



Multidrug-resistant tuberculosis in Myanmar

Progress, Plans and Challenges



Dr Tin Mi Mi Khaing, Dr Myo Zaw, Dr Thandar Hmon, Dr Michael Rich and Dr Phyu Noe review MDR-TB patient records at Aung San TB Hospital in Yangon, March 2012.

The total cost of scaling up MDR-TB management is US\$ 55 million, out of which US\$ 41 million is yet to be raised. While the top priority remains preventing MDR-TB by sustaining and improving basic TB control, the Ministry of Health is working with technical and financial partners towards the goal of universal access to MDR-TB diagnosis, treatment and care.

Background

MDR-TB, which is defined as TB resistant to at least isoniazid and rifampicin, the two most powerful anti-TB drugs, is a serious threat to the fight against TB. In 2012, there were an estimated 650,000 cases of MDR-TB among the world's 12 million TB cases.

MDR-TB emerges as a result of underinvestment in basic TB control, including stock-outs and the use of poor-quality or counterfeit anti-TB drugs, improper treatment of TB patients and transmission of drug-resistant strains. MDR-TB does not respond to the standard six-month regimen with first-line anti-TB drugs. Instead, it takes two years to treat with drugs that are less effective, more toxic and cost at least 100 times more.

Improper use of second-line anti-TB drugs can lead to the development and transmission of XDR-TB, caused by MDR-TB strains that are also resistant to treatment with any fluoroquinolone and any of the injectable second-line anti-TB drugs. By 2012, XDR-TB cases were reported from 70 countries, including Myanmar. Treatment options for XDR-TB are severely limited and fatality rates are high, especially in patients co-infected with HIV. A few countries have also found patients that are resistant to all available anti-TB drugs, bringing TB back to the pre-antibiotic era.

The MDR-TB burden in Myanmar

In 2011, WHO estimated that about 180,000 adults and children developed TB, including 20,000 infected with HIV and 9,000 suffering from MDR-TB. Myanmar is one of the world's 27 high MDR-TB burden countries, and the MDR-TB rate among new cases is the highest in South-East Asia. WHO estimates that in 2010 there were more than 5,000 MDR-TB cases among the notified pulmonary TB cases (Table 1).

Two nationwide drug resistance surveys have been carried out, and a third started in September 2012. The first survey, 2002-2003, showed an MDR-TB rate of 4% among new cases and 15.5% among previously treated cases. In the second survey, 2007-2008, the proportion of MDR-TB was 4.2% among new cases and 10.0% among previously treated cases.

The World Health Organization (WHO) estimates that 9,000 multidrug-resistant tuberculosis (MDR-TB) cases occur in Myanmar each year. Extensively drug-resistant TB (XDR-TB) has been reported since 2007.

In 2011, only 2% of MDR-TB cases received adequate diagnosis, treatment and care. Undiagnosed or mismanaged MDR-TB cases lead to further spread of the disease.

The Ministry of Health is committed to fighting MDR-TB. In 2009 the National TB Programme (NTP) and Médecins Sans Frontières (MSF) launched an MDR-TB pilot project in 10 townships in Yangon and Mandalay.

Following excellent initial results, the NTP is taking MDR-TB management to scale. The 2011-2015 MDR-TB expansion plan will enable treatment of nearly 10,000 MDR-TB cases in 100 townships.

Table 1: MDR-TB estimates in Myanmar

New TB cases with MDR-TB	4.2% (3.1 - 5.6)
Retreatment TB cases with MDR-TB	10.0% (6.9 - 14)
Estimated MDR-TB cases among new pulmonary TB cases notified in 2010	4,200 (3 100 - 5 600)
Estimated MDR-TB cases among retreated pulmonary TB cases notified in 2010	1,000 (710 - 1 400)

Source: Global Tuberculosis Control, 2011, WHO



Ko Han Zaw is 35 years old and lives in North Okkalapa Township in Yangon. After nine months of MDR-TB treatment his condition has greatly improved.



