%)	44.6	52.5	59.5	58.9	57.7
H+ resistance (%)	13.7	12.8	13.4	11.7	12.3
R+ resistance (%)	0.4	1.0	0.6	0.4	0.2
MDR-TB (%)	9.5	10.9	9.2	11.2	11.6
Other patterns (%)	31.9	22.7	17.3	17.8	18.2
Previously treated cases:					
Cases with DST results	567	675	541	527	503
Sensitive to all first-line drugs (%)	33.3	35.6	42.0	38.3	38.0
H+ resistance (%)	13.6	12.3	10.7	9.9	9.5
R+ resistance (%)	0.5	1.3	0.6	0.0	1.4
MDR-TB (%)	31.4	31.7	31.2	38.1	39.2
Other patterns (%)	21.2	19.1	15.5	13.7	11.9

Source: NCTLD/NRL *(9).*

As with first-line DST, access to second-line DST improved markedly: from 2011 to 2013 over 90% of confirmed MDR-TB cases had DST results for both fluoroquinolones and second-line injectables (Fig. 13).

Fig. 13. Number of MDR-TB patients detected, MDR cases with second-line DST results and proportion of MDR-TB patients with second-line DST results, Georgia, 2007–2013
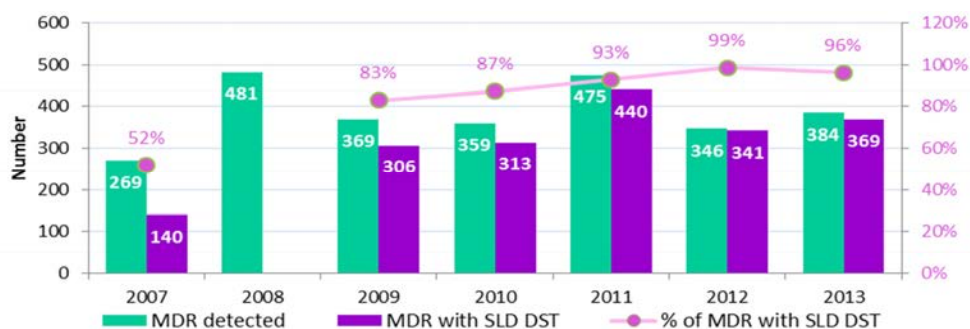
Source: WHO *(6).*

Between 2009 and 2012, about 28 to 32 extensively drug-resistant (XDR)-TB cases were detected each year among confirmed MDR-TB cases with second-line DST results equivalent to an XDR-TB rate of 6–10%. In 2013, there was an unexpectedly sharp increase in XDR-TB cases: in total, 71 XDR cases (about 19% of MDR-TB cases) were notified. Thus, about one in five MDR-TB cases notified is diagnosed with XDR-TB (Fig. 14).

Fig. 14. Number of MDR cases with second-line drugs DST results, number XDR-TB cases detected and proportion of XDR with among MDR-TB cases, Georgia 2007–2013

Source: WHO *(6).*

The pool of XDR-TB cases is shaped mainly by cases that are resistant to kanamycin (Km) and ofloxacin (Ofx) (Table 4).

Table 4. Pattern of second-line DST results among MDR-TB patients with DST results to any of Km, Cm and Ofx, Georgia, 2013 (n=401)

Profile of resistance	No.	%
Any resistance to Km, Cm or Ofx	230	57.4
No resistance to Km, Cm or Ofx	171	42.6
Resistance to Km only	92	22.9
Resistance to Cm only	11	2.7
Resistance to Ofx only	41	10.2
Resistance to Km and Cm	13	3.2
Resistance to Km and Ofx	45	11.2
Resistance to Cm and Ofx	5	1.2
Resistance to Km, Cm and Ofx	23	5.7

Source: NCTLD/NRL *(9).*

Levels of resistance to Km were fairly stable during 2010–2013, varying between 36.3% and 38.1% in new cases and 43.6% and 47.3% in retreatment cases, while resistance to capreomycin (Cm) decreased from 22.3% in 2010 to 13.4% in 2013 (Fig. 15). Resistance to Ofx, which was stable during 2010–2012 at around 20%, rose substantially in 2013 to 28.4%.

Second-line TB treatment has been available since 2007. In 2009, universal coverage with second-line drugs treatment was achieved for all patients notified with MDR-TB. The ratio of notified to enrolled MDR-TB cases in 2009 was 136%. The ratio of enrolled to notified cases reached 192% before decreasing to 132% in 2013. The proportion of presumptive TB cases among all those enrolled in second-line treatment across the recent four years varied from 12.0% to 17.6% (Fig. 16).

Fig. 15. Percentage of MDR cases with resistance to Km, Cm and Ofx among MDR-TB patients with second-line DST results, Georgia, 2010–2013
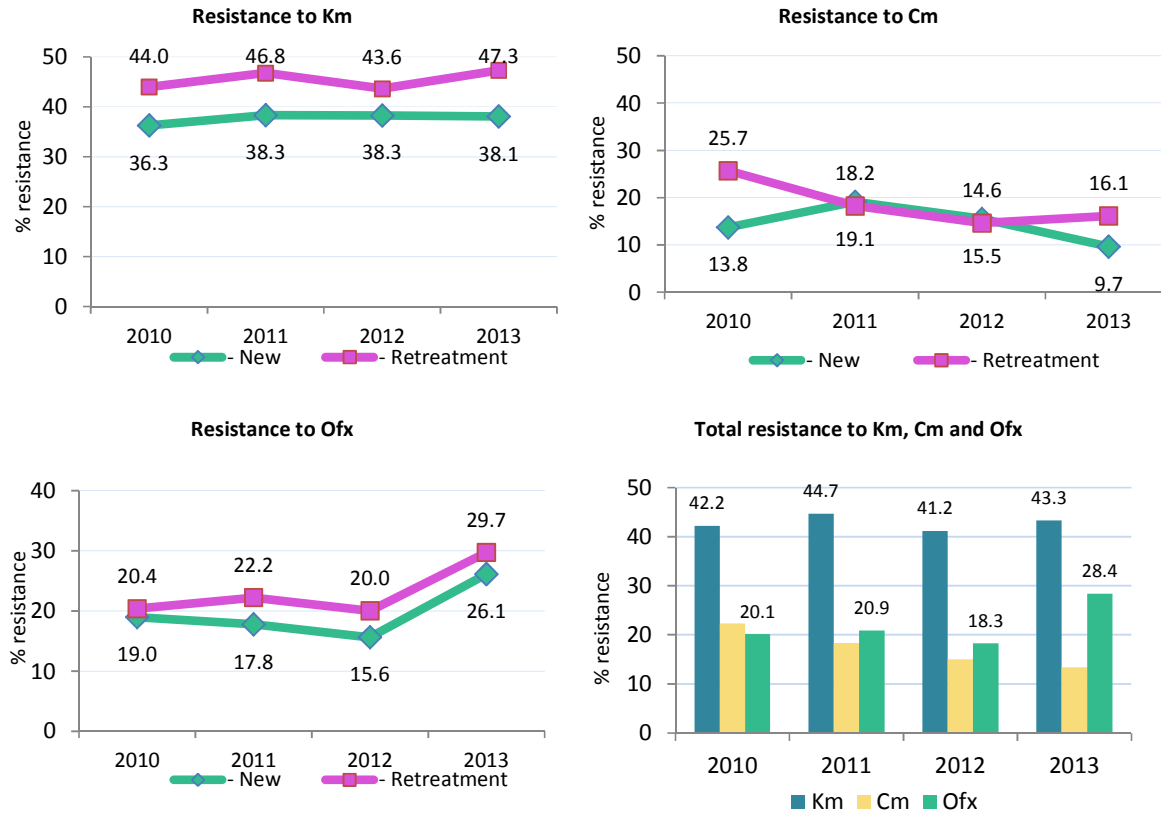
Source: NCTLD/NRL *(9)*.

Fig. 16. Number of pulmonary MDR-TB cases detected and number of all confirmed and presumptive MDR-TB cases enrolled in MDR-TB treatment, Georgia, 2005–2013
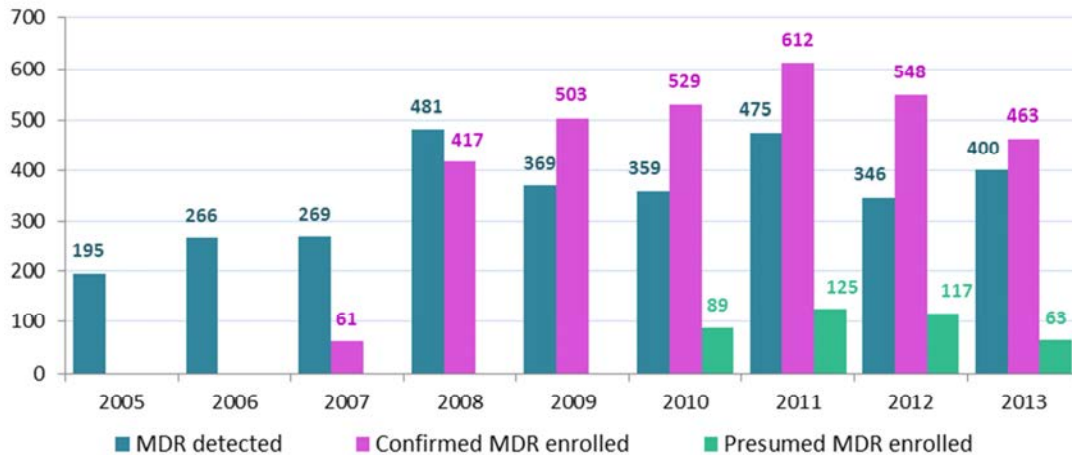
Source: WHO *(6)*.

The difference between notified and enrolled confirmed MDR cases has several reasons: TB cases notified in previous years and confirmed with MDR in the following reporting period are

not included in MDR notification. In addition only pulmonary MDR cases are reported per WHO data collecting form, while in Georgia extrapulmonary cases with confirmed MDR-TB also are enrolled into second-line treatment. Another group of patients are those that already were treated with MDR-TB and again are recruited into second-line drugs treatment (relapse of MDR treatment, or interruption of MDR treatment). And another reason is that the patients with several attempt of treatment are not renotified (prevalent TB cases), however if DST indicates MDR they are recruited into second-line drugs treatment.

TB in prisons

In 2014, the average annual number of detainees in the penitentiary system (all facilities, including pre-trial detention centres) was about 10 370 against 24 100 in 2011 (a 2.3-fold decrease). TB remains an important health problem in prisons, although the absolute number of TB cases, all forms, in the system decreased from 1172 in 2011 to just 145 in 2014.

In the same years, the number of new cases decreased from 800 to 66. TB notification rates fell from 4860 to 1400 per 100 000 of prison population (all cases) and from 3320 to 640 per 100 000 (new cases). TB notification rates in the penitentiary system are, however, much higher than in the civilian sector, exceeding them by 8.5 times (for new cases) to over 30 times (for all cases).

In 2013–2014, there were no lethal cases among TB patients in prisons, compared to 50 deaths in 2011 and 21 in 2012. MDR-TB prevalence in 2013 accounted for 9.2% of new culture-positive cases and for 53.1% of retreatment cases; in 2014 (preliminary data), it was 7.7% and 40.8%, respectively.

HIV/TB coinfection

The Joint United Nations Programme on HIV/AIDS estimates that at the end of 2013, about 6400 people of all ages were living with HIV (range 5000–8000), with an HIV prevalence rate of 0.3% in the adult population aged 15–49 years. Since the first HIV case was detected in 1989, the annual rate of new HIV infections increased steadily to 10.9 per 100 000 population in 2013. As of the end of 2014, a total of 4695 individuals were diagnosed with HIV in the country. In 2014, 564 new HIV infections were detected (compared to 490 in 2013 and 526 in 2012).

Although the infection is mainly found among males, the proportion of women affected by HIV is rising and reached 31% in 2014. HIV remains largely concentrated among the key affected populations: men having sex with men, people who inject drugs and sex workers. The highest rates of recent HIV infections are found among men having sex with men; HIV prevalence in this risk group increased from 7% in 2010 to 13% in 2012. Between the various groups among the estimated 45 000 people who inject drugs in Georgia, HIV prevalence ranges from 0.4% to 9.1%. In prisons, a significant decrease in HIV prevalence has been documented (from 1.4% among inmates in 2008 to 0.35% in 2012). HIV prevalence among pregnant women and blood donors (0.04% in both sub-populations) is lower than in the general population. Coinfection with hepatitis C virus is common; hepatitis C virus antibodies are detected in up to half of the registered people living with HIV in Georgia.

HIV testing coverage increased fivefold compared to 12% in 2004, suggesting an impressive improvement over time, although it is still far below the regional target of 100% HIV testing coverage. The proportion of TB patients with known HIV status remains low: in 2013 it was 62% (2698 patients out of a total of 4320 were tested for HIV (Fig. 17)). HIV prevalence among TB patients is low compared to other countries in the Region; during 2010–2013, it varied from 1.9% to 2.3% among TB cases, all forms, tested for HIV. Among MDR-TB patients, however, HIV/TB coinfection is more frequent: 5.3% of MDR-TB cases were HIV-positive in 2012–2013.

Fig. 17. Number of notified HIV/TB coinfections and HIV testing coverage among notified TB patients, Georgia, 2004–2013
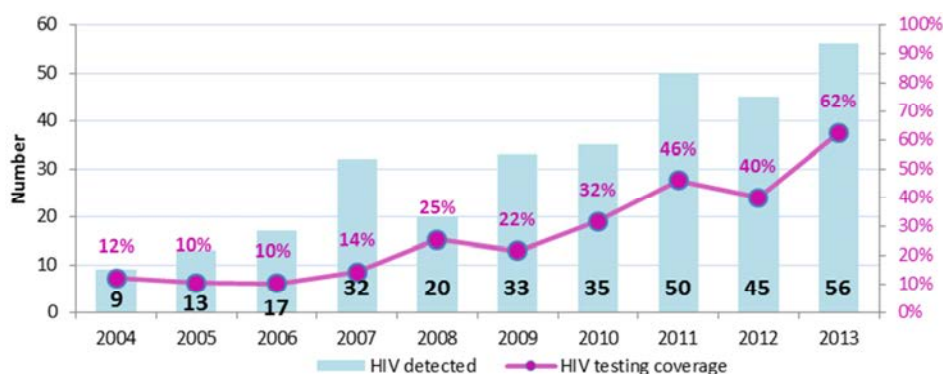
Source: WHO *(6).*

In 2013, national surveillance data showed that 2.1% of TB patients with documented HIV test results were HIV-positive. The level of HIV/TB coinfection peaked in 2007 at 3.8% then fluctuated widely over the years between 1.3% and 2.6% with no clear trends. Such a fluctuation is due to limited HIV testing coverage leading to selection bias. According to WHO, the estimated percentage of HIV/TB coinfections increased from 0.61% in 2004 to 1.9% in 2013. Of an estimated 97 HIV/TB cases (range: 69–130), only 56 were notified in 2013, resulting in an average 57.7% HIV/TB detection rate (Table 5).

Table 5. TB/ HIV collaborative activities, Georgia, 2004–2013

Year	Notified TB cases	HIV tests among TB cases	HIV detected	HIV-positives among TB cases (%)	No. of HIV/TB cases with antiretroviral therapy (ART)	No. of HIV/TB cases with cotrimoxazole preventive therapy (CPT)
2004	5967	726	9	1.2	9	5
2005	6448	674	13	1.9	13	7
2006	6311	649	17	2.6	9	10
2007	5912	842	32	3.8	21	21
2008	5836	1482	20	1.3	17	17
2009	5978	1289	33	2.6	18	18
2010	5796	1841	35	1.9	27	22
2011	5533	2550	50	2.0	38	28
2012	4974	1992	45	2.3	36	36
2013	4319	2698	56	2.1	50	50

On the other hand, TB is frequent among HIV-infected individuals. During 2011–2013, 1440 newly diagnosed people living with HIV were screened for TB and active disease was found in 252 cases (17.5%). TB is the leading cause of mortality among these people, currently accounting for 21% of the total number of deaths in this population group.

ART is a critical intervention for reducing the risk of TB among people living with HIV. It reduces the individual risk of HIV by 65% and, in combination with isoniazid preventive therapy (IPT), can greatly prevent TB in HIV cases *(10)*. In Georgia, ART as well as CPT coverage increased from 55% in 2009 to 89% in 2013.

NTP

The implementation in Georgia of the internationally recommended TB control strategy based on directly observed treatment, short course (DOTS) started in 1995. Countrywide DOTS coverage was achieved in 1999, including the penitentiary sector.

TB control interventions are guided by the National Tuberculosis Strategy and Operational Plan for Georgia 2013–2015 *(11)*. The goal of the Strategy is to stop the spread of TB in Georgia and reduce its burden, including that of M/XDR-TB, with a consequent impact of reducing TB mortality, reducing the level of M/XDR and HIV in TB patients, and reducing the number of health workers with TB. The interventions are organized around seven strategic areas: (i) TB diagnosis; (ii) TB treatment; (iii) governance, financing and monitoring; (iv) human resources; (v) infection control; (vi) empowering TB patients and communities; and (vii) HIV/TB coinfection collaborative treatment and care. A new national TB strategic plan is being developed for 2016–2020. This was due to be finalized by July 2015, together with the new TB application to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

Georgia has made a strong political commitment to protect its population from TB. The MoLHSA bears the overall government responsibility for public health issues, including TB control. It undertakes this function in close interaction with other relevant state entities and collaborates with nongovernmental organizations and international partners in the planning, implementation, monitoring and evaluation of TB control activities. The Georgian Country Coordinating Mechanism for TB, HIV/AIDS and Malaria is the high-level body entrusted to facilitate horizontal links with and participatory governance in disease control programmes. This Mechanism includes representatives from different governmental entities, external development assistance agencies and civil society. A specific important function of the Mechanism is to oversee the implementation of support from the Global Fund.

TB control services have undergone substantial changes over the last decade and are provided by both public and private health care institutions. TB laboratories have been downsized and integrated into the network of public health laboratories under the management of the NCDC. Currently, these include six regional laboratory surveillance stations (LSS) in Akhaltsikhe, Gori, Ozurgeti, Poti, Telavi and Zugdidi and two zonal diagnostic laboratories (ZDL) in Batumi and Kutaisi. The entire network is supervised by the NCTLD/NRL in Tbilisi.

Otherwise, TB care delivery is integrated into the general health care services which have been reorganized and restructured through privatization since 2012. TB services are provided by specialized TB units as well as by primary health care units. There are 69 outpatient specialized TB units at district and regional level, which are organizationally part of private health care provider institutions. In addition, six specialized TB inpatient facilities function in the civilian sector: in Abastumani, Batumi, Kutaisi, Poti, Tbilisi (NCTLD) and Zugdidi, with a total capacity of 466 beds (170 of them for treatment of M/XDR-TB cases). There are about 870 staff in the specialized TB service, including 184 TB doctors, 379 nurses and 25 laboratory personnel.

Passive case-finding is the main method of TB detection. Primary health care providers are responsible for identifying TB suspects and referring them to specialized TB service units for diagnosis. Diagnosis of TB is established by direct sputum smear microscopy and GeneXpert MTB/RIF, supported by X-ray in cases with negative microscopy/GeneXpert results and confirmed by culture. Transport of sputum specimens is organized from district TB units to the LSS and thence to the ZDL in Kutaisi or the NRL. The Kutaisi laboratory is a regional centre for western Georgia for culturing, while DST is currently only performed at the NRL. The NRL performs the full range of TB laboratory investigations and is responsible for laboratory quality assurance countrywide. The novel GeneXpert MTB/RIF diagnostic technology was introduced in 2013 and is being expanded; at present 17 instruments are operational in the country, including in the penitentiary system.

Case classification and definition of treatment category are done in the specialized TB service units. Treatment regimens are administered according to WHO recommendations. An uninterrupted supply of quality anti-TB drugs is ensured countrywide. Procurement of TB drugs is carried out with financial support from the Global Fund. There are established procedures for port clearance, storage, distribution to service delivery sites, monitoring of stocks and replenishment.

The majority of infectious TB patients are hospitalized during the intensive phase of treatment. TB units and primary health care facilities follow up patients and dispense drugs during outpatient treatment. Ensuring direct observation of treatment is the goal for all TB patients; with support from the Global Fund and the government, patients are given monetary incentives to increase their adherence to treatment.

The standardized TB recording and reporting system, which has been upgraded to include the latest WHO recommendations and additional country needs, is used. Since 2006, individualized recording and reporting is in place and is incorporated in the national electronic TB database.

The Ministry of Corrections, through its Medical Department, is responsible for TB control activities in the penitentiary system. Case detection in the penitentiaries combines passive and active case-finding (on entry and through regular screening). TB treatment in prisons is provided at the TB Prison Hospital in Ksani (Shida-Kartli region) and at the Central Prison Hospital in Gldani (Tbilisi). These institutions also have TB laboratories carrying out microscopy and GeneXpert MTB/RIF.

Systematic HIV/TB collaborative activities between the NTP and the National AIDS Programme were initiated in 2005 and continue through: (i) joint programming and technical consultations; (ii) adjustment of guidelines and case management protocols; and (iii) collaboration and coordination of activities related to the provision of HIV counselling and testing for TB patients, screening for active TB among people living with HIV, administration of ART to patients with HIV/TB coinfection, data exchange and integration of monitoring and reporting systems, as well as through alignment and coordination of interventions among high-risk groups, including interventions implemented with Global Fund support.

Over the last decade, significant progress has been achieved countrywide in treatment outcomes of sensitive TB cases. The treatment success rate of all TB cases rose from 62.5% in the 2004 cohort to 78.0% in the 2013 cohort, and the proportion of patients interrupting treatment during the same period fell from 16.3% to 10.7% (among new acid-fast bacilli-positive cases – from 12.7% to 7.5%).[1] The full treatment results of the 2013 cohort of new acid-fast bacilli-positive cases are the following: treatment success – 81.5%, default – 7.5%, failure – 3.7%, death – 3.5%, transfer out – 0.5%, not evaluated – 3.3%.

As regards the management of drug-resistant TB, Georgia conducts routine drug resistance surveillance as a continuation of the first nationwide representative drug resistance survey, carried out in 2005–2006. The DST data for 2010–2014 are presented in Table 3 above. Although lower than in other countries in the Region, the burden of resistance to anti-TB drugs is high, representing a key challenge for effective TB control in the country.

The programmatic management of MDR-TB started in 1998 with support from Médecins Sans Frontières France for treatment of drug-resistant TB patients in Abkhazia, which was expanded in November 2006 to the Samegrelo region. National TB programme started expanding countrywide access to MDR-TB treatment according to international standards in November 2006, based on its application to WHO's Green Light Committee for access to quality second-line drugs at concessionary prices. From then until May 2015, over 4300 patients were enrolled in second-line TB treatment. With the support of international partners, the country ensures universal access to diagnosis and treatment of all forms of TB, including treatment of extensively-resistant (XDR) forms of the disease (pre-XDR and XDR-TB) with the application of newly developed anti-TB drugs such as bedaquiline, the use of which will be expanded to all patients in need from June 2015 through the global donation programme supported by the manufacturer and the United States Agency for International Development (USAID).

At the same time, the treatment results for M/XDR patients are worrying and represent a major concern for the NTP. In total, for the completed M/XDR-TB treatment cohorts for 2008–2012, only 51.2% of patients were successfully treated, 8.4% died, 4.9% failed treatment, 28.6% defaulted and 7.3% of cases were not evaluated at the end of treatment. The very high rates of treatment interruption are attributed not only to patients' difficulties in completing the lengthy (up to two years) course of therapy due to social and economic circumstances, but also to insufficient support for adherence as well as medical complications from treatment related to comorbid conditions and adverse drug reactions caused by second-line TB drugs and the failure by health care providers to manage these complications effectively.

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[1] The rates are presented according to WHO's revised classification of TB treatment outcomes *(12)*.

Main achievements of the NTP

The following are considered the main achievements of the NTP since the start of DOTS implementation.

- There has been remarkable successes in the uptake and implementation of contemporary international strategies and guidance in TB control. All of the main components of the Stop TB strategy are in place and the country is continuously developing, upgrading and developing its practices to align them to the emerging challenges of the TB epidemic and approaches to ensure an effective national TB response.

- Visible improvements have been documented in recent years in relation to the TB burden, proved by the decreasing number of TB cases and falling TB rates, including the reduction in TB cases in children. The prevalence of drug-resistant forms of TB has been consistently contained at levels substantially lower compared to other countries in the Region.

- Universal access is ensured to diagnosis and treatment of all forms of TB, including M/XDR-TB. The use of novel rapid diagnostic methods for TB and drug-resistant TB, as well as of newly developed drugs, is being scaled up.

- As a key indicator of the positive developments in the NTP, treatment outcomes of sensitive TB cases are improving, including a steady decrease in the proportion of patients lost to follow-up.

- TB control in the penitentiary system is fully integrated into the overall NTP. The effectiveness of TB control measures in prisons is shown by the decreasing incidence of active TB and improvement in treatment results, consistent with the overall trend in the country.

- Georgia is considered as a regional leader in aligning its TB care delivery system to the epidemiological challenges and international best practices. In particular, this refers to the implementation of predominantly outpatient TB case management, with reduced frequency and duration of hospitalization as a result of the optimization and downsizing of the TB hospitals' capacity.

- External funding support (from the Global Fund and other partners) has been implemented effectively, with a reliance on effective and professional collaboration and coordination with international agencies as well as national stakeholders.

Key challenges for TB control

Despite the important positive developments achieved in TB control listed above, a number of serious challenges remain to be addressed.

- TB remains an important public health issue and the overall TB epidemiological situation continues to be worrying, above all due to the high burden of drug-resistant TB which threatens to reverse the recent positive trends and further increase the overall economic and social burden of the disease.

- While there was a decreasing trend in TB notifications during 2012–2014, primary attention should be given to ensuring an effective system for TB case detection/diagnosis, which should address the issue of undiagnosed and/or late diagnosed TB and provide for rapid detection of drug resistance.

- Poor outcomes of treatment for M/XDR-TB cases are a big issue. They need to be addressed both through novel treatment approaches reliant on the revised treatment regimens (including scaling up the use of new drugs) and through strengthening the application of patient-centred approaches with appropriate support for patients, which is not limited to provision of incentives but covers a broader set of determinants of adherence.

- The burden and impact of HIV/TB coinfection is underestimated and needs to be properly addressed through a set of strengthened collaborative activities between the national TB and HIV/AIDS programmes, including more active involvement by civil society, especially in addressing the needs of the population groups most at risk.

- TB control interventions need to be effectively integrated into all developments affecting the organization and management of the overall health system as a main public health function of the government in view of its priority objective of ensuring a universal health coverage system. As well as a strengthening of the governance and management of the NTP and adjustment of the financing and allocation arrangements, proper attention should be given to the development of the human and infrastructure resources required to provide essential TB services to the entire population.

- Georgia is currently heavily dependent on external support (above all the Global Fund) in financing key TB control activities, including the procurement of drugs, laboratory equipment and supplies and support for adherence, as well as in supporting essential functions of the NTP such as training and supervision. In view of the fact that external funding support is decreasing with time, there is an urgent need to assure a substantial and rapid increase in government financing of these components, especially those related to complex and costly drug-resistant TB management interventions.

Case-finding and diagnosis

The achievements in case-finding and diagnosis are as follows.

- TB laboratory diagnosis is based on smear microscopy, GeneXpert and culture examination on solid and liquid media. Sensitivity testing of TB drugs for *M. tuberculosis* is carried out in the NRL. Molecular genetic tests have been in use since 2011 and are a priority for rapid diagnosis of MDR-TB.

- All laboratories are equipped with modern sophisticated equipment. External quality assurance of DST for first- and second-line drugs is conducted regularly.

- A national TB laboratory strategic plan has been developed, and training courses have been conducted for staff involved in sputum smear microscopy (SSM) investigations in peripheral and intermediate laboratories.

