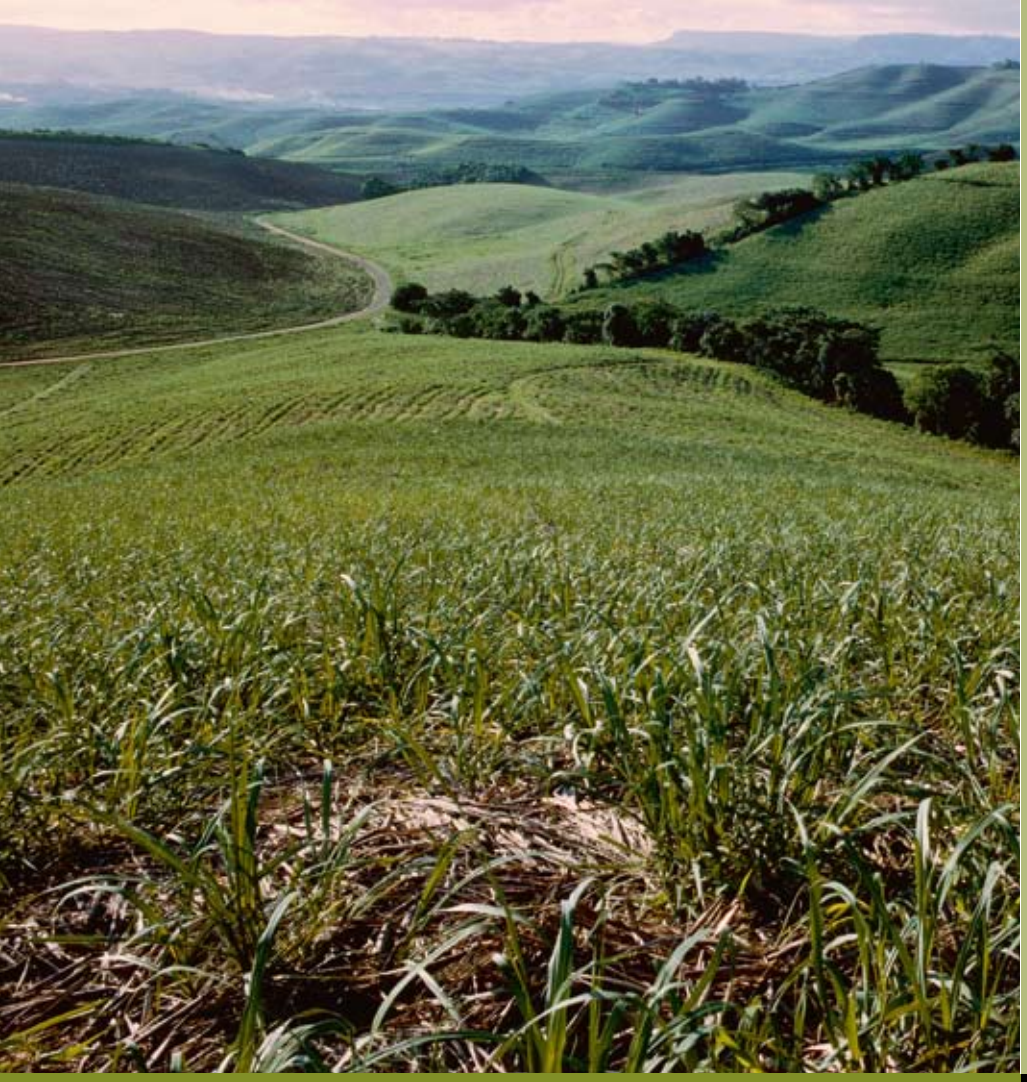

TUBERCULOSIS MDR/XDR

The Msinga Experience

Lessons learnt from South Africa

2005-2009

Contents

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January 2009

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Summary

Drug resistant tuberculosis has emerged as a serious public health issue around the world. Recent global estimates put the number of reported cases for 2006 at close to half a million. This represents 4.8 percent of all notified TB cases worldwide. An estimated 1.5 million people died from TB in 2006.

In 2006, an outbreak of a deadly and almost incurable form of TB was reported in Msinga, Umzinyathi district, a remote and rural part of KwaZulu-Natal province in South Africa. The extensively drug-resistant TB or 'XDR TB' as it became known largely occurred among HIV-infected people, in particular those with terminal AIDS.

Patients who were co-infected with XDR TB and HIV stood little chance of survival. The XDR strain was resistant to almost all available TB drugs, severely reducing treatment options. Fifty-three patients were diagnosed

Since the beginning of 2008, the number of drug resistant TB cases has been decreasing, giving hope that we are moving in the right direction.

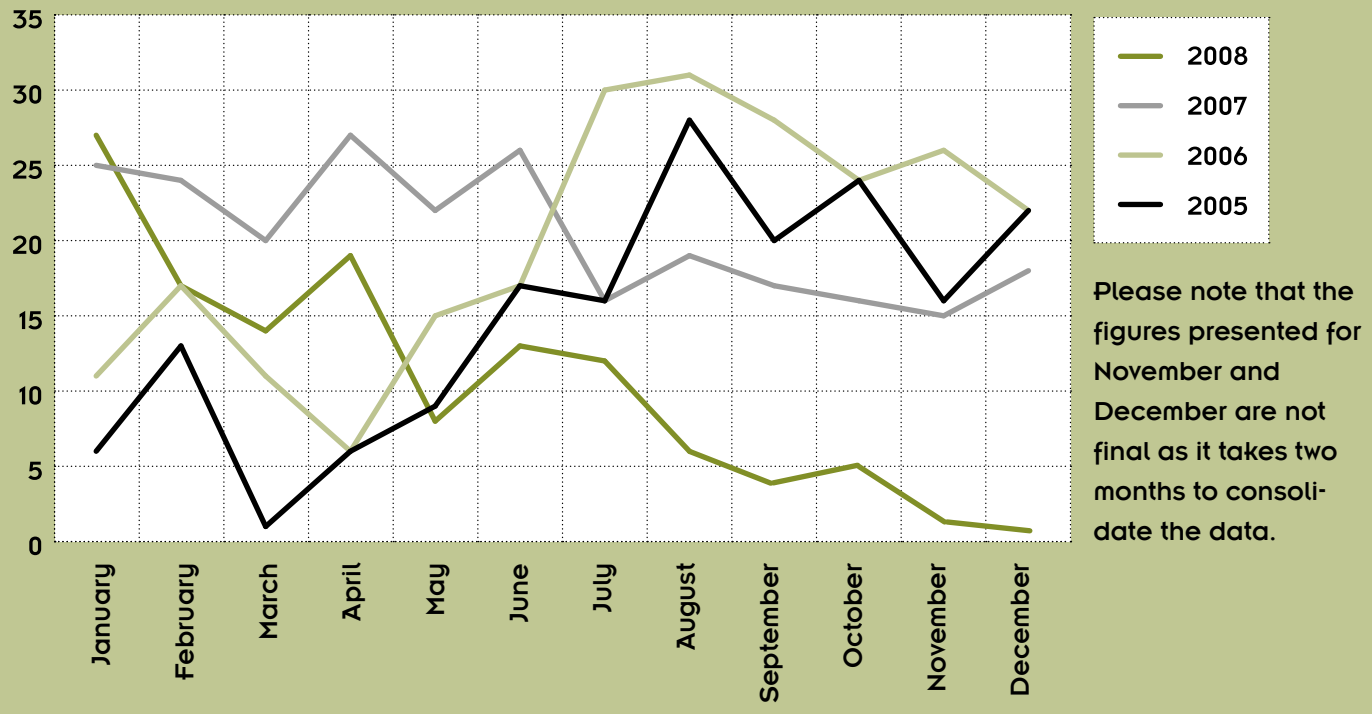
Factors behind the decline in drug resistant TB in Msinga:

- The commitment of the Umzinyathi health district management team ensured that TB control was placed at the top of the district's agenda and that adequate resources were allocated to tackle the disease.
- The management of TB patients was aggressively addressed by providing refresher training for nurses and introducing appointment diaries to track patients.
- An increase in the nurse-to-patient ratio also played an important role in improving treatment outcomes and preventing defaulting.
- Tracer teams were increased and provided with GPS to map MDR/XDR TB households. Tine tests were performed and containers with sputum samples were sent to the laboratory for analysis.
- TB suspects in the community were identified through strict surveillance and contact tracing.
- Measures were taken to bolster infection control at COSH to reduce hospital transmission of MDR/XDR TB.
- Public information campaigns helped to sensitise the community on the dangers and prevention of TB.

with the disease at the time of the outbreak; only one survived. The others died on average within 16 days of diagnosis. XDR TB was believed to be transmitted mainly in the Church of Scotland Hospital (COSH), the rural hospital serving Msinga, as most of the patients had a history of hospitalisation at COSH.

Following the report, questions emerged as to whether transmission may have also taken place in the community. Few studies have evaluated the rate of transmission of drug resistant TB among family contacts in high HIV prevalence settings. Since October 2006, the KwaZulu-Natal Department of Health has been implementing an innovative and intensive community surveillance system in Msinga with technical support from the 'Istituto Superiore di Sanita' and funding from the Italian Cooperation. Results have shown that the transmission rate of drug resistant TB among adults in the households is low. However, children living in the households have a much higher incidence of TB.

Measures have been taken to turn the tide of the epidemic in Msinga (see box). Since the beginning of 2008, the number of drug resistant TB cases has been decreasing, giving hope that we are moving in the right direction. We need to continue monitoring the situation and strengthening ongoing efforts to contain the epidemic.



Please note that the figures presented for November and December are not final as it takes two months to consolidate the data.

Monthly MDR and XDR cases (up to January 2009)

HIV & AIDS in South Africa

5.3 million

The number of South Africans between the ages of 15 and 49 living with HIV and AIDS.

27%

The national HIV prevalence among pregnant women attending antenatal clinics.

37.4%

The HIV prevalence among pregnant women attending antenatal care in KwaZulu-Natal.

31.7%

The HIV prevalence among pregnant women attending antenatal care in Umzinyathi district.

43 years

The life expectancy at birth in KwaZulu-Natal.

Source: The National HIV and Syphilis Prevalence Survey South Africa 2007, National Department of Health, 2008; Mid-year population estimates 2007, Statistics South Africa, July 2007; Biennial Report on the State of the South African HIV/AIDS Epidemic, Actuarial Society of South Africa, November 2006.

The deadly synergy between tuberculosis and HIV

At no time in recent history has TB been as great a concern as it is today. Despite highly effective drugs, morbidity and mortality due to the disease are increasing and are being fuelled by the AIDS epidemic.

In countries with high rates of HIV prevalence such as South Africa, TB is often the first sign of HIV infection and the leading cause of death in people living with HIV and AIDS. The country contributes to 80 percent of the global burden of tuberculosis, along with 22 other 'high-burden' countries.[1] An estimated 60 percent of all new TB cases in South Africa are among HIV-positive individuals.[2] Mortality rates of up to 40 percent per year have been reported in patients co-infected with TB and HIV who are receiving treatment for TB, but not for HIV.[3]

TB incidence and death rates have increased three fold in South Africa since the disease was declared a national emergency in 1996.[4] This comes despite a concerted effort to reform TB control, including improvements made in line with the internationally recommended DOTS* strategy.

* DOTS stands for 'Directly Observed Treatment, Short-course' and is a global emergency framework for TB control developed by WHO in 1994. DOTS is seen as the most effective strategy available for controlling the worldwide TB epidemic.

The cost of treating MDR/XDR TB

Normal or drug sensitive TB

R80/month

MDR TB

+/- R1,650/month

XDR TB

+/- R3,600/month

More than 400,000 cases of TB require treatment every year[5] but cure rates barely reach 50 percent,[6] reflecting the classic mistake made in TB control programmes of identifying cases but not treating them properly. Barriers to effective TB control include the exploding HIV epidemic, constraints on human resources in the public healthcare system and deteriorating socioeconomic conditions among people already vulnerable to diseases of poverty.

Paradoxically, the driving force for TB transmission in the community is HIV-negative, smear-positive people because of their fairly long duration of infectiousness and apparent lack of symptoms of active TB disease. Though more susceptible to getting TB because of their compromised immune systems, HIV-positive individuals, most of whom are smear-negative, progress to symptomatic TB much quicker. Co-infection with HIV and TB contributes greatly to death but it might contribute much less to disease transmission. This combination of "*exquisite vulnerability to disease by HIV-positive individuals and prolonged transmission from HIV-negative patients with tuberculosis together fuel the escalating incidence of tuberculosis in areas of high HIV prevalence.*"[7]

The rise of a new disease

Of great threat to public health in South Africa is the development of a 'new' and deadly form of TB. Mutant TB strains have been identified that defy the most potent antibiotics available to treat the disease. South Africa has the highest burden of multi-drug resistant tuberculosis (MDR TB) on the continent, another sign that tuberculosis control is weak.[8] And even more alarming is the rise of an extremely lethal form of MDR TB – extensively drug resistant TB or XDR TB. XDR TB is virtually untreatable and especially virulent in people with end-stage AIDS.

MDR/XDR TB: how does it develop and spread?

MDR TB, like other cases of antibiotic resistance, is a man-made amplification of a natural phenomenon. One in three people in the world are infected with dormant TB bacteria[10]. TB bacteria become active when a person's immunity is weakened by advancing age, a medical condition or HIV.

TB is usually treated with a six to eight-month course of four standard, or first-line antibiotics. If these drugs are misused or mismanaged, for example, when a patient is not properly supported to complete their full course of treatment, a relapse in normal or drug-sensitive TB can occur or the TB bacteria mutate and develop resistance to those drugs, creating MDR TB. MDR TB takes longer to treat with second-line drugs (around two years), which are more expensive and have more toxic side effects. XDR TB can develop when these second-line drugs are also mismanaged and become ineffective. Because XDR TB is resistant to both first and second line drugs, treatment options become seriously limited. Treating MDR/XDR TB and HIV simultaneously can also be frustrating for health practitioners and patients because of drug interactions and the potential for many strong side effects. The other way of becoming infected with MDR/XDR TB is to contract an already drug resistant strain from another person.

TB is an airborne disease and is spread by coughing, sneezing or simply talking. A person only needs to breathe in a small number of TB germs to become infected though only a small proportion of people actually become ill. The spread of TB depends on several factors such as the number and concentration of infectious people in any one place together with the presence of people who are more susceptible to infections such as those with HIV. The risk of infection increases the longer the time an uninfected person spends in the same room as the infected person and in closed environments with stagnant air, such as overcrowded and poorly ventilated hospitals, homes and prisons.

