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Review of the national tuberculosis programme in Romania

10–21 March 2014

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Review of the national tuberculosis programme in Romania, 10–21 March 2014

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ABSTRACT

Romania has the highest incidence of TB in the European Union (EU)/European Economic Area (EEA), representing one quarter of the EU/EEA TB burden. A review of the national TB programme in Romania was jointly organized by the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control, with WHO leading all operations, from 10 to 21 March 2014. The review acknowledged the high rates of detection and treatment success achieved among patients with drug-susceptible forms of TB; it also pointed to the large proportion of patients with multidrug-resistant TB who are not detected or are poorly treated. The review identified major challenges to be addressed at programme level as well as at health system level and gave the Ministry of Health and the national TB programme 14 main recommendations for improvement.

Keywords

DELIVERY OF HEALTH CARE
HEALTH POLICY
NATIONAL HEALTH PROGRAMS
ROMANIA
TUBERCULOSIS
TUBERCULOSIS, MULTIDRUG-RESISTANT

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CONTENTS

Page

Acknowledgements v

Abbreviations vi

Executive summary vii

Introduction 1

General information 2

TB epidemiology 2
- Recommendations 4

NTP strategies, structure, budget and main achievements 4
- Strategies 4
- Structure 4
- Budget 8
- Main achievements 8
- Recommendations 10

Case-finding and diagnosis 11
- Case-finding 11
- Diagnosis 12
- Recommendations 17

Treatment and case management 19
- Treatment 19
- Case management 19
- Recommendations 20

TB in children 20
- Recommendations 21

HIV-related TB 21
- Burden 21
- Organization of services and coordination 22
- Reducing HIV among TB patients 23
- Reducing TB among PLHIV 23
- Recommendations 24

Drug-resistant TB 24
- Burden 24
- Programmatic management 26
- Case management 27
- Recommendations 29

TB control in prisons 30
- Recommendations 31

Other vulnerable populations and social determinants 32
- Poor people and those living in rural areas 32
- Roma 32
- People who inject drugs 33
- Homeless people 33
- Migrant workers 34
- Recommendations 34

TB infection control 34
Administrative measures 36
Environmental measures 36
Personal protection 37
Recommendations 37
Management of medicines 38
Financing 38
Procurement and registration 38
Quantification 40
Storage, distribution and quality assurance 41
Pharmacovigilance 41
Recommendations 41
Monitoring and evaluation 42
Recommendations 43
Human resources development 44
Recommendations 45
Operational research 46
Recommendations 46
Ethics and human rights 47
Access to TB diagnosis 47
Access to TB treatment 47
Compassionate use of and expanded access to new anti-TB drugs 48
Palliative care 48
Patients who refuse treatment 49
Recommendations 49
Advocacy, communication, social mobilization 50
Recommendations 52
Health system and TB control 53
Service delivery 53
Health system governance 55
Health system financing 57
Health system workforce 62
Medical products and technology 64
Health information 64
Recommendations 64
References 65
Annex 1 Members of the review team 70
Annex 2 Programme overview 71
Annex 3 Field teams: programmes 73
Annex 4 People interviewed 75
Annex 5 Epidemiological impact assessment 80
Annex 6 Profiles of patients interviewed 85
Annex 7 TB reporting 89

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Abbreviations

ACSM	advocacy, communication and social mobilization
ART	antiretroviral therapy
ASPTMR	Association for the Support of MDR-TB Patients
BCG	Bacillus Calmette-Guérin
CHPS	Centre for Health Policies and Services Foundation
DOT	the basic strategy that underpins the Stop TB Strategy
DR	drug-resistant
DST	drug susceptibility testing
ECDC	European Centre for Disease Prevention and Control
GDF	Global TB Drug Facility
GDP	gross domestic product
GLC	Green Light Committee
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
MDR	multidrug-resistant
MGIT	mycobacteria growth indicator tube
NHIH	National Health Insurance House
NRL	national tuberculosis reference laboratories
NTP	national tuberculosis programme
PAS	4-aminosalicylic acid
PLHIV	people living with HIV
PWID	people who inject drugs
RAA	Romanian Angel Appeal
TB/HIV	HIV-related TB
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme
UNOPA	Union of Organizations for People Affected with AIDS
XDR	extensively drug-resistant

Executive summary

Romania is one of the WHO European Region's 18 high-priority countries for TB control. The national TB programme (NTP) has achieved good rates of detection and successful treatment of new drug-susceptible TB cases but poor rates among the new multidrug-resistant (MDR) TB cases. The National Plan to Prevent and Control M/XDR-TB 2012–2015 was officially launched by the Prime Minister on 2 October 2012, on the occasion of a visit by the WHO Regional Director for Europe and the European Union (EU) Commissioner for Health and Consumer Policy. The implementation of this plan has, however, had to be delayed due to a lack of financial resources. Since the visit, a number of missions have been conducted jointly by WHO and the European Centre for Disease Prevention and Control (ECDC) to provide technical assistance. Important opportunities to improve performance are now offered by the new funding mechanism of the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), the Norwegian Financial Mechanism and other international support.

The current review took place from 10 to 21 March 2014. Eleven international and eight national experts participated, visiting 18 counties. The team members conveyed their main findings and recommendations at the end of the mission to the Minister of Health.

Main findings

A number of achievements were observed since the previous review of the NTP in 2009 and follow-up missions by WHO, the ECDC and the European Commission. There are fewer notifications of TB cases, plans and guidelines had been developed, rapid diagnosis of drug-resistant TB has been established in the two national TB reference laboratories (Bucharest and Cluj), an increasing number of patients with MDR-TB are being treated, drug procurement has been revised, a countrywide drug resistant survey has been started and patient associations have been established.

Despite the steady decrease in TB cases notified to the NTP, WHO estimates that 20 000 new cases occur every year, giving the country the highest TB incidence in the European Economic Area (EEA)/EU (six times higher than average) and representing one quarter of the TB burden in the EEA/EU. The great majority of these cases are drug-susceptible forms of TB that are detected and treated successfully. It is estimated, however, that there are also 800 new MDR-TB cases a year (estimated for 2012), of whom only 62% are detected and, of these, only 20% are treated successfully. Extensively drug-resistant (XDR) TB cases are occurring.

Current and future external funding is an important source of support for the Ministry of Health in implementing the National Strategy for Health 2014–2020 and the National Plan to Prevent and Control M/XDR-TB 2012–2015. In addition to the procurement of the necessary drugs, this funding gives an important opportunity to implement many of the recommendations of this review.

TB services are delivered through an extensive network of laboratory and treatment facilities and by a number of dedicated and committed health staff. These services are, however, tailored more to the providers than to the patients with their needs for rapid diagnosis, effective treatment and support in their social vulnerability. The major challenges that need to be addressed are that:

- patients have to wait a long time to see a family doctor and frequently seek emergency medical care in hospital; diagnosis is late and drug resistance not tested in half of the patients; and diagnosis is not supported by standardized quality laboratory procedures;
- patients are unnecessarily admitted and kept in hospital for a long time, sharing the same environment with non-TB and other TB patients regardless of their infectious status – good conditions for the nosocomial transmission of TB among patients and hospital staff, with a potential for litigation and financial compensation by the hospital administration;
- many patients do not receive supervised treatment and most do not get the necessary support to continue their treatment outside hospital;
- many patients with drug-resistant TB receive only some of the drugs necessary for their cure;
- patients who suffer more economically and socially from TB do not receive adequate social support;
- the general population has little awareness about TB and the local authorities lack political commitment in supporting TB control.

Additional challenges at the level of the health system are that:

- the Ministries of Health and Justice are highly dependent on external funding to provide basic TB services;
- negative incentives promote the hospitalization of patients, the mixing of TB and non-TB patients in the same environments, an inefficient laboratory network and limited access to family doctors;
- health care for different pathologies within the same patient is fragmented across the various specialized services;
- the governance of the national public health programmes is unclear;
- recording and reporting required for administration are complicated, cumbersome and insufficiently used for decision-making in supporting TB services;
- there is an imbalance in the number and distribution of human resources (including for TB) and a lack of support through coherent training.

Main recommendations

The review team has the following recommendations for the Ministry of Health and the NTP.

Ministry of Health

1. Prevention and control of TB and M/XDR-TB should be considered as a public health priority. Sufficient and sustainable funding and necessary changes in the health system should be ensured. The draft National Strategic Plan for TB control should be finalized and approved in line with the recommendations of this review. No delays should occur in the approval of future norms (secondary legislation) necessary to implement the NTP consistently.
2. The second TB project under the Norwegian Financial Mechanism should be revised in line with, and in support of the effective implementation of, the recommendations of this

review, taking into account the technical assistance required. A working group should be established as soon as possible to draft the concept note required to access further support from the Global Fund. The current composition of the Country Coordinating Mechanism should be revised to ensure the direct involvement of the Ministry of Health.

3. Effective centralized procurement and the uninterrupted supply of all internationally recommended anti-TB drugs (first, second and third line) should be ensured, including for their compassionate use. Free ancillary drugs should be ensured for both in- and outpatients. The benefits of international procurement should be assessed through a cost-effectiveness study.

4. The payment system under the National Health Insurance House should be revised so as to: prevent unnecessary hospitalization of patients, promote administrative measures for TB infection control, ensure the appropriate distribution of laboratories, and provide TB outcome-based incentives to family doctors in the package of minimum services currently under discussion.

5. TB infection control measures should be introduced urgently in diagnostic and treatment facilities and in congregate settings by revising Ministry of Health Order No. 916 of 26 July 2006 and the current system of health facility accreditation and including specific measures for the prevention of airborne TB transmission.

6. The governance of the NTP should be clarified in the spirit of the recent law establishing the National Agency for Health Programmes and aiming to ensure ownership by, and accountability to, the Ministry of Health.

7. TB outreach services (identification of cases for diagnosis and prevention, directly observed therapy and patient support) should be strengthened among socially and economically disadvantaged people and vulnerable population groups through the involvement of community nurses, Roma mediators, nongovernmental workers and lay people (for example, school teachers and religious leaders).

8. TB control should be maintained as a priority in the prison sector and sustainable funding provided for the National Administration of Penitentiaries to implement the TB control plan in the penitentiary system, including after the end of the Global Fund grants.

9. A national strategy and plan for advocacy, communication and social mobilization with regard to TB should be developed by the National Institute of Public Health, together with the NTP, with clear roles and responsibilities for all partners (including the Ministry of Education), timelines and an assured budget from diverse sources.

NTP

10. Universal access should be ensured to rapid diagnosis of TB and MDR-TB by using cartridge-based nucleic acid amplification techniques in selected lower level laboratories and/or sputum collection points with high rates of TB and/or MDR-TB (such as prisons, selected hospitals, HIV centres) and line probe assay in geographically representative regional laboratories. The TB laboratory network should be redesigned and rationalized by the end of 2015.

11. The national TB/HIV coordination committee should be activated and effective regional TB/HIV coordination committees established so as to ensure the integrated diagnosis and continuum of care for all TB/HIV patients focused on their needs. The National TB/HIV

Collaborative Protocol should be revised to ensure isoniazid preventive treatment for people living with HIV. All TB/HIV patients should be treated in pulmonology facilities.

12. The prevention, diagnosis, treatment and care of TB in children should be improved by ensuring that they receive Bacillus Calmette-Guérin vaccination, tuberculin skin testing and paediatric formulations of anti-TB drugs, and that their parents/caregivers can stay with them while in hospital free of charge.
13. The recording and reporting system should be rationalized and the national TB database revised to improve the processing of patients' data and ensure their analysis and use for policy decisions.
14. A national plan should be developed for human resources for TB that is consistent with the laboratory and treatment networks and includes adequate formal, in-service and continuing medical education according to the NTP guidelines.

Introduction

Romania is one of the WHO European Region's 18 high-priority countries for TB control *(1)*. The national TB programme (NTP) has achieved good rates of detection and successful treatment of new drug-susceptible TB cases but poor rates among multidrug-resistant (MDR) TB cases. The National Plan to Prevent and Control M/XDR-TB 2012–2015 *(2)* was officially launched by the Prime Minister on 2 October 2012, on the occasion of a visit by the WHO Regional Director for Europe and the European Union (EU) Commissioner for Health and Consumer Policy. The implementation of this plan has, however, had to be delayed due to a lack of financial resources. Since the visit, a number of missions have been conducted jointly by WHO and the European Centre for Disease Prevention and Control (ECDC) to provide technical assistance, especially with the establishment of central procurement of anti-TB drugs through the available international mechanisms, such as the Global TB Drug Facility (GDF). Important opportunities to improve performance are now offered by the New Funding Mechanism of the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), the Norwegian Financial Mechanism and other international support. Among the supporting documents for applications to the New Funding Mechanism, the Global Fund requires a national strategic plan for TB and a concept note. These are both to be built in from a recent review of the TB epidemiology and organization, functions and deliveries of the NTP.

Previous NTP reviews were conducted by WHO in 2005 and in 2009. On 19 December 2013, the Ministry of Health requested the WHO Regional Office for Europe to support a third review in 2014. A similar request, dated 16 January 2014, was also sent to the ECDC.

This NTP review was jointly organized by WHO and ECDC from 10 to 21 March 2014, with 11 international and eight national experts and limited participation by three other experts (Annex 1). Under the leadership of WHO, the team members: analysed relevant background documents (including publications, studies and previous assessment reports); visited health facilities and institutions selected to give a balanced representation of the different epidemiological, geographical and health service delivery conditions in the country; and interviewed policy-makers, health care providers, TB patients (through in-depth interviews and focus groups) and the main national and international partners at national and county levels. The team members developed a number of tools to collect data in advance in order to guide their field observations and interviews.

Annex 2 gives an overview of the review programme and activities. During the first week, the members divided themselves into three field teams, each coordinated by an international expert, which visited a total of 18 counties (Annex 3). Each team produced an analysis of strengths, weaknesses, opportunities and threats and discussed it with the other teams. All reviewers spent the second week in Bucharest attending visits and meetings at the central level and working on the various sections of the final report. The complete list of persons interviewed is in Annex 4.

The review also gave an opportunity for a joint monitoring visit on behalf of the Green Light Committee (GLC) for the WHO European Region and the GDF. These reports, and an epidemiological assessment supporting the concept note for the Global Fund (Annex 5), were produced separately. The most significant profiles of patients interviewed are summarized in Annex 6.

The team members conveyed their key findings and recommendations at the end of the mission to the new Minister of Health, Dr Nicolae Banicioiu, in the presence of all review members and the head of the WHO country office in Romania.

General information

Romania is bordered by Hungary and Serbia to the west, the Republic of Moldova and Ukraine to the east and northeast, and Bulgaria to the south. It is the ninth largest country by area (238 391 km^2) with the sixth largest population (21 754 741 inhabitants) in the EU and European Economic Area (EEA) *(3)*. Fifty-seven percent of the population live in urban areas. More than 10% of the population in 2011 was represented by minorities, mainly Hungarians (6.5%, concentrated in Transylvania) and Roma (3.3%, concentrated in Calarasi and Mures counties). Romania joined the EU on 1 January 2007.

Gross domestic product (GDP) per capita is US$ 9499 (2013) and the country is classified as having an upper-middle income economy *(4)*. The annual growth in GDP (restarted in 2013 with +2.2%) is the result of incentives to private investment, industrial and agriculture production and exports. In 2012, the unemployment rate was only 7% but the low average monthly wage (the lowest in the EU) has led to emigration to other EU countries among Romanians in various social groups, including doctors and nurses.

Life expectancy at birth is 71 years for men and 78 years for women (2013). Important causes of death are cardiovascular diseases and cancer. In 2011, however, infant mortality was 9 per 1000 live births and maternal mortality was 11 per 100 000 live births, the highest and second highest rates in the EU.

TB epidemiology

According to the latest WHO estimates, the incidence of TB per 100 000 population in 2012 was 94 (77–112), TB prevalence was 144 (67–251) and TB mortality was 5.6 (5.5–5.6) *(5)*. Based on the drug resistance survey of 2004, the proportion of MDR-TB is currently estimated at 2.8% (1.8–4.2%) among newly diagnosed and 11% (8–15%) among previously treated TB patients. A second countrywide drug resistance survey was launched on 1 March 2014, the results of which are expected to be available in 2015. A prospective study of drug resistance carried out for 756 MDR-TB cases collected between October 2009 and January 2010 revealed extensively drug-resistant (XDR) TB in 9.9% of the newly diagnosed and 11.6% of the previously treated MDR-TB patients.

Translating these rates into case numbers, it is estimated that in 2012 there were 20 000 (17 000–24 000) new TB cases, 1200 (1200) new deaths from TB and 800 (610–980) new MDR-TB cases. On the basis of these figures, Romania is included among the 18 high-priority countries for TB control in the WHO European Region but is not considered as one of the 15 high MDR-TB burden countries in the Region.

The notification rate of new and relapsed TB cases varies across the counties (Table 1), which may indicate actual differences in TB epidemiology as well as in the local performance of the NTP.

Table 1. Notification rate of new TB cases and relapses by county, 2010–2013

County	2010[a]		2011		2012		2013[a]	
	No.	Per 100 000 population	No.	Per 100 000 population	No.	Per 100 000 population	No.	Per 100 000 population
Alba	224	60.2	178	48.0	201	54.5	182	49.3
Arad	543	119.4	488	107.5	448	99.0	392	86.6
Argeș	526	82.3	480	75.4	441	69.6	464	73.2
Bacău	784	109.7	684	96.0	687	96.9	627	88.4
Bihor	404	68.2	358	60.4	321	54.4	296	50.1
Bistrița-Năsăud	202	63.7	144	45.4	134	42.4	135	42.7
Botoșani	465	104.0	406	91.3	411	93.2	408	92.5
Brașov	317	53.0	261	43.6	233	38.8	244	40.7
Brăila	356	99.5	340	95.7	320	90.8	295	83.7
Buzău	355	73.9	308	64.5	304	64.1	266	56.1
Caraș-Severin	356	111.0	331	103.9	277	87.6	267	84.4
Călărași	297	95.2	309	99.5	252	81.3	238	76.8
Cluj	345	49.9	338	49.0	313	45.3	289	41.8
Constanța	822	113.6	784	108.2	738	101.9	651	89.9
Covasna	85	38.2	92	41.5	80	36.2	60	27.1
Dâmbovița	439	82.9	387	73.2	393	74.3	375	70.9
Dolj	990	141.0	910	130.4	859	123.7	791	113.9
Galați	779	127.9	641	106.0	597	99.0	579	96.0
Giurgiu	401	143.2	342	122.5	330	117.6	302	107.7
Gorj	371	98.6	374	99.7	381	102.2	339	91.0
Harghita	89	27.4	96	29.6	95	29.4	84	26.0
Hunedoara	392	84.9	345	75.3	335	73.8	301	66.3
Ialomița	229	79.8	235	82.2	203	71.4	171	60.1
Iași	889	107.7	748	91.1	732	87.3	684	81.6
Ilfov	338	105.3	305	91.2	341	98.0	331	95.1
Maramureș	403	78.9	398	78.2	379	74.6	384	75.6
Mehedinți	370	127.1	364	126.0	324	112.9	268	93.4
Mureș	507	87.4	380	65.6	385	66.7	293	50.7
Neamț	562	100.0	574	102.4	452	81.2	446	80.1
Olt	703	151.9	590	128.7	612	134.6	493	108.4
Prahova	677	83.3	620	76.6	510	63.3	464	57.6
Satu Mare	319	87.6	311	85.7	365	100.8	274	75.6
Sălaj	158	65.6	152	63.3	125	52.2	127	53.0
Sibiu	195	45.8	182	42.7	163	38.3	199	46.7
Suceava	511	72.1	500	70.5	437	61.7	491	69.3
Teleorman	511	128.4	443	112.7	459	118.1	431	110.9
Timiș	771	113.4	649	95.5	648	95.0	623	91.3
Tulcea	262	106.5	247	101.2	194	80.0	225	92.8
Vaslui	480	106.8	439	98.1	387	86.9	344	77.2
Vâlcea	313	77.0	299	73.8	295	73.1	296	73.3
Vrancea	328	84.2	305	78.4	321	82.8	261	67.3
București	1 327	68.3	1 335	69.6	1 286	67.3	1 236	64.6
Total	19 395	90.5	17 672	82.77	16 768	78.7	15 626	73.3

[a] Data for 2010 and 2013 are still preliminary and not validated.
Source: NTP database (unpublished information).

According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), between 14 000 and 21 000 people were living with HIV in Romania in 2012 *(6)*. Many of them are, however, unaware of their HIV status: only 237 HIV cases were registered in the country in January 2013, mostly among individuals in key populations and their partners. The estimated HIV prevalence among TB incident cases in 2012 was 2.9% (2.9–3.0%), or 660 (490–720) new HIV-related TB (TB/HIV) cases per year.

Recommendations

Ministry of Health

1. Prevention and control of TB and M/XDR-TB should be considered as a public health priority.

NTP strategies, structure, budget and main achievements

Strategies

The Ministry of Health started piloting the WHO-recommended DOTS strategy (the basic package that underpins the Stop TB strategy) in 1997. By 2005 this was being implemented countrywide. The full Stop TB strategy was then adopted and implemented through the Tuberculosis National Strategic Plan 2006–2010 *(7)*. Different draft versions of a plan for continuing the strategy after 2010 were updated, until the current draft Tuberculosis National Strategic Plan 2013–2017. In this draft, the NTP aims to reduce the mortality, morbidity and transmission of TB until it is no longer a national public health problem. Three targets are to be met by 2017: (i) to reduce TB prevalence and mortality by 50% (2002 baseline); (ii) to maintain a case detection rate of new smear-positive pulmonary TB cases over 70%; and (iii) to maintain the treatment success rate among new pulmonary TB sputum-positive cases of 85%. The six major areas of intervention correspond to the six components of the Stop TB strategy. The Tuberculosis National Strategic Plan 2013–2017 is supposed to incorporate the National Plan to Prevent and Control M/XDR-TB 2012–2015, which was officially launched by the Prime Minister in October 2012 on the occasion of a visit by the WHO Regional Director for Europe and the EU Commissioner for Health and Consumer Policy, but its implementation has been delayed due to a lack of financial resources. Approval by the Ministry of Health of such a plan is conditional on the approval of the National Health Strategy 2014–2020, which has a chapter on TB in line with the Stop TB strategy. Before this can be finalized and approved, however, it has to undergo a public hearing, a process which has taken many months. The TB Control Implementation Regulations and the National Plan for TB Infection Control were updated by the NTP some time ago and given to the Ministry of Health in 2013 for approval as secondary legislation required for implementation.[1]

A National Commission of Pulmonology, Allergology and Clinical Immunology, with members nominated by the Ministry of Health, meets twice a year and advises the Ministry on TB policies and guidelines.

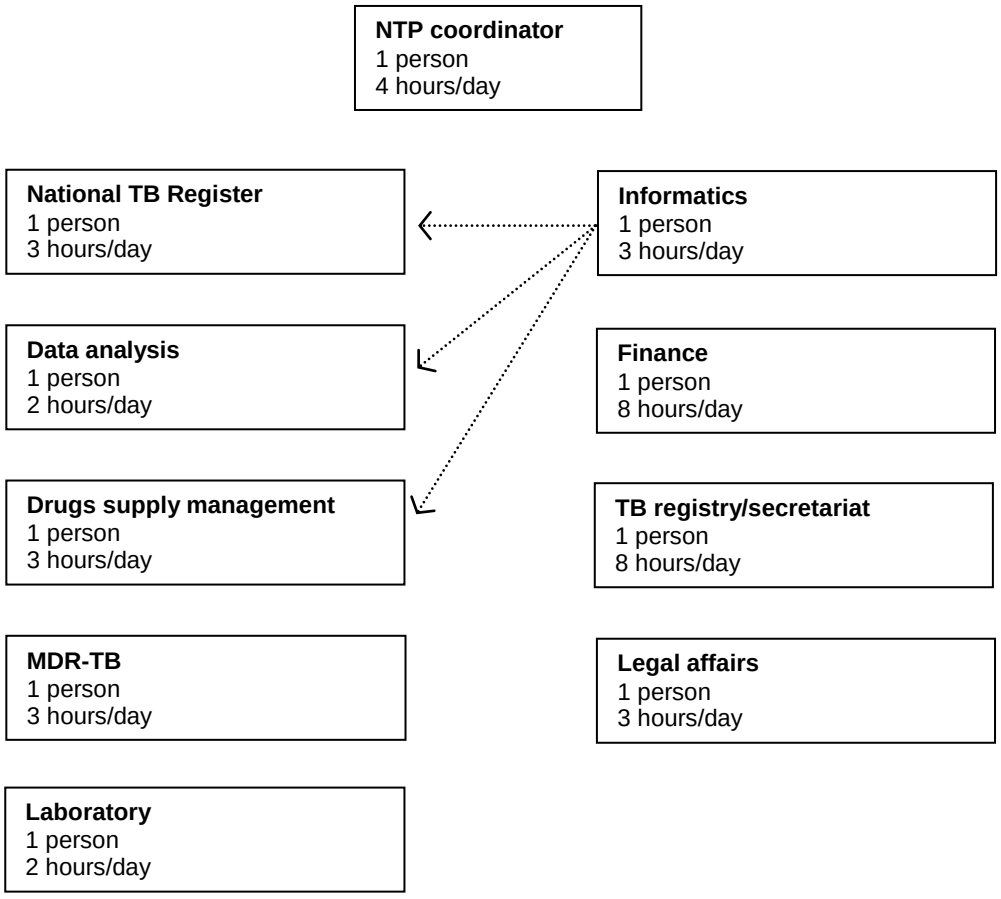
Structure

The NTP has a central unit hosted by the Marius Nasta National Institute of Pulmonology. It was established in 2002 by the charismatic then director of the Institute and accommodated in the Institute's premises, which were renovated through the first TB grant from the Global Fund Round 2. The staff of the NTP central unit are on the payroll of the Institute for their clinical work and receive a salary bonus from the Global Fund grant implemented by the Romanian Angel Appeal Foundation (RAA) for work additional to their clinical duties. In these conditions, the staff of the NTP central unit (those with a steering role for the programme) can potentially be

[1] As requested by Ministry of Health Order No. 422 of 29 March 2013 on Technical Norms of the National Public Health Programmes for 2013–2014 *(8)*.

influenced by both the Director of the Institute and the RAA. In April 2013, for the first time in years, the Ministry of Health issued the terms of reference of the NTP central unit (Ministry of Health Order 422/2013 *(8)*), officially appointed its members and introduced a system of payment for a maximum of 71 working hours per person per month for work in addition to clinical duties At the time of the review, 10 people were employed in the NTP central unit (Fig. 1); only two of them were full time and not involved in clinical duties (an economist and a secretary). Although acknowledging the important step forward in increasing the capacity of the NTP central unit, the review team noticed the difficulty the staff were having in working extra hours in addition to their clinical duties at the Institute.

Fig. 1. Organizational chart of the NTP central unit



In December 2013, the Government issued Decision No. 993/2013 laying down new functions for the Ministry of Health, including the creation of a new National Agency for Public Health Programmes, with the aim of strengthening the governance of public health programmes and limiting the amount of delegation to national institutes, including the Marius Nasta Institute. This agency was intended to be staffed with full-time personnel (a programme manager and a team for each major national programme, including the NTP) with responsibility for planning, budgeting and providing standards to the National Health Insurance House (NHIH) for service delivery, monitoring and evaluation. Meanwhile, other important functions for good NTP governance (development of clinical guidelines, coordination of TB laboratory activities, provision of training and field supervision) could have been effectively contracted out to the Marius Nasta Institute. At the time of the review, the National Agency for Public Health

Programmes was still not active and the recently appointed Minister of Health was considering how to move forward. Such an agency would offer an opportunity to improve the governance of the NTP by increasing its ownership by the Ministry of Health, its public health vision and collaboration with other health programmes (such as for HIV/AIDS), services (primary health care) and the NHIH, and the ability of the NHIH to reinforce clinical practices through its purchasing mechanism for services and accountability. On the other hand, the new agency would need consistent financial resources and other means to operate effectively, all yet to be found.

Below the NTP central unit, there are 42 TB coordinators (one for each county and for Bucharest) paid by the NTP, with responsibilities for local coordination and management (of human resources, drugs and laboratory commodities provided directly by the NTP) and supervision. The TB county coordinators work with hospital directors, managing the funds for TB channelled through the NHIH. The role of the TB coordinators will have to be reconsidered if in future all TB funds will be channelled through the NHIH. Moreover, the Ministry of Health is considering creating eight regional health hubs (based on historical factors), which will move TB coordination to that level.

TB inpatient services are delivered through a network of 33 pulmonology hospitals, 80 pulmonology departments in general hospitals, two TB sanatoria for adults and two sanatoria for children. The total capacity is 5625 hospital TB beds, including 100 MDR-TB beds of which 49 are in the Marius Nasta Institute and 51 in Bisericani. In addition, 12 infectious disease hospitals can care for TB patients (even if they are not HIV-related), while there are 20 hospital TB beds under the Ministry of Defence and 164 under the Ministry of Justice.

TB outpatient services are delivered through 184 pulmonology dispensaries.

Many inpatient facilities (such as the Pulmonology Hospital in Brasov) and outpatient facilities providing TB services are situated in private properties expropriated between 1945 and 1989 but now to be returned to their original owners (see section on Health system and TB control, p. 53) or be compensated. This uncertain situation is preventing the major investments required for rationalizing and upgrading the facilities and consequently their infection control measures.

In addition to the tertiary and secondary levels of care, TB services should also be delivered at primary health care level in accordance with Government Decision No. 400/2014 requesting family doctors to identify communicable diseases presumed relevant to public health, including TB, and refer them to a specialist. Unfortunately, since financial incentives from the NHIH for TB stopped in 2009, family doctors' collaboration with the NTP has been quite limited and often based on personal relations between medical professionals (see section on Health system and TB control, p. 53).

The review team understood that the future shape of the health system, which will have a major impact on the way NTP services will be organized and delivered, may be influenced by the results of the European elections in May and presidential elections in November 2014.

Romania has a large network of nongovernmental organizations, many operating under the Global Fund grant (either for TB or HIV) and supporting the NTP (Table 2). All main nongovernmental organizations, working with either TB or HIV/AIDS, are represented in the Country Coordination Mechanism, although there has been no representative of the Ministry of Health for a long time. The large nongovernmental organizations, in particular the RAA (which

is active in many health programmes, including in TB as the principal recipient of Global Fund grants since 2007), have provided essential support to the management of the NTP especially in view of the frequent turnover in managers of the programme, directors of the Marius Nasta Institute and ministers of health as well as the political situation in the country since 1989. It is difficult to imagine how the NTP would have functioned without the RAA, which gives rise to concern on the part of the review team as to the extent of ownership of the NTP by the Ministry of Health, and the long-term commitment of the Ministry in fighting TB.