- Wide-ranging collaboration with international partners in the field of TB diagnostic research, development of molecular methodologies and genotyping of *M. tuberculosis* has been established.

- The capacity of the NRL (surfaces, equipment) will be expanded and additional technologies will be implemented. The new building for the NRL was due to be finished in 2015.

The following challenges remain.

- The unequal distribution of the laboratory network in regard to the population, number of patients and geographically limits access to TB diagnostic investigations in remote areas and leads to delays in diagnoses.

- There are no key performance indicators for all organizations/participants involved in TB diagnostics.

- The number of SSM investigations fell during the last two to three years and do not cover all symptomatic patients

- Culture methods investigations and DST cover only 65% of those needed.

- Neither the NRL nor the regional reference laboratories (RRL) carry out quality control for culture methods.

- The algorithms for TB diagnostics and DST need to be revised, implemented and maintained.

- Financing is heavily dependent on external donors.

- The surveillance system and monitoring of microbiological investigations are duplicated.

The review teams made the following overall recommendations.

- An adequate infrastructure should be established, a stable and well-trained work force should be developed and supported, and a systems approach should be implemented to

maximize the efficiency and proficiency of laboratory TB diagnostics. The laboratory network should be adjusted according to the number of patients and geographical distribution and the courier system for sputum transportation should be maintained and improved. Accessibility for all TB symptomatic patients to treatment should be improved and delays in receiving the results removed.

- Performance indicators for TB coordinators, primary health care and laboratory workers should be drawn up, implemented and monitored regularly. Close collaboration between different structures involved in TB diagnostics should be established. Consideration should be given to ensuring coverage of all patients with early diagnosis and accurate results of monitoring of treatment.

- The current TB laboratory service needs to be comprehensively analysed. The tasks and responsibilities of laboratories at all levels (workload, area of service, microbiological indicators, correct requests for laboratory tests, proper use of reagents and consumables, staff qualifications) should be clearly established, bearing in mind the implementation of GeneXpert in level I laboratories and DST in the level II (intermediate-level) laboratory (the RRL in Kutaisi). Effective policies are needed for decentralizing diagnostic capacity.

- The algorithm for microbiological investigations of symptomatic patients and follow-up of treatment could be revised to include different levels of complexity (SSM, GeneXpert, line probe assay, culture and DST) for rapid diagnosis of MDR-TB (lists of patients at risk of MDR should be drawn up and approved). Laboratory indicators should be monitored regularly.

- The agenda for training courses for TB laboratory network staff should be revised and continue to be implemented at all laboratories.

- A plan for external quality assurance for culture methods (Löwenstein Jensen and mycobacteria growth indicator tube (MGIT)) for the NRL and RRL should be drawn up and implemented urgently.

- Guides for culture, DST, rapid methods and quality control should be drawn up. Standard operating procedures should be revised regularly according to specific conditions. Standard operating procedures for GeneXpert should be drawn up and distributed.

- MTBDR*sl* assays should be performed in line with the possibilities for rechecking sensitive results by MGIT as per the Centers for Disease Prevention and Control and international practice *(13)*.

- WHO does not recommend routine DST for group 4 drugs (ethionamide, prothionamide (Pto), cycloserine (Cs), terizidone, p-aminosalicylic acid (PAS)) and for group 5 drugs (clofazimine (Cfz), amoxicillin-clavulanate (Amx/Clv), clarithromycin (Clr), linezolid (Lzd)).

- Delays in sputum transport and SSM, GeneXpert and line probe assay results should be reduced. SSM results should be delivered to the responsible physician within one or two days.

- Countrywide coverage of smear microscopy laboratories should be increased, and the SSM laboratories in Rustavi and Marneuli should be re-opened.

- Access to quality TB diagnosis and treatment should be improved by strengthening the capacity of the private health care sector to train and educate facility managers and clinicians according to international standards for TB care.

Background

The laboratory plays a critical role in the diagnosis and management of drug-resistant TB. Test results must be available in a period that allows clinicians to make prompt patient management decisions.

Georgia is facing a growing problem of drug-resistant TB. In view of the need to control the continued spread of MDR-TB, a strong laboratory service for rapid diagnosis and monitoring of treatment should be established. To begin treatment correctly, the rapid method and systematic external quality assurance for conventional methods of DST should be implemented. Delays in TB diagnoses can lead to delays in start of treatment and missed opportunities to stop the spread of infection, and incorrect or overdue DST results can lead to inappropriate treatment.

Most essential and expensive laboratory activities (such as SSM, culture, rapid methods and maintenance) are funded by the Global Fund for AIDS, Tuberculosis and Malaria, the Swiss non-profit organization FIND, USAID and other projects. Government funding for a small part of these activities should be increased.

Organizational structure of the TB laboratory service

During the, TB control (including laboratory services for TB diagnostics) was provided as a vertical programme headed by the NCTLD. Each region had TB clinics and TB doctors working through TB dispensaries. In 2012, in response to the real threat and high incidence of MDR-TB, the MoLHSA decided to reorganize the laboratory network to strengthen TB laboratory services with the aim of providing prompt and reliable laboratory results.

The laboratory network is now divided into three levels, as follows (Fig. 18):

- nine laboratories for sputum smear microscopy in the civilian sector (in Akhaltsikhe, Batumi, Poti, Gori, Ozurgeti, Telavi and Zugdidi districts and Kutaisi and Tbilisi cities) and two in the prison system (the TB Prison Hospital in Ksani and Central Prison Hospital in Gldani, Tbilisi) (level I);

- the RRL, located in the ZDL in Kutaisi (level II);

- the NRL, located in the NCTLD in Tbilisi (level III).

Fig. 18. Structure of the TB laboratory network, Georgia, 2013
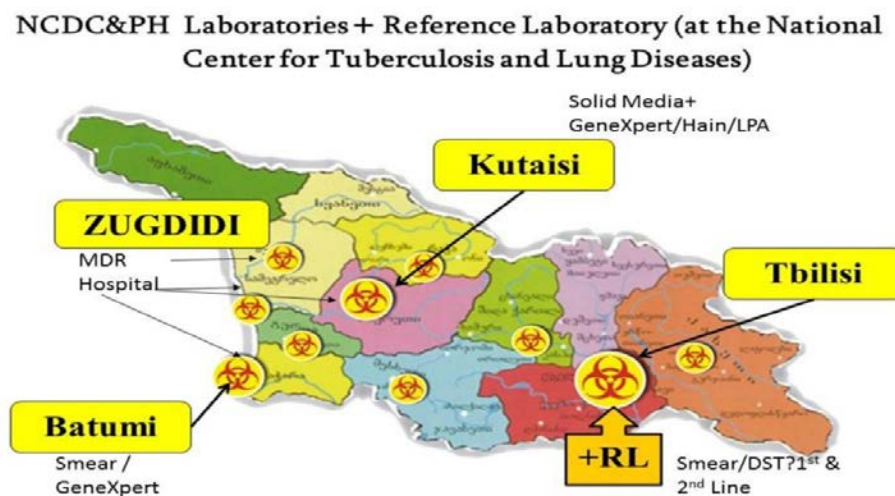
Level I laboratories for sputum smear examination

The main task of level I laboratories involved in TB control is to find new bacillary patients among TB symptomatic patients and carry out rapid diagnoses for MD-TB. They should be located at the district level in TB doctors' clinics. One laboratory should cover a population of around 100 000 people so that their services are located close to patients and TB doctors. This would make it easy to examine all symptomatic patients in real time: 30 minutes for SSM or two hours for GeneXpert) and the investigations could be repeated the same day if the first result is not enough to make the diagnosis. Thus, for TB doctors, the microscope and GeneXpert are indispensable medical technologies for rapid and correct diagnosis of disease.

Eight of the laboratories (Akhaltsikhe, Batumi, Poti, Gori, Ozurgeti, Telavi, Zugdidi and Kutaisi) are located in LSS and are part of the NCDC system. The two laboratories in the prison medical system (Ksany and the Central Prison Hospital) are responsible to the medical service of the Ministry of Corrections. Another direct smear microscopy (DSM) laboratory is located in the NCTLD in Tbilisi and is responsible to the NRL.

Specimens are collected in 65 local TB clinics and samples are transported to level I laboratories for smear microscopy, as well as to the RRL and NRL for culture and DST. These laboratories are equipped with microscopes, reagents and other essential supplies for Ziehl Neelsen and fluorescence microscopy investigations. The laboratories in Tbilisi, Kutaisi and Batumi are also equipped with GeneXpert machines.

The tasks and responsibilities of level I laboratories are:

- to receive specimens for sputum smear examination
- to prepare and stain the sputum smears

- to carry out Ziehl Neelsen and fluorescence microscopy examinations

- to carry out GeneXpert MBT/RIF for TB diagnosis and DST (only three laboratories)

- to receive, store and transport sputum samples for culture and DST to the RRL and NRL

- to report/record results (electronic surveillance)

- to manage reagents and supplies

- to carry out internal quality control

- to participate in external quality control for sputum smear examination.

Workload and staff

The level I laboratories employ 25 laboratory technicians in total. In six laboratories only one person is employed, making it difficult to organize uninterrupted work during the summer holidays, training courses or in cases of sickness. Only three laboratories carrying out SSM have more than one trained laboratory technician: Batumi has two laboratory technicians, Kutaisi has six and Tbilisi has 13. More laboratory staff should be trained for SSM investigations (as reserve personnel) in laboratories where only one specialist is trained to examine smears.

The level I laboratories have different workloads and are geographically unequally distributed (Table 6, Fig.18).

Table 6. Workload of level I laboratories, Georgia, 2013

Regions	DSM tests	No. of staff	DSM tests per laboratory technician	Share of all tests (%)	Population
Akhaltsikhe LSS	1 255	1	1255.0	1.9	214 000
Batumi LSS	8 650	2	4325.0	12.8	395 000
Poti LSS	2 706	1	2706.0	4.0	48 000
Gori LSS	3 353	1	3353.0	4.9	183 600
Kutaisi ZDL	7 283	6	1213.8	10.8	749 000
Ozurgeti LSS	1 515	1	1515.0	2.2	138 800
Tbilisi NRL	35 153	13	2704.1	51.9	1 797 000
Telavi LSS	2 733	1	2733.0	4.0	404 000
Zugdidi LSS	5 091	1	5091.0	7.5	430 500
Total	67 739	25	2709.6	100.0	4 359 900

Because samples are not transported daily, the laboratory sometimes receives 45 specimens in one day. This is too many to be processed in a day. There should be at least two slides per day and a maximum of 20–25. Staff workload in microscopy laboratories needs to be calculated based on the sample amounts submitted per day.

In 2013, Tbilisi laboratory performed about 52% (n=35 151) of all SSM investigations (n=67 739) in the country. This laboratory covers 1 787 000 people, or about half the civilian population.

In the eight regions south of Tbilisi (Rustavi, Gardabani, Marneuli, Tetritskharo, Tsalka, Bolnisi, Dmanisi), covering a population of over half a million people and with more than 400 TB patients a year, the laboratories for TB screening could be closer to the TB clinics so that screening can be organized in real time for all symptomatic patients. In discussion with the

head of the NRL it was agreed that the mission would evaluate the possibility of organizing two additional laboratories for screening TB symptomatic patients and monitoring TB treatment in Kvemo Kartli region, where there is at present no laboratory.

Access to diagnostics could be increased were some level I laboratories to reopen. The evidence of symptomatic patients would be conducted in real time, avoiding the need to transport samples and shortening the turnaround time for the results of investigations.

In view of the size of the population, the number of annual notifications of TB patients and the volume of investigations required, it has been decided to set up microscopy laboratories for the detection of *M. tuberculosis* in Rustavi and Marneuli. The infrastructure for a new laboratory exists in Rustavi but not in Marneuli. The local possibilities should be assessed and the problem solved with the local administration, with the request addressed to the NTP and MoLHSA. At some point in the future, these laboratories could be equipped with GeneXpert MBT/RIF (Annex 1).

Another opportunity to reduce the delay in SSM/GeneXpert results could be to organize a laboratory in Chiatura district (30 000 population), which is a long way from Kutaisi. It is planned to place the TB clinic in a building which is undergoing renovation, with an additional room allocated to a laboratory. This laboratory, too, could be equipped with the GeneXpert machine.

There has recently been a decrease in the indicators for TB screening and confirmation of patients with pulmonary TB by microscopy. Thus, in 2007 the confirmation rate by SSM among pulmonary TB patients was 67.5%, but by 2013 this had dropped to 55.3% (Fig. 19).

Fig. 19. TB confirmation by SSM among pulmonary TB cases, Georgia, 2007–2013

Region/year	No of TB pulmonary patients 2007				No of TB pulmonary patients 2013			
	SSM+	SSM-	Total	%	SSM+	SSM-	Total	%
Tbilisi	866	371	1237	70	641	425	1066	60.1
Mtskheta-Mtianeti	70	39	109	64.2	46	20	66	69.7
Kakheti	157	77	234	67.1	129	57	186	69.4
Shida Kartli	142	59	201	70.6	98	81	179	54.7
Kvemo Kartli	269	103	372	72.3	174	125	299	58.2
Imereti	316	149	465	68	193	155	348	55.5
Guria	62	54	116	53.4	47	58	105	44.8
Samegrelo	361	207	568	63.6	221	190	411	53.8
Samckhe-Javakheti	40	103	143	28	29	51	80	36.3
Adjara	239	182	421	56.8	222	277	499	44.5
Racha-Lechkhumi					17	5	22	77.3
Prison	476	97	573	83.1	96	105	201	47.8
Total	**2998**	**1441**	**4439**	**67.5**	**1913**	**1549**	**3462**	**55.3**

The number of symptomatic patients screened for TB in 2011 was 26 162, resulting in the finding of 3036 new bacillary patients.

In 2013, 17 067 symptomatic patients were screened for TB and 1668 new bacillary patients were found (Table 7). The rate of SSM-positive detection among symptomatic patients from the various regions is very high (Khashuri 20.8%, Dedoflistskaro 21.4%, Ambrolauri 25.0; Akhalgori, Mestia 28.6%), indicating that patients are referred for diagnosis too late, when they are already infectious and have probably been transmitting the disease. In other areas, however, this indicator is too low (Adigeni 1.3%; Aspindza 1.5%, Lentekhi 2.4%). In the Akhalkalaki district 32 symptomatic patients were examined in 2013, but no positive SSM results were found. In 2011, in the same district, 13 patients were examined of whom 12 (97%) were SSM-positive.

According to WHO's recommendation, the detection rate by SSM among symptomatic patients should be around 10%; in other words, to find one new TB patient, 10 TB symptomatic patients

should be examined. This means that in the last few years the number of TB symptomatic investigations is just about half the recommended level.

Table 7. Screening of TB symptomatic patients by SSM, rate of SSM+ among TB symptomatic patients, Georgia, 2013

Regions	Total	Sputum smear-positive	Percentage (%)
Samstke-Javakheti	436	14	3.2
Imereti-2	542	34	6.3
Ajara	3 533	222	6.3
Poti town	937	63	6.7
Shida Kartli	1 091	88	8.1
Imereti-1	1 963	160	8.2
Guria	468	39	8.3
Mingrelia-Zemo Svaneti	1 505	182	12.1
Mtskheta-Mtianeti	300	38	12.7
Tbilisi City	4 563	587	12.9
Kakheti	694	95	13.7
Kvemo Kartli	1 045	146	14
Georgia	17 077	1 668	9.8

The reasons for this situation, in the opinion of specialists from the TB service, are the new conditions of TB clinics in the private sector and the reduction in the number of laboratories for SSM, as well as their unequal geographic distribution.

Issues of motivation and performance need to be addressed in the private sector clinics, which now house the former government TB clinics. The TB specialists and service staff feel disempowered and are not motivated to perform at their previous levels. Private TB clinics receive a fixed fee, based on TB suspect identification. However, they are generally not interested in providing diagnostic services beyond sputum collection.

To improve this situation, the laboratory network should be adjusted according to the number of patients and their geographical distribution, the courier system for transporting sputum should be maintained and improved, accessibility for all TB symptomatic patients should be improved and delays in receiving results should be reduced.

Additional activities should be provided to improve access to quality TB diagnosis and treatment. Periodic training courses should be organized for the private health care sector and facility managers and clinicians educated according to international standards of TB care.

Performance indicators for TB coordinators, primary health care and the laboratory service should be drawn up and implemented, close collaboration between different structures involved in TB diagnostics should be established, and coverage of all patients with early diagnosis and accurate results of monitoring of treatment could be considered. The performance indicators should be monitored regularly.

Sputum collection room
Sputum collection usually takes place in a designated room or outside the building (for TB outpatients). In some sites visited, these rooms had inappropriate infection control: they were too small and the ultraviolet lamp was old, not cleaned regularly and ineffective (Tbilisi Centre

dispensary). In Tbilisi and Zugdidi hospitals the sputum collection rooms were large, with ultraviolet lamps and positive and negative pressure.

Only the TB doctors can refer patients for sputum collection and SSM examination. A nurse is responsible for collecting sputum specimens.

Courier system

The courier system for transporting samples is funded through the Global Fund grant.
In 2013, the postal service took on the function of courier for sputum transport in two regions in the western part of the country. This service has reduced delays in transportation. Unfortunately, in the rest of the country, inefficient sputum transport logistics combined with the difficulty of reaching many towns and villages in the mountains (especially in winter) is resulting in inequitable access to TB diagnosis and testing results. This creates problems with initiating the correct treatment or changing the treatment schedules for individual patients. Special transport boxes with ice packs are used to transport the specimens. The postal courier system is also used to send laboratory results from the NRL and RRL to TB doctors and level I laboratories.

Recommendations

- The laboratory network should be adjusted according to the number of patients and their geographical distribution.

- Laboratories for SSM at level I should be reopened in line with needs and taking into account the geographical distribution of hospitals and NCDC laboratories.

- The courier system for transporting sputum should be maintained and improved, access for all TB symptomatic patients improved and delays in results reduced.

- Performance indicators for TB coordinators, primary health care and laboratory service should be drawn up and implemented, close collaboration between different structures involved in TB diagnostics should be established, and early diagnosis for all patients and accurate results of monitoring of treatment should be considered. The performance indicators should be monitored regularly.

- Infection control measures should be strengthened in places for sputum collection in level I areas, and accessibility for patients to TB laboratory diagnostics improved.

- Short training courses should be conducted periodically for dedicated staff for sample collection (on-site training).

- Other laboratory staff should be trained for SSM investigations (as reserve personnel) in areas where only one specialist is trained to examine smears.

RRL at Kutaisi ZDL

The roles, tasks and responsibilities for the level II RRL at Kutaisi for TB diagnostics include:

- diagnosis of TB by culture (Löwenstein Jensen + MGIT)

- line probe assay (MTBDR*plus*)

- reporting /recording of results

- management of reagent and supplies

- internal quality control

- collection, storage and transport to the NRL of strains for second-line DST.

The RRL is responsible to the NCDC and can carry out its role efficiently and effectively. It is equipped with modern apparatuses and equipment, which allow for the implementation of sophisticated, rapid methods of TB diagnostics and DST for first- and second-line drugs. If these activities were performed in this laboratory, DST results would be available much more quickly.

The RRL does not participate in external quality control for culture. The NRL should implement such quality control for culture and DST urgently.

The culture and line probe assay laboratory has enough staff (two specialists in molecular genetics investigations and two microbiologists).

NRL

The NCTLD is responsible for the NRL and the prison laboratories. This laboratory took the leading role in organizing the TB laboratory service and developing protocols for laboratory diagnosis, training and supervision. It is adequately resourced and demonstrated proficiency in TB bacteriology, with 100% accuracy for proficiency testing (external quality assurance) for DST conducted by the supranational reference laboratory in Antwerp.

The roles, tasks and responsibilities of the level III NRL include:

- diagnosis of TB by culture (Löwenstein Jensen + MGIT);

- DST for first- and second-line drugs;

- line probe assay (MTBDRplus);

- support and supervision of microscopy centres for external quality assurance of SSM;

- external quality assurance for DST;

- development of protocol and guides;

- organization of training courses;

- monitoring and evaluation visits to the RRL (Kutaisi ZDL) and microscopy centres (LSS);

- organization and conduct of drug resistance surveillance;

- conduct of operational research.

The NRL plans to develop, with international technical assistance, a national TB laboratory strategic plan in 2014 for approval by the MoLHSA and implementation.

Training courses in laboratory methodologies for laboratory staff at all levels have been held. The NRL conducts regular training courses for staff involved in SSM investigations, GeneXpert MBT/RIF, culture methods and DST. A description of their role in quality control of smear microscopy and training has been drawn up.

The NRL has established broad collaboration with international partners in the fields of TB diagnostic research, development of molecular methodologies and genotyping of *M. tuberculosis*.

The capacity of the NRL (surfaces, equipment) is to be increased and additional technologies implemented – it is planned to finish the NRL's new building in 2015.

Equipment and supply
The NRL is equipped with, among other things: two MGIT machines, two Hain instruments, three GeneXpert machines, three class 2 biosafety cabinets, two freezers -80 °C and three thermostats.

Procurement of equipment and supplies is financed under Global Fund, FIND and USAID projects. Plans for the procurement and distribution of supplies and equipment are available. The NRL takes part in the procurement system and has been involved in developing the plan for the procurement and distribution of laboratory reagents, consumables and equipment. The government has not so far allocated funding for these activities but plans to participate in the procurement of laboratory supplies starting from 2015.

The NRL is responsible for estimating the requirements at various levels and making final decisions as to quantities and suppliers, reagents and equipment.

Workload

The NRL is understaffed and does not have the capacity to carry out all its activities, including the implementation of new diagnostic methods, monitoring, supervision, training and operational research. Some activities, such as DST for first- and second-line drugs, could be done by the level II laboratories. In 2013, the NRL performed SSM for about 47% of the TB patients countrywide and diagnosed about 50% of the smear-positive new cases notified (Tables 8, 9).

Table 8. NRL culture investigations, Georgia, 2013

Microscopy result	Not in treatment (new and relapsed cases only)				Treatment/follow-up started				Grand total
	Positive	Negative	Confirmed	Total	Positive	Negative	Confirmed	Total	
Positive	1168	59	42	1269	876	320	74	1270	2 539
Negative	500	3274	200	3974	468	4016	344	4828	8 802
Total	1668	3333	242	5243	1344	4336	418	6098	11 341

Table 9. NRL: workload of laboratory workers for DSM, culture and DST, Georgia, 2013

No. of smears/staff	Smear	Culture	DST
No. of staff per laboratory	13	3	5
No. of smears/staff	35 153/10	11 341/3	4 496/5

Conclusions and recommendations

- A comprehensive analysis needs to be conducted of the current situation of the TB laboratory service.

- The tasks and responsibilities of all laboratories (workload, area of service, microbiological indicators, correct requests for laboratory tests, proper use of reagents and consumables, qualifications of staff) should be clearly established in view of the implementation of GeneXpert in level I laboratories and DST for the level II laboratory. Effective policies for decentralizing diagnostic capacity are required. The costs of the TB laboratory network should be analysed and a budget plan developed, including further rationalization of the network, maintenance of laboratory equipment and scaling-up of logistics.

- There is a disproportion in TB treatment and care facilities compared to TB diagnostic facilities, with only a few laboratories and microscopy centres in proportion to the population and case-load, especially as concerns MDR-TB.

- No TB laboratories exist in the private sector, even though privatization is a key strength of the MoLHSA's reforms to the health system.

- Effective coordination is lacking for general quality management and, in particular, laboratory quality issues between the NCDC/NCTLD.

- The maintenance of existing laboratory equipment should be planned. Only officially certified experts should be contracted for annual maintenance of equipment, which they should document.

- A sustainable diagnostic samples transport system should be developed using all means of transport and communication.

Policy guidelines and procedures

TB laboratory diagnosis is based on SSM, line probe assay and culture investigations (Löwenstein Jensen and MGIT). DST of *M. tuberculosis* on solid and liquid media is only carried out by the NRL. Rapid diagnostic tests and tests based on molecular biology have been in use since 2011 and are now a priority for the NTP.

Diagnostic methods

DSM
All the laboratories visited perform smear examination by the Ziehl Neelsen method. Fluorescence microscopies are used in the NRL and Kutaisi RRL. In general, the quality of sputum smear preparation is satisfactory, although some smear slides are too small and thin. The quality of the stains (carbolic fuchsine and methylene blue) was good and is provided from central level. The staining solutions are procured by the Global Fund and distributed to all laboratories in the country, which ensures the standard quality of the stains in all smear microscopy centres.

All laboratories have been provided with binocular microscopes. Positive smear results are reported according to the WHO-recommended grading scale. Positive and negative smears are kept in laboratories for three months until the next monitoring visit by the NRL.

Recommendation
The quality of smear preparation should be improved by periodic training and retraining courses for the staff involved in smear examination.

Culture
The NTP recommends culture examination for diagnosis and follow-up for TB cases, in the expectation that culture and DST will provide prompt diagnosis and adequate treatment of drug-resistant cases and prevent the development of MDR-TB.

The methodology of culture examination is standardized for both Löwenstein Jensen and MGIT methods for culture laboratories. For decontamination, the recommended N-acetyl-L-cysteine-sodium hydroxide method is MycoPrep solution from Becton, Dickinson and Company. The NRL uses solid medium from a Löwenstein Jensen base. Internal quality control of each prepared batch is carried out regularly.

Identification of positive culture
A Ziehl Neelsen and Becton, Dickinson and Company MGIT™ TBc identification test is used to identify a positive culture.

Sputum samples received within four days of collection are inoculated in MGIT and then the decontaminated samples are inoculated on Löwenstein Jensen solid media. Usually specimens are brought twice a week, so that about one third of specimens either arrive too late or other problems make liquid media testing impossible.

The recent Green Light Committee (GLC)-GDF mission recommended that consideration should be given to increasing the number of TB diagnostic laboratories so as to shorten patient and laboratory turn-around times.

DST

According to the NTP, only the NRL in Tbilisi performs conventional DST methods. The TB registry carries out countrywide drug resistance surveillance annually. DST results are registered for all patients. The DST results for first-line drugs are presented in Annex 2, which shows that in 2013, the prevalence of MDR-TB among TB new cases was 11.2% and among retreatment cases 36.8% (as against 6.4% and 32.7%, respectively, in 2007).

The NRL does not carry out DST for all TB and MDR-TB patients. The number of DST investigations fell by 25% in 2013 compared with 2011.

The NRL participates in international external quality assurance proficiency testing for phenotypic and genotypic DST. Twice a year, the Supranational Reference Laboratory from Antwerp conducts external quality control for DST first- and second-line drugs (see Annex 3 for the results).

Line probe assay and GeneXpert MBT/RIF methods

Molecular genetic methods have been implemented at the NRL in Tbilisi and the ZDLs in Kutaisi and Batumi. At levels II and III, line probe assay MTBDR*plus* ver.2 (Hain) and GeneXpert MTB/RIF with four modules have been implemented. In Batumi LSS two GeneXpert MTB/RIF machines are installed, procured under a FIND project to help identify MDR-TB cases more rapidly. The typical schedule of once a week sputum transport causes many delays in examination and treatment for TB and, more noticeably, particularly long delays to obtain molecular tests and DST results that are only available in the two reference laboratories mentioned above.

Sputum samples for molecular testing (Hain) from three of eight LSS are send to NRL. The other five LSS send specimens to Kutaisi.

Samples are batched and tested twice a week. Results are provided on the day after testing. NCDC laboratories send specimens to Tbilisi for culture, molecular examination or DST as requested by the TB doctor. This referral system is not optimal: delays occur at all levels as well as late diagnosis of TB and MDR-TB.

The NTP plans to procure additional GeneXpert MBT/RIF machines for the level I laboratories (funded by the Global Fund). The new algorithm for microbiological investigations should be revised and approved, in view of changes in the laboratory network when additional GeneXpert machines are brought into use.