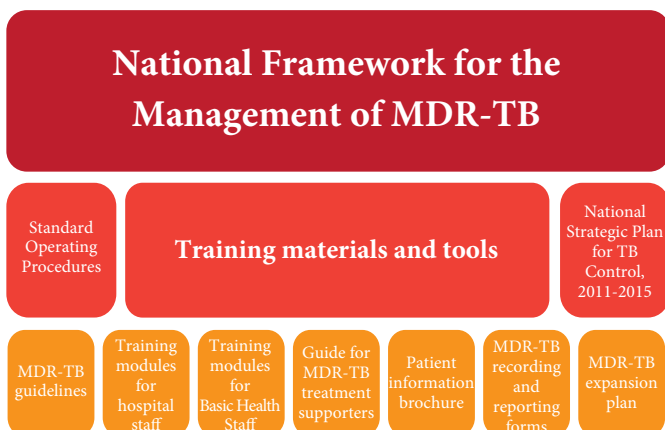
Daw Tin Tin Nwet, a midwife from Mandalay, delivers home-based care to Ma Yin Yin Mya from Aung Myay Thazan township. Ma Yin Yin Mya was cured from MDR-TB in September 2011.

Policy, strategy and coordination

The Ministry of Health has established structures for managing drug-resistant TB (DR-TB), ensuring coordination from the national level down to the hospital and township levels for programme and patient management:

National DR-TB Committee	<ul style="list-style-type: none"> - Overall policy and strategy guidance - Meets bi-annually
Expert DR-TB Committee	<ul style="list-style-type: none"> - Oversees Hospital DR-TB Committees - Provides expert advice to National DR-TB Committee - Meets biannually
Region/State DR-TB Committee	<ul style="list-style-type: none"> - Interdepartment coordination, operational support - Meets biannually
Hospital DR-TB Committee	<ul style="list-style-type: none"> - Clinical patient management, links with community DOTS, local program management - Meets monthly

The NTP has developed a number of documents as part of the National Framework for the Management of MDR-TB. The National Strategic Plan for TB Control, 2011-2015, has recently been updated with a more ambitious MDR-TB expansion plan.



Achievements

A Green Light Committee-approved MDR-TB pilot project was initiated in 10 townships of Yangon and Mandalay in July 2009. The pilot project was made possible with financial support from the Three Diseases Fund (3DF), United States Agency for International Development (USAID), UNITAID (an international facility for the purchase of diagnostics and drugs for HIV/AIDS, TB and malaria) and MSF. Two years later, 275 MDR-TB patients were enrolled, and by June 2012, the first 87 MDR-TB cases in Myanmar were cured. Following the successful pilot of MDR-TB management in 2009-2011, the NTP is committed to take MDR-TB management to scale. Key achievements since 2009 are outlined in the following sections.



Daw Hnin Moe Tun delivers food to hospitalized MDR-TB patients at Aung San TB Hospital in Yangon.

Treating and caring for people affected by MDR-TB

All MDR-TB patients are treated with quality-assured second-line anti-TB drugs provided free of charge. A standardized treatment regimen is used for two years. Laboratory investigations and ancillary drugs, to manage frequent and sometimes life-threatening side-effects, are also provided free of charge.

During the pilot phase, all MDR-TB patients were hospitalized for the initial two to three months to ensure that the treatment was tolerated. Following the hospitalization, daily home-based care was delivered by Basic Health Staff. In 2011, the NTP shifted its policy to hospitalize only severely ill patients and patients with social problems. Home-based care continues to be provided by Basic Health Staff and increasingly also by nongovernmental organizations (NGOs) and volunteers. To ensure adherence to the lengthy and toxic treatment, the NTP and MSF provide food to MDR-TB patients hospitalized at the Aung San TB Hospital in Yangon and Patheingyi TB Hospital in Mandalay. In addition, MDR-TB patients receive socioeconomic support, enablers to cover for transportation charges to and from clinics, as well as counselling and psychosocial support. Basic Health Staff are also compensated for travel costs to deliver home-based care to MDR-TB patients.

Human resources

- The National Strategic Plan for TB Control, 2011-2015, sets clear directions for increasing staff with the support of NGOs, community workers and volunteers, as well as training and providing technical assistance.
- Health-care staff at all levels have received extensive training on MDR-TB diagnosis, treatment and counseling, recording and reporting and infection control.
- Myanmar experts have benefited from study tours and international training in Indonesia and the Philippines for TB infection control, Nepal, India and Thailand for MDR-TB clinical management, and India and Thailand for MDR-TB diagnosis.
- Six expert MDR-TB monitoring missions have been carried out since the launch of the pilot project, providing technical assistance on programmatic and clinical MDR-TB management.
- With technical support from WHO and with funding mainly from the Global Fund to Fight AIDS, Tuberculosis and Malaria, the NTP has added 75 staff to support the TB and MDR-TB programme implementation, including field officers, data assistants and laboratory technicians.



