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What are Factors that contribute to favourable MDR-TB treatment outcomes in Eastern Europe/Central Asia (EECA)

Findings from Romania



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List of abbreviations

AIDS	Acquired Immunodeficiency Syndrome
CBO	Community-Based Organizations
CHW	Community Health Workers (nurses in Romania)
CSO	Civil Society Organization
DQA	Data Quality Assessment
DR-TB	Drug-resistant tuberculosis (i.e. all kinds of resistance patterns)
EECA	Eastern Europe and Central Asia
FD	Family Doctor
FGD	Focus Group Discussion
HF	Health Facility
HIV	Human Immunodeficiency Virus
IDU	Injecting Drug User
MDR-TB	Multidrug-resistant tuberculosis
MDT	Multi-Disciplinary Teams
MOH	Ministry of Health
NTP	National TB Control Program
NGO	Non-Governmental Organization
PHC	Primary Health Care
PLWH	People Living With HIV
PR	Principal Recipient
RFP	Request For Proposal
RR-TB	Rifampicin-resistant tuberculosis
SCIH	Swiss Centre for International Health
Swiss TPH	Swiss Tropical and Public Health Institute
TB	Tuberculosis
WHO	World Health Organization

1 Background

1.1 Drug-resistant Tuberculosis (DR-TB) in Romania

The Global Fund mandated the Swiss TPH to conduct a study on factors that contribute to favorable MDR-TB treatment outcomes in Eastern Europe/Central Asia (EECA). Field work for the study was conducted in five countries in the EECA region: Romania, Ukraine, Belarus, Tajikistan and Azerbaijan.

Romania has the highest TB incidence in entire European Union. There are specific challenges for MDR/RR - even when the rate of MDR-TB is 2% for new cases and 17% for previously TB cases, the absolute number of MDR/RR TB cases is the highest in WHO Europe region (more than 500 cases detected each year).

In 2015, the incidence rate of MDR/RR-TB in Romania, a country of 20 million inhabitants, was estimated at 4.8 per 100'000. There were an estimated 670 MDR/RR-TB cases among notified pulmonary TB cases. 3% of new TB cases and 12% of previously treated cases were estimated to have MDR/RR-TB. Among the notified cases, 48% of the new cases and 64% of the previously treated cases were tested for rifampicin resistance. 330 MDR/RR-TB cases were tested for resistance to second-line drugs. There were 576 laboratory-confirmed MDR/RR-TB cases and 53 laboratory-confirmed XDR-TB cases in 2015. The 601 MDR/RR-TB patients who began second-line treatment in 2013 had a treatment success rate of 41%; among the 56 XDR-TB cases of 2013, the treatment success rate was only 16%. For 2016, the national TB budget amounted to slightly more than 17 million USD; only approximately 6 million was from domestic funding. Approximately 3 million remained unfunded.

2 Objectives

The overall objective of the study in Romania is to better understand the factors that influence MDR-TB treatment outcomes in general, and amongst special groups, in order to enable the national TB program of Romania, in collaboration with the Global Fund and other partners, to prioritize interventions for better treatment outcome among drug-resistant TB cases.

Specific objectives are two-fold:

- (1) To understand the factors that influence DR-TB treatment outcomes in general and amongst special groups:
 - at county, health facility (HF), community and individual levels,
 - in migrants, People Living with HIV (PLWH), drug users.
- (2) To establish and assess the role of NGOs (Non-Governmental Organizations) and their efforts regarding community-based treatment in the care of DR-TB patients.

3 Methodology

The study was carried out in close collaboration with the National TB program (NTP) in Romania. The study in Romania consisted of a **high level assessment of the NTP with a focus on drug-resistant TB (DR-TB)**¹. Both quantitative and qualitative methodologies were used to collect data for the study, as detailed below.

¹ To make clear that patients with resistance patterns other than resistance to rifampicin and isoniazid are included (e.g. rifampicin-resistant TB cases and extensively drug-resistant TB cases) we use the term DR-TB cases.

The Marius Nasta Institute of Pulmonology is currently playing the role of NTP, and has assumed the responsibility for planning, implementing, monitoring and evaluation of all TB-related activities in the country. The Marius Nasta Institute granted permission to the research team to conduct all study-related activities such as field visits to counties, interviews with health care officials, as well as community representatives, visiting the health care facilities, conducting observations, and reviewing patients' charts from the 2013 cohort. An Ethical Committee permission letter was received as well, allowing the research team to interview TB patients.

The research team included two Swiss TPH consultants who, over 11 days of field work, visited 6 healthcare facilities, conducted 24 oblast-level interviews, 18 health facility-level interviews, 18 community-level interviews, 6 observations, as well as 8 patient interviews and FGDs with patients who completed treatment. The researchers were supported by Marius Nasta Institute representatives, Dr. Misu Stefan, Dr. Cristina Popa and Mr. Andrei Dobre from the Romanian Angel Appeal (Principal Recipient of the Global Fund Grant).

