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Extensive review of tuberculosis prevention, control and care in Armenia
17–25 July 2014

ABSTRACT

The tuberculosis (TB) epidemiological situation remains a public health issue in Armenia and a matter of concern for the Ministry of Health, community and other stakeholders. Armenia remains in the top 10 out of the 27 countries globally with a high burden of MDR-TB. A review of the TB situation and interventions to prevent and control TB and MDR-TB was carried out by a team of international experts led 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 compared to the extensive programme review conducted in 2011; (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.

Keywords

ARMENIA
EPIDEMIOLOGY
PUBLIC HEALTH
SURVEILLANCE
TUBERCULOSIS

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Acknowledgements

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Abbreviations

ACSM	advocacy, communication and social mobilization
ARCS	Armenian Red Cross Society
ARV/T	antiretroviral therapy
AUA	American University of Armenia
CPT	co-trimoxazole preventive therapy
DOT	directly observed therapy
DR-TB	drug-resistant tuberculosis
DST	drug susceptibility test
GDF	Global Drug Facility
GDP	gross domestic product
GLC	Green Light Committee
Global Fund	Global Fund to Fight AIDS, TB and Malaria
ISO	International Organization of Standards
LPA	line probe assay
MC	microscopy centre
MDR-TB	multidrug-resistant tuberculosis
MGIT	mycobacteria growth indicator tube
MSF	Médecins Sans Frontières-France
MTB	*Mycobacterium tuberculosis*
NaOH	Petroff's sodium hydroxide
NCAP	National Centre of AIDS Prevention
NRL	National Reference Laboratory
NTC	National Centre for Tuberculosis Control
NTP	national tuberculosis control programme
PDR	polydrug-resistant
PLWH	people living with HIV
RTBD	Republican Tuberculosis Dispensary
TB	tuberculosis
USAID	United States Agency for International Development
XDR-TB	extensively drug-resistant tuberculosis

Executive summary

A review of the tuberculosis (TB) situation and interventions to prevent and control TB and drug-resistant (DR) TB was carried out in July 2014 by a team of international experts, led by the WHO Regional Office for Europe, with the participation of national experts. The Global Fund to Fight AIDS, TB and Malaria supported the review and its experts participated as observers.

Both TB notifications and mortality have been decreasing in the last five years by an average of 9% per year. TB notifications fell to 41 new and relapsed TB cases per 100 000 population and a detection rate of 80% of the estimated TB incidence. The prevalence of HIV among notified TB cases is 4.7% (67 cases in 2013). The treatment success rate of new and relapsed TB patients is 81%, below the WHO target of 85%. Ten percent of new and relapsed TB patients in the 2012 cohort were lost to follow-up and 6% died.

Armenia remains in the top 10 out of the 27 countries globally with a high burden of multidrug-resistant (MDR) TB. According to the latest representative 2007 Drug Resistance Survey, 9.4% of new cases and 43.2% of previously treated cases were multidrug-resistant. Of these, 4% were extensively-drug-resistant (XDR) TB cases. Detection of MDR-TB remains at 37%. Even though in 2013 all detected MDR-TB cases were enrolled in MDR-TB treatment, the treatment success rate among the 2011 MDR-TB cohort remained 51%, with 26% of patients who defaulted (mainly due to migration) as the main reason for the poor outcomes; the other outcomes were 17% still in treatment, 5% died and 1% failed. Nevertheless, a pilot project with Médecins Sans Frontières France (MSF-France), which is strongly supported by the government and is being carried out by the national TB control programme (NTP), is showing promising results among MDR-TB cases with the compassionate use of bedaquiline.

Despite some achievements in TB control, the epidemiological situation remains an important public health issue and a matter of concern for the Ministry of Health, the community and other stakeholders.

A team of experts led by WHO visited Armenia from 17 to 24 July 2014 to conduct a comprehensive review of the NTP. The review aimed to:

- document the progress and shortcomings in TB prevention, control and care in comparison with the extensive programme review conducted in 2011;
- assess the health care network, including laboratories, and report on the quality of TB services delivery;
- assess the links, synergies and opportunities for TB control in relation to health financing, health system strengthening and other disease-specific interventions;
- assess partnerships in TB care and coordination and collaboration with the NTP (intra- and inter-departmental, national and with international stakeholders such as the Ministry of Justice).

The review team visited TB programmes in three regions (Armavir, Shirak and Yerevan), evaluated three administrative levels (national, province and local), and had full access to

information throughout the country. They had meeting with the leading agencies developing public health strategy and health financing, the National Centre for AIDS Prevention, the narcological dispensary and in the prison sector, observing the structure, resources and practices of the NTP. The team noted the main strengths and weaknesses of the NTP and proposed key recommendations for action to improve its effectiveness.

The team concluded that the NTP is performing well overall and can be a model for other countries in reforming its governance, financing and service delivery. In June 2014, the Republican TB Dispensary and the former NTP management central unit were merged into the National Centre for Tuberculosis Control (NTC). The new entity now defines the policy, control, prevention, treatment and care for TB, and is responsible and accountable for the provision of medical care and services in collaboration with the primary health care sector, the national AIDS programme (for the civil population) and the Ministry of Justice (for the prison population). Key international collaborators include MSF-France, which is supporting efforts relating to MDR-TB, childhood TB interventions and the compassionate use of new anti-TB medicines, the United States Agency for International Development and the Global Fund.

The following are the important findings and recommendations for the improvement of the NTP.

Organization and management

- The Armenia Development Strategy for 2014–2025 was endorsed in March 2014 following the development of The Republic of Armenia Health System Development Concept Paper 2013–2020 (HSDC). The latter has not, however, been finalized or approved by the government. It should also be improved to take account of the following comments, before being approved by a high-level normative act (a government decree).
  - The regulation of intersectoral cooperation is of the utmost importance since health care issues unrelated to the Ministry of Health require a significant input from other ministries and agencies. It is, therefore, recommended that a section regulating intersectoral cooperation should be included in the HSDC.
  - The HSDC consists of summaries of vertical programmes (such as maternal, child and reproductive health, communicable diseases and health of elderly people) and lacks clearly defined integrative approaches, such as a strategy for the integration of vertical programmes (including TB) into primary health care, development of a unified health information system and reform of the hospital infrastructure. The revised HSDC should address this gap by defining criteria and methodologies for the horizontal integration of health care services delivery and specialized programmes.
- Health care providers should be made more aware of health system reforms. Their low level of awareness hinders the success of many progressive reforms. One such was performance-based financing in primary health care facilities, where the lack of knowledge on the part of facility managements and care providers led to no improvement in performance.
- The structure of the newly organized NTC should continue to be rationalized to achieve a more effective and cost-efficient management of the overall NTP.

Financing

- The Armenia Development Strategy for 2014–2025 assumes that public expenditure on health care will increase to 1.8% of gross domestic product by 2017 and around 2.7% by

2025. Health care financing parameters should be re-evaluated and broadened so as to bring the financial levels up to international standards.

- The Ministry of Health budget is segregated into about 50 programmes. There is a need to consolidate the budget and reduce the number of programmes.

Introduction

This report presents findings and recommendations of an extensive review of the prevention, control and care of tuberculosis (TB) in Armenia conducted by WHO on 17–25 July 2014 at the request of the Minister of Health of Armenia. The review was led by the WHO Regional Office for Europe with support from the WHO Country Office for Armenia, in close collaboration with the National Centre for Tuberculosis Control.

The review team was comprised of 10 international experts, including representatives from the WHO Green Light Committee and the Global Drug Facility. Short biographies of review team members are in Annex 1. Two representatives from the Global Fund to Fight AIDS, TB and Malaria (Global Fund) participated in the review as observers.

The review methodology included: surveillance data quality audit; revision of relevant technical reports (list of documents reviewed in Annex 2), surveillance data, national reports and epidemiological data; interviews with Ministry of Health, National Centre for Tuberculosis Control and provincial health authorities, chief hospital doctors and TB physicians, health care staff and representatives of state sanitary and epidemiological services, nongovernmental organizations and people affected by TB; field visits to specialized TB facilities and general health facilities caring for TB patients, including hospitals, rural health centres (outpatient health facilities), TB laboratory services and the HIV/AIDS centre. Team members also met prison health authorities and visited TB prison services and administrations. The programme is in Annex 3.

Epidemiology

A comprehensive review of the TB epidemiology, assessment of the TB surveillance system, levels and trends in the TB disease burden and analysis of specific interventions related to TB in Armenia and their impact on TB-related statistics were conducted before the review.

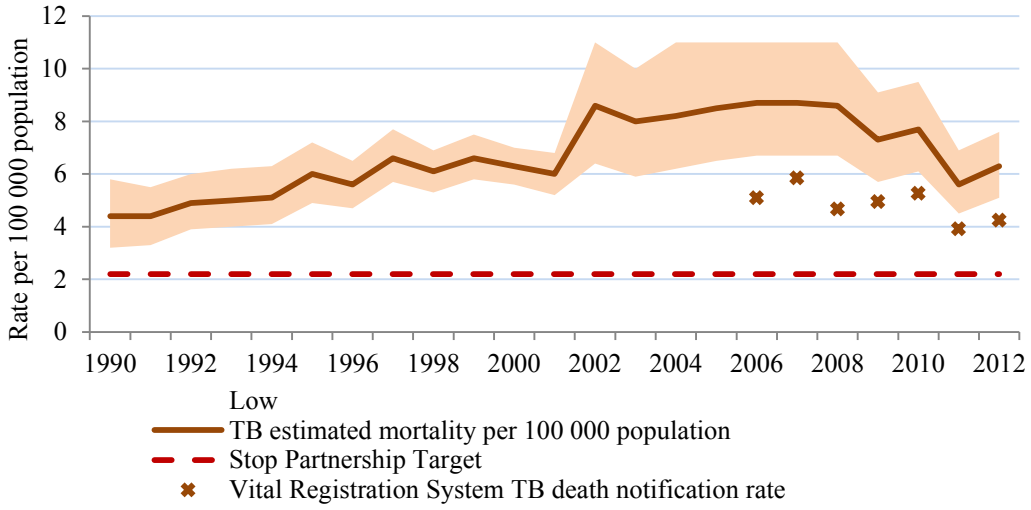
TB incidence and mortality

From 1990 to 2006, TB mortality increased from 4.4 to 8.7 per 100 000 population but declined from 2008. In 2012, the estimated TB mortality was 6.3 per 100 000 population, far below the Millennium Development Goal 6 target to halt the TB mortality rate compared with the 1990s (Fig. 1).

According to the WHO Global TB report for [2013] *(1)*, TB prevalence in Armenia peaked in 2005–2006 at 118 cases (range 55–195) per 100 000 population (Fig. 2). It then fell by an average of 6.3% per year to 79 cases (range 37–137) per 100 000 population in 2012. This is far higher than the Millennium Development Goal 6 targeted prevalence of 14 per 100 000, although there is considerable uncertainty with indirect estimates of TB prevalence.

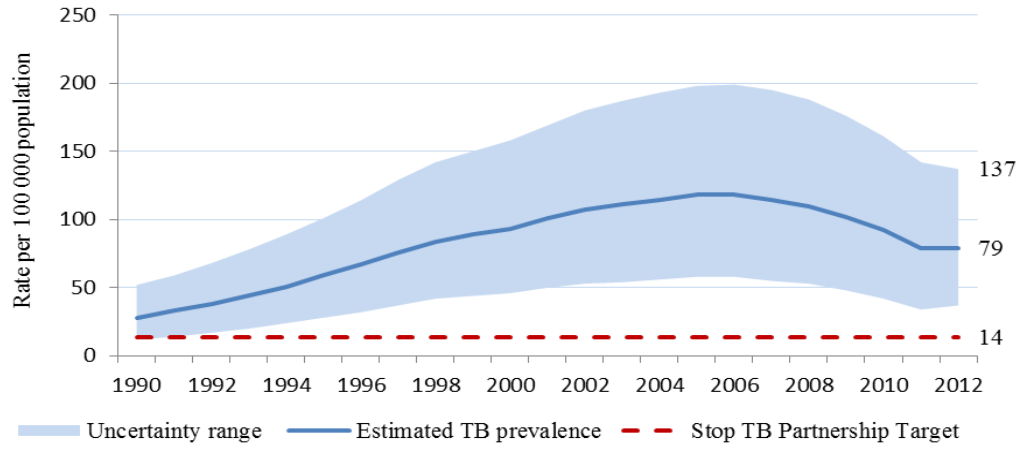
TB incidence rose sharply to a peak of 77 cases per 100 000 in 2005–2006 (Fig. 3) and fell again from 2008. The gap between notification and estimated incidence has narrowed considerably in recent years, indicating improved case detection: in 2012 the estimated TB incidence was 52 (range: 43–61) and notification of incident TB cases was 41 per 100 000.

Fig. 1. Estimated TB mortality rate (excluding TB/HIV mortality) per 100 000 population, Armenia, 1990–2012



Source: Global TB database *(2)* and vital registration system.

Fig. 2. Estimated TB prevalence rate per 100 000 population, Armenia, 1990–2012

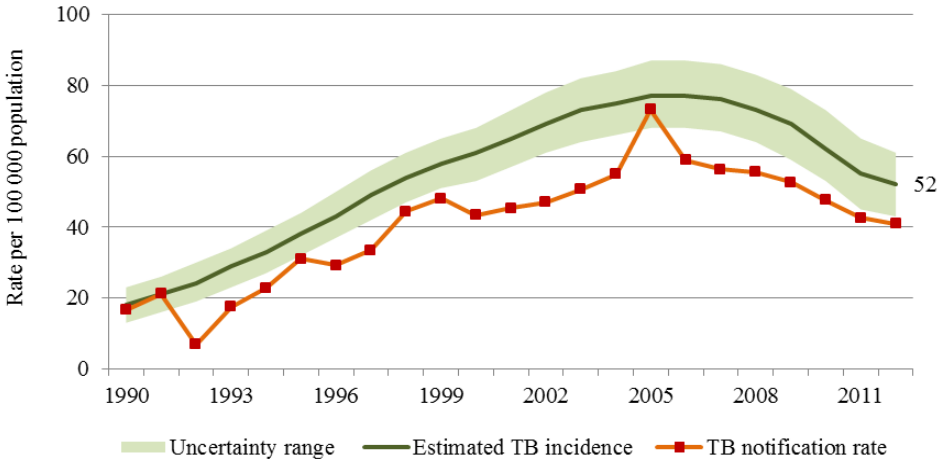


Source: Global TB database *(2)*.

At the national level, the number of notified TB cases (all forms) increased from 1570 cases (equivalent to 51.7 per 100 000) in 2003 to a peak of over 2300 (77.0 per 100 000) cases in 2005 (Fig. 4). After 2005, the number of notified TB cases steadily declined. In 2013, a total of 1457 TB cases (48.9 per 100 000) were notified (Fig. 5). This is the lowest number and level of TB cases recorded over the last decade.

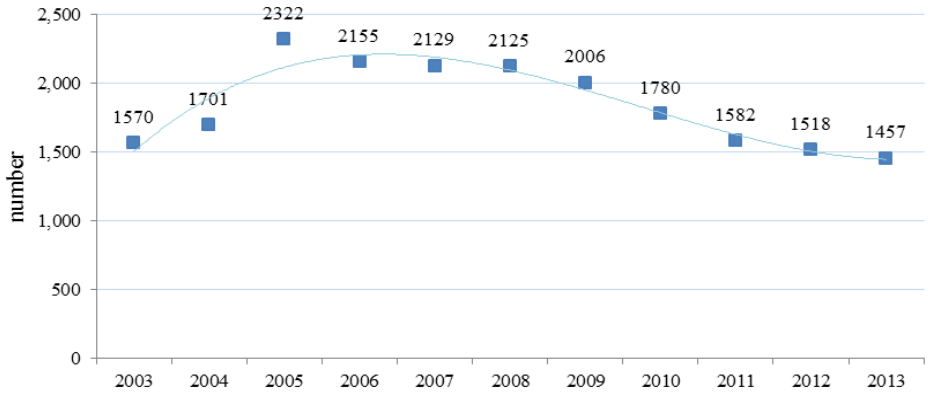
The decline is observed across all geographical areas in the recent five years, although in some areas (the prison sector, Tavush and Syunik provinces) the decline is very sharp, while in others the change is smaller (Kotayk and Yerevan provinces).

Fig. 3. Estimated TB incidence rate and notification of incident TB cases (new and relapsed), Armenia, 1990–2012



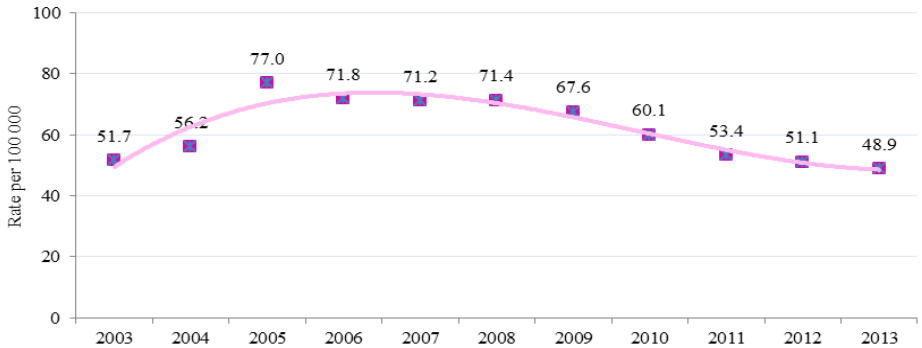
Source: Global TB database *(2)*.

Fig. 4. No. of notifications of TB (all forms), fitted with polynomial trendline, Armenia, 2003−2013



Source: Global TB database *(2)*.

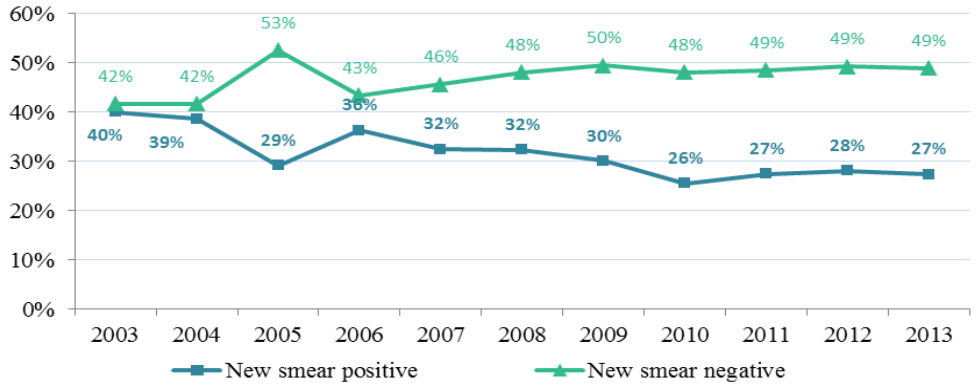
Fig. 5. Notification of TB rate per 100 000 population, fitted with polynomial trendline, Armenia, 2003−2013



Source: Global TB database *(2)*.

The relative numbers of new smear-positive TB cases among all new TB cases varied notably over time (Fig. 6). The proportion of smear-positive TB cases among all new cases fell from 40% in 2003 to 27% in 2013 with some sharp year-on-year fluctuations suggesting some weakness in surveillance. A review of the national reference laboratory (NRL) database for 2013 indicated that the proportion of bacteriologically confirmed cases accounting for culture and GeneXpert MTB/RIF[1] results is 60–70%, but because of the incomplete recording of laboratory results in the TB and electronic registers, there is no easily generated accurate information on the proportion of bacteriologically confirmed cases.

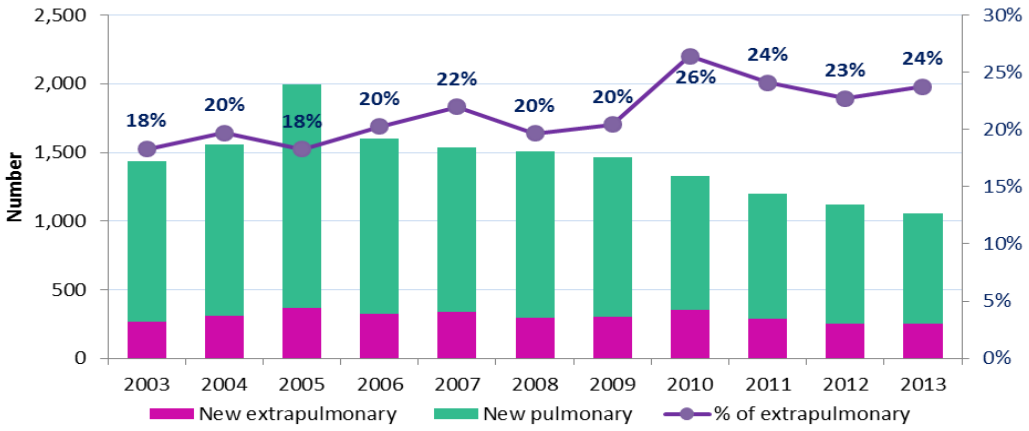
Fig. 6. Proportion of new smear-positive and smear-negative pulmonary TB cases among all new TB cases, Armenia, 2003–2013



Source: Global TB database *(2)*.

The percentage of new extrapulmonary cases increased gradually from 18% in 2003 to 24% in 2013, with a sharp fluctuation in 2009–2010 (Fig. 7).

Fig. 7. Trend in notification number of new pulmonary and extrapulmonary TB cases and proportion of extrapulmonary TB among new TB cases, Armenia, 2003–2013



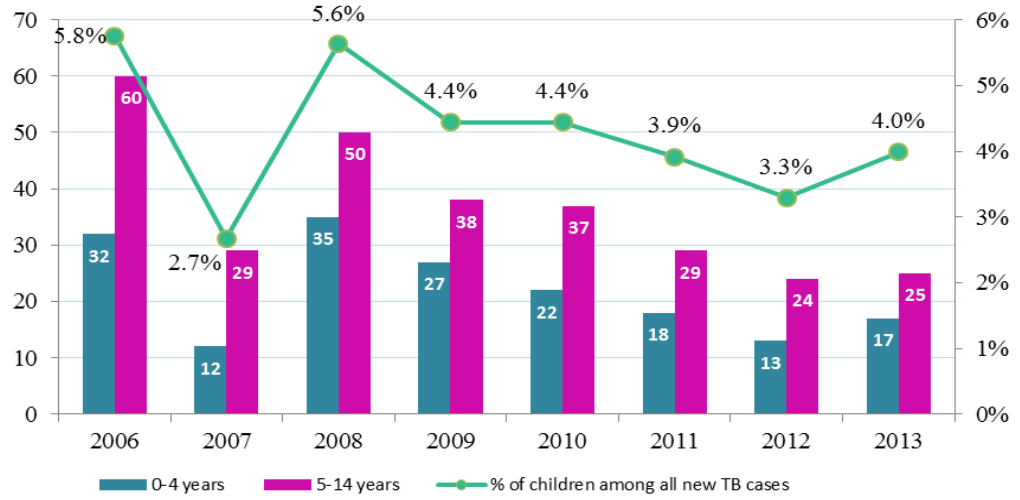
Source: Global TB database *(2)*.

[1] Cartridge-based automated diagnostic test to identify *Mycobacterium tuberculosis* DNA and resistance to rifampicin by nucleic acid amplification technique.

In 2013, according to the NRL database, 181 suspected cases with extrapulmonary TB were investigated for bacteriological confirmation by microscopy and culture, while a total of 250 new extrapulmonary TB cases were reported by routine surveillance system. Of the 181 suspected cases, only 10 (5.6%) were confirmed bacteriologically. The proportion of cases with bacteriological confirmation among extrapulmonary TB cases is very low, suggesting over-diagnosis of extrapulmonary TB cases and/or suboptimal quality and sensitivity of the laboratory diagnostic methods used.

The absolute number of paediatric TB cases almost halved from 82 in 2006 to 42 in 2013. The relative number of child TB cases also fell in the same period from 5.8% to 4.0% (Fig. 8). The year-on-year change in numbers is quite sharp, although this can be partly explained by the small number of paediatric TB cases resulting in large stochastic variations. The sharp reduction and increase in the number of child TB cases in 2007 is obviously an artefact caused by weakness in reporting.

Fig. 8. Trend in notified number of TB cases in children and proportion of child TB among all new TB cases, Armenia, 2006–2013

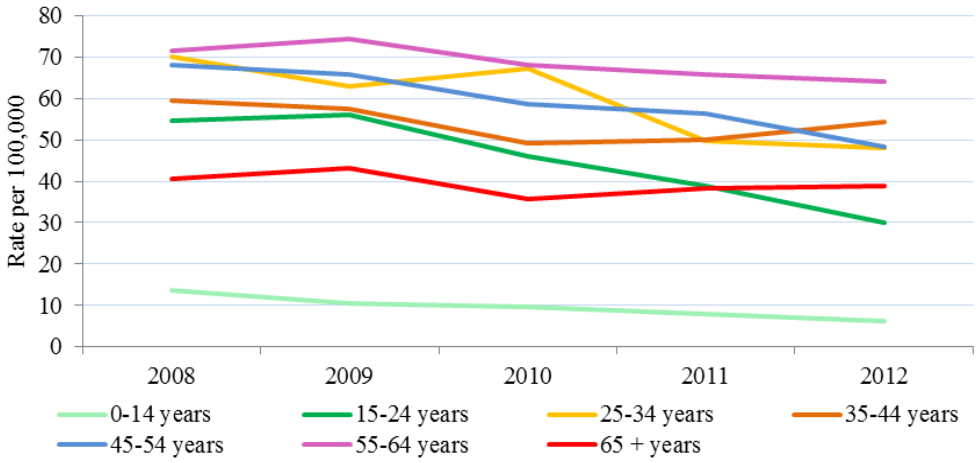


Source: Global TB database *(2)*.

In 2012, the percentage of children among new smear-positive pulmonary TB patients was 0.32%, among smear-negative new pulmonary TB patients -1.83% and among new extrapulmonary TB cases -10.2%. The proportion of extrapulmonary TB cases among children was 54.1% and the male-to-female ratio among children was 3.63. Such a high male-to-female ratio in children is puzzling and contradicts universal observations. Because of similar risk factors and exposure, TB in children is evenly distributed in both the sexes. A skewed population structure caused by sex-selective abortions alone cannot explain such a high sex ratio; most probably it is related to weakness in case detection and diagnosis.

Fig. 9 shows the trends in age-specific notification rates of new TB cases from 2008 to 2012. The age-specific notification rate fell consistently in all age groups except among those aged over 65 years, with an especially notable decrease in the young age groups.

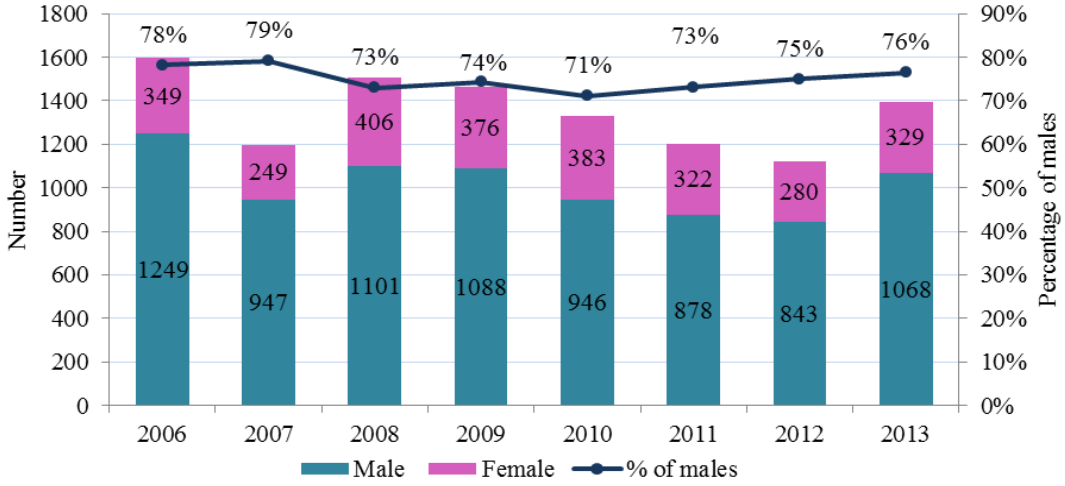
Fig. 9. Age-specific TB notification rate in new TB cases, Armenia, 2008–2012



Source: Global TB database *(2)*.

Between 2006 and 2013, the proportion of male TB patients was more or less stable, ranging from 71% to 77% among new TB cases (the 2013 data include relapsed cases). It was highest in 2006–2007, fell to 71% in 2010 and gradually rose again up to 2013 (Fig. 10).