Table 2. Nongovernmental organizations collaborating with the NTP

Name	Description
Bucharest Medical Students' Association	Global Fund sub-recipient (under the Centre for Health Policies and Services Foundation – CHPS) for TB education and screening in rural communities and among students in Bucharest.
Centre for Health Policies and Services Foundation – CHPS	Established in 1999 as the spin-off Public Health Program of the Open Society Foundation/Soros Foundation. Active in policy analysis, promotion of community participation and patient empowerment in a number of programmes, such as mother and child health, cervical cancer communicable diseases, healthy lifestyle, community-based care. In TB context, subrecipient of the Global Fund grant for ACSM, outreach to the most vulnerable, training and research.
Association for the Support of MDR-TB Patients– ASPTMR	Formed in 2011. Consists of 35 former and current M/XDR-TB patients, three psychologists and one psychiatrist. Global Fund subrecipient (under Union of Organizations for People Affected with AIDS – UNOPA) in the project Support Network for MDR-TB Patients which ran from January 2013 to September 2014 and provided food vouchers and counselling to M/XDR-TB patients.
Romanian Angel Appeal Foundation – RAA	Established in 1991 by Olivia Harrison and the Beatles' wives and Elton John with the mission to improve the quality life of children abandoned in Romanian institutions. It has evolved into an organization with recognized quality management systems, fully committed to saving lives and supporting the children and young people affected by HIV/AIDS, TB and other chronic conditions facing social exclusion and discrimination. Current work is focused on improving medical and social services, conducting research and building capacity among a variety of medical and social professionals. One of the founders of the Romanian STOP TB Partnership. The Principal Recipient of the Global Fund grants since 2007, currently involved in NTP planning (Global Fund New Financial Mechanism, Norwegian Financial Mechanism, Swiss grants), procurement and supply of diagnostic materials and anti-TB medicines.
Romanian Children's Humanitarian Foundation	Works in collaboration with the University Hospital of Pulmonology in Iasi on TB education in schools and rural areas.
Romanian Red Cross	Has provided support to TB patients as subrecipient of the Global Fund grants in rounds 2 and 6.
Romanian TB Patients' Association	Works mainly on TB education and awareness for the general public (World TB Day) and collection of food, toys and other items for children admitted to the TB ward in Bucharest.
Save the Children	Global Fund subrecipient for TB education and awareness and facilitating access to TB diagnosis among the homeless and poor in Bucharest, Dolj, Iasi and Timis.
Union of Organizations for People Affected with AIDS – UNOPA	Global Fund subrecipient. Works with ASPTMR in providing support to TB patients through a network of volunteers among people living with HIV.

Many more nongovernmental organizations operate in Romania and some of them could be considered by the NTP for partnership, such as Act for Involvement, ARAS – Romanian Association Against AIDS, Carusel Association, New Horizons, Ovidiu Rom Foundation, Romani Criss (Centrul Romilor pentru Interventie Sociala si Studii [Roma Centre for Social Intervention and Studies]), Romanian College of Physicians, Romanian Harm Reduction Network, Romanian Nurses and Midwives Organizations, Romanian Orthodox Church, Romanian Respiratory Society, The Roma Center for Health Policies – Sastipen and World Vision.

Budget

For 2013, the NTP reported to WHO an expenditure of more than 9 million Romanian Leu, of which 5.5 million Leu came directly from the government and 3.5 million Leu (39%) came from international donors. The actual budget for all NTP activities should be considered much more as the TB services are integrated with other services at the different levels of care and are paid through the NHIH. The review team was not able to calculate such an overall budget. In general, the Ministry of Health budget is decided on historical bases and past consumption, which may limit proper planning based on new challenges and estimated needs and gaps. There is a general call in the country to raise funds for certain services, such as the procurement of second-line anti-TB drugs that would be necessary to ensure the universal access to MDR-TB treatment foreseen in the four-year National Plan to Prevent and Control M/XDR-TB, 2012–2015 (with a total budget of €23 million or €5.75 million/year) that was officially launched by the Prime Minister in October 2012 but only covered partially by the limited resources at the disposal of the Ministry of Finance. For 2014, the NTP budget was increased to 29.4 million Leu.

Currently, Romania receives a €3.7 million grant under the Global Fund Transitional Funding Mechanism (January 2013–March 2015) with RAA as the principal recipient. The country is also eligible for an additional grant of up to €8.4 million under the Global Fund New Funding Mechanism. Moreover, a 32-month grant (1 October 2013–30 April 2016) of €4.2 million has been agreed (but not yet implemented) from the Norwegian Financial Mechanism, with the Marius Nasta Institute as principal recipient. Both grants from the Global Fund and from Norway are mainly directed to the procurement of second-line drugs for the treatment of the MDR-TB patients currently detected by the NTP. Current negotiations are for the use of an additional €4.5 million grant extension of the Norwegian support, expected to be implemented from 1 September 2014 to April 2016. Moreover, the United States European Command is interested in supporting the Ministry of Health, especially in the areas of strengthening the TB laboratories and surveillance *(9)*. All these external sources of funding represent a golden opportunity for the Ministry of Health to implement many of the recommendations made by this review.

Main achievements

In 2012, the NTP reported to WHO/ECDC that 18 197 TB cases had been registered for treatment. Among the 13 888 new TB cases, 2472 (18%) were extrapulmonary, and 62% of the remaining 6987 (pulmonary) cases were sputum smear-positive *(10)*.

During the period 2008–2012, the notification rates of new/relapsed TB cases showed a steady decreasing trend. MDR-TB notification also decreased (Table 3).

Table 3. Number and rate of reported TB cases, 2008–2012

Year	Population	New and relapsed TB		MDR-TB	
		No. of cases	Per 100 000 population	No. of cases	Per 100 000 population
2008	21 964 962	21 724	98.9	816	3.7
2009	21 913 311	20 643	94.2	624	2.8
2010	21 861 476	18 590	85.0	574	2.6
2011	21 808 931	17 045	78.2	579	2.7
2012	21 754 741	16 107	74.0	530	2.4

During the last five years, the detection rates of new/relapsed TB cases remained fairly stable, reaching 80.5% in 2012. The detection rate of MDR-TB cases, on the other hand, fluctuated with a low of 66.3% among notified TB cases in 2012 (Table 4).

Table 4. Detection rate of new and relapsed TB cases and MDR-TB cases, 2008–2012

Year	New and relapsed TB			MDR-TB		
	No. estimated (best)	Detected		No. estimated among notified TB cases (best)[a]	Detected	
		No.	%		No.	%
2008	27 000	21 724	80.5	1100	792	72.0
2009	25 000	20 643	82.6	1020	624	61.2
2010	24 000	18 590	77.5	930	574	61.7
2011	22 000	17 045	77.5	850	579	68.1
2012	20 000	16 107	80.5	800	530	66.3

[a] MDR-TB estimates are taken from the Romania TB country profiles published annually by WHO *(10)* and based on the drug resistance survey of 2004.

The notification rate of pulmonary culture-positive TB cases (new and previously treated TB cases) decreased during 2008–2012, while the proportion of MDR-TB among them remained fairly stable (Table 5), which could be explained by a lack of improvement in the laboratory diagnosis. Meanwhile, the notification rate of all pulmonary TB cases (new and previously treated) showed a reduction over the same period.

Table 5. Number and rate of all pulmonary TB cases, culture-positive and MDR-TB cases, 2008–2012

Year	Population	All pulmonary TB		Culture-positive TB		MDR-TB		
		No. of cases	Per 100 000 population	No. of cases	Per 100 000 population	No. of cases	Per 100 000 population	%
2008	21 964 962	24 786	112.8	10 079	45.9	816	3.7	8.1
2009	21 913 311	23 164	105.7	11 299	51.6	624	2.8	5.5
2010	21 861 476	21 059	96.3	10 039	45.9	574	2.6	5.7
2011	21 808 931	19 205	88.1	9 331	42.8	579	2.7	6.2
2012	21 754 741	18 197	83.6	8 812	40.5	530	2.4	6.0

In 2011, the NTP successfully treated 85% of new TB cases, 73% of relapsed cases, 38% of cases retreated after loss to follow-up and 40% of cases retreated after failing category I treatment.[2] Death and loss to follow-up, however, made up a significant proportion of the unsuccessful treatment outcomes and a significant number of cases were transferred to category IV treatment[3] because they were found to have M/XDR-TB (Table 6).

The treatment outcomes did not change much during the last five years among both new pulmonary sputum smear-positive TB and MDR-TB patients (see Tables 7, 8).

[2] 2HRZE/4HR: two months of isoniazid, rifampicin, pyrazinamide and ethambutol followed by four months of rifampicin and isoniazid.

[3] Treatment with first-line and second-line anti-TB drugs based on DST results.

Table 6. Treatment outcomes among pulmonary sputum smear-positive TB patients by treatment history, 2011

Treatment outcome	New		Relapse		After loss to follow-up		After failure	
	Cases	%	Cases	%	Cases	%	Cases	%
Cured	5228	71.7	1176	60.8	135	26.3	157	31.7
Treatment completed	963	13.2	231	11.9	58	11.3	41	8.3
Died	462	6.3	140	7.2	71	13.8	64	12.9
Treatment failed	262	3.6	159	8.2	52	10.1	135	27.3
Lost to follow up	371	5.1	218	11.3	190	37.0	86	17.4
Still in treatment	19	0.3	11	0.6	8	1.6	12	2.4
Transferred out	0	0.0	0	0.0	0	0.0	0	0.0
Not evaluated	0	0.0	0	0.0	0	0.0	0	0.0
Subtotal	7289	100.0	1935	100.0	514	100.0	495	100.0
Transferred to category IV treatment	106	1.4	132	6.4	82	13.8	183	27.0
Total cases registered	7395	100.0	2067	100.0	596	100.0	678	100.0

Table 7. Treatment outcomes among new pulmonary sputum smear-positive TB patients, 2007–2011

Year	No./%	Success	Died	Failed	Lost to follow-up	Still in treatment	Transferred/ unknown
2007	No.	9532	456	445	672	142	0
	%	*84.8*	*4.1*	*4.0*	*6.0*	*1.3*	*0.0*
2008	No.	8504	467	389	556	169	0
	%	*84.3*	*4.6*	*3.9*	*5.5*	*1.7*	*0.0*
2009	No.	9168	475	415	610	69	0
	%	*85.4*	*4.4*	*3.9*	*5.7*	*0.6*	*0.0*
2010	No.	7915	441	379	538	172	0
	%	*83.8*	*4.7*	*4.0*	*5.7*	*1.8*	*0.0*
2011	No.	7616	412	301	470	91	1
	%	*85.7*	*4.6*	*3.4*	*5.3*	*1.0*	*0.0*

Table 8. Treatment outcomes among MDR-TB patients, 2007–2010

Year	No./%	Success	Died	Failed	Lost to follow-up	Still in treatment	Transferred/ unknown
2007	No.	125	141	227	138	41	1
	%	*18.6*	*21.0*	*33.7*	*20.5*	*6.1*	*0.1*
2008	No.	129	179	259	166	59	0
	%	*16.3*	*22.6*	*32.7*	*21.0*	*7.4*	*0.0*
2009	No.	102	119	229	126	48	0
	%	*16.3*	*19.1*	*36.7*	*20.2*	*7.7*	*0.0*
2010	No.	115	98	231	106	24	0
	%	*20.0*	*17.1*	*40.2*	*18.5*	*4.2*	*0.0*

Recommendations

Ministry of Health

1. Sufficient and sustainable funding should be ensured.
2. The draft National Strategic Plan for TB control should be finalized and approved in line with the recommendations of this review. No delays should occur in the approval of the future norms (secondary legislation) necessary to implement the NTP consistently.

3. The second TB project under the Norwegian Financial Mechanism should be revised in line with, and in support of the effective implementation of, the recommendations of this review, taking into account the technical assistance required.
4. A working group should be established as soon as possible to draft the concept note required to access further support from the Global Fund. The current composition of the Country Coordinating Mechanism should be revised to ensure the direct involvement of the Ministry of Health.
5. The governance of the NTP should be clarified in the spirit of the recent law establishing the National Agency for Health Programmes and aiming to ensure ownership by, and accountability to, the Ministry of Health.

Case-finding and diagnosis

Case-finding

Active case-finding

Active TB case-finding has been limited in Romania to contact-tracing and screening of prisoners and health workers.

TB contact-tracing starts from the hospital where a patient is diagnosed with TB and follows a procedure requiring the collaboration of three services, the district epidemiologist, the family doctor and the pulmonology dispensary (Ministry of Health Order No. 8 of 2000). The hospital fills out the contact information form in collaboration with the epidemiologist; the family doctor (or the occupational health doctor for the patient's workplace) identifies the patient's contacts and informs the pulmonology dispensary; the pulmonology dispensary invites by letter all contacts to report for a medical check. There are no specific guidelines for these checks and no strict obligation to keep records. Often no tuberculin skin test is available so none is made. Some children with presumptive TB are sent to Bucharest for diagnosis. However it is organized, such screening is not effective and misses many TB contacts who do not come to the pulmonology dispensary (even if the Public Health Authority may be involved) or are screened in another facility somewhere else or in the private sector without proper registration.

Among the population groups at higher risk, only prisoners and health workers are screened annually for TB. Save the Children has been running a project for TB education and screening among homeless and poor people. This has yielded 799 people referred for TB diagnosis, 228 of them confirmed with TB, in 2008–2010 and 130 people referred with 36 cases confirmed in 2013. There have been discussions in recent years about arranging a mobile unit with digital X-ray and geneXpert to screen the population.

Passive case-finding

Passive TB case-finding relies on symptomatic patients self-reporting to family medicine services or, even more frequently, directly to TB services. Family medicine services are free only for those under the daily quota of consultations reimbursed by the National Health Insurance House. Other patients have to pay or go directly to the emergency services of the nearby hospital, which are provided free. This seems to be the main cause in delays in self-reporting and explains the frequent observation of severe forms of TB at the time of diagnosis. The private

sector is well-established but it is only used by a few patients and then mainly for chest X-ray diagnosis, followed by referral of presumptive TB patients to the public sector.

Diagnosis

In principle, patients are diagnosed based on clinical presentation and the laboratory and radiology results. In some cases, bronchoscopy or other investigations are also requested. Most TB cases are diagnosed during hospital admission. Not all TB services are following Ministry of Health Order No. 916 of 27 July 2006 which states that radiological investigation is not obligatory for TB diagnosis.

Laboratory network and services

The national TB laboratory network consists of 105 laboratories: 14 level I provide only direct microscopy), 48 level II provide direct microscopy and bacteriological culture and 43 level III provide direct microscopy, bacteriological culture and anti-TB drug susceptibility testing (DST). Among the latter are the two TB laboratories in Bucharest and Cluj, which function as national TB reference laboratories (NRL), and the two TB laboratories in Jilava and Targu Ocna prisons. Level I laboratories are usually located on the premises of TB dispensaries, while levels II and III laboratories are in hospitals. The geographical distribution of the laboratories is uneven, with some counties over-served and some under-served. Clinical samples should be transported daily in cool boxes to laboratories for culture and DST using cars bought in 2005 through the Global Fund grant. The review team observed that such transport works well in the south-west of the country but less well in other regions.

Most laboratories perform microscopy by using Ziehl-Neelsen staining, while a few use auramine staining and fluorescence microscopy. Light-emitting diode microscopy is only available in Bisericani hospital. In some places there were reports of irregular supplies of microscopy reagents (supplied by Sanimed) and sometimes laboratories prepared their own reagents.

Level III laboratories perform DST to first-line anti-TB drugs such as isoniazid and rifampicin applying the absolute concentration method, while NRLs expand the testing through the proportion method to ethambutol and streptomycin and to some main second-line anti-TB drugs (kanamicyn, amikacin, capreomycin, ofloxacin and ethionamide).

In general, culture laboratories use the commercial Löwenstein-Jensen medium (supplied by Sanimed and Cantacuzino) and those that perform DST use the commercial ready-to-use Löwenstein-Jensen media containing 0.2 µg/ml isoniazid or 40 µg/ml rifampicin (Sanimed). The quality of these commercial media appears to be good but a whole country relying on two suppliers is a weak point, considering that if the supplier should experience problems in the delivery or the quality of the media, it will be a countrywide problem. The culture results are obtained through three automated systems: eight laboratories have the mycobacteria growth indicator tube (MGIT), six laboratories have MB/BacT and the laboratory in Bucharest has VersaTrek, but all these are rarely used because of lack of funds to procure the necessary consumables. The laboratories regularly experienced stock-outs of Löwenstein-Jensen media for DST of isoniazid and rifampicin because of organizational problems, and at the end of 2013 there were also stock-outs of materials for second-line DST. Confirmation of the presence of *M. tuberculosis* complex is done by using the Standard Diagnostics TB Ag MTP64 rapid test for

identification of TB, but this test is not available in all culture laboratories because of the lack of the specific reagents due to budget constraints.

Romania has embarked on the implementation of rapid molecular diagnosis of TB and drug resistance. Since July 2013 (with support from the Global Fund and training by WHO/ECDC), line probe assays have been in use for the molecular detection of *M. tuberculosis* complex and resistance to isoniazid and rifampicin (MTBDR*plus* assay, Hain Lifescience) and resistance to selected second-line drugs (MTBDR*sl* assay, Hain Lifescience). Since then, 1462 MTBDR*plus* analyses have been performed in four laboratories (Brasov, Bucharest, Cluj and Constanta) and 228 MTBDR*sl* analyses in Bucharest and Cluj (the two NRLs). There are plans to introduce cartridge-based nucleic acid amplification techniques (GeneXpert platform) testing of high-risk communities and TB outbreaks.

The two NRLs have been working in this capacity since 1997, even though they have never officially been recognized as such by the Ministry of Health. Their terms of reference from the NTP include, in addition to work for their hospitals, the external quality control and supervision of the TB laboratory network. These activities are paid from the budgets of the hospitals where they are located. The national coordinator of the laboratory network is the head of the NRL in Cluj, working on a voluntary basis and with no financial compensation. Under these conditions and despite the goodwill, the supervision of lower-level laboratories was necessarily limited to only a very few in recent years. In fact, the last supervision of level II laboratories countrywide took place in 2011.

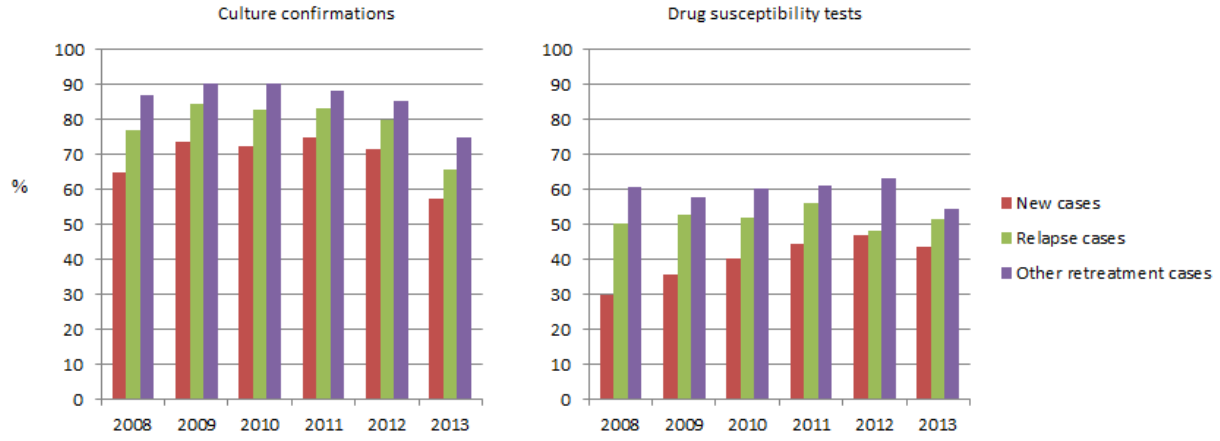
A TB laboratory national working group was established in 2003 and recognized by the NTP in 2006 and the Ministry of Health in 2010. The working group currently consists of nine members and has in its terms of reference the analysis of the country's needs for laboratory equipment and consumables, the development of national laboratory plans, the development of standard operating procedures and their reinforcement, the updating of training curricula and training of laboratory staff and the development of standardized checklist for supervision.

The standard operating procedures developed by the TB laboratory national working group require three sputum samples for direct microscopy in a patient with presumptive TB and two sputum samples in a patient during TB treatment. Three culture tubes are also taken. However, the review team observed that the number of sputum samples investigated per patient varied from one to six, with six samples as routine practice in various sites. Moreover, in some laboratories poorly stained sputum smears were observed.

Laboratory output, staff and workload

In the last six years, the number of culture-confirmed TB cases has decreased slightly (Fig. 2a) but the number of cases with DST has not convincingly increased (Fig. 2b). The level of DST in Romania is among the lowest in the Region and far from the 100% target set by the Consolidated Action Plan to Prevent and Combat M/XDR-TB in the WHO European Region 2011–2015 *(11)* and by the ECDC Framework Action Plan to Fight Tuberculosis in the European Union *(12)*. Long delays occur in receiving the laboratory results; it can take three weeks to one month to receive the results of the bacteriological culture, one additional month to receive the DST results for first-line anti-TB drugs and even three to seven months to receive the DST results for second-line anti-TB drugs. Moreover, the review team observed high contamination rates in culture.

Fig. 2. TB cases by history of previous treatment: (a) confirmed by bacteriological culture and (b) investigated with DST, 2008–2013



The assessment of the laboratory network conducted by the NTP in 2013 found 67 physicians (average age 49 years, range 30–65 years), 66 biologists/biochemists (average age 44 years, range 29–65 years) and 257 technicians (average age 47 years, range 26–64 years).[4] Only a few members of staff had received training in the previous years, mostly informally on-the-job or through participation in expensive conferences paid by them. The assessment documented quite different workloads between level I, level II and level III laboratories in the number of direct microscopy investigations carried out per month as well as of bacteriological cultures (see Table 9), and a similar quite large variance in positivity rates of the investigations. The low workload in some laboratories cannot support good quality practice and clearly calls for a significant decrease in the number of laboratories and a fairer distribution of the workload between them.

Table 9. Number of laboratory tests and their positivity rates[a] in the national TB laboratory network, Romania, 2013

Data	Laboratory level I	Laboratory level II	Laboratory level III
No. of laboratories assessed	14/14	46/48	43/43
Direct microscopy			
Tests during the year (N)	14 116	95 353	366 114
Range (N)	39–2 707	842–3 684	1 689–20 442
Positivity rate (% mean)	4.7	8.1	8.8
Positivity rate (% range)	0.0–10.3	2.0–21.0	3.8–16.0
Bacteriological culture in solid media			
Tests during the year (N)	–	91 003	361 985
Range (N)	–	248–3 684	1 689–20 442
Positivity rate (% mean)	–	11.3	13.2
Positivity rate (% range)	–	3.3–21.5	5.0–18.3
Bacteriological culture in liquid media			
Tests during the year (N)	–	–	4 633
Range (N)	–	–	23–1 368
Positivity rate (% mean)	–	–	13.1
Positivity rate (% range)	–	–	4.9–94.7

[a] The positivity rate is calculated as the percentage of total examinations (sputum smears or cultures) which were found with mycobacteria.

[4] Homorodean D. Annual assessment of the TB laboratory network. Cluj Napoca: Pulmonology Hospital; 2013 (unpublished information, available on request from the Tuberculosis and M/XDR-TB Programme, WHO Regional Office for Europe).

The low positivity rates may be due to a number of reasons: too many respiratory patients investigated for presumptive TB, poor quality of sputum samples sent to the laboratory, poor quality of the laboratory investigation. A most remarkable finding of the review team was the too low centrifugation speed for primary isolation of the mycobacteria, mainly due to the inadequacy of the centrifuges in use. Definitely, a centrifugation speed which is above 3000 × g can lead to more bacteriologically confirmed cases. The relatively high positivity rates in some of the laboratories could be due to their location in hospitals where patients with presumptive TB were selected by a specialist, but laboratory cross-contaminations could also play a part. These conditions were often observed in laboratories by the review team, and the possibility should be confirmed by specific operational research.

Plan to rationalize laboratory services

Past consultancy missions have repeatedly recommended that the TB laboratory network should be reduced, and in fact the total number of laboratories of 188 in 2000 has been progressively decreased to the current 105. However, this is still too many and past plans to decrease the number have never been implemented. The latest draft National TB Strategic Plan (not yet approved) envisages eight regional laboratories with good quality and biosafety, but neither the process for achieving this is described nor is their location. In 2011, the TB laboratory national working group recommended the closure of all level I laboratories, but by the end of 2013 only three of them (out of 17) were actually closed. As well as the problem of managing staff after the closure of a laboratory (including their relocation to other laboratories not entitled to provided salary bonuses linked to the TB occupational risk), another important reason could be financial arising from the fact that hospitals receive funding for laboratory activities based on the number of hospital beds and not on their workload (see section on Health system and TB control, p. 53).

In the Global Plan to Stop TB 2006–2015 *(13)*, one microscopy laboratory per 100 000 population and one culture laboratory per five million population are envisaged, with possible variations between countries. Based on this and on its population (22 million), Romania should have 220 microscopy laboratories and five culture laboratories. However, considering the TB epidemiology in the country and the need for more DST, the eight regional level III laboratories and the two NRLs (which also perform DST for second-line anti-TB drugs) envisaged in the current draft National TB Strategic Plan are reasonable. The ideal numbers of level I and level II laboratories should be based on an analysis of the workload. Table 9 shows that 103 laboratories reported that they had performed 475 583 direct microscopic examinations and 452 988 bacteriological cultures in solid media in 2013. Extrapolating this workload to the existing 105 laboratories, it can be said that the total workload in 2013 was around 485 000 samples for both microscopy and culture. Such a workload is the result of the collection of three sputum smear samples (or even more) from each patient for microscopy and three for culture. If the WHO recommendations of only two microscopic examinations and cultures per patient were to be implemented, the workload would decrease by roughly one third to 323 500 microscopic examinations and cultures per year. In 2013, the 43 level III laboratories performed 361 985 bacteriological culture on solid media, with an average of 8500 cultures per laboratory. Therefore, with the current capacity and the expected number of samples after implementation of the WHO recommendations (323 500/8500), 38 culture laboratories would be needed. However, the country has 41 counties plus the municipality of Bucharest, thus the initial reduction in culture laboratories from the current 91 to 42 seems reasonable to ensure universal access to culture. In summary, it looks as if a revised national TB laboratory network should be composed of the following:

- eight level III laboratories at regional level (performing microscopy, culture and DST of first-line anti TB drugs) and two NRLs also performing DST for second-line drugs instead of the current 43 level III laboratories;
- a minimum of 30 and maximum of 35 level II laboratories (performing microscopy and culture and referral of all positive cultures to level III laboratories for DST) evenly distributed across the country and equipped with GeneXpert platform based on the local TB and MDR-TB incidence, physical accessibility, presence of population risk groups, availability of equipment and staff;
- no level I laboratories (the existing 14 laboratories to be closed).

Laboratory quality assurance

Quality assurance in the TB laboratory network is based both on internal and external cross-checking (Table 10). The review team observed that many laboratories were cross-checking all sputum smears of the day instead of a monthly sample, creating an unnecessary workload while appropriate external quality assurance was lacking. The external quality assurance of sputum microscopy and bacteriological culture is provided through a mix of rechecking by another TB laboratory and/or by LABQuality, a Finnish company contracted for these activities. For microscopy, five positive and five negative slides are chosen randomly twice a year and sent for blind cross-checking. For bacteriological culture, two samples are sent two/four times a year. In 2013, 17 (17%) laboratories did not participate in external quality assurance for microscopy. All laboratories checked for culture by LABQuality scored a "good result" (an unclear definition). The review team observed that the quality of sputum samples was quite variable (0–35% was useless saliva; in one laboratory this was 70%), indicating the need to improve sputum collection. High contamination rates of cultures in Löwenstein-Jensen medium (up to 18%) were also observed, suggesting inappropriate decontamination or inoculation under non-sterile conditions.

Table 10. Participation in external quality assurance by TB laboratories, 2013

Laboratories participating in the survey		Microscopy			Culture by LABQuality
		Rechecking	Rechecking+LABQuality	LABQuality only	
Level I	14/14	6			
Level II	46/48	29	4	4	46
Level III	43/43	4	30	9	43
Total	103/105	39/103	34/103	13/103	89/89

Source: Homorodean D. Cluj Napoca: Pulmonology Hospital; 2013 (unpublished data).

Countrywide external quality assurance of DST for rifampicin and isoniazid was only carried out in 2009 and 2012 by the NRL in Cluj (10 and 20 strains, respectively, tested from each of the 42 level III laboratories checked). In 2012, the results for rifampicin were 100% concordant between the laboratory being checked and the NRL in 20 laboratories, 95% in 19 laboratories, 90% in one laboratory and 85% in two laboratories. For isoniazid, 100% concordance was found in 39 laboratories and 95% in three laboratories. Training was recommended for the staff working in the laboratories with unsatisfactory results.

The external quality assurance of DST (first and second-line anti-TB drugs) is also conducted every year by the Supranational Reference Laboratory in Stockholm, Sweden, for the NRLs; both of them reached 100% concordance of results in the last round of 2013. There has been

good collaboration with the Supranational Reference Laboratory since 2003 covering, in addition to external quality assurance, the development of standard operating procedures, identification of Bacillus Calmette-Guerin (BCG) and design of drug resistance surveys. Both NRLs are also collaborating with the INSTAND Project for Central and Eastern European Countries initiated by the Supranational Reference Laboratory in Borstel, Germany *(14)*, the European Tuberculosis Laboratory Initiative of the Regional Office *(15)* and the European Reference Laboratory Network for TB of the ECDC *(16)*. External quality assurance of the recently introduced line probe assay diagnostics will be conducted in the country through the European Reference Laboratory Network for TB.

There is a national accreditation body, RENAR, for all medical activities, including laboratory activities. Thirty-five TB laboratories were accredited by RENAR, at €2500 per each accreditation. RENAR appears to be well-organized and ensures the presence of the requirements for quality and competence in medical laboratories as specified under the International Organization for Standardization 15189. RENAR accreditation does not, however, mean that the laboratories are appropriately equipped for TB investigations. In fact, most of the RENAR-accredited laboratories visited by the review team did not have appropriate centrifuges for the isolation of TB and their biosafety cabinets were not being properly maintained.

Biosafety

Biosafety in the TB laboratories is governed by Ministry of Health Order No. 1302 of 2007, which indicates the mandatory use of a class II biosafety cabinet but not its characteristics, including the airflow speed which should be checked by the Romanian Bureau of Legal Metrology. This Order is enforced by the public health agency of each county; in practice, TB laboratories are allowed to work even if they are not compliant with the biosafety rules, through six-monthly permissions and further extensions by the public health agency. On paper, 2/14 level I, 33/48 level II and 43/43 level III laboratories have biosafety cabinets. However, the review team found level III laboratories performing culture and DST with no proper cabinets. Maintenance was very poor and there was no replacement of the high-efficiency particulate air filters almost everywhere. Most of the laboratories visited did not have centrifuges with safety buckets, and staff were using inappropriate respirators/masks.

Recommendations

NTP

1. Guidelines should be developed and introduced for conducting contact investigation according to international standards.
2. Universal access should be ensured to rapid diagnosis of TB and MDR-TB by using cartridge-based nucleic acid amplification techniques in selected lower level laboratories and/or sputum collection points with high rates of TB and/or MDR-TB (such as prisons, selected hospitals, HIV centres) and line probe assay in geographically representative regional laboratories. The TB laboratory network should be redesigned and rationalized by the end of 2015.
3. The laboratory network should be redesigned to consist of eight regional level III laboratories, the two NRLs and a maximum of 35 level II laboratories. Eight level III laboratories are assigned to perform liquid culture and first-line drug DST and rapid detection of resistance to isoniazid and rifampicin by line probe assays, while the two NRLs also ensure second-line drug DST for the whole country. The level II laboratories

should only perform microscopy and culture and refer the positive cultures to the level III laboratories for DST. The existing level I laboratories should be closed.