The roll-out of new diagnostics (GeneXpert MTB/RIF at level I and MTBDR*sl* at level II in Kutaisi) and implementation of additional DST at the NRL (such as pyrazinamide, Lzdand other drugs for future MDR/XDR-TB treatment) underlines the need for a long-term laboratory-specific strategic plan, to include coordination with partners across the health system, for the effective implementation of TB diagnostics.

GeneXpert MTB/RIF investigations should be used as an add-on test following SSM. If testing capacity is limited, clear priority should be given to testing TB suspects, including at least all MDR-TB suspects and HIV-infected individuals in a particular population. Other groups to consider are: children with TB symptoms (especially in contact with people with TB-MDR); prisoners and former prisoners; vulnerable groups such as homeless people, drug users and immunosuppressives; relapsed cases of TB; medical workers caring for MDR-TB patients; and patients with TB meningitis.

The diagnostic algorithm should be revised to include the GeneXpert MTB/RIF assay and line probe assay results for first- and second-line drugs. The clinical guidelines and laboratory strategic plan should be adjusted accordingly. It will be necessary to establish an expert working group, including laboratory representatives and clinicians, which can assess the line probe assays, GeneXpert and conventional DST for first- and second-line results and make the correct decisions.

Laboratory and clinical staff should be trained in the new molecular genetic investigations.

MTBDR*sl* method
Accurate and rapid tests for TB drug resistance are critical for improving patient care and decreasing the transmission of drug-resistant TB *(13)*. Genotype®MTBDR*sl* is the only commercially available molecular test for detecting resistance in TB to the fluoroquinolones (Ofx, moxifloxacin (Mfx) and levofloxacin (Lfx)) and the second-line injectable drugs (amikacin, Km and Cm), which are used to treat patients with MDR-TB.

In adults with TB, a positive MTBDR*sl* result for resistance to fluoroquinolones and second-line injectable drugs or to XDR-TB can be treated with confidence. However, MTBDR*sl* does not detect approximately one in five cases of fluoroquinolone-resistant TB or approximately one in four cases of TB resistant to second-line injectable drugs. Of the three second-line injectable drugs, MTBDR*sl* has the poorest sensitivity for resistance to Km. It will miss between a quarter and a third of XDR-TB cases. Its diagnostic accuracy is similar when done using either culture isolates or smear-positive sputum. As the location of the resistance causing mutations can vary on a strain-by-strain basis, further research is required as to the accuracy of tests in different settings and, if genetic sequencing is used as a reference standard, all resistance-determining subnational areas hould be examined. Given the confidence it is possible to have in a positive result, and the ability of the test to provide results within a matter of days, MTBDR*sl* may be used as an initial test for second-line drug resistance. However, when the test reports a negative result, clinicians may still wish to carry out conventional testing.

The results show that a positive MTBDR*sl* result for resistance to fluoroquinolones or second-line injectable drugs is reliable evidence that the person has drug-resistant TB and further conventional drug-resistance testing is not required.

The WHO Expert Group has recommended that:

• the MTBDR*sl* assay should not be used as a replacement test for conventional phenotypic DST;

- MTBDR*sl* may be used as a rule-in test for XDR-TB but cannot be used to define XDR-TB for surveillance purposes;

- as cross-resistance between the second-line injectables is incomplete, MTBDR*sl* cannot be used to identify individual drugs to be used for treatment;

- MTBDR*sl* may be used to guide infection control precautions while awaiting confirmatory results from conventional phenotypic testing.

Recommendations

- Laboratory methods and reporting, especially for susceptibility to second-line drugs, should be standardized and implemented in Kutaisi RRL.

- The algorithm for microbiological investigations for symptomatic patients and follow-up of treatment should be revised to include different levels of complexity (SSM, GeneXpert, line probe assay, culture and DST) for rapid diagnosis of MDR-TB, and a list of patients at risk of MDR should be drawn up approved. The performance of laboratory indicators should be monitored regularly.

- The roles and responsibilities of laboratories at all levels should be defined and collaboration established between the different levels to clarify roles and responsibilities in different partner-supported activities.

- The NTP and NRL should asses staffing needs and develop a training plan for each laboratory in the network.

- The agenda for training courses for the TB laboratory network should be revised and continue to be implemented at all levels.

- Guidelines for culture, DST, rapid methods and quality control should be drawn up. Standard operating procedures should be revised regularly according to specific conditions, and standard operating procedures for GeneXpert should be drawn up and distributed.

- MTBDR*sl* assays should be performed in line with the possibilities for rechecking sensitive results by MGIT as per the Centers for Disease Prevention and Control and international practice *(9)*.

- WHO does not recommend routine DST for group 4 drugs (ethionamide, Pto, Cs, terizidone, PAS) and for group 5 drugs (Cfz, Amx/Clv, Clr, Lzd).

- Guidelines for culture methods and DST should be developed and put into practice.

- Kutaisi ZDL should carry out DST methods for first- and second-line drugs.

- Training in DST should be arranged for the staff of the Kutaisi ZDL.

- Operating and other procedures and documentation in all laboratories of the network should be standardized in collaboration with the Supranational Reference Laboratory.

Laboratory quality control, biosafety

The NTP guidelines for quality assurance of SSM are only available in Georgian.

In SSM level I laboratories, new reagents are controlled but there is no regular maintenance for the microscopes. Controls are carried out once a week, positive and negative controls daily.

All laboratories participate in proficiency testing organized by the NRL, which carries out on-site evaluations during monitoring visits. The method used for external quality control of microscopy investigations is based on the lot quality assurance system. This is a method to determine an optimum sample size which, when applied properly, yields statistically acceptable samples to assess quality of work, in this case, the work of the laboratory technicians. One quality management person is responsible for external quality control of SSM for all level I and II laboratories. Monitoring visits are planned at least twice a year.

Analysis of results always includes a check on validity of the controls. If any corrective action were to be necessary, the respective responsible person will supervise the method in question, training will be planned for the relevant people and there will be more monitoring visits in the immediate future.

The results of external quality assurance were presented in the laboratories visited. Annex 3 contains a summary report of external quality control of SSM results in level I laboratories conducted by the NRL.

External quality control activities for culture methods in NRL and RRL laboratories have not been developed and, therefore, were not provided to the mission.

The NRL was well-organized and biosafety issues were well-covered (biosafety cabinets, gowns, masks, gloves, waste disposal and disinfection).

Biosafety cabinets are in use in laboratories at all levels. A sufficient number of respirators are available. The procurement system for disinfectants, alcohol (75%) and bleach for surface cleaning is centralized.

Recommendations

- A plan for external quality assurance for the culture method (Löwenstein Jensen and MGIT) for the NRL and RRL should be drawn up and implemented urgently.

- The national strategic plan on development of the TB laboratory services should be finalized and implemented.

- A laboratory quality manual should be developed to include a section on the selection and analysis of laboratory quality indicators as part of the development and implementation of a comprehensive quality management system at all levels of the TB laboratory network.

- A clear communication and coordination plan between all structures involved in TB diagnostics should be developed and implemented.

- Current laboratory capacity is inadequate to implement the new TB and MDR-TB diagnostic algorithm, developed in response to the new algorithm proposed by WHO for implementation, in particular the culture examination of all TB symptomatic patients.

Treatment and case management

TB treatment is governed by the TB management guideline and the nine associated protocols endorsed by the MoLHSA in June 2013.

The review team was provided with an English summary of the 108 main recommendations, which are considered to be equivalent to the original text. Childhood TB is treated in line with the recent paediatric guideline and the associated MoLHSA-approved protocols. The guidelines are in accordance with the best available international evidence and WHO recommendations. They have already been the subject of training programmes for TB specialists, paediatricians, family medicine practitioners and nurses, and their application is now common practice.

According to data in the *Global tuberculosis report for 2014 (4)*, 4319 new and relapsed cases and pulmonary and extrapulmonary disorders were notified in 2013. It is estimated that 11% of the new cases and 38% of the relapsed cases were MDR-TB-related. In 2013, second-line treatment for 526 such patients was introduced. The data show the scale of the problem and the heavy burden of MDR-TB in a population of 4.3 million.

The differences in treatment responses are also highly relevant. The first-line treatment success rate for new and relapsed cases was 85% in 2012. A 50% success rate was declared for MDR-TB patients who began treatment in 2011, while for the 19 XDR-TB cases the success rate was 11% (even though the cumulative success rate for the 149 XDR-TB patients registered during 2008–2011 was 29.5 %, that is, 44 patients).

A few elements characterize the therapeutic context:

- the all-access policy is working, including for MDR-TB cases;

- the necessary treatment for all types of TB is fully provided through external funding and predictable sources (Global Drug Facility);

- the health services have been almost entirely privatized, which has had a severe impact on the TB network;

- the recent widespread amnesty transferred part of the TB problem in prisons from a closed carceral system to a civil system which is unprepared to manage the considerable number of additional cases.

From a clinical point of view, the major goal is "to optimize patient cure: curing patients will prevent death, relapses, acquired drug resistance and the spread of TB in the community" *(14)*. Dedicated to this fundamental purpose and strictly from a therapeutic angle, the health care system has a central component represented by the NCTLD in Tbilisi, a regional level of control and coordination (nine regions) and a peripheral level of 74 TB service delivery points (TB dispensaries) through private general medical facilities and more than 2000 primary care physicians and nurses.

In state hospitals 422 beds are available, of which 243 are assigned to drug-susceptible TB cases, 159 to MDR-TB and a limited number to palliative care. The NCTLD provides 250 of these

beds. The funding system is based on daily hospitalization fees, but this does not seem to serve as a perverse incentive to prolong admission.

Although the initial hospitalization of patients with TB is still common practice, the average length of hospitalization is 10 days for smear-negative and extrapulmonary cases, 25 days for smear-positive cases and 75 days for MDR-TB.

Accordingly, the significant commitment towards the outpatient community-based model is obvious.

Drug-susceptible TB

The symptomatic patient, with compatible imagery and bacteriologically confirmed through sputum smear and/or culture in the case of respiratory forms or with morphological and/or bacteriological evidence from samples adequate to the extrapulmonary forms, is usually hospitalized.

For drug-susceptible TB, a standard regimen is configured as: 2HRZE/4HR.[2] The same regimen is applied to new and relapsed cases, which are expected to have full sensitivity to all four prescribed drugs. The minimum duration of treatment is six months. Streptomycin (S) is not used given the high rates of resistance to the drug and the systematic elimination of category II drugs in the country. The resistance rate varies from, in 2007, a discouraging 76.1% in patients who had never been treated with S and 83.6% in those previously treated with it to 35.2% and 54.2%, respectively, in 2013, which makes this drug unusable.

This characteristic underlines the need for the large-scale use of modern molecular techniques such as GeneXpert MTB/RIF, which allow for diagnosis of resistance to R or, even better (though with logistical difficulties), GenoType MTB-DR plus which on positive smear can also highlight resistance to H with a reasonable degree of sensitivity. Smear-positive samples and quick strain sensitivity confirmation through molecular techniques allow the application of the standard regimen. Extrapulmonary TB is treated according to the same regimen. Because of the severity of this illness, special features of the regimen are applied to meningitis TB, which may be treated with a scheme of four drugs for 12 months, and to bone and joint TB which responds to four drugs over a period of nine months.

The schemes applied, regardless of their duration, have an initial intensive phase of about two months during which four drugs (H,R,Z,E) are administered, followed by a four months continuation phase (although seven months of treatment are required for bone and joint TB and 10 months for TB meningitis) in which two drugs (H,R) are prescribed.

Daily drug administration is recommended for the entire duration of the treatment. New case monitoring consists of SSM procedures on sputum samples harvested two months after the beginning of the treatment (at the end of the intensive stage). If results are positive, testing is resumed in the third month. Culture and DST should be carried out. The same procedure should

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[2] H=isoniazid, R=rifampicin, Z=pyrazinamide, E=ethambutol.

be applied in the third month for previously treated cases, with re-evaluation for later treatment if necessary.

Adverse effects of standard therapy are recorded on the observation sheets, but there is no national drug safety system (one should be created urgently). A standard approach to adverse effects is explicitly provided in the recommendations.

Initial treatment is administered in the hospital in separate treatment rooms for drug-susceptible TB and MDR-TB, together with the ancillary drugs that are generally available.

Explicit recommendations are given for drug-susceptible TB in special circumstances: pregnancy and breastfeeding (S, which is already contraindicated for pregnant women, is not used because of high resistance rates); liver disease with an alpha-1 antitrypsin protein three times the normal value for which regimens with a limited number of potentially hepatotoxic drugs are used; and renal failure, for which the standard scheme is applied three times per week for the entire duration of the treatment.

In HIV-positive patients with drug-susceptible TB, the recommendations apply to the daily administration of the standard scheme in association with the appropriate antiretroviral drug treatment and CPT and vigilant monitoring of side-effects.

The recommendations are consistent with those set out in the 2010 *Treatment of tuberculosis guidelines, fourth edition (10)*.

Once released from hospital, the patient will continue treatment in central, regional or peripheral outpatient facilities. Apart from sometimes extreme infrastructure quality issues, these facilities offer specialized medical practices and so-called "DOT-spots" (directly observed treatment) for drug-susceptible TB and MDR-TB, where treatment is provided directly by trained TB nurses.

One consequence of the privatization of the health care services is the reduction in TB-spots from 21 to five, associated with the five outpatient facilities in Tbilisi. These services are accessed through referral by primary health care providers as well as directly as long as TB doctors and nurses are concerned. This is done free of charge regardless of the patient's medical insurance status. There are enough medical staff to provide assistance at home and at the medical facilities.

The TB-spots are open five days a week for drug-susceptible TB assistance and six days a week (including legal holidays) for M/XDR-TB, with extra pay offered to the personnel. This makes it possible to administer daily treatment schemes recommended for both the intensive and the continuation stages.

A distinctive feature, which seems to be common, is the administration of the standard treatment under direct observation for three days a week, with the patient left to administer

his/her medication the following day supervised by the patronage[3] nurse at home. The team was able to observe DOT implementation in rural PHC facilities, where the challenge from TB is limited. The treatment can be administered exclusively in outpatient facilities in smear-negative patients or in patients who refuse admission.

The final bacteriological evaluation (in the fifth month) concludes the treatment.

The success rate of standard first-line treatment results for the smear-positive and/or culture-confirmed cases from the 2012 cohort is 84%, which is in line with WHO's recommendations and with the generally accepted rates of 6.1% lost to follow-up, 4.4% failure, 2.2% death and 3.3% not evaluated, and which has had a positive impact on the endemic dynamics (in obvious decline) in recent years.

Recommendations

- Since Georgia depends partly on external resources for the proper functioning of TB control activities, a good start would be for the Ministry of Health to purchase first-line drugs from the government budget and with a predictable source of revenue (Global Fund). These medications have an optimal cost–efficiency ratio and the treatment has positive results (85% success rate), with the obvious consequence of a reduction in the TB burden as a threat to public safety.

- Given the existence of a unique standard regimen for drug-susceptible TB, widespread access to rapid bacteriological (molecular and phenotypic on liquid medium) techniques becomes relevant not only for the definition of drug resistance but also for confirmation of mycobacterium strain sensitivity.

- In view of the high M/XDR-TB resistance rate characteristic for Georgia, a full and rapid bacteriological diagnosis of all previously treated patients regardless of their category (relapsed, failed, lost to follow-up) is a priority in starting treatment, the distinction between drug-susceptible and M/XDR-TB being essential for the therapeutic regimen applied.

- The standard regimen in outpatient facilities administered in the continuation phase should be rethought in order to avoid the mixture of DOT and self-administration that seems to be current practice. WHO recommends three times a week administration in the continuation phase, provided that each dose is directly observed. Field staff thus released could be redirected towards prevention of failure and default.

- Smear-positive sputum persistence at the end of the intensive phase should lead to the reassessment of the regimen, once the bacteriological investigation (culture, DST) and the terms of treatment administration are completed.

- Rapid recognition and standard management of adverse events can avoid failure and default.

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[3] An outreach nursing system delivering preventive and curative care outside the health systems in south-east Europe.

DR-TB

DR-TB other than MDR-TB

These terms will be used in their generally accepted meaning of resistance to one first-line drug (monoresistance) or resistance to at least two first-line drugs but not to both isoniazid and rifampicin (polyresistance). The correct treatment of these forms of disease prevents the development of M/XDR-TB and should take into account the frequency and resistance profile, limitations of bacteriological investigations and the possible acquisition of new resistances after the treatment is administered.

According to the data provided to the mission, several issues were relevant for 2013. A total of 2156 DST were performed on 1629 new cases and 527 on previously treated patients. In 627 cases, resistance to H was present (29.1%), 23% in new cases and 48% in previously treated cases; of these, 384 were associated at least with resistance to R and, therefore, classified as MDR-TB cases. The remaining 243 fell within the definition of monoresistance to H (100, 4.6%) and polyresistance to H (143, 6.6%). In 860 of the 2156 cases (39.9%), there was a significant occurrence of mono- and polyresistance to S that prevented the use of that drug in standard schemes. This, however, represented a marked decrease in resistance to S from the level of 78.3% in 2007, which was probably related to the exclusion of the drug from standard TB therapy.

These data shed light on the magnitude of the problem. Invariably, the figures available for previously treated patients are much higher than those for new patients, illustrating the impact of the treatment on the acquisition of chemoresistance – an artificial phenomenon featuring in the preliminary stages of types of M/XDR-TB.

Another relevant factor is the limited share of R+ resistance (monoresistance and polyresistance other than MDR). Of 390 (18.1%) cases of resistance to R, monoresistance was encountered in four (0.2%) and non-MDR R polyresistance was observed in two (0.1%). These figures provide answers (at least for Georgia) to questions about the usefulness of GeneXpert MTB/RIF devices in diagnosing MDR-TB and thus in determining therapy for resistance to R, particularly given their remarkable stability over the period 2005–2013.

GeneXpert cannot, however, specify possible associations of resistance to H, which is emphasized by molecular techniques such as GenoType MTBDR-plus with a sensitivity of 80% or by rapid phenotypic techniques in liquid medium and on solid medium (conventional approach) techniques involving another logistics.

Once the MDR nature of the disease is ruled out, the standard scheme also covers the initial period of treatment when resistance to H (±S) occurs. If resistance to H is identified, the scheme involves the administration of an RZE regimen for a period of nine months. For the other forms of polyresistance to H, the schemes administered are in accordance with the recommendations in international guidelines. A distinct feature of the Georgian recommendations is that they preserve different schemes for mono- and polyresistance to R, unlike the current recommendations for full MDR-TB regimen plus H *(15)*.

Recommendations

- Rapid GeneXpert MDR/RIF type methods should be generally used; these allow not only the identification of resistance to R but also, in case this type of resistance is not found, the start of the standard regimen until resistance to H can eventually be identified with conventional techniques.

- In the case of resistance to R, MDR-TB regimens should be applied in accordance with international guidelines (especially as local data suggest that resistance to R is almost always associated with resistance to H).

- Problems with logistics, which sometimes delay the GeneXpert MTB/RIF results up to 10 days, should be resolved.

- The development of resistance should be monitored via DST in cases of positive sputum persistence or positive sputum after initial conversion and therapy reorientation.

M/XDR-TB

According to the available data, the prevalence of MDR-TB is increasing among both new and previously treated patients. This is proof of the continuing spread of the disease in the community as well as of the consequences of inefficient therapy on the increase in resistance to drugs.

Between 2006 and 2013, the prevalence of MDR-TB in new cases increased from 6.8% to 11.2% and in previously treated patients from 26.4% to 38.1%. An apparent paradox is that this evolution occurred despite the introduction of MDR-TB treatment in 2004 and the provision of universal access to TB diagnosis and treatment in 2009, and even though there was an obvious improvement in the general endemic framework during the same period, with TB notifications decreasing from 6311 (143‰) in 2006 to 4320 (96‰) in 2013.

Other significant data relate to the 2008–2011 cohorts and to the difference in final treatment outcomes for MDR-TB and XDR-TB patients. The increase in size of cohort is significant: 466 patients in 2008, 636 in 2009, 633 in 2010 and 743 in 2011, with varying success rates for MDR-TB and XDR-TB.

The success rate for MDR-TB fell gradually from 56.4% in 2008 to 51.2% for 2011 (average 54%), while for XDR-TB the success rate varied from a maximum of 39.1% for the 2009 cohort to 10.5% for the 2011 cohort (average 29.5%), although the results are so far difficult to interpret in the absence of full treatment coverage of XDR cases. At the same time, the rates for death and failure were relatively stable with low values (9% average death rate and 4.9% average failure rate for the period). The increase in those lost to follow-up is striking in both absolute and relative terms, from 95 (20.4%) in 2008 to 256 (34.5%) in 2011.

The available data, which include the limited success rate and the lost to follow-up rate, suggest a kind of "therapeutic fatigue". Thus Georgia seems to be an example of the most feared scenario: the translation of the fall and rise curve from the individual to the endemic, with a major impact on the perspectives for therapy.

Another limitation was the incomplete coverage of DST to H and R in registered cases. In 2011, however, the rate for new cases was better at 83% than for retreatments (52%), even though the prevalence of MDR among the latter was four times higher.

According to the 2013 DST data on first-line antibiotics, of the 183 (11.2%) new MDR-TB cases and 201 (38.1%) previously treated patients, 146 (9%) and 172 (32.6%), respectively, had acquired resistance to all four tuberculostatic drugs on which testing is usually performed (H, R, E and S) and, as a consequence, most likely to Z as well, which makes any antibiotics in this category irrelevant. To this is added a high incidence of resistance to second-line drugs, according to tests carried out on patients from the 2012 and 2013 cohorts. A special case is that of E, which had an 85–90% resistance rate and a refusal rate of 70%. However, an evaluation performed on a number of patients from the west of the country led (affirmatively) to much lower values after a comparison of resistance to the same strains via different DST techniques (conventional and liquid medium). High resistance rates were encountered for Km (40–45%), Ofx (17–27%) and PAS (15%). Until the results of DST to second-line drugs are available, the empirical regimen which initiates therapy is obtained through the association of Z, Km, Lfx, Pto and Cs (PAS), which illustrates the obvious obstacles in treatment and the increasing need for therapy.

In most cases, treatment for MDR-TB is initiated in hospital. As well as the NCTLD, which has 97 beds organized in different sections for pulmonary drug-resistant TB, MDR-TB and XDR-TB, treatment for drug-resistant TB is available in Abastumani and Zugdidi hospitals.

In the NCTLD, a national consilium meets twice a week to analyse drug-resistant TB cases and propose the therapy scheme, where it should take place (Tblisi or other places) and any eventual modifications to it. The NRL, also situated in the NCTLD, assimilates rapid and conventional methods which underpin the bacteriological diagnostics as a basis for recommended regimens.

Once conversion is complete, patients continue their treatment in outpatient facilities, in which separate DOT-spots for MDR-TB are organized and individual treatment is assured six days a week, or in rural care centres. Occasionally, home-based DOT can be organized.

Bacteriological monitoring is done monthly until conversion, and then quarterly by repeating DST in cases of positive sputum persistence or positive sputum after initial conversion.

Despite all these efforts (a centralized approach, all-access policy, enough beds for treatment of specialized conditions, constant access to a reasonable number of good quality second-line drugs via external financial funds, a coherent ambulatory assistance system-outpatient TB unit, and rewards such as reimbursement of transport costs, food vouchers and monthly cash incentives), results are at the limit of relevance (with a 50% success rate) and incompatible with controlling the disease.

A major characteristic of treatment for MDR-TB is the high rate of loss to follow-up: 34.5% in 2011. The mission saw a published analysis of the risk associated with loss to follow-up concerning MDR-TB patients. This study looked at 1240 patients with MDR-TB enrolled in treatment during 2009–2011; 395 (29%) were, in the end, lost to follow-up. A number of high-

risk characteristics for patients lost to follow-up were identified: male gender, history of incarceration, illicit drug use, tobacco use, previous anti-TB treatment, pulmonary disease, higher baseline smear-positive results and a significantly lower culture conversion rate of two per month. Forty-one percent of patients gave up within the eight-month limit, with a conversion rate of only 37%, thus continuing to be active factors in the propagation of the disease. Another study covering half the MDR-TB patients showed that treatment-related adverse events were the major cause of loss to follow-up.

An observation in the first study also suggested that overstretch on the part of the assistance services (as the number of MDR-TB patients steadily increases, with half of them starting treatment in Tblisi) was a possible explanation for the increase in loss to follow-up.

The recommendations of this study could form the basis of a rational approach to the problem. As regards M/XDR-TB therapy, the recommendations are in accordance with those in the 2011 update to WHO's *Guidelines for the programmatic management of drug-resistant tuberculosis (16)* and with all the previous versions.

The therapeutic regimen includes Z, a fluoroquinolone, a second-line injectable, Pto, Cs (or PAS if Cs cannot be used) or, in other words, at least four line drugs (including an injectable) as well as Z during the intensive phase of treatment. Individual recommendations refer to fluoroquinolones, in the sense of using later generation drugs and Pto in the scheme.

In accordance with WHO's recommendations, treatment is given for an eight-month intensive phase and a total period of at least 20 months, although a maximum duration of 32 months is advised. If anti-TB treatment is considered to have failed, the palliative care model should be used.

These recommendations are debatable. An excessively long period is not necessarily associated with increasing positive results and avoiding recurrence of the illness (the recommendation is valid rather for previously treated patients). Taking into account the high frequency of loss to follow-up, it is clear that the situation could be influenced by re-evaluating the regimen, motivating the patient, strictly applying DOT and not relying on palliative care.

Specific recommendations for XDR-TB had recently been made available. The only group 5 drugs available until recently for pre-XDR-TB and XDR-TB were Cfz, Clr and Amx, which was mainly relevant because it contains Clv. At present and in the near future, concordantly with the 2013 and 2014 visits by the GLC, access to group 5 medicine has been extended through the use of imipenem/cilastatin (Imi/Cls), the acquisition of Lzd via compassionate use programmes for bedaquiline (Bdq) since 2011 and through a clinical trial with the inclusion of Bdq and delamanid for which discussions between the MoLHSA and Médecins Sans Frontières are continuing.

In July 2014, the GLC was motivated by the new conditions to make a visit dedicated to treatment strategies. Their report included the following:

- an important recommendation to replace the current empirical regime Z, Km, Lfx, Pto, Cs (PAS) with Z, Cm, Mfx, Lzd, Cs, PAS until full DST is obtained to orient the therapy, with

the arguments that should trigger the suggested regimen changes and the observation that their application should be tested at the NCTLD and then gradually introduced nationwide;

- an attempt to rank group 5 drugs according to data on drug efficiency, safety, costs and logistics issues; and

- regimens adapted to the various therapeutic situations: resistance to fluoroquinolones, resistance to aminoglycosides, XDR-TB.

The schemes to be considered are:

resistance to fluoroquinolones:	Cm – PAS – Cs – Lzd – BDQ – Z
resistance to aminoglycosides:	Lfx – PAS – Cs – Lzd – BDQ – Z
XDR-TB:	PAS – Cs – Lzd – BDQ – Cfz – Z

Consequently those advanced by the NCTLD are:

MDR (simple):	8 Z – Cm(Km) – Mfx(Lfx) – Cs – PAS – Pto(Lzd)/12 Z – Mfx(Lfx) – Cs – PAS – Pto(Lzd)
Pre-XDR (resistance to fluoroquinolone):	10 Z – Cm –Cs-PAS – Lzd – (Mfx, Cfz) – Bdq/14 Z – Cs – PAS – (Mfx, Cfz)
Pre-XDR (resistance to Cm and Km):	10 Z – Mfx(Lfx) – Cs – PAS(Clr) – Lzd(Cfz) – Bdq/14 Z – Mfx(Lfx) – Cs – PAS(Clr, Cfz)
XDR-TB	10 Z – Cs – PAS – Lzd – Bdq – Cfz – Imi/Cls(Clr) – Amx/Clv/14 Z – Cs – PAS – Cfz – Imi/Cls(Clr) – Amx/Clv.

Changes to regimens are made according to full DST results and to the potential adverse effects.