3.1 Study areas and site selection

The selection of the study areas in Romania was done in two stages: first, counties were selected depending on their treatment success rate, and second, within selected counties, the health facility with the highest volume of drug-resistant TB (DR-TB) patients in the 2013 cohort was selected. In all selected counties, the research team reviewed the treatment outcome of three additional health facilities based on the data provided by NTP, but only one was visited, as envisioned in study protocol. Decision was made based on practicality and distance.

The counties identified were Arges, Dolj, Ilfov, Olt and Iasi counties. Bucharest was also selected as a separate entity at county level. Six territories were thus identified and visited between 17th and 26th May 2017. The final list of healthcare facilities visited by the research team is as follows:

County	Type of facility	Name of facility/city
Bucharest	City TB Dispensary	Sector 6
Arges County	TB Dispensary	Pitesti
Dolj county	TB Dispensary	Craiova
Olt County	TB Dispensary	Scornicesti
Ilfov County	City TB Dispensary	Sector 2
Iasi County	TB Dispensary	Iasi

3.2 Data collection overview

As per the study protocol, quantitative and qualitative data collections were performed.

There were three quantitative approaches:

- (i) collecting patient information from archived DR-TB patient charts in one HF of each selected county;
- (ii) review of the 2013 cohort treatment outcomes in 3 HFs in each selected county; and
- (iii) Data Quality Assessment by comparing reported versus recorded treatment outcomes (see chapter 0 for details).

Qualitative approaches included semi-structured interviews with providers and DR-TB patients, short interviews/observations at different levels (national, regional health facility as well as community level), and Focus Group Discussions (FGD).

3.3 Study populations and study approach

3.3.1 Key informant interviews at national and county level, health facility and community level

The study team carried out **Key Informant Interviews** with the main stakeholders at national and county level. At the national level, interviews were conducted with representatives of:

- Ministry of Health
- the Marius Nasta Institute of Pulmonology
- the World Health Organization
- the Global Fund Principal Recipient: Romanian Angel Appeal Foundation
- the Center for Health Policies and Services
- the Association for Supporting MDR-TB patients
- ARAS: Romanian Association Against AIDS

These respondents were selected on the basis of working at the whole country level, relevance to the topic of the study, and also availability during the time of the visit.

At the county level and community level, the team had met with various specialists from the TB health facilities, including administration, TB coordinators, TB and MDR-TB doctors and nurses, as well as representatives of community (NGOs staff and supporters, Roma community mediators). When opportunity allowed, other specialists were also interviewed, such as representatives from Matei Bals Institute (HIV System), Save the Children Romania - that works with homeless people, and Dr. Jonathan Stillo, a medical anthropologist studying tuberculosis in Romania. All these accounts helped to contextualise the state of TB response in Romania, TB system organization and community involvement.

3.3.2 Interactions with people affected by the disease

FGDs with DR-TB patients

A FGD with ten DR-TB patients who completed their treatment was held at the Marius Nasta Institute.

Interviews with DR-TB patients

A total of seven individual interviews with former patients were held in Bucharest and in the counties. One interview was with an HIV positive former IDU and one interview was with an HIV positive patient. Oral informed consent was obtained prior to each interview. HIV positive patients were informed about the study protocol and willingly disclosed their HIV status. All interviews were confidential.

Interviews with family members

No family members of DR-TB patients were interviewed during this mission.

3.3.3 Quantitative approaches

There were three quantitative approaches:

1. Collecting patient information from archived DR-TB patient charts in the each visited HFs. From these charts, information was extracted into a pre-designed Excel worksheet on the following: demographics, employment, body weight and body height, history of treatment, time spent in hospital, mode of treatment supervision, chest X-ray result at baseline, sputum examination results at baseline and at two months of treatment, co-morbidities, adverse drug reactions and treatment outcome.
2. Documentation of the treatment outcome of the 2013 cohort [treatment success, died, treatment failure, loss to follow-up, other treatment outcome (mostly transfer out)] of three HFs belonging to each county visited, as found in the reports at the county.
3. Data quality assessment was done in one HF of each of the three following counties: Bucharest, Arges, Dolj. The assessment consisted of a comparison of the treatment outcome as documented in the HF report with the treatment outcome as re-counted by the study team in the source recording tool (TB register) of the HF (i.e. the study team checked the treatment outcome of the patients belonging to the 2013 cohort as seen in the DR-TB patient register).

4 Findings

4.1 Findings from the desk review of reports on TB and DR-TB control in Romania

4.1.1 Overview and vulnerable populations

In the desk review, six reports (three of them rGLC reports) were reviewed. These reports were written in the time span 2014 to 2016 (we did not receive reports from the years 2010 to 2013). The following marginalised patient sub-populations were mentioned:

- People living with HIV/AIDS in 5 reports
- Prisoners in 4 reports
- Homeless patients in 4 reports
- Unemployed patients in 2 reports
- Migrants in 2 reports
- Users of illicit drugs in 1 report

4.1.2 Main challenges of the DR-TB programme hindering treatment completion

All in all, various main challenges were mentioned 12 times in the analysed reports:

- Five challenges related to financial and/or management issues. Two examples: (i) from a report of 2014: “ensure sufficient and sustainable funding and the required changes in the health system” and (ii) from a report of 2016: “Ensure adequate financing and uninterrupted supply of drug procurement for first- and second-line drugs at all treatment sites”.
- Two challenges related to programme management in general (e.g. from a report of 2014: “Centralize the drug procurement system for first and second-line anti-TB medications as an urgent measure”)

- Also two challenges related to economic hardship of patients (e.g. from a report of 2016: “in 2013, 10.4% of Romanians reported unmet health care needs because care was too expensive, it was too far to travel or there was a waiting list”).
- There were three further challenges related to various issues, e.g. to ancillary drugs: “Consider developing mechanisms for covering the ancillary medicines for side effect management through the new mechanism of financing through the MOH, especially for the ambulatory sector”

4.1.3 Patient enhancers for supporting treatment

Patient enhancers were mentioned only once, namely that former DR-TB patients who are cured have been connecting in an informal manner with current XDR patients to encourage them and help them through the process. The report added the following remarks: “It has been invaluable for the Romanian patients to see the former patients, now healthy and happy.” Also, a recommendation to give antiretroviral therapy to all patients with HIV and drug-resistant TB can also be considered a patient enhancer.

4.1.4 Provider enhancers for supporting treatment

Provider enhancers were mentioned once only: it was recommended (in a report of 2014) to provide TB outcome-based incentives to family doctors under the package of minimum services currently under discussion.

4.1.5 Recommendations related to treatment outcome

In the 6 reports, we found 37 recommendations related to treatment outcome. There were various categories of recommendations:

- 14 referred to programme management. Some examples:
 - Develop strategies aimed on improving patients’ adherence to treatment using the principles of patient-centered approach to address the problem of high rate of default from treatment (report of 2014).
 - Address the issue of excessive hospitalization at TB inpatient facilities by creating criteria for admission to the hospital and strengthening the ambulatory care program, including aspects of adherence to treatment (report of 2014).
 - DOT should be mandatory for all drug-resistant TB patients and implemented through patient-centred packages of services as an alternative to hospitalization (report of 2014)
 - Support the update and endorse the updated National Guidelines on PMDT and make it mandatory for implementation at all inpatient and outpatient institutions nationwide involved in the management of TB and DR-TB, including penitentiary sector (report of 2015).
- 7 recommendations referred to the design/composition of the regimen. Some examples:
 - Regimens for patients diagnosed with DR-TB should be designed in accordance with updated version of the National Guidelines (in report of 2014 and of 2015).
 - Strictly prohibit the use of Streptomycin in the regimens for patients with DR-TB, unless there is documented resistance to Cm, Km, AM but sensitivity to Streptomycin.
 - Consider introducing an update of the National Guidelines for Programme Management of Drug-resistant Tuberculosis (PMDT) in line with recently released recommendations by the WHO on PMDT, especially on new groups of TB drugs and regimen design for M/XDR-TB (in report of 2016).

Related to this, there was another recommendation (of 2015), namely to create a Technical Working Group as an advisory board to the National TB Coordination Committee to oversee technical aspects related to access to new TB and Group 5 drugs.

- 4 referred to management issues that have a financial dimension. Some examples:
 - Consider developing mechanisms for covering the ancillary medicines for side effect management through the new mechanism of financing through the MOH, especially for the ambulatory sector (in report of 2015)
 - Develop strategy to ensure allocation of adequate financing of drug procurement past 2018 for the management of M/XDR-TB (in report of 2015 and of 2016)
- 3 referred to side effects/ancillary drugs. Some examples:
 - Develop a list of possible ancillary medicines used in the management of DR-TB, to be updated on a regular basis.
 - Perform recording of the frequency of adverse reactions to at least SLD and the use of ancillary medicines
- Finally, there were two recommendations related to training:
 - Consider clinical rotation rounds for county TB coordinators at two MDR-TB Centers to improve their capacity to manage MDR-TB.
 - Ensure distribution of the updated version of the National Guidelines on PMDT and training of all healthcare providers involved in management of patients with DR-TB.

4.2 Findings from the interviews and other qualitative approaches

4.2.1 A short description of the DR-TB programme

TB system organization: In Romania, the DR-TB program is a part of the national TB Program. Romania has a strong TB network built as a pyramid. At the base of the system, there are family doctors which refer the patient to the TB system, or if necessary directly to TB hospitals.

At county level, TB departments in hospitals and TB dispensaries are coordinated by one TB county coordinator. County-level TB specialists meet monthly to share and analyze news cases, relapses and surveillance statistics for the county.

At the top of the pyramid is the technical assistance and management unit of the National TB Program located at the Marius Nasta Institute of Pulmonology in Bucharest which coordinates the national TB Program. The NTP has managerial oversight of all issues related to TB but the MoH is responsible for policy and strategic decision-making. The NTP is an intermediary between the MoH and health facilities. The MoH itself is under structural changes and the MoH was changed several times over the past years.