4. Access to TB diagnosis should be ensured through sputum collection points and prompt transport of samples, bearing in mind that the vehicles currently being used will need replacement within five to 15 years.
5. The national diagnostic algorithms should be revised to include the rapid detection of TB and MDR-TB and to ensure the consistent retraining and education of staff, including family doctors.
6. Light microscopes needing replacement should be replaced with more sensitive light-emitting diode microscopes.
7. All level II and level III laboratories should be equipped with centrifuges with safety buckets operating at 3000 × g.
8. DST should be scaled up so that all new and previously treated pulmonary TB patients are bacteriologically confirmed tested for resistance to rifampicin isoniazid.
9. The WHO guidelines for the isolation of TB (two sputum samples and an appropriate centrifugation speed) and for the quality control of microscopy should be implemented *(17)*.
10. Collaboration with RENAR should be undertaken to include in their assessment the appropriateness and biosafety of TB isolation procedures, the appropriateness and maintenance of equipment (especially the biosafety cabinets) and other biosafety aspects.
11. TB laboratory specialists should receive international training in the maintenance of biosafety cabinets.
12. A detailed TB laboratory development plan should be prepared by the end of 2014 to describe the process and timeframe of the rationalization of the network and consider the upgrading and maintenance of laboratory equipment, biosafety, quality assurance and supervision and the training of staff.
13. Possible new funding opportunities for the TB laboratory network should be prioritized as follows:
    - to ensure sufficient consumables and reagents for currently available equipment for liquid culture (MGIT) system and rapid diagnosis of drug resistance (line probe assays);
    - to optimize biosafety by ensuring proper and certified maintenance of biosafety cabinets;
    - to scale up the rapid diagnosis of drug resistance;
    - to obtain appropriate centrifuges for the isolation of TB (3000 × g and safety buckets);
    - to procure other equipment, reagents and training.
14. Because of the infrastructure and low workload at the laboratory in the penitentiary system in Bucharest, consideration should be given to implementing the cartridge-based nucleic acid amplification technique in the prison TB departments and sending specimens for culture and DST to the NRL.
15. The capacity of the NRL in Cluj should be expanded to perform laboratory network supervision.

Treatment and case management

Treatment

NTP treatment regimens are designed in category I[5] and III[6] for new TB cases with sputum-positive pulmonary TB and sputum-negative or extrapulmonary TB, respectively, and category II[7] for retreatment TB cases. These regimens are maintained until DST identifies an anti-TB drug resistance profile requiring a different treatment. Despite the revised WHO recommendations published in 2010 *(18)* and the recommendations of previous missions of the regional GLC, the category III regimen has been maintained instead of category I being used for all new TB cases. In addition, the intermittent intake of drugs (every second day) has not been replaced by a daily intake during the maintenance phase of treatment.

Case management

Once diagnosed with TB, patients are hospitalized in a TB hospital for at least that part of the intensive phase of treatment reimbursed by the NHIH, that is, 37 days for drug-susceptible and 120 days for drug-resistant patients (see subsection on Health system financing, p. 58). After discharge from hospital, they are referred to pulmonology dispensaries, where their treatment continues usually with intermittent self-administered-treatment (drugs to be taken every second day) through a weekly/monthly supply of anti-TB drugs to patients, or supervised treatment (DOT) by the pulmonology dispensary, or by the family doctor if he/she has agreed to collaborate with the dispensary. Collaboration with family doctors has been limited since the NHIH stopped paying financial incentives for TB/related activities in 2009. Home-based treatment and tracing of patients lost to follow-up are infrequent, due to the limited number of dedicated nurses and the small budgets that TB dispensaries have for transport (with cars supplied about 10 years ago under the Global Fund grant).

The review team noticed the extensive hospitalization of TB patients, including patients with non-severe and non-infectious TB disease. The implications of and reasons for such extensive use of hospital TB beds are explained elsewhere in this report (see subsection on Health system financing, p. 58). The review team also noticed the widespread practice of separate hospital admissions for co-pathologies. Under the NHIH framework contract (and its need to forecast case load and control payments for each condition), a TB patient with diabetes mellitus has to be treated in an endocrinology hospital, which may disrupt the continuum of care for the patient.[8]

[5] Two months of isoniazid, rifampicin, pyrazinamide and ethambutol followed by four months of isoniazid and rifampicin (2HRZE/4HR). During the second phase of treatment (maintenance), drugs are given every second day.
[6] Two months of isoniazid, rifampicin and pyrazinamide followed by four months of isoniazid and rifampicin (2HRZ/4HRE). During the second phase of treatment (maintenance), drugs are given every second day.
[7] 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 (2HRZES/1HRZE/5HRE). During the second phase of treatment (maintenance), drugs are given every second day.
[8] The review team came across one patient who had been admitted to a pulmonology hospital for presumptive TB, discharged, admitted to an endocrinology hospital for treatment of diabetes mellitus (diagnosed at the pulmonology hospital) and registration in the national database, discharged, and then traced by and readmitted to the pulmonology hospital after confirmation of TB disease by culture. Had this patient been treated for diabetes in the pulmonology department, the TB treatment would have been initiated earlier with less discomfort for the patient and fewer costs for the health system.

Self-administered treatment through family members is quite popular, as in other countries, but is at the same time in contradiction with the opinion reported by most of the doctors that DOT in hospital is the best way to ensure treatment compliance and completion *(19,20)*. Meanwhile, the support offered to patients to compensate the lack of supervision of their treatment is very limited.

Under the Global Fund Round 4 grant, food vouchers for a value of 50 Leu per month were given to treatment-compliant TB patients in 13 counties (and Bucharest) through Doctors of the World and Red Cross volunteers. The Global Fund Round 6 grant covers similar services, although only in two counties. These projects are widely viewed as successful in reducing loss to follow-up treatment but even so they were not expanded by the NTP. At the time of the review, the only patient support provided was to MDR-TB patients in a limited number of sites under the Global Fund Transition Funding Mechanism through UNOPA and ASPTMR. This project includes the provision of a package of food vouchers, psychological support and counselling via telephone. The review team encountered several M/XDR-TB patients in Bucharest, Iasi and Piatra Neamt who were enrolled in the project and all had positive opinions of such support. While the UNOPA/ASPTMR project is promising, it was due to end in September 2014. Because it was only implemented for one year, it will be difficult to measure an impact and, therefore, to justify its expansion in future Global Fund grants.

One of the great challenges for the NTP is the continuation of interventions established under international funding such as the Global Fund. In the case of Red Cross and Save the Children (see previous section on Case-finding and diagnosis), support for outreach and treatment among homeless people had to stop in the entire country for nearly three years between the end of the Global Fund Round 6 grant and the start of the Global Fund Transitional Funding Mechanism.

Recommendations

NTP

1. The national guidelines for TB treatment should be updated according to the most recent WHO recommendations. In particular:
    - category III should be abandoned; category I regimen should be considered for all new patients regardless of their disease location (pulmonary or extrapulmonary) and infectiousness (sputum smear-positive or -negative);
    - the retreatment patients, especially those with a high likelihood of MDR-TB, should be guided by sputum culture and DST instead of a standardized category II regimen;
    - the treatment regimen of all patients with positive sputum samples at the end of the intensive phase should be reassessed and guided by sputum culture and DST;
    - intermittent treatment should be replaced by daily treatment during the continuation phase, especially when it is not supervised, and the number of patients under DOT should be expanded through the use of family doctors.

TB in children

In line with the decrease of TB transmission in Romania over the years, the notification rate of TB among children aged 0–14 years also dropped from 47 new TB cases per 100 000 children in 2002 to 24 in 2011, with similar variations across counties as seen among adults. In 2011,

however, as many as 65 children were diagnosed with disseminated forms of TB (meningitis, miliaris or massive pulmonary damage). While such cases are indicative of ongoing TB transmission in the community, it could also be suspected that notification is not really indicative of the actual TB incidence in this population but the result of the well-known difficulty in diagnosing TB in children and the reported shortage of tuberculin skin tests.

BCG vaccination takes place under the national vaccination programme, which is financed by the Ministry of Health and implemented by the Communicable Disease Control Department of the National Institute of Public Health. The reported increase in adverse reactions (lymphadenitis) after BCG vaccination (vaccine manufactured by the State Serum Institute in Denmark) in November 2012 convinced the Ministry of Health to suspend the vaccinations as a precautionary measure and to ask for a risk assessment. This was conducted jointly by WHO and ECDC in the same month and ended with the recommendation to continue BCG.[9]

National guidelines for TB in children are available but have not been updated since 2006 to take into consideration the latest WHO recommendations (issued in 2010) *(21)*. All children are admitted to hospital until at least the completion of the intensive phase of TB treatment, which disrupts their social and family lives and may place them at risk of TB suprainfection through nosocomial transmission because of poor infection control. Moreover, parents of children aged more than three years have to pay for their stay in hospital.

Paediatric formulations of drugs, either in single or fixed-dose combination, are not included in the essential drug list. There are plans to apply to the GDF for a specific grant.

Recommendations

NTP

1. The prevention, diagnosis, treatment and care of TB in children should be improved by ensuring that they receive Bacillus Calmette-Guérin vaccination, tuberculin skin testing and paediatric formulations of anti-TB drugs, and that their parents/caregivers can stay with them while in hospital free of charge.
2. The national guidelines for TB in children should be updated according to the latest WHO recommendations, and doctors should be trained in the new guidelines.

HIV-related TB

Burden

At the end of 2013, 12 273 people living with HIV (PLHIV) were registered in Romania, with a cumulative total of 19 261 HIV/AIDS cases recorded since 1985 *(22)*. More than half of these people are aged 20–24 years, as the result of the diffuse nosocomial infection that occurred among orphans and hospitalized children (through transfusion of unscreened blood and injections with improperly sterilized equipment) during the mid-1980s and beginning of the 1990s. The number of HIV cases registered annually remained stable at around 400 new cases per year between 2004 and

[9] Johansen K, Vermeer-de-Bondt P, Muzafarova N, Salvi C. WHO/ECDC joint support mission to Romania to assess reports of adverse events following immunization with BCG vaccine in current use, 26–30 November 2012 (unpublished document available on request from the Tuberculosis and M/XDR TB Programme, WHO Regional Office for Europe).

2009, before increasing to 531 new cases in 2010, 720 in 2011, 821 in 2012 and 797 in 2013. Such an increase can be explained by the increasing number of people who inject drugs and of the HIV infections among them: 14 new HIV cases in 2010, 131 in 2011, 252 in 2012 and 233 in 2013. TB is the main AIDS-indicative disease, with 160 cases reported in 2013.

Organization of services and coordination

The National AIDS Programme is led by the National Commission to Fight AIDS based at the Matei Bals Institute of Infectious Diseases in Bucharest. There are nine HIV centres for HIV diagnosis, treatment of HIV and its coinfections and copathologies, case registration and reporting, and programme evaluation. Each centre is attached to an infectious disease hospital: the Victor Babes Clinical Hospital for Infectious and Tropical Diseases and the Matei Bals National Institute of Infectious Disease in Bucharest and the seven infectious disease hospitals in the counties of Brasov, Cluj, Constanta, Craiova, Iasi, Targu-Mures and Timisoara.

Since 1998, universal ART has been available and given free to all PLHIV with a CD4 count of $<500/mm^3$. ART is available in every infectious diseases hospital and TB hospital, although monitoring of the viral load and the immunological evaluation of the patients is only performed in the nine regional HIV/AIDS centres. Access to ART has been affected by the economic crisis in recent years and many nongovernmental organizations working with PLHIV have reported shortages and interruptions of ART in different parts of the country. A 2011 study on access to ART for PLHIV in Romania by UNOPA and the University of Bucharest, supported by UNICEF, reported that 65% of the respondents interrupted their treatment and only 35% received treatment regularly *(23)*. Concerns are also raised about adherence to treatment, as only about 40% of the long-term surviving PLHIV (infected during the 1980s and now young adults) are adhering to ART.

A National TB/HIV Collaborative Protocol was signed in April 2011 by the Ministry of Health, the National Commission to Fight AIDS and the NTP with the aim of strengthening collaboration between the two national programmes and with the specific objectives of: (i) defining the collaboration between the two programmes; (ii) agreeing on the methodology for testing, recording and reporting both infections; (iii) describing the TB/HIV clinical management; and (iv) establishing a connection between the TB and HIV national recording and reporting systems.

In addition to this Protocol, the draft TB National Strategic Plan 2013–2017 (which has not yet been endorsed by the Ministry of Health) includes the following TB/HIV activities:

- all TB patients (bacteriologically-confirmed and not) are to be tested for HIV following the methodologies defined in the National TB/HIV Collaborative Protocol;
- all PLHIV are to be screened for TB at the infectious diseases hospitals and any person with presumptive TB is to be referred to the national pulmonology network for further investigation;
- when TB is confirmed, the anti-TB treatment is to start with priority over anti-retroviral treatment (ART); smear-positive TB patients are to be treated for both TB and HIV in pulmonology facilities, while smear-negative and extrapulmonary TB patients are to be treated in infectious diseases facilities;
- isoniazid preventive therapy is only to be given to PLHIV at high risk of TB infection.

Despite the existence of the National TB/HIV Collaborative Protocol and the experience gained in responding to the HIV dramatic epidemic which started in the mid-1980s, the review team observed sub-optimal collaboration between the two national HIV and TB programmes.

The National TB/HIV Commission envisaged for the coordination, monitoring and evaluation of the implementation of the National TB/HIV Collaborative Protocol has not yet been established. TB/HIV prevention, diagnosis, treatment and care are fragmented, so that avoidable referrals are frequent between different services. There are no centres where the complete harm reduction package is provided in one stop, including opioid substitution therapy and prevention, diagnosis and treatment of TB. Only a few nongovernmental organizations are involved in both TB and HIV national programmes and ensuring low-threshold services.

Reducing HIV among TB patients

In 2012, Romania reported to the Joint ECDC-WHO Reporting TB Platform that 9922 (54%) of 18 197 TB patients registered in that year were tested for HIV and 232 (2%) of them were found with HIV infection. While it has gradually increased in recent years, the coverage of HIV testing is far behind the 90% target by 2017 indicated in the draft TB National Strategic Plan. For the same year, Romania reported that 90% of TB/HIV patients had been placed on ART and 76% on cotrimoxazole preventive treatment.

According to the HIV/AIDS Monitoring and Evaluation Department Report *(24)*, 14 115 HIV tests were performed among TB patients in 2012, with only 143 HIV infections detected. The difference between this number and the 232 TB/HIV patients reported through the Joint ECDC-WHO Reporting TB Platform during the same year highlights how discrepancies arise between the two national TB and HIV registers, not linked to each other, and how difficult it is to document the burden of and interventions for TB/HIV in Romania.

Reducing TB among PLHIV

In accordance with the National TB/HIV Collaborative Protocol and practice observed by the review team, PLHIV are screened for TB at the infectious diseases hospitals and those with presumptive TB are sent to pulmonology services for further evaluation. Information on the prevalence of latent TB in PLHIV is scarce, and PLHIV are in general not provided with isoniazid preventive therapy. The roles and responsibilities of TB and HIV services in the prescription, monitoring and evaluation of isoniazid preventive therapy are not defined.

When TB is confirmed, anti-TB treatment is provided in pulmonology hospitals for patients with smear-positive pulmonary TB and in infectious diseases hospitals for patients with smear-negative pulmonary or extrapulmonary TB. Collaboration between the different specialists is not institutionalized but based on personal relations. The review team observed competition between specialized hospitals (pulmonology, infectious diseases and internal medicine) for TB patients, who are admitted without infection control measures.

The national AIDS programme has received significant support from the Global Fund since 2004. However, according to the new eligibility criteria, Romania can no longer apply for support in the area of HIV/AIDS. This is inappropriate in view of the worrying recent increase in HIV infections from injecting drug users. Closer collaboration, including in sharing resources, must be developed between the HIV/AIDS, harm reduction and TB services and civil society

organizations. An important HIV component should be welcomed in the formulation of future TB project applications to the Global Fund.

Recommendations

Ministry of Health

1. The National TB/HIV Commission should be activated and effective regional TB/HIV coordination committees established so as to ensure integrated diagnosis and a continuum of care for all TB/HIV patients focused on their needs.
2. The National TB/HIV Collaborative Protocol should be revised to ensure isoniazid preventive treatment for PLHIV. All TB/HIV patients should be treated in pulmonology facilities.

NTP

3. Formal collaboration should be established between TB and HIV facilities with effective consultancy visits by the respective experts.
4. Adequate capacity and resources for HIV testing and counselling should be ensured, as should the correspondence in the number of TB patients knowing their HIV status between the national HIV and TB databases.
5. The capacity for diagnosis of active and latent TB in infection disease hospitals and the initiation and monitoring of isoniazid preventive therapy should be strengthened.
6. The number and capacity of nongovernmental organizations working with specific hard-to-reach groups at high risk of TB/HIV coinfection should be expanded.

Drug-resistant TB

Burden

Even if it is not listed among the 15 high-burden MDR-TB countries in Europe, Romania should acknowledge that MDR-TB is one of its major public health challenges. The NTP reports a decreasing number of MDR-TB cases over recent years (see section on NTP strategies, structure, budget and main achievements, above), but this trend does not reflect the actual situation because of the limited access to DST. For example, in 2012, the NTP tested only 3654 out of 9112 (40%) newly diagnosed patients and only 1864 out of 3452 (54%) previously treated patients with bacteriologically confirmed TB. Those found with MDR-TB were 114/3654 (3%) and 416/1864 (22%), respectively. Of those 530 found with MDR-TB, 495 (93%) were placed in treatment, with only 284 MDR-TB patients with DST for second-line anti-TB drugs. Thirty-two (11%) patients were found with XDR and 30 were placed in treatment, but most of them received inadequate treatment regimens due to the lack of Group 5 and new anti-TB drugs. The overall gap in accessing MDR-TB diagnosis and treatment is summarized in Fig. 3.

The stratification of M/XDR-TB patients by history of past exposure to treatment shows a higher frequency of drug resistance among relapsed and chronic patients (Table 11).

Fig. 3. Number of MDR-TB patients estimated, detected and treated, 2012

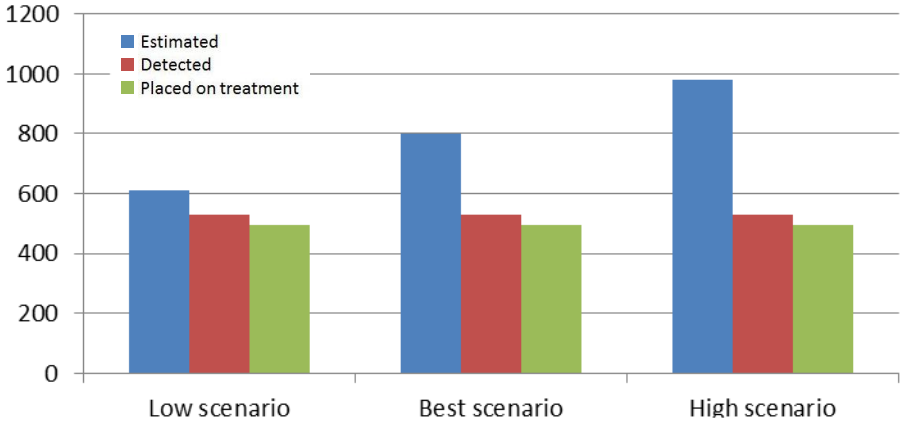


Table 11. M/XDR-TB patients by treatment history; 2012–2013 (January–September)

Year	No./%	New	Relapse	After failure	After loss to follow-up	Chronic	Total
2012	No.	114	142	85	74	144	415
	%	*27.5*	*34.2*	*20.5*	*17.8*	*34.7*	*100.0*
2013	No.	77	97	52	60	66	286
	%	*26.9*	*33.9*	*18.2*	*21.0*	*23.1*	*100.0*

Based on the available records, the MDR-TB patients among all TB patients undergoing treatment each year (newly and previously diagnosed and in treatment) represent an increasing percentage and burden for the NTP (Table 12).

Table 12. Prevalence of MDR-TB, 2007–2012

Year	No. of TB cases under treatment	MDR-TB cases	
		No.	%
2008	43 726	1 505	3.44
2009	43 277	1 586	3.66
2010	40 030	1 552	3.88
2011	36 455	1 528	4.19
2012	34 098	1 425	4.18

Over the past three years, the percentage of XDR-TB has remained around 10% of all incident MDR-TB cases. However, the number of XDR-TB cases seems to be underdiagnosed due to the fact that not every diagnosed case with any resistance to rifampicin is being tested for second-line DST. Assuming an average of 10% of all MDR-TB cases to have resistance to an injectable agent and fluoroquinolone, this constitutes a reservoir of around 150 patients with XDR-TB whose treatment is currently almost impossible due to poor access to an adequate XDR-TB regimen with later generation fluoroquinolones (capreomycin and Group 5 drugs). Over the past year, only eight patients out of 19 diagnosed with XDR-TB have started treatment with a regimen containing moxifloxacin (Table 13).

Table 13. Registered XDR-TB cases by type, 2011–2013 (January–September)

Type of XDR-TB case	2011	2012	2013 (January–September)
Resistant to Group 2 second-line anti-TB drugs (pre XDR-TB)	61	64	34
Resistant to Group 3 second-line anti-TB drugs (pre XDR-TB)	1	9	8
Resistant to isoniazid and rifampicin, any fluoroquinolones and at least one injectable second-line anti-TB drug (XDR-TB)	34	30	20

The number of MDR-TB patients registered for treatment does not reflect the actual number of those who started an adequate treatment regimen, even if such a number is increasing under the Global Fund support and the procurement of second-line anti-TB drugs through GDF (Table 14).

Table 14. MDR-TB and XDR-TB patients registered for treatment with category IV regimens, 2011–2013

Cohort of patients	2011	2012	2013
MDR-TB patients	622	601	357
XDR-TB patients with moxifloxacin	1	9	8

Programmatic management

Romania received the Global Fund Round 6 TB grant for the period 2007–2012. With this grant it became possible to scale up MDR-TB control with 523 MDR-TB patients starting treatment with quality-assured second-line drugs (of 480 targeted). An additional 165 patients (138 already enrolled, 300 target) were considered under the Global Fund Transitional Funding Mechanism for the period October 2012–September 2014.

Treatment outcomes of GLC cohorts enrolled in the MDR-TB treatment programme with Global Fund Rounds 2 and 6 funding show comparatively good performance (Table 15).

Table 15. MDR-TB treatment outcomes under Global Fund support by cohort of patients enrolled during 2004–2011

Treatment outcome	Cohort 1 (2004–2005)		Cohort 2 (2006–2007)		Cohort 3 (2009)		Cohort 4 (2010–2011)	
	No.	%	No.	%	No.	%	No.	%
Patients enrolled	200	100.0	200	100.0	145	100.0	339	100.0
Still in treatment	0	0.0	0	0.0	0	0.0	205	60.5
Success	118	59.0	150	75.0	96	66.2	46	13.6
Failure	31	15.5	20	10.0	17	11.7	28	8.3
Lost to follow-up	22	11.0	16	8.0	10	6.9	23	6.8
Died	25	12.5	13	6.5	21	14.5	27	8.0
Lost to follow up/excluded from the cohort[a]	4	2.0	1	0.5	1	0.7	3	0.9

[a] Patients excluded from the cohort analysis are those who emigrated to another country before the completion of treatment.

Treatment outcomes in the cohorts of patients outside the Global Fund support (the non-GLC cohorts) have, however, been extremely poor in recent years (Table 16). In 2010, a total of 570 MDR-TB patients were treated outside the Global Fund support: 115 (20%) were successfully treated, 231 (40%) failed, 106 (18%) were lost to follow-up, 98 (17%) died and 24 (4%) were

not evaluated. The highest treatment success rate (29.3%) was achieved among the new cases and the lowest (9.6%) among those lost to follow-up.

Table 16. MDR-TB treatment outcomes outside Global Fund support by cohort of patients with different history of previous treatment

Cohort	No./%	Patients enrolled	Success	Failure	Lost to follow-up	Died	Not evaluated
New	**No.**	116	34	46	16	15	5
	%	*100*	*29.3*	*39.7*	*13.8*	*12.9*	*4.3*
Relapsed	**No.**	140	35	50	24	24	7
	%	*100*	*25.0*	*35.7*	*17.1*	*17.1*	*5.0*
Lost to follow-up	**No.**	83	8	26	32	14	3
	%	*100*	*9.6*	*31.3*	*38.6*	*16.9*	*3.6*
After failure of categories I and II treatment	**No.**	86	20	29	17	17	3
	%	*100*	*23.3*	*33.7*	*19.8*	*19.8*	*3.5*
Other or unknown retreatment	**No.**	149	18	80	17	28	6
	%	*100*	*12.1*	*53.7*	*11.4*	*18.8*	*4.0*
Total	**No.**	574	115	231	106	98	24
	%	*100*	*20.0*	*40.2*	*18.5*	*17.1*	*4.2*

Delayed diagnosis and initiation of therapy, improper treatment and poor patient management are the causes of MDR-TB *(25)*. There is limited access to DST; stockouts of injectable agents (aminoglycosides and capreomycin) and fluoroquinolones (ofloxacin and levofloxacin) occurred and ciprofloxacin was used. Hospitalization is often unnecessary and prolonged, without infection control measures, and patients are not supported during their treatment. The reservoir of anti-TB drug resistance is increased by TB patients with treatment failure and those lost to treatment follow-up. Similarly, shortages of second-line anti-TB drugs have already led to the creation of XDR-TB reservoirs, especially at county level. Currently, the absence of adequate range of second-line drugs and Group 5 agents, the unregulated approach to diagnosis and management of patients with pre-XDR-TB (resistance to either fluoroquinolones or an injectable agent alone) and the nosocomial transmission of bacteriological strains are major obstacles to effective action by the NTP.

Case management

The NTP has designated two centres of excellence for drug-resistant TB in Romania: the Marius Nasta Institute and the MDR-TB Hospital in Bisericani, Neamt County. Each of them covers half of the country and has a committee (consilium) of trained experts (drug-resistant-TB committee) responsible for the evaluation of patients found with drug-resistant TB and decisions as to their clinical management, hospital admission and discharge, treatment regimen and follow-up, management of adverse reactions and surgical care. All patients enrolled in the GLC cohort are initially treated in one of these two centres and then referred to the pulmonology dispensary in their county of residence. The patients in the non-GLC cohort are treated in the pulmonology hospitals and (in the case of those with HIV coinfection) the infectious disease hospitals available in each county.

The review team found that the treatment regimens prescribed for the patients in the GLC cohort follow the latest WHO guidelines and include the combination of pyrazinamide, an injectable agent (capreomycin, kanamycin), a fluoroquinolone (ofloxacin, levofloxacin or moxifloxacin) and an oral bacteriostatic agent (ethionamide or prothionamide, cycloserine and/or 4-aminosalicylic acid (PAS)).

For the last GLC-approved cohort of 150 MDR-TB patients (enrolment started in October 2013), the intensive phase of treatment has been increased to the minimum of eight months. The plan is to treat these patients (as reflected in the order to GDF) for a 10 months intensive phase with capreomycin (as injectable of choice) or kanamycin (50% of patients), levofloxacin as fluoroquinolone, and PAS as oral bacteriostatic agent only to be added for 30% of them (those with extensive disease). The criteria to decide the completion of the intensive phase treatment (clinical improvement and two consecutive negative cultures) do not really correspond to those suggested by WHO (clinical improvement and at least four months sputum conversion) but can be considered adequate.

The GLC cohort also includes 19 XDR-TB patients. Their treatment regimens can also be considered adequate, designed to be for 24 months, with a 10 months intensive phase, including capreomycin or kanamycin (50% of patients), moxifloxacin as fluoroquinolone, prothionamide and cycloserine and PAS as bacteriostatic agents and any of the Group 5 agents (clofazimine, linezolid, imipenium/cilastatin and amoxicillin-clavulanate).

For the patients in the non-GLC cohort, the intensive phase is limited to an average of six months with amikacin and streptomycin used as injectable agents (without capreomycin because it is not registered in the country and with streptomycin even though it is not recommended). Ofloxacin is used as the first choice fluoroquinolone due to the higher price of levofloxacin on the local market; ciprofloxacin is not in use but is still on the list of essential medicines. PAS is also not registered in the country. Withdrawal of second-line anti-TB drugs is decided on the basis of adverse reactions but without proper documentation.

When in hospital, MDR-TB patients receive second-line anti-TB drugs every day, including weekends. Consultations with other specialists may also be required and are variously available in the counties (ear, nose and throat, psychiatry, ophthalmology, dentistry, internal medicine, surgery). Palliative care is limited by the unavailability of proper facilities. In ambulatory settings, the drugs are given five days a week at the health facility, and self-administered on Saturdays. Some family doctors may agree to take responsibility for such MDR-TB patients by giving them a one or two weeks' supply of drugs for self-administration: this practice is completely unacceptable and increases the risk of amplifying drug resistance in the patient and of him/her not being cured but continuing to transmit MDR-TB in the community.

To monitor the MDR-TB treatment, sputum smear microscopy and culture are repeated every month during the intensive and continuation phases. Chest radiography is also done every quarter. A positive microscopy and/or culture after four months is not, however, an indication for DST for second-line drugs. Adverse reactions to anti-TB drugs are monitored by periodic clinical examinations including general blood and urine tests, biochemical analysis (bilirubin, liver function test, urea, uric acid, electrolytes, creatinine and glucose).

The review team found that most of the recommendations from previous GLC missions[10] had been implemented, at least at national level, although the old NTP clinical guidelines (2005) are still widely used in the counties. In 2013 they were revised by a group of international experts but now need updating and rapid approval in order to: support the banning of second-line drugs in drug-susceptible TB patients; promote drugs prescribing according to patients' weight and

[10] Yedilbayev A. Green Light Committee monitoring mission, 23–28 April 2013 (unpublished document available on request from the Tuberculosis and M/XDR TB Programme, WHO Regional Office for Europe).

further adjustments; properly monitor the effectiveness of treatment during the intensive phase; indicate the proper management of adverse reactions (for example, discontinuation of injectables because of hearing loss and local pain or use of pyridoxine); improve the management of laboratory-confirmed pre-XDR-TB and XDR-TB cases; and guide the compassionate use of new anti-TB drugs such as bedaquiline and other Group 5 agents (this has already started in the Marius Nasta Institute). Training of staff at all levels will be required to ensure compliance with the new guidelines.

There is a well-developed system of pharmacovigilance under which adverse reactions to any drug are notified to the National Agency for Medicines and Medical Devices on standardized yellow forms. The system for accreditation of physicians includes points for such notifications, basically encouraging the use of the pharmacovigilance notification system. It is, however, monitored by the National Agency for Medicines and Medical Devices and notifications are usually used for serious reactions that cause a temporary or permanent withdrawal of drugs.

Recommendations

NTP

1. DST for first-line anti-TB drugs should be ensured for at least all bacteriologically-confirmed TB patients, and DST for second-line anti-TB drugs should be ensured for all MDR-TB patients.
2. Streptomycin and ciprofloxacin should not be used for the treatment of drug-resistant TB patients. Levofloxacin should be used as first-choice fluoroquinolone in MDR-TB patients and moxifloxacin in M/XDR-TB patients with any resistance to fluoroquinolones. Group five agents (linezolid, clofazimine, imipenem/cilastatin) should be considered for the routine management of XDR-TB patients.
3. The national list of essential drugs should be updated accordingly to include only those medications used by the NTP.
4. Any use of second-line drugs should only be authorized by the drug-resistant TB committees to avoid improper management of patients and further amplification of drug resistance. Regimens for patients diagnosed with drug-resistant (DR-) TB (monodrug-resistant (mono-DR), polydrug-resistant (PDR), MDR and XDR) should be designed in accordance with the updated version of the national guidelines.
5. The compassionate use of new anti-TB drugs should be expanded and the guidelines for the use of bedaquiline should be matched with the WHO recommendations.
6. DOT should be mandatory for all drug-resistant TB patients and implemented through patient-centred packages of services as an alternative to hospitalization.
7. ART is recommended irrespective of CD4 cell-count and as early as possible (within the first eight weeks) from the initiation of anti-TB treatment in patients with HIV and drug-resistant TB coinfection.
8. The interruption of adequate M/XDR-TB treatment due to adverse reactions to drugs should be limited through proper pharmacovigilance, information on the use of ancillary drugs and their inclusion under the national health insurance schemes.