In view of the predictable incidence and remarkable diversity of adverse reactions, the above-mentioned report suggests a standard approach in administration of the drugs and minimum ancillary support. From the experience of the WHO review team, the problem is mainly seen at the regional and peripheral levels, suggesting logistical issues. Occasionally patients must pay for their own medication (usually for vitamins and food supplements, according to the interviews).

Treatment for M/XDR-TB in special situations (pregnancy, breastfeeding, hepatic affections, renal insufficiency, diabetes and AIDS) benefits from express recommendations in the national TB management guideline, in accordance with WHO's *Guidelines for the programmatic management of drug-resistant tuberculosis. Emergency update 2008 (17)*.

A novelty is the introduction of elementary recommendations concerning the indications for and decisions about surgery, the optimum time for the intervention, the period of anti-TB treatment in the postoperative period and contraindications for surgical treatment.

Finally, the problem of MDR-TB treatment is being handled in a difficult context involving a variety of factors: the growing burden of the disease, increasing resistance, financial limitations, dependence on external funding, uncertainties regarding sustainability, extended privatization

of health care services and, above all, rapid progress in therapies and methodological changes which force fast decisions. This is only possible with dedicated and motivated staff.

Recommendations

• The sustainability of the various components of therapy should be assured through the progressive introduction of M/XDR-TB treatment to address a major problem of TB control in the country.

• The financial and legal administrative framework should be structured to facilitate the new patient-centred therapeutic approach and provide extra motivation for the medical staff.

• The working framework of the NTP, which is essential for the modernization of therapy, should be reorganized.

• In the current context, the existence of a strong methodological centre such as the NCTLD and the retention of an evenly distributed network of outpatient facilities can assure the efficiency of the NTP policies.

• The central consilium at NCTLD level must keep its responsibilities for rationalizing therapeutic regimes, controlling drug use to avoid improper management and further amplification of drug resistance, initiating and monitoring the various pilot and clinical trials and implementing new therapies.

• If necessary, consideration will be given to organizing new councils in units that have the necessary expertise and access to complete bacteriological investigations.

• In view of the rapid changes occurring in X/MDR-TB therapy, an important task for the NTP in the near future will be to re-evaluate the national guidelines, protocol and recommendations to bring them into line with WHO's updates (*Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis (15)*, *Interim policy guidance for new drugs (Bdq and Dlm), Policy implementation package for new TB drug introduction (18)*) and with the recommendations of the GLC visit in 2014.

• The new therapeutic strategies should be gradually introduced from correctly monitored test studies at NCTBL level, combined with training for medical staff in new regimens and drugs and their particularities of use and side effects. Some drugs, such as Amx/Clv, Imi/Cls, meropenem and delamanid, are administered twice or three times a day which is difficult in outpatient facilities.

• DST for first-line drugs (genotypic and phenotypic rapid tests) should be the basis for early MDR case diagnosis, and DST for first- and second-line drugs should be the basis of TB treatment.

• Administration of M/XDR-TB treatment under direct supervision is mandatory and should be done through a patient-centred approach at the outpatient facilities level.

• The declining success rate (50%) for MDR-TB and the increasing rate (34.5%) for loss to follow-up suggest a lack of efficiency. The risk factors associated with loss to follow-up among MDR-TB patients should be well defined in a local evaluation that can form the

basis of an approach to the problem. The proposed measures are expensive, time-consuming and with limited efficiency but unavoidable.

- Adverse reactions are frequent in M/XDR-TB treatment and trigger at least half of the loss to follow-up. It is essential that they are recognized, standard monitoring is introduced and they form part of the elementary training of the medical staff in line with the development of the pharmacovigilance system.

- Structures and staff should be prepared for the changing nature of the specialty, while avoiding too limited specializations.

Childhood TB

The data provided on the dynamics of the epidemic in the group aged 0–14 years shows a remarkable decrease in the absolute number of cases from 1105 (88.8‰ incidence) in 1998 to 188 (24.5‰ incidence) in 2013. The number of meningitis cases also dropped from a peak of 28 cases in 2003 to 0 in 2013, although the team came across one case of meningitis with optic chiasma compression and permanent blindness. Both incidence data as well as the decreasing number of meningitis cases are proof of the significant weakening of the TB epidemic in children, a more important improvement than that of the TB epidemic in adults.

There has, however, been a dramatic decrease in the population of children from 1 245 000 to 766 000 in this period. Diagnostic difficulties characteristic of TB in children and the need for uniform practice in line with WHO recommendations have led to the development of evidence-based child- and parent-centred paediatric TB guidelines and protocols, which have already been approved by the MoLHSA.

The guidelines cover diagnosis, treatment, management of adverse effects and control tracing for drug-susceptible TB and MDR-TB and have been the object of training. Essentially, regular TB is treated with a standard H,R,Z,E association and the M/XDR-TB cases are treated according to the resistance type of the source case.

Paediatric formulations have been available but they become out of date and had to be thrown away, which caused a temporary shortage.

In 2013, there was no purified protein derivative tuberculin for the Mantoux test (this has since been resolved). Bacillus Calmette-Guérin vaccination is done at birth with a 96% coverage. One problem is the precarious state of the NCTLD paediatric ward, the main facility for childhood TB diagnostic and treatment in the country.

Recommendations

- Prevention, diagnosis and TB treatment in children should be improved by ensuring Bacillus Calmette-Guérin vaccination, tuberculin skin testing and adapting paediatric formulations of anti-TB drugs.

- The infrastructure of the central paediatric TB ward should be improved and access to the technical NCTLD platform maintained.

HIV-associated TB

The achievements in the field of HIV-associated TB are as follows.

• Universal coverage with TB symptom screening of adults and children enrolled in HIV care has been achieved.

• HIV, TB and harm reduction services are coordinating well at hospital level. ART and methadone substitution therapy are provided in TB hospitals if needed.

• ART coverage of TB patients rose from 54% in 2009 to 89% in 2013.

• CPT among patients with TB and HIV coinfection increased from 56% in 2011 to 89% in 2013.

The following challenges remain.

• Integrated TB and HIV services are seriously underfunded (95% gap based on the National TB Strategy and Operational Plan for Georgia for 2013–2015).

• There is no joint TB and HIV strategy and coordination body, and coordination between HIV and TB services at regional and district levels is inadequate.

• Coverage with HIV counselling and testing among notified TB patients is low (62%).

• Screening of TB among people living with HIV is performed in TB facilities, which exposes them to an increased risk of infection.

• Coverage with IPT is still low (21%, or 92 out of 439 patients) despite a recent increasing tendency from 16% in 2011 to 18.6% in 2012.

• Low TB treatment success rate among HIV-positive TB and M/XDR-TB patients.

TB was the leading cause of death among HIV-infected individuals in the period 1989–2012, accounting for 21% of the total deaths reported (Fig. 20) *(19)*. Universal access to ART has significantly reduced mortality among HIV-infected patients, although overall mortality rates remain high, primarily due to late diagnosis, and TB remains a significant cause of death. Improving rates of early HIV diagnosis and ART initiation may further decrease mortality as well as prevent new HIV and TB infections.

Fig. 20. Causes of death among people living with HIV
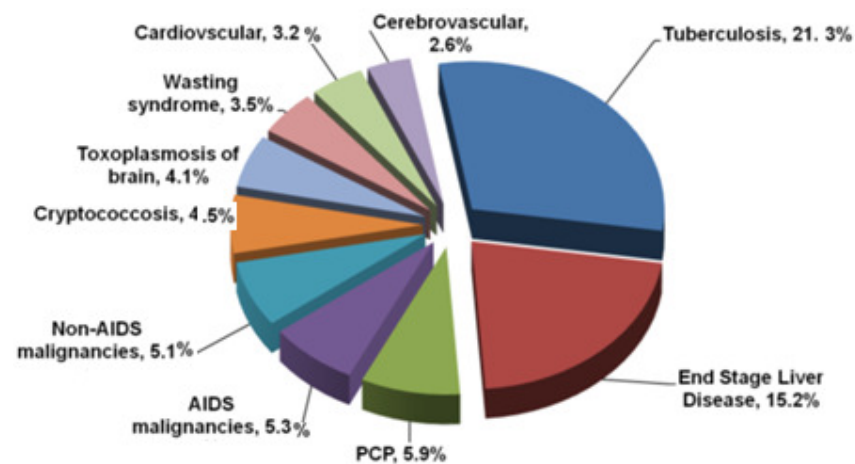
PCP= *Pneumocystis* pneumonia

Almost all doctors, physicians and nurses in primary health care and TB doctors and nurses have been trained in the management of TB and HIV coinfection by a USAID-funded project. But in reality their knowledge and understanding are inadequate and sometimes contradictory (see below).

Mechanisms for delivering integrated TB and HIV services

No separate joint TB and HIV strategy exists to address the collaborative HIV/TB services in the next few years with a situational analysis; terms of reference for each service; models to deliver client- and family-centred TB and HIV services at facility and community levels; a joint training plan; job descriptions for health workers; baseline and target indicators; and the budget needed, available and the gap between the two. The National TB Strategy and Operational Plan for 2013–2015 (NSP) does, however, have a separate objective for strengthening HIV and TB collaborative activities with defined outcome indicators. As highlighted in the NSP, the overall purpose of the country policy for HIV/TB collaborative activities is to ensure a reduction in the burden of TB and HIV. The NSP has outcome indicators (TB patients with known HIV status, clients screened for TB), an impact indicator (reduced level of HIV among TB patients), and baseline statistical and target data.

The National HIV/AIDS Strategic Plan for 2011–2016 does not have a separate objective but addresses collaborative activities through different objectives with the following defined indicators:

- implementation of provider-initiated HIV counselling and testing of patients in narcology, sexually transmitted infections and TB clinics and antenatal care clinics (TB and antenatal care clinics are covered by routine surveillance);

- integration of HIV and TB services (one stop service);

- percentage of HIV/TB patients who receive treatment for both TB and HIV (baseline data 67%; target 95% by 2016);

- percentage of HIV patients with latent TB infection who receive preventive treatment for TB (no target and baseline).

There is no detailed plan of action and budget for collaborative activities attached to the NSP on TB and HIV/AIDS. However, based on the NSP, the total planned budget needed for 2013–2015 is US$ 568 000, with a considerable budget gap of 95%. No government contribution was identified for collaborative activities. TB and HIV collaborative activities are highly reliant on external technical support and financial assistance, mainly from the Global Fund. During the interview with key informants, the team found that activities are covered under other budget lines such as procurement, training and drug components. Almost all collaborative activities are covered by the Global Fund grant.

A national guideline for collaborative TB and HIV activities was approved in 2013, as well as a clinical protocol on HIV/TB which is in line with the revised WHO HIV/AIDS clinical protocols.

Despite good collaboration between the TB and HIV services there is no coordinating body or mechanism for HIV/TB coordination, joint planning, and the monitoring and evaluation of joint activities. The team found that a TB and HIV technical working group existed at national level in the past but has stopped working due to privatization of the services and the lack of interest by the private service providers in supporting TB and HIV services. Coordination and information exchange between the two services at regional and district level is inadequate. It is very important that a strong joint national HIV/TB coordinating body functions at all levels to ensure effective collaboration. The body should represent both programmes, people at risk of or affected by both diseases, and other ministries (such as those working on harm reduction and prisons). Its responsibilities should include the governance, planning, coordination and implementation of collaborative HIV/TB activities and the mobilization of financial resources.

Surveillance of HIV among TB patients and surveillance of active TB disease among people living with HIV is conducted at national level in order to inform programme planning and implementation. Both TB and HIV programmes have electronic databases. The HIV/AIDS programme has an online database (the HIV/AIDS register) which includes data on TB and HIV coinfected patients and is protected by coded password and secured. The TB database also has information on TB and HIV coinfected patients. Although the team was told that information exchange between the two programmes is good at national level, in the regions and districts visited they observed that data on the HIV status of TB patients is not reported to staff in the TB clinics and rural ambulatories who are involved in providing DOT. This was explained as ensuring the confidentiality of patients' HIV status.

There is no integrated national monitoring and evaluation mechanism for collaborative HIV/TB activities. Information on HIV/TB coinfection is reported on HIV form N1: the data are submitted to the database managers monthly by facilities where voluntary counselling and testing specialists conduct HIV testing (mainly in the national and three regional HIV/AIDS centres and 12 voluntary counselling and testing sites at primary health care institutions).

Recommendations

- National policies/strategies/plans should be developed to address HIV/TB coinfection for the next few years with a situational analysis; terms of reference for each service; models to deliver client- and family-centred TB and HIV services at facility and community levels; a joint training plan; job descriptions for health workers; baseline and target indicators; and the budget needed, the budget available and budget gap.

- A detailed budget should be developed with funds ensured and a schedule for their disbursement against the funding requirements for the collaborative HIV/TB programme. A separate component to support the collaborative HIV/TB service should be included in the new application to the Global Fund.

- A HIV/TB coordinating body or mechanism (working group) should be re-established to be effective at all administrative levels of the health services, with representation from all the major stakeholders in collaborative HIV/TB activities (including civil society/ nongovernmental organizations, the population affected and the penitentiary sector), to meet at least quarterly and with clear terms of reference and functions.

- Information exchange should be ensured between TB and HIV services at regional and district levels, and in particular information on the HIV status of TB patients should be available for doctors providing TB treatment.

- Monitoring and evaluation for collaborative HIV/TB activities should be included in the terms of reference of the national and regional monitoring teams. The results of the monitoring and evaluation visits should be reported to both national TB and HIV centres and the NCDC.

Reducing the burden of TB among people living with HIV
The national policy dictates that all adults and children enrolled in HIV care should be covered with TB symptom screening. The country reported 100% coverage with TB symptom screening since 2011; in 2013, 2369 out of 2369 people living with HIV were screened for TB. However, HIV-infected patients with suspected TB are referred to TB facilities for further investigation which increases the risk of acquiring TB disease. The exceptions are patients hospitalized with HIV, for whom sputum is collected by a nurse and sent to a TB facility for further investigation.

The HIV/AIDS service should consider measures to decrease this risk by adopting one of the following scenarios:

- implementing GeneXpert MTB/RIF machines in HIV facilities, at least at national and regional HIV centres; procurement of GeneXpert MTB/RIF machines can be added in the new Global Fund grant;

- organizing an effective sputum collection and transport system to TB laboratories.

They could also establish a half-time position of TB doctor in HIV facilities so as to reduce referrals to TB facilities and the consequent risk of TB transmission.

The proportion of TB patients with an HIV-positive status in 2013 was 2.1% or 56 patients. There is a rising tendency in the number of TB and HIV coinfected patients: 33 in 2009 and 56 in 2013.

However, the low TB case detection rate (68%), insufficient testing coverage for most-at-risk groups (12% among people who inject drugs, 13.4% among sex workers and 5.4% among men who have sex with men), and the low proportion of TB patients tested for HIV suggest that the burden of TB and HIV coinfection is higher than the notified rate.

Data from the national HIV/AIDS Centre show that 100% of registered HIV/TB patients received TB treatment in accordance with the national TB treatment regime in 2013.

Coverage with IPT still remains low (21%, or 92 out of 439) despite the national target in the NSP of 70% by 2015. Although it has increased from 16% in 2011 to 18.6% in 2012, it is not enough to achieve the defined target. IPT is supplied by the government (TB service) and administered by HIV/AIDS centres.

Despite the recently adopted national guideline for collaborative TB and HIV activities (which is in line with the latest WHO recommendation), there is a discrepancy in implementation: in some facilities visited, IPT was prescribed when the CD4 count was less than 50 cells/mm^3. Insufficient IPT coverage was explained by a lack of funds to procure tuberculin to perform tuberculin skin tests to detect latent TB. In addition, there is concern about the increased risk of developing Z-resistant TB as a result of IPT. Based on the latest WHO recommendation, all adults and adolescents living with HIV who do not have active TB should be offered IPT for six months, and concerns regarding the development of resistance to Z should not be a barrier to providing IPT.

The mission found that there is no TB infection control plan in HIV/AIDS care facilities.

Recommendations

- To decrease the risk of TB transmission, the referral of people living with HIV to TB facilities for screening should be discontinued by considering/adopting one of the following scenarios:

  - implementing GeneXpert MTB/RIF machines in HIV facilities, at least at national and regional HIV centres; procurement of GeneXpert MTB/RIF machines can be added in the new Global Fund grant;

  - organizing an effective sputum collection and transport system to TB laboratories.

- A part-time position of TB doctor in HIV facilities, or TB specialist as consultant in HIV facilities, should be established.

- Coverage with IPT should be increased to 100% through Ministry of Health regulation and enforcement of the implementation of the recently adopted national guideline on management of TB and HIV coinfection at all TB and HIV care facilities across the country. The lack of tuberculin to perform tuberculin skin tests to detect latent TB, CD4 counts, as well as the risk of developing Z-resistant TB should not be a barrier to IPT.

- Each HIV/AIDS facility should develop a TB infection control plan, which includes administrative, environmental and personal protection measures to reduce the

transmission of TB in health care and congregate settings, and surveillance of TB disease among workers.

Reducing the burden of HIV in patients with presumptive and diagnosed TB
The proportion of TB patients with known HIV status is low (62%, or 2698 patients out of 4319 in 2013 *(4)*. As laid down in the national guideline on management of TB and HIV coinfection, HIV testing should be offered to all TB patients at the time they start TB treatment.

In reality, provision of HIV testing and counselling is limited and is provided in infectious diseases hospitals, the AIDS and Clinical Immunology Research Centre and some regional TB hospitals. Some hospitals collect blood from hospitalized patients and transport it to HIV centres for testing. Some private clinics providing treatment to TB patients do not offer HIV testing at all. No HIV rapid tests are available at TB clinics for ambulatory-treated TB patients. In many cases TB doctors do not referring TB patients for HIV investigation because HIV tests are not free at nearby hospitals. Moreover, HIV testing is expensive (around US$ 13) and presents an extra financial burden for patients. Patients are not keen to travel to HIV centres to get free testing. A ministerial decree or regulation is needed in order to ensure that all TB clinics in the country routinely offer free HIV testing.

HIV testing and counselling for patients with presumptive TB is not practised. WHO strongly recommends offering routine HIV testing both to patients with diagnosed TB and those with presumptive TB and their partners.

A considerable increase in CPT among patients with TB and HIV coinfection was observed at national level from 56% in 2011 to 89% in 2013. The mission was told that at national level, all TB hospitals provide CPT to all HIV/TB coinfected patients, ambulatory patients receive CPT from the HIV/AIDS service and co-trimoxazole is procured by the NCTLD. In reality, CPT was only available in one facility visited; a lack of co-trimaxazole prevented it. In some HIV clinics, the team was told that CPT was prescribed when the CD count was lower than 200 cells/mm^3. Coverage with CPT should be increased to 100% (in accordance with the target in the NSP) and it should be prescribed regardless of CD4 counts to improve the survival of patients with coinfection.

ART coverage of TB patients has considerably increased since 2009 from 54% (18 out of 33 patients with coinfection) to 89% in 2013 (50 out of 56 patients with coinfection). It should be increased to more than 95% to improve the survival of patients with coinfection. Another concern is the low success rate of TB treatment and the high rates of failure and default among HIV-positive TB and M/XDR-TB patients (Table 10).

Table 10. Treatment outcomes of TB, M/XDR-TB and HIV coinfected patients, 2009–2014 cohorts

	Succeeded (%)	Failed (%)	Defaulted (%)	Died (%)	Not evaluated (%)
Non-DR-HIV/TB coinfected cases (86 cases, 2009–2014)	58.1	17.4	9.3	8.1	7
MDR-HIV/TB coinfected cases (65 cases, 2009–2014)	30.8	4.6	29.2	26.2	9.2
XDR-HIV/TB coinfected cases (5 cases, 2009–2014)	–	–	40	60	–

Source: NCTLD *(7)*.

One of the reasons for the low treatment success rate and high level of default and death among coinfected patients is late initiation of ART. Of 10 patients with the coinfection who

were hospitalized in the NCTLD, the level of CD4 at the start of ART treatment was lower than 50 cells/mm^3 in six cases (>50%); the start of ART was delayed in three cases and there was no ART in the rest. These patients are eligible to start ART within two weeks after TB treatment has been started.

Recommendations

• The Ministry of Health should issue a regulation directing that routine HIV testing rate in patients with TB should be increased to more than 95%, and implementation of the revised guideline on management of TB and HIV coinfection and its routine introduction in all TB care facilities across the country should be ensured. HIV testing should be free. Routine and free rapid HIV tests should be added in the current grant and the new funding model of the Global Fund.

• The Ministry of Health should direct that coverage with CPT should be increased to 100% and reinforce the implementation of the revised national guideline on management of TB and HIV coinfection by all TB and HIV care facilities across the country. CPT should be prescribed regardless of CD4 counts to improve the survival of patients with coinfection.

• The latest WHO recommendation regarding in-time initiation of ART in patients with TB and HIV coinfection should be reinforced and its implementation ensured. In particular, coinfected patients with a CD4 cell count of less than 50ml/mg should start ART within two weeks after start of TB treatment.

• Operational research should be conducted to investigate the high levels of treatment default and death.

Supply and management of anti-TB drugs

The NCTLD is the head facility for TB control, administering and implementing the NTP with the aim of reducing the spread of TB. It is subordinate to the MoLHSA, which has overall responsibility for TB control. TB management is carried out through a network of specialized TB service institutions and primary health care services. The NTP is structured on three levels: national (NCTLD), regional (regional TB facilities including TB dispensaries in Tbilisi) and district (TB units and primary health care facilities).

Since the health reform of 2012, significant changes have been made to the TB control system which have had a big impact on the common health care structure. All primary health care facilities were sold to private investors because a lack of funds meant the government was unable to maintain them. As a result, TB dispensaries at district level were absorbed by private general medical facilities and continuity between levels of TB services became complicated. Most of the TB service employees lost their jobs, although TB services continue to be provided by TB specialists working in multidisciplinary teams based at general health facilities. These teams, consisting of the regional TB coordinator and TB nurse belonging to the NCTLD and primary health care supervisor belonging to the NCDC, are responsible for TB services including drug management in the relevant regions. There is no drug management position in the system.

At national level, some responsibilities for the running of the NTP have been transferred from the NCTLD to the NCDC. As before, the NCTLD cannot keep full control of drugs distributed to the regional and primary health care levels because health care facilities at primary health care level are in the private sector. From the moment they receive the drugs, the primary health care facilities own them. The poor control of anti-TB drugs consumption is a weak point in the system. There are no clearly written procedures in the interaction between the public and private sectors. The central pharmacy unit of the NCTLD, which is responsible for drug management activities (storage, inventory management, distribution and supervision of TB drugs at all levels) could have used its skilled staff to render technical assistance to primary health care facilities in making assessments, discovering shortcomings in drug management in privatized primary health care facilities, making analyses and, based on the results, providing on-the-job training for primary health care workers. It could have been positive to monitor primary health care facilities at least once a quarter to see if the forecasting and quantification of needs are well-defined, what the consumption of anti-TB drugs is, what needs to be approved and so on. In general, there is a need for legislation to provide for an efficient mechanism for the smooth interaction between the public and private sectors in drug management.

Selection

Currently, the selection of anti-TB and ancillary drugs is the responsibility of a group consisting of the clinicians, managers and pharmacists at the NCTLD and the principal recipient staff at the NCDC. All anti-TB drugs, including fixed-dose combination forms, are included in the revised national essential drugs list, which was approved by the MoLHSA in 2012 based on the

recommendations in WHO's model list of essential medicines (Table 11). Clinical protocols for all forms of TB approved by the MoLHSA include standard regimens given with the drugs included in the national essential drugs list. At present, in line with the approved treatment regimens, only fixed-dose combination forms of anti-TB drugs are used for treatment of sensitive TB in adults and children. Drugs for treatment of resistant TB were selected according to the national treatment guidelines, in line with WHO's recommended standards for TB control and national DST data. Due to high resistance to second-line anti-TB drugs, the treatment regimens for M/XDR-TB were revised in accordance with the recommendations of the GLC mission in July 2014. The so-called group 5 drugs, including new drugs, will be widely used for treatment of all resistant TB. In view of the new approaches in treatment of resistant TB, the national guidelines for M/XDR-TB will be revised in 2015. For new drugs to be included in the national drug register, the procedures for their registration in Georgia should be stated.

Table 11. Anti-TB drugs for treatment of all forms of TB

First-line drugs	Second-line drugs
RHZE 150/75/400/ 275 mg tablets	Km 1g vial
RH 150/75 mg tablets	Cm 1g vial
E 400 mg tablets	Paser (acid/sodium) 4 g sachet
Z 400 mg tablets	Pto 250 mg tablets
E 100 mg tablets	Cs 250 mg cap
Z 100mg tablets	Lfx 250 mg tablets
Z 300mg tablets	Moxifloxacin 400 mg tablets
R 150 mg tablets	Clr 250 mg tablets
	Lzd 600 mg tablets
	Amx/Clv 875/125 mg tablets
	Imipenem/Cilastatin 500 mg+500 mg
	Cfz 100 mg (Cfz)

Procurement

The Procurement Law, which was updated in September 2013, regulates procurement of pharmaceutical products. There is no special clause in the procurement law and decrees regulating the procurement of essential medicines. The new state procurement system was established in December 2010 on the following principles:

- transparency

- non-discrimination

- fair selection

- facilitated procedures

- less paperwork.

The State Procurement Agency was assigned to create, introduce and run the electronic system of state procurement. The main advantage of the system is its simplicity and transparency. When logged onto the system, any person can see:

- annual procurement plans;

- announcements of tenders;

- approximate value of procurements;

- documentation for tenders, specifications and amendments made to them;

- supplier's tender proposal and its price;

- minutes of the tender commission meetings, correspondence with the supplier and contracts and amendments made to them;

- information on payments made.

The main objectives of the State Procurement Agency are to:

- supervise and monitor the legality of state procurement procedures;

- secure the principles of publicity, transparency, fairness and non-discrimination when carrying out state procurements, and ensure precise procedures and calculations as defined by law, fair competition and the rational and free choice of participants in state procurements;

- support the working of the unified electronic system for state procurement and boost public trust in it;

- improve legislation regulating competition and state procurement, ensuring its compliance with internationally recognized standards and best practice.

At present, the Global Fund grant is the sole source for procurement of first- and second-line anti-TB and ancillary drugs for the NTP carried out through the GDF by direct procurement for 2014–2016. The government is planning to take over the procurement of first-line drugs from 2015. By that time, regulations need to be in place to ensure the procurement of quality-assured fixed-dose combinations, preferably through the GDF.

An uninterrupted supply of TB drugs of guaranteed quality and ancillary drugs for treatment of adverse reactions is ensured through the financial support of the Global Fund. This is one of the main achievements of the NTP.

The principal recipient staff get permission to import medicines before they arrive in the country and legalize the shipment. It takes 20 days to obtain all the permissions necessary to import medicines. In addition, a Special Commission assesses the status and quality of anti-TB drugs and the compliance of accompanying documents for the cargo (airway bill, invoice, good manufacturing practice (GMP) certificates of analysis, freight prepaid certificate (FPP), etc.) provided by the principal recipient staff to the MoLHSA. If the preparatory work for customs clearance and obtaining all the required papers and approvals of local authorities is carried out in advance, drugs can be delivered promptly to recipients without damage.

In September 2014, an order for procurement of first- and second-line anti-TB drugs for 2015–2016 by direct purchase was submitted by the NCDC to the Global Fund under the Procurement Supply Management Plan. The procurement order for the first-line TB drug includes a two fixed-dose combination (2FDC) drug HR 75/150 and monodrugs (Z,E,H) for treatment of sensitive TB, including polyresistant cases with selective sensitivity to the first-line drugs. The procurement order does not include a four fixed-dose combination (4FDC) drug with fixed

doses for intensive phase treatment. As there was a 20-month supply of the drug in the country (enough to meet the demand in treating sensitive forms of TB until the end of 2015), it was not ordered. The GDF mission in July 2014 recommended that calculations should be made and an order placed for 4FDC together with 2FDC in February 2015.

