The effects of tuberculosis on PLWHA

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TUBERCULOSIS

and HIV

A Global Emergency

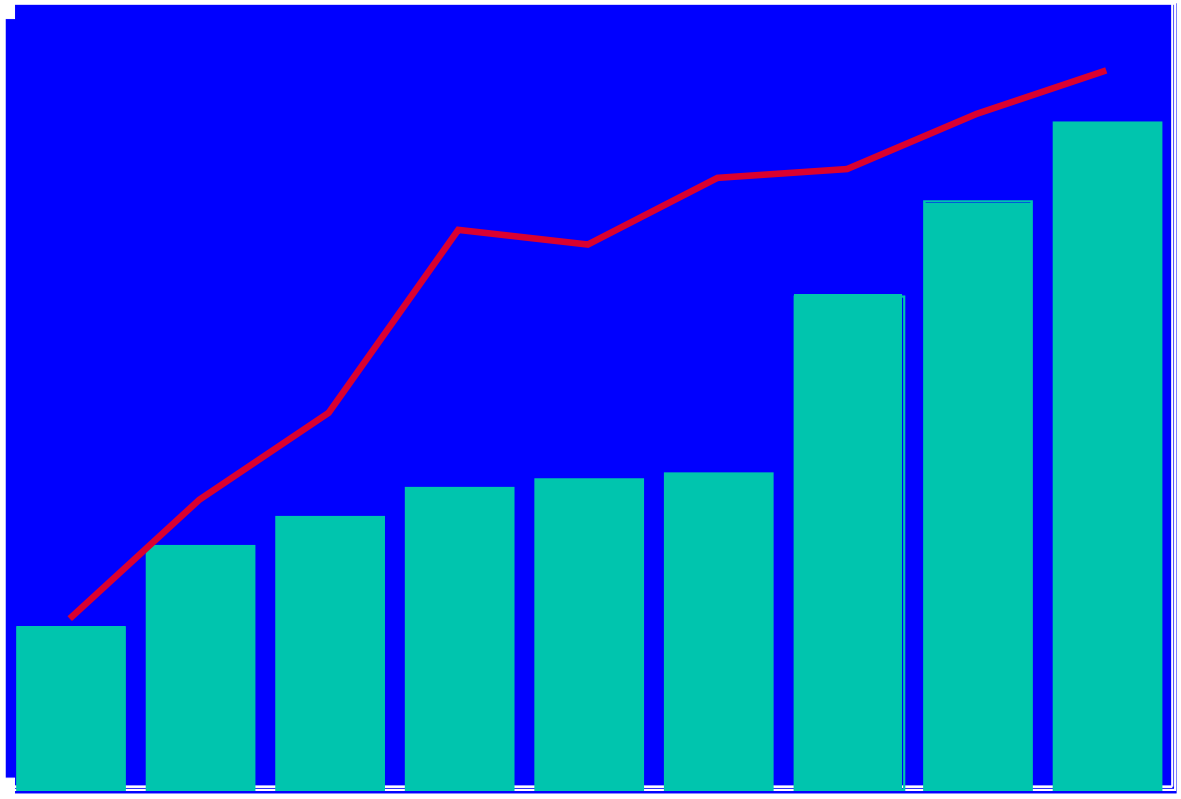
3 leading causes of natural death in age group 15-49

Cause on death certificate	1997			1999			2001		
	Rank	No.	%	Rank	No.	%	Rank	No.	%
Tuberculosis	**1**	13396	11.9	**1**	23448	15.2	**1**	37917	19.0
HIV disease	2	5029	4.5	3	8197	5.3	5	7564	3.8
Influenza / Pneumonia	3	4467	4.1	2	9830	6.4	2	18632	9.3

Source: Stats SA

Trends in TB and HIV in South Africa

(Source: Department of Health, 2004)

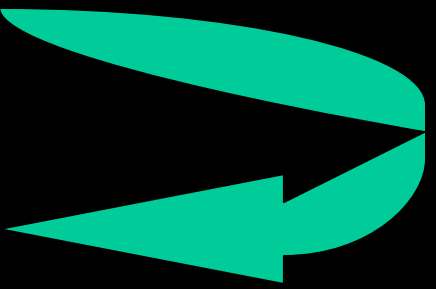


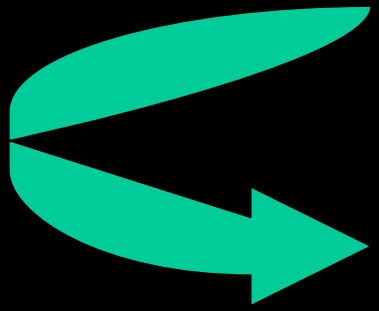
HIV and TB dual epidemic

- Incidence of TB cases in SA rose with 276% over last 10 years (187 to 524/100 00 population)
- TB is most common opportunistic infection
- In SA >55% of TB patients are co-infected with HIV
- Progression of latent to active TB increased from 10% to 50%
- Risk of TB if HIV+ is 10% yearly versus 10% lifetime if HIV negative

TRANSMISSION OF TUBERCULOSIS

EXPOSURE





INFECTION

DISEASE

Challenges

- Access of services to communities
- Delays in diagnosis and treatment
- Poor monitoring and outcