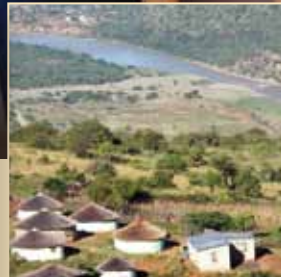


Taking Action against MDR/XDR TB & HIV in Tugela Ferry, South Africa

RESEARCH, CLINICAL AND PROGRAMMATIC RESPONSE



UNCOVERING AN EPIDEMIC

In 2005, South African and US clinicians and researchers identified a large number of cases of a deadly and almost untreatable form of tuberculosis (TB) at the Church of Scotland Hospital (COSH) in Tugela Ferry, a rural and desperately poor part of KwaZulu-Natal province in South Africa. The extensively drug-resistant TB or 'XDR TB' they uncovered occurred among HIV-infected individuals, and was resistant to almost all anti-TB drugs available in South Africa, severely limiting treatment options.

Of fifty-three patients diagnosed during the first year of surveillance for XDR TB only one survived. Patients with XDR TB died on average within 16 days of presenting for medical attention at COSH. Some of those who died were hospital staff and 67 percent had been hospitalized in the preceding two years, which led the team to believe that transmission of XDR TB had likely occurred in the overcrowded wards of COSH. The 350-bed hospital is the major source of medical care for 172,000 people living in the Msinga sub-district surrounding Tugela Ferry in Umzinyathi district, KwaZulu-Natal province—an area of extremely high HIV and TB prevalence.

These diagnosed cases were the largest cluster of HIV-associated XDR TB ever recorded in the world. The emergence of XDR TB—with its extremely high mortality, limited treatment options, co-infection with HIV, and potential to spread widely—appropriately alarmed medical and public health officials worldwide. It became clear that a major coordinated and comprehensive effort would be critical to combat this unprecedented epidemic.



JOINING FORCES



TF CARES/Philanjalo

PHILANJALO, a local NGO based at Tugela Ferry, was established in 1998 to mitigate the impact of HIV/AIDS in this resource poor area by providing home-based care, voluntary counseling and testing and the management of opportunistic infections in the years before the launch of the South African anti-retroviral (ARV) program. This was done hand in hand with the Department of Health to provide a continuum of care for patients from hospital to home.

A partnership between Philanjalo, Yale University and University of KwaZulu-Natal was formed in 2002 to provide ARV treatment to patients co-infected with HIV and TB using the existing infrastructure of the Directly Observed Treatment, Short course (DOTS) program. It was during this project that XDR TB was found to be a major cause of death among HIV/TB co-infected patients. An international collaboration of partners developed rapidly to jointly address the challenges of drug-resistant TB in order to understand the complexities of the epidemiology, faster diagnosis, treatment, control and programmatic management of this serious epidemic.

TF CARES (The Tugela Ferry Care and Research Collaboration) emerged formally to coordinate these efforts, involving a partnership between Philanjalo, Yale University, Albert Einstein College of Medicine and the University of KwaZulu-Natal. TF CARES has worked closely with the KwaZulu-Natal Department of Health and the Italian Cooperation since 2006 to devise strategies and programs to combat the drug-resistant TB epidemic in KwaZulu-Natal.

SOUTH AFRICA'S VULNERABILITY

With 18 percent of its adult population infected with HIV in 2009, South Africa is home to one of the world's largest HIV epidemics and one of the highest burdens of TB. Despite an advanced public health system and far greater capacity for TB drug resistance surveillance than any other sub-Saharan country, the HIV epidemic has overwhelmed and disrupted an already faltering TB control program. This has led to increases in TB treatment failure and default and greater opportunities for drug-resistant TB to emerge and spread among HIV-infected and uninfected people.

HOW DOES DRUG RESISTANT TB DEVELOP AND SPREAD?

An airborne disease, TB is spread through coughing, sneezing or simply talking. The risk of transmission increases where there is a high concentration of TB bacteria – in overcrowded and poorly ventilated settings where people congregate including houses, hospitals, waiting rooms, offices and prisons. Those with compromised immune systems – such as HIV – are at very high risk of contracting and developing TB disease.

TB can usually be treated with a standard course of four first-line anti-TB drugs. If these drugs are misused or mismanaged, multidrug-resistant TB or 'MDR TB' can develop. MDR TB takes longer to treat with second-line drugs (usually two years), which are more expensive and have more toxic side effects.