The procurement order for second-line TB drugs was submitted in September 2014 for 643 MDR-TB patients enrolled in 2014, 80 of them with pre-XDR and XDR-TB and 520 with MDR-TB. Of the latter, 166 had pre-XDR and XDR-TB. The immediate delivery was scheduled for January 2015, the regular delivery for was scheduled half for March 2015 and half for November 2015. The order included the group 5 drugs: Amx/Clv, Clr, Cfz, Lzd, Imi/Cls, Bdq.

Currently, there is no dosage of TB drugs for children in Georgia. The 2014 GDF mission reported that the country would not make an order for a paediatric grant, even though the 2013 TB reports showed that children with TB weighing 5 kg accounted for 20% (50–60 cases) of all the newly detected TB cases. The WHO team therefore recommends that paediatric dosages for 50 cases of children with TB weighing up to 5 kg should be purchased under the new funding model concept note (June 2015).

Ancillary drugs for the treatment of adverse reactions are provided free with support from the Global Fund (Table 12). All resistant TB cases undergoing inpatient or outpatient treatment are fully covered by ancillary drugs. The availability of these drugs for sensitive TB cases is an important issue in treatment. They should be made much more widely available so as to increase patient adherence for better outcomes of treatment.

Table 12. Ancillary drugs supplied by the Global Fund

Name	Dosage/form
Amiodarone	200 mg tablets
Cetirizine	10 mg tablets
Domperidone	20 mg tablets
Flavamed (Ambroxol)	300 mg tablets
Fluconazole	150 mg tablets
Hyoscine butylbromide(Buscopan)	10 mg tablets
Loperamid	2 mg tablets
Meloxicam	2 mg tablets
Metoclopramide hydrochloride	10 mg tablets, and sol. inj. 10 mg/2ml
Omeprazol	20 mg tablets
Promethazine	12.5 or 25 mg tablets
Pyridoxine hydrochloride	Solution for injection/tablets
Zopiclone	7.5 mg tablets

Registration

According to the Law on Drugs and Pharmaceutical Activity, all drugs may be manufactured, sold and used if they are registered in the country. Marketing authorizations are issued by an authorized state agency, such as the State Regulation Agency for Medical Activities (SARMA) (under the MoLHSA), and form the basis for entering registered drugs into the register. The list of registered drugs is available on the Agency's website *(20)*.

In October 2009, the Law on Drugs was amended to simplify the drugs registration procedures (Decrees Nos. 344/n and No 325/n of the MoLHSA). Medicines are registered in two ways: national procedures (for branded medicines and generics) and recognition procedures. For the national procedure, a manufacturer or importer must submit a set of registration documents based on which the agency will then carry out administrative, scientific and technical reviews. The registration process takes an average of three months and costs 500 lari (US$ 300).

The recognition procedure covers medicines that are formally recognized by the European Medicines Agency and certain other countries. WHO prequalification is not a recognized practice. An applicant manufacturer or importer has to submit a limited number of documents to SARMA for administrative review; within seven days a certificate of approval is issued to the applicant and information about legalization of the product is published in the Agency's register. The cost of registration under the recognition procedure is 2500 lari (US$ 1500).

Most anti-TB drugs are registered in Georgia, but the first- and second-line anti-TB drugs delivered with funds from the Global Fund through the GDF are not. Currently a waiver issued by the MoLHSA exempts all anti-TB drugs procured through the GDF. However, from 2015 the procurement of anti-TB drugs (first-line drugs) will gradually be transferred to state funds, in line with the quality requirements in operation. At present a parallel import system is permitted which, while it improves the availability of medicines and positively affects market competition, risks penetration by counterfeit drugs and a lack of control of the origin and quality of drugs.

Priority should be given to developing regulatory mechanisms for the import of anti-TB drugs. This was widely discussed at the meeting with officials in SARMA. The necessity for mandatory registration of anti-TB drugs used by the NTP, including new medicines, was taken into account.

Distribution

The distribution system for anti-TB drugs is not integrated into the national supply system for basic remedies Once the Director of the NCTLD has approved the requests from the districts, the anti-TB drugs (including medicines for treatment of adverse reactions) are distributed to all regions and primary health care facilities by the NCTLD (central pharmacy unit) as well as to the regional TB coordinators authorized to distribute medicines. The central pharmacy unit uses the following data to assess the need for anti-TB drugs: monthly and quarterly reports from TB service facilities which include the balances at the beginning and end of the quarter, the quantity of medicines received and used, expiry dates and information on the number of notified cases. The quantity of drugs delivered is determined on the basis of the needs in one quarter plus a buffer stock (100%) minus the available reserve for first-line anti-TB drugs. For second-line drugs, the estimated deliverable quantity is usually modified depending on the number of patients in treatment, treatment regimens and reported data on stocks at the facility and hospital level and may include the needs for one, two or three months without a buffer stock. The regional NTP units distribute drugs to TB services and primary health care facilities once a month. Reports on the consumption of anti-TB drugs and the available stock are used in allocating distribution.

A supervisor in the relevant region distributes the drugs to the service delivery point. The supervisor has the schedule for drugs deliveries, which is based on patients in treatment. It could be useful to establish a patient database at the regional level giving information about possible shortages in drugs or interruptions in treatment, to which other people could have access in the absence of a supervisor.

Once a quarter, a regional supervisor delivers the order for the first-line drugs with 50% buffer stock, and once a month the order for second-line drugs without a buffer stock, to the service delivery point. Usually up to a week passes from the placing of the order to the arrival of the drugs. Orders from the regional level are sent to the central level each quarter, and delivery of the anti-TB dugs takes one to three days. Regional drug distribution to the low levels is practised through a pull system.

When drugs are distributed to private primary health care facilities, they need to be authorized by the management team of the general health financial system. Even when drugs procured via the Global Fund grant are delivered to primary health care facilities, they become the property of the private sector. As a result, they cannot be redistributed from one facility to another. Private facilities are not interested in the management of anti-TB drugs. When a TB patient dies or interrupts treatment, the unused drugs accumulate and dates for their use expire.

To deal with this problem, a more efficient mechanism should be created for unlimited movement of anti-TB drugs, including ancillary drugs, within the TB service network. Some administrative options should be worked out by both sides, state and private. The most important thing is to create conditions in which TB patients will have access to diagnosis and adequate treatment.

Storage and inventory management

The NCTLD and the NCDC are responsible for storage and inventory management of drugs and other health commodities and products supplied with Global Fund financing.

The NCTLD central warehouse is spacious, well-equipped and meets international standards for storage of a large volume of medicines, including temperature and humidity control. Drugs requiring a cold chain are kept in a separate space. Regional storehouses visited have appropriate conditions for keeping anti-TB drugs. Treatment facilities, however, are a much greater cause for concern. They are frequently housed in old, dilapidated buildings completely inappropriate for health care and storage of drugs. A dialogue should be started as soon as possible between all the stakeholders (MoLHSA, NCTLD, NCDC, partners, private health sector) with the aim of providing guaranteed access for TB patients to qualified TB services in better conditions as well as proper storage of anti-TB drugs (to avoid damaging them).

The first expiry/first out method is used to control expiry dates and establish a system of regular stock tracking and reporting, but monitoring of consumption and management of expiry dates are weak. Both the June 2014 GDF mission and this mission in November 2014 found drugs that had expired or were at risk of expiry. All expired drugs were isolated from other drugs and the procedure for their disposal begun. Although national standards (No. 124/1438 from 10/10/2009) apply to the disposal of expired drugs, no special body is charged with this

task. Usually, a tender for disposal of expired drugs is announced among eligible organizations and the work is carried out by the body awarded a contract as a result of the tender. Unfortunately, the disposal procedure requires much paperwork and the signature or approval of certain authorities, which takes a long time and can entail more drugs expiring.

Coordination between clinical subdivisions of the NTP (such as the consilium) and a central pharmacy unit should be improved so as to enable a rapid response to risks related to expiry of drugs and medical commodities. At regional level, the inventory management system should be improved and conditions created for reallocation of anti-TB and ancillary drugs among primary health care facilities.

Use of TB medicines

Treatment of all forms of TB follows the national treatment guidelines, which were updated in 2013 in accordance with the latest WHO recommendations and introduced at all levels of the system. The NTP planned to revise the guidelines in early 2015 following new WHO recommendations *(15)*. Treatment of all forms of TB in children was revised and approved in 2014.

The NTP is using 2HRZE/4HR for adults and children. S is omitted from the treatment regimen. In 2012, the GDF paediatric grant covered child formulations, but the mission found no anti-TB drugs for children. The June 2014 GDF mission reported that no further orders for paediatric grants would be made. However, as stated above, since in 2013 it was reported that children with TB weighing 5 kg accounted for 20% (50–60) of all newly detected TB cases, the WHO team recommends that the new funding model concept note (at the end of 2015) should include the purchase of paediatric formulations for 50 cases of children with TB weighing up to 5 kg.

Treatment strategies and approaches for the management of M/XDR-TB are in accordance with the WHO recommendations. The standard treatment regimen is used and then adjusted once all DST results are received. Decisions regarding the start of treatment are made through the national MDR-TB consilium at central level. The GDF mission noted that treatment success rates are extremely poor (about 50%) and that loss to follow-up rates are 25–30%; data from 2014 show a loss to follow-up rate of 38% as a result of poor outcomes. A high rate of resistance to second-line drugs is also noted, which requires the immediate revision and optimization of the treatment regimen for drug-resistant TB with the use of new TB drugs (Bdq, delamanid). Following the recommendations of the GLC mission (in July 2014), the number of regimens has been severely pruned from 13 (GDF mission report, June 2014) to six (GLC mission report, July 2014).

To encourage adherence to treatment, M/XDR-TB patients receive monthly payments if they do not miss doses. Monitoring of drugs consumption is through the completion of individualized patient-specific reports for M/XDR-TB by supervisors at district and regional levels. These are aggregated by regional coordinators based on patient treatment monitoring cards and reported to the central level monthly. The report contains relevant information for each M/XDR-TB patient on second-line anti-TB treatment and includes the name and number of each drug

prescribed to the patient during the reporting month per indication as well as actual consumption.

Most patients receive ambulatory treatment. There are 188 MDR-TB beds and approximately 600 M/XDR-TB patients registered for treatment per year. The outpatient/community-based model of care is provided by the district TB specialist. If a patient lives in a remote area, local medical staff ensures delivery of DOT drugs by a TB specialist.

Pharmacovigilance

Pharmacovigilance is included in the law on drugs and pharmaceutical activity, which regulates the monitoring of adverse reactions. The Pharmacology Committee of the SARMA under the MoLHSA is responsible for the monitoring of adverse reactions to drugs permitted for medical use. The Committee has one specialist in charge of pharmacovigilance for the country.

Since 2007, Georgia has been an associate member of the WHO Programme for International Drug Monitoring and reports to the Uppsala Monitoring Centre on Adverse Drug Reactions. All information on adverse reactions received by the national pharmacovigilance officer must be sent to the WHO database in Uppsala.

The reporting form (yellow card) for spontaneous adverse drug reactions was approved by the MoLHSA. Doctors and pharmaceutical companies are responsible for sending adverse drug reaction reports to SARMA. However, the system is barely working because of insufficient authority and resources, the absence of a clear system for reporting adverse reactions, poor involvement by public health programmes and weak involvement by health providers; as a result, no reports are being sent to the WHO database in Uppsala. But at a meeting with officials from SARMA, the team was informed that the Agency had prepared a package of documents to enter additions to the Law on Drugs and Pharmaceutical Activities related to pharmacovigilance. If it is approved, significant improvements will be expected in that area.

The treatment of TB patients, particularly for resistant TB, is accompanied by manifestations of adverse reactions to varying degrees. It is well-known that anti-TB drugs are toxic, of poor tolerability and with a high probability of interaction between themselves.

Adherence to treatment remains problematic in TB care and interruptions associated with adverse reactions to medication are known to be often to blame. The NTP registers adverse reactions on the medical cards of TB patients and provides treatment in accordance with the national TB treatment guidelines. These include a separate chapter on management of adverse drug reactions, which is in line with WHO's recommendations. The NTP also registers adverse reactions in the special side-effects form for M/XDR-TB patients. These data are not, however, sent to SARMA and remain in the NTP. Ancillary drugs at inpatient and outpatient levels for M/XDR cases are provided through the Global Fund project, but the availability of drugs for treatment of adverse reactions for sensitive TB, particularly at outpatient level, remains a big problem which needs to be resolved as fast as possible.

Georgia was one of the first countries in the region to start using new anti-TB drugs (Bdq) through the compassionate use programme. It had been planned to start treating 40 pre-

XDR/XDR-TB patients, but the manufacturer approved significantly fewer patients. All adverse reactions were registered on the form provided by the manufacturer and sent to it. At present, the NTP is planning to continue selecting patients for treatment with the new anti-TB drugs using new treatment regimens in the settings of the programme. In this connection, the NTP has been making a great effort to ensure a clear pharmacovigilance system at all levels and its mandatory integration into the general TB surveillance system and the national system of pharmacovigilance. At the same time, the NTP needs technical assistance in defining the organizational structure and operational plan, developing guidelines for pharmacovigilance, and helping pharmacovigilance personnel improve their skills and competences to support the collection, analysis and reporting of data.

Quality assurance

SARMA is responsible for state quality control of the safety of pharmaceutical products. The existing provision on pharmaceutical manufacturing covers only some elements of good manufacturing practice (GMP) and there is no certifying agency that reviews or provides GMP certification. SARMA reviews, tests and certifies individual drugs, conducts selective control inspections and issues licences to manufacturers but does not issue any kind of GMP-type certification for the manufacturing process itself. The government has announced that it would adopt GMP standards by 2016 (that is, include GMP standards in legislation and establish a certifying body). It is currently developing policies and plans for adopting such a certifying agency; however, it was not known at the time of the mission whether these will be WHO's GMP standards or the European Union and Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme standards.

There is no provision and procedure for acceptance of WHO prequalified medicines, although following a recent consultation with the Regional Office, SARMA has signed a collaborative agreement with the WHO Prequalification Programme which will ensure the establishment of a fast tracking mechanism for WHO prequalified products. The team received an assurance from SARMA to help speed up the registration of anti-TB drugs, including new drugs supplied via the GDF with funds from the Global Fund. At present, all drugs are procured, in accordance with the requirements of the Global Fund quality assurance policy, from sources prequalified by WHO or the stringent regulatory authorities or approved by the Global Fund Expert Review Panel. The GMP certificate of WHO standards, as well as a certificate of analysis for each consignment, proves that the anti-TB drugs are of high quality. The NCDC as principal recipient bears responsibility for monitoring the quality of the drugs delivered. There is no post-marketing quality control system. In this connection, the mission recommends that the NCDC as principal recipient includes the monitoring of quality control of drugs to be procured with grant funds in its activities listed in the Global Fund new funding model concept note.

TB drug information management

The NCTLD receives regular and comprehensive reports from the regions and Tbilisi city regarding both patients and inventory data. In turn, the principal recipient (NCDC) receives the same reports from the NCTLD. This includes aggregated information, including on the number of patients in treatment at the time of the report, the treatment regimens and number of patients on each regimen, drug consumption during the reporting period and patient

enrolment. Reports are also submitted on first- and second-line drugs, anti-TB drugs and drugs for adverse reaction management. This information is updated monthly for second-line drugs and quarterly for first-line drugs. A double review of reports enables mistakes to be minimized and decisions to be taken promptly.

The standardized recording and reporting forms for drug management (opening stock, receipts, consumption, closing stock) are used by all TB services. Regional and district levels provide reports to the NCTLD monthly on a specially designed form that includes individualized patient-specific data and a summary report for the month for second-line drugs. Summary reports for first-line drugs are submitted quarterly and provide the balance of stock at the beginning and end of the quarter, the quantities received and consumed; the expiry dates, and the number of patients by treatment category notified for the reporting quarter. The central unit pharmacy possesses all the information (reports from the regions and on the stocks in store) necessary to make a consolidated report, but they do not aggregate the data and consolidated data are made available only when needed.

As explained above (Use of TB medicines), individualized patient-specific reports for M/XDR-TB are completed at facility (district) and regional levels by supervisors. They are aggregated by regional coordinators based on the patient treatment monitoring cards and are reported to the central level monthly. The reports contain relevant information for M/XDR-TB patients on second-line anti-TB treatment and include the name and number of each drug prescribed to the patient during the reporting month per indication as well as the actual consumption. This is a good primary source to measure adherence to treatment regimens.

The monthly and quarterly reports from all over the country are merged at the central unit pharmacy and updated according to the reporting schedule. The central unit pharmacy itself has an electronic supply chain management program that records stock levels, receipts and issues but only at the NCTLD level (there is no electronic connection between the regional and district units). The program is updated on a daily basis and provides information at any time about the existing stocks, including batch numbers, expiry dates, strength, packaging, quantity, unit price and total cost, manufacturer's name and country of origin. The two systems (reports and supply chain) complement each other and provide complete information on drug management countrywide, although it is acknowledged that there is no single national logistics management information system for TB.

Recommendations

• The submission for the pharmacovigilance system should be sent for governmental endorsement/approval as soon as possible.

• Finance should be guaranteed by the government for the continuous supply of high-quality first-line anti-TB drugs to treat sensitive TB after 2015.

• Regulations should be drawn up for the import of quality-assured anti-TB drugs and the avoidance of useless drugs (WHO prequalified and authorized for use by the stringent regulatory authorities).

• Regulations should be identified or laid down to allow the redistribution of medicines between facilities.

- Manufacturers and relevant partners should be engaged to facilitate the registration of new TB drugs (Bdq, delamanid) to ensure their safety.

- The status, scope of work, roles and responsibilities of the NCTLD central pharmacy unit should be specified.

- Human resources capacity at central and regional levels should be strengthened in the area of inventory management through training and monitoring.

- The GDF and manufacturers should be asked to cooperate in facilitating the registration of quality-assured anti-TB medicines to ensure the availability of international sources of quality-assured TB medicines for the country when it switches to government-funded procurement.

- Standard operating procedures should be developed for anti-TB drug management within the existing system of TB service provision. The distribution and inventory management systems and the storage and supervisory practices should be unified and standardized.

- Procurement of paediatric doses for 50 cases of children with TB weighing up to 5 kg should be included in the new application to the Global Fund (to be submitted in July 2015).

- The post-marketing monitoring of quality control of drugs to be procured for treatment of all forms of TB should be included in the activities listed in the Global Fund new funding model concept note.

- Coordination should be improved between the clinical subdivisions of the NTP (consilium) and the central pharmacy unit so as to enable a rapid response by the NTP to the risks related to expiry of drugs and medical commodities. At regional level the inventory management system should be improved to control expiry dates, and conditions created for anti-TB and ancillary drugs to be reallocated among primary health care facilities.

- A pilot project for pharmacovigilance should be developed and implemented at the NCTLD, in cooperation with SARMA and other partners engaged in this field, and gradually rolled out countrywide.

- A working group should be established to develop an operational plan for pharmacovigilance in NTP settings in cooperation with SARMA.

- A protocol on pharmacovigilance should be developed, including recording and reporting forms, registers and communication tools.

- Training in pharmacovigilance should be conducted for everyone (clinicians, health providers, nurses) involved in monitoring adverse drug reactions.

- Technical assistance should be given to the SARMA and NCTLD in developing active pharmacovigilance.

- It is suggested that the GDF might:
  - assist the MoLHSA and NCTLD in the planning and execution of procurement of first-line drugs with government funding for 2015;
  - supply prompt updates to the NTP/Global Fund principal recipient in relation to orders placed;
  - assist with registration of anti-TB drugs, including new drugs.

Infection control

The development and implementation of comprehensive infection control measures through the NTP should be one of the main components of proper service delivery and the key to ensure a safe environment in health care facilities. As an airborne-transmitted disease, TB can present a big risk of nosocomial transmission of disease in facilities without proper TB infection control measures.

Effective infection control practices are critical to prevent the transmission and further spread of MDR- and XDR-TB in health care and other congregate settings.

Georgia has taken very important steps toward improving infection control measures in specialized TB facilities. In the past two to three years, the NCTLD building has been renovated, including the departments for MDR-TB and sensitive TB treatment, and overall environmental improvements have been made. Posters on TB infection control are prominent in corridors and waiting areas at the NCTLD. Different categories of patient are distributed between different rooms.

In MDR-TB departments in the NCTLD and Zugdidi hospital, negative and positive pressure ventilation is in place. Separation of patients in wards is adequate and is organized according to resistance, smear conversion status and results of DST.

Good infection control practices were generally observed in wards: doctors and nurses used personal protective equipment correctly and patients using masks, especially when leaving their rooms and going outside the building. Respirators and gowns are available for visitors. The visiting policy is strict.

Patient triage in outpatient departments is working well. The NCTLD outpatient department has a separate entrance where TB suspects, follow-up cases, and contacts are seen. Triage is done by at least one nurse in the outpatient waiting area, who identifies coughing patients and gives out surgical masks. Severe coughers are fast- tracked. The outpatient waiting area relies on natural ventilation and ultraviolet germicidal irradiation.

Shielded ultraviolet germicidal irradiation fittings have been installed throughout the NCTLD hospital.

A national plan for TB infection control was drawn up in 2010 but has not been revised or approved. This is explained by the lack of effective coordination in the general management of the NTP and, in particular, in infection control issues between the NCDC and NCTLD. No coordinating mechanism (team) for infection control with the capacity to develop a national policy on infection control centred specifically on infection control in TB facilities has been established. The infection control plan should be revised and submitted to the government for endorsement; it is recommended that it be included in the national M/XDR-TB response plan.

Most of the TB units visited only have draft infection control plans which have not been approved by internal regulation.

No infection control committee has been established, and none of the facilities visited had a responsible person dedicated to infection control activities.

One major risk of integrating TB care into primary health care is the potential nosocomial spread of TB to the general population. Facilities have been given infection control standards, but they are unclear as to how or if they will be able to meet them. Site assessments revealed dangerous conditions for both TB patients and those seeking other services in primary health care facilities.

Additional training courses for TB specialists and primary health care workers will be necessary. The agenda for such courses should be revised and continue to be implemented. Plans and tools oriented towards improving infection control should be developed, together with a detailed plan for supervising and supporting infection control activities in primary health care facilities.

Recommendations

- At national level, a coordinating mechanism (team) should be identified for infection control with the capacity to develop a national policy on infection control, centred on the specific infection control measures that are needed in TB facilities to implement the prioritized recommendations.

- A comprehensive analysis should be conducted of the current situation regarding TB infection control.

- The national infection control plan for airborne diseases should be reviewed and updated annually to include: the current situation, activities for possible improvements, timelines, responsibilities, indicators and the budget to reflect the costs of implementing the plan, and plans to develop human resource capacity.

- Infection control practices should be monitored in TB facilities. A questionnaire should be developed for infection control, and supervision of infection control practices carried out regularly.

- Curricula should be developed for courses in TB infection control lasting two to three days, with specific elements for administrative, environmental and personal protection (for TB managers, epidemiologists and microbiologists).

- The training courses in infection control for all staff working in TB facilities and involved in the diagnostics, treatment or care of TB patients (nurses, technical staff) should be revised and extended for all personnel in TB facilities.

- Informational materials should be designed, printed and distributed to TB patients to improve their education in infection control (cough etiquette, leaflets, banners).

- Better opportunities should be found for improving infection control in TB institutions and the community.

- Administrative infection control measures should be strengthened in all TB and MDR-TB health facilities. Patients must use masks and personnel must use respirators. Infectious

patients must be isolated in special departments. Clean zones must be established for personnel. Where appropriate (in places attended by infectious patients), shielded ultraviolet lamps should be installed.

- A national TB infection control working group, a national infection control working plan and national infection control guidelines should all be approved.

- Monitoring mechanisms for infection control measures at facility level should be developed or updated with the involvement of all responsible organizations in the working group.

- Action-oriented plans and tools to improve infection control and a detailed plan for supervising and supporting infection control activities in primary health care facilities should be developed.

Surveillance, monitoring and evaluation

Surveillance system

The achievements in surveillance are as follows.

- A well-established TB surveillance system is in place, including human resources, a smooth flow of data and information and the consistent use of standard recording and reporting across different levels of the TB system.

- A functional real-time web-based electronic TB register is in place with countrywide coverage which allows the generation of standard and user-defined reports.

- The penitentiary surveillance system is well-integrated into national TB surveillance.

- Data quality assurance procedures are consistently applied from the peripheral units up to the national level.

- There is extensive coverage of routine first- and second-line drug resistance testing.

The following challenges remain.

- The proportion of deaths coded for ill-defined cause of death is very high, suggesting that the vital registration system is weak and its data cannot, therefore, serve as a direct measure of TB mortality (one of the key impact indicators of the burden of TB).

- Limited access to TB diagnostic services, resulting in a low case detection rate, suggests that some TB cases are not diagnosed or detected by the health care system. Thus, surveillance data cannot serve as a direct measure of the number of TB cases.

- Coverage of HIV surveillance among TB cases is restricted.

- There is no system of pharmacovigilance and, in general, a lack of awareness as to the level and burden of adverse events.

- The classification of treatment outcomes of MDR-TB cases is not in line with WHO's recording and reporting guidelines.

Surveillance structure

TB is a notifiable disease in Georgia and all detected TB cases are the subject of compulsory notification. The TB surveillance system consists of three vertical reporting/ administrative levels: national, regional and local TB units. Seventy local TB units (including the penitentiary system) are responsible for sputum collection, diagnosis, monitoring treatment and reporting the monitoring and treatment outcome information to regional centres on paper forms. Regional TB facilities are responsible for the collection of paper forms (on notification, treatment outcome and HIV) from the local TB units and entering data into the electronic register, as well as for monitoring the quality of data provided by the local TB units. The surveillance team at regional level includes nine regional data managers (one for each region and one in the penitentiary system) and four in Tbilisi. Overall oversight of the surveillance

system at national level is the responsibility of the NCTLD. The national surveillance team consists of the head of the surveillance department, an epidemiologist and a data manager. They are responsible for the maintenance of the electronic register at national level, validation of the data and checking their quality, staff training, development of guidelines and instructions on data management, development of recording and reporting forms, coordination of data exchange with the AIDS centre, NRL and other laboratories, and monitoring the functioning of the surveillance system.

Aggregated annual surveillance data related to notification, treatment outcome and routine drug resistance surveillance are posted on the NCTLD website *(21)* in the form of tables without any analysis, interpretation or recommendations for further informed action and decision-making.

A parallel system of recording and reporting functions through the public health units which collect single reports on new infectious TB cases detected and contact information, and forward the aggregated data annually to the NCDC.

Recommendation

• The NTP is advised to develop an annual analytical surveillance report taking into account recent WHO recommendations *(22)* and disseminate it widely, including posting it on the website for the better use of data for decision-making and advocacy purposes.

Vital registration system

Presidential Decree 31 of December 10, 2002 on Civic Registration is the main policy document regulating the current system of vital registration.

The civil registration of deaths relies primarily on a hand-delivery system. Once a death occurs, the relatives of the deceased ask his/her physician to provide medical notification of death. The death is recorded and a death certificate is issued by the State Office for Statistics based on the medical notification provided by physician. The registrar at the State Office for Statistics submits the certificate to the State Department of Statistics for filing under the national civil registration system. In parallel, aggregate health information, including births and deaths registered by health institutions, is sent to the Centre for Medical Statistics and Information under the MoLHSA. A second copy of the medical notification of death is sent to the public health centres at district and regional levels, who in turn send it on to the State Department of Statistics (Fig. 21).

Fig. 21. Death registration information flow, Georgia
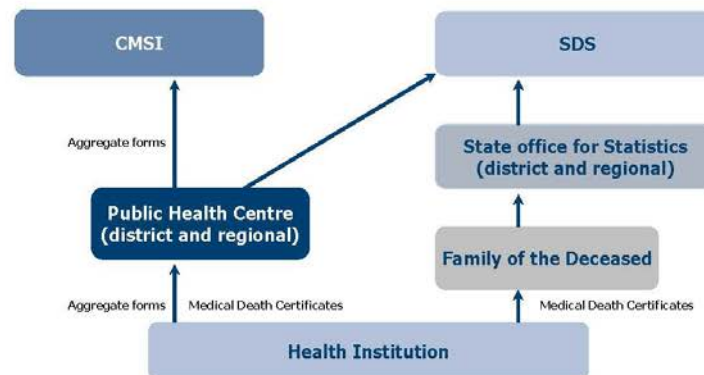
Source: Tefft *(23)*.

Since 2002 and with the support of international organizations, the government has undertaken a number of activities to improve the coverage and quality of the vital registration system, including establishing a web-based real-time electronic database and training health providers in certification of death with International Classification of Diseases codes and registration of death.

The Georgian medical death certificate was designed in line with WHO recommendations. It includes both the immediate and underlying causes of death. The underlying cause is most commonly used in the analysis and statistical tabulations of mortality data.

The electronic system is enhanced with a drop-down menu of International Classification of Diseases codes in Georgian, thus enabling all registrars to set the cause of death.

Completeness of death registrations has significantly improved. At national level annual statistics are generated on deaths and causes of death by sex and age for national and all subnational levels. These are published in the yearbooks produced by the National Statistics Office of Georgia *(24)* and in the yearbooks on health statistics produced by the NCDC *(25)*.

Based on World Bank data sources *(26)*, the estimated completeness of death registration in Georgia is close to 100%. Nevertheless, there are no quality assurance procedures in place for validating the causes of deaths. According to the annual reports of the vital registration system in 2012, 33.8% of causes of death in Georgia are classified as "Ill-defined and unknown causes of mortality" as defined in Chapter XVIII of the 10th revision of the International Classification of Diseases *(25)*.

Poor quality of recording of cause of death is explained by the fact that authorities and policy-makers are more interested in the prompt reporting and recording of all deaths for the management of social and administrative issues, such are regulating the payment of pensions, health insurance and subsidies. The existing regulatory system is not geared towards ensuring

the quality of recording of cause of death (only a short time is allocated for the reporting of death and there is no possibility of revising the cause of death in the system).

Thus, the vital registration system cannot serve as a reliable source for TB mortality surveillance unless action is taken to improve the coverage and quality of death registration.

Recommendation

• Even though the vital registration system is beyond the sphere of influence of the NTP, the MoLHSA could play an active role to improve it by initiating a dialogue with the governmental bodies and stakeholders involved to develop an action plan and proposal for legislative changes to improve the quality of death registration.

Recording, reporting and electronic registers

All service delivery points systematically use standardized TB data collection forms and tools. Data collection forms enable reports to be generated according to WHO recommendations covering all core variables, including age, sex, bacteriological confirmation, previous history, anatomical site of disease and year of registration. In addition, each TB case is assigned case identifiers which allow it to be linked to individual patient information from various data sources. The NTP has not yet made the transition to WHO's 2013 definitions and reporting framework for TB *(27)* and the previous recording and recording forms are still in use. However, because of the availability of case-based data at NTP level, it is possible to generate most of the revised indicators according to the 2013 revised framework.

The TB surveillance system is based on paper forms for entry on to the electronic case-based register designed for TB and M/XDR-TB individual case notification and treatment outcome monitoring. The application was developed with the support of the French company MEDES. It is a real-time web-based application with nationwide coverage, including the penitentiary system. The electronic TB register allows for the generation of national surveillance statistics on TB case notification disaggregated by core variables, MDR notification and regular rifampicin-resistant/MDR and XDR-TB treatment outcomes.

Once a patient is confirmed with TB, an individualized TB form (TB-10/12) is completed which serves as the main data source for transferring information into the national electronic register. The first page of the form includes data related to the patient's identity, demographics and laboratory test results. It is completed once the patient is diagnosed with TB, and is sent by courier to the regional TB centre for data entry into the electronic register. The second page is completed by the TB facility where the patient completes his/her treatment. Once the treatment outcome is known, the second page is sent to the regional data manager for data entry into the electronic register. The third page, which contains identical information to the second page, is filed at the local TB facility. The main data source for the national electronic register for MDR-TB notification and treatment outcome monitoring is the hospital admission form and the important dates form (for second-line treatment). These are individualized forms for patients who start second-line treatment, and contain broader information including health and risk factors (such as smoking, diabetes and employment status).

The other standard recording and reporting forms used are individual TB treatment forms for regular (TB 01) and MDR-TB patients (TB 01 MDR), the TB facility register (TB-03), the second-line treatment register for TB facilities (TB 02) and HIV forms (N1). The latter is used to submit HIV test results from voluntary counselling and testing centres to regional database managers. Reporting forms include the quarterly case notification form (TB 07) and the quarterly treatment outcome form (TB 08), which are submitted quarterly by all district-level TB facilities to regional NTP units for onward transmission to the NCDC. Paper reports are, however, used for cross-checking aggregated data with the reports generated by the electronic register. National surveillance statistics are generated by the NCTLD surveillance unit following the data validation process. There is no interim analysis of treatment outcome monitoring either for regular or MDR-TB cases. This makes it difficult to detect problems quickly (such as hot-spots of loss to follow-up) in order to take appropriate measures and evaluate the effectiveness of treatment algorithms. Neither does the system allow for the collection of information on delays in starting TB and MDR-TB treatment, as recommended by WHO *(15)*, which could serve as an important indicator to detect regions with suboptimal programmatic performance. As there is also no system for monitoring adverse events, the burden and causes of drug side-effects on TB management remains unknown.

The NRL and the second-level culture laboratory in Kutaisi have maintained a web-based electronic laboratory register since 2008. This register includes fields required for the patient's identity, purpose of testing, treatment of category, results for microscopy, culture and DST per methodologies (solid liquid media) and corresponding dates, as well as results for new rapid diagnostic technologies such as GeneXpert and line probe assay. Laboratory request forms serve as the main data source to enter patient-related data into the register. The laboratory register is not linked to the electronic TB register, so the DST results from the laboratory register have to be entered manually into the TB register, requiring additional effort and delays in data transfer.

A further drawback to the surveillance system is that it has no module for drug management. Modifications to the electronic system require the services of an external consultant.

To improve the existing electronic recording system, an electronic TB health information system platform was developed by a local information technology company under the USAID-funded TB Prevention Project. The server will also be maintained locally. New software includes five interlinked modules: registration, treatment monitoring, laboratory results, drug management and statistics. The platform permits geographic allocation and the application of time-tagging functions. The module will allow a quick data exchange between clinicians and epidemiologists on newly registered patients, contacts to be screened and DOT compliance. It is in line with the revised WHO recording and reporting framework. The new TB information system was being piloted at the time of the mission. With the introduction of the new electronic recording system, the number of users should increase significantly. However, piloting of the software, distribution of information technology equipment, training, internet connections and maintenance of the system are fully covered by the donor organization, which raises some concerns related to its sustainability and continued maintenance.

Recommendations

• The NTP is advised to ensure the transition to the WHO 2013 revised definition and reporting framework. This should include the revision of recording and reporting forms, followed by their printing and distribution, training of the staff engaged in data recording and analysis, and revision of the monitoring and evaluation plan.

• The NTP should continue piloting the new electronic platform and, in close collaboration with USAID/URC, should plan for the smooth and transparent transition to the new system with the mandatory addition of pharmacovigilance, laboratory and pharmaco-management modules. The transition plan should be based on a careful assessment of the feasibility of engaging such a large number of data users and their literacy in information technology, as well as the prospects for long-term sustainability including the necessary financial and human resources with, ideally, a reliance on domestic funds.

Data quality

To assess the quality of the data produced by the surveillance system, the WHO-recommended checklist for standards and benchmarks was used. Of 12 standards for TB surveillance applicable to Georgia, five were met, four were partly met and three were not met (Table 13). A more detailed description of the checklist is provided in a separate report; here some of the key findings from field visits are outlined.

Table 13. Summary of standards and benchmarks for TB surveillance, Georgia, November 2014

	Standard	Met	Partly met	Not met	Not applicable
B1.1	Case definitions consistent with WHO guidelines	X			
B1.2	TB surveillance system designed to capture a minimum set of variables for reported TB cases	X			
B1.3	All scheduled periodic data submissions received and processed at the national level	X			
B1.4	Data in quarterly reports are accurate, complete and internally consistent				X
B1.5	Data in national database are accurate, complete, internally consistent and free of duplicates	X			
B1.6	TB surveillance data are externally consistent	X			
B1.7	Number of reported TB cases internally consistent		X		
B1.8	All diagnosed cases of TB are reported		X		
B1.9	Population has good access to health care			X	
B1.10	Vital registration system has high national coverage and quality			X	
B2.1	Surveillance data provide a direct measure of drug-resistant TB in new cases		X		
B2.2	Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases		X		
B2.3	Surveillance data for children reported with TB are reliable and accurate			X	

Several procedures ensure the quality of data collected at various levels: At district and regional levels, they include regular monitoring visits from national to regional and from regional to district level, recalculation, rechecking the data and cross-checking the paper registers with electronic registers and laboratory registers. Other data quality assurance considerations at

regional level are related to the design of the electronic databases: thus, the electronic database is designed so that during data entry some data validation checks are undertaken to prevent errors. Validation of the data at national level includes de-duplication and checking for consistency and completeness.

Despite the application of various methods of data quality management, the surveillance system has no formal standard operating procedures to detect problems related to data quality. It was found that at the regional level each data entry specialist had his/her own way to check data quality. Detected and corrected errors are not recorded.

Data tabulation of notified TB cases during the first quarter of 2013 indicated that all key variables were fully complete and consistent. For the whole year 2013, however, 116 potential duplicates (patients with the same surname, name and age but different identifiers) were detected (2.7% of all cases). Cross-checking of the electronic database with the paper TB registers at the sites visited showed that all cases recorded in the electronic database were also in the paper registers. The surveillance data generated were in general complete for core variables and consistent and allowed for the provision of up-to-date statistics, which form the main source for the national statistics on TB.

Year-on-year changes of all TB notification rates for the period 2009–2013 disaggregated by geographic areas were in general within ±10% for all TB cases (with some not substantial exceptions), indicating internal consistency (Fig. 22). However, there was a very sharp (about 19%) decrease in the number of new smear-positive pulmonary TB cases at the national level between 2011–2012 and 2012–2013. At regional level unusual fluctuations in new smear-positive TB cases were observed in Kakheti (-37%), Imereti and Samckhe-Javakheti (-23% in each) and in prisons (more than -50%), which is unusual for TB epidemiology in the absence of major external factors.

Fig. 22. Year-on-year change in rate of notification of new smear-positive pulmonary TB cases disaggregated by regions, Georgia, 2009–2013
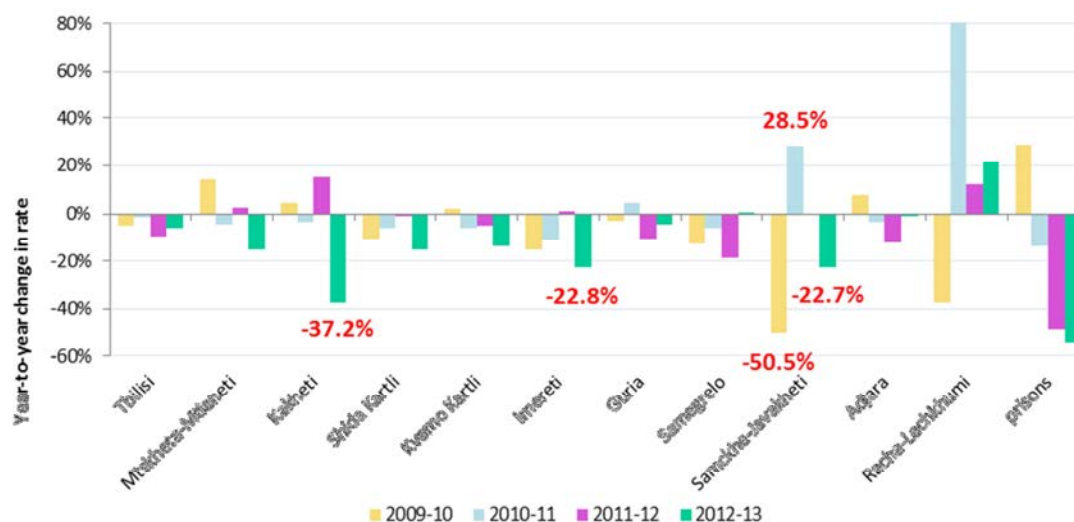
One of the explanations for such a decrease at national level, according to local experts, was the amnesty in the penitentiary system, which accommodated about 21% of the TB cases notified in 2012. The release of the vast majority of prisoners, combined with frequent cycles of active screenings of TB cases and a decrease in overcrowding in prisons, led to a dramatic decrease in the number of TB cases in the penitentiary sector, which was reflected in national surveillance as the share of prison TB in national notification was substantial. However, because the sharp decrease in TB in the civilian population across all geographic regions coincided with the privatization of health services, there is concern that the decrease in notification of smear-positive pulmonary TB cases is not related so much to a true decrease in the number of TB cases so much as to increased under-detection and barriers to diagnostic services.

The population has limited access to health care: the levels of out-of-pocket payments and under-five mortality are high, indicating that access to health care may not be adequate. This means that many cases of TB remain undetected by the health systems and surveillance data cannot provide a direct measure of TB cases occurring in the population. Thus, the ratio of presumptive to diagnosed TB cases is extremely low: in 2011 it was only 2.0 in the civilian population and despite a small increase to 2.7 in 2013, the number of presumptive TB cases remains extremely low. At the TB facilities visited by the mission, up to 30–40% of presumptive TB cases had been diagnosed with TB, indicating that only patients with apparent clinical signs and symptoms are referred TB facilities for diagnosis. This suggests that TB is rarely considered a possible diagnosis for patients with cough at primary health care level and probably a considerable proportion of TB patients remain undiagnosed or only diagnosed after a delay.

Despite a notable increase in HIV testing coverage in recent years, only 62.5% of TB cases have documented HIV test results.

TB surveillance in children does not meet the WHO benchmarks of the ratio for the age groups 0–4 to 5–14 years being within the range of 1.5–3.0. According to routine notification data, of 183 children diagnosed with TB in 2013, 51 were aged under five years and 132 were aged 5–14 years. The number of children diagnosed with TB aged 0–4 years is, therefore, much lower than the number of children aged 5–14 years. Thus, the ratio of TB cases in the groups aged 0–4 to 5–14 years is 0.4. This is far below the expected level, suggesting that many cases of TB in children aged under five years probably remain undetected.

While all definitions applied were in line with WHO recommendations, issues were noted in the current classification of treatment outcome. The main reason for unfavourable treatment outcomes of MDR-TB cases was loss to follow-up: more than one in three patients enrolled into second-line treatment was reported as lost to follow-up. However, it was noted that many patients classified as lost to follow-up interrupted their treatment due to adverse events. Patients with persistent positive smear who interrupted their treatment after several months of intensive treatment were also classified as lost to follow-up: under the WHO revised framework such patients would be classified as failed.

Recommendations

- The NTP is advised to develop standard operating procedures (other than cross-checking) for data validation and cleaning for each reporting level and ensure that they are implemented.

- Consideration should be given to conducting operational research (data quality audit) according to WHO guidelines to evaluate the extent of the underreporting of diagnosed TB patients.

- The trends in notifications from routine surveillance should be carefully analysed, disaggregated by geographic administrative levels and other core variables. Regions reporting unusually sharp changes in notification should be assessed carefully for possible gaps in human resources, accuracy of surveillance data, quality of diagnostic services or access to services for prompt interventions.

- There is ample room to increase HIV testing coverage. The introduction of rapid HIV tests might improve the situation. The TB and AIDS centres should work more closely to exchange HIV/TB data.

- Reasons for the small number of children aged under five years should be investigated and potential reasons should be hypothesized jointly with paediatric experts. The NTP should focus on childhood TB diagnosis and organize training in childhood TB and its diagnosis for paediatricians throughout the country. The NTP should strengthen collaboration with the Integrated Management of Childhood Illnesses programme to promote application of the programme's diagnostic algorithms for children with cough and severe disease.

- Operational research should be conducted to assess the reasons, risk factors and delays in TB diagnosis.

- To improve appropriate differential diagnostics, case management and prompt referral of patients with respiratory infections, including TB, at primary health care level, the MoLHSA is advised to introduce, develop and implement the practical approach to lung health (PAL) strategy. This could include the establishment of a national working group on PAL, adaptation and development of national PAL guidelines and training materials and a baseline survey on respiratory care management.

- TB doctors should be made more aware of the importance of correctly classifying the treatment outcomes of MDR-TB patients in line with WHO case definitions.

Supervision, monitoring and evaluation of the NTP

The achievements in supervision, monitoring and evaluation of the NTP are as follows.

- Regular field supervision and monitoring visits are organized across the country

- The National TB Strategy and Operational Plan for 2013–2015 in general applies sound standard indicators that accurately reflect the performance of all components of the NTP.

- In 24 of 39 programme performance indicators with available data, progress towards the target or target was achieved.

The following challenges remain.

- Monitoring of HIV/TB collaborative activities is not included in the scope of supervisory monitoring visits.

- The monitoring and evaluation component is fully financed by donors, which raises some concerns regarding its long-term sustainability.

- Despite the existence of a performance plan for 2013–2015, no programme performance report has been produced by the NTP to assess the trends towards the targets set.

- Monitoring of the treatment outcome of MDR-TB cases is questionable due to overestimation of cases lost to follow-up.

- In 15 of 39 programme performance indicators with available data, the mid-term value of the performance indicator showed a negative trend compared to the baseline (value of indicator deviated from the target set) or there was no change compared to the baseline.

Field supervision

The monitoring and evaluation system works on three levels: district, regional and national levels. A functional monitoring system includes staff (epidemiologist/clinician, laboratory and pharmacy management officer), frequency, tools and a feedback system. Supervisory visits from national to district level are made regularly by team of specialists using standards checklists. Quarterly supervisory visits are made by regional TB coordinators to each of the district TB facilities.

Checklists are used to monitor each level of service covering aspects such as clinical management, data management, infection control, and laboratory and drug management. Supervision of HIV/TB collaborative activities is not, however, part of supervisory field visits. The checklists are used to provide feedback and recommendations. A copy of the checklist is retained at the facility so that it can be followed up.

Supervisory visits are fully covered by donor funding, which raises some concerns related to their sustainability.

Recommendation

- Monitoring for collaborative HIV/TB activities should be included in the scope of work of national and regional monitoring teams. The results of the monitoring and evaluation visits should be reported to the national TB and HIV centres and the NCDC.

Monitoring and evaluation of TB control

According to the National Tuberculosis Strategy and Operational Plan 2013–2015, TB control is supposed to be monitored through a set of 55 indicators covering all aspects of TB control. The vast majority of these are adopted from the WHO regional M/XDR response plan and are sound enough to evaluate the progress of TB efforts. However, there was no report available at national level on the annual performance of the NTP against the targets. Comments (if any) for specific indicators are included in Table 14.

Table 14. Monitoring and evaluation framework of TB control, Georgia, 2013–2015

No.	Indicator / Description	Baseline 2011	Target 2015	Mid-term progress	Comments
1	No. of deaths attributable to TB (all forms) registered in a specified period per 100 000 population	4.5 in 2012	4.2	7.0 ↑	WHO no longer recommends setting estimates as programme performance targets because of large uncertainty. However, TB death rate could be an excellent indicator in countries with good quality and coverage of vital registration system.
2	Percentage of previously treated TB patients with MDR	32%	12%	38% ↑	
3	Percentage of MDR-TB cases with XDR	6%	Decrease	19.2 ↑	
	TB case detection				
4	Notification rate of new and relapsed cases	105	102	79 ☺	The definition of relapsed cases changed, but this report does not take account of this revision. Data are comparable.
	TB case detection in general medical facilities				
6	No. of patients with suspected TB referred from primary health care providers	Unknown	20% increase	N/A	
7	No. of suspected TB cases with sputum examined	13 410 (9 575 only civilian)	No target	11 553 (21%) ↑	Comparison is done for presumptive cases in civilian population only (assuming 9 575 in 2011).
8	Percentage of smear-positives among suspected cases with sputum examined	2 148 1 552/9 575 =16.2%	No target	1 289/ 11 553 =11.1% ↑	Because number of microscope examinations was available for civilian population only, the numerator was also taken for civilian cases
	TB case detection in contacts				
9	No. of TB cases identified among contacts	104	No target	102 ☺	
10	No. of contacts of smear-positive TB cases screened for TB	3 475	No target	4 823 ↑	
	TB case detection in prisons				
11	No. of TB cases notified from prisons	1 172	No target	228 ↓	Rate instead of number is recommended (rate was reduced from 4.9% to 2.3%).
12	No. and percentage of prisoners screened for TB at entry	8 446 (97%)	97%	N/A	
	Detection of drug resistance				
13	MDR-TB cases detected as percentage of those estimated among TB notifications	63%	85%	55.6% (400/720) ↓	
14	Percentage of previously treated patients with first-line DST at the start of retreatment	52%	100%	87.5% (527/602) ↑	100% target set is unfeasible. Always will be pulmonary TB cases without

Indicator		Baseline 2011	Target 2015	Mid-term progress	Comments
No.	Description				
					bacteriological confirmation.
15	Percentage of new patients with first-line DST at start of treatment	83%	100%	67.5% (1 629/2 412) ↓	100% target set is unfeasible. Always will be pulmonary TB cases without bacteriological confirmation.
16	Percentage of MDR-TB patients with second-line DST	93%	100%	92.3% (369/400) ☺	
	Laboratory				
17	No. of smear microscopy laboratories for which external quality assurance was carried out; percentage of all laboratories performing smear microscopy	29 (100%)	100%	11 (100%) ☺	
18	No. and percentage of smear microscopy units for which external quality assurance was carried out that demonstrated acceptable performance	29 (100%)	not applicable	10 (90.9%) ↓	
19	No. of culture laboratories for which external quality assurance was carried out, percentage of all laboratories performing culture	2 (100%)	not applicable	0 (0%) ↓	No external quality assurance of culture is done.
20	No. of culture laboratories for which external quality assurance was carried out, percentage of all laboratories performing culture	2 (100%)	not applicable	N/A	No external quality assurance of culture is done.
21	DST laboratories with external quality assurance according to international standards	1 (100%)	100%	1 (100%) ☺	
22	Percentage of DST laboratories achieving >95% proficiency for Z and R (via external quality assurance)	100%	100%	100% ☺	
23	No. and percentage of TB patients with a sputum culture performed at diagnosis via automated MGIT on liquid media	2 834 (65%)	90%	N/A	
24	Percentage of pulmonary cases that are culture-positive	71%	Increase	72.1% (2 173/3 014) ↑	
	Treatment				
25	Percentage of new smear- and/or culture-positive pulmonary TB patients successfully treated	76%	85%	74.4% ↓	Indicator needs to be revised to be aligned with the WHO 2013 revised framework.
26	Percentage of new TB patients lost to follow-up, transferred or not evaluated	10.4%		8.0% ↓	
27	Percentage of previously treated TB patients successfully treated	61%	Increase	73.8% ↑	Relapse not included in 2012 cohort per revised reporting framework.
28	No. and percentage of TB patients on first-line TB treatment receiving food vouchers at least once in the reporting period	3 071 (56%)	76%	N/A	
29	Treatment success rate, laboratory confirmed R-resistant TB and/or MDR-TB	52% in 2010	58%	50% (305/611) ↓	
30	Percentage of MDR-TB patients dying during treatment	8%	<10%	5% (31/611)	

No.	Indicator Description	Baseline 2011	Target 2015	Mid-term progress	Comments
				↓	
31	Percentage of MDR-TB patients whose treatment fails	6%	<10%	3% (18/611) ↓	Concerns related to validity of data (see data quality section).
32	Percentage of MDR-TB patients lost to follow-up, transferred out or not evaluated	31%	<5%	36% (221/611) ↑	Concerns related to validity of data (see data quality section).
33	Interim treatment success of MDR-TB patients	Not available	75%	N/A	
34	Percentage of confirmed MDR-TB cases starting MDR treatment in programmes following international guidelines	Unknown	100%	100% ☺	
35	Treatment success rate among prisoners with new laboratory-confirmed pulmonary TB	84%	85%	71.4% ↓	
36	No. of MDR-TB patients receiving incentives	300 (42%)	80%	N/A	
37	Stockouts of first- or second-line drugs	None	None	None ☺	
38	No. of health facilities with TB care protocols	Unknown	100%	N/A	
39	No. of health facilities conducting TB clinical audits	Unknown	50%	N/A	
	Governance				
40	Gap in financing of core elements of TB control	Unknown	Decrease	No gap reported	
41	Percentage of total annual funding needs financed by domestic sources	41%	≥70%	48% in 2012 ↑	
42	Reporting units submitting prompt reports according to national guidelines	100%	100%	100% ☺	
	Human resources				
43	Percentage of TB service delivery points that provide excellent/good performance during performance evaluation visits	Unknown	95%	N/A	
44	Percentage of penitentiary facilities with appropriate practices for TB detection and DOT documented during performance evaluation visits	Unknown	95%	N/A	
	Infection control				
45	Ratio of TB notification rates in health care workers versus general population	Unknown	≤1	4.4 (428/96) ↓	4 TB cases in health care workers reported out of 935. 4320 TB cases in general population (4 487 200).
46	No. of facilities with infection control plans based on risk assessment	Unknown	100%	N/A	
	Empower people with TB and their communities				
47	No. of TB patients provided with DOT by trained community members	Unknown	No target	0	Only health care workers provide DOT.
48	No. of small grants implemented by nongovernmental organizations	Unknown	10	N/A	
	7. HIV/TB				
49	Percentage of TB patients who are HIV-	2%	Decrease	2.1%	

No.	Indicator Description	Baseline 2011	Target 2015	Mid-term progress	Comments
	positive			☺	
50	Percentage of notified TB cases tested for HIV	46%	100%	62% ⬆	
51	Percentage of HIV-positive TB patients receiving ART	76%	>95%	89% ⬆	
52	Percentage of HIV-positive TB patients receiving cotrimoxazole	56%	100%	89% ⬆	
53	Percentage with treatment success among HIV-positive new TB cases	40%	Increase	57.1% (12/21) ⬆	
54	No. of intravenous drug users screened for TB	1230	1 750	N/A	
55	No. and percentage of people living with HIV attending HIV care services who were screened for TB at the last visit	387 (100%)	100%	100% (2 369/2 369) ☺	
56	No. and percentage of people living with HIV starting IPT	61 (16%)	70%	21% (92/439) ⬆	

Recommendations

• Key policy documents, including a monitoring and evaluation plan and the NTP strategy and operational plan should be updated according to the WHO revised definitions and reporting framework to include the full minimum set of M/XDR core indicators, including: median delay in MDR detection, median delay in start of MDR treatment and treatment interim indicators (proportion of MDR patients converted at the sixth month after start of R-resistant/MDR treatment). Such modifications would allow prompt identification of the gaps in the management of cases and enable prompt interventions. Performance indicators should also be revised according to the revised definitions and reporting framework.

• NTP performance targets should not be set based on estimated indicators (such as the estimated mortality rate or the incidence rate) because of considerable uncertainty. Instead, the NTP should set targets that are directly measurable. The performance framework should include annual target indicators to enable the annual evaluation of progress against interim targets.

• Monitoring for collaborative HIV/TB activities should be included in the scope of work of national and regional monitoring teams. The results of the monitoring and evaluation visits should be reported to the national TB and HIV centres and the NCDC.

• Basic indicators for pharmacovigilance (the surveillance of adverse effects of treatment) should be included in the monitoring and evaluation framework to quantify treatment-related harm.

• A strategic analysis framework should be developed for TB data, including applications for public health policy and action. Data should be analysed accordingly and interpreted and distributed widely (including posting on the website).

Health system and TB control

Health system

The achievements in the health system and TB control are as follows.

- The basic benefit package was extended to the whole population in 2013.