Diagnosis and treatment: TB patients are diagnosed at county-level TB ambulatory facilities (bacteriological exam for Mycobacterium tuberculosis microscopy, tested for drug resistance, DST for isoniazid and rifampin is performed as well as; chest X-ray and other tests) and treated. Drug resistant TB is diagnosed by rapid molecular tests (GeneXpert, or Hain) or classical method – standardized DST on liquid/solid media. Regional laboratories are performing rapid tests for neighbouring counties. Contagious TB patients are hospitalized in specific TB departments. The TB network has 190 TB ambulatories and 60 hospitals with TB departments. The TB system however focuses more on hospitals, rather than on ambulatory service.

Individualized treatment is initiated after the DR-TB patient's case is discussed at one of the 2 MDR-TB Commissions (Bucharest and Bisericani). The two commissions also perform intermediate evaluation of MDR-TB patients. DR-TB patient can start the treatment in his own county, but often is hospitalized in one of the 2 specialized centers for MDR-TB (one in Bucharest and one in the northeastern part of Romania in Bisericani, Neamt county).

The treatment regimen is established by MDR-TB Commission according to DST to second line drugs, whenever possible (only 60% of MDR/RR TB patients have this result). Hospitalization period is depending on the patient infectiousness, in average 3 months, or longer for XDR-TB patients. After discharge and for up to 24 months, the patient continues treatment in TB ambulatory or through family doctor in a rural area. On a case-by-case basis, support options at community-level may exist and can be sought for.

Romania has a National Electronic Register for the TB patients since 2006. A subset of this database is specifically for drug-resistant tuberculosis cases. Numerous variables are recorded such as demographic information, clinical and radiological forms, HIV testing, types of regimens, adverse events, weight, sources of treatment, etc. The Register is still being developed to further improve its functionality.

Funding and drug availability: In the last 13 years Romania received several GFATM grants and more than 2000 MDR-TB cases were treated. The second line drugs were provided by the Global Drug Facility. In the last 2 years, 150 pre-XDR/XDR-TB patients were treated with tailored regimens including Linezolid, Imipenem, Clofazimine, Bedaquiline. The rest of MDR/RR TB patients received treatment through national TB program, but with a limited list of TB drugs. As a result this created two distinct TB patients' cohorts – one receiving Government drugs, another one receiving GF drugs.

In recent years funding from the Government, from the GF, the Norwegian Government and from European structural funds have increased but remain low. City or County administrations sometimes cover the costs of specific items. Many respondents agreed that with the exception of infrastructure, the funding level for TB is enough. Romania has one of the lowest rates of healthcare funding (as a percentage of Gross Domestic Product) in the entire European region. From a financing perspective, TB does not seem to be a health priority.

Legal environment: In Romania there is no TB law yet, but there is reportedly a law in preparation and currently under discussion. There are mixed opinions about the relevance of this law and whether or not it can be a plausible solution to persisting deficiencies. Several documents give strategic orientations and delineate the responsibilities in the TB field: the National Health Strategy for 2020, the National TB program, the Strategy for TB and the TB Action plan in accordance with general health policy. Various guidelines are also being developed, some of which are pending approval by the MoH. The existing legislation is reportedly rather inadequate and lacking internal alignment.

Intersectoral collaboration: The TB system has established collaboration with other entities such as penitentiary, Ministry of Justice, or Ministry of Social Affairs among others. Collaboration is reportedly satisfactory but seems to be more based on personal relationships rather than on sustainable institutionalization of collaborative processes.

4.2.2 Enablers and other NTP factors promoting completion of DR-TB treatment

Group 5 medicines are on the so-called C2 list (list of the MOH for essential TB drugs), but they are not procured through national tender (unlike the other TB drugs). Most of the Group 5 medicines are available on the local market but they are not covered by the NTP budget. There is evidence

that only patients treated in the two DR-TB hospitals in Bucharest and Bisericani are receiving these group 5 medicines.

TB-specific Multi-Disciplinary Teams (MDTs) were set up through a collaboration between the NTP (TB facilities) and NGOs. The first 4 MDTs started with EU structural funds and expanded with GF grants to 6 counties in total. MDTs include at minimum a social worker, a psychologist, and a doctor-pneumologist.

With funding received from foreign aid, the NGO “Association for Supporting MDR-TB patients” hires social workers and psychologists dedicated to TB patients. These specialists are based in the TB department of county hospital and collaborate with TB health providers on case evaluation and risk assessment. Case evaluation assesses social status, comorbidities, treatment and risk for non-adherence.

Risk assessment classifies (DR) TB patients in two groups:

- Patient at average risk of defaulting receive DOT, counselling, social assistance (referral to other services), participation to group support meetings led by a psychologist and so-called *social tickets* (50 lei; this corresponds to 11 EURO) if adherent at the end of each month.
- Patient at higher risk of defaulting: receive DOT, counseling, social assistance and support, peer support (phone-based from cured patients), and *social tickets* (80 lei) if adherent at the end of each month.

Social tickets, although of very modest value, have reportedly proven to support treatment adherence among vulnerable groups.

Social workers and psychologists from the MDTs provide face-to-face and phone-based support in the hospital where they are based, in the other TB dispensaries of the county where they are based and occasionally do outreach support at patients' place of residence. Other forms of support include the *social tickets*, support for the establishment of missing documents, or for state benefit application, especially for medical pensions of TB patients. MDTs also refer patient to have DOT in dispensaries/communities, close to their place of residence.