XDR TB can develop when these second-line drugs for MDR TB treatment are also misused or mismanaged and, therefore, also become ineffective and lead to amplified resistance. With XDR TB, the most powerful first-line and second-line TB medications are no longer effective, thereby severely limiting the chance of treatment success and cure-take out for these patients. Both MDR TB and XDR TB can spread to others, through the airborne route, rapidly increasing the number of cases and dire consequences to epidemic levels.

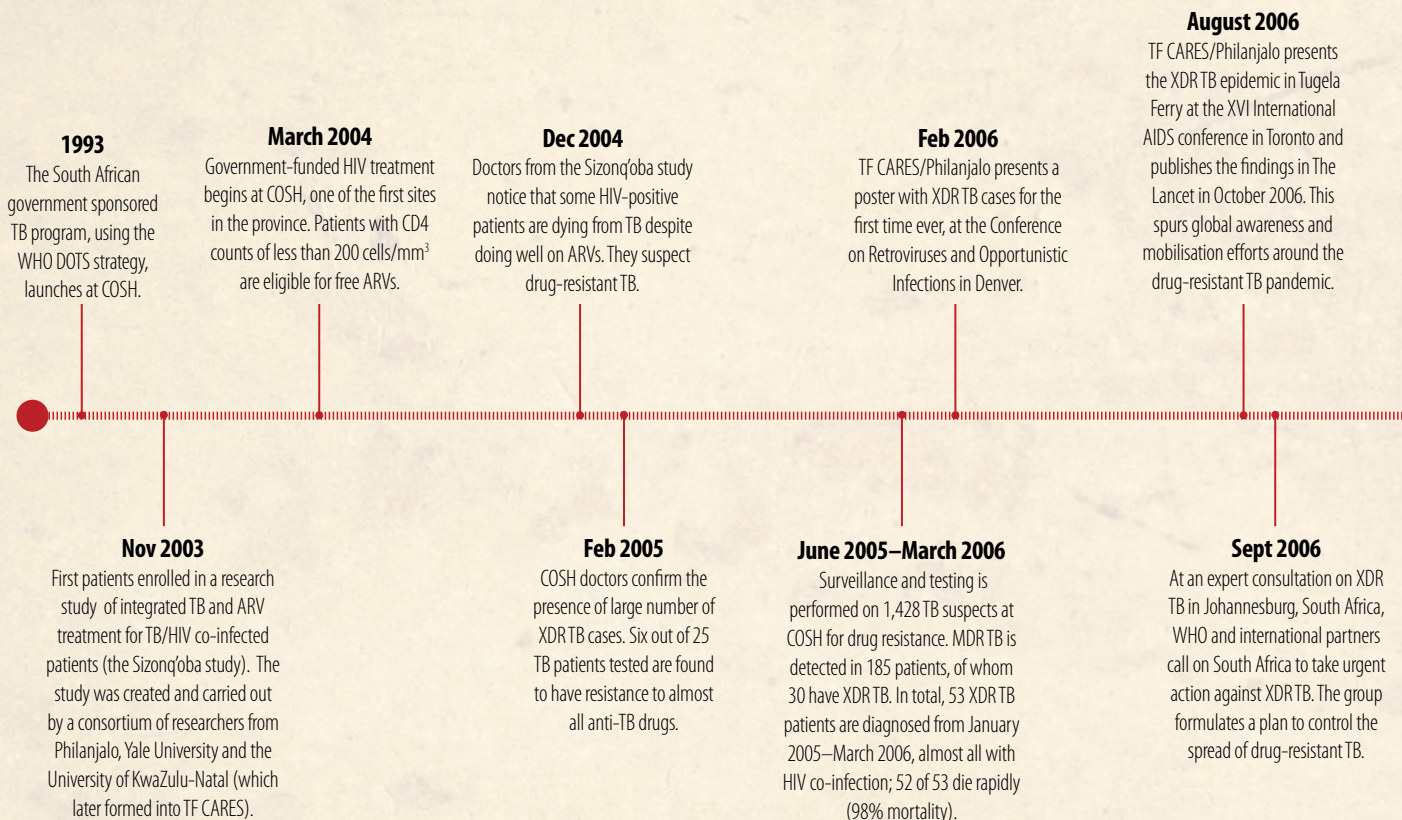


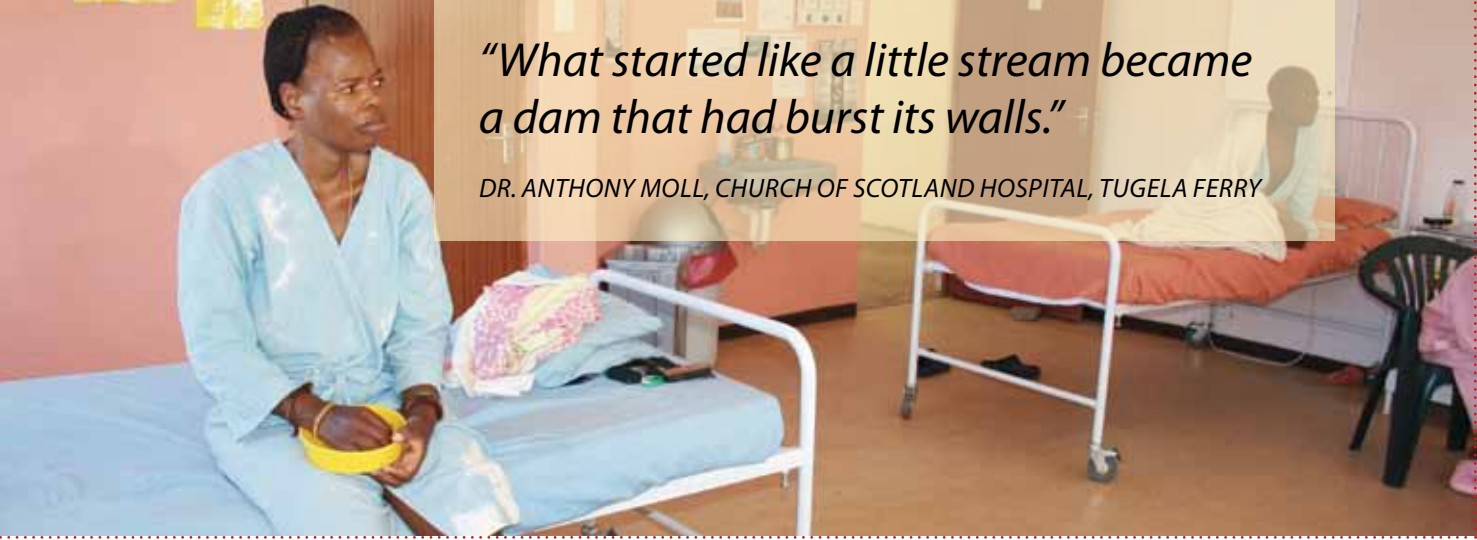
RAPID SPREAD OF A DEADLY DISEASE

The convergence of TB, HIV and XDR TB has created a new and dangerous major epidemic. The number of cases of both XDR TB and MDR TB has continued to increase. XDR TB is now present in all nine South African provinces and its neighboring countries and has been reported in nearly 60 countries worldwide. The largest number of cases remains in the Tugela Ferry area with over 500 cases reported as of December 2009. In addition, many more cases have been suspected but not diagnosed, due in part to delays in patients presenting for medical care and limitations in diagnostic tests for TB.

In addition to the dangers to individual patients, the spread of MDR/XDR TB could derail recent advances in TB control and HIV treatment, especially in areas of sub-Saharan Africa, like Tugela Ferry, with high HIV infection rates. Scientific predictions indicate that the number of cases will continue to escalate upwards unless a comprehensive and coordinated response, directed at both TB and HIV, is rapidly implemented.

CHRONOLOGY OF IDENTIFYING AND COMBATING THE EPIDEMIC IN TUGELA FERRY





“What started like a little stream became a dam that had burst its walls.”

DR. ANTHONY MOLL, CHURCH OF SCOTLAND HOSPITAL, TUGELA FERRY

Sept–Dec 2006

The Italian Cooperation and the Department of Health evaluate Tugela Ferry and surrounding Umzinyathi district's TB control program. TB indicators are validated and programmatic improvements are made.

Jan 2007

Airborne infection control program established at COSH, including administrative, environmental and personal control strategies.