- The Social Security Agency provides a firm basis to develop a more active purchasing role for the health services and to manage more complex payment methods.

- The current mandate to manage several public policies beyond the health policy makes it possible for the MoLSHA to create effective intersectoral collaboration for improving health.

- All important health system functions are covered by a dedicated governmental organization.

- Several organizational mechanisms enable stakeholders to take part in the decision-making process.

- Ambulatory care has been integrated into the general health care system.

- In all key institutions there is a good understanding of advanced health policy concepts, including the possibilities and constraints of health finance.

The following challenges remain.

- The stewardship roles of the key stakeholders involved are blurred and accountabilities are not comprehensively clarified and regulated.

- Unresponsiveness can be observed from the responsible organizations, especially as regards quality.

- Although human resources and care facilities are widely available, there are wide variations in the quality of infrastructure in both the private and public sectors.

The health system has undergone several radical changes in recent years. First, a mandatory social health insurance system was introduced and operated from 1995 to 2004. Subsequently the social health insurance system was privatized and multiple insurance companies became the norm for purchasing prepaid health services, although out-of-pocket payments remained the dominant form of paying for health services (HF1). In fact, the level out-of-pocket payments was already very high under the social health insurance system. The shortcomings of that system in collecting adequate resources to pay for the public health services was used as one of the arguments for introducing a multiple insurance system. Finally, following the election in 2013, the new government decided to try again to set up a single non-profit-making mandatory health insurance fund *(28).*

In parallel with the privatization of the social health insurance system, from the second part of the 1990s the government incrementally eliminated the restrictions on private ownership and centralized hospital governance and opened the way for the privatization of the health facilities. After 2007 all state-owned hospitals were privatized. One comparative health system

review states that insurance companies own more than 40% of all hospitals in Georgia *(28)*. In 2012, TB ambulatory care was integrated into the network of private health facilities, while the state sustained its full ownership in the TB-specific hospitals.

In order to replace the dominant reason for out-of-pocket payments in the system, which caused high inequalities in access to care, the government decided to expand basic coverage of health care for the whole population. From 2008 to 2013, state-funded medical insurance covered only households living below the poverty threshold, but in 2012 other social groups with limited or no income such as students, children and disabled people were included, extending the coverage to 45% of the population *(28)*. Finally, between February and July 2013 both the scope and breadth of the benefit package under the universal health coverage programme was extended to all the formerly uninsured population and included primary health care services, some selected specialized services and emergency medical care *(28)*. The introduction of this minimum basic benefit package, coupled with the increase in public expenditure on health, undoubtedly addressed the low take-up of health services and was an important milestone in increasing access to these services.

The mission observed that although human resources and care facilities are widely available, there are wide variations in the quality of the infrastructure in both the private and public sectors. Poor conditions in some facilities indicate very low responsiveness from the owners in some places and low effectiveness of quality control in some aspects of the care.

Privatization also involved wide variations in the salaries of medical professionals as pay was no longer regulated centrally. These variations make TB an especially unattractive field to work in, which raises concerns for the sustainability of adequate human resources.

Fig. 23 and Table 15 summarize the key stakeholders with their most important responsibilities and shows the most important relationships between the key stakeholders in the health system (see more in the section on governance below).

Fig. 23. Chart of the overall health system, Georgia, 2014
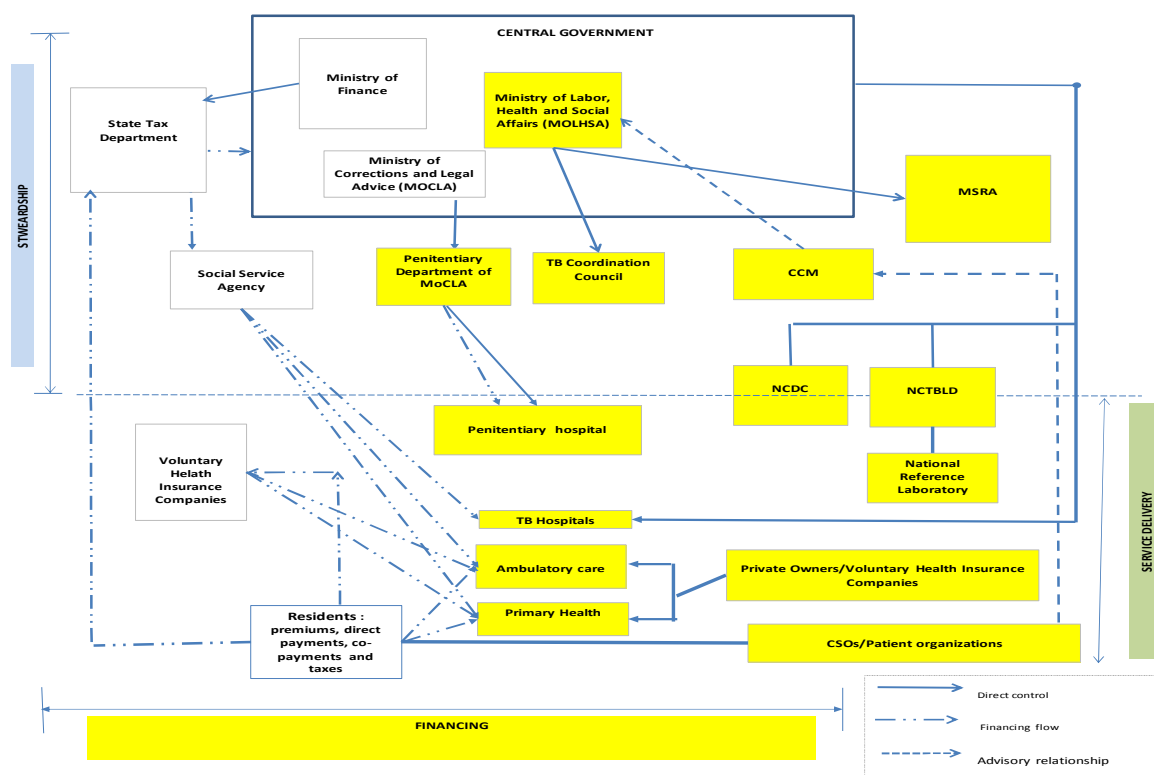
Table 15. Key stakeholders in TB control in the health system perspective

Key actors	Key responsibilities
MoLHSA	Oversight and evaluation of the NTP. Regulation and overall strategic planning.
Social Service Agency	Acts as third party payer for public services under the aegis of the MoLHSA
NCTLD	Provides tertiary care. Acts as leading agency to develop professional standards for treatment and supervise the work of the regional coordinators. According to the NTP strategy dated January 2013, the NCTLD is supposed to act as the central unit of the NTP. Compiles international and national reports.
NCDC	Responsible for contact-tracing as well as for part management of TB surveillance and programme evaluation. Compiles national reports.
Ministry of Corrections	Responsible for providing and financing care in prisons under the supervision of the NCTLD.
SARMA	Issues licences and permits for health care facilities. Investigates patients' complaints.
Public TB hospitals	Provide tertiary care.
Private ambulatory care and primary health care integrated into the general health care system.	Provides ambulatory care.
Civil society organizations	Advocacy, communication and social mobilization.

With specific reference to TB care, the self-reported data in Table 16 for the estimated percentage of new smear-positive, smear-negative, extrapulmonary and MDR cases from the

countries reporting through the WHO data collection form show marked variations between the countries. The data in Table 16 do not, however, reflect the true extent of hospitalization as they do not take into account the possible hospitalization of suspected cases and of readmitted cases. In 2013, the hospitalization of new smear-positive cases was 70%, but the average length of stay was very short (25 days) compared to other countries. The reported data for the number of visits need to be revised as the NTP reported the cumulative number and not the average number of visits by a patient.

Table 16. Self-reported indicators on utilization of services in TB control, Georgia, 2014

Countries	Average number of visits by a patient during treatment			Estimated percentage of cases that are hospitalized (%)			Average length of stay in hospital (days)		
	New smear-positive	New smear-negative/ extrapulmonary	MDR-TB	New smear-positive	New smear-negative/ extrapulmonary	MDR-TB	New smear-positive	New smear-negative/ extrapulmonary	MDR-TB
Armenia	112	104	312	94	78	75	60	50	90
Azerbaijan	NA	NA	NA	NA	NA	NA	NA	NA	NA
Belarus	180	180	540	100	80	100	60	30	180
Georgia	**NA**	**NA**	**NA**	**70**	**30**	**90**	**25**	**10**	**60**
Kazakhstan	80	70	220	95	84	35	80	60	120
Kyrgyzstan	104	104	560	60	34	100	84	84	146
Republic of Moldova	116	116	336	95	50	96	56	40	140
Tajikistan	168	168	604	50	30	30	56	70	180
Turkmenistan	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ukraine	100	120	480	100	30	100	90	50	180
Uzbekistan	168	168	612	70	60	40	56	56	90

Recommendations

• Providers should be subject to stronger quality control to improve their responsiveness in TB control.

• More should be invested in creating more effective collaboration with other public policy sectors. Sick payments and workplace protection together with cash assistance to those in prolonged treatment would be highly important.

Governance and management

The achievements in governance and management are as follows.

• A well-designed strategy with specific targets and baselines was approved by the Global Fund country coordinating mechanism in January 2013. The strategy includes an action plan and a detailed table of accountability and responsibilities in TB control.

• A network of central and regional coordinators of the NTP has been set up with the technical and financial support of the Global Fund.

• A new coordination committee was officially established at the time of this NTP review.

The following challenges remain.

- Although both the NTP strategy 2013 and the national health care strategy 2011–2012 emphasize the importance of health performance assessment, no comprehensive performance assessment is carried out or, therefore, published annually either by the MoLHSA or the NTP.

- The NCTLD has no clear authority as to how to control the quality of care, how to initiate corrective action or how to coordinate action to improve performance. A lack of clarity in roles and responsibilities was also seen in the NTP strategy 2013–2015.

- The mission understood that the new committee does not involve the focal points or representatives of other public health programmes or public policies in its work.

The main elements of governance and the policy cycle of TB control are illustrated in Fig. 24. The strategy is well-designed, with specific targets and baselines, and was approved by the Global Fund country coordinating mechanism in January 2013. The Minister of Health chaired sessions of a special working group of the Country Coordinating Mechanism. It is not clear, however, in what way other ministries will support this strategy.

Fig. 24. Main stakeholders in the policy cycle of TB control, Georgia, 2014
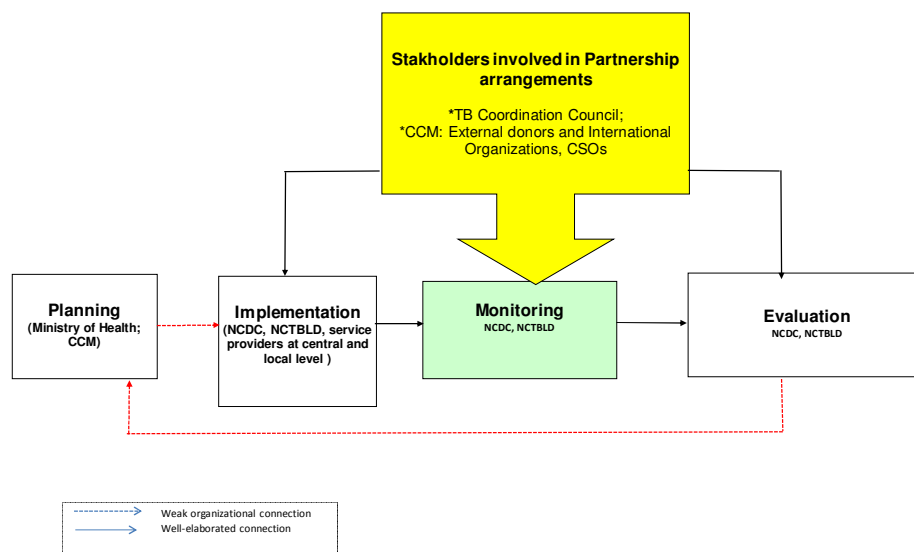
Although the health system performance assessment has been institutionalized in Georgia, it is only occasionally used in evaluating and reporting on the overall performance of the health system. TB control and strategy is not evaluated regularly by the MoLHSA. Monitoring and evaluation of the epidemiological situation is carried out jointly by the NCTLD and NCDC. The NTP strategy includes a well-designed monitoring and evaluation framework covering the most important health outcomes, and many output indicators for service delivery but few for health finance and other important aspects of performance such as efficiency and responsiveness. There is thus no annual published report that would include a more detailed analysis of aspects such as efficiency and responsiveness. Such a report would also make possible an external appraisal of the performance of and progress and bottlenecks among the stakeholders involved in the implementation of the NTP. Even though it would be important, the MoLHSA lacks the capacity to carry out regular evaluations of the TB control services.

The reliance on market mechanisms in service delivery and integration of the NTP in the general health system have resulted in fragmentation of the governance and management of the NTP and a blurring of accountability as well as the mandate of the key central institutions. Under the approved strategy, the director of the NCTLD was nominated as a specific senior focal point accountable for TB control nationwide, but some responsibilities were shared with the NCDC so that there is now no clear definition of authority for the NCTLD with regard to implementation of the NTP. For instance, there is no clear dedicated authority for the NCTLD as to how to control the quality of care, and how to initiate corrective action or coordinate action to improve performance A lack of clarity in roles and responsibilities was also seen in the National Tuberculosis Strategy and Operational Plan 2013–2015 *(11)*.

The NCTLD, which is supposed in part to coordinate the NTP at central level, has to focus primarily on providing hospital services at tertiary level. It can contribute to assessments of the providers' performance but it has a limited role in the management and coordination of the NTP at regional and local level. There are no performance incentives for the coordinators of the NTP.

A network of central and regional coordinators of the NTP has been set up with the technical and financial support of the Global Fund to supervise the implementation of TB control. In 2014, 10 regional coordinators paid from with funding from international donors were working part-time to check adherence to treatment guidelines and to provide supervision. They report both to the NCTLD and NCDC. Their findings are neither summarized nor appraised in the framework of a more systematic evaluation at policy level. It is not clear how the SARMA, the government body accountable for the quality of care, reports and evaluates the performance of quality of the TB control.

There is no consistent line for accountability in the organizational framework of TB control for the overall performance of the NTP. To improve oversight of the implementation of the NTP, a new coordination committee was officially established at the time of this review. The mission understands that this committee does not involve the focal points or representatives of other public health programmes or public policies in its work.

In sum, many elements of the policy cycle are working in an occasional and unpredictable manner not based on well-designed and stable institutional processes. Neither has any governance mechanism been established to prioritize expenditure financed by the funds saved and how to convert it to finance ambulatory care.

Recommendations

- Accountability should continue to be improved through the nomination of a central coordinator of the NTP. Approval should be given to a basic document describing the responsibilities, authorities and accountabilities for all the main stakeholders involved in TB control, which should be annexed to the ministerial decree on the new coordinating committee for TB control.

- A results-based managerial approach and capacities should be established for the overall management of the NTP.

- Appointment of the NTP managers should be based on merit and on a performance-based contract with financial incentives linked to the implementation of the NTP strategy and action plans.

- The performance framework assessment and capacities should be strengthened both at the central level of the NTP and at ministry level.

- The new committee for TB control should involve representatives of other public policies, even on an occasional basis.

- An annual report on TB with an assessment of all aspects of performance, including efficiency, quality and responsiveness beyond health outcomes, is important to create sound and good governance for TB.

- Overall performance assessments of the NTP should also rely on external appraisal in the framework of assessments of the performance of the general health system at system level, to avoid a natural conflict of interest stemming from self-assessment by those stakeholders that are also in charge of coordinating and implementing TB control activities.

- A sub-committee should be set up in the framework of the new TB Coordination Council, including representatives of the Social Service Agency, to follow up the financing of the NTP for health and especially to design proposals as to how the funds saved in the planned downsizing of hospital care should be spent on ambulatory care. The recommendations of this committee should be approved by the MoLHSA, and the Social Service Agency should ensure the technical reallocation of the resources.

- The current participatory approach for horizontal governance should continue and, where necessary, be strengthened, especially through cooperation with other public health and non-health programmes addressing the social determinants of health.

Financing and allocation

The achievements in financing and allocation are as follows.

- TB services are free of charge.

- Ambulatory care finance provides a good base for incentivizing ambulatory care treatment.

- The Social Service Agency and providers in hospitals as well as at ambulatory care level have adequate information technology capacities and knowledge to manage more complex payment methods such as case payments.

- In 2014, WHO estimated that the cost per patient for cases of susceptible TB in 2012 was US$ 2246, which is quite moderate compared to other countries.

The following challenges remain.

- Public expenditure on health was very low between 2005 and 2012: in 2012, it was only 1.7% of gross domestic expenditure. The national health account for 2013 could well show, however, that since 2013, when the government introduced a basic benefit package for all residents, public expenditure on health has increased significantly.

- Expenditure on TB as reported on the 2013 WHO data collection form also seems to be low as a share of public expenditure on health (excluding funding from external donors) at 0.9% and, in 2012, 0.16% of total expenditure on health.

- No overall health account for TB has been compiled which could be used to identify the allocation patterns of resources across the main health service categories and to calculate the efficiency of their overall performance.

- Sick pay for patients is paid by employers up to one month. This is a very limited time, especially for M/XDR patients. Patients do not receive cash benefits during treatment apart from the Global Fund's financial incentives.

- The average salary for TB doctors was estimated about 350 lari. Providers usually pay the expected minimum salary of 300 lari per month (Marneuli Multiprofile private centre), which is far lower than the salaries of other health professionals.

Health finance

While total expenditure on health as a percentage of gross domestic product is one of the highest in the Region, peaking at 10.1% in 2010, by 2012 it was 9.2%. At that time 77% of expenditure stemmed from private sources (Table 17).

Table 17. Main indicators of health finance, Georgia, 1995–2012

Indicators	1995	2000	2005	2010	2011	2012
Total health expenditure as a percentage of gross domestic product	5.1	6.9	8.6	10.1	9.4	9.2
General government expenditure on health as a percentage of gross domestic product	-	1.2	1.6	2.3	1.7	1.7
Private expenditure on health as a percentage of total health expenditure	94.8	83.0	80.8	77.2	81.9	82.0
General government expenditure on health as a percentage of general government expenditure	2.5	6.9	6.2	6.6	5.3	5.2
Social security funds as a percentage of general government expenditure on health	39.2	46.0	45.6	78.7	68.8	68.8
Out-of-pocket expenditure as a percentage of private health expenditure	100.0	99.4	95.0	89.5	79.3	78.9
Out-of-pocket expenditure as a percentage of total health expenditure	94.8	82.5	76.8	69.1	64.9	64.7
Total expenditure on inpatient care as a percentage of total health expenditure	-	-	23.9	-	-	-
Total expenditure on health per capita at exchange rate	29.0	44.7	123.2	266.6	309.6	333.3
General government expenditure on health per capita exchange rate	1.5	7.6	23.6	60.7	56.1	60.0

Source: WHO *(29)*.

Public expenditure on health was, however, very low between 2005 and 2012: in 2012, it was only 1.7% of gross domestic product. The national health account for 2013 could well show, however, that since 2013, when the government introduced a basic benefit package for all residents, public expenditure on health has increased significantly.

In 2012, spending on health in the overall government budget was 5.2%. This indicates a weak commitment, in comparison with other countries in the Region, on the part of the government to distribute a fair share of the national budget to the health system.

An output-based payment mechanism based on a case payment approach in ambulatory care sends clear incentives to the provider to increase activities, although this might be difficult to translate into increased performance as TB doctors and nurses have some of the lowest salaries in the health care system. Case payment is made on a monthly basis and includes all necessary medical interventions and diagnoses. Monthly payments are 65 lari for sensitive cases and 125 lari for non-sensitive cases. The Social Service Agency has the right to monitor contracts and the validity of providers' reports on output; the mission understood that this happens in practice.

The average salary for TB doctors was estimated about 350 lari. Providers usually pay the expected minimum salary of 300 lari per month (Marneuli Multiprofile private centre), which is far lower than the salaries of primary health care professionals (650 lari per month for doctors and 450 lari per month for nurses in the Krtsanisi primary health care facility) and other professionals, including pulmonologists.

TB services are free. One provider visited by the mission was uncertain whether the regulation intended that suspected but not subsequently diagnosed patients should make a copayment to the providers for the medical examination. If other institutions are using the same interpretation, the respective regulation should be modified to exclude this possibility.

Currently there is no pay for performance element in the payment methods used.

No overall health account for TB has been compiled which could be used to identify the allocation patterns of resources across the main health service categories and to calculate the efficiency of their overall performance. Nevertheless, the data collection and financial reports from the providers to the Social Security Agency would make it easy to compile a detailed health finance report.

Daily payments per case in hospital settings increase the length of stay, although some overall summary data on hospitalization indicate that new smear-positive patients only stay for a fairly short period.

Payment mechanisms in ambulatory and inpatient care are not aligned to each other in their expected impact. Whereas ambulatory care finance provides a good base for incentivizing ambulatory care treatment, the current payments to hospitals encourage prolonged hospital treatment. Nevertheless, a representative of the central hospital explained the current relatively short average length of stay in hospital, reported in the WHO data collection form, by the relatively low number of hospital beds.

Sick pay for patients is paid by employers up to one month. This is a very limited time, especially for M/XDR patients. Patients do not receive cash benefits during treatment apart from the Global Fund's financial incentives. They can thus easily be faced with catastrophic financial consequences with regard to their household income.

In 2014, WHO estimated that the cost per patient for cases of susceptible TB in 2012 was US$ 2246, which is quite moderate compared to the costs in other countries.

Public expenditure on health was very low between 2005 and 2012: in 2012, it was only 1.7% of gross domestic expenditure. The national health account for 2013 could well show, however, that since 2013, when the government introduced a basic benefit package for all residents, public expenditure on health has increased significantly. Taking into account the expenditure on TB funded by international donors together with public expenditure on health, spending on TB was 2.31% as a share of public expenditure and 0.42% of the total expenditure. This level is very low in compared to other countries with a high burden of TB.

The NTP is still heavily dependent on international donors, including the Global Fund. In 2012, 62% of total funding came from international donors. The government financed only the professionals' salaries, a small proportion of the cost of laboratory supplies and equipment, the cost of hospitalization and some other infrastructure expenditure. The current domestic funding level for the NTP is not enough to scale up MDR-TB prevention and control activities to achieve full MDR-TB country coverage as well as to replace funding from external donors for first- and second-line drugs.

Spending on management and supervision as well as incentives for better performance seem to be limited and neglected.

Recommendations

- A report on TB-specific health accounts should be compiled by using the health account production tool recommended by WHO.

- Performance-based financial incentives should be created for TB doctors and nurses, especially in ambulatory care, to improve their performance in selected fields such as contact-tracing and the adherence of patients to treatment. This could be piloted and managed either by the Social Service Agency or by a possible central coordination unit with clear responsibilities and authority.

- Sick payment should be introduced for patients who are employed and who would lose their income because of the disease.

- The salaries of professionals involved in TB control should be increased at least to the level of those working in primary health care.

- The impact of daily payments on length of stay should be assessed in detail and consideration given to moving towards a global budget or a case payment method or a well-planned combination of both payment methods in hospital settings.

Human resources

The achievements as regards human resources are as follows.
- TB and pulmonology specialities have been integrated into one service.

- Standard curricula for under- and postgraduate education is being implemented with the most recent TB knowledge and skills by the TB department of Tbilisi State Medical University for both private and public medical educational institutions.
- Health care professionals in cross-disciplinary specialties (internal medicine, obstetrics-gynaecology, orthopaedics, endocrinology, paediatrics) are being trained in the diagnosis and differential diagnosis of pulmonary, extrapulmonary and childhood TB as part of the URC research project.

The following challenges remain.
- There is no comprehensive plan for human resources development for the health sector in general and the TB control service in particular, with a situational analysis, future plan and defined budget.
- No sustainable mechanism for accreditation and no professional development scheme exist for health personnel.
- Division of the tasks and responsibilities of TB and primary health care doctors and nurses is not well defined.
- TB doctors and nurses have the lowest rates of pay. The government decree N279 on the minimum pay for TB doctors and nurses (not less per month than 360 lari for doctors and 280 lari for nurses) is a barrier to increasing or revising the salary scale.
- TB doctors are on average aged over 55 years. The TB specialty is not attractive for newly graduated medical doctors.
- The cost of postgraduate education of TB doctors (1650 lari/year) is a financial burden and barrier to young doctors who wants to choose this specialty.

Policies and plans

Human resources for TB control are addressed in strategic area No. 4 of the national TB strategy and operational plan for Georgia, 2013–2015. It consists of a number of activities to ensure that human resources are available at each level with the appropriate professional competences and support to meet the NTP's targets and defined indicators. A number of activities have not, however, been implemented owing to insufficient funding (only 51% of the funds needed were available). The mainly components covered are training and salaries. The Plan does not provide a situation analysis, identify existing gaps and challenges or provide a detailed action plan for the sustainable development of human resources for TB control. A detailed plan of action needs to be developed and supported by the budget, which should include monitoring and evaluation and be part of the national TB strategy and national plan for human resource development for health.

The mission observed that the MoLHSA does not have comprehensive information on health personnel and there is no plan for the sustainable development of human resources for health. The Ministry staff explained that since the mass privatization of health facilities (about 99% of health facilities have been privatized), decisions on health staffing are now the responsibility of the private facilities. This situation needs to be addressed urgently and a mechanism should be developed to involve the Ministry fully in the planning and development of human resources in order to ensure the quality of the health care service.

Many actors are involved in TB control, including the TB service, some primary health care facilities, HIV/AIDS and the narcological service. Health care professionals in cross-disciplinary specialties (internal medicine, obstetrics-gynaecology, orthopaedics, endocrinology, paediatrics) are being trained in the diagnosis and differential diagnosis of pulmonary, extrapulmonary and childhood TB as part of the URC research project. The division of tasks and responsibilities between TB and primary health care and other actors is not, however, well-defined and, as a result, the proportion of patients with suspected TB referred to the TB service is very low and there is a different approach to TB and HIV screening at peripheral level and an inefficient use of human resource capacity. Thus, a clear division of responsibility between the TB and other services, including primary health care, should be developed for each member of staff at each level of service provision.

Staffing, recruitment

Staffing with physicians for TB service (the ratio of established to occupied posts) is relatively sufficient based on the current staffing norm: 189 established posts in 2013 have been occupied by 184 positions (97.3%). These posts are occupied by 184 doctors, which means that one doctor occupies one post. Of 381 nurse posts, 379 are occupied (99.5%). According to the data provided by the NCTLD, almost all district-level TB dispensaries have at least one TB doctor and one nurse providing DOT. Four districts, however, do not have a TB doctor, resulting in inadequate access for TB patients to TB care and support, especially as the primary health care services do not on the whole get involved in the provision of DOT.

The available information shows that the average age (56 years) of TB doctors in hospitals is relatively old (52–62). In the TB dispensaries the average age is even higher: in nine units 11 doctors are aged over 75 years. The average age of TB nurses is 47 years. The country does not oblige health personnel to retire.

There is an increasing risk of understaffing by TB doctors in the near future, taking into account the absence of staffing norms, under-provision of TB doctors and nurses in some districts, relatively old age structure of TB doctors and unattractiveness of the TB specialty. It is very important to develop and implement a human resources development plan for the TB service.

The mission was unable to see a document describing staffing norms for health personnel, including for the TB service (particularly TB dispensaries), and so could not conclude whether the staffing, norms and workload are sufficient for the current system of TB service provision.

TB doctors have complained about the burden of administrative paperwork. They would be able to focus on their primary responsibility far more effectively if secretaries or administrative staff were employed to carry out this work.

Pay, motivation and incentives

After privatization, in order to protect TB doctors and nurses, the Government issued decree N279 on the minimum pay for TB doctors and nurses to guarantee monthly salaries of not less than 360 lari for doctors and 280 lari for nurses (from which 20% is deducted for social taxes). This, however, has become a barrier to getting higher salaries, resulting in TB doctors and nurses having the lowest salaries among all health personnel. In comparison, the gross salaries

of primary health care doctors and nurses are 650 and 450 lari, respectively. This is another factor in making TB as a specialty unattractive for young doctors and nurses. The TB service is not entitled to premiums on salaries or other incentives as is common in other countries.