The MDT can refer DR-TB patients to **other NGO or NGO-led projects**:

- The Centre for Health Politics and Services (CPSS) which trains Community Health Workers (community nurses) and some other volunteers (e.g. family doctors) to be DOT supporters and who provide social tickets to (DR) TB patients living far from the dispensaries (in 5 counties);
- ARAS in collaboration with PARADA Foundation provide harm reduction services for IDU, rapid test for HIV and hepatitis, supports active identification of TB cases among IDUs, and introduce methadone substitution programme, IEC, peer support, active identification, transport of suspect cases to dispensary for testing, referral to other medical and social services, counselling, DOT by peer supporters, and *social tickets*. (in Bucharest and Ilfov);
- UNOPA - The National Federation of Associations of PLWHIV in collaboration with MDR-TB Patient Association provides DOT and social tickets at the level of dispensaries (in 6 counties), working with volunteers.
- Peer support is provided by the MDR-TB patient association since 2013. After discharge, MDR-TB patients in selected counties can receive phone-based support by former MDR-TB to prevent default.
- Save the Children (Salvati Copiii) provides to homeless TB patients (only in Bucharest) a full package of services: IEC, peer support, TB active identification, calendar of screening, transport of suspect cases to dispensary for testing, referral to other services, counselling, juridical assistance, DOT by peer supporters, and social tickets (if adherent).

The NGO involvement in TB treatment and care has led to a form of integrated support services for TB patients which is widely appreciated by patients and providers. NGO interventions are making up for the State inactivity in this field, and provide a much needed support to patients. However, the readability of Romanian NGO intervention in the TB field is difficult due to its multiple layers of interventions, multiple actors involved, and the partial geographical coverage of their actions which raises the question of equal access to care.

To a certain extent, NGO-led TB services developed parallel systems to public institutions: the NGO-supported social workers do not belong to the Ministry of Labour and Social Affairs and have not institutional linkage to the cadre of public social workers accountable to city halls. Collaboration between the two cadres of social workers takes place but seems to depend on personal initiatives. In general, the NGOs involved in TB care focus on specific topics, such as HIV/AIDS, homelessness, IDUs, for instance the “Association for Supporting MDR-TB patients”.

These community-based support functions by social workers/psychologists, community health workers (CHW), and peer supporters each provide valuable services in their own areas but being funded and coordinated by different NGOs as part of distinct projects, the collaboration and exchange of information between them are not automatic and seem to depend on personal relationships. They function as parallel systems.

In addition, the role of CHW (nurses) in Romania is still under development after evolving from office-based medical nurses to field workers. There is still a low understanding of their role and their outreach possibilities are limited.

TB patients can be entitled to **short-term medical pension** and receive salary for up to one year. However, they are no longer covered after one year, which makes the situation of DR-TB patients particularly difficult. Medical pensions are granted by a county-level Medical Committee. For TB patients, application for this state benefit is often facilitated by social workers.

4.2.3 NTP challenges and other factors hindering treatment completion

Funding mechanisms and drug public procurement procedures are not adapted for MDR-TB: the flexibility needed to react to new emerging cases of DR-TB is limited by the decentralization of drugs procurement at level of each institution, by budget planning done on the basis of historical budgets, and by limiting thresholds for procurement procedures. NGOs are subject to specific procurement procedures.

DR-drug availability in the future: the Norwegian Funds stopped in 2017 but DR-drugs were procured to complete the treatment of the current cohort. The GF will be providing treatment for 400 MDR and 80 XDR prospective patients.

Family doctors (FD) are marginally involved in the TB response. There is no official coordination of TB services with family doctors and no systematic collaboration between dispensaries and FD. When it takes place, it mostly depends largely on personal relationships. FD support is often limited to contact referral of suspect cases (passive identification) and contact tracing. FD being private providers in Romania, the overall coordination with this cadre of workers is an issue. FD used to be involved in the TB response when this service was incentivized but this stopped in recent years. With GF funding, NGOs incentivize FD and nurses working in primary care practices to perform DOT. Overall the network of FD and CHW (nurses) is not dense enough and many villages do not have nurses.

DOT is not strictly performed at PHC level or in TB dispensaries in Romania. Most patients often come weekly to dispensaries where doctors give them doses for several days. When FD are involved in DOT, they give weekly treatment to patients for self-administration.

Financing: Financing system seems to be having difficulties in terms of using historic estimates for next year budget, not real calculating based on needs. The MOH takes only historical data, budget is coming with delays, and finance allocation may not be related to the real needs of the NTP. Issues come from a beyond the funding issue, which became less acute in recent years. The lack of alignment of the legal and regulatory framework keeps preventing patients from getting the needed treatment. The health insurance covers several costs related to TB except the TB drugs. In addition, as DR-TB drugs were procured only through foreign aid contribution, a major issue for the future will be the continuous procurement of DR-TB drugs when funding from development partners stop. By the time of the research, the Norwegian funding had stopped but had ensured the procurement of the entire treatment for the current cohort. The main challenge seems to be the following: over the the last years, the budget gap was covered by grants (Global Fund and Norwegian), but for next year the costs for drugs, rapid diagnosis (GeneXpert and LPA) and liquid media will not be covered by the MOH (even though the NTP asks for this).

