Background

Multidrug-resistant tuberculosis in EU/EEA countries

Countries in the European Union (EU) and European Economic Area (EEA) reported 1 421 patients with multidrug-resistant tuberculosis (MDR TB) in 2012, which is 5% of the 31 004 patients for whom there were drug susceptibility test results [1].

The history of treatment was known for 28 054 patients. MDR TB was found in 580 (2%) of the 23 859 new TB patients and 750 (18%) of the 4 195 patients who had been previously treated for TB.

As in previous years, the highest rates of MDR TB among new patients (11–20%) were found in the three Baltic countries, Estonia, Latvia and Lithuania.

The five EU/EEA countries with the highest reported numbers of MDR TB patients were Romania with 530 patients; Lithuania, 271 patients; Latvia, 106 patients; the United Kingdom, 81 patients; and Italy with 74 patients.
Treatment outcomes

The treatment of MDR TB is lengthy, toxic, expensive, and has generally poor outcomes [2]. Inadequate treatment can lead to unfavourable outcomes for the patient, while increasing the risk of transmission and the development of extensive drug resistance [3].

The aim of the Stop TB Partnership Global Plan is that by 2015 at least 75% of MDR TB patients should be treated successfully [4]; the target for EU countries is at least 70% treatment success for new pulmonary MDR TB cases [5]. In 2010, the treatment success rate in the World Health Organization (WHO) European Region for notified MDR TB patients was only 49%; the proportion of successfully treated MDR TB patients across the EU/EEA was even lower at 34% [1]. In the EU/EEA overall, 18% of MDR TB patients died, the treatment failed for 20% and 20% of patients defaulted. Six per cent of patients were reported as still on treatment after 24 months, and for 3% the outcome of treatment was not reported.

This study was conducted to identify which factors of a healthcare system influence the outcome of treatment, in order to contribute to better treatment for MDR TB patients.

Methods

Case studies were conducted in four EU countries by experts from the KNCV Tuberculosis Foundation, based in the Netherlands, in January and February 2014. The selection criteria were based on the number of MDR TB patients notified in 2009 for which treatment outcome was reported in 2011 (≥20), a geographical distribution of selected countries (one central, one eastern, one southern and one western EU country) and different treatment success rates of the 2009 MDR TB cohort (i.e. high, low or unknown) [6].

The study objectives were to identify and better understand the role that various factors of a healthcare system play in achieving a good outcome from MDR TB treatment under different conditions, without intending to give a full picture of TB control in the EU/EEA. Countries were selected by ECDC and asked to participate. Institutions and individuals for the interviews were selected by the national TB programme’s contact persons in each country.

A guide for semi-structured interviews was developed for use at different levels of the healthcare system: the ministry of health, national TB programme, healthcare facilities and civil society organisations. The guide was tested in Belgium, an EU country not included in the study. Interviews were conducted face-to-face by two consultants. The responses were analysed and organised following the six building blocks for health systems from ‘Strengthening health systems to improve health outcomes: WHO’s framework for action’: service delivery; health workforce; information; medical products, vaccines and technologies; sustainable financing and social protection; leadership and governance [7].

Results and discussion

ECDC selected Austria, Bulgaria, Spain and the United Kingdom for the case studies. All four countries agreed to participate. Their healthcare systems vary from a centralised governance structure to an autonomous regionalised one; with different financing structures from general taxation to national health insurance schemes, and one country receiving support from the Global Fund to Fight AIDS, TB and Malaria (the Global Fund). Generally, national governments are responsible for the regulation and planning of TB control and local and regional governments for the provision of TB services, including public health actions.

Service delivery

Diagnosis of MDR and XDR TB

Rapid molecular testing (Xpert/MTB or line probe assays) is not available in some hospitals in the four countries. Criteria for rapid molecular testing for drug resistance are not available in most of the countries and testing depends on the decision of the individual clinician.

