

HATiP

HIV & AIDS Treatment in Practice

Issue 166 | 08 October 2010



In this issue:

Decentralised, patient-centred models of delivering treatment and palliative care for people with M/XDR-TB; by Theo Smart *page 2*

- Managing MDR-TB in the community
- Treating MDR-TB in the community is possible
- Models of care for drug-resistant TB
- The many downsides of hospital-based TB care in a resource limited setting
- The risks of transmission in hospitals versus within the community
- Ensuring high quality care and adherence outside hospital-based DR-TB management
- Leveraging the community and technical partners in Lesotho
- Staged decentralisation in KwaZulu Natal
- Ambulatory MDR-TB care in Nepal
- Clinic-based community care in Khayelitsha... and the Western Cape
- Adapting a more community-based approach in other settings

Decentralised, patient-centred models of delivering treatment and palliative care for people with M/XDR-TB

By Theo Smart

This clinical review was kindly supported by the Stop TB department of the World Health Organization and the Diana, Princess of Wales Memorial Fund.

Thanks to the reviewers of this edition: Dr Haileyesus Getahun, Dr Ernesto Jaramillo, Dr Christian Gunneberg (WHO Stop TB department), Dr Bhawana Shrestha (Genetup Clinic, Katmandu, Nepal), Dr Helen Cox, Dr Gilles Van Cutsem (MSF Khayelitsha).

Managing MDR-TB in the community

This HATIP is part of a series of articles on the management of multi-drug resistant tuberculosis in the community.

This HATIP looks at how treatment and palliative care for MDR-TB can be delivered, focusing on the various models of more decentralised patient-centred TB care that are being implemented in Lesotho, KwaZulu Natal and Khayelitsha, South Africa, as well as in Nepal and India. The next issue will address what should be the role of empiric treatment; the need for optimised treatment regimens; the management of serious side effects (that appear to be more common in people with HIV) and common clinical conditions in people with M/XDR-TB — as well as what to do when treatment fails.

Treating MDR-TB in the community is possible

"It's now over a decade ago that Partners in Health (PIH) began treating patients with multidrug resistant tuberculosis (MDR-TB) in Peru, when no one else was treating MDR-TB as per WHO guidelines at that time," said Professor Edward Nardell of Harvard University and PIH during a plenary at the 2nd South African TB Conference in June.

"And I think from the get-go, we actually got it right. We used high-dose drugs, we used multiple drugs and we did it, from the beginning, in the community and not in hospitals. Now in PIH-Lesotho, in Karachi, in Cambodia and in many other sites, community-based treatment is the way that MDR-TB is being treated. And in Lima, Peru only 10% of patients are hospitalised now. Community-based treatment is highly effective, with less opportunity for institutional transmission."

The much-celebrated work of PIH and its Peruvian affiliate, Socios En Salud (SES), in the shantytowns outside of Lima, Peru was the first demonstration that community-based treatment for MDR-TB could succeed in a resource-poor setting. It was done at a time when many, including the Peruvian Ministry of Health, considered MDR-TB treatment impractical and unaffordable.

Socios En Salud pioneered the directly observed therapy (DOTS)-plus approach, which included training and hiring people from the community to accompany patients during up to two years

of MDR-TB treatment. They achieved very high cure rates of around 83% among those who completed at least four months of treatment in the initial report.¹ Since that time, the strategy has been expanded to deliver MDR-TB care and treatment throughout Peru. A subsequent report from the country has reported cure rates of 66.3% (out of 400 patients who initiated treatment), and relatively high cure rates for XDR-TB (60.4%).²

A few years ago, the approach was adapted to deliver community-based MDR-TB care in Lesotho, a setting with a high burden of HIV coinfection distributed across remote, mountainous terrain. Preliminary results in Lesotho sound just as promising.³ In fact, the experience in Lesotho guided the development of [a field guide on the Management of MDR-TB](#) authored by Dr Kwonjune Seung and Dr Hind Satti, that has been produced by PIH and WHO, (and which serves as much of the basis for sequence of care for MDR-TB described later in this edition of HATIP).

This is the third in a series of HATIP articles on M/XDR-TB, the [first](#) of which described the growing public health importance of the disease, particularly in countries and communities with a high burden of HIV, and the [second](#) of which looked at laboratory capacity and screening practices needed to improve case detection.

Regardless of the model of care delivery, we would argue that the palliative care approach is an essential part of the patient-centred approach. As always, we should note that palliative care is an holistic approach, that should start as soon as a person presents for care, and which tries to alleviate the pain and suffering of people with, and families affected by a life-threatening illness.

Many of the clinic and community-based MDR-TB care initiatives meet some of the key criteria for palliative care, in recognising that people with MDR-TB and their families have a right to maintain a reasonable quality of life over the entire course of illness. The programmes described in this article attempt to help patients and their families deal with the emotional, economic and psychosocial consequences of having a highly stigmatised infection.

But a palliative care approach emphasises patient and family-centred care over the entire course of illness. Unfortunately, a cure is not always possible, and many TB care providers are unsure of what to do when it is clear that all treatment options have been exhausted — when or whether to stop treatment and how to best provide end-of-life care. Models of care that do not sufficiently engage the patient and his or her family in a 'treatment' partnership may be particularly poorly equipped to manage this aspect of illness — and some programmes appear to be failing in this regard.

Models of care for drug-resistant TB

WHO's Guidelines for the Programmatic Management of Drug-resistant Tuberculosis (PMDT) refers to three basic models to deliver treatment and care for people with drug-resistant TB: hospitalisation, clinic-based care and community-based care.⁴

Hospitalisation:

In many industrialised countries, and even some middle-income countries such as South Africa, strict hospitalisation of patients with drug-resistant TB is still deemed necessary, at least until the case becomes culture-negative. When well-resourced, these facilities ought to serve as centres of excellence, able to employ a well-trained staff, with experts who can manage difficult cases, maintain high standards for infection control and provide access to rapid diagnostics, drug sensitivity and second-line TB drugs. Perfectly realised, they should also provide decent living conditions,

with recreational activities to prevent boredom over the long months of isolation, education for children and adequate food.