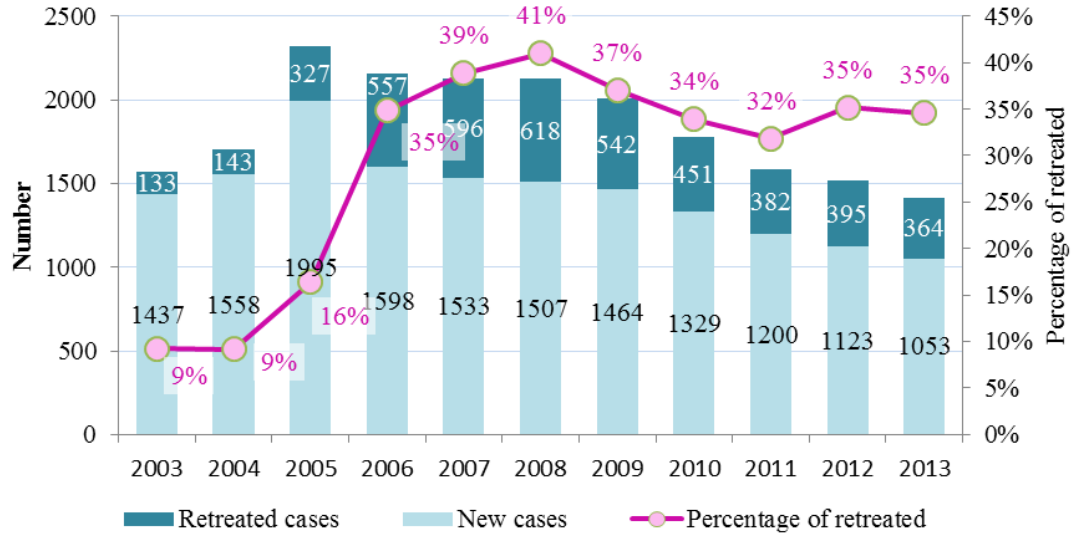
Fig. 10. No. of notified new TB cases by sex and proportion of cases who are male, Armenia, 2006–2013



Note: 2013 data include new and relapsed cases.
Source: Global TB database *(2)*.

The proportion of retreated TB cases among all notified TB cases at national level increased markedly from 9% in 2003 to 41% in 2008. The sharp year-on-year changes in the proportions of notified retreated TB cases between 2004–2005, 2005–2006 and 2008–2009 indicated weak surveillance. Notification of retreated cases during 2009–2013 is free of such sharp variations, suggesting an improvement in the surveillance system (Fig. 11).

Fig. 11. No. of notified new and retreated TB cases and proportion of previously treated TB cases, Armenia, 2003–2013

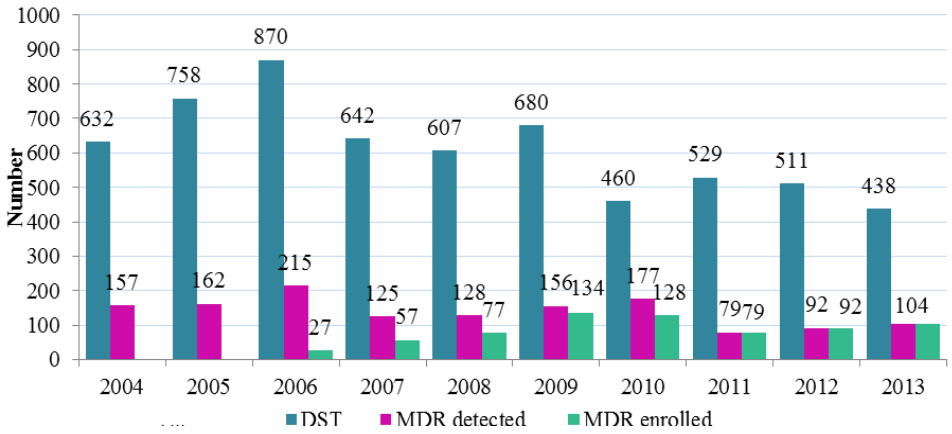


Source: Global TB database *(2)*.

Drug-resistant TB

All TB patients detected according to the current national protocol undergo culture and drug susceptibility testing (DST) at the NRL. The NRL database shows that in 2013, of 456 patients with positive culture/GeneXpert MTB/RIF results, 438 (96%) had documented DST results; 104 (21%) of those with DST results were identified as rifampicin-resistant/multidrug-resistant (MDR) TB cases (Fig. 12).

Fig. 12. No. of cases with DST, MDR-TB detection and treatment, Armenia, 2004–2013

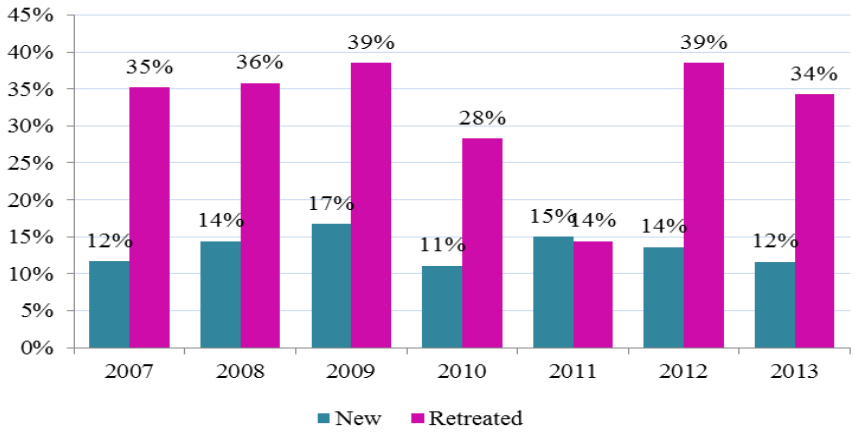


Source: Global TB database *(2)*.

According to routine drug resistance surveillance results, in 2013 the percentage of MDR-TB among new registered cases was 11.6% (43/371), with 34.3% (23/67) among previously treated cases (Fig. 13). The proportion of MDR-TB among new and previously treated cases remains more or less stable. It is important that the total number of MDR-TB patients detected in the last

three consecutive years remains around 100. The wide variations in the percentage of MDR-TB patients among new and previously treated cases between some consecutive years (2009–2010, 2010–2011) and implausible results in 2011 (MDR-TB among new and retreated cases are equal) are most probably related to weaknesses in the accuracy of classification of patients' treatment history and double counting. Even accounting for this fact, it could be concluded that the absolute number of MDR-TB patients fell by an annual average of 22% between 2009 and 2013. Universal access to MDR-TB treatment since 2010 (even with a moderate treatment success rate), access to early drug resistance testing and administration of drug-resistant (DR) TB treatment to prevent further amplification are likely to be the main contributing factors for the stabilization of MDR-TB prevalence among TB patients and reduction in the absolute number of MDR-TB cases observed in Armenia in recent years.

Fig. 13. Percentage of MDR-TB patients among new and previously treated pulmonary TB patients with DST results, Armenia, 2007–2013



Source: Global TB database *(2)*.

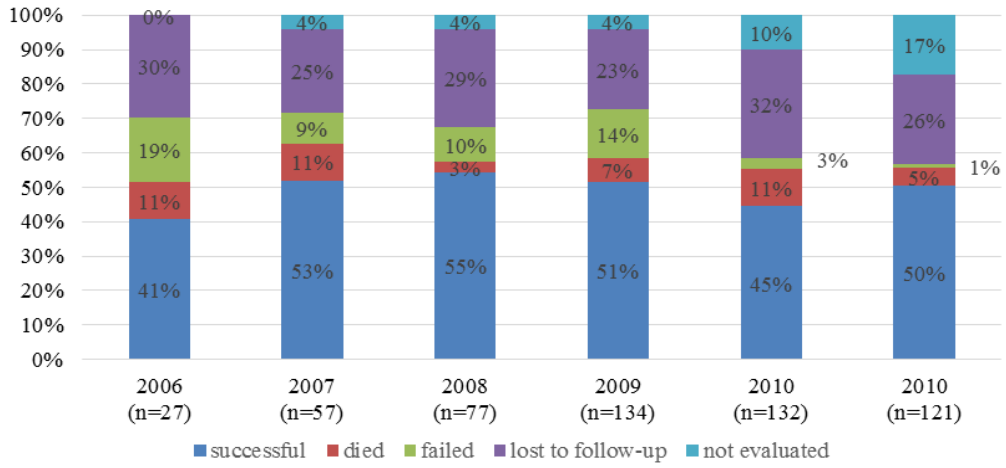
According to the national TB control programme (NTP) database at provincial level, the highest proportion of rifampicin-resistant/MDR-TB cases among TB patients is observed in Armavir, Tavush and Vayots Dzor provinces.

MDR-TB treatment became available from 2006, although with limited coverage. Since 2011, it has been accessible for all notified TB patients. The MDR-TB treatment success rate since 2006 varies between 45% and 55% without any clear trend. The main reason of the poor treatment outcome is interruption of treatment: about one in four patients is lost to follow-up (Fig. 14).

TB/HIV co-infection

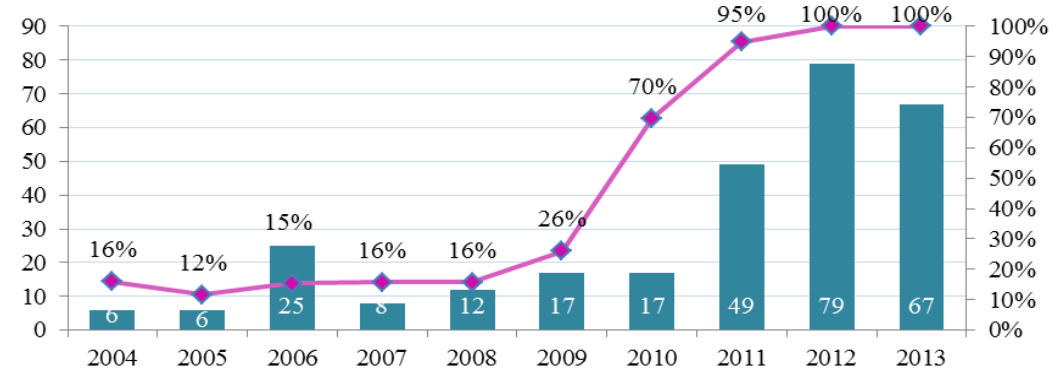
In recent years the number of recorded cases of co-infection with TB/HIV increased sharply, although this might be an artefact associated with the increased coverage of HIV testing among TB patients. In general, there has been major progress in implementing TB/HIV interventions, such as testing TB patients for HIV and providing co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) to HIV-positive TB patients. Coverage of HIV testing is high: in 2011–2013 over 95% of TB patients had documented HIV results. The proportions of HIV-positive people among notified TB patients in 2011, 2012 and 2013 (when coverage was reasonably high) were 3.3%, 5.2% and 4.7%, respectively (Fig. 15).

Fig. 14. Treatment outcomes of MDR-TB patients, Armenia, 2006–2010



Source: Global TB database *(2)*.

Fig. 15. No. of notified TB/HIV co-infections and HIV testing coverage among notified TB patients, Armenia, 2004–2013



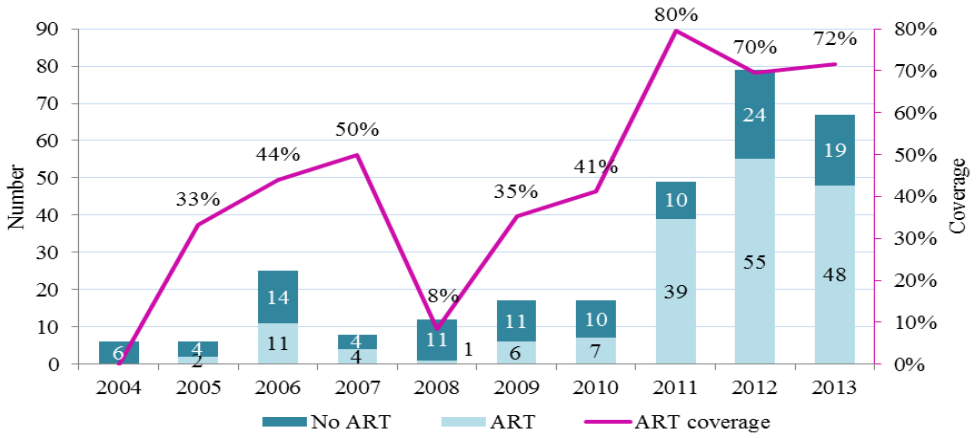
Source: Global TB database *(2)*.

According to the Global TB database *(2)*, of 67 HIV-positive TB patients notified in 2013, 49 patients (71.6%) were enrolled on CPT and the same number of patients started ART. Before 2010, however, coverage with both ART and CPT was quite limited (Figs. 16, 17).

Treatment outcomes

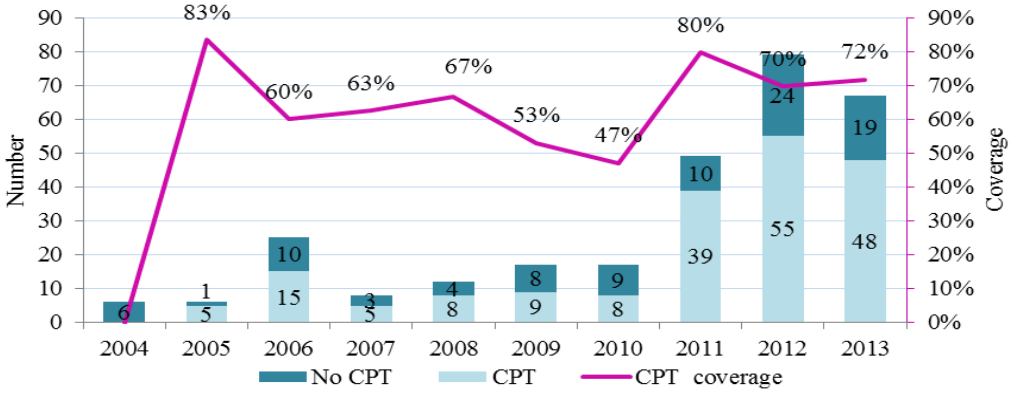
According to NTP records, the treatment success rate among new smear-positive pulmonary TB patients fell from 79% in 2002 to 63% in 2011. Some of the decrease is probably linked to the increased MDR-TB burden among TB cases as well as the increase in the percentage of patients with TB/HIV co-infection. It is, however, difficult to draw conclusions about the real trends in treatment outcomes on the basis of the NTP data. Discussions with NTP staff and a review of records indicated widespread non-adherence to recording and reporting guidelines. In particular, patients detected as MDR-TB were not assigned as treatment failure. This situation improved somewhat in 2010 and 2011 (following the previous review), which explains the sharp increase in treatment failure in the 2010 and, especially, 2011 cohorts. At the same time, it is noteworthy that the proportion of, for instance, defaulters fell markedly (Fig. 18).

Fig. 16. No. and percentage of HIV-positive TB cases enrolled in ART, Armenia, 2004–2013



Source: Global TB database *(2)*.

Fig. 17. No. and percentage of HIV-positive TB patients enrolled in CPT, Armenia, 2004–2013



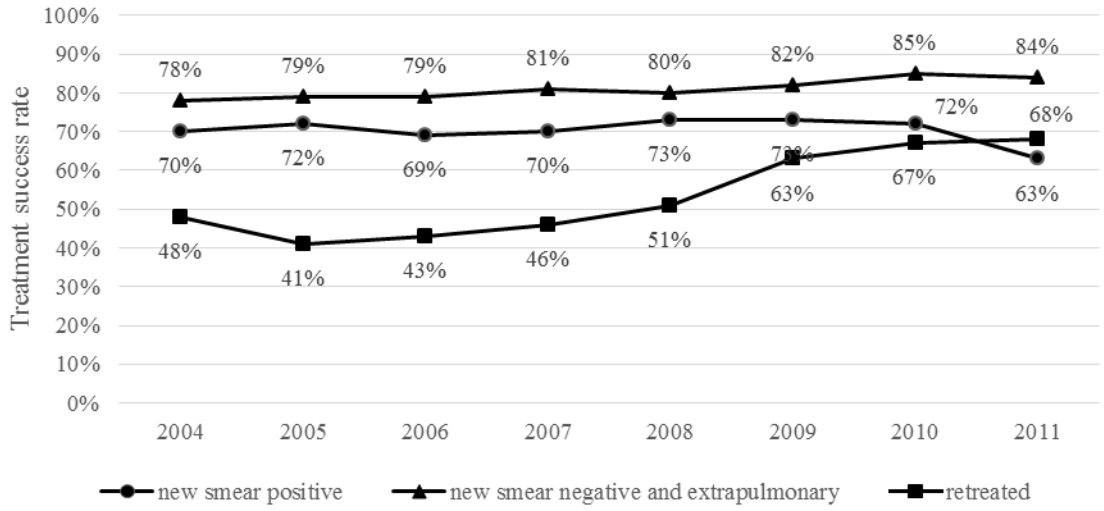
Source: Global TB database *(2)*.

Fig. 18. Treatment outcomes in new sputum smear-positive TB cases, Armenia, 2002–2011

Source: Global TB database *(2)*.

Treatment outcomes of smear-negative/extrapulmonary TB cases and retreated cases in 2004–2011 improved from 78% to 84% in smear-negative/extrapulmonary TB patients and from 48% to 68% in retreated TB cases (Fig. 19). The increase in favourable outcomes of retreated cases is probably associated with improved access to MDR-TB diagnosis and DR-TB treatment.

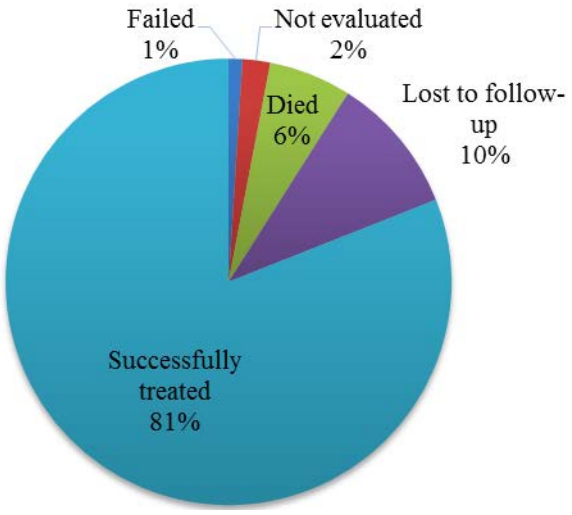
Fig. 19. Treatment success rate among new smear-positive, smear-negative/extrapulmonary and retreated TB cohorts, Armenia, 2004–2011



Source: Global TB database *(2)*.

Fig. 20 shows the treatment outcomes of all new and relapsed cases (bacteriologically confirmed or clinically diagnosed, pulmonary or extrapulmonary) of TB patients notified in 2012 according to the WHO revised recording and reporting framework and case definitions *(3)*. According to the new case definitions, the success rate in new regular TB cases is 81% and the failure rate is only 1%.

Fig. 20. Treatment outcome of new and relapsed TB cases (all forms) notified in 2012, Armenia (n=1350)



Source: Global TB database *(2)*.

Organization and management

Stewardship

TB control is prioritized at the highest political level in the Ministry of Health and by the Minister, who chairs the Country Coordination Mechanism. The top priority given to TB control has led to significant changes and important documents that have been introduced in the strategic management of the health care system in recent years.

On 27 March 2014, the National Armenia Development Strategy for 2014–2025 *(4)* was introduced and adopted by Government Decree #442-N. This strategy defines development priorities for all sectors of the economy, including health care (Chapter 21). Three major components related to health care in the Development Strategy include health situational analysis, definition of priorities for implementation and budget allocations for implementation of key priorities. The following priorities for health sector development are defined in the Development Strategy:

- improving population health through better access, affordability and quality of health care services;
- focusing on the prevention, early diagnosis and treatment of diseases (particularly reversing negative trends in morbidity and mortality of noncommunicable diseases);
- improving and enhancing primary health care;
- developing and implementing quality standards for health care services, ensuring specialized inpatient care for socially vulnerable and special groups;
- guaranteeing emergency cardiac surgery for all citizens;
- improving access to and quality of maternal and child services and prenatal care;
- establishing a haematology hospital that meets European standards;
- improving the accessibility and affordability of medicines;
- increasing public expenditure on health;
- improving the current monitoring, evaluation, recording and reporting systems.

In terms of ensuring the efficient use of resources allocated to health care, the strategy prioritizes the financing of primary health care: "… around 35–40% of state financing allocations to the sector will again be channelled to primary health care services. Thereafter, starting from 2017–2018, increases in overall state allocations to primary health care and hospital services will be distributed with the ratio of 65:35, with the larger share going to hospital services" *(4, p. 105)*.

The Ministry of Health has developed a strategic plan for the health sector entitled The Republic of Armenia Health System Development Concept Paper 2013–2020 (HSDC) *(5)*, which takes into consideration the recommendations of the 2011 review of the national TB control programme *(6)*. The document includes a situational analysis; development strategies for health services to address noncommunicable diseases; maternal, child and reproductive health; communicable diseases (including TB); health for elderly people; mental health; a safe

environment; key priorities in health reforms; strategies for increasing the quality of health care; and human resources in health and a budget.
A significant achievement in advancing accountability, responsibility and institutional capacity was the government decision adopted in March 2014 merging the national TB control programme and the Republican TB Dispensary (RTBD) into the National Centre for Tuberculosis Control (NTC). This reform was recommended by WHO, the World Bank and other donors. As a result of the merger, the NTC has strengthened its roles in TB policy development and implementation and the coordination of work among all stakeholders in the TB system.

Recommendations

The National Armenia Development Strategy is an extremely important document. Not only does it formulate goals and objectives for reforms and development in health and other sectors and define milestones for their implementation, it can also become a basis for developing strategies in different areas. It will, however, be strengthened by the following recommendations.

- Since the Development Strategy was adopted after the Health System Development Concept Paper was developed and approved, the latter should be reviewed and synchronized with the Development Strategy to ensure that the two strategic documents are consistent.
- A chapter(s) should be added to the Health System Development Concept Paper on strategies for integration of vertical programmes in primary health care, development of an integrated health information system and increases in the efficiency of the hospital system. The Health System Development Concept Paper has well-defined strategic priorities for vertical programmes and the main principles for health system performance, but the objectives of its integration with the health system and the directions of organizational reforms of the system are not sufficiently defined.
- A chapter(s) should be added to the Health System Development Concept Paper on intersectoral collaboration and the document adopted by the highest level regulatory act. The goals of intersectoral collaboration are not made sufficiently clear in the Health System Development Concept Paper. The regulation of intersectoral collaboration is extremely important as public health in general implies the involvement of other sectors (ministries/governmental agencies). Currently, many cross-cutting issues are dealt with through personal contacts and other informal mechanisms; this is not a sustainable approach and needs formalization.
- The long-term structural planning of the NTC should be considered, including the possible gradual replacement of TB services with a greater focus on lung and other diseases. Expansion of the hospital profile will provide solutions for many issues, including the possible resistance of TB doctors to the implementation of reforms, the efficient involvement of specialized staff (surgeons) and the full utilization of capacity. Infection control issues should be closely monitored.

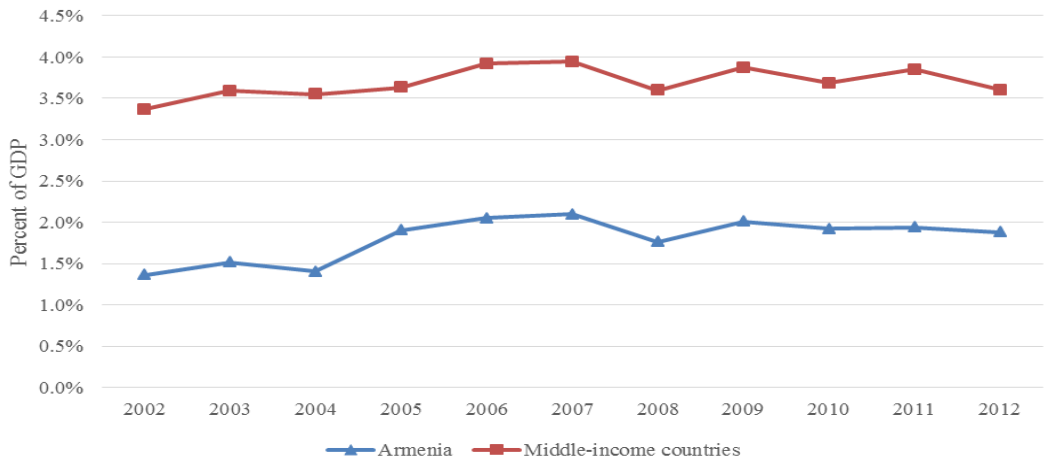
Financial aspects

Financing

Public financing of health care is at an extremely low level compared to other World Bank-classified middle-income countries (Fig. 21). According to ADP, the country plans to increase public expenditure on health care to 1.8% of gross domestic product (GDP) by 2017, rising to around 2.7% of GDP by 2025. To achieve these targets, it is planned to increase the public

expenditure/GDP ratio by 0.1–0.2 percentage points annually. During the ten years 2002–2012, the average annual increase of public expenditure on health as a percentage of GDP was 1.6% in other middle-income countries, widening the gap between Armenia and other countries with similar income levels. At the same time, during the current programme period, the nominal average annual GDP growth in United States dollars will be around 9%, as a result of which GDP per capita will triple in 2025 compared to 2013 and will constitute about US$ 9500 *(4, p. 24)*. This means that the expected increase in expenditure on health care is significantly behind the trends in overall economic development and can lead to poor fulfilment of economic demands in terms of, for example, qualified labour, a decrease in the accessibility and quality of health care services and a continued increase in informal payments.

Fig. 21. Health expenditure as percentage of GDP, Armenia and middle-income countries, 2002–2012



Source: World Bank *(7)*.

Budgeting

Input-based budget planning is an important financial aspect. The budget is not formally separated from infrastructure and general indicators. Every year the Ministry of Health develops a budget proposal based on expenditure on such items as infrastructure, network and workforce. Consequently, there is a risk of reductions in the budget for structural reforms, increased efficiency of the system and/or improved reporting. For example, the creation of a database showing the population covered by primary health care organizations revealed that the total catchment population was lower than the total population according to the National Statistical Service, so the Ministry of Finance announced a reduction in the financing of primary health care based on the new (reduced) data on population coverage. Although at the time of the review this cut had not happened, public health leaders are cautious about this, which hinders initiation of radical reforms.

Pooling

Budget pooling can be viewed as the institutional, geographic and programmed pooling of resources. Institutional and geographic pooling of funds and risks is conducted by the State Health Agency, which acts as a third-party player, pooling and allocating public funds and managing more than 80% of public health resources. At the same time, the State Health Agency receives a budget for more than 50 state-funded budget lines (programmes). This reduces

flexibility in resource management and in operational reallocation of funds (for example, between hospital and primary health care levels and other priority programmes).

Purchasing

Primary health care services included in the basic benefit package are purchased by the State Health Agency according to a simple capitation formula that is weighted for age. Since July 2014, the capitation payment for adults of 18 years and older has been 2185 Armenian drams per person aged over 17 years per year, and double (4380 Armenian drams per person per year) for those aged 17 years and under. In the past, capitation payments were allocated according to the catchment population; now they are paid according to the number of patients enrolled in the primary health care facility. There is no differentiation by gender, and actual expenditure is not considered in the calculations.

TB surgeries and TB doctors in outpatient facilities are also financed on a per capita basis (116 Armenian drams per capita, based on the State Health Agency calculations).

Since July 2014, there has been an increase in per capita financing of primary health care facilities (an average of 34% compared to January–June 2014), reflecting the increased priority given to primary health care by the Ministry of Health.

Hospital and specialist outpatient services included in the basic benefit package are funded through overall budgets as part of a prospective payment system based on an agreed number of hospital cases. The overall budget is set as a ceiling defined by the availability of funds, historical expenditure and the number of cases. Hospital cases are differentiated according to clinical specialty or condition and the type of care required (inpatient/outpatient, average length of stay). When a hospital underspends, the State Health Agency can appeal the budget and reallocate the funds to ensure that the total health budget is spent.

Until recently, TB dispensaries were financed on a bed occupancy basis, which created a negative motivation to increase the length of hospitalization and unnecessary hospitalization. There was no mechanism for financing outpatient services for patients referred for diagnostic tests from outpatient facilities. In order to receive reimbursement for diagnosing patients referred from primary health care facilities, the TB dispensaries tend to hospitalize TB suspects for up to six days.

Several progressive reforms recommended by the previous review mission and other WHO and international donors' reviews have been implemented by the Ministry of Health. Some of these reforms were initiated in recent months and were in the piloting phase during the mission.

New model of TB outpatient financing

The new model of financing outpatient treatment for TB, psychiatric disorders and substance abuse cases was adopted by Government Decision # 1515-N on 26 December 2013. According to this model, finances are allocated in two streams: a global budget (approximately 70%), which includes fixed expenses such as utilities and health personnel salaries, and variable expenses (approximately 30%) which includes medicines and medical supplies, food and other expenses. A similar model is already implemented in organizations providing psychiatric treatment. During the mission the NTC was in the process of adopting this model of financing for TB care. In three TB units in regional hospitals the new financing mechanism will not be implemented due to a lack of calculations for segregating the global budget for TB units from the overall budget of the regional health facility (in two regions TB units are included in regional infection hospitals, and in one region the unit is in the general regional hospital).

Improving the performance-based financing model in primary health care

In 2010, Armenia began piloting the performance-based financing system in primary health care. Initially, the system was based on 10 indicators, for the performance of which a bonus payment was added to the per capita payment of a primary health care facility. This system stimulated data collection, document circulation and testing of selected indicators. To motivate primary health care providers to improve TB detection, the indicator "proportion of confirmed TB cases out of total number of TB suspects referred to TB clinic" was added to the system.

On the other hand, the small size of the bonus (up to 3% of per capita budget), suboptimal interval for payment of bonuses (once a year) and low awareness of performance-based financing in primary health care facilities on the part of management and care providers, the incentive did not result in improved performance.

