MISSION REPORT

Report of the joint ECDC and WHO review of the national tuberculosis programme in Bulgaria

2–9 June 2014

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This joint report of the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO) was coordinated by Marieke J. van der Werf.

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Abbreviations

Am	Amikacin
BCG	Bacillus Calmette-Guérin
BDA	Bulgarian Drug Agency
Cm	Capreomycin
Cs	Cycloserine
CSO	Civil society organisation
DOT	Directly observed treatment
DST	Drug susceptibility testing
E	Ethambutol
EQA	External Quality Assessment
FLD	First line drug
FFP	Filtering face pieces
GDF	Global Drug Facility
GF	Global Fund
H	Isoniazid
HIV	Human Immunodeficiency Virus
IC	Infection Control
Km	Kanamycin
Lfx	Levofloxacin
LPA	Line Probe Assay
LTBI	Latent TB infection
Lzd	Linezolid
MDR TB	Multidrug-resistant tuberculosis
Mfx	Moxifloxacin
NGO	Non-governmental organization
NRL	National Reference Laboratory
NTP	National Programme for Prevention and Control of Tuberculosis
Ofl	Ofloxacin
PAS	Para-Aminosalicylate Sodium
PMU	Project management unit
Pto	Protionamide
R	Rifampicin
RHI	Regional Health Inspectorate
RRL	Regional Reference Laboratory
S	Streptomycin
SLD	Second line drug
SM	Smear microscopy
SRL	Supra national reference laboratory
TB	Tuberculosis
TLD	Third line drug
TST	Tuberculin skin test
WHO	World Health Organization
XDR	Extensively drug-resistant
Z	Pyrazinamide

Executive summary

The Minister of Health of Bulgaria, Dr Tanya Andreeva, invited the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization Regional Office for Europe (WHO Regional Office) to jointly conduct a review of the Bulgarian National Tuberculosis Control Programme. The terms of reference of the review were discussed and agreed upon by the Department of 'Specialized Donor-funded Programmes' and ECDC. From 2 to 9 June 2014, a team of nine experts visited Bulgaria to perform the review. The programme of the review included visits to national institutions involved in tuberculosis (TB) prevention and control, primary healthcare facilities, regional hospitals including laboratories, the hospital for treatment of multidrug-resistant TB, a prison hospital, regional health inspectorates, and non-governmental organisations. The team was supported by national experts.

Tuberculosis epidemiology

Bulgaria is one of the 18 TB high priority countries in the WHO European Region and one of the six countries in the European Union reporting more than 20 TB cases per 100 000 population. In 2013, 1 932 tuberculosis (TB) cases were notified in Bulgaria, i.e. 27 per 100 000 population. Since 2006, the number of TB cases and the TB notification rate have been declining.

A national drug resistance survey conducted in 2010 showed that multidrug-resistant TB (MDR TB) was detected in 2.1% of new TB cases and 11.1% of previously treated TB cases. In 2013, 27 MDR TB cases were identified through the national TB register, this is less than expected.

Of all TB cases notified in 2012, 86% were treated successfully. Of the MDR TB cases notified in 2011, 67% were treated successfully.

National Tuberculosis Programme

For the period 2012–2015, the National Programme for Prevention and Control of Tuberculosis (NTP) in the Republic of Bulgaria has as its main objective reducing the transmission of tuberculosis and the emergence and development of drug resistance. The plan is implemented through nine operational objectives:

- ensuring effective management and coordination of the NTP
- timely diagnosis and control of tuberculosis
- successful treatment of tuberculosis in Bulgaria
- successful treatment and control of multi-resistant and extensively-resistant tuberculosis
- control of child tuberculosis
- reduction of the transmission of tuberculosis in Bulgarian prisons
- restriction of the spread of tuberculosis in the Roma community and in groups at risk
- diagnosis and treatment of persons with latent tuberculosis infection
- raising public awareness.

Key observations and recommendations

The team focused on seven objectives for the review of the National TB Programme of Bulgaria. For each objective key observations and recommendations are provided below.

A general observation is that the Bulgarian TB prevention and control programme contains a number of essential components that are dependent on Global Fund (GF) funding for implementation:

- management of the National TB Programme
- drugs for MDR TB treatment
- incentives for patronage nurses for field work
- support for transport and food coupons for TB patients
- laboratory activities necessary for MDR TB
- non-governmental organisations (NGOs) activities on screening.

Since the Global Fund funding is temporary, the sustainability of the implementation of the components mentioned above is not guaranteed. Discontinuation of the implementation of these components will seriously jeopardise the success of TB prevention and control in Bulgaria. Continuous successful implementation of TB prevention and control needs the inclusion of funding of the above components in the national budget for TB prevention and control.

Objective 1: Assessment of the current performance and sustainability of the Programme and development of recommendations for future activities

- The TB programme has a good structure and effective management of the programme. It has national coverage and in 2013 the main programme outcome indicators were reached.
- The government of Bulgaria shows commitment to TB prevention and control through funding of TB activities in the State budget. However, specific essential activities of the TB programme are highly dependent on GF funding.
- Not all TB prevention and control activities have a strategy or a standardised approach, or if available they are not universally implemented. Strategies should be developed for all relevant TB prevention and control activities and these strategies should be implemented.
- There is poor practice in the follow up of patients receiving Isoniazid (H) preventive treatment. Patients are exposed to repeat tuberculin skin tests and chest X-rays at three and six months after the start of preventive treatment. This practice is not supported by current evidence. The use of tuberculin skin testing and chest X-ray to monitor response to preventive treatment should be abandoned
- Patients receiving treatment for TB or MDR TB are hospitalised for extensive periods of time during the intensive phase of treatment. There is no evidence that supports long hospitalisation. Therefore, it is recommended to develop ambulatory care from the start of treatment by involving general practitioners, patronage nurses, and NGOs in a coordinated manner, for patients who so wish and are in a position to adhere to daily observed treatment.
- There are difficulties in providing early and active case-finding, adequate support to ensure adherence to treatment, and follow-up among Roma and other vulnerable population groups. It is suggested to increase activities among vulnerable groups, through a coordinated approach involving community/social workers and NGOs, and through a proper diagnostic algorithm based on analysis of the epidemiology, behaviour, and feasibility for each risk group.
- Children are vaccinated with Bacillus Calmette-Guérin (BCG) at birth. The vaccine scar is checked when children are aged 7 months, 7 years, 11 years and 17 years. If there is no scar and if the Tuberculin skin test (TST) result is negative, children are re-vaccinated with BCG. This schedule is not supported by the scientific evidence. The schedule should be changed at the national level, avoiding unnecessary toxicities and saving human and economic resources

Objective 2: Assessment of the TB surveillance system and analysis of the epidemiological data

- The TB surveillance system is adequate and provides information that can be used for monitoring and evaluation, and policy development.
- The surveillance system is paper and digital-based for the collection, storage and analysis of data with consequential high workload and risk of error. To improve surveillance data collection, a patient web-based surveillance system should be developed. This will also facilitate the exchange of information between hospitals, National Reference Laboratory (NRL), Regional Health Inspectorate, prisons, and national level, etc.
- Annually the national TB surveillance report is published on the TB control website. However, there is no in-depth analysis of surveillance data, and the surveillance outcomes seem to be insufficiently used at the local and national level. To fully use the potential of surveillance it is recommended to perform in-depth analysis of data at the national level using appropriate software and to use the information for action.
- The surveillance system does not collect information on risk factors. Therefore, it is not possible to identify the population groups most at risk for TB. To support TB prevention and control in the future, the surveillance system should include relevant risk factors to be able to identify the populations most at risk.

Objective 3: Assessment of the implementation of the National MDR/extensively drug-resistant (XDR)-TB plan in Bulgaria and assessment of achieved results and obstacles

- Most MDR TB cases are detected and all cases that need treatment can be treated. For MDR TB management, international guidelines are closely followed with the assistance of the MDR TB treatment commission. The second line TB drugs are provided by the GF and are available in adequate quantities and variety. These favourable conditions result in good MDR TB treatment outcomes. To ensure adequate MDR TB treatment in the future, the Ministry of Health budget must include budget lines for MDR TB drugs and laboratory expenses necessary for testing and treating all MDR TB patients in Bulgaria.

- All MDR TB patients are hospitalised in the M/XDR TB hospital in Gabrovo during the intensive phase of treatment. There are no opportunities to receive intensive phase MDR TB treatment in an ambulatory setting. Many patients may have social and personal problems that make hospitalisation during the intensive phase of treatment beneficial, also with respect to training their skills of adherence. However, for patients, hospitalisation is often difficult in view of their family and economy situation, and means a substantial amount of opportunity costs. It is therefore desirable to aim at discharging the patient for ambulatory care as soon as this is feasible for the individual patient. Therefore, it is recommended to develop ambulatory care from the start of treatment, by involving general practitioners, patronage nurses, and NGOs in a coordinated manner.
- Long delays before establishing that a patient is an MDR TB case were observed, even among retreatment TB cases. To ensure quick diagnosis of MDR TB, rapid diagnosis for all TB patients with a high risk of MDR TB should be implemented and the tests should be free.

Objective 4: Assessment of the anti-TB drug supply management

- Quantification and procurement of quality first line drugs needs is done properly by the NTP. First line TB drugs are distributed through a pull system with sufficient buffer stock at peripheral level. Quantification of second line drug needs was done inadequately and resulted in excessive stocks of MDR TB drugs. The Ministry of Health should place a second line drugs order so that there are two shipments per year for all second line drugs (and paediatric drugs if adopted) to prevent excessive stocks.
- Bulgaria does not have fixed dose combinations for TB drugs available for adults or children. Also, the strength of the first line drugs are not according to the strengths recommended by WHO. For drugs not registered in Bulgaria there is a possibility to obtain a waiver of registration (regulation 10). A waiver of registration was obtained for second line TB drugs, third line TB drugs, and streptomycin. The Ministry of Health and the National Council on Prices and Reimbursement of Medicinal Products should register adult and children Fixed Dose Combinations, GeneXpert equipment and cartridges.
- A pharmaco-vigilance system is in place but not used for TB. The NTP should promote the use of the pharmaco-vigilance system for TB drugs.
- The paediatric regimen is not in line with WHO rapid advice guidelines because of the use of streptomycin, lower dosage of several drugs, and lack of paediatric formulation. The TB Expert Group and National Consultant should consider updating the guidelines for adult TB treatment to include fixed dose combinations in accordance with the recent WHO guidelines, and for paediatric TB treatment to make them in line with WHO guidelines.

Objective 5: Assessment of the microbiological diagnostics of TB and MDR TB in the country and operation of the laboratory network

- The TB laboratory network is established, a quality assurance system is in place and training on infection control and laboratory techniques are regularly organised by the NRL and the hospitals. Infection control plans and standard operating procedures are available, personal protective equipment is used and recent certificates of equipment maintenance were presented.
- In 2013, first line drug susceptibility testing was only performed on 78% of the new TB pulmonary cases with positive culture and 82% of the retreatment cases with positive culture. Drug susceptibility testing should be performed for all culture-positive TB cases.
- Rapid molecular tests to detect antibiotic resistance are mainly used for confirmation of MDR TB after obtaining drug susceptibility testing results. These tests are rarely performed directly for suspected MDR TB cases. The algorithm for use of rapid molecular tests developed by the NRL (also in the Regional Reference Laboratories) should be implemented and sputum of all MDR TB suspects should be analysed with GeneXpert.
- The laboratory part of the TB surveillance system is underused and not designed to extract data and make reports. The system should be adapted for use by the NRL and it should be adapted to improve its usefulness for the laboratory.
- There is a high turnover of laboratory staff. Several heads of TB laboratories reported that this is due to low salary levels. To ensure adequate staffing of TB laboratories a human resources strategy for the TB laboratories should be developed.

Objective 6: Assessment of current engagement with non-governmental organizations (NGOs) and patient groups, and of the extent to which their potential contribution to the detection, treatment and care of individuals with TB is maximised

- The NTP operates an innovative way of engaging local NGOs, extending the ability of the NTP to undertake screening and case finding within risk group populations. There is an exceptionally close relationship between health services and NGOs not seen in other countries, leading to a significant increase in screening and contact tracing. It was reported that NGOs are especially helpful to healthcare services in facilitating access to hard-to-reach groups.

- The current structure of NGOs and patronage nurses linked to Regional Health Inspectorates and TB hospitals should continue. To ensure future sustainability of this structure, it is recommended that the contractual and work position of patronage nurses be reviewed. Their hospital workload should be such that time outside the hospital is possible as a regular part of their activity. Furthermore, national processes need to be developed that will allow continuation of NGO involvement in TB control.
- NGOs have some informal interaction between themselves but it is patchy and not organised. As a result, their ability to share learning amongst themselves, to interact with the NTP, and to engage in any broader advocacy, is limited. NGOs engaged in TB activities should look to improve these three areas for example by improving networking among themselves. The NTP could welcome and encourage this. Encouragement should also be given to the development of TB patient group(s) and their use in advocacy and awareness activities.
- Health promotion organised by the Regional Health Inspectorates is regular but limited and does not focus enough on key and vulnerable populations. The Ministry of Health should encourage an approach involving NGOs and other health service stakeholders that emphasises TB within the Regional Health Inspectorate health education programme and encourages a more practical focus on key populations in each region.

Introduction

The European Centre for Disease Prevention and Control (ECDC) and the World Health Organization Regional Office for Europe (WHO Regional Office) regularly collaborate on tuberculosis (TB) surveillance, prevention and control in the European Union. Following a request from the Ministry of Health of the Republic of Bulgaria, dated 20 February 2014, ECDC and WHO Regional Office conducted a joint country visit – in collaboration with the Bulgarian national counterparts – from 2-9 June 2014. The visit followed agreed terms of reference (Annex 1).

The aim of the review was to assess the Programme's contribution to TB prevention and control in Bulgaria, to identify the gaps in the implementation of the present Programme and to make recommendations for needed improvements in the Programme's implementation as well as for future strategic planning of TB prevention and control activities.

The objectives of the review of the National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria, 2012–2015 (NTP) were:

- assessment of the current performance and sustainability of the Programme and development of recommendations for future activities
- assessment of the TB surveillance system and analysis of the epidemiological data
- assessment of the implementation of the National MDR/XDR-TB plan in Bulgaria and assessment of achieved results and obstacles
- assessment of the anti-TB drug supply management
- assessment of the microbiological diagnostics of TB and MDR TB in the country and the operation of the laboratory network
- assessment of current engagement with civil society organisations (CSOs) and patient groups, and of the extent to which their potential contribution to the detection, treatment and care of individuals with TB is maximised
- present specific recommendations regarding the actions and priorities for the next stage of the National TB Programme and National Health Strategy for the period 2014–2020.

The evaluation team used qualitative and quantitative methods for collection of information, including an analysis of TB surveillance data. Before the field visit, the team members studied documents made available to them by the national counterparts and relevant documents obtained from the public domain. During the review in Bulgaria the team of experts conducted visits and had meetings and one-on-one interviews with relevant stakeholders at the national and local level (Annex 2: Programme for the Bulgaria National TB Programme Evaluation and Annex 3: People and organisations contacted and met). The collected evidence was discussed within the evaluation team and observations and recommendations were agreed upon. On 9 July 2014 the team debriefed the deputy minister Professor Chavdar Slavov and the national technical experts and experts of the department of 'Specialized Donor-funded Programmes' of the Ministry of Health.

Background information

Bulgaria is situated in southeast Europe in the eastern part of the Balkan Peninsula. The country has borders with Romania to the north, Serbia and the former Yugoslav Republic of Macedonia to the west and Greece and Turkey to the south. To the east the Black Sea is a natural border. Bulgaria covers an area of approximately 111 000 square kilometres. The country is divided into 28 districts, while six regions were also created by the 2008 Law of Regional Development (North-western, North-central, North-eastern, South-western, South-central South-eastern).

Bulgaria is a parliamentary democracy with a multi-party system and free elections. The constitution introduced and enforces the principle of the separation of powers divided between the legislative, executive and judiciary branches of government.

Bulgaria has a population of 7 284 552 [1], with 49% of the population male. The ethnic background of the population is Bulgarian 76.9%, Turkish 8%, Roma 4.4%, other 0.7% (including Russian, Armenian, and Vlach), other (unknown) 10%. In the last 25 years, demographic development has been characterised by population decline, a low crude birth rate, a low fertility rate, a high mortality rate and an ageing population. The most important causes for the population decline are the negative net international migration and negative population growth. Life expectancy at birth was 70.9 years for males and 77.9 for female in 2012 (Eurostat). The crude birth rate per 1 000 inhabitants decreased from 10.4 in 2008 to 9.5 in 2012.

The main causes of death are diseases of the circulatory system (592 death per 100 000, 2011) and neoplasms (156 deaths per 100 000, 2011) [2].

Public health services, including TB treatment, are funded by the Ministry of Health [3]. The Ministry of Health is also responsible for planning and ensuring human resources for the health system, the development of medical science, and collecting and maintaining data on the health status of the population and the national health accounts. Each region has Regional Health Inspections (RHI). The RHI's tasks include the collection, registration, handling, storage, analysis and provision of health information; overseeing the registration and quality of healthcare providers; implementing information technology in health; organising action plans for natural disasters and accidents; coordinating activities regarding the implementation of national and regional health programmes; and conducting research into the demand for human resources in healthcare.

