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Review of the national tuberculosis programme in former Yugoslav Republic of Macedonia

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By:
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ABSTRACT

The WHO Regional Office for Europe conducted a comprehensive review of the national tuberculosis programme (NTP) of the former Yugoslav Republic of Macedonia from 29 August to 5 September 2016. This review followed a similar review conducted in 2007 and preceded the end of support from the Global Fund to Fight AIDS, Tuberculosis and Malaria. Five international and six national experts visited several facilities and institutions and met health providers and patients across the. The NTP has been effective in bringing down the incidence of tuberculosis and will now need to make further efforts to eliminate this disease. Intensified action is called for which should be sustainable and receive long term support.

Keywords

TUBERCULOSIS – prevention and control
NATIONAL HEALTH PROGRAMS
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Abbreviations

CCM	Country Coordinating Mechanism
CXR	chest X-ray
DOTS	directly observed treatment
DST	drug susceptibility testing
ECD COR	Early Child Development Consulting and Research
EDL	essential drugs list
EU	European Union
GDP	gross domestic product
GP	general practitioner
HERA	Health and Education Research Association
HIF	Health Insurance Fund
HOPS	Healthy Options Project Skopje
IGRA	interferon-gamma release assays
ILDTB	Institute of Lung Diseases and Tuberculosis
LDTB	lung diseases and TB
MDR	multidrug-resistant
MERC	Centre for Medicine, Ecology and Research
MGIT	mycobacteria growth indicator tube
NRL	national reference laboratory
NTP	national tuberculosis programme
PAL	practical approach to lung health
PHC	primary health care
PLWH	people living with HIV
PTB	pulmonary tuberculosis
RIF	rifampicin
SEEHN	South-Eastern Europe Health Network
TB	tuberculosis
TST	tuberculin skin test
XDR	extensively drug-resistant

Executive summary

The last comprehensive review of the national tuberculosis programme (NTP) of the former Yugoslav Republic of Macedonia was organized by the WHO Regional Office for Europe in November 2007. The Ministry of Health was the principal recipient of the US$ 6.4 million tuberculosis (TB) grant for "ensuring high quality and sustainable DOTS interventions in the Republic of Macedonia" from the Global Fund to Fight AIDS, Tuberculosis and Malaria, which was due to end on 30 September 2016. The extension of the grant to 31 March 2017 was being discussed at the time of the review.

The NTP review is part of the technical assistance requested by the Ministry of Health from the Regional Office by letter dated 19 April 2016. It was funded under the current Global Fund TB grant.

From 29 August to 5 September 2016, five international experts visited 34 facilities and institutions in the country to assess the epidemiological situation of TB and the features and performance of the NTP.

The main findings are listed below, followed by recommendations for the Ministry of Health that would strengthen the NTP and at the same time contribute to a more efficient use of resources.

Main findings and recommendations

TB action plan for the WHO European Region

The former Yugoslav Republic of Macedonia has subscribed to the Health 2020 European Policy Framework, the global End TB Strategy and the Tuberculosis Action Plan for the WHO European Region 2016–2020. The country now needs to align its national TB strategy to the global End TB Strategy and European Tuberculosis Action Plan.

Recommendation. There is an urgent need for the Ministry of Health to update the national TB strategic plan to bring it into line with the Tuberculosis Action Plan for the WHO European Region 2016–2020.

NTP central unit

The former Yugoslav Republic of Macedonia has intermediate-to-low TB incidence, with low rates of drug-resistant TB and of TB/HIV coinfection. Despite the achievements in TB control in previous years, there are still threats that may have a negative influence on ending the TB epidemic and eliminating TB in the country.

An immediate threat is the end of the Global Fund grant and its financial contribution to key elements of the NTP.

A threat that has not been completely recognized is the possible increase in multidrug-resistant (MDR) TB and TB/HIV coinfection in the future. The finding that the majority of identified MDR-TB cases are new cases and some of them are lost to follow-up suggests that MDR-TB transmission is ongoing. An increase in HIV infections among men having sex with men has been observed in recent years.

For TB to be eliminated, an aggressive and concerted approach is needed in which targeted activities are planned, coordinated and monitored. This would exceed the capacity of the staff of the NTP central unit, located in the Institute for Lung Diseases and Tuberculosis in Skopje, which is also charged with clinical duties in the Institute.

Recommendation. The Ministry of Health should officially nominate an NTP central unit with positions covering programme management, surveillance, coordination for training and supervision and TB laboratory services as well as advocacy, communication and social mobilization.

Optimizing the TB facility infrastructure

The present system of identification and treatment of TB patients underuses the primary health care facilities, makes inefficient use of intermediate TB facilities (dispensaries) with a low case load and overburdens the Institute for Lung Diseases and Tuberculosis in Skopje, which in the light of scarce human resources leads to a highly inefficient use of the available resources.

Recommendation. The Ministry of Health should consider closing a number of intermediate TB facilities (TB dispensaries and hospital departments) and increasing the involvement of the remaining intermediate TB facilities and primary care providers in TB case management.

Human resources

Many TB doctors are near retiring age and will be difficult to replace. The same applies to microbiologists. In the short term this may lead to the interruption of essential services.

Recommendation. The Ministry of Health should take steps to realign human resources with the proposed revised network of TB services, and adapt job descriptions to the different roles and responsibilities. Discussion should start with medical faculties on the content of undergraduate training, taking into account the new approach towards the control and elimination of TB and the use of new technologies.

Outreach activities

Outreach activities that have been successfully implemented by nongovernmental organizations may not be sustainable when the Global Fund financial support ends. These outreach activities are, however, essential to assure the successful completion of treatment.

Recommendation. The Ministry of Health should ensure that all outreach TB activities that are currently being implemented by patronage nurses and nongovernmental organizations will be continued after the end of the Global Fund grant. Social contracting could be considered.

Vulnerable populations

For a variety of reasons vulnerable people often avoid medical facilities. A serious challenge to the elimination of TB arises from the continued transmission of the disease among people living in poor conditions, who thus continue to be a reservoir of TB infections.

Recommendation. In order to eliminate TB, the Ministry of Health should vigorously target some of its interventions towards vulnerable populations that act as reservoirs of TB.

Infection control

Awareness of the risk of TB transmission in most facilities is low. This is especially a risk in facilities that deal with both TB and HIV patients.

Recommendation. The Ministry of Health should improve TB infection control in the facilities providing TB services and HIV services by training and retraining staff, reinforcing adherence to standard operating procedures and increasing cooperation between the TB and HIV services.

Introduction

The last comprehensive review of the national tuberculosis programme (NTP) in the former Yugoslav Republic of Macedonia was organized by the WHO Regional Office for Europe in November 2007. The Ministry of Health is the principal recipient of the US$ 6.4 million TB grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria for "ensuring high quality and sustainable DOTS interventions in the Republic of Macedonia", which was due to end on 30 September 2016. Its extension to 31 March 2017 was under discussion at the time of the review.

The Ministry of Health asked for the assistance of the Regional Office by letter dated 19 April 2016 to conduct a review of the NTP, to be funded under the current Global Fund TB grant. This review took place from 29 August to 5 September 2016 and had the following objectives:

- to assess the TB epidemiological situation in the country and the features of the NTP with reference to the analysis and recommendations of previous WHO missions, the global End TB Strategy and the TB Action Plan for the WHO European Region 2016–2020;
- to develop specific recommendations for improving TB control and combating drug-resistant TB and ensuring their sustainability once international funding is phased out;
- to prepare a comprehensive report of the review (this report);
- to prepare a separate report for the Green Light Committee for the European Region.

Five international and six national experts participated in the review (Annex 1). They analysed all relevant documents available, conducted site visits and interviewed patients, health providers and policy-makers in a number of areas chosen to reflect a range of epidemiological situations as well as the geographical distribution and organization of TB services (programme in Annex 2).

Two teams were organized to work in the field, each coordinated by an international expert. Logistics support was provided by the WHO Country Office in Skopje and by the national and regional health authorities. The first part of the review was spent in visiting the regions, while the second part was spent in Skopje with meetings and visits at central level and working on the first draft of the review report. To be effective, the two teams divided into smaller groups when appropriate. In this way the reviewers were able to meet a wider variety of people (Annex 3).

On behalf of the European Green Light Committee, the review also monitored interventions for the programmatic management of drug-resistant TB.

At the end of the mission, and accompanied by Dr Pierpaolo de Colombani (Medical Officer of the Joint TB, HIV and Hepatitis Programme at the Regional Office), the review team presented an overview of the main findings and recommendations at a formal meeting with representatives of the Ministry of Health.

Background information

The former Yugoslav Republic of Macedonia lies in south-eastern Europe, north of Greece. It is landlocked and forms the major corridor from western and central Europe to the Aegean Sea and from southern to western Europe. It is bordered by Albania, Bulgaria, Greece, Kosovo (in accordance with United Nations Security Council Resolution 1244 of 1999) and Serbia. The climate is warm with dry summers and autumns and relatively cold winters with heavy snowfalls. The terrain is mountainous with deep basins and valleys *(1)*.

The country was admitted to the United Nations in 1993 and became a candidate member of the European Union (EU) in 2005. It has 70 municipalities and one city, Skopje, which comprises 10 of the 70 municipalities.

Demography

In 2016, on the basis of a national census conducted in 2002, the total population was estimated to be slightly over two million inhabitants (2 100 025) *(1)*. This figure is not necessarily reliable as many people have left the country since 2002 to work abroad. A study from the University of Skopje stated that labour migration started in the mid-1960s and quoted the World Bank estimate of 447 138 Macedonian citizens spread all over the world in 2010 *(2)*. According to the European Statistical Agency (Eurostat), around 230 000 people left the country to live abroad legally in the period between 1998 and 2011*(2)*. In these 14 years, more than 10% of the country's population emigrated *(3)*. Taking this into account, a better estimate would be a total population of 1 886 400. During the refugee crisis from 2015 to June 2016, an estimated 472 903 refugees and migrants arrived *(4)*. It is unclear if these people are still in the country or have travelled through to other countries. The rates used in this report are based on the population size officially used by the government.

There are two major ethnic groups: Macedonian 64% and Albanian 25%. The remainder are Turkish 4%, Roma 3%, Serb 2% and other 2%. The two official languages are Albanian and Macedonian. There is a high level of literacy: 98% of the population over 15 years of age can read and write.

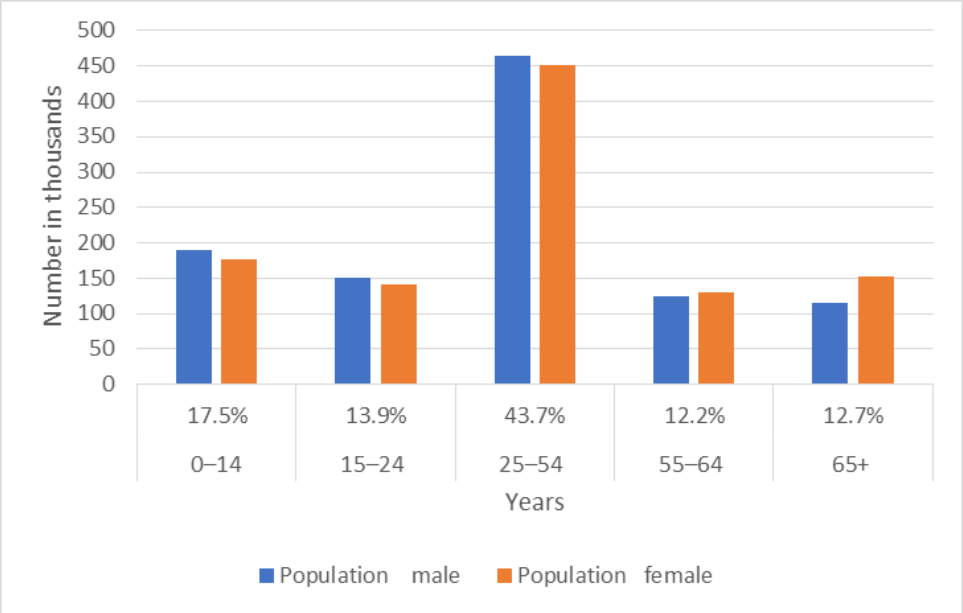
The distribution of the population by age group and sex (2015 estimates) shows an almost equal number of men and women in all age groups. The economically active age groups represent about half the population (Fig. 1).

The economy

According to the World Bank classification, the former Yugoslav Republic of Macedonia is an upper-middle-income country that has made great strides in reforming its economy over the last decade *(5)*. While the country has made significant progress in its economic development, efforts across a range of areas are still needed to generate economic growth that will create jobs and improve living standards for all.

Growth in the gross domestic product (GDP) reached 3.7% in 2015, supported by rising private consumption and higher public spending *(5)*. The main contributors to the GDP are agriculture (10%), industries (25%) and services (65%). The continued expansion in economic activity reflects the labour market as unemployment dropped from 28.1% in 2014 to 26.1% in 2015. By the end of 2015, public debt was 40.3% which, although low for the Balkan region, is significant for a small economy.

Fig. 1. Population distribution by age group and sex, the former Yugoslav Republic of Macedonia, 2015



Source: NTP TB register (unpublished).

Some 30.4% of the population lives below the poverty line of US$ 4 per day *(6)*. The gross national income per capita is US$ 11 520 *(7)*. According to the International Monetary Fund, almost 20% of the population is economically dependent on remittances *(3)*.

Governance

Transparency and accountability are crucial to good governance and equitable, socially inclusive development. A study published in May 2016 showed the indicators used to determine whether an agency was practising good governance with marks for compliance. Among the country's 19 central government institutions, the Health Insurance Fund and the Parliament scored the best marks (41% and 40%, respectively) for adopting the principles of good governance. The average score for all institutions is 31%, so the study concluded that there is room for improvement in all categories of good governance.

Looking at processes, the study found a compliance of 60% (the highest level) for parliamentary oversight but much lower for monitoring regulations and reporting *(7)*. Monitoring and evaluation are, of course, cornerstones of NTPs (see the section on monitoring and evaluation).

Health status

The major burden of illness comes from cardiovascular diseases and diabetes mellitus, followed by cancers and neuropsychiatric diseases expressed as 250 000, 120 000 and 100 000 quality-adjusted life-years, respectively. HIV, TB and malaria contribute a far smaller number: fewer than 5000 quality-adjusted life-years combined *(8)*.

The main health indicators are listed in Table 1.

Table 1. Major health indicators

Indicator	Value	Year of estimate
Maternal and child health		
Total fertility rate (children per woman)	1.6	2015
Mother's mean age at first birth (years)	26.2	2011
Maternal mortality rate (deaths per 100 000 live births)	8	2015
Number of live births (live births per 1000)	22.5	2013
Infant mortality rate (deaths per 1000 live births)	7.7	2015
Life expectancy at birth		*2015*
Total population (years)	76.0	
Male (years)	73.4	
Female (years	78.8	
Health expenditure as proportion of GDP (%)	6.4	2013
Physicians (number per 1000 population)	2.6	2009
Hospital beds (number per 1000 population)	4.5	2011
TB		
Total cases notified (number)	285	2014
Mortality (deaths per 100 000 population)	2.3	2014
HIV/AIDS		*2013*
Prevalence among adult population ((estimated %)	0.01	
People living with HIV/AIDS (estimated number)	200	
Mortality (estimated number)	< 100	

Source: Central Intelligence Agency *(4)*.

TB epidemiology

According to WHO estimates, TB incidence in 2015 was 13 (12–14) per 100 000 inhabitants and mortality was 0.41 (0.38–0.45) per 100 000. The estimated number of MDR-TB cases was 10 *(9)*. Table 2 shows the trend in TB incidence and mortality as estimated by WHO over the period 2010–2015.

Table 2. WHO estimates for TB incidence and mortality per 100 000 population, the former Yugoslav Republic of Macedonia, 2010–2015

Year	Population	All TB cases		Mortality	
		No.	Per 100 000 population	No.	Per 100 000 population
2010	2 062 443	430 (380–490)	21 (18–24)	34 (33–36)	1.7 (1.6–1.7)
2011	2 065 888	380 (330–430)	18 (16–21)	30 (29–31)	1.5 (1.4–1.5)
2012	2 069 270	390 (340–440)	19 (17–21)	31 (30–32)	1.5 (1.5–1.6)
2013	2 072 543	360 (320–410)	17 (15–20)	29 (28–30)	1.4 (1.3–1.4)
2014	2 075 625	320 (280–360)	15 (13–17)	24 (23–25)	1.1 (1.1–1.2)
2015	2 078 453	270 (260–280)	13 (12–14)	8.5 (7.8–9.3)	0.41 (0.38–0.45)

Source: WHO *(10)*.

When compared with the above WHO estimates, the TB incidence and mortality notified by the NTP confirm a decreasing TB burden over the same period but also show variability in TB notifications (Table 3). This probably indicates the need to revise upwards WHO's estimates for 2015.

Table 3. TB incidence and mortality per 100 000 population as notified by the NTP, the former Yugoslav Republic of Macedonia, 2010–2015

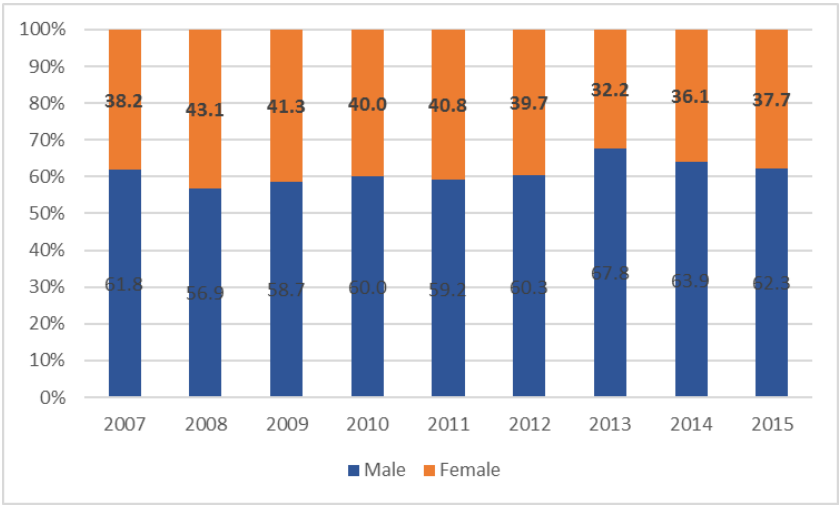
Year	All TB cases		Mortality	
	No.	Per 100 000 population	No.	Per 100 000 population
2010	420	20.4	34	1.7
2011	362	17.5	19	0.9
2012	355	17.2	28	1.4
2013	323	15.6	24	1.2
2014	285	13.7	18	0.9
2015	284	13.7	18	0.9

Source: NTP TB register (unpublished).

The above rates are calculated on the basis of the population estimates derived from the 2002 census. As mentioned above, studies have estimated emigration as varying from 10% to 20%. Although this would influence the calculation of rates, making them 10–20% higher than reported, but importantly the declining trend is not affected.

Over the years there has been a stable distribution by gender, with notifications from 1.5 times more men than women (male : female = 3 : 2) (Fig. 2).

Fig. 2. Notification rate by gender, the former Yugoslav Republic of Macedonia, 2007–2015



The distribution of notifications by age shows an increase in rates towards the older age groups, which is a typical pattern for a low-incidence country (Fig. 3). This is also illustrated by the greater decline in the group aged 0–14 years (8%) compared to the overall decline of 6%. This finding is probably reliable, given the active case-finding among household contacts and the absence of TB meningitis in recent years.

The geographical distribution of notified new/relapse TB cases shows that there were remarkable fluctuations between the regions over the period 2011–2015 (Fig. 4 and Annex 4). The large proportion of cases notified in Skopje (absolute number of cases 110: 18 per 100 000) are not included in Fig. 4 as the Skopje region is an outlier compared to the other regions.[1]

[1] TB cases are registered for treatment according to the dispensary in the area where the patient lives and not where the diagnosis is confirmed (which is quite often done by the ILDTB in Skopje).

Fig. 3. Notification rate by age group, the former Yugoslav Republic of Macedonia, 2007 and 2015

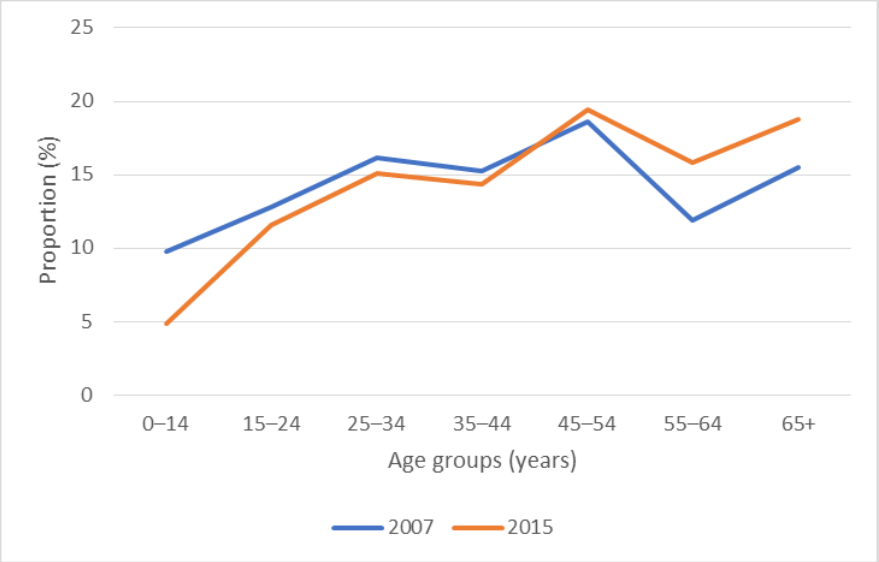
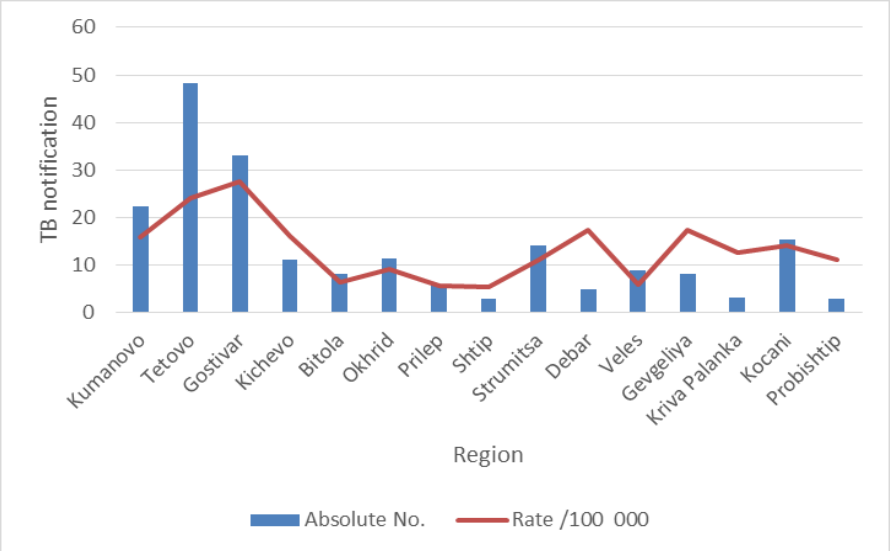


Fig. 4. Average TB notification by region (absolute numbers and rates per 100 000),[a] the former Yugoslav Republic of Macedonia, 2011–2015



[a] Without Skopje, which is an outlier.
Source: NTP TB register (unpublished).

In considering the geographical distribution of workload, if the cut-off point for a low workload is taken as 10 cases per year, only Gostivar, Kocani, Kumanovo, Ohrid, Skopje, Strumitsa and Tetovo have a high workload. The other eight regions have lower caseloads. Caseload is important for maintaining proficiency. When looking at notification rates per 100 000 population and taking 10 per 100 000 population as the cut-off point, Debar, Gevgeliya and Kitchevo are also higher-incidence regions. These latter findings are important when optimization of the infrastructure is discussed in the NTP.

