



## Is the TB epidemic showing signs of stabilising in the Western Cape?

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The estimated incidence of TB is increasing in South Africa and TB is one of the main causes of death with more than 55,000 people dying from TB annually. However, in the Western Cape, each year fewer people are treated for TB (figure 1) and there has been a steady increase in the cure rate of new smear positive TB cases (66.5% in 1995 to 75.7% in 2006 to 81.5% in 2012).

These are welcome trends in the TB programme, but many challenges remain as can be seen from the routinely collected data from the TB programme:

- An unacceptable high proportion of smear positive cases (27%) are retreatment cases
- Cure rate of these smear positive retreatment cases was 66.8% in 2012 – exactly what the cure rate for new smear positive cases was in 1995
- Each year more MDR and XDR TB cases are diagnosed

The Western Cape has a huge advantage that there are many research institutions doing very good research on TB and there is close collaboration between these research institutions and the Western Cape Government Health Department. However, operational research identifies gaps in the health services for example:

- Claassens et al<sup>1</sup> recently documented unacceptably high mean initial default rates of 25% in five provinces in SA, and in early studies similar high initial default rates have been found in the Western Cape and are still present - this presents a serious challenge to TB control
- Welfare et al states, on page 2 of this newsletter, that there is poor integration between TB and HIV services
- Poor linking to primary health care for patients diagnosed in hospitals is commonly reported in the literature and is highlighted in the study by du Preez et al on page 5.

We would like to see the Western Cape Government Health Department lead the way and set an example to other provinces by responding rapidly to such operational research findings. This might not be an easy task as there is a tremendous shortage of resources and skills in the Department leading to staff not coping with what they are expected to do due to competing demands, such as multiple programmatic changes in TB diagnostics and modifications to M&E systems.



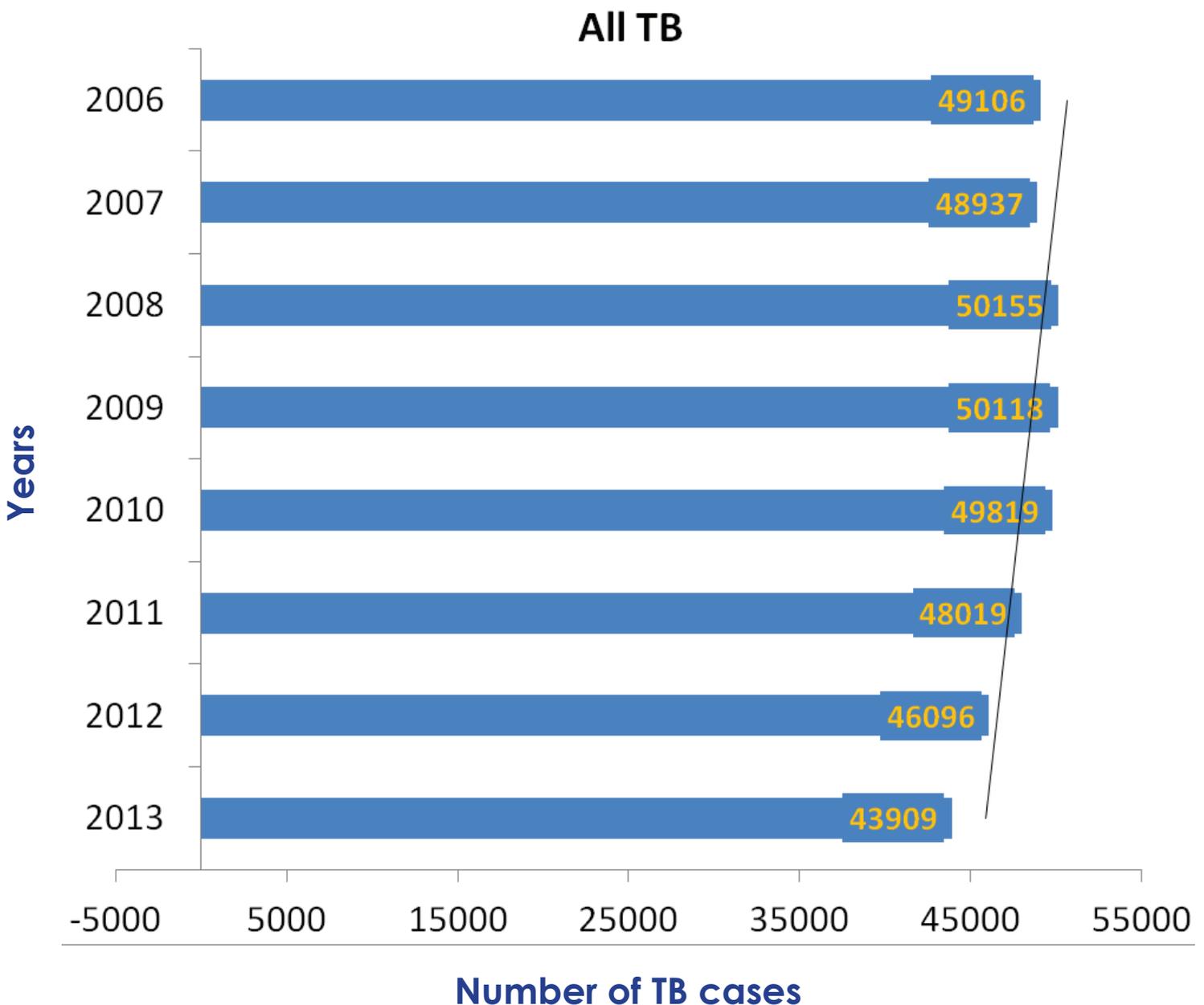
**Prof. Nulda Beyers**  
(Picture taken by Damien Schumann)

In conclusion, the Provincial and local government TB Control Programmes should be applauded for the downward trend in cases and high cure rates of new smear positive TB cases. However, we should not be complacent as there still are many challenges. The TB Programme should continue its focus on new smear positive cases, but also calculate and reports the cure rates for all smear positive TB cases (new plus retreatment), devise a strategy to ensure that resource and skills shortages are addressed and translate operational research findings into action.

**Reference:**

1. Claassens MM, du Toit E, Dunbar R, Lombard C, Enarson DA, Beyers N, Borgdorff MW. Tuberculosis patients in primary care do not start treatment. What role do health system delays play? *Int J Tuberc Lung Dis.* 2013 May;17(5):603-7.
2. Botha E, den Boon S, Lawrence KA, Reuter H, Verver S, Lombard CJ, Dye C, Enarson DA, Beyers N. From suspect to patient: tuberculosis diagnosis and treatment initiation in health facilities in South Africa. *Int J Tuberc Lung Dis.* 2008; 12(8):936-941.

**Fig. 1 Annual trend in TB cases in the Western Cape Province 2006 - 2013**



# Assessing TB and Human Immune Virus (HIV) service integration in primary care clinics in Khayelitsha, South Africa: identifying and overcoming barriers to service integration.

**By: R. Welfare, G. Patten, P. Saranchuk, V. de Azevedo, D. Coetzee, N. Mantangana, G. van Cutsem & D. Garone**

Tuberculosis (TB) is already a large Public Health problem in the Western Cape, but realizing that it is closely associated with human immune virus (HIV) infection adds further concerns. South Africa has the greatest number of HIV-infected individuals and among the highest TB new cases worldwide. We urgently need better ways to manage the twin epidemics in the country.

A study was carried out in 11 clinics at Khayelitsha, a highly deprived community, burdened by both TB and HIV. A multi-method cross-sectional assessment of TB and HIV services was conducted. One day was spent in each clinic conducting the assessment. The assessment involved the collection of routine data, observation of HIV and TB consultation rooms, a folder review and assessments of the Monitoring and Evaluation system and TB infection control. Staff completed self-administered questionnaires on training and clinical practices.

An interview to capture staff knowledge and perceptions on TB and HIV service integration was also conducted. In total, self-completed questionnaires were completed by 38 doctors, 22 counsellors, 11 facility managers and 7 community-care workers; and interviews conducted with forty five doctors, including 7 facility managers and 3 doctors, plus 23 counsellors and community care workers were interviewed. All clinics were assessed for TB infection control practices.

Of the eleven clinics, only 3 could be considered as providing combined services. Primary Health Care centres (PHCs) were more likely to provide a combined HIV/TB service while Community Health Centres (CHCs) were only partially integrated or

collaborative. Nursing personnel were the category of health providers most likely to be trained in both HIV and TB (63%), while 42% of them were trained to initiate clients on anti-retroviral therapy (ART). As a consequence nurses trained in both HIV and TB had a greater burden of clinical practice. To sustain and expand such integrated health services would require more healthcare providers that are trained in both HIV and TB.

Evidence from this study suggests that the high burden of TB and HIV in Khayelitsha requires a clear plan to enhance service integration. The results also show that TB and HIV services are gradually being combined in Khayelitsha, with 3 of the 11 clinics providing a combined service for patients with both TB and HIV. Notwithstanding the existence of forward-looking policies and strategic plans on TB/HIV combination in South Africa, implementation remains a big challenge.



## Use of linezolid for complicated drug-resistant TB: experience in HIV infected and uninfected patients in Khayelitsha, Cape Town.

By: J. Hughes, H. Cox, J. Daniels, V. Cox

Drug-resistant TB is the result of interrupted, or inadequate TB treatment, and its spread is undermining efforts to control the scourge in South Africa. This condition may also develop when people with TB stop taking their medicines before the disease has been fully cured or cleared from their body. Patients tend to interrupt their treatment owing to the lengthy period they have to take the treatment.

This form of tuberculosis is fast becoming an additional burden disease on top of the quadruple disease burden in the Western Cape Province. Approximately 10% of the 10,000 cases of multidrug-resistant tuberculosis (MDR-TB) notified in South Africa in 2011 are infected with extensively drug-resistant TB (XDR-TB). Nationally, 65% of MDR-TB cases are HIV infected. With limited treatment options available for DR-TB, the investigators sought to describe the use of linezolid as part of a treatment programme for (MDR)/(XDR-TB) among both HIV-infected patients requiring antiretroviral treatment (ART) and HIV-uninfected patients in the decentralized drug-resistant TB programme in Khayelitsha.

All patients who were diagnosed with second line TB drug resistance and who have been

assessed by an expert clinical committee to receive linezolid (600mg oral dose (OD) as part of an individually specific treatment programme were included in the study. All drugs other than linezolid were given according to South African national guidelines. HIV testing was strongly encouraged and all HIV-infected patients were offered ARV regimens modified according to known or possible interactions with second line TB drugs.

Thirteen (13) patients, 4 of them HIV-infected were treated with linezolid-containing treatment regimens for a period of 4 months. Three HIV-infected patients were on first-line ART; the fourth was on a second-line regimen; all were virally suppressed. Eight patients, including three HIV-infected participants receiving linezolid for more than 4 months. Of these, 6 converted sputum cultures to negative (75%) and are still receiving treatment and 2 of them HIV infected. Two patients were HIV negative and had developed anaemia as possible side effect. One HIV-infected patient had severe peripheral neuropathy resulting in permanent withdrawal of linezolid after 3 months.

The investigators concluded that HIV infection and ART do not appear to reduce the efficacy or increase the side effects of linezolid in an individually tailored treatment regimen for DR-TB. Although included in current DR-TB management guidelines, more widespread use of linezolid in individually tailored regimens would require registration of linezolid for DR-TB treatment in South Africa and procurement of the drug at provincial level.

## Linking Hospital to Community TB Care in Children.

By: K du Preez, HS Schaaf<sup>2</sup>, R Dunbar, H Finlayson, A Swartz, A.C Hesselning

Linkages between the care of children with tuberculosis (TB) treated at the hospital to treatment in community-based facilities is major challenge.

The investigators in this article have previously shown that reporting of childhood tuberculosis (TB) managed in hospital settings is incomplete.

This study aimed to estimate the total burden of childhood TB at a tertiary hospital, and to improve continuity of TB care for children from hospital to primary care services at community level.

Daily hospital-based surveillance by dedicated personnel in the paediatric wards at Tygerberg Children's Hospital, Cape Town, South Africa is crucial to getting full paediatric TB management. Health system strengthening interventions included counselling of caregivers of TB patients, and contacting TB personnel at identified PHCs to ensure continuation of TB treatment upon discharge.

## Barriers to Implementation of Tuberculosis Infection Control amongst South African Health Care Workers.

By: O Adeleke\*

Health care providers are at the fore front in the battle against Tuberculosis (TB), and are at increased risk of acquiring TB infection from their work environments. Although Tuberculosis Infection Control (TBIC) measures put in place in clinics may reduce infection transmission, implementation remains a major challenge.

This study aimed to assess barriers to implementation of TBIC among Health care providers in two South African primary care clinics in a Cape Town township with a high TB prevalence.

The researcher applied a case study approach to recruit and interview groups of Health providers. Data were collected by direct observation, key informant interviews, semi-structured interviews, focus group discussions and document review, and analysed using thematic and interpretive analysis.

The study found that barriers and enablers to TBIC implementation were linked to health systems and healthcare provider motivation. Some of the barriers were inadequate healthcare provider training on TBIC, a non-responsive compensation policy and the perception that a busy clinic schedule leaves

no time for TBIC implementation. On the other hand, resource availability, adequate human resources and leadership enabled healthcare providers to implement TBIC. Measures such as use of respirators and masks tend to be prioritized by providers ahead of administrative and environmental measures that are potentially more effective in reducing TB infection.

The investigator came to the conclusion that healthcare provider motivation plays a crucial role in consistent implementation of TBIC measures. In-service training and leadership characterized by delegation with supervision could motivate healthcare providers to do the right thing.



Outcomes were measured by comparing the proportion of children recorded pre- and post-intervention in the provincial electronic TB registers, using electronic probabilistic record linking. During January through June 2012 the investigators identified 199 children (median age 2.8 years, IQR 1.2-5.3; 106(54%) male) who were routinely diagnosed or treated for TB.

They compared the proportion discharged to community-based primary healthcare clinics pre-intervention (133 out of 199 or 68%) to that after intervention and found an overall improvement in reported referral to 91/106 (86%). Culture-confirmed children with drug-

susceptible TB who were referred to PHCs were 3.2 times more likely to be included into routine reporting systems during the intervention period (125/183 (68%) vs 28/32 (88%)(OR 3.2; 95%CI: 1.1-13.3; p-value=0.03).

The investigators concluded that, tertiary hospitals carry a large burden of childhood TB disease. Given the need for improved surveillance and reporting of childhood TB, a dedicated TB service in large hospitals should be considered to ensure continuation of care for children between hospital discharge and community-based TB care.

# Changing the Ways TB Drugs are Developed.

By: C. van Niekerk

The current levels of the TB epidemic in South Africa call for innovative and radical measures to stop spread of TB. The author(s) describe the contribution of drug research to a world where no one has to die of tuberculosis. They outline opportunities for developing new, better, and faster-acting tuberculosis drug regimens. The Global Alliance for TB Drug Development (TB Alliance) was established in 2000 as a not-for-profit product development partnership to lead the search for new cures.

The drug development model advanced by the TB Alliance aims to reduce the time needed to develop improved TB cures. The approach to novel treatment development is to start with animal model(s) to identify most promising course of therapy, conduct full pre-clinical, Phase I and Phase II early bactericidal activity [EBA] evaluations of each individual drug followed by studies exploring drug-drug interactions and, as appropriate, preclinical toxicology of combinations. At the end,

the plan is to take combination regimens into clinical development (Phase II, III). This approach evaluates novel combinations of TB drugs from the start - instead of single drugs - as part of a single development programme. It offers the potential to reduce the time needed to develop a novel treatment regimen by up to 75%, shortening the clinical development from decades to years. It will end the treatment distinction between multi-drug resistance (MDR) DS TB: DS and MDR T8 treated with the same combination regimen.

The TB Alliance believes that it is in a unique position to bring together TB drug developers under the Critical Path to TB Drug Regimens (CPTDR) initiative to test their drugs together and advance the best TB regimens, regardless of sponsor.

## Molecular characteristics and global spread of Tuberculosis with a Western Cape F11 Genotype.

By: TC Victor, PEW de Hass, AM Jordaan, GD van de Spuy, M Richardson, D VAN Soolingen, PD van Helden, R Warren

In order to fully understand the global tuberculosis (TB) epidemic it is important to investigate the population structure and dissemination of the causative agent that drives the epidemic.

Several strains of *Mycobacterium tuberculosis* have been identified including the Beijing and F11 strains. Beijing strains are speculated to have a selective advantage over other *Mycobacterium tuberculosis* strains because of increased transmissibility and virulence.

*Mycobacterium tuberculosis* strain family 11 (F11) genotype isolates (found in 21.4% of all infected patients) are at least as successful as the Beijing genotype family isolates (16.5%) in contributing to the TB problem in some Western Cape communities of South Africa.

This study describes key molecular characteristics that define the F11 genotype. A data-mining approach coupled with additional molecular analysis showed that members of F11 can easily and uniquely be identified by PCR-based techniques such as spoligotyping and dot blot screening for a specific *rrs491* polymorphism.

Isolates of F11 not only are a major contributor to the TB epidemic in South Africa but also are present in four different continents and at least 25 other countries in the world. Careful study of dominant compared to rare strains should provide clues to their success and possibly provide new ideas for combating TB.

# Confinement for extreme drug-resistant TB: Balancing protection of individual rights and the public's health.

By: L London

In the context of an expanding TB and HIV epidemic in South Africa, enforcing involuntary admission for XDR TB raises many ethical and human rights dilemmas, mainly because it trades off the human rights of individuals for the public good. However, we can just as well think about this contradiction as being about competing rights claims and rights obligations of the state to control infectious diseases.

The analyses of the ethical and rights issues in managing drug-resistant TB patients are often superficial and may result in actions that (i) do not consider carefully the purpose of involuntary admission, (ii) the likely effectiveness of forcible admission and (iii) whether there are less intrusive ways to achieve the intended objectives. This approach may be more likely to do harm than good.

This paper argues that we should develop policy in a way that can accommodate dialogue about these difficult choices,

provide a more careful human rights analysis, and use established analytical frameworks to identify criteria that could justify limitation of individual rights.

When such analyses are applied, it is usually only in very restricted situations, where there is a clearly defined risk to one or more third parties, based on evidence, and conditional on careful consideration of available alternatives, that involuntary admission be considered.

Community-based strategies will need to be developed to cope with infection control without forced admission for most cases, particularly in high prevalence settings typical of many developing countries. Even in the exceptional cases when involuntary admission is indicated, strict adherence to fair administrative procedures are required.

Importantly, as a strategy for the broader control of the epidemic, confinement has little role since it will drive the epidemic underground and undo many of the gains made to date. Control of Drug-Resistant TB is contingent on sustained commitment to improved health system functioning and action to address the abysmal investment in research and development for drugs for neglected diseases worldwide.



# UPCOMING EVENTS

## **3rd Annual ARESA Seminar in Health Research Ethics**

*When: 18 & 19 September 2014*

*Venue: Southern Sun Hotel, Newlands*

*For enquiries e-mail: [kelseyf@sun.ac.za](mailto:kelseyf@sun.ac.za)*

*Send Registration to: fax: +27 21 938-9731*

## **20<sup>th</sup> International AIDS Conference**

*When: 20-25 July 2014*

*Venue: Melbourne, Australia*

*URL: <http://www.aids2014.org/>*

The AIDS 2014 programme will present new scientific knowledge and offer many opportunities for structured dialogue on the major issues facing the global response to HIV. A variety of session types - from abstract-driven presentations to symposia, bridging and plenary sessions - will meet the needs of various participants.

## **10<sup>th</sup> Public Health Association of South Africa**

*When: 3-6 September 2014*

*Venue: Polokwane*

*URL: <http://www.phasa.org.za/10th-phaasa-conference-2014/>*

The 10th anniversary of the Public Health Association of South Africa (PHASA) conference will be celebrated with the hosting of the conference in Polokwane (Limpopo) from 3 to 6 September 2014. The workshops will take place on the 3rd, the actual conference on the 4th and 5th, and the student symposium on the 6th of September.

## **Third Global Symposium on Health Systems Research**

*When: 30 September to 3 October 2014*

*Venue: Cape Town, South Africa*

*URL: <http://hsr2014.healthsystemsresearch.org/>*

The theme of the symposium is the science and practice of people-centred health systems, chosen to enable participants to address current and critical concerns of relevance across countries in all parts of the world. Researchers, policy-makers, funders, implementers and other stakeholders, from all regions and all socio-economic levels, will work together on the challenge of how to make health systems more responsive to the needs of individuals, families and communities.

## **4<sup>th</sup> Provincial Health Research Day**

*When: 24 October 2014*

*Venue: Lentegeur Hospital, Events Centre*

*Mitchells Plain, Cape Town, South Africa*

*Enquiries: [Health.Research@westerncape.go.za](mailto:Health.Research@westerncape.go.za)*