Tuberculosis epidemiology

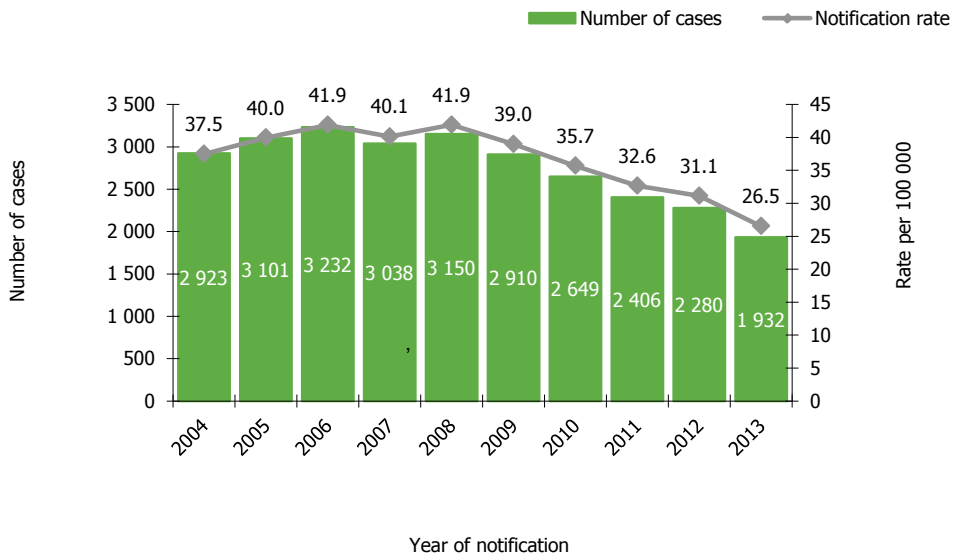
The data on tuberculosis presented below were provided by the National Centre for Public Health and Analysis in Bulgaria or extracted from the ECDC European Surveillance System TB database (as of 1st July 2014). All data presented, except when specified, are based on information collected through the National TB Register in Bulgaria.

Number of cases and notification rate

In 2013, the total number of TB cases notified in Bulgaria was 1 932 (26.5 per 100 000 population). In the last five years, the TB notification rate has steadily declined, by 7.2% on average between 2008 and 2012 and by 14.8% between 2012 and 2013 (Figure 1). This sharp decrease in 2013 should be interpreted with caution as, according to the Bulgarian TB team, it may reflect in part a change in case detection methods compared with the previous year. If the average annual decline of 7.2% observed between 2008 and 2012 had continued in 2013, the TB rate would have been 28.9 per 100 000 population and Bulgaria would be a TB low incidence country (notification rate <20/100 000 population) by 2018 according to the ECDC definition.

In the latest Global TB report (2013), WHO has provided estimates of the TB incidence of 32 per 100 000 population (uncertainty range 28–36) in 2012 and of the TB prevalence of 43 per 100 000 (uncertainty range 17–80).

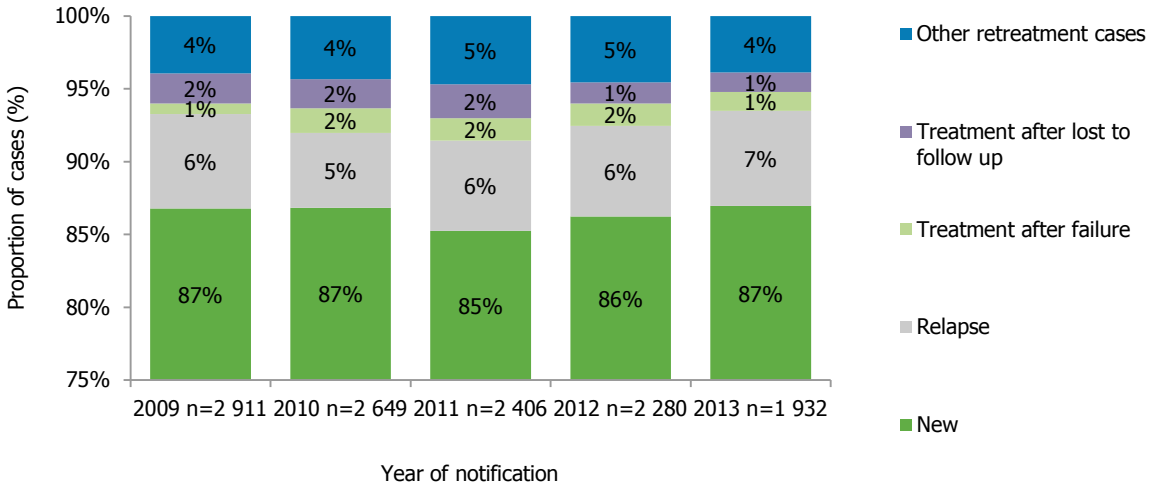
Figure 1. Number of tuberculosis cases (all cases) and notification rate, Bulgaria, 2004–2013



Sources: ECDC-Tessy for TB cases, Population figures extracted from Eurostat, 27 June 2014

In 2013, new TB cases were 1 680 (87%), relapses 126 (7%), treatment after failure 25 (1%), treatment after the case was lost to follow up 26 (1%) and other retreatment cases were 75 (4%). This distribution was close to that of previous years (Figure 2).

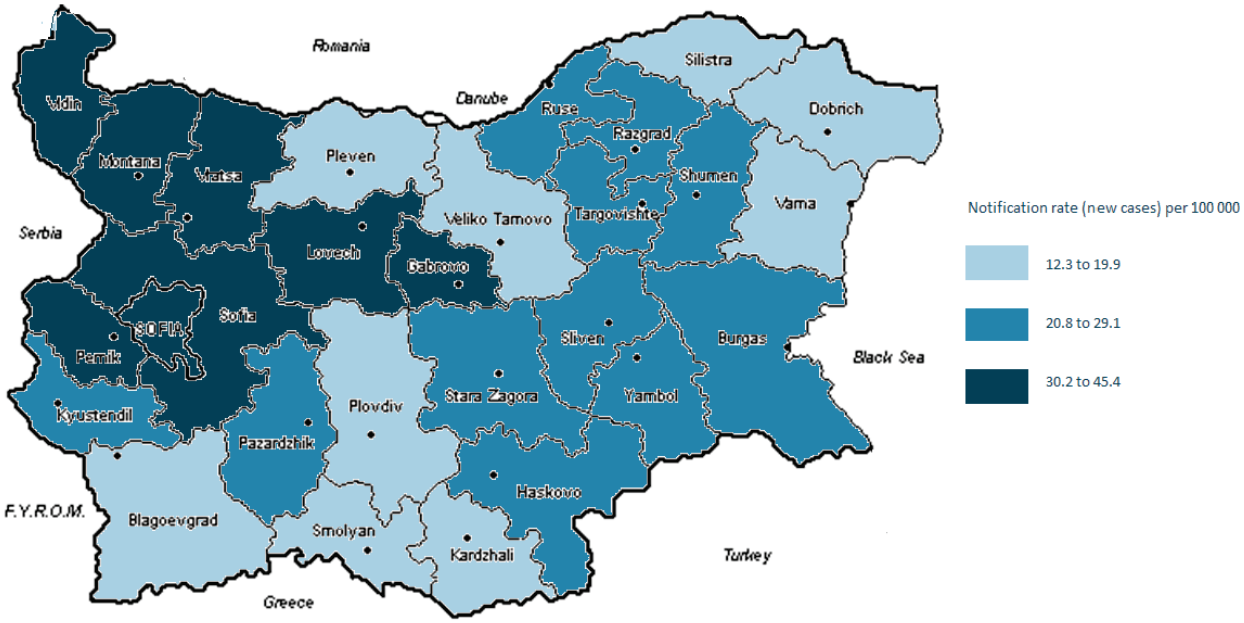
Figure 2. Distribution (%) of tuberculosis cases (all cases) by category, Bulgaria, 2009–2013



Source: ECDC

Notification rates differ by region. In 2013, the TB notification rate of new cases was below 20 per 100 000 in nine of the 28 regions, 20 to 29.1 per 100 000 in 12 regions and over 30 (up to 45.4) in seven regions. These seven are situated in the north west of the country (Map 1). In the last three years (2011 to 2013), the TB notification rate (new cases) has declined or remained relatively stable in 15 of the regions with a rate of 20 or more per 100 000, but has increased by more than 5% on average in four regions (Yambol + 6%, Haskovo + 13%, Stara Zagora and Sofia region + 14%).

Map 1. Tuberculosis notification rate (new cases) by region, Bulgaria, 2013



Sources: Bulgaria, National Centre for Public Health and Analysis, National TB Register

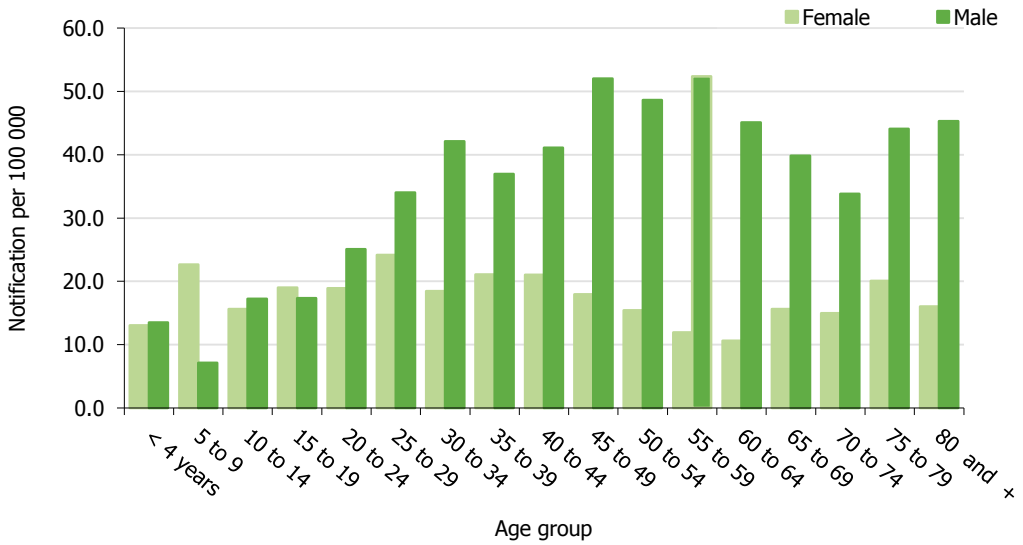
Age, gender and place of birth

In 2013, sixty six percent of TB cases were in males and 34% in females (Figure 3).

Seven percent of TB cases were notified in children below the age of 15 years. Eight percent were aged 15 to 24 years, 66% were aged 25 to 54 years and 19% were 65 years or over.

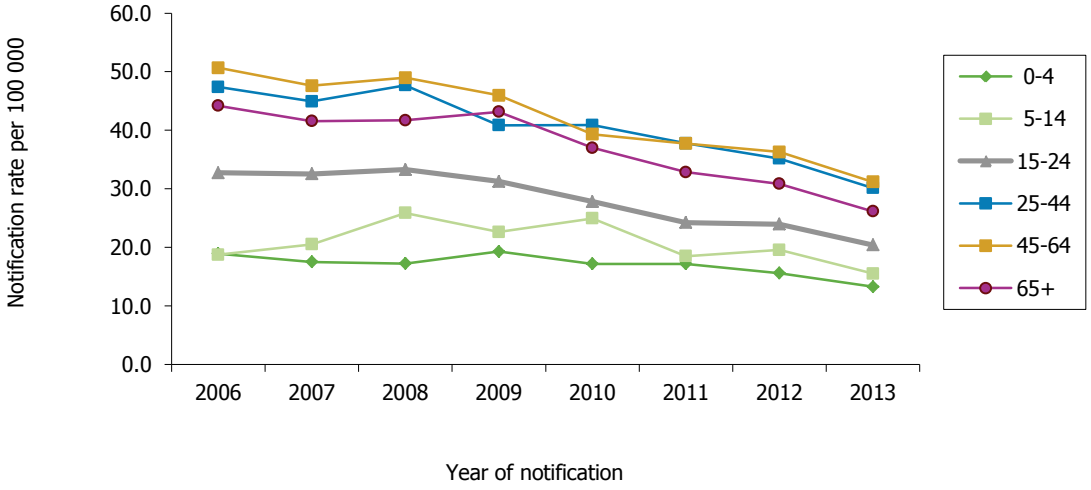
Except in age groups below 10 years and from 15 to 19 years, the TB notification rate was higher in males than in females. The notification rate in males was over 30 per 100 000 population in those aged 30 years and over, peaking at over 50 per 100 000 population in the age groups 45 to 49 and 55 to 59. In females, the highest notification rates ranged from 20 to 24.6 and were observed in age groups 5 to 9, 25 to 29, 35 to 44 and 75 to 79 years. Between 2006 and 2013, age group specific notifications rates have decreased in all age groups (Figure 4).

Figure 3. Tuberculosis (all cases) notification rate by gender and age group, Bulgaria, 2013



Sources: Bulgaria, National Centre for Public Health and Analysis, National TB register for TB cases, Population figures extracted form Eurostat, 27 June 2014

Figure 4. Tuberculosis (all cases) notification rate by age group, Bulgaria, 2006–2013



Sources: ECDC-TESSy for TB cases, Population figures extracted from Eurostat 27 June 2014

Persons born in Bulgaria represented 99.5% of the TB cases reported in 2013 and persons born abroad 0.5% (ranging each year from 0 to 0.3% in the past five years).

Site of disease and bacteriological results

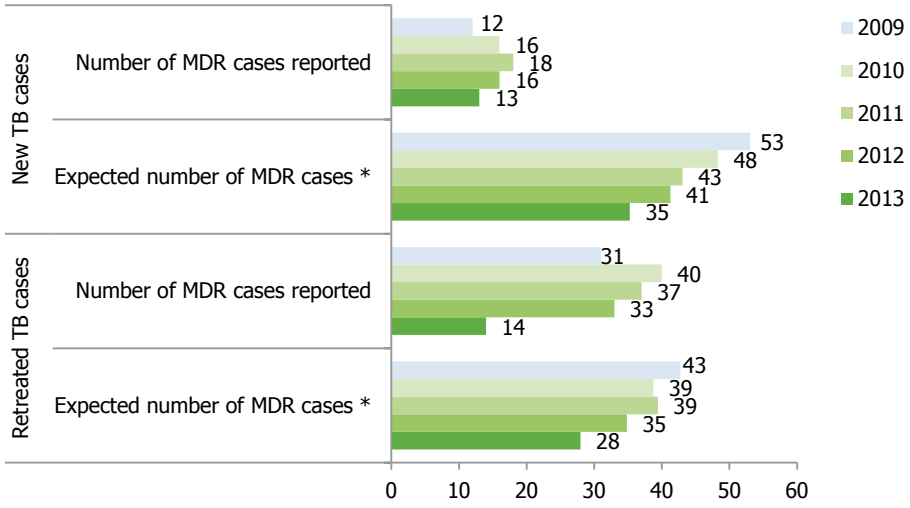
Pulmonary TB cases (with or without other sites of disease) accounted for 74% of all TB cases reported in 2013 of which 58% were reported to be sputum smear positive. Meningeal TB was reported in three cases in 2013 (0.20%). In the past five years, the proportion of TB meningitis per year ranged from 0.2 to 0.3%.

In 2013, culture result was reported for 85% of the TB cases reported to the national TB registry (97% in pulmonary cases vs. 51% in extra pulmonary cases). Among cases with reported results, the proportion of positive culture was 58% (67% in pulmonary cases vs. 10% in extra pulmonary cases).

Resistance to anti-tuberculosis drugs

Of the 1 932 TB cases reported in 2013, 951 were culture positive of which 734 (77%) had a drug susceptibility testing (DST) result reported for first line anti TB drugs. The proportion of H-resistant TB was 6.1% in new cases and 23.0% in cases with previous history of TB treatment (calculated among cases with DST known results). Multidrug-resistant (MDR) TB cases (resistant to isoniazid (H) and rifampicin (R)) accounted for 27 cases in 2013 and the proportion of MDR TB cases was 2.1% in new cases and 12.8% in retreatment cases The number of MDR TB cases was much lower in 2013 compared with previous years (27 vs. 43 to 56 each year since 2009). This may reflect a possible underreporting. A national drug resistance survey conducted in 2010 showed that MDR TB was detected in 2.1% of new TB cases and 11.1% of previously treated TB cases. Using these proportions to recalculate the expected number of MDR TB cases would result in 63 MDR TB cases in 2013 of which 35 new cases and 28 cases with a previous history of TB treatment. From 2009 to 2013, the expected number of MDR TB cases would be each year 1.5 to 2.3 times higher than the reported number with a trend showing a decrease of MDR TB cases in Bulgaria both for new cases and retreatment cases (Figure 5).

Figure 5. Multidrug-resistant tuberculosis cases, Bulgaria, 2009–2013



** Based on results of 2010 Drug Resistance Survey*

Source: Bulgaria, National Centre for Public Health and Analysis, National TB Register

Vulnerable population

The TB register collects information on HIV status. Of the 1 932 TB cases reported in 2013, 1 874 (97%) were tested for HIV infection of which 4 (0.2%) were found to be positive.

Additional information provided by the Department Management of Specialized Donor-Funded Programmes of the Ministry of Health showed that the number of TB cases reported in prisons was 48 in 2013, accounting for 2.5% of all TB cases reported (3.3% in 2012).

Treatment outcome monitoring

Of all TB cases notified in 2012, 84% were treated successfully within 12 months following the start of treatment. The proportion of treatment success was 81% among laboratory-confirmed (microscopy of culture) pulmonary cases (Table 1). The proportion of treatment success in new pulmonary laboratory-confirmed cases has exceeded 85% since 2009 and was 86.1% in 2013.

Of the 55 MDR TB cases notified in 2011, 67.3% were successfully treated, 12.7% died, 16.4% were lost to follow up and 3.6% had treatment failure.

Table 1. Treatment outcome at 12 months of cases reported in 2012, Bulgaria

Outcome category	All tuberculosis cases n=2 280	Pulmonary sputum smear or culture positive n=1 133	New pulmonary sputum smear or culture positive n=948
Treatment success	84.0%	80.8%	86.1%
Lost to follow up	5.1%	6.4%	4.5%
Death	7.9%	7.3%	6.9%
Failure	1.0%	1.9%	0.9%
Still on treatment at 12 months	1.6%	3.2%	1.3%
Outcome not reported	0.4%	0.4%	0.3%

National Tuberculosis Programme

The National Programme for prevention and control of tuberculosis in the Republic of Bulgaria for the period 2012–2015 is the follow-up of the National Programme for prevention and control of tuberculosis in the Republic of Bulgaria for the period 2007–2011. The programme was approved with Protocol n. 25 of the session of the Council of Ministers of the Republic of Bulgaria on 28th June 2007.