On 12 July 2010, the biosafety level 3 laboratory in Yangon was officially opened in the presence of HE Minister of Health and the Chief Executive Officer of the Foundation for Innovative New Diagnostics.

Laboratory strengthening and new diagnostic tools

- UNITAID has financially supported the EXPAND-TB project to upgrade capacity at the National TB Reference Laboratories in Yangon and Mandalay. Extensive technical support has been provided by the Foundation for Innovative New Diagnostics (FIND), while WHO has facilitated the importing of all equipment and supplies and has ensured coordination among partners. The new TB diagnostic tools include liquid culture, first-line drug susceptibility testing (DST), rapid immunoassay for species identification and line probe assay for rapid diagnosis of MDR-TB.
- Excellent concordance between conventional and new laboratory methods has paved the way for rapid diagnosis of MDR-TB.
- As of August 2012, five Xpert MTB/RIF machines are available in Myanmar. The WHO-endorsed Xpert MTB/RIF tool is fully automated, requires limited infection control measures and can be used at the level of point of care. *Mycobacterium tuberculosis* and rifampicin resistant TB can be diagnosed within 90 minutes.
- Quality control for drug susceptibility testing, technical assistance and collaboration for capacity-building continue with support from the WHO-designated supranational TB reference laboratory in Bangkok, Thailand.



Dr Moe Zaw reviews the X-ray of an MDR-TB patient at Aung San TB Hospital.



Two reference laboratories are equipped with liquid culture and drug susceptibility techniques as well as nucleic acid amplification tests to rapidly detect MDR-TB.



Ma Lei Yin Win, medical technologist, is using Xpert MTB/RIF to rapidly detect TB and MDR-TB at the Upper Myanmar TB Center in Mandalay.



MSF built a new ward at Aung San TB Hospital in 2009 with single occupancy and well ventilated rooms to ensure infection control.

Infection control

- Infection control practices were assessed and an infection control plan was developed in 2010.
- With support from MSF, a new MDR-TB ward has been built at Aung San TB Hospital in Yangon. There are separate men's and women's wards with excellent infection control measures. The Patheingyi MDR-TB Hospital in Mandalay has also been completely renovated to ensure minimal transmission of TB and MDR-TB.
- Infection control upgrading has been ensured in 10 townships, and by the end of 2012, 22 township health facilities will be upgraded.
- Airborne infection control has been incorporated into routine clinic policies and practices, with posters advising on cough hygiene, regular provision of N-95 respirators to health-care workers and masks to patients, outdoor TB waiting areas and separate screening and registration areas for TB patients.

Results of the MDR-TB pilot project

The treatment of MDR-TB cases started in July 2009 in Yangon and Mandalay regions in a total of 10 out of 325 townships, with a target to enrol 275 patients. As of August 2012, there were 459 patients enrolled in the programme in 22 townships, with outcomes available for 122 patients (Figures 1 and 2). The MDR-TB pilot project has proven feasible with good cure rates (71%), despite protracted and severe disease among all patients.

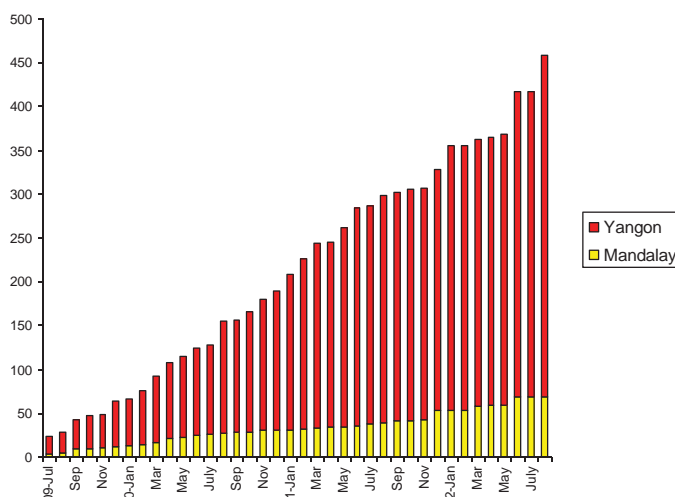


Figure 1: From July 2009 to August 2012, 459 MDR-TB patients have been enrolled on treatment with quality-assured second-line anti-TB drugs.