9. The national guidelines for the management of drug-resistant TB should be updated, approved by the Ministry of Health and their implementation reinforced in all inpatient and outpatient facilities nationwide, including the penitentiary system.
10. The implementation of the national guidelines for the management of drug-resistant TB should be promoted through the training of the TB county coordinators and the further cascade training of other medical providers (doctors and nurses). Short residencies for the TB county coordinators at the two MDR-TB centres of excellence should be considered.

TB control in prisons

In December 2013, a total of 33 434 inmates (167 inmates per 100 000 general population) served time in the prisons of Romania. The number of inmates has progressively increased from the 26 212 reported in 2008 by the National Administration of Penitentiaries of the Ministry of Justice. Even so, only 160 TB cases were reported in prisons during 2013, with a notification rate that decreased remarkably from 2967 per 100 000 detainees in 2002 (20.8 times higher than in the total population) to 479 per 100 000 detainees in 2013 (only 6.5 times higher), much faster than in the general population.

The number of PLHIV in prisons increased from 76 positive in 2010, to 99 in 2011, 194 in 2012 and 288 in 2013. This reflects the increasing number of people who inject drugs and of HIV infections in this group observed since 2011. Of the PLHIV reported in 2013, only 125 (43%) were known to have HIV infection before their detention. It is claimed that an increasing number of inmates are infecting themselves to take advantage of the financial benefits given to PLHIV.

There are 38 penitentiary centres in Romania: 16 of the prisons are open or half open, 17 are closed and high maximum security prisons, and 23 have units with remand sections. In each prison there is a small medical unit where the medical screening and consultations are performed at the start of and during imprisonment. There are six prison hospitals, two of which have TB beds where all TB cases are referred (in Bucharest[11] and in Targu-Ocna).

All inmates are assessed on entry into prison through a questionnaire and clinical examination, which is repeated annually. When TB is presumed, sputum samples are sent to the laboratory of a local pulmonology facility (dispensary or TB prison hospital) while chest X-rays may be performed by referring the patients to the same facilities. Those with confirmed TB are referred to the two TB prison hospitals and stay there throughout their treatment unless their sentence ends first. Any other inmates or prison staff in contact with a TB patient within the previous three months should be screened for TB and sent to a local pulmonology dispensary or the TB prison hospital. Sending many prison contacts to the local pulmonology dispensary may be challenging and the review team was not able to understand clearly to what extent this was actually done.

When prisoners are released from prison before their TB treatment is finished, they are referred to the local pulmonology dispensary with notification sent to the NTP. The pulmonology

[11] Jilava prison in Bucharest visited by the review team has a 391-bed hospital with 120 beds dedicated to TB (two wards), two laboratories (for haematology/biochemistry and for bacteriology) and one radiology department. There are four pulmonology doctors, one laboratory doctor, one radiology doctor, 10 nurses, two laboratory nurses and one psychologist.

dispensary has to confirm to the prison the arrival of the patient, who may be referred on to a family doctor but with follow-up and final evaluation still under the responsibility of the pulmonology dispensary. The review team was not informed of any patient lost to TB treatment follow-up during the process of referral from the penitentiary to the civilian system.

Some nongovernmental organizations have carried out harm reduction activities in the prison system, for example the Association ARAS. The experience of this collaboration with nongovernmental organizations/civil society has been positive as they work with the target population both inside and outside the prison and can have a positive impact on the inmates by building trust.

With the support of the Global Fund since 2002, the National Administration of Penitentiaries has achieved very satisfactory results in recent years. It collaborates closely with the NTP, adopting the same guidelines and being supplied with all anti-TB drugs from the Ministry of Health budget. In 2012, the National Administration of Penitentiaries endorsed a National TB Plan (National Administration of Penitentiaries' Decision No. 672 of 21 September 2012) that outlines all TB prevention and control activities to be undertaken in prisons. The implementation of this plan is linked to support from the Global Fund grant and its implementation timeframe. The support of the Global Fund has been very effective in reducing transmission of TB in prisons. An effective system of coordination, planning and monitoring is in place which is endorsed by the TB infection control plan. An important part of the activities is the health education programme, which has provided training to more than 4000 prison security staff since 2006. Since 2004, a total of 840 prison guards, social workers and nurses have been also trained as health educators to provide education and information to the inmates.[12]

There is, however, no official collaboration between the NTP and the National HIV Programme under the National Administration for Penitentiaries. HIV, hepatitis B and C counselling and testing is not offered at all times and systematically in prisons, but only occasionally and depending on the implementation of specific projects funding these forms of activity. All those found with HIV rapid test-positive are sent to Matei Bals or Victor Babes HIV/AIDS centres for confirmation and provision of ART according to national protocols. PLHIV are eligible for isoniazid preventive therapy only if found with positive tuberculin skin test. Opiate substitution therapy is available in 12 prisons under the budget of the National Administration of Penitentiaries, either in continuation of a past prescription or a new prescription. Some nongovernmental organizations are implementing harm reduction inside and outside prisons.

Recommendations

Ministry of Health

1. TB control should be maintained as a priority for the prison sector and sustainable funding provided for the National Administration of Penitentiaries to implement the TB control plan in the penitentiary system, including after the end of the Global Fund grants.

[12] An e-learning platform, funded by the Global Fund since 2006, supports a health education programme (including on TB) that gives points to the participating inmates which count towards earlier release from prison. Unfortunately, there is only limited access to this platform (one computer is available in Poarta Alba prison and one in Jilava prison) and only a few inmates can participate at once in such a health education training course.

NTP

2. A joint TB/HIV commission should be created at the National Administration of Penitentiaries to formalize the work around HIV and TB in the prison setting, or the national TB/HIV commission should work on prison-specific activities.
3. Testing for HIV and hepatitis B and C should be scaled up in prisons.
4. The coverage of, and opportunities for inmates to take part in, e-learning for health education should be increased.
5. Consideration should be given to working more closely with nongovernmental organizations and civil society organizations that work with inmates on information, education and communication as well as for social integration and harm reduction activities for inmates who are intravenous drug users.

Other vulnerable populations and social determinants

Poor people and those living in rural areas

The patients who suffer the most economically and socially from TB are not receiving adequate social support to get access to and complete their treatment. Several rural and marginalized population groups suffer from inadequate access to health care, which has implications for rapid TB diagnosis and support to complete their treatment. The problem is mainly how to reach poor people and the rural population and the lack of primary care services in these regions.

Many of these people are self-employed or unemployed, and consequently not eligible for sick pay while on TB treatment; their families are not supported when the breadwinner is hospitalized or not able to work. When employed, the length of sickness benefit may not match the length of TB treatment. There is no social protection scheme.

Roma

According to national census data *(26)*, 619 000 Roma people were living in Romania in 2011, which is most probably an underestimate since many Roma do not disclose their ethnicity due to social stigma. In fact, the EU estimates the Roma population to be much more, about 1.85 million, while some sources have even proposed 2.5 million *(27)*. Similarly, the information about TB among the Roma could be imprecise. One prevalence study found that 27 000 per 100 000 Roma people were infected with TB.[13] In 2000, the incidence of TB disease was documented as more than twice as high among the Roma as in the general population *(28)*. The Roma people suffer from inadequate access to early diagnosis and treatment of TB.

Over the years, a number of projects and programmes funded by different international organizations in partnership with the NTP have targeted the Roma people to improve both access to and quality of care for them and raise their awareness of TB and health issues. This has been done by local outreach in Roma communities through training peer health educators (Roma mediators) and setting up community centres for educational and advocacy activities, often involving the local health services. While there are good examples of best practice in working with local communities, there is limited national coverage and capacity.

[13] Gheorghe N et al. TB prevalence in Roma communities in Bihor and Arad counties (Operational research conducted under the Round 6 TB Grant) (unpublished document).

People who inject drugs

The estimated number of people who inject drugs (PWID) and other drug users in Romania has increased compared to previous years *(29)*. It is reported that the PWID in Bucharest doubled in just one year (from 10 000 in 2011 to 20 000 in 2012, that is, 20 per 1000 population aged 18–49 years). The prevalence of viral infections has reportedly increased among PWID from 2010 to 2012: hepatitis B virus rose from 13% to 25%, hepatitis C virus from 64% to 82% and HIV from 4% to 25%. Such increases are thought to be partly linked to the increasing use of ethnobotanical drugs[14] and to the decreasing coverage of harm reduction services as consequence of the economic crisis. The data considered by the review team at the Victor Babes Clinical Hospital of Infectious and Tropical Diseases in Bucharest confirm the rapid increase of hepatitis C virus and HIV infections among the PWID hospitalized during 2010–2013, and of the association with TB, especially in its extrapulmonary and disseminated forms.

The treatment of drug addiction has been provided since 2007 by about 50–60 centres for drug prevention, evaluation and counselling and five addiction integrated care centres. Coverage with opioid substitution therapy is, however, low with only 742 clients registered in 2011. A group of nongovernmental organizations associated in the Romanian Harm Reduction Network provide services (needle exchange, condom distribution, opioid substitution therapy, HIV testing, referral to TB screening at TB dispensaries and hospitals, outreach) in Bucharest and a few other main cities. Unfortunately, more than half of the staff stopped working in 2011 following the withdrawal of Global Fund support. As of today, there are 3000–4000 beneficiaries of harm reduction services, about half the number in 2010. Mention should be made of the project Empowering the Public Health System and Civil Society to Fight the Tuberculosis Epidemic among Vulnerable Groups (TUBIDU) *(30)*, which was active in increasing awareness of TB among PWID and PLHIV in Romania until it ended in May 2014.

Homeless people

The Romanian Academy National Institute of Research on the Quality of Life has estimated that approximately 11 000 children, young people and adults are homeless, about 5000–6000 of them in Bucharest. In 2011, a study showed a prevalence rate of 6700 TB cases per 100 000 homeless people in Bucharest, about 50 times higher than in the general population *(31)*.

Under the Global Fund support, a number of projects targeted homeless people for TB active case-finding and treatment support, with Save the Children Romania as grant subrecipient. Building on the experience achieved and the information from a knowledge-attitude-practice survey conducted in 2010 *(32)*, two additional projects were included in the Global Fund Transition Funding Mechanism targeting homeless people, street children and youngsters in Bucharest, Craiova, Iasi and Timisoara. Outreach staff from Save the Children evaluate the risk of TB and assist those with presumptive TB to report to their family physicians and TB physicians for diagnosis. Information and education on TB is also given in day and night shelters. In view of the very high proportion (80–90%) of street children and homeless people who use drugs, attempts are being made to establish links with harm reduction and drug treatment services.

[14] Ethnobotanic drugs are herbal remedies. Although they are illegal substances in Romania, their intravenous use is documented for the treatment of opportunistic ailments of HIV/AIDS.

Migrant workers

A frequently mentioned problem is the number of TB patients who move abroad and are lost to follow-up. Those who emigrate to the EU have access to TB services, but not much information is available regarding those who emigrate to other countries. Operational research may be needed.

Recommendations

Ministry of Health

1. TB outreach services (identification of cases for diagnosis and prevention, DOT and social support) should be strengthened among socially and economically disadvantaged and vulnerable population groups through the involvement of community nurses, Roma mediators, nongovernmental workers and lay people (for example, school teachers and religious leaders).
2. The Ministry of Labour and Social Protection, in collaboration with the Ministry of Health and the NTP, should develop a system of social protection for TB patients and their families.

NTP

3. Support should be sustained for the continuance of activities connected with preventing the transmission of TB and providing social support to homeless children, youngsters and adults.
4. The sickness benefit for salaried patients should be extended at least to match the treatment duration for MDR-TB (24 months) and XDR-TB (36 months). Unemployed or self-employed patients should automatically receive a pension equivalent in value to an illness pension contingent upon the satisfactory progress of their treatment.
5. Adequate resources should be ensured to sustain the activities of Roma community centres, and consideration should be given as to how activities in the different counties can be expanded and offer wider coverage of the Roma population.
6. TB and HIV services should be integrated and linked with drug dependence treatment services to ensure access to the full harm reduction package and expand collaboration with nongovernmental organizations working with PWID at low-threshold level.

TB infection control

TB infection control has been recognized by national and international experts as a priority area for improvement.[15] Important steps have been taken in recent years in terms of developing methodological documents and infection control plans at facility level as well as conducting training courses.[16] Unfortunately these activities were not supported by the necessary legislation and most of the recommendations from past technical missions have been ignored.

[15] Crudu V. Tuberculosis infection control in Romania: report of a mission, 15–22 July 2011(unpublished document available on request from the Tuberculosis and M/XDR TB Programme, WHO Regional Office for Europe).
[16] In 2014, the ECDC supported a two-day infection control meeting with a multidisciplinary group of experts (TB coordinators, epidemiologists, clinicians and laboratory personnel). In the same year, nine trainers were educated and 42 staff were trained in infection control during a two-day course.

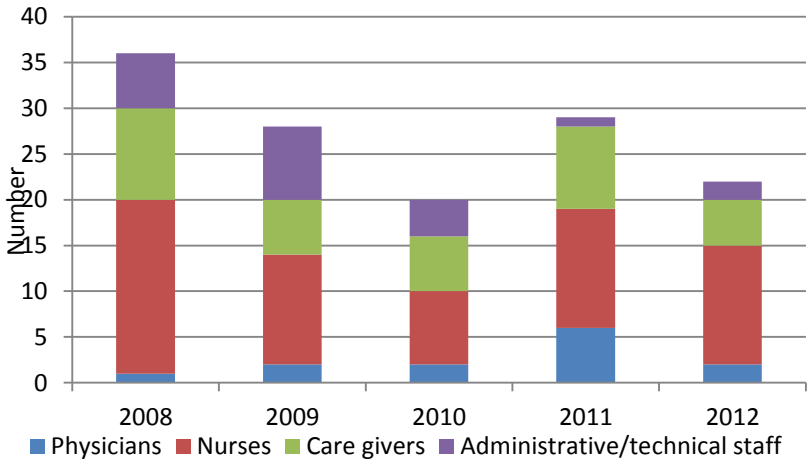
Infection control in health facilities is regulated by Ministry of Health Order No. 916 of 26 July 2006 on Surveillance, Prevention and Control of Nosocomial Infections in Health Care Facilities and Government Resolution No. 355 of 11 April 2007 on Workers' Health Surveillance. However, none of these documents consider airborne infection control and TB, which is not classified among the nosocomial infections.

Each health facility is directly responsible for the reinforcement of the existing infection control legislation, while the county public health departments are responsible for monitoring and evaluation/accreditation. The Public Health Institute in Bucharest only provides methodological guidelines to guide county health authorities but does not participate in monitoring visits and/or accreditation. The process of accreditation is different for hospitals, outpatient facilities and laboratories. It does not require any airborne infection control, although special conditions for disinfection may be required for some hospitals, including prison hospitals.

Airborne infection control interventions were drawn up by the NTP in 2011 in line with international recommendations and included in a national infection control plan for TB for 2011–2015, which has, however, never been endorsed by the Ministry of Health. The NTP has one coordinator for infection control and a team of 20 specialists at county level to supervise each facility every year following a standardized checklist. The supervisors usually provide specific recommendations in a written report, but these are usually ignored.

The Government Resolution on Workers' Health Surveillance does not include TB surveillance. The only information about TB among health care workers comes from a study[17] conducted in the Marius Nasta Institute showing that 135 staff were diagnosed with TB during 2008–2012, corresponding to an average annual incidence of 307 TB cases per 100 000 workers and a relative risk of TB disease 2.84 times higher than in the general population. The incidence of TB per 100 000 population was on average 310 cases among physicians and 430 cases among nurses (Fig. 4). Fluctuations in the number of TB cases over the years does not show any trend but calls for checking and probably improving this kind of hospital record.

Fig. 4. Number of staff diagnosed with TB by type of employment, Marius Nasta Institute, 2008–2011



[17] In 2013, the NTP infection control coordinator conducted a study for the Lung Disease network which included an analysis of the records of Marius Nasta Institute for the period 2008–2012 and questionnaire interviews with staff diagnosed with TB.

Administrative measures

The review mission has major concerns about the extensive and unnecessary hospitalization of TB patients and their accommodation in mixed rooms, including with non-TB respiratory patients. This applies to all facilities visited by the teams. Some facilities have infection control plans, but these usually lack clear activities, timelines and responsibilities and are in any case disregarded. Many facilities use different colours to show the types of TB patient staying in the rooms and the consequent risk of TB transmission. However, bacteriologically-confirmed TB patients usually share rooms before their DST results are known and patients with presumptive TB share rooms with non-TB respiratory patients. The common service areas (cafeterias, toilets, corridors, waiting areas, diagnostic rooms) are used by all types of respiratory patient (TB and non-TB) without any infection control measures. The risks of nosocomial transmission of TB and cross-contamination of different forms of drug-resistant TB are very high and are further enhanced by the usual long hospitalization (three months and more).

Many pulmonology hospitals are located in residential properties expropriated during the period 1945–1989. When such properties consist of separate buildings, it would be easy to separate non-TB from TB patients, and TB patients by type of infectiousness and level of drug susceptibility. Unfortunately, the organization of work among physicians and the incentive of a salary compensation for exposure to TB encourage the sharing of accommodation between TB and MDR-TB patients (see section on Health system and TB control, p. 53). Only in the Marius Nasta Institute are there separate wards for the treatment of drug-resistant TB patients with different DST profiles. In the TB sanatoria visited by the review teams, the separation of patients with different DST profile by floors was observed. Major improvements in infection control administrative measures (compared with previous technical consultancy missions) were, however, noted in the Jilava Prison hospital: the rooms were no longer overcrowded and patients were separated by smear/DST status, regardless of their crime/sentence.

Environmental measures

Most of the facilities had no mechanical ventilation, apart from the Marius Nasta Institute, which had a ventilation system in its MDR-TB ward that had not, however, functioned since 2006. Ultraviolet lamps are largely not available and those in place are not shielded and thus cannot be used safely for 24 hours a day.[18] A number of hospitals and dispensaries expropriated during 1945–1989 are now listed buildings (with limitations on major renovation work). Another major concern of the review team concerns biosafety in laboratories. Although some biosafety cabinets were serviced by a number of private companies contracted by county administrations, where such service arrangements existed they were not found to be meeting the real needs. Certification, measurements of airflows and replacement of the high-efficiency particulate air filters had not been carried out since the biosafety cabinets had been installed. In one laboratory the review team found that a positive-pressure (for media preparation) cabinet had been installed instead of a negative-pressure biosafety cabinet and was happily being used by the unaware

[18] To be effective, ultraviolet lamps should have enough power (20 W lamp/20 m^2 in high-risk zones) and safe enough for 24-hour use (upper room shielded). Such lamps used around the clock need spare bulbs at least every two years. The number of ultraviolet lamps needed should be calculated only after a specific assessment (exceeding the terms of reference of this review). A rough estimate from the status quo could be an average of 12 lamps for each of the 42 hospitals, five lamps for each of the 184 TB dispensaries and some additional ones to compensate for confined spaces, making about 1500 ultraviolet lamps in all. However, in view of the urgent need for infection control administrative measures aimed at reducing the number and mix of patients in hospitals, a rationalization of hospital beds is anticipated which will decrease the need for such environmental interventions.

laboratory technician. Most of the laboratories visited had centrifuges without a proper closed bucket swing rotor. Sputum collection rooms are only available in TB hospitals (established with Global Fund support).

Personal protection

The NTP guidelines consider the use of respirators for staff caring for TB patients and facial masks for the TB patients themselves. The review team found that respirators and facial masks were available in most of the facilities. However, the fit test was not practised and the appropriate equipment was not available.

Recommendations

Ministry of Health

1. TB infection control measures should be introduced urgently in diagnostic and treatment facilities and in congregate settings by revising Ministry of Health Order No. 916 of 26 July 2006 and the current system of health facility accreditation and including specific measures for the prevention of airborne TB transmission.

NTP

2. The national infection control plan 2011–2015 should be updated.
3. Basic TB infection risk assessments should be conducted in all major hospitals and their specific plans revised accordingly.
4. Upper room shielded ultraviolet lamps should be procured, including spare parts and maintenance for all hospital facilities providing TB care in the civilian and penitentiary systems, based on the new network designed in consideration of the revised criteria for hospitalization and the NHIH payment scheme.
5. Measuring equipment for airborne infection control should be procured, such as one anemometer for each country and one ultraviolet electromagnetic radiation subtype C meter for the Marius Nasta Institute.
6. The proper maintenance of engineering control measures should be ensured for ventilation, ultraviolet lamps and biosafety laboratory equipment. This could be done through the contracting out of private services to qualified engineers and certification against specific technical requirements.
7. Fit-testing equipment should be procured in each county and each member of staff should be fit-tested at least annually.
8. Mandatory TB surveillance should be established among health workers, with regular monitoring and mechanisms for prompt intervention, either by establishing a mechanism to request information retrospectively from staff or by improving data collection in the national TB database (where a field for specifying the occupation of the patient already exists).
9. Health care workers, including staff in pulmonology health facilities and family medicine centres, should receive continuing education.

Management of medicines

Financing

Anti-TB drugs are procured through the state budget and with additional funds from international donors.

The drugs financed by the state budget are supplied through the NHIH, according to Ministry of Health Order No. 1047 of 20 December 2013 on National Programmes for Communicable Diseases, which includes medicines under 100% of coverage (section on the treatment of TB patients).[19] Some additional second-line anti-TB drugs are also listed in the section on treatment of HIV/AIDS (levofloxacin (no longer recommended), linezolid and imipenem/cilastatin), but only patients with TB/HIV coinfection can be reimbursed for these drugs.

The main international donors are GDF, the Global Fund and Norway. Under the Global Fund grant, the direct procurement from GDF of second-line anti-TB drugs for 129 MDR and 19 XDR-TB patients was planned for 2014. An additional supply of drugs is envisaged under the New Financial Mechanism of the Global Fund, which is likely to start in 2015. Financial support is also expected from the Norwegian Financial Mechanism for the treatment of 1000 M/XDR-TB patients during the period between the signature of the agreement (which had not happened at the time of the review) and 31 January 2016. GDF may agree to provide a one-year grant in kind for the treatment of children with paediatric formulations of anti-TB drugs.

Procurement and registration

Only drugs currently registered in Romania can be procured under the state budget. These are all first-line anti-TB drugs but with only one fixed-dose combination (rifampicin 300 mg + isoniazid 150 mg) and without paediatric formulations. Many second-line anti-TB drugs are also registered, with the important exclusion of capreomycin and PAS. All first-line anti-TB drugs used in Romania are manufactured by the Romanian company S.C. Antibiotice S.A., which was recently included in the list of WHO prequalified manufacturers for all its seven products and can now participate in GDF global tenders. Many second-line anti-TB drugs are registered in Romania and are imported through local dealers.[20] In the case of capreomycin and PAS, their manufacturers are not interested in registering them because of the limited market in Romania.

Procurement through the state budget has changed over the years. In 2007, the management of health services was decentralized to the counties and their financing delegated to the NHIH. This also implied the decentralization of all health supplies, including anti-TB drugs. During the six years up to 2013, every pulmonology hospital had to arrange a local tender, which caused high administrative burdens and drug stockouts in a number of counties for reasons such as the absence of the local suppliers for specific drugs, poor planning and delays in budget allocations.[21]

[19] Medicines covered by the NHIH are categorized in three levels of reimbursement (A, B and C). The C2 drugs are those in use by the national health programmes (for treatment of, for example, TB, HIV/AIDS, certain tumours, multiple sclerosis and diabetes mellitus) but only available above the patient's insurance budget ceiling and only through hospitals and outpatient pharmacies.

[20] The good quality of second-line anti-TB drugs is assured by registration after assessment by the National Medicines and Medical Devices Agency and (for some of them) marketing authorization in the EU.

[21] Muzafarova N, Evans P. Report on procurement and supply management, 25 February–1 March 2013 (unpublished document available on request from the Tuberculosis and M/XDR TB Programme, WHO Regional Office for Europe).

In March 2013, the Ministry of Health decided (under Order No. 422 of 27 March 2013) to recentralize the procurement of supplies for all public health programmes. Under the current procurement model, the Ministry of Health Unit for Central Procurement (for medicines, medical equipment, sanitary devices and so on) signs framework contracts with suppliers selected from a national tender, while local hospital administrations place the actual orders and pay from their own budgets. In view of the current limited capacity of the Ministry of Health, the Marius Nasta Institute was asked to specify the drug needs, evaluate the bids and select the suppliers. The tender was launched and the suppliers selected by June. From the beginning of 2014, all the TB facilities were in a condition to sign contracts with their suppliers.

In preparation for the national tender, the list of drugs reimbursable by the NHIH was updated to include six first-line anti TB drugs (isoniazid 100 mg and 300 mg tablets, rifampicin 150 mg and 300 mg, rifampicin and isoniazid fixed combination 300 mg + 150 mg, ethambutol 250 mg and 400 mg, pyrazinamide 500 mg, streptomycin 1 g vial for injection), eight second-line anti-TB drugs (kanamycin 1g vial; amikacin 500 mg; ofloxacin 200 mg; moxifloxacin 400 mg; ciprofloxacin 100 mg, 250 mg, 500 mg, 750 mg and 1000 mg; cycloserine 250 mg; prothionamide 250 mg; clarithromycin 250 mg and 500 mg) and two ancillary drugs for the management of adverse reactions to anti-TB drugs (pyridoxine, prednisone). Products not registered in Romania could not be included for the national tender (capreomycin, PAS, first-line anti-TB drugs in fixed-dose combinations and paediatric formulations). Moreover, while some ancillary drugs are included in the list of drugs reimbursable by the NHIH, none of the newly-developed anti-TB drugs are included (for example, bedaquiline, delamanid and linezolid), even though they are available on the international market for the compassionate treatment of patients.

Direct procurement from GDF follows the Global Fund policy on purchasing quality medicines. This specifies the need for: WHO pre-qualified second-line anti-TB drugs or authorized by a stringent regulatory authority, compliance with good manufacturing practices, a batch analysis certificate and a minimum shelf-life for the medicines delivered. Because not all second-line drugs supplied by GDF are registered in Romania, the shipments of medicines should be accompanied by: a good manufacturing practices certificate or a US Food and Drug Administration licence for each manufacturer and for each drug and, for each drug, a marketing authorization, summary of product characteristics, drug information leaflets and certificate of analysis.

As a consequence of the national tender, all the prices have dropped compared to the past when only one supplier was selected for every medicine. The national tender clearly introduced an economy of scale not possible when smaller quantities are purchased through local tenders. Table 17 documents the significance of the price reduction especially for ofloxacin, clarithromycin, cycloserine, ethambutol and rifampicin (150 mg tablets). Only in Bucharest was the difference in prices not so significant because of the usual large quantities purchased by the Marius Nasta Institute.

The prices obtained through the national tender were still higher than those offered under the GDF. However, while the former include the costs of storage and transport in counties, the latter include neither those costs nor the costs of overseas shipment and import taxes. Moreover, not all GDF drugs are registered in Romania, which is a condition required by Romanian law on public procurement. The advantages of buying drugs directly from GDF with state funds in future will, therefore, have to be carefully assessed and ways found to reduce the costs for their registration, such as a waiver on the registration charges by the National Medicines and Medical Devices

Table 17. Price of anti-TB drugs purchased through the national tender and local tenders at county level, 2013

Drug/strength	Unit	Local tender as assessed in the sites visited by the review team (Leu)	National tender (Leu)	Price difference (%)
Isoniazid 100 mg	Tablet	0.08	0.08	–
Isoniazid 300 mg	Tablet	0.2	0.2	–
Rifampicin 150 mg	Tablet	0.18	0.12	- 50
Rifampicin 300 mg	Tablet	0.47	0.47	–
Isoniazid and rifampicin 150/300 mg	Tablet	0.6	0.53	- 13
Ethambutol 250 mg	Tablet	0.18	0.18	–
Ethambutol 400 mg	Tablet	0.28	0.16	- 75
Pyrazinamide 500 mg	Tablet	0.31	0.24	- 29
Streptomycin 1.0 g	Vial	3.04	2.47	- 23
Amikacin 1.0 g	Vial	5.61	N/A[a]	–
Kanamycin 500 mg	Vial		N/A[b]	–
Capreomycin[c]	Vial	–	–	–
Ofloxacin 200 mg	Tablet	0.92	0.27	- 241
Moxifloxacin 400 mg	Tablet	12.22	10.45	- 17
Cycloserine 250 mg	Tablet	4.63	2.39	- 94
Prothionamide 250 mg	Tablet	1.07	0.98	- 9
PAS[c]	Tablet	–	–	–
Clarithromycin 500 mg	Tablet	1.81	0.69	- 162

[a] No supplier of amikacin was selected during the national tender due to the lack of a commercial offer for amikacin 1 g.
[b] There were no commercial offers for kanamycin in the national tender.
[c] Not registered in Romania.

Agency or on the registration itself (as happens when capreomycin, PAS, levofloxacin cycloserine, prothionamide, pyrazinamide and moxifloxacin are procured through the Global Fund). Such a decision has to be taken urgently for capreomycin and PAS, which are procured only in limited quantities and only for the cohort of patients agreed under the Global Fund grant.

Although there has been a decrease in costs, the procurement of anti-TB drugs is only partly centralized since the counties have been left with full responsibility for purchasing. The county TB coordinators still find it a challenge to deal with the heavy administrative burden of preparing multiple contracts and the long wait to get them approved by the NTP and the Ministry of Health. The risk of stockouts is still there, depending on the budget and managerial skills available in the counties.

Quantification

Each hospital has a two-year contract with the NHIH that includes the purchasing of anti-TB drugs within a budget range calculated on past consumption and what is available in store. Buffer stocks, lead times and the compliance coefficient for anti-TB drugs are not considered. This method of quantifying needs and budgeting decides the local availability of drugs for the treatment of patients, which is often limited for very expensive drugs (such as moxifloxacin). The review team observed that all first line anti-TB drugs were available in practically all the TB facilities visited, apart from a lack of amikacin in some of them and of moxifloxacin in most of them. The review team also documented stockouts at county level during 2013 of pyrazinamide (in at least one TB hospital for two months) and of second-line anti-TB drugs for one to six months. No stockouts were observed in Bucharest.

The calculation of second-line anti-TB drugs needed from GDF, as opposed to those purchased with the state budget, is based on estimated morbidity and following standard GDF procedures. The review team did not observed any shortage of such drugs during the treatment of the cohorts of MDR-TB patients under the Global Fund support.

Storage, distribution and quality assurance

The drugs purchased with the hospital budget are delivered by the local suppliers on a monthly basis, without a buffer stock. Every hospital has a pharmacy responsible for the registration, storage and further distribution of anti-TB drugs within the hospital departments and to the TB dispensaries. There is no possibility of a redistribution of medicines between TB hospitals in cases of shortages or surpluses.

The anti-TB drugs purchased under the Global Fund grant are imported, stored and distributed under the care of UNIFARM *(33)*, a national company contracted by RAA, the principal recipient of the Global Fund grant. UNIFARM has a good warehouse in Bucharest from where it distributes drugs to all hospitals and TB dispensaries on a quarterly basis, with a buffer stock of one month. Standard operating procedures are in place and followed.