In 2003, the internationally-recommended Directly Observed Treatment, short-course (DOTS) Strategy, the basic package that underpins the Stop TB Strategy [4], was approved and implemented countrywide. The National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria for the period 2007–2011 was prepared following the WHO Stop-TB Strategy, adapting it to the national context. In 2007, Bulgaria endorsed The Berlin Declaration on Tuberculosis [5] of the WHO European Ministerial Forum 'All against tuberculosis' and was included in the Plan to Stop TB in 18 high-priority countries in the WHO European Region, 2007–2015 [6].

In 2009 a national plan for control of MDR TB in Bulgaria was issued and the GF to fight against AIDS, tuberculosis and malaria started supporting the management of drug-resistant cases with second-line drugs.

In 2011, Bulgaria was selected for the inclusion in The Consolidated Action Plan to Prevent and Combat M/XDR TB in the WHO European Region, 2011–2015 [7].

Objectives of the National Tuberculosis Programme, 2012–2015

The main aim of the Bulgarian National Programme for prevention and control of TB (NTP) is to reduce the transmission of *Mycobacterium tuberculosis* in the community and in congregate settings and to decrease the probability of emergence and spread of drug-resistant *M. tuberculosis* strains.

The operational objectives can be summarised as follows *(Source NTP)*:

- to ensure effective management and coordination of the NTP
- to diagnose early and control tuberculosis cases
- to treat successfully tuberculosis cases
- to treat successfully and control multi- and extensively-drug resistant tuberculosis (M/XDR TB) cases
- to control childhood tuberculosis
- to reduce the transmission of *Mycobacterium tuberculosis* strains in Bulgarian prisons
- to reduce the transmission of *Mycobacterium tuberculosis* strains in the Roma community and in groups at risk of developing tuberculosis
- to diagnose and treat persons with latent tuberculosis infection
- to raise public awareness on tuberculosis.

The performance of the NTP was assessed using the epidemiological indicators adopted by WHO and by ECDC to specifically identify the impact of the clinical and public health measures implemented and scaled-up at national, regional, and local level (Table 2).

Table 2. Performance of the National Tuberculosis Programme of Bulgaria against WHO and ECDC indicators .

Indicator	Year	Achieved	Expected indicators
TB notification rate	2012	31.1 per 100,000	29 per 100,000
MDR TB case detection rate	2012	49%	80%
Treatment success rate of new culture-confirmed cases	2012	86.4%	>85%
Lost to follow up rate of new culture-confirmed cases	2012	3.2%	4%
Treatment success rate of MDR TB cases	2012	67%	46%
Indicators not included in the National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria for the Period 2012 -2015			
Antiretro-viral therapy coverage	2012	>75%	-
Percentage of laboratories with external quality assurance	2012	28.6%	-
Estimated MDR TB among notified new TB cases	2012	2.3%	-
Cases with known HIV status	2012	66.4%	-
Treatment success rate of previously-treated culture-confirmed cases	2012	51.6%	-
Lost to follow up rate of previously-treated culture-confirmed cases	2012	16.3%	-
Percentage of MDR among retreated TB cases	2012	23	-

Source: European Centre for Disease Prevention and Control/WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2014. Stockholm: European Centre for Disease Prevention and Control, 2014

The main programme outcome indicators as defined in the NTP in Bulgaria for the period 2012–2015 were reached. The notification rate was 27 per 100 000 in 2013 (target for reduction of the number of diagnosed tuberculosis cases, equal to or less than a rate of 28 patients per 100 000 population), the treatment success rate of new, culture-confirmed, pulmonary TB cases was 86% (target > 85%) and for MDR TB cases 67% (target > 46%).

Specific essential clinical and public health activities of the TB programme, which are highly dependent on the GF funding, are at risk of being reduced. This can decrease the quality of the implementation of TB prevention and control in Bulgaria (e.g. contact tracing in high risk groups).

The political commitment is demonstrated by including tuberculosis among the priorities of the national health system and by financially supporting the NTP with funds from the State budget. Furthermore, the commitment of the State is shown indirectly by the good structure and management of tuberculosis at the national, regional, and local level.

The management of tuberculosis in Bulgaria is carried out by 36 medical institutions, financed by the Ministry of Health. In particular, 16 specialised hospitals are focused on the care off TB cases, five hospitals are specialised for rehabilitation, one ward is in a psychiatric hospital, and there is one specialised hospital for prisoners. Twenty-nine medical institutions work on a district level financed by the Global Fund to fight against AIDS, tuberculosis, and malaria. The main players of the program are: The National Centre of Infectious and Parasitic Diseases; The National Centre of Drug Addiction; The National Centre of Public Health and Analysis; Regional health inspections; Institutions of the Ministry of Justice; Non-governmental organisations and foundations with health-social purpose; Civil associations; and Medical institutions for inpatient and outpatient care. These medical institutions can be divided into University hospitals; Specialised hospitals for the active treatment of pulmonary/ pneumo-physiatric diseases; Multi-profile hospitals for active treatment; Medical centres for pneumo-physiatric diseases; Specialised hospitals for long-term treatment; State psychiatric hospital; Facilities for specialised outpatient medical support; and General Practitioners.

Numerous ministries and institutions have a direct and indirect role in TB control: National Health Insurance Fund; Ministry of Interior; Ministry of Labour and Social Policy; State Agency for Refugees; District and municipal authorities (regional and municipal directorates for 'Social assistance'); Bulgarian Union of Physicians; Bulgarian Respiratory Society; Bulgarian Association for Pediatric Pulmonary Diseases; and International organisations.

Bulgaria does not have a national human resources plan for TB human resources in the hospitals and laboratories. Retirement, recruitment of healthcare workers in programmes focused on chronic diseases, and migration of the youngest generations to high income countries can create a national human resource emergency for the National Tuberculosis Programme in the future. The unavailability of a sufficient number of health workers in a hospital-centered system can favour a gap, whose consequences might result in inadequate tuberculosis control. Several stakeholders pointed out this relevant issue which necessitates a strong political commitment from the central government, the ministries of health, the university, and the national scientific societies.

The national infection control (IC) strategy is not fully implemented in all facilities. This is shown by the fact that not all facilities, particularly in the periphery, have a facility IC plan available. In addition, non-adherence to the use of personal protective equipment and environmental measures was observed in some places. National IC guidelines follow the WHO recommendations and were distributed countrywide. However, in some circumstances the national recommendations were not adapted to the local situation. In particular, environmental measures and personal protective interventions should be improved; in some nosocomial settings the awareness of the healthcare workers, the patients, and the visitors does not seem adequate. Training and educational activities are not always adequately planned by the local IC committee. The control activities of the local IC committees are not sufficient to fill the above-mentioned gaps in a few cases.

Recommendations

- Include funding in the national budget of all components essential for TB prevention and ensure that components currently covered by GF funding will be covered by the national budget when the GF funding ends.
- Develop a human resources plan including a strategy to retain staff for TB services. Recruitment of the new generations with professional and economic incentives will support the system. The collaboration at a national level of the central government, the ministries of health and of the universities can identify a new approach to reinforce TB human resources planning and management. The enforcement of new strategies focused on the recruitment of the younger generations, starting from an improvement of the monthly salary, is needed to support TB prevention and control in Bulgaria.
- Develop facility IC plans where those are not in place, and continue with providing proper training to all staff and ensure use of personal protective equipment and implementation of environmental measures. The knowledge of the healthcare workers, the patients, and the visitors about the *Mycobacterium tuberculosis* risk should be increased. Educational activities for patients and visitors should be performed and standardised in the hospital educational plan. A strict monitoring performed by the IC committee should be in place.

Tuberculosis laboratory diagnosis

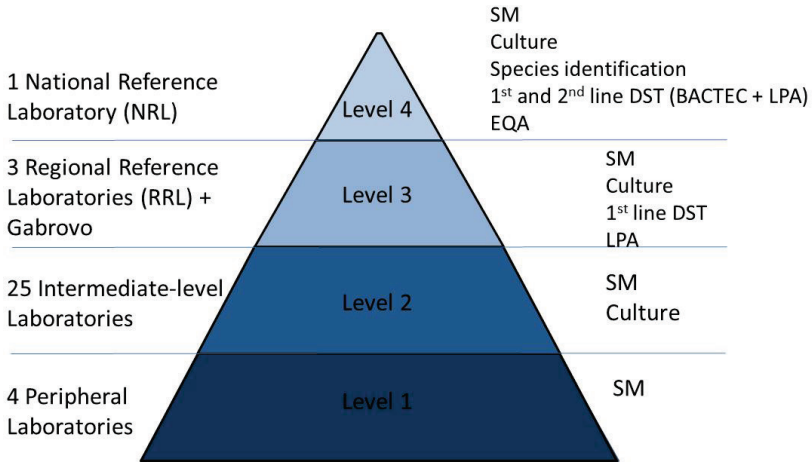
Tuberculosis laboratory network

The TB laboratory network in Bulgaria includes 34 laboratories organised in a pyramidal structure with four different levels:

- Level 4: National Reference Laboratory (NRL) performing microscopy, cultures on liquid and solid media, species identification (MGIT TBc Identification Test, Genotype CM/AS), 1st line and 2nd line DST (Bactec MGIT, Genotype MTBDR plus and Genotype MTBDRsl). The NRL confirms the MDR TB cases detected by other laboratories performing 1st line DST and organises the External Quality Assessment (EQA).
- Level 3: 3 Regional Reference Laboratories (RRL) (Plovdiv, Pleven and Sofia University hospital) + laboratory in Gabrovo, performing microscopy, culture on solid and liquid media and 1st line DST (Bactec MGIT and Genotype MTBDRplus, except for Gabrovo were molecular tests are not yet implemented).
- Level 2: 25 intermediate-level laboratories performing smear microscopy (SM) and cultures on solid medium.
- Level 1: 4 peripheral laboratories performing only SM.

The levels and the performed techniques are summarised in Figure 6.

Figure 6. Organisation of the tuberculosis laboratory network in Bulgaria.



SM=smear microscopy, DST=Drug susceptibility testing, LPA=Line Probe Assay, EQA=External Quality Assessment.

The 34 laboratories are situated in:

- Multi-profile hospitals – 12
- Specialised hospitals for Active Treatment of Lung Diseases – 16
- Medical center – 1
- Specialized hospitals for Prolonged Treatment of Lung Diseases – 3
- State Psychiatric Hospital with ward for patients with active tuberculosis – 1
- TB NRL – 1

Laboratory techniques

All the laboratory techniques used in the different laboratories in Bulgaria are explained with practical details in a 'microbiological standard' document.

Decontamination: All samples are decontaminated using the Petroff or the NALC-NaOH methods (as described in the 'Microbiological Standard'). Contamination rates between 3% and 10% were reported by the heads of the visited laboratories. This range of percentages is just outside the limits of what is acceptable and needs attention.

Smear microscopy: Standard Operating Procedures for smear preparation, staining and smear examination were presented. Only light microscopy is used. Staining is performed according to the standard Ziehl-Neelsen method. The slides are not reused.

Culture: The three RRLs and the laboratory in Gabrovo hospital (level 3) and the NRL (level 4) perform cultures using liquid media (Bactec MGIT) and solid media (Löwenstein Jensen egg-based medium). The 25 intermediate level laboratories (level 2) perform culture on solid medium only. The use of solid medium by the 25 intermediate-level laboratories is leading to a significant delay in diagnosis of MDR TB. This is because it takes time for a culture to grow on solid medium, and thereafter positive cultures need to be sent to the NRL or a regional laboratory in order to perform DST testing.

In some laboratories the Bactec MGIT 960 system is used far below its capacity. The resources needed for maintenance of the incubator are the same for Bactec MGIT 960 systems used frequently and infrequently. Thus the under use results in high relative cost of one liquid culture in laboratories that use the system below its capacity. Laboratories that do not use the Bactec system frequently should consider the introduction of the manual Bactec MGIT system. Alternatively, samples can be sent to a laboratory that can perform detection of Mycobacteria by liquid culture.

Currently, the regional laboratories are underused for the realisation of DST. An order must be signed that peripheral laboratories have to send all their positive cultures to the closest RRL for DST.

Species identification: Some laboratories (e.g. NRL, Plovdiv, Pleven) use the rapid 'BD MGIT TBc Identification test' based on the detection of the MPB64 protein secreted by *M. tuberculosis* complex in liquid medium. Other laboratories (performing culture only on solid medium) use the nitrate reductase and niacin tests. The positive cultures that are nitrate reductase/niacin negative or negative with the BD MGIT TBc test are considered as non tuberculosis mycobacteria suspected and are sent to the NRL to perform Genotype CM/AS. Some reports of non tuberculosis mycobacteria identification received back from NRL were observed during the visits. In 2011: 52 non tuberculosis mycobacteria strains were identified by the NRL. The most represented species are *M. fortuitum* followed by *M. chelonae*, *M. mucogenicum*, *M. peregrinum* and *M. abscessus*.

First line DST – molecular tests: Only four laboratories (3 RRL + NRL) perform DST first line drugs (FLDs) with the Bactec MGIT technology (liquid media) and rapid molecular tests (Genotype MTBDRplus - Hain). The hospital laboratory in Gabrovo performs also DST FLD but by using solid medium (Löwenstein Jensen) according to a Standard Operating Procedure based on international standards.

All MDR TB strains detected in Bulgaria are referred to the NRL for confirmation.

In 2013, FLD DST was only performed on 78% of the new pulmonary TB cases with positive culture (and 82% of the retreatment cases with positive culture), Table 3. It's an improvement from 2011 where the percentage was only 68%, but DST should be performed for all culture positive TB cases.

Currently, rapid molecular tests to detect antibiotic resistance are mainly used for confirmation of MDR TB after obtaining DST results. Despite the existence of an algorithm (indications) for the use of the molecular tests on 'New patients suspected for MDR TB' and 'Previously treated patients', these tests are rarely performed directly for suspected cases (before detection of the MDR by DST).

GeneXpert: Currently, GeneXpert is not available in Bulgaria. The use of GeneXpert to analyse sputum of all MDR TB suspects could reduce the delay for the detection of MDR TB cases.

Table 3. Microbiological confirmation of tuberculosis in Bulgaria, 2011–2013

TB cases	2011	2012	2013
Incidence (all TB cases/100 000)	32.6	31.1	26.5
All TB cases per year	2 406	2 280	1 932
MDR TB – New	3.1%	2.3%	2.1%
MDR TB – Retreatment	25.5%	23.2%	12.8%
MDR TB – Total	7.5%	5.9%	3.7%
All TB cases, C +	1071 (44%)	1094 (48%)	951(49%)
All TB cases, C +, with DST	745 (68%)	843 (77%)	734(77%)
TB cases with PT	1723(72%)	1625 (71%)	1425(74%)
New TB cases with PT	1423 (83%)	1359 (84%)	1209 (85%)
New TB cases with PT, SM +	716(50%)	741 (55%)	691 (57%)
New TB cases with PT, SM/C+	920 (65%)	948 (70%)	838 (69%)
New TB cases with PT, C+	853 (60%)	896(66%)	792 (66%)
New TB cases with PT, C+, with DST	579 (68%)	688 (77%)	619 (78%)
All TB cases, with PT, C +	1043 (60%)	1065 (66%)	924 (65%)
All TB cases, with PT, C + , with DST	724 (69%)	830 (78%)	728(79%)

TB: tuberculosis, MDR TB: multidrug-resistant tuberculosis, PT: Pulmonary tuberculosis, C+: positive culture, SM+: positive smear microscopy, DST: drug susceptibility testing.

Sources: Bulgaria, National Centre for Public Health and Analysis, National TB register for TB cases and National Reference Laboratory, Dr. Batchiiska.

Second line DST: is performed by the NRL for all MDR TB patients identified in Bulgaria (~50/year). The NRL is accredited for this technique and participated successfully in proficiency testing organised by the supra national reference laboratory (SRL) of Italy.

Molecular tests (Genotype MTBDRsl) are also used by the NRL in order to detect mutations associated with resistance to second line drugs (SLDs).

Turnaround time

Microscopy results are produced within 24 hours during working days. The Löwenstein Jensen results (culture on solid medium) take 6–8 weeks. The MGIT 960 results (culture in liquid medium) are produced in 2–3 weeks. The DST results for FLDs are provided in two to four weeks after the positive culture. The results from NRL are provided approximately ten days after sending a culture to the NRL. The NRL provides the MGIT result by phone and letter.

Some patient registers at the healthcare facility showed longer delays regarding the SLD DST results. It seems that the SLD DST is not always performed by rapid test.

Quality assurance system

TB laboratories in Bulgaria have to participate in the EQA schemes organised by the NRL. Two times per year, the NRL sends panels for testing of proficiency in SM, culture investigations, and DST for FLDs to the concerned laboratories. The level of proficiency of the 33 peripheral laboratories seems to be acceptable. For the last round of EQA performed, the percentages of correct results were between 80 and 100%. In addition to the panel testing, the NRL also realizes 'on site evaluation' and 'blinded rechecking of microscopy results' (1 time per year) for the 33 TB laboratories.

The NRLs participates in EQA schemes of external organisations. The NRL has participated successfully in INSTAND's EQA TB scheme since 2006, for microscopy, culture, species identification, Nucleic Acid Amplification Test and DST for FLDs (SLDs since 2011). Moreover, in 2007, 2010 and 2013 the NRL participated successfully in 3rd, 4th and 5th rounds of proficiency testing for DST (FLDs and SLDs) organised by the SRL in Italy.

Infection control measures

An IC plan specific for the laboratory was available in the visited places. Regular training on IC and laboratory techniques is organised by the hospitals and by the NRL for the laboratory staff.

Personal protection

Respirators (filtering face pieces 2 (FFP) and FFP3) were available in all sites visited. Since there was no work done in the laboratories during the visits the team could not observe the use of the respirators. Nobody using a respirator was ever tested for efficacy of the respiratory protection (fit testing).

Laboratory coats, gloves and overshoes are routinely used when laboratory personnel manipulates biological material. Adequate disinfectants were available in the different visited laboratories.