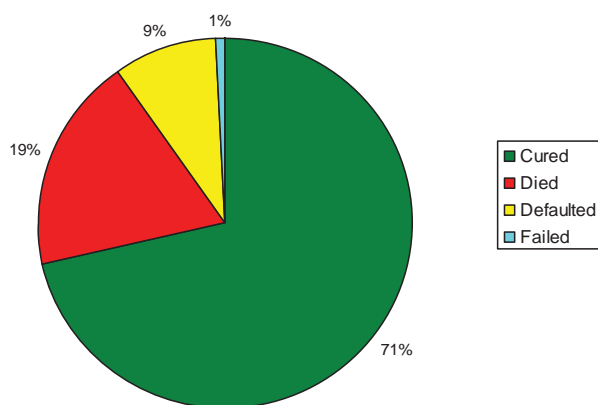


Figure 2: Treatment outcomes for patients enrolled between July 2009 and June 2010 in the Myanmar MDR-TB pilot project (n=122).

MDR-TB scale-up plan

Building on the success of the pilot project, an Expansion Plan for the diagnosis and treatment of MDR-TB has been developed as an addendum to the National Strategic Plan for TB Control, 2011-2015. The goals of the Expansion Plan are threefold:

1. Diagnosis of MDR-TB in all groups of patients at risk for MDR-TB
2. Diagnosis of MDR-TB in all HIV-infected patients with TB
3. MDR-TB treatment for all patients diagnosed with MDR-TB under WHO-endorsed treatment protocols

Table 2: Goals for MDR-TB management in Myanmar

Indicator	Baseline (2010)	Target (2015)
Percentage of previously treated TB patients tested for MDR-TB	Less than 10%	100%
Percentage of new TB patients tested for MDR-TB	Less than 1%	20%
Ratio of culture laboratories to population	1 per 25 million	1 per 10 million
Percentage confirmed cases of MDR-TB enrolled in treatment according to international guidelines	Not known	100%
Number of confirmed cases of MDR-TB enrolled in treatment according to international guidelines	200	4,000
Treatment success rate among confirmed cases of	Not available	≥75%

From 2011-2015, almost 10,000 MDR-TB cases will be enrolled in treatment. The annual number of MDR-TB patients to be enrolled and the scale-up of diagnostic and clinical facilities are presented in Table 3.

By the end of 2015, 100 townships (nearly a third of Myanmar's townships) will have MDR-TB facilities, covering 42% of the country's population.

Table 3: Geographical scale-up of MDR-TB management

Year	MDR-TB patients enrolled in treatment	Reference diagnostic labs with culture/ with DST	Centers with Xpert MTB/RIF	Regions or states with TB/ MDR-TB treatment centre	Townships with MDR-TB treatment centre	Townships covered	Population covered
2010	200	2/2	0	2	10	3.1%	3.9%
2011	500	2/2	5	2	22	6.8%	9.3%
2012	1,200	5/2	7	5	37	11.4%	14.6%
2013	1,800	5/2	12	10	62	19.7%	26.3%
2014	2,400	5/5	12	10	72	23.7%	31.6%
2015	3,395	5/5	19	10	100	30.8%	41.5%

Funding needs, availability and gaps

The cost of MDR-TB patient management is calculated at nearly US\$ 5,000 per patient, including second-line anti-TB drug costs of US\$ 2,500. The ambitious MDR-TB expansion plan will cost an estimated US\$ 53 million over a five-year period (2011-2015). This figure includes all aspects of the programme: second-line anti-TB

drugs and ancillary drugs, socioeconomic support to patients and travel allowances, enablers to treatment supporters, laboratory capacity and diagnosis, infection control, training, supervision and monitoring and evaluation.