Nov 2007

TF CARES evaluates a rapid diagnostic test strategy using MODS assay in over 900 TB suspects, primarily HIV co-infected. The tests exhibit high sensitivity and specificity with rapid turnaround time.

Jan 2008

The Department of Health starts healthcare and community-based intensive case finding program for drug sensitive and resistant TB and HIV.

Feb 2008

TF CARES/Philanjalo and the KwaZulu-Natal Department of Health establish a community-based MDR TB treatment program in Tugela Ferry and the Msinga district.

April 2010

TF CARES/Philanjalo begin expansion of the community-based intensive case finding program to reduce mortality and TB transmission.

Sept–Oct 2006

The Italian Cooperation and the Department of Health begin household contact tracing. Tracing teams visit, screen and evaluate 725 households with MDR/XDR TB patients in the Tugela Ferry area, including 3,206 adult and pediatric household contacts.

July 2007

TF CARES initiates program to provide medical support for clinical programs at COSH and Philanjalo in Tugela Ferry.

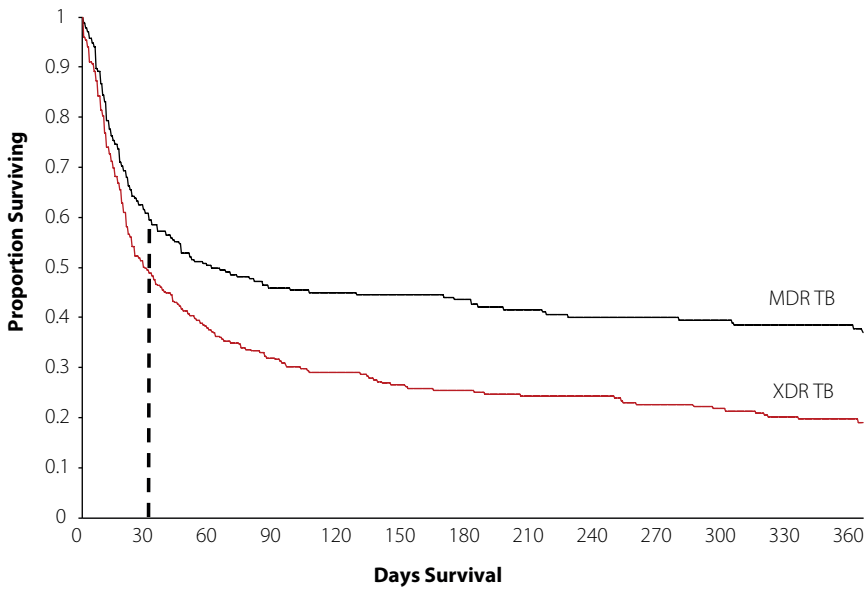
July 2009

TF CARES/Philanjalo launch an enhanced pediatric TB diagnosis initiative to improve diagnosis of TB and drug-resistant TB in children. Over 100 childhood TB suspects enrolled to date, including screening for pediatric contacts of MDR and XDR TB adults.

2009

The South African National TB Program, in collaboration with TF CARES/Philanjalo and Médecins Sans Frontières, explores the feasibility of implementing community management of MDR TB as a treatment approach.

HIGH MORTALITY AMONG MDR TB AND XDR TB PATIENTS IN THE HIGH HIV PREVALENCE SETTING OF TUGELA FERRY, SOUTH AFRICA



At the end of one year, 71 percent of MDR TB patients and 83 percent of XDR TB patients died in large part due to late appearance for care, delay in diagnosis of TB and HIV and limitations of therapy for drug resistant TB. The majority of deaths occurred within the first 30 days after sputum collection: 40 percent of MDR TB patients and 51 percent of XDR TB patients died within the first 30 days, most before the results of their culture and drug-susceptibility tests were available.



“Rapid diagnosis of TB and TB drug resistance is key to improving survival and reducing transmission of MDR and XDR TB.”

DR. SARITA SHAH, ALBERT EINSTEIN COLLEGE OF MEDICINE

WHAT IS BEING DONE TO CURB THE MDR/XDR TB AND HIV EPIDEMICS?