Screening of laboratory staff for LTBI and disease is routinely done (about once a year) in the TB facilities. Staff of the TB laboratories are usually tested by TST but they were also tested by interferon gamma release assay last year as part of a project.

Environmental control measures

Ultra violet-lamps are used in the TB laboratories. They are used before and after manipulations.

Biosafety cabinets were available in all visited TB laboratories. They are used for specimen decontamination and inoculation of cultures. Recent maintenance certificates were presented for the Biosafety cabinets, and also for the MGIT machine, centrifuges, microscopes, etc.

The transport of positive cultures/specimens is realised by using specific containers and a transport company paid by the GF.

Contaminated waste is sterilised using an autoclave. Thereafter, the sterilised waste is collected by an external company for incineration.

Different types of ventilation were observed in the laboratories in Bulgaria. Some laboratories use natural ventilation (windows), e.g. the laboratory in Ruse, some laboratories have an air cleaner (the laboratory in Plodiv), some have mechanical ventilation but without negative pressure (the laboratories in Gabrovo and Trojan), and some labs have mechanical ventilation and negative pressure (the laboratory in Pleven and the NRL).

The new building for the NRL was visited. Renovations are well advanced, and planned to be finished in two to three months. The NRL will then be fully equipped and the flow of operations will be better. Indeed, currently the molecular tests are realised in only one room. In the new building, on the first floor, there will be one room to prepare the mix and to realise the polymerase chain reaction amplifications and another one to realise the work on amplified DNA. The ground floor of the new facility will be dedicated to bacteriology with several rooms for registration, to perform smears, cultures and DST. This space is equipped with a double door autoclave and a mechanical ventilation system (already installed).

The new building for the TB hospital and laboratory in Plovdiv was also visited. Renovations are in progress Mechanical ventilation will be available in this new building.

Human resources

The number of staff members for the volume of work carried out is acceptable but near to the lower limit. The turnover rate among laboratory staff is a problem described by the heads of all the visited laboratories. For example, in the NRL, seven people left during the last nine years. People are trained to work in the TB laboratory and then they leave the laboratory and the training must be done again with another person. The low salary and the risk linked to the work seem to be the main reasons for leaving. In addition, some laboratory staff members are close to retirement.

The recruitment of qualified workers is reported to be problematic by the heads of the laboratories. In general, a lack of microbiologists was reported in Bulgaria.

Training

The head of the NRL regularly organises training for the staff of the peripheral laboratories. These trainings are organised in the infrastructure of the NRL for small groups of people. The mains topics of these trainings are the laboratory techniques and the IC measures. All the trainings organised and the participants are recorded by the NRL and by the different laboratories (lists seen in visited places). All new staff members must follow training.

In addition to this, the laboratory staff also participates in trainings organised by the hospital to which they belong. During our visits, we saw records of training organised by the hospitals on the use of biosafety cabinet and on the use of the information register.

Data management: recording/reporting

A computerised registering/monitoring system is implemented in all the TB laboratories (seen in places visited). In this system, the members of the laboratories can see the patient data entered by the medical doctor and they can complete the fields concerning the laboratory results. Concretely, they have access to the following data: name of the patient, date of sputum collection, code given to the patient, tests requested by the physician, reason for the requested test, name of the doctor, and they can enter their laboratory results. The access to the register is password protected.

All laboratories use this information system except the NRL who still uses an Excel file for their database. It seems that the system is not well designed for use by the NRL and for the tests performed by the NRL. Other laboratories visited also reported some practical problems with the use of this national information system. For example, it is not possible for the laboratories to extract data from the information system in order to prepare their activity report or to produce a result report. Therefore, all the visited laboratories also use a written laboratory book (and sometimes also an Excel file) in addition to the information system. Currently, all the result reports provided by the different laboratories are prepared using a form completed by hand, which is time consuming. Positives results are immediately reported to the doctor by phone.

Funding

All visited laboratories reported that it will be difficult to carry out the current activities after the end of the GF funding. Currently, a large part of the laboratory activities are financed by the GF. For example, in the NRL, the cultures in liquid medium (Bactec MGIT), DST for FLDs and SLDs, species identification (MTC/NTM), molecular tests for detection of mutations of antibiotic resistance, genotyping, training courses, EQA, new equipment and transport of the cultures are paid by the GF. Only the reagents and materials for SM and culture on solid media are paid by the NTP.

- Key observations
- The TB laboratory network is established, quality assurance system is in place and training on IC and laboratory techniques are regularly organised by the NRL and the hospitals. IC plans and standard operating procedures are available, personal protective equipment is used and recent certificates of equipment maintenance were presented.
- The order on the organisation of the laboratory network has not been signed and is therefore not implemented.
- In 2013, FLDs DST were only performed on 78% of the new TB pulmonary cases with positive culture and 82% of the retreatment cases with positive culture.
- Rapid molecular tests to detect antibiotic resistance are mainly used for confirmation of MDR TB after obtaining DST results. These tests are rarely performed directly for suspected MDR TB cases
- GeneXpert is not available.
- Laboratory diagnosis algorithm should be fully implemented.

- Reagents are stored adequately and no shortage occurred in the last years, but currently some laboratories work with reagents exceeding the expiration date.
- The laboratory part of the TB information system is underused and not designed to extract data and make reports.
- High turnover of laboratory staff due to low salary levels is reported by several laboratories.
- Renovation of buildings for the NRL and the laboratory in Plovdiv are well advanced. They will have mechanical ventilation (with negative pressure) and the flow of operations will be better.
- Respirators are available for lab staff members but nobody using a respirator is ever fit tested.

Recommendations

- Sign order that peripheral laboratories send all their positive cultures to the closest RRL for DST.
- Implement the algorithm for use of rapid molecular tests developed by the NRL (also in the RRLs).
- Procure GeneXpert machines for the NRL and RRLs.
- Analysis of sputum of all MDR TB suspects with GeneXpert is recommended. The number of GeneXpert machines should be determined based on a needs assessment ensuring full country coverage.
- Resolve the problems that lead to expired laboratory reagents.
- GeneXpert DST should be performed for all culture positive TB cases in order to early detect R resistant cases. Based on the GeneXpert result, the conventional first or second line DST should be performed, preferably by MGIT.
- The laboratory part of the surveillance system should be adapted for use by the NRL.
- Develop computer applications to improve the usefulness of the laboratory part of the information system for the laboratories activities (e.g. automatic generation of results reports).
- Develop a human resources strategy for the TB laboratories.
- Ensure sufficient mechanical ventilation in the TB laboratories.
- Perform respirator fit testing for each person using a respirator.

Tuberculosis treatment and case management

The internationally accepted DOTS strategy for TB treatment and management (the basic package that underpins the Stop TB Strategy) has been implemented in Bulgaria since 2003.

The department for 'Specialized Donor-funded Programmes' was created as the project management unit (PMU) with the Ministry of Health being the primary recipient of a GF Grant in Round 6, and later the 'Specialized Donor-funded Programmes' successfully applied for a GF grant in Round 8. With its very energetic, efficient and highly competent staff the PMU assisted by national TB specialist consultants has managed to consolidate rational TB control with all its important components of the DOTS strategy.

The WHO guidelines have been translated to Bulgarian, disseminated and with the GF contribution from Round 6, hospital doctors, nurses and general practitioners involved in TB control have been trained accordingly. The main standard forms for TB registration and daily management have been adopted (Patient Treatment Cards, District Register books, Lab Registers) together with additional items (e.g. Register of Suspects, standard hospital files etc).

Patients are categorised along the conventional lines of 'New' or 'Retreatment Cases', receiving either CAT 1, CAT 2, and CAT 3 treatment with regimens of 2HR Pyrazinamide (Z) ethambutol (E)/4HR or 2SHRZE/1HRZE/5HRE for the sputum smear positive infectious patients and retreatment cases respectively.

Sputum microscopy results after two and three months for category (CAT) 1 and CAT 2 respectively, and are used to decide whether the continuation may be started or the intensive phase should be prolonged for another month. By definition the treatment in this phase is fully supervised.

Management of adult non-resistant TB is essentially decentralised to the county level, and in each of the 28 counties and the metropolitan area of the capital Sofia, there are facilities for in-patient care either in so-called Specialised Hospitals for TB and Lung Diseases, or in multi-profile hospitals with some TB wards.

The total number of hospital TB beds is approximately 650 at present, which is a very high number compared with the number of notified TB cases (approximately 1 930 TB patients in 2013). If the average stay of a TB patient in hospital is assumed to be two and a half months, there would be a need for 400 TB beds. Approximately two thirds (68%) of the total TB budget for 2012 corresponds to hospital costs for TB patients.

Drug-susceptible TB cases are hospitalised for at least two months, and MDR TB patients are hospitalised for at least the intensive phase of treatment. This practice of very long hospitalisation is not evidence-based. The current international recommendations suggest a duration of the hospitalisation correlated with the contagiousness of the patients and as needed for the recovery of the clinical conditions. The long duration of hospitalisation significantly increases the human and economic resources needed for TB control. These resources can be better applied for community-based assistance, particularly for those activities which can be helpful to decrease the burden of TB patients and latently TB infected individuals (i.e. case-finding and contact-tracing activities). An increased hospital turn-over and shorter duration of hospitalisation can avoid unpleasant and at-risk conditions where patients are admitted in large rooms; in particular, risk of cross-transmission.

So far no attempt has been made to differentiate between the TB patients that obviously need and benefit from being in hospital for the whole of the intensive phase, and the probably many TB patients who should stay in hospital only for the first 14 days of treatment only to render them non-infectious, or could be treated as out-patients from the start. Reimbursement systems to the hospital from the Ministry of Health/Health Insurance for TB in-patients may, together with a long standing tradition for in-patient treatment in Bulgaria, explain the long duration of hospitalisation. Reduction of the duration of hospitalisation is an obvious opportunity for savings and for introducing a more user friendly TB treatment modality without compromising treatment outcomes.

Whereas all patients are kept as in-patients in hospital during the intensive phase, also if sputum smear negative, in the continuation phase their control and follow-up will normally be done by the county TB dispensary. The patronage nurses will take care of the follow-up, and patients are also seen monthly by the pulmo-phthisiologist. Thus, the TB follow up system is DOTS without DOT for the continuation phase as patients only come on a monthly basis to collect their drugs for the following month. Home visits by the patronage nurses to TB patients in the continuation phase appeared to occur on a regular basis, in some places even weekly. Unfortunately the phase 2 of the Round 8 of the GF grant was subject to budget cuts, and financing interrupted for fuel for the county car (also bought for GF money) used by patronage nurse for field work.

If the patient lives far away from the county TB dispensary the TB follow-up is delegated to general practitioners that are rewarded with some extra consultation salary for seeing the patient through to the completion of her/his treatment. This option seems to have been used fairly little and interviewed general practitioners have expressed that they feel that TB patients should be seen by specialists. On average a general practitioner with 1 500 registered patients could expect to encounter a TB patient within her/his group of patients every 2.5 years.

Treatment outcomes in terms of treatment success rate of new sputum smear positive patients have generally been very satisfactory and remarkably stable over time, with a treatment success rate of 85–86% on TB cases reported from 2009 to 2012 (Table 4). Although the total number of TB patients has decreased from 2 910 to 1 932 (33%) in five years (2009–2013) the relative proportions of relapses and of total number of retreatment cases have not changed at all during this same period, being 6.5% and 13% respectively. Death rates are high (6–8%) and may indicate that a number of patients are diagnosed too late. Data allowing an evaluation of diagnostic delay are not available.

Table 4. Tuberculosis treatment outcomes of tuberculosis cases in Bulgaria, 2009–2012

New sputum smear positive tuberculosis patients														
Year	Total		Cured		Treatment completed		Death		Failure		Lost to follow up		Not evaluated *	
	N	%	n	%	n	%	n	%	n	%	n	%	n	%
2009	896	100%	699	78.0%	71	7.9%	70	7.8%	12	1.3%	33	3.7%	2	0.2%
2010	805	100%	664	82.5%	23	2.9%	68	8.4%	13	1.6%	29	3.6%	8	1.0%
2011	716	100%	587	82.0%	25	3.5%	59	8.2%	11	1.5%	25	3.5%	9	1.3%
2012	741	100%	610	82.3%	25	3.4%	55	7.4%	8	1.1%	31	4.2%	9	1.2%
Retreatment tuberculosis cases (all cases)														
Year	Total		Cured		Treatment completed		Death		Failure		Lost to follow up		Not evaluated *	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2009	384	100%	121	31.5%	145	37.8%	44	11.5%	17	4.4%	32	8.3%	18	4.7%
2010	348	100%	113	32.5%	109	31.3%	46	13.2%	20	5.7%	41	11.8%	16	4.6%
2011	355	100%	107	30.1%	129	36.3%	32	9.0%	19	5.4%	40	11.3%	27	7.6%
2012	314	100%	99	31.5%	109	34.7%	27	8.6%	13	4.1%	41	13.1%	24	7.6%

**include patients still on treatment and transferred out*

Sources: Bulgaria, National Centre for Public Health and Analysis, National TB register for TB cases

Although the overall treatment success rate is more than 85%, the treatment success rate of re-treated cases is much lower, i.e. 64–66% (Table 4). This poses a risk for development of MDR TB. International studies [8–10] show that most cases that relapse are individuals whose adherence to anti-tuberculosis drugs is poor. The surveillance system does not include information on treatment adherence and does therefore not allow identifying the size of the problem in Bulgaria. This hampers the development of an evidence-based strategy for reducing relapse.

Based on a prevalence survey, the proportion of MDR TB cases among previously treated TB patients during the period 2011–13 was estimated to be 11.1%, and the number of MDR TB cases expected to arise among the retreatment cases in 2012 was 35.

Patients with mono-and polyresistant TB are treated according to the Programmatic Management of Drug Resistant TB WHO guidelines at county level. No analysis of DST patterns for this group of TB patients is available to explain why the retreatment cases have relatively poor outcomes, but risk groups such as those of Roma ethnicity may at least account for part of the high rate (11–12%). Loss to follow up among non-resistant new TB patients is on the other side satisfactorily low. The patronage nurses with legal help from the Regional Health Inspectors are responsible for bringing back the absconders. Also here, the disappearance of extra funds from the GF for the purpose of retrieval of cases who are lost to follow up may result in higher lost to follow up rates.

Individuals identified with an immunological diagnosis of latent TB infection (LTBI) are treated with the internationally recommended H preventive therapy. Adults are considered to have LTBI if they have a TST result of ≥15 mm. If they have specific risk factors and are considered to be at high risk of developing active TB preventive treatment is initiated if the TST result is above 5 mm. All treated persons, including children, are evaluated with tuberculin skin test (TST) and X-ray at three and six months after the start of preventive therapy to monitor the response to preventive treatment of LTBI. The team was informed that the aim of the follow up examinations of children and adults with proven LTBI is to determine the positive effect of the chemoprophylaxis and the absence of lung x-ray symptoms in case there is resistance to H. This practice is not supported by current evidence. The inappropriate exposure to X-rays in at-risk categories (e.g. children) could be avoided. The financial savings can be relevant, shifting important economic and human resources to other fields of the tuberculosis management.

Key observations

- The 'Specialized Donor-funded Programmes', the PMU for the GF fund money, has been very effective in consolidating the TB control for non-resistant TB in Bulgaria along the lines recommended by WHO.
- In the intensive phase of treatment, adherence is good as all patients stay in hospital during this period.
- Hospitalisation of all TB patients during 2–3 month is expensive and for many TB patients not necessary nor is it for these persons patient friendly.

- Treatment outcomes for new TB cases are satisfactory.
- High death rates and less satisfactory treatment results among retreatment cases has been a constant phenomenon over the last five years.
- Bulgaria is practicing DOTS without DOT apart from monthly control visits in the continuation phase.
- There is no special provision for poor and vulnerable non-resistant TB patients (e.g. compensation of transport costs or food tickets).
- Patronage nurses seem to be vital for the follow-up of TB patients and field work has previously been financed through the GF grant.

Recommendations

- Develop ambulatory care from start of treatment for patients who so wish and are in a position to adhere to treatment, to decrease the duration of hospitalisation, by involving general practitioners, patronage nurses, and NGOs in a coordinated manner. The coordination of the stakeholders should be performed at a national and local level, involving the public health organisations. Individuals and organisations who could support the ambulatory phase should be adequately trained. The directly observed treatment (DOT) can represent an option to be implemented in specific high-risk categories, avoiding the hospital model (i.e. longer hospitalisation stay to improve the adherence).
- The substantial group of retreatment patients with poor outcome (e.g. lost to follow up) should be analysed closely (Operation Research) with a view to enhance relevant aspects of case holding and supervised treatment to achieve more satisfactory outcomes.
- Increase DOT for retreatment cases involving all stakeholders to decrease the lost to follow up rate. The shift of the healthcare assistance to the ambulatory phase can strengthen all the measures which should be implemented to increase the adherence to anti-tuberculosis therapy, particularly in those individuals with a poor compliance (e.g. Roma community members, intra-venous drug or alcohol abusers).
- Social help and incentives should be introduced for the most vulnerable TB patients (e.g. Roma persons) and NGOs involved in these aspects.
- Closer control (DOT) should be given to vulnerable TB patients and field work (i.e. home visits to TB patients by patronage nurses) should be financed by the Ministry of Health in absence of external funds.
- Stop the TST and x-ray to monitor response to preventive treatment. Every clinical and public health practice should be evidence-based. The savings could be allocated to other essential TB prevention and control activities.

Drug-resistant tuberculosis

Multidrug-resistant tuberculosis in Bulgaria - short background

The successful application to the GF Round 8, entailing an agreement of procurement of SLDs through the Green Light Committee mechanism enabled the Bulgaria NTP to start recruiting MDR TB patients for treatment. This was preceded by the adoption of guidelines similar to the WHO Programmatic Management of drug-resistant TB guidelines, training of staff and the refurbishment of an appropriate part of the old sanatorium at Gabrovo, which in the meanwhile functioned as the county Specialized Hospital for TB and Lung Diseases. All these activities were financed by the GF grant. The initial provision of drugs was for 50 MDR TB patients in 2009 recruited with a little delay and thus formed the first cohort (2009–2010). Subsequently, annual cohorts of 55–60 were planned to a maximum of 240 MDR TB patients. In 2014, the fifth cohort was being recruited.