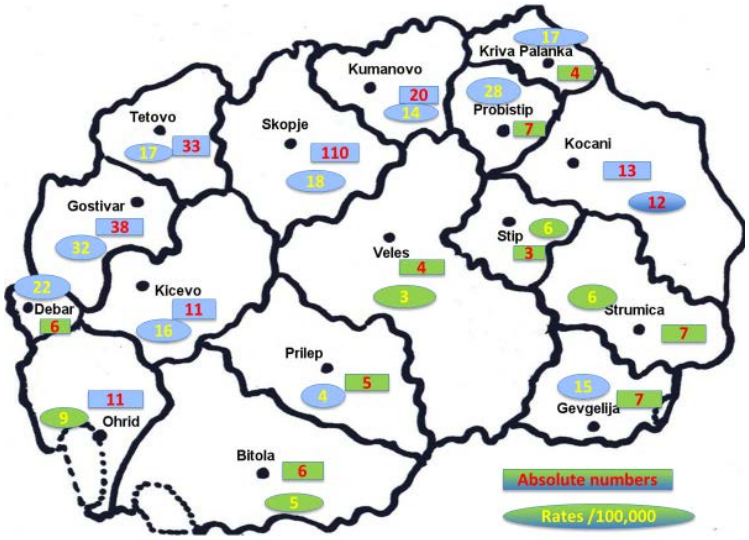
There is a clear difference in notification rates between the major ethnic groups. The NTP register shows a notification rate among people of Albanian ethnicity about three times higher, and among Roma people almost four times higher, than among people of Macedonian ethnicity (Table 4).

Table 4. Absolute number of notifications and the average notification rates among three ethnic groups, the former Yugoslav Republic of Macedonia, 2013–2015

Year	Macedonian	Albanian	Roma
2013	133	153	19
2014	122	134	17
2015	96	158	20
Average (per 100 000)	8.7	28.3	32.9

The map of the country shows an apparent increasing gradient in notification rates from west to east, with the exception of Gevgelija and Kocani (Fig. 5).

Fig. 5. TB notifications in absolute numbers and rates per 100 000 population, the former Yugoslav Republic of Macedonia, 2015



Source. Prepared by review team based on data in the NTP TB register.

These findings are important when consideration is being given as to which TB facilities could be closed for reasons of access, efficiency and maintenance of proficiency.

Recommendations

NTP

1. Even though the country is moving towards a low incidence of TB, the NTP should pay serious attention to those regions and ethnic groups where prevalence is higher when optimizing the structure of the programme.
2. The NTP should collect data on vital registration and report these to WHO so that the current estimates of TB mortality can be revised.

NTP

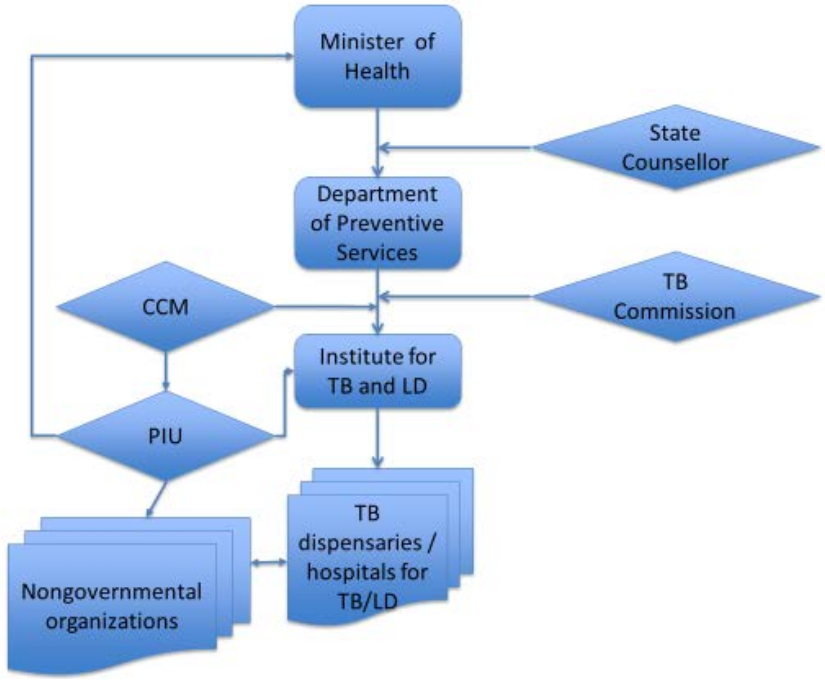
The NTP was introduced in 1929 and was one of the first programmes for disease control ever to be implemented in the former Yugoslavia. The programme was updated in 1964, 1977 and 1986. The DOTS strategy[2] was introduced in 1996 and the Stop TB strategy in 2008.

The Ministry of Health subscribed to the TB action plan for the WHO European Region 2016–2020, which was endorsed in Regional Committee resolution EUR/RC65/17. However, the process to align the national TB action plan with the regional one has not yet started.

Organization

The Minister of Health has a decisive role in all matters of health policy (Fig. 6). The state counsellors advise the minister and are pivotal in policy-making in all aspects of health, including both the TB and HIV control programmes. The Ministry of Health includes: (i) the Department of Preventive Services, which (among other things) is in charge of the NTP and provides the funds for procuring anti-TB drugs; and (ii) the Commission for Tuberculosis Control, whose 16 members are appointed by the Ministry of Health (on the basis of recommendations by the national coordinator for TB) to oversee and approve programmatic and organizational activities in TB control. Although the Commission's role is advisory, no activities are implemented without its consent.

Fig. 6. Organigram of the Ministry of Health and its TB stakeholders, the former Yugoslav Republic of Macedonia, 2016



CCM = Global Fund Country Coordinating Mechanism.
PIU = Global Fund Programme Implementation Unit.
LD = lung diseases.

[2] The core approach underpinning pillar 1 of the End TB Strategy, launched in 2016.

The Country Coordinating Mechanism (CCM) was established in 2003, as a prerequisite for an application to the Global Fund. It was initially established as an alliance of the TB and HIV/AIDS national committees, which were the original policy-makers for the TB and HIV programmes, respectively. In 2009, the CCM amended its role to increase active monitoring and evaluation in the interests of faster and more effective decision-making regarding implementation. At the same time, it reduced its membership from 52 to 32 and established a secretariat. The membership includes government officials, representatives of nongovernmental organizations (40%), one person affected by TB and one by HIV. The CCM plans to continue its work after the Global Fund grant has come to an end, in order to ensure the sustainability of the TB (and HIV) programme(s). How its advisory role will dovetail with that of the TB Commission is unclear.

The Ministry of Health also includes the Project Implementation Unit, as the Ministry is the principal recipient of the Global Fund grant. The Project Implementation Unit oversees the implementation of the project proposal for which the grant was intended and as such is monitored by the Global Fund. To achieve its objectives, the Unit needs to be in close contact with the Minister of Health, the Institute for Lung Diseases and Tuberculosis (ILDTB) in Skopje and the implementing nongovernmental organizations (subrecipients of the Global Fund grant). Its role will finish when the grant ends.

The NTP is not a legal entity but a functional unit within the ILDTB. Strategic directions for TB control are given by the director of the ILDTB. Staff members of the Institute act as a management team for the NTP but have no formal mandate for this purpose. The NTP proposes changes in laws and regulations related to TB, and plans, implements, monitors and evaluates TB control activities, which are based on international standards. The University Pulmonology Clinic is supposedly responsible for developing guidelines and protocols, but it lacks up-to-date information on international developments in TB control.

The NTP management team consists of the director of the Institute (national coordinator), a national clinical affairs coordinator, the head of the department for preventive activities, the coordinator for supervision, monitoring and evaluation (who is also the head of the central TB register), a coordinator for training and health education and a drugs coordinator. The director nominates the members of the national team, who are subsequently approved by the Commission for TB control.

All these activities are carried out by individuals alongside their clinical duties. The risk is a high burden of work and less attention given to the core activities of the NTP. If TB is to be eliminated, a concerted approach is needed whereby various activities are coordinated, planned, implemented and monitored.

Financing

In general, health services are paid for by the Health Insurance Fund (HIF). Primary health care services are paid per capita of the catchment population, but these services do not include outreach activities for TB. Secondary and tertiary care are paid by the HIF, based on a diagnosis-related groups costing system. The funding of hospital care and staff costs for TB patients and maintenance of TB facilities is based on the length of hospital admission, for which three categories exist. Anti-TB drugs are not, however, included; these are paid for by the Department of Preventive Services, which also covers programmatic costs related to TB control.

The cost of TB control has been estimated at around two million US dollars annually. The government contributes about 40% of that amount. From 2011 to end September 2016 the gap was filled by the Global Fund grant of US$ 6.1 million. A no-cost extension was envisaged until March 2017, after which date the country was expected to cover the costs of the NTP from its own resources.

In June 2014, initiated by the nongovernmental Centre for Medicine, Ecology and Research and with the support of the CCM, a TB Coalition was established *(11)*. The first of its kind in south-eastern Europe, this Coalition aims to develop a transition plan that ensures the domestic funding of Global Fund-supported activities by defining priorities for intervention and making proposals for the integration and coordination of services.

The transition plan was developed through an open and consultative process and finalized by the Project Implementation Unit but it has not yet been endorsed by the government or the Ministry of Finance. Concerned about the major delays and the level of the government's commitment, the TB Coalition started a process of parliamentary advocacy focusing on HIV and leading to a public hearing in December 2015 *(12)*. The Parliamentary Commission on Health committed itself to hold another hearing after six months (in June 2016) to assess progress in the transition processes. Unfortunately, the uncertain political situation prevented such a public hearing and makes any advocacy initiative rather difficult.

The CCM hired a consultant to develop a crowd-funding website to mobilize resources from citizens and the private sector *(13)*. The website had generated €800 by September 2016, although it is not dedicated to raising funds for the NTP.

TB infrastructure

TB services are provided at three levels:

(i) primary health care facilities, where general practitioners (GP) trained in the practical approach to lung health (PAL) only refer patients with presumptive TB for further diagnosis and treatment but are not involved in any other TB activity;

(ii) 16 secondary level facilities for TB: TB dispensaries, TB departments at lung diseases hospitals and the ILDTB (Table 5);

(iii) tertiary level, represented by the University Pulmonology Clinic.

Although the ILDTB coordinates the activities of the NTP and hosts the TB department, the national TB register and the TB drugstore, it is considered a secondary level facility. The reason for this is the absence of university clinic status implying responsibility for teaching students and updating national TB protocols. The University Pulmonology Clinic, which is a tertiary level facility, developed the last update of the national protocol on TB diagnostics, but it is not in line with WHO recommendations *(14)*. Currently there is a list of documents requiring revision, including the TB control guideline, guideline on latent TB infection, TB/HIV protocol and infection control guideline/plan. This again underlines the need for a mandated NTP central unit.

The present system of identification and treatment of TB patients underuses the primary health care facilities, makes inefficient use of intermediate TB facilities (dispensaries) with a low case load and overburdens the services of the ILDTB which, in view of the scarcity of doctors, leads to a highly inefficient use of financial and human resources.

Table 5. Hospitals and their TB facilities, the former Yugoslav Republic of Macedonia, 2016

City	Public Health Facility	Unit
Skopje	Health Centre	Dispensary for lung diseases and TB
Kumanovo	General Hospital	Internal diseases, TB dispensary
Tetovo	Clinical Hospital	Dispensary for lung diseases and TB
Gostivar	General Hospital Dr Ferit Murat	Dispensary for lung diseases and TB
Kicevo	General Hospital	Dispensary for lung diseases and TB
Bitola	Clinical Hospital Dr Trifun Panovski	Department for pneumophtisiology and Dispensary for lung diseases and TB
Ohrid	General Hospital	Dispensary for lung diseases and TB
Prilep	General Hospital	Dispensary for lung diseases and TB
Stip	Clinical Hospital	Internal disease ward
Strumica	General Hospital	Internal disease ward
Debar	General Hospital	Internal disease ward
Veles	General Hospital	Dispensary for lung diseases and TB
Gevgelija	General Hospital	Dispensary for lung diseases and TB
Kriva Palanka	Health Centre Dr Dimitar Artov	Dispensary for lung diseases and TB
Kocani	Health Centre	Dispensary for lung diseases and TB
Probishtip	Donevska Dr Paca	Private department for ambulatory pulmonary and TB care

NTP partners

Six nongovernmental organizations are subrecipients of the Global Fund grant and are thus involved in various aspects of patient support (Table 6).

Table 6. Nongovernmental organizations subrecipients of the Global Fund

Name	Description
Centre for Medicine, Ecology and Research (MERC)	Active in the fields of TB prevention, education, advocacy and research.
Health and Education Research Association (HERA)	Established in 2000 and focused initially on HIV prevention and support for people living with HIV. Its mission is to promote human rights related to sexual and reproductive health based on social justice and gender equality principles, the use of strategies for advocacy, provision of education and services and continuous and systematic research and development. It specifically targets young people, PLHIV and vulnerable populations. It has also taken on TB-related education for these groups at risk.
Doverba (Trust)	For 20 years has supported vulnerable populations such as drug users and TB and HIV patients by providing social packages, educational brochures and face-to-face health education.
Healthy Options Project Skopje (HOPS)	Aims to prevent HIV/AIDS and other blood or sexually transmitted infections, by re-socialization, rehabilitation and improvement of the health and social status of drug users, sex workers, their partners and families. HOPS provides harm reduction services and offers harm reduction and drug policy training to professionals, decision-makers and nongovernmental organizations. It advocates the right to health of injecting drug users and sex workers.
Early Child Development Consulting and Research (ECD COR)	Works with children and mothers.
Red Cross of the former Yugoslav Republic of Macedonia	Works with the Roma population, people living in poverty and schoolchildren. The municipal offices of the Red Cross work with the national office of the Red Cross and carry out a number of local campaigns. Representatives from the Roma council and TB doctors and nurses are Red Cross volunteers and are involved in community activities.

Main achievements

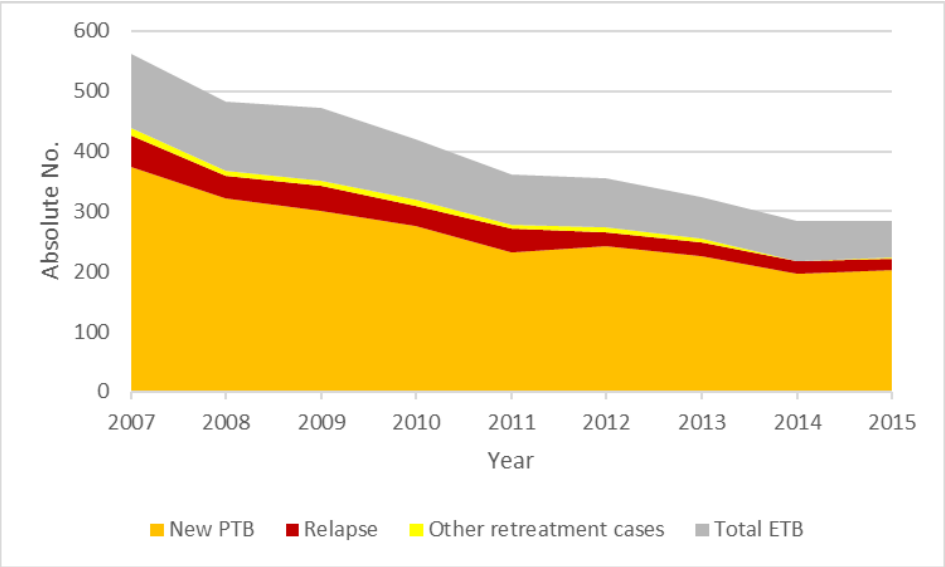
The TB strategy has been successful, as shown by the declining incidence and mortality, the high treatment success rates and the low prevalence of MDR-TB and TB/HIV coinfection. Although socioeconomic conditions have improved over the years, its contribution to the success of the NTP has probably, however, been small given the still high unemployment rate of 26% and the high proportion (30%) of the population living below the poverty line.

In 2015, the NTP registered a total of 284 TB cases (all cases), including 255 pulmonary TB (PTB) cases, of whom 105 (41%) were bacteriologically confirmed PTB.

The proportion of new cases among all notified cases is around 90%, up from 87% in 2007 to 92% in 2015. Bacteriological confirmation among PTB cases increased from 66% in 2007 to 88% in 2015 (Annex 4, Table 4.2).

The decline in notifications is apparent for all categories of TB (Fig. 7).

Fig. 7. Pulmonary TB case notification by category, the former Yugoslav Republic of Macedonia, 2007–2015

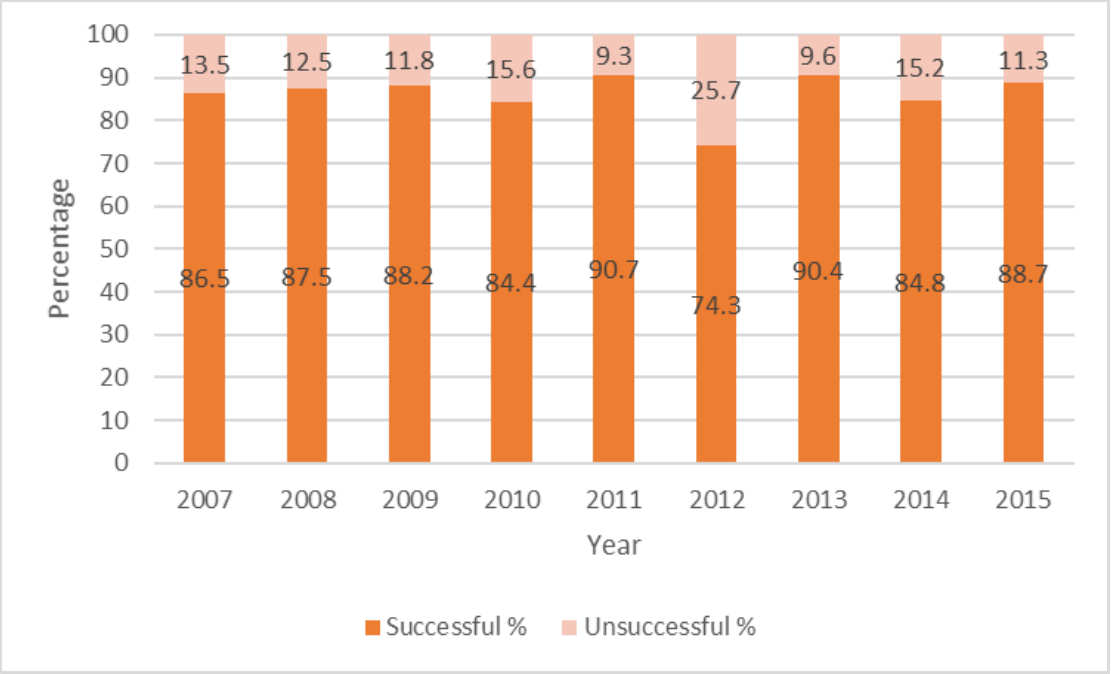


ETB = extrapulmonary TB.
Source: NTP TB register (unpublished).

The treatment success rate among new and relapse pulmonary TB cases is reported as around 90% between 2007 and 2014 (Fig. 8). In 2012, there was a significant drop with unsuccessful treatment in 25% of cases, but it is not clear what the reason was.

Treatment success rates in 2015 were 89% in new PTB cases and 62% among relapses. The reason for the low success rate among relapses in 2015 is the three deaths (23%) that occurred, but the small numbers allow of no further conclusions. Table 7 compares the treatment outcomes in 2015 and 2014 and shows that failure and lost to follow-up rates were low in both new and relapse cases.

Fig. 8. Treatment success in new pulmonary TB cases, the former Yugoslav Republic of Macedonia, 2007–2014



Source: NTP TB register (unpublished).

Table 7. Treatment outcome for new and relapse cases, the former Yugoslav Republic of Macedonia, 2014–2015

Outcome	2014				2015			
	New PTB SS+[a]		Relapse		New PTB SS+		Relapse	
	No.	%	No.	%	No.	%	No.	%
Notified	115		17		105		13	
Cured	61	53.0	6	35.3	39	37.1	2	15.4
Completed	41	35.7	8	47.1	53	50.5	6	46.2
Death	7	6.1	2	11.8	10	9.5	3	23.1
Failure	1	0.9	0	0.0	0	0.0	1	7.7
Lost to follow-up	5	4.3	1	5.9	3	2.9	1	7.7
Not evaluated	0		0		0		0	0

[a] SS+ = sputum smear-positive.

Recommendations

Government/Ministry of Finance

1. The government and the Ministry of Finance should, as soon as possible, endorse the transition plans of the TB and HIV programmes so as to ensure that sufficient finances will be available for the transition from Global Fund to domestic funding in order to avoid endangering the decline in the TB epidemic.

Ministry of Health

2. The Ministry of Health should urgently update its national TB strategic plan to bring it in line with the TB action plan 2016–2020 for the Region.

3. The Ministry of Health should officially designate an NTP central unit with positions covering guideline development, programme management, surveillance, coordination for training and supervision, TB laboratory services, and advocacy, communication and social mobilization.
4. The Ministry of Health should decide on the roles and responsibilities of the two advisory bodies (TB Commission and CCM). One could be strategic, the other clinical, or they could be merged to become one advisory mechanism.

NTP

5. The NTP should revise and update a number of national guidelines, such as the TB control guidelines, guidelines on latent TB infection, TB/HIV protocol, and infection control guidelines and plan.

TB case-finding and diagnosis

Case-finding is based on active and passive strategies in both the general population and vulnerable groups (detainees, asylum-seekers, refugees, ethnic minorities). In 2015, a few cases were identified by active screening, mainly in vulnerable groups, through outreach activities by nongovernmental organizations or by contact-tracing around TB cases carried out by primary health care (PHC) centres (see section on vulnerable populations).

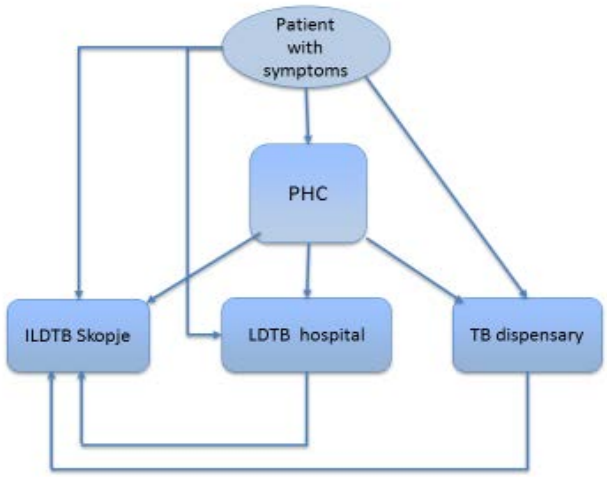
Case-finding

Passive case-finding

Passive case-finding in patients with symptoms follow various pathways. GPs working at PHC centres have been trained in the PAL, which should allow them to recognize a spectrum of lung diseases in patients with respiratory symptoms, including TB. The manuals used in the PHC centres represent general guidelines for diagnosing several diseases but do not include TB, so in practice GPs refer all individuals with respiratory symptoms as presumptive TB cases to a higher level. This means there is little chance to lose TB cases but it results in a wide selection of presumed TB cases of which only 5% are eventually diagnosed as TB (the norm is 10%).

Respiratory patients are referred to a lung diseases and TB (LDTB) dispensary, an LDTB hospital or the ILDTB in Skopje (Fig. 9). Presumptive TB patients may also present directly to an LDTB dispensary. The LDTB dispensaries are usually located in general hospital facilities which offer further laboratory analyses (blood, clinical chemistry) and chest X-rays (CXR). If there is a high suspicion of TB, two biological sputum samples are collected and examined by smear microscopy (not all TB dispensaries have a microscopy facility – see the section on the TB laboratory network). The combination of physical examination, CXR, sputum smear microscopy and blood chemistry (if requested) helps clinicians at the dispensaries decide whether to refer the individual as a presumed TB case or dismiss TB from the differential diagnosis. If TB is suspected, any individual from anywhere in the country is sent to the ILDTB in Skopje for diagnosis and confirmation.