In one country, the time between the initial diagnosis of TB and the MDR TB diagnosis can be as long as 4–5 months.

National TB programmes should consider developing clear criteria and guidance for rapid molecular drug-resistance testing to assure timely diagnosis of MDR and XDR TB and ensure its implementation.
MDR TB treatment
Some countries have published national MDR TB guidelines, while others use the 2008 or 2011 update of the WHO guidelines for the programmatic management of drug-resistant tuberculosis [8]. Despite the availability of global guidance, clinicians tend to rely on recent literature and/or a mix of professional insights and experience.

Many of the clinicians interviewed do not complete the injectable second-line drugs (aminoglycosides/polypeptides) for the full eight months that WHO recommends, because of frequent adverse effects (ototoxicity) in patients.

In some countries, category five drugs (especially linezolid) are used more widely than recommended in the WHO guidelines.

- In countries with health systems that can afford more expensive MDR TB drugs and where side effects can be monitored closely, specialists may adapt MDR TB treatment according to the latest literature and their own insights.
- There is a need for endorsed national or European MDR TB guidance, appropriate for the region’s socio-economic circumstances. This would serve as a better professional reference and guide for clinical management of MDR TB in EU/EEA countries than the current WHO guidelines. The guidance should be elaborated based on a wide range of expert opinion and needs to take into consideration the diverse experience of clinicians in the EU.

Duration of hospitalisation
Two countries have a TB hospital ward where about 80–90% of the country’s MDR TB patients were treated, with about 20–40 new MDR TB admissions annually. In these two countries, either the hospital continues to monitor patients intensively after discharge or an MDR TB Expert Committee monitors the ambulatory treatment, which provides a complete or nearly complete overview of patients under ambulatory care. By contrast, in the other two countries, in-patient MDR TB treatment is dispersed over many hospitals with clinicians hospitalising and treating about 1–5 cases annually and providing follow-up care for these patients during ambulatory treatment.

Initial hospitalisation of MDR TB patients is utilised for controlled initiation of treatment and good preparation for treatment adherence after discharge, thus contributing to better treatment results.

The timing and criteria for discharging MDR TB patients vary widely, and there is no available guidance on the optimal duration of hospitalisation.

Some clinics have introduced a hospital discharge plan for MDR TB patients that includes sections on clinical condition, housing facilities, community management and infection control.

- Concentration of in-patient MDR TB treatment could be considered in countries with low numbers of MDR TB patients. In addition to providing more specialised care, it also facilitates monitoring during ambulatory treatment after discharge.
- EU-wide criteria need to be developed to rationalise the duration of hospitalisation.
- A well-designed discharge plan, including social aspects of care, is viewed as a good tool to achieve a successful outcome for MDR TB patients. Patients should be involved in the development of the discharge plan.

Multidisciplinary teams
In some situations MDR TB Expert Committees have been established to decide or advise on treatment and management of all MDR patients in its catchment area, including initiation of treatment (choice of regimen), management of side effects, monitoring of treatment progress and compliance, regimen changes, and the end of treatment. One country has established an MDR TB Clinical Advice Service.

Elsewhere, there are formal and informal in-hospital team meetings to discuss management of MDR TB in-patients, often held on a weekly basis.

Countries take different approaches to monitoring patients during ambulatory care, varying from monthly evaluation by the MDR TB Expert Committee to consultation room discussions between the medical doctor, the patient and the nurse accompanying the patient during these visits.

Multidisciplinary decision-making on treatment regimens and treatment adjustments can be essential for good MDR TB care.

Cross-border MDR TB case management
Some MDR TB patients seek care in other countries, because treatment is insufficiently available in their home country. Some EU countries face an increase of MDR TB patients from eastern EU and non-EU countries with sometimes XDR TB and several episodes of previous treatment.
Migrant MDR TB patients, e.g. students and workers from EU or non-EU countries, frequently return to their home country during the lengthy MDR TB treatment, which lasts a minimum of twenty months.

