To assist international efforts to address major gaps in the availability and accessibility of quality diagnosis and treatment for multi-drug resistant tuberculosis, Médecins Sans Frontières has adapted an approach combining three sets of interlinked strategies: direct provision of medical care, operational research, and public health advocacy. The activities undertaken are reviewed each in turn, with stress on the ways that they impact upon and consolidate each other. In spite of new opportunities, including technologies which significantly improve diagnosis and new, more patient-centred approaches, a much broader international mobilization is needed in order to confront MDR-TB. It is also questionable as to whether existing technologies are successful enough to provide a solid basis for expanded national programs.

Keywords: tuberculosis, multi-drug resistant tuberculosis, diagnosis, treatment, research, advocacy, humanitarian, non-government organization

Background

The major gaps that exist in the availability and accessibility of quality diagnosis and treatment of multidrug-resistant tuberculosis (MDR-TB) are some of the important drivers of the epidemic of this disease. Fewer than 5% of new and previously treated TB patients were tested for drug resistance in 2010 [1]. Only 10% of the estimated caseload of MDR-TB patients among notified TB cases in 2009 had access to treatment [2]. Drug-resistant TB is especially prevalent in the countries of the former Soviet Union: the nine countries with MDR-TB rates in new TB cases higher than 12% are all former Soviet countries [3]. There are 31,914 total confirmed cases of MDR-TB in the former Soviet countries [4].

Commitment by governments and the international public health community to tackling the MDR-TB epidemic appears to be growing. In the Berlin Declaration of 2007 [5], ministers of member states in the WHO European region committed to concerted action to implement the Stop TB Strategy [6]. The Beijing Call to Action of 2009 [7] was issued by WHO member states affected by M/XDR-TB (extensively drug-resistant TB) that resulted in a World Health Assembly resolution on the prevention and control of these forms of TB [8]. Governments committed to “moving urgently towards universal access of diagnosis and treatment of M/XDR-TB by 2015,” including through the introduction of a comprehensive approach incorporating improved diagnosis systems and infection control policies, proper adherence to treatment protocols, improved drug supply and sustainable financing and human resourcing.

The role of Médecins Sans Frontières

For Médecins Sans Frontières (MSF), a non-governmental medical-humanitarian association, the primary response to the MDR-TB epidemic in the countries of the former Soviet Union is through direct provision of quality diagnosis and treatment to patients. MSF has been involved in the diagnosis and treatment of MDR-TB in the former Soviet countries for more than a decade and was a founder of the Green Light Committee, which supports countries in the management of MDR-TB. Using the experience from these activities, MSF decided to address the wider efforts being undertaken by governments in the region and by other international public health institutions in the hope of assisting the development of a larger response. MSF’s approach to MDR-TB treatment in the former Soviet countries has three components (Box 1).
Advocacy on tuberculosis in the former Soviet Union

MSF’s Medical Programs

Location and history

MSF is providing diagnosis and treatment for MDR-TB patients in six countries: Armenia, Georgia, Kyrgyzstan, the Russian Federation, Tajikistan, and Uzbekistan. A program is soon to start in Ukraine. The longest-running continuous TB program started in Uzbekistan in 1998 and began treating MDR-TB in 2001. Two new programs were initiated in 2011, in Tajikistan and the Kara Suu district of southern Kyrgyzstan. The largest program, in terms of expenditures, staff and patient numbers, is in Karakalpakstan in Uzbekistan with 869 patients with drug-resistant TB and 228 with drug-susceptible TB in treatment on May 31, 2012. At the end of 2011, MSF was treating approximately 1500 patients for tuberculosis in the former Soviet Union.

Patient-centred model of care

MSF’s model of care is based on a comprehensive and patient-centred approach: diagnosing and treating all cases; and addressing the high default rates common with MDR-TB treatment (Box 2). A strong focus has been the introduction of high-quality laboratories with rapid drug-susceptibility testing to enable the rapid initiation of correct treatment. Also, heavily emphasized is ambulatory treatment, if possible from the first day, in order to lower default rates by bringing treatment closer to where the patient lives and reduce the chance of nosocomial transmission of drug resistance. All programs are carried out jointly with the Ministry of Health inside public facilities.