WHAT DO THEY MEAN?

MDR TB – multi-drug resistant tuberculosis, defined as resistance to the first line drugs – isoniazid and rifampicin.

XDR TB – extensively drug resistant tuberculosis, defined as resistance to at least isoniazid and rifampicin, in addition to any fluoroquinolone, and to at least one of the following second line injectable drugs: amikacin, kanamycin and capreomycin.

Index Case – the first person that has been diagnosed with MDR/XDR TB in a household.

Contact – everyone living in the same household as the first person diagnosed with MDR/XDR TB.

Contact tracing – locating people who have been in contact with a person with TB or MDR/XDR TB.

Cure rate – the percentage of smear-positive TB patients who are cured of the disease.

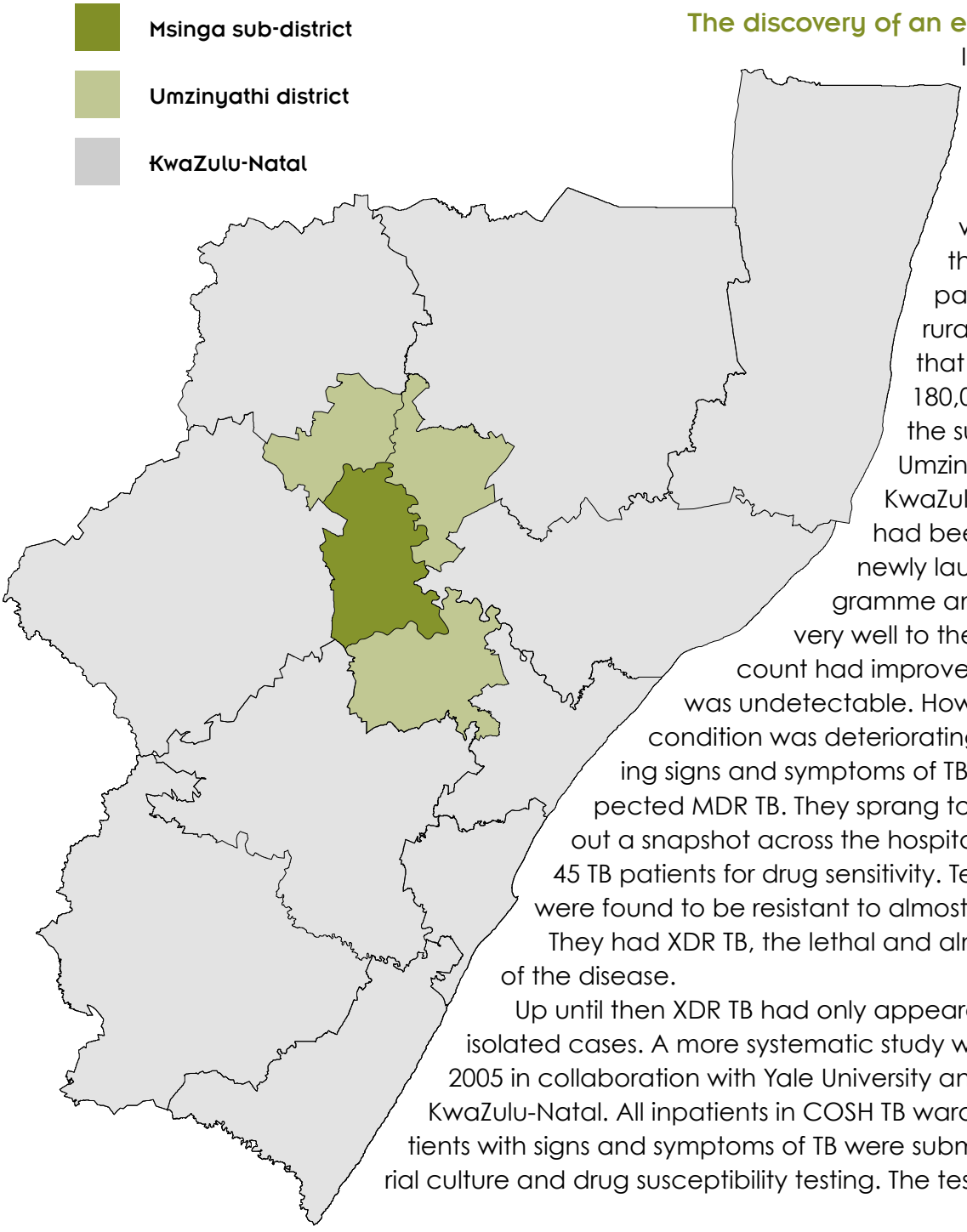
Default rate – the percentage of TB patients who interrupt their treatment.

Patients who are co-infected with HIV and XDR TB have been reported to die within 16 days of diagnosis.[9] Since the recent discovery of an epidemic of XDR TB/HIV co-infection in a remote rural part of KwaZulu-Natal province, it has raised serious concerns about the success of treatment programmes for TB and HIV.

Treatment for HIV under threat

The era of highly active antiretroviral therapy (ART) ushered fresh hope that the fight against TB would be won. Findings from several different countries show that antiretrovirals (ARVs) reduce the likelihood of an HIV-positive person becoming infected with TB by 80 percent or more.[11] However, TB is an aggressive opportunistic infection that arises at higher median CD4 counts than other AIDS-defining disorders. This means that the potential effect of ART in protecting people from TB is diminished because many HIV-infected patients develop active TB before ARVs are prescribed. Any reduction in HIV-associated illness and death is blunted if efforts are not taken to improve collaboration between TB control and HIV treatment programmes.

With the promise of life from ART undermined by the lethal alliance of HIV and TB, South Africa has reason to be concerned. The national ARV programme, in which billions of Rand have been invested and on which hundreds of thousands of HIV infected people rest their hopes, is at risk of being seriously compromised by TB. The country is also paying the price for an ARV treatment programme that started late – by the time the Government began rolling out the programme in 2004, the country had a mature HIV epidemic. WHO estimates that 460,000 South Africans were receiving ARVs at the end of 2007, equating to 28 percent of those in need of treatment.[12] This means that TB threatens the lives of approximately 1.3 million HIV-positive people who need ARV treatment but are not getting it.



The discovery of an epidemic

In 2004, doctors at the Church of Scotland Hospital (COSH) started noticing that something was wrong with two of their HIV-infected patients. COSH is a small rural hospital of 335 beds that serves around 180,000 people living in the sub-district of Msinga, Umzinyathi district in KwaZulu-Natal. The patients had been enrolled in the newly launched ARV programme and had responded very well to the treatment. Their CD4 count had improved and their viral load was undetectable. However, the patients' condition was deteriorating rapidly with worsening signs and symptoms of TB. The doctors suspected MDR TB. They sprang to action and carried out a snapshot across the hospital's TB wards, testing 45 TB patients for drug sensitivity. Ten of the patients were found to be resistant to almost all anti-TB drugs. They had XDR TB, the lethal and almost incurable form of the disease.