The review team found good storage conditions in most of the pharmacies visited. Their recording and reporting system is also good, based on a special software package able to produce monthly reports for the NHIH with specified quantities and costs of all drugs received, distributed and in stock. However, not all the pulmonology dispensaries have such a system, so the drugs situation cannot be monitored at that or at central level. Every quarter, the NTP central unit receives from all TB services a report on the drugs received and consumed that are used to decide the next quarterly distribution through UNIFARM. A proper database is needed.

The NTP central unit currently uses an Excel spreadsheet to monitor the drugs for the treatment for MDR-TB patients under the Global Fund grant. It registers the patient's identification data, dates of enrolment in treatment and actual start, treatment regimen and drug doses prescribed, and the dates and results of check-ups.

Pharmacovigilance

The government has introduced regulations on good laboratory practice, good manufacturing practice, good distribution practice and good pharmacy practice. Recently, the National Agency for Medicines and Medical Devices approved guidelines on good pharmacovigilance that are in line with the EU law on pharmacovigilance of 2012. Despite this, the review team was informed that information concerning side effects is not submitted regularly to the National Agency for Medicines and Medical Devices.

Recommendations

Ministry of Health

1. Effective centralized procurement and the uninterrupted supply of all internationally recommended anti-TB drugs (first-, second- and third-line) should be ensured, including for their compassionate use.
2. Free ancillary drugs should be ensured for both in- and outpatients.

3. The benefits of international procurement should be assessed through a cost-effectiveness study.
4. The essential drugs list should be regularly updated in supporting the treatment regimens adopted by the NTP, in alignment with the drugs registered in the country and to allow the revision of the list of drugs that can be reimbursed by NHIH.
5. Proper documentation should be made of needs and a waiver of the fees charged by the National Agency for Medicines and Medical Devices should be introduced so as to encourage manufacturers to apply for the registration of capreomycin and PAS in the country. The Ministry of Health should find a way to procure non-authorized anti-TB drugs through an emergency mechanism.

NTP

6. A comprehensive electronic information system should be created to ensure the monitoring of distribution and availability of all drugs in all facilities within the same county and the possibility of submitting data to the NTP central unit for analysis and informed planning.
7. The calculation of drug needs should be improved in order to consider buffer stock levels, lead periods, rational stocks and the coefficient of treatment compliance.
8. UNIFARM should also be used for the distribution of drugs procured centrally from the state budget.

Monitoring and evaluation

The legal basis for TB data recording and reporting is in Government Decision No. 589 of 13 June 2007 establishing the methodology for data recording and reporting for surveillance of infectious diseases and Ministry of Health Order No. 1577 of 16 September 2008 on Methodological Norms for TB Control Programme Implementation *(34)*. Data are processed through a web-based TB surveillance system (SOFT) which produces the National TB Registry. Data are entered by all pulmonology dispensaries, all TB units (in 41 counties and six sectors of Bucharest) and different ministries (three facilities under the Ministry of Justice, one under the Ministry of Defence and one under the Police). The National TB Registry is kept at the NTP Central Unit in the Marius Nasta Institute. The first data validation is carried out at county level, with a further daily check at central level. Crosschecking with the National TB Laboratory Register (70% of all TB laboratories entering the positive laboratory results) is also possible. The National TB Register has had an operational link with the National HIV Register since 2013, although it is not legally official, and TB and HIV data are crosschecked every year. The National Institute of Public Health uses the data produced by the NTP quarterly and annually for its epidemiological analysis and publications *(35)*. The NTP reports regularly every year to the Joint ECDC-WHO Reporting Platform.

Supervision of the facilities with TB services at county level is carried out by the Supervisory Commission of the NTP from the Marius Nasta Institute in Bucharest and by the TB county coordinators. The supervision of laboratories should be ensured by the Laboratory Working Group and by the county TB laboratory coordinators

The National TB Register is maintained at the NTP Central Unit (see Fig. 1) by three people employed part-time: the head, data manager/server administrator and public health analyst, who consistently have to work overtime to ensure data quality, analysis and reporting.

All paper forms and registers used by the NTP can be seen in the document on the Implementation of the DOTS Strategy to Control TB in Romania issued in 2005 *(36)*. The TB electronic database is divided into five modules: (i) patient' data; (ii) diagnostic characteristics; (iii) treatment data (including laboratory and treatment regimen); (iv) automatically generated quarterly and annual reports; and (v) administrator's module. For data extraction and analysis, a specific program in Fox Pro and Excel 2003 is used, but preparation of the reports is both time- and resource-consuming and only some functionalities are included in the reports (tables) that are automatically produced.

The application software includes some enhanced protection mechanisms against undesirable access or loss of data (user' rights defined for each level, firewall, antivirus, register's application and program in separate servers). Weaknesses can, however, be found, such as servers not being secure locations, backups archived in the same room as the server, the user manual not updated since 2005, codes for case registration only partially documented and no confidentiality declaration requested. The TB electronic database has needed upgrading for many years but has been kept on hold because of the high costs asked for modifying the application software from the copyright-protected MS SQL Server platform.[22] It is now planned under the Norwegian Financial Mechanism using the MySQL Database open-source platform.

Parallel to the electronic recording, the NTP maintains its old system of forms and registers on paper, justifying this with the need to cross-check the data and keep paper records as requested by law. The review team crosschecked data on paper (local TB forms and registers) with the data entered in the National TB Register and found some discrepancies in TB laboratory and HIV testing. This does not justify doing away with such a parallel system of recording but it does show the need for more effective use of computers in reducing the workload and improving data quality. Since TB-related activities have to be reported monthly, quarterly and yearly to local and national authorities (epidemiological, programmatic and administrative data), this creates a complex reporting system which is unclear for local and county policy-makers to use (Annex 7). The National TB Registry is not linked to other existing national databases (such as for population or mortality).

The review team found that supervision is poor. Supervision is not part of the activities reimbursed by the NHIH and the NTP does not have specific funds other than the Global Fund grant. There are no clear terms of reference and standard operating procedures for the TB coordinators in counties. Supervisors at all levels operate without a clear mandate from the Ministry of Health giving them authority and accountability.

Recommendations

NTP

1. The recording and reporting system should be rationalized and the national TB database revised to improve the processing of patients' data and ensure their analysis and use for policy decisions.
2. Paper-based recording and reporting should be abandoned in favour of the exclusive electronic processing of TB data aimed at reducing the workload and improving the quality of data.

[22] Several missions organized by the GLC have recommended that the National TB Register should be upgraded but this has never happened because of the estimated cost in excess of US$ 50 000.

3. A legal framework should be defined to ensure accountability by the TB services to the supervision carried out by the NTP at all levels.
4. The National TB Registry should be improved by:
    - including MDR-TB according to the latest international recommendations;
    - establishing official an link with the National HIV Register, the national vital register and the national population register;
    - expanding automatically generated reports with the introduction of statistical analysis tools able to produce analyses better tailored to the needs of each level of coordination;
    - requesting a data confidentiality declaration from all SOFT users;
    - hosting servers in special locked and protected rooms with fire and security alarms;
    - hosting server backups and copies of the database in separate locked safe deposit boxes;
    - implementing standards of practice for data protection and confidentiality;
    - compiling a data dictionary so as to expand data analysis to all available entry codes;
    - replacing the database server of the National TB Registry with an open-source platform and obtaining an expert assessment of the MySQL platform with particular attention paid to data protection functionalities.
5. The use of SOFT should be promoted for proper monitoring and planning at all levels.
6. Monitoring and supervision should be strengthened at county level, with clear terms of reference and standard operating procedures for the TB coordinators and adequate funds for supervisory visits from the Ministry of Health and NHIH.

Human resources development

TB services are delivered through a network of laboratory and treatment facilities with a variety of dedicated and other staff, such as pulmonology doctors and nurses, microbiologists and other laboratory staff, paediatricians, family doctors and other staff. There are around 750 pulmonologists, 70 000 nurses and 17 000 family doctors, although it is not clear how many nurses and family doctors are actually involved in the delivery of TB services. After the Government Emergency Ordinance No. 162 of 3 December 2008 and the transfer of responsibilities from the Ministry of Health, around 1000 community nurses moved to be under the administration of the local authorities. These nurses are also supposed to provide TB care, although the review team understood that their work could differ considerably from their job descriptions (and not necessarily remain in the area of health), at the decision of the local authorities and local dynamics.

After six years of medical school, doctors have four years postgraduate education in pulmonology (five years if they are doing internal medicine or surgery). Continuing education is mandatory to practise medicine and fixed at 40 credits per year. There are no specific conditions attached to these credits; they are acquired by activities such as attending congresses and conferences, publishing articles and lecturing at workshops. Training courses should be paid by the doctors themselves.

Microbiologists need a master's degree in laboratory medicine and a membership certificate for practice from the College of Physicians and Order of Biochemists, Biologists, Chemists in the Sanitary System. Continuing education is again mandatory and fixed at 40 credits per year.

Laboratory technicians, nurses, midwives and medical assistants are trained for three or four years, depending whether they are in college or at university. After graduation they need to obtain a licence to practise and a membership certificate issued by the Order of Nurses, Midwives and Medical Assistants in Romania, according to the Government Emergency Ordinance 144/2008. Nurses also undergo a programme of continuing education based on the acquisition of 30 credits per year, of which 15 credits should be from participation in training courses on nosocomial transmission (every year), on the specific field of their current employment (every year) and on cardiopulmonary resuscitation (every three years). Part of such training is paid by the Order. In the current review of the national programme for continuing medical education, the Order is considering introducing some TB training. The NTP is not a registered provider of continuing medical education, so no credits could have been obtained from attending its training courses.

Continuing education for all staff does not specifically include TB and, as a result, many staff working in TB services have not received TB training during the last five years.

While the number of staff could be enough to provide good TB services, their unequal distribution contributes to the shortcomings of the NTP described in other parts of this report. Moreover, the staff are ageing: many pulmonologists in the public sector are at the end of their careers and young ones are working in the private sector. There are also fewer paediatricians. The migration of medical staff to other countries is a threat to the running of TB services (10–15% of doctors have emigrated or are considering doing so).

Recommendations

NTP

1. A national plan should be developed for human resources for TB that is consistent with the laboratory and treatment networks and includes adequate formal, in-service and continuing medical education according to the NTP guidelines. Such a plan should:
    - include a comprehensive view of all staff and level of services;
    - forecast the numbers and levels of staff needed in the future, identify current and future gaps and plan to fill those gaps;
    - revise and reassign tasks to favour ambulatory care over hospital care;
    - describe the training of target groups and learning objectives consistent with the national plans/guidelines;
    - revise training methods and material;
    - consider the costs and travel for the trainees and the possibility of distance education (e-learning).
2. TB should be included in the continuing medical education of doctors and nurses.
3. The NTP should be accredited as a provider of continuing medical education.

Operational research

Operational research is an integral part of the Stop TB strategy and of the Global Strategy and Targets for TB Prevention, Care and Control after 2015. Programme-based operational research is already included in the draft National Strategic Plan for TB Control 2012–2016 as a major intervention. Funding foreseen from the Global Fund and Norway should give an opportunity to enhance it in future. The design and conduct of locally relevant operational research can help to identify problems in the NTP, determine workable solutions, test them in the field and plan for scale-up as needed. New tools (such as vaccines, diagnostics and drugs) may become available in future which should be rapidly introduced into routine field practice, for which collaboration between programme managers and researchers is essential. Romania is home to many academic and public health institutions that have the necessary skills to help the NTP initiate operational research. The review team has identified a number of priority areas for future operational research by the NTP.

Recommendations

NTP

1. A focal point should be established in the NTP Central Unit and an ad hoc task force assigned to list the priorities in operational research that address the main challenges in the NTP and to match them with available funding.
2. Formal collaboration agreements should be established with academic and public health institutions to assist the NTP technically and financially (streamlining of resources) with the undertaking of operational research.
3. The following topics (not in order of priority) should be considered in the process of setting priorities for operational research:
    - effectiveness of contact-tracing;
    - reasons for diagnostic delay;
    - risk factors and social determinants, including migration;
    - Xpert MTB/RIF assay (effectiveness of the patient risk assessment, impact on case detection, impact on access to care, effectiveness and cost-effectiveness);
    - genotyping of drug-resistant versus drug-susceptible isolates;
    - standards of care;
    - perspectives and expectations of patients as regards TB care;
    - cross-contamination in laboratories;
    - nosocomial transmission;
    - new financing mechanisms to discourage unnecessary hospitalization;
    - financial incentives to family doctors;
    - formal and in-service training of staff (doctors, nurses);
    - advocacy, communication and social mobilization activities targeting local authorities and communities and the general population.

Ethics and human rights

Ethical values refer to how individuals, professionals and corporations choose to interact with one another. Human rights are legal guarantees that protect individuals and groups against actions that interfere with fundamental freedoms and human dignity: they are concrete legal expressions of ethical values. Because human rights are legally binding, they provide an overarching ethical framework that governments and international organizations are obligated to respect *(37)*. Major issues associated with TB, both from an ethical perspective and realization of human rights are: universal access to good quality services (as defined by the International Standards for Tuberculosis Care) *(38)*, healthy occupational and environmental conditions, involvement of patients *(39)* and communities, and research *(40)*.

Access to TB diagnosis

The weak performance and uneven distribution of family doctors and TB laboratory services in Romania limits access to TB diagnosis, which adds a major ethical concern to the technical considerations. The review team visited counties in which all patients had DST results and other counties where fewer than 10% did, highlighting how where people live in Romania has a disproportionate influence on the TB services they receive. People in rural and hard-to-reach areas experience a shortage of family doctors, who prefer to work in towns. Even the presence of a family doctor in one's community does not guarantee access, as these doctors have a threshold number of patients they can see and be reimbursed for by the NHIH. This leads to delays in the time taken to seek care, late diagnosis and more severe forms of TB. Patients who live too far from a hospital (where they can access free emergency care) have to choose between buying drugs from the local pharmacy for self-medication and paying the local family doctor for a private consultation.

Rapid diagnosis of TB and drug-resistant TB is only available in Bucharest and Cluj, while DST through traditional solid-media culture is provided to less than half of all TB patients in the country, including those more likely to have MDR-TB. Access to DST for second-line anti-TB drugs is even more limited. The weeks waiting for DST results are the cause of long stays in hospital, with severe economic and social consequences especially for farmers, day labourers and women with small children who are not eligible for sick pay. Poor infection control in hospitals, meanwhile, exposes patients to TB superinfections in proportion to their length of stay. Limited access to DST for first- and second-line anti-TB drugs leads to inappropriate treatment and possible amplification of drug resistance.

Access to TB treatment

Drug stockouts are a major violation of patients' right to be cured and a threat to the prevention and control of MDR-TB in the country. The availability of PAS and capreomycin, which the national tender failed to procure, is fully dependent on GLC/GDF procurement and only available for about 20% of the total number of M/XDR-TB patients in the country. Those outside the GLC treatment cohort have a less than 20% treatment success rate, while those included have more than 66%. The threefold difference in treatment success could be explained by the failure of the treatment regimen to contain these drugs, as well as by the conditions required for GLC treatment, which are a long stay of many months in one of the two MDR-TB hospital centres where this is possible (Bucharest and Piatra Neamt), usually hundreds of kilometres from the patient's home and family. Medication stockouts and shortages in outpatient facilities result in

the readmission of patients to hospital instead of enabling them to receive emergency supplies of medications so that they can continue outpatient treatment with far less disruption to their lives.

The Romanian MDR-TB guidelines have not been officially updated since 2005 and contain selection criteria for GLC-supported treatment that are too selective and depend on subjective interpretation. M/XDR-TB treatment should be made available to all through a clear case management algorithm.

Special mention should be made of the treatment for XDR-TB patients who have been prescribed the same second-line anti-TB drugs given to MDR-TB patients with the addition of moxifloxacin (if available). The treatment success rate most recently reported for these patients is only 3.3%. Of the Group 5 anti-TB drugs, only clarithromycin is widely used to treat TB in Romania, while linezolid is not in the list of essential drugs although it is available in the local market at very high cost. While this has convinced some patients to buy the generic formulation of this drug over the internet or from other countries, poor patients cannot consider such options, leading to a divide between patients with the same condition but different capacities for treatment.

Since 2012, two websites (Medicamente-lipsa and Lipsa Tratament) have documented the availability of medications for all diseases in Romania *(41,42)*.[23] They have not, however, been widely advertised or formally adopted, despite a recommendation by a GLC mission. There is a demonstrated need for the TB services and the Ministry of Health to know in real time when there are shortages or stockouts of anti-TB drugs. The present paper-based monitoring system does not allow this. There is also an urgent need for patients and their civil society allies to know about medicine stockouts so that they can advocate effectively for them to be rectified.

Compassionate use of and expanded access to new anti-TB drugs

At the time of the review, only bedaquiline was available in Romania for compassionate treatment of two XDR-TB patients, and another XDR-TB patient was treated with it in Italy. However, many more patients might benefit from the treatment with bedaquiline in conjunction with other drugs with probable efficacy (Group 5), such as linezolid and clofazimine *(44)*. The review team was informed of the plan to expand the access to new anti-TB drugs by purchasing linezolid and other Group 5 anti-TB drugs for 19 patients through GLC/GDF and for 79 patients through the Norwegian funds. This initiative is very welcome.

Palliative care

When patients' treatment options are reduced, they are unable to buy expensive additional drugs or refuse drugs that give them side effects, they receive "compassionate" treatment (not to be confused with the "compassionate use of new anti-TB drugs") consisting of the compassionate prescription of one/two anti-TB drugs just to keep the patient on drugs and justify his/her hospitalization. Such a practice should not be considered ethical, as it offers false hopes to patients while exposing hospital staff and other patients to higher risks. A decision should be taken as to whether to ensure that all conditions are present for effective treatment or to withdraw all TB medicines and arrange dignified palliative care in a protected facility.

[23] Lipsa Tratament, an open-source non-profit project, was a winner of the Restart Romania competition in 2012. Review member Jonathan Stillo was one of the creators, inspired by the Stop Stockouts website *(43)* developed with the same purpose in South Africa. The project is run by the RAA.

Romania lacks a palliative care strategy for TB patients. When patients are deemed to be without therapeutic options they may be sent home (or sign themselves out) or remain in hospital, although the vast majority of hospitals cannot properly house these patients due to their limited space and infection control. In practice, patients move back and forth between home and hospital with related ups and downs in status. Patients who are contagious pose a threat to their caregivers and other patients. Until such time as the full range of anti-TB drugs is available to treat these patients, it is preferable to organize domiciliary care for them with only minimal infection control measures to protect their relatives and neighbours (such as facial masks and ventilation of the home). For patients with poor living conditions, isolated houses with proper infection control within or close to the hospital premises may be required.

Patients who refuse treatment

It is common for patients to refuse certain second-line anti-TB drugs. Patients complain often of severe nausea from oral medications and severe pain and hearing loss from the injectable ones. Doctors often say that "being deaf is better than being dead", underestimating the different measures that can be taken to prevent nerve damage and relief from painful injections. It is also common practice to get patients to sign for their refusal to receive a medication even in the absence of proper counselling, following which treatment is continued without a drug that cannot be replaced. While it is understood that patients have the right to refuse treatment, it is felt that additional efforts are necessary to educate them as to the consequences of interrupting or refusing treatment, possibly through a team of doctors, psychologists and social workers.

Recommendations

1. Every effort should be made for access to TB diagnosis and treatment to be universal. This is only possible if providers at all levels of care, including family doctors and community workers, are involved in delivering TB services. Patients should be able to choose their site of diagnosis and treatment.
2. Access to rapid, quality TB diagnosis, including DNA-based methods, should be made available to everyone regardless of geographic location or socioeconomic status.
3. All M/XDR-TB patients detected should have access to all the anti-TB drugs they require, regardless of the source of funding for their purchase. All treatments should meet the International Standards for Tuberculosis Care, regardless of patients' geographic location or social status.
4. The exclusion of patients from M/XDR-TB treatment should be limited to extreme clinical conditions and palliative care should be organized as close as possible to patients' homes and needs. National guidelines for palliative care should be developed.
5. The practice of prescribing "compassionate regimens" should be ended. All patients with multiple treatment failures and/or returning after loss to follow-up should receive treatment based on full DST and proper counselling to understand the importance of the new treatment.
6. All TB patients, including those to be treated in the two M/XDR-TB centres of excellence, should receive treatment enablers (transport) and social support to help them complete their treatment successfully.
7. Access should be ensured to effective treatment for pre-XDR and XDR-TB, including linezolid and other Group 5 drugs, and the registration and introduction facilitated of new

anti-TB drugs as well as medications not yet registered for use on a compassionate basis for patients without other therapeutic options.

8. The work of the National MDR-TB Commission should be properly documented (patients evaluated, patients approved for treatment and actually enrolled, patients excluded from treatment and reasons for exclusion) and disclosed in the public domain.
9. Pharmacovigilance should be strengthened to monitor adverse reactions to anti-TB drugs during both inpatient and outpatient treatment. The national guidelines to prevent and mitigate such reactions, which are so important for ensuring patients' adherence to treatment, should be strengthened.
10. An electronic system should be established for the mandatory reporting of first- and second-line drug shortages and stockouts and such reporting made public through the Lipsa Tratament and Medicamente-lipsa websites.

Advocacy, communication, social mobilization

Nearly all advocacy, communication and social mobilization (ACSM) activities for TB control in Romania have been funded by the Global Fund. While national awareness (and community involvement) activities have taken place around health-related issues in recent years (for example, human trafficking, mother and child health, end of life care), there has been nothing of this kind in relation to TB.

Most of the TB educational materials were developed from the Global Fund grants under Round 6 and even Round 2. The last national TB awareness and education campaign, which ended in 2007, was conducted with funds from Global Fund Round 2, the United States Agency for International Development and Doctors of the World (the latter two organizations stopped working in Romania in 2007). For that campaign, educational material, video and short television spots were created. Such material, currently in use, was designed for the general public and has little information on patients' rights regarding the TB services that must be provided by the Ministry of Health. The Charter for TB Patient Care was translated into Romanian but is rarely available. In 2012, Romania received a small grant from the Global Fund Transitional Financial Mechanism that included a budget for patients' education and destigmatization.

The largest ACSM project currently taking place is conducted by CHPS and The Bucharest Medical Students' Association, with funds from the Global Fund. This project uses caravans to bring TB education to rural and underserved populations (such as poor people and Roma communities) and reached 41 923 people in 32 counties (especially in Calarasi) and Bucharest during 2008–2013. While this achieved an increase in knowledge about TB, the beneficiaries of the project clearly represent only a tiny fraction of the country's population.

Other advocacy and educational initiatives are those sponsored by the United States Embassy in Bucharest, such as the activities of a TB working group since 2011, the education campaign We all Breathe the Same Air in schools and universities conducted in six counties during 2011–2012, and the dialogue and collaboration with the United States military.

An example of ACSM activities with no international funding is the Romanian TB Patients' Association, which contributes with its own funds to the awareness activities during World TB Days and to the links between various nongovernmental organizations (such as the Bucharest Medical Students' Association and the Carusel Harm Reduction).

The vast majority of nongovernmental organizations active in TB are based in Bucharest.[24] Some large nongovernmental organizations such as CHPS, Save the Children and Romanian Red Cross have or have had projects (on outreach, education, patient support) outside Bucharest, but these are based on Global Fund support and are likely to be disrupted when such support ends.

Four knowledge, attitude and practice surveys took place in 2004, 2007, 2010 and 2012 (the first by Doctors of the World, the others by CHPS), all of them with support from the Global Fund. Differences in methodology and coverage, however, make it difficult to compare the results. The 2004 survey covered only two counties, although it studied specific groups more deeply such as poor people, Roma communities, former TB patients and families and TB nurses. Many respondents in all groups (including patients and nurses) believed that TB can be spread by sharing dishes/utensils, food and physical contact. The knowledge, attitude and practice surveys in 2007 and later years used representative samples of the general population. A significant proportion of the people interviewed had no knowledge of TB, its transmission and curability, which highlights the need for mass media campaigns targeting the general population, improving their understanding of TB and addressing the social stigma associated with it.

The review team only found TB educational material in TB dispensaries and pulmonology hospitals, combined with a varying quality and amount of information given by the treating physicians. No TB educational material was seen at any family doctor practice visited. In the educational material for MDR-TB patients, reference was found to totally drug-resistant TB which is an unnecessary reminder of the possibility of no cure for TB. Discussions with patients revealed a wide range of knowledge about TB among them, with many still thinking they got TB from exposure to cold or damp.

As a whole, national ACSM activities are limited. The possibility of using the mass media (television, radio) through the National Institute of Public Health Television is unclear, considering its current focus (on healthy food and water) and the cost of air-time.

No nationwide TB education has occurred in schools, which would have required collaboration with the Ministry of Education, but some such education has taken place depending on the local goodwill of some school administrators and family doctors, sometimes with the support of the Romanian TB Patients' Association, the Bucharest Medical Students' Association and the United States Embassy.

One major challenge for ACSM in Romania is how to reach the local authorities. Since the reform, mayors and local councils health and social welfare departments are represented on hospital boards and decide health and social support budgets. They are a key target for advocacy to divert available local resources towards effective TB control interventions. A positive example is in Brasov County, where the local council funds a social/medical rehabilitation centre for TB patients to continue their treatment and for former TB patients in need (such as homeless and/or disabled people or those without families).

There are a number of relatively low-cost interventions which could be made, such as local TB education, media outreach and small events. It is unclear why these sorts of activity have been neglected by Romanian civil society organizations in favour of more attention given to project-

[24] A notable exception is the Romanian Children's Humanitarian Foundation, a small Dutch organization which is based in Iasi, a northern city near the Republic of Moldova, and which carries out TB education and anti-poverty activities in rural communities.

based longer-term funding and development of professional advocates. Former patients, students and other volunteers across civil society are willing to contribute but lack organization and coordination. Small projects implemented by local nongovernmental organizations and volunteers, such as local advocacy campaigns, could have a large impact with small budgets mainly covering educational material and transport, rather than staff salaries and office rentals.

The last major social mobilization campaign around TB was the STOP TB campaign in summer 2012[25] when the Romanian STOP TB Partnership was launched at a press conference attended by many media. The Partnership, established and housed by RAA with support from the Global Fund, has been active in organizing some ad hoc activities with national and international partners. However, it works mainly on a case by case basis, lacking proper governance and funding. Its last major initiative was an open letter released after publication on The Sun website in April 2013 of a hostile article describing the time bomb represented by Romanian immigrants bringing drug-resistant TB to the United Kingdom *(45)*. The Partnership is still very much in its infancy and, if it is to grow and be of real added value, it needs a clear structure and legal status, and transparent and democratic management.

Civil society in Romania should work with and inform policy-makers but also criticize the health system when necessary. The vertical structure of TB services in Romania and the Global Fund funding may create dangerous proximity where the civil society organizations receiving the Global Fund grant may forget that one of their roles is to stimulate national and international pressure on the Ministry of Health. This may be why the Romanian civil society organizations were shy in reacting to the well-documented stockouts of second-line drugs and very poor M/XDR-TB treatment outcomes. Other civil society organizations were much more active and vocal in publicly decrying actual and potential ART stockouts. Given the weak voice that Romanian TB patients have nationally and internationally, it makes sense to build more capacity in the Romanian patients' associations, especially in advocacy and the promotion of international links with, for example, Stop TB, the TB Europe Coalition, the Global Coalition of TB Activists and others.

Recommendations

Ministry of Health

1. A national strategy and plan for advocacy, communication and social mobilization with regard to TB should be developed by the National Institute of Public Health, together with the NTP, with clear roles and responsibilities for all partners (including the Ministry of Education), timelines and an assured budget from diverse sources.

NTP

2. TB educational material should be revised and updated consistently with regard to the transmission, prevention, diagnosis, treatment and care of TB. Patients' rights and responsibilities and latest international standards of care should be included and widely promoted.
3. TB educational material should be made available in a variety of locations other than TB treatment units, especially in general hospitals and family doctors' surgeries, to promote early health care-seeking behaviour and reduce the social stigma attached to TB.

[25] The Stop TB Campaign in 2012 was initiated by the RAA on a wave of concern after the death of an XDR-TB patient.

4. ACSM should be strengthened and expanded, especially at county level and with the involvement of all national and locally available partners. Preferential partners are the TB patients and former patients and their relatives, who should be encouraged to participate in patient organizations for ACSM interventions. Key targets for advocacy are the local authorities.
5. A special grant programme should be developed to foster the development of small projects by local organizations and groups of individuals able to ensure effective ACSM interventions with small budgets that exclude staff salaries and office rentals.
6. ACSM should also be conducted at the national level with the involvement of different components of civil society such as communities, faith organizations, former TB patients' associations, professional societies and school administrations. When appropriate, public governmental and nongovernmental organizations and private partnerships should be encouraged.
7. The Romanian STOP TB Partnership should be strengthened and expanded to include all current and new partners. For this, a recognized legal status, clear structure and mechanisms for democratic participation are required.
8. A single up-to-date TB website should be developed in Romanian, similar to that produced by the National AIDS Programme, addressing the general public and patients and showing the most recent NTP statistics.

Health system and TB control

The current structure and characteristics of the Romanian health system are the result of a long transition, beginning in December 1989, from the Semashko model, which was already showing shortcomings in the 1970s and 1980s.

Service delivery

Health care services in Romania are delivered through a network of family medicine practices and facility-based outpatient services with specialists and inpatient hospital services. In addition, the public health network devoted to health promotion, prevention and environmental health and a small network of civil society organisations involved in outreach activities are mainly concentrated in large cities and depend on external funds.

Family medicine practices

Primary health care in Romania is provided through family doctors. Ideally, all Romanian residents either covered by the NHIH or from a protected population group[26] should be registered with a family doctor. These doctors have a gatekeeping role, which was reinforced in 1999 with the introduction of compulsory payments for specialized and hospital services (except for emergencies) if they were not prescribed by a family doctor. Family doctors own or rent their premises and operate independently under a framework contract with the NHIH to serve a population of 2000 people, although the current average is about 1600 people.

[26] Until 2004, five million people (almost one quarter of the population) were paying to the NHIH *(46)*. Then exemptions were limited to: pregnant women, children below 18 years of age, students below 26 years, war veterans, people without an income or very low income, people with disabilities, and people with conditions of public health relevance such as TB and HIV. Elderly people have to pay, unless they have a pension below a specific ceiling. Even so, only 6.5 million people are contributing to the NHIH *(47)*.

Contracts with the NHIH have a fixed number of consultations per day. If the number of these consultations is exceeded the family doctor cannot invoice for such services and is not paid for them. Thus people seeking care but who arrive after the daily quota has been exceeded may be charged by the family doctor directly. As consequence, it is quite common for patients to bypass family doctors and seek care directly in the hospital emergency room, where services cannot be charged and from which patients can be referred to specialists, also free.

Family doctors may collaborate with county public health departments for public health interventions such as the investigation of epidemics and TB contact-tracing. In practice, however, such cooperation is the exception because there are no incentives in the framework contracts. There are, however, a few examples of cooperation in active case-finding using funding and resources from motivated local authorities *(48)*.

A number of family doctors were trained in the Practical Approach to Lung Health under a specific project implemented by CHPS during 2008–2011 with Global Fund support. Unfortunately, the operational guidelines developed for the Practical Approach to Lung Health were never officially adopted and rolled out in the country *(49)*.

