3. Providing M/XDR-TB management and care

Countries are facing major challenges the management of M/XDR-TB. This paper will focus on the challenges related with the models of care (hospital-based vs. outpatient care) selected to treat patients with MDR-TB and the proposed measures to tackle those challenges, namely, the balance between hospital-based and out-patient care in the context of social support and community-based care, ethics of treatment and care, involvement of all health-care providers (including hospitals), and the needs of persons with HIV.

3.1 Hospital-based versus outpatient care

The problem

Treatment and care of MDR-TB is demanding, relatively complex, and costly. MOHs are quite often relying on models of care that are not suitable to the needs of patients, are not in line with WHO guidance, reduce the impact of treatment, and/or are not cost-effective. The chief demands come from the length of therapy (two years) and the need to deliver directly observed treatment (DOT) using a patient-centered approach. The complexity stems from the following facts:

- Second-line anti-TB drugs (SLDs) produce a higher frequency and more severe adverse reactions than first-line anti-TB drugs (FLDs), especially during the first six to twelve weeks of treatment. Poor management of adverse drug reactions contributes to high treatment default and extended period of transmission of M/XDR-TB.
- Coinfection with HIV may require frequent or lengthy hospitalization.
- Proper infection control measures should be available in hospitals whenever TB patients are hospitalized; and at the household level to reduce contamination of air with the bacilli; but these practices should not promote or increase stigma.
- Monitoring of the response to treatment is based on culture and not only smears.
- Public hospitals and the private health sector are quite often the initial, single or intermittent provider of M/XDR-TB care.
- Protecting the community and health-care workers from infection while treating patients raise major ethical issues.
- Case-holding is complicated when patients migrate to settings with uneven capacities in place to manage M/XDR-TB.

The high cost of MDR-TB management is mostly the result of the cost of SLDs; use of hospitalization (up to 50% of the total cost of treatment in middle income countries); and the size of the workforce necessary to diagnose, treat and care.
The solution

Countries have been tackling demands, complexity, and costs of M/XDR-TB management by implementing one or two different models of care:

- **Out-patient care**, which consists of treating patients on ambulatory basis from the start of treatment and hospitalizing only for medical reasons. The chief advantage of this model is the social acceptability by patients; its lower cost; and the lower risk of nosocomial transmission. The successful implementation of this model depends, to a large extent, on i) the availability of a strong social support network to promote adherence to treatment through information and education on the disease, psychological counseling, and enablers to deal with socio-economic barriers; and ii) on the availability of a network of primary health-care facilities with health-care workers properly trained on M/XDR-TB management.

- **Hospital-based care**, which consists of hospitalizing patients until they become culture negative (usually during the first six months of treatment); followed by outpatient care. The main advantages of this model are the easier implementation of DOT; the probable lower transmission of infection to household contacts and community in general; and the easier training of health-care workers that are not familiar with SLDs. The successful implementation of this model depends on the availability of funds and beds to support hospitalization for long periods; proper infection control measures in hospital wards; and the implementation of basic ethics and legal principles that guarantee respect and promotion of human rights. The higher frequency of other medical conditions among those co-infected HIV makes more frequent the need to hospitalize these patients.

Out-patient care happens in both models since hospitalizing for two years is not an option for obvious reasons, ranging from costs to social acceptability. Despite the high costs, M/XDR-TB treatment is cost-effective compared to international benchmarks and measured in disability adjusted life years (DALYs) averted, both in settings using hospitalization during the initial phase of treatment and in those treating on out-patient care basis during the full course of treatment. However, there are no studies looking at the cost-effectiveness of hospital-based care in low resource settings. One model is not necessarily better than the other, and both may coexist. However, depending on the patient needs and the capacity in place, one model may be preferred over the other. In a small size country, for example, that plans to treat thousands of cases every year, it is very unlikely that there is hospital capacity ready available to properly treat these patients, making out-patient care the preferred option. However, hospitalization may be the preferred choice in the case of HIV infected patients during the initial phase of treatment; in the absence of social support networks that promote treatment adherence; or when primary health-care workers properly trained in the management of adverse effects are lacking or insufficient.
Urgent actions needed

