

# thibela tb

## highlights

- Thibela TB is being funded by CREATE and the Mine Health and Safety Council in South Africa to research strategies to improve the control of TB in the South African gold mining industry.
- Thibela TB was launched nationally in October followed by regional launches in November 2005.
- Thibela TB has the committed support of all stakeholders including: Organised labour, employers, the Departments of Minerals and Energy, Health and Labour, local government and other national and local interest groups.
- HealthScanX, the new digital health screening vehicle which enables digital capturing and the remote assessment of a patient's medical status, was launched in June 2005.



**THIBELA**  
Team up against TB



## OVERVIEW

During the 1990s, it became clear in the South African gold mining industry that despite meeting World Health Organisation (WHO) targets for tuberculosis (TB) detection and cure, the incidence of TB among employees had risen sharply and was the principal cause of death in the workforce. It was noted too that the five-fold increase in the rates of TB coincided with the onset of the HIV epidemic in South Africa. A comprehensive TB-prevention programme which included all aspects of the WHO's TB-control strategy together with x-ray screening was not succeeding in reducing the incidence of TB. It thus became imperative that an alternative approach be investigated and plans were formulated to research the likely effects of community-wide TB preventative therapy on the incidence rate of TB in the South African gold mining industry.

The rationale supporting this approach is that all individuals at risk of developing TB in a population would be treated rather than just those identified as being high-risk, for example those who are HIV positive or who have silicosis. If successful, such a programme would have the added advantage of reducing the transmission of TB between people, resulting in fewer cases of TB, which would in turn lead to improved control of the disease.

The aim of the Thibela TB study is to establish whether community-wide isoniazid preventative therapy (IPT), administered to a whole at-risk community, is more effective than TB preventative therapy that is given to high-risk individuals only, particularly those with HIV/AIDS or silicosis.

Thibela TB's primary objective is to accomplish a 60% reduction in the incidence of TB in the community-wide IPT arm, compared to the control arm in months 13 to 24 after enrollment, at 90% power.

While the Thibela TB study is being overseen and managed by Aurum Institute in South Africa, this study is one of three designed by the Consortium to Respond Effectively to the AIDS/TB Epidemic (CREATE), of which Aurum is a member. (see box).

The research being conducted by Aurum, under the auspices of the Mine Health and Safety Council (MHSC) and CREATE, follows extensive consultation, and collaboration, with several South African gold mining companies, including AngloGold Ashanti, Gold Fields and Harmony, and the Departments of Health, Labour and Minerals and Energy. Extensive discussion and debate has also been held with representatives from the National Union of Mineworkers and other labour unions representing mineworkers to obtain their support for the study.

Since the start of the project in South Africa several key appointments have been made, including that of Programme Director. Other key positions, such as those of regional project managers, social scientist and project administrator have been filled, while 200 additional staff are currently being recruited.

In all, around 65,000 volunteer participants will be involved in the study.

## GENERAL DESCRIPTION OF STUDY

This is an open cluster-randomised study, comparing clusters projected to remain operational for at least five years. In the intervention clusters, community-wide IPT will be offered to all employees without evidence of active TB.

Each of the 15 clusters recruited, with shaft sizes ranging from 1 000 to 10 000 men, will have sufficient power to address the study objectives.

In addition to the primary objective stated above, various secondary objectives have been formulated to:

- ✦ Achieve at least a 40% reduction in TB case notification rates in the community-wide IPT arm, compared to the control arm in months 0 to 24 following enrollment.
- ✦ Accomplish a 60% reduction in the sputum culture prevalence of TB among HIV-infected individuals in the community-wide IPT arm compared to the control arm at the end of follow up.
- ✦ Identify and communicate trends in TB case notification following the intervention, safety of community-wide IPT, all-cause mortality and the prevalence of isoniazid resistance among TB cases

There are four pilot studies currently running, from which results and findings will lead the way for the parent study:

- ✦ **Pilot study A: Attitudes to TB and TB preventive therapy.**  
This cross-sectional qualitative study serves to establish attitudes towards, and perceptions of TB and associated therapies. Observations will center around how communities respond to research being done on the disease in order to plan and coordinate community education programmes for Thibela TB, which will inform communities about the studies and their aims.  
Participants in this pilot study include mine employees and 'key informants', including team leaders, union representatives, hostel leaders, and ex-employees who are medically boarded due to TB but still live in the surrounding community.
- ✦ **Pilot study B: Prevalence of radiological TB disease, silicosis, and latent TB infection.**  
This study employs a cross-sectional method in order to establish an approximate eligibility for TB preventative therapy from a representative sample of mineworkers by screening for TB symptoms. It further acts as a forerunner for the parent study's enrolment procedures. Secondly this pilot study serves to establish the prevalence of latent TB among a representative sample of mineworkers by means of voluntary tuberculin skin testing (TST) which is read after 72 hours.  
The sample size is approximately 400 participants which will be adequate to estimate the current latent TB infection rate. Participants are asked to complete a questionnaire and for their consent to review their medical records, in particular their latest occupational screening chest x-ray to check for radiological TB (active TB and previous TB) and silicosis
- ✦ **Pilot study C: Validation of the Arkansas method of urine testing for isoniazid**  
Arkansas urine testing will be a significant measure of adherence to isoniazid preventative therapy in the parent study. This study serves to establish the sensitivity and specificity of the Arkansas method of urine testing for INH in a population of miners in South Africa.



### CREATE

*The Consortium to Respond Effectively to the AIDS/HIV Epidemic (CREATE) was established in response to increasing awareness by TB and HIV experts that innovative and even radical approaches to TB control will be necessary to reverse the alarming trends of the incidences of these diseases which have been exacting a devastating toll on societies in the developing world. CREATE aims to co-ordinate, organise, implement and evaluate novel strategies to reduce the incidence of TB and related mortality in communities with high HIV infection rates.*

*CREATE is led by the Johns Hopkins University (School of Medicine, Centre for Tuberculosis Research); research partners are Aurum Institute for Health Research, the London School of Hygiene and Tropical Medicine, the Municipal Health Secretariat (Brazil) and the World Health Organisation. The University of Stellenbosch is also involved.*

*At the XV International AIDS Conference in Bangkok in July 2004, The Bill and Melinda Gates Foundation announced the award of a \$45 million grant to CREATE which will conduct three, large-scale community studies (including the one conducted by Aurum in the South African gold mining industry) over seven years in Africa and South America. As part of this grant, the Aurum Institute will receive \$14 million over five years.*

*When announcing the three studies, Richard E. Chaisson, professor of medicine at Johns Hopkins University and principal investigator of CREATE stated, "CREATE's community-level studies will assess bold new approaches for driving down skyrocketing rates of TB in areas with severe HIV epidemics."*

*The findings of the CREATE research portfolio will be used to develop new global policies to combat TB/HIV, a key criterion of projects supported by The Bill and Melinda Gates Foundation. CREATE will make a major contribution to identifying effective strategies to reduce suffering and death from HIV-related TB worldwide.*



138 in-patient participants, currently receiving isoniazid for TB or as preventive therapy, are being tested at 6-, 12- and 24-hour intervals after ingestion of a 300mg dose of INH to determine the sensitivity of the Arkansas test. The specificity of the Arkansas test is established from 60 in-patient participants not currently receiving isoniazid.



#### Pilot study D: Estimation of TB case notification rates

Using a cross-section of participants, a system for data collection of TB episodes is being piloted. Approximate TB case notification rates will be determined for each mine shaft participating in the overall programme.