The epidemic of MDR/XDR TB and HIV co-infection has been a wake-up call to the public health community in South Africa and globally. Through our work in Tugela Ferry, TF CARES/Philanjalo has responded to the urgent need for prevention, diagnosis, care and treatment of TB and HIV. Our aim is to provide the evidence-base for sound public health and clinical policy to address the combined epidemics of TB, HIV and drug-resistant TB in South Africa. We are committed to clinically relevant and ethical research, capacity building through education and training, and the highest quality of compassionate and comprehensive care for communities with HIV/AIDS and TB.

Our initiatives include prevention of TB transmission, earlier diagnosis of TB and drug resistance and strengthening of TB and HIV care and treatment programs. Since the effective treatment of XDR TB is and will remain limited for the near future, our efforts are directed towards reducing the generation and transmission of TB, particularly MDR and XDR TB.

We provide clinical support and technical assistance to the KwaZulu-Natal Department of Health and to the physicians, nurses and staff at COSH and Philanjalo. We link clinical care and operational research to increase program effectiveness and to inform policy and practice.

STRENGTHENING THE ROUTINE TB PROGRAM, INTEGRATING TB AND HIV CARE

After uncovering the XDR TB epidemic in Tugela Ferry, TF CARES/Philanjalo shared the findings with policy makers at the local, regional and international level in order to mobilise a response to the epidemic. The KwaZulu-Natal Department of Health and the Italian Cooperation made the critical first step of strengthening the regular TB control program in Tugela Ferry's Umzinyathi district. The aim was to improve outcomes and reduce the likelihood of generation of drug-resistant TB. As a result of this intervention, the treatment default rate in the area dropped to zero and the treatment success rate rose to 85 percent, achieving international standards for TB control.

TF CARES/Philanjalo has provided technical assistance to the Department of Health in the areas of infection control, ongoing surveillance of MDR/XDR TB, intensive case finding and community management of TB. These approaches, which were first demonstrated in Tugela Ferry, are being adopted throughout the province.



Prior to the XDR TB epidemic, in 2002 and 2003, TF CARES/Philanjalo first demonstrated that TB and HIV care could be integrated with successful outcomes even in rural, low-resource areas. Following the epidemic, our site has served as a demonstration program for integration of care and treatment for MDR/XDR TB and HIV co-infection. We have shown how testing, co-treatment, active case finding and community-based treatment are feasible approaches in rural areas.

REDUCING TRANSMISSION OF MDR AND XDR TB

Standard TB diagnostic methods are no match for today's drug-resistant strains. Clinicians need diagnostic tools that can provide real-time information about the presence of drug-susceptible or drug-resistant TB in their patients. TF CARES/Philanjalo is developing and testing multiple strategies for a more rapid diagnosis of MDR/XDR TB (see box below).

STRATEGIES TO IMPROVE DIAGNOSIS

TF CARES has tested and demonstrated the feasibility and effectiveness of the Microscopic Observation Drug Susceptibility (MODS) test at COSH. MODS is a simple and inexpensive procedure that uses existing lab equipment and yields results in one week.

We are studying the value of blood cultures and body fluids as a diagnostic tool for patients with suspected drug-resistant TB.

We are also working to improve TB and drug-resistant TB diagnosis in children by strengthening specimen collection procedures and practice for blood, gastric aspirate, sputum and urine samples.

In consultation with the National Health Laboratory Service, TF CARES/Philanjalo and the Foundation for Innovative New Diagnostics are working on plans to decentralise laboratory facilities for rapid molecular and culture-based TB diagnosis by early 2011.

HOUSEHOLD CONTACT TRACING

People are often sick with both TB and HIV long before they seek medical attention. During that time, those with TB run the risk of infecting their spouses, children and other community members. Early identification and treatment of TB both improve the chances of successful treatment and survival and can interrupt transmission to others.

The Italian Cooperation and the Department of Health designed and started implementing household contact tracing for MDR/XDR TB in 2006. Tracer teams visit households to screen family contacts for signs and symptoms of the disease. Between 2005 and 2009, close to 4,200 family contacts were screened – 70 were diagnosed with drug-resistant TB, of which 60 percent had XDR TB.

An innovative community surveillance system is closely monitoring the evolution of the epidemic in Tugela Ferry. Tracer teams collect GPS coordinates of all households of patients diagnosed with MDR/XDR TB, which are then used to map the distribution and numbers of affected households. Mapping is an important tool for household contact tracing, especially in rural areas like Tugela Ferry.