Since July 2014, the performance-based financing system has been significantly modified. New indicators have been introduced and a decision made to allocate funds for bonuses to health care facilities twice a year. An increase in the budget for primary health care and the proposed 70% increase in salaries will contribute to improved motivation. An indicator on successful treatment outcome for TB has been added to the list for the system to motivate TB doctors working in regional outpatient clinics.

Autonomy for providers and decentralization of management

The operation and ownership of health services have been devolved to regional/province and local governments (with the exception of the State Hygiene and Anti-Epidemic Inspectorate and some tertiary care hospitals). Devolution of financial responsibility means that individual providers now have financial autonomy and are increasingly responsible for their own budgets and management, including the ability to retain and reinvest any profits. The 11 province governments (10 in the regions plus the capital city of Yerevan) continue to monitor the care provided while the Ministry of Health formally retains regulatory functions, although the effective coordination and planning of this decentralized system is still developing.

Most hospitals in Yerevan, almost all pharmacies, the majority of dental services and medical equipment support facilities have been privatized. The regulatory base of the NTC does not, however, allow for the provision of paid services and introduction of special payment mechanisms for selected categories of health providers (such as surgeons).

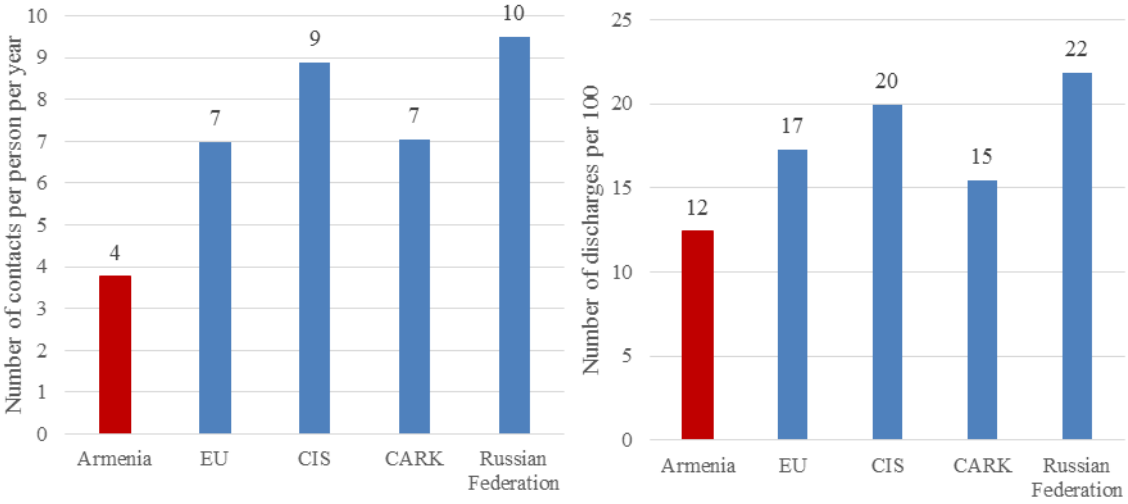
Utilization of health care services

The take-up of health care services is extremely low at both primary and secondary health care levels. Fig. 22 shows the numbers of visits to primary health care facilities and hospitals in Armenia in comparison with European and neighbouring countries.

This low take-up of health care can be explained by multiple factors, affordability being the most important *(9)*. National experts and medical professionals have also identified gaps in the registration system showing high levels of self-referral by patients to familiar/known doctors at both primary and secondary levels without such visits being registered and/or services provided in the statistics system. If this assumption is true, there is a need to raise the level of involvement

and sensitize a wider spectrum of medical personnel at all levels of health care, including private clinics, to TB.

Fig. 22. Utilization of primary and secondary health care services, Armenia, 2014

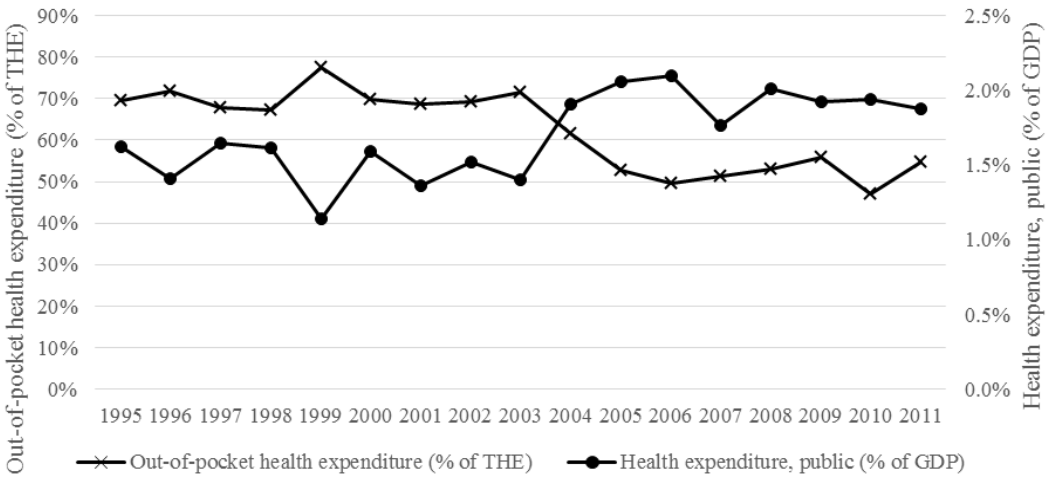


EU = European Union
CIS = Commonwealth of independent states
CARK = Central Asian Republics and Kazakhstan
Source: WHO *(8)*.

Correlation between out-of-pocket expenditure and public health expenditure

As in other countries, the correlation between out-of-pocket health expenditure and total health expenditure is evident (Fig. 23.)

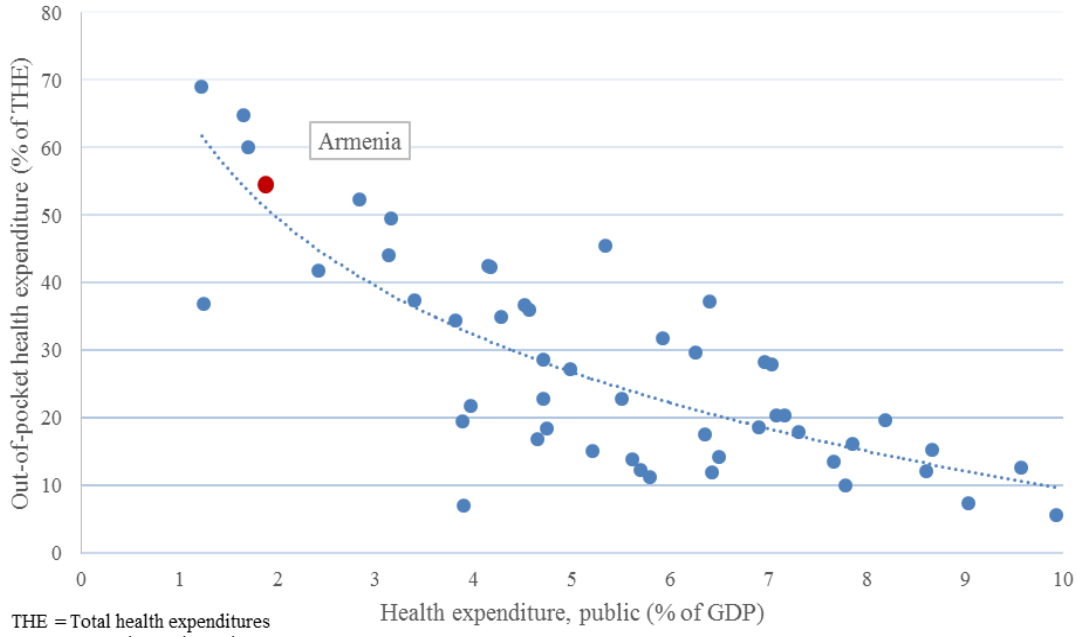
Fig. 23. Correlation of out-of-pocket health expenditure with public health expenditure, Armenia, 1995–2011 [colours?]



THE = Total health expenditures
GDP = Gross domestic product
Source: World Bank *(7)*.

As shown in Fig. 24, a similar correlation exists in other counties: with lower levels of governmental health expenditure there are higher rates of out-of-pocket health expenditure.

Fig. 24. Correlation of out-of-pocket health expenditure and public health expenditure,, 2012



THE = Total health expenditures
GDP = Gross domestic product
Source: World Bank *(7)*.

Thus, without an appropriate increase in governmental health financing it would be extremely difficult to reduce out-of-pocket health expenditure, particularly unofficial expenditure, as well as to increase the affordability of health care in general and for TB in particular (Box 1). "Many patients avoid seeking care because of the costs involved and the perceived level of quality, preferring to wait until a more specialized level of care is needed. The necessity of making informal payments was the main source of patient complaints." *(9)*

Recommendations

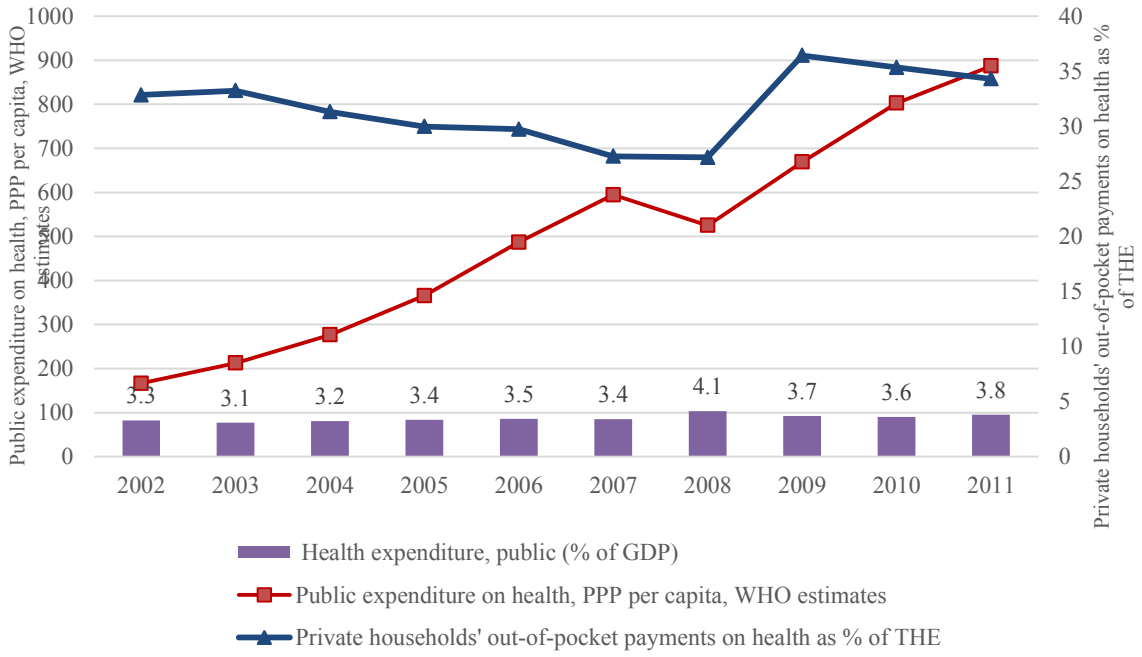
- A policy dialogue should be conducted with the government and other stakeholders with the aim of increasing expenditure on health care and aligning it with international tendencies and projected economic growth rates. In accordance with the requirements of modern social health systems, "… it is unacceptable that people become poor as a result of ill-health" *(10)*. A second aim would be to reduce out-of-pocket expenditure as part of overall health system financing.
- Implementation of the principles of reinvestment of funds for the entire public health system and separate priority areas is one of the key conditions of success in health system reforms. If there is a risk that budgets might be sequestered as a result of network optimization. implementation of reforms, introduction of mechanisms which optimize resources and other interventions, health managers will not be motivated to make changes and develop an effective infrastructure. The possibility of legal regulation of health financing (for example, as a percentage of GDP or governmental expenditure, per capita expenditure) should be explored with the aim of ensuring the reinvestment of funds and stimulation of reforms in public health. Lithuania offers an example in its law on the health system: "The annual base

amount of funding for the Lithuanian national health system, including the state and local government budgets, as well as essential (compulsory) health insurance must be no less than five percent of DGP".

Box 1. Example of correlation between growth of absolute health expenditure and private payments

When discussing planning for health financing, the national partners often expressed the opinion that despite the projected low increase in health expenditure as a percentage of GDP, the absolute amount of health expenditure is expected to increase rapidly. International experience shows, however, that given a low level of health expenditure as a percentage of GDP, the growth in absolute health expenditure does not lead to an adequate reduction in private payments. In the Russian Federation, for example, private payments did not decrease (but even increased slightly) from 2002 to 2011, regardless of a 6.2-fold increase in per capita health expenditure during that period (Fig. 25).

Fig. 25. Correlation between public health expenditure and private payments, Russian Federation, 2002–2011



THE = Total health expenditure
PPP = Purchasing power parity
Source: World Bank *(7)*.

- TB subaccounts should be part of the national health accounts system so that the actual funds for allocation to financing of TB services can be estimated. This will allow for a realistic estimate of the size and structure of the budget to be allocated for TB services and for the development of a system to ensure sufficient funding for TB in future. This is especially important in the light of the reforms related to reallocation of resources from inpatient services to outpatient care.
- A proposal should be made to the Ministry of Finance to reduce the number of government-funded programmes, so as to increase the flexibility and effectiveness of the Ministry of Health in resource management. The process can be implemented in phases with an annual decrease in the number of programmes. The recommendation does not imply termination of detailed reporting by the Ministry of Health on the main expenditure lines; rather it suggests shifting the focus towards delegating more power to the Ministry of Health in making operational decisions on the use of resources.

Financing of primary health care system

- The incentive for per capita allocation should be increased based on a stimulating component of up to 10–15% (currently about 3%). Outcome-based financing of primary health care is an optimal solution which has been widely introduced internationally with an incentive/bonus component of, generally, 10–20% of the total per capita payment. A smaller percentage of per capita financing as motivation is generally not efficient.
- Bonus payments should be made quarterly. In the pre-2014 model, bonus payments were allocated annually based on end-of-year performance analysis. A one-year delay in paying bonuses failed to motivate service providers to improve their performance.
- The sources for data collection on outcome-based financing should be optimized. Information on the performance of TB indicators should be collected from the NTC rather than primary health care providers. This will increase the validity of the data (data will be generated by an independent organization), reduce the paper work of primary health care physicians, and increase the role of the NTC and the efficiency of using an e-TB Manager.
- Primary health care facility managers and health care providers should be made more aware of incentive-based financing and their roles within this system. The following activities are suggested: (i) analysis and presentation to primary health care facilities of the results of quarterly performance monitoring, with the possibility for facilities to compare their performances with those of similar organizations; (ii) publication of reports on the Ministry of Health website for public access; and (iii) identification and dissemination of successful implementation of strategies leading to achievement of positive outcomes.
- Those recommendations of the previous National TB Control Programme review on the use of incentives for patients and health care providers which had not been introduced by the time of the mission should be carried out *(6)*.

Financing at hospital level

- The treatment of different forms of TB should be costed in accordance with WHO classifications and the results used to estimate the size of the global budget for providers. The move to financing TB hospitals from the global budget is an innovative step directed towards improving the efficiency of outpatient TB care. The next step could be to introduce a performance-based coefficient into the global budget, which would align the budget with the types of hospital patient. Calculation of these coefficients could be based on the proposed costing study. This measure is directed towards the development of financial incentives for TB hospitals to ensure the validity of hospitalization and optimization of the structure of treated patients, as well as stimulating prompt discharge of patients on achievement of positive treatment outcomes. These recommendations have been made in a number of other studies and reports *(11,12)*. In addition, the Ministry of Health will, on the basis of the results of the recommended costing study, be able to segregate the budget for TB departments of general hospitals in three regions and move to global budget-based financing (similar to the NTC).
- A regulatory basis should be provided to enable TB hospitals to provide paid services, such as medical check-ups of foreign citizens.
- The NTC (TB inpatient clinic) should consider the implementation of mechanisms for per service financing of outpatients referred by polyclinics and/or other hospitals. Such mechanisms will reduce hospitalization for diagnoses and stimulate outpatient diagnosis.

- A regulatory basis should be provided for NTC managers to determine staff salaries. Informal payments for different categories of health workers generally differ. For example, "those working in psychiatry or TB care are not well placed to elicit informal payments whereas gynaecology and cardiology have the potential to be much more profitable branches of medicine" *(13)*. As a consequence, there is no prestige attached to working in the NTC, which makes it difficult to attract qualified personnel such as surgeons.
- The NTC should develop and distribute widely a manual for physicians.

Service delivery

Laboratory and diagnostic services

To evaluate the NTP laboratory network and diagnostics services, the review team visited TB laboratory services at national and regional levels, and interviewed management and staff of the NTC, NRL, regional laboratories, Médecins Sans Frontières (MSF)-France and prisons and regional TB coordinators.

TB laboratory network

The TB laboratory service aims to diagnose TB cases and monitor treatment. It includes one NRL and 26 microscopy centres (MC), distributed throughout the country and the prison system (Table 1). The NRL has facilities to conduct culture testing, molecular diagnosis of drug resistance (with line probe assay (LPA) and GeneXpert MTB/RIF) and DST. There are three GeneXpert MTB/RIF machines in the country, two of them located in NRL and one in the Yerevan City tuberculosis dispensary. The laboratory network does not possess any sputum collection centre.

Table 1. Laboratory facilities, Armenia, 2014

Level of the service	No. of facilities conducting:			No. of functioning facilities
	acid-fast bacteria microscopy	GeneXpert MTB/RIF	culture	
Central	1	1	1	1
Intermediate	1	1	0	1
Peripheral	25	0	0	25
Total	26	2	1	26

Source: NTP and NRL data.

WHO criteria for laboratory coverage require one MC per 100 000 population and one culture/ DST laboratory for five million population. In Armenia one MC is designated for an average population of 128 579 and one culture laboratory for three million.

TB diagnostics are done through smear microscopy confirmed by culture inoculated in both solid and liquid media. LPA and GeneGeneXpert MTB/RIF were introduced in 2010 and 2013, respectively, and are in use.

Overall the system is functioning without an overarching strategic document, such as a laboratory strategic plan, regulating laboratory services. The plan of laboratory activities is reflected in the national TB working plan and MDR-TB response plan for 2012–2015.

An informal committee, consisting of a consultant from the NTC, the head of the NRL and microbiologists from the NRL, functions as a task force to guide the NTC's laboratory-related activities. It is not, however, formalized and there is no formal national laboratory committee.

Recommendations

- A strategic plan should be developed and approved for the NRL that will reflect a vision, goals, detailed objectives, strategies and a (realistic) list of activities for the next five years for TB laboratory services in line with the directions of the NTP.
- A comprehensive analysis should be made of the current TB laboratory service, including staff workload and qualifications, microbiological indicators, proper requests for laboratory tests according to national algorithms, and proper usage of reagents and consumables. This assessment should become a basis for the NRL strategic plan.

Policy guidelines and procedures

At the time of the review there was no final and approved NRL manual or guideline, although such a document is being developed. Once the current draft has been revised by a Ministry of Health specialist, the document is to be translated into English for revision by international experts.

National algorithms for diagnosis of TB infection have been drawn up but not yet approved and introduced for implementation. Some health facilities visited lacked current TB algorithms.

Standard operating procedures and short instructions for main laboratory procedures are available and in use in the NRL.

The draft version of generic standard operating procedures drawn up by the NTP for the main laboratory activities in MCs (such as the Ziehl-Neelsen method, and the use and maintenance of optical microscopes) are in use in some of them. These documents have not, however, been adapted for each MC.

Recommendations

- The capacity of the NRL should be strengthened with a focus on policy, planning, coordination, monitoring, specialized testing and research.
- Laboratory guidelines should be finalized, approved, disseminated and implemented.
- National algorithm for TB diagnostics should be approved by the Ministry of Health, distributed and followed by all TB physicians.
- Standard operating procedures for MCs should be drawn up for specific local conditions and approved by the local medical authorities.
- To coincide with the planned rollout of GeneGeneXpert MTB/RIF throughout the country, standard operating procedures for GeneGeneXpert MTB/RIF should be drawn up and distributed to local MCs.

Laboratory network

The TB laboratory service and laboratory network are structured at central and regional levels, and the responsibilities and interactions between levels and designated facilities have been defined. The courier system for sputum transfer is working properly.

The NRL was established in 2002. It is supervised by the Supranational Reference Laboratory in Borstel, Germany, although there is no formal agreement between the NRL and the Supranational Reference Laboratory. The NRL is not accredited nationally or internationally. The work of the NRL includes: performing culture, DST and molecular tests covering the entire country; supervising all MCs; providing external quality assurance to staff of the MCs to ensure quality diagnosis; conducting monitoring visits and providing technical training for technicians from MCs.

Sputum microscopy diagnostic services under NTP are provided by designated *MCs*. Following the reorganizations in 2010 and 2013, there are now 26 MCs: one or two in each province (18 in all), five in Yerevan, one in the RTBD and two in the prison system. The functions of the MCs include screening TB suspects using microscopy, monitoring treatment and performing the main biochemical tests for TB patients. The workload of the laboratories visited seems to be low.

There are no *sputum collection centres*. Following the reorganization of the TB services several TB clinics remained without an MC. In these areas, patients are referred to the nearest TB clinic with an MC. This creates concerns in terms of access to TB testing, especially for patients (from socially vulnerable groups) who may refrain from travelling to the nearest TB clinic/MC for TB diagnoses.

Recommendations

- Access to TB laboratory diagnostics should be improved for patients in areas with no MCs.
- Consideration should be given to opening peripheral sputum collection centres at all TB clinics (this does not mean reopening MCs). This is a low-cost intervention (sputum collection centres may be located outside the health facility building).
- Samples, but not patients, should be referred to laboratories. The collection sites should be included in the courier system and samples transported to the nearest MC or the NRL.
- Staff involved in sputum sample collection in MCs and sputum collection centres should be trained in methods of sputum collection.

Courier system

The Global Fund to Fight AIDS, TB and Malaria grant provides support to the NTP for the transport of sputum. Each region has one car to transport samples from the province to the NRL (twice a week from provincial MCs to the NRL and three times a week from Yerevan MCs to the NRL). This courier system is also used to send laboratory results from the NRL back to MCs. Overall the system is working well although there are delays in feedback and communication of test results from the NRL to some MCs. These delays may create problems with initiation of the correct treatment and/or change of the treatment schedule for individual patients.

Recommendations

- The courier system should be maintained and a search started for domestic funds to ensure proper functioning of the system in case the Global Fund grant is terminated. The plan for the courier system should be incorporated into the NRL strategic plan (recommended for development).
- The laboratory results reporting system should be improved by:
  - ensuring proper submission of the results on paper forms from the NRL to regional MCs so as to avoid delay in confirmation and/or treatment initiation of TB;
  - ensuring that the test result is entered into the national electronic database and made accessible for physicians; this will improve the communication of test results from the NRL to health care providers.

Infrastructure

The physical infrastructure of MCs should allow at the least appropriate space, water and the possibility to decontaminate infectious materials. Some MCs have limited space allocated to them. In general, the majority of MCs have dedicated areas for main activities only. For example, in one facility the autoclave was located on the stairs and the microscope was in the hall. Some of the facilities have not been renovated and lacked furniture, air conditioning and internet access. The efforts of the MC staff to keep the facility clean were noted, but the infrastructure needs basic improvement. When GeneXpert MTB/RIF is rolled out, some MCs will be in need of space to place the GeneXpert MTB/RIF machines.

Space is available in the NRL for all the main activities, although at the time of the visit some rooms (for the LPA test) were flooded and in need of renovation.

Recommendations

- MCs should have a sufficient area and facilities for main activities. The proper allocation of space in MCs should be thoroughly considered in anticipation of the rollout of GeneXpert MTB/RIF.
- Some MCs and the NRL should be renovated urgently. Current needs for the renovation of MCs and identification of funds from local authorities, Ministry of Health, NTP, the Global Fund or other donors should be evaluated.
- It is important to consider installation of air conditioning systems and ensure internet access in the MCs, prioritizing the sites planned for GeneXpert MTB/RIF machines.
- New furniture should be procured for some MCs.

Staff

Overall, the MCs and the NRL have adequate staff, although there is a shortage of medical technicians in some regional MCs and in the NRL. The average age of the staff working in the regions is above retirement age, and the system has difficulties in attracting and retaining younger personnel. The review identified the following issues related to medical personnel in the laboratory services.

- Around 70% of the overall laboratory personnel have more than 10–15 years of experience and 30% have from 5–15 years (based on the findings from the MCs visited).

- No new staff (such as microbiologists) have been employed at the NRL, apart for one technician who joined in 2009.
- At the national level, there is no registry of all the staff involved in the TB laboratory service.
- At the moment the laboratory network is sufficiently staffed, although there is a need for backup. In some laboratories work stops when the permanent staff are on annual leave.
- There is no general training plan for laboratory technicians. Training in laboratory methods was conducted two years ago with support from the Global Fund, but there has been no refresher training since. Most of the issues identified in the laboratory service can, however, be addressed during on-site monitoring visits.
- New staff are trained on the job or at the NRL.
- There is a five-year cycle of competence assessment scheme for bacteriologists, recommended by the Ministry of Health.
- Two laboratory specialists have been trained at the Supranational Reference Laboratory in Borstel and are currently employed as a laboratory consultant and a microbiologist in the NRL.

Recommendations

- The NTC should be responsible for the continuous professional development of the laboratory network staff.
- Motivational mechanisms need to be developed and implemented to recruit, train and retain laboratory staff.
- Together with the NRL, the NTC should develop a registry for the laboratory personnel (technicians and microbiologists) involved in TB laboratory service. The registry should include information on the training status and staff training needs.
- The training needs of the laboratory network staff should be identified and a training plan drawn annually based on training needs.
- A specific budget should be designated for training laboratory staff (from, for example, the Global Fund or domestic funds, or from courses at Yerevan State Medical University or medical colleges).
- New personnel, such as graduates and students of medical colleges and universities, should be motivated and involved in the NRL.

Equipment

Most MCs are equipped with biosecurity clinics for performing smear and Ziehl-Neelsen staining and each MC has a binocular microscope, with an average lifespan of five to eight years, procured with support from the Global Fund. The NRL is equipped with biosecurity clinics class II, two mycobacteria growth indicator tube (MGIT) BACTEC 960 machines, equipment for LPA, two four-module GeneXpert MTB/RIF machines, an autoclave, several incubators, a refrigerated centrifuge and a vortex. Almost all the equipment was procured through the Global Fund grant.

Maintenance of equipment is one of the most important prerequisites to ensure the quality and validity of laboratory results. A key challenge is the lack of routine monitoring of equipment to

ensure that it functions correctly and that malfunctions (with, for example, the air flow for biosecurity clinics, temperature records for refrigerators and the temperature for the centrifuge) are detected promptly. The following issues with maintenance of the laboratory equipment were identified.

- There is no plan for procurement and maintenance of equipment (such as biosecurity clinics, HAIN equipment and autoclaves) at the NTP, and no contract between the NRL and companies/individuals for regular equipment maintenance.
- No funds have been designated for maintenance of the MGIT equipment.
- The Hain Company does not maintain the LPA equipment because the thermocyclers were procured from another company.
- There is no company (and thus no contract) that could perform maintenance and certification of the biosecurity clinics. The most recent certification of the biosecurity clinics was done in 2013 by an engineer from the German LKK Klimatechnik company.
- The NRL does not have a contract with a company providing maintenance and repair services for other general equipment. The NRL equipment (autoclaves, centrifuges and freezers) is checked by an engineer from RTBD.
- The lack of bioengineers at the MCs also creates challenges in repairing microscopes and changing lamps, so no maintenance is done for biosecurity clinics.

Recommendations

- A national plan for the procurement, maintenance and replacement of equipment should be developed and reflected in the strategic plan for the NRL.
- Resources should be identified for the maintenance of equipment (such as contracts with external companies and/or engineers).
- Maintenance issues with the LPA thermocycler and the MGIT machine should be solved.
- Options should be identified for calibration and maintenance of the GeneXpert MTB/RIF machine, and be reflected in the new Global Fund proposal.
- Standard operating procedures and short instructions for all types of equipment should be developed by the NRL and daily technical records should be available.

Workload

Although WHO recommends that two samples should be taken for TB diagnosis and follow-up, the national algorithm requires the collection of three samples per patient (arguably because of the poor quality of the samples collected). This increases the workload for MCs and leads to the overconsumption of reagents and consumables without improving the quality of microbiological tests. The majority of MCs (except the RTBD and the Yerevan City Tuberculosis Dispensary) have a workload of less than five sputum samples per day for both diagnostic and follow-up purposes. Usually, for diagnostic purposes, the MCs have one to two new TB suspects per day (confirmed by TB physicians). This observation was confirmed by facility visits (Table 2).

If the workload is reduced by 30% (taking two samples instead of three) the MCs could be used more effectively, especially if sputum collection sites are opened and maintained and the courier system improved.

Table 2. Daily workload of the MCs visited, Armenia, 2014

Name of MC	Samples per day	Total		Diagnostic		Follow-up	
		Total	Positive No. (%)	Total	Positive No. (%)	Total	Positive No. (%)
RTBD	29	7281	1066 (14.6)	4740	474 (10)	2541	592 (23.3)
Yerevan City Tuberculosis Dispensary	14	3739	170 (4.5)	2678	129 (4.8)	1061	41 (3.9)
Vagharshapat	4.1	1025	53 (5.2)	470	27 (5.7)	555	26 (4.6)
Vanadzor #2 hospital	4.5	1146	105 (9.2)	613	60 (9.8)	533	45 (8.4)
Shirak infection hospital	6.6	1652	95 (5.7)	961	50 (5.2)	691	45 (6.5)

Source: Annual reports of MCs and NRL.