Lack of alignment of the legal and regulatory framework: at national and decentralised level (county and city hall), laws and regulations are not aligned and prevent a coherent TB response. As an example, TB patients without Identification Documents (ID) cannot receive the Health Card. These patients still get TB treatment; the challenge is that for patients without identification security number or valid Health Card, their hospital is not reimbursed from National Insurance House for hospitalization days. It also needs to be noted that late registration procedure to obtain ID papers exists; however, this takes on average two years to complete. Another example is that there is a perception that only family doctors and nurses should administer DOT (some even have the believe that a law limits DOT to family doctors and nurses). This makes facilitation of alternative modes of DOT difficult. Laws around drug procurement and budgeting are also counterproductive for continuous procurement of TB drugs. Regulations governing the Medical Pension Commission do not permit enough flexibility for TB patients; there also was a perception that in Romania, social benefits are provided in exchange for community work which is not feasible for TB patients. However, social benefits are provided to all patients eligible to receive them, depending on the risk evaluation. Also, the research team was informed that a new law on TB care is currently being drafted.

Quality of care: During field work, the research team performed a number of observations of facilities infrastructures and equipment. The conclusion was that almost all of the facilities visited are fully equipped, with exception of X-ray, and have access to uninterrupted supply of water and electricity. Most of them have laboratories which are well equipped. The facilities have all means of communication including internet, waste disposal, infection control and supplies procedures are in place. There are cars available (from GF) in some places, with fuel. TB drugs supplies were calculated in advance, and have at least one month of stock. However, a number of infrastructure and equipment issues were reported during the research. For example, TB departments do not always have the adequate measures of infection control implemented (isolation rooms, adequate circuits, separation of patients, ventilation, masks and respirators). Some TB facilities have poor infrastructure conditions and issues around building property rights forces TB dispensaries to identify new premises. When TB dispensaries are hosted in hospitals or public health facilities, the NTP provides consumables, salaries, and treatment but administrative costs are covered the county council. There is a shortage of TB health providers.

Access issues: Due to decentralisation issues, there are disparities in the coverage and quality of TB services between counties, especially in rural areas. A reduction of the number of beds is happening, risking that some facilities may have to close. Local versus central administration does not seem to be more effective. There are access issues for patients (not only TB patients) without medical insurance or living in remote rural areas. Roma communities are particularly marginalised from the health system in general and the TB care system in particular. The lack of proper identification documents, a frequent issue among Roma communities, is often an obstacle for hospitalisation (while such patients are still hospitalised, the costs are not reimbursed by the county insurance house). The mandatory administrative registration of citizens by place of residence often creates challenge for hospitalisation of patients in other counties. Very few hospitals accept TB patients without document or insurance.

Mental health, addictions, economic and social factors among patients from vulnerable or marginalized groups were reported as the main reasons for not completing treatment. Patients with addictions are facing specific challenges. Addictions can be a major obstacle to treatment adherence, especially during hospitalization phase which limits possibilities to procure narcotics or alcohol. Providers noted that TB patients on methadone substitution therapy have better chance to complete treatment. Overall, health providers from TB facilities are not adequately trained to deal with at-risk groups.

Patients refusing hospitalisation: providers report that some MDR-TB patients refuse hospitalization for various reasons (distance from families, fear of isolation, duration of treatment, work opportunity abroad, etc.).

Lack of solutions for the reintegration of cured patients with socio-economic vulnerabilities: the links between reintegration, chronic re-infection and re-treatment are not sufficiently explored and taken into consideration. Solutions are missing for the reintegration of homeless former TB patients or cured patients from a family with repeated re-infection cases.

4.2.4 Patients' perspectives

Challenges

From the patients' perspectives, but also reported from health providers or NGO, a major factor that negatively impact of a DR patient treatment outcome is the **length of treatment**. The DR-TB treatment is deemed too long and has a considerably disruptive impact on their life (interruption of work, family ties are strained, etc.). Patients wish they had more options to choose from such as home-based treatment, from community workers, or self-administration through video-observed treatment.

"TB is not only a disease: it's 2 years of your life, you need help to cope, it's not like you are pausing your life." (Bucharest FGD with former DR-TB patients)

Treatment side effects and their management came up frequently. During hospitalisation, patients often experiment with drug timing or drug and food combination for an easier uptake of all drugs and easier management of their side effects under health providers' supervision. At ambulatory stage, drugs for treating side effects, when available, have to be purchased by patients and are not covered by medical insurance. Another options for side effect management is re-hospitalisation of patients.

"When in treatment it is very hard to do certain things, because side effects can last 10 hours." (Bucharest FGD with former DR-TB patients)

"It would take me 40 min to take all the pills." (Bucharest FGD with former DR-TB patients)

“It’s important that doctors let patient experiment with their treatment administration, such as mixing pills with foods. Patients should not to be forced to take drugs with water”. (Bucharest FGD with former DR-TB patients)

DR-Drug availability: prior to GF and Norwegian funding, there was second-line drug commonly used for XDR patients available in Romania. Patients would need to procure it from abroad and pay for it themselves.