Responding to research data

MSF’s programatic approach has varied and developed with experience and new data. For example, the program in Uzbekistan initially focussed on DOTS implementation. In 2003, a drug susceptibility study found high levels of drug resistance, leading to the initiation of a DOTS-Plus program, treating only drug-resistant forms of the disease. While outcomes were acceptable, it became clear that drug resistance was becoming more prevalent, caused in part by the inappropriate treatment of drug-susceptible cases. In response, in 2010, MSF and the Ministry of Health initiated a comprehensive program with the aim of improving the cohesiveness of the program, and in particular the early diagnosis and treatment of MDR-TB in the Republic of Karakalpakstan. A study on the amplification of MDR-TB into XDR-TB led to greater concentration on, and improvements in, infection control [9]. A study of community-based care in South Africa has modified the approach towards decentralising care in Karakalpakstan [10].

Box 1. MSF’s approach to MDR-TB treatment in the former Soviet countries

| Diagnosis: Rapid diagnosis of TB and drug susceptibility testing |
| Treatment: |
| - Comprehensive – drug-susceptible and drug-resistant TB |
| - Decentralised – preference for community based treatment, even from day 1 |
| - Hospitalisation still required for some patients: XDR, severe side-effects, late stage and/or severely ill, patients for whom ambulatory care is not feasible or not preferred |
| - Children should also be diagnosed and treated |
| Infection control: |
| - Based on early diagnosis and effective treatment |
| - Implementation of administrative, environmental and personnel protective measures |
| Psychosocial support: Individual and group education and counselling, defaulter tracing, incentives and enablers (such as reimbursement of patients’ transport costs, food parcels) |
| Human resources: strong clinical supervision and training |
| Drug supply management |

XDR = extensively drug-resistant TB
Specialised programs

While most programs provide services to the general population, two have focussed on specific populations. In Kyrgyzstan, TB is diagnosed and treated in the prison system, a significant locus of infection throughout the Eastern European and Central Asian region. The planned program in Ukraine will also focus on prison populations. In Tajikistan, a paediatric TB program was started because TB in children had been neglected in this country, and indeed worldwide. There is a lack of appropriate TB drug formulations or diagnostic techniques available for children, and few means of diagnosing or treating them for drug-resistant disease.

MSF’s Research

Programmatic research

MSF has focused on documenting the scale of the problem (such as through involvement in two drug susceptibility surveys with the Uzbek Ministry of Health in 2003 and 2011), documenting the response to MDR-TB with international protocols and the limitations of these (for example, default rates in MDRTB [11]), and the wider issues that may influence program outcomes [12]. The foundation of MSF’s research in TB has been the description and analysis of its own cohorts and its experiences in the introduction and implementation of particular technologies, e.g. GeneXpert in diagnosis. This research has two main aims. Firstly as part of routine monitoring and evaluation to ensure that treatment outcomes and implementation meet required MSF as well as international standards. Secondly to propagate practices, technologies and models of care, in the hope that strong evidentiary backing will lead to them being adapted by other health providers. See Box 3 for examples of MSF research in MDR-TB.

Wider research issues

MSF clinicians and epidemiologists have also sought to investigate wider phenomena, including the causes of default, the incidence of XDR-TB and the availability of TB drugs outside the regulated market. Research is presently being conducted by anthropologists and health economists into the social and economic aspects of TB and the relevant aspects of health systems.

MSF’s Public Health Advocacy

Why advocacy is essential

The numbers of patients within MSF programs is small compared with the numbers treated by Ministries of Health in the countries of the region, let alone compared with the numbers who are undiagnosed or untreated. Further, the success of control endeavours depends strongly on the effectiveness of available technologies. Therefore MSF engages in public health advocacy with governments, international organisations, researchers and the pharmaceutical industry, in order to address the limitations in current practice and in the hope of mobilising wider efforts (Box 4).