It is expected that one GeneXpert MTB/RIF machine will be procured for each MC so that all 26 MCs have a GeneXpert MTB/RIF available on site.

Recommendations

- The sputum sample collection algorithms should be revised to two samples of sputum per patient instead of three.
- The quality of the samples collected in peripheral centres should be improved through training designated staff and routine monitoring of the quality of the samples.
- The MCs' workload and WHO's recommendations for GeneXpert MTB/RIF should be considered in the process of budgeting for and procurement of new GeneXpert MTB/RIF machines.

Biosecurity

The team made the following observations regarding biosecurity in the MCs.

- In general, the ventilation system in most MCs is natural. In some MCs biosafety clinics class 1 (air extraction clinics) are used to perform smear preparation and staining procedures. Maintenance of these biosafety clinics is a challenge, given that they are not verified and certified according to WHO recommendations.
- A sufficient number of respirators was available in most of the facilities visited.
- A centralized procurement system is used for disinfectants, alcohol (75%) and bleach for surface cleaning in the 26 MCs. The MCs can also receive disinfectants from local medical institutions.
- Used sputum containers and other contaminated materials are collected in the MCs and discarded according to the regulations of the medical institutions (autoclaving or incineration). Some facilities contract a specific service company to collect and destroy medical waste.
- There are no generic standard operating procedures or regulations for decontamination of medical waste in TB MCs, which can pose a risk for staff in some MCs. For example, the practice of putting disinfecting solution into the sputum container and then discarding the solution into another (bigger) container or sewage can lead to the generation of aerosols or contamination of the environment.
- The Global Fund has supported the procurement of small autoclaves and their installation in some MCs to help deal with the challenge of decontaminating medical waste.

- As far as possible, working places were being kept clean.

The following observations were made in the NRL.

- The NRL has no mechanical ventilation with negative pressure. Biosecurity procedures are observed through good microbiological practice and work in biosecurity clinics type II.
- As stated above, the most recent evaluation and certification of biosecurity clinics in the NRL was conducted in 2013 by an engineer from German LKK Klimatechnik company, supported by the Global Fund. One biosecurity clinic has not been certified because of failure and cannot be used since it presents a biohazard to the staff. The filters need to be changed, but these types of filter are no longer in production.
- Proper refrigerating centrifuges are in use in the NRL. Centrifuges contain aerosol-tight caps for tube buckets that are not used permanently.
- Ultraviolet germicidal irradiation lamps are in place and properly used.
- There is no plan to train NRL staff in biosecurity procedures (such as biological accidents in- and outside biosecurity clinics; the use, maintenance and cleaning of centrifuges; and the use of disinfectants).

Recommendations

- A local company should be identified to maintain and certify existing biosecurity clinics according to WHO recommendations (at least once a year).
- The filters of uncertified biosecurity clinics should be changed or (preferably) additional filters procured for at least one biosecurity clinic for the NRL (possibly through the Global Fund project).
- The NRL should identify and train a biosecurity officer (possibly from the existing staff) in the main biosecurity procedures and infection control principles in a TB laboratory. He/she should then provide routine training for laboratory staff and regularly monitor laboratory practice for all staff working at the NRL (including use of the cap for centrifuge buckets, procedures to minimize aerosol, biological accidents and use of the respirators).

Financing

Funding for the TB laboratory service is allocated by the State Health Agency (for salaries and the facilities' running costs such as water, electricity and waste decontamination) and donors (for reagents, consumables and equipment). Substantial funding over the last three years also came from international donors, particularly the International Committee of the Red Cross, GOPA (a German technical agency, with funds provided through the German Development Bank) and the Global Fund. The NRL was built using donations from the International Committee of the Red Cross and equipped with support from the Global Fund. The Global Fund also supported the procurement of binocular microscopes for MCs as well as the purchase of registers, submission forms, reagents and consumables. There are no other funds available to cover the needs of the TB laboratory service. The government plans to apply for a new Global Fund grant for 2015–2017 to cover all the costs of the laboratory network for the next few years.

Further assessment is needed of the generally limited understanding of the costs of the TB laboratory service.

Recommendations

- The current overall needs and associated costs of the TB laboratory network should be identified.
- Funding should be ensured either from domestic sources (negotiations with the Ministry of Health and the State Health Agency) or from other partners (such as donors, research projects or clinical trials) to cover the needs of the laboratory service.

Data management

Two separate laboratory registers (for microscopy and for culture) are in use by the NRL and MCs. This creates difficulties in following up the laboratory results for the same sample (microscopy, GeneXpert MTB/RIF, culture, DST).

Quarterly reports from MCs are regularly submitted to the NTC, whose laboratory consultant has data regarding workload and laboratory indicators from all MCs. The reports do not include GeneXpert MTB/RIF test results.

A national electronic database (e-TB Manager) has been launched countrywide, based on individual patient records with clinical and laboratory components. However, there is no systematic data entry of the laboratory results (culture and DST) into the database; data are occasionally entered into the system by staff of either the NRL or MCs. The lack of clarity and/or protocols as to which organizational unit is responsible for data entry – the NRL or MC – means that the test results are not available when they should be in the electronic database. Validation and quality assurance of the data have not been properly done and the database needs a major upgrade.

Monitoring and supervision of MCs is conducted from the central level. Monitoring visits are carried out by microbiologists from the NRL. Supervisory laboratory visits are performed separately by monitoring and clinical teams. No records for visits conducted in 2013–2014 were available in any of the MCs visited during the review. Reports of monitoring visits are archived in the NRL with no copy given to the facility in question. The staff in MCs and administrative departments of medical institutions are not familiar with the recommendation of the national consultant who visited the facility.

Recommendations

- A comprehensive data flow should be created for the national electronic database. Data entry operator(s) responsible for data entry and validation should be identified or designated. Monitoring and supportive supervision should be improved by reorganizing monitoring visits to:
  - consider joint monitoring and supervision visits (by clinicians and laboratory staff) to address common problems;
  - provide feedback to MC staff and administration on the issues identified and recommendations made during the monitoring visit, with a copy of the monitoring report left in the facility.
- The quarterly reports from MCs should be modified to include a separate line for reporting GeneXpert MTB/RIF test results (in view of the plans to roll out GeneXpert MTB/RIF).
- Consideration should be given to unifying and optimizing laboratory registers in MCs.

Procurement and distribution of supplies and equipment

There is no specific plan for procurement of laboratory equipment and reagents. Up to now, the purchase of all equipment and supplies has been financed by the Global Fund. There is no agreement or signed document as to the government's intention to take over the procurement of reagents and/or laboratory supplies. Neither the NTC laboratory consultant nor any other laboratory staff have been involved in the procurement system (including in the estimation of requirements and choice of quality materials) up to 2014.

Reagents and consumables are procured centrally in coordination with the NTC and with the support of the Global Fund project. No other source of procurement existed at the time of review. Reagents and consumables are stored at the NTC.

Local TB coordinators estimate the needs for supplies and reagents and send quarterly requests to the NTC laboratory coordinator. Following review by the NTC laboratory coordinator, the reagents and consumables are taken to regional MCs by car (for drugs) or during monitoring visits. No problems have been reported in the distribution of supplies at any level.

The NRL receives some of the powder for reagents (fuxin, methylene blue), prepares the solutions and distributes them to the MCs. The team observed that reagents prepared by the NRL and distributed to MCs were not properly labelled, with no note on preparation date and validity time. Some expired reagents were still in use.

There are no systematic and unified procedures for management of the stock and inventories of consumables and reagents in the MCs. Each MC uses different inventory forms. The team did observe, however, that in the facilities visited the reagents and consumables were properly kept.

During the review an interruption of TB rapid diagnosis was observed resulting from a shortage of reagents. The GeneXpert MTB/RIF was held in customs waiting for clearance for more than two months, while the GenoType MTBDRpl assay, which the NRL had ordered six months earlier, was interrupted for more than a month before it reached the laboratory.

Recommendations

- A continuous cycle for procurement and supply of reagents and consumables should be organized to avoid shortages.
- The NTC should identify domestic funds for procurement of reagents and consumables.
- A space should be designated in the NTC for storage of reagents and consumables (following relocation of the NTP central office to RTBD).
- The quality of prepared reagents should be ensured by controlling the quality of each batch and submitting the certificate of quality together with the reagents to each MC. The NRL should distribute reagents in proper vessels and with correct labelling (including the name of the reagent, date of preparation, date of expiry and responsible person).

Case-finding

There is no active TB case-finding: patients are referred individually to the primary health care system (general physicians) based on complaints of cough or other respiratory symptoms. General practitioners usually start antibacterial treatment with a broad spectrum of antibiotics for two to

three weeks. If the symptoms continue the patients are referred to TB doctors, who refer TB suspects for laboratory tests (microscopy, GeneXpert MTB/RIF/LPA, culture) and often prescribe anti-TB treatment before receiving microbiological confirmation. At the same time, not all physicians are familiar with the case definition of and main symptoms for suspecting TB, which leads to a number of patients being referred for TB laboratory diagnostics without TB-related symptoms.

The team observed that a number of patients were diagnosed with TB and treatment initiated on the basis of clinical assessment. A number of TB patients did not have microbiological confirmation (microscopy, GeneXpert MTB/RIF/LPA, culture), which means that some patients received unnecessary, incorrect or suboptimal treatment.

Additionally, the laboratory indicators show that real TB suspects are not referred to microscopy, GeneXpert MTB/RIF, MGIT tests. For example, according to the MC reports the positive rate for microscopies done for diagnostic purpose is below 10% – the standard recommended by WHO (Table 2). The positivity rate of MGIT culture is around 15%.

Recommendations

- Case-finding of microbiologically confirmed TB patients should be improved.
- The definition of TB suspect/TB clinical/TB confirmed case and algorithm for diagnosis should be revised, approved and implemented, and its implementation regularly monitored.
- Physicians' knowledge about TB should be improved (target training).
- The quality of sample collection should be improved (recommended in 2011).
- TB diagnosis should be ensured through quality-assured bacteriology tests (GeneXpert MTB/RIF/LPA, MGIT BACTEC).
- The differential diagnosis of respiratory diseases should be improved by implementing the practical approach to lung health.

Samples

Different materials are collected for TB laboratory diagnosis. Sputum is usually collected on two consecutive days, once in the morning. In addition to sputum, the NRL also receives different extrapulmonary samples.

It is well-documented that reliable laboratory results depend on the quality of the material collected. The quality of the sputum was noted during the 2011 review and continues to be of concern now. Not all the staff in the MCs visited know how to collect sputum correctly and to explain the procedure to patients. According to the MCs quarterly and annual reports, poor quality samples are received by the MCs and the NRL (10–30% of all samples are saliva or have low volume). Laboratory tests are performed using these poor quality samples, leading to a lack of reliable microbiological results and inefficient use of reagents, consumables and staff work. There seems to be limited evidence of efforts to correct this problem since it was reported in 2011.

Recommendations

- The quality of the material collected for laboratory diagnosis should be improved.

- Procedures should be developed and staff trained in sputum collection.
- Information material regarding sputum collection should be created and displayed visibly in sputum collection sites.

Laboratory methods

Ziehl-Neelsen method

- All TB MCs conduct testing using the Ziehl-Neelsen method directly from samples. The fluorescent assay method is not available in Armenia. The NRL prepares concentrated smears.
- Incorrect reporting of Ziehl-Neelsen results in MCs was observed during the review. Reporting of microscopy results should be standardized and based on the WHO recommendation.

Decontamination procedure

- Decontamination is conducted based on the recommended NaLC sodium hydroxide (NaOH) method, for which the MycoPrep solution from Becton Dickinson is used. The speed of the centrifuge is 3000 g. Pipettes are used for preparation of suspensions.

Culture method

- Solid and liquid media are used for inoculation and isolation of *M. tuberculosis*.

Löwenstein-Jensen media

- A homemade Löwenstein-Jensen medium made from the Löwenstein-Jensen powder base is used in the NRL. There is no routine quality control of each prepared batch. The NRL does not perform DST on solid Löwenstein-Jensen media.

  Before 2014, the NRL experienced problems with the contamination rate on solid media (7–8% in 2013). To reduce the contamination rate, a mixture of antibiotics was added to the solid culture media (the name and concentration of the antibiotic was discussed with the Supranational Reference Laboratory, similar to PANTA[2] from Becton, Dickinson and Company). Very few contaminated tubes or tubes with colour changing were observed during the visit.

Liquid MGIT media

- Two BACTEC 960 MGIT machines are installed in the NRL. At the time of the visit they were not fully loaded. There is an adequate number of reagents and consumables for MGIT liquid tests.

Identification of positive culture

- A Ziehl-Neelsen and BD TB Id test is used for identification of a positive culture.

[2] Polymyxin B, amphotericin B, nalidixic acid, trimethoprim, azlocillin (BACTEC 460 TB System).

Molecular tests

HAIN test (LPA)

- Cross-contamination is prevented by using the three-room concept and laboratory coats and equipment in each room. Bleach is used for cleaning of the surfaces.
- At the time of the visit, the room for mixture was not in use due to water leaking from the ceiling. The procedure was conducted in the room for media preparation.
- For DNA extraction the genolyse method is recommended and used. At the time of the visit the reagents for the HAIN test were not available, although (according to the NRL) the request had been submitted well in time.

GeneXpert MTB/RIF

- Three four-module GeneXpert MTB/RIF machines are in use and there are plans to obtain two more machines with the support of MSF-France.
- At the time of the visit the reagents for GeneXpert MTB/RIF had not been available for around two months, as they were being held in the local customs warehouse due to a problem with customs clearance.
- GeneXpert MTB/RIF has not been used in the Yerevan City Tuberculosis Dispensary since April 2014 due to the high number of errors produced by the machine. Additional modules had been requested but at the time of the visit they were not available or had not been installed.

Recommendations

- Funds should be rationalized for the preparation of self-made decontamination NALC-NaOH reagents.
- Quality control should be carried out for each batch of reagents and an internal quality control system introduced to ensure the quality of the decontamination procedure.
- A solution should be found for the problems with failed modules in the Yerevan City Tuberculosis Dispensary.

Laboratory performance indicators

Conventional and new methods are used to diagnose TB. According to the medical files reviewed in the RTBD, the treatment is initiated properly based on molecular rapid test results (LPA and GeneXpert MTB/RIF), when such results exist.

New molecular methods (GeneXpert MTB/RIF, LPA) have been started successfully. However, efforts to implement the rapid methods and decrease the probability of earlier TB diagnosis and initiation of treatment have been dramatically reduced by problems such as the failure of GeneXpert MTB/RIF modules in the Yerevan City Tuberculosis Dispensary together with shortages of cartridges for more than two months as well as reagents for the MTBDRpl assay for more than one month and the MTBDRsl assay for more than six months.

For quality control purposes, all specimens tested for GeneXpert MTB/RIF are inoculated on MGIT and on Löwenstein-Jensen.

GeneXpert MTB/RIF

The yield from the use of GeneXpert MTB/RIF should have a considerable impact given the low number of rifampicin-resistant/but isoniazid-susceptible strains circulating in Armenia (2.4% according to 2013 surveillance data). Detection of rifampicin-resistant TB means that in 98% of cases the patient was infected with an MDR-TB strain. It also has an operational implication in terms of infection control: patients infected with a rifampicin-resistant strain, detected by GeneXpert MTB/RIF, should not be accommodated in a hospital together with patient(s) infected with a susceptible strain.

GeneXpert MTB/RIF is used in the NRL for HIV-positive patients for early detection of TB/MDR-TB. It is not, however, widely used in the country, including the prison system. GeneXpert MTB/RIF results should be available before detainees enter a prison. Results of X-ray and smear microscopy are not enough to interrupt the transmission chain.

From the total number of GeneXpert MTB/RIF tests performed, it appears that 10–20% were conducted to evaluate the outcome of treatment and some positive tests were repeated several times without reasonable grounds. During the period of GeneXpert MTB/RIF implementation, 1491 tests were performed in the RTBD and the Yerevan City Tuberculosis Dispensary. Around 9.4% of them were positive, which seems lower than the WHO-recommended standard of 10% for diagnostic purposes. It seems that patients referred to GeneXpert MTB/RIF testing are not well-defined: for example, in the Yerevan City Tuberculosis Dispensary, it was observed that around 20% of the tests were performed for in order to monitor treatment, and some of them were repeated several times without well-defined reasons.

The percentage of invalid and error results for GeneXpert MTB/RIF in the NRL was 4–7%, indicating that the tests performed were of relatively good quality. A second laboratory, located in the Yerevan City Tuberculosis Dispensary, faced some problems with GeneXpert MTB/RIF equipment, with a percentage of errors of 11.3% (Table 3) (the most common errors were those with codes 5007 and 5011[3]). Owing to the high rate of errors in the Yerevan City Tuberculosis Dispensary, it was decided to stop testing and request new GeneXpert MTB/RIF modules. At the time of the visit the module had been held in customs for over two months.

Table 3. GeneXpert MTB/RIF tests, 2013–2014

Tests	Total	Positive No. (%)	Negative No. (%)	Error No. (%)
RTBD (NRL), sputum	777	77 (9.7)	664 (85.4)	33 (4.2)
RTBD (NRL), other samples	167	5 (3.0)	154 (92.2)	8 (4.7)
Yerevan City Tuberculosis Dispensary	547	59 (10.8)	426 (77.9)	62 (11.3)
Total	1491	141 (9.4)	1244 (83.7)	103 (6.9)

Source: [1]NRL reports; [2]data collected directly from the GeneXpert MTB/RIF machine in Yerevan City Tuberculosis Dispensary.

From 51 positive GeneXpert MTB/RIF samples performed for diagnostic reasons with available microscopy results, 12 were microscopy-positive and 39 were microscopy-negative, resulting in a 76% increase of bacteriological value, which shows that the new rapid implementation method was having a good impact. From all 81 positive GeneXpert MTB/RIF tests in the NRL, 18 (22%) were rifampicin-resistant (Table 4).

[3] Error 5007 is related to the sputum viscosity and/or volume, the reaction tube being filled improperly or probe integrity problem detected. Error 5011 = signal loss detected.

Table 4. GeneXpert MTB/RIF tests, NRL, 2013

Tests	Total investigated	Positive			Negative	Error
		Rifampicin-susceptible	Rifampicin-resistant	Rifampicin-indeterminate		
Sputum	777	53	18	5	664	33
Other samples	167	4	-	1	154	8

Source: NRL reports.

Liquid culture

In 2013 the NRL performed 5412 MGIT tests, 63% for diagnostic purpose and 37% for treatment follow-up. The positivity rate was 16% (14.6% for diagnostic and 18.8% for follow-up), which seems lower than the recommended standard. It can be assumed that the problem lies in the incorrect evaluation of TB suspect cases that were (unnecessarily) referred for laboratory tests. Nontuberculous mycobacterium was diagnosed in five cases. The contamination rate was 7%, which is within the recommended range.

Quality of decontamination procedures

The proportion of microscopy-positive/MGIT-negative results shows the quality of decontamination procedures in the laboratory. According to the data provided by the NRL, this indicator for all samples (collected for both diagnosis and treatment follow-up) is 1.9%; for diagnostic purposes it is 0.6%; and for treatment follow-up 4.0% (this seems slightly higher than the recommended 2% standard for such an indicator).

DST

In 2013, the NRL performed 573 DST for fist-line drugs, 97 (17%) of which were MDR-TB-positive (Table 5).

Table 5. Drug susceptibility tests, NRL, 2013

Results	No.	%
Invalid	31	5.4
Susceptible	307	53.7
Resistant		
Mono-rifampicin	15	2.6
Mono-isoniazid	29	5.1
All MDR (isoniazid and rifampicin)	97	17.0
All other	94	16.4
Total	573	100

Source: NRL reports.

The consistency of rifampicin results between MGIT and GeneXpert MTB/RIF was within a reasonable range and did not create difficulties in providing final results to clinicians.

From 478 patients with available DST results in 2013, 406 (85%) were new cases and 72 (15%) were previously treated cases. Of 478 reported cases with DST results, 305 (63.8%) were drug-susceptible and 173 (36.2%) were drug-resistant cases (Table 6).

Of 406 new cases, 272 (67.0%) were susceptible, 67 (16.5%) were monodrug-resistant, 24 (6%) were polydrug-resistant and 43 (11%) were MDR-TB cases. Of 72 previously treated cases, 33 (45.8%) were susceptible, 14 (19.4%) were monodrug-resistant, two (2.8%) were polydrug-resistant and 23 (31.9%) were MDR-TB cases.

Table 6. DST profile of notified TB cases, 2013

Profile	New cases No. (%)	Retreated cases No. (%)	Total No. (%)
Susceptible	272 (67.0)	33 (45.8)	305 (63.8)
Monoresistant	67 (16.5)	14 (19.4)	81 (19.9)
Polyresistant	24 (5.9)	2 (2.8)	26 (5.4)
MDR-TB	43 (10.6)	23 (31.9)	66 (13.8)
Total DSTs done	406 (85.0)	72 (15.0)	478 (100.0)

Source: NRL reports.

In 2013, in total according to the drug susceptibility profile, 66 (13.8% out of all TB cases) were confirmed as MDR-TB. Of 66 MDR-TB confirmed cases, 43 (65%) were new cases and 23 (35%) were previously treated cases (Table 6).

According to data from the NTP and the TB Epidemiological and Impact Analysis report *(14)*, 169 TB patients notified in 2013 were enrolled in treatment with second-line drugs, although the evidence of microbiological confirmation of MDR-TB existed for only 66 patients (based on NRL data). This means that for about 60% of cases, MDR-TB treatment was initiated empirically, without microbiological confirmation.

Recommendations

- Laboratory indicators should be regularly monitored.
- The various steps in the decontamination procedure (percentage of NaOH solution, exposure time with NaOH solution) should be carefully evaluated to identify the reasons for the high proportion of microscopy-positive/MGIT-negative results in samples collected from previous cases.
- GeneXpert MTB/RIF should be used according to the national algorithms. Its use for treatment monitoring should be limited.
- GeneXpert MTB/RIF testing should only be conducted for TB suspects and should include all TB suspects. A sufficient number of tests should be procured to enable all TB suspects to be tested.
- TB treatment should be started according to microbiological test results.
- There should be more reasons for initiation of empirical MDR-TB treatment, including microbiological confirmation. Empirical treatment of MDR-TB patients should be reduced.

Quality assurance system

At the time of the review the NRL was not accredited at the national level in the quality management system according to the International Organization of Standards standard 15189. Some elements of the quality management system are present in the laboratory but the NRL should be implementing the system fully to improve the quality and credibility of the results. The NTP guidelines for quality assurance of laboratory procedures are not available.

As regards internal quality control for smear microscopy, there are no daily or weekly controls in the MCs to check the performance of reagents and technicians and no regular maintenance is organized for the microscopes, while at central level positive and negative controls are not carried out on time.

The NRL is responsible for the external quality assurance of smear microscopy. Monitoring visits are planned by the Monitoring and Evaluation Department of the NTC and carried out by a laboratory specialist at least once a year. The visitor should take microscopy slides on each visit (minimum 10 positive and 20 negative slides) to be rechecked at the national level. In cases of inconsistency, another person from national level conducts a final check.

The team noticed that monitoring visits were not being conducted by central laboratory staff to MCs; only smears were being submitted to central level for rechecking/validation.

There is no routine feedback of the results of external quality assurance or onsite supervision. Original reports of supervisory visits are kept at the NTC and no copy is sent to the relevant facility. There were no reports of supervisory visits during 2013–2014 at the MCs visited.

There is no internal quality control for culture using positive and negative culture for MGIT.

Indications of contamination rate are monitored: the reported rate is 6–7% for liquid culture and 7–8% for solid media (2013).

The NRL participates in the DST external quality assurance with strains that are sent from Supranational Reference Laboratory. The results from 2011 and 2012 were acceptable for first- and second-line drugs. The results from 2013 external quality assurance have not been yet submitted by the Supranational Reference Laboratory.

Even if the NRL demonstrates permanent proficiency and qualification through external quality control, it should show commitment to continuous improvement in line with implementation of the quality management system according to International Organization of Standards standard 15189.

Recommendations

- TB laboratory management should be strengthened towards accreditation.
- International Organization of Standards requirements should be implemented leading to a functional quality management system and eventual accreditation to produce quality, accurate and reliable results on time.
- The NRL should identify and train a person responsible for the quality management system to be involved in implementing and monitoring it.
- Internal quality control should be introduced for all laboratory methods covering weekly positive and negative strains and, for DST, the minimum weekly susceptible strain and monthly resistance strain.

Treatment

Treatment of DR-TB

DR-TB is managed in accordance with the national guidelines on programmatic management of drug-resistant tuberculosis, which are updated annually. The current version of the guidelines is for 2012, which was updated based on the latest WHO Guidelines on programmatic management of drug-resistant tuberculosis of 2011 edition but lacks some of the latest information on new TB drugs and Group 5 agents. However, the NTC updated the old version and planned to seek

approval from the Ministry of Health later in 2014. Technical assistance on updating the guidelines was provided by a group of international experts including MSF-France and WHO. The new version will include the diagnostic algorithms required, protocols on side-effect management, and the required registration and treatment forms.

MSF-France continues to provide technical assistance in the management of DR-TB patients in six provinces and, partially, in Yerevan. MSF-France remains a main technical assistance agency on TB and DR-TB for the NTP, which values its support and assistance; it is recommended that this should continue in the longer run. Since 2014 MSF-France has no longer been responsible for enrolment of MDR-TB patients in Yerevan city and pilot provinces, with responsibilities fully delegated to the NTP. MSF-France continues to support and implement a series of activities, including development of protocols for palliative care, management of nontuberculous mycobacterium infection, compassionate use of new drugs and management of XDR-TB (procurement of clofazimine and bedaquiline), and support for the management of polydrug-resistant (PDR) TB through procurement of monocomponent rifampicin.

DR-TB treatment regimens, including for PDR-TB and compassionate use programmes, are designed by the DR-TB Committee (NTC and MSF-France), with weekly meetings taking place at the NTC (starting from 2014). The role of the committee includes designing the treatment strategy for DR-TB, as well as diagnosis, referrals and defining the outcome. Approaches for case definitions match the WHO criteria and are based on the site of the disease, prior treatment history and type of drug resistance. DST guides the treatment regimens for MDR-TB and XDR-TB patients, with every patient being given information on drug resistance to at least first-line drugs by the start of therapy. Algorithms for DST, including rapid molecular diagnosis (GeneXpert MTB/RIF and LPA) are available and included in the updated version of the national guidelines on programmatic management of drug-resistant tuberculosis.

The criteria for the duration of the intensive phase and of the whole course of chemotherapy match the WHO recommendations of 2011, with the duration of the intensive phase no less than eight months and duration of the whole course of treatment no less than 20 months for patients never treated before for MDR-TB. For patients who have already been treated for DR-TB and those with massive pulmonary damage the whole duration of treatment exceeds 20 months. The criteria for stopping the injectable agent are based on strong evidence of culture conversion – up to four consecutive negative cultures – and clinical response to treatment. There are no limitations for prolonging the duration of the intensive phase and the whole duration of treatment.

The requirements for clinical monitoring of a DR-TB patient's dynamic are clear and include sputum smear microscopy and culture at the start of treatment, repeated on a monthly basis during the intensive and continuation phase. Clinical examinations cover essentials, including liver and kidney function tests, as well as instrumental screening of patients for diagnosis during the whole course of therapy. Chest radiography examinations are available at central and regional levels, with access to computer tomography scanning. Diagnosis and management of adverse reactions is being performed adequately with clinical algorithms available and ancillary medicines purchased by the NTP (through the Global Fund grant) and MSF-France. Side-effects are recorded on the special forms for further entry into e-TB Manager and analysis. However, regular monitoring of the treatment of DR-TB patients in all provinces requires improvement to ensure the adequate management of adverse reactions, patient referrals and monitoring.

MDR-TB regimens include an injectable agent (kanamycin/amikacin/capreomycin), fluoroquinolone, Group 4 agents (protionamide, cycloserine, *p*-aminosalicylic acid) and pyrazinamide with maximum dosages according to the patient's weight and tolerance. Treatment is administered seven days a week in inpatient and six days a week in outpatient settings, regardless of the phase of treatment. Ethambutol is used in M/XDR-TB regimens only if it is susceptible by DST results. Pyrazinamide is used for the whole duration of therapy. Minimum duration of the use of an injectable agent is eight months for MDR-TB and 12 for XDR-TB. Kanamycin/amikacin is the choice of an injectable agent if susceptible, as they are considered more potent agents than capreomycin. Levofloxacin serves as the fluoroquinolone of choice for all MDR-TB patients in maximum dosages (750 mg =<70 kg, 1000 mg = >71 kg). Moxifloxacin is used in when DST shows resistance to fluoroquinolone. In certain circumstances (diabetes mellitus, HIV coinfection, massive pulmonary damage, other) moxifloxacin is used to strengthen the regimen. *P*-aminosalicylic acid is routinely added to the majority of M/XDR-TB regimens. Group 4 agents are present in the majority of MDR-TB regimens. Ethionamide is not included once it is resistant according to the DST or in XDR-TB regimens or as part of compassionate use because of the history of previous use and low confidence as to its effectiveness.