Overall, the countries should select models of care to manage M/XDR-TB after having conducted a thorough analysis of, at least, the following factors:

- Patient needs and his/her preferred options to adhere to treatment
- Local law and ethics standards
- Engagement of private sector and public hospitals in M/XDR-TB management
- Hospitals with infection control measures in place
- Estimated number of patients to treat and hospital-bed capacity
- Funding to guarantee the health-care workforce needed to deliver DOT
- Primary health-care workforce properly trained on MDR-TB management
- Burden of HIV among MDR-TB patients to be treated and level of collaboration established with HIV control programmes
- Laboratory capacity in place to monitor response to treatment
- Attitudes of caregivers to the different options of care
- Social support networks that facilitate a patient-centred approach to DOT
- Capacity to educate, and not only to train, patients on hygiene and infection control measures at household level
- Geographical access to points of M/XDR-TB care

WHO, Stop TB Partnership and technical agencies to assist countries in conducting the analysis to create models of care that meet the needs of the patients and are feasible and cost-effective in the health system.

The WHO Guidelines for the programmatic management of DR-TB define a framework for M/XDR-TB treatment drawing on the five components of the DOTS strategy.\(^1\) The Green Light Committee Initiative of WHO and the Stop TB Partnership supports the piloting and scaling up of MDR-TB management, and promotes the best standards of care drawing on WHO guidelines.\(^2\) In the next sections, we discuss in more depth some fundamental components of that framework that should be carefully examined when selecting and implementing a model of M/XDR-TB care and their respective challenges.

3.2 Ensuring that TB treatment and care are consistent with ethics and human rights norms and promote social justice

The problem

In some circumstances, personal dignity and rights of patients have been compromised in the process of TB care and control, and fundamental ethical norms for public health and clinical practice may not have been applied. Steps taken by some Governments, service

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facilities and providers in the interest of protecting public safety may have included measures that have not effectively balanced the protection of the health and rights of the public and those of persons suspected to have TB or with confirmed TB. In the face of worries about M/XDR-TB, public emotions linked to poor information and stigma, severely strained manpower and resources, all may further complicate and compromise careful decision-making. In some instances this has led to severe restrictions on rights, such as broad rather than exceptional use of involuntary detention or isolation. Ethically-compromised practices may also be linked closely to inequitable access to, and quality of, prevention, care and health promotion related to TB and other health challenges. Poor, vulnerable and highly marginalized groups are most likely to become infected with TB and to suffer poor outcomes when illness occurs.

Many NTPs may currently have incomplete answers and policies to questions relevant to the ethical design and conduct of services, particularly in light of MDR-TB, for example: (a) what are best practices for care of patients and infection control if M/XDR-TB is suspected and diagnostic tests and second-line medicines are not yet readily available? (b) if adequate TB infection control practices are not yet in place in major hospitals where should infectious TB patients be initially treated? (c) what are the limits of health-care workers’ “duty to treat”, especially when proper infection control measures are absent? (d) what human rights principles and local laws are being applied in decision-making regarding the use of involuntary detention? (e) are the International Standards of TB Care, the Patients Charter for Tuberculosis Care, International Health Regulations, and ethical standards in TB research and surveillance being applied?3,4,5 Though the answers to some of these questions may vary with local context, capacity ready available to answer these questions under a sound ethical framework is weak or may even be absent in some countries.

The solution

To help prevent or address such problems, countries should:

• pursue overall aims of primary health care, universal health coverage, and the upholding of human rights, social justice and development;

• apply all six components of the Stop TB Strategy for effective TB detection, diagnosis, treatment and prevention, and with recognition of the need to address all forms of TB and to serve all persons in need, and especially the poor and vulnerable;

4 The patients’ charter for tuberculosis care. World Care Council/Conseil Mondial de Soins, 2006 (www.worldcarecouncil.org/).
strengthen capacities to develop and apply ethically-based TB care and control policies, drawing on all available guidance and best practices. This includes involving ethics advisory bodies at the national or facility level, seeking technical assistance.