Participants in the study will be asked to complete a questionnaire survey and asked for their consent to access their medical records for data regarding TB episodes



#### Parent Study

The parent study consists of the following

- A baseline survey of clusters where in both intervention and control clusters, a sample of 1 000 individuals per cluster will be asked to participate in a baseline survey of radiological TB and silicosis.
- The IPT Intervention in intervention clusters including participant screening and follow up over 9 months.
- TB Prevalence survey at the end of the follow-up period (month 24). A cross-sectional survey will be carried out to determine the prevalence of TB based on culture of a sputum specimen. A random sample of 750 employees will be selected from each cluster.
- TB episodes will be ascertained from routine data collected on TB patients treated by the mine health services.
- The Foundation for Innovative New Diagnostics (FIND) sub-study has funded a laboratory based sub-study that will run for 24 months after the first cluster starts enrolling.

## REVIEW OF PROGRESS – 2005

Since project initiation in October 2004, there have been numerous highlights, of which the following deserve particular mention:



Various stakeholders have reconfirmed their support and commitment to Thibela TB, including the MHSC and the Department of Health.



Approval was obtained from the ethics committees of both the University of KwaZulu-Natal and the London School of Hygiene and Tropical Medicine.



Research clusters were randomly selected as either intervention or control during March 2005.










Four pilot studies were initiated in preparation of the final protocol for the Thibela TB study. These studies are at various stages and should all be concluded by June 2006.









A project communication strategy was implemented to facilitate the mobilisation of community activities around Thibela TB, as a result of which the project was branded. This brand was used to launch it by means of various initiatives and activities, such as luncheons, concerts and video screenings.



HealthScanX, the new digital health screening vehicle which enables digital capturing and the remote assessment of a patient's medical status, was launched in June 2005. This digital diagnostic radiology unit has several benefits. Firstly, it reduces the radiation dose by 80% from that necessary with other forms of x-ray equipment and is able to transmit the digital x-ray electronically to a central assessment and storage point, and secondly, these vehicles enable people to be examined at their places of work.

-  The supply of isoniazid was offered by Sanofi-Aventis who kindly agreed to re-start local manufacture of the drug and supply the medication to the study at access prices.
-  A regional office was established in Carletonville and regional teams are also present in Orkney and Welkom.
-  A data management strategy and associated IT infrastructure was defined and agreed upon for implementation. The IT infrastructure is in place undergoing final testing before the roll-out.
-  Various project procedures have been identified and SOPs developed.
-  A project training programme was rolled out to facilitate project- specific training. 66 training opportunities have been delivered through this program to date.
-  The first study centre was established at TauTona, a mine belonging to AngloGold Ashanti Limited, and the first mobile study centre is under construction.
-  A delegation from CREATE as well as the Bill and Melinda Gates Foundation visited Aurum in October 2005 and provided positive feedback on study progress and initiatives.

## CHALLENGES

-  Stakeholder relationship management was an ongoing challenge throughout 2005. Various and ongoing negotiations, at times facilitated by external expert facilitators, took up many hours of senior management's time but concluded with desirable outcomes and culminated in the MHSC reinforcing their support for Thibela TB.
-  Community mobilisation of participating communities has proved to be an onerous task, which requires many hours of investment before results are seen. This was confirmed by other CREATE projects where it has been estimated that up to one year is required to prepare a community for a study of this nature.
-  Key to the success of this project is collection and data management of a large volume of data, i.e. 1.4 million data fields. The data management strategy adopted is based on Electronic Data Capture which is a challenge in itself within this environment.
-  Stakeholder consultation and data management strategy implementation have posed the biggest delays within the set of project timelines. A contingency plan is being implemented to bring the overall project back onto the original schedule.
-  Communication with a remote project team is an ongoing challenge and various plans are in place to ensure effective project communication.
-  Documentation of project activities outside of participant data collection is crucial to managing the project and various strategies and systems are being considered on an ongoing basis.

## FUTURE PLANS AND OPPORTUNITIES

Various opportunities for sub-studies are vested within the current project, which need to be explored and have funding secured. If proven successful, a community wide roll-out of this program will have to follow and early phase planning should be initiated during 2006.

The Thibela TB project is still in its initiation phase and the delivery objectives for 2006 will place high demands on the team – demands they are eager to meet.