Overall, there is a concern that treatment outcomes of MDR-TB cohorts are not high. Of 99 MDR-TB patients who started treatment in 2011, only 54.5% were considered as effectively treated (33.3% cured, 21.2% treatment completed) and more than 30% defaulted. A similar situation was noted in previous years. More than 90% of patients who defaulted were found to have migrated. The high rates of second-line drug resistance, especially among patients with a previous or unknown history of treatment, are also considered a serious threat to the effectiveness of the MDR-TB programme. In 2013, drug resistance to ethionamide was up to 40% of patients, which puts the drug at high risk of low confidence in its effectiveness, especially among previously treated cases. The NTP has reported a growing tendency towards any resistance to fluoroquinolones, which increases the chances of further amplification of drug resistance and development of unfavourable outcomes.

Management of mono- and PDR-TB is regulated by the clinical protocol, which is based on Partners in Health-MSF Guidelines on Tuberculosis (2013) *(15)*. Treatment regimens for mono- and PDR-TB patients are based on the assumption that a full baseline DST is performed before or at the start of treatment with first-line drugs (Table 7).

Table 7. Resistance pattern and recommended treatment schemes

Resistance category	Isoniazid	Rifampicin	Ethambutol	Streptomycin	Treatment scheme
Isoniazid-rifampicin-susceptible	Susceptible	Susceptible	Susceptible	Res.	New case regimen
	Susceptible	Susceptible	Susceptible	Susceptible	New case regimen
	Susceptible	Susceptible	Resistant	Susceptible	New case regimen
	Susceptible	Susceptible	Resistant	Resistant	New case regimen
Isoniazid resistance	Resistant	Susceptible	Susceptible	Susceptible	PDR scheme A[a]
	Resistant	Susceptible	Susceptible	Resistant	PDR scheme A[a]
	Resistant	Susceptible	Resistant	Susceptible	PDR scheme B
	Resistant	Susceptible	Resistant	Resistant	PDR scheme B
Rifampicin resistance	Susceptible	Resistant	Susceptible	Susceptible	PDR scheme C
	Susceptible	Resistant	Susceptible	Resistant	PDR scheme C
	Susceptible	Resistant	Resistant	Susceptible	PDR scheme C
	Susceptible	Resistant	Resistant	Resistant	PDR scheme C

[a] Except previously treated patients, for whom PDR scheme B + ethambutol is preferred.

Treatment regimens for mono- and PDR-TB have been included in the latest version of the national guidelines, which are awaiting approval by the Ministry of Health. However, the guidelines need to be revised to take account of the presence of access to rapid molecular diagnosis of drug resistance (GeneXpert MTB/RIF assay). According to the 2014 Companion Handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis: "All TB patients infected with strains resistant to rifampicin should be treated using a full MDR-TB regimen, with isoniazid being added to/included in the regimen until DST results to isoniazid are available and appropriate adjustments to the regimen can be made. If DST results to isoniazid shows susceptibility, isoniazid can be continued in the MDR-TB regimen" *(16)*. Thus, the NTP should consider revising the national protocol and phasing out PDR-TB regimen C.

Approaches to the management of XDR-TB are similar to those for MDR-TB, with regimens based on DST pattern and history of previous treatments. XDR-TB regimens include the longer use of injectable agents, fluoroquinolone of a later generation (moxifloxacin) and the other second-line drugs with pyrazinamide. Group 5 drugs are available and used to reinforce the regimens: clofazimine, linezolid, imipenium/cilastatin and amoxicillin-clavulanic acid. Regimens for XDR-TB include a minimum of two Group 5 drugs in XDR-TB regimens.

Since spring 2013, patients have been treated with bedaquiline (TMC 207) under the compassionate use programme. The programme is supported by MSF-France, which guarantees access to bedaquiline and other Group 5 agents, including clofazimine and imipenium-cilastatin. Since the start of the programme 35 patients with resistance to fluoroquinolone have been enrolled. Suggested regimens vary and include an injectable agent if susceptible according to DST, pyrazinamide, cycloserine, clofazimine, bedaquiline, linezolid, imipenem/cilastatin and amoxicillin/clavulanic acid (linezolid, imipenem/cilastatin and amoxicillin/clavulanic acid are not used in every regimen). The clinical protocol for the compassionate use programme is available with regimens assigned for every patient according to DST and history of previous use of second-line drugs, and essential requirements for clinical monitoring. Issues of pharmacovigilance are included in the clinical protocol and well addressed.

As from 2015, Armenia will become a part of the end-TB project financed with UNITAID,[4] which will be jointly implemented by MSF-France and the NTP, to access the new drugs (bedaquiline, delamanid and Group 5 agents) for treatment of MDR-TB and patients with resistance to fluoroquinolone. It is expected that 96 patients will be enrolled in Armenia over these years.

Not all DR-TB patients with HIV coinfection receive ART, possibly due to the existing regulation of the CD4 threshold of 200 cells. All ART medicines are self-administered. The team discussed with the members of the DR-TB committee whether all patients with DR-TB and HIV coinfection should receive ART, no matter the level of CD4 cells. In the RTBD, doctors had noticed a high rate of DR-TB patients coinfected with hepatitis C and B (incidence of up to 14%), and viral hepatitis was noticed as being more common among patients with treatment failure outcome. Thus, clinical approaches towards the management of hepatitis C would be of benefit for treatment outcomes.

[4] A global health organization that uses innovative financing to increase funding for greater access to treatments and diagnostics for HIV/AIDS, malaria and tuberculosis in low-income countries.

The issue of nontuberculous mycobacterium infection is addressed with the nontuberculous mycobacterium protocol developed by MSF-France since the previous mission. Previous Green Light Committee missions described how nontuberculous mycobacterium infections are not considered contagious, unlike TB. There is no evidence that the infection can be transmitted from one person to another. While the NTP should respect issues of infection control, treatment of nontuberculous mycobacterium should be considered at ambulatory settings and in the general health care network.

Treatment of DR-TB

Treatment of drug-sensitive TB patients is according to WHO recommendations, with new cases starting treatment with a Category I regimen and retreatment cases with Category II. Cohort analysis is performed and submitted to WHO on a regular basis for drug-sensitive TB, and data collection from every treatment facility is centralized at the NTP. As recommended by the previous mission, the NTP considered phasing out Category III treatment from the treatment protocol and replacing it by a Category I regimen. Discussions at treatment sites and those sites visited showed that the optimal dosing frequency for new patients with pulmonary TB was daily throughout the course of therapy provided under direct observation. The national guidelines on TB have been updated in accordance with the WHO Guidelines on TB, 4th edition *(17)*, as recommended by the Green Light Committee.

Treatment outcomes for regular TB among new smear-positive cases (from 2011 and 2012) showed a good success rate (78.9%) but a high rate of default (11%), possibly due to migration (Table 8). Among retreatment pulmonary cases (smear-positive and -negative, excluding extrapulmonary cases), the treatment success rate was 65.2% with a higher rate of default (15.9%) and a relatively high rate of patients who died (7.1%).

Treatment outcomes for children showed a high success rate of 93.3% in 2010 (60 cases): no patients died, two defaulted and one was considered as a treatment failure. In 2011, of 15 cases diagnosed with TB, 80% completed treatment and were considered cured, nobody died and 13.3% were reported as treatment failures. Treatment approaches available for paediatric TB cases match the WHO recommendations of 2006 but are not institutionalized in the national guidelines by a separate chapter. Prophylactic treatment with six months of isoniazid is given to child contacts (aged 0–14) years of sputum smear-positive cases, with 350–400 TB contacts covered a year. Single dose formulations of isoniazid are available (in blister packs). The NTP is planning to revise the national guidelines in accordance with the interim dosing instructions received last year from the Global Drug Facility (GDF).

Treatment of TB and DR-TB in the ambulatory sector

The management of DR-TB covers all provinces with 100% directly observed therapy (DOT) for all DR-TB patients reported by the NTP. The majority of patients are hospitalized for the start of treatment in specialized DR-TB wards at the NTC then, given sputum smear/culture conversion, discharged to outpatient facilities. The rapid expansion of the DR-TB programme to new provinces in 2010–2011 required that the NTP strengthen all programme activities, including monitoring and evaluation, capacity and infrastructure building, as well as technical assistance from partners. MSF-France provided all possible technical and financial assistance to the NTP in building the capacity and sustainability of the DR-TB programme. Despite the positive achievements of the programme, however, there is still a high treatment default rate, which is mostly due to migration. Despite the availability of options for DOT in Armenia, no system has been established to measure the effectiveness of the efforts undertaken.

Table 8. Treatment outcomes for regular TB, Armenia, 2011 and 2012

	Treatment completed	Cured	Death	Default	Failure	No TB	Transferred out	Total
2011								
Sputum-smear-positive	62	144	20	21	37	1	45	330
Sputum-smear-negative	474	0	21	36	16	8	30	585
EP	254	0	5	15	5	8	2	289
Total new	*790*	*144*	*46*	*72*	*58*	*17*	*77*	*1204*
Relapsed sputum-smear-positive	8	15	4	4	5	1	17	53
Relapsed sputum-smear-negative	53	0	4	10	1	0	0	69
Default Sputum-smear-positive	1	2	1	2	4	0	1	11
Default sputum-smear-negative	1	0	0	0	0	0	0	1
Failure	4	4	0	0	0	0	2	10
Other	108	0	7	31	2	3	6	157
EP	64	0	0	11	3	1	1	80
Total retreatment pulmonary	*239*	*21*	*16*	*58*	*15*	*5*	*27*	*381*
TOTAL	**1029**	**165**	**62**	**130**	**73**	**22**	**104**	**1585**
2012								
Sputum-smear-positive	66	127	16	26	5	0	0	240
Sputum-smear-negative	421	0	36	60	5	7	9	538
EP	210	0	9	14	0	5	8	246
Total new	*697*	*127*	*61*	*100*	*10*	*12*	*17*	*1024*
Relapsed sputum-smear-positive	10	28	3	5	1	0	0	47
Relapsed sputum-smear-negative	161	0	15	35	0	5	4	220
Default sputum-smear-positive	1	1	0	4	1	0	0	7
Default sputum-smear-negative	0	0	1	0	0	0	0	1
Failure	2	3	1	1	0	0	0	7
Other	0	0	0	0	0	0	0	0
EP	76	0	3	8	0	0	1	88
Total retreatment pulmonary	*250*	*32*	*23*	*53*	*2*	*5*	*5*	*370*
TOTAL	**947**	**159**	**84**	**153**	**12**	**17**	**22**	**1394**

The options for delivering DOT to TB and DR-TB patients are widely presented with adherence and patient-centred approach used. The majority of patients are covered with DOT by volunteers from the Armenian Red Cross Society (ARCS) in the provinces, as are those coming for treatment to TB clinics at selected polyclinics in Yerevan, TB clinics in provincial centres and rural ambulatories.

Home-based treatment is another option available in Yerevan for patients with disabilities, elderly people and children. First initiated by MSF-France, the programme was delegated to the NTP to cover patients with DR-TB as well as those with regular TB. The initiative is primarily focusing on patients at high risk of abandoning treatment due to behavioural and social challenges, and on elderly people and people with disabilities. In May 2013, the NTP signed a contract for one year with the local nongovernmental agency Yerevan Home Care, which was already providing care for elderly people and people with disabilities who did not have TB. The contract was financed from the Global Fund grant to provide DOT six days a week for 20 patients a month by two DOT teams (one team for DR-TB and the other for regular TB).

The ARCS is continuing to act as a sub-recipient of the Global Fund grant with the main responsibilities of providing standardized types of incentive and enabler to TB patients. The Society delivers social support to patients with regular TB and DR-TB in treatment at ambulatory settings countrywide, including patients hospitalized at the NTC. Regular TB patients receive food baskets and hygiene packages once a month; inpatients with DR-TB receive one food baskets a month, and those in ambulatory settings receive two food baskets and a hygiene package per month, with a total cost of around €50. As a new initiative, the Society

has started providing support for patients hospitalized at the NTC, including weekly supplies of fresh fruits and vegetables. The Global Fund supported the proposal by the ARCS to provide alternative social support for TB and DR-TB patients. Thus, from the winter of 2013 the Society started paying 15 000 Armenian drams (US$ 36.6) for three and a half months towards the electricity and gas bills of patients needing additional assistance due to social challenges. The Society also organizes group of volunteers to visit patients in their homes to deliver social support and information. The volunteers are paid around 35 000 Armenian drams (US$ 85.4) monthly from the Global Fund grant. At present this initiative is possible for both DR-TB patients and those with drug-susceptible TB.

Recommendations

- The prevention and control of TB and DR-TB should be considered a public health priority. Sufficient and sustainable funding and required changes to the health system should, therefore, be ensured.
  - The national M/XDR-TB response plan for 2013–2015 should be revised in line with the forthcoming end of the consolidated Global Fund grant, taking into consideration the 6–12 month no-cost extension and close-out periods. Once the concept note for the Global Fund is finalized, however, the NTP should consider developing an extension of the response plan for 2016–2018 to include all aspects of programmatic management of DR-TB and activities scheduled for implementation by national and international partners (Global Fund, MSF, the United States Agency for International Development (USAID), WHO and others).
  - The 2013 national guidelines on DR-TB should be updated with a chapter on new anti-TB medicines and Group 5 agents for them, including a list to facilitate the procurement and use of the drugs for the management of patients with XDR-TB and those with resistance to fluoroquinolones. The update should be done in line with WHO's interim policy guidance *The use of bedaquiline in the treatment of MDR-TB (18)* and *The use of delamanid in the treatment of MDR-TB (19)*. Chapters should be included on the management of coinfection with HIV/AIDS and palliative care. The chapter on TB in children should be updated in line with WHO's *Guidance for national tuberculosis programmes on the management of tuberculosis in children,* 2nd ed. *(20)*.
  - Case-finding of DR-TB at province level, and prompt referral for the start of treatment through increased access to rapid molecular diagnosis of DR-TB should both be strengthened.
  - Consideration should be given to phasing out the Category II regimen for retreatment cases. National guidelines on TB as well as drug procurement orders for first-line drugs require updating once the national guidelines on TB have been revised.
- A national TB/HIV coordination committee should be established to ensure the integrated diagnosis and continuum of care for all TB/HIV patients with a focus on their needs. Isoniazid preventive treatment should be ensured for people living with HIV.
- Consideration should be given to improving pharmacovigilance in the management of patients with DR-TB, especially for those on compassionate use therapy.
- The capacity of health providers should be improved at all levels of the management of TB and DR-TB, including in the prison sector, primary health care and HIV/AIDS services in line with updated national guidelines.

- The prevention, diagnostics and treatment of paediatric TB should be improved through the introduction of algorithms for the integrated management of childhood illnesses.
- The monitoring and supervision system should be improved for the programmatic management of DR-TB in patients with TB and DR-TB at NTP and province levels.
- The hospitalization of TB suspects with unknown TB/DST status in TB inpatient facilities should be addressed.
- Early diagnosis of TB and DR-TB should be improved, especially among risk groups. Screening with the use of mobile radiography methods could be considered an option for risk groups.
- A system should be introduced to measure programme performance for ambulatory care, especially for home-based treatment.

Infection control

Improving infection control is a priority of the NTP. Infection control activities are regulated by Ministry of Health Decree N-21-N of 20 October 200, epidemiological control 3.1.1-010-08 sanitary-epidemiological norms. An epidemiologist acting as coordinator of infection control, who has been trained in the programmatic management of DR-TB and infection control on international training courses, is available in the NTC, but there is no position for an engineer responsible for infection control in addition to the epidemiological aspects covered by the epidemiologist. The NTC has developed the national guidelines on infection control according to the most recent WHO recommendations. Translated into English and Russian, these were submitted for review to WHO and international experts. They were endorsed by the local sanitary and epidemiological services and further endorsed by the Ministry of Health in 2013. At the time of the visit, the NTC was in the process of conducting a comprehensive infection control assessment of each facility involved in the management of patients with TB and DR-TB. A list of questions on infection control had been compiled and included in the monitoring and evaluation checklists separately for inpatient and outpatient facilities.

In 2013, with technical assistance from the WHO Country Office in Armenia and the WHO Regional Office for Europe, the NTC started to develop a strategic document to address the issue of excessive hospitalization of TB suspects and patients in inpatient facilities. The NTC has closed the TB departments in three regional inpatient facilities which did not meet modern standards of infection control. All patients diagnosed with any form of DR-TB are hospitalized in specialized DR-TB departments at the NTC (formerly RTBD). Patients with drug-susceptible TB from across the country (apart from Yerevan) are hospitalized in TB wards at the NTC. The average hospitalization for drug-susceptible TB last for up to two months and for DR-TB up to three months. The duration of stay may, however, be prolonged by a physician if the patient is homeless or requires medical assistance and care, or there is uncertainty about his or her adherence to DOT at the place of residence.

Both drug-susceptible TB and DR-TB patients are subject to extensive and long periods of hospitalization, lasting on average for three months. Moreover, patients with unknown TB or DST status spend an average of up to two weeks in hospital (aggravated since May 2014 by the delays in GeneXpert MTB/RIF assay testing). An increased risk of undiagnosed TB and DR-TB had been found in the ward for TB patients with psychiatric disorders, which was housing both patients with DR-TB and drug-susceptible TB patients. Even where they had separate rooms and had been reported as smear- and culture-negative, MDR-TB patients were sharing the bathroom

and cafeteria. The rest of the patients were smear-negative, but the quality of sputum collection from the ward was reported as poor, thus there is a risk of unconfirmed DR-TB cases being present in the ward. Patients with psychiatric disorders are usually hospitalized for the whole of their anti-TB treatment because of problems with clinical monitoring in ambulatory settings. The NTC is strongly recommended to consider the possibility of treating DR-TB patients with psychiatric disorders in the DR-TB ward.

A similar situation was found in the specialized department for drug-susceptible TB patients at the NTC, where patients are hospitalized once they have been diagnosed with TB. Even with increased access to rapid diagnosis of TB and DR-TB, the risks of nosocomial transmission of infection in inpatient facilities is present due to the hospitalization of all TB suspects and the lack of cartridges to perform GeneXpert MTB/RIF assay. The team noticed that sputum for culture and DST is usually collected when a patient is admitted to hospital, with several cases of DR-TB diagnosed over the previous few months and referred to the specialized DR-TB ward for DR-TB treatment. Before their diagnoses, these patients were sharing facilities such as the cafeteria, bathroom, corridor and even rooms. It should become mandatory to roll out and rationalize access to GeneXpert MTB/RIF and to hospitalize patients with a known diagnosis and DST, and conduct further triage according to DST status. The approach to infection control when patients with known DST status are hospitalized should be considered an essential tool to decrease the nosocomial transmission of infection.

DR-TB patients at the NTC are hospitalized in special 100-bed DR-TB wards located on two floors of the NTC, with triage available according to DST and smear/culture status. All sections of the DR-TB ward are equipped with mechanical ventilation and upper-level ultraviolet germicidal irradiation lamps. In order to decrease the risks of possible nosocomial transmission, patients receive food and medicines in their rooms and each room has a separate washroom. Similarly, patients with drug-susceptible TB are hospitalized in specialized drug-susceptible TB wards at the NTC and separated administratively from those considered as TB suspects. However, as confirmation of diagnosis by MGIT is now taking two to three weeks, there is a high risk of nosocomial transmission of TB or exposure to TB of non-TB suspects. All sections of the drug-susceptible TB wards as well as the corridors are equipped with upper-level ultraviolet germicidal irradiation lamps, but a qualified engineer specialized in infection control is needed to carry out regular maintenance and evaluation of all lamps installed in all inpatient facilities, including in the prison sector.

The NRL is in the grounds of the RTBD in a separate new building with ventilation. Personal protection measures are followed properly, with respirators available for all medical and non-medical personnel, medical robes and hats and gloves. No incidence of TB and DR-TB among laboratory personnel has been reported since the last visit. Second-class biosafety clinics are available for all culture and DST methods used in the laboratory with infection control monitoring implemented on a regular basis, including filter exchange and air flow at biosafety clinics. The contamination rate for testing on liquid media is lower than 5%, and on solid media it averages 3%, which is relatively good. The administrative separation of the infectious and clean zones is adequate, and there is a separate entrance for sample collection. The sterilization of materials, utilization of disposables and cleaning of rooms with detergents and disinfectants are carried out according to existing sanitary-epidemiological regulations, which are adequate. A specialist (engineer) from MSF-France monitors infection control on a regular basis.

There are slight improvements in infection control measures in the Central Hospital for Detainees, in comparison with the previous years, directly associated with a general decrease in

the number of TB patients detained in the hospital. All were on appropriate treatment regimens and all achieved a positive therapeutic response. Thus, a limited risk of nosocomial transmission was identified. All DR-TB patients were detained in specialized TB wards with a separate entrance; no contact with other detainees was noted. Infectious patients are administratively isolated from those with smear/culture converted. Upper level ultraviolet germicidal irradiation lamps had been installed in the TB unit (corridor and rooms) and doctors' offices, but an independent assessment of their capacity and efficiency should be carried out.

Recommendations

- Early diagnosis of TB and DR-TB should be improved, especially among risk groups. Screening with the use of mobile radiography stations could be considered as an option to improve early diagnosis of TB.
- The capacity of specialists (engineers) involved in TB infection control should be improved and a system of monitoring and evaluation of the national infection control plan should be set up in inpatient and outpatient facilities, including in the prison sector.
- Consideration should be given to hospitalizing patients with known DST status in any inpatient facility. The use of rapid molecular diagnosis of drug resistance should guide further administrative triage of patients according to DST status.
- Consideration should be given to purchasing sputum induction equipment for the NTC to be used for adult patients from wards where the quality of sputum is reported as poor.
- Consideration should be given to purchasing different types of respirator for health personnel at the NTC and fit-testing them prior to use.
- Upper-room ultraviolet germicidal irradiation lamps are recommended for 24/7 use at patients' presence at least in all inpatient facilities (wards, corridors, procedure rooms, DOT points), including in the prison sector. Regular monitoring of performance and appropriate use of upper-room ultraviolet germicidal irradiations is essential. Consideration should be given to installing a new generation of upper-room ultraviolet germicidal irradiation equipment, at least in sputum smear-positive TB and DR-TB wards in the Central Hospital for Detainees (repeated recommendation).
- Health personnel of the Central Hospital for Detainees should wear respirators in the presence of any infectious patients and patients in all inpatient facilities should wear surgical masks (at the least) and follow cough etiquette. In collaboration with the prison sector, the NTP should conduct regular monitoring of infection control in the Central Hospital for Detainees and other prison inpatient facilities (repeated recommendation).
- Health and administrative personnel of health facilities and bacteriological laboratories where there is a high risk of nosocomial infection of TB and DR-TB should use personal respirators of biosafety class no lower than FFP2 (or N95 according to the US Standard 42CFR84). At least two types of respirator are recommended for use by health and administrative personnel in health facilities and bacteriological laboratories. The fit test should be considered the gold standard by every health and administrative worker before using the new form of respirator. The use of surgical masks is strongly recommended for TB and DR-TB patients at least in inpatient facilities (repeated recommendation).

TB/HIV collaborative activities

Coordination of TB/HIV collaborative activities

The NTC and the National Centre for AIDS Prevention, coordinated by the Ministry of Health, carry out collaborative TB/HIV activities within their areas of work. The Country Coordination Mechanism ensures joint monitoring and evaluation of these collaborative activities.

The National Centre of AIDS Prevention (NCAP) is located in Yerevan. It has six units/ departments (Prevention Department; HIV Surveillance Department; Department of Laboratory Diagnostics, including HIV Reference Laboratory; Immunological Laboratory; Polymerase chain reaction, Microbiological and Virology Laboratory; Biochemical and Clinical Laboratory; Psychosocial Counselling Department; Medical Care Department; Administration). The NCAP has 89 employees, including 10 doctors in the Medical Care Department, four psychologists in the Psychosocial Counselling Department and nine laboratory specialists. On average, 30 patients receive medical care there daily (three or four patients per physician).

A national HIV/TB strategic plan has been developed, targeted at reducing TB/HIV coinfection through the prevention, diagnosis and treatment of HIV among TB patients and through the prevention, diagnosis and treatment of TB among people living with HIV (PLWH). The involvement of civil society organizations in developing and implementing this document was limited and the plan is not widely implemented due to weak monitoring and evaluation mechanisms for the collaborative TB/HIV activities.

Reducing the burden of TB among PLWH

Intensified TB case detection should be offered to HIV-positive patients every time they visit a health care facility, especially the NCAP. The team noted that the symptomatic screening tool is not commonly used at the NCAP to identify TB suspects among PLWH and prevent other patients being exposed to TB. According to the current national guidelines, PLWH should be screened for TB every year through clinical examination, chest X-ray and sputum microscopy, but in 2013 only 233 out of 1041 (22.3%) PLWH were tested for TB.

Isoniazid preventive treatment is not being implemented in routine practice despite the recommendations of the 2011 NTP review and the national TB/HIV strategic plan. None of the HIV-positive patients received this treatment in the period 2011–2014. Isoniazid preventive treatment must be prescribed to PLWH without symptoms of active TB but with positive tuberculin skin test result.

To improve the diagnosis of TB in HIV-positive people, the 2011 NTP review recommended the establishment of a TB diagnostic facility at the NCAP with support from the Global Fund *(6)*. The Global Fund provided an GeneXpert MTB/RIF assay machine and an X-ray system to the NCAP, but the TB diagnostic unit was not working at the time of the current review. There is no sputum collection unit at the NCAP.

HIV testing and counselling among TB patients and suspects

According to the national HIV guidelines, HIV counselling and testing should be offered to all patients suspected of and diagnosed with TB, but the review noted that this service is offered only to confirmed TB cases. In accordance with the Ministry of Health order on HIV counselling and testing, in 2012–2013 all TB patients received provider-initiated HIV testing and

counselling, most of whom were tested for HIV in the inpatient department of the NTC clinic (the former RTBD).

During 2011–2013 progress was made in HIV testing for TB patients; in 2012 and 2013 all TB patients were tested, but no information was available about HIV testing of TB suspects.

The organization and implementation of HIV testing in the inpatient department of the NTC clinic also needs improvement. During the first week of hospitalization the patient receives HIV counselling and his/her blood sample is transported to the NCAP laboratory for testing. The test results are generally available on the next day and communicated by the NCAP to the NTC by telephone, which implies a certain risk of disclosure of an HIV diagnosis (telephone communication is at risk of unauthorised access and/or use). If the HIV test is positive, an AIDS specialist talks to the patient and tells him/her about the diagnosis.

The HIV testing and counselling services are regulated by the HIV testing and counselling procedure approved by the Ministry of Health. The relevant protocol regulates mechanisms and issues related to mandatory, provider- and patient-initiated HIV testing and counselling, although not all primary health care facilities apply a systematic approach to voluntary counselling and testing services. Some of the health care facilities provide such counselling and testing only for pregnant women, not for TB patients. For example, in one of the clinics visited the team noted that the infectionist [staff member responsible for infection control conducts voluntary counselling and testing; when she/he is not available, patients are referred to the NCAP for testing. In another polyclinic HIV testing is available only for pregnant women as part of the strategy to prevent mother-to-child transmission, because only the gynaecologist provides voluntary counselling and testing. TB doctors in that polyclinic have to refer TB patients to the NCAP for HIV testing, and no follow-up mechanisms are in place to ensure that the patient referred actually reaches the HIV services.

One of the key problems in the general HIV/AIDS system in Armenia is late HIV diagnoses, as is inferred from the available statistics: over 60% of the new HIV cases identified in 2013 were in the AIDS stage.

CPT

According to the national guidelines, CPT should be given to all TB/HIV patients throughout their TB treatment regardless of their CD4 count level. During the last three years, CPT coverage did not exceed 80% (80% in 2011, 70% in 2012 and 72% in 2013).

HIV treatment and care is the responsibility of the NCAP specialists. ART is free and indicated for all PLWH with active TB infection and should be started from the second to the eighth week of TB treatment. In 2013, only 72% (48 out of 79) of TB/HIV coinfected patients received ART.

At the time of the mission's visit to the NTC clinic, there were nine TB/HIV patients: four had been screened for HIV in the TB clinic (the other five had been screened in the NCAP between December 2013 and June 2014) and their CD4 levels were 3, 11 and 136 cells/ (this can be another proof of assumption of late diagnosis of HIV/TB coinfection). CPT and ART were provided to three of these patients, and the one of them was enrolled in ART in 2012. ART must be prescribed during the fourth, fifth and seventh weeks (and not later than the eighth week) of TB treatment.

Monitoring of ART needs to be improved. According to current practice, patients receive a three-months' supply of ARV drugs (based on the results of the laboratory test usually conducted about earlier). In such a situation, there is a very high risk of losing control of the side-effects of the drugs.

HIV prevention among TB patients

The review noted that TB care providers in hospitals and TB clinics in polyclinics lack information materials on the prevention, care and treatment of HIV. No nongovernmental organizations implement HIV prevention activities among TB patients or suspects.

Services for intravenous drug users

According to the Republican Narcological Centre, the estimated number of intravenous drug users is 42 000: 30 000 cannabis users and approximately 12 700 opioid intravenous drug users. Officially 5200 intravenous drug users are registered (2700 opioid intravenous drug users and 2500 cannabis users). The Centre provides methadone substitution therapy for opioid injecting drug users. It currently covers 237 patients, including 60 and 80 patients, respectively, in the towns of Gyumri and Vanadzor.