Facility-based outpatient services with specialists

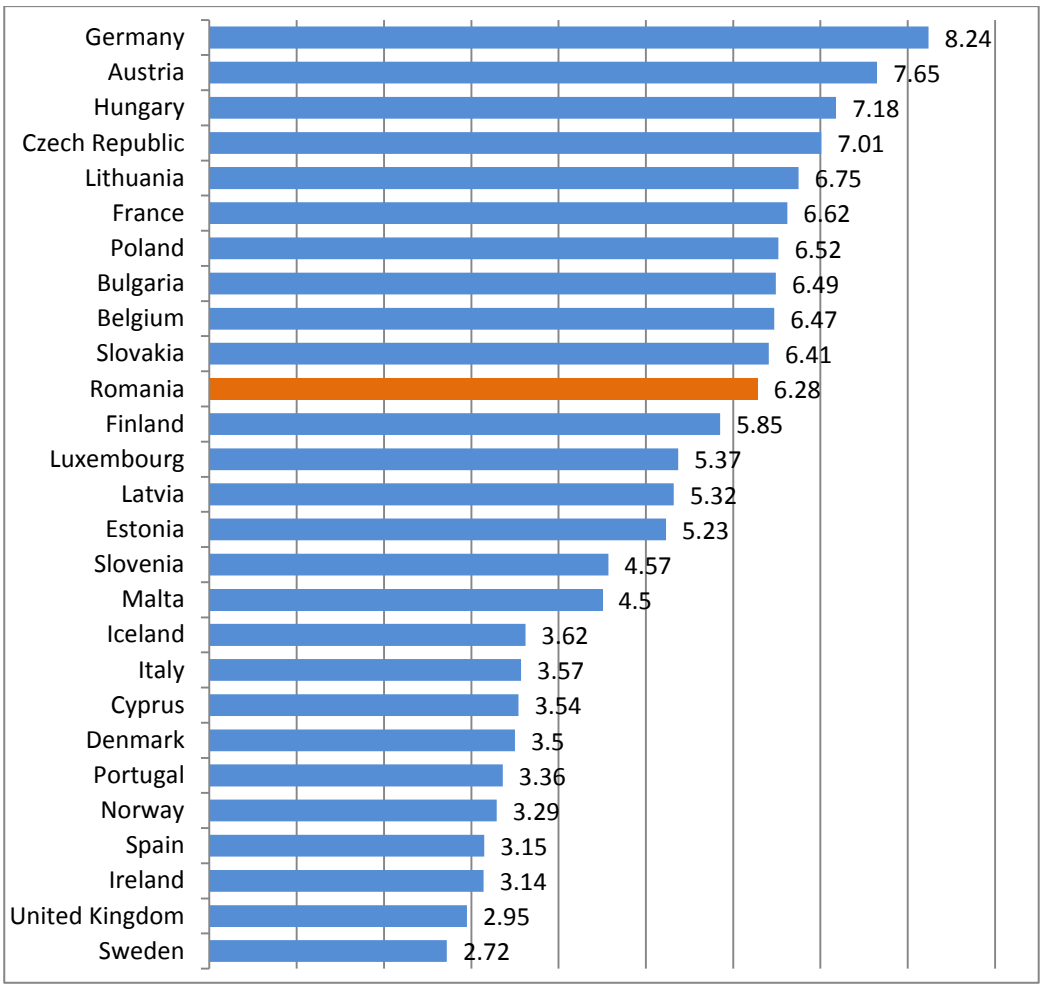
These services are provided from outpatient departments in hospitals and other outpatient facilities depending administratively from them but in separate premises. Such premises were called polyclinics (facilities for non-hospital-based specialists) under the Semashko model.

Inpatient hospital services

The inheritance from the Semashko model means that there is still an excess of inpatient services whose management now exceeds the financial capacity of the country. Current legislation promotes a shift to an ambulatory model of care, which was expected to continue progressively over the years. This has not, however, happened: 416 hospitals were registered in 1980, increasing to 422 in 2003 and 461 in 2013 *(50)*. Such a paradox can be explained by the disaggregation of large hospital complexes into smaller specialized hospitals (including TB hospitals). Behind the number of hospitals, there was the effective closure of almost 28 000 beds that reduced the ratio of hospital beds per 100 000 population from 8.9 in 1991 to 6.69 in 2011 *(46)*. An additional 9200 beds in 66 hospitals are earmarked for closure in the future *(51)*. The inpatient care capacity in Romania remains high in the EU/EEA member states (Fig. 5, 6). A further reduction is planned under the National Strategy for Hospital Rationalization through the development of regional and national plans for hospital care and a national integrated system of health information *(52)*. The World Bank and the European Commission are giving their support to such a process.

Hospitals are classified in five types (Table 18) based on the level of services provided *(54,55)*. Type one hospitals are the largest, with all the clinical specialities and most advanced technologies (digital radiology, computerized tomography, magnetic resonance imaging, a defined list of equipment), working as national/regional reference and active in academic teaching and scientific research. The hospitals at this level that cover only one medical specialty, such as the Marius Nasta Institute, are classified as subtype 1M. Type two hospitals are county reference hospitals, able to perform most laboratory investigations and equipped with a defined list of equipment. Type three hospitals are also at county level but provide fewer services. Type four hospitals are local and municipal hospitals with surgery and a few other specialties. Type five hospitals are for chronic patients. In the case of TB, these are sanatoria.

Fig. 5. Hospital beds per 1000 population, EU/EEA countries, 2010



Note. Greece and the Netherlands did not report.
Source: WHO European health for all database *(53)*.

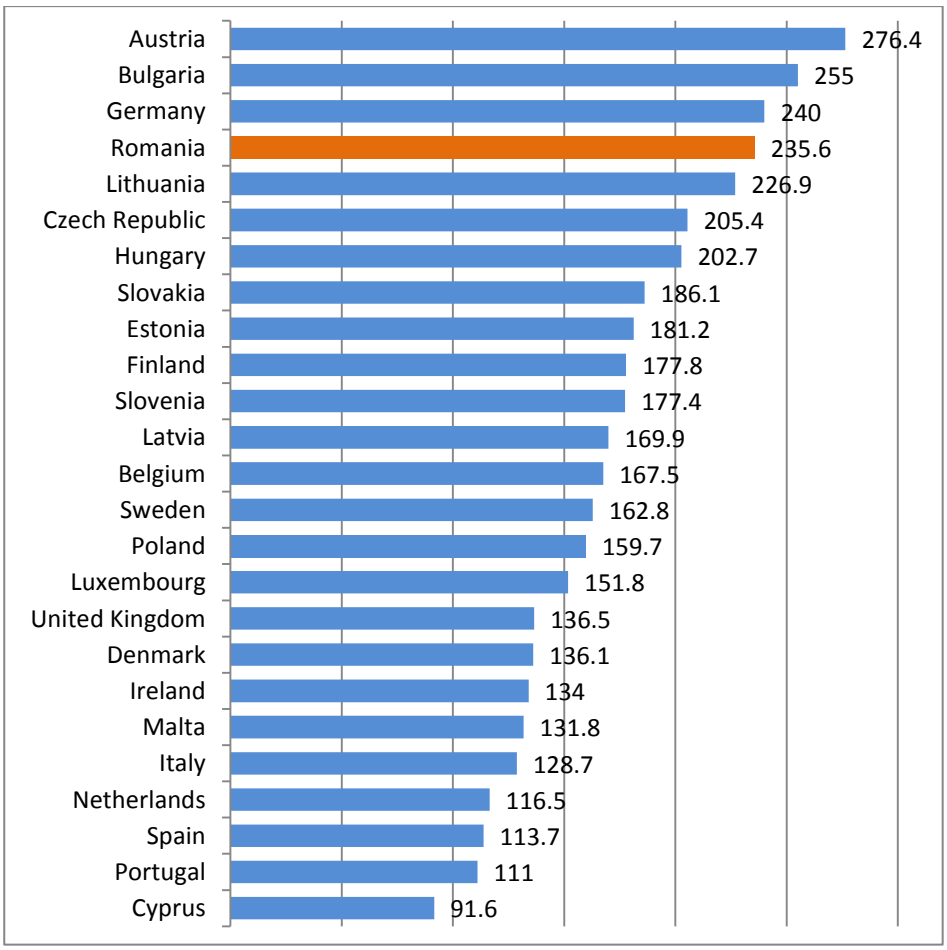
The NHIH refers to this classification, based on a standardized capacity for delivery of services (diagnosis and treatment) for issuing framework contracts with the hospitals.

The need to preserve their budgets from the NHIH forces hospitals to maintain their large numbers of hospital beds and thus to compete for patients, who may not only be admitted without a real need but may also be referred from one hospital to another and thus receive fragmented care (as described above). Moreover, having a laboratory able to investigate TB is a key feature in the classification of a hospital and its level of framework contract budget, which is an important financial disincentive to closing TB laboratories as part of downsizing the over-large national TB laboratory network.

Health system governance

There are two essential legislative milestones in the reform of the health system in Romania: the Health Insurance Law approved by the Parliament in 1997 *(56)* and the Health Reform Law passed in 2006 *(57)*.

Fig. 6. Hospital discharges per 1000 population, EU/EEA countries, 2010



Note. France, Greece, Iceland and Norway did not report.
Source: WHO European health for all database *(53)*.

Table 18. Number of hospitals by type, 2012

Type	Level	No.
1	National	30
2	Best county hospitals	64
3	Other county hospitals	50
4	Municipal or town hospitals	169
5	Chronic care hospitals	147
Not classified		1
Total		461

The Health Insurance Law introduced a public health system funded through payroll contributions and administered through the relatively independent Casa Nationala da Asigurari de Sanatate (NHIH). This represented a diversion away from central taxation and direct management by the government by transferring the government-owned health care institutions to multiple ownership, replacing central planning with direct contracts between the NHIH (purchasing services) and the health facilities (providing services) and employing health personnel with contracts through health institutions and/or private contracts rather than civil service appointments. Other small health insurance schemes survived to cover specific populations such as civil servants, the army, police and railway workers.

In 2006, nine years after the establishment of the NHIH, the Health Reform Law laid down new directions in line with a modern and effective health system, including a focus on prevention and primary health care, enhancement of a minimum package of care, more effective emergency services, clear relations with the private sector and improved links between the public health care and social assistance systems for better policy development. Unfortunately, the directions set out in the Health Insurance and Health Reform Laws encountered serious difficulties that shaped the system as it is today.

Most hospitals are no longer owned by the Ministry of Health but by the counties or municipalities as individual, legally-established institutions. Each of them has a board with political representatives and a chief executive officer (director) appointed by and accountable to the board. The Ministry of Health retains a stewardship role for the health of the population by establishing policies and guidelines that must be followed by all institutions either under a framework contract with the NHIH or a private contract. The Ministry of Health also directly funds interventions for the prevention and control of public health diseases, including the procurement of essential commodities (drugs) and the direct payment of health care institutions providing TB-dedicated services.

In reality, hospitals and health care institutions are less flexible than they should be in an ideal decentralized and pluralistic system. Hospitals still operate according to rigid Ministry of Health rules under which, for example, opening or closing a hospital ward or changing the contract of health staff require the authorization of the Ministry of Health *(46)*. The Ministry of Health can also decide to increase staff pay scales, which increases the hospital's expenditure and budget gap. The hospital directors interviewed by the review team disclosed the difficulties they were having in moving away from historical suboptimal clinical practices to better ones as the result of such administrative rigidity and of the inadequate legal environment and contradictory financial incentives (see the following sections).

An additional problem comes from the many properties confiscated during the previous regime from rich families, churches and other associations that now have to be returned to their original owners and their heirs *(58,59)*. In 2013, the government passed new legislation *(60)* under which the original owners of a currently state-owned property can receive points for the nominal value of the property and use them in the public auctions of that property. Such arrangements, bypassing restitution, is opposed by most owners in view of the market interest that many of their past properties currently have due to their historical design, central location and land. Many are hospitals or other health care facilities, and many are TB-dedicated. The ferocious and lengthy legal disputes for restitution/compensation, with uncertainty as to final ownership, prevent the government from allocating the necessary funds for their physical renovation and the prevention of nosocomial infections.

Health system financing

Health expenditure

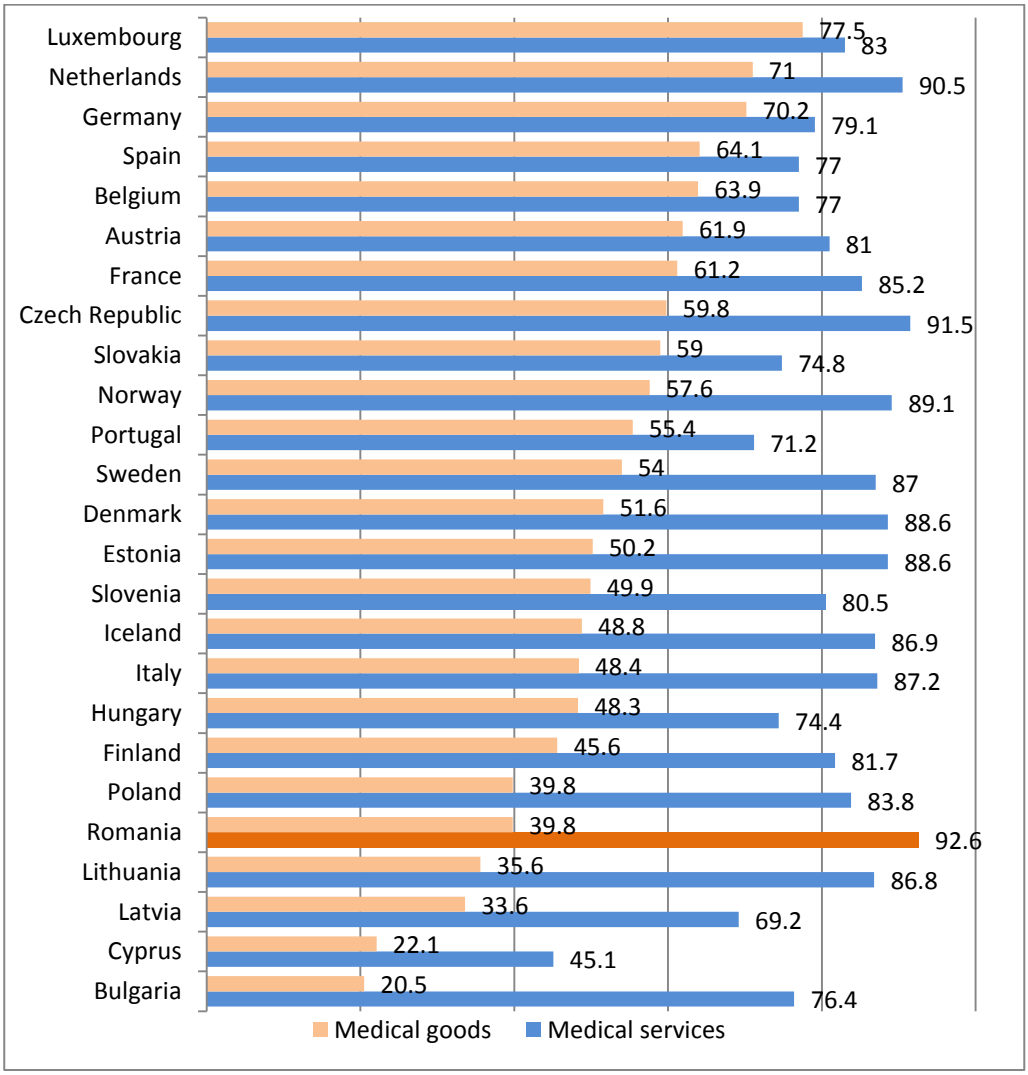
Although total health expenditure increased progressively after the introduction of the Health Insurance Law in 1997, it is still only 5.6% of GDP, the lowest in the EU *(61)*.[27] This is in spite of the efforts of the government, which maintained during 2000–2010 the higher annual average

[27] Figures refer to 2010 or nearest available year.

growth in health expenditure per capita of 5.4% (less than 4% the EU average) while GDP per capita grew by only 3.8% *(62)*.

According to the OECD, public funding through direct government expenditure and health insurance funds represents 80% of total health expenditure in Romania *(62)*. Public funds cover 93% of expenditure on medical services but only 40% of expenditure on medical goods (drugs and devices, see Fig. 7), which means that patients in Romania pay the most out of pocket in the EU for drugs and other medical goods.

Fig. 7. Public share of health expenditure on medical services and goods, EU/EEA countries, 2010



Note. Greece, Ireland, Malta and the United Kingdom did not report.
Source: OECD *(62)*.

Coverage and private payments

The national health insurance is designed to cover all residents of the country, with compulsory payments. Free insurance coverage is, however, offered to non-wage earners, persons with disabilities, war veterans, people with conditions of public health relevance such as TB and HIV, pregnant women and children below 18 years of age *(47)*. Twenty percent of total health expenditure is private and used for payment for services in the private sector, official

copayments in the public sector for some services and delivery of goods (such as drugs) and informal payments in the public sector.

Private health services are growing and used by those who can afford it. Private TB services are, however, marginal.

Official copayments are charged for a number of tests, most of the drugs, some surgical interventions and most of the hospital care. They range from a symbolic token of €2 for hospital admission to much more for tests and medicines, which have to be paid at a rate of 50–100% of market value according to their category of reimbursement. As the price of a test/medicine increases, so does its absolute cost within the same percentage of reimbursement, a fact well-known by international experts and considered socially regressive. Informal payments continue to be offered as in the past; they are also asked for to level up the low salaries of the healthprofessionals. A survey conducted in 2007 found that 60% of hospital patients had made unofficial payments and estimated that informal payments represented 41% of the total costs paid by patients *(63)*. Informal payments are a well-known deterrent to seeking health care when a person experiences symptoms *(64)*. Although copayments are excluded from basic TB diagnostic and treatment services, such payments can take place before TB is diagnosed. Moreover, patients have to make copayments for additional tests required when diagnosis is difficult and for any non-specific drugs to treat clinical complications.

As informal payments are requested according to the perceived capacity of patients to pay, they may not be asked of a large proportion of TB patients, who often suffer from low socioeconomic conditions. Still, anecdotal evidence from the review suggests that informal payments for basic TB tests may be charged in some localities.

Paying providers

Health providers in Romania, whether they work in an institution or are independent contractors (such as family doctors), are paid according to a framework contract with the NHIH that describes all the services to be provided as well as the official copayments that can be charged up to a maximum amount per insured person of around 600 Leu/year (about €135/year). The payment system and its consequences on behaviour and possible solutions for improvement vary for each type of provider.

Inpatient care

All hospitals have an annual contract with the NHIH determining the number of hospital cases to be admitted or discharged and the price for each type of case depending on the type of the hospital and the method for adjusting the cost per case based on clinical complexity according to the diagnosis-related group system.[28] The more complex the cases, the bigger the budget given to the hospital, without regard to the length of admission. In many countries, such a payment system has promoted shorter hospital admissions and more patients treated per hospital bed. In other countries, including Romania, it did not. The level of flexibility in hospital management is considered key. For example, the diagnosis-related group system may increase the number of patients that can be treated per bed but also create an anti-economic surplus of beds that are not

[28] The diagnostic-related group system is a standard system of measuring case mix in an institution. It is based on aggregating hospital discharges in groups of patients with similar clinical conditions and sharing similar costs (or weight, as described in the system). Adding the weights of all discharges allows the calculation of an average for each hospital, and complexity (as a proxy of cost) can be compared across hospitals using the same funding system. Romania uses standard software used widely in Europe.

needed but cannot be closed by the hospital administration. In such conditions, the marginal cost of keeping patients longer in hospital and having all beds occupied is lower than the cost of diagnostic procedures and treatment for new patients.

TB cases are excluded from the diagnosis-related group system, probably as the result of the past policy that was maintained with the intention of isolating TB patients from the community and providing shelter to those in need. The NHIH reimburses TB care in hospitals for a maximum of 37 days (non-resistant TB cases) or 120 days (drug-resistant TB cases) at a flat fee of 200 Leu (€45) per day (160 Leu (€36) in the sanatoria). It is evident that such a system represents an economic incentive to keep patients in hospital for the maximum number of reimbursable days even if their clinical conditions would support earlier discharge.

This number of days might not, however, be sufficient bearing in mind that the first phase of TB treatment, which is more intense and care-demanding, is recommended for 60 days for non-resistant TB patients, 160 days for MDR-TB patients and even longer for XDR-TB patients. Such differences were used to justify the readmission of patients on the day after their discharge from the first admission in many of the hospitals visited by the review team.

A diagnosis-related group system applied to TB patients would have forced hospitals to dramatically reduce the length of stay of these patients to close to the average for all patients.[29] It is also true that any payment system could not be enough to change clinical practices unless there is a synergy with the institutional clinical leadership. In either system, whether a diagnosis-related group system or one for TB, hospital managers have limited control of expenditure since many costs are fixed (salaries) and others are decided by the Ministry of Health, although they do have full control of the income produced by reimbursements from the NHIH (see the budget for the Marius Nasta Institute, Table 19). Playing with the length of hospital admission is one of the few instruments left to hospital managers to maximize their budgets for investment in technologies and staff salaries.

Table 19. Budget of the Marius Nasta Institute by hospital department (Leu), 2013

Department	Total income	Expenditure				Balance
		Direct		Indirect	Total	
		Human resources	Other			
Department 1	6 101 365	1 190 063	1 406 153	2 427 934	5 024 150	1 077 215
Department 2 (Medical oncology)	156 048	75 513	119 887	182 031	377 431	-221 383
Department 3	4 193 077	1 322 734	876 114	2 056 181	4 255 029	-61 952
Department 4	4 245 915	1 073 817	873 468	1 820 310	3 767 595	478 320
Department 5	4 531 091	1 256 037	1 003 127	2 112 585	4 371 749	159 342
Department 6	3 587 182	193 990	1 427 202	1 815 182	2 009 172	1 578 010
Department 7	3 982 675	966 925	959 013	1 802 363	3 728 301	254 374
Department 8	5 390 005	1 118 174	1 047 531	2 025 415	4 191 120	1 198 885
Department 9	3 570 268	1 200 947	265 887	1 371 642	2 838 476	731 792
Department 10	5 610 597	1 111 598	454 976	1 463 939	3 030 513	2 580 084
Department 11 (MDR-TB)	2 682 071	1 199 198	1 015 647	2 071 564	4 286 409	-1 604 338
Department 12 (Thoracic surgery)	5 400 264	2 130 695	4 804 567	6 489 022	13 424 284	-8 024 020
TOTAL	49 450 558	13 734 843	11 931 218	25 638 168	51 304 229	-1 853 671

[29] On the impact of the diagnosis-related group system in reducing length of stay, see Mathauer & Wittenbecher *(65)*.

Outpatient TB-dedicated care

TB outpatient care is provided from the TB dispensaries. Their budgets come from the Ministry of Health through the NTP. Until 2012, their budget sources were split between the Ministry of Health (for some salaries and prevention activities) and the NHIH (diagnosis and treatment provided under their framework contract). In 2013, with the national centralization of drugs procurement, their budgets moved back under the Ministry of Health. The different budget sources and the changes in system resulted in complex management and were the cause of some breakdowns in services (such as drug stockouts). There is a plan to move all the budgets to a new framework contract with the NHIH in the near future. Such a change and integration might possibly simplify administration and increase the efficiency of and accountability for the services provided.

Primary health care

The NHIH contract with family doctors envisages payments based on a capitation fee, that is, a fixed amount received for each insured person enlisted, and a fee for every consultation. There is a limit of two visits per month reimbursable per each insured person, and a guideline average time per visit of 15 minutes, which leads to a theoretical ceiling of 22 visits reimbursable by the NHIH per working day. These rules were designed to limit the number of unnecessary consultations but they clearly impede DOT and undermine the early detection of TB cases. Until 2009, the framework contract with the NHIH included a financial incentives scheme calculated on 20 points given for the detection of a TB case and 40 points for the completion of a DOT course.[30] The incentives were subsequently removed and only a few family doctors continued to provide TB services that were not reimbursed by the NHIH. The review took place when the framework contract was being renegotiated between the Ministry of Health, the NHIH and the Family Doctors Association. The negotiations were about the inclusion of financial incentives for the provision of a minimum package of services covering five conditions of public health relevance (hypertension, chronic bronchitis, renal failure, kidney diseases and asthma) and linking them to specific outcomes instead of outputs. The inclusion of TB in the package of reimbursable services by family doctors is an opportunity that cannot be missed to decentralize TB control and strengthen DOT countrywide. The review team met all three parties to the negotiations; when specifically questioned, they assured the team of their firm intention to include TB. In contrast to the situation before 2009, the performance indicators to be included are the number of TB contacts traced, patients cured and patients who completed their TB treatment. Successful examples could be used to pilot the involvement of family doctors in the screening of communities with known risk of TB.[31]

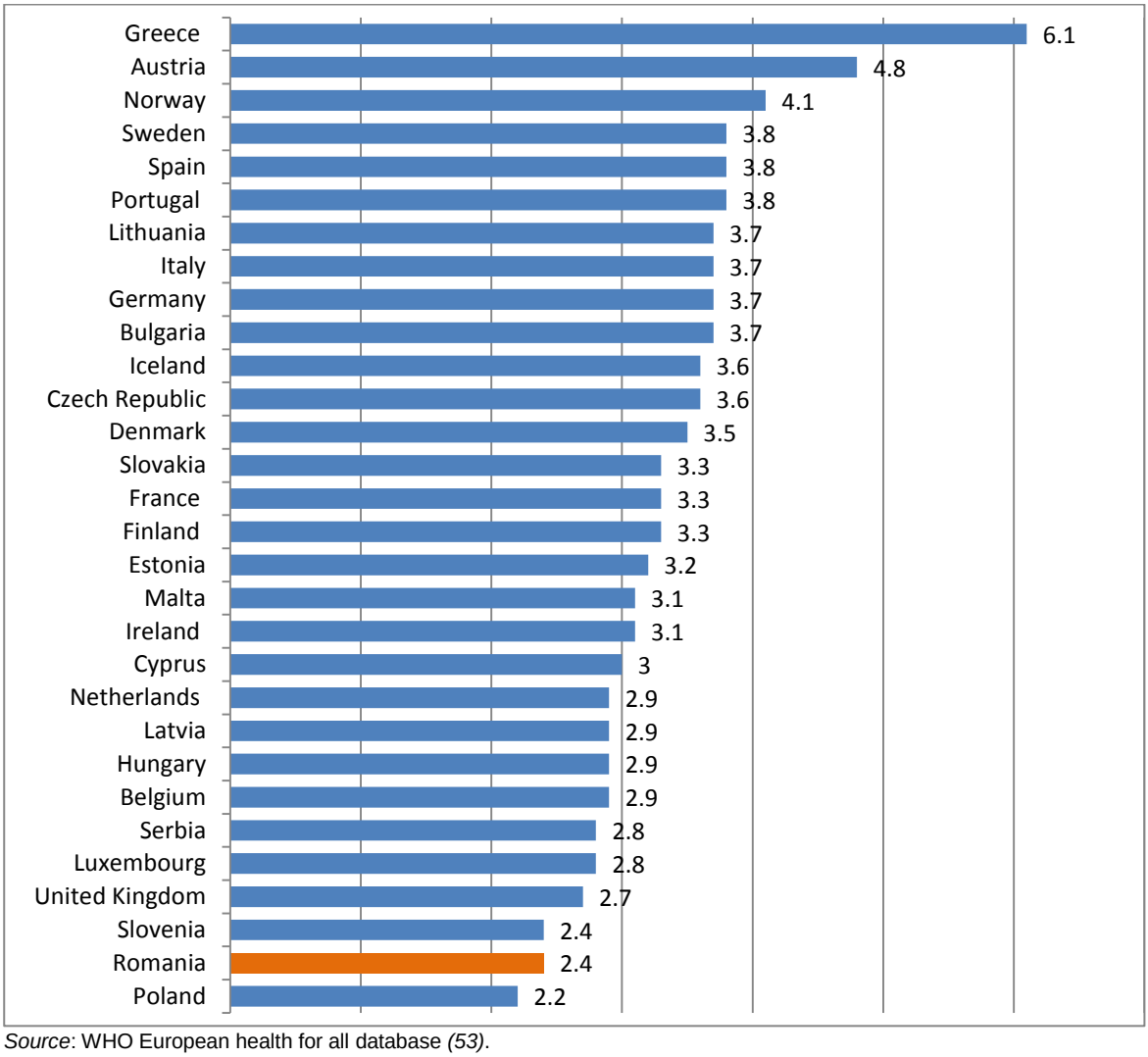
The review team understood that the government will soon move the budget for NTP services from joint administration by the Ministry of Health and the NHIH to direct administration by the NHIH. Such an arrangement will have the advantage of mainstreaming TB funding and service delivery but may incur dangerous breakdowns during the transition from one system of purchasing TB services to another.

[30] The value of a point in money changes depending on the number of points produced by the system. In 2009, points were probably reimbursed in a range of 3.85 Leu per point; 40 points gave 154 Leu (approximately €38).
[31] See Dumitra G *(48)*. Past examples of the integration of Romanian family physicians in screening, such as for cervical cancer, reinforce the view that their further involvement in TB care is both feasible and effective.

Health system workforce

In 2010, there were 2.4 practising doctors per 1000 population, the second lowest number of doctors (after Poland) within the EU/EEA (Fig. 8). Of these, about one third (11 400) were family doctors with an average of 1600 people enrolled for the NHIH. There are no updated data for more recent years, but the situation seems to have deteriorated in the last three years as a result of emigration by doctors (especially to France, Germany, Italy and the United Kingdom) looking for better conditions and facilitated by the free movement of health workers within the EU *(66,67)*.

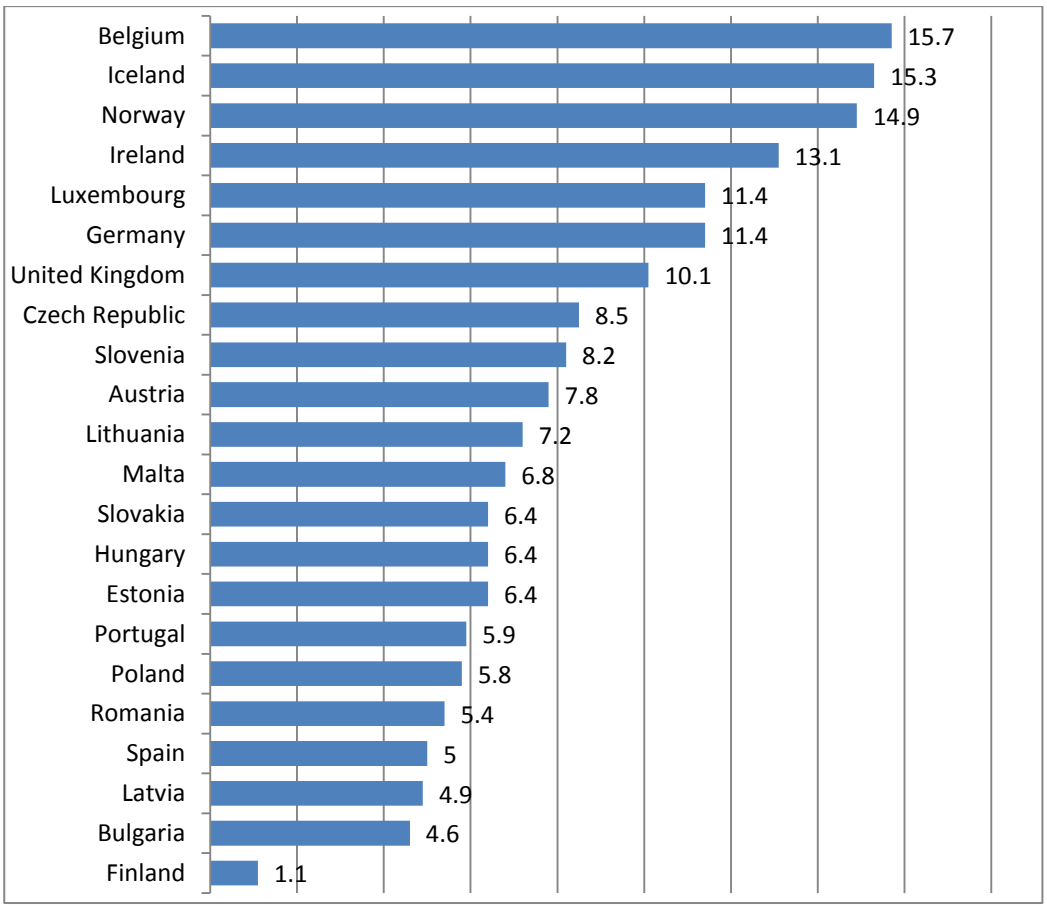
Fig. 8. Practising doctors per 1000 population, EU/EEA countries, 2010



Source: WHO European health for all database *(53)*.