Back then I bought some of the drugs from Canada, a 5 month dose. After that I received the treatment free of charge from the Nasta Institute. The doctors did a lot for me to have the necessary drugs. (Bucharest FGD with former DR-TB patients)

Co-morbidities are often inadequately addressed. As the treatment duration for MDR/RR TB can take up to 24 months, patients with comorbidities (HIV, viral or toxic hepatitis, diabetes, psychiatric disorders, etc.) need special arrangements that allow them to complete treatment. HIV-positive patients with pulmonary TB are treated in the TB system (they are hospitalised in TB facilities and receive their HIV treatment there). If an HIV-positive patient has extra-pulmonary TB, the patient can be treated in the HIV system.

There is also an issue in the way **patients (and more widely the population) are educated and informed about TB and its treatment**. Written information material and posters exist in hospitals but there is a general lack of accurate information about TB in Romania, contributing to myths and stereotypes. Providers are not adequately trained to adapt health education and promotion to groups with special needs.

Stigmatization of TB patient is high in Romania in all sectors of society. Roma TB patients bear a double burden of stigmatization with the marginalization of their communities. Roma mediators often play the role of social workers and treatment observers.

Poor **provider-patient interactions** can sometimes hinder treatment completion. Reasons can be providers’ demotivation due to high workload and low salaries, lack of time to dedicated sufficient attention to patients, or individuals’ attitudes.

The **economic situation** of (DR) TB patient has a major influence on treatment completion. Given the length of the treatment, especially at hospitalization stage, patients must interrupt their work which can place the entire households in a critical situation when the patients are the main economic pillar of the family. Medical pension is very low. It is important for DR-TB patients to be relieved from additional burdens in order to focus on the recovery:

“During treatment the only preoccupation of TB patients should be the treatment. All the other problems should be taken care of by someone else... When you are on a treatment like this, you have to eat very well. If you do not have what to eat, you cannot continue treatment.” (Former XDR-TB Patient, Pitesti)

“You need to take out financial issue out of the equation to help you focus on health” (FGD Bucharest) (Bucharest FGD with former DR-TB patients)

Economic migrants often interrupt their treatment, especially at ambulatory stage, to seize a work opportunity abroad.

While most respondents were satisfied with the level of information they received at the start of their treatment, they all agreed on the **poor health information, education and prevention system** in Romania:

“There is a large gap in prevention activities in Romania, we lack information in schools, we know that the flu can be cured, but it is not known that TB can be cured. With this lack of information, patients assume they will die, and therefore won’t bother taking treatment.” (FGD Bucharest) (Bucharest FGD with former DR-TB patients)

“People do not know that people can be treated. Previous experience with TB in their family may lead them to think that TB is a chronic disease, a disease that cannot be cured.” (FGD Bucharest) (Bucharest FGD with former DR TB patients)

According to respondents, the government does not communicate enough on the TB situation in Romania and there is also insufficient or misleading media coverage of this issue, contributing to stigma and wrong perceptions of the disease.

“It makes no sense to spend so much money on MDR-TB treatment. They should invest in prevention!” (Bucharest FGD with former DR-TB patients)

Enablers

Family members play in major role in supporting patients to adhere to treatment. Supportive family members bring moral as well as material support (food, taking on economic support for other family members, etc.) and increase the chance of treatment completion. The role of family members as carers of (DR) TB patients at ambulatory stage is critical and more attention should be placed on supporting carers, for example through training, to increase treatment adherence. On the contrary, it was reported that the most marginalized DR-TB patients whose adherence to treatment is the most difficult, are often those with limited family ties (IDUs, homeless people, etc.).

A holistic approach to patients and their treatment is critical. It is important at the start of hospitalization to assess the patient not only a medical point of view but understand their circumstances (family, social environment, education or work commitments, economic situation, etc.). The post-treatment period should be given more attention as long-term consequences of treatment can still affect former-patients. Depression, even after treatment completion or cure, was often mentioned as a long term consequence of patients’ lives:

“After 3 months of hospitalization, I developed a severe depression and since then I am on anti-depressive drugs. The depression was so severe that I could not speak to the psychologist of the Institute. (...) [After discharge] I went to see a private psychologist. (...) Because of the depression, I could not take any pills and I became again positive.” (Former XDR-TB patient, Pitesti)

According to respondents, **psychological support is as much important as material support.** Professional psychosocial support provided by hospitals and NGOs is very much appreciated by TB patients. Material support (food parcels, travel vouchers, clothes) provide a significant relief to the poorest households with TB patients.

“The psychologist was very important. I discussed a lot with her; these discussions continued during ambulatory phase, she gave me a lot of information, not only about the TB treatment but also for my personal development, on how to cope with the treatment; it helped me be a better person.” (Bucharest FGD with former DR-TB patients)

Keeping busy and avoiding boredom during treatment: former patients reported that having an activity during treatment is critical to focus the mind on something else than the disease and the treatment. Former patients explained how they started to practice physical activity at ambulatory stage of treatment and how it was helpful with recovery.