Fig. 9. Flow of presumed TB patients for TB diagnosis, the former Yugoslav Republic of Macedonia



Active case-finding

Active case-finding is done by contact-screening of children and other close contacts of TB cases by using the tuberculin skin test (TST), the interferon-gamma release assays (IGRA) test and CXR. LDTB dispensaries coordinate active case-finding. In 2015, 84% (511) of all registered contacts were screened. Prisoners are screened on entry to prison by questionnaire, physical examination and, when indicated, by CXR at the nearest Ministry of Health facility, and by annual CXR in the mobile X-ray unit (see the section on TB in prisons). With help of the Global Fund, the mobile X-ray unit is also used for targeted CXR screening among groups at risk, such as Roma people or intravenous drug users, often with the help of nongovernmental organizations.

In 2015, the Ministry of Health Prevention Programme stepped up active case-finding: 2000 individuals in various unspecified risk groups were screened by CXR and up to 50 paediatric TB suspects were tested by the QuantiFERON test. For 2016, 4000 CXRs have been forecast and at least the same number of QuantiFERON tests has been planned as well.

Contact-screening

The country has a policy of active case-finding among identified contacts. Most of those are children. Table 8 shows that the number of contacts identified per bacteriologically confirmed case (two to three) is rather low. Given the normal size of a family this number should be twice as high.

Table 8. Number of contacts identified per bacteriologically confirmed case, the former Yugoslav Republic of Macedonia, 2011–2015

Year	Bacteriologically confirmed cases	No. of contacts	Contacts per case
2011	214	709	3.3
2012	216	436	2.0
2013	211	527	2.5
2014	188	505	2.7
2015	196	605	3.1

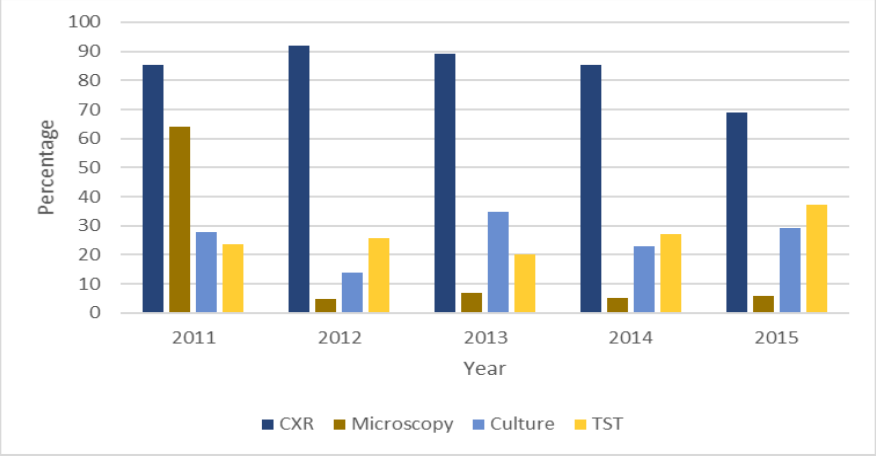
From 2011 to 2015, a total of 2782 contacts were identified, of whom 2167 (78%) were screened, yielding 39 (1.8%) active TB cases and 175 (8%) cases of latent TB infection (Table 9).

Table 9. Results of contact-screening in aboslute and relative numbers, the former Yugoslav Republic of Macedonia, 2011–2015

Year	2011		2012		2013		2014		2015	
	No.	%	No.	%	No.	%	No.	%	No.	%
Total registered close contacts	709		436		527		505		605	
Screened contacts	472	66.6	357	81.9	423	80.3	404	80.0	511	84.5
Identified TB cases	10	2.1	4	1.1	9	2.1	7	1.7	9	1.8
Latent TB infection	35	7.4	22	6.2	27	6.4	54	13.4	37	7.2

The yield from screening also depends on the methods chosen to identify TB and latent TB infection. Contacts are screened either by CXR, sputum smear and/or culture (Fig. 10). The majority are screened by CXR; since 2012, sputum smear microscopy was done in only a small percentage of cases (on average 5.7% over 2012–2015). Culture is performed in a quarter of screenings (25.7%), but the yield is low with an occasional positive result. Surprisingly, TST is done in only 26% of screenings, probably because many children have been vaccinated, causing false positive results. Positive tests were recorded in 39% of those tested.

Fig. 10. Proportion of screening methods among contacts screened, the former Yugoslav Republic of Macedonia, 2011–2015



Diagnosis

Smear microscopy

Sputum smear microscopy by Ziehl-Neelsen staining performed by the LDTB dispensary laboratories is the first step in the diagnostic algorithm. The sample is not concentrated by centrifugation. This is the methodology with the lowest sensitivity. Except for Lesok LDTB Clinic, which has a high positivity rate (30.5%), the positivity rates for sputum smear microscopy across the country are very low (1.7–6.1%). This may be due to the intrinsic low

sensitivity rate of the test performed, but probably also to the over-selection of patients with respiratory symptoms not necessarily indicative of TB.

Smear microscopy laboratories performing direct smear are underused and most of them have a daily workload below the acceptable number of tests to maintain proficiency. Data from all smear microscopy laboratories were not available, but from the data collected in the TB dispensaries visited during the review, the daily workload on average ranges from 0.75–1.5 smears per day. These numbers include smears for diagnosis and treatment monitoring. The low sensitivity of direct smear microscopy, the low daily workload and the referral system with duplication of testing at the national reference laboratory (NRL) raises concerns about the efficacy of all these smear microscopy laboratories in the network.

Culture

Three laboratories (Bitola, Kozle and NRL Skopje) do culture on solid media. Kozle can also use liquid media.

Kozle is the only hospital with diagnosis and treatment fully dedicated to paediatric presumed TB cases and TB patients. The new laboratory in the hospital (since January 2016) performs smear microscopy and cultures on both solid and liquid media (BacT/Alert donated by Rotary). Positivity rates of microscopy and culture are very low. The review found the quality of sputum samples collected to be poor and the yield of other biological samples (such as gastric aspirates and bronchial aspirates) is low. In the five years that the laboratory has been using BacT/Alert, no positive case has been found.

At the NRL, all diagnostic procedures are performed both by conventional methods and by polymerase chain reaction-based methods. The diagnostic workflow includes fluorescence smear microscopy (light-emitting diode microscopy) and culture on solid media (Loewenstein-Jensen) for every sample collected. Although the laboratory has one 960-position and one working 320-position Bactec mycobacteria growth indicator tube (MGIT), liquid culture is not routinely performed, since it is only done at the request of clinicians (and they do not make such requests for unclear reasons).

Identification of a positive culture is done by an immunochromatographic test. Positive cultures isolated in Bitola and Kozle are sent to the NRL for drug susceptibility testing. Bitola has only one or two samples per day. Not all presumed TB cases have a culture done: some centres do not send smear-negative samples to NRL for further testing.

Molecular techniques

In general, clinicians can request samples to be sent to the NRL for Xpert *M. tuberculosis* (MTB)/rifampicin (RIF) testing. A four-module Xpert MTB/RIF machine is present in the laboratory. According to the estimate based on annual working days, the laboratory collects and processes about 25 samples every day.

Drug susceptibility testing

On positive cultures, the NRL performs drug susceptibility testing (DST) for first-line drugs only (excluding pyrazinamide). Conventional DST for second-line drugs is neither done nor requested from a supranational reference laboratory. The NRL uses the proportional method on solid media for DST. Media are home-made.

On receipt of a specific request the laboratory performs Xpert MTB/RIF and line probe assay genotype MTBDR*sl*. Genotype MTBDR*sl* is the only assay available for the detection of determinants of resistance to second-line drugs (fluoroquinolones and aminoglycosides) in MDR-TB patients.

Diagnostic algorithms

Country diagnostic algorithm

A diagnostic algorithm for TB (the country algorithm) is under consideration by the TB Commission (Annex 5), but has not yet been approved.

The algorithm recommends that, for every presumptive TB case regardless of the CXR findings, 100% of samples will be smeared for microscopy and cultured. Once smeared and cultured, every sample is tested by Xpert MTB/RIF.

This algorithm raises the following issues.

- The inclusion of smear microscopy seems questionable if, regardless of the CXR results, all samples will be cultured and Xpert-tested. According to this algorithm, smear microscopy will be superfluous.
- According to the diagnostic algorithm chosen, all samples of presumed TB patients should be tested by Xpert MTB/RIF. This unconditional use is, however, arguable. In an optimal situation it would be a good solution, but in the former Yugoslav Republic of Macedonia account had be taken of the Global Fund project that was due to finish in 2016 and the cost of the entire diagnostics workflow if this algorithm is followed. The concern is about the unbalanced cost of diagnosis if the cartridges have to be bought at a non-negotiable price of about €50 per cartridge.

Alternative diagnostic algorithm

In 2014, a diagnostic algorithm was developed by a visiting laboratory consultant, implying a rational use of Xpert MTB/RIF for selected categories. The algorithm only refers to the diagnostic workflow at the NRL in Skopje: it should be integrated into the country algorithm. Screening for symptoms and CXR are still the initial steps in the algorithm, but the use and role of smear microscopy and Xpert MTB/RIF should be revised (Annex 6). Comparing the two algorithms the differences in approach are evident: in the country algorithm all suspects will be screened by Xpert MTB/RIF (Annex 5), while in the new diagnostic algorithm (Annex 7) a strict selection of presumed TB cases will be tested by Xpert MTB/RIF. The choice of algorithm should be discussed by several stakeholders, including the TB Commission and representatives of the Ministry of Health, and should be based on a cost–benefit analysis.

TB laboratory network

The TB laboratory network has a pyramidal and centralized structure with the NRL in the ILDTB in Skopje at the top of the pyramid. The network consists of six laboratories performing direct smear microscopy (Gostivar, Jacenovo, Kozle, Lesok, Skopje, Tetovo) and three performing cultures (Bitola, Kozle and NRL). Only the NRL performs further testing, including molecular assays. Smear microscopy laboratories are located within the LDTB dispensaries and general hospitals. They are not only dedicated to TB diagnosis: their activities include tests for

other diseases. Moreover, in some dispensaries smear microscopy is only adopted for patient monitoring (Gostivar), while for diagnostic purposes the individual is referred or (less often) samples are delivered to the NRL.

Quality assurance

The NRL organizes external quality assessment for smear microscopy in the country. Once a year, a panel of 10 slides is sent from the NRL to participating laboratories. In 2015, all laboratories passed the test. Files on external quality assessment are archived at the NRL. Two on-site visits per year are planned, during which slides for rechecking are collected.

For international external quality assessment the NRL participates in the European Centre for Disease Prevention and Control Proficiency Testing scheme (Instand e.V.), with satisfactory results for culture, identification, conventional and molecular DST as well as the detection of *M. tuberculosis* complex by molecular assays.

The NRL produces an annual report on basic laboratory indicators, which is sent to the director and epidemiologist of the ILDTB. There are no quarterly reports.

The laboratory indicators produced do not take into account other important indicators suggested in previous country visits (Table 10). Annex 8 contains a list of suggested indicators.

Table 10. NRL performance indicators, the former Yugoslav Republic of Macedonia, 2015

Indicators	No.	Positive result	
		No.	%
Microscopy			
Presumptive TB screened (including extrapulmonary TB suspects)	3664	99	**2.7**
Patients follow-up	491	42	8.5
Samples tested (total)	6022	205	3.4
Samples for diagnosis	5040	163	3.2
Samples for follow-up	982	42	4.3
Culture			
Total samples	6435	356	5.5
Contaminated samples	182		2.8
Patients investigated (either for diagnosis or treatment follow-up)	3692	192	**5.2**
DST (all TB patients)			
DST performed and confirmed MDR	202[a]	4	**1.9**
DST performed and rifampicin-resistant	202[a]	1	**0.5**
DST performed and DST *pan*-susceptible	202[a]	192	**95**

[a] Positive cultures include 192 at the NRL and 10 from Bitola and Kozle.

From Table 10, it can be seen that only 2.7% of the patients with presumptive TB were actually confirmed by positive sputum smear microscopy, which may be explained by a poor selection of respiratory patients for such investigation. The data on bacteriological culture are difficult to interpret as there is no differentiation for diagnosis and follow-up.

Indicators for molecular testing are missing for 2015 because in that year and the first months of 2016, procurement and supply of consumables was interrupted. The Xpert MTB/RIF results reported on the TB registers at different LDTB dispensaries show that there are huge differences in terms of availability of Xpert MTB/RIF results. In some dispensaries up to 50% of TB cases

have been confirmed by Xpert MTB/RIF whereas in others this percentage is much lower (5%). The Xpert MTB/RIF is mainly used at the request of clinicians. This unbalanced data from some dispensaries could come from a lack of awareness that a molecular test can be requested, or even from scepticism regarding new molecular tools.

Biosafety

The TB laboratory network has smear microscopy rooms, where the only biosafety measure is natural ventilation.

The new TB laboratory is situated on the first floor of the NRL with many rooms. According to international standards three rooms for molecular biology are present (pre- and post-polymerase chain reaction, and the DNA loading room). The most hazardous methodologies with viable bacteria are performed in the mycobacteriology department, accessible through a double door into an anteroom. Inside the laboratory, biosafety equipment and personal protective devices are available: two biosafety cabinets, refrigerated centrifuges with lids, respirators (N95; FFP2) and disposable laboratory coats.

Human resources

At the NRL, the staff include the manager and two technicians. The most the urgent topic to deal with is the scarcity of human resources. The head of the laboratory was supposed to retire in 2016 but was asked to stay on for one more year. One of the technicians retired in 2015 and was not replaced. No plans have been made to replace these staff members. There is no shortage of staff in the rest of the laboratory network.

Recommendations

Ministry of Health

1. The Ministry of Health should include laboratory staff when preparing an adequate human resources plan. Steps to replace the laboratory manager and another technician should be taken urgently.
2. The Ministry of Health should negotiate the cost for Xpert MTB/RIF cartridges and should ensure the regular procurement and supply of consumables and reagents for conventional and genotypic methods for TB detection once the Global Fund project has expired.

NTP

3. The NTP should ensure universal access to high-level microbiological diagnosis of TB, according to a sustainable national algorithm based on 100% culture of presumptive TB cases and access to new molecular tools for a higher number of these cases according to the algorithm chosen.
4. The NTP should consider harmonizing the flow of presumed TB cases from the primary level (GPs) to higher levels of diagnosis and care by optimizing the activities of intermediate facilities. Rationalization of smear microscopy laboratories should be included.
5. Culture at the laboratory in Bitola and the Bact/Alert in Kozle should be terminated (according to the new diagnostic algorithm).
6. Laboratory and programme indicators should be used in accordance with Annex 8.

7. The NRL should test all diagnostic samples from MDR and rifampicin-resistant TB cases for susceptibility to second-line drugs and pyrazinamide, or should consider sending cultures to internationally recognized TB laboratories as part of international collaboration with a supranational reference laboratory.

TB treatment and case management

The national policy guarantees free treatment for TB patients (in the framework of the Preventive TB programme funded from the state budget and implemented by the Ministry of Health) *(15)*. This is regulated for those who have health insurance (coverage 86%) and for refugees/asylum-seekers. Patients who have no health insurance or an income below 2300 dinars are assisted by the Ministry of Labour and Social Protection through the provision of health insurance and additional financial and social support.

The country uses the regular WHO recommended standard first-line drugs treatment category 1 for new cases[3] and category 2 for retreatment cases.[4]

Category 2 treatment with added streptomycin was previously recommended for patients with a high likelihood of rifampicin-resistant TB. When rapid molecular tests are used that prove the absence or presence of rifampicin-resistant TB, there is no need to use streptomycin in previously treated cases. Although rapid molecular tests are available in the NRL, their use is limited.

Case management

All TB cases are hospitalized during the intensive phase of treatment. Patients may, however, refuse hospitalization and start ambulatory treatment from the first day of treatment. From 2011 to 2015, about one third of all registered patients preferred to start on ambulatory treatment. Approximately 80% of patients hospitalized were admitted to the ILDTB (Table 11).

Directly observed treatment is not used outside hospitals; patients on ambulatory treatment are given a monthly stock of anti-TB drugs until the next treatment follow-up. The Global Fund grant pays for six patronage nurses[5] follow up patients in four cities with the highest burden of TB: Gostivar, Kumanovo, Skopje (Pit Bazar) and Tetovo. The doctor usually selects the patients for inpatient treatment. The most important criterion is infectiousness of the patient. Additional criteria are relapse, chronicity, co-morbidity, social vulnerability, likelihood of future loss to follow-up and poor access to the LDTB dispensaries (in practice, these criteria cover the majority of patients). The frequency of home visits varies from daily to once monthly. Drug intake is indirectly monitored by counting the remaining drugs for the months and calculating the accuracy of intake. But the main activity of patronage nurses is psychological support and health education to convince the patient to adhere to the treatment.

[3] Two months of isoniazid, rifampicin, pyrazinamide and ethambutol followed by four months of isoniazid and rifampicin.
[4] Two months of isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin followed by one month of isoniazid, rifampicin, pyrazinamide and ethambutol and five months of isoniazid, rifampicin and ethambutol.
[5] A patronage or community nurse encourages patients and mediates in the provision of material help.

Table 11. Number of TB patients hospitalized for treatment, the former Yugoslav Republic of Macedonia, 2011–2015

Place of treatment	2011	2012	2013	2014	2015
Institute at Kozle	30	22	17	15	13
ILDTB	154	157	140	129	146
Infectious diseases clinic	3	6	5	3	3
Department at Bitola	12	9	15	5	6
Department at Shtip	0	0	0	0	0
Psychiatric clinic, Demir Khisar	1	1	0	2	0
Psychiatric clinic, Negorci	1	1	1	1	5
Psychiatric clinic, Skopje	2	1	2	2	0
Special facility, Demir Kapija	0	0	1	0	0
Special hospital, Jasenevo	9	2	1	5	1
Special hospital, Leshok, Tetovo	14	18	18	19	13
Other facilities	8	5	6	6	4
Patients hospitalized for initial phase	234	222	206	187	191
Patients starting ambulatory treatment	128	133	117	98	93
Total patients registered	362	355	323	285	284
Proportion starting ambulatory treatment (%)	35.4	37.5	36.2	34.4	32.7

Adherence to treatment by TB patients is further assured by support from different sources. Under the Global Fund grant, socially disadvantaged patients are eligible for food packages (€40 a month) and a transport fee (€10 a month). The Ministry of Labour and Social Protection, municipalities and a range of nongovernmental organizations may also provide additional support.

Of the 254 new cases notified in 2014, 16 (6%) cases died. All the patients who died (12 men and four women) suffered from co-morbidities. None was rifampicin-resistant, their ages varied from 25 to 84 years and the median time of treatment from start to death was 14 (0–126) days. Co-morbidity is thus an important factor for fatalities, but a median of two weeks delay in starting treatment cannot be considered a system problem.

According to the NTP guidelines, cases of latent TB infection should receive isoniazid preventive treatment daily for six months. In practice, latent TB infection is mostly diagnosed and treated in children (see section on childhood TB).

The TB facility infrastructure needs to be optimized. There are 16 TB facilities in the country, half of which identify fewer than 10 cases a year (Table 12).

Given the low patient load of many facilities and the problem with the decreasing number of doctors, the NTP should consider increasing the number of facilities providing TB services. When optimizing the system it should, however, take into account the regional differences in notification rates that are probably based on ethnic patterns. Probably five TB/pulmonary hospitals are enough for the country.

Patients with pulmonary symptoms seen by the GP should be evaluated according to the PAL protocol and, when needed, referred to the specialist in the nearest TB facility for diagnostic confirmation of TB and a prescription for treatment. When TB is suspected, sputum samples can be sent to the laboratory in Skopje. The results will be reported to the requesting specialist, who will decide if the patient should be admitted to the regional hospital (if infection control

Table 12. Number and average rate per 100 000 population of registered TB cases by health facility, the former Yugoslav Republic of Macedonia, 2011–2015

Facility	Average number of registered cases 2011–2015	Average rates per 100 000 population of registered cases 2011–2015
Skopje LDTB Dispensary	122	20
Kumanovo Internal diseases -TB Dispensary	22	16
Tetovo LDTB Dispensary	28	24
Gostivar LDTB Dispensary	33	28
Kicevo LDTB Dispensary	11	16
Bitola Pneumophtisiology	8	6
Ohrid Pneumophtisiology	11	9
Prilep Pneumophtisiology	6	6
Stip Internal Disease Ward	3	5
Strumica Internal Disease Ward	14	8
Debar Internal Disease Ward	5	17
Veles Consultative Clinic for Ambulatory Pulmonary and TB Care	9	6
Gevgelija Consultative Clinic for Ambulatory Pulmonary and TB Care	8	17
Kriva Palanka LDTB Dispensary TB	3	13
Kocani LDTB Dispensary	15	14
Probishtip Consultative Clinic for Ambulatory Pulmonary and TB Care	3	11

measures are adequately implemented there – see section on infection control) or can start ambulatory treatment. For the ambulatory phase of treatment the patient will be referred to the PHC services near his/her home. Outreach services should be available. The final results of such arrangements will be that: patients will not have to use time and money travelling long distances; the number of respiratory patients investigated for presumptive TB will be filtered by the specialist; the workload in the laboratory of the ILDTB will decrease; and the remaining TB facilities will have fewer staff vacancies and operating costs (cleaning, bedding, food for patients).

Recommendations

NTP

1. The Ministry of Health should consider closing a number of intermediate TB facilities (TB dispensaries and hospital departments) and increasing the involvement of the remaining intermediate TB facilities and the primary care providers in TB case management.
2. Outreach services such as patronage nurses should be used more intensively for follow-up to improve treatment outcomes in vulnerable patients, for example, retreatment cases.
3. The algorithm for diagnosis and treatment of latent TB infection should be critically reviewed and updated if it proves to be old. Adherence to the revised protocol needs to be supervised.
4. The use of streptomycin in the first-line drugs regimen for previously treated TB patients should be discouraged as there is no justification for its use given the availability of rapid diagnosis of rifampicin resistance.

Childhood TB

The (draft) NTP strategy 2013–2017 aims to examine all children aged up to 14 years who have been in contact with TB patients, to examine 250 children with presumed TB that have not been in contact with TB patients and to treat 35–40 children with various forms and localization of the disease per year.

Every year 500–600 contacts are identified, of whom 80% undergo screening and 40–60 cases of latent TB infection are identified.

Kozle Children's Hospital is the facility where all children of the country are investigated and treated for TB. Children are referred here when they have a history of contact with an infectious TB patient (usually a household contact). Diagnosis is based on CXR and TST and bacteriological confirmation is through microscopy, culture and DST from gastric lavage or sputum induction when sputum cannot be collected. Xpert MTB/RIF is not used even though it has been recommended by WHO *(16)*.

From January to July 2016, the hospital tested 96 TB paediatric patients (three smears and one culture each) without finding any positive case. In 2015, only one out of 150 suspects (0.7%) tested was positive to culture. Clinicians can request samples to be sent to the NRL for Xpert MTB/RIF testing but rarely do so. The occasional positive cultures are sent to the NRL for DST.

The hospital has a TB ward with eight beds for children and the same number for mothers. Day-hospital admission is possible, giving children the possibility to spend the night at home.

The treatment regimen is the same as category 1 for adults, but dosages are adapted to the weight of the children. The Global TB Drug Facility has provided paediatric drug formulations free for the last few years. The procurement of paediatric formulations has been budgeted for in 2017.

The number of notified cases in the country more than halved from 2011 to 2015 and so did the number of admissions (Table 13). In 2012–2014, however, the proportion of admissions declined by an additional 10–15% owing to the renovation of the hospital.

Table 13. Children notified with TB, and the number and proportion admitted to Kozle Children's Hospital, the former Yugoslav Republic of Macedonia, 2011–2015

Year	Notified	Admitted	%
2011	33	30	90.9
2012	29	22	75.9
2013	23	17	73.9
2014	19	15	78.9
2015	14	13	92.9

Latent TB infection

Preventive treatment for latent TB infection is only provided in the TB ward of the Kozle Children's Hospital and only to children aged up to 15 years and with a tuberculin skin test (TST) result of 10 mm or more. The regimens used are three months rifampicin and isoniazid or six months isoniazid.