Providing such care doesn't come cheap — it could comprise up to 50% of the total price of treatment in middle-income countries.⁵ That's quite a lot when one considers that the cost of a course of treatment for MDR-TB is approximately US \$30,000 for countries that receive no drug procurement assistance from Unitaids and the Project Green Light Committee.

Clinic-based treatment:

Some programmes offer treatment within a clinic setting, which clearly requires the person with DR TB travelling to a clinic each day to receive their treatment. Such a system can be patient-centred provided the clinic is located close by — and in densely populated settings, the approach may actually be less stigmatising than having community-based teams visiting the patient's household each day. The PMDT guidelines stress that clinics must practice high standards of infection control — and take care that people with HIV are not exposed to drug-resistant TB.

Community-based care:

As already noted, programmes in Peru, Lesotho and other settings have demonstrated that multidisciplinary teams, including trained lay and community health workers (CHWs) can deliver care to the person with DR TB within their own home and achieve comparable results to hospital-based care.

The PMDT guidelines also stress that clinic and community-based care must emphasise education of the person with DR TB and his or her family, including how to improve infection control in the home.

"In practice, the distinctions between these approaches are becoming somewhat blurred — with programmes using components of each approach. As a review of the Khayelitsha programme makes clear, clinic-based care can also be community-based in that the clinic is within the community, and care is heavily reliant upon community-based TB treatment supporters. Meanwhile, KwaZulu Natal is decentralising in stages, relying on hospital based care initially, and then using mobile teams to provide care to people in their own homes (see descriptions of these programmes below).

The many downsides of hospital-based TB care in a resource limited setting

In addition to the expense, studies presented at recent conferences highlight a number of reasons why hospital-based care for TB (any TB) may be a poor option outside of the very well resourced settings. A survey of patients and care providers by Krause, Gwyther and Gould noted the extremely negative feelings associated with long-term hospitalisation — which also had an impact on the healthcare staff.⁶

"Hospitalisation led to estrangement between the patient and the caregiver which ultimately affected the caregiver's quality of life," the authors wrote. Such negative feelings are understandable, especially when parents and breadwinners are taken away from their families, sometimes leaving no one to care for their children.

"TB is all about case retention. If you can't keep your patients in the treatment programme and cure them, you're wasting your time," Bruce Margot, who is the TB programme manager in KwaZulu Natal for decentralising care said at the 2nd South African TB Conference (SATB) in Durban. "And if you profile the patients, 6 months hospital policy was certainly no good."

As reported in [HATIP #162](#), Dr Margot also noted that lack of hospital beds to handle the increasing numbers of people with M/XDR-TB was a leading reason cited for decentralising care. Delays getting lab results back and waiting to get a bed in the hospital for treatment could have increased community transmission of MDR- and XDR-TB strains, since patients continue to be infectious without effective treatment. In addition, it resulted in a high rate of mortality.

"We see between about 45 and 55% who die before the treatment programme actually starts," he said.

Dr Gilles Van Cutsem, working with Médecins sans Frontières (MSF) in Khayelitsha, made a similar point at the World AIDS Conference in Vienna:

"When MSF reviewed DR-TB in Khayelitsha in 2007, we found a difficult situation where patients had to wait very long for treatment because it was a centralized system. Every patient had to be admitted for six months in a central hospital which had a capacity of 350 beds while there were more than one thousand DR-TB cases per year in the Western Cape. So you had long waiting times," he said, adding that treatment outcomes were very poor. "There was less than 25% treatment success. But most importantly only 38% of the DR-TB patients were HIV-infected."⁷

He went on to point out that the actual burden of HIV-infected TB patients in the setting is much higher — the low number that were in treatment was likely a result of the fact that they were dying before they could be hospitalised and receive care.

"What was also important, was that there was a high (39%) default rate from the centralised hospital — which defeats the purpose of centralised management of DR-TB," he added. Finally, he pointed out that because its care was centralised, clinicians at the primary care level had very limited knowledge of DR-TB. So case detection in the clinic setting was limited, which was quite a serious problem since "infection control was virtually non-existent at the primary care level," he said.

The risks of transmission in hospitals versus within the community

But at the 2nd SATB conference, Prof Nardell proposed that the real risk of transmission in a healthcare setting is when drug resistance goes unrecognised. He believes that many of the cases of active disease, and much of the spread of highly resistant strains, may actually be the result of reinfection, sometimes with a more virulent or a more drug-resistant strain.

"If transmission is as important as I think it is; if reinfection is a big part of this, we need to get people out of hospitals and get them into the community for treatment," he said. To support this, he first cited data from Madras (now Chennai), India,⁸ where the very first clinical trials of ambulatory TB treatment found no more household conversions after the start of treatment when patients were sent home.

"Most household contacts had been exposed for months before the diagnosis was made," he said, "so susceptible household contacts unfortunately were probably already infected, and the patients who returned on therapy appeared not to be infectious."

Then he noted that early studies of the guinea pig model for transmission (which involves ventilating all the air from a TB ward into a chamber housing guinea pigs, which are highly susceptible to TB) showed that only a small number of patients — those who were drug-resistant and on inadequate therapy — had transmitted TB to the infected guinea pigs.⁹ A subsequent study found that untreated patients would transmit the most TB, while treated patients (who

were admitted to the ward *at the time of treatment initiation*) were only 2% as infectious.¹⁰ Even drug-resistant TB patients on treatment were less infectious than untreated patients.

“The treated patients were *admitted to the ward at the time treatment was initiated* and were generally removed before the sputum became completely negative. Hence the decrease in infectiousness *preceded* the elimination of the organisms from the sputum, indicating that the effect was prompt as well as striking,” the authors of that study (Riley et al) noted.

In other words, the available data measuring transmission indicate that although smear-positive patients are generally thought of as being infectious, this may not be the case once they have started effective TB treatment — even before they convert to smear negative.

Prof. Nardell described subsequent guinea pig studies that he has helped conduct at the Airborne Infectious Research (AIR) facility in Witbank, Mpumalanga (established in 2005 to study various infection control interventions). The first pilot test was to see how infectious MDR-TB would be in treated patients — and he was initially concerned that it might not work because of the data from Riley et al. However, 74% of the guinea pigs became infected.

“So we thought MDR-TB is really infectious and we proceeded to design tests for various interventions,” he said. But they went on to discover that the guinea pigs “were infected, the genotyping told us, by two patients only. Those two patients had unrecognised, untreated XDR-TB. None of the MDR patients - smear-positive, cavitary, coughing, on standard South African treatment - infected any guinea pigs.”

In subsequent studies, choosing people with MDR-TB who they thought most likely to be infectious, they continued to have trouble infecting significant numbers of guinea pigs, unless one or more of the patients turned out to have XDR-TB.

“What I’m suggesting here is that if this were a General Medical Ward, an Orthopedic Ward, an Obstetrics Ward or a Psychiatric Ward, it’s going to be the unsuspected TB patient that’s going to transmit. They may be drug-susceptible, they may be drug-resistant, but those are the patients that are infectious,” he said. “So in a TB hospital, there’s no unsuspected TB but what there is, is unsuspected untreated drug-resistant TB; and those are the patients that are transmitting because everyone else is on TB therapy — standard TB therapy. And if it’s an MDR-TB hospital — as our facility in Witbank is where everyone is on MDR-TB treatment, it’s the XDR-TB patients that are unsuspected and untreated that are transmitting. So this has enormous implications for rapid diagnostics and for traditional control measures.”

Indeed, as we described in HATIP 163, in settings with a high burden of MDR-TB, rapid drug susceptibility testing (DST) must be rolled out as soon as possible because at present months typically pass before drug resistance is detected. If people with DR-TB are in the wards, even if they are on treatment, it currently takes months to discover that they are an infection control risk. So, because there are no rapid tests at all for XDR-TB, people in TB hospitals — whether patients or staff — are at risk of becoming infected or reinfected with extensively resistant strains of TB.

“But the patients with MDR-TB who are started on effective therapy — you should have *no* hesitations sending them back in to the community, especially since there are many, many, unsuspected, untreated patients in the community. The risk comes

from [the ones] you don’t know about in the community,” Prof Nardell concluded.

Ensuring high quality care and adherence outside hospital-based DR-TB management

Of course, to deliver treatment and care, monitor treatment and guarantee adherence outside of a hospital setting, adequate systems must be put into place — particularly for the poorly tolerated second-line TB regimens that must be taken for up to 24 months. But there is a growing evidence base suggesting that it is possible to design and implement community- and clinic-based models that are cost-effective for the health system and that meet the needs of patients. The following section describes some of the lessons learned in some of the vanguard M/XDR-TB treatment programmes in resource-limited settings.

Leveraging the community and technical partners in Lesotho

“Community-based MDR-TB/HIV/TB programmes allow for rapid enrolment and closer monitoring of side effects. But the key to a successful programme is the training of healthcare workers and the training of community health workers to support the programme,” Dr Hind Satti of PIH Lesotho said during a session on MDR-TB at the 40th Union World Conference on Lung Health last December in Cancun, Mexico.

Lesotho has very limited numbers of medical personnel: only 89 doctors and 1,123 nurses are in practice for a population of 1.98 million.¹¹ In addition, there simply isn’t the hospital capacity to provide care for Lesotho’s high burden of M/XDR-TB patients — approximately 78% of whom are HIV co-infected; and Dr Satti explained that requiring patients to come in daily for clinic-based care would be impossible.

“The patients are very poor and coming from very rural areas. For many, it is around 5 to 6 hours walking distance to the nearest health centre — the patients live either up in the mountains, down in the valley or anywhere in the country” she said. “In addition, we observed very high adverse effects due to very high HIV prevalence among these patients. So we have to recognise side-effects quickly and manage them aggressively. So we overcome this challenges by working with the communities and the community health workers.”

The community health workers supervise treatment, observing each dose (twice daily). Since the patients live too far to travel to the clinic, the community health workers even provide injections.

“They have been trained for two months and they have been monitored and supervised on how to give injections,” said Dr Satti. “We’ve also trained them to identify early side-effects and they also accompany the patient to all clinical evaluations, even if there is any unscheduled clinical visit due to side-effects.”

Upon enrolment into the programme, patients are assigned to a community nurse who completes a detailed questionnaire regarding the patient’s psychosocial and socioeconomic circumstances. This questionnaire provides insight for the community staff regarding what to expect when they visit the patient.¹²

The first visit is made immediately after admission, and community staff screen all the household contacts for HIV and MDR-TB to identify suspects and TB patients. For instance, Dr Satti said that around 30% of the MDR-TB patients are miners coming from the neighbouring countries who had already been initiated on 2nd-line TB medication — but once they came home, they did not inform any health facilities that they had an active case of MDR-TB.

"We find out about them through the community health workers," she said. "They also offer psychosocial support to the patient and the family, and reinforce the messages that we provide to them, through the training, about TB/HIV and MDR-TB. They also track defaulters, if there is any."

"We know each and every MDR patient enrolled within the community. And each and every patient has got a community health worker. So the community health worker usually takes care of maximum 5 MDR-TB patients," said Dr Satti.

The community health workers are non-immune-compromised individuals, some of whom were previously HIV testing counsellors, but others have had little or no previous health training. They should be respected in the community, and need to be accepted by the patient and their family and to live close by. They must commit to support the patient for at least 2 years, including accompanying the patient on every clinical visits (even unscheduled ones). They also have to successfully complete training and be willing to attend monthly refresher trainings at the nearest health facility.

The initial training is 2 hours long using training materials appropriate for a low-literacy community with limited previous health related training, a poster at the 2nd SATB described the process in more detail.¹³ The training includes lectures, exercises and demonstrations on primary care, prevention, TB and MDR-TB treatment, drug resistance, management of side effects, DOT, and sputum collection. During the monthly refresher trainings, there is a monthly assessment of the treatment supporters, which tests the knowledge of MDR-TB medication, side effect recognition and management, checks proper filing of the recording forms, proper administration of the drugs, and rates the relationship between the treatment support, patient & family. According to the poster, "treatment supporters should be paid. Job creation and job training at the community level provides socioeconomic support and a viable work option for community members."

The programme provides comprehensive services for MDR-TB/HIV and even other chronic diseases. "Each and every MDR-TB suspect is tested for HIV," said Dr Satti, "and we initiate antiretrovirals as early as possible and usually this takes around 10 to 21 days, regardless of the CD4 cell count."

The programme in Lesotho is all the more remarkable for how quickly it was scaled up — with comprehensive care decentralized to all 10 districts in the country within the nine months of starting the programme. One member of the audience at the Union World Lung Conference in Cancun referred to it as a 'Rolls Royce' programme — and how could any other poor country hope to replicate it. And indeed, although it was established by the Lesotho Ministry of Health and Social Welfare, Dr Satti stressed that they received a lot of help from partner organisations. Technical assistance was provided by PIH and WHO, who also worked with the Foundation for Innovative Diagnostics to renovate the National TB Reference Laboratory, streamlining conventional culture and drug susceptibility testing (DST) and introducing modern TB diagnostic methods (liquid culture and line probe assays).¹⁴ A small high facility with state of the art infection control was built for people with MDR-TB who need hospitalization. Patient care was funded by the Open Society Institute for the first two years of the programme.

Dr Satti said that the cost per patient was approximately US \$1200, including payment for the community health workers, transportation fee and food packages for the entire period of treatment (24 months). But the [second-line TB] drugs were actually supported by UNITAID [and procured through the Green Light Committee Initiative (GLC)]. "So the \$1200 includes only the drugs for side effects, which the majority of our patients they take a

lot of, and also includes investigations, which have to be done very frequently especially for patients with renal toxicity and so on," she said.

More about the Lesotho model and early outcomes of the programme can be read in a recent article in PLoS One.¹⁵

Note: the Green Light Committee Initiative helps countries gain access to quality assured second-line anti-TB drugs so they can provide treatment for people with multidrug-resistant tuberculosis (MDR-TB) in line with the WHO guidelines, the latest scientific evidence and country experiences. More information on applying for GLC assistance is [available on the WHO website](#).

Staged decentralisation in KwaZulu Natal

"In 2005, we had already started discussing decentralisation because of poor case retention, high default rates, and refusal of treatment," Dr Margot said at the 2nd SATB Conference in Durban. Initially, the idea was to set up decentralized sites with satellite centres in parts of the province that were too far from King George V Hospital, the 'Centre of Excellence,' in Durban. The plan was that the decentralised site would provide full patient management, diagnosing, registering and commencing treatment, and providing follow-up, while the satellite centres would basically just house the patient.

"But community-based management was really thrust upon us by the outbreak in Tugela Ferry," said Dr Margot, noting that in this rural province, that meant relying on mobile injection teams.

"We officially started running the community-based management programme in 2007 in KwaZulu-Natal and it was restricted mainly to the Msinga district but it's now expanded right across the whole of the Msinyati district; and we've got it in small pockets in other parts of the province," said Dr Margot.

King George V Hospital remains the centre of excellence in Durban that manages difficult patients, cases that need surgery and the XDR-TB case are still being sent there at present. (However, Dr Margot said that the management of "XDR-TB is going to have to be decentralized as well because the personal and social issues are even more pressing in the XDR-TB patients because of the length of time they stay.")

Decentralised sites have been set up in districts depending on the patient load and the geography. Upon diagnosis, patients are traced, then admitted, registered, counselled and put on to treatment as an inpatient at the decentralised site. Contact tracing and education of the patient and the households/contacts occurs while the patient is still hospitalised.

"You don't want to educate a patient going back into an uneducated household, everybody needs to be educated around what the treatment is, the side-effects, understand the journey of the patient and also around infection control issues," said Dr Margot.

The patient is hospitalised at the decentralised site for 2 to 4 weeks or a bit longer if there is a clinical reason.

"That gives you time to do the education, start the treatment, monitor the side-effects early and do your adjustments. So by the time you release the patient, you're releasing, hopefully, a relatively stable patient that started on their treatment, you adjusted the side-effects or whatever you need to do with the treatment and you release them back into the community — a relatively safe patient to go back to community-based management," he said.

Once the patients are discharged, they are visited daily in their own home by the mobile injection team (trained nurses provide the injections). Dr James Brust of the Montefiore Medical Centre, who

has working with the programme in KwaZulu Natal, described this process in a bit more detail at the 2nd SATB in Durban.

“An injection team visits patients daily to provide intramuscular injection of kanamycin, to observe oral dosing of medications and to provide care and support and adverse event monitoring,” said Dr Brust. “Patients identify a family treatment supporter, and all patients and their supporters are given extensive treatment literacy support. We created a cartoon flip chart to educate patients about drug resistant TB, about HIV, infection control, the importance of adherence and so forth, translated into Zulu.”

“Patient education needs to be really strong in these units and I think it is one of the keys. We need to set up, once you move to community-based care, a good system with well-trained staff and a good system monitoring the side-effects for patient safety,” said Dr Margot.

Monthly follow-up is then conducted at the decentralised MDR-TB unit on an outpatient basis. According to Dr Brust, during each monthly visit, patients are seen by their doctor/medical officer; they have their routine laboratory tests and a monthly sputum culture/DST. They have CD4/viral load monitoring, chest x-rays and TSH (thyroid stimulating hormone) done every six months. Audiology assessments are done at baseline, two months, six months and periodically thereafter.

Once the intensive phase of treatment ends (when the injection team is no longer required), a lay health worker/home-based carer is employed to serve as the direct observed therapy supporter. The DOT supporter goes daily and reports about any adverse events or disease progression on a weekly basis.

Dr Margot listed a number of key services that are needed to support the decentralized units and community-based management of MDR-TB in KwaZulu Natal, including good clinical, laboratory and pharmacy support.

Patient monitoring can be improved with chest X-Ray, and audiology (the capacity to monitor for hearing loss sometimes associated with second-line treatment). Patients and their families benefit from having a good social worker, physio and occupational therapy as well as psychiatric support. Good infection control is important for both the healthcare facilities and home. The programme needs support from a surveillance officer and data capturer to monitor the stats and handle all the paperwork. The decentralised unit should also have strong linkages or integration with HIV services (for HIV testing and counselling and ART. Outreach Community Teams (Tracing/Injection teams) with one TB community officer and one staff nurse are obviously necessary – as is good management support to pull all these elements together.

“You need to look at the stability of your doctor-base for the decentralised unit, it proves to be a problem, so you need to look at that carefully. And your outreach teams need to be people with really big hearts that are really interested in their work, because a lot of them work under very extreme conditions. So you need a really dedicated team,” said Dr Margot.

As for the cost for the vehicles, petrol, staffing etc – Dr Margot presented calculations showing that to manage 30 patients on the community-level, it would cost around R77,837.00 a month (US \$11,000) (not including drug costs). Hospital care for the same 30 patients at the decentralised unit would cost almost 10 times as much – while the cost of care at King George V would be close to 1 million rand a month (US \$140,000).

“And the terrain - it's not easy. The patients are spread far, the terrain is heavy on vehicles and you can only do so many patients in

a day unlike in urban areas. So if things can be done in this area at these kinds of costs, it's going to be even more cost-effective in an urban area,” said Dr Margot.

The data coming out of three out of four of the decentralised sites, regarding death, default/failure and culture conversion are quite good. One extremely rural and under-resourced site which has had trouble with physician coverage, Thulasizwe, is struggling a bit, with a 26% death rate, and a failure rate is 3%, a 1% defaulter rate, and a 58% culture conversion rate.

“But, [apart from Thulasizwe], what is significant is that the death rates are much lower than what we're seeing in the standardised, centralised control programmes in the country. The defaulter rate is significantly different to what we've been seeing in the centralized treatment centres. And we're starting to see some really good conversion rates coming out of the decentralised sites,” said Dr Margot.

The Health Department plans to continue decentralisation to other districts in the province where the need exists. The programme is also looking at nurse initiated MDR-TB care and decentralising to the clinic level.

“We obviously struggle with doctors in rural areas, and to find a doctor that will work with just TB is far more difficult. But I think probably 50 to 60% of the patients have straightforward MDR-TB and if we can up-skill nurses to do ART we can do the same thing with MDR, there's no reason why we can't break the load on the doctors and do a lot of the patients through the nurses,” said Dr Margot. “When there is no doctor, they are doing it anyway already so we may as well train them, skill them, and get their skill recognized.”

So the province has launched a partnership with Johns Hopkins School of Medicine, and the Medical Research Council (MRC). The partnership is timely because the nursing regulations (section 56) are changing in South Africa to expand the scope of practice for nurses with appropriate training to prescribe ART and other drugs (potentially including TB drugs), and there is also a movement to decentralise more care to the primary health care levels.

Assistant Professor Jason Farley of Johns Hopkins University, who is also a nurse practitioner, described the partnership in more detail at the 2nd South African TB Conference.¹⁶ He noted that preliminary data on nurse-based management for HIV and TB in South Africa and other settings was positive, with good patient satisfaction but that “the identification of what is appropriate training is quite different in different parts of the country... and that there is a high staff turnover in those clinics.”

In other words, it can be a challenge to maintain the nurses in those sites once they have been given additional training and responsibilities.

He cited findings from the Lusikisiki Model of decentralised care which showed that scale up of nurse-based prescribing must include:

- Ensuring an adequate budget for a full complement of clinic staff
- Recruitment of adequate administrative staff to ensure that nurses' time is optimised towards direct patient care rather than non-nursing tasks (taking away administrative and secretarial duties that would otherwise consume nurse time).
- Accreditation and increased remuneration of nurses
- Acknowledging the great disparity between non-urban settings by paying rural allowances to staff working in the most challenging rural areas.¹⁷

Taking these factors into consideration, the partnership has designed a study of nurse-initiated/managed intensive MDR-TB treatment which aims to develop nurse-based capacity at Thulasizwe and another site, and compare outcomes between these sites and King George V Hospital. The success of this trial and partnership could dictate how quickly the province can down-refer to other facilities and to the primary care level where there is limited doctor support.

Eventually, Dr Margot says the plan is to down-refer some functions to the clinic level. The clinics would begin to provide the monthly follow-up and may begin to initiate treatment in non-complicated MDR-TB cases.

“But that would be in targeted areas/select areas where there are high case loads and where we’ve capacitated the clinics to do the work — a little further down the road once we’re strengthened and got the decentralized sites running completely,” he concluded.

Ambulatory MDR-TB care in Nepal

Nepal began delivering MDR-TB treatment under direct observation on an entirely ambulatory basis through a decentralised network of clinics in 2005 — patients are only hospitalised if they have a serious clinical problem.¹⁸ [A recent retrospective analysis of the first twelve months of the programme, published in PLoS One](#), reported high cure rates (~70%) using a standardised treatment regimen (see below), and default rates comparable to those reported by other programmes (though there were problems at some sites). By July 2009, over 600 people with MDR-TB had started treatment in a network consisting of 10 primary treatment centres and 34 sub-centres located in the more densely populated parts of the country (half of the people in the programme are from around the Kathmandu region).