Box 3. Examples of MSF’s research publications in MDR-TB


Box 4. Examples of MSF’s advocacy in MDR-TB

Organising symposia:
Central Asian medical symposium, ‘Uniting to scale up TB care’. Tashkent, Uzbekistan, April 2011
Kyrgyzstan regional symposium planned for late 2012

Publication of reports:
Treating drug-resistant TB: what does it take? Comprehensive TB Care for All: the Karakalpak Experience

Input into the drafting of Order 1224, by the Ministry of Health of the Republic of Chechnya, which provides the framework for TB diagnosis and treatment. December 2011

Input into the drafting of new infection control guidelines for all Ministry of Health TB facilities, in the Republic of Karakalpakstan, Uzbekistan

Developing a paediatric TB protocol for Tajikistan planned to be disseminated regionally through WHO

Partnerships
MSF’s principal partner is the Ministry of Health in the country it is working in. Many countries of the former Soviet Union have been involved in (often difficult) reform processes within their health systems [16] and have been seeking to modernise their approaches to TB care. MSF has participated in review processes conducted by national health authorities for TB care strategies, protocols and prikaz (government regulations), with the aim of incorporating new technologies (such as rapid drug-susceptibility testing) and new approaches (such as Day 1 ambulatory treatment for MDR-TB patients) into government policy and practice. At the national and local levels, MSF has provided recommendations on implementation plans and strategies. MSF has also sought to encourage the exchange of experiences and practices between regional health officials through symposia, conferences and public reports.

Global efforts
In November 2011, the board of the Global Fund to fight AIDS, TB and Malaria cancelled its next scheduled funding round (‘Round 11’). Given that the Global Fund provides 82% [17] of external funding for TB, MSF is concerned that the decision could halt progress towards universal access to diagnosis and treatment. MSF has advocated the Global Fund implementing appropriate transitional measures to maintain existing national TB cohort sizes and donor countries maintaining previous commitments to assist TB control efforts. The Global Fund introduced a Transitional Funding Mechanism, which was a way of opening up funding requests for maintenance of current programs until the next round of funding is available in 2014/2015, but there is still considerable uncertainty about the medium-term future of TB funding. MSF also seeks to share its experiences and work with global public health institutions, such as WHO, the Stop TB Partnership and the International Union against Tuberculosis and Lung Disease.

New technologies
While the availability of rapid drug-susceptibility tests is an important breakthrough for diagnosis, in the field of new treatments the pipeline has been empty for the past 40 years [18]. Existing courses of treatment for MDR-TB have serious side-effects and are lengthy (at least 20 months), in large part because the drugs themselves are only weakly effective. The length and difficulty of treatment seems to be a major driver of high default rates. There are now some promising candidates for new drugs, including several entering phase 3 trials [19]. MSF has long sought to accelerate this process through its Access Campaign, through advocacy efforts with the pharmaceutical industry and with public–private partnerships for product development. It seems unlikely that the MDR-TB epidemic can be contained without significant improvement in the technologies available, making treatment courses more effective, shorter, and easier to tolerate for the patient.

Conclusion
Successful control of the epidemic in the region is still far away – and the Berlin and Beijing Declarations remain just that, declarations. Further, there is a question over whether the existing tools, especially the drugs available to treat MDR-TB, are successful enough to serve as the foundation for successful treatment programs of sufficient scale. So far, the international community has failed in its attempts to ensure access to effective, well tolerated treatment.

However, new opportunities need to be recognised. The advent of rapid drug susceptibility testing is a significant step forward, addressing what was previously a major rate-limiting factor, the difficulty of quickly diagnosing drug resistance. Further, an international consensus is building in favour of innovative approaches to treatment, such as the new emphasis on ambulatory treatment, which may allow both scaled-up efforts and improved outcomes.

As a non-governmental medical-humanitarian association, MSF will only ever have the resources to diagnose or treat a small number of cases. While the organisation sees its own direct efforts as a humanitarian necessity, it also sees the need for a wider mobilisation to universalise access to diagnosis and treatment. Indeed, MSF hopes that its experiences will help the adaption of new technologies and approaches, either constituting a ‘model’ for wider replication or serving as a catalyst for change.
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