All countries have difficulties in ensuring continuation of treatment for patients migrating to other countries.

Although in some cases clinicians successfully refer patients on MDR TB treatment to clinics in other countries, and nurses closely monitor the continuation of treatment by email, these patients are by definition classified as ‘transferred out’ and thus, according to the ECDC reporting system, have an unsuccessful treatment outcome.

**MDR TB treatment should be universally accessible in all EU and non-EU countries.**

**Referral and exchange of information needs to be facilitated between (EU) countries, including the possibility to report (MDR) TB treatment outcome of patients crossing borders during treatment.**

### Health workforce

**Health workforce providing patient-centred services**

Although all four countries have different ambulatory care arrangements for MDR TB patients, they have in common that healthcare workers (community-based or hospital-based nurse) or social workers are assigned as case managers for patients during ambulatory care.

Healthcare workers (including social workers) provide emotional, psychological and social support tailored to patient needs, are capable of building ‘trustful relationships’ and are very committed, engaged and dedicated to their work.

**The interaction between the healthcare worker and the patient is a key factor in successful MDR TB treatment and should be organised in all countries, in accordance with the country’s health system and the patient’s social needs, such as housing, as well as their clinical needs, like co-management of substance dependencies and other co-morbidities.**

**Motivated and devoted healthcare workers are important to support and guide MDR TB patients during treatment. Healthcare workers need training, the mandate and the means to develop individual, patient-centred approaches to support their patients towards treatment success.**

### Health information

**Diversity of MDR TB populations**

The characteristics of MDR TB patients vary strongly between countries, and even within countries between regions. Migrants can make up as much as 90% of the MDR TB patients; their origin differs widely per country.

Extensive drug resistance and drug and alcohol dependency are risk factors for poor treatment outcome in some countries.

**Patient support needs to be tailored in line with the patients’ specific characteristics, culture, language and socio-economic environment.**

**Information-based decision making**

All four countries have TB surveillance systems in place to collect MDR TB treatment outcome data. Three countries have collected data long enough to be able to analyse and report the results.

MDR TB surveillance data, including treatment outcome data, are collected and reported to ECDC and the Global Fund, but some gaps have been identified in terms of use for programme monitoring.

One country uses a systematic approach to regularly review all TB patients on treatment, including those with MDR TB.

**Analysis and use of MDR TB cohort data could be strengthened in EU/EEA countries.**

**Systematic analyses of the time period between bacteriological diagnosis and diagnosis of MDR TB and interim cohort analyses could benefit some of the MDR TB programmes.**
Medical products, vaccines and technologies

**Uninterrupted MDR TB drug supply**

None of the four countries currently faces problems procuring MDR TB drugs although one country has only had MDR TB drugs, and thus MDR TB treatment, available since 2009 with Global Fund support.

Some countries have centralised management of MDR TB drugs including the distribution of drugs to the penitentiary sector and for ambulatory care.

One good country practice is that the MDR TB drugs kit follows the patient irrespective of the place of treatment.

In other countries each individual (hospital) pharmacy procures MDR TB drugs.

The quality of MDR TB drugs is the domain of pharmacists and National Medicine Boards and clinicians are not involved in the debate over quality issues.

A coordinated approach to procuring MDR TB drugs with an overview at country level, including the quality, may benefit MDR TB management.

**Sustainable financing and social protection**

**Financing mechanisms for MDR TB services**

State health insurance, regional or central government budgets cover the costs of TB care. In one country the allocation of health funds, including TB services, was determined by decentralised specialised groups. One other country has achieved remarkable results with support from the Global Fund, but there are concerns and uncertainties about the sustainability of funding, once this support ends.

All four countries have a system (or are moving towards it) with centralised and ear-marked budgets for (MDR) TB. Some hospitals report inadequate funding for in-patient care, e.g. because of fixed budgets per TB patient/bed without specific arrangements for MDR TB patients. However, this does not interrupt services or make them unavailable, because the MDR TB numbers are small.