Dr Pushpa Malla and other representatives of the National Tuberculosis Centre (NTC), and the Ministry of Health and Population in Nepal told HATIP a bit more about how this programme works in practice at the 39th Union World Lung Conference in Paris in 2008.

Treatment is supervised daily at the clinic by middle level healthcare workers (nurses, clinical officers), who have undergone five days of specialised training. The healthcare staff monitor for side effects and perform follow-up, and a doctor is available if there are complications.

Treatment is entirely voluntary, and the programme has little problem getting people to come in for treatment. “People in Nepal have good health-seeking behaviour,” said Dr Malla, with perhaps the exception of some cases of substance users. However, as with almost any other condition, it becomes harder to encourage good adherence once people begin to feel better on treatment. So each patient nominates a treatment support person, who may be a family member, who receives training and education to help the patient adhere to treatment. An active defaulter tracing system is in also place and implemented locally by the clinics with support and supervision from the District TB/Leprosy Officers.

There are a limited number of sites in the country (the programme has prioritised those areas with a greater burden of MDR-TB. To be in the programme, many people have to relocate to live near their treatment centre — often without work.

“They have to stay somewhere in the rented houses and this is a problem, and sometimes they are accompanied by family members,” said Dr Malla. “Food also they have to buy for themselves. For the last two years, they are getting about 300 Nepalese rupees per month from the programme — which amounts

to nothing, perhaps tea or something else. But now it is going to be increased to 1000 rupees per month from the government to help support the patient. For my patients who are attending our clinic, we are supplying from our side something for the patients’ transportation cost. But they don’t get that everywhere.”

The patients are given free treatment for side effects, in particular, ranitidine is used to help with gastrointestinal symptoms. The Green Light Committee has helped the country access high quality affordable second-line treatment.

Of note, the programme is using a standardised second-line treatment regimen, based upon surveyed drug resistance patterns in the country — as opposed to individualising regimens when the DST results become available). In the *PLoS One* paper, Malla et al wrote that an individualised treatment regimen would have been logistically difficult for them to introduce: “The utilization of a standardized regimen makes training, drug forecasting, and management of adverse events much easier, in addition to reducing significantly the overall cost of treatment.”

One concern about such standardised regimens is that they may not prove optimal for individual patients who could then go on to develop XDR-TB. As the *PLoS One* paper went to press, XDR-TB cases made up about 7% of the MDR-TB cases in the country — but the programme is uncertain when those cases became extensively drug-resistant due to lack of access to routine drug susceptibility testing (DST) for second-line drugs.

The country is scaling up laboratory services, however, the terrain makes getting timely results more challenging. To get to the centralised lab, many of the sputum samples must be flown in.

The results achieved by the programme are remarkable considering the setting — however, there are indications that outcomes are not quite as good in some districts. “Unfavourable outcomes are not evenly distributed across different areas of the country. The sub-optimal outcomes in the Eastern region is a result of poor performance at the NATA clinic in the region, which has a greater proportion of defaulters... [and which] serves a very large catchment area. More MDR-TB clinics have been recently opened in that area to improve access to services in the most remote areas,” Malla et al wrote.

Clinic-based community care in Khayelitsha... and the Western Cape

Late in 2007, another pilot project in ambulatory care decentralising and integrating the care of drug-resistant TB into the primary TB programme was implemented in Khayelitsha.

“The aim of doing this was to develop a model of care that would improve the care and treatment of people with DR-TB in Khayelitsha in a way that puts the patient at the centre of their treatment,” said Dr Helen Cox of MSF at the 2nd South African TB Conference. “Rather than doing things to the patient, we’re trying to work with patients to help them to get cured. We also wanted a model of care that was replicable elsewhere and that could provide a model for scale-up so that all of the patients who need 2nd-line DR-TB treatment could actually access that treatment.”

Khayelitsha is a very large community of nearly half a million people that is part formal, part informal settlement. It has one of the highest rates of TB in the world, with a case notification rate of about 1200 per hundred thousand people. Every year, there are at least 400 new cases of MDR-TB emerging in the community — this is despite good outcomes for drug-sensitive TB. In fact, the cure rate is 78% and the success rate is 83.5%. There are about 10 health facilities providing TB diagnosis and treatment in the community

Again, “the heart principle of this model was to be patient-centred and to treat patients at clinic level, primary care and in the community at home,” said Dr Van Cutsem, giving an overview of the programme at the AIDS 2010 conference in Vienna. But he added that additional aspects of the pilot project were to perform operational research, monitor and evaluate programme performance and to conduct advocacy.

Activities to support the project include the training of staff, NGOs and community workers at primary care level. The programme has worked to establish good infection control, not only at the facility level, but also within the home and community.

The programme has also established a number of mechanisms to provide patient support. These include support groups, assistance getting social grants, and counselling services with special MDR-TB counsellors who go to every single family and house of MDR patients to inform them about treatment but also about infection control measures that can be taken in the home setting, and community workers to perform default tracing. The same workers perform contact identification and refer them for screening at the clinic. The programme has also established community awareness programmes.

The programme has expanded the range of clinical services available within the community for people with MDR-TB. For instance, they have installed a sound proof booth, and trained a community worker to provide an audiology service (to assess for hearing loss associated with kanamycin).

The programme has opened a small sub-acute in-patient facility ‘Lizo Nobanda’ with 12 beds for patients who would be too sick to be treated at home, so that they could be admitted for short periods without leaving the community (this includes a couple of beds for end-of-life care). The programme has made efforts to optimise the treatment regimen (even purchasing moxifloxacin – which is currently too expensive to be used widely in South Africa). New patient and paediatric review meetings are held each month, along with the meeting of the DR TB task team.

Several of the staff and lay community health workers involved in the programme gave presentations on their work at the 2nd SATB Conference in Durban – making it clear that this programme really is of, by and for the community.