Multidrug-resistant tuberculosis epidemiology in Bulgaria

The provision of SLDs financed by the GF was originally thought to offer only a partial coverage of the real and expected number of some 400 new MDR TB cases annually building on older WHO estimates presuming that Bulgaria was a high MDR TB prevalence country. However, the national drug resistance survey from 2010 proved these assumptions wrong and exaggerated. Estimations using the results of the drug resistance survey of 2.1% MDR TB cases among new TB cases and 11.1% among previously treated patients result in an expected annual number of 63 MDR TB cases.

The actual number of detected MDR TB cases is shown in Table 5. In 2013, only 27 MDR TB cases were detected. Leaving alone the surprising low figure for 2013, the annual detection of MDR TB cases seems stable from year to year. Also the number of XDR TB patients has remained stable, in 2013 three new cases were detected.

Table 5. Multidrug-resistant tuberculosis in Bulgaria, 2009–13

	2009			2010			2011			2012			2013		
Patient Category	New	Re-Tx	Total	New	Re-Tx	Total	New	Re-Tx	Total	New	Re-Tx	Total	New	Re-Tx	Total
No. of cases with Culture (+) tested with DST	717	128	845	803	164	967	600	145	745	700	143	843	625	109	734
No. (%*) of MDR TB cases	12 1.7%	31 24%	43 5%	16 2%	40 24.4%	56 5.8%	18 2.7%	37 25.5%	55 7.4%	16 2.3%	33 23.1%	49 5.8%	13 2%	14 12.8%	27 3.7%
No. of XDR TB cases	0	0	0	1	3	**4	2	3	***5	0	3	****3	2	1	*****3

Data from Ministry of Health.

Re-Tx=re-treatment; No=number; DST=Drug Sensitivity Testing; MDR TB=multidrug-resistant tuberculosis; XDR TB=extensively drug resistant tuberculosis

** In 2008 Bulgaria was included in the group of 27 High M/XDR TB burden countries, based on WHO prognostic model: 9.4% MDR TB cases out of new TB patients, and 37% - out of re-treatment cases.*

*** In 2010, four XDR TB cases were confirmed by WHO-SRL in Italy, out of all MDR TB cases registered in 2007 and started treatment with SLD in the first MDR TB cohort.*

**** In 2011 NRL-TB confirmed 3 XDR TB cases out of MDR TB cases registered in 2007, one XDR TB case, registered in 2008, and one XDR TB case registered in 2010.*

***** In 2012 NRL-TB confirmed 3 XDR TB cases out of MDR TB cases – one registered in 2009 and two registered in 2012.*

****** In 2013 NRL-TB confirmed 3 XDR TB cases out of MDR TB cases – one registered in 2010, one registered in 2012 and one registered in 2013*

Diagnosis and treatment coverage for multidrug-resistant tuberculosis

In Bulgaria, with its extensive network of laboratories performing culture, DST is performed on all culture positive samples. Yet, it should be noted that in 2013 only, 37% (625/1680) of all new TB cases were confirmed by culture and had a DST performed. For retreatment cases the corresponding figure was 43% (109/252). The large proportion of sputum smear negative/culture negative may indicate 'over-diagnosis' of TB in Bulgaria. Therefore, it is plausible that the actually detected number of MDR TB cases may be close to the real number. So far all detected MDR TB patients have been offered treatment.

A major issue is the problem of delay in the MDR TB diagnosis. Culture is generally done on solid media, and this is also often true for the DST. Although there is in the NRL an algorithm for rapid diagnosis given preference for rapid diagnostic methods (fluid media, line probe assay [LPA]) to TB suspects who are contacts to MDR TB cases and to all retreatment cases, this algorithm does not seem to be applied for the patients where the file has been reviewed. Even in re-treatment cases often three to four months may elapse from their start of CAT 2 treatment until their real status as MDR TB patients is revealed. In the meanwhile these patients are treated in lung hospitals where IC measures are not optimal, while they are getting worse due to the inappropriate treatment.

Case holding by the health system

All MDR TB patients are treated as in patients in the MDR TB facilities at Gabrovo hospital. After diagnosis the patient is counselled locally in his own county, and then s/he will be invited to Gabrovo for another counselling during which the patient will sign a contract that s/he is willing to stay in the hospital during the intensive phase. Very few patients refuse, 15 patient rooms of which 11 with negative pressure, offer a sufficient number of beds and isolation facilities for the current MDR TB patient load even if most patients will stay for eight months or longer in the hospital depending of the need for a prolongation of the intensive phase due to late sputum conversion. The majority of patients convert to negative culture (and microscopy) during the first 2–4 months (data not presented) and will be given injectable medicine until some four months after sputum conversion depending on the total clinical development. Sputum control samples are examined at the local laboratory at the Gabrovo hospital that has Bactec culture facilities.

Once the patient is ready to be discharged to her/his own county, the patient file and SLDs packed patient-wise are sent in advance to the county TB dispensary which is notified about the patient. The continuation phase is generally 12 months depending on the intensive phase and the sputum culture development. Observations during field visits seem to corroborate a directly supervised follow up for 6/7 days a week. Once a month the patient will be seen at the TB dispensary, biochemistry performed according to guidelines, and a sputum sample is produced by the patient. Criteria for cure, completion, failure, lost to follow up etc. follow the conventions of WHO. Ancillary drugs seem to be available, both at the hospital and in the TB dispensaries for addressing side effects of the TB drugs. Most MDR TB patients are supervised by the nurses of the dispensary, but examples were seen where the patient's general practitioner supervised her/his MDR TB client through the last part of the treatment against an extra fee of €30/months (paid with money from GF grant).

Of the first three cohorts (165 patients in total) up to now 18 (11%) MDR TB patients have been lost to follow up. In case of loss to follow up from Gabrovo Hospital or after start of ambulatory treatment patients have been searched for by different organisations: the outreach workers of NGOs working with the TB programme and financed by the GF; social services; RHIs; and occasionally by the police. When traced, NTP staff have tried to persuade patients to stay on treatment. During the continuation phase the tracing is initially done by the patronage nurse, who is also paid an extra salary from GF money. This nurse has at her disposition a vehicle, delivered by the GF and running costs (fuel etc.) likewise financed by the grant from the GF in the beginning, but these funds have now been suspended due to reduction of the GF funding.

The stay and the food at Gabrovo hospital are free of charge. During the out-patient time MDR TB patients are given food vouchers at the end of a week's complete adherence which seems to be a significant contribution to the small public (sick) pension which a TB patient is entitled to receive while under treatment. Also food vouchers are paid for by the GF.

Multidrug-resistant tuberculosis treatment

As soon as the patient is diagnosed as a MDR TB patient the Treatment Commission will be notified and the commission will review the case history, the patient will be hospitalised and started on an empirical treatment until the availability of SLD susceptibility testing results. Until 2014, the SLD DST would come after one to two months and be done on liquid media (Bactec). Now, in a few cases LPA results (Kanamycin [Km], Amikacin [Am], Capreomycin [Cm], Ofloxacin [Oflx]) were available, in one case within a week after the start of hospitalisation.

For the intensive phase the empirical treatment includes: Am, Levofloxacin (Lfx), Protionamide (Pto), Para-Aminosalicylate Sodium (PAS), Cycloserine (Cs), and Pyrazinamide (Z). The individualised treatment regimen, which is designed by the Treatment Commission, will in MDR TB patients with no further resistance often be: Am, Lfx, Pto, PAS, Z, and E. If additional resistance is detected a modified regimen according to actual resistance pattern will be prescribed.

At the present visit the file of one XDR-TB case was reviewed. His regimen was Moxifloxacin (Mfx), Linezolid (Lzd), Amoxicillin- Clavulanic acid, E, Cs, PAS, Pto.

Treatment outcome for multidrug-resistant tuberculosis cases

The first cohort of MDR TB cases recruited in 2009–10 consisted of the backlog of chronic pulmonary patients, and the mortality among this group after start of treatment was high (38%). In the following two years the mortality was 12% and below 2% respectively (Table 6). Treatment success increased from 48% in the first cohort to 67% in the following cohort (Table 6). Of the 2011 cohort, 67.3% finished treatment successfully, 12.7% died, 16.4% were lost to follow up, and 3.6% failed.

Table 6. Treatment outcomes for multidrug-resistant tuberculosis cohort 2 (2011).

Registration group	Cured	Treatment completed	Died	Failed	Lost to follow up	Not evaluated[1]	Total
New	9	6	1	0	4	0	20
Relapse	12	4	1	1	4	0	22
After lost to follow up	2	0	2	0	1	0	5
After failure of Category I treatment	1	2	3	1	0	0	7
After failure of Category II treatment	1	0	0	0	0	0	1
Other or unknown retreatment[2]	0	0	0	0	0	0	0
Total	25	12	7	2	9	0	55

[1] Not evaluated = cases registered - sum of treatment outcomes, 'Not evaluated' includes 'transferred out', 'still on treatment' and any other registered case where the treatment outcome has not been evaluated.

[2] Unknown retreatment is a previously treated cases but without information on outcome of previous treatment

Key observations

- The MDR TB management follows international guidelines closely.
- Detection rate of MDR TB cases seems to be high.
- All diagnosed patients can be and are being treated.
- Still long delays before establishing that a patient is a MDR TB case, even among retreatment TB cases.
- No ambulatory treatment opportunities in the intensive phase.
- Enthusiastic leadership and good team work in an effective treatment commission.
- Adequate and appropriate treatment facilities at the MDR TB Hospital in Gabrovo.
- Insufficient social and psychological support for the patients.
- Even though Gabrovo offers good IC measures the long hospital stray offers no active or constructive. stimulation, training or entertainment for patients
- Sufficient quantity of SLDs and appropriate treatment regimens.
- Fully observed treatment,- also in the continuation phase.
- Acceptable to good treatment outcomes, 67% in 2011 Cohort.
- All major activities necessary for the continued MDR TB management depend on the GF grants, thus when the GF stops the following issues will arise:
  - no financing arrangement so far for MDR TB drugs (approximately € 100 000 per year)
  - patronage nurses no longer receive incentives for field work (supervision, retrieval of absconders etc)
  - patients will receive no more social support for transport and food coupons
  - all laboratory activities necessary for programmatic management of MDR TB (Culture, DSTs, rapid diagnostic tests and other lab test for diagnosis) and maintenance of laboratory equipment will immediately suffer.

Recommendations

- The Ministry of Health budget must include budget lines for MDR TB drugs and laboratory expenses necessary for treating all MDR TB patients in Bulgaria.
- Rapid diagnosis for all TB patients with a high risk of MDR TB should be implemented (LPA, GeneXpert) and the tests should be free.
- Many patients may have social and personal problems that make hospitalisation during the intensive phase of treatment beneficial, also with respect to training their skills of adherence. However, for patients hospitalisation is often difficult in view of their family and economy situation, and means a substantial amount of opportunity costs. It is therefore desirable to aim at discharging the patient for ambulatory care as soon as this is feasible for the individual patient. Therefore, it is recommended to develop ambulatory care from start of treatment, by involving general practitioners, patronage nurses, and NGOs in a coordinated manner.
- Ensure fully observed treatment during continuation phase for all MDR TB patients and retrieval of cases lost to follow up (up to 16% of registered outcomes).
- Implement an activity programme for MDR TB patients in Gabrovo hospital.

Tuberculosis in vulnerable populations

General

There is no clear strategy for case-finding among high-risk groups based on epidemiological data. The missing epidemiological support of key variables that would allow identifying those at high risk of being infected or developing tuberculosis disease hampers case-finding among high risk groups. This may result in cases being missed and continuing transmission of *Mycobacterium tuberculosis* strains.

Recommendation

- Increase early and active case-finding activities among vulnerable groups, through a coordinated approach involving community/social workers and NGOs, and through a proper diagnostic algorithm based on the epidemiology, behavior, and feasibility per risk group.

Childhood tuberculosis

In Bulgaria, there is centralised management of all childhood TB cases (0–18 years) with a comprehensive diagnostic algorithm following international guidelines. Diagnosis and treatment is available at no cost, and covers the paediatric population including the most vulnerable. The management of childhood TB is performed by dedicated staff. Currently, there is one resident physician in training to become specialist in childhood TB. The conditions for the children at the Sofia University Children's hospital for Respiratory Diseases are good. No child-friendly drugs formulations are available for the treatment.

Preventive treatment is offered to all asymptomatic paediatric contacts, independent of TST results. Isoniazid for six months is the standard regimen, but regimens tailored to index case's DST are often used and they have performed studies on the effectiveness of different regimens for MDR TB contacts. There is a practice to perform TST and X-ray at three and six months after the start of preventive treatment to monitor response to preventive treatment of LTBI. This practise is not supported by any current scientific evidence. It is common practice to change the preventive treatment regimen or duration if there is an increase in the size of TST reaction. This practice is not part of any national guidelines, and is not in line with international guidelines or current evidence based practice.

Bulgaria practises an extensive BCG vaccination programme that does not follow the current international and WHO guidelines. The programme includes a first immunisation at birth, followed by four re-immunisations at 7 months, and 7, 11 and 17 years of age if the child does not have a BCG scar and the TST result is negative.

Recommendations

- The need for a Bacillus Calmette-Guérin (BCG) revaccination programme should be carefully assessed, taking into account the evolving epidemiological situation in the country, the current international guidance and cost-benefit analyses.
- Availability of child-friendly drugs formulations should be ensured to maximise treatment adherence and effectiveness.
- Practices such as the use of TST to monitor response to preventive treatment should be carefully reconsidered in view of current international recommendations and existing evidence.

Tuberculosis in prison

Bulgaria has specific guidelines for TB treatment and control in the penitentiary system. These guidelines build on the Ministry of Health TB Guidelines for the civilian population, but specifically address the practices in the prison. There are annual trainings of all medical staff on the guidelines for TB control in prisons. However, it seems challenging to retain expertise and to encourage qualified staff to join the penitentiary health service in general and the TB penitentiary service in particular.

At the level of the Ministry of Health and Ministry of Justice there is good collaboration between the civilian and penitentiary system. This is through the activities funded by the GF project on TB control in prisons.

At entry into prison, all inmates go through a medical examination. This examination includes a questionnaire for TB. If TB is suspected, TST and sputum collection are done directly, and an X-ray is performed either at the local hospital or in one of the prison hospitals. There are good collaborations established between the prisons and the regional hospitals and microbiological laboratories for microscopy and culture. Sputum collection and transport of sputum to regional laboratories is well organised. The follow up of TB patients ending their sentence and continuing treatment in the civilian sectors does not seem to be rigorously organised.

Through the GF, sputum collection rooms have been established in each medical centre and the two prison hospitals. The prison hospital for TB patients in Lovech has been renovated, and the clinic has got a new MDR TB section, and more equipment including digital X-rays. The GF project also supports monitoring visits to all prisons two times per year following a standardised checklist. Screening campaigns of prisoners by fluorography supported by the Ministry of Health are also supported by the GF grant (GF in 2011-2012). However, these campaigns are irregularly implemented without clear reasons.

Good statistics and data are available for all TB cases in the penitentiary system. These data show that there was a marked decrease in the number of new TB cases from 2005 to 2006 (by 50%). Thereafter, the number of cases has been rather stable at around 60 to 90 per year. The treatment outcomes show a high rate of transfer out. This is due to end of sentence with insufficient follow up of treatment outcome.

Information and educational material for prison inmates is available and information campaigns around world TB day are implemented.

Recommendations

- More active follow up to ensure that patients ending their sentence during treatment really continue their treatment, and to obtain treatment outcomes of the transferred out patients.
- Ensure sustainability of the TB screening upon entry into the prisons and maintain good contacts with regional hospitals and laboratories.
- Continue the good collaboration between Ministry of Health and Ministry of Justice.
- Assess the annual screening campaigns by fluorography, taking into account the cost-benefit and the yield of those screenings campaigns versus the case detection activities under the GF project

Tuberculosis/HIV

At the Ministry of Health level there is good collaboration between the TB and HIV/AIDS programmes. However, there is a varying degree of formal collaboration between the HIV and TB specialists in the regions, especially in regions with less experience of TB/HIV co-infection. Several NGOs run joint TB and HIV activities funded by the GF, e.g. in street children and Roma populations.

HIV testing and counselling should be offered to all TB patients as per the national guidelines. The coverage of HIV testing among TB patients is suboptimal. Although several clinics report that all patients are tested, it is not reflected in the surveillance system. The percentage of patients with a known HIV status was 66% for the 2012 cohort.

There is a streamlined process for referral of TB patients to the infectious disease hospital in Sofia for evaluation and management of HIV.

Recommendations

- Strengthen the systematic collaboration between TB and HIV specialists in all the regions.
- Increase the coverage of HIV testing, e.g. by putting more efforts in the counselling of the patients to reduce refusals.

Roma populations

Roma, but also other marginalised groups of the population suffer from inequitable access to healthcare which has implications for rapid TB diagnosis and support to complete the treatment.

There are difficulties in providing adequate support to ensure adherence and follow-up among Roma, and other vulnerable population groups.

Under the GF project, a functional network between the outreach workers of the NGOS, patronage nurses from the hospitals, the TB dispensaries and the RHI is in place in order to better serve high-risk groups, including Roma.

Recommendations

- Continue with activities for case finding and case holding among the Roma population.

Tuberculosis contacts

Bulgaria does not seem to have implemented a standardised approach to contact tracing and guidelines for contact tracing were not presented to the review team. It seems to be unclear what the responsibilities are of the Regional Health Inspectorates (RHI), hospitals and non-governmental organizations (NGOs) with regards to contract tracing. The risk is an inadequate allocation of human resources and economic resources. Furthermore, the inappropriate distribution of the tasks can favor the under-diagnosing and under-reporting of TB cases and of latently-infected cases, particularly those in hard-to-reach groups.