Up until then XDR TB had only appeared in the province in isolated cases. A more systematic study was carried out in early 2005 in collaboration with Yale University and the University of KwaZulu-Natal. All inpatients in COSH TB wards as well as all outpatients with signs and symptoms of TB were submitted to microbacterial culture and drug susceptibility testing. The tests were done at the

provincial laboratory at Inkosi Albert Luthuli Central Hospital in Durban.

The results confirmed the worst.

MDR TB was found in 221 patients of whom 53 had XDR TB. The prevalence of both diseases was substantially higher than those previously reported (only 347 cases of XDR TB were identified worldwide from 2000 to 2004)[13]. An epidemic of extensively drug resistant TB, characterised by co-infection with HIV, had been uncovered in a remote rural corner of South Africa (see panel on 'Chronology of an epidemic').

Furthermore, XDR TB was rapidly – and almost uniformly – fatal. Fifty-two of the 53 XDR TB patients died; their average survival period was 16 days from the time of diagnosis. All 44 patients with XDR TB who had been tested for HIV were infected with the virus. They had very low CD4 counts, implying that XDR TB was the last nail in the coffin for these patients already suffering from terminal AIDS.

What led to the XDR TB outbreak in Msinga?

Transmission in the community

More than half of the 53 XDR TB patients had never been previously treated for TB, suggesting that they had contracted the disease from other people who already had the drug resistant strain. The patients had no prior contact with each other apart from receiving healthcare from the same hospital. None of the patients had family members who had been sick with TB before their illness. The majority of patients with XDR TB were infected with a genetically similar strain, unique to KwaZulu-Natal, that had first been reported in 1996. At that time, the strains had been fully sensitive or had resistance to only first-line TB drugs.[14] Resistance to second-line drugs was not seen until recently, further supporting the notion of recent transmission of XDR.

Hospital transmission

It is also probable that *recent* transmission of XDR TB occurred in health facilities. The majority of the XDR TB patients at COSH had been recently hospitalised before the onset of the disease. Two of the 53 XDR TB patients were health workers and four other health workers died of what was suspected to be MDR TB. Infection control at COSH was weak with overcrowded TB wards, inadequate ventilation and poor respiratory hygiene and cough etiquette, all factors that help the spread of the airborne TB bacteria.

Weaknesses in the TB control programme

Although the current outbreak is now believed to be due in large part to transmission from person to person, particularly in healthcare settings, the *initial* XDR TB case must have developed as a result of the evolution of drug resistance in persons receiving first and second-line TB treatment.

A likely origin of XDR TB was incomplete treatment of MDR patients who were transferred to King George V Hospital (KGV) in Durban before 2004 and were treated with second-line drugs. As many of these referred patients defaulted and returned to their communities in Msinga, they were likely to have developed XDR TB, beginning the chain of transmission and passing on the deadly strain to highly vulnerable contacts, especially children and people living with HIV and AIDS.

At the time of the XDR TB outbreak, Umzinyathi district reported that 19.2 percent[15] of TB patients had defaulted on their treatment or had not been evaluated in 2004. This means that almost a fifth of patients diagnosed with TB – 4,572 that year – were lost and became a potential reservoir of MDR/XDR TB.

King George V Hospital

KGV is the referral specialised hospital for MDR TB and has 320 beds. Because of the rising number of MDR cases, the KwaZulu-Natal Department of Health began decentralising the MDR TB unit to district hospitals in 2008. One of these facilities is located in Greytown, Umzinyathi district, and has 30 beds. Of critical importance is the ability of KGV to follow all MDR TB patients who are transferred or discharged to home-base care to avoid generating XDR. The Italian Cooperation is supporting the development of an electronic system to manage and monitor these patients and has also provided video-conferencing equipment to facilitate consultations between Greytown hospital and KGV.

Collision between HIV and TB

KwaZulu-Natal has borne the brunt of the interconnected HIV and TB epidemics. The provincial rates of both are among the highest in the Southern Africa. The prevalence of TB doubled over a four-year period, from 400 cases/100,000 people in 2000/1 to 800/100,000 people in 2003/4 and now reaches 1,054 cases/100,000.[16] Up to 80 percent of new tuberculosis cases in the province are co-infected with HIV.[17] MDR/XDR TB is mostly diagnosed among inpatients and almost all of them are infected with HIV. Mortality is high for both MDR and XDR TB, suggesting that the main risk factor is related to a person's low immunity caused by HIV infection rather than the type of TB strain. In fact, 'normal' TB is just as contagious as MDR/XDR TB.

The convergence of the HIV and TB epidemics is placing great strain on healthcare services in the country. Health facilities cannot cope with the sheer number of people seeking treatment. There are not enough hospital beds, especially for the growing caseload of patients with TB, and medical workers are overstretched and cannot provide the individual attention and close follow-up needed to manage diseases such as TB. This state of affairs threatens to overturn the gains made by the national TB control and ARV treatment programmes and opens the door for an explosion of MDR/XDR TB.

The link with poverty

An important contributing factor to the spread of MDR/XDR TB in Msinga is the deep poverty in which most inhabitants live and their lack of access to basic services. Msinga is part of Umzinyathi district, one of the most disadvantaged districts in a province that already has some of the worst socioeconomic indicators in the country. Eighty percent of the district population lives in remote, rural and underdeveloped areas. MDR/XDR TB households in Msinga are among the poorest of the poor, living in deplorable conditions that increase their vulnerability to diseases of poverty.

A wake-up call

"HIV-related disease has emerged as the dominant challenge in sub-Saharan Africa, with the size of the epidemic calling for a response beyond the traditional boundaries of tuberculosis control."
(The Lancet, Vol 367, March 18 2006)

The outbreak of XDR TB in Msinga marked a turning point in the fight against TB and re-awakened interest in strengthening TB control strategies. The findings of the study on the Msinga epidemic were presented at the XVI International AIDS Conference in Toronto in August 2006 and published in The Lancet in October.

Since then WHO, the Centre for Disease Control in Atlanta, South African health authorities and other partners have met several times to find ways of containing and preventing the spread of the deadly disease, especially in high HIV prevalence areas.

WHO and its partners have organised task forces around different aspects of XDR TB, including defining XDR TB cases, updating guidelines for infection control in health facilities and devising communications strategies.

A global survey on drug resistant TB was published in 2008, revealing that XDR TB has been found in 45 countries and threatens to derail ten years of progress in TB control and HIV management.[18]

In August 2005, the Italian Cooperation and the 'Istituto Superiore di Sanita' (ISS), the leading technical and scientific body of the Italian National Health Service, began supporting the TB programme in Umzinyathi. A public health specialist came on board to give technical assistance to all aspects of TB control in the area.

CHRONOLOGY OF AN EPIDEMIC

1993 – Government-sponsored TB treatment programme, using the WHO DOTS strategy, launched at COSH. Patients receive free TB treatment by home-based directly observed therapy, administered by volunteer community health workers.

March 2004 – State-funded HIV treatment programme begins at COSH. Patients with CD4 counts of less than 200 are eligible for free ARVs. By October 2008, nearly 3,595 patients are receiving ARVs from COSH.

2004 – Doctors at COSH begin noticing that some HIV-positive patients are dying from TB despite doing well on ARV treatment. They suspect MDR TB.

February 2005 – COSH physicians do a snapshot across the hospital's TB wards. Ten out of the 45 patients tested are found to have resistance to almost all anti-TB drugs. This uncovers the presence of XDR TB in Msinga.