In 2015, 500 children were tested for latent TB infection; 67 children with a mean age of 7.3 (1–15) years and an average TST result of 9.5 (0–50) mm, were put on preventive treatment: 23 on three months rifampicin and isoniazid and 44 on six months isoniazid. Of 41 children with a TST ≥5 mm, 30 were unnecessarily retested with IGRA (QuantiFERON). Seventeen results were negative, yet all 41 children were put on treatment.

This indicates either a poor latent TB infection algorithm or poor adherence to a good algorithm. There is no need for preventive treatment for latent TB infection if both tests are negative, and there is no need for a confirmation test if the results do not influence the interventions.

Vaccination with bacille Calmette-Guérin

Vaccination with bacille Calmette-Guérin is performed at birth. The strategy for TB control 2013–2017 (which has still not been approved by the Ministry of Health) includes revaccination at the age of seven years, but the review team understood that this is not done.

Recommendations

NTP

1. Samples of all paediatric presumed TB cases should be tested by Xpert MTB/RIF.
2. The NTP should develop an algorithm that deals with the use of TST and IGRA in establishing the diagnosis and defining the correct criteria for treatment of latent TB infection in children. Adherence to the revised protocol needs to be supervised.
3. The policy for revaccination at the age of seven years, which is included in the draft strategy for TB control 2013–2017, should be revised.

HIV-related TB

Burden

The country has a low prevalence of HIV/AIDS. The first HIV/AIDS case was diagnosed in 1987. Between 2006 (first year of reporting) and 2015, a total of 126 people living with HIV (PLWH) were reported, with an increase during 2013–2014 *(17)*. In 2015, the reported modes of HIV transmission were heterosexual contact (48%), men having sex with men (39%), injecting drug use (5%), transfusion (2.5%), mother-to-child (2.5%) and other/undetermined (2.1%). In general, diagnosis occurs late, suggesting that many cases are missed at an early stage *(18)*.

During the last two years the rate of men having sex with men rose from 0% in 2010 to 44% in 2012 and 67% in 2014.[6]

Of all registered cases in the country, 75% were from the six municipalities: Skopje 108 (47%), Tetovo 23 (10%), Kumanovo 14 (6%), Prilep 10 (4%), Ohrid 9 (4%) and Kicevo 8 (4%), plus a total of 10 (4%) registered cases from abroad.

[6] Oral communication from Dr Vladimir Mikic, Sector for Prevention and Control of Communicable Diseases, Institute of Public Health, Skopje.

Almost 87% of PLWH were being given antiretroviral therapy.

Like the NTP, the national HIV/AIDS programme is under the Department of Preventive Services. The programme has received support from the Global Fund since November 2004, but as the country is classified as upper-middle-income, it is no longer eligible for funding.

In 2003, at the suggestion of the Global Fund, a national multisectoral HIV/AIDS Commission was formed, at the suggestion of the Global Fund, with membership drawn from governmental, nongovernmental and United Nations organizations. This Commission is accountable for the development and oversight of the national HIV/AIDS strategy, which focuses on prevention services for the populations most at risk, early testing and admission to health care, antiretroviral therapy for all in need, closing the link between the HIV and TB services, and strengthening surveillance and community systems. Cooperation between the TB and HIV programmes has been established.

Since 2011, payment for HIV counselling, testing and treatment has been covered by the Ministry of Health. The Ministry also finances antiretroviral drug susceptibility testing, aiming to cover all PLWH before they start antiretroviral therapy.

Many public or private health facilities provide HIV counselling and testing. Free services are available at the University Clinic of Infectious Diseases, the Institute of Public Health, public health centres and two youth centres managed by the Health and Education Research Association. Civil society organizations provide fast screening tests; the University Clinic and the Institute of Public Health use enzyme-linked immunosorbent assay tests. The final confirmation test can only be done at two facilities: the University Clinic and the Institute of Public Health *(19)*. Antiretroviral treatment is only provided by the University Clinic of Infectious Diseases, and is free.

Reducing HIV among TB patients

The proportion of TB patients tested for HIV has increased over recent years to 65% in 2015; only one tested positive between 2010 and 2015 (Table 14). This may indicate that TB/HIV coinfection is not yet a problem. All coinfected patients received antiretroviral therapy.

Table 14. Proportion of TB patients tested for HIV and proportion testing positive, the former Yugoslav Republic of Macedonia, 2010–2015

Year	All notified TB cases	Tested for HIV		HIV-positive	
		No.	%	No.	%
2010	420	40	9.5	0	0
2011	362	45	12.4	0	0
2012	355	146	41.1	0	0
2013	323	207	64.1	0	0
2014	285	168	58.9	1	0.6
2015	284	185	65.1	0	0

Blood samples from TB patients all over the country are sent to the Institute of Public Health for HIV testing. Confirmation tests are done at the University Clinic of Infectious Diseases and Institute of Public Health. Antiretroviral treatment starts at the University Clinic of Infectious Diseases and the stock of antiretroviral drugs is kept there. Testing of TB patients has stepped up since 2012, but

although it is said that all TB patients receive voluntary counselling and testing, coverage of HIV testing in 2015 was only 65% (Table 14). HIV testing is not proposed for children.

Cotrimoxazole preventive treatment for TB/HIV co-infected patients has been introduced for PLWH who have a positive IGRA test.

Reducing the TB burden among PLWH

All persons detected with HIV infection are sent to the ILDTB for a CXR and the collection of a sputum sample. This practice places PLHIV at high risk for TB as the Institute has limited airborne infection control measures (see chapter on infection control). There are plans to introduce annual screening for TB among all PLWH.

Isoniazid preventive treatment for PLWH with a positive QuantiFERON test is in place, paid for by the Preventive Programme.

Recommendations

NTP/national HIV/AIDS programme

1. PLWH should not be screened at the ILDTB but referred to the radiological clinic next to the University Clinic of Infectious Diseases for a CXR. A sputum sample should be collected at the HIV centre and sent to the NRL. It is important for the current referral system to be revised soon in view of the planned introduction of annual screening for TB among all PLWH.
2. Coverage of HIV testing among TB patients should be stepped up to reach 100%.

Drug-resistant TB

The burden of drug-resistant TB is relatively light. Since 2007, on average there have been seven to eight new cases annually with monoresistance to isoniazid, two new cases of polyresistance and four to five new cases of MDR-TB. From 2007 to 2015, a total of 42 MDR-TB cases were identified. In 2015, no cases of polyresistance and five cases with MDR-TB were notified. One of these cases was proved to have extensively drug-resistant (XDR) TB. In 2016, only one MDR-TB patient had been diagnosed by the time of the review.

All culture-confirmed TB cases undergo DST for first-line drugs by liquid testing at the NRL. In 2015 the DST coverage was 100% (202/202). Rapid testing is not routinely performed on all MDR suspects but is based on requests from clinicians or from the Consilium (group of experts composed of two clinicians, a laboratory specialist and the head of the NTP register) when there is a high suspicion of MDR-TB.

The policy is for all MDR or rifampicin-resistant cases to be tested for second-line drugs, but second-line drug resistance testing is not routinely performed at the NRL. In the past MDR-TB isolates were sent to the laboratory in Slovenia to be tested. In 2015 no strain was sent abroad for second-line drug resistance testing. The data on rapid testing for second-line drugs (Hain Genotype MTBDR*sl*) held by the NRL were not considered reliable by the review team.

All MDR-TB cases start treatment in the ILDTB in Skopje. The ILDTB acts as the MDR-TB expert centre. The Consilium discusses each case of MDR-TB and chooses the treatment regimen based on the expected resistance pattern. Hospitalization lasts until sputum culture conversion. In rare cases treatment is ambulatory from the first day, but directly observed treatment should be ensured.

During 2012–2015 a total of 13 MDR-TB patients were notified. Of these patients, two had been treated successfully and five were still in treatment; three had died (23%) and three (23%) were lost to follow-up.

The medical files of the six MDR-TB patients notified in 2015 and 2016 were examined by the review team. Five patients were newly detected and one patient had previously been treated; one had died, two had been lost to follow-up and three were still in treatment. The fact that five out of six MDR-TB patients were newly detected indicates ongoing MDR-TB transmission rather than the result of inappropriate previous TB treatment. Only one of these six patients had DST to second-line drugs, and this patient had XDR-TB.

Based on the recommendation from the most recent visit by the Green Light Committee for Europe (21–23 December 2015), the intensive phase of treatment for new rifampicin-resistant TB cases is now eight months, as per WHO guidelines *(20)*. However, the review team observed that some MDR-TB cases were receiving streptomycin as an injectable agent even though it should only be included when other injectables (amikacin, capreomycin or kanamycin) cannot be used and there is a proved strain susceptibility for streptomycin.

Almost all regimens contained ethambutol and some had 4-aminosalicylic acid (para-aminosalicylic acid or PAS). These are included in the add-on group of anti-TB drugs with limited efficacy/long-term safety and should be replaced by core second-line drugs.

Some patients were receiving ofloxacin, which is no longer recommended for MDR-TB treatment. Some regimens contained suboptimal dosages of prothionamide and amikacin.

The conclusion is that the treatment regimens are not in line with WHO guidelines.

Recommendations

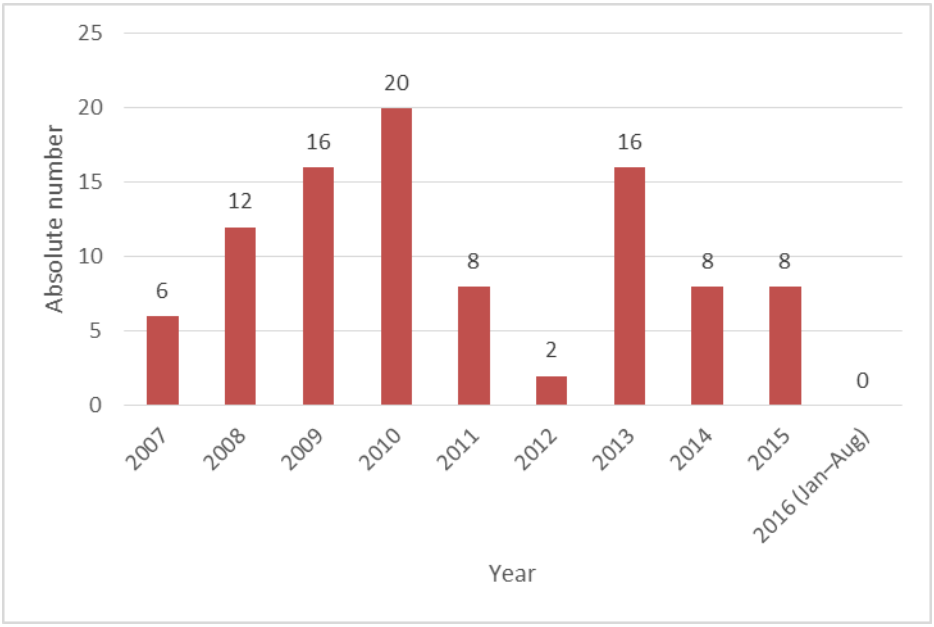
NTP

1. All rifampicin-resistant patients should have DST for second-line drugs, either tested on the spot or sent to supranational reference laboratories.
2. The MDR-TB treatment protocol should be revised in accordance with the latest WHO *Treatment guidelines for drug-resistant tuberculosis*.
3. Directly observed treatment should be ensured for all MDR-TB patients, either in or out of hospital.

TB control in prisons

TB cases reported in the penitentiary system have averaged 10 a year in recent years with wide annual fluctuations (Fig. 11). At the time of the review there were no TB cases in the penitentiary system.

Fig. 11. No. of TB cases diagnosed in the penitentiary system, the former Yugoslav Republic of Macedonia, 2007– August 2016



Note: no distinction is made between cases in pre-trial and prison institutions.
Source: NTP TB register (unpublished).

Between 2005 and 2012, a total of 41 prisoners with TB were registered; 34 (83%) were new and seven (17%) were retreatment cases; 24 (58%) were aged 15–34 years, 38 (93%) were male and 15 (37%) of all patients were drug users. Only one patient was diagnosed with MDR-TB and none was coinfected with HIV. Of the 41 TB patients, 36 (88%) had been treated successfully, one patient had died, three had interrupted their treatment and one was lost to follow-up *(21)*.

Penitentiary facilities fall under the Directorate of Prison Administration, which is part of the Ministry of Justice. There are 12 penitentiary facilities in the country: 10 mixed type penitentiary facilities (pre-trial + prison), one prison (Idrisovo in Skopje) and one juvenile correction centre. The official capacity is 2519. The overall population of detainees given to the review team was approximately 2600 but the number reported in the World Prison Brief (at 1 January 2016) was 3427, which corresponds with 166 prisoners/100 000 general population *(22)*. Of these, 10% were remand prisoners, 3% were females and 0.3% were juveniles. The review team was not able to visit the remand section of the prison in Skopje but observed no apparent overcrowding in the prison side.

All penitentiary facilities have a health care unit. In 2013, the decision was taken to shift the responsibility for health care services in penitentiary facilities from the Ministry of Justice to the Ministry of Health but this has only been partially implemented. Currently, six facilities have

permanent medical staff employed by the Ministry of Justice (Bitola, Idrissova, Kumanovo, Skopje, Stip and Tetovo) and six other facilities have temporary medical staff (visiting twice a week) employed by the Ministry of Health.

In the last few years, the Prison Administration has developed several departmental documents on health care: Health care Protection in Prison Strategy, a Guideline on Health Care Screening, Protocols for the Prevention of TB, HIV, Viral Hepatitis and Sexually Transmitted Diseases and a Policy on the Methadone Substitution Therapy. Despite having prison coordinators, the NTP does not carry out routine supervisory visits to the penitentiary facilities. Visits were, however, made to the two largest prisons in the country (Skopje Idrisovo and Skopje Sutka) in 2015 and 2016 with the support of the Global Fund. Supervisory visits are planned to all prisons in 2017, paid for by the Department of Preventive Services.

When a detainee enters a penitentiary facility he/she is interviewed through a questionnaire and, if symptomatic, selected for medical examination to be conducted within 24 hours after admission. Prisoners with TB symptoms are referred to a nearby civilian CXR facility as there is no X-ray equipment in the penitentiary system. All detainees are offered HIV counselling and testing and hepatitis C testing by the local branch of HERA. There is, however, no record of proposed and performed TB and HIV services, which complicates monitoring and evaluation of the association's performance.

The ILDTB organizes annual mass screenings for TB in all penitentiary facilities with a mobile X-ray machine.

Presumptive TB detainees are referred to the Ministry of Health hospital for further diagnosis and treatment. During this period, and based on a risk assessment by TB specialists, the sentence may be interrupted and resumed after cure. Only detainees from Idrisovo prison may be sent to Arestanko, a secure prison facility located on the premises of the ILDTB.

Recommendation

The NTP should include the penitentiary facilities in routine supervisory visits and use these visits to improve the implementation of the new TB guidelines in prisons.

Other vulnerable populations and social determinants

In 2015, there was an estimated incidence of 13 (12–14) new TB cases per 100 000 inhabitants (see section on TB epidemiology), the result of a steadily decreasing trend. The country will hopefully soon join those with low incidence where additional efforts are requested to eliminate TB, such as prevention and care among all vulnerable populations *(23)*.[7] As well as the PLWH and the population in the penitentiary system, some additional vulnerable population groups could be considered for targeted TB efforts.

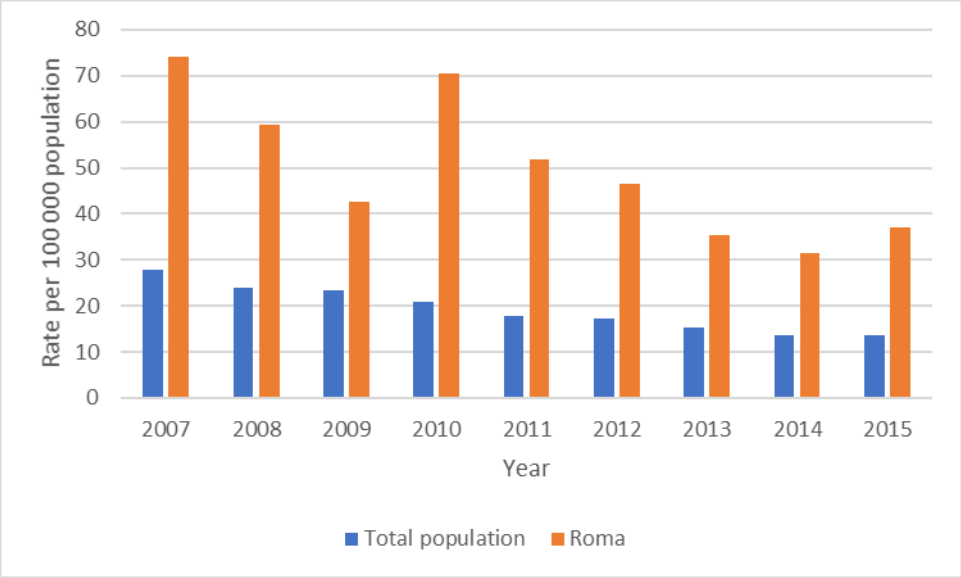
[7] A low-incidence country is when there are ≤10 new TB cases per 100 000 population per year, pre-elimination is with ≤1 new TB case per 100 000 population per year, and elimination is with ≤0.1 new TB case per 100 000 population (≤1 per million population) per year.

Roma

The Roma are a well-known disadvantaged community in Europe with poor health status and access to health care *(24)*. Despite improvements, poverty is widespread among Roma in the former Yugoslav Republic of Macedonia and they are excluded from various aspects of social and economic life. Most Roma continue to live in settlements isolated from the rest of society in conditions well below the minimum standard of living *(25,26)*.

The incidence of TB is reported to be higher among the Roma than in the general population. The reliability of the data reported is, however, questionable as the Roma are not a stable population. Notification rates are derived from a standard denominator of 53 870 Roma population (2002 census). Data from a more recent published study (2007–2012) *(27)* and the register (2013–2015) show that ,in general, notifications are two or three times higher among the Roma than in the general population (Fig. 12).

Fig. 12. Notification rate of new TB cases per 100 000 total and Roma population, the former Yugoslav Republic of Macedonia, 2007–2015



A project for Roma health mediators started in 2013 as a cooperative effort between the Ministry of Health and the civil sector. The goal of the project is to improve the health status of the Roma population through easing their access to health and social services, establishing an upper level of trust in a patient –doctor relationship and establishing habits for taking care of their own health conditions *(25)*.

Refugees

On 22 December 2015, the International Organization for Migration announced that over one million migrants and refugees had entered Europe in the record-breaking year of 2015 *(28)*. The former Yugoslav Republic of Macedonia recorded 412 351 people passing through from June 2015 to mid-January 2016 *(29)*, placing it among the top countries in the Balkan region for migrants transiting through. The closure of the Balkan route towards northern Europe on 8 March 2016 (by closure of the borders in the former Yugoslav Republic of Macedonia, Croatia

and Slovenia) stranded some 300 refugees, mainly women and children, in the two dedicated centres in the country: the Vinojug Reception Centre in Gevgelija (Fig. 13) near the southern border with Greece, and the Transit Refugees Centre in Tabanovce, close to the northern border with Serbia *(30)*. At the time of the review team's visit, there were 140 refugees in Gevgelija and 70 refugees in Tabanovce. The team was told that the Gevgelija centre would be closed but not where the refugees would be moved to.

Fig. 13. Vinojug refugee transit centre in Gevgelija, the former Yugoslav Republic of Macedonia, 30 August 2016

Photographs courtesy of Jaap Veen.

The refugees in these two centres come from Syria (58%), Iraq 36% and Afghanistan (6%). Health care in the centres is ensured through two separate health points providing primary health care services free, one supported by the Red Cross and Project Hope and the other supported by the International Committee for the Red Cross and Red Crescent. If there is a need for a specialist consultation or an emergency the patient is referred to the nearest hospital.

In the centres, there is no medical screening for communicable diseases and patients are expected to report to the health point when sick. No TB cases have been reported from the two centres.

People addicted to alcohol

In the last few years, the government has become concerned about the growth in numbers of those who can be classified as having an addiction to alcohol. About 250 000 (12%) suffer from an ongoing alcohol addiction, and 60 000 (3%) can be categorized as alcoholics *(31)*.

Of 22 TB deaths (70% males) that occurred in the ILDTB in 2010–2013, alcoholism was seen as a contributing risk factor in 23% *(32)*.

The NTP reported a total of 94 TB patients with alcoholism from 2010 to 2016 (nine in 2010, 12 in 2011, 11 in 2012, 24 in 2013, 20 in 2014, 10 in 2015 and eight in 2016).

People who use drugs

The country lies almost directly in the path of one of the world's major heroin trafficking routes, from Afghanistan through Turkey and Bulgaria on its way to Europe. It is estimated that 80 tons of heroin travel this route every year *(31)*.

In 2010 various methods were used to estimate the prevalence of injecting drug use. An extrapolation of the results from the population of injecting drug users in Skopje to the country as a whole results in an estimated 10 200 such users. Estimates by the national focal point for drug use of the number of problem drug users (mainly opiate users) for the country as a whole show about 8000 injecting heroin users. This figure corresponds to a rate of 1.5 per 1000 inhabitants aged 15–64 years. *(33)*. However, evidence in literature shows that they have a higher risk of TB infection and active disease independently from HIV infection (Table 15) *(34)*.

Table 15. TB cases among drug users by gender, the former Yugoslav Republic of Macedonia, 2010–2015

Sex	2010	2011	2012	2013	2014	2015
Male	9	5	3	6	2	5
Female	1	1	2	0	1	1

Source: NTP TB register (unpublished).

Psychiatric patients

There are four psychiatric institutions in the country: Demir Hisar, Demir Kapija, Negorci and Skopje. The team visited the psychiatric hospital in Negorci. It was built as a barracks for the army in 1972 and at present has eight buildings, of which five are meant for patients. Most buildings have been refurbished, general conditions are good and there is no overcrowding (213 patients for 220 beds available). One ward is designated as a detention facility, with 35 beds and 25 detainees diagnosed with a psychiatric illness during their judicial process. The hospital has a staff of 100 people, of whom 80 are medical, including five psychiatrists, two social workers and two psychologists. The most common diagnoses are schizophrenia and affective disorders, while a number of patients are substance abusers (alcoholics, narcomaniacs).

The review team reviewed the records of the Negorci hospital and found four TB patients, three of whom had an infectious form of the disease. All three had converted their sputum smear to negative. To prevent transmission, TB patients are housed apart from other patients. The ILDTD in Skopje follows up the patients, while the TB dispensary in Gevgelija supervises their treatment.

Staff and other patients are examined as contacts of an infectious case after a diagnosis has been made.

Only a few TB cases were found among psychiatric patients during the period 2007–2015 (Table 16).

Table 16. Number of TB patients notified in psychiatric institutions, the former Yugoslav Republic of Macedonia, 2007–2015

Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	Annual average
Skopje	6	2	6	0	1	1	2	2	1	2.3
Demir Hisar	2	1	0	0	1	1	0	2	0	0.8
Negorci	1	0	0	1	1	1	1	1	5	1.2
Demir Kapija	1	2	3	3	0	0	1	0	0	1.1
Total	10	5	9	4	3	3	4	5	6	5.4

The number of psychiatric patients is not known, so it is impossible to calculate rates. As in prisons, the populations of psychiatric institutions fluctuate, with some patients staying for short (and sometimes repeat) periods and others for a very long time. Assuming that Negorci hospital, with its 220 beds, has a stable population of 220 patients annually, the notification rate is around 550/100 000. With all its uncertainties about the real number it is clear that psychiatric patients form a formidable group at risk.