Urgent actions needed

- NTPs should explicitly consider ethical issues related to policy and service provision.

- WHO, with the assistance of a WHO Task Force on Ethical Issues in TB Control and broad stakeholder consultation, to complete guidelines by early 2010 to help support sound ethical practice in TB control for use by NTPs, all stakeholders involved in TB prevention, treatment and care.

- Ministries of health and NTPs may wish to create their own task forces on ethical issues to consider key immediate questions as they develop MDR-TB response plans. Relevant legislation may also be required.

3.3 Involving all health-care providers, including public hospitals

NTPs in many high TB-burden countries have not had the capacity to treat M/XDR-TB patients. Many of these patients were managed, and continue to be managed, outside NTPs. Countries with a large burden of M/XDR-TB do have the capacity to diagnose M/XDR-TB cases in the private sector. For example, a network of private laboratories in India diagnosed about a thousand MDR-TB cases in 2007. Laboratories in large hospitals in China and Indonesia are also equipped to diagnose drug-resistant TB. In the absence of any formal links with NTPs, the quality of diagnosis, treatment and care by these private providers remains questionable.

The market for SLDs in high M/XDR-TB burden countries is large. However, unlike FLDs, a large proportion of which are bulk-purchased by NTPs, most if not all SLDs are sold in the private retail market. The prescribers and the receivers of MDR-TB medicines are not known to NTPs and efforts are rarely made to identify them.

There are concrete examples of private institutions undertaking M/XDR-TB management. The Aga Khan University hospital in Karachi, Pakistan, has a good working programme on MDR-TB management. Indus hospital, a state-of-the-art, multi-speciality, philanthropic hospital in the same city, financed by expatriates, recently set up a community based MDR-TB management programme on the lines of that run by Partners in Health in Peru. A few NGO and private hospitals in India undertake proper management of MDR-TB patients. A remarkable example has been the Tropical Disease Foundation hosted by Makati Medical Centre -- a modern private multi-speciality hospital -- in the Philippines, which was the very first project approved by the Green
Light Committee. Almost every care provider can play important role in the management of drug susceptible TB. However, in view of the complexities involved, treatment and care of M/DR-TB has to be undertaken by specialist care providers affiliated to institutions equipped to provide the support required. Treatment supervision may be community-based but it has to be backed up by expert support. Public-private mix initiatives need to be tailored to the requirements of programmatic management of MDR-TB.

The emergence and spread of M/XDR-TB is likely to be checked only through a rapid scale up of programmatic management of M/XDR-TB. This is unlikely to happen if NTPs focus their attention on public sector institutions alone. A sequential approach of waiting to first strengthen public sector laboratories and treatment centres and then begin supporting non-programme structures may not help achieve the necessary pace either. NTPs ought to take a more comprehensive approach of identifying, strengthening and making operational, an adequate number of selected facilities from all sectors: public, voluntary, private or corporate. For example, following the Philippines example, if addressing quality or other related issues in some NGO or private institutions is likely to take time or investment than setting up a public sector institution from the scratch, work must begin on both fronts simultaneously. If there is no capacity in the public sector to undertake both, capacity outside the programme must be harnessed at the same time to meet the requirements.

**Urgent actions needed**

- TB technical partners should help NTPs undertake a situation assessment of M/XDR-TB diagnosis, treatment and care in the country encompassing all public, private, corporate and voluntary sectors.
- NTPs should conduct a mapping to understand the sources of M/XDR-TB patients and the places where they are currently diagnosed and treated.
- NTPs should understand M/XDR-TB diagnosis and treatment practices among other laboratories and care providers and assess their appropriateness.
- NTPs should assess the strengths and weaknesses of non-programme laboratories and care providers and their potential to collaborate in scaling up M/XDR-TB management.
- NTPs should undertake phased involvement of willing non-programme laboratories and institutions in M/XDR-TB management by first establishing linkages with them and harnessing their capacity to deliver.