INTENSIVE CASE FINDING

We have established intensive case finding programs in the hospital and community settings. Patients entering the hospital and clinics are routinely screened by 'cough officers' to identify TB suspects. TF CARES/Philanjalo has also launched a TB and HIV screening program at congregate settings throughout the community. These include 'pension pay points' where monthly

grants are distributed, schools, and taxi ranks. Close to 600 individuals have been screened to date; 9 percent have been found to be HIV infected and 3 percent have had active TB, including drug-resistant TB.

“Practical and feasible strategies can be implemented to reduce TB transmission risk in hospitals and clinics, even in resource-limited settings”

DR. GERALD FRIEDLAND, YALE UNIVERSITY



INFECTION CONTROL

Inadequate infection control in health care facilities such as hospitals and clinics puts patients and staff in danger in the very place they expect to find help. Since the epidemic of MDR/XDR TB is fueled by healthcare-related transmission, TF CARES/Philanjalo has developed, implemented and monitored simple, feasible, effective and low cost strategies of airborne infection control at COSH. However, due to the old hospital buildings and overcrowded TB and other wards, serious challenges to airborne infection control remain. These need to be addressed adequately through the construction of a new, improved and safer TB ward and other facilities.

However, due to the old hospital buildings and overcrowded TB and other wards, serious challenges to airborne infection control remain.

IMPROVING INFECTION CONTROL

TF CARES/Philanjalo has helped to develop and implement infection control policies by working closely with designated infection control nurses appointed by the Department of Health. This carefully monitored program has been associated with a decrease of MDR/XDR TB on the COSH hospital wards.

- **Ventilation has been improved in waiting rooms, the TB ward and other sites through an open window policy that promotes natural ventilation, and through the installation of mechanical extractor fans.**
- **All patients in the ARV and other clinics and waiting rooms are screened for cough and other TB symptoms and those who are suspected of having TB are separated from others and evaluated.**
- **Staff risk has been reduced by the provision of N95 respirator masks for all staff, infection control education and training, and encouragement of HIV counseling and testing, access to ARVs, if positive, and transfer to safer hospital areas.**

COMMUNITY-BASED CARE OF MDR TB AND HIV

TF CARES/Philanjalo has developed and is testing one of Africa's first community-based treatment programs for patients who are co-infected with MDR TB and HIV. The goal is to improve treatment outcomes for MDR TB and limit the generation and transmission of XDR TB.

The single provincial TB referral hospital became overwhelmed by drug resistant cases. Due to the scarcity of hospital beds and desire to improve outcomes, a decentralized community-based model of treatment for MDR TB is key to helping patients complete their treatment successfully. Nurses conduct daily home visits to give second-line anti-TB drugs by injection to their patients and observe doses of oral TB medications and ARVs. TF CARES/Philanjalo developed an innovative treatment literacy education curriculum for patients and their family members to teach the importance of medication adherence and how to prevent MDR TB and HIV transmission. Home visits provide close monitoring for any treatment-related adverse effects or disease progression.

“We're seeing patients every day in their homes, so we can ensure they remain adherent to their treatment and we can detect and treat adverse events rapidly and effectively.”

***DR. NEEL GANDHI, ALBERT EINSTEIN
COLLEGE OF MEDICINE***

Home-based care is cost-effective compared to hospitalization. We have shown that community-based treatment can yield successful outcomes for patients. Default rates in our program are extremely low and 18 of our patients have now been cured of MDR TB while receiving treatment at home. This year we successfully demonstrated that MDR patients can be cured through community-based treatment.

The community-based treatment program has had a significant impact at the patient and policy level. Our program design and educational materials have been adopted by other districts in the province and are being used in the design of a national program by the South African Department of Health.