Recommendations

- Implement a standardised approach to contact tracing and develop guidelines for contact tracing if not available.

Other vulnerable populations (migrants, street children)

There is a successful collaboration between NGOs running shelters and day centres and the local patronage nurses. This collaboration benefits the health of street children and homeless children.

There is a good safety net created between government and NGOs to cover treatment and care for refugees and migrants (including undocumented migrants), also the collaboration with patronage nurses is a crucial component.

The sustainability of all activities targeting Roma, street children, homeless and migrants is threatened as it fully relies on the GF funding and engagement of NGOs for the specific target groups.

Recommendations

- To ensure sustainability and state funding of the activities for TB screening, and patient support to ensure timely case detection, diagnosis and adherence to treatment for all individuals, also the vulnerable groups most at risk of TB.

Supply management of anti-tuberculosis drugs and diagnostics

Quantification

The National Programme for Prevention and Control of Tuberculosis is responsible for quantifying the need on a yearly basis for FLD and SLD, laboratory reagents and supplies for the country, including the penitentiary system. Quantification is based on TB morbidity (TB and MDR TB notification of previous year) with a buffer stock of six months for FLD, and on consumption for laboratory supplies with buffer. The NTP follows the technical specification provided by the 'TB Expert Group and National Consultant' defining TB regimen, strength and posology. FLD includes R 300 mg, H 100mg, Z 500 mg, E 250 mg, and streptomycin (S). SLD are Lfx 250 mg, Pto 250 mg, Cs 250 mg, (PAS 4 g, Amk 500 mg, Cm 1g. Third Line Drugs (TLD) are Mfx 400mg and Lzd 600.

Quantification of TB drugs aims at treating all TB and MDR TB in the country without the risk of running out of stock. FLD does not include Fixed Dose Combinations (adult and paediatric) nor paediatric formulation and is using non WHO recommended strength for FLD. The use of a loose tablet of Rifampicin is not recommended by WHO as it increases the risk of MDR TB. Using strength not in line with the WHO recommendation may limit to some extent the interest of manufacturers to be registered.

Based on the consumption observed in the previous year and taking into account the trend of previous years the NRL prepares the tenders for the Ministry of Health for consumables/reagents for all the TB laboratories of the country.

Procurement and funding

First Line drugs are procured with State budget under the Public Procurement Law (National Procurement Act for TB). The Ministry of Health carries out the national tender independently without international bidding following the technical specification of the 'TB Expert Group and National Consultant' the quantification made by the NTP and the national legislation on quality of products (Good Manufacturing Practice rule, United States or EU pharmacopae certification, authorization in other countries of EU, analysis of batch). The Bulgarian Drug Agency (BDA) also gives its opinion to the Ministry of Health on procurement.

Rifampicin, (R), Isoniazid (H), Ethambutol (E) are procured through Bulgarian manufacturers (Actavis for R, Mieve for E and H) and a Slovenian manufacturer for Z (Krka). Strepromycin (S) is procured through the Global Drug Facility (GDF) under Direct Procurement mechanism since 2007 after the Bulgarian manufacturer stopped its production.

All SLD are procured through GDF/IDA supplier following GF quality policy and benefitting from concessional prices and good quality of the products.

The TB drugs and laboratory supplies are funded by the national budget for FLD and TST and by the GF for SLD and laboratory supplies (Table 7). The yearly average budget and expenditure for TB drugs is about 75 000€ for FLD and 180 000€ for SLD and TLD representing about 33 € per FLD treatment and 3 600€ per S/TLD treatment (3 900€ in 2015 with Cm).

Table 7. Funding of anti-tuberculosis drug and laboratory consumables in Euros by source; 2009–2014

Euro	Expenditure					Budget
	2009	2010	2011	2012	2013	2014
TOTAL	713 770	513 101	518 106	762 283	213 038	884 164
Ministry of Health budget	156 851	218 109	253 062	150 359	122 040	163 082
First Line drugs	65 524	88 067	118 346	54 349	37 952	74 789
PPD-tuberculin	91 327	130 042	134 716	96 009	84 088	88 293
GF budget	556 919	294 992	265 044	611 924	90 997	721 082
Rd6 SLD and lab	556 919	244 122	158 127	417 164		
Rd8 SLD and lab		50 870	106 917	194 760	90 997	721 082

FLD drugs currently purchased on national and Balkan market have a price about 30% higher than what is offered by GDF. The Ministry of Health could benefit from lower prices if using WHO recommended strength and presentation in Fixed Dose Combinations and WHO prequalification drugs through the GDF procurement mechanism using same regulation path as for S.

The NRL takes part in the national procurement system. Laboratory supplies amounting to about 150 000€ per year should increase with use of Xpert with quantity to be defined according to diagnosis algorithm.

The Ministry of Health does not allow international tenders nor direct procurement with the exception of emergencies and drugs and equipment under regulation 10 which currently include all SLD and TLD and S. The Ministry of Health should consider adding adult and paediatric Fixed Dose Combinations and Xpert machines and cartridges on regulation 10 list allowing procuring quality-assured and concessional priced products from the existing TB international mechanisms such as GDF.

Registration and quality control

The National Council on Prices and Reimbursement of Medicinal Products is the regulation authority which registers the products on the Positive Drug List (PDL), approves the specification, indication, prices and reimbursement by Health Insurance and controls the sale with approved prices. The sale does not apply for TB drugs distributed only in TB hospitals and free of charge for patients. Loose TB drugs (R, H, Z, E) are registered meeting the required quality standard (GMP rule, US or EU pharmacopae certification, authorisation in other countries of EU, analysis of batch). Other TB drugs which are not registered are procured through GDF with batch control upon arrival.

Most TB drugs except R, H, Z, E receive a waiver for registration (regulation 10). Due to the size of the market it is not attractive enough for manufacturers to initiate a registration procedure. The registration process takes about six months and there are no particular conditions encouraging new supplier to enter into the small market of Bulgaria.

BDA houses the quality control laboratory for all drugs and is operating under ISO17075 certification. A drug quality control system exists, and no quality failure was recently reported for TB drugs. BDA also perform market surveillance and no event was found in recent years. BDA supervises safety of medical devices through a pharmacovigilance system.

The ancillary drugs to support the TB treatment are procured by Gaborovo hospital with its own local budget and are made available free-of-charge to the hospitalised patients.

Distribution, storage, and rationale use of drugs

The review team visited 11 of the 29 TB hospitals in the country.

Distribution

TB drugs are distributed through a pull system mechanism with sufficient buffer stock in place in all 29 TB hospitals. Each TB hospital places an order for FLD TB drugs every two months based on previous consumption, taking into consideration the stock and one month buffer. It takes two to four weeks to receive the drugs after the order is sent. No shortage of TB drugs was mentioned in any of the sites visited during recent years (since 2007). No expiring TB drug was observed during the visit and first in, first out procedure was applied.

The delivery of the laboratory supplies is done directly by the providers to the different laboratories. The NRL doesn't participate in the distribution of supply. No interruption in laboratory work occurred in the last year as a result of shortage of supplies but all the laboratories visited reported a slow and heavy tender procedure taking about five months. Because of this, last year, there was a small delay in the realisation of genotyping of the MDR strains in the NRL caused by a lack of MIRU-VNTR kits, and currently the Löwenstein-Jensen tubes used by the laboratory of Ruse and the MGIT kits used in Pleven have exceeded the expiration date (May 2014). Moreover, the Genotype MTBDRplus kits observed in the laboratory of Pleven had expiration dates of 2013 and 2012.

Storage

The storage conditions for FLD were found to be satisfactory with proper computerised recording and a very good drug inventory tool at TB hospital level, facilitated by the fact that only a limited amount of drugs were kept. There is no storage of TB drugs at the central level except for S kept at Saint Sofia Hospital (specialised hospital for active TB and lung disease). Most TB drugs are distributed directly from the manufacturer/supplier to the TB hospitals.

SLD TB drugs storage conditions were not optimum. They are stored in the Gabrovo hospital pharmacy which is located on the last floor of the building under the roof. There are no shelves, boxes are laying directly on the ground without palette, in contact with one wall which is presenting some moisture. Another location should be found in a more suitable place with more space and with shelves. The mission notices an overstock of Lfx due to a decrease of MDR TB case notification and use of a single shipment of MDR TB in 2013. The SLD order was placed through Global Drug Facility (GDF) with excessive quantity for MDR TB due to too high quantification. The next delivery is correctly planned with two shipments except for injectable drugs.

Concerning the management of the supply in the laboratory, the laboratories keep the delivery documents provided by the manufacturers with the date of delivery and the list of received reagents. In the NRL, an 'inventory visit' is also realised once a year by the person responsible for financial aspects. Reports of these visits containing the list of reagents, expiration date, price, etc. were available.

Reagents were found to be stored adequately.

Rational use

All anti-TB drugs are provided free-of-charge including the ancillary drugs. Although all patients are on a daily treatment regimen for category 1 and 2, the treatment guidelines still include a three times weekly category I treatment regimen during the entire treatment which is no longer recommended by WHO (and not used in the country).

Patients are receiving the proper dosage of TB drugs and MDR TB drugs. However, as already mentioned before, the availability of single loose drugs in different forms creates opportunities for many physicians to deviate from the national treatment protocols and for the patients to assume incomplete treatment and amplify drug resistance. Another problem in the rational use of drugs is the unavailability of paediatric anti-TB drugs formulations which forces providers to crash tablets, open capsules and roughly calculate doses. Another concern regards the use of S for children (2SRHZ/4RH). Lastly, dosages for children are similar to those for adults which is not conform the WHO rapid advice guidelines.

The review team visited few private pharmacies, it was unable to buy first-line anti-TB drugs but able to buy some of the second-line ones (Lfx, Ofxn, Km). However, a medical prescription was always requested.

The Bulgarian Drug Agency has established a system of pharma-covigilance that routinely collects the information on adverse drug reactions. However, no event has been reported so far for TB drugs although a severe case of adverse reactions were mentioned during visit. The review team observed that adverse reactions are recorded in TB patient cards but are not reported to BDA.

Recommendations

- The Ministry of Health and the National Council on Prices and Reimbursement of Medicinal Products should register adult and children Fixed Dose Combinations (RHZE 150/75/400/275, RHE 150/75/275, RH 150/75, RHZ 60/30/150, RH 60/30, RH 60/60), GeneXpert equipment and cartridges.
- The TB Expert Group and National Consultant should consider updating the guidelines for adult and paediatric TB treatment to include Fixed Dose Combinations in accordance with the recent WHO guidelines (paediatric rapid advice guidelines).
- The Ministry of Health should procure Fixed Dose Combinations for FLD for children and adults, and GeneXpert under regulation 10, from the existing TB international mechanisms such as GF. Children FLD should be procured with 2 shipments per year given its short shelf life.
- The Ministry of Health should place a SLD order with two shipments per year for all SLD (and paediatric if adopted).
- NTP should promote the use of the pharmaco-vigilance system for TB drugs.

Assessment of the tuberculosis surveillance system

Overall description of the tuberculosis surveillance system

The principles and legal framework for TB surveillance in Bulgaria are based on Ordinance N°21 of 18 July 2005 on procedure for registration notification of communicable disease. Methods (variables and reporting forms) were standardised based on an Ordinance of the Minister of Health No RD09-426 of 10 August 2009. In the 2012–2015 TB programme, one of the operational objectives of the action plan is specifically: 'to provide effective management and coordination of the NTP of TB'.

At the national level, the TB surveillance system is coordinated by the Directorate for Prevention and Control of AIDS, Tuberculosis and STIs at the Ministry of Health. Within the National Centre for Public Health and Analysis, a specific unit is working on HIV, TB and Sexually Transmitted Disease surveillance and is responsible for collecting and analysing data obtained through the routine TB surveillance. Three persons are working on TB including:

- two medical doctor epidemiologists (working part time) on TB surveillance
- one database manager working full time on TB surveillance.

A TB register with patient-based information was implemented in 2008 based on information collected from the TB hospitals, prisons and military settings and the national level.

The RHIs are involved in controlling the implementation, the methods and the results of TB contact investigation but are not directly involved in the TB surveillance process.

Methods of data collection for tuberculosis surveillance

The case definition used for surveillance was changed in 2008 to be consistent with the one used at the European Union level and includes all TB cases whether or not they are laboratory confirmed. The change in 2008 was according to Ordinance №21. Cases are classified as 'definite' (isolation of *M. tuberculosis* complex from a clinical specimen or positive sputum smear if culture not routinely performed) or 'other than definite' (based on clinical criteria, without laboratory confirmation).The case definition and algorithm for TB surveillance are included in a national guideline that has been disseminated in all hospitals and is also used by the RHI.

At the hospital level, clinicians are entering information on TB patients in a paper register and in a dedicated Excel application. This application is standard and is used at the hospital both by the clinicians and laboratories and at the national level.

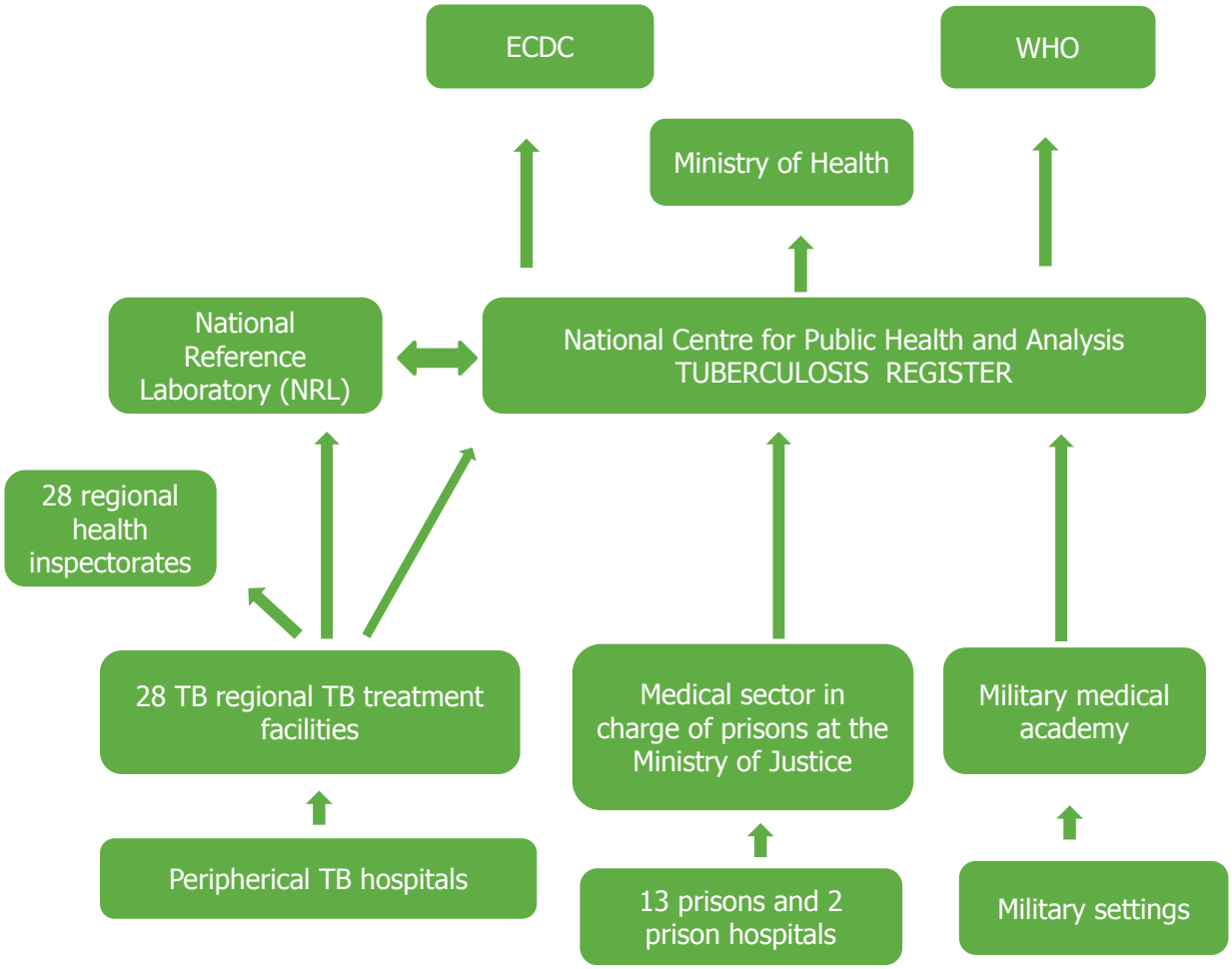
Case-based information on TB cases is sent by hospitals quarterly through Excel spreadsheets to the national level (Figure 7). Information on TB cases is also provided separately by the 13 prisons and two prison hospitals and military medical settings to the national level. The prisons and prison hospitals are under the authority of the Ministry of Justice and the Military Medical Academy is under the authority of the Ministry of Defence. If a case moves from hospital to prison, information on the TB case will be sent by prison to the national level but the hospital that was initially in charge of the patients may not necessary be informed of the updated information on the patient.

The 35 laboratories performing TB diagnosis are submitting information to the NRL quarterly in Excel spreadsheet (Figure 7). At the NRL level, data are entered into a paper register (mandatory) and then entered into an excel spreadsheet. Data on MDR TB cases are transmitted monthly to the national TB register.

In addition to flow of information for the national TB register, hospitals have to send:

- quick notice on TB case to RHI and general practitioner
- information on TB cases monthly to RHI
- information on contacts to RHI and national level.

Figure 7. Information flow for TB surveillance



Sources: Bulgaria, National Centre for Public Health and Analysis

Completeness and validation of data

Validation of the TB register at the national level includes standard controls for errors and inconsistencies. The persons responsible for surveillance may contact hospitals for corrections. To improve the data quality of the TB register, the national level experts pay regular visits (at least once a year) to each hospital to discuss TB surveillance.

According to the national Unit in charge of TB surveillance, the system records all TB cases diagnosed in Bulgaria. There is a good completeness (over 80%) on most information collected in the TB register.