The number of nurses also ranks low by European standards (Fig. 9) and migration of the best trained nurses to many western European countries and beyond is a problem *(68)*.

Fig. 9. Practising nurses per 1000 population, EU/EEA countries, 2010



Note. Cyprus, Denmark, France, Greece, Italy, Netherlands and Sweden did not report.
Source: WHO European health for all database *(53)*.

There are 11 state-owned and two private universities providing undergraduate medical training and postgraduate training in 52 medical specialties, including pulmonology and family medicine. Some of the universities also take students from other countries, including the EU.

Approximately 3700 students graduate each year in Romania and around 1400 go on to specialize. On the other hand, a significant number of newly-graduated doctors move to work abroad (1100 and 1700 during the first eight months of 2010 and 2011, respectively) and an unknown number find employment in a non-medical sector *(69–71)*. Although it was not possible to find more recent data, medical emigration is perceived as a major problem for the sustainability of the system.

All staff working in hospitals are subject to a national pay scale and a scheme of salary bonuses for specific professional risks. The bonus for exposure to TB is high (60–75% of the basic salary) and only paid to physicians and other staff caring for patients with TB.[32] As it is now, the bonus is a major incentive for the scattered distribution of TB patients, which ensures that all staff receive the bonus but discourages better arrangements for nosocomial infection control, such as keeping TB patients in different hospital wards according to their degree of

[32] A senior pthisiopulmonologist receives a basic monthly salary of €500–600. Even with the bonus, this is widely considered insufficient.

infectiousness. In fact, the review team observed in most of the sites visited that TB patients are competed for by different doctors and in different wards of the same hospital (pulmonology, infectious diseases and internal medicine), with the result that patients with presumptive TB share rooms with non-TB respiratory patients, patients with confirmed TB share common spaces (such as cafeterias, toilets, corridors, waiting areas and diagnostic rooms) with non-TB respiratory patients and patients with different forms of TB share the same wards regardless of their infection status (apart from MDR-TB patients, but even then only after their drug resistance has been identified by culture).

Medical products and technology

Registration of medical products and technologies is under the authority of the National Drug Agency in line with EU directives. Purchasing and procurement in the public health system is regulated by Government Emergency Order 34/2006 regarding public acquisition contracts, public works concession contracts and services concession contracts (amended by Government Emergency Order 77/2012) applicable to all institutions owned either by the state or by local authorities. Central Ministry of Health procurement is maintained for some public health programmes (see section on Management of medicines, above). Accreditation is also an important tool for ensuring structural standards of health care. It is implemented by the Comisia Nationala de Acreditare a Spitalelor (National Commission for Hospital Accreditation) acting as an autonomous agency. Hospitals do not, however, receive specific funds for meeting accreditation requirements and doubts were raised as to the relevance of such a system if it is not linked to a comprehensive hospital master plan[33] that ensures the matching of epidemiological needs with the distribution of facilities and types of technology (for example, for the rapid diagnosis of MDR-TB).

Health information

The contract with the NHIH requires hospitals to collect and report quite a large amount of data documenting the services provided and reimbursable. It represents a big burden for the administration and competes with the collection and reporting of other data sets needed for the monitoring and evaluation of TB patients and the performance of NTP. Moreover, hospital records are not linked to records kept by family doctors. There is, however, a plan to introduce the unique integrated information system, which has components on finance, accounting, investments, purchase, payroll, buildings and maintenance.

Recommendations

Ministry of Health

1. The payment system under the NHIH should be revised so as to prevent unnecessary hospitalization of patients, promote administrative measures for TB infection control, ensure the appropriate distribution of laboratories and provide TB outcome-based incentives to family doctors in the package of minimum services currently under discussion.

[33] The National Hospital Rationalization Strategy in 2011 *(52)* was a first attempt to revise the current hospital capacity and reduce the size of some major facilities, but it was not carried out.

References

1. Plan to stop TB in 18 high-priority countries in the WHO European Region, 2007–2015. Copenhagen: WHO Regional Office for Europe; 2007 (http://www.euro.who.int/__data/assets/pdf_file/0005/68180/E91049.pdf, accessed 9 October 2014).
2. National plan for multidrug resistant TB prevention and management in Romania 2012–2015 [Planul National de Prevenire si Management al Tuberculozei Multidrog-rezistente in Romania 2012-2015]. Bucharest: Ministry of Health; 2012.
3. 2012 Demographic yearbook. New York: United Nations; 2013 (http://unstats.un.org/unsd/demographic/products/dyb/dybsets/2012.pdf, accessed 13 October 2014).
4. Country and lending groups [website]. Washington (DC): World Bank; 2013 (http://data.world bank.org/about/country-and-lending-groups#Upper_middle_income, accessed 9 October 2014).
5. Global tuberculosis report 2013. Geneva: World Health Organization; 2012 (http://apps.who.int/iris/bitstream/10665/91355/1/9789241564656_eng.pdf, accessed 9 October 2014).
6. UNAIDS report on the global AIDS epidemic 2013. Geneva: Joint United Nations Programme on HIV/AIDS; 2013 (http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf, accessed 9 October 2014).
7. Tuberculosis national strategic plan 2006–2010 [Strategia naţională pentru controlul tuberculozei în România 2006 – 2010]. Bucharest: Ministry of Health; 2006.
8. Ordin 422/2013 privind aprobarea Normelor tehnice de realizare a programelor naţionale de sănătate publică pentru anii 2013 şi 2014 [Order No. 422 of 29 March 2013 on Technical Norms of the National Public Health Programmes for 2013–2014]. Bucharest: Ministry of Health; 2013 (http://www.lege-online.ro/lr-ORDIN-422%20–2013-(146475).html, accessed 10 October 2014).
9. Coordinating Tuberculosis Control Efforts Workshop [website]. Bucharest: Embassy of the United States; 2014 (http://romania.usembassy.gov/policy/media/pr-03192013.html, accessed 3 December 2014).
10. Tuberculosis country profiles [website] (Romania). Geneva: World Health Organization; 2014 (http://www. who.int/entity/tb/country/data/profiles/en/index.html, accessed 9 October 2014).
11. Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant TB in the WHO European Region 2011–2015. Copenhagen: WHO Regional Office for Europe; 2011 (http://www.euro.who.int/__data/assets/pdf_file/0007/147832/wd15E_TB_ActionPlan_111388.pdf, accessed 9 October 2014).
12. Progress towards TB elimination in the EU [website]. Stockholm, European Centre for Disease Prevention and Control, 2014 (http://ecdc.europa.eu/en/healthtopics/Tuberculosis/progress-tb-elimination/Pages/index.aspx, accessed 30 December 2014).
13. The Global Plan to Stop TB 2006–2015 [website]. Geneva: World Health Organization; 2014 (http://www.who.int/tb/features_archive/global_plan_to_stop_tb/en/, accessed 14 October 2014).
14. National Reference Center (NRC) for Mycobacteria [website]. Borstel: Research Center Borstel, Leibniz-Center for Medicine and Biosciences; 2014 (http://www.fz-borstel.de/cms/en/science/ national-reference-center-for-mycobacteria.html, accessed 9 October 2014).
15. European TB Laboratory Initiative (ELI) core group members selected [website]. Copenhagen: WHO Regional Office for Europe; 2014 (http://www.euro.who.int/en/health-

topics/communicable-diseases/tuberculosis/news/news/2012/7/european-tb-laboratory-initiative-eli-core-group-members-selected, accessed 9 October 2014).
16. ERLN-TB [website]. Stockholm: European Centre for Disease Prevention and Control; 2012 (http://www.erlntb.eu/, accessed 9 October 2014).
17. Global Laboratory Initiative. Mycobacteriology laboratory manual, first edition. Geneva: World Health Organization; 2014 (http://www.stoptb.org/wg/gli/assets/documents/gli_ mycobacteriology_ lab_manual_web.pdf), accessed 9 October 2014).
18. Treatment of tuberculosis guidelines, fourth edition. Geneva: World Health Organization; 2010 (http://apps.who.int/iris/bitstream/10665/44165/1/9789241547833_eng.pdf?ua=1, accessed 9 October 2014).
19. Moonan PK, Weis SE. Caveat emptor? Meta-analysis of studies comparing self-observed therapy and directly observed therapy for tuberculosis. Clin Infect Dis. 2013;57(7):1062–3. doi: 10.1093/ cid/cit431.
20. Volmink J, Garner P. Directly observed therapy for treating tuberculosis (Review). Cochrane Database Syst. Rev. 2007;(4):CD003343 (http://www.thecochranelibrary.com/ userfiles/ccoch/ file/CD003343.pdf, accessed 9 October 2014).
21. Rapid advice: treatment of tuberculosis in children. Geneva: World Health Organization; 2010 (http://whqlibdoc.who.int/publications/2010/9789241500449_eng.pdf, accessed 3 December 2014).
22. Evoluția infecției HIV/SIDA în România – 31 decembrie 2013 [The evolution of the HIV/AIDS epidemic in Romania 31 December 2013]. Bucharest: National Institute for Infectious Diseases "Matei Bals", Monitoring and Evaluation Department; 2013 (http:// www.cnlas.ro/ images/doc/rom_31122013en.pdf, accessed 9 October 2014).
23. Buzducea D, Lazăr F. The access to antiretroviral therapy for people living with HIV in Romania. Copenhagen: United Nations Children's Fund and Bucharest: Uniunea Naţională a Organizaţiilor Persoanelor Afectate de HIV/SIDA [National Union of People Affected by HIV/AIDS]; 2011 (http://www.unicef.org/romania/The_access_to_antiretroviral_therapy. pdf, accessed 9 October 2014).
24. Evolution of HIV/AIDS infection in Romania 31 December 2012. Bucharest: National Institute for Infectious Diseases "Matei Bals", Monitoring and Evaluation Department; 2014 (http://cnlas.ro/images/doc/romania31dec2012eng.pdf, accessed 5 December 2014).
25. Asociatia Pentru Sprijinirea Pacienţilor cu Tuberculoză Multi-Drog Rezistentă [MDR-TB Patients Association – ASPTMR]. Mapping of Romanian TB patients' needs. Report. Bucharest: Romanian Angels Appeal; 2014.
26. Comunicat de presă 2 februarie 2012 privind rezultatele provizorii ale Recensământului Populaţiei şi Locuinţelor – 2011 [Press release of 2 February 2012 on the provisional results of the population and housing census – 2011]. Bucharest: Comisia Centrală Pentru Recensământul Populaţiei Şi Al Locuinţelor [Central Commission on the Population and Housing Census]; 2012 (http://www. recensamantromania.ro/wp-content/uploads/2012/02/ Comunicat_DATE_PROVIZORII_RPL_ 2011_.pdf, accessed 9 October 2014).
27. Roma and travellers [website]. Strasbourg: Council of Europe; 2014 (http://www.coe.int/t/ dg3/ RomaTravellers/Default_en.asp, accessed 9 October 2014).
28. Ionita M, Nastase M, Mihailescu T. Tuberculosis in a rural gypsy community – Romania. Eur Respir J. 2001;18(Suppl. 33):323s.
29. Romania. New developments, trends and in-depth information on selected issues. 2013 National report (2012 data) to the EMCDDA by the Reitox National Focal Point. Bucharest: Ministry of Internal Affairs; 2013 (http://www.ana.gov.ro/rapoarte%20 nationale/en/National%20Report%20 on%20Drugs%202013.pdf, accessed 9 October 2014).

30. Tubidu. Project description [website]. Tallinn: Tervise Arengu Instituut [National Institute for Health Development]; 2014 (http://www.tai.ee/tubidu/project-description, accessed 9 October 2014).
31. Ibraim E, Cioran N, Popescu N, Furtunescu F L. Approaching tuberculosis in a vulnerable group. Eur Respir J. 2012:40(Suppl. 56):2866 (http://erj.ersjournals.com/content/40/Suppl_56/P2866, accessed 9 October 2014).
32. Annual report 2008. Bucharest: Save the Children; 2008 (http://www.salvaticopiii.ro/upload/p00060005_Annual_Report_2008_Save_the_Children_Romania.pdf, accessed 8 November 2014).
33. UNIFARM [website]. Bucharest: C.N. Unifarm S.A.; 2014 (http://unifarmromania.ro/, accessed 13 October 2014).
34. ORDIN Nr. 1577 din 16 septembrie 2008 pentru aprobarea Normelor metodologice de implementare a Programului national de control al tuberculozei [Order No. 1577 of 16 September 2008 on Methodological norms for the implementation of the National Tuberculosis Programme]. Bucharest: Ministry of Health; 2008.
35. Evoluţia Tuberculozei În Anii 1999 – 2012 În România. Bucharest: Centrul Naţional de Statistică şi Informatică în Sănătate Publică [National Centre for Public Health Statistics and Informatics]; 2013 (http://www.ccss.ro/public_html/, accessed 9 October 2014).
36. Ghid metodologic de implementare a programului naţional de control al Tuberculozei 2007-2011 [Methodological guide for implementation of the national TB control programme 2007–2011] Bucharest: Ministry of Public Health; 2007.
37. Guidance on ethics of tuberculosis prevention, care and control. Geneva: World Health Organization; 2010 (http://whqlibdoc.who.int/publications/2010/9789241500531_eng.pdf?ua=1, accessed 16 October 2014).
38. International standards for tuberculosis care. Diagnosis, treatment, public health. Second edition. The Hague: Tuberculosis Coalition for Technical Assistance; 2009 (http://www.who.int/tb/ISTC_Report_2ndEd_Nov2009.pdf, accessed 16 October 2014).
39. The Patients' Charter for Tuberculosis Care. Viols-en-Laval: World Care Council; 2006 (www.who.int/tb/publications/2006/istc_charter.pdf, accessed 9 October 2014).
40. Stillo JJ. "All my problems started with tuberculosis:" an ethnographic analysis of treatment failure in Romania. Washington: IREX; 2012 (scholar research brief).
41. Medicamente-lipsa. In: Monitorizarea lipsei unor medicamente esentiale in Romania [Monitoring the lack of essential drugs in Romania] [website]. Bucharest: Medalert; 2012 (www.medicamente-lipsa.ro, accessed 13 October 2014).
42. Lipsa Tratament [website]. Bucharest: Romanian Angel Appeal; 2013 (www.lipsatratament.ro, accessed 13 October 2014).
43. Stop Stockouts [website]. Guateng: South Africa: Monitoring Essential Medicines Consortium; 2014 (www.stockouts.org, accessed 13 October 2014).
44. The use of bedaquiline in the treatment of multidrug-resistant tuberculosis. Interim policy guidance. Geneva: World Health Organization; 2013 (http://www.who.int/iris/bitstream/10665/84879/1/9789241505482_eng.pdf?ua=1, accessed 9 October 2014).
45. TimeBomb. Migrants to bring drug-resistant TB superbug to UK. The Sun. 29 April 2013 (http:// www.thesun.co.uk/sol/homepage/features/4861619/Time-Bomb-immigrants-to-bring-drug-resistant-TB-superbug-to-UK.html, accessed 9 October 2014).
46. Vladescu C, Scintee G, Olsavszky V. Romania: health system review. Health Systems in Transition. 2008;10(3):1–181 (http://www.euro.who.int/__data/assets/pdf_file/0008/95165/E91689.pdf, accessed 9 October 2014).

47. Holt E. Romania redrafts health-care law after violent protests. The Lancet. 2012;379 (9815):505 (http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(12)60214-1/fulltext, accessed 9 October 2014).
48. Dumitra G. Relation between GP network and National Control Programme of Tuberculosis. Bucharest: Asociatia Medicilor de Familie [National Society of Family Physicians]; 2014.
49. Practical Approach to Lung Health [web site]. Geneva: World Health Organization; 2013 (www.who.int/tb/health_systems/pal/en/, accessed 9 October 2014).
50. Clasificarea spitalelor [Classification of hospitals] [website]. Bucharest: Ministry of Health; 2011 (http://www.ms.ro/upload/CLASIFICAREA%20SPITALELOR-1.pdf, accessed 10 October 2014).
51. Ciutan M, Preda A, Chiriac ND, Dosius M, Vlădescu C. The evaluation of hospital services using after implementation of restructuring measures in Romania, May 2011. Management in health. 2012;16(4):13–23.
52. Hotărâre Nr. 303 din 23 martie 2011 pentru aprobarea strategiei naţionale de raţionalizare a spitalelor [Decision No . 303 of 23 March 2011 approving the national strategy for rationalization of hospitals]. Bucharest, Ministry of Health, 2014 (http://www.ms.ro/?pag=207, accessed 10 October 2014).
53. European health for all database (HFA-DB) [online database]. Copenhagen: WHO Regional Office for Europe; 2013 (http://data.euro.who.int/hfadb/, accessed 9 October 2014].
54. Clasificarea spitalelor din România [Classification of hospitals in Romania]. In: News [website]. Bucharest: Adevarul Holding; 15 June 2011 (http://adevarul.ro/news/eveniment/clasificarea-spitalelor-romania-1_50ad66317c42d5a663946acb/index.html, accessed 10 October 2014).
55. Raportul Comisei de Selectie a Unitatilor Sanitare cu paturi care nu pot incheia contracte cu Casele de Asigurari de Sanatate [Selection Committee report that sanitary units with beds may conclude contracts with health insurance funds] [web-page]. Bucharest: Ministry of Health; 2011 (www.ms.ro/documente/Anexa%201_485_962.doc, accessed 10 October 2014).
56. Lege nr.145 din 24 iulie 1997 Legea asigurărilor sociale de santate) [Law No. 145 of 24 July 1997 Health Insurance Law]. Bucharest: Ministry of Health; 1997.
57. Legea nr. 95/2006 privind reforma în domeniul sănătăţii [Law No. 95/2006 on health care reform. Bucharest: Ministry of Public Health; 2006 (http://codfiscal.net/act-pdf/legea-95-2006-reforma-domeniul-sanatatii-vconsolidata-05-01-2009.pdf, accessed 8 November 2014).
58. AHF calling for church and property restitution in Rumania [website]. Baltimore (MD): The American Hungarian Federation; 2013 (http://www.americanhungarianfederation.org/news_ rumania_churchconfiscation_kerry.html, accessed 9 October 2014).
59. Stan L. The roof over our heads: property restitution in Romania. Journal of Communist Studies and Transition Politics. 2006;22(2):180–205 (http://www.academia.edu/183374/The_Roof_over_ Our_Head_Property_Restitution_in_Romania, accessed 9 October 2014).
60. 2013 Country reports on Human Right Practices – Romania. In: Refworld [website]. Washington (DC): United States Department of State; 2014 (http://www.refworld.org/docid/53284a82b.html, accessed 9 October 2014).
61. World Health Statistics 2013. In: Global Health Observatory [website]. Geneva: World Health Organization; 2014 (http://www.who.int/gho/publications/world_health_statistics/2013/en/, accessed 10 October 2014).

62. OECDiLibrary [website]. Health at a glance: Europe 2012. 5.6 Financing of health care. Paris: Organisation for Economic Co-operation and Development; 2014 (http://www.oecd-ilibrary.org/ sites/9789264183896-en/05/06/index.html?contentType=%2fns%2fChapter%2c%2fns%2f StatisticalPublication&itemId=%2fcontent%2fchapter%2f9789264183896-56-en&mimeType=text %2fhtml&containerItemId=%2fcontent%2fserial%2f23056088&accessItemIds=, accessed 9 October 2014).
63. Mihaescu Pinta C. An update on the implementation of patient co-payments in Romania. Bucharest: Scoala Nationala de Sanatate Publica, Management si Perfectionare in Domeniul Sanitar [National School of Public Health, Management and Training in the Field of Health]; 2007 (http://www.assprocee2007.com/SeminarASSPROCEE2007MAY1618BudapestAbstractCPintia2.pdf, accessed 9 October 2014).
64. Lewis M. Informal payments and the financing of health care in developing and transition countries. Health Affairs. 2007;26(4):984–97.
65. Mathauer I Wittenbecher F. Hospital payment systems based on diagnosis related groups: experience in low- and middle-income countries. Bull World Health Organ. 2013;91:746–56 (http://www.who.int/bulletin/volumes/91/10/12-115931.pdf, accessed 9 October 2014).
66. Stancu E. Mass exodus: Why corruption in Romania's healthcare system is forcing its doctors to work abroad. The Independent. 2 January 2014 (http://www.independent.co.uk/news/world/europe/mass-exodus-why-corruption-in-romanias-healthcare-system-is-forcing-its-doctors-to-work-abroad-9035108.html, accessed 9 October 2014).
67. Chiscop E. Tackling the brain drain from Romania's health workforce. Problem analysis and policy recommendations. Revista Română de Bioetică [Romanian Journal of Bioethics]. 2013;11(3):92–106 (http://www.bioetica.ro/index.php/arhiva-bioetica/article/view/503, accessed 9 October 2014).
68. Vladescu C, Olsavsky V. Migration of nurses: the case of Romania. Management in health 2009;13:4 (http://journal.managementinhealth.com/index.php/rms/article/viewFile/91/187, accessed 9 October 2014).
69. Chiriac M. Brain drain of doctors worsens in Romania. In: BalkanInsight [website]. Sarajevo: Balkan Investigative Reporting Network; 6 October 2011 (http://www.balkaninsight.com/en/ article/more-romanian-doctors-go-abroad-for-better-pay, accessed 9 October 2014).
70. Borcean G. Doctors' emigration. Bucharest: Romanian College of Physicians; 2012 (http://www. ceom-ecmo.eu/sites/default/files/documents/doctors_emigration_in__romania_0.pdf , accessed 9 October 2014).
71. Romanian health service in crisis as doctors leave for UK and other states. The Guardian. 7 February 2014 (http://www.theguardian.com/world/2014/feb/07/romanian-health-service-crisis-doctors-uk, accessed 9 October 2014).

Annex 1

MEMBERS OF THE REVIEW TEAM

International

Pierpaolo de Colombani	Medical Officer, TB and M/XDR-TB Programme, WHO Regional Office for Europe, Copenhagen, Denmark *(Leader)*
Vahur Hollo	Tuberculosis Surveillance Officer, ECDC, Stockholm, Sweden
Niesje Jansen	Senior Nurse Consultant, ECDC, Stockholm, Sweden
Kristin Kremer	TB laboratory scientist, Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands
Soleil Labelle	Technical Officer, Global TB Programme, WHO headquarters, Geneva, Switzerland
Mavluda Makhmudova	Consultant, Global TB Drug Facility, Geneva, Switzerland
Oriol Ramis	Specialist in Community Medicine, Barcelona, Spain
Andreas Sandgren	TB expert, ECDC, Stockholm, Sweden
Jonathan Stillo	Anthropologist, City University of New York, United States
Nestan Tukvadze	Head of Research Unit, National Centre for Tuberculosis and Lung Diseases, Tbilisi, Georgia
Askar Yedilbayev	Medical Officer, Partners in Health, Boston, United States

National

Marlene Crişan Umbriţa	Manager, County TB Programme, Oradea
Manuela Gheorghiu	Manager, County TB Programme, Bucharest
Daniela Homorodean	National TB Reference Laboratory, Pulmonology Hospital, Cluj Napoca
Roxana Mindru	National TB Reference Laboratory, Marius Nasta Institute, Bucharest
Adriana Socaci	Manager, County TB Programme, Timis
Adriana Sorete	Manager, County TB Programme, Iasi
Victor Spanu	Chief, MDR-TB Department, Marius Nasta Institute, Bucharest
Cristina Vladu	RAA consultant

Other members

Cassandra Butu	National Professional Officer, WHO Country Office, Bucharest
Victor Olsavszky	Head, WHO Country Office, Bucharest
Mihaela Stefan	Project Coordinator, RAA Foundation, Bucharest

Interpreters

Cristina Enache
Ioana Pricop
Florin Rosu

Annex 2

PROGRAMME OVERVIEW

Sunday 9 March 2014

19.00–20.00 ▪ Meeting of the international reviewers

Monday 10 March

10.00–11.00 ▪ Briefing with Ministry of Health

11.30–13.00 ▪ Meeting with the NTP (all international and national reviewers): review of the agenda of visits/ meetings scheduled during the first week; TB epidemiology, the NTP structure, objectives, targets, management, progress; international funding

14.00–17.00 ▪ Meeting with the NTP (continued) ▪ Marius Nasta Institute

17.00 Departure of Field Team 1, Field Team 3 and Field Team 4

Tuesday 11–Friday 14 March. Field work

Saturday 15 March

Discussion of the field work: presentation by each field team and discussion in plenary; review of the agenda of visits/meetings scheduled during the second week; distribution of experts (international and national) for the visits/meetings and into groups working around the thematic areas and chapters of the final review report; finalization and circulation of each field team report. Venue: Marius Nasta Institute

Monday 17 March

09.00–13.00 ▪ Save the Children Project ▪ Drug Users Centre ▪ HIV Clinic, Matei Bals Institute ▪ Family physician's office ▪ NHIH ▪ Marius Nasta Institute

14.30–16.45 ▪ Pulmonology dispensary Sector 2 ▪ Marius Nasta Institute

17.00–18.00 Wrap up: conclusions and recommendations. Venue: Marius Nasta Institute

Tuesday 18 March

09.00–12.00 ▪ Jilava Prison ▪ Victor Babes Hospital of Infectious and Tropical Diseases ▪ Marius Nasta Institute

14.00–16.45 ▪ Drug Regulatory Agency and Central Drug Warehouse ▪ International Organization for Migration, United Nations High Commissioner for Refugees ▪ Parliamentary Commission for Health ▪ National Association of Primary Physicians ▪ Marius Nasta Institute

17.00–18.00 Wrap up: conclusions and recommendations. Venue: Marius Nasta Institute

Wednesday 19 March

09.00–10.30 ▪ Ministry of Justice, National Administration of Penitentiaries

09.30–10.30 ▪ Nurses and Midwives Association

▪ Ministry of European Funds

10.00–11.00 ▪ National Public Health Institute

10.30–12.00				▪ Ministry of Health, Department for Structures and Department for Central Procurement
11.00–12.00	▪ Prime Minister Counsellor for Health	▪ University Medicine, Department of Pneumology	▪ TB children's hospital	
14.00–16.45	▪ Roundtable with main nongovernmental organizations and civil society: CHPS, UNOPA, Filantropia Foundation, Association for Supporting MDR TB Patients, RAA, Romanian Harm Reduction Network, Romanian Orthodox Church, Save the Children, Society of Medical Students, United States Embassy Venue: National Institute of Public Health		▪ Marius Nasta Institute	
17.00–18.00	Discussion of main findings and recommendations. Venue: National Institute of Public Health			

Thursday 20 March

09.00–20.00 Discussion of main findings and recommendations, logistics and future coordination. Venue: Marius Nasta Institute

Friday 21 March

09.00–10.30 Debriefing with the Minister of Health: main findings and recommendations of the review

Annex 3

FIELD TEAMS: PROGRAMMES

Field team 1 (Brasov, Mures, Cluj, Bihor)
P de Colombani (Coordinator), S Labelle, O Ramis, D Homorodean, M Crisan, C Enache (Interpreter)

Tuesday 11 March	Brasov county. **Brasov** town: Pulmonology Dispensary, TB Laboratory,
09.00 – 16.00	Pulmonology Hospital. **Feldioara** village: family doctor
Wednesday 12 March	Mures county. **Targu Mures** town: Pulmonology Dispensary,
09.00 – 16.30	Pulmonology Hospital, Infectious Diseases Hospital
Thursday 13 March	Cluj county. **Cluj-Napoca** town: Pulmonology Dispensary, Roma
09.00 – 16.00	mediator, Pulmonology Hospital, National TB Reference Laboratory. **Savadisla** village: TB sanatorium
Friday 14 March	Bihor county. **Oradea** town: Pulmonology Dispensary, TB Laboratory,
09.00 – 17.00	Pulmonology Hospital, Municipality Hospital

Field team 2 (Prahova, Buzau, Calarasi, Constanta, Dambovita)
A Sandgren (Coordinator), N Tukvadze, N Jansen, M Gheorghiu, C Vladu

Tuesday 11 March	Prahova county. **Ploiesti** town: Pulmonology Dispensary. **Floresti**
08.00 – 18.00	village: TB sanatorium. Dambovita county. **Moroeni** village: TB sanatorium
Wednesday 12 March	Buzau county. **Buzau** town: Pulmonology Dispensary, Pulmonology
09.00 – 17.30	Hospital. **Smeeni** village: family doctor. **Pogoanele** village: Pulmonology Dispensary
Thursday 13 March	Calarasi county. **Calarasi** town: Pulmonology Dispensary,
08.30 – 17.00	Pulmonology Hospital. **Roseti** village: family doctor. **Obor** village: community centre, Roma community
Friday 14 March	Constanta county. **Constanta** town: Pulmonology Hospital,
09.00 – 17.00	Pulmonology Dispensary, TB Laboratory. **Poarta Alba** village: prison hospital

Field team 3 (Vaslui, Iasi, Suceava, Neamt)
A Yedilbayev (Coordinator), M Makhumodova, J Stillo, A Sorete, R Mindru, M Stefan

Tuesday 11 March	Vaslui county. **Barlad** town: Pulmonology Dispensary, Pulmonology
08.00 – 17.30	Hospital. **Perieni** village: family doctor. Village of **Stefan Cel Mare** town: Pulmonology Hospital
Wednesday 12 March	Iasi county. **Iasi** town: University of Medicine, Pulmonology
08.00 – 16.00	Department; Pharmaceutical Industry "Antibiotice"; Pulmonology Hospital
Thursday 13 March	Suceava county. **Suceava** town: Pulmonology Hospital, Pulmonology
09.00 – 14.00	Dispensary
Friday 14 March	Neamt county. **Bisericani** town: MDR-TB Hospital; **Piatra Neamt**
09.00 – 17.00	town: Pulmonology Dispensary

Field team 4 (Arges, Vilcea, Timis, Gorj, Teleorman)
V Hollo (Coordinator), K Kremer, A Socaci, V Spanu, F Rosu (interpreter)

Tuesday 11 March	Arges county. **Pitesti** town: Pulmonology Dispensary
08.00 – 17.00	Vilcea county. **Vilcea** town: Pulmonology Dispensary
	Mihaesti village: Pulmonology Hospital, family doctor
Wednesday 12 March	Timis county. **Timisoara** town: Pulmonology Hospital, Infectious
08.00 – 13.30	Diseases Hospital

Thursday 13 March 09.00 – 16.00	Gorj county. **Targu Jiu** town: Pulmonology Dispensary, Pulmonology Hospital. **Runcu** village: family doctor
Friday 14 March 08.30 – 17.00	Teleorman county. **Rosiorii de Vede** town: Pulmonology Dispensary, Pulmonology Hospital

Annex 4

PEOPLE INTERVIEWED

BUCHAREST

Drug Regulatory Agency and Central Drug Warehouse

Nicolae Fotin	Pharmacist
Felicia Marinescu	Pharmacist

Hospital of Infectious and Tropical Diseases "Victor Babes"