“One of the DR-TB programme objectives is to reduce the time between diagnosis and the start of treatment. It is hoped that this will reduce mortality among patients before treatment can be started,” said Johnny Daniels, the programme’s data manager.

Experience elsewhere has shown that the time between sputum collection and treatment can be considerable. For instance, in Peru, using the MODS assay, the time was relatively short (42 days) though the time between getting the result and going on treatment was actually 17 days.¹⁹ A study in KwaZulu Natal reported that the time between sputum collection to starting MDR-TB treatment was 109 days for people with ‘centralised management’ (at King George V Hospital) versus 84 days for community management,²⁰ while in the Western Cape, Van Rie et al reported that a time between sputum collection and treatment of 94 days.²¹

At the Khayelitsha clinic the time between sputum sampling and treatment was around 71 days in 2007, going down to 50 days in 2008 and 40 days in 2009. This was thanks, in part, to the use of new laboratory technology. In a more detailed analysis of the last six months of 2008, and the first six months of 2009, Daniels found that the median time had gone down from 46 days to 37 days. However, the median time to starting treatment after getting the results back from the lab had dropped from 17 days in the end of 2008 to just 8 days in 2009.

“Although there is a reduction in time, high mortality still occurs before start of treatment,” he said. In fact, about 9% of patients are dying before getting onto treatment.

Andiswa Vazi described the process of contact screening in the community – which she pointed out not only improves early diagnosis of MDR-TB but also offers an opportunity “to educate households on TB symptoms and the need for early diagnosis and also TB transmission and how to reduce the risk in homes.”

She said that to improve contact screening:

- Data recording forms were developed to collect information on close contacts and the outcomes of screening.

- Contacts are identified through household visits.

- All DR-TB contacts are offered screening, focusing on those at high risk, such as children less than 5 years of age, people with HIV staying with patients with DR-TB and also people with chronic illnesses.

- Those at high risk are encouraged to go for sputum screening and others to attend clinic if symptomatic.

- Contacts are given a letter advising the HCW to screen for DR-TB, if the individual presents to a clinic for TB screening.

Contact screening identified a fair number of children with TB. Among the individuals over the age of 5 only about 1% of people were found to have MDR-TB, however, 3% of household contacts were found with drug-sensitive TB, indicating that among older contacts at least, one can’t assume that the contacts have DR-TB which has important implications for empiric treatment.

This method of trying to encourage people to go into the clinic for screening did miss some active cases however.

“Not all contacts go for screening, they often only go when they are sick,” said Vazi. “And contacts with negative results on initial screening often don’t return for follow-up screening.”

Debra Bonkolo, who referred to herself as previously unskilled non-health staff described how she was trained to provide the audiometry service in Khayelitsha. The facility was built for about 50,000 rand but it can service the entire sub-district. Clients are assessed at baseline at then during monthly visits to look for the subtle beginnings of hearing loss due to kanamycin and other aminoglycoside drugs used in second-line TB treatment..

Busisiwe Beko explained the need for community-based counsellors, described the counselling process and the factors that they had observed were associated with default at the facility.

“Many HCWs lack understanding of the difficulties facing patients,” she said. “I know it from experience.”

Patients receive at least two formal counselling sessions: soon after diagnosis when the patient is received at the clinic, and before initiating treatment, and a home visit (which is combined with contact screening, family education and infection control assessments). In addition, all DR-TB patients are encouraged to join the DR-TB support group at their local clinic. Beko said that the support groups offer an opportunity to correct misperceptions about toxicity and other issues confronting patients.

But some still default, and the team performed a survey to assess the key reasons why.

“The most significant factors associated with default were the stigma associated with DR-TB and difficulties associated with the lack of a stable home and consequent travel back and forth from the Eastern Cape [where many of the residents of Khayelitsha are originally from]. Other relevant factors were excessive alcohol use by either patients or close household members leading to household instability; poor rapport with clinic staff, difficulties with hospitalization, the need to work and financially support others; and feeling better,” she said.

Yvonne Xhaso described a study investigating delays and difficulties assessing disability grants for people on MDR-TB treatment in Khayelitsha.

“Patients need financial assistance immediately after they start treatment because they are often not allowed to work, but many patients take more than 6 months to access grants,” she said. Sometimes the problem is due to poor access to social services doctors, or loss of the paperwork by social services. There is also a requirement for the patient to request the paperwork in person — which can be difficult if they are ill.

“DR-TB patients need financial support to stay on treatment, particularly at treatment initiation,” she said. “Strategies to streamline access to disability grants for DR-TB patients are urgently needed, and we recommend that Social Services monitor their processes to streamline their services.”

As a result of the experience in Khayelitsha, the Western Cape Province is expanding clinic-based MDR-TB care at least within the urban and periurban settings — with some modification.

“The model of care here is for Khayelitsha. It’s going to need to be changed and adapted for elsewhere in the province and country,” Dr Cox told HATIP.

“Beyond Khayelitsha, we need to concentrate on rural models. The Khayelitsha model, I think, is very replicable to other peri-urban settings. But for rural settings, you need different approaches i.e. what they are doing in KwaZulu-Natal with mobile teams. That is fantastic where you get injection teams going to the villages,” Dr Van Cutsem told HATIP.

Adapting a more community-based approach in other settings

Although there is increasing evidence that community and clinic based approaches to MDR-TB care can work, many TB experts and others are worried about rushing to adopt them.

“My name is Numsa Mphe and I’m from the Northwest Province,” one woman said during the discussion of one session at the 2nd SATB. “We all agree that community-based management of MDR-TB is the way to go, and it has been happening in the Tugela Ferry. What lessons are we learning from this experience so that we are able to deal with things that are coming out that may be undesirable? Because surely, I don’t want to believe that everything is ‘hunky-dory’. There could be challenges here and there, taking into consideration the environment within which these things happen.”

Simangele Mgcombela, TB programme manager from the Northwest Province, told HATIP some of their worries.