June 2005–March 2006 – Yale University, the University of KwaZulu-Natal and COSH carry out a study and test all TB suspects at COSH for drug susceptibility (a total of 1,539 patients). MDR TB is detected in 221 patients, of whom 53 have XDR TB, characterised by co-infection with HIV and high mortality.

September–December 2005 – A survey team visits all health facilities in Umzinyathi district to validate TB indicators and evaluate the TB control programme. They discover that the TB cure rate, reported as 47 percent, has been miscalculated. The real cure rate in the district for 2004 is 71 percent, though there is a high variation among clinics. The percentage of patients who defaulted and were not evaluated is 19.2 percent. The analysis shows that

Evaluating the TB programme

One of the first steps taken was to evaluate the regular TB control programme in the district. Between September and December 2005, a survey team visited all health clinics in the district to gather information on the state and operation of TB clinics, including staffing, infrastructure and access. The team found that clinics were in good condition, around 70 percent were accessible by public transport and more than one quarter reported an increase in MDR TB. However, strategies to trace defaulting TB patients were weak. When nurses were asked if they knew how many TB patients were scheduled for that day, only a few could reply.

At the same time, the district's TB indicators for 2004 were validated to provide a more solid baseline against which to compare the progress of the programme over time. Validation simply means that the accuracy of the indicators was verified by recalculating them. Reported TB cure rates in Umzinyathi had consistently been low, and in 2004 had been reported as 47 percent.[19] After tackling coding and methodological problems, the real cure for the district was 71 percent, a much better outcome than previously thought.

Cure rates however varied quite considerably across clinics. Rural clinics that dealt with smaller annual numbers of TB patients reported better indicators than busy, overcrowded urban facilities. The survey team found that the most important factor influencing cure rates was the number of patients per nurse. A clinic in which a nurse is responsible for about 40 TB patients per year is likely to have a cure rate of around 70 percent.[20] Any higher and the nurse

the most important variable influencing the cure rate is the number of patients per nurse.

August 2006 – The findings on the XDR TB epidemic in Msinga are presented at the XVI International AIDS Conference in Toronto and published in The Lancet in October. This causes a stir among medical and public health experts. Media coverage is unprecedented.

September 2006 – Officials from the Centre for Disease Control in Atlanta, WHO and African governments meet in Johannesburg for a conference on XDR TB in South Africa. WHO calls on South Africa to take urgent action against XDR TB, seen as a threat to global health and security. A plan is formulated to control the spread of the killer disease.

October 2006–ongoing – Mapping of all households with MDR/XDR TB patients in Msinga sub-district is carried out, using GPS. The tracing teams cover 725 households, including 3,206 family contacts.

POVERTY PROFILE OF MDR/XDR TB HOUSEHOLDS

72 percent live in homes made out of mud

75 percent are headed by women

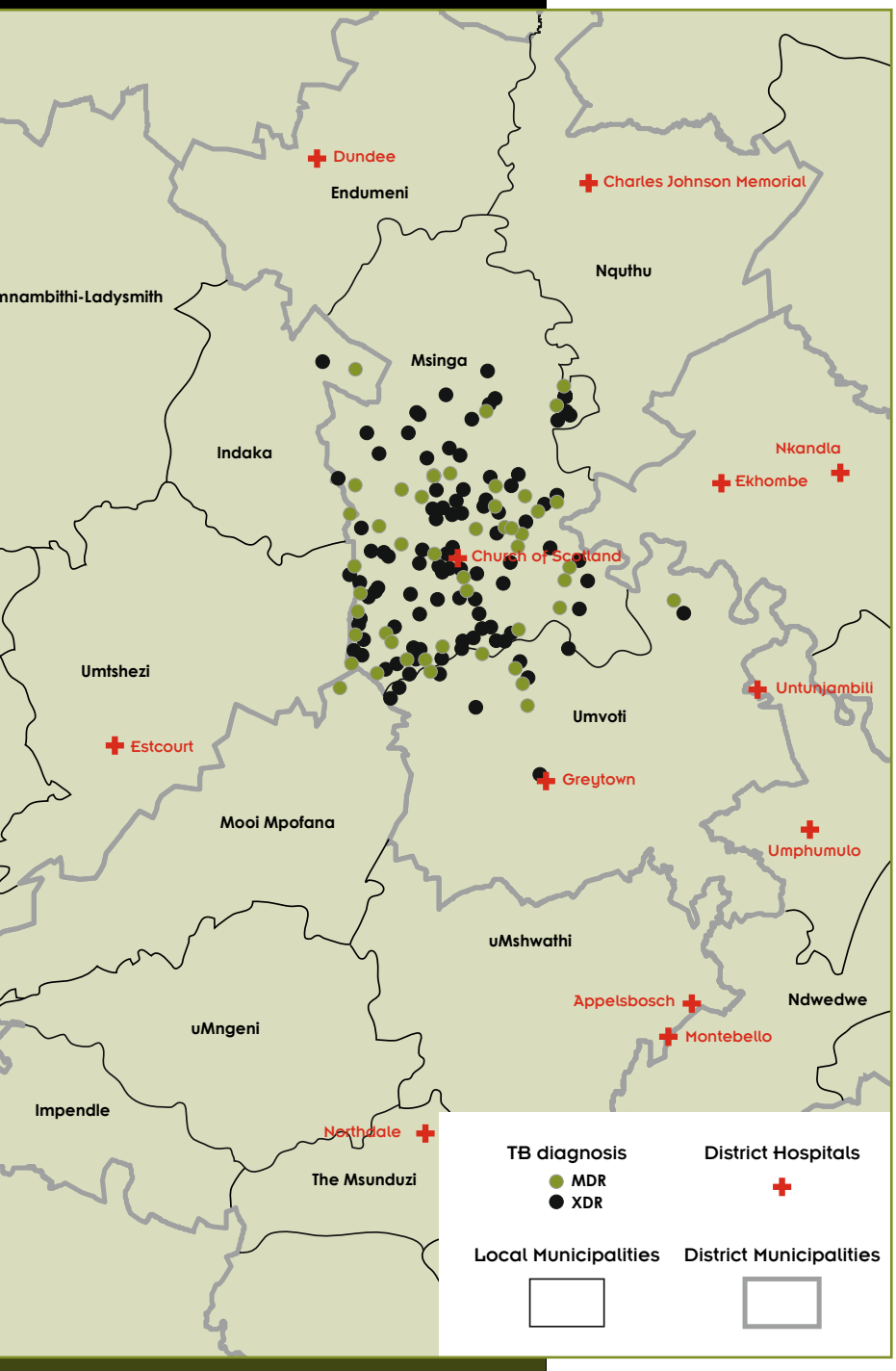
11.5 percent have formal employment

89 percent depend on social grants for survival

11 percent have electricity

2 percent have adequate sanitation

98 percent travel on foot to the nearest health centre, which is on average 4.4km away



Location of MDR/XDR index cases In Msinga

(based on map produced by the GIS unit, DoH, KwaZulu-Natal)

cannot provide the necessary follow-up needed to prevent patients from defaulting on their treatment, which lowers the cure rate. This pointed to the need of increasing staff in the busiest, mainly town-based clinics.