Systems with ear-marked budgets facilitate (MDR) TB treatment and care and need to be maintained.

Countries with Global Fund support for (MDR) TB control activities should develop long-term financing strategies in which domestic funding gradually increases while the Global Fund support phases out.

**Treatment for all MDR TB patients**

All four countries have health and financial systems that provide free treatment for TB and MDR TB patients, including uninsured or undocumented migrants. Different forms of legislation guarantee free TB treatment, including, in some countries, coverage of prescription fees for medication or the transport costs to receive daily intravenous MDR TB treatment, or daily food vouchers.

Systems that provide accessible and affordable MDR TB services for all patients in need have to be maintained.

**Leadership and governance**

**Intersectoral collaboration and partnerships**

In most of the reviewed countries, a social support system is in place, although often limited to the country’s own citizens or EU citizens.

Encouraging examples show drug substitution programmes for people with substance dependencies and antiretroviral treatment for HIV-infected MDR/XDR patients. Social workers, paid by the municipality, guide the ambulatory TB treatment and provide social support. Community-based initiatives are in place that aim to increase community awareness, case-finding and treatment support, particularly among hard-to-reach communities. Non-governmental organisations are involved in housing MDR TB patients and supporting them in obtaining work, including migrants, as well as lobbying to enhance political commitment, and indirectly contributing to good treatment outcomes.
Conclusions

For EU/EEA countries, with relatively low numbers of MDR TB patients, treatment success of MDR TB is unacceptably low [1,4]. Only one in three patients diagnosed in 2010 in the reporting EU/EEA countries finished MDR TB treatment successfully. This study assessed the contribution that certain key components of the health system in four selected EU countries make to the treatment results of MDR TB patients.

Financial systems in the countries studied are favourable for the treatment of MDR TB. However, social support is in some situations not accessible to some groups of migrants. Notably, some governments have moved from decentralised health insurance funding schemes towards more ear-marked and protected budgets for (MDR) TB (and other infectious diseases) to ensure that TB treatment is accessible and free for all patients, including those without insurance or legal status.

Health services in the four countries are generally well equipped to diagnose and treat MDR TB. Several obstructing system factors were identified such as insufficient access and use of rapid molecular testing, limited expertise and limited sharing of expertise between professionals, lack of treatment guidance and protocols, long duration of hospitalisation and difficulties ensuring continuation of treatment and care for patients crossing borders. The importance of these factors has been stressed in several international policy documents [8–15]. In one country, MDR TB drugs were only secured in 2009, with many patients with advanced disease awaiting treatment. As a result, the first treatment success rates in that country were low.

Good practices include a well-designed hospital discharge plan for MDR TB patients that includes the social aspects of care, and an MDR TB Expert Committee that decides on all aspects of MDR TB management. Motivated and devoted healthcare workers with a sufficient mandate and means to support patients are a strong enabling factor for successful MDR TB treatment.

The following actions could be considered by EU/EEA countries and at EU level to improve the success of treatment for MDR TB patients: i) timely diagnosis of MDR and XDR TB in all EU/EEA countries; ii) development of European guidance on treatment regimen design; iii) development of EU-wide criteria for hospitalisation of MDR and XDR TB patients; iv) implementation of a minimum package of cross-border (MDR) TB control and care and development of collaboration mechanisms to ensure a continuum of care between countries, including reporting of treatment results; v) implementation of patient-centred approaches encompassing the social needs of MDR TB patients and sharing successful examples with other countries; and vi) development of long-term sustainable financing strategies to ensure prevention, diagnosis, treatment and care for MDR TB patients. This is particularly important for countries with a high burden of MDR TB that have lower levels of income per capita. Domestic funding has to be increased for those EU countries that currently receive Global Fund support, to make the programme activities less donor-dependent.
References


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