“We have such poor outcomes with drug-sensitive TB. If our healthcare staff can’t manage that, how are they going to properly manage MDR-TB, which is considerably more difficult? Without proper training and the allocation of resources, I’m afraid that we might simply generate XDR-TB,” she said.

Indeed, there were posters at the 2nd SATB suggesting that many healthcare staff felt very unprepared to deal with MDR-TB and nurses felt they didn’t have enough training or support from doctors in the health system. Clearly, training and resources must be made available that are commensurate to the challenge.

As anyone following the healthcare worker strike in South Africa knows, many staff are burnt out to the point of having little or no empathy for clients. This is all the more reason to engage community health workers and supporters in the treatment programme.

In the end, there really is no choice but to treat MDR-TB and XDR-TB as public health emergencies. The low case detection, and delayed access to treatment and potential for the nosocomial spread in an under-resourced, centralised hospital-based system increases the risk of turning most TB into drug-resistant TB.

The models suggest that there are viable alternatives. According to the WHO STOP TB website, “WHO and its partners have scores of experts who can offer technical assistance to countries as they build their response to MDR-TB.

The GLC has been established to allow access to high-quality second-line drugs to treat MDR-TB — and the Global Fund to Fight AIDS, Tuberculosis and Malaria has committed billions to TB control programmes.

Furthermore, WHO member states committed at the 62nd World Health with achieving universal access to diagnosis and treatment of MDR-TB. This bold goal reflects the fundamental changes in global policy for MDR-TB management. Tackling the weaknesses of the health care system are essential to accelerate the achievement of this [goal](#).

Obviously funding gaps persist.

But as Dr Mario Raviglione, Director of WHO’s Stop TB Department has said, the organisations are “aware of those gaps and working closely with governments, the Global Fund, UNITAID and other funding agencies to mobilise needed funds.”

References

- [1] Mitnick C et al. Community-based therapy for multidrug-resistant tuberculosis in Lima, Peru. *N Engl J Med* 348:119-28, 2003.
- [2] Mitnick C et al. Comprehensive treatment of extensively drug-resistant tuberculosis. *N Engl J Med* 359:563-574, 2008.
- [3] Seung KJ et al. Early outcomes of MDR-TB treatment in a high HIV prevalence setting in Southern Africa. *PLoS ONE* 4(9): e7186. doi:10.1371/journal.pone.0007186, 2009.
- [4] WHO. Guidelines for the programmatic management of drug-resistant tuberculosis. Emergency Update. Geneva, 2008.
- [5] WHO. Multidrug and extensively drug-resistant TB (M/XDR-TB). 2010 Global report on surveillance and response. Geneva, 2010.
- [6] Krause R, Gwyther L, Gould T. An evaluation to assess the holistic care of tuberculosis patients with palliative care needs in the Western Cape, South Africa. 2nd SATB Conference, Durban, 2010.
- [7] McDermid C et al. A decentralised model of care for drug resistant tuberculosis in a high HIV prevalence setting. *AIDS* 2010, Vienna, 2010.
- [8] Kamat SR et al. A controlled study of the influence of segregation of tuberculosis patients for one year on the attack rate of tuberculosis in a 5-year period in close family contacts in South India. *Bull World Health Organ* 34:517-32, 1966.
- [9] Riley RL et al. Aerial dissemination of pulmonary tuberculosis: a two-year study of contagion in a tuberculosis ward. *Am. J. Epidemiol.* 142(1): 3-14, 1995 (reprinted from *Am J Hyg*; 70:185-196, 1959).
- [10] Riley RL, Mills CC, O’Grady F, et al. Infectiousness of air from a tuberculosis ward. *American Review of Respiratory Disease* 85: 511-525, 1962.
- [11] Nkuebe M. Home assessment in the management of MDR-TB/HIV patients in Lesotho. 2nd South African TB Conference, Durban, 2010.
- [12] Ibid.

- [13] Lethetsa M. Community-based treatment of MDR-TB patients in Lesotho. 2nd South African TB Conference, Durban, 2010.
- [14] Paramasivan CN et al. Experience establishing tuberculosis laboratory capacity in a developing country setting. *INT J TUBERC LUNG DIS* 14(1):59–64, 2010.
- [15] Seung KJ et al. Early outcomes of MDR-TB treatment in a high HIV-prevalence setting in southern Africa. *PLoS ONE* 4(9): e7186. doi:10.1371/journal.pone.0007186, 2009.
- [16] Farley JE. Building partnerships and capacity to effectively address nurse-initiated MDR-TB/HIV treatment in KwaZulu Natal South Africa. 2nd South African TB Conference, Durban, 2010.
- [17] Bedulu M et al. Implementing antiretroviral therapy in rural communities: the Lusikisiki model of decentralized HIV/AIDS care. *J Infect Dis.* 196(Suppl 3):S464-S468, 2007.
- [18] Malla P et al. Ambulatory-based standardized therapy for multi-drug resistant tuberculosis: experience from Nepal, 2005–2006. *PLoS ONE* 4(12): e8313. doi:10.1371/journal.pone.0008313, 2009.
- [19] Fhogartaigh N et al. Physician-initiated courtesy MODS testing for TB and MDR-TB diagnosis and patient management. *IJTB LD* 12(5):555-560, 2008.
- [20] Heller T et al. Community-based treatment for multidrug-resistant tuberculosis in rural KwaZulu-Natal, South Africa. *IJTB LD*, 14(4): 420-426, 2010.
- [21] Van Rie A et al. Transmission of a multidrug-resistant *Mycobacterium tuberculosis* strain resembling "strain W" among noninstitutionalized, human immunodeficiency virus-seronegative patients. *JID* 180(5):1608-15, 1999.

about HATiP

A regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings.

The newsletter is edited by Theo Smart (Cape Town) and Keith Alcorn, NAM's Senior Editor (London).

For further information please visit the HATiP section of aidsmap.com