The district health management in Umzinyathi has since made concerted efforts to improve TB programme. In January 2006, a new tool to address defaulting was introduced. Special attention was given to Msinga, the epicentre of the MDR/XDR TB epidemic. Nurses were provided with diaries in which they could register appointments with TB patients. If a patient did not show up, a TB tracer team was sent to find the patient and bring them to the clinic. The number of dedicated TB nurses and tracer teams was also increased in the district.

Household surveillance, data collection and service delivery

In October 2006, the district management, in agreement with the provincial Department of Health, launched an innovative MDR/XDR TB community surveillance system in Msinga. ISS provided technical support and funding came from the Italian Cooperation. Since the sub-district has such a high number of HIV/XDR TB co-infected patients, the surveillance system is the first of its kind in Africa and provides a comprehensive package of interventions, including early identification of positive contacts, early initiation of treatment, health education and improved access to healthcare for affected households.

The system involved:

Reviewing data on MDR/XDR TB – two research assistants from the Italian Cooperation were stationed at COSH to plan, organise and review the data collected during household visits.

Tracing MDR/XDR households – tracing teams were provided with GPS to collect coordinates of all households of patients diagnosed with MDR/XDR TB. These coordinates will be used for future tracing.

Mapping MDR/XDR households – the GIS unit of the provincial Department of Health used the GPS coordinates to produce maps with the exact location of MDR/XDR TB households. Mapping is an important tool to plan follow-up visits.

Household visits – the tracer teams visited the households to identify cases of MDR/XDR TB among family contacts. All children below 15 received the tine test. Adults were asked to produce sputum to be sent to the lab for culture and drug susceptibility testing. The team interviewed all household members using a structured questionnaire. TB suspects and those with signs and symptoms of TB who could not produce sputum were referred to COSH for X-rays.

Systematic Voluntary Counselling and Testing (VCT) for children – tracing teams strongly recommended VCT for children. If the parents or caregivers agreed, the children were brought to COSH. Since September 2008, VCT has been provided as a home-based service.

Improving infection control

The presence of MDR/XDR TB is a sign of inadequate infection control in healthcare settings. Measures have been taken to address infection control in all four of Umzinyathi's district hospitals. A multidisciplinary approach was used to identify areas where transmission was likely to occur and standardised minimum requirements to make hospital environments safer were established.

In COSH, an 'open window' policy was implemented in TB wards and waiting rooms to improve ventilation. An extractor fan was installed in the TB ward in 2006. In waiting rooms, patients who are coughing are separated from others and requested to wait in a well-ventilated area or placed at the front of the queue to provide care quickly and reduce the amount of time that others are exposed to them.

Home-based care for MDR TB

Because of insufficient bed capacity at KGV, community management of MDR TB has been introduced. Mobile medical teams provide, to date, home-based care to 35 patients and collect information on side effects and other issues. This initiative is proving to be very cost-effective and amounts to approximately 10 percent of the cost of hospitalisation.

The importance of laboratories

The ability of laboratories to accurately diagnose MDR/XDR TB in a timely and efficient manner is paramount to the success of TB control. The only lab in KwaZulu-Natal that can perform drug susceptibility testing (DST) is in Durban. It carries out more than 12,000 DST tests a month and works to full capacity. Peripheral laboratories in the districts conduct sputum smear microscopy and are also overstretched, with some of them performing more than 100 AFB (acid-fast bacilli) tests a day. The link between laboratory services and the TB programme needs to be strengthened in order to achieve better performance in TB control.

Table 1: Age and gender distribution of the 725 index cases diagnosed with MDR and XDR in Msinga

	MDR				XDR			
Age	**Males**	**Females**	**Total**	**%**	**Males**	**Females**	**Total**	**%**
0-4			0	0		1	1	0
5-9	2		2	1	2	2	4	1
10-14	4	1	5	2	3	1	4	1
15-19	1	5	6	2		7	7	2
20-24	7	16	23	7	6	21	27	7
25-29	27	27	54	17	26	47	73	18
30-34	36	26	62	20	45	51	96	23
35-39	39	20	59	19	40	35	75	18
40-44	19	21	40	13	30	32	62	15
45-49	18	8	26	8	13	9	22	5
50-54	6	4	10	3	12	10	22	5
55-59	6	3	9	3		5	5	1
60-64	1		1	0	5	2	7	2
65-98		2	2	1		5	5	1
Missing age	8	3	11	4	2	3	5	1
Total	**174**	**136**	**310**	**100**	**184**	**231**	**415**	**100**

Table 2: Age and gender distribution of the 58 household contacts diagnosed with MDR and XDR

	MDR				XDR			
Age	**Males**	**Females**	**Total**	**%**	**Males**	**Females**	**Total**	**%**
0-4	1		1	4			0	0
5-9			0	0	1		1	3
10-14	1	2	3	12	1	1	2	6
15-19	3		3	12	2	2	4	12
20-24		4	4	16	1	1	2	6
25-29	1		1	4	1	3	4	12
30-34	1	3	4	16	4	5	9	27
35-39	1	1	2	8	2	4	6	18
40-44		2	2	8		2	2	6
45-49	1		1	4	1		1	3
50-54		1	1	4			0	0
55-59		1	1	4		1	1	3
60-64		1	1	4		1	1	3
65-98		1	1	4			0	0
Total	**9**	**16**	**25**	**100**	**13**	**20**	**33**	**100**

Table 3: Age and gender distribution of the 68 children contacts who were diagnosed with TB

Age	**Males**	**Females**	**Total**	**%**
0-4	13	19	32	47
5-9	20	11	31	46
10-12	3	2	5	7
Total	**36**	**32**	**68**	**100**

Surveillance results

Between October 2006 and October 2008, surveillance teams visited 725 households in Msinga and screened 3,206 household contacts twice after the diagnosis of the index case. Table 1 shows the number and percentage of MDR TB and XDR TB index cases by age and sex.

Table 2 shows the number and percentage of positive family contacts in the households by age and sex.

Thirty-five of the 58 positive contacts were still alive by the end of October 2008 and are being closely monitored. Some are receiving home-based treatment while others have been hospitalised or are being monitored without treatment.