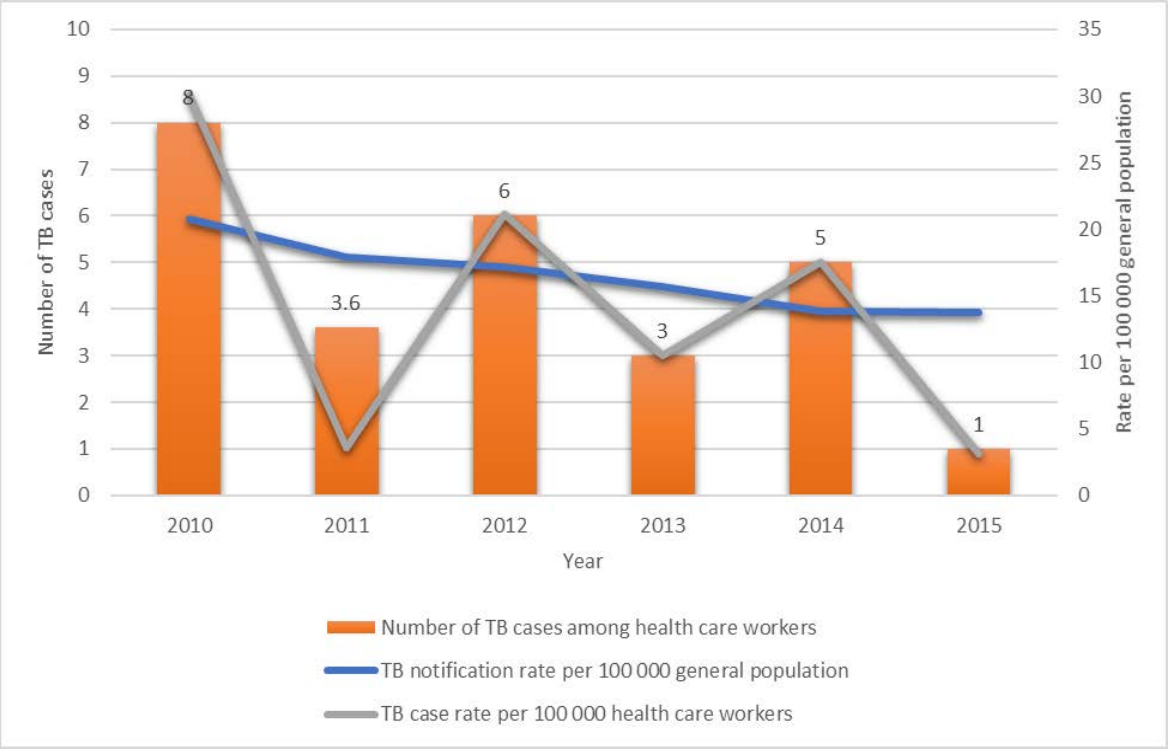
Recommendation

The Ministry of Health should target specific interventions towards the vulnerable populations that are reservoirs of TB.

Infection control

From 2010 to 2015, 24 TB cases were identified among health care staff (Fig. 14). Spikes have been observed over the years, which may correspond to irregular implementation of mandatory annual TB screening or to occasional outbreaks. Still, the rate of TB in health care workers has been lower than in the general population. A surveillance system was introduced in 2015 to monitor the risk of occupational infection with TB.

Fig. 14. Absolute number of TB cases and TB rate per 100 000 health care workers compared to the general notification rate, the former Yugoslav Republic of Macedonia, 2010–2015



Each health facility is responsible for the implementation of infection control measures in accordance with the general infection control guidelines that are based on the Health and Social Care Act 2008 Code of practice of the prevention and control of infections and related guidance

(35). As TB transmission is not specifically addressed in the guidelines, facilities in general are not much concerned.

There are no national TB specific infection control guidelines, and the national infection control plan for TB has not yet been endorsed by the Ministry of Health and thus not implemented countrywide. Some interventions are, however, taking place at a few facilities.

Administrative procedures

None of the hospitals visited had an infection control plan. The national regulation implies hospitalization of all TB cases during the intensive phase of treatment, irrespective of their infectiousness. Although all the sites visited had separate rooms for TB and non-TB respiratory patients, the patients were free to move around which increases the risk of TB transmission.

MDR-TB patients are only treated at the ILDTB in Skopje as it has separate isolation rooms for these patients.

Patients with presumptive TB, non-TB respiratory patients and TB patients in the continuation phase of treatment visit LDTB dispensaries.

Environmental measures

Influx-exhaust ventilation systems exist in the rooms for MDR-TB patients in the ILDTB in Skopje and in the rooms for infectious patients in the TB department of the Jasenevo LDTB Hospital. Some hospitals have ultraviolet germicidal lamps, but they are not shielded and not properly maintained. The remaining facilities only use natural ventilation.

Personal protection

Respirators are often not available, and when they are, the review team observed the reluctance of the LDTB staff to wear them. Staff are not tested for the fit of their respirators.

Recommendations

Ministry of Health

1. The Ministry of Health should finalize and endorse the national TB infection control guidelines aligned with international recommendations, followed by the endorsement of the national infection control plan, with basic risk assessments and the development of facility-specific infection control plans.
2. The Ministry of Health should supply all TB facilities with shielded ultraviolet germicidal lamps. Regular maintenance of these lamps should be introduced and their effectiveness checked regularly with an ultraviolet dosimeter.

NTP

3. The NTP should make respirators for personal protection available for all health staff working in potential areas at risk for nosocomial TB infection. Each staff member should be fit-tested at least annually.

Management of medicines and other commodities

The head nurse of the TB ward in the ILDTB is responsible for managing the supply of anti-TB drugs. She keeps the stock and distributes it to the TB ward or to other TB facilities. Another nurse in the Institute is responsible for managing all other commodities.

Most anti-TB drugs are available and 70% of the first-line drugs are in fixed-dose combinations. First-line drugs are not, however, on the essential drug list (EDL). Group 5 drugs (linezolid, clofazimine) are not available. Ancillary drugs for supporting patients during their TB treatment are only available at the ILDTB. Including anti-TB drugs in the EDL would guarantee their availability as a priority for budget allocation.[8]

Using the Global TB Drug Facility forecasting tool and based on historical data, the director of the ILDTB calculates the need for first-line drugs, with an additional buffer stock of 30%.

The TB head nurse at the ILDTB records the expiry dates of drugs and, when needed, asks facilities to cooperate in their redistribution. Even so, in August 2016 the Kozle children's hospital was holding a stock of expired rifampicin tablets. In other facilities some first-line drugs (isoniazid-rifampicin; isoniazid-rifampicin-pyrazinamide-ethambutol; ethambutol) had limited expiry dates or had expired.

For laboratory reagents and consumables, the NRL provides quantification and procurement of Ziehl-Nelsen solutions for staining. No stock-outs had been reported. In 2015, a shortage of consumables occurred at the NRL for the molecular tests (Xpert MTB/RIF and Genotype MTBDR platform). This was mainly due to administrative rather than financial problems.

All anti-TB drugs are procured locally from the government budget and through a national tender. Even so, a single supplier (MacLeods) seems to have been providing anti-TB drugs manufactured in India for years. The drugs are paid for through the budget of the Department of Preventive Services of the Ministry of Health. The amount budgeted for 2017 was €73 000, which is considered to be sufficient. Drugs are ordered for the period of one year. From 2017 onwards it is also planned to procure paediatric formulations. No drugs are supplied through the Global TB Drug Facility: the direct procurement mechanism was excluded because the Global TB Drug Facility requires full payment in advance, which posed an insurmountable administrative barrier.

The head of the NRL asks the ILDTB management to procure laboratory consumables, or the NTP if the consumables are paid for by the Global Fund project (consumables for molecular tools).

Anti-TB drugs, as well as all other drugs, are stored in the ILDTB store in its basement. It is not a proper warehouse, but temperature and humidity fluctuations are reportedly small. Stock cards are available for all products and are well-kept. The head nurse also has an electronic system of stock-keeping in the computer on her desk. The first in first out principle is practised.

[8] The EDL lists the most efficacious, safe and cost–effective medicines for priority conditions. It is the responsibility of the HIF to ensure that these drugs are always available in the country.

Peripheral facilities (dispensaries, hospitals) request drugs based on the numbers of patients in care. The nurse in charge of TB drugs checks with the head of the registry if the amounts requested are appropriate and, if so, the facility is asked to collect these drugs. There is no regular transport for drug distribution (pull-system). The drugs are given to the patients from the dispensaries.

There is no system for pharmacovigilance. Adverse events are rarely entered in patients' records and no systematic analysis is done.

Recommendations

Ministry of Health and the HIF

1. The Ministry of Health and the HIF should consider placing first-line anti-TB drugs on the essential drugs list.

NTP

2. The NTP should ensure the availability of linezolid and/or clofazimine for rifampicin-resistant TB cases.
3. The NTP should introduce a register for active drug safety monitoring.

Monitoring and evaluation

The NTP has a mainly paper-based recording and reporting system updated with the latest WHO definitions. When a TB patient has been diagnosed, information is sent to the dispensary that is responsible for the region where the patient lives. This information contains the diagnosis and treatment procedures. The dispensary records the patient in the patient register. When treatment has been completed, the dispensary doctor sends a report (Form TB 10) to the ILDTB, where the information is entered into the national electronic TB register. Only four TB dispensaries (Gostivar, Kumanovo, Skopje Pit Bazaar and Tetovo) can enter their data in the NTP register via the internet.

The head of the registry checks the data case by case, verifies consistency by quarterly cross-checks with on-site source registers, and in cases of possible errors uses the telephone to verify the data. The NTP register is backed up every day.

The NTP register was developed in 2006 and has its limitations. It cannot generate user-defined tables, which limits the routine evaluation of the data collected. Neither is it possible to export registry data for analysis in statistical software, which would allow further analysis to enable improvements in the delivery of TB services. The possibilities for operational research are limited. The NTP register does not include pharmacovigilance.

Recently the NRL (laboratory) electronic database has been linked to the NTP register. Through the internet, the head of the NTP register can connect to the NRL database and import the patient data needed to complete the patient's file.

The NTP sends annual reports (on paper) to the Institute of Public Health.

The ILDTB is responsible for supervision of all TB activities in the country but does not have the legal status to reinforce its recommendations. Supervisory staff act as technical advisers who document their findings and recommendations in reports which are shared with the facilities visited in the hope that these will be considered.

All TB facilities should be supervised once a year by an ILDTB team. The supervisory visits to TB dispensaries are mainly meant to review the records with a special focus on drug management. The quality of record-keeping varies noticeably between the TB dispensaries, with staff often showing a limited understanding and poor practice in treatment monitoring. The common perception of the staff is that supervision is control and punishment of mistakes, instead of an opportunity to clarify errors and build capacity.

Since the visits to the facilities are infrequent, the NTP mainly evaluates the TB activities in the country through analysis of the data in the central TB register. The analysis is limited to simple descriptive epidemiology which could also be biased by the uncertain population figures for the regions which are used to calculate many indicators.

Recommendations

Ministry of Health

1. The Ministry of Health should invest in upgrading the TB registry software to allow for the creation of custom tables and reports and for the extraction of raw data from the registry, in order to support the creation of further evidence that can be used for operational research to improve patient care and performance of the NTP.
2. The Ministry of Health should make electronic data entry available at all TB dispensaries and in the long term also include data on (daily) medication distribution to patients in the registry.
3. The Ministry of Health should ensure that supervision is based on a legal foundation to effectively allow ILTDTB staff to monitor work processes in TB facilities.

Development of human resources

Health workforce in TB

The available data retrieved by the review team on NTP human resources show that in 2014, a total of 14 specialists and 35 nurses were working in 16 TB dispensaries, and 32 specialists (including two microbiologists) and 46 nurses were working in five LDTB hospitals. Of the nurses, three in the ILDTB in Skopje and three at the specialized hospital for LDTB in Lesok were working primarily with TB patients (Table 17).

The retirement age is 64 years for men and 62 years for women, which can be voluntarily extended by two years. In the TB dispensaries, three women specialists based in Skopje and Tetovo have passed the retirement age. The other 11 specialists are aged between 58 and 60 years, and the three male specialists are aged 60 or 61 years. This means that all TB doctors are close to or past retirement age.

Table 17. Number and sex of doctors and nurses and average workload by TB dispensary, the former Yugoslav Republic of Macedonia, 2014

TB dispensary	Doctors			Nurses		Registered TB cases per year, doctor and nurse (average of the last 5 years)		
	No.	Age (years)	Sex	No.	Sex	Per year	Per doctor	Per nurse
Skopje (ILDTB)	2	64	F	3	F	122	61	41
		65	F					
Kumanovo	1	58	F	4	F	22	22	5
Tetovo	3	65	F	3	F	28	9	9
		60	M					
		60	M					
Gostivar	2	59	F	3	F	33	16	11
		61	M					
Kichevo	0			1	F	11		11
Bitola	1	60	F	7	F	8	8	1
Ohrid	1	59	F	1	F	11		11
Prilep	1	60	F	4	F	6	6	2
Shtip	0			1	F	3		3
Strumitsa	0			1	F	14		14
Debar	0							
Veles	2	Both 59	F	3	F	9	4	3
Gevgeliya	0			1	F	8		8
Kriva Palanka	0			1	F	3		3
Kocani	0			1	F	15		15
Probishtip	1	58	F	1	F	3	3	3

Source: NTP TB register (unpublished).

The average case load per doctor shows considerable variability, from 61 TB cases/doctor/year in the ILDTB to three TB cases/doctor/year in Probishtip. In seven dispensaries there were no doctors at all (Debar, Gevgeliya, Kichevo, Kocani, Kriva-Palanka, Shtip and Strumitsa).

The NTP plans to reduce the number of dispensaries in the country, which could lead to a redistribution of TB doctors. This will require careful planning and a projection of health workforce needs to prevent future shortages of skilled personnel. Based on a needs assessment, new job descriptions for health care workers (in TB services or services with integrated TB) should be developed after which new positions can be opened.

Nineteen of the 32 specialists in the LDTB hospitals and dispensaries are women and 15 specialists are 60 years or older (Table 18). All the nurses are women; their ages were not available.

Table 19 shows how many of the specialists currently employed are close to retirement. There are no new TB doctors in the pipeline. In the near future this may lead to the interruption of essential medical services in TB case and programme management.

Human resources for TB services are determined by the heads of health institutions. Turnover is nearly non-existent, and doctors and nurses tend to stay in their jobs indefinitely.

Although the ILDTB has information on the number of doctors and nurses working on TB across the country, there is no routine monitoring process to track the workforce or to evaluate future demand. This is a real challenge for the NTP. Human resource development plans have not been developed. Although the ages of doctors are known, no information is available on the ages of nurses and when they will retire.

The team was informed that medical students are not choosing studies leading to working in the TB field due to the poor working conditions, the high occupational risk, the low professional prestige and the limits on private practice.

Table 18. Doctors and nurses by age and sex per LDTB, the former Yugoslav Republic of Macedonia, 2014

TB hospitals	Doctors				Nurses
	No.	Age (years)	Sex		No.
			Male	Female	
ILDTB Skopje	15	> 60	1	3	18
		55–60		3	(3 in TB dep)
		40–50	1	6	
		30	1		
Kozle ILD children	2	62		1	5
		60	1		
Bitola Department for Pneumophtisiology	5[a]	60	2	2	
		53		1	7
	2[b]	60	1	1	
Lesok specialized hospital for LDTB	3	50		1	12
		61	2		(3 in TB dep)
Jasenovo specialized hospital for LDTB	5	57		1	
		60	1		3
		50–60	3		

Note: patients are only registered in TB dispensaries, so no inference can be made for numbers of staff and caseloads in the hospitals.
[a] Pneumophtisiologists.
[b] Microbiologists.
Source: NTP TB register (unpublished).

Table 19. Summary of TB doctors by age and sex, the former Yugoslav Republic of Macedonia, 2014

Age group (years)	Women	Men
60 and above	7	8
51–60	4	3
41–50	8	1
31–40	0	1

Source: NTP TB register (unpublished).

Working conditions

Doctors and nurses at the ILDTB work seven hours a day. Administrative personnel work eight hours and hygienists work shifts. Doctors, nurses and other medical personnel work eight hours a day in all other facilities in the country.

The personnel are offered a maximum of 26 days of annual leave a year, rising to 29 days for staff over 56 years of age. Staff working in infectious diseases receive a bonus of three extra days of leave and a salary increase of 3% for the occupational risk of infection. The number of hours worked and the benefits offered are in keeping with general working conditions for health workers in the country. TB doctors and nurses are entitled to the same amount of sick leave and pensions as other medical staff across the health care system.

Training

Undergraduate training

There are three medical schools. Medical school takes six years after secondary school.

For many years, the ILDTB was part of the medical faculty of SS Cyril and Methodius University. This ensured that students received adequate training in TB. But a disconnect has arisen between the Institute and the University Clinic. Despite this, the ILDTB is still the only institute in the country to which patients with presumptive TB are referred for diagnosis and initial treatment for TB. Thus the students at the medical faculty and attending the University Clinic do not receive any practical training in TB. The ILDTB is reviewing the current legislation with the assistance of a legal adviser in the Ministry of Health, looking for a legal technicality that will again allow the Institute to provide undergraduate training related to TB.

Physiotherapists, nurses and laboratory technicians can obtain a diploma following four years of training after secondary school. The diploma allows a nurse to be employed in patient care but not in therapeutic practice. Theoretically, to become a therapeutic nurse needs an additional three years of study, but for the time being this requirement has been waived.

Postgraduate training

An additional six years is required for specialization in internal medicine and pulmonology, two channels to enhance TB medical education. Another specialization with relevance to TB is in public health.

Doctors who are employed can have their specialization sponsored by their employers (which is used as a professional incentive), but they have to commit themselves to working in the relevant institution for several years. Studying for specialization privately costs up to €10 000.

Pulmonology has been offered as a specialization from 2015. Four hours of theory on TB is included in pulmonology (including one hour on paediatric pulmonology and one hour on pharmacology), which is part of the internal medicine course. Students gain practice through seeing cases admitted to the ILDTB clinic. The course content for nursing includes one to two hours on TB. The shift from phtisiology to pneumophtisiology and then to pulmonology changes the work description of lung specialists. TB still seems to be regarded as a disease solely for phtisiologists. This may result in their having insufficient knowledge of recent WHO TB guidelines.

In-service training

Every year, the ILDTB organizes quarterly training seminars for specialists, GPs, nurses, social workers and laboratory technicians funded through the Global Fund grant. . Each hospital has at least one social worker employed under the Ministry of Labour and Social Protection who is in charge of delivering food packages to patients and their families. The ILDTB maintains a central database in which trainers, trainees and seminar topics are recorded to ensure that new developments reach all health care workers. It also prevents duplication and facilitates future planning of in-service training courses.

Each training seminar organized lasts one and a half days, excluding travel time to Skopje. Examples of seminar topics include the protection of TB patients' personal data and practical work on evaluating the living conditions of TB patients.

Topics for seminars are revised every year. Course information is updated regularly. GPs and specialists attending the seminars receive points towards the periodic renewal of their licences. The Chamber of Physicians approves each training seminar for specialists and GPs. In future, training seminars for nurses will also need approval for accreditation (see Annex 10 for the training topics in 2015).

All personnel, including hygienists, have to pass a test on infection control. Staff from the children's hospital in Kozle and immunization centres in the country are trained annually in contact-tracing and the diagnosis and treatment of latent TB infection.

TB experts and civil society representatives participate in international meetings and conferences with the aim of increasing the capacity for managing the control of TB. NTP staff also visit neighbouring countries (Croatia, Serbia, others) to share experiences. No e-learning courses have been developed.

Recommendations

Ministry of Health

1. The Ministry of Health should take steps to realign human resources with the proposed revised network of TB services, and instigate a national TB human resources development plan.
2. A national TB human resources development plan should be part of the NTP strategy and support its goals. The plan should be based on changing job descriptions and a needs assessment, taking into account future developments in epidemiology and health systems. Routine monitoring and evaluation of the workforce should be part of the plan.
3. The Department of Preventive Services should budget for in-service training to allow for its continuation after the Global Fund grant ends.

NTP

4. Undergraduate training should be revised together with the medical faculty, taking into account the new approach towards TB control and elimination and the use of new technologies.
5. All training curricula dealing with TB should be in line with the latest WHO guidelines.

Operational research

Operational research is part of the third pillar of the End TB Strategy with the purpose of optimizing implementation and impact and promoting innovations *(36)*.

The Global Fund grant included as Objective 4 (SDA 4.1): "Enabling and promoting operational research aimed at evidence based policy decisions by developing the capacity and the

environment for Operational Research". Under this objective, the following activities were planned but have so far only been partially implemented:

- training of 10 people in operational research by an international expert;
- development of a research agenda by the NTP manager in collaboration with the operational research experts, based on the most urgent needs to analyse ongoing or new interventions, to define at least two studies annually;
- development of protocols by trained operational research experts indicating study subjects, identification of study participants, development of a data collection form (questionnaire), determination of the variables to be collected, determination of sample size;
- training for a data manager in the Statistical Package for the Social Science software and epi-info and provision with an infrastructure (computer, printer, internet, relevant software);
- training in biostatistics.

Some operational research studies have been subcontracted to nongovernmental organizations which have experience in specific fields. HOPS reported that it had undertaken a knowledge, attitude and practices study but the results were not made available to the review team.

Most recently, the project implementation unit plans to do a fast method of modelling study that will help the Ministry of Health to set priorities after the Global Fund support has ended in 2017.

A number of TB-related operational studies have been performed in the last decade.

- A study was published on the comparison of outcomes between TB patients treated in hospital and in ambulatories *(37)*. The conclusion was that there are no statistically significant differences in sputum conversion and treatment outcomes between inpatients and outpatients with TB or outpatients only. However, the length of inpatient treatment was statistically significant regarding its effect on the treatment outcome. Such a study has a potential impact on the treatment process and is an example of operational research.
- A descriptive analysis of TB in prisons in the country led to the conclusion that the NTP must make an effort and take measures in order to identify and solve the risk factors for developing TB in Macedonian prisons *(38)*. This study recognizes the determinants of TB in prisons but does not study the interventions that can improve the situation.
- An assessment of the occupational risk and characteristics of TB among health care workers employed at health institutions in the country from 2007 to 2011 turned out to be a description of the characteristics of 16 health care workers that had been identified. The conclusion seems to be that health care workers in TB institutes are less at risk due to better infection control in those institutes. The study is descriptive and cannot been seen as operational research, as there is no proper study protocol and analysis *(39)*.
- A case-control study was conducted in 2013 among households of TB patients and non-TB patients, which showed the basic social determinants of the health of TB patients implying that TB patients are mostly male, of lower socioeconomic status, less educated and unemployed and that TB is clustered in certain ethnic groups. The conclusion was that the study documented the basic determinants of TB patients and provided useful baseline information aimed at facilitating the determination of future efforts. This is an example of operational research that can have impact on the TB control processes *(40)*.

- To identify barriers to health care in four districts and to improve the quality of the NTP's performance, a knowledge, attitude and practices study was undertaken in 2008. The study revealed gaps in routine recording and reporting and in diagnostic services and a need for improved routine data management, adaptation of the PAL and new strategies to improve knowledge among people with TB. Since then the data management system has improved; the other aspects are more difficult to judge. This is an example of operational research that directly influenced the performance of the NTP *(41)*.
- Another knowledge, attitude and practices study was undertaken in 2010 to identify what TB patients know about how TB is transmitted. It led to the recommendation that the NTP should consider strategies to improve the knowledge of TB patients, such as training in client–provider communication skills, and developing a standard set of written materials regarding diagnosis, treatment and infection control for new TB patients with key messages and broader communication campaigns aimed at the general population *(42)*.
- A good example of an operational research study is the determination of the cut-off point of the tuberculin skin test in children aged 0–14 years that was undertaken in the period 2003–2007. The study showed the cut-off point to be at >=5 mm irrespective of the presence of an (anti-TB) vaccination with bacille Calmette-Guérin. A clear programme guideline emanates from this study *(43)*.

Another (not so) recent study on TB in prisons was descriptive and not meant as operational research *(44)*.

The introduction of innovative approaches, tools and technologies will require considerable operational research. At the Institute of Public Health in Skopje, no operational research activities have been planned even though the Institute could offer good support for these kinds of activity.

A coherent national TB research plan that includes a country-specific prioritized research agenda across a continuum from basic to operational research is a core requirement for the development of TB research capacity in countries with a moderate or high burden from TB. One of the easier approaches is proper cohort analysis that helps to identify where support for patients can be most effective. The introduction of new tools in the diagnostic algorithm can also be a source of new applied research studies.

Operational research is not something to be done easily. While a national capacity has not been developed, cooperation with international institutions can help in developing protocols and in-service training.