Data analysis and dissemination

Analysis of national data from the register is done manually with Excel and is mainly based on standard tables. A report including these standard tables is disseminated on the TB control website. There is no in-depth analysis of surveillance data and results seem to be insufficiently used at the national and local level. The register provides the main epidemiological information that can be used for monitoring and evaluation, and policy development. Information is also provided to ECDC and WHO. Dissemination of national data is done through a report posted each year on the TB control website and national and regional results are sent to the RHI.

The information collected gives a good description of the national TB epidemiological situation in Bulgaria. Data are collected on place of birth and HIV status. However, analysis on risk factors is very limited and the system does not include information that would provide relevant information on most at risk population groups for Bulgaria, such as the homeless, prisoners, persons in congregate settings or other vulnerable groups. National regulation on ethics and confidentiality is limiting the collection of information on ethnic groups. Since the surveillance system does not collect information on risk factors, it is not possible to identify the population groups most at risk for TB.

Monitoring and evaluation of the Global Fund project

Besides the routine surveillance system for TB, a monitoring and evaluation system has been implemented as part of Global Fund grants. The National TB Programme manages a web-based system for collection, aggregation, processing and analysis of results achieved by sub-recipients (mainly NGOs). Reporting to this system consists of regular reporting from the local level to the regional, from the regional to the national level. It aims to monitor and evaluate the interventions of all stakeholders. Data collected includes information on TB control activities and information on TB suspects, including on risk factors. However, for the moment, information on total population by sub group is lacking. It is, therefore, not possible to use the information to calculate the TB incidence and to identify the population groups more at risk.

Key observations

- Dedicated unit for TB surveillance at the national level.
- Information collected is case based.
- Paper and digital means used to collect, store and analyse data with risk of error and high workload.
- Good collaboration between national level and hospitals.
- Dissemination of national data done through report posted on TB control website.
- Lack of in depth analysis including on trends.
- Insufficient and heterogeneous use of surveillance data at local and national level.
- Good completeness of most collected information.
- Sensitivity of the register very good according to the epidemiologist in charge.
- Partly duplication of system (RHI have their own TB register).
- Lack of information on risk factors which allows to identify the most at risk population group.

Recommendations

- To improve exchange and linkage of information, timeliness and to limit the workload and the risk of error when using paper or digital means, it is recommended to develop a patient web-based system. This could avoid possible duplication of systems (for example with a possibility for RHI to have access to their data) and facilitate linkage of information of the TB register and of the NRL.
- To fully use the potential of surveillance it is recommended to develop in depth analysis of data stored at national level using appropriate software and to consider developing training on analysis of data for the national team in charge of TB surveillance.
- To identify the population groups most at risk of TB, it is recommended to increase the use of surveillance information, especially to identify key populations and vulnerable groups and to develop the data collection on relevant risk factors either in the TB register or through ad hoc surveys.

Non-Governmental Organisation engagement

Terminology

The terms 'civil society organisation' (CSO) and 'non-governmental organisation' are largely interchangeable, both meaning organisations that are neither governmental nor commercial. In international usage 'NGO' tends to be used for larger and international agencies while 'CSO' is used for smaller, localised bodies. In Bulgaria, however, 'NGO' is used in both cases. As the primary audience for this report is Bulgaria, their practice is followed and 'NGO' is used throughout.

Use of NGOs

At the time of accessing GF funds in 2008, a strategic decision was taken by the NTP to supplement formal health service capacity by engaging NGOs in accessing risk groups. Consultations took place, risk areas were agreed, and in three waves since then, the NTP has recruited NGOs by inviting Expressions of Interest, going through a selection process and entering into contracts with, at present, around 26 NGOs.

The review team met 12 of these NGOs, four together in Sofia, and eight individually in the course of visits to other parts of the country. The picture described by these agencies was remarkably consistent. They spoke of good working relations with both the NTP and their local health services, clear understanding of their functions as increasing awareness of TB in the risk groups within which they worked, screening for TB, facilitating access to risk communities by formal health staff, notably the 'patronage nurses' (described below) and RHI staff, and assisting with compliance by individual patients.

The majority of the contracted NGOs are small local bodies active within their own communities such as Roma, injecting drug users or mental health groups; although there are a few larger ones like the Bulgarian Red Cross working in more than one area. Most had little or no involvement with TB beforehand and are unlikely to have become active on TB without being recruited and receiving funds (from GF budgets) for this work.

Responding to risk

The system of contracted NGOs can be flexible. For example, by using NGOs, the NTP has been able to respond rapidly to the influx of Syrian refugees experienced by Bulgaria over the past three years.

Similarly, an NGO was contracted to increase TB awareness among the increasing influx of Russian retirees moving to settle on the Bulgarian coast. However, due to the method of involving NGOs by contracting, the work has been continued despite developing evidence that TB risk in this community of relatively well-off individuals is low. On the other hand, the same NGO works with homeless individuals, sees evidence among them of significant TB risk, but is not contracted to increase TB awareness in this other group.

Engaging individuals with personal experience of tuberculosis

No TB patients' organisations appear to exist in Bulgaria either at the national or local level.

No NGO appears to have made any particular effort to recruit a cadre of current or recent TB patients to assist in their TB work. Some NGOs were able to refer to one or two individuals among their staff or volunteers who had personal experience of TB.

Patronage nurses

A key component linking the work of NGOs and that of the formal health services is the cadre of patronage nurses. 'Patronage' in Bulgarian refers to home care. Each TB hospital designates a couple of experienced nurses to spend a part of their working time visiting patients in the community and supporting the activity of NGOs. In effect, they ensure a skilled medical backbone to the community outreach work of NGOs.

It was noticeable that when asking such nurses what added value was brought by the NGOs, all said access to hard to reach individuals and communities. They recognised that without the NGOs they would be limited to the extent that they are accepted by individuals and groups who are often suspicious of professionals from official public services.

Both NGOs and patronage nurses reported good working relations with each other. There were indications that this harmony had not been so at the outset. It had been achieved by conscious training and other efforts by the NTP bringing the two sides together when the NGOs were first recruited. It is also possibly helped by the fact that the salary supplements and costs associated with work outside the hospital are paid to them by the NGOs, thus making the patronage nurses in part employees of and dependent on the NGOs.

Tuberculosis and the regional health inspectorates

For each county there is an RHI responsible for a range of public health functions. As regards TB these include registration and monitoring of individual TB cases, and also public information communications about TB.

Like the patronage nurses, RHI staff are appreciative of NGOs assisting them achieve access to hard to reach patients. Collaboration between NGOs and RHI staff has become a normal, accepted part of work patterns.

Collaboration and advocacy among NGOs

No mechanism exists for regular interaction among NGOs engaged in TB activity. There is no network of TB-interested NGOs or any version of a national Stop TB Partnership.

Some of the NGOs meet in the context of other networks such as those engaged in HIV activity or those working in Roma communities. TB-NGOs based in Sofia have made one attempt to jointly talk to the Mayor about TB in the city but this attempt was not successful.

The NTP is currently deeply engaged in preparation by mid-August of a Concept Note for submission to the GF. If successful, it is from these funds that NGO TB activity will be funded for the next three years. NGOs expect to be consulted by the NTP once a tentative draft is available but they have not met or otherwise discussed what issues of interest to NGOs they want to press for to be included in the Concept Note.

Long-term sustainability of the NGO role in support of the NTP is dependent on funding. Indeed several significant aspects that currently make the NTP effective are dependent on GF funding. While it is probable that GF funds will be available for a further three years, government or alternative external funding will be required after that. So far, TB-active NGOs have not focused on this as an advocacy issue either as regards to funding of their own role or the broader issue of maintenance of NTP effectiveness at maintaining the current rate of decline in TB incidence in Bulgaria.

Key observations

- The NTP has devised and operates an innovative way of engaging local NGOs, extending the ability of the NTP to undertake screening and case finding within risk group populations.
- This has led to an exceptionally close relationship between health services and NGOs not seen in other countries, leading to a significant increase in screening and contact tracing.
- Sustainability of this system is dependent on continued funding. NGOs report that if not contracted, they might maintain some focus on TB but screening activity would definitely cease.
- Identification of risk groups has been effective and flexible but occasionally slow to adapt to changing data.
- There is a lack of patient groups with a focus on TB; and a lack of recognition by both NTP and NGOs that people with personal experience of the disease can be exceptionally effective in building community awareness of TB, training of health staff, and advocacy.
- Patronage nurses are a key component of NTP action at field level, and in linking NGOs and health services. Sustainability, however, is fragile as their outreach role is dependent on temporary funding.
- RHIs undertake some TB awareness building and health promotion activity but it is limited and not sufficiently focused on key and vulnerable populations.
- Interaction among TB-active NGOs is occasional and informal. There is no mechanism through which they might increase their ability to share learning, interact with the NTP, and engage in broader advocacy for action on TB.

Recommendations

- The process of contracting NGOs to facilitate access to at-risk and vulnerable populations and to undertake screening and awareness work is important and should be continued.
- Similarly, the current structure of NGOs and patronage nurses linked to RHIs and the TB hospitals should continue.
- To ensure future sustainability of this structure, it is recommended that the contractual and work position of patronage nurses be reviewed. Their hospital workload should be such that time outside the hospital is possible as a regular part of their activity.

- Resources should be switched when data emerges showing a group not to be as much of a TB risk as first thought; and vice versa when evidence arises of a risk group such as the homeless, not currently acted on by the NTP through NGOs.
- Efforts should be made to identify individuals who are current or recent TB patients who are willing to be drawn into TB field activity, probably as staff or volunteers of NGOs. Should national or local patient groups emerge, they should be encouraged an supported.
- RHIs should intensify their TB communications activity, focusing on key and vulnerable populations. They are well-placed to develop comprehensive approaches to all the challenges faced by each group and to incorporate TB activity as part of a broad spectrum of health and social interventions.
- NGOs engaged in TB activity should look to improve networking among themselves in order to share learning and techniques amongst themselves, interact more effectively with the NTP, and engage in broader TB advocacy. The NTP should welcome and encourage this.

Conclusions and recommendations

Specific recommendations are provided in the chapters above. Below we summarise the main issues considered essential for successful TB control in Bulgaria.

The Bulgarian TB prevention and control programme contains a number of essential components that are depending on GF funding for implementation

- management of National TB Programme
- drugs for MDR TB treatment
- incentives for patronage nurses for field work
- support for transport and food coupons for TB patients
- laboratory activities necessary for MDR TB
- NGO activities on screening.

Global Fund funding is temporary and therefore the sustainability of the implementation of the components mentioned above is not guaranteed. Discontinuation of the implementation of these components will seriously jeopardise the success of TB prevention and control in Bulgaria. Continuous successful implementation of TB prevention and control needs the inclusion of funding of the above components in the national budget for TB prevention and control.

Bulgaria has made great progress in TB prevention and control. Many activities are implemented. However, some activities remain to be implemented and others should be fully implemented. Below we list these activities:

- Strategy for early and active case-finding among key risk groups.
- Use of rapid diagnosis test for all MDR TB presumed cases (suspects) to speed up the start of MDR TB treatment.
- Re-organisation of the laboratory network (signing of Order).
- Xpert first line DST testing for all culture positive TB patients.
- National infection control strategy.
- Standardised approach to contact tracing activities.
- HIV testing among TB patients.
- Use of the pharmaco-vigilance system for TB drugs.

In addition the programme would benefit from making the following changes:

- Reduce duration of hospitalisation for TB and MDR TB patients.
- Develop web-based surveillance system that also collects information on risk factors.
- The Ministry of Health and the National Council on Prices and Reimbursement of Medicinal Products should register adult and children Fixed Dose Combinations, GeneXpert equipment and cartridges.
- Abandon follow up TSTs and chest X-ray at three and six months after the start of TB preventive treatment.
- Abandon BCG re-vaccination policy.

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Annex 1. Terms of reference

Review of the National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria 2012-2015

Aim

The aim of the review is to assess the Programme's contribution to TB prevention and control in the Country, to identify the gaps in the implementation of the present Programme and to make recommendations for needed improvements in Programme's implementation as well as for future strategic planning of TB prevention and control activities.

Objectives

The objectives of the review of the National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria, 2012-2015 ("NTP") are:

1. Assessment of the current performance and sustainability of the Programme and development of recommendations for future activities;
2. Assessment of the TB surveillance system and analysis of the epidemiological data;
3. Assessment of the implementation of the National MDR/XDR-TB plan in Bulgaria and assessment of achieved results and obstacles;
4. Assessment of the anti-TB drug supply management;
5. Assessment of the microbiological diagnostics of TB and MDR TB in the country and the operation of the laboratory network;
6. Assessment of current engagement with civil society organisations (CSOs) and patient groups, and of the extent to which their potential contribution to the detection, treatment and care of individuals with TB is maximized;
7. Present specific recommendations regarding the actions and priorities for the next stage of the National TB Programme and National Health Strategy for the period 2014 – 2020.

During the review of the National TB Programme the following documents are taken into account: the Millennium Development Goals, the WHO Strategy to Stop TB, the Global Plan to Stop TB 2006 – 2015; the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug Resistant Tuberculosis in the WHO European Region, 2011-2015; the Framework Action Plan to Fight Tuberculosis in the European Union,

Background Information

The National Programme for Prevention and Control of Tuberculosis in Bulgaria 2012-2015 was adopted by Council of Ministers of the Republic of Bulgaria on 2 May 2012.

The main goal of the Programme is to reduce the transmission of the tuberculosis infection and to limit the development of drug resistance.

Achieving this goal can be reached by means of:

1. Strengthening the infrastructure, the management and coordination between the separate elements of the healthcare system which are involved in the control of tuberculosis in the country.
2. Performing adequate epidemiological surveillance, timely diagnosis of TB and LTBI and efficient tuberculosis treatment.
3. Timely tuberculosis diagnostics, treatment and care of MDR TB and XDR-TB cases;
4. Timely tuberculosis diagnostics in children and chemoprophylaxis;
5. Timely TB case finding and diagnosis among vulnerable groups;
6. Treatment in line with the international standards.

The National programme has 9 operational objectives:

1. Ensuring effective management and coordination of the NTP;
2. Timely diagnostics and control of tuberculosis;
3. Successful treatment of tuberculosis in Bulgaria;
4. Successful treatment and control of multi-resistant and extensively-resistant tuberculosis;
5. Control of child tuberculosis;
6. Reduction of the transmission of tuberculosis in Bulgarian prisons;
7. Restriction of the spread of tuberculosis in the Roma community and in groups at risk;
8. Diagnostics and treatment of persons with latent tuberculosis infection;
9. Raising public awareness.

The expected results of the implementation of the National Programme for Prevention and Control of Tuberculosis in the Republic of Bulgaria for the period 2012-2015 are:

- reducing the TB incidence;
- improving the treatment outcome of the newly discovered smear – positive patients;
- reducing the percentage relapse and patients on re-treatment;
- reducing the chronic cases and patients with MDR TB and XDR-TB;
- improving the knowledge of the population about the problems related to tuberculosis;
- increasing tolerance and concern of society and institutions to the risk groups;
- positive change among groups–at-risk to seek medical aid.

This will contribute to achieving the main objective of the National Programme: to reduce the transmission of tuberculosis and the development of drug resistance.

Specific objectives of the review

Objective 1: Assessment of the current performance and sustainability of the Programme, and development of recommendations for future activities.

Specific objectives:

1. To assess the efficiency of the activities and the implementation of the Programme, as well as the achievements and/or the obstacles;
2. To identify the main problems faced by the National Programme at different levels: national, regional, institutional level;
3. To assess the availability, accessibility, utilization and quality of the services (activities for prevention and control of tuberculosis, activities for prevention of the development of resistant forms of tuberculosis, stigma and discrimination, direct observation of treatment in the continuation phase, contact investigation in the most at risk and general population);
4. To identify the gaps and opportunities for collaboration between the different institutions.

Objective 2: Assessment of the TB surveillance system and analysis of the epidemiological data.

Specific objective:

1. To assess the epidemiological surveillance, the registration and reporting of TB cases;
2. To assess the quality, accuracy and suitability of the TB surveillance system.

Objective 3: Assessment of the implementation of the National MDR/XDR-TB plan in Bulgaria and assessment of achieved results and obstacles.

Specific objectives:

1. To assess the results and achievements in the implementation of the National M/XDR-TB plan in terms of:
    - Diagnosis of M/XDR-TB;
    - Ensuring treatment;

- Ensuring directly observed treatment in the continuous phase;
- Role of the social services in the support and motivation for treatment;
- Role of the local municipal structures in the support of patients with tuberculosis and their families;

2. To identify how the health system works and what could be improved in the health system in order to obtain better results in M/XDR-TB treatment.

Objective 4: Assessment of the anti-TB drug supply management.

Specific objectives

1. As part of the overall review of the National TB programme, to assess all different aspects of drug supply management, including first, second and third-line anti-TB drugs, either from national or international sources, and ancillary drugs;
2. To review the GDF current support and adherence to GDF terms and conditions, and provide technical support in drug management (including quantification of drug needs).

Objective 5: Assessment of the microbiological diagnostics for TB and MDR TB in the country and the operation of the laboratory network.

Specific objectives

1. To identify what microbiological diagnostics are used at what level;
2. To assess the functioning of the laboratory network;
3. To assess quality of microbiological diagnosis, including the internal and external quality assurance system;
4. To assess the management (including supply, procurement) of consumables for microbiological diagnosis of TB and M/XDR-TB.

Objective 6: Assessment of current engagement with civil society organisations (CSOs) and patient groups, and of the extent to which their potential contribution to the detection, treatment and care of individuals with TB is maximized.

Specific objectives:

1. To assess the scale, nature and geographic coverage of the contribution to TB detection and care by CSOs.
2. To assess the nature of coordination between the NTP and CSOs, and by CSOs amongst themselves.
3. To assess the support available to CSOs for work relating to TB and to TB/HIV co-infection.
4. To assess in what ways the voice of people with personal experience of the disease is facilitated and heard.