The TB service was combined with pulmonology in February 2014. It is expected that this will broaden the expertise of practitioners and make the profession more attractive to younger doctors.

No information was available on staff turnover. The mission therefore advises that the current mechanism of payment for of TB service providers should be revised and consideration given to performance-based payments, extra incentives and motivation premiums to attract doctors and nurses to the TB specialty.

Training and skills building

There are about 15 public and private medical educational institutions and faculties providing undergraduate education. Postgraduate medical education in TB is only available at Tbilisi State Medical University, an independent institution accredited by the Ministry of Education for undergraduate education and by the MoHLSA for postgraduate education. Under its contract, it uses private clinics as university clinical bases. In 2015 the first multifunctional governmental university clinical base will be launched. The NCTLD serves as the clinical base for TB doctors.

TB is the subject of a two-week course in the fifth year of the undergraduate curriculum. Postgraduate education includes: three years residence in TB (this will soon be replaced by TB with pulmonology); one- and two- month courses on continuous education for TB doctors; short requalification courses for other specialties who want to become TB doctors (duration depends on continuity of employment); and a seven-day standard course on TB for other specialties. The curricula for all courses are revised by the TB department of the University every two years and approved by the MoLHSA.

Family physicians have taken short-term residencies to enhance their knowledge and skills in TB care in the past. In 2013 the Ministry revised the regulation on specialties and stopped these residencies because family medicine is no longer considered a cross-disciplinary specialty. The mission strongly recommends the re-introduction of TB courses into the curricula of family doctors.

Medical education is not free. The cost of a residence in TB is about 1650 lari a year, a financial burden and one of the barriers for young doctors who want to choose this specialty. The number (quota) of places for TB residencies is decided by the MoLHSA based on the capacity of the clinical bases – six places at present. An expansion in the clinical bases' capacity and removal of the fee for TB postgraduate education would increase the number of TB residencies.

International agencies such as the Global Fund, together with the USAID-funded TB prevention project, have made a considerable investment in the development of health personnel by providing short courses in different aspects of TB control for primary health care and TB service personnel and by giving technical assistance with the development and revision of guidelines and protocols.

Professional development scheme

Since 2007 there has been no system for professional development and quality control. The government has stopped recertifying health personnel and introduced lifetime certification. This will affect the qualification of health personnel. The mission recommends that a professional development scheme be implemented with regular and credit-based accreditation linked to in-service training. Postgraduate and continuing professional education for phthisio-pulmonologists should be free to motivate young doctors to choose this specialty.

A private health company runs an annual test of the knowledge and skills of health personnel for the purpose of extending their contracts. Of 4000 test questions, around 400 are about TB. Private facilities should be obliged to invest in the training of human resources and the MoLHSA and TB department of the Medical University should be involved in the testing mechanism. TB-related questions in the test should be revised and brought into line with internationally recognized and nationally adopted recommendations and practices.

Recommendations
- A needs assessment should be conducted for human resources for TB and a national human resources plan developed that includes a training component with short-, medium- and long-term interventions and a budget, taking into account the service delivery model and further integration of TB services into primary health care.
- Focal points on human resources should be appointed at the NCTLD and TB regional centres, and clear terms of reference drawn up for them to coordinate the implementation of a national human resources plan of action and training activities.
- Staffing norms should be developed and implemented for the more effective division of responsibilities between the TB service and primary health care, and clear terms of reference should be written for personnel at each level.
- A professional development scheme should be implemented with regular and credit-based accreditation linked to in-service training. Postgraduate and continuing professional education for phthisio-pulmonologists should be free to motivate young doctors to choose this specialty.
- In-service training in cross-disciplinary specialties should be continued and institutionalized in order to increase the TB case detection rate.
- The current payment mechanism for TB service providers should be revised and consideration given to performance-based payments, incentives and/or motivation premiums to attract doctors and nurses to the TB specialty.
- The MoLHSA regulation should be revised and barriers removed so that other specialties can attend requalification courses in TB. A TB course should be re-introduced into the curricula for family doctors.
- Access should be ensured to all recent guidelines at peripheral level through the printing and dissemination of guidelines to all staff and provision of training in each subject.

Civil society engagement, advocacy, communication and social mobilization

Civil society organizations benefit from a small grants programme, thanks to URC which is currently running a USAID-funded TB prevention project. The aim of these grants is to support civil society involvement in projects, allowing them to improve the quality of TB treatment facilities. They are also responsible for advocating the greater availability of TB services as well as patient awareness regarding their entitlement to TB treatment. At present, a range of services is being provided through local nongovernmental organizations including training, awareness raising activities, production of information materials, TB quality improvement tools and operational assessment. Civil society involvement has reached all levels of society: school teachers, pupils and students have been mobilized to fight TB, while the First Lady, the Georgian Patriarch, artists, painters, photographers, celebrities, nongovernmental organizations and the private sector have also participated in these activities. In addition, meetings with local health care, media and church representatives have also been organized.

These activities have been spearheaded by the NCTLD, NCDC and the URC TB prevention project. During the review, the TB Georgian Coalition was established to allow greater involvement by community-based organizations and patients in the management of the TB control system. The Coalition will also support the country dialogue and the concept note writing process in the framework of the Global Fund new funding mechanism. The Coalition is striving to become the main facilitator in the mobilization of, and collaboration among, civil society organizations and to fulfil the same role between civil society organizations and the NTP on the one hand, and civil society organizations and the local authorities on the other. Eleven local nongovernmental organizations have joined the Coalition and are currently working on project proposals with the aim of attracting funds to implement their action plan.

Nongovernmental and civil society organizations remain heavily reliant on external donor aid. The gradual phasing out of Global Fund support and the ending of USAID programming are leading to uncertainty regarding the future funding of advocacy, communication and social mobilization activities.

The achievements as regards civil society engagement, advocacy, communication and social mobilization are as follows.

- Local nongovernmental organizations are significantly involved in TB care and control and advocacy, communication and social mobilization activities through grant programmes supported by the URC TB prevention project, focus areas and achievements within completed or ongoing small grants programs in 2013 and 2014.

- Coordination of local nongovernmental organizations by the URC TB prevention project, duplication of activities avoided.

- Local nongovernmental organizations have access to the penitentiary system to provide assistance and support (TB prison hospital in Ksani).

- Education materials are available and used for counselling former prisoners. Family members of former prisoners are engaged in advocating adherence to treatment.

- The National TB Strategy and Operational Plan for Georgia 2013–2015 encourages local nongovernmental and community-based organizations to participate in advocacy, communication and social mobilization activities and TB care. The TB Georgian Coalition has been established and unites nongovernmental organizations, representatives of doctors from the NCTLD and people affected by TB. A former TB patient and member of the Club of Winners (part of the Coalition) is producing a documentary film as a tool to challenge the stigma surrounding TB.

- High-profile social mobilization events such as World TB Day and the White Flower Day campaign have been arranged with the involvement of Georgian celebrities. Other activities include:

  - media advocacy and mobilization (the TV Against TB project);

  - sports events to mobilize pupils and students (Healthy Body – Healthy Breath project);

  - theatre and arts festival "TB in the Arts" (Strong Souls to Fight TB project).

- In terms of advocacy, TB was successfully included in earlier legislative measures, such as the 1997 Law of Georgia on Health Care, the 2003 Economic Development and Poverty Reduction Programme of Georgia, and the 2006 Law of Georgia on Public Health.

The following challenges remain.

- The provision of TB care in the regions of Abkhazia and South Ossetia is problematic.

- Domestic funding is lacking for advocacy, communication and social mobilization activities.

- There is no national strategic plan for advocacy, communication and social mobilization, including a detailed budget and a monitoring and evaluation plan. Earlier a comprehensive national strategy for advocacy, communication and social mobilization in TB control for 2011–2013 was developed with technical support from the Programme for Appropriate Technology in Health and financial support from USAID. Despite a 2012 update in the system of funding for advocacy, communication and social mobilization and the NTP, large parts of the strategy have not been implemented. When the policy changed, advocacy, communication and social mobilization activities were conducted through local nongovernmental organizations in collaboration with international partner organizations.

- More patients are interrupting their treatment and emigrating to other countries. In part this is due to a lack of adequate social, economic and psychological support for patients, and in part to the lack of adequate and regular public information about TB.

- Stigma remains dominant and a constant background barrier to all TB control efforts. In spite of lectures, meetings and communication campaigns, accurate knowledge among the general population about TB transmission, epidemiology and prevention remains at a low level while stigma remains high.

Recommendations

- Nongovernmental organizations should be helped to coordinate their service delivery, including in Abkhazia and South Ossetia, through the MoLHSA.

- A central advocacy, communication and social mobilization thematic working group should be established as a central hub of communication and coordination at the NTP. This would serve the purpose of recruiting former TB patients/activists as well as members of the Coalition for the national advocacy, communication and social mobilization network.

- A national advocacy, communication and social mobilization operational plan should be developed with a detailed budget and a monitoring and evaluation plan.

- Former TB patients should be involved in stigma reduction and treatment adherence activities by promoting the sharing of experience and providing psychological support.

- Volunteers for TB advocacy, communication and social mobilization should be mobilized among university students (for academic credit), social workers or former TB patients through small incentive programmes such as vouchers for transport or telephone cards.

- As adherence counsellors' posts have been abolished, TB staff and primary health care providers should be motivated and retrained to improve their skills in interpersonal communication and adherence counselling.

- Government co-funding should be ensured for the Coalition to allow for the engagement of civil society organizations.

- Coverage of TB on television should be increased with greater accuracy and frequency to reinforce positive messages about TB. The Georgian National Communications Commission could promote a national health TV channel which would regularly advocate the prevention of and care for TB and inform the general public, and health care workers in particular, about TB and other diseases.

- The social media should be used for advocacy. The mission encourages the creation of a TB in Georgia hashtag. Greater use of new media technologies, in particular web-based and social networking channels, should be prioritized in this context.

- World TB Day should be marked with patients and community-based nongovernmental organizations and the organization of public action and sports events nationwide.

Ethics and human rights

The achievements as regards ethics and human rights are as follows.

- The Constitution adopted in 1995 includes a catalogue of human rights and fundamental freedoms, some of which are relevant in the context of TB control and management. The Public Defender, who is elected for five years by members of parliament (Article 43), supervises the implementation of the human rights provisions of the Constitution. The Public Defender's Office is already aware of the human rights implications of TB control and management policies.

- Discussions concerning the financial sustainability of the NTP and the improvement of TB control legislation are conducted at government level. A draft law on TB control is already under discussion in parliament. Clarifications regarding the institutional structure of the response to TB have been made through the governmental order adopted on 11 November 2014, which created the National TB Council as the central coordination body for TB control. The Council is specifically in charge of the coordinated development and implementation of a long-term strategy in line with international standards. The purpose of the draft law for TB control is to define the instruments necessary "for the protection of individual and public health through effective control of TB" (Article 1 of the draft law). According to the draft, human rights are basically to be respected. Article 3.3 of the draft law uses a broad formulation and requires the "respect for and protection of individual, social and patients' rights".

The following challenges remain.

- Interviews revealed that TB patients are not familiar with the Patients' Charter for Tuberculosis Care *(30)*.

- As a result of a high degree of stigmatization, people with TB face challenges including losing their jobs. They do not take sick leave for TB treatment as they face rejection when they return to work, even after full completion of their TB treatment. As some patients acknowledged during interviews, they had decided to continue working until their health deteriorated.

Recommendations

- Parliament should adopt a specific law on TB. Current legislation for the control of contagious diseases does not offer a sufficient legal basis for the management and control of TB. A specific law on TB should be adopted in order to strengthen the political and financial engagement of the political authorities in this field.

- The law on TB control should include provisions concerning, for instance, patients' right to work or the obligations and responsibilities of patients with infectious TB towards other individuals.

- The patients' charter should be included in the education of and counselling for patients. TB staff and primary health care providers should be trained in its use.

Operational research

There is good institutional capacity for both operational research and surveillance-based (epidemiological) research. The two main institutes (NCTLD and NCDC) that handle data have a recent history of performing epidemiological and operational research. The special research department within the NCTLD is well organized and has good collaboration with national partners (NCDC, AIDS centre, State Medical University) and international partners (such as Emory University in Atlanta (GA), United States of America). The NCDC collects a large amount of good quality surveillance data that can be used to inform further operational research studies. All research currently conducted at the NCTLD is project-funded (through external international grants). In order to ensure sustainability and political commitment to the End TB Strategy, the MoLHSA is to allocate specific annual funds from the established national TB budget for research in TB control.

In addition, the review team recommends that:

- a national agenda should be developed for TB operational research, based on epidemiological trends and national priorities for TB, and incorporated into the new national strategic plan and the new application to the Global Fund;

- a national TB research plan should be developed by 2016;

- the research department of the NCTLD should be formalized as the national TB research centre.

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Annex 1

PROPOSED LABORATORY NETWORK FOR TB DIAGNOSTICS
IN KVEMO KARTLI REGION
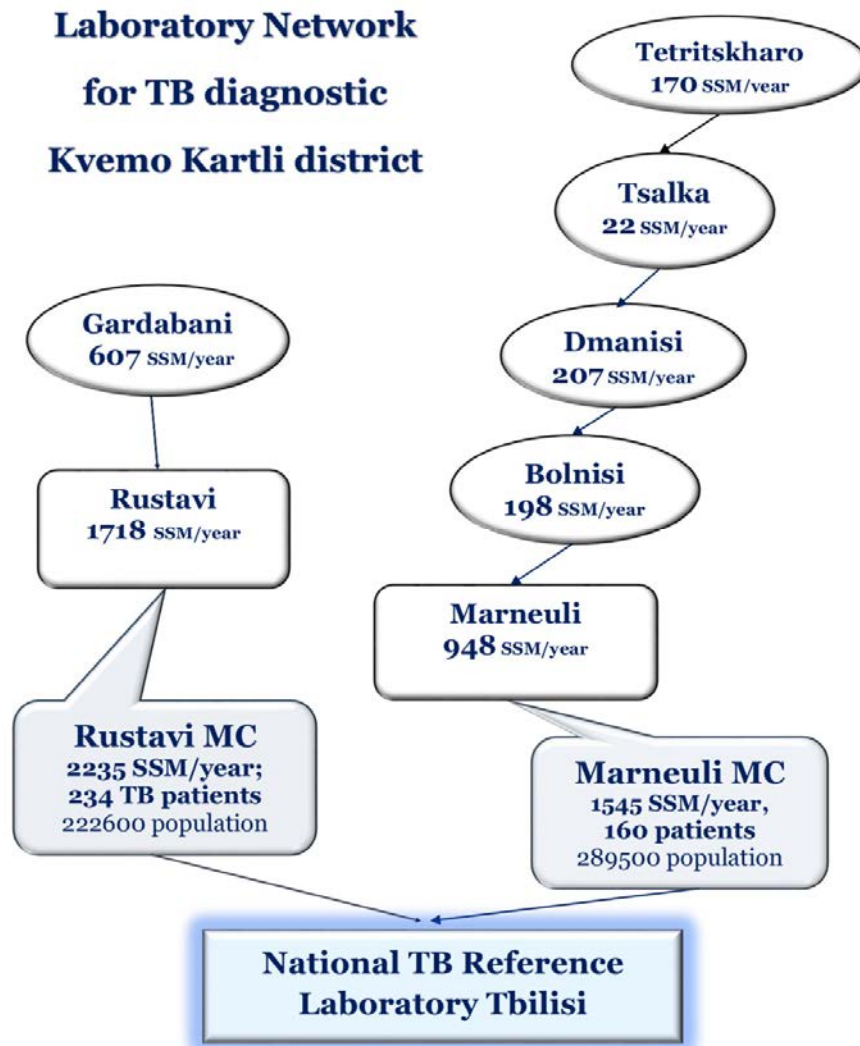
Annex 2

TB RESISTANCE, NEW AND RELAPSED CASES

	2013				2012				2011			
	New cases		Relapsed cases		New cases		Relapsed cases		New cases		Relapsed cases	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total cases	**1629**		**546**		**1931**		**541**		**2197**		**675**	
Sensitive	959	58.9	221	40.5	1149	59.5	227	42	1154	52.5	240	35.6
A H	374	23	253	46.3	435	22.5	227	42	521	23.7	297	44
A R	189	11.6	201	36.8	189	9.79	172	31.8	262	11.9	223	33
A E	179	11	179	32.8	203	10.5	159	29.4	249	11.3	211	31.3
A S	573	35.2	287	52.6	648	33.6	283	52.3	921	41.9	387	57.3
H	73	4.48	27	4.95	107	5.54	23	4.25	86	3.91	29	4.3
R	4	0.25	0	0	7	0.36	1	0.18	9	0.41	3	0.44
E	6	0.37	3	0.55	13	0.67	2	0.37	13	0.59	5	0.74
S	278	17.1	69	12.6	317	16.4	82	15.2	483	22	121	17.9
Total monoresistant	361	22.2	99	18.1	444	23	108	20	591	26.9	158	23.4
HR	11	0.68	7	1.28	1	0.05	3	0.55	6	0.27	9	1.33
HRE	2	0.12	1	0.18	1	0.05	1	0.18	1	0.05	2	0.3
HRS	24	1.47	21	3.85	22	1.14	14	2.59	38	1.73	17	2.52
HRES	146	8.96	172	31.5	153	7.92	151	27.9	194	8.83	186	27.6
Total MDR	**183**	**11**	**201**	**37**	**177**	**9.2**	**169**	**31**	**239**	**11**	**214**	**32**
HE	1	0.06	0	0	4	0.21	1	0.18	7	0.32	0	0
HS	99	6.08	22	4.03	121	6.27	30	5.55	160	7.28	39	5.78
HES	18	1.1	3	0.55	26	1.35	4	0.74	29	1.32	15	2.22
RE	0	0	0	0	1	0.05	0	0	0	0	0	0
RS	2	0.12	0	0	4	0.21	2	0.37	12	0.55	6	0.89
RES	0	0	0	0	0	0	0	0	2	0.09	0	0
ES	6	0.37	0	0	5	0.26	0	0	3	0.14	3	0.44
Total polyresistant	126	7.73	25	4.58	161	8.34	37	6.84	213	9.7	63	9.33

	2010				2009				2008			
	New cases		Relapsed cases		New cases		Relapsed cases		New cases		Relapsed cases	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total cases	**1988**		**567**		**1777**		**594**		**1685**		**720**	
Sensitive	886	44.6	189	33.3	880	49.5	201	33.8	917	54.4	226	31.4
A H	461	23.2	255	45	417	23.5	270	45.5	452	26.8	392	54.4
A R	196	9.86	181	31.9	194	10.9	189	31.8	208	12.3	301	41.8
A E	370	18.6	191	33.7	208	11.7	166	27.9	159	9.44	219	30.4
A S	911	45.8	322	56.8	776	43.7	357	60.1	653	38.8	437	60.7
H	81	4.07	24	4.23	85	4.78	25	4.21	91	5.4	40	5.56
R	2	0.1	1	0.18	4	0.23	2	0.34	8	0.47	3	0.42
E	94	4.73	19	3.35	23	1.29	4	0.67	5	0.3	0	0
S	469	23.6	85	15	432	24.3	108	18.2	289	17.2	91	12.6
Total monoresistant	646	32.5	129	22.8	544	30.6	139	23.4	393	23.3	134	18.6
HR	2	0.1	10	1.76	3	0.17	5	0.84	5	0.3	8	1.11
HRE	2	0.1	1	0.18	1	0.06	0	0	1	0.06	2	0.28
HRS	23	1.16	23	4.06	30	1.69	32	5.39	53	3.15	75	10.4
HRES	162	8.15	144	25.4	149	8.38	148	24.9	131	7.77	205	28.5
Total MDR	**189**	**9.5**	**178**	**31**	**183**	**10**	**185**	**31**	**190**	**11**	**290**	**40**
HE	9	0.45	1	0.18	5	0.28	0	0	3	0.18	4	0.56
HS	152	7.65	42	7.41	129	7.26	53	8.92	155	9.2	50	6.94
HES	30	1.51	10	1.76	15	0.84	7	1.18	13	0.77	8	1.11
RE	1	0.05	0	0	0	0	0	0	2	0.12	0	0

	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
RS	3	0.15	2	0.35	6	0.34	2	0.34	8	0.47	8	1.11
RES	1	0.05	0	0	1	0.06	0	0	0	0	0	0
ES	71	3.57	16	2.82	14	0.79	7	1.18	4	0.24	0	0
Total polyresistant	267	13.4	71	12.5	170	9.57	69	11.6	185	11	70	9.72

	2007				2006				2005			
	New cases		Relapsed cases		New cases		Relapsed cases		New cases		Relapsed cases	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Total cases	**1366**		**556**		**1135**		**587**		**799**		**515**	
Sensitive	299	21.9	69	12.4	492	43.3	169	28.8	406	50.8	175	34
A H	265	19.4	268	48.2	226	19.9	240	40.9	187	23.4	243	47.2
A R	123	9	196	35.3	85	7.49	163	27.8	61	7.63	147	28.5
A E	97	7.1	141	25.4	51	4.49	83	14.1	33	4.13	56	10.9
A S	1040	76.1	465	83.6	586	51.6	392	66.8	330	41.3	299	58.1
H	20	1.46	13	2.34	41	3.61	17	2.9	49	6.13	28	5.44
R	5	0.37	4	0.72	4	0.35	2	0.34	4	0.5	4	0.78
E	2	0.15	0	0	2	0.18	0	0	3	0.38	0	0
S	746	54.6	199	35.8	405	35.7	169	28.8	193	24.2	91	17.7
Total monoresistant	773	56.6	216	38.8	452	39.8	188	32	249	31.2	123	23.9
HR	0	0	3	0.54	7	0.62	6	1.02	6	0.75	6	1.17
HRE	0	0	0	0	1	0.09	0	0	0	0	2	0.39
HRS	23	1.68	51	9.17	31	2.73	72	12.3	27	3.38	83	16.1
HRES	64	4.69	128	23	38	3.35	77	13.1	21	2.63	50	9.71
Total MDR	**87**	**6.4**	**182**	**33**	**77**	**6.8**	**155**	**26**	**54**	**6.8**	**141**	**27**
HE	0	0	2	0.36	2	0.18	1	0.17	1	0.13	1	0.19
HS	147	10.8	67	12.1	100	8.81	64	10.9	78	9.76	70	13.6
HES	11	0.81	4	0.72	6	0.53	3	0.51	5	0.63	3	0.58
RE	0	0	0	0	0	0	0	0	0	0	0	0
RS	29	2.12	9	1.62	4	0.35	5	0.85	3	0.38	2	0.39
RES	2	0.15	1	0.18	0	0	1	0.17	0	0	0	0
ES	18	1.32	6	1.08	2	0.18	1	0.17	3	0.38	0	0
Total polyresistant	207	15.2	89	16	114	10	75	12.8	90	11.3	76	14.8

Annex 3

EXTERNAL QUALITY ASSESSMENT FOR SPUTUM SMEAR MICROSCOPY

Name	Microscopy result	SSM+	SSM-
2012			
NRL	SSM+	57	
	SSM-		548
Kutaisi ZDL	SSM+	27	1
	SSM-		246
Batumi ZDL	SSM+	14	2
	SSM-		231
Zugdidi LSS	SSM+	7	3
	SSM-	1	142
Poti LSS	SSM+	3	1
	SSM-		96
Ozurgeti LSS[a]	SSM+		
	SSM-		
Gori LSS	SSM+	11	2
	SSM-		149
Akhaltsikhe LSS	SSM+	41	
	SSM-		55
Telavi LSS	SSM+	33	1
	SSM-	3	52
CPH laboratory	SSM+	8	
	SSM-		71
Ksani laboratory	SSM+	23	
	SSM-		63
2013			
NRL	SSM+	118	
	SSM-		819
Kutaisi ZDL	SSM+	26	
	SSM-		353
Batumi ZDL	SSM+	18	
	SSM-		331
Zugdidi LSS	SSM+	19	2
	SSM-	4	156
Poti LSS	SSM+	4	
	SSM-		182
Ozurgeti LSS	SSM+	3	
	SSM-		103
Gori LSS	SSM+	34	3
	SSM-	1	170
Akhaltsikhe LSS	SSM+	38	
	SSM-		60
Telavi LSS	SSM+	7	
	SSM-		73
Central prison hospital laboratory	SSM+	9	
	SSM-		85
Ksani laboratory	SSM+	14	
	SSM-		86

[a] In 2012 the Ozurgeti LSS laboratory did not work.

External quality assessment for DST, NRL, Tbilisi, Georgia, 2013

Strain duos	Strain code no.	Reported results: phenotypic tests					Score (SRLN discordant results excluded				
		R = resistant S = susceptible NR = not reported		NG = no growth, or contaminated NTM = non-TB mycobacterium			1=correct 0 = incorrect R = false resistant S = false susceptible			NA = excluded	
Lab code 113		Drugs tested							Drugs tested		
Tbilissi, Georgia		Km	Ak	Cm	Ofx		TB / NTM	Km	Ak	Cm	Ofx
1A	6795	S	NR	S	S		1	1	NR	1	1
2A	5793	S	NR	S	S		1	1	NR	1	1
3A	5679	R	NR	R	S		1	1	NR	1	1
4A	1200	S	NR	S	R		1	1	NR	1	1
5A	389	S	NR	S	R		1	1	NR	1	1
6A	5790	S	NR	S	R		1	1	NR	1	1
7A	5582	R	NR	R	S		1	1	NR	1	1
8A	2758	R	NR	R	S		1	1	NR	1	1
9A	813	S	NR	S	R		1	1	NR	1	1
1B	2734	S	NR	S	S		1	1	NR	1	1
2B	4614	S	NR	S	S		1	1	NR	1	1
3B	2400	NG	NG	NG	NG	Wrong	NA	NG	NG	NG	NG
4B	3615	S	NR	S	R	strain	1	1	NR	1	1
5B	5597	S	NR	S	R		1	1	NR	1	1
6B	3468	S	NR	S	R		1	1	NR	1	1
7B	848	R	NR	R	S		1	1	NR	1	1
8B	3284	R	NR	R	S		1	1	NR	1	1
9B	2551	S	NR	S	R		1	1	NR	1	1
19	4923	R	NR	S	S		1	1	NR	1	1
20	1446	R	NR	R	R		0	NTM	NTM	NTM	NTM
						TOTAL CORRECT R	18	18	0	18	18
	Method used:		6*			TRUE RESISTANT		6	0	5	8
1*	Proportion method LJ					FALSE RESISTANT		0	0	0	0
2*	Proportion method agar					TRUE SUSCEPTIBL		12	0	13	10
3*	Absolute conc. LJ					FALSE SUSCEPTIBLE		0	0	0	0
4*	Absolute conc. agar					SENSITIVITY		100%		100%	100%
5*	Resistance ratio					SPECIFICITY		100%		100%	100%
6*	MGIT					PREDICTIVE VALUE RES.		100%		100%	100%
7*						PREDICTIVE VALUE SUSC.		100%		100%	100%
	Arrival:	strains	12-Nov-13			ACCURACY	95%	100%		100%	100%
		results	28-Mar-14			REPRODUCIBILITY		100%		100%	100%

Source: SNRL Antwerp, *Department of Biomedical Sciences, Mycobacteriology Unit, Prince Leopold Institute of Tropical Medicine*
http://www.itg.be/itg/generalsite/Default.aspx?WPID=796&MIID=649&UnitCode=5321&L=E

Annex 4

MAP OF ANTI-TB MEDICINES SUPPLY SYSTEM

Second Line Anti-TB drugs	First Line Anti-TB drugs	Ancillary drugs

Source of Funds	Global Fund
Procurement Agent / Body / Organization	PR GFATM
Point of 1st warehousing	
Point of distribution	TB facility → PHC
	PHC / Patient