Table 4: Estimated total MDR-TB expansion plan cost over five-year period, 2011-2015

Year	Patients enrolled	Direct patient costs (US\$ 4,740/patient)	Estimated programme costs (US\$)	Total (US\$)
2011	500	2,370,000	1,269,273	3,639,273
2012	1,200	5,688,000	1,538,191	7,226,191
2013	1,800	8,532,000	1,750,320	10,282,320
2014	2,400	11,376,000	2,015,236	13,391,236
2015	3,395	16,092,300	2,221,697	18,313,997
Total		\$44,058,300	\$8,794,717	\$52,853,017

The available resources for MDR-TB control, excluding human resources and infrastructure contributed by the Government, include:

- Global Fund: the majority of funding for MDR-TB management is from the Round 9 grant which contains about US\$ 11 million for MDR-TB, including second-line anti-TB drugs for 1,800 patients.
- 3DF: substantive funding supports human resource development, socioeconomic support and allowances to patients, as well as enablers for basic health staff and volunteers ensuring MDR-TB treatment adherence.
- UNITAID: has supported second-line drugs, upgrading of two reference laboratories and Xpert MTB/RIF machines and cartridges. UNITAID will supply the reference laboratories with reagents and commodities for rapid MDR-TB diagnosis until the end 2013.
- USAID: supports WHO with technical assistance for MDR-TB management, policy development, capacity-building, laboratory strengthening, community involvement and infection control. In addition, in 2011 USAID launched an MDR-TB project in Myanmar through FHI360.



MDR-TB patients in Insein township, Yangon, are counseled on MDR-TB treatment and care.

There is an estimated US\$ 14 million for MDR-TB management available for 2011-2015, leaving a significant funding gap of US\$ 41 million.

Without proper management, MDR-TB diagnosis and treatment would be provided either by general practitioners who might not abide by the NTP's MDR-TB treatment protocols; or by self-treatment through the purchase of inadequate quantities and combinations of medicines due to financial constraints.

The purchase of anti-TB drugs from pharmacies and drug shops could also lead to the use of counterfeit and poor-quality drugs. Such practices would lead to the development, amplification, and spread of MDR-TB. More severe drug resistance patterns, including XDR-TB, would render the standardized MDR-TB treatment regimen useless. Instead, individualized/tailor-made second-line drug regimens would be required, resulting in escalating human and financial resource needs and worse treatment outcomes.



Ko Min Min, 38 years old, was a successful shop owner in Aung Myae Thar Zan township, Mandalay, but when he was diagnosed with MDR-TB, he had to sell his business. His younger sister and brother passed away from TB as a result of treatment failure six years ago. Thanks to the MDR-TB programme, Ko Min Min had access to diagnosis, treatment and care and after two years of rigorous treatment, he was declared cured on 15 July 2011. Today he's looking forward to getting back to business.

Next steps on MDR-TB prevention and control in Myanmar

- The first priority remains to prevent MDR-TB by strengthening basic TB control and expanding the successful public-private mix programme. Private general practitioners working with the Myanmar Medical Association and Population Services International should be further involved in MDR-TB prevention, diagnosis, referral and care.
- Better knowledge of the MDR-TB situation and trends will be available following the third nationwide drug resistance survey.
- Expanded eligibility for drug susceptibility testing and treatment enrollment will improve MDR-TB cure rates.
- Additional technical partners will be engaged to allow for the expansion of MDR-TB management, including in prisons.
- Further involvement of NGOs and volunteers in community-based MDR-TB care will ensure sufficient capacity to manage close to 10,000 MDR-TB cases by the end of 2015.
- Active resource mobilization efforts will be pursued, targeting:
 - Future funding opportunities with the Global Fund
 - UNITAID for the scale-up of rapid diagnostic tools
 - Three Millennium Development Goals Fund (successor to 3DF)
 - USAID for continued support to MDR-TB technical assistance through WHO and support to FHI360 for MDR-TB prevention and control
 - Japan International Cooperation Agency for continued and increased laboratory strengthening and expansion of public-private mix



Ma Thin Thin Wai is 30 years old and lives in Hlaing Township, Yangon. She is married to a trishaw driver and has one daughter and one son. Ma Thin Thin Wai was suffering from TB for more than five years and she was treated without success two times before she had access to quality-assured second-line anti-TB drugs. On 20 July 2011 she was declared cured from MDR-TB.

The inability to scale up MDR-TB management as a result of lack of funding would be devastating to MDR-TB patients, their families and the community and would jeopardize the gains made in TB control in Myanmar.

The following partners are gratefully acknowledged for their support for MDR-TB control in Myanmar:

