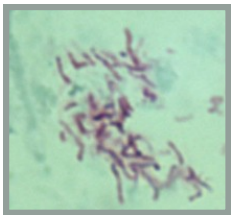
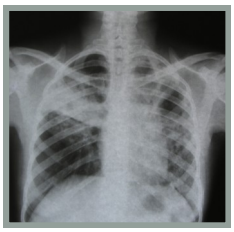
Research Briefing
Drug Resistant TB

This briefing explains drug resistant tuberculosis and presents research from TARGETS, a DFID funded Research Programme Consortium that generates knowledge, tools and strategies to control and contain communicable diseases of poverty and vulnerability.





TB is caused by Mycobacterium tuberculosis, a slow-growing bacteria with a lipid rich cell wall that is naturally resistant to many antibiotics. Treatment lasts at least six months using a cocktail of four or five drugs for the first two months.

TB is highly infectious, spreading from person to person via small airborne droplets (aerosols) created during coughing sneezing, or even when speaking. Effective treatment kills most of the bacteria in the first few weeks. greatly reducing infectiousness. If however the bacteria are resistant to the drugs then patients may remain infectious despite treatment and can easily pass on (transmit) the drug resistant strain to others.

MDR and XDR-TB

Drug resistant TB arises through the selection of naturally occurring mutations in the bacterial genes by inadequate treatment. TB that is resistant to both rifampicin and isoniazid, two of the key drugs is termed multi drug-resistant tuberculosis or MDR-TB.

Treatment of MDR-TB is expensive and difficult. Its requires at least 18 months treatment with drugs of heightened toxicity. Daily injections are required for the first phase of treatment which may last for several months. If resistance also develops against these second line drugs then the treatment options are very limited.

MDR-TB strains that are also resistant to any of the fluoroquinolones such as ciprofloxacin and one the injectable drugs (Amikacin, Kanamycin or Capreomycin) are called extremely drug-resistant or XDR-TB.

MDR-TB half a million cases...

XDR-TB found in over 40 countries...

How big is the problem?

Global data on drug resistance is incomplete, with many countries in Africa and Asia unable to overcome technical and logistical obstacles to conducting national surveys. The prevalence of drug resistance is usually expressed as the proportion of TB cases that are resistant. Using this measure it is countries of Eastern Europe and the former Soviet Union that are seen to have the biggest problem, where in some places over 10% of all TB patients require treatment for MDR-TB.

The low proportion of MDR cases identified in Africa previously meant that it was not considered a priority by international policy makers. Analysis published by TARGETS scientists suggested that this situation be reassessed as when expressed in terms of the whole population, the incidence and subsequent risk of infection with MDR-TB in some African countries appears to be amongst the highest in the world. An outbreak of XDR-TB in South Africa has also highlighted the issue and international policy now supports the roll out of treatment for MDR-TB in Africa.

Monitoring Resistance in Tanzania

Patients frequently live long distances from the sophisticated microbiological facilities needed to test for drug resistance. A novel sample collection strategy was tested in Tanzania where SMS messaging and partnership with a private bus company were utilized to deliver specimens for testing at the national reference laboratory. The strategy was implemented successfully during a nationwide survey which found low levels of resistance to anti-TB drugs in Tanzania.

Drug Resistance in Sudan

TARGETS scientists assisted a Sudanese PhD student to investigate drug resistance in Sudan. Initial studies raised the possibility that a single 'outbreak' strain might be responsible for a large proportion of MDR-TB in Sudan. Further work showed this was not the case and that MDR was arising independently in different regions pointing to a need to improve treatment delivery across the country.

MDR-TB in Uganda

TARGETS joined with a team of Ugandan and international partners funded by the Wellcome Trust to investigate strategies to control MDR-TB in the referral TB clinic of the Ugandan National TB Control Program.

We discovered much higher levels of drug resistance in re-treatment cases than previously expected. A quarter were resistant to isoniazid and nearly 13% (52/409) had MDR-TB. Mortality was significantly higher among those with MDR-TB. We found evidence of amplification of resistance in patients treated in the standard re-treatment program. HIV was not associated with resistance.

In addition to highlighting the seriousness of the situation in Africa we developed and field-tested effective tools to assist control of drug resistant tuberculosis in Kampala. Uganda has adopted a policy to implement detection and treatment of MDR-TB. The findings from this study will also contribute to the international debate on strategies to control MDR-TB in Africa. The TARGETS Consortium has already enabled scientists from the Zambian TB reference lab to visit Kampala to learn from their experience.

We implemented enhanced clinical care and developed a nutritional program for hospitalized patients and their families. We developed a sustainable, evidence-based 'infection control' policy. Expertise in clinical management of MDR-TB was developed at Mulago Hospital and community health workers were trained to provide the necessary care (DOTS-Plus).

We compared tests for rapid detection of drug resistance for accuracy, turnaround time and cost. Direct testing of sputum for resistance to rifampicin was implemented. Testing of 2nd line drugs was also implemented .

We obtained approval from the WHO Green Light Committee for procurement of second-line drugs to treat MDR-TB

The success of this project was due to the co-operation and collaboration of Ugandan and international experts with a broad range of expertise and skills providing the framework for a comprehensive assessment of the situation and development of a strategy appropriate to the setting. Partners included Makerere University; National Tuberculosis and Leprosy Program; Old Mulago Hospital; Joint Clinical Research Center; New Jersey Medical School-UMDNJ (USA); London School of Hygiene & Tropical Medicine (UK); Case Western Reserve University (USA) and Medical Research Council/Uganda Virus Research Institute.

TARGETS

Team for Applied Research Generating Effective Tools and Strategies for Communicable Disease Control

DFID Department for International Development

TARGETS is an international Consortium of research scientists funded by the Department for International Development (UK) from 2005-2010.

The Consortium brings together researchers based at seven key international institutions and includes world leaders in research on malaria and tuberculosis.

The aim of the Consortium is to contribute to poverty reduction and achievement of the Millennium Development Goals (MDGs) through the production and uptake of technologies and policies that will improve the health of the poor and vulnerable.

TARGETS works with local, national and international stakeholders. The core funding provided has enabled leverage of substantial funds from other sources and the development of an extensive network of collaborative activities with TARGETS scientists involved in over a hundred research projects.

Strengthening of research capacity is an essential feature and TARGETS partners benefit from enhanced training opportunities and through North-South and South-South dialogue and shared experience.

IFAKARA HEALTH INSTITUTE research | training | services

INDEPTH · INDEPTH · INDEPTH ·

LONDON SCHOOL OF HYGIENE & TROPICAL MEDICINE

KNCV TUBERCULOSEFONDS

Zambart Project

THE MAHARASHTRA ASSOCIATION OF ANTHROPOLOGICAL SCIENCES

The TARGETS RPC is formed by seven partner organisations:
Ifakara Health Institute, Tanzania; MAAS CHRD, India; ZAMBART, Zambia; INDEPTH Network, Ghana;
Makerere University, Uganda; KNCV TB, The Netherlands and the
London School of Hygiene and Tropical Medicine, UK.
For more information about TARGETS research contact Alexandra.Hyde@lshtm.ac.uk

Prepared and published by Ruth McNerney and Alexandra Hyde for TARGETS. The findings, views and recommendations contained in this document are those of the authors and do not necessarily represent those of the Department for International Development

www.targetsconsortium.org