3.4 **Collaborating with HIV programmes to strengthen both TB and HIV control**

**The problem**

People living with HIV have a higher risk of M/XDR-TB, with an increased mortality up to 90% or more, and greatly reduced survival time. Early diagnosis and treatment of drug
resistant TB is thus essential but complicated. Management of drug-drug interactions with antiretroviral therapy (ART) and anti-TB treatment is also a major challenge, due to frequent severe toxicities and adverse events experienced when combining SLDs and ART.

Of the 27 MDR-TB priority countries, 12 are also TB/HIV priority countries. These countries contain ¾ million HIV related TB cases, 54% of all HIV related TB globally.

HIV is probably accelerating the spread of M/XDR-TB, especially in countries where prevalence of infection with M/XDR-TB is high. New HIV infections are stable or on the rise in those countries with higher proportions of MDR-TB cases including China, the Russia Federation, Ukraine and Latvia necessitating urgent actions to address the overlapping epidemics. Although not well studied the problem is a public health concern in sub-Saharan Africa also.

The solution

In order to obtain a better understanding of the extent and magnitude of the overlap between HIV and TB drug resistance we must incorporate HIV status in drug resistance surveys. We must also explore synergies between HIV and TB drug resistance surveillance.

By 2007, only 11% of all TB patients in the 27 MDR-TB priority countries were tested for HIV, which is up from 2% in 2004. One out of four (25%) of those tested for HIV were found to be positive and almost a third (29%) of these were placed on antiretroviral therapy (ART). Building further on this experience, nationwide scale up of collaborative TB/HIV activities through strengthened collaboration between national TB and AIDS control programmes need to ensure:

- HIV testing of all TB patients and suspects, including those with both drug susceptible and drug resistant strains;
- intensified and prompt TB case finding mainly by HIV service providers;
- early diagnosis and treatment of drug susceptible and drug resistant cases among people living with HIV;
- TB prevention once active disease has been excluded;
- the institution of TB infection control measures in all HIV care settings.

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6 China, the Democratic Republic of the Congo, Estonia, Ethiopia, India, Indonesia, Myanmar, Nigeria, the Russian Federation, South Africa, Ukraine and Viet Nam.
In settings where there is extensive overlap between drug resistance and HIV, and where early diagnosis is difficult, provisions to put patients on empirical treatment for drug resistant TB will avert unnecessary death of people living with HIV.

Enhanced access to better and quicker TB diagnosis (including culture technologies and molecular tests), particularly among people living with HIV, will identify drug susceptible and resistant strains for appropriate treatment. Exploring synergistic opportunities between HIV and TB laboratory initiatives will benefit both sides.

For all of this to happen there will need to be improved collaboration between TB and HIV stakeholders to include MDR-TB and XDR-TB in TB and HIV strategic planning and to generate the political commitment for action and resource allocation. Increased engagement of community groups will empower communities to act to prevent the spread of TB and generate demand for collaborative TB/HIV services, including prompt TB prevention, diagnosis and treatment.

Operational research on optimal models of care for people living with HIV, including clinical trials for shorter and more efficacious co-treatment (anti-TB medicines and ART), is also part of the solution.

**Urgent actions needed**

- To map extent of the problem by including HIV testing as a standard in national TB drug resistance surveys.
- Nationwide scale up collaborative TB/HIV activities.
- Scale up the access for better TB diagnostic capacity in PLHIV including culture technologies and molecular tests.
- Increased engagement of community groups.
- Improved collaboration between TB and HIV stakeholders and political commitment.
- Basic and operational research on optimal models of care in HIV related M/XDR TB.