Opioid substitution therapy is provided according to national legislation. The criteria for enrolling patients in the programme include several failed attempts for drug dependence treatment through detoxification for people aged over 18 years. The legislation also gives priority to opioid substitution therapy for people with HIV, TB and/or hepatitis.

At the time of the review, 17 HIV-positive patients and 13 TB patients were receiving opioid substitution therapy. All TB patients in the inpatient department in need of opioid substitution therapy received the treatment with the support of a mobile ambulatory service. There is an increasing risk of treatment interruption during the continuation phase of TB treatment because patients have to visit two different health care settings.

Recommendations

- A collaborative TB/HIV strategic plan should be developed (with the participation of the Ministry of Justice and civil society organizations) to foster collaboration between the HIV and TB services on both national and local levels.
- Monitoring and evaluation of joint TB/HIV activities should be ensured.
- The quality of medical care for TB/HIV coinfected patients should be ensured by through the implementation of the national guidelines on management of TB/HIV patients in all HIV and TB facilities, and training of HIV and TB specialists in the prevention, diagnosis and treatment of TB/HIV.
- Access for HIV testing and counselling services should be expanded in primary health care facilities for TB suspects and TB patients so as to improve early HIV diagnosis by involving and motivating TB suspects, the general population, the population most at risk and, primarily, migrants in HIV testing.
- TB case-finding (symptomatic screening, tuberculin skin testing) among HIV patients should be implemented in the NCAP's daily practice.
- The NCAP should launch TB detection services (GeneXpert MTB/RIF assay, laboratory and X-ray diagnostics) and ensure their operation by using internal resources.

- Isoniazid preventive treatment should be initiated for all cases of latent TB among people living with HIV. It could be prescribed and monitored by an infectious diseases specialist in close coordination with a TB specialist. The NTP should arrange for the NCAP to receive the required amount of tuberculin and isoniazid and organize training for the staff.
- CPT should be prescribed for all TB/HIV patients (by TB specialists) simultaneously with TB treatment.
- Infection control should be ensured in HIV and TB settings, especially at the NCAP (infection control for PLWH suspected of having TB, in the smear collecting room and in the TB laboratory).
- Mechanisms should be developed to ensure follow-up HIV and TB treatment and care among TB/HIV coinfected patients after their discharge from hospital.
- Integrated services for patients with double/triple problems (TB/intravenous drug users or TB/HIV/intravenous drug users) should be organized at opioid substitution therapy centres to ensure DOT for intravenous drug users during the continuation phase (TB treatment during the continuation phase should be given at opioid substitution therapy centres).
- Consideration should be given to procuring rifabutin for HIV/TB patients to ensure their effective treatment and the prevention of drug interactions in cases where there are contraindications to the use of ART with efavirenz (for example, for TB/HIV patients with hepatitis C coinfection).

TB control in prisons

The penitentiary system is under the Criminal Executive Department of the Ministry of Justice. This Department includes a health care unit that coordinates medical care for prison inmates. The unit implements heath care approaches in accordance with the national guidelines and standards approved by the Ministry of Health. Currently the health care system of the Ministry of Justice is in a transitional stage. There are 160 full-time positions for health care staff in prisons, of which approximately 25% are vacant.

A key reform in the prison health sector would be to abolish the rank of officer for health personnel (most health staff in the prison system hold the rank of officer). This would increase both the independence of physicians in taking medical decisions and the confidence of prison inmates in medical staff. To ensure the quality of medical care in the prison system, the health care unit is planning to retrain prison physicians as family doctors.

Following a reform of the criminal legislation, the prison population decreased from 6000 in 2011 to approximately 4000 in 2014. As a result, the majority of institutions are no longer overcrowded (as was the case during the 2011 review). A reform of the judicial and prison systems has been launched. Currently, 90% of court decisions result in imprisonment, which is expected to drop by 30%. A probation service will be established in place of the present criminal-executive inspectorate to implement alternative punishments.

In recent years, the prison health system has been strengthened through cooperation with the Global Fund, the Ministry of Health, NTP and nongovernmental organizations such as MSF-France.

The main principles of the European Prison Rules of the Council of Europe were integrated into the revised prison legislation, such as a guarantee of equal quality and range of health care services for inmates as for the general public, the integration of prison health policy into national health policy, and ensuring the professional independence of prison health care staff.

Police offices are under the Ministry of the Interior. Police temporary detention facilities hold people who have been arrested for 24–72 hours, after which they must either be released or transferred to a pre-trial institution for prosecution. Medical care for such people is provided by public health institutions.

The penitentiary system consists of 12 penitentiary institutions, including one for women. The Abovian penitentiary institution for women includes a pre-trial facility, a prison and a unit for women with children aged under three years.

Erebuni prison in Yerevan will be closed and detainees will be transferred to a new prison in Ashtarak, together with 85 prisoners from Nubarashen prison who are serving life sentences.

Nubarashen prison consists of two sections: a prison and a pre-trial unit, and approximately 95% of all offenders await their court decisions there. The other 11 institutions take sentenced prisoners, although in the remote areas some of them also include small pre-trial facilities.

The Ministry of Justice TB control programme in prisons is part of the National Ministry of Health NTP. The TB coordinator in the Department of Penitentiary Institutions ensures collaboration with the NTP.

In accordance with national guidelines, all new detainees are screened on entry (medical examination and chest X-ray). Active and passive case-finding methods are used to detect TB among prisoners. The number of TB cases detected decreased from 33 in 2011 to 27 in 2013 (-22.8%).

TB control in prisons is also designed in accordance with international guidelines. All new detainees are screened on entry via medical examination and chest X-ray. Smear microscopy takes place in the prisons (in Nubarashen prison and the Hospital for Detainees), but sputum specimens can also be sent to the NRL for bacteriological, culture and GeneXpert MTB/RIF tests. Regular TB patients in Nubarashen receive treatment in TB wards (segregated according to smear status). If DR-TB is detected, the patient is transferred to the Hospital for Detainees. Prisoners and prison staff are regularly (twice a year) screened for TB with chest X-ray.

Two institutions provide a full course of TB treatment. The Hospital for Detainees is the only institution that treats DR-TB, with support from MSF-France which will be gradually taken over by the NTP. At the time of the visit there were 27 TB patients in the hospital: five TB suspects; one who had refused treatment; one TB/HIV coinfected; 14 TB and six DR-TB patients.

The Medical Department of the Criminal Executive Department collaborates with the NTP to ensure uninterrupted treatment for prisoners after their release. In 2013, only four TB patients were released and all of them continued treatment in public health TB settings; in 2014 only one patient (citizen of Georgia) was released and returned to Georgia.

Medical care for other patients

Harm reduction programmes are implemented routinely in prisons. Opioid substitution therapy is available for intravenous drug users in prisons. In 2014, 75 inmates received methadone. Condoms are available, particularly in rooms for long visits.

There are 30 HIV patients in the penitentiary system, including 10 coinfected patients (one with active TB and nine successfully treated); follow-up and ARV treatment was organized under the control of the NCAP. The control of immunological status and viral load is carried out every three to six months in the prisons where the inmates are. The majority of inmates with HIV-positive status (24 to 30) are located in the infection department of the hospital, despite the high risk of exposure to nosocomial and opportunistic infections.

Recommendations

- Financing of health care, based on national approaches, should be ensured to provide a full range of medical care in prison facilities and in the public primary health care network. A network including the different prison health units and health facilities in the civilian sector should be established to facilitate easy contact and exchange of medical data.
- Separate budget lines should be added for the prison system (including for purchase of equipment and training of personnel) in the Global Fund concept note for new programme funding.
- The NTP should develop a separate section on TB control in prisons.
- Isoniazid preventive treatment for HIV-positive patients should be implemented in prisons to reduce the burden of TB among HIV-positive prisoners. Inmates are for TB on entry, and isoniazid preventive treatment will prevent the development of TB during incarceration.
- The capacity of prison TB laboratories should be strengthened by introducing GeneXpert MTB/RIF systems to improve early case detection in all penitentiary institutions.
- Infection control should be improved in penitentiary institutions:
  - the position of infection control engineer should be included in all health care units to control and improve the environmental infection control in the prison system, and he/she should be trained in infection control in an international training centre;
  - ventilation should be improved in TB wards, cells and smear collecting rooms and its quality supervised;
  - staff, patients and family members should be encouraged to wear masks, if needed.

Health workforce

A number of recommendations made during the 2011 programme review were followed up during the 2014 extensive review of the NTP. It was observed that major efforts had been made since 2011 for the development of human resources, particularly in primary health care. The recommendations of the last review had been implemented by the NTP and the Ministry of Health. In addition, a number of new areas for action were identified based on visits and interviews with the Ministry of Health and Yerevan State Medical University and information gathered during field visits to polyclinics and TB dispensaries.

The Ministry of Health is in the process of finalizing a five-year human resources development strategy which will include specific components for TB specialists. For example, it is planned to gradually increase the remuneration for TB specialists, as well as to make residency and recertification more affordable (Annex 4). The mission was informed that the in-service training model for TB is currently being updated with the aim of potentially moving to a continuing medical education model.

There is good communication between the Ministry of Health and the NTC regarding the development needs for TB health care providers. Given the new restructuring and merger of the RTBD and the NTP, there are several opportunities for human resources development.

Since the 2011 review, the NTP has appointed a dedicated coordinator for continuing education and training. With the decentralization of TB services to the primary health care level, in-service training is geared towards primary health care practitioners. A standardized training curriculum was developed in 2011 in line with WHO recommendations and is to be updated every three to four years. Training is currently conducted in detection and diagnosis, treatment, and recording and reporting. New topics will be incorporated into the training curricula once the national guidelines have been updated. Additional special training has, however, been conducted in DR-TB as well as training of trainers for GeneXpert MTB/RIF. Standardized training in DR-TB was to begin in 2014 or 2015 and should be included in the curricula. Five core training courses are offered each year: three from the NTC and two from Yerevan State Medical University.

It was unclear at the time of the review how many training courses take place each year, although in 2013, 430 doctors and 736 nurses had been trained this way. Letters are sent out from the NTC manager (formerly from the NTP) to the heads of regional public health departments asking how many doctors and nurses need to undergo training. The NTC then organizes the courses by calling for tenders from all collaborating institutions which can deliver them, except in Yerevan, where the courses are conducted directly by the NTC. Priority for training is given to health care providers who have not yet participated in any training.

The NTC currently has no long-term or specific human resources development plan. Neither have all clinical health care staff undergone training in TB offered by the NTC, especially those in rural ambulatory health care clinics. This is primarily due to issues of coverage of patient care, lack of salary during the training courses or courses not being conducted in certain regions. As a result, many participants attend only part of the training programme but not all of it. Training is also dependent on cooperation by the heads of regional public health departments. It was evident during one field visits that it had not been possible to arrange training because of a lack of priority or support from the regional public health department.

Upgrade training or reaccreditation is handled by the National Institute of Health in collaboration with Yerevan State Medical University. Training takes seven weeks for doctors and five weeks for nurses. All health care providers need to complete this training once every five years.

The following challenges were observed during visits and interviews.

- There appear to be late diagnoses and missed cases of TB due to a lack of recognition and training among subspecialists other than primary health care physicians. Underdiagnosis of TB and DR-TB in children was also found during the epidemiological review.

- Training in TB offered by the NTC is not reaching specialists other than those in primary health care.
- There is a need for training in paediatric TB and extrapulmonary TB.
- The cost of the five-year reaccreditation is a financial burden on those health care staff who need to undergo this training.
- TB doctors are ageing, and there are not enough incentives for young doctors to go into or stay in TB practice. This is largely due to inadequate remuneration and the stigma or fear of becoming infected with TB. As a result there is a shortage of TB physicians, especially in rural areas.

Recommendations

- In-line with Pillar 1 (Integrated patient-centred care and prevention) of the Post-2015 Global Tuberculosis Strategy Framework *(21)*, a TB training component should be included in the five-year reaccreditation and in-service training curricula for other subspecialties, in addition to primary health care. This should be initiated through direct cooperation between the Yerevan State Medical University and the NTC. Such a strategy would improve the capacity for diagnosis of all forms of TB and rapid referral to TB specialists for treatment.
- In order to incentivize primary health care and other subspecialists and reinforce their TB training, and in line with Health 2020 and the strengthening of health systems, it is recommended that in-service training should be linked with reaccreditation as in, for example, the continuing medical education model. Such a model should be credit-based, so that health care staff can accrue a standard number of credits upon successful completion of each module, which are then counted towards the five-year reaccreditation requirement. Such a model would give an incentive to staff to complete the annual in-service training and alleviate some of the time and financial burden of the five-year reaccreditation process.
- To address the shortage of TB doctors, and given that many pulmonologists also have qualifications in the TB specialty (after upgrade training), it is recommended that the NTC and Yerevan State Medical University should discuss the possibility, feasibility and sustainability of potentially merging the TB and pulmonology specialties.
- The NTC should carry out a national comprehensive assessment of training needs for both clinical care and monitoring and evaluation at both the NTC and the clinical service levels, with particular attention to rural ambulatory care clinics.
- Based on the needs assessment, the NTC should develop a long-term plan for developing the capacity of human resources, including a financial component.
- Components covering extrapulmonary, paediatric and DR-TB should be added to the standard in-service training curricula. The NTC should consider training trainers in these topics.

Medical products, vaccines and technologies

Management of TB medicines

The drug management unit of the NTP was established following a recommendation of the 2011 review mission. It consists of three pharmacists, who are responsible for forecasting the NTP's

needs for anti-TB drugs and medicines for management of adverse reactions, preparation of requests, receipt of shipments after customs clearance by the Republican Centre for Humanitarian Assistance, storage, inventory and distribution of these medicines to TB facilities, including in the penitentiary sector, in coordination with the Global Fund project coordination team. The drug management unit also coordinates all activities related to procurement and supply chain management with MSF-France and other partners. Laboratory equipment, reagents and supplies for diagnosis of TB are quantified, procured and managed through the laboratory unit, led by the NRL coordinator.

Selection

Medicines for treatment of TB are selected by the NTC in coordination with technical partners and in accordance with the national treatment guidelines, which are in line with WHO recommendations. Since 2003, the NTP has rapidly increased the use of fixed-dose combinations and almost 90% of patients with susceptible forms of TB are currently treated with these combinations at all levels. Owing to the high incidence of drug-resistant forms of TB, the NTP still requires 5–7% of single-dose formulations to adjust regimens when drug resistance is identified. In only a few cases have side-effects leading to withdrawal of fixed-dose combinations from treatment been reported and observed by the health facilities. Since the 2011 review, the NTP has shifted from an intermittent to a daily regimen, which has led to the replacement of 150 mg rifampicin/150 mg isoniazid in the continuation phase of treatment with 150 mg rifampicin/75 mg isoniazid.

Following repeated recommendations by technical partners, the National Drug Regulatory Authority has included most of the first-line drugs on the national essential medicines list, which is revised every two to three years. Key second-line drugs in Groups 2, 3 and 4 have already been included on the list, or there are plans for them to be included. It is hoped that when the revised national drug policy or drug law is approved, inclusion of lifesaving medicines in Group 5 on the list will become easier and quicker. Products on the national essential medicines list are prioritized for procurement with government funding.

Procurement

The Procurement Law regulates all aspects of public procurement. Public sector procurement is centralized and the state procurement agency procures all public goods. This agency organizes the procurement of medicines and supplies determined by the Ministry of Health in accordance with the national essential medicines list/priority list and carries out calls for tenders for the individual health facilities, which are then reimbursed by the Ministry of Health. The public sector tender bids are publicly available and known. However, the high cost and unknown quality of the products due to the limited size and fragmented market (facility-based) make public procurement practices unreliable and almost unsustainable.

The procurement of anti-TB medicines has been fully dependent on donors for over a decade and requires coordination between multiple players. At the time of the review, all anti-TB drugs other than those used in the MSF-France supported project are procured with Global Fund grants through the GDF direct procurement mechanism.

During 2003–2010, all first-line TB medicines were procured directly from the GDF by the German Agency for Development Cooperation with funds provided by the German Development Bank. Since then, procurement has been through three rounds (5, 8 and 10) of the Global Fund grant. The Global Fund has committed itself to provide funds for procurement of first-line drugs

until the end of 2015 and the government will take over procurement of quality-assured first-line drugs through the GDF direct procurement mechanism from 2016 onwards. The team held a meeting with GDF staff to clarify the requirements for procurement with government funds, and a follow-up discussion took place early in 2015 to ensure that procurement requests are prepared well in time and orders placed to avoid shortages of drugs and interruption of treatment.

The current procurement procedure regarding anti-TB drugs and medicines for adverse drug reactions is as follows: the NTC uses all available tools to select the drugs, provide a specification which includes dosage, formulation and packaging, quantify the needs per year and prepare the draft order. The Global Fund project coordination team finalizes the drug order, signs a technical agreement with the GDF and coordinates the disbursement of funds to the GDF procurement agent. Countrywide drug orders are usually placed once a year, with two deliveries planned every six months to ensure the prompt arrival of medicines and replenishment of all stocks at the central warehouse (Annex 6). By using the GDF drug calculation sheet, the NTP has quantified its needs well for first-line drugs without shortages and losses/expiries. Ad hoc changes were made in procurement requests for first-line drugs during the period 2012 –2014 to reflect changes that had occurred due to resistance patterns (use of isoniazid, ethambutol and pyrazinamide).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The mission raised concerns about the low intake of paediatric formulations nationwide. The TB doctors still refrain from prescribing these formulations to all children at the main Republican TB hospital, visited by the mission, where children with TB start their treatment. Despite the efforts of the NTC team to promote the use of child-friendly formulations, adult drugs are still being used (as indicated in this picture). Underdetection and underreporting of TB in children would be another reason why substantial amounts of paediatric formulations were due to expire by September 2014 unless they were used for adult patients. The estimates for TB in children would have to be further adjusted for 2015 to avoid products expiring. There is a need for the NTC to give priority to familiarizing and training paediatricians to improve diagnoses of TB in children and the use of child-friendly formulations for treatment.

Second-line TB medicines are procured by the NTP in coordination with the Global Fund project coordination team. Initially it was anticipated that DR-TB treatments would be made available through various rounds of Global Fund grants as follows: 300 in round 5; 360 in round 8 and €2.5 million in round 10, which were adjusted as rapid diagnostic tools became available and more patients were recruited for treatment. Due to a lack of comprehensive calculation tools and limited experience in the management of complex treatment regimens, the procurement of second-line drugs did not run as smoothly for the NTP during the initial phase of DR-TB treatment initiation. However with more guidance, rapid support and the direct involvement of technical partners (MSF, GDF, Green Light Committee, Management Sciences for Health), the situation has stabilized and no shortages of second-line drugs for DR-TB treatment have been reported over the last two years. Currently there is no buffer stock provision made for second-line drugs, while for first-line drugs it is 50%.

MSF-France has been one of the key partners of the NTC over the past decade contributing to the decrease of the reservoir of DR-TB in the country. MSF-France procures some of the Group 5 anti-TB drugs together with bedaquiline with their own funds and through the GDF

direct procurement mechanism for the Armenia programme, which includes the compassionate treatment of pre/XDR-TB. MSF-France also provides single-dose rifampicin for treatment of DR-TB patients for the NTC and ancillary drugs for their project. Jointly with other partners, MSF-France was planning to initiate the treatment of 24 pre/XDR cases a year with regimens consisting of bedaquiline from January 2015 to December 2019. This MSF-France regional project is supported through a UNITAID grant covering over 17 countries globally. In addition, MSF-France has its own plan of activities focused on technical assistance, programme monitoring, operational research and capacity-building.

Ancillary drugs for managing the side-effects of DR-TB treatment are procured locally and/or internationally by the Global Fund grant and MSF-France and provided to most health facilities. Box 2 shows the latest list of key ancillary medicines that were provided to TB health facilities. The list is not exhaustive, and TB hospitals and dispensaries procure additional medicines for management of adverse reactions and other symptomatic treatments. Lists of these medicines, with information on funds spent to procure them, were made available to the team at the hospitals and TB dispensaries. Since procurement of these drugs is usually put together with other goods required for the hospitals it was impossible to single out the costs of the medicines accurately. Due to the limited market size (facility-based), domestic procurement has not been so smooth. Delays with signing contracts and disbursement of funds, together with poor product quality, were mentioned by a few facilities. All ancillary drugs are provided free of charge to patients at the hospital or ambulatory levels. Despite all the issues, no shortage of ancillary medicines was reported in the health facilities visited or mentioned by the patients interviewed.

Box 2. List of main medicines procured for treatment of side-effects of DR-TB treatment

1. Aluminium hydroxide 400 mg/magnesium hydroxide 400 mg (Maalox)
2. Omeprazole, 20 mg
3. Ondansetron,
4. Promethazine hydrochloride, 25 mg
5. Paracetamol (acetaminophen), 500 mg
6. Nystatin, 500.000 IU
7. Ibuprofen, 400 mg
8. Diklofenac sodium, 25 mg/ml -3.0 ml
9. Salbutamol, 200 puffs, 0.1mg/puff, inhaler
10. Multivitamin
11. Pyridoxine, 10 mg
12. Dicynone, 250 mg
13. Metoclopramide, 50 mg
14. Rehydron powder, dose of 18.9g package
15. Fluconazole, 50 mg
16. Fluconazole, 100 mg
17. Co-trimoxazole (sulfamethoxazole+trimethoprim), 480 mg
18. Carbolen

Registration

Requirements for registration are based on current legislation. Medicines are registered either by their international non-proprietary name or by this name together with the brand name. A fee must be paid for a medicines market authorization (registration) based on the application, varying according to the requirements for new and/or additional dosage/strength. The standard registration of a generic product may take as long as 180 days and cost US$ 2000; registration of an innovative product takes even longer and costs US$ 3500. A description of the processes and lists of documents required can be found on the national drug regulatory authority website.[5]

Formal registration is not required for medicines imported or arriving as humanitarian aid: for every shipment, a special waiver is obtained through the Ministry of Health and the national drug regulatory authority. The first- and second-line drugs procured through the GDF had not yet been

[5] The Scientific Centre of Drug and Medical Technologies Expertise [website]. Yerevan: The Scientific Centre of Drug and Medical Technologies Expertise; 2015 (http://www.pharm.am/index.php/en/, accessed 12 July 2015).

registered. Currently, very few products prequalified by WHO and/or authorized by the stringent regulatory authority are registered.

The Scientific Centre for Drug and Medical Technology Expertise (the national drug regulatory authority) is responsible for registration of medicines. At a meeting with the director of the Centre it was confirmed that the Ministry of Health has agreed to register the drugs procured by the GDF at no cost in the country as per the fast tracking procedure. The agreement for the fast-track registration procedure was signed by the Centre with WHO in 2012. The procedure can be exercised at any time and can be carried out for WHO prequalified products and medicines authorized for use by the stringent regulatory authority, meaning that these medicines can be registered within 30–45 working days in Armenia. It is important that the NTP initiates registration of anti-TB medicines jointly with the GDF as early as possible.

The last joint review mission commented on double standards for registration of medicines manufactured in former Soviet states (relaxed) versus those produced in the rest of the world (restricted). These comments were taken into consideration by the Scientific Centre for Drug and Medical Technology Expertise and, with technical support from partners, relevant provisions were included in the revised national drug policy a few years ago. Since this is still waiting for government endorsement, the mission made it a key recommendation to the Ministry of Health to expedite approval and facilitate implementation of these provisions. The Ministry of Health and the Centre have already confirmed and made a commitment to procuring anti-TB medicines with domestic funding through the current quality requirements (WHO product quality plan or stringent regulatory authority) and as per the specifications for international bidding. There is, therefore, no threat to the availability, accessibility and affordability of quality assured anti-TB medicines to patients. Since legal provisions supporting these requirements are included in the national drug policy, its early governmental endorsement will certainly facilitate the rapid implementation of these provisions.

Since the 2011 review, only a few of the WHO-recommended anti-TB medicines, formulations and strengths had been registered (Annex 7). Many of these products are authorized by the stringent regulatory authority and one has been prequalified by WHO. None of the medicines procured through the GDF had been registered in the country, as issuance of a waiver remained an easier option and has thus been extensively used. With the possibility of fast-track registration and simplified legal provisions included in the national drug policy, registration of all anti-TB medicines will have to be requested and supported by both the GDF and the NTP.

Distribution and storage

First- and second-line TB medicines arrive by air and are stored in the customs warehouse. Each shipment requires a special waiver and takes an average of 30–45 working days to clear customs, which is too long for lifesaving medicines. The shipments are then cleared tax-free by the Humanitarian Aid Department and stored at its warehouse pending further information and action from the NTP.

The distribution system for TB medicines is separate from the national supply system for essential medicines. The NTP drug management unit stores and distributes medicines to all TB facilities in the country. Almost half the TB facilities send quarterly reports and requests for replenishment of orders to the central or NTP drug management unit; they then pick up the first-line drugs quarterly and second-line drugs (mainly) monthly. The rest of the facilities receive their stock during visits by supervision vehicles or on an ad hoc basis (for example, combined

with deliveries of laboratory equipment and supplies and sputum collection). Although the health facilities visited did not complain about difficulties with deliveries, the NTC should look into the possibilities for improving the arrangements within the overall health system as soon as possible.

The drug management team: (i) checks and verifies the quantities of stock versus the request forms and corrects, where necessary, the total quantities to be issued, and (ii) conducts regular analyses of the consumption of medicines. The NTP practises the pull system (based on actual or consumed demand) for the distribution of anti-TB drugs to avoid the complications in returning medicines to the central NTP. This system allows for internal redistribution among health facilities, although this does not often happen.

The storage of all anti-TB medicines is to some extent consolidated at central level, which simplifies inventory management and distribution (one-stop pick-up for the district facilities). Owing to limitations on space, however, some of the TB shipments are kept at the Humanitarian Aid warehouse, which is 15 km away from the NTC store. Storage conditions at the NTP central and district facilities store visited were adequate except in the RTBD, where space was very limited and hygienic conditions were poor (cracked walls, floors, doors and broken shelves). The staff responsible for stock management are well trained and familiar with basic storage and inventory principles such as first expired, first out and regularly updating books and ledgers and stock cards.

The health facilities keep stock records in two types of standard ledger: (i) consumption by patients and individuals, and (ii) medicines received/medicines utilized by drug names. The facility staff report the numbers quarterly to the NTC when they pick up the next supply. According to NTP guidelines, a 100% buffer stock of first-line drugs must be maintained at central level and about a three-month stock at facility level. In practice these have not been maintained. The team noted that the buffer stock was below 50% at central level and less than 30% at health facilities for first-line drugs and almost no buffer stock for second-line drugs as they were distributed monthly. It may, however, not be necessary for a 100% buffer stock to be held centrally due to the short distances between the referral stores, good infrastructure and established inventory management system for first-line drugs.

Technical assistance in pharmaceutical management has not been available to the NTP on a regular basis. Some ad hoc assistance has been provided during GDF missions and NTP staff have attended regional drug management workshops, but the high staff turnover has rendered this assistance inefficient.

There are still no standard operating procedures for handling the import, transport, storage and distribution of TB medicines: activities are carried out according to the previously established practices. It is, therefore, crucial that the NTC drug management team develops standard operating procedures as soon as possible in view of the forthcoming changes and familiarizes health facility staff with the procedures in advance. With the move of the central NTP units to premises in Abovian planned for the next 12–18 months and the anticipated procurement of first-line drugs by government funds through the GDF, the procedures for procurement, registration, recording, reporting, storage and distribution will certainly change and the team will need to be ready to respond rapidly and to implement the changes.

Use of TB medicines

The treatment of drug-susceptible TB is carried out according to WHO recommendations and includes the treatment of new and retreatment cases. The Category III regimen was phased out in 2012 and replaced by a regimen for the treatment of new cases. A daily regimen was introduced in 2013 and the NTP is aiming to implement DOT for all TB cases throughout the course of therapy. The team recommended that the treatment regimens should be simplified and standardized by phasing out the Category II regimen.

The medical management of DR-TB is carried out in accordance with WHO recommendations. All treatment regimens for DR-TB cases are designed by the treatment Committee, but doctors at treatment sites are permitted to change regimens. Currently 13 treatment regimens are used for DR-TB treatment, including the options with bedaquiline. All the treatment sites visited were carrying out treatment under strict DOT and had adequate defaulter tracing and social support systems in place. Patient support programmes, including mobile home visits, reimbursement of transport and a monthly package of food and hygiene products, had been designed to ensure treatment adherence. The social support is being funded through the Global Fund grant, and there are no plans for the government to take over this support at present.

Legal provisions are in place for pharmacovigilance activities, for which the national drug regulatory authority at the Scientific Centre for Drug and Medical Technology Expertise is responsible and leads the implementation of related activities. In accordance with the registration requirements, marketing authorization holders must continuously monitor the safety of their products and report adverse drug reactions to the national drug regulatory authority. There is a national pharmacovigilance centre at the Scientific Centre for Drug and Medical Technology Expertise with three full-time staff. An official form for reporting adverse drug reactions was recently revised and is available for use (Annex 8) and there is a national adverse drug reactions database. On average, 220 adverse drug reaction reports are sent annually to Uppsala, the WHO collaborating centre. Over 10% of these were related to first- and second-line anti-TB drugs (rifampicin, kanamycin, pyrazinamide, particle acceleration by stimulated emission of radiation, protionamide and cycloserine). The pharmacovigilance centre has published at least one analysis in the last two years and it regularly publishes an adverse drug reactions bulletin.