PUBLICATIONS AND PRESENTATIONS

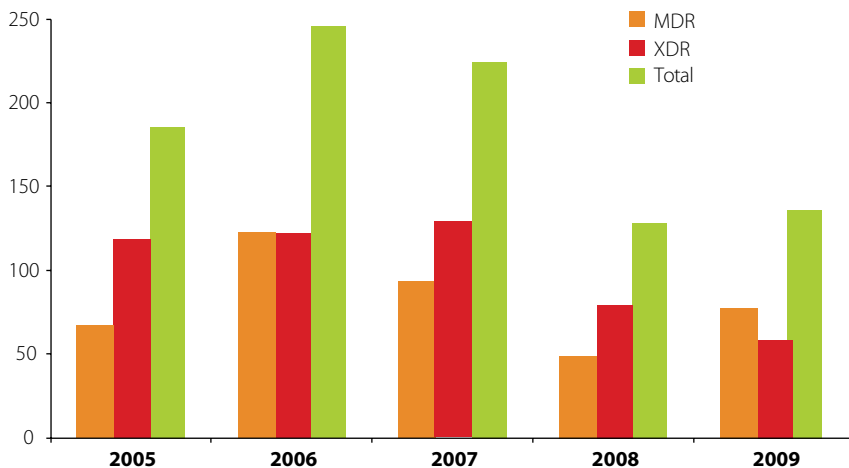
TF CARES/Philanjalo conducts operational research in Tugela Ferry that improves prevention, diagnosis, care and treatment of TB, drug-resistant TB and HIV co-infection. To date, our members have published over 20 research papers in leading international medical journals and made more than 50 presentations at national and international medical meetings in an effort to raise awareness and improve the standard of care for TB patients not only in KwaZulu-Natal, but also throughout sub-Saharan Africa and beyond.



THE WAY FORWARD

TF CARES/Philanjalo has made great strides in turning the tide of the MDR/XDR TB epidemic in Tugela Ferry, by developing, implementing and demonstrating the effectiveness of a comprehensive approach to tackling this epidemic. There is still much to be done to see a definite and sustained reversal of the epidemic. In 2008, the number of diagnosed cases declined but 2009 saw an increase in cases, making it clear that the epidemic remains volatile and requires a sustained and aggressive response.

REDUCTION BUT CONTINUING REPORTED CASES OF MDR AND XDR TB IN TUGELA FERRY



COMPREHENSIVE PROGRAM TO ADDRESS THE DRUG-RESISTANT TB EPIDEMIC

PREVENTION

- Strengthen susceptible TB treatment program to ensure high rates of cure/treatment completion and minimise treatment failure and default.
- Implement a comprehensive and effective TB infection control program based on international standards.

DIAGNOSIS AND SURVEILLANCE

- Perform continuous surveillance for MDR and XDR TB by testing all TB suspects with culture and drug-susceptibility testing.
- Minimise delay in diagnosing MDR and XDR TB by using new rapid diagnostic assays and decentralizing laboratory diagnosis to Tugela Ferry.
- Perform active case-finding in healthcare and community settings to identify patients at earlier stages of TB and HIV disease to reduce mortality and TB/HIV transmission.

TREATMENT

- Improve effectiveness of both susceptible TB and MDR TB treatment, by creating integrated TB and HIV treatment programs in Tugela Ferry.
- Improve access to MDR TB treatment by creating a community-based treatment program in Tugela Ferry.

FUTURE ACTION

Since 2006, TF CARES/Philanjalo has worked to implement many of the necessary facets of this comprehensive drug-resistant TB program as described in this publication. Although much work remains to reach the necessary targets to dramatically reduce MDR and XDR TB incidence, many of these components have been developed and implemented. Two key areas for further development over the next year are:

- Further improvement in TB infection control at COSH, by structurally modifying the existing 40–70 bed congregate wards.
- Introduction of rapid TB assays in Tugela Ferry by decentralizing laboratory capacity.

TF CARES /Philanjalo has been at the forefront of identifying, characterizing and addressing the MDR and XDR TB epidemics in South Africa. We intend to continue our leadership in responding to this epidemic. We are committed to scaling up our programming and innovative current strategies to keep ahead of the drug-resistant TB epidemic. This will require the further strengthening and implementation of a comprehensive and integrated TB and HIV program, continued development, improvement, dissemination of established and new prevention diagnosis and treatment programs, and development and testing of additional strategies. To accomplish this, we require continuing commitment to research, clinical care, training, capacity building and substantial additional resources.

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For more information and to learn what you can do to help, contact:

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We would like to add a special thanks to the KwaZulu-Natal province and the Umzinyathi district Departments of Health and the Church of Scotland Hospital for collaboration and support in addressing this epidemic. It is only through a true public-private partnership such as ours that an effective and lasting solution to this epidemic can be developed and widely implemented.

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