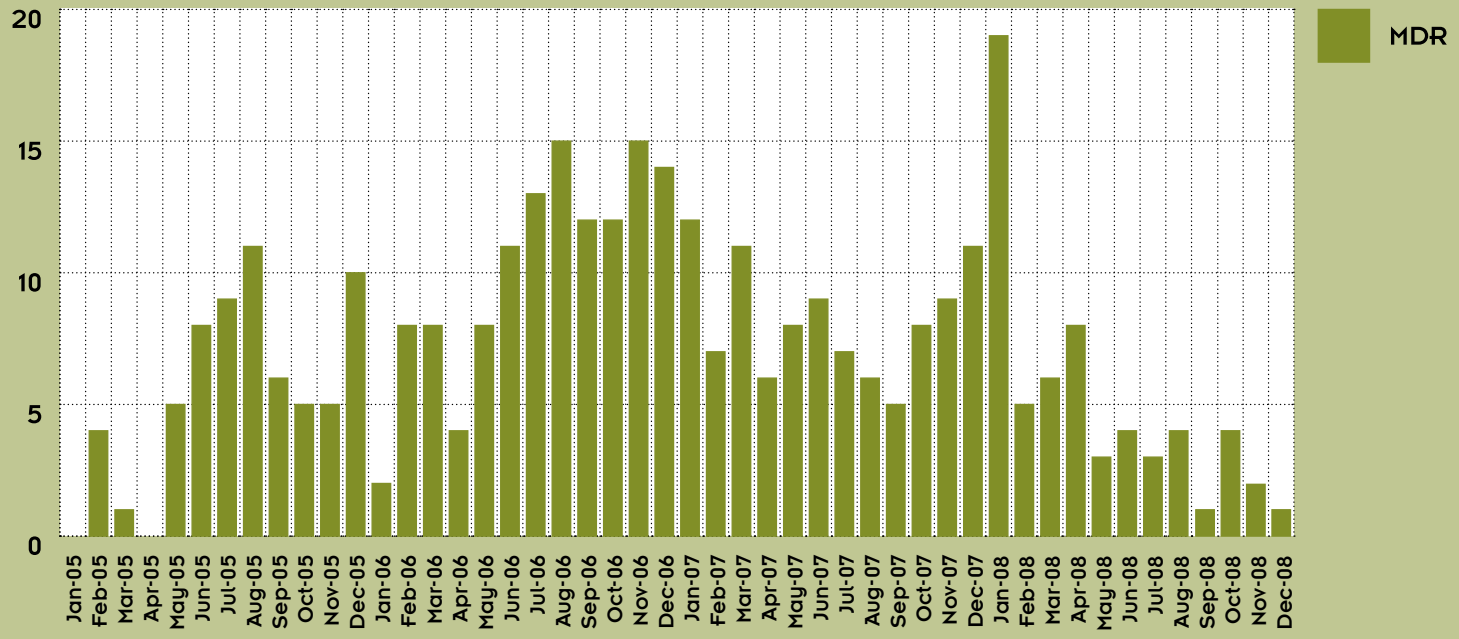
Table 3 shows the number and percentage of children who tested positive for TB as diagnosed by the tine test and chest X-rays. All the children have received a six-month course of first line drugs and are under close observation.

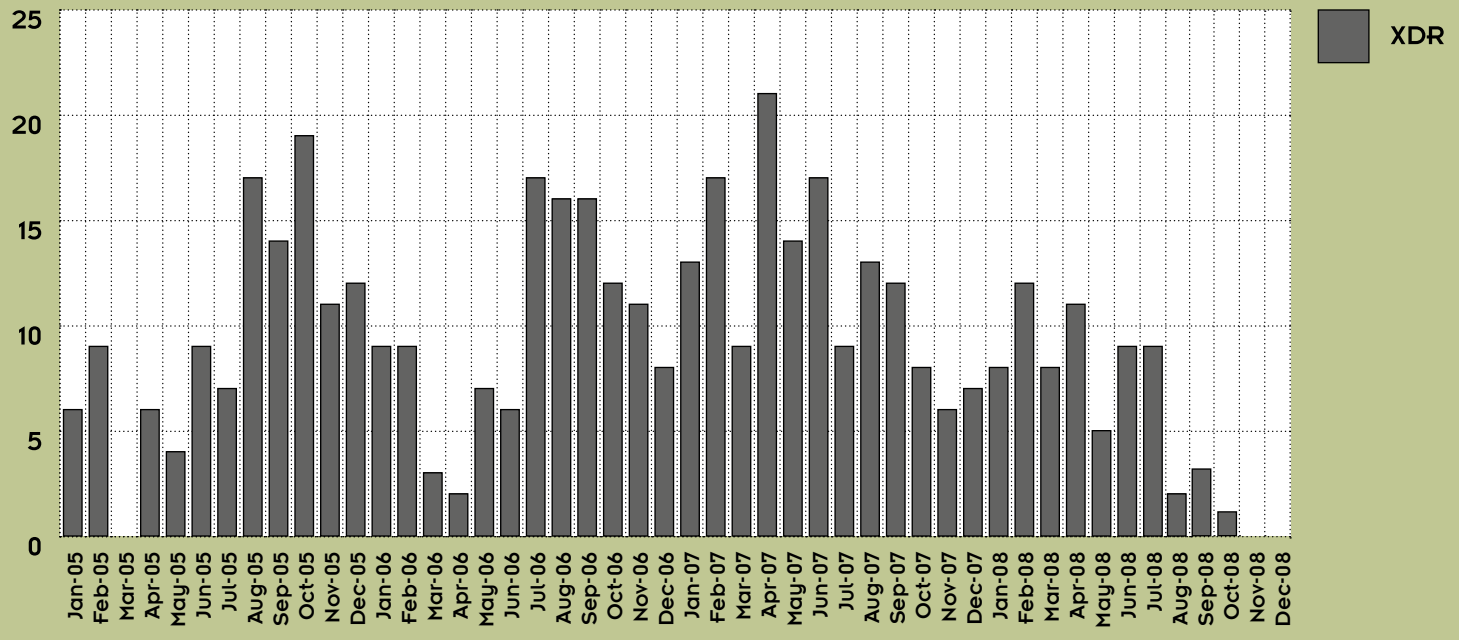
MDR TB cases represented 1.2 percent of the total sample sent to lab while XDR TB stood at 1.4 percent. This low rate of transmission in the affected households is most likely due to the fact that most MDR/XDR TB patients were co-infected with HIV, were not highly contagious (smear negative) and died quickly, limiting the spread of the deadly disease to their closest contacts at home. Fatality in patients with XDR TB is greater than that of those with MDR TB.

Ten percent of all children in the households were diagnosed with TB. Though the vast majority is HIV negative, children are generally at greater risk of contracting infectious diseases because of their developing immune systems. Special measures need to be put in place to protect children from contracting TB. Isolation from a positive family member, for example, is a must. Strict monitoring is under way to ensure that children are kept safe.

The results of the surveillance were presented at the first South African TB conference in Durban from 1–4 July 2008, and at the 39th Lung Health conference in Paris from 16–20 October 2008.

Special measures need to be put in place to protect children from contracting TB.





MDR and XDR cases diagnosed monthly (2005–2008)

MDR/XDR TB cases decrease

Dramatic progress was made in lowering the default rate, from a high of 19.2 percent in 2004 to close to zero percent in 2007.

In 2008, TB programme managers started noticing a drop in the number of MDR and XDR TB cases diagnosed on a monthly basis (please refer to graphs on page 3 and 16).

What was behind this decline?

- The commitment of the Umzinyathi health district management team ensured that TB control was placed at top of the district's agenda and that adequate resources were allocated to tackle the disease.
- The management of TB patients was aggressively addressed by providing refresher training for nurses and introducing appointment diaries to track patients.
- An increase in the nurse-to-patient ratio also played an important role in improving treatment outcomes and preventing defaulting.
- Tracer teams were increased and provided with GPS to map MDR/XDR TB households. Tine tests were performed and containers with sputum samples were sent to the laboratory for analysis.
- TB suspects in the community were identified through strict surveillance and contact tracing.
- Measures were taken to bolster infection control at COSH to reduce hospital transmission of MDR/XDR TB.
- Public information campaigns helped to sensitise the community on the dangers and prevention of TB.