Guidelines for managing side-effects are included in the TB treatment guidelines and the ancillary medicines are made available through the Global Fund grant or MSF-France project. Temporary or permanent withdrawal of second-line drugs from the regimen is possible only after severe side-effects. Comments to this effect are usually included on the reporting form and the patient treatment card, but do not yet have to be reported to the pharmacovigilance centre. This information is provided to the drug management unit on a monthly basis and captured by the quantification tool DR Koch Tail database .

Table 9 refers to the most frequent adverse drug reactions observed by the health facilities and reported to the NTP in 2013. Protionamide and pyrazinamide were indicated as the main medicines causing a high rate of adverse drug reactions across the country (the details were not available to the mission). It is, therefore, crucial that all observed adverse drug reactions are fully reported to the pharmacovigilance centre on a regular basis and forwarded to the Uppsala centre for a full review and analysis.

Table 9. Frequency of adverse drug reactions reported to the NTP, Armenia, 2013

Anti-TB agent	Adverse drug reaction reported

	%
P-aminosalicylic acid	4
Streptomycin	1
Protionamide	11
Kanamycin	1
Ethambutol	1
Pyrazinamide	10

Source: NTP.

Anti-TB drugs are on unrestricted sale in pharmacies despite the Ministry of Health order of 2012 banning the over-the-counter dispensing of anti-TB medicines and other antimicrobials. Eight pharmacies were visited during the mission and six of them had at least two or three anti-TB medicines available for dispensing without a prescription. Among first-line drugs, rifampicin is mostly demanded and among second-line drugs, the kanamycin injection and fluoroquinolone tablets are in high demand. These medicines are mostly used and misused for non-TB indications and/or for veterinary purposes, leading to further amplification of drug resistance. It is, therefore, imperative that the Scientific Centre for Drug and Medical Technology Expertise of the Ministry of Health joins other ministries and departments in banning the registration of non-WHO-recommended formulations and combinations of anti-TB medicines and the use of rifampicin for non-TB indications. The revised national drug policy provides for the introduction of severe measures to reinforce the ban on over-the-counter sales of rifampicin and other antimicrobials from pharmacies.

The use of tuberculin tests for mass screening to identify latent TB in adults aged over 15 years is another example of timeworn and irrelevant practices that require a change. It currently costs the Ministry of Health over €85 000 a year and should be abandoned, in accordance with the latest WHO recommendations.

Quality assurance

Good manufacturing practices are a legal requirement for registration of medicines, and local and foreign manufacturers are inspected for compliance with them. The legal requirement for the GDP is included in the revised national drug policy document. The Scientific Centre for Drug and Medical Technology Expertise informed the team that their medicine quality control testing laboratory had recently been ISO-certified and plans were being made for the laboratory to becoming WHO-prequalified soon. The laboratory undertakes responsibility for post-marketing surveillance. For most medicines, samples are collected by government pharmaceuticals inspectors on registration for quality post-marketing monitoring and in case of complaints. Samples should be taken from pharmacies or warehouse stocks – inspectors have the authority to make unexpected inspections and/or sampling post-marketing. Based on the testing results, the product is permitted or rejected from further use in the country. According to the Centre, no anti-TB drugs failed quality control testing in 2013 or 2014. Owing to limited financial resources and inadequate and irrelevant legal provisions, the inspectors are unable to carry out their responsibilities to the full. Substantial positive changes are, however, expected when the national drug policy is approved.

TB drug information management

The management of information about TB drugs is organized through monthly (for second-line drugs) and quarterly (for first-line drugs) reports and all data are entered in the log at regional and health facility levels. Once the reports reach the NTC drug management unit, data are

entered into the Access or DR Koch Tail databases (note the picture of modules the database covers, the two tools used in the country for monitoring and quantification purposes in addition to the GDF drug calculation sheet. The following data and reports (PDF only) are currently available through the NTC used tools: received lots/stock level, consumption/ distribution data, stock-out periods, inventory data, shelf life/expiry date, expired products, dispensing to patient, anticipated consumption, forecasting module and prediction for patient enrolment.

These tools are only used by the NTC drug management unit at central level and it is anticipated that a computerized drug management module will be made available to NTP for countrywide use by mid–2015, which will link the drug management database with the NTC full database.

Recommendations

- The Ministry of Health should expedite submission of the revised national drug policy document (the drug law) for government approval.
- The Ministry of Health should urgently develop mechanisms and ban over-the-counter sale of all antibiotics and anti-TB medicines so as to reduce the spread of drug resistance across the country.
- The Ministry of Health should restrict the registration and procurement of anti-TB medicines to quality assured products (prequalified by WHO and authorized for use by stringent regulatory authorities).
- The Ministry of Health should ensure that financial resources are available to procure first-line anti-TB medicines from 2016 onwards.
- Within the next four months, a staged plan should be developed for the procurement of first-line anti-TB medicines with government funds. An order was to be finalized and placed not later than March–April 2015. An estimated US$ 200 000 will be required to cover the NTP's buffer stock needs, including all related costs (shipment, pre-shipment inspection, quality control, fees and insurance).
- TB doctors and paediatricians at all levels should be informed and sensitized urgently to the availability of child-friendly formulations and their use for treatment of TB in children.
- Supportive supervisory visits (programmatic/laboratory/medicines) should be conducted jointly to regions and primary health care facilities. There is a need to reduce the frequency of such visits, improve their quality and ensure the provision of written feedback and follow-up visits.
- The rational use of antibiotics should be promoted through sensitization of and collaboration between the private pharmacy network and the Ministry of Health/ pharmaceutical inspectors/Scientific Centre for Drug and Medical Technology Expertise.
- The collection and reporting of adverse drug reactions should be supported and facilitated for all second-line anti-TB medicines from TB treatment facilities and the central NTC and their prompt provision to the pharmacovigilance unit.
- Standard operating procedures should be developed for important aspects of TB medicines management such as selection, inventory control, ordering, storage and distribution.
- The mass screening of adults aged over 15 years with tuberculin skin test should be discontinued.

- The NTC, GDF and WHO should initiate and facilitate fast-track registration of all anti-TB medicines in accordance with the standard treatment guidelines (free registration).
- Partners should assist the development of action plans for implementation of new and revised polices as defined in the national drug policy.
- The GDF should assist the Ministry of Health and NTC with planning and executing the procurement of first-line drugs with government funding for 2016.
- The GDF should provide prompt updates to the NTC and the Global Fund grant principal recipient for placed orders.

Partnership, advocacy, communication and social mobilization and community involvement

In general, advocacy, communication and social mobilization (ACSM) are being developed with the establishment of civil society organizations and patient groups, and a TB patient group led by an MDR-TB survivor has been set up recently. This is an informal structure that needs support and capacity-building. It is considered a significant step in making the voices of people affected by TB heard and their needs articulated.

The involvement of former patients in patient education started in June 2014. The NTC has identified and supported a former MDR-TB patient, psychologist by profession, to initiate peer-to-peer education for patients with regular TB. At least three more former TB patients are willing to be involved in social mobilization activities.

Nongovernmental organizations involved in TB control in Armenia (to differing extents) are: the ARCS, MSF-France, Mission East Armenia, Yerevan Home Care, Foundation For the Sake of Children's Health, Real World Real People and Positive People Armenian Network. Information provided by representatives of these organizations, TB patient groups and the NTC was used to review existing partnerships and civil society involvement in TB activities.

There is no well-developed strategy or clear budget for implementing ACSM campaigns. There is no ACSM working group, although there is a focal person for ACSM in the NTC. A national ACSM strategy should be developed with activities, timeline for implementation and budget. Collaboration with local nongovernmental and community-based organizations as important actors in community involvement should be clearly defined and stated.

Over 20 medical staff have been trained in ACSM. From 2012 to mid-2014, the NTC's ACSM focal point conducted face-to-face counselling sessions for over 300 patients with regular TB, using TB information materials and individual assessment lists. ACSM campaigns are, however, limited: the campaigns guided by the NTC focal point were limited to Yerevan, and TB-related information activities on television only happen on World TB Day. The use of social media as an ACSM tool is also underutilized.

Several nongovernmental organizations are involved in TB-related ACSM activities in Armenia. *Mission East* is an international nongovernmental organization working to build capacity among the most marginalized and vulnerable people with interventions in TB prevention and improving access to education and health care services. *Real World Real People*, since its foundation in

2003, has been working to increase the quality of life for PLWH and their families and uniting the community by providing direct psychological, social and legal services, as well as advocating universal access to treatment, care, support and testing for HIV/AIDS. *Positive People Armenian Network* has, since 2006, worked to free society of stereotypes about PLWH. The organization conducts large-scale events and mass campaigns. Although the main target of these organizations is HIV, they extend their focus to people coinfected with TB and HIV in TB facilities. Human rights and stigma-related issues are of great concern to them, and they cooperate closely in implementing their activities with other Armenian nongovernmental organizations focusing on human rights.

Real World Real People and Positive People Armenian Network have signed memorandums of collaboration with state institutions only for HIV interventions, but they are carrying out TB-related interventions beyond the most at risk populations, such as referring HIV-positive people with TB symptoms to TB facilities and visiting them in these institutions.

For the Sake of Children's Health, formed mostly of doctors and nurses, has worked in the TB sector for 16 years. Since its foundation, it has conducted interventions on TB prevention with the support of municipal authorities, including interventions to increase awareness about TB in eight (out of 11 provinces) targeting children, pregnant women, students and the general public.

The ARCS, MSF-France and Yerevan Home Care are the three key organizations that work with TB patients using ACSM tools such as psychosocial assistance and provision of information, education and counselling activities.

Childhood TB interventions and peer support activities for DR-TB patients are conducted regularly by MSF-France according to the implementation plan. Food parcels are distributed in prisons for DR-TB patients. MSF-France nurses and counsellors are continuously retrained in patient education and psychosocial support through the expertise of an international counsellor.

Access to new drugs and treatment regimens is important in TB treatment, care and support. The contribution of MSF-France in good partnership with the NTC has resulted in a new TB drug (bedaquiline) being made available for M/XDR-TB patients through the compassionate use programme. Between April 2013 and July 2014, 38 DR-TB patients were enabled to have access to bedaquiline in the programme. This includes the prison sector, where two DR-TB patients have been enrolled in the compassionate use programme since January 2014. From a human rights perspective this is an important step in ensuring access to new available drugs and regimens.

The ARCS carries out a number of ACSM activities, planned and funded by the Global Fund grant. These activities mostly concern retraining of the ARCS social workers and education sessions for TB patients. Through the current programme, Social Support to TB Patients in Armenia, the ARCS delivered motivational packages to 96–99% of all TB patients, reimbursed their transport costs and covered the cost of heating for three and a half winter months for the 96–99% of all TB patients during 2011–2014. The results of this programme are encouraging: according to the Ministry of Health assessment conducted in 2013, 98% of TB patients received motivational packages, 96.1% of whom consider them (motivational packages) satisfactory. About a quarter of TB patients (27.4%) reported returning to treatment because of the motivational packages and 87.3% considered them extremely important. It can, therefore, be concluded that patient motivation is very important and should be fully supported by the NTC.

Since 2013, the NTC, as a subrecipient of the Global Fund grant, has mobilized Yerevan Home Care to deliver treatment and social support services to over 108 TB patients with difficulties or problems with mobility who were unable to come daily to TB clinics for DOT. To improve the service, Yerevan Home Care staff have received special training in TB and criteria have been developed to define the group of TB patients for home-based DOT.

TB stigma

Patients often have a confused understanding of TB. Some key actors present a hygienic lifestyle (the use of personal tableware, towel and kitchen utensils) as a preventive measure in controlling TB. This is highly confusing and feeds the existing stigma for TB patients. Information materials should be consistent with the recommended international standards for controlling TB and reducing stigma. Interviews conducted during the review showed low TB literacy and high stigma from TB among patients, who preferred to keep their TB status undisclosed and not to communicate with other TB patients.

No surveys or assessments of the perception of and stigma from TB between TB patients and the general population have been conducted and the NTP lacks data on the issue. For programme activities to be planned successfully, there is a need for reliable and valid information on the perception, knowledge and stigma of TB as between TB patients and the general population.

The staff of TB facilities should be able to identify and respond properly to rumours. During the initial treatment phase, it is very important for the staff, at the same time as focusing on the management of side-effects from drugs, to properly address any rumours circulating among the patients, especially any related to DR-TB. The staff need to apply their communication skills to prevent interruptions to treatment due to rumours, miscommunication and lack of information.

TB patients have a high appreciation of the health staff who, in most cases, are friendly, patient and accurate in ambulatory treatment.

In general, TB-related information campaigns are not widespread. There are no specially designated places in TB facilities at any level to display information, education and counselling materials for patients and the general population. Access to such materials is very limited.

Medical and social support are very important and there is space for community involvement in information, education and communication interventions. TB awareness should be strengthened with the main focus on dissemination of information related to TB among the patients and reduction of stigma and self-stigma between patients and the general population.

The team encouraged any partnerships directed towards increasing the efficiency and effectiveness of such activities as advocacy, public education, de-stigmatization and patient support. Nongovernmental and community-based organizations should develop their capacities to increase their involvement in TB control.

Recommendations

- A national ACSM strategy with an operational plan including a budget should be developed in line with the national strategic plan for TB control. The strategy should promote new partnerships by involving grass roots nongovernmental organizations in TB control.

- Community actors should build their capacity to play their roles in service provision, social mobilization, monitoring and advocacy.
- The Patient Charter for TB Care should be made available and widely distributed among patients via peer-to-peer support activities.

Operational research

Intensified research and innovation is one of the three pillars of the Post-2015 Global Tuberculosis Strategy Framework. In addition, operational research is one of the Stop TB Strategy components, which is aimed at improving programme performance; assessing the feasibility, effectiveness and impact of new strategies or interventions in TB control; and collecting evidence to guide policy recommendations on specific interventions. In line with the Post-2015 strategy, national TB control programmes should prioritize their topics for research and set an operational research agenda which takes into account the researchers and institutions that can perform the particular studies, the time involved and the amount it will cost. An operational research agenda can be developed in Armenia based on the findings of recent studies and this programme review.

The NTP in Armenia currently collects a large amount of data through the monitoring and evaluation department, and most of the research carried out to date is centred on surveillance data. The national TB surveillance system is good and major efforts in capacity-building for surveillance have taken place since the last programme review in 2011.

Data are collected at the clinic level from all TB clinic inpatient departments as well as ambulatory services. Case-based registry data are also collected. Data are validated through the check functions used when data are entered. All clinic-level reporting is paper-based, although some clinics report on paper forms as well as electronically through e-TB Manager. Capacity is currently being built for the use of e-TB Manager, with plans to migrate fully to electronic reporting in the future. The NRL database is linked with the monitoring and evaluation database; the NRL receives paper-based reporting forms and data are then entered into the electronic system. There is, however, no long-term research plan to use the surveillance data collected through the monitoring and evaluation system, and there are no non-routinely collected data. A full description of TB surveillance and the monitoring and evaluation system is available in the separate report on the epidemiological review carried out by the mission.

The NTC has good capacity for conducting operational research. The head of the NTC monitoring and evaluation department has been trained through (and has facilitated) the WHO-led Structured Operational Research and Training Initiative course. In addition, the NTC has supervised several American University of Armenia (AUA) masters' students using national TB data for their projects.

The NTC has a good working relationship with key partners in research such as the AUA's Centre for Health Services Research and Development. In consultation with the NTC, the AUA has initiated TB projects looking at TB among migrants and the risk factors for TB. The AUA is also working on a cluster randomized trial investigating psychosocial support with modified DOT. This study is being conducted in close collaboration with WHO and the Global Fund. The team also found that the Yerevan State Medical University actively supports collaboration between its medical students, the NTC and AUA for research projects.

With the recent merger of the NTP and the RTBD, both the Ministry of Health and the NTP expressed interest in eventually building the capacity of the NTC to make it into a regional research and training centre. This would combine greater development of human resources and training plans with operational research. The team supports this eventual initiative, which is integrated into the recommendations for operational research. In addition, priority areas for operational research have been identified based on the current review and the corresponding epidemiological review.

Priority topics for operational research

The following are priority topics for operational research:

- evaluation of financial reforms against performance indicators and TB case-detection rates;
- reasons for the low TB case-detection/notification rates, including paediatric TB (this may include an evaluation of TB detection capacity and methods, including patterns of detection and DST);
- risk factors (including social determinants) for M/XDR-TB;
- risk factors for unfavourable treatment outcomes among patients with TB and M/XDR-TB, such as socioeconomic factors and/or the presence of comorbidities (for example, diabetes mellitus);
- the prevalence of irrational use of anti-TB drugs, such as rifampicin, for non-TB-related treatments and diseases;
- the burden and management of side-effects from TB treatment;
- TB in the prison sector: burden, management and treatment outcomes of prisoners with TB and M/XDR-TB;
- TB among migrants: burden of TB and M/XDR-TB and risk factors for unfavourable treatment outcomes;
- TB/HIV: evaluation of screening for latent TB infection and TB detection among people living with HIV and those on isoniazid preventive therapy and co-trimoxazole preventive therapy;
- molecular epidemiology: TB strain patterns in Armenia.

Recommendations

- The NTP should develop an operational research plan, including priority topics for study, in line with Pillar 3 (intensified research and innovation) of the Post-2015 Global Tuberculosis Strategy Framework *(21)*. The research plan should be incorporated into the national strategic plan and aligned with the Global Fund TB grant work plan for 2015–2017.
- The NTC should capitalize on its new structure and cross-cutting with human resources development to develop a formal link between operational research and activities for human resources development/training (such as a research and training development unit or centre). This link will optimize the use of strategies, interventions, tools or knowledge to enhance the quality, coverage, effectiveness or performance of TB health services.
- An additional staff member should be allocated to the NTC to oversee the implementation of the research plan and activities with collaborative institutions.

- The NTC should consider strengthening research collaboration with the AUA and Yerevan State Medical University, with the support of NTP partners such as WHO, MSF-France, USAID and the German Company for International Cooperation (GIZ). Capacity-building for carrying out the operational research plan will benefit from identified investigators being trained through the Regional Office Structured Operational Research and Training Initiative or other international training in operational research.

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Annex 1

SHORT BIOGRAPHIES OF REVIEW TEAM MEMBERS

Dr Andrei Dadu (Team Leader, epidemiological review, reporting and recording, monitoring and evaluation)
Technical officer (TB epidemiology and surveillance) in the TB and M/XDR-TB Control Programme (TBM) of the Division of Communicable Diseases and Environment, WHO Regional Office for Europe, Copenhagen. Expertise in TB surveillance, monitoring and evaluation of TB control programmes and field supervision, recording and recording, e- and mobile health. Responsible officer for managing the TB surveillance network; focal point for drug resistance surveys, intensified case finding, TB elimination and millennium development goals; focal point for TBM for south Caucasus and Baltic states.

Colleen Acosta (operational research, human resources, human resource development)
Epidemiologist and public health expert. Extensive experience in epidemiological and public health and field operational research in TB and M/XDR-TB. Working with TBM on the Compendium of Best Practices in Prevention, Control and Care for Drug-resistant Tuberculosis in the WHO European Region, and studies on childhood TB policies in the Region. Joined TBM in 2014 as focal point for research, training and collaborating centres. Currently leading the Regional Office's Structured Operational Research and Training Initiative in Eastern Europe and Central Asia.

Nigorsulton Muzafarova (drug and supply management, pharmacovigilance)
Product Quality Assurance Officer of the Global Drug Facility (GDF), Stop TB Partnership, WHO based in Geneva. Pharmacist and drug management expert working with national TB control programmes globally to address drug and supply chain management issues. Participated in several programme reviews and technical assistance missions in the Region, and helped countries to streamline planning, budgeting, financing and procurement requirements for first- and second-line anti-TB medicines and laboratory supplies.

Arax Hovhannesyan (epidemiological review)
WHO temporary adviser responsible for aspects of the epidemiological review, including data collection system, data quality, analysis and interpretation. Wide experience in health care systems, especially development and planning, implementation and monitoring of health projects. Experienced in providing technical support to NTPs to carry out TB drug resistance surveys, participated in programme reviews in eastern Europe and assisted the Regional Office in developing regional annual surveillance and monitoring reports.

Dr Askar Yedilbayev (Green Light Committee, treatment, MDR-TB, infection control)
Medical doctor and public health specialist from Kazakhstan. Programme Director for Russia and Medical Officer at Partners In Health (PIH). Has worked extensively with PIH's DR-TB programmes around the world providing technical assistance on programme and medical management of TB and DR-TB DR-TB, and focusing on the prison sector, building best practices of clinical care and ambulatory treatment. WHO consultant on Green Light Committee monitoring missions in European Region and international trainer in related fields. On behalf of PIH, participated in development of the Consolidated Action Plan to Prevent and Combat MDR-

TB and XDR-TB in the European Region for 2011–2015. Represents PIH on the Green Light Committee of the WHO European Region for DR-TB.

Dr Alexandra Solovyeva (Green Light Committee, treatment, MDR-TB, infection control)
Experienced in clinical, administrative and public health work in general medical service. Tomsk City Programme Coordinator for Partnership in Health – Russia covering the development and management of patient-oriented approaches in the treatment of TB in Tomsk, and the organization and coordination of programmes on reducing alcohol problems in TB patients and on TB control among people living with HIV/AIDS in the Tomsk Region, including operational research in the latter. Organized and trained groups of nurses and doctors in the clinical and programmatic management of TB and TB/HIV.

Alexandr Katsaga (health system strengthening, health financing)
Health policy, financing and health information system expert with extensive practical experience mainly in eastern Europe and central Asia. Worked with multiple clients, including USAID, World Bank, Asian Development Bank and WHO, as well as governments and ministries. Participated in developing large-scale country-level health policy strategies and reform programmes and payment methods for hospital and primary health care services, and provided training programmes for health care managers.

Elena Romancenco (diagnosis and case detection, laboratory services)
Medical microbiologist from Republic of Moldova. Extensive practical experience as laboratory consultant for diagnosis of infectious diseases (establishment of laboratory network, National Reference Laboratory, implementation of new laboratory methods and staff training). Participated in establishment of reference laboratories in Republic of Moldova for influenza (through World Bank programme in Moldova), viral hepatitis (through USAID programme) and TB (through Global Fund, Foundation for Innovative New Diagnostics and TB Reach programme). Responsible for monitoring and evaluation of TB laboratory service, including forecasting and procuring reagents, consumables and equipment, monitoring visits, writing national reports for donors, staff training, writing guidelines and procedures and implementation of quality management system in TB National Reference Laboratory and TB Microscopy Centre). Worked with multiple clients, including Global Fund, FIND, WHO, USAID as well as local counterparts.

Ms Oxana Rucsineanu: advocacy, human rights, community involvement
Vice-President of Moldova National Association of TB patients, member of the Moldova National Platform of Community-Based Organizations Working in the Field of TB, member of Steering Committees of Global Coalition of TB Activities and TB Europe Coalition. Focuses on rights and responsibilities of TB patients. Personal experience of DR-TB and realization of the importance of patient-centred treatment and support led her (together with other TB patients) to start a patient organization. Committed to advocating partnerships between TB patients, medical staff and authorities to make treatment more efficient, improving universal access to TB/MDR/XDR treatment and making the voices of TB-affected people heard in the global response to the disease.

Dr Nataliia Moisieieva (partnership, advocacy, communication and social mobilization, TB/HIV, TB in prisons)
Experienced in public health in Ukraine specializing in issues of HIV and TB/HIV, including prevention and treatment of HIV coinfection and management of TB/ HIV training for medical workers and public health policy development. Extensive experience with nongovernmental

organizations at local and national levels. Involved in projects aimed at prevention of HIV and TB among prisoners and prison staff, providing access to diagnosis and treatment of TB and TB/HIV for prisoners. Formerly programme manager for HIV/TB of the Stop TB in Ukraine programme of the Development of Ukraine Foundation. Main activities included revision of national legislation on TB/HIV, advocacy for access to ART for TB/HIV patients and prevention of TB among most at risk populations. Expert on TB/HIV coinfection with the TB Tuberculosis Technical Assistance Mechanism (TBTEAM).

Annex 2

LIST OF BACKGROUND DOCUMENTS

1. Country TB Profile
2. Last TB Programme Assessment Mission Report (April–May 2011)
3. National TB Control Programme for 2007–2015
4. National TB Monitoring and Evaluation Plan for 2010– 2015
5. National MDR-TB Response Plan in Armenia, 2009–2013
6. TB Epidemiological Control and Sanitary Epidemiological Regulations and Norms, 2008
7. Norms and Regulations for the Implementation of the State-funded TB Activities in Armenia, 2009 (package of documents with Appendices)
8. TB Infection Control Guidelines 2013
9. National Response Plan to Combat DR TB
10. TB Laboratory Diagnostics Training Guidelines 2013 (Armenian version is available)`
11. TBTEAM Technical Assistance to the National TB Program of Armenia in the Area of Laboratory Strengthening, mission report, February 2011 (not available yet, draft report is being finalized)
12. TB Control Programme in Prisons: International Committee of the Red Cross Hand Over – Take Over (HOTO) Report, December 2008
13. Analysis of the TB Control System in Armenia in both the Civilian and Penitentiary Sectors, September 2008 (also available as part of the HOTO report)
14. Anonymous Survey on Knowledge, Attitude and Practice towards TB among prisoners and prison staff in Armenia, 2006 (also available as part of the HOTO report)
15. TB Infection Control Consultancy Visit (TBCAP, USAID funded project, KNCV TB Foundation) by Arch. Thea Zuccotti, Nestan Tukvadze, October 2009
16. TB Infection Control Consultancy Visit (TBCAP, USAID funded project, KNCV TB Foundation) by Johannes Mulder, Nestani Tukvadze, July 2010
17. Framework for Reorganization (Optimization) of the TB Laboratory System in Armenia, 2008
18. Pay for Performance Scheme for Ambulatory TB in Armenia, 2009, by Michael Borowitz
19. Public Expenditures on Health (draft chapter October 2011)
20. Short Policy Paper on TB in Armenia, 2009, by Michael Borowitz
21. Assessment of Financial Mechanisms of TB Services within Health System in Armenia, 2009
22. National Programme on the Response to HIV Epidemic in the Republic of Armenia for 2013 – 2016, including
    a) Operational Plan of the Implementation of the National Programme in Response to HIV Epidemics
    b) Budget of the National Programme on the Response to HIV Epidemic
    c) Monitoring and Evaluation Plan of the National Programme on the Response to HIV Epidemic
23. National Guidelines on Management of TB/HIV Patients, approved by the Ministry of Health on 29 July 2010 (Google translation into English available)
24. Protocols for Organization of Voluntary HIV Testing and Counselling in Primary Health care Facilities, approved by the Ministry of Health on 22 April 2004 (Google translation into English available)
25. Voluntary HIV Testing and Counselling (National Guidelines), approved by Ministry of Health on 11 December 2002 (Google translation into English)
26. Provider Initiated Counselling and Testing in Primary Health care Facilities, approved by Ministry of Health on 22 May 2008 (Google translation into English)
27. National TB/HIV Strategic Plan, 2010–2014 (update for 2013–2015 available in Armenian)
28. National Protocol on Management of HIV and TB, 2010 (Armenian version available)

29. Manual on TB Control in Prisons, 2009 (Armenian version available)
30. Update on the current situation of the prison health system with more focus on TB programme, December 2010 (not available yet, draft report is being finalized)
31. Report on TB Laboratory Assessment, by Kiebooms Ludo, December 2009
32. Assessment of DR TB Unit Ventilation System and Proposal for Its Improvement, by MSF-F
33. Programmatic Management of Drug Resistant TB, Green Light Committee Monitoring Report, June 2012 (package of documents with appendices)
34. Programmatic Management of Drug Resistant TB, Green Light Committee Monitoring Report, May 2013 (package of documents with appendices)
35. The Global Drug Facility Mission Report 2010
36. The Global Drug Facility Mission Report 2012
37. Health Systems in Transition, Armenia Health System Review, 2013
38. Armenia Demographic and Health Survey 2010
39. Effectiveness of the "Social Assistance and Information for TB Patients" Project in c. Abovyan, Armenia: a Pilot Study, by Karine Kentenyants, October 2007
40. Predictors of time to sputum culture conversion in MDR TB patients enrolled into second-line TB treatment programme in Armenia: Analysis of dataset, Master Thesis Project by Arax Hovhannesyan, September 2010
41. New XDR TB treatment combination with Bedaquiline: Interim outcomes from the Armenian National Tuberculosis Control Program (conference abstract)
42. Draft Concept Note for Global Fund Application
43. Post-2015 WHO documents
    - Draft global strategy and targets for tuberculosis prevention, care and control after 2015, 67th World Health Assembly, Report by the Secretariat, 14 March 2014
    - Global strategy and targets for tuberculosis prevention, care and control after 2015, 67th World Health Assembly, 21 May 2014
    - Global strategy and targets for tuberculosis prevention, care and control after 2015, Post-2015 Global Tuberculosis Strategy Framework, 67th World Health Assembly, 21 May 2014