Olimpia Nicolaescu	Infectious diseases physician
Cristiana Oprea	Infectious diseases physician

Jilava Prison

Liliana Ilasi	Physician

Institute for Infectious Diseases "Matei Bals"

Mariana Mardarescu	National HIV/AIDS Focal Point
Adrian Streinu Cercel	National HIV/AIDS Programme Manager

International agencies

Peter Wijninga	United Nations High Commissioner for Refugees
Mircea Mocanu	International Organization for Migration
Hilde Berit Eide	Counsellor EEA and Norway Grants
Kendra Pace	United States Embassy
Victor Stefan Olsavszky	Head, Country Office, WHO
Cassandra Andreea Butu	National Professional Officer, Country Office, WHO

Medical Association of Family Physicians

Sanda Adalgiza	Vice President
Gindrovel Dumitra	Family physician

Ministry of Health

Nicolae Banicioiu	Minister of Health
Alexandru Rafila	Personal Counsellor to the Minister of Health
Amalia Serban	Deputy Director, Directorate of Strategies in Public Health
Iuliu Todea	Counsellor
Michaela Bardos	Director, Agency of Public Health Programmes
Marieta Bardut	Department of Health Structures

Ministry of European Funds

Daniela Tala	Programmes Coordinator

Ministry of Justice (National Administration of Penitentiaries)

Lucia Mihailescu	Physician

National Health Insurance House

Anci Popescu	Chief Medical Officer
Gheorghe Radu Ţibichi	President

National Institute of Public Health

Adriana Pistol	Director
Odette Popovici	Epidemiologist

Marius Nasta National Institute of Pulmonology

Ioan Cordos	Director
Gilda Popescu	Pulmonology physician and Manager of the NTP
Mariana Andrei	Project Coordinator for the NTP
Domnica Chiotan	Pulmonology physician and expert on TB surveillance for the NTP
Andreea Dumitrescu	Psychologist
Roxana Mindru	Director of laboratory and of the National TB Reference Laboratory
Cristian Popa	Pulmonology physician and infection control expert for the NTP
Cristina Popa	Pulmonology physician and MDR-TB expert for the NTP
Ruxandra Spataru	Head of the Paediatrics Department and expert on TB in children and drug management for the NTP
M/XDR-TB patients	Focus group with five men and two women aged 18–57 years undergoing M/XDR-TB treatment in the Marius Nasta Institute

Nongovernmental organizations

Catalina Constantin	President, Association for MDR-TB Patient Support
Stefan Radut	Vice-President, Association for MDR-TB Patient Support
Marian Ursan	President, Carusel Association
Silvia Asandi	General Manager, RAA Foundation
Mihaela Stefan	Project Coordinator, RAA Foundation
Maria Georgescu	President, Romanian Anti-AIDS Association
Dana Farcasanu	Executive President, Centre for Health Policies and Services
Dorel Nicolae Motoc	Executive Director, Filantropia Federation
Valentin Simionov	Director, Romanian Harm Reduction Network
Marius Dumitru	President, Romanian TB Patients' Association
Daniela Ilascu	Project Coordinator, Impreuna Invingem Tuberculoza
Catalina Zaharia	Project Coordinator, UNOPA
Leonard Andreescu	Child protection expert, Save the Children
Anca Stamin	Project Coordinator, Save the Children
Radu Neuman	Patriarchal Counsellor Coordinator, Orthodox Church

Nurses and Midwives Association

Mircea Timofte	President

Parliamentary Commission for Health

Nassar Rodica	President
Cristian Horia	Vice-President
Irimie Vicenţiu-Mircea	Vice-President
Popescu Dumitru-Iulian	Vice-President
Buicu Corneliu-Florin	Member
Roşca Lucreţia	Member
Bîrsăşteanu Florică	Member
Rădulescu Constantin	Member
Uioreanu Elena-Ramona	Member

Prime Minister's Counsellor for Health

Vasile Cepoi	Physician

Pulmonology Dispensary Sector 2

Adrian Stefanescu	Pneumology physician

University of Medicine "Carol Davila"

Miron Bogdan	Pneumology physician, Professor, Department of Pneumonology
Florin Mihaltan	Pneumology physician, Professor, Department of Pneumonology
Florentina Furtunescu	Public health expert, Professor, Department of Public Health

COUNTIES

Arges

Marioara Micu	TB County Coordinator, Pulmonology Dispensary, Arges

Bihor

Marilena Umbrita Crisan	TB County Coordinator, Pulmonology Dispensary, Oradea
Marcela Vigdorovici	Director, Pulmonology Dispensary, Oradea
Cornelia Barbulescu	Director Nurse (Assistant), Pulmonology Dispensary, Oradea
Ecaterina Berinde	Statistician, Pulmonology Dispensary, Oradea
Daniela Rahota	Director, Public Health County, Bihor
Diana Moldovan	Pulmonologist, Pulmonology Hospital, Oradea
Natalia Zaporojan	Head, TB laboratory, Pulmonology Hospital, Oradea
Marilena Umbrita Crisan	Head, Paediatrics Department, Municipal Hospital, Oradea
Claudia Cladovan	Director, Municipal Hospital, Oradea
Anca Brad	Head, Financial Department, Municipal Hospital, Oradea

Buzau

Elena Brâncuş	TB County Coordinator, Pulmonology Dispensary, Buzau
Cornelia Neagu	Family physician

Brasov

Carmen Tania Macavei	TB County Coordinator, Pulmonology Dispensary, Brasov
Corin Olimpia	Director, Pulmonology Dispensary, Brasov
Ionela Sorina Muntean	Head, TB Laboratory, Pulmonology Dispensary, Brasov
Elena Barbu	Head, Paediatrics Department, Pulmonology Hospital, Brasov
Gabriela Proca	Epidemiologist, Pulmonology Dispensary, Brasov
Dan Moraru	Director, Pulmonology Hospital, Brasov
Elena Bodean	Family doctor, Feldioara
TB patients	Interview with one man and one woman undergoing treatment for TB in the Pulmonology Hospital, Brasov

Calarasi

Spiridon Dumitrescu	TB County Coordinator, Pulmonology Dispensary, Calarasi
Iuliana Nicolae	Laboratory physician
Dan Nitulescu	Pulmonology physician

Cluj

Vasile Muresan	Director, Pneumology Hospital, Cluj
Mihaela Cirstoniu	Manager, County TB Programme, Cluj

Mirela Stoian	Epidemiologist
Carmen Monica Pop	Professor, University of Medicine Cluj Napoca
Marioara Simon	Bronchology Department
Daniela Homorodean	Director, NRL Cluj
Andreea Melinda Jodal	NRL Cluj
Liliana Paduraru	Director, Savadisla Sanatorium
Rodica Cretiu	Pulmonologist, Savadisla Sanatorium

Constanta

Elena Dantes	TB County Coordinator, Pulmonology Dispensary, Constanta
Oana Cristina Arghir	Pulmonology physician
Emanoil Vasiliu	Pulmonology physician

Dambovita

Virginia Dumitrescu	Manager, County TB Programme, Dambovita

Gorj

Maria Popescu	Manager, County TB Programme, Gorj

Iasi

Traian Mihaescu	Pulmonology physician
Adriana Sorete Arbore	Manager, County TB Programme, Iasi
Mihaela Diculencu	Head of laboratory, laboratory physician
M/XDR-TB patients	Focus group with four men aged 40–50 years undergoing M/XDR-TB treatment in the Pulmonology Hospital, University of Medicine, Iasi
TB patients	Interview with two men in early to mid-twenties, one with indicative and the other with confirmed TB, admitted to the Pulmonology Hospital, University of Medicine, Iasi
TB patients	Interview with one man and one woman undergoing outpatient TB treatment in the Pulmonology Hospital, University of Medicine, Iasi

Mures

Mihaela Patraulea	Manager, County TB Programme, Mures
Lilla Lorinczi	Professor (Conferentiar) University of Medicine Targu Mures, TB laboratory director
Monica Ianosi	Pulmonologist, Pneumology Hospital
Carmen Chiriac	Professor (Conferentiar), University of Medicine Targu Mures, Director of HIV Regional Centre Mures
TB patient	Interview with one man undergoing treatment for TB in the Pulmonology Hospital, Targu Mures

Neamt

Elena Botezatu	Manager, County TB Programme, Neamt
Victor Kilileanu	Pulmonology physician
M/XDR-TB patients	Interview with one man and three women aged 34–59 years undergoing M/XDR-TB treatment in the MDR-TB Hospital, Bisericani

Prahova

Dana Bolgiu	TB County Coordinator, Pulmonology Dispensary, Prahova

Suceava

Maria Muha	TB County Coordinator, Pulmonology Dispensary, Suceava

Teleorman

Mihail Năstăsescu	TB County Coordinator, Pulmonology Dispensary, Teleorman
Silvia Ghetu	Pulmonology physician
Rodica Niculescu	Pulmonology physician
Ionela Neagu	Pulmonology physician

Timis

Adriana Socaci	TB County Coordinator, Pulmonology Dispensary, Timis
Dorin Vancea	Pulmonology physician
Voicu Tudorache	Pulmonology physician
Adriana Dan	Pulmonology physician
Camelia Nita	Pulmonology physician
Minerva Gherman	Chemist

Vaslui

Cristina Barbu	TB County Coordinator, Pulmonology Dispensary, Vaslui

Valcea

Cornelia Vultur	TB County Coordinator, Pulmonology Dispensary, Valcea
Viorica Mincu	Pulmonology physician
TB patients	Interview with three men undergoing TB treatment in the Mihaesti Pulmonology Hospital
TB patient	Interview with one man undergoing TB outpatient treatment by the family doctor in Mihaesti village

Annex 5

EPIDEMIOLOGICAL IMPACT ASSESSMENT

As part of the review, and in view of the requirements to apply to the Global Fund New Funding Mechanism, a specific assessment was conducted to understand the current national TB surveillance and vital registration systems with regard to their capacity to measure the levels of and trends in TB epidemiology in Romania. The checklist and user guide from the WHO Global Task Force on TB Impact Measurement was used for this assessment.

Of the 10 standards and associated benchmarks recommended by WHO, six were completely met, three were partly met and one standard could not be assessed. None of the three supplementary standards were met (Table 5.1).

Table 5.1. Performance against WHO standards and benchmarks for assessing TB surveillance system, Romania, 2014

Standard		Met	Partly met	Not met	Not applicable
No.	Name				
B1.1	Case definitions are consistent with WHO guidelines	X			
B1.2	TB surveillance system is designed to capture a minimum set of variables for all reported TB cases	X			
B1.3	All scheduled periodic data submissions have been received and processed at national level (not applicable to web-based reporting)				X
B1.4	Data in quarterly reports (or equivalent) are accurate, complete and internally consistent (for paper-based systems only)				X
B1.5	Data in the national database are accurate, complete, internally consistent and free of duplicates (F electronic case-based or patient-based systems only)	X			
B1.6	TB surveillance data are externally consistent	X			
B1.7	TB surveillance data are internally consistent over time	X			
B1.8	All diagnosed cases of TB are reported		X		
B1.9	Population has good access to health care		X		
B1.10	Vital registration system has high national coverage and quality[a]				X
B2.1	Surveillance data provide a direct measure of drug-resistant TB in new cases			X	
B2.2	Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases			X	
B2.3	Surveillance data for children reported with TB are reliable and accurate, and all diagnosed childhood TB cases are reported			X	

[a] Not assessed during the review.

To be sure that the national TB surveillance and vital registration systems provide reliable data, some improvements should be considered.

- A data dictionary should be compiled for the National TB Registry and standard operating procedures for data quality assurance at all levels of reporting.
- The structure of the national TB database should be upgraded and its user manual updated.
- Reports should be published on data quality and surveillance evaluations.

- The completeness of TB reporting should be directly assessed using the recommended WHO guidelines.
- Health care services should be strengthened, through long-term planning for increased funding and the recruitment and retention of well-trained staff.
- All MTB strains should be routinely tested for drug resistance.
- HIV testing and counselling should be given to all patients with presumptive or diagnosed TB.
- Possible misdiagnosed cases of TB in children should be investigated and feedback given to health workers on the TB diagnosis.

Standard B1.1. Case definitions are consistent with WHO guidelines.

Benchmarks (all to be satisfied).

- *Laboratory-confirmed cases are distinguished from clinically diagnosed cases.*
- *New cases are distinguished from previously treated cases.*
- *Pulmonary cases are distinguished from extrapulmonary cases.*

The electronic case-based TB surveillance system in Romania was introduced as a pilot project in 2005 and implemented countrywide in 2006. Reporting takes place at the county and district (dispensary) level. Pulmonary TB cases are distinguished from extrapulmonary cases. Case classification is consistent with the EU case definition and WHO's new case definition, that is, culture-confirmed, smear-positive and clinical cases are differentiated. A difference is made between new and retreatment cases. A further distinction is made for retreatment cases with previous failures and previous cases lost to follow-up. All three benchmarks, and therefore the standard, are met.

Standard B1.2. TB surveillance system is designed to capture a minimum set of variables for all reported TB cases.

Benchmarks.

- *Data are routinely collected for at least each of the following variables for all TB cases: (i) age or age group; (ii) sex; (iii) year of registration; (iv) bacteriological results; (v) history of previous treatment; (vi) anatomical site of disease; (vii) a patient identifier (for case-based systems only).*

Data are routinely captured by programme recording and reporting (reporting is mandatory within 48 hours after diagnosis). The information on age, sex, year of registration and all three case types (new, pulmonary and laboratory-confirmed) and patient identifier are reported. The standard is met.

Standard B1.3. All scheduled periodic data submissions have been received and processed at national level (for electronic systems that import data from subnational feeder systems).

Dispensaries, laboratories, health care facilities and other providers inside and outside the NTP enter their individual TB case records directly into a national database. The standard is not applicable.

Standard B1.4. Data in quarterly reports (or equivalent) are accurate, complete and internally consistent (for paper-based systems only).

The standard is to be applied to paper-based systems only. The standard is not applicable.

Standard B1.5. Data in the national database are accurate, complete, internally consistent and free of duplicates (for electronic case-based or patient-based systems only).

Benchmarks: all benchmarks should be met to reach this standard.

- *Data validation checks are in place at the national level to identify and correct invalid, inconsistent and/or missing data in the minimum set (standard B1.2).*
- *For each variable in the minimum set (standard B1.2), >90% of case records are complete, valid and internally consistent for the year being assessed.*
- *Less than 1% of case records in the national dataset for the year being assessed are unresolved potential duplicates.*

Data validation checks are conducted monthly by TB county managers and daily, quarterly and annually by the National TB Register central unit. Database completeness needs to be improved, especially for DST data and HIV test results. Data completeness for the minimum set of variables is high, the registration year is mandatorily variable, therefore reported 100%; in fewer than 0.1% of cases is the age unknown; only three cases are recorded with unknown gender; microscopy test results are available for 98% of pulmonary cases; culture results are missing for 12% of all reported cases in 2012. The national identity number works well for avoiding and checking the duplicates. There are very few people without national identity numbers (0.5%). Database completeness needs to be improved for culture results. The standard is partly met.

Standard B1.6. TB surveillance data are externally consistent.

Benchmark.

- *Among new TB cases, the percentage of children diagnosed with TB is between 5% and 15% in low- and middle-income countries, and <10% in high-income countries*

In Romania, 5.2% of reported TB cases are among children based on 2012 data. The standard for low- and middle-income countries is met.

Standard B1.7. TB surveillance data are internally consistent over time.

Benchmarks. If vital registration data are available, the following benchmark should be satisfied for this standard to be met.

- *Year-on-year change in the national number of reported TB cases is consistent with the year-to-year change in national TB mortality (HIV-negative, from national vital registration), that is trajectories with the same direction.*

Year-on-year change in rates 2003–2012 in the National TB Registry and mortality data from the Romanian Vital Registry are mutually consistent with the mean annual change of percentage –6.0% and -5.9%, respectively. The standard is met.

Standard B1.8. All diagnosed cases of TB are reported.

Benchmarks (all to be met).

- *TB reporting is a legal requirement.*
- *≥90% of TB cases are reported to national health authorities, as determined by a national-level investigation (such as an inventory study conducted in the past 10 years).*

In Romania, notification of TB cases has been mandatory since 1965. All forms of TB are notifiable by physicians under the technical norms of the National Public Health Programmes for 2013–2014. Countrywide aggregated data have been available since 1965 and case-based data since 1995.

The Technical Assistance and Management Unit of the NTP uses inventory methods to assess whether all cases of TB are reported to the NTP, comparing with other data sources such as the laboratory database, individual patient records and local TB registers. The results of the inventory studies are not, however, available. The standard is partly met.

Standard B1.9. Population has good access to health care.

Benchmarks (all to be met).

- *Under-five mortality rate (probability of dying by age 5 per 1000 live births) is <10 per 1000 live births.*
- *Out-of-pocket expenditure is less than 25% of total health expenditure.*

According to WHO data, the under-five mortality rate was 33/100 000 population in 2012. A rate under 10/100 000 demonstrates good access to health care. The WHO national health account database reports that out-of-pocket payments represented 21% of total health expenditure in 2009 (most recent available data)[1] (benchmark satisfied). The standard is partly met.

Standard B1.10. Vital registration system has high national coverage and quality.

Benchmarks (both to be met).

- *Cause of death documented in ≥90% of total deaths is recorded in: (a) the national vital registration system or (b) the sample vital registration system.*
- *<10% of deaths have ICD codes for ill-defined causes (defined as ICD-9 780–799 and ICD-10 R00–R99).*

The assessment of this standard was beyond the scope of the NTP review and it was not, therefore, assessed.

[1] WHO Global health expenditure atlas. Geneva: World Health Organization; 2012 (http://apps.who.int/nha/atlas final.pdf, accessed 19 October 2014).

Standard B2.1. Surveillance data provide a direct measure of drug-resistant TB in new cases.

Benchmarks (only one benchmark to be met).

- *Rifampicin susceptibility status (positive/negative) is documented for ≥75% of new pulmonary TB cases.*
- *Rifampicin susceptibility status (positive/negative) is documented for a nationally representative drug resistance survey of new pulmonary TB cases.*

Of 11 416 previously untreated pulmonary TB cases reported in 2012, 3856 (34%) had DST results available for rifampicin. The last nationally representative drug resistance survey was in 2004 and another is currently in progress, with results expected by the end of 2014. The standard has not been met.

Standard B2.2. Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases.

Benchmarks (only one benchmark to be met).

- *HIV status (positive/negative) is documented for ≥80% of all notified TB cases.*
- *HIV status is available from a representative sample from all TB cases notified in settings with a low-level epidemic state or where it is not feasible to implement routine surveillance.*

Of 18 197 TB cases reported in 2012, 9922 (54%) had a documented HIV status. No representative HIV status surveys have been carried out in the last five years. The standard has not been met.

Standard B2.3. Surveillance data for children reported with TB are reliable and accurate, and all diagnosed childhood TB cases are reported.

Benchmarks (both to be met).

- *The ratio of the groups aged 0–4 years to 5–14 years is in the range 1.5–3.0.*
- *≥90% of childhood TB cases are reported to national health authorities, as determined by a national-level investigation (such as an inventory study, conducted in the past 10 years).*

Of the 718 child TB cases (under 15 years) reported in 2012, 271 were below five years and 447 over five years. The ratio of the groups aged 0–4 years to 5–14 years was 0.6, below the standard. Possible over- or under-diagnoses should be investigated by an inventory study. The standard has not been met.

Annex 6

PROFILES OF PATIENTS INTERVIEWED

The review team held two focus groups (at the Marius Nasta Institute in Bucharest and the Pulmonology Hospital of the University of Medicine in Iasi) and interviewed 15 TB and MDR-TB patients (in Brasov, Iasi, Mures, Neamt and Vilcea). Patients were selected according to their TB condition and their availability. After they gave their informed consent to participate in the focus groups or interview, the staff of the facility were asked to leave and the dialogue was conducted in Romanian with interpretation from/to English. Below are some of the stories collected.

Dona is a 25-year-old woman coming to hospital for DOT. She is in the continuation phase of her MDR-TB treatment. In the past she had moved from her village to town for her undergraduate and postgraduate education and then found a job with a private call centre working for a multinational company. Many months ago, after coughing for more than a week, she saw her family doctor, who prescribed her some antibiotics; she did not improve so her doctor decided on a chest X-ray, which showed some shadows indicative of lung cancer or TB. One of her uncles died of MDR-TB 10 years ago and another has been treated for MDR-TB. However, Dona has a different drug susceptibility pattern from that of her uncle, and thinks she has caught TB from customers during her work or in the dormitory of her university where she sometimes slept in the past. Dona began treatment on first-line drugs and started to feel better; after her DST showed resistance to isoniazid and rifampicin, amikacin was added to her treatment (no fluoroquinolones) to which she became soon resistant. At this point, her doctor decided to include her in the GLC cohort, which made it possible to expand her treatment regimen with capreomycin and a fluoroquinolone. Treatment has been difficult for Dona: she has had gastritis and pain in her tendons, dizziness after taking her pills and has experienced depression: *"I didn't have any friends. I had my laptop and the internet"*. Because of the painful injections and buzzing in her ears, Dona has decided to discontinue capreomycin. She is now back living with her boyfriend and his family; she receives 80 Leu (about €18) per month in food vouchers and psychological support from UNOPA/ASPTMR through telephone counselling. She is very positive about her food vouchers: *"Food vouchers were included in my job benefits, I feel now like I am still working".* Dona wants to return to work as soon as she can and says that some of her friends and work colleagues know that she has TB.

Adrian is a 28-year-old man coming to hospital for DOT. He is the father of an eleven-month-old baby. Before his sickness, he was working in a firm managing EU-funded projects. The first symptom that Adrian paid attention to was coughing blood: he immediately went to the emergency room of his hospital and was admitted. Adrian was very afraid of catching MDR-TB from other patients and left the hospital after only 10 days. He is smear- and culture-negative and his doctor describes him as very cooperative; his family and friends are not stigmatizing him because of the disease. He badly wants to go back to his office, from where he can reach the hospital in only five minutes and receive DOT there every day.

Sorin and Dan are brothers and were admitted together to the county pulmonology hospital. Sorin is in his late twenties. He had been admitted to hospital five weeks earlier after suffering respiratory symptoms for a long time and weight loss. He is smear-positive and was treated with

first-line anti-TB drugs while waiting for the DST results. His lungs are badly damaged. The investigation of Sorin's close contacts resulted in his younger brother Dan and their father being admitted to hospital. Dan is smear-negative and had never had symptoms, unlike their father **Dorel**, who was treated several times in the past for XDR-TB and lost to follow-up. Dan is waiting for the results of his sputum culture. Dorel is hospitalized in an external section of the same county hospital. He is annoyed at being brought back to hospital after his son was diagnosed with TB because he does not live with him or see him much; he is also sputum-negative. Dorel thinks his elder son is spending too much time in the bar drinking beer and was infected with TB there. He does not intend to stay in hospital much longer because he is sputum smear-negative. His bacteriological culture documented resistance to many drugs and he was offered treatment as part of the GLC cohort at the MDR-TB Hospital in Bisericani. However he refused: *"That hospital is too far and too expensive to go to"*. Dorel is sharing a room with three other middle-aged male patients with "chronic" TB (that is, with pre-XDR or XDR-TB): one excluded from the GLC cohort and treated with only pyrazinamide; one with pre-XDR-TB resistant to fluoroquinolones (who complained to the review team that the law has changed and TB is no longer recognized as a condition for a disability pension); and one with impaired hearing and a possible psychological disorder who was unable to understand and participate in the discussion.

Elena is a 34-year-old woman from a small remote village with the nearest family doctor 20 km away. Elena only has a sixth grade education and was living from the food she managed to grow and a small social pension given by the local mayor's office. Her home lacks running water and sanitation and is heated by a wood stove. Elena's husband left her some time ago and her four children (aged 5–14 years) had to be sent to live with her brother following her diagnosis since both her parents died two years ago. She was found with TB during a prenatal visit and admitted to the county hospital where, after treatment with first-line anti-TB drugs, it was found that she had MDR-TB. She was enrolled in the GLC cohort and sent to Bisericani Hospital where after two months, a second culture unfortunately found that she had XDR-TB. The long time it took to be diagnosed and the indefinite nature of her hospitalization have been difficult for her. She misses her children and badly wants to go home, but she also says that if there was a possibility to receive a better treatment, she would even move to Bucharest.

Grigore is a 59-year-old man. He is a machinist and was diagnosed with TB as part of an annual screening at work. His first TB diagnosis and treatment was in 2007. In 2009, he was admitted again to the local hospital, where he spent 12 months before being referred to Bisericani Hospital in June 2010. Sent home, he stopped his continuation phase treatment. He again felt ill, was admitted to hospital and found to have highly infectious XDR-TB (sputum smear 3+ at direct microscopy). Grigore's wife left him in 2008 because of his TB. He discontinued his TB treatment several times because of adverse drug reactions and a lack of support and supervision. Grigore lives in a large county with few family doctors, where most TB patients self-administer the drugs they collect once a month from the pulmonology dispensary, including their injectable medications.

Tudor is a 51-year-old German/Romanian man. Tudor said after he developed TB, he became homeless. He worked as a carpenter, including for five years in a workshop in Germany: *"My life was beautiful before I got get TB. I had friends and family. Now I have nothing"*. Tudor was firstly diagnosed with TB and treated in 2005. Then he was diagnosed with MDR-TB in 2008, enrolled in the GLC cohort and treated at Bisericani Hospital. He continued his treatment in a special social-medical centre designed specifically for pulmonology patients and offering many

leisure activities, the only one of its kind in Romania. Today, Tudor is on his third treatment course for TB and second treatment course for MDR-TB, having relapsed multiple times. He has chronic pancreatitis and kidney problems and recently refused capreomycin because of the painful nodes at the place of the intramuscular injections. Tudor is looking forward to continuing his treatment in the social-medical centre, but after this, he will, as before, have to go back to living on the street. He is convinced that this was the cause of his relapses.

Nicolae is a 26-year-old man whose mother died when he was 18 years old, most probably due to MDR-TB. He was twice sent to a sanatorium for children during his mother's relapses, where he received four months' isoniazid preventive treatment. He shares an apartment in Bucharest with a roommate. He is trained as a psychologist and owns a media company which used to collaborate with a major Romanian TV station. Nicolae started to cough a lot, to have fever and nausea from any smell. After five months, he went to a private hospital for some tests, was referred to the Marius Nasta Institute with presumptive TB and was found with MDR-TB. Nicolae's media company, very successful in the past, now exists in name only. All his friends have disappeared. After three months in hospital, he wants to continue his treatment at home but he is also concerned to return to work, which will not be possible if he has to come to the dispensary daily for treatment. The best would be to work and to take the pills himself. Nicolae complains about the monotony and poor quality of food in hospital (boiled potatoes and chicken, no fresh fruit and vegetables), and how ancillary drugs to treat adverse reactions from MDR-TB treatment have to be paid for by the patients if they are outside hospital. Nicolae considers that TB patients should receive the same support as PLHIV, such as a disability pension and other benefits, including free public transport.

Stefan is a 22-year-old man who was previously living and working in a factory in Germany. He managed to save enough money to buy an apartment, took classes at the university and was going to return to Germany for another work contract, this time a longer-term one requiring a medical certificate. The chest X-ray revealed a large shadow and doctor wanted to hospitalize him; Stefan looked for other doctors but after two months and two haemoptysis, he started treatment for TB, initially as an ambulatory patient. Eventually, he was admitted to hospital weighing 69 kg weight (he now he weighs 94 kg). He thinks he got his XDR-TB from a friend. Stefan is willing to appear on TV in Romania to increase awareness about TB. He wanted to tell other Romanians that *"drug-resistant TB is an awful, but curable disease".*

Amalia is an 18-year-old woman. She interrupted her final year of high school because she was diagnosed with TB. She had never met anyone with TB and has no idea how she could have got the disease. She went to her family doctor after suffering from a very productive cough and night sweats. She was told that she had bronchitis and was sent home with medicine. Her symptoms did not improve so then she went to a private clinic for a chest X-ray. Based on the results, she was referred to the pulmonology hospital where TB was diagnosed and she shared a room for three months with another young girl who was eventually found with the same drug resistance pattern. She was treated for three months with first-line drugs before being referred to the Bucharest MDR centre. When her TB was confirmed, all her high school classmates were checked with tuberculin skin tests and her family members had X-ray examinations. Luckily, no one was infected.

Simona is a 57-year-old woman. Before being diagnosed with TB at the age of 45, she worked in construction: *"We were eating very well, working 10–12 hour days, but I was very well nourished"*. Then, she started to sweat, lose weight and feel weak but *"I did not lose much*

weight and I assumed the symptoms were associated with pre-menopause". Simona went to the doctor, who made all kinds of analyses and prescribed some medicines for a cold, which she bought over the counter. However, the medications did not make her feel better; she was hospitalized after a haemoptysis, diagnosed with TB and treated with first-line drugs for six months. She then felt ill again and was treated with first-line anti-TB drugs for a further nine months (retreatment regiment). One and a half years ago, she relapsed again. Again she began taking first-line drugs without feeling any better and her culture again became positive. Despite this, her doctor noted improvements in her chest X-ray and kept her on first-line treatment. She has now been diagnosed with MDR-TB and is receiving treatment with second-line drugs through the GLC programme.

Annex 7

TB REPORTING

TB-related information is reported by various units through eight different reports (Table 7.1).

Table 7.1. TB-related reports by unit, timeframe and type of report

From \ To	Hospital	Pulmonology dispensary	TB coordinator (county)	Public health directorate (county)	NTP	Ministry of Health
Hospital	–		A (m/q/y)	B (m) C (q/y) H (y)	D (m) E (m)	
Pulmonology dispensary		–	A (m/q/y)	C (q/y) H (y)	D (m) E (m)	
TB coordinator (county)			–	A (m/q/y) B (m)	D (m) E (m)	
Public health directorate (county)				–	A (q/y) H (y)	
NTP			F (q/y) G (y)		–	F (q/y) G (y) H (y)
Ministry of Health						---

m = monthly; q = quarterly; y = yearly.

Report A. Content: information on individual TB patients (including diagnosis and treatment). Source: other than the National TB Registry. Reporting: all TB services (hospitals, dispensaries) report monthly/quarterly/annually to their TB coordinator, who reports monthly/quarterly/ annually to the public health directorate of the county, which forwards reports quarterly/annually to the NTP.

Report B. Content: financial data. Source: other than the National TB Registry. Reporting: TB services (hospitals) and TB coordinators report monthly to the Public Health Directorate.

Report C. Content: activities and efficiency indicators, including budget disbursement. Source: National TB Registry. Reporting: all TB services in the county (hospitals, dispensaries) report quarterly/annually to the Public Health Directorate.

Reports D and E. Content: information on the use of the NTP cars. Source: other than the National TB Registry. Reporting: all TB services (hospitals, dispensaries) and TB coordinators report monthly to the NTP.

Report F. Content: TB case-finding (new and relapsed cases). Source: National TB Registry. Reporting: the NTP reports quarterly/annually to the Ministry of Health, National Institute for Public Health and TB coordinators.

Report G. Content: all TB indicators. Source: National TB Registry. Reporting: the NTP reports annually to the Ministry of Health, the National Centre for Communicable Diseases and the National Institute for Health Statistics and TB coordinators.

Report H. Content: all activities. Source: National TB Registry (in theory but not possible now as the registry has to be updated). Reporting: all TB services (hospitals, dispensaries) report annually to the Public Health Directorate, which forwards the reports to the NTP which in turn reports to the Ministry of Health.

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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