Recommendations

NTP

1. The NTP should introduce a regular ongoing system of operational research that will provide evidence-based information for both the TB expert community and national decision-makers.
2. The NTP should consider collaboration with international institutions in the field of operational research.
3. The NTP should conduct a modelling study that will help the Ministry of Health to set priorities after the Global Fund support has ended.

Ethics and human rights

Article 39 of the constitution states that all citizens have the right and duty to protect and promote their own health and the health of others *(45)*. The underlying principles and values of the national health strategy 2020 are:

- equity, which means that the whole population has financial and geographical access to a package of basic health services;
- responsibility, meaning that citizens, the government, all health care institutions providing health services, public and private enterprises and nongovernmental organizations are responsible for the health of the population;
- health insurance, which creates mutuality and solidarity between sick and healthy, poor and rich, and young and old *(46)*.

An example is EGAL, a nongovernmental organization that provides support to the lesbian, gay, bisexuals and transgender community in addition to advocating the promotion and protection of the culture, identity and human rights of these communities. The goal is to eliminate all forms of discrimination and inequality based on sex, gender, sexual orientation, sexual identity, gender identity, gender expression and intersexual characteristics.

TB diagnosis and treatment is free for all citizens whether in formal employment and registered with the health insurance or unemployed or with an informal low-income job asked to advance the cost of TB services and later reimbursed. Patients do, however, have to pay their travel expenses to Skopje in order to be diagnosed, which may deter people with a low income and those who are unemployed and not registered with the HIF. Patients also stand to lose their daily wages when they take time off to visit the GP and the TB facility.

Patients are not entitled to sick leave for diagnostic purposes. This too, may act as a deterrent to TB testing. The current law on TB prohibits certain workers (teachers, health care staff, food handlers) to work until they are cured of TB. Although patients' salaries are partially reimbursed while they are on sick leave, and legally they may not be fired during this period, it may still be an obstacle to access the TB services.

Notwithstanding the existence of the HIF, 36.7% of all health expenditure comes from out-of-pocket payments (2014 data).

Nongovernmental organizations, such as the Red Cross, assist low-income families with money for travelling to Skopje for diagnosis and support them in applying for assistance from the local government or through social welfare mechanisms set up by the Ministry of Labour and Social Protection.

Health providers are respectful of minorities, particularly the Roma. Poverty appears to be a greater barrier than lack of respect for culture or ethnicity.

In many facilities, the staff are not well protected from nosocomial TB infection because infection control measures are poorly implemented.

A number of health care facilities will soon face shortages in TB doctors which, without an adequate human resources development response, may mean that TB patients will not in future receive quality care.

Closely related to quality of care is the issue of access to essential drugs, since the official list does not at present include anti-TB drugs.

Patients have the right to refuse treatment, and contagious patients cannot be isolated against their will. Because of this, the national strategy for TB control (2013–2017) includes the creation of a legal basis for compulsory isolation of patients with MDR/XDR-TB during the initial phase of their disease. While such an approach is understandable and has been adopted in a number of countries in the Region, it should be enforced only as a last resort after all possible efforts have been made to convince the patient to be treated under proper isolation and supervision. Following discharge, MDR/XDR-TB patients have to continue treatment at the ILDTB, regardless of the inconvenience (and costs) involved.

The *International standards for tuberculosis care* describe a widely accepted level of care that all practitioners, public and private, should seek to achieve in managing patients who have, or are suspected of having, TB *(47)*. The basic principles of such care are the same worldwide. An accurate diagnosis should be established promptly, standardized treatment regimens of proved efficacy should be used with appropriate support and supervision, the response to treatment should be monitored and the essential public health action should be carried out. All providers who evaluate and treat patients with TB should recognize that they are not only delivering care to an individual, they are also assuming an important public health function that entails a high level of responsibility to the community. The country has not yet adopted the *International standards for tuberculosis care*.

The former Yugoslav Republic of Macedonia has not yet adopted the *Patients' Charter for Tuberculosis Care*, which outlines the rights and responsibilities of people with TB *(48)*.

Recommendations

Ministry of Health

1. The Ministry of Health should develop a social protection mechanism that prevents low-income people from paying diagnosis-related costs in advance for a service that is free, to prevent financial barriers to access health services.
2. The Ministry of Health should revise the law on TB to allow patients who adhere to treatment and who are physically fit to resume their work after sputum smear conversion to negative has been achieved.
3. *The International standards for tuberculosis care* should be adopted and the *Patients' Charter for Tuberculosis Care* should be introduced.
4. When legislation is revised to include the possibility of involuntary isolation, this should be done with full respect for the internationally adopted patients' rights (including the use of alternative treatment options first, the issuing of a court order and periodic reassessments).

Advocacy, communication, social mobilization

Most advocacy, communication and social mobilization activities are dependent on external funding, primarily the Global Fund grant.

In 2015, the Global Fund reduced its funding for these activities. With the ending of the Global Fund grant in 2016, it is uncertain where the budget for future such activities will come from. Nongovernmental organizations' activities, primarily educational events in schools and seminars with social workers, will be the first to be affected *(49)*.

The Strategy for TB Control in the former Yugoslav republic of Macedonia 2013–2017, inspired by the Stop TB Strategy, includes as one of its six goals support for patients (advocacy, information, communication, education), their families, the general population and patients' rights, with a number of objectives and activities. The pursuing of these goals and objectives is not, however, supported by a comprehensive strategic plan for advocacy, communication and social mobilization. Such a strategy is necessary for a TB control programme to be effective. It should coordinate all engaged partners, include strengthening the partnership between the public and private sectors (public-private mix), be in line with the TB elimination framework for action and prioritize vulnerable populations. Although several nongovernmental organizations have some form of experience with advocacy, communication and social mobilization activities, additional technical assistance may be needed for the development of a comprehensive strategy.

Advocacy

A young Macedonian woman from the Albanian community, who was cured of TB, is one of the 16 members of the TB Commission. She acts as a role model and TB advocate with the mass media.

Communication

The NTP has produced a number of educational materials (booklets, pamphlets, posters) in Macedonian targeting patients. The team had the opportunity to see such material in all ILDTB and LDTB dispensaries but not in any of the PHC centres visited. The Red Cross has produced also such materials in Albanian and Roma.

The ILDTB has organized training on stigma in TB. The last seminar was held in 2013 for specialists and demonstrated communication with TB patients and talking about TB in schools, to parents and to managers of schools. The seminar also included an exchange of experience.

Social mobilization

The celebration of World TB Day and of one national anti-TB week is organized every year. Television and radio programmes dedicated to TB are broadcast and provide the most recent facts and figures. The radio programmes have included phone-ins with answers given by TB experts. At local level, the Red Cross has supported educational programmes in schools and police stations with the participation of TB doctors and nurses. HOPS also initiated a knowledge, attitude and practices study in 2016 but no results were available.

Stigma is inherent in the general population. A cross-sectional study undertaken in 2014 documented that 17% of patients diagnosed with TB were not assisted by their family and close friends, and 8% were even treated badly by them, for example they left the patient completely alone, refused to talk or disclosed the patient's TB status to other people *(50)*.

The ILDTB in Skopje and the LDTB hospital in Bitola carry out patient satisfaction surveys.

Recommendations

Ministry of Health

1. The Ministry of Health should facilitate the development of a comprehensive advocacy, communication and social mobilization strategy that should coordinate all engaged partners and include strengthening partnerships between the public and private sectors (public-private mix). Technical assistance should considered.

NTP

2. The NTP should designate a focal person for advocacy, communication and social mobilization in the NTP management unit.
3. The NTP, in collaboration with all stakeholders, should develop key messages and advocacy activities (strategies, material) tailored to the different targets (policy-makers, academia, international partners) in supporting the TB Coalition and its efforts to ensure the long-term sustainability of NTP activities after the end of Global Fund support.

Health system and TB control

The level of compulsory state-funded health care, which is available free to all citizens and registered long-term residents, is improving. Private health care is also available. All citizens are entitled by law to equal access to health care. They can take out additional private insurance to cover services not provided by the state system but are not allowed to opt out of the compulsory state system. Only a few citizens, however, have the means to take out private health care *(51)*.

The country inherited a Semashko type health care system, in which regional and financial access to services is centralized along with a heavy reliance on specialist care and detailed central planning and management of service provision.

Health system governance

The law on health care, first adopted in 1991, stressed the principles of solidarity, mutuality and citizens' participation. The law meant to retain the aspects of the former health care system that were seen as positive and advantageous, such as control of communicable diseases, strong delivery of preventive services and access to health services free at the point of delivery. At the same time, it opened the market to private provision of services initially in specialist care (and some other areas), until reforms in the mid-2000s also changed primary care provision from public to private. As a result, all primary care providers were obliged to obtain private ownership of their practices, which are governed by the HIF through a contractual mechanism.

The two central institutions in the health care system are the Ministry of Health and the HIF.

The Ministry of Health is responsible for health policy-making, the organization of the health care system and the enforcement of health legislation, although all policies go through a process of consultation and agreement with other relevant ministries and agencies within the regulated legal procedures. Regional and local governments have almost no role in health policy development and service provision *(52)*.

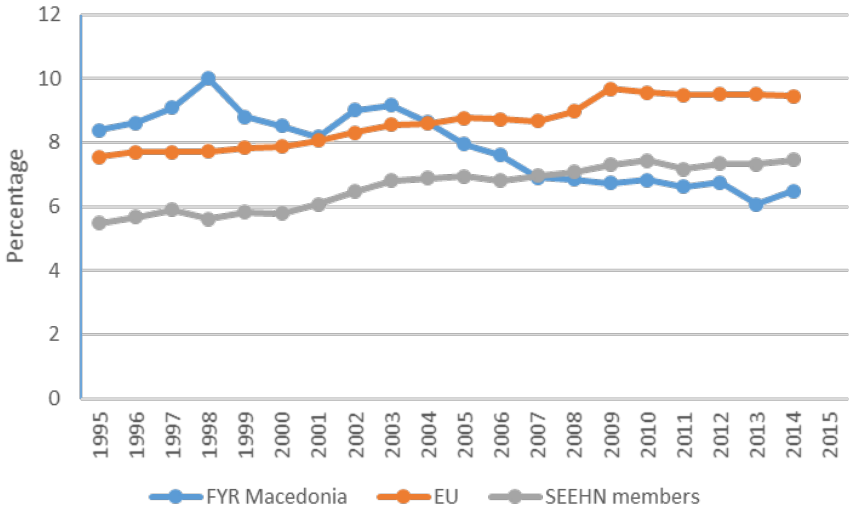
The HIF is responsible for the purchase of services from both public and private providers *(52)*. It was created by the health insurance law adopted in 2000, and acts as a semi-autonomous agency. At present the Ministry of Health manages the public hospital sector. Not long ago the public and private hospitals functioned as parallel systems, but now the HIF can contract private hospitals as well following changes in the law of health care in 2012 that allow the partial incorporation of private hospitals into the public system *(52)*.

The 2012 law on health care also established a new plan for a hospital network, with a geographical and functional scope defined by the government and operated and monitored by the Ministry of Health. The volume (and services) provided by each health care institution are based on this hospital network plan. Public hospitals that do not meet the service provision criteria (for example, the infrastructure or competence) are put on a government programme to upgrade medical equipment, infrastructure and/or the recruitment of professional staff, to ensure the provision of services close to a patient's home and to reduce patient referrals to the next levels of care *(52)*. As a result, the provision of care is less efficient than is desirable, and there is a risk of reduced quality of care as individual providers in the regions and localities do not have an adequate volume of practice to maintain high levels of preparedness.

Health expenditure

The overall health expenditure was approximately 6.5% of GDP in 2014 (Fig. 15) with a steady decline from 10% in 1998 according to WHO estimates *(53)*. In contrast, the average level of health expenditure as a proportion of GDP in 2014 was 7.5% for the countries in the South-Eastern Europe Health Network (SEEHN) and 9.5% on average for the whole EU (both with a steady increase over the years).

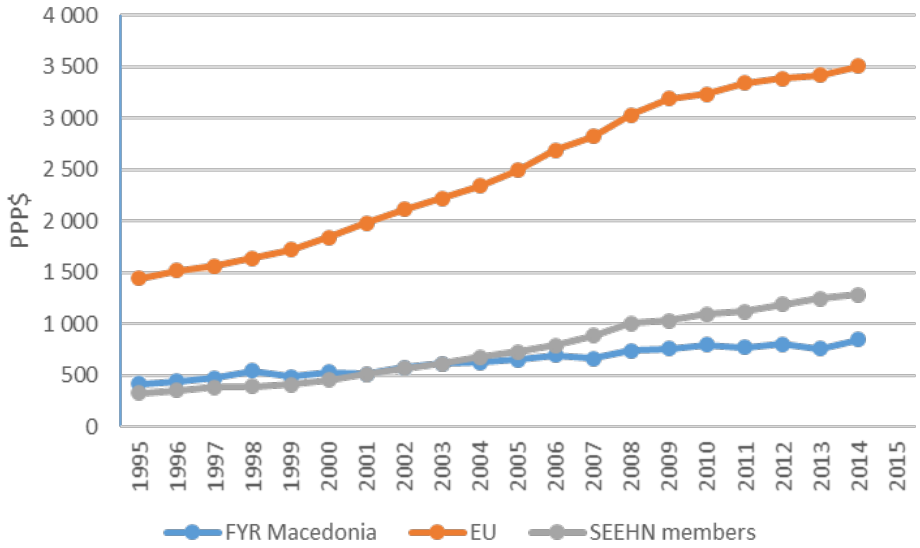
Fig. 15. Total health expenditure as a percentage of gross national income (GDP), the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53)*.

The total health expenditure in the country per capita in US dollars, adjusted for purchasing power parity ($PPP, which takes into account differences of purchasing power in different countries), was US$ 851 PPP in 2014 (Fig. 16) with US$ 1287 PPP and US$ 3509 PPP, respectively, for SEEHN and EU countries in the same year *(53)*. More importantly, health expenditure has been stable since 2008 with a minimal increase in 2014 while it increased in both SEEHN and EU countries over time.

Fig. 16. Total health expenditure per capita, US$ adjusted to purchasing power parity ($PPP), the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53)*.

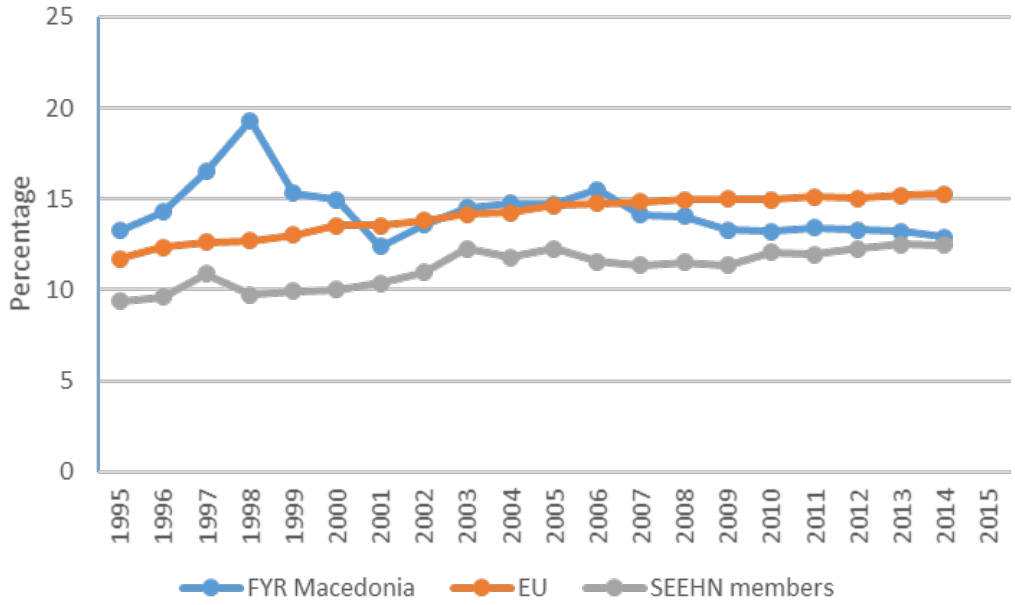
The proportion of health expenditure from GDP and the per capita expenditure illustrates the overall declining level of investment in the health sector, and the proportion of health expenditure compared to all public expenditure shows that the importance of health for the government is decreasing. There were significant fluctuations in this indicator between 1995 and 2005 (between 19.3% and 13.3%) but there has been a steady decline from 15.5% in 2006 to 12.9% in 2014, according to WHO estimates (Fig. 17) *(53)*. This proportion of decreasing health expenditure in total public expenditure is still, however, above the (increasing) SEEHN average of 12.5% while being below the EU average of 15.8% in 2014.

Health system financing and coverage

Health system financing is divided into two main components: public financing ranging from 60–70% and private financing by out-of-pocket payments by patients. Public spending is mostly from the HIF with additional transfers and direct payments from the Ministry of Health.

The main source of funding for health insurance are contributions from salaries and transfers from other agencies for specific population groups (unemployed, retired persons, persons receiving social assistance), which altogether account for 90% of total HIF revenues. The HIF purchases health services as specified in the broad basic benefit package, which covers almost all treatments and rehabilitation services for all residents eligible for compulsory insurance coverage. There are, however, some challenges with insurance coverage among, for example, the Roma community or in cases where proof of citizenship is missing.

Fig. 17. Public sector expenditure on health as a percentage of total government expenditure, the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53).*

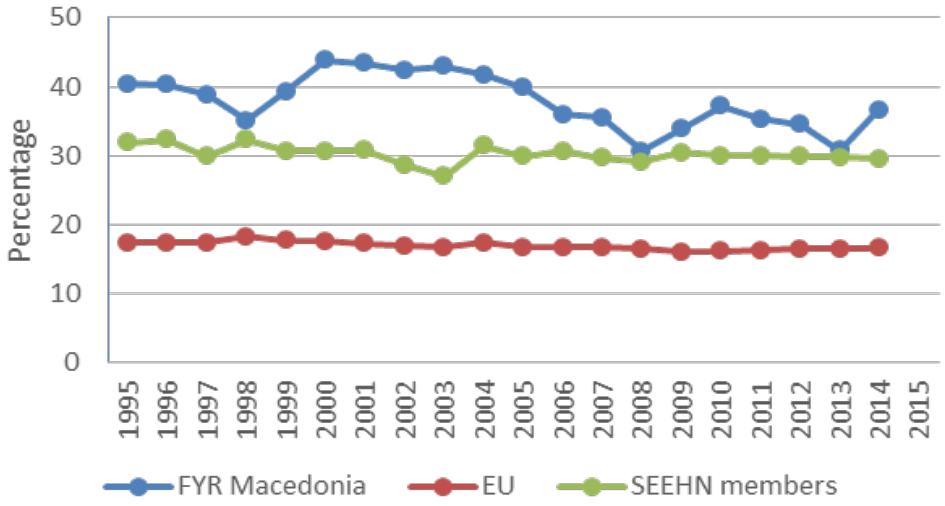
In addition to the health services, insured persons are entitled to compensation for sick and maternity leave, which is covered by the Ministry of Labour and Social Affairs and administered through the HIF. Paid sick leave amounts to 70% of the average income in the previous six months (85% for malignant neoplasms) and is paid partly by the HIF and partly by the employer, in different percentages and schemes depending on the disease category.

The Ministry of Health finances investments in public health providers (for facilities and medical equipment) and implements preventive and public health measures through the annual health programmes financed directly from the Ministry of Health budget *(52)*. A small percentage of the health care financing can be attributed to donors and nongovernmental service delivery organizations, but in the case of HIV/AIDS and TB, the Global Fund is the major donor to the health budget.

Out-of-pocket payments are mostly co-payments for health care services (capped at 20% per contact, resulting in an average 8% co-payment for services covered by the HIF) and direct payments for private hospital services, pharmaceuticals and medical devices that are not covered by the health insurance *(52)*. Although out-of-pocket spending decreased significantly from 43.8% in 2000 to 30.7% in 2008, the following years saw large fluctuations (Fig. 18) and by 2014 the proportion of out-of-pocket payments in total health expenditure rose to 36.7% again *(53)*. To ensure wide access to the health system at the primary level, services are available without any co-payments, including services for general practice that are free at the point of delivery.

Individuals usually pay themselves if they are not insured, if they choose to not use their health insurance due to waiting times, if they consider the quality of services to be inadequate or because they wish to be examined by a specific physician (without referral). Direct payments also have to be made for medicines not on the essential drug list or obtained with a private prescription not covered by the HIF. Informal payments are very difficult to estimate and it is

Fig. 18. Private household out-of-pocket payments on health as a percentage of total health expenditure, the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53).*

assumed that total out-of-pocket spending may be much higher than the above conservative estimates *(52)*.

As in many health systems with a high level of out-of-pocket expenditure, informal payments constitute a significant part of direct expenditure for patients: in 2010, over 40% of the population made informal payments for health services, with over 20% stating that they usually or always made these kinds of payment *(52)*. In particular, informal payments are made for expensive diagnostic or medical procedures and services that are limited in volume or have long waiting lists.

TB treatment is exempt from any co-payments. Primary care is provided without co-payments, but specialist services before the diagnosis of TB has been ascertained are not exempt.

Paying providers

When the primary care providers became private providers in 2005 they had to sign a contract with the HIF for payment per registered patient. However, part of the payment (30%) is in essence a performance payment which is not reimbursed to providers if they fail to achieve set performance targets. These targets focus on rational prescribing below the set budget ceiling for prescription, and rational referrals aiming to reduce referrals to the next levels of care and preventive services, with early detection of deformities in children and malignancies, cardiovascular diseases, diabetes or renal disorders in adults.

Contracts for the purchase of services from secondary and tertiary level providers are based on an analysis of the business plans submitted by each health care provider, including plans for type and volume of health services, plans for reaching goals and other required documentation. The HIF negotiates the conditions and volumes for each service. The usual practice is that the planned volume for specific services is distributed among providers who meet the conditions, but the allocation formula is not very strictly defined.

Outpatient services are reimbursed using global budgets and a capped fee-for-service payment system. The HIF contracts providers based on an annual volume of services for a predefined sum of the contract, based on both previous year's performance and expected service volume for the forthcoming period. Payments to public providers cannot fall below 80% of the agreed budget, even if they invoice a lower volume of services, but there is no such safety net for contracted private providers.

Hospitals are paid using a combination of diagnosis-related groups and conditional budgets. The latter require hospitals to provide a minimum set of health services according to the protocols adopted and standards that are monitored quarterly. Based on these, budgets are reduced or increased depending on whether the hospital fails to achieve or exceeds the set targets. The conditional budgets are intended for the provision of care while at the same time control is kept of overall hospital expenditure and part of the planned budget can be retained. The planned amount of the conditional budgets for 2014 was €9.6 million.

When primary care providers are private entrepreneurs, they are free to choose their preferred workforce payment mechanisms, similar to private specialist service providers. In the public domain, providers receive salaries as exactly defined in the collective agreement.

Service delivery

Health care services are provided at three levels of care. Primary care is full outpatient care, while at secondary and tertiary levels both specialist outpatient and inpatient care is provided.

Primary care providers (GPs, paediatricians, gynaecologists and dentists) play the gatekeeper role in the health care system. Patients register with a primary care physician of their choice; twice a year they have an opportunity to switch to a new one.

Secondary care consists of outpatient services provided either by health centres (34 in total) or various types of hospital that also provide inpatient care. In 2014, there were 18 general and clinical hospitals (one providing TB inpatient care) and 20 specialized hospitals, of which four provided TB care. As indicated above, one of the leading priorities in the organization of the secondary level of care is good regional coverage to provide care as close to the patients' homes as possible.

The type and volume of specialist consultative services delivered at the health centres is defined at state level according to historical data, health care needs and financial arrangements, with the capacity for emergency response, availability of the workforce and financial sustainability additionally taken into account for hospitals.