Objective 7: Provide specific recommendations regarding the actions and priorities for the next stage of the National TB Programme in line with the WHO strategies on TB and MDR TB microbiological diagnosis, treatment and control as well as with the National Health Strategy for the period 2014 – 2020.

Scope of the work

The evaluation team will use qualitative and quantitative methods for collection of information, including an analysis of TB surveillance data.

Desk review:

Before the field visit the team will study documents made available to them or relevant documents obtained from the public domain. These documents can cover:

- Programmatic data, i.e., number and kind of services provided; size of population, people reached by the programme, by vulnerable groups and geographic areas; facility data on services utilization;
- National strategic documents and policies related TB and MDR TB;
- Financing data, i.e., committed budget, disbursement and expenditure against disease burden;
- Existing surveys and surveillance reports and documents on number and type of offered services, and use of services and the health system; as well as relevant studies;
- Population size by target groups, known factors facilitating and inhibiting the programme implementation; best practices from national programme and other international programmes.

Interviews with stakeholders, service providers, clients etc. during field visits:

During the review in Bulgaria the team of experts will conduct visits and have meetings and one-on-one interviews with relevant stakeholders at national and local level:

1. At national level: TB Programme staff, Ministry of Health structures: National Center of Infectious and Parasitic Diseases, The National Reference Laboratory for TB, Unit in charge of procurement of drugs, Centres responsible for management, storage and delivery of drugs, National drug regulatory authority, Organization responsible for customs clearance, Partners/donors working in TB and drug distribution, others as identified;
2. At local level: service providers in health care system (TB treatment centres including hospital and clinics at central, intermediate and peripheral levels, Microbiological laboratories, Service providers for vulnerable populations, Civil society organizations, Centres responsible for management, storage and delivery of drugs, Private sector- GPs Pharmacies, Partners/donors working in TB and drug distribution, Local TB Drug Manufacturers (if applicable), others as identified.

Collection of data and analysis of information:

- Each expert in the review team will be assigned responsibility for specific objectives;
- Expert conducts the data collection and analysis in accordance to a plan;
- Expert presents his/her main findings to the review team;
- Review team discusses findings and clarifies any inconsistencies or collects additional information;
- Expert develops draft suggestions for action for his/her area(s) of responsibility;
- Review team discusses all draft suggestions for action and experts agree on formulation of final suggestions for action.

Reporting, finalization and dissemination:

- Each expert drafts his/her chapter(s) for the report;
- Team leader collects all draft chapters and circulates the draft report for comments to the review team members;
- Team leader compiles the comments on the draft report;
- If needed a teleconference is organized with the review team to finalize the draft report;
- The draft report is submitted to the Ministry of Health of the R. Bulgaria for their review;
- Review team incorporates suggestions from the Ministry of Health of the R. Bulgaria in a final version of the review report;
- Review report is edited and submitted to the Ministry of Health of the R. Bulgaria.

Composition of the review team

A multidisciplinary team of experts will carry out the above mentioned activities.

Name	Organization	Objective
Marieke J. van der Werf (team leader)	ECDC, Stockholm, Sweden	Objective 7
Giovanni Sotgiu	WHO Regional Office for Europe (external consultant), University of Sassari, Italy	Objective 1 and 3
Sören Thybo	WHO Regional Office for Europe (external consultant), University Hospital Rigshospitalet, Copenhagen, Denmark	Objective 1 and 3
Pierre-Yves Norval	Global Drug Facility, Geneva, Switzerland	Objective 4
Paul Sommerfeld	WHO Regional Office for Europe (external consultant), London, United Kingdom	Objective 6
Andreas Sandgren	ECDC, Stockholm, Sweden	Objective 1
Csaba Ködmön	ECDC, Stockholm, Sweden	Objective 5
Vanessa Mathys	ECDC (external consultant), Scientific Institute of Public Health, Brussels, Belgium	Objective 5
Delphine Antoine	ECDC (external consultant), Institut de Veille Sanitaire, Paris, France	Objective 2

Deliverables

1 Debriefing presentation
2 Draft evaluation report
3 Evaluation report

Report

The report on the review of the National TB Programme of Bulgaria will be in English.

The report will contain:

- Title
- Table of contents
- List of acronyms and abbreviations
- Executive summary with key suggestions for action
- Introduction
- General information
- Evaluation approach and methods
- Findings and suggestions for action by objective
- Annexes (including agenda of review mission)

Annex 2. Programme for the Bulgaria National TB Programme Evaluation, 2–9 June 2014

Group	Participants	Mon, June 2	Tue, June 3	Wed, June 4	Thu, June 5	Fri, June 6	Mon, June 9
Group 1	Giovanni Sotgiu, Andreas Sandgren, Vanessa Mathys Prof. Osmanliev Prof. Minchev Blagovesta Gadjeva	Sofia (see p.2)	Sofia Plovdiv Hospital RHI NGO "Roma" Sofia	Sofia Ruse Hospital TB Lab NGO "Center Dinamika"	Ruse Pleven Hospital TB Lab Sofia	Sofia	Debriefing
Group 2	Pierre Yves Norval, Soren Thybo, Csaba Kodmon Dr Maria Zamfirova Prof. Stefanova Kristian Hristov	Sofia (see p.2)	Sofia Lovech Prison Hospital Trojan Hospital TB lab Gabrovo	Gabrovo Hospital (MDR sector) Pharmacy NGO "Social Dialogue 2001" PHC Sofia	Sofia Vratsa Hospital NGO "New way" PHC/RHI Sofia	Sofia	Debriefing
Group 3	Paul Sommerfeld, Delphine Antoine, Marieke van der Werf Dr. Vladimir Milanov Yuliya Stankova Bahtiyar Karaahmed	Sofia (see p.2)	Sofia Haskovo Hospital RHI Refugee Center – NGO "Ikar" Haskovo	Stara Zagora Hospital NGO "World without borders" RHI Burgas	Burgas RHI NGO "Caritas" NGO "Dose of Love" Sofia	Sofia	Debriefing

Programme for the Bulgaria national TB programme evaluation, 2–9 June 2014

Monday, June 2

	Group A: Pierre Yves Norval, Soren Thybo	Group B: Giovanni Sotgiu, Paul Sommerfield, Andreas Sandgren, Marieke van der Werf	Group C: Csaba Kodmon, Vanessa Mathys, Delphine Antoine
9:00 – 12:00	Meeting with the Department of "Specialized Donor-funded Programmes" at MoH (Conference room) Presentations on organisation of health system, TB programme, overview on TB prevention and control in Bulgaria, human resources and budget for TB control		
Lunch break			
13:00 – 16:00	Meeting at Drug Policy Directorate, MoH Dr Velkovska Dr Varleva	Meeting at Regional Health Inspectorate (RHI), Sofia Dr. Ognyan Ivanov, Director of RHI and Dr. Ilonka Maeva, Director of „Control of Infectious Diseases " Directorate	Meeting at the National Reference Lab, NCIPD Dr Bachijska, Head of the NRL Staff
16:00 – 18:00	Meeting to prepare the field visit (data collection, field visit debrief format, mission report format, else) Conference room		

Friday, June 6

	Pierre Yves Norval	Delphine Antoine, Marieke van der Werf	Soren Thybo, Vanessa Mathys, Paul Sommerfield, Andreas Sandgren, Giovanni Sotgiu
9:00 – 10:00	Meeting with Kosta Yannis, focal point on drug supply and management for the GLC Drugs	Meeting with Dr Maria Zamfirova and Dr Maria Tufekchieva, focal points for the National TB Surveillance Programme	
10:00 – 11:00	Meeting with Bahtiyar Karaahmed, focal point for the supply of Streptomycine drug		Meeting at the St Sofia Hospital for Lung Diseases, Children TB clinic
11:00 – 12:00	Meeting at the Executive Agency on Drugs, responsible for the Quality Assurance of GLC drugs		
Lunch			
13:00 – 15:00	Meeting with NGOs at the Department of "Specialized Donor-funded Programmes" at MoH (Conference room) "Initiative for Health" Foundation, Obj. 5 "Bulgarian Red Cross" Association, Obj. 4 Patients' organization		
15:30 – 17:00	Debriefing between teams (Conference room)		

Monday, June 9

10:00 – 11:00 11:30 – 14:30	Debriefing with deputy minister –prof. Chavdar Slavov Debriefing with the Department of "Specialized Donor-funded Programmes" at MoH, Tonka Varleva, Maria Zamfirova, Maria Tjufekchieva, Plamen Ivanov, Yulia Stankova, Anna Keshelava

Annex 3. People and organisations met and contacted

Name	Organisation
Elizabeta Bachiyska	TB National Reference Laboratory, NCIPD
Petko Minchev	Hospital for Lung Diseases 'St Sofia', Sofia
Vyara Georgieva	Chief Expert, Ministry of Health Department MSDFP
Plamen Ivanov	Manager 'Monitoring and Evaluation' PMU, Ministry of Health
Donka Stefanova	Hospital for Lung Diseases 'St Sofia', Sofia
Mariya Zamfirova	State Expert Ministry of Health Department MPSDFP
Kristiyan Hristov	Assistant 'Monitoring and Evaluation' PMU, Ministry of Health
Bahtiyar Karaahmed	Expert, Directorate 'International projects and specialized donor-funded programme', Ministry of Health
Vladimir Milanov	Clinician, TB Clinic, University Hospital for Lung Diseases 'St Sofia'
Blagovesta Gadzheva	Programme Assistant, PMU
Tonka Varleva	Directorate 'International projects and specialized donor-funded programme', Ministry of Health
Yuliya Stankova	Directorate "International projects and specialized donor-funded programme', Ministry of Health
Rositsa Krumova Valyova	Expert, 'Epidemiological Control' Department, 'Surveillance of communicable diseases' Directorate, Regional Health Inspectorate, Sofia
Kostadinka Ivanova Pacharuzova	Head of 'Hospital Hygiene and Epidemiology' Department, 'Surveillance of communicable diseases' Directorate, Regional Health Inspectorate, Sofia
Ilonka Maeva	Director, 'Surveillance of Communicable Diseases' Directorate, Regional Health Inspectorate, Sofia
Doncho Nenchev	Deputy Director, Regional Health Inspectorate, Sofia
Veselin Kalfov	Director of Specialized hospital for active treatment of pneumo-phthisiatric diseases and District TB Coordinator, Haskovo
Boyka Guzgunova	Head of Microbiological Laboratory, hospital Haskovo
Yanka Raeva	Patronage nurse, hospital Haskovo
Snezhana Ivanova	Director, 'Control of Infectious Diseases' Directorate, RHI, Haskovo
StanislavaTananova	Deputy Director, RHI, Haskovo
Nina Nikolova	Chief Expert, 'Public Health' Directorate, RHI, Haskovo
Dimka Staleva	Patronage nurse, Specialized hospital for active treatment of pneumo-phthisiatric diseases, Haskovo
Mariana Delchevska	Coordinator, IKAR Association, Haskovo
Plamen Kolev	Outreach worker, IKAR Association, Haskovo
Maria Peteva	Outreach worker, IKAR Association, Haskovo
Petya Tancheva	Outreach worker, IKAR Association, Haskovo
Lyubomir Lyubenov	Director of Specialized hospital for active treatment of pneumo-phthisiatric diseases and District TB Coordinator, Stara Zagora
Vanya Ventsislavova	Head of Microbiological laboratory, hospital Stara Zagora
Tsvetana Rireva	Pharmacy Stara Zagora
Irina Lekova	Pharmacy Stara Zagora
Svetlan Mihaylov	MD clinician and on surveillance, hospital Stara Zagora
Ivaneta Alexandrova	MD clinician entering data on electronic register, hospital Stara Zagora
Fani Ahmed	Patronage nurse, hospital Stara Zagora
Elena Kaneva	Director, Regional Health Inspectorate, Stara Zagora
Bozhidarka Kayrakova	Director, 'Surveillance of Communicable Diseases' Directorate, RHO, Stara Zagora
Tanya Perchemlieva	Head of 'Epidemiological Control' Department, RHI, Stara Zagora
Vanya Karaboyteva	Chief Expert, 'Disease Prophylaxis and Health Promotion' Directorate, RHI, Stara Zagora
Galina Dimitrova	Chief Expert, Psychologist, 'Disease Prophylaxis and Health Prevention' Directorate, RHI, Stara Zagora
Gancho Iliev	Chair, 'World Without Borders' Association
Milena Ilieva	Outreach worker, NGO World Without Borders, Stara Zagora
Margarita Valcheva	Outreach worker, NGO World Without Borders, Stara Zagora
Mariyka Mineva	Outreach worker, NGO World Without Borders, Stara Zagora

Name	Organisation
Valentin Uzunov	Outreach worker, NGO World Without Borders, Stara Zagora
Daniela Georgieva	Director of Directorate 'Control of Infectious Diseases', RHI, Burgas
Velichka Georgieva	Epidemiological Control Department, RHI, Burgas
Ludwila Hristova	Epidemiological Control Department, RHI, Burgas
Vessa Jeljazkova	Epidemiological Control Department, RHI, Burgas
Diana Dimova	Health Promotion and Disease Prevention, RHI, Burgas
Mariana Kofinova	Director of Directorate 'Health Promotion and Disease Prevention' , RHI, Burgas
Emilia Svetoslavova	Epidemiological Control Department, RHI, Burgas
Nela Ivanova	Project Coordinator Intravenous Drug Users, NGO Dose of Love, Burgas
Antoaneta Radeva	President, NGO Dose of Love, Burgas
Kamen Penkov	Project Coordinator Men having Sex with Men, NGO Dose of Love, Burgas
Asena Mateeva	Project Coordinator Commercial Sex Workers, NGO Dose of Love, Burgas
Irina Bulanova	Coordinator Information Centre, Information Centre for Immigrants, International Organisation of Migration, Burgas
Violeta Stoeva	Coordinator Information Centre, Information Centre for Immigrants, International Organisation of Migration, Burgas
Mima Kochevska	Outreach worker, NGO Caritas, Burgas
Bistra Daeva	Outreach worker, NGO Caritas, Burgas
Natalia Sharbanova	Coordinator, NGO Caritas, Burgas
Velkovska	Director, Drug policy directorate , Sofia, Ministry of Health
Zlatina Georgieva	Deputy executive Director, Bulgarian Drug Agency, Sofia, Ministry of Health
Neli Agapova	Head of Department, Analyses of Medical Products, Bulgarian Drug Agency, Sofia, Ministry of Health
Maria Popova	Head of Medicines, Use Control Department, Bulgarian Drug Agency, Sofia, Ministry of Health
Lyudmila Angelova	Head of Department, Control of Medical Products, Bulgarian Drug Agency, Sofia, Ministry of Health,
Kosta Yannis	SLD management, PMU, Sofia, Ministry of Health
Bahtiyar Karaahmed	Streptomycine management, State expert vulnerable group, Sofia, Ministry of Health
Aneta Stavrova	Director, Vrasta, Regional Health Inspector, Ministry of Health
Veli Petrova	Vrasta, Regional Health Inspector, Ministry of Health
Muponsoo Suogopol	Vrasta, Regional Health Inspector, Ministry of Health
Mirolyub Todorov	Vrasta, Regional Health Inspector, Ministry of Health
Keti Tsenova	Vrasta, Regional Health Inspector, Ministry of Health
Petar Dimitrov	General Practitioner, Vrasta
Mariana Stoyanova	Director Dispensary Pneumo-Phtysiatry, Vrasta, Ministry of Health
Bilana Vasileva	Dispensary Pneumo-Phtysiatry, Vrasta, Ministry of Health
Lydia Nikolova	Patronage nurse, Dispensary Pneumo-Phtysiatry Vrasta, Ministry of Health
Nina Metodieva Marinova	Patronage nurse, Dispensary Pneumo-Phtysiatry Vrasta, Ministry of Health
Svetla Peneva	Chair of the executive baord of Social dialogue 2001, Vrasta,
Venelin Velchev	Coordinator of Social dialogue 2001, Vrasta, psychologst
Maya Aurosa	Food nutrition, Social dialogue 2001, Vrasta
Dpapanolova	Food nutrition, Social dialogue 2001, Vrasta
Tsvetomila Dedevska	Director , Specialized hospital for active treatment of pulmonary diseases, Trojan
Bozhkov	DOTS manager, Trojan
Sretoslav	General Practitioner, Trojan
Jordanka Popska	Biologist, laboratory hospital Trojan
Mihajl Mihajlov	Chair of the Board, NGO New Road, Hajredin , Vrasta
Daniela Kostova	NGO New Road, Hajredin , Vrasta
Spaska Petrova	NGO New Road, Hajredin , Vrasta
Marln Kalcheevsky	Director of prison, Lovech, Ministry of justice
Marguerita Trifonova	TB coordinator prison, Lovech, Ministry of justice
Vladimir Tikov	Director of prison hospital, Lovech, Ministry of justice
Mapravta	Nurse of prison hospital, Lovech, Ministry of justice
Antoaneta Gzolgeva	Biologist, laboratory hospital Gabrovo
Tania Spasova	Chief nurse, patronage nurse, Plovdiv hospital

Name	Organisation
Veselin Davchev	Director Plovdiv hospital
Margarita Tsolova	Head of microbiological laboratory, hospital Plovdiv
Tsetsa Penkova	Senior Lab technician, hospital Plovdiv
Denmo Osmanliev	Associate Professor
Asen Antonov	NGO 'Roma'
Anton Karagyozov	NGO 'Roma'
Angel Mihaylov	NGO 'Roma'
Sasho Yuyukov	NGO 'Roma'
Asem Mihaylov	NGO 'Roma'
Milko Stoyanov	NGO 'Roma'
Lora Deneva Tsonevska	Head of microbiological laboratory, hospital Ruse
Tatyana Nedrova Simeonova	Nurse, Pleven hospital
Anelia Atanasova	Nurse, Pleven hospital
Sashka Mihajlova	Doctor, laboratory hospital Pleven
Petjo Trifonov	Lab technician, laboratory hospital Pleven
Minchev	Childrens hospital, Sofia
Veneta Milenova	Childrens hospital, Sofia
Sokolova	Childrens hospital, Sofia
Simeonova	Ministry of Justice