Annex 3

PROGRAMME

Time	Activity	Place	Participants
17 July			
10:30–12:00	Preparatory work by the mission members in the WHO Country Office Mission internal briefing	AUA Business Centre	A. Dadu C. Acosta A. Solovyeva N. Muzafarova A. Katsaga E. Romancenco O. Rucsineanu N. Moisieieva V. Zemlyanska
13:30–15:30	Initial briefing by the mission – round table with the Ministry of Health, NTP and other national and international partners	AUA Business Centre	Chairperson Dr Vahan Poghosyan, Deputy Minister of Health Ministry of Health, NTC, WHO, MSF-France, USAID, Global Fund, other stakeholders V. Petrosyan, translator
15:30–16:00	Meeting with Dr Vahan Poghosyan	AUA Business Centre	WHO team members H. Karapetyan, translator
16:00–18:00	Meeting with the NTC	AUA Business Centre	WHO team members H. Karapetyan, translator
18 July			
9:30–13:00	Visits to polyclinics and pharmacies in Yerevan – Polyclinic # 12 – Polyclinic #19 – Pharmacies		A. Dadu C. Acosta E. Romancenco O. Rucsineanu A. Martirosyan S. Arakelyan H. Margaryan
9:30–13:00	Visits to polyclinics and pharmacies in Yerevan – Polyclinic # 16 – Nor Aresh Polyclinic – Pharmacies		A. Yedilbayev A. Solovyeva N. Moisieieva N. Muzafarova M. Hovhannisyan A. Sahakyan
09:30–11:00	Meeting at the State Health Agency, purchaser of health services, Saro Tsaturyan, Head	State Health Agency	A. Katsaga G. Ghukasyan V. Zemlyanska
11:30–13:00	Meeting with Sergey Khachatryan – Deputy Minister of Health	Ministry of Health	A. Katsaga G. Ghukasyan V. Zemlyanska
13:45–15:45	Meeting with the Global Fund project coordination team, Dr Hasmik Harutyunyan and the team	Ministry of Health	A. Dadu C. Acosta A. Yedilbayev A. Solovyeva N. Muzafarova A. Katsaga E. Romancenco O. Rucsineanu N. Moisieieva V. Zemlyanska

Time	Activity	Place	Participants
16:15–18:00	Meeting with nongovernmental organizations (ARCS, Mission East, Real World Real People, Positive People Armenian Network, For the Sake of Children Health and others)	AUA Business Centre	O. Rucsineanu N. Moisieieva V. Zemlyanska
16:15–18:00	Meeting at MSF-France	MSF-France Office	A. Dadu A. Yedilbayev A. Solovyeva N. Muzafarova E. Romancenco
16:15–17:30	Meeting at the Scientific Centre of Drugs and Medical Technology Expertise	Drug Agency	N. Muzafarova A. Sahakyan
16:00–17:00	Meeting with Samvel Soghomonyan, Head, Human Resources Department	Ministry of Health	C. Acosta
16:00-16:45	Meeting with Armen Karapetyan, Ministry of Health, Head health financing, TB financing	Ministry of Health	A. Katsaga K. Davtyan
16:50–17:30	Meeting with Hrair Aslanyan, Head, Public Health Unit	Ministry of Health	A. Katsaga K. Davtyan
19 July			
10:00–11:00	Meeting with Deputy Minister of Justice Mr Suren Krmoyan	Ministry of Justice	A. Yedilbayev A. Solovyeva O. Rucsineanu N. Moisieieva E. Romancenco M. Hovhannisyan V. Zemlyanska
10:00–16:30	Meetings at the NTC – Programme management – Treatment – Surveillance, monitoring and evaluation – Laboratory services – Pharmacy – Continuing education/training	NTC	A. Dadu C. Acosta N. Muzafarova A. Katsaga H. Karapetyan, translator A. Yedilbayev A. Solovyeva E. Romancenco O. Rucsineanu N. Moisieieva
21 July			
09:30–17:30	Visit to the RTBD/NTC – Laboratory department – Diagnostic department – NRL – Dispensary department – Inpatient department – Central pharmacy of NTP and RTBD	RTBD/NTC, Abovian city Kotayk region	A. Dadu C. Acosta A. Yedilbayev A. Solovyeva N. Muzafarova A. Katsaga E. Romancenco O. Rucsineanu N. Moisieieva H. Margaryan
15:00–16:30	Meeting at the NCAP, Samvel Grigoryan, Director	AIDS Centre	A. Dadu N. Moisieieva G. Ghukasyan M. Hovhannisyan
16:30–17:30	Meeting at the Republican Narcological Centre	Narcological Centre	A. Dadu N. Moisieieva G. Ghukasyan V. Grichechkina
15:00–16:30	Meeting with Parunak Zelveyan, Head, National Institute of Health and Alexander Bazarjyan, Head, National Information Analytical Centre, National Institute of Health	National Institute of Health	A. Katsaga
15:00–16:30	Meeting, AUA, Centre for Health Services Research and Development, Varduhi Petrosyan, Director	AUA	C. Acosta K. Davtyan V. Zemlyanska

Time	Activity	Place	Participants
17:00–18:00	Meeting with Mikayel Narimanyan, Rector, Yerevan State Medical University	Yerevan State Medical University	C. Acosta
22 July			
08:30–18:00	Visits to TB sites in regions – Gyumri regional health department – Gyumri regional hospital TB dispensary/TB unit – Gyumri Red Cross polyclinic – Horom village rural medical ambulatory	Shirak region	A. Yedilbayev A. Solovyeva C. Acosta V. Grichechkina V. Zemlyanska A. Martirosyan
08:30–18:00	Visits to TB sites in regions – Echmiadzin polyclinic/TB clinic – Arax village rural medical ambulatory	Armavir region	A. Dadu N. Muzafarova E. Romancenco O. Rucsineanu G. Tsaturyan H. Margaryan
10:00–14:00	Visit to the Hrazdan Criminal-Executive Institution		N. Moisieieva M. Hovhannisyan
23 July			
09:30–13:00	Meeting with the with TB Coordinator of the Criminal-Executive Department of the Ministry of Justice, Dr Ara Hovhannisyan Visits to the TB wards of the Central Hospital for Detainees	Central Hospital for Detainees	A. Yedilbayev O. Rucsineanu N. Moisieieva V. Grichechkina V. Zemlyanska A. Martirosyan
09:30–12:00	Visit to the Yerevan City TB Dispensary		C. Acosta N. Muzafarova E. Romancenco A. Solovyeva K. Davtyan H. Margaryan
14:00–18:00	Visit to the Nubarashen Criminal-Executive Institution		O. Rucsineanu N. Moisieieva E. Romancenco M. Hovhannisyan
14:00–18:00	Yerevan Home Care Company (Home-based care programme for TB patients), Zaven Koloyan, Director		A. Yedilbayev A. Solovyeva V. Grichechkina V. Zemlyanska M. Hovhannisyan
14:00–17:30	Work on report/preparation for the debriefing	WHO Country Office	A. Dadu C. Acosta N. Muzafarova
17:00-18:00	Meeting with the Minister of Health	Ministry of Health	T. Hakobyan H. Kluge A. Dadu
24 July			
09:00–10:00	Work on report/preparation for the debriefing	WHO Country Office, AUA Business Centre,	WHO team members
10:00–13:00	Official debriefing of the mission – round table meeting with the Ministry of Health, NTC and other national and international partners	AUA Business Centre	Chairperson: Dr Vahan Poghosyan
14:00–15:00	Debriefing with Dr Vahan Poghosyan	WHO Country Office	WHO team members V. Grichechkina V. Zemlyanska
15:00–16:30	Debriefing with the NTC	AUA BC Business Centre, WHO Country Office	WHO team members

Annex 4

HEALTH CARE HUMAN RESOURCES DEVELOPMENT STRATEGY

E X C E R P T

FROM PROTOCOL N 5
OF THE REPUBLIC OF ARMENIA GOVERNMENT SESSION

6 February 2014

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1. ON APPROVAL OF THE HEALTHCARE HUMAN RESOURCES DEVELOPMENT STRATEGY AND THE LIST OF ACTIONS

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1. Hereby I order to approve
1) The RA Health care Human Resources Development Strategy according to Annex 1, and
2) The Action Plan of the RA Health care Human Resources Development Strategy according to Annex 2.

PRIME MINISTER OF THE REPUBLIC OF ARMENIA
TIGRAN SARGISYAN

13 February 2014
Yerevan

Annex 1
Of Protocol N 5
of the RA Government Session of February 6, 2014

STRATEGY

HEALTHCARE HUMAN RESOURCES DEVELOPMENT

CONTENT

Annex N 2
Of Protocol N 5
of the RA Government Session of February 6, 2014

LIST OF ACTIVITIES AIMED AT IMPLEMENTATION OF THE HEALTHCARE HUMAN RESOURCES DEVELOPMENT STRATEGY

Description of the activity	Responsible agency	Coordinator	Deadline	Budget
Strategic direction 1. Armenia health care human resources development strategy				
1. Analysis of the capacity of public and territorial administration bodies as regards health care human resources planning and management.	RA Ministry of Health (Ministry of Health)	RA Ministry of Territorial Administration (MTA)	2014	Sources not prohibited by the RA legislation
2. Establishment of HR Development Observatory and development and submission of recommendations on the status thereof	Ministry of Health	MTA	2015	Sources not prohibited by the RA legislation
Strategic direction 2. Improvement of human resources planning and utilization				
1. Founding a taskforce responsible for the development of Health care HRD Plan	Ministry of Health	RA Ministry of Labour and Social Affairs (MLSA)	2014	Does not require funding
2. Development and adoption of Health care HRD Plan for the coming 20 years, based on a. Current provider (doctor, nurse)/hospital bed correlation according to results of the revision of specialties b. Workload assessment at a representational health care facility using WHO methodology on Workload Indicators of Staffing Needs c. Definition of staffing needs based on findings of relevant WISN studies and the entire system staffing needs (both public and private settings)	Ministry of Health	MLSA	2014–2015	Sources not prohibited by the RA legislation
Strategic direction 3. Workplace quality: Moral and material incentives				
1. Expanding performance-based remuneration mechanisms to cover inpatient care providers	Ministry of Health		2014	Sources not prohibited by the RA legislation
2. Development and submission of recommendations on additional incentives	Ministry of Health		2014	Does not require funding
Strategic direction 4. Management of health care human resources				
1. Definition of the list of needed specialties (including their educational level and skill mix) in line with medium- and long-term health care needs of the country.	Ministry of Health	RA Ministry of Education and Science (MES)	2015	Sources not prohibited by the RA legislation
Strategic direction 5. Implementation of health care workers performance qualification system				
1. Development and submission of recommendations on definition of control-permission procedures for professional activities (medical), which will ensure simultaneous assurance of various	Ministry of Health	MLSA	2015	Does not require funding

components of continuing professional education of health care workers				
2. Development of a nominal list of medical, pharmaceutical, dental and public health specialties (basic and narrow specialties), development of job (professional positions) descriptions	Ministry of Health		2015	Sources not prohibited by the RA legislation
Strategic direction 6. Improvement of human resources management information system				
1. Revision of human resources planning indicators	Ministry of Health	-	2015	Sources not prohibited by the RA legislation
2. Development and adoption of a list of indicators for local and national situations as regards health care human resources	Ministry of Health		2015	Sources not prohibited by the RA legislation
3. Organization of trainings for capacity-building of organization/ unit responsible for health care human resources information vis-à-vis data collection, verification and analysis.	Ministry of Health	-	2015	Sources not prohibited by the RA legislation
Strategic direction 7. Increasing the role of professional associations				
1. Submission of recommendations and organization of discussions on defining the role and functions of professional associations as regards health care human resources planning, development and management.	Ministry of Health		2014	Does not require funding

Annex
Of Decree 696-A
of the RA Minister of Health
issued 4 April 2014

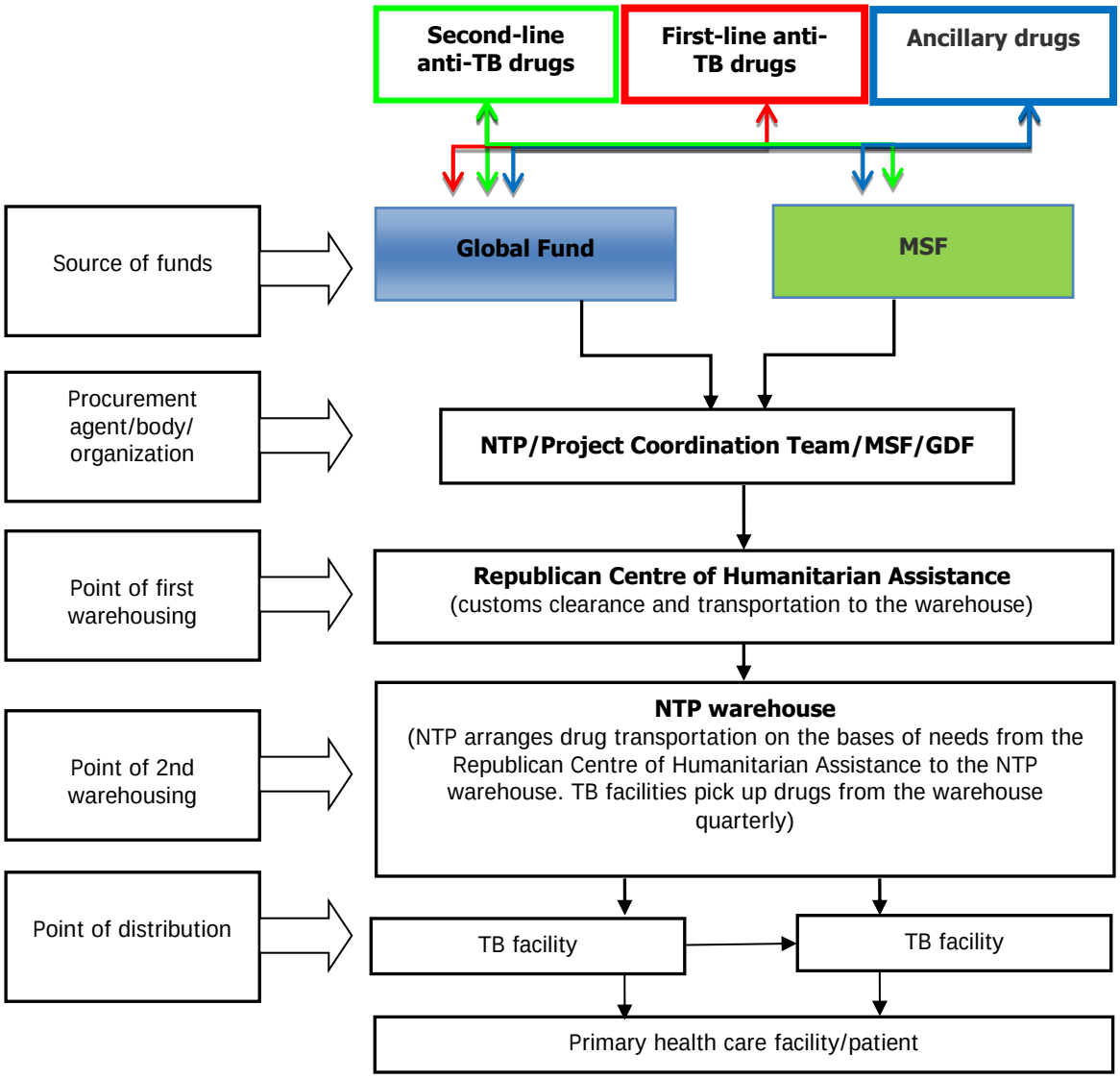
LIST OF AGENCIES RESPONSIBLE FOR IMPLEMENTATION OF THE HEALTHCARE HUMAN RESOURCES DEVELOPMENT STRATEGY AND THE ACTIONS PROVIDED FOR BY THE STRATEGY

No.	Description of the activity	Deadline	Responsible agency	Deputy Minister of Health in charge of coordination of the specific area
1.	Analysis of the capacity of public and territorial administration bodies as regards health care human resources planning and management.	2014	National Institute of Health of the Ministry of Health Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan
2.	Establishment of HR Development Observatory and development and submission of recommendations on the status thereof	2015	National Institute of Health Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan
3.	Founding a taskforce responsible for the development of Health care Human Resources Development Plan	2014	Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan
4.	Development and adoption of Health care Human Resources Development Plan for the following 20 years, based on a) current provider (doctor, nurse)/ hospital bed correlation according to results of the revision of specialties b) Workload assessment at a representational health care facility using WHO methodology on Workload Indicators of Staffing Needs c) Definition of staffing needs based on findings of relevant WISN studies and the entire system staffing needs (both public and private settings)	2014–2015	National Institute of Health Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan
5.	Expanding performance-based remuneration mechanisms to cover inpatient care providers	2014	State Health Agency	T. Sahakyan
6.	Development and submission of recommendations on additional incentives	2014	State Health Agency	T. Sahakyan

7.	Definition of the list of needed specialties (including their educational level and skill mix) in line with medium- and long-term health care needs of the country.	2015	Human resources Management Department of Ministry of Health Staff	T. Sahakyan
8.	Development and submission of recommendations on definition of control-permission procedures for professional activities (medical), which will ensure simultaneous ensuring of various components of continuing professional education of health care workers.	2015	Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan
9.	Development of nominal list of medical, pharmaceutical, dental and public health specialties (basic and narrow specialties), preparation of job (professional positions) descriptions.	2015	Human resources Management Department of Ministry of Health Staff	T. Sahakyan
10.	Revision of human resources planning indicators	2015	National Institute of Health Human resources Management Department of Ministry of Health Staff	T. Sahakyan
11.	Development and adoption of a list of indicators for local and national situations as regards health care human resources	2015	National Institute of Health Human resources Management Department of Ministry of Health Staff	T. Sahakyan
12.	Organization of trainings for capacity-building of organization/unit responsible for health care human resources information vis-à-vis data collection, verification and analysis.	2015	National Institute of Health Public Health Division of Ministry of Health Staff	T. Sahakyan
13.	Submission of recommendations and organization of discussions on defining the role and functions of professional associations as regards health care human resources planning, development and management.	2014	Human resources Management Department of Ministry of Health Staff Public Health Division of Ministry of Health Staff	T. Sahakyan

Annex 5

MAP OF ANTI-TB MEDICINES SUPPLY SYSTEM IN ARMENIA



Annex 6

LIST OF ANTI-TB DRUGS REGISTERED IN ARMENIA (AUGUST 2014)

	Medicine recommended by NTP guideline	Product description	GDF eligible manufacturer	Description of product registered in the country	Manufacturer
First-line drugs					
1.	Isoniazid (30 mg) + Rifampicin (60 mg)	H30R60	Macleods Pharmaceuticals Ltd	None registered	None registered
2.	Isoniazid (30 mg) + Rifampicin (60 mg) + Pyrazinamide (150 mg)	H30R60 Z150	Macleods Pharmaceuticals Ltd	None registered	None registered
3.	Isoniazid (60 mg) + Rifampicin (60 mg)	H60 R60	Macleods Pharmaceuticals Ltd	None registered	None registered
4.	Isoniazid (75 mg) + Rifampicin (150 mg)	H75 R150	LUPIN LTD	Iso-Eremfat 150/ 300 (H150R300)	Fatol, Riemser Arzeimittel AG
5.	Isoniazid (150 mg) + Rifampicin (150 mg)	H150 R150	Macleods Pharmaceuticals Ltd	None registered	None registered
6.	Isoniazid (75 mg) + Rifampicin (150 mg) + Pyrazinamide (400 mg) + Ethambutol (275 mg)	HRZE75/ 150/400/275	LUPIN Ltd	None registered	None registered
7.	Ethambutol (400 mg)	E400	Cadila Pharmaceuticals Ltd	EMB-Fatol 400	Fatol, Riemser Arzneimittel AG
8.	Isoniazid (100 mg)	H100	Macleods Pharmaceuticals Ltd	None registered	None registered
9.	Isoniazid (300 mg)	H300	Macleods Pharmaceuticals Ltd	Isoniazid 300 combined with B6	Fatol, Riemser Arzneimittel AG
10.	Pyrazinamide (400 mg)	Z400	Macleods Pharmaceuticals Ltd	Pyrafat 500	Fatol, Riemser Arzneimittel AG
11.	Rifampicin (150 mg)	R150	Sanofi-Aventis	Rifampicin 150	Belmedpreparaty, Minsk
12.	Rifampicin (300 mg)	R300	Medochemie Ltd	Rifampicin 300	Antibiotiche, Romania
				Eremfat 300	Fatol, Riemser Arzneimittel AG
13.	Streptomycin (1 g)	S1	Laboratirio REIG JOFRE, SA Spain	Streptomycin 1000	Kievmedpreparati, Ukraine
Second-line drugs					
14.	Amoxicillin (875 mg) + Clavulanic acid (125 mg)		Medochemie Ltd	Panklav 875/125	Xenofarm
				Augmentin 875/125	Bichem group
				Kamox Clav 875/125	Flamingo, India
				Amoxiklav 875/125	Lek, Slovenia
				Amoxiklav - Denk 875/125	Denk Pharm, Germany
				Clavomed 875/125	World Medicine
				Rapiclav 875/125	Ipca Laboratories, India
				Flemoclav 875/125	Astellas
15.	Levofloxacin (250 mg)		Macleods Pharmaceuticals Ltd	Levoflacin 500 - Asteria	Hongong, Korea, Pharmaceutical Co.
				Zolev - 250	EfDiSi
				Levo-Denk 250	Denk Pharma, Germany
				Hileflox 250	HiGlans, India
				Tavanic 250	Sanofi, France

	Medicine recommended by NTP guideline	Product description	GDF eligible manufacturer	Description of product registered in the country	Manufacturer
				LeVITRONN 250	Insepta Pharmaceuticals
16.	Kanamicin (1 g)		Panpharma	Kanamycin 1000	Kievmedpreparati, Ukraine
17.	Capastat/capreomycin (1 g)		Acorn Inc.	None registered	None registered
18.	Clofazimine (100 mg)		Novartis Pharma	None registered	None registered
19.	Moxifloxacin (400 mg)		Bayer Pharma AG	Moxin 400 Avelox 400	GM Pharmaceuticals Bayer, Shering
20.	Paser (4 g)		Jacobus Pharmaceuticals Co.	None registered	None registered
21.	Prothionamide (250 mg)		Fatol, Riemser Arzneimittel AG	None registered	None registered
22.	Cycloserin (250 mg)		Macleods Pharmaceuticals Ltd	Cycloserin 250	Biocome, Russian Federation

Annex 7

ADVERSE DRUG REACTION/SERIOUS ADVERSE EVENT FORM

Armenia

TMC207 CU PROGRAM
(Program ID: TMC207TBC3002)

ADVERSE DRUG REACTION/SERIOUS ADVERSE EVENT FORM

PLEASE COMPLETE ALL PAGES AND FAX WITHIN 24 HOURS OF BECOMING AWARE OF A SERIOUS ADVERSE EVENT OR ADVERSE DRUG REACTION TO:
SAFETY UNIT Fax: + 7 495 580 91 75
Email: DrugSafetyRU@its.jnj.com

EVENT: CHECK ALL THAT APPLY

☐ SERIOUS ADVERSE EVENT ☐ NON-SERIOUS ADVERSE DRUG REACTION

No of PAGES: ☐ INITIAL REPORT x☐ FOLLOW-UP REPORT

PHYSICIAN INFORMATION

Patient Date of Birth: d d M O N y y y y

Country where ADR/SAE occurred: Armenia .....

Date of Report: 2 0 d d M O N y y

Date reporter became aware of ADR/SAE: d d M O N y y

Treatment with TMC207
Describe why the patient is receiving or received TMC207 (indication):

Participating Physician's Name: .....

Physician's Address:
.....

Telephone: ..... *(country code)* Fax: ..... *(country code)*

ADR/SAE DESCRIPTION

FOR CONCOMITANT THERAPY, MEDICAL HISTORY, AND RELEVANT LAB RESULTS PLEASE COMPLETE PAGE 4 OF THIS ADR/SAE REPORT AND/OR ATTACH RELEVANT RECORDS.
Please remove any patient identifiers from any submitted reports or records.

Indicate pages that are attached: ☐ Relevant Labs
☐ Other, specify: .....

Reporter's Narrative (Describe the course of events, timing and suspected causes):
.....
.....
.....
.....
.....
.....

FOR COMPANY USE ONLY

Date ADR/SAE report received: d d M O N y y

GMS Reference Number: .....

PV Contact Person who received this report: .....
(please print name clearly)
Contact's Telephone Number, please include country code: .....

Additional information requested? ☐ No ☐ Yes, please specify
.....

TMC207 CU PROGRAM
(Program ID: TMC207TBC3002)
NON-SERIOUS ADVERSE DRUG REACTION/SERIOUS ADVERSE EVENT FORM (continued)

☐ Initial Report ☐ Follow-up Report

Patient	Sex: ☐ Male ☐ Female	Height: [ ][ ][ ] ☐ cm ☐ in	Weight: [ ][ ][ ] ☐ kg ☐ lb	Date of Birth: d d M O N y y y y
AE Diagnosis	ADR/SAE (If diagnosis unknown, list symptoms) ……… ……… ………	ADR/SAE (If diagnosis unknown, list symptoms) ……… ……… ………	ADR/SAE (If diagnosis unknown, list symptoms) ……… ……… ………	
Onset	d d M O N y y	d d M O N y y	d d M O N y y	
Severity	☐ Mild ☐ Moderate ☐ Severe	☐ Mild ☐ Moderate ☐ Severe	☐ Mild ☐ Moderate ☐ Severe	
NCI toxicty	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5	
ADR/SAE Seriousness Category	☐ Serious AE/ADR please specify category ☐ Non-Serious ADR ☐ Death[1] ☐ Hospitalization required[2] ☐ Prolonged hospitalization ☐ Life threatening ☐ Persistent/significant disability ☐ Congenital anomaly/birth defect ☐ Other medically important condition	☐ Serious AE/ADR please specify category ☐ Non-Serious ADR ☐ Death[1] ☐ Hospitalization required[2] ☐ Prolonged hospitalization ☐ Life threatening ☐ Persistent/significant disability ☐ Congenital anomaly/birth defect ☐ Other medically important condition	☐ Serious AE/ADR please specify category ☐ Non-Serious ADR ☐ Death[1] ☐ Hospitalization required[2] ☐ Prolonged hospitalization ☐ Life threatening ☐ Persistent/significant disability ☐ Congenital anomaly/birth defect ☐ Other medically important condition	
Relation to TMC207	**ONLY APPLICABLE FOR SERIOUS AE's/ADR's** ☐ Not Related ☐ Possible ☐ Doubtful ☐ Probable ☐ Very likely	**ONLY APPLICABLE FOR SERIOUS AE's/ADR's** ☐ Not Related ☐ Possible ☐ Doubtful ☐ Probable ☐ Very likely	**ONLY APPLICABLE FOR SERIOUS AE's/ADR's** ☐ Not Related ☐ Possible ☐ Doubtful ☐ Probable ☐ Very likely	
Outcome	☐ Recovered/ resolved ☐ Recovered/resolved with sequelae Recovery date d d M O N y y ☐ Fatal[1] ☐ Recovering/resolving ☐ Unknown ☐ Not recovering/ not resolved	☐ Recovered/ resolved ☐ Recovered/resolved with sequelae Recovery date d d M O N y y ☐ Fatal[1] ☐ Recovering/resolving ☐ Unknown ☐ Not recovering/ not resolved	☐ Recovered/ resolved ☐ Recovered/resolved with sequelae Recovery date d d M O N y y ☐ Fatal[1] ☐ Recovering/resolving ☐ Unknown ☐ Not recovering/ not resolved	

[1] Record further death information on the following page in the 'SAE General' section.
[2] Record hospital admission date on the following page in the 'SAE General' section.

TMC207 CU PROGRAM
(Program ID: TMC207TBC3002)

NON-SERIOUS ADVERSE DRUG REACTION/SERIOUS ADVERSE EVENT FORM (continued)

☐ Initial Report ☐ Follow-up Report

Patient Date of Birth: | | | | | | | | | |

SAE General

Date of Death | | | | | | | | (d d M O N y y)

Primary cause of death (if known): .....

Was autopsy performed? ☐ No ☐ Yes (If yes, attach copy of report if available)

Hospital Admission Date | | | | | | | | (d d M O N y y)

Hospital Discharge Date | | | | | | | | (d d M O N y y)

DOSING OF TMC207

Start Date | | | | | | | | (d d M O N y y)

Stop Date | | | | | | | | (d d M O N y y)

Action taken re TMC207
☐ None
☐ Dose adjusted
☐ Temporary stop
☐ Permanent stop

TMC207	Batch/Lot No.	Dose	Unit	Frequency	Route
	.....	.....	.....	.....	.....

REPORTING

Reporter's Statement

Note: Please ensure Page 4 is completed prior to signing

I have verified the data on this ADR/SAE report and have determined they are accurate and compatible with clinical notes.

Reporter's Name: ..... *(Please print)*

Signature (required): .....

Date: | | | | | | | | (d d M O N y y)

CONTINUE ON THE NEXT PAGE

TMC207 CU PROGRAM
(Program ID: TMC207TBC3002)

ADVERSE DRUG REACTION/SERIOUS ADVERSE EVENT FORM (continued)

☐ Initial Report ☐ Follow-up Report		Patient Date of Birth:

MEDICAL HISTORY

Briefly describe disease and concurrent illness:

CONCOMITANT MEDICATIONS

Relevant Concomitant medications (include medications taken within 2 weeks prior to the first event):

Drug	Dose	Frequency	Route	Start Date	End Date	Indication

LAB DATA

Test	Unit	Ref Range	Date	Result