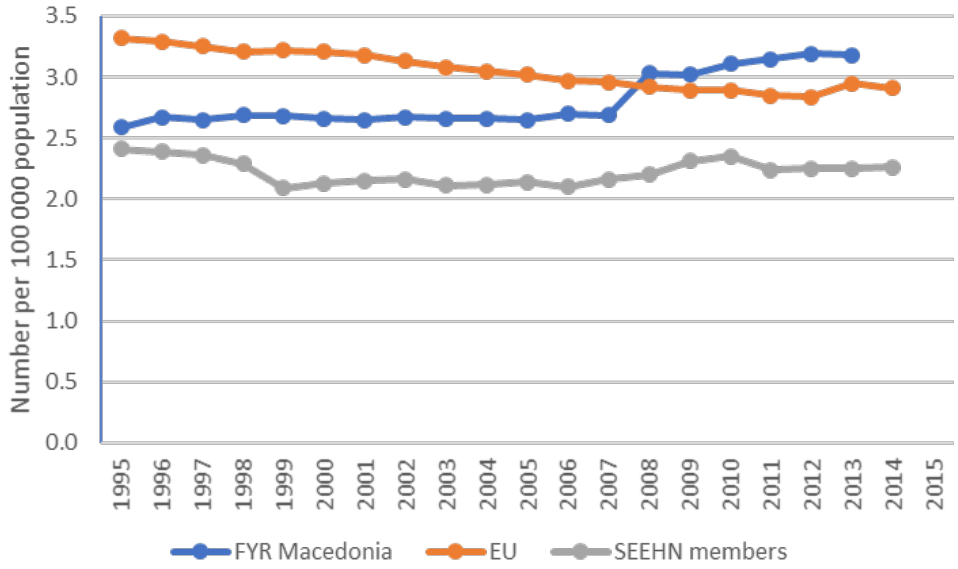
Tertiary care is provided at the University clinics in Skopje (28 in total in 2014) which are also the teaching clinics for medical professionals. TB care is not, however, provided at the tertiary care level. The secondary level ILDTB is the highest level provider of TB care.

Efficiency of service delivery in specialist care

As the number of beds per 100 000 population in the country has been declining – from 560 in 2000 to 442 in 2013 – while the number of hospitals has increased, it can be deduced that the hospitals are small and becoming even smaller (Fig. 19). But even those beds that are available

are not used; there is a very low bed occupancy rate (59.7% in 2013), meaning that the available hospital resources are not used to their full capacity.

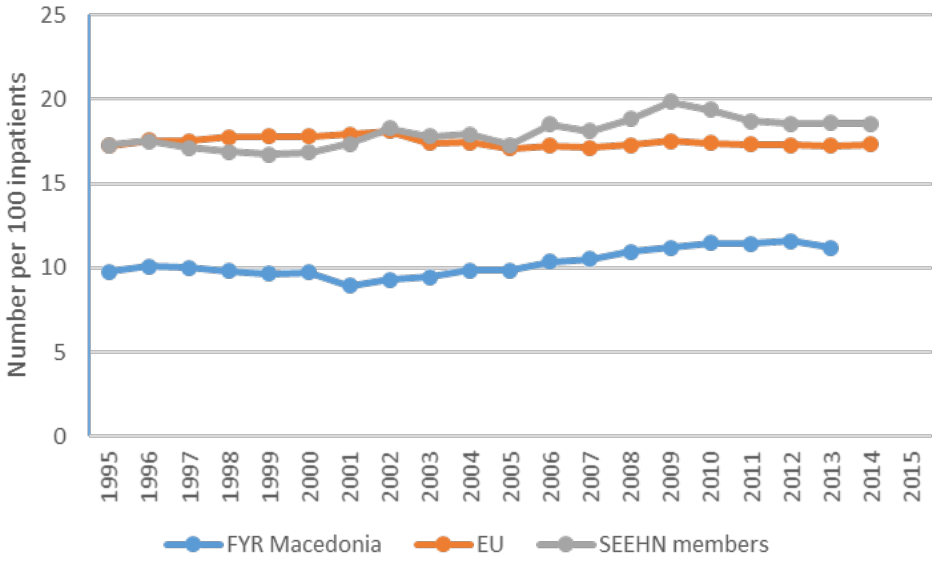
Fig. 19. Number of hospitals per 100 000 population, the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53).*

At the same time there is also a low rate of patient discharges (Fig. 20), further highlighting the inefficient use of resources, while the average length of stay decreased from 11.4 days in 2003 to 7.9 days in 2013.

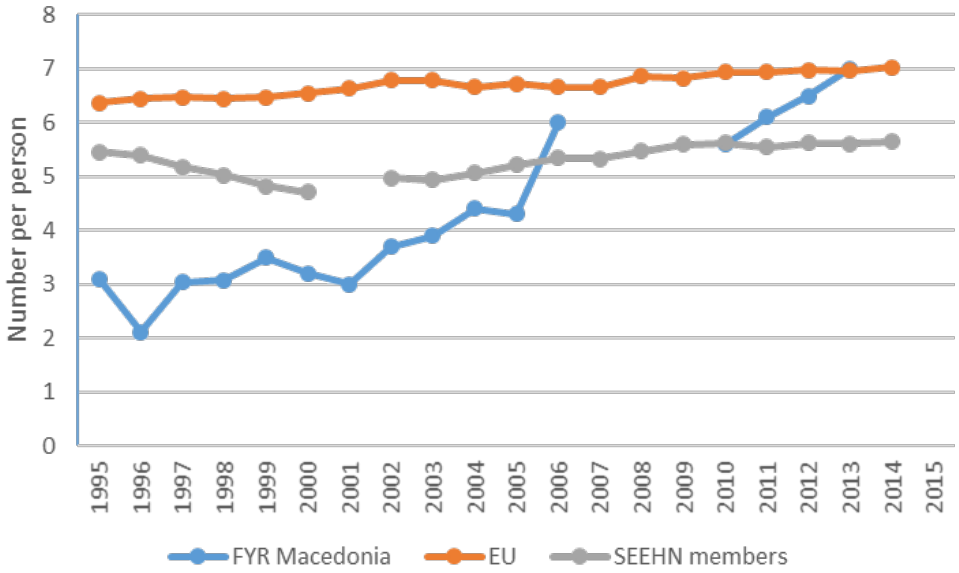
Fig. 20. Number of discharges per 100 inpatients, the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53).*

The number of outpatient contacts (both primary and specialist outpatient care) has been increasing rapidly in recent years (Fig. 21) and has almost surpassed EU levels. While the country has made a strong commitment to reduce waiting times in health care, the high number of outpatient visits does not necessarily imply an improvement in the health of the population as increases in the number of contacts can, in principle, also be due to high levels of referral in situations where there is weak coordination and care pathways are fragmented.

Fig. 21. Outpatient contacts per person per year, the former Yugoslav Republic of Macedonia, EU and SEEHN, 1995–2014



Source: WHO *(53)*.

Referral behaviour of providers and TB patient pathway

Primary care providers have the role of gatekeepers to prevent overuse of secondary and tertiary care services *(52)*. One of the components of the primary care performance payments directly incentivizes non-referral to the next levels of care. There are also treatment algorithms available for most chronic diseases (but not for TB) that lay out the general patient pathway through the health system.

However, a recent assessment of the system for treatment of noncommunicable diseases found that consecutive referrals to the highest levels of care still happen throughout the country, leaving primary care possibilities significantly underused and the possible role of specialist outpatient care partly underused *(54)*. This is due to multiple factors across all levels of care, such as the low status of GPs compared to specialists, the primary care payment mechanism that incentivizes referral through capitation and penalizes initiatives through negative performance incentives, low managerial autonomy in hospitals regarding infrastructure investment and personnel, salary payments in specialist care that do not incentivize increases in performance, and the combination of fee-for-service/diagnosis-related group and budget-based financing of specialist care which is an incentive to increasing the volume of service provision instead of improving health outcomes.

The current assessment found that the role of primary care in the provision of treatment for TB is minimal, which is in line with the study by Lai et al. *(54)*. GPs were said to refer most of the pulmonary suspects to TB dispensaries and/or other specialist consultants (pulmonologist or internist) in the nearest hospitals.

Use of resources in TB care

In the provision of TB care it seems that specialist care (especially at the highest level) is overused and primary care is underused. The gatekeeping function of primary care seems to be minimal and GPs are not involved in the delivery of medication and everyday monitoring of TB patients, creating a higher than necessary workload at the next levels of care.

Similarly, it is unnecessary to hospitalize all patients in the ILDTB in Skopje, especially when they are not contagious, as treatment could be started at the regional level. Further, the dispensaries are part of hospitals but duplicate the equipment in those hospitals to a degree (for general laboratory tests and X-rays, for example). Most of the bacteriological tests done in dispensaries have no effect on the diagnosis and treatment as patients are referred to the next level regardless of the results of the tests. There are also dispensaries staffed only by nurses where the physicians' positions are vacant. This makes such dispensaries virtually non-functional in regard to TB diagnosis and treatment while using resources for infrastructure, salaries and so on. At the same time, the hospitals where these dispensaries are located have internists available who are not currently involved in TB treatment.

Moreover, due to the declining numbers of TB cases in the country, the actual workload in the dispensaries is quite low, which has implications for the maintenance of a high quality of service and effective use of resources. The same applies to the specialist hospitals providing TB inpatient care where only a few patients really receive TB treatment and yet the infrastructure, equipment and so on have to be maintained. Here it is also worth recalling that the budget for public hospitals cannot be reduced below 80% of the agreed budget even if no cases are treated. This finding is also supported by the generally low occupancy rate of hospital beds, most likely caused by the high priority given to the local availability of all services in combination with a strong (albeit declining) reliance on (inpatient) specialist care.

e-Health

An electronic health data management system has been introduced with the intention of collecting health data on time, maximizing the use of health care equipment and resources, and (at first) reducing waiting times in public facilities. The MyAppointment (Moj Termin) software platform was later gradually extended from initial online, real-time appointment management (doctors selecting appointments for patients that needed referrals) to include e-services such as an electronic patient file for doctors, an electronic health insurance card, a number of electronic registries and the reporting of financial information to the national health insurance fund *(52)*.

The electronic medical record, which is still being developed, is envisaged to integrate all existing and future developments such as an e-diary for doctors, e-prescriptions and e-referrals into one system available to both patients and their doctors. At the moment, the e-services in health care are still mostly used for recording and reporting, while the potential of the information for care management is still largely untapped *(54)*. For instance, the assessment of health service outcomes and quality of care is still in the preliminary phase due to the lack of

systematic data collection (and analysis) of outcome data *(52)*. Similarly, there are no dedicated tools to support physicians in clinical decision-making, planning of care and management.

Doctors treating a TB patient may see that a patient has been contacted in another facility through the MyAppointment system, but not the content or results of the contact. Moreover, their own patient records are contact-based (with data for every contact recorded separately) and in text format. There are significant barriers to obtaining an overview of the treatment progression of a particular patient or an overview of the overall performance of a doctor or a facility, which result in a significant unused potential for the improvement of quality or continuity of care.

The TB registry is not linked to the rest of the e-health services and thus has to rely solely on the information provided by TB dispensaries without the possibility of enriching the registry data from other possible types and sources of data such as the overall health service and outcome data of the patients.

Recommendations

Ministry of Health

1. The Ministry of Health should consider closing a number of intermediate TB facilities (TB dispensaries and hospital departments) and increasing the involvement of the remaining intermediate TB facilities and the primary care providers in TB case management.
2. The Ministry of Health should facilitate the integration of the TB register with the rest of the e-health system in order to create the possibility for a treating doctor to have an integrated overview of a patient's health.

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Annex 1

LIST OF PARTICIPANTS IN THE REVIEW

International review members

Elmira Gurbanova	Green Light Committee Expert, Head of the WHO Collaborating Centre on Prevention and Control of Tuberculosis in Prisons, Baku, Azerbaijan
Sampreethi Aipanjiguly	Expert on advocacy, communication, social mobilization, Copenhagen, Denmark
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Jaap Veen	Independent Senior Tuberculosis Control Adviser, The Netherlands *(Team leader)*

National review members

Biljana Ilievska	Medical Director, ILDTB, Skopje, and Manager of the NTP
Anita Popovska	Economy Director, ILDTB, Skopje
Maja Zakovska	Head of the Central Unit for recording and reporting of TB cases
Cveta Vragoterova	Head of the National Reference Laboratory (NRL)
Nikola Milanovski	Head of TB department
Marina Efremova	Head nurse and responsible for TB drug management

Other members

Pierpaolo de Colombani	Medical Officer, Joint TB, HIV and Hepatitis Programme, WHO Regional Office for Europe, Copenhagen, Denmark

Interpreters

Nela Klimenta
Ivona Kostelova

Annex 2

OVERVIEW OF THE PROGRAMME

Monday 29 August 2016

09:00–11:30	ILDTB, Skopje	Biljana Ilievska Poposka, Medical Director Anita Popovska, Economy Director
12:00–12:30	Ministry of Health, Skopje	Jovanka Kostovska, State Councillor

Monday 29 – Wednesday 31 August, in the field

Thursday 1 September

09:00–12:00	ILDTB, Skopje	Nikola Milanovski, Head, TB Department Cveta Vragoterova, Head, NRL Marina Efremova, Head nurse, responsible for TB drugs Maja Zakoska, Head, Central Unit for Recording and Reporting Irina Teodosievska, responsible for Central Drug Warehouse
	Faculty of Medicine, Ss. Cyril and Methodius University, Skopje	Daniela Miladinova, Vice Dean
14:00–15:00	Ministry of Health, Skopje	Zoran Stojanovski, Head, Preventive Programme Department Djemile Alili, Preventive Programme Department
15:30–16:30	Institute of Public Health, Skopje	Gordana Kuzmanovska, Head, Department for Communicable Diseases Control and Prevention Golubinka Bosevska, Head, Laboratory for Virology and Molecular Diagnostics
17:00–18:00	Round table with nongovernmental partners	Aneta Trgacevska, Health Coordinator Red Cross Hristijan Jankulovski, Executive Director, HOPS Bojan Jovanovski, Executive Director, Health and Education Research Association Biljana Ancevska, Early Child Development Consulting and Research Kiril Solevski and Darko Iliev, Merck

Friday 2 September

09:00–10:00	Ministry of Justice	Elisaveta Sekulovska, Counsellor, Sanctions Department
10:30–11:30	Ministry of Labour and Social Protection	Suzana Anova, Head of Department
12:00–13:00	HIF, Skopje	Saso Stefanovski, Director Orhan Ramadani, Director
13:30–16:00	Prison Skopje	Aleksandar Gjorgievski, Director Nikola Pilovski. Head, TB department Sasko Lazarevski, Commander Zoran Aleksoski, Supervisor
16:30–17:30	Project Implementation Unit, Global Fund	Daniela Dukovska, Head Emilija Lokvenec, Legal/Procurement Officer

Saturday 3 September – Sunday 4 September

09:00–17:00	Working on the main findings and recommendations	

Monday 5 September

09:30–10:15	WHO Country Office	Snezana Cicevalieva, Head
10:30–11:30	Ministry of Health	Aleksandra Eftimova, Cabinet of the Minister

Annex 3

PROGRAMME IN THE FIELD

Team 1

Jaap Veen (Coordinator)
Sampreethi Aipanjiguly
Biljana Ilievska Poposka
Ivana Kostelova (interpreter)

Monday 29 August

14:00–15:30	Institute for Lung Diseases and TB in Children, Kozle	Oliver Zafirovski, Director Mirjana Dilberova, Head, TB Department Trajanka Ilievska, Head, TB Laboratory
16:00–17:00	Health Department Arestanko, Skopje	Elisaveta Sekulovska, Counsellor, Department of Sanctions (Ministry of Justice)

Tuesday 30 August

10:00–11:30	Psychiatric Hospital, Negorci	Petar Kangov, Director
12:00–13:30	Temporary transit centre for refugees, Gevgelija	
14:00–16:00	Hospital and dispensary for LDTB, Bitola	Mile Nasev, Head Vladimir Radevski, Head TB Laboratory

Wednesday 31 August

09:00–11:00	Dispensary for LDTB, Ohrid	Slavica Petrovska, Head
11:30–12:00	PHC practice, Ohrid	Mirce Grozdanovski, GP
12:30–13:00	PHC practice, Struga	Ami Mamudi, GP
14:00–16:00	Dispensary for Lung Diseases and TB, Kicevo	Zaklina Nicolovska, nurse; responsible for dispensary

Team 2

Elmira Gurbanova (Coordinator)
Emenuele Borroni
Nela Klementa (interpreter)
Taavi Lai
Anita Popovska

Monday 29 August

14:00–15:30	Clinic for Infectious Diseases, Skopje	Zvonko Milenkovik, Director
16:00–17:30	Dispensary for LDTB, Bit Pazar	Slavjanka Doneva, Head

Tuesday 30 August

09:00–10:30	Dispensary for LDTB, Gostivar	Suzan Ismail, Head
11:00–12:30	Dispensary for LDTB, Tetovo	Zorica Bilbiloska, Head
14:30–16:00	Hospital for LDTB, Lesok	Verica Teofilovska, Director
16:30–17:30	PHC practice, Tetovo	Bekim Ismaili, GP

Wednesday 31 August

09:00–10:00	Temporary transit centre for refugees, Tabanovce	Responsible person at the Centre
10:30–12:00	Dispensary for LDTB, Kumanovo	Svetlana Talevska, Head
14:00–15:30	Hospital for LDTB, Jasenovo	Goce Buzalkov, Director
16:00–17:00	PHC practice, Tetovo	Marija Stolevska, GP

Annex 4

LIST OF PERSONS MET

Name	Position	Institution	Location
Djemile Alili	Preventive Programme Department	Ministry of Health	Skopje
Zoran Aleksoski	Prison supervisor	Ministry of Justice	Skopje-Sutka
Biljana Ancevska	Representative	Early Child Development Consulting and Research	Skopje
Suzana Anova	Head of department	Ministry of Labour and Social Protection	Skopje
Djevdet Bedjeti	Pneumophtisiologist	Dispensary LDTB	Tetovo
Zorica Bilbiloska	Pneumophtisiologist, Head	Dispensary LDTB	Tetovo
Hrisula Blazevska	Patronage nurse hired by Global Fund	Dispensary LDTB	Bit Pazar, Skopje
Golubinka Bosevska	Head, Laboratory for Virology and Molecular Diagnostics	Institute of Public Health	Skopje
Verica Bozinovska	Main nurse	Hospital LDTB	Lesok
Sabani Burak	Counsellor for Primary Health Care	Dispensary LDTB	Bit Pazar, Skopje
Goce Buzalkov	Director	Hospital LDTB	Jasenovo
Borislava Cali	Nurse, TB department	Hospital for LDTB	Lesok
Snezana Cicevalieva	Head	WHO Country Office	Skopje
Dragan Dacevski	Head, TB Department	LDTB children	Kozle
Femi Demiri	Pneumophtisiologist	Hospital LDTB	Lesok
Slavjanka Donevska	Head	Dispensary LDTB	Bit Pazar, Skopje
Daniela Dukovska	Head, Project Implementation Unit	Ministry of Health	Skopje
Marina Efremova	Head nurse, responsible for central store of anti-TB drugs	ILDTB	Skopje
Aleksandra Eftimova	Cabinet of the Minister	Ministry of Health	Skopje
Ljazime Ejupi	Patronage nurse hired by Global Fund	Dispensary LDTB	Gostivar
Nermina Fakovik	Preventive Programme Department	Ministry of Health	Skopje
Ana Filipovska	Executive Secretary of CCM	Ministry of Health	Skopje
Aleksandar Gjorgievski	Prison Director	Ministry of Justice	Skopje- Sutka
Valentina Goricanec	Main nurse	Health Unit	Bit Pazar, Skopje
Mirce Grozdanovski	GP	PHC	Ohrid
Trajanka Ilievska	Head, Laboratory for TB, second level	LDTB children	Kozle
Bekim Ismaili	GP	PHC	Tetovo
Jagoda Jakimoska	Laboratory technician	Dispensary LDTB	Gostivar

Name	Position	Institution	Location
Hristijan Jankulovski	Director	HOPS	Skopje
Petar Kangov	Director	Hospital for Psychiatric Diseases	Negorci
Jovanka Kostovska	State counsellor	Ministry of Health	Skopje
Aneta Kovacki	Head, pneumophtisiologist	Dispensary LDTB	Veles
Sasko Lazarevski	Prison commander	Ministry of Justice	Skopje-Sutka
Emilija Lokvenec	Legal/Procurement Officer, Project Implementation Unit	Ministry of Health	Skopje
Atmi Mamudi	GP	PHC	Velesta, Struga
Suzana Manevska	Head, Department for Secondary and Tertiary Health Care	Ministry of Health	Skopje
Lindita Mehmeti	Head nurse	Dispensary ILDTB	Tetovo
Vladimir Mikic	Sector for Prevention and Control of Communicable Diseases	Institute of Public Health	Skopje
Daniela Miladinova	Vice Dean	Faculty of Medicine, Ss Cyril and Methodius University	Skopje
Nikola Milanovski	Head, TB Department	ILDTB	Skopje
Zvonko Milenkovik	Director, National HIV/AIDS programme manager	University Clinic for Infectious Diseases and Febrile Conditions	Skopje
Ramija Muca	Head nurse	Dispensary ILDTB	Gostivar
Mile Nasev	Pneumophtisiologist, Head, Department of Pneumophtisiology	Dr Trifun Panovski Clinical Centre and Dispensary LDTB	Bitola
Zaklina Nikolovska	Head nurse	Dispensary ILDTB	Kicevo
Nikola Pilovski	Prison medical doctor	Ministry of Justice	Skopje-Sutka
Mirjana Pehcevska Popiliev	Managing Director	University Clinic for Infectious Diseases and Febrile Conditions	Skopje
Anita Popovska	Economy Director	ILDTB	Skopje
Biljana Ilievska Poposka	Medical Director, NTP manager	ILDTB	Skopje
Elena Popovska	Specialist in internal medicine	Dispensary ILDTB	Kicevo
Vladimir Radevski	Microbiologist, TB Laboratory, second level	Dr Trifun Panovski Clinical Centre and Dispensary LDTB	Bitola
Orhan Ramadani	Director	HIF	Skopje
Ljupco Ristevski	Director	Dispensary ILDTB	Kicevo
Jelica Saraginovska	Dispensary nurse	Dispensary ILDTB	Gostivar
Elisaveta Sekulovska	Counsellor, Department for sanctions	Ministry of Justice	Skopje
Milena Stefanovik	Responsible for Programme for HIV/TB activities	University Clinic for Infectious Diseases and Febrile Conditions	Skopje

Name	Position	Institution	Location
Saso Stefanovski	Director	HIF	Skopje
Zoran Stojanovski	Head, Preventive Programme Department	Ministry of Health	Skopje
Marija Stolevska	GP	PHC	Tetovo
Keti Todorova	Representative	Doverba	Skopje
Verica Tofilovska	Director, Internal medicine specialist	Hospital ILDTB	Lesok
Vasilka Salevska Trajkova	Cabinet of the Minister	Ministry of Health	Skopje
Ramona Trajkovska	Pneumophtisiologist	Dr Trifun Panovski Clinical Centre and Dispensary LDTB	Bitola
Svetlana Trajkovska	Main nurse	Dispensary ILDTB	Bit Pazar, Skopje
Pece Trajkovski	Laboratory technician	Dispensary ILDTB	Bit Pazar, Skopje
Aneta Trgacevska	Representative	Red Cross	Skopje
Ismail Vaiti	Pneumophtisiologist	Hospital LDTB	Lesok
Meri Vasilevska	Pneumophtisiologist, Head	Dispensary LDTB	Bitola
Jasmina Velickovska	Social worker	Dispensary LDTB	Bit Pazar, Skopje
Cveta Vragoterova	Head, NRL	ILDTB	Skopje
+Oliver Zafirovski	Director	LDTB children	Kozle
Maja Zakoska	Head, National TB Register	ILDTB	Skopje

Annex 5

EPIDEMIOLOGICAL TABLES

Table 4.1. Notification of all TB cases by new and relapse and case fatality by absolute numbers and rates per 100 000 population, the former Yugoslav Republic of Macedonia, 2007–2015

Year	Population	All TB cases		New and relapse cases		Mortality	
		No.	Per 100 000 population	No.	Per 100 000 population	No.	Per 100 000 population
2007	2 043 559	563	27.5	549	26.9	38	1.9
2008	2 046 898	483	23.6	474	23.2	28	1.4
2009	2 050 671	473	23.1	465	22.7	17	0.8
2010	2 055 004	420	20.4	408	19.9	34	1.7
2011	2 063 819	362	17.5	354	17.2	19	0.9
2012	2 066 356	355	17.2	345	16.7	28	1.4
2013	2 072 543	323	15.6	318	15.3	24	1.2
2014	2 075 625	285	13.7	284	13.7	18	0.9
2015	2 068 453	284	13.7	282	13.6	18	0.9

Source: NTP TB register (unpublished).