Post TB life: NGO support and former-patient involvement as volunteers in NGO was frequently mentioned as a positive factor for reintegration after cure.

“There should be more NGO initiative like this one [raising money and visiting TB patient for Christmas]. To show that somebody cares.” (Bucharest FGD with former DR-TB patients)

“I am now a volunteer of the MDR patient association, the one in Bucharest.” (Former XDR-TB patient, Pitesti)

“After TB you are never the same as you were before.” (Former XDR-TB patient, Pitesti)

Former DR-TB female patients mentioned the need for more information about the impact of the treatment on their fertility and their possibility to be pregnant in the years following cure.

4.3 Findings from the quantitative studies

4.3.1 An analysis of charts of DR-TB patients, cohort 2013

In the frame of this study, data from charts of DR-TB patients were gathered from *five* countries. The results will be presented from all five countries together in the overall study report to be sent to the Global Fund.

Findings from a single country are not very useful, though for Romania, the sample size is relatively large (77). A few comments are warranted for the patient data of Romania:

- High-level resistance was quite common: thirty (39%) had either XDR (n = 14) or pre-XDR (n = 16; three of them with resistance to a fluoroquinolone and the remaining 13 with resistance to an injectable).
- Only two of the 77 patients were HIV-positive (and for eight patients, the record regarding HIV was not clear).
- Only one patient had diabetes mellitus. And for five patients, this record was not clear.
- The body mass index could be calculated for only 16 cases (weight and height was indicated for only 16 patients). Six of them (37.5%) had a body mass index of below 18.5 kg/m² (indicating a poor nutritional status).
- Eighty percent of the 75 pulmonary cases had at least one cavity and 59% of the 75 pulmonary cases had not only at least one cavity but also bilateral lung involvement (i.e. X-ray findings indicating TB in *both* lungs).
- Twenty-four of the 77 (31.2%) regularly drank alcoholic drinks during the time when DR-TB was diagnosed. Homelessness and illicit drug use was very rare (in 4 and 2 cases, respectively).

4.3.2 Treatment outcome as collected at the counties

In the six visited counties, the treatment outcome of a total of 134 cases was collected from 36 health facilities. Only 41% of them had successful treatment outcome (41 were cured and 14 had “treatment completed”). Death was common (28.4% died; 38/134). Loss to follow-up was the outcome of 15% (20/134) and failure the treatment outcome of 13.4% (18/134).

4.3.3 Data verification: treatment outcome in visited health facilities

The comparison of the treatment outcome according to two sources revealed full concordance in two health facilities. In the third health facility where this data assessment was performed, there was a small discrepancy: the size of the analysed DR-TB cohort was reported as 13 but in the re-count, only 12 DR-TB cases could be counted. Accordingly, there was a discrepancy of one regarding the number of DR-TB cases that did not have successful treatment outcome (8 versus 7).

5 Recommendations

At the end of field work, a debriefing session was conducted at the Marius Nasta with several representatives of the NTP, WHO and the Global Fund PR (RAA). An overview of field work was presented as well as preliminary findings.

The following recommendations are made by the research team:

- A systematic analysis of the legal and regulatory environment is needed to identify and address the difficulties created by unaligned regulations, especially around drug procurement.
- Solutions engaging the Government of Romania must be found to ensure long-term, adequate, sustainable procurement of rapid diagnostic tools as well as the medicines needed for the treatment of DR-TB (i.e. second-line drugs, ancillary drugs and drugs addressing co-morbidities).
- Further support should be provided to the MDT mechanisms but a reflection should take place on further integration of the specialists in the system to avoid parallel structures.
- The NGO interventions in the TB field, especially social supports through social tickets, should be continued and supported, with a focus on increased coordination and integration on interventions into the public system. It is important that Government increases its involvement in and ownership of community-based integrated TB services.
- It is critical that the support provided by NGOs in selected counties be scaled up nationally to ensure equal access to quality TB service across the country.
- It is necessary to have a coherent strategy for the involvement of the PHC in the TB response, for FDs and CHWs (nurses). The National Health Insurance Company should propose mechanisms to increase participation of FD in active TB detection and DOT.
- Take co-morbidities into consideration when deciding on treatment.
- Although already being implemented, methadone therapy has to be offered for all patients with drugs addiction problems.
- In the light of the fact that there is a methadone substitution programme and the mental health challenges that some TB and DR-TB patients have, a special program for mental health seems warranted.
- Keep on improving approaches for ensuring treatment completion, such as offering treatment at the place of where patients live (although it is difficult). Advocate for the introduction of video-observed (virtually observed) therapy.
- The post-treatment period should be part of a larger re-integration plan for cured DR-TB patients, with more attention placed to the long-term consequences of the disease and the treatment. This is especially important for patients with addictions (alcohol, narcotics) and homeless patients.

The NTP formulated two recommendations:

- Continuous financial and advocacy support from the GF is needed.
- Continuous technical support and follow-up of the situation with DR-TB, especially through sharing of information and recommendations from other countries.