Efforts to hem in the spread of MDR/XDR TB resulted in an improvement in the district's cure rate, from 71 percent in 2004 to 83 percent in 2007. Dramatic progress was made in lowering the default rate, from a high of 19.2 percent in 2004 to close to zero percent in 2007. This meant that the TB control programme was no longer losing patients who would have otherwise developed resistance and added to the pool of MDR/XDR TB sufferers. These indicators are to date the best in South Africa. They demonstrate that the TB programme's success depends on a provincial health system with a solid foundation, which can be built upon and strengthened.

An opportunity for expansion

The Global Fund has launched its Round 9 Call for Proposals and provides a golden opportunity for the KwaZulu-Natal Department of Health to scale up community surveillance and home-based care for MDR/XDR TB, based on the lessons learnt in Msinga.

HOW IS TB DIAGNOSED?

Addressing the MDR/XDR TB epidemic effectively rests on the accurate diagnosis of the disease. Since the discovery of the TB bacterium in 1882, microscopy, culture testing, skin testing and radiology have been the mainstay of TB control programmes worldwide. Laboratories have therefore played a pivotal role in the fight against TB. Without a lab, physicians can only suspect that a patient has TB and have no way of knowing what kind of strain they are dealing with. Early and accurate diagnosis is critical for early treatment, which greatly improves a patient's chances of survival and helps to break the chain of transmission. The development of new and rapid diagnostic technologies promises to revolutionise the way MDR/XDR TB is managed, especially in resource-poor settings where access to laboratories is limited.

Tine Test – the test involves injecting a small amount of tuberculin antigen just under the skin. A positive result is read by measuring the size of the papule – a red and swollen area on the skin. A negative tine test does not necessarily exclude TB disease.

Chest X-ray – the lungs are the most common site of TB disease. An X-ray can detect chest abnormalities that may suggest TB infection/disease.

Diagnostic microbiology AFB – a *sputum smear* (mucus/phlegm coughed up by patient) is examined with a microscope for presence of TB bacteria. If the result is positive, the person is said to be smear positive. The test's accuracy in identify TB infection in HIV-infected patients is low.

Culture testing with drug sensitivity (DST), in which a culture of TB bacteria is grown in a solid/liquid media, is the golden standard for both diagnosis and drug sensitivity testing. However, it takes up to eight weeks to produce results.

Hain Test – this test is part of the drive to develop new diagnostic tools to address MDR/XDR TB. The Hain test is an improved molecular test, which is used on smear positive isolates and gives a MDR TB diagnosis in two hours.

TB diagnosis in children

Diagnosing TB in children is difficult because children under the age of 10 years usually cannot cough up sputum for analysis. The diagnosis is thus largely based on the clinical features of coughing, weight loss, fever, with a history of contact with an infectious adult TB patient. Tine test results from children have been evaluated according to the size of the reaction and a negative result does not rule out exposure to TB.


DSCOPE
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The way forward

The decline in MDR and XDR TB cases in Msinga is a promising sign that a comprehensive and aggressive approach to TB control is able to begin turning the tide of the MDR/XDR TB epidemic. The impressive work done to date by the Umzinyathi district management needs to be sustained and further improvements have to made to maintain the downward trend. In particular:

- The commitment by the district management needs to stay strong and focused.
- Household surveillance has to continue with an additional component of aggressive infection control at household level.
- More funds need to be provided to address infection control in healthcare settings so that hospitals and health centres become healthier and safer environments for patients and health workers alike.
- VCT uptake needs to be increased so that co-infection with HIV and TB can be dealt with promptly.
- ARV treatment needs to reach greater numbers of people living with HIV and AIDS to reduce their susceptibility to virulent diseases such as MDR/XDR TB.
- The home-based care unit at COSH needs to be strengthened and connected with the ARV programme to ensure a coordinated approach to treatment for TB and HIV.
- Child contacts have to be monitored closely and continuously so that children who test positive for TB can be referred for prompt treatment.
- KGV must have a dedicated unit to monitor patients on home-based care so that patients are not lost once they are discharged.
- The quality of services provided by the National Health Laboratory Service needs to be strengthened and services linked with the TB programme.

Cover photographs:
(left) © Freeman Patterson/Radius Images
(right) © Les Cunliffe/Dreamstime.com

Endnotes

1 Global Tuberculosis Control, WHO Report 2008
2 'Case Study: South Africa', Karin Weyer, WHO Bulletin, Volume 85, Number 5, May 2007
3 'Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural areas of South Africa', Neel R Ghandi, Antony Moll, A Willem Sturm, Robert Pawinski, Thiloshini Govender, Umesh Lalloo, Kimberly Zeller, Jason Andrews, Gerald Friedland, The Lancet 2006; 368:1575-80
4 'Case Study: South Africa', Karin Weyer, WHO Bulletin, Volume 85, Number 5, May 2007
5 Ibid
6 Ibid
7 Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment, Elizabeth L Corbett, Barbara Marston, Gavin J Chruchyard, Kevin M De Cook, The Lancet, Vol 367, March 8, 2006
8 'Case Study: South Africa', Karin Weyer, WHO Bulletin, Volume 85, Number 5, May 2007
9 'Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural areas of South Africa', Neel R Ghandi, Antony Moll, A Willem Sturm, Robert Pawinski, Thiloshini Govender, Umesh Lalloo, Kimberly Zeller, Jason Andrews, Gerald Friedland, The Lancet 2006; 368:1575-80
10 K. Mlambo, R.M. Warren, X. Poswa, T.C. Victor, A.G. Duse, E. Marais, Int. J Tuberc Lung Dis 12(1):99-104
11 'Frequently asked questions – XDR TB', www.who.int/tb/xdr/faqs/en/index.html
12 'Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in an era of antiretroviral treatment', Elizabeth L Corbett, Barbara Marston, Gavin J Churchyard, Kevin M De Cook, The Lancet, Vol 367, March 18, 2006
13 Towards Universal Access: Scaling up priority HIV/AIDS interventions in the health sector, Progress Report June 2008, WHO, UNAIDS, UNICEF, 2008
14 'XDR TB – An emerging global threat to TB control', Dr. James P.T., Institute of Chest Diseases, Medical College, Calicut, Pulmon 2006: 8:2:41-42
15 'Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural areas of South Africa', Neel R Ghandi, Antony Moll, A Willem Sturm, Robert Pawinski, Thiloshini Govender, Umesh Lalloo, Kimberly Zeller, Jason Andrews, Gerald Friedland, The Lancet 2006; 368:1575-80
16 Electronic TB Register, Umzinyathi District, 2004/5
17 KwaZulu-Natal Department of Health
18 'Uncovering XDR TB associated with HIV Infection in KZN. Experience in KwaZulu-Natal, South Africa', presentation made by Dr. Tony Moll to the 4th Regional Advisory Panel & Regional Clinical Coordination Sub-Committee Meeting in Accra, Ghana, January 19 2007
19 Anti-Tuberculosis Drug Resistance in the World, Forth Global Report, The WHO/IUALTD Global Project on Anti-tuberculosis Drug Resistance Surveillance, 2002-2007, WHO, 2008
20 Validation of the TB indicators in Umzinyathi District, KwaZulu-Natal Epidemiology Bulletin, KwaZulu-Natal Department of Health, Issue 12, December 2005
21 Evaluation of the TB control programme in Umzinyathi District, KwaZulu-Natal Epidemiology Bulletin, KwaZulu-Natal Department of Health, Issue 13, March 2006

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Stop TB Partnership