

## **INFORMATION FOR PROPOSED UCT PRESS RELEASE**

**Title of study to be published in the Lancet next week:** Long term outcomes of patients with extensively drug resistant TB in South Africa: A cohort study

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Tuberculosis (TB) remains one of the foremost public health problems in South Africa. Almost half a million cases of tuberculosis are treated annually, it has substantial impact on the national GDP, and is officially the commonest cause of death in South Africa. TB is easily treated with antibiotics but a strain of TB called MDR-TB or multi-drug-resistant TB has emerged, and is resistant to two main TB antibiotics. This type of TB strain requires treatment for two years with at least six months of injections, and even then favourable outcome rates are approximately 50%. Almost 8 000 MDR cases are treated in the country annually and it is likely that we are only detecting about half of the approximately 16 000 prevalent cases. This has now been eclipsed by a strain called XDR-TB, which is resistant to the four major classes of antibiotics used to treat TB. Many of these strains have resistance beyond XDR-TB (also XXDR-TB or TDR-TB, i.e. totally drug-resistant tuberculosis).

Annually between 500 and 1 000 patients with XDR-TB are diagnosed or treated in South Africa. There is little information about the prognosis and natural history in patients with XDR-TB. This is required for rational design of plans to fight the disease and for appropriate resource allocation. We also know from clinical experience that many patients with XDR-TB, and resistance beyond XDR-TB, fail to respond to treatment (continue to be sputum TB culture positive), but the natural history of disease in treatment failures remains unknown. It is critical that solutions are found to preventing and containing drug-resistant TB as the associated costs are unsustainable. For example, in South Africa, we have shown (Pooran & Dheda, PLoS ONE, 2013) that despite drug-resistant TB forming less than 3% of the total TB burden in South Africa, it currently consumes almost 40% of the total national TB management budget (in the region of R1.5 billion).

Investigators at the University of Cape Town, in collaboration with others at Gordon Hospital in the Northern Cape, researchers at the University of Stellenbosch, and at co-workers at Sizwe Hospital in Johannesburg, followed a group of 107 XDR-TB patients from three provinces in South Africa, who were put on treatment between August 2002 and February 2008, for a period of several years until 2012.

More than 60% of the TB strains tested were found to be resistant to eight or more drugs. Despite these patients being treated with an average of eight drugs (between six and ten drugs), the prognosis and treatment outcomes of these patients were unfortunately dismal. After five years of follow-up, only 11% had a favourable outcome. The rest had died or failed treatment. Out of 107 patients, 45 patients were eventually discharged from hospital. Just under half of these patients (19 out of 45) were treatment failures (they were alive, but still had culturable TB bugs in their sputum). These treatment failures, because of limited bed space in hospitals and lack of appropriate facilities that could house them, were discharged back to their homes in the community. In the community setting these patients survived for an average of approximately 20 months with some patients continuing to survive for more than four years. Worryingly, a third of these treatment failures were discharged back into the community had smear positive disease (had a very high concentration bugs in the sputum), which made them at high risk of transmitting disease. There are several key implications of the findings:

- i) Patients with failed XDR-TB and resistance beyond XDR-TB are being discharged on a country-wide level back into the community, where they are transmitting the disease. A co-ordinated national strategy is urgently required which combines a home care package, long community stay facilities (modern sanatoria), and palliative care facilities so that these patients can be appropriately accommodated, thus prevent spread of disease within the community. At present, the responsibility

and containment of disease spread is left almost entirely to the patients with XDR-TB, who come from disadvantaged and resource poor communities.

- ii) The poor prognosis of patients with XDR-TB and the growing problem implies that newer TB drugs such as bedaquiline, linezolid, and delamanid, which are already available in Europe and the United States, need to be urgently trialled and made available to TB programmes in Africa. In this way newly diagnosed patients, who often come from the economically productive age groups, can be rapidly treated, rendered non-infectious, and cured.
- iii) This is a serious reminder for healthcare workers, planners, and policy makers that prevention of TB and drug-resistant TB is paramount. South Africa treats almost 8 000 MDR-TB cases per annum compared to less than 100 in the United States, which has a population approximately eight times that of South Africa. Preventing and treating HIV, alleviating poverty and over-crowding, and addressing factors that will strengthen and improve the functioning of the national TB programme, including staff training, provision of drugs, and ongoing research is critical if further cases of drug-resistant TB are to be prevented.

Governing bodies and policy makers in South Africa have limited resources and many healthcare priorities to attend to including HIV, maternal and child health, pneumonia, gastrointestinal diseases, and non-communicable diseases, amongst others. Much is being done through the Health Ministry to combat TB, including patient education, healthcare worker training, resourcing the national TB programme, and the recent introduction of new TB diagnostic technologies such as the GeneXpert PCR system. Decentralisation of MDR treatment has recently been implemented and better versions of drugs such as moxifloxacin have been made available. Major progress has been made by the government in combatting HIV, making available anti-retroviral therapy, and combatting poverty and over-crowding. However, more needs to be done to tackle and to prevent the growing problem of drug-resistant TB.