Table 4.2. Notifications by category, the former Yugoslav Republic of Macedonia, 2007–2015

Year	All notified cases					All PTB									Extrapulmonary TB		
	Total	New cases		R cases		Total	B confirmed		New		Relapse		Other R cases		Total	B confirmed	
	No.	No.	%	No.	%	No.	No.	%	No.	%	No.	%	No.	%	No.	No.	%
2007	563	492	*87.4*	71	*12.6*	438	288	*65.8*	374	*85.4*	53	*12.1*	11	*2.5*	125	1	*0.8*
2008	483	427	*88.4*	56	*11.6*	368	268	*72.8*	321	*87.2*	38	*10.3*	9	*2.4*	115	4	*3.5*
2009	473	417	*88.2*	56	*11.8*	351	279	*79.5*	301	*85.8*	42	*12.0*	8	*2.3*	122	12	*9.8*
2010	420	368	*87.6*	52	*12.4*	319	249	*78.1*	276	*86.5*	33	*10.3*	10	*3.1*	101	7	*6.9*
2011	362	307	*84.8*	55	*15.2*	278	214	*77.0*	231	*83.1*	40	*14.4*	7	*2.5*	84	7	*8.3*
2012	355	319	*89.9*	36	*10.1*	274	216	*78.8*	243	*88.7*	22	*8.0*	9	*3.3*	81	6	*7.4*
2013	323	290	*89.8*	33	*10.2*	254	211	*83.1*	225	*88.6*	24	*9.4*	5	*2.0*	69	3	*4.3*
2014	285	261	*91.6*	24	*8.4*	218	188	*86.2*	197	*90.4*	20	*9.2*	1	*0.5*	67	11	*16.4*
2015	284	261	*91.9*	23	*8.1*	224	196	*87.5*	203	*90.6*	19	*8.5*	2	*0.9*	60	11	*18.3*

R = retreatment cases
B = bacteriologically confirmed
Source: NTP TB register (unpublished).

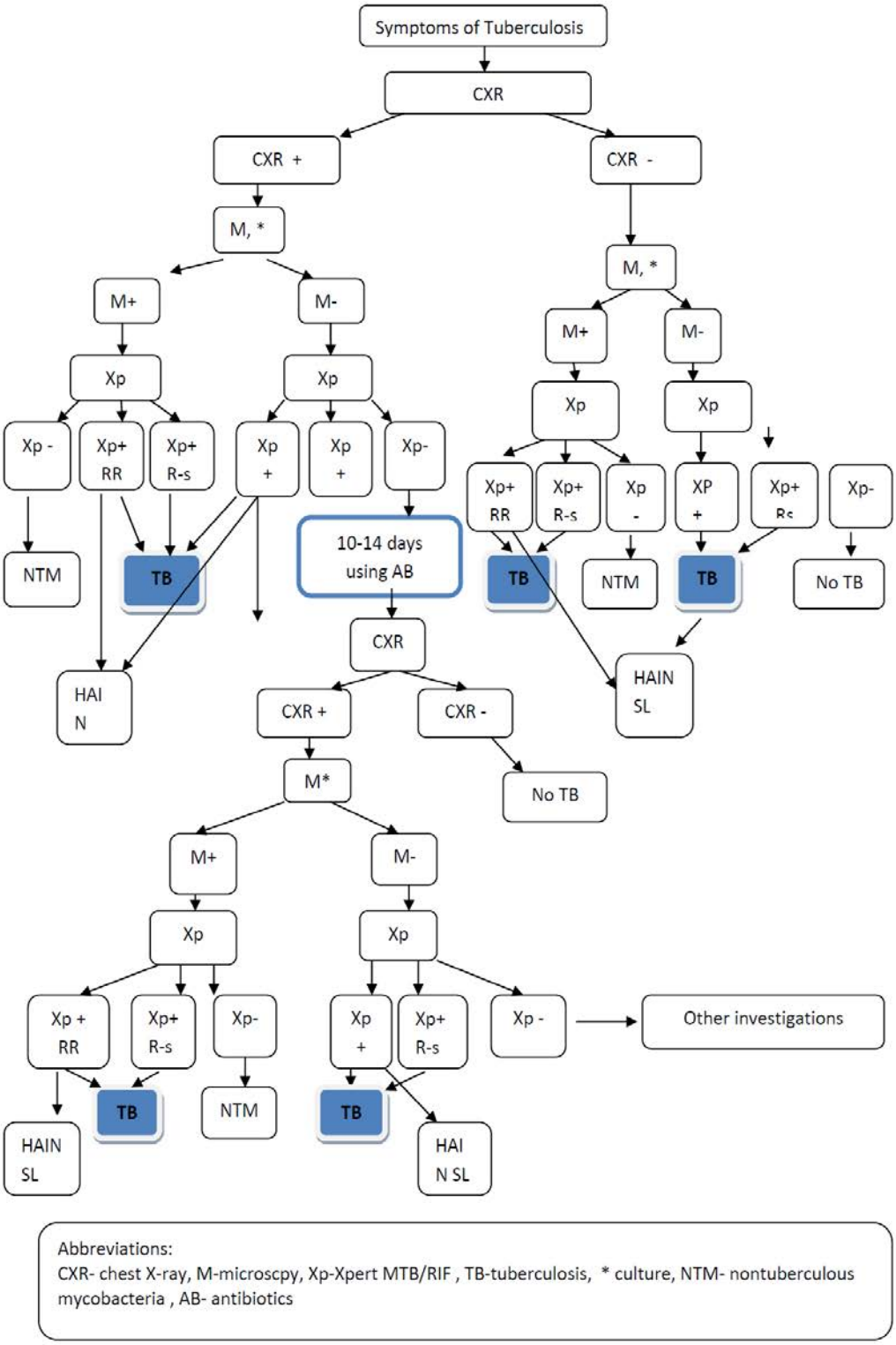
Table 4.3. TB notification for 16 regions, the former Yugoslav Republic of Macedonia, 2011–2015

Region	2011		2012		2013		2014		2015	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Skopje	142	23	150	24	105	17	104	17	110	18
Kumanovo	31	22	24	17	18	13	19	13	20	14
Tetovo	53	27	63	32	52	26	40	20	33	17
Gostivar	35	29	36	30	28	23	28	23	38	32
Kichevo	7	10	10	15	19	28	8	12	11	16
Bitola	8	6	6	5	12	9	8	6	6	5
Okhrid	15	12	10	8	9	7	12	10	11	9
Prilep	6	6	3	3	10	10	6	6	4	4
Shtip	3	6	2	4	2	4	4	8	3	6
Strumitsa	14	11	18	14	13	10	19	15	7	6
Debar	6	22	4	14	5	18	3	11	6	22
Veles	12	8	7	5	13	8	8	5	4	3
Gevgeliya	5	11	6	13	13	28	9	19	7	15
Kriva Palanka	7	29	1	4	2	8	1	4	4	17
Kocani	17	15	14	13	20	18	13	12	13	12
Probishtip	1	4	1	4	2	8	3	12	7	28

Annex 6

COUNTRY ALGORITHM FOR THE DIAGNOSIS OF PULMONARY TB IN ADULTS

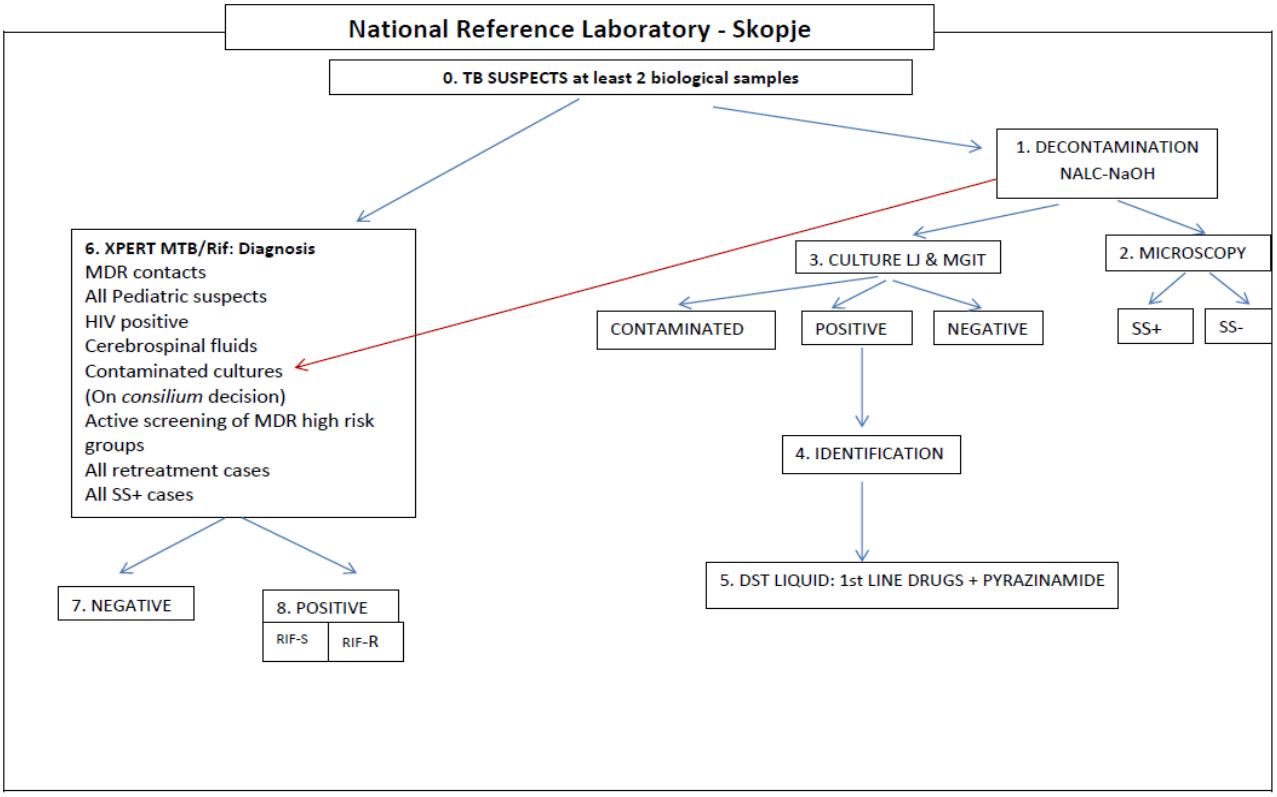
The review team proposed the following algorithm for the diagnosis of pulmonary TB in adults.



Abbreviations:
CXR- chest X-ray, M-microscpy, Xp-Xpert MTB/RIF , TB-tuberculosis, * culture, NTM- nontuberculous mycobacteria , AB- antibiotics

Annex 7

ALGORITHM FOR LABORATORY DIAGNOSIS



NALC- NaOH = n-acetyl-L-cysteine- sodium hydroxide.

Description

Xpert MTB/RIF should be used directly on biological samples (fresh sample). It could be used after samples have been decontaminated, but it is preferable to test fresh and untreated samples. At least two specimens are required when introducing Xpert MTB/RIF in the algorithm. If the sample is not going to be tested by Xpert, proceed as usual by decontaminating samples and inoculating them on both liquid and solid media (BBL® MycoPrep™ MGIT and Loewenstein-Jensen).

1. Decontaminate with n-acetyl-L-cysteine (NALC)- sodium hydroxide (NaOH) for use compatible with liquid cultures.
2. For infection control purposes, microscopy is still necessary to discriminate between infectious cases and smear-negative cases when Xpert MTB/RIF is not performed. If line probe assay is available at the NRL, tests could be carried out on smear-positive cases with a high risk of being MDR-TB or to confirm resistances (rifampicin resistance only) found by Xpert MTB/RIF. Do not duplicate tests for confirmation of susceptible cases.
3. Inoculate one BBL® MycoPrep™ MGIT tube and one Loewenstein-Jensen medium for each incoming sample, both at the time of diagnosis and at follow-up. If *M. bovis* infection becomes more common, it is possible to inoculate another solid medium enriched with pyruvate.
4. Identification should follow a first screening by Ziehl-Neelsen microscopy to verify the presence of acid-fast bacilli. Chord formation could be a good marker of the presence of *M. tuberculosis* complex, but identification cannot be based on that. Identification of positive cultures by immunochromatographic assay (Capilia Neo-TB™; SD Bioline™; BD Identification test™) is

recommended. This can discriminate between *M. tuberculosis* complex or nontuberculous mycobacteria in 15 minutes.

5. Test drug susceptibility in liquid media only. Once laboratory skills have been acquired for DST in liquid (BacTEC MGIT960), this should be the only method for DST testing. It should also include pyrazinamide testing. If the sample has already been tested by Xpert MTB/RIF and the result is RIF-susceptible there is no need to test first-line drugs again but only to test pyrazinamide.

6. Using Xpert MTB/RIF™.

- The selection of samples to be tested by this method is summarized in Box 6 in the diagram of the diagnostic algorithm. Xpert testing is only recommended for diagnostic purposes.
- It is possible to use Xpert for follow-up on special occasions: when, after the intensive phase of treatment or during the continuation phase of a first-line regimen, the patient still has a positive culture, it is important to know possible resistance to rifampicin immediately.
- Xpert could also be used on decontaminated samples. Do not waste pellets of decontaminated samples until culture testing is over. If cultures are contaminated, it is possible to use Xpert on frozen decontaminated samples.
- All other categories in Box 6 are those recommended by WHO.[1]

7. Xpert Result: NEGATIVE. Negative results do not exclude the diagnosis of TB. A definite negative result for TB should only be given when culture results are available. If the Xpert is negative but the culture positive, consider the culture results as the final microbiological confirmation of TB.

8. Xpert Result: POSITIVE. According to new WHO definitions,[2] a positive test must be considered as TB microbiologically confirmed. Thus a positive result confirms TB. Treatment should be initiated immediately.

- Rifampicin susceptibility. No need for reconfirmation.
- Rifampicin resistance. Although new data on the test reveal that rifampicin-resistant strains should not be reconfirmed, confirmation of resistance to rifampicin would be advisable. Discordant results must be seen one by one, depending on the case.
- If the Xpert test is positive but the culture negative, the following checks are advisable:
  - confirm that the patient is a new patient and is not taking any treatment;
  - check for culture decontamination procedure (or any other sudden event that might have occurred);
  - check the TB register for cross-contamination; for example, on a particular day all Xpert tests were positive and only one culture was positive, or two Xpert tests were positive consecutively and the first one was 3+ at smear microscopy while the other was smear-negative.

Comments

- DST and Xpert testing are not duplication. A TB rifampicin-susceptible case detected by Xpert should be tested for pyrazinamide resistance when the culture becomes positive. However, the

[1] Using the Xpert MTB/RIF assay to detect pulmonary and extrapulmonary tuberculosis and rifampicin resistance in adults and children. Expert group meeting report. Geneva: World Health Organization; 2013 (http://apps.who.int/iris/bitstream/10665/112659/1/WHO_HTM_TB_2013.14_eng.pdf?ua=1, accessed 18 February 2017).

[2] Definitions and reporting framework for tuberculosis – 2013 revision (updated December 2014). Geneva: World Health Organization; 2014 (http://apps.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf?ua=1, accessed 10 March 2017).

clinician should be informed about the positive Xpert test immediately after the Xpert results become available. There is no need for confirmation of rifampicin susceptibility.

- If the laboratory receives only one adequate biological sample for TB testing, it should be decontaminated and cultured according to conventional methods. The remaining pellet (after decontamination) could be used for Xpert MTB/RIF testing according to the manufacturer's instructions.
- The proposed algorithm is valid both for diagnosis and patient follow-up (except for Xpert/MTB RIF™).

Annex 8

LABORATORY INDICATORS

Laboratory process indicators should be updated on a quarterly basis (Table 8.1).

Table 8.1. Procedure for updating laboratory process indicators

Sputum smear microscopy		
Indicator 1		
Positivity rate for sputum smear microscopy done – (general indicator)	*Number of smears positive/ Total number of smears x 100*	TB suspects and TB patients should be calculated separately (diagnosis vs. follow-up)
Indicator 2		
Positivity rate for TB suspects screened [i]	*Number of TB suspects positive/ Total number of TB suspects screened x 100*	TB suspects and TB patients should be calculated separately (diagnosis vs. follow-up)
Primary cultures		
Indicator 3		
Positivity rate for cultures done [ii]	*Number of cultures positive/ Total number of cultures x 100*	TB suspects and TB patients should be calculated separately (diagnosis vs. follow-up)
Indicator 4		
Positivity rate for TB suspects that had their sputum cultured [ii]	*Number of TB suspects culture-positive/Total number of TB suspects tested x 100*	TB suspects and TB patients should be calculated separately (diagnosis vs. follow-up)

[i] This is independent of the number of sputum smears made for each TB suspect. (For example: if only 1 out of 3 of a suspect's sputum smears are positive, he/she must be considered positive.
[ii] When BacTec MGIT is routinely introduced, indicate the total number of MGIT-positive compared to Loewenstein Jensen-positive.

Comparison between microscopy and culture

From the collected data, calculate the rates (Table 8.2), using the following classification of specimens from adult pulmonary TB patients investigated for diagnosis:

a smear-positive and culture-positive
b smear-positive and culture not done
c smear-negative and culture-positive
d smear-positive and culture-negative
e smear-positive and culture contaminated
f smear not done and culture-positive

Table 8.2. Calculating rates of indicators

Indicator 5	
Contribution of culture to diagnosis	$\frac{c + f}{a + b + c + d + e + f} \times 100$
Indicator 6	
Contribution of culture to diagnosis over microscopy [i]	$\frac{c}{a + c + d + e} \times 100$
Indicator 7	
Percentage of smear-positive and culture-negative diagnostic cases [ii]	$\frac{d}{a + c + d + e} \times 100$
Indicator 8	
Contamination rate [iii]	*Number of contaminated tubes/all inoculated tubes x100*

[i] Culture is more sensitive than smear microscopy and is expected to contribute at least 20% to the bacteriological confirmation of adult pulmonary TB cases.
[ii] This percentage should be very low, typically around 2–3 %. In exceptional cases, patients are found with persistent smear-positive and culture-negative diagnostic specimens. These are usually undisclosed treatment control specimens. Higher percentages could be the result of decontamination procedures that are too harsh or of transport delays.
[iii] The contamination rate is a valuable indicator of the efficiency of procedures used for specimen processing. It is calculated as the percentage of contaminated tubes among all inoculated tubes or vials and not as the percentage of samples

Signals of cause for alarm

The indicators in Table 8.3a are valid for specimens from adult pulmonary TB patients investigated for diagnosis (but do not apply to follow-up). If indicators are much higher or lower than the normal value, actions should be investigated as in Table 8.3b.

Tabe 8.3a. Indicators of culture performance

Indicators of culture performance	Normal value (%)	Much higher: investigate	Much lower: investigate
Contribution of culture to bacteriological diagnosis of TB	20	A	B and C
Percentage of smear positive/culture negative specimen	2–3	C and D	Not a problem
Percentage of contaminated tubes	2–8	E	F

Table 8.3b. Actions to be investigated if indicators are much higher or lower than normal value

A	• Smear microscopy reading errors: false negative smears • High percentage of incipient pulmonary TB and paediatric TB cases are being tested (not a problem)
B	• Inadequate use of culture: patients who are not TB suspects are being examined, rather than incipient TB cases
C	• Excessive delay between collection and processing of specimens • Over-harsh specimen decontamination procedures (excessive concentration and/or too long a contact time with the decontaminant) • Low relative centrifugal force or overheating of centrifuge • Low culture media sensitivity (lack of homogeneity, overheating during inspissation, too much malachite green, too acidic pH in liquid medium) • Incubation at too high or too variable temperatures • Misclassification of follow-up specimen
D	• Smear microscopy reading errors: false positive smears
E	• Unrefrigerated storage of specimen • Excessive delay between collection and processing of specimen • Low concentration of decontaminant • Too short a contact time between decontaminant and specimen • Deficiency in the sterilization procedure • Careless use of the biological safety cabinet, generation of draughts by fans or air-conditioning system
F	• Too high concentration of decontaminant • Too long contact time of the specimen with the decontaminant • Poor specimen neutralization • Too high concentration of malachite green in the culture medium • Incubation at too high or variable temperatures

Annex 9

INDICATORS OF THE CAPACITY OF THE NTP

Indicator	Description	*Notes*
Indicator a Percentage of notified new and relapse TB cases with bacteriological confirmation	Number of notified new and relapse TB cases with bacteriological confirmation/ number of notified new and relapse TB cases × 100	*Target 2020:* 80% (relapse 90%) *Target 2025:* 90% (relapse 95%)
Indicator b Patient cost involved	Does the national policy indicate that TB diagnostic and follow-up tests provided through the NTP are free of charge or that fees can be fully reimbursed through health insurance, or both, for all people with signs and symptoms of TB?	
Indicator c Universal access to DST (yes/no)	Do the national policy and the diagnostic algorithm indicate that there is universal access to DST?	
Indicator d Percentage of notified bacteriologically confirmed TB cases with DST results for rifampicin	Number of notified, bacteriologically confirmed TB cases with DST results for rifampicin/number of notified bacteriologically confirmed TB cases × 100	*Target 2020:* 100% of cases
Indicator e Percentage of notified rifampicin-resistant TB cases with DST results for fluoroquinolones and second-line injectable agents.	Number of notified rifampicin-resistant-TB cases with DST results for fluoroquinolones and second-line injectable agents/number of notified rifampicin-resistant-TB cases × 100	*Target 2020:* 100% of cases
Indicator f Percentage of diagnostic testing sites that monitor performance indicators and are enrolled in an external quality assessment system for all diagnostic methods performed	Number of diagnostic testing sites (stratified by type of diagnostic testing) that monitor performance indicators and are enrolled in an external quality assessment system for all diagnostic methods performed/number of testing sites (stratified by type of diagnostic testing) × 100	*Target 2020* 100% of sites

Source: Framework of indicators and targets for laboratory strengthening under the End TB Strategy. Geneva: World Health Organization; 2016 (WHO/HTM/TB/2016.18; http://apps.who.int/iris/bitstream/10665/250307/1/9789241511438-eng.pdf?ua=1, accessed 18 February 2017).

Annex 10

TOPICS COVERED BY TRAINING

For GPs

- Epidemiology of TB in the world and in the Republic of Macedonia
- Clinical features of TB
- Etiology and pathogenesis of TB
- Transmission of TB
- Latent TB infection
- Diagnosis and treatment of TB
- The role of GPs in TB control
- TB and HIV infection
- Practical work – presentation of different cases with TB

For TB specialists (pneumophtisiologists, pulmonologists, paediatricians, infectiologists)

- Latent TB infection and Quantiferon test
- News in bacteriological diagnosis of TB
- MDR-TB
- Practical work – active case-finding, overview of contacts
- Practical work – monitoring of TB patients during treatment
- Practical work – HIV protocol and sending samples for HIV testing

For nurses

- Epidemiology of TB
- Etiology and pathogenesis of TB
- Diagnosis and monitoring of TB patients
- HIV protocol
- Practical work – sending samples for HIV testing
- Practical work – estimating drugs needs and preparing procurement plan

For social workers

- Epidemiology of TB
- Etiology and transmission of TB
- Medical social work – economic and social factors, targets, principles, techniques
- Current legislation on protection of personal data
- Medical social work – TB: stigma, prejudice, discrimination
- Practical work – the role of the social worker in the NTP; motivating patients for more effective treatment.

For laboratory technicians

- Practical work in the laboratory – smear-making, colouring and microscopy
- Microscopy of acid-resistant bacillus
- Microscopy quality control
- Collecting samples (sputum smear)
- Transporting samples
- Practical work

For prison staff (infection control)

- Epidemiology of TB
- Etiology and pathogenesis of TB

- TB diagnosis and treatment
- TB control in prison facilities in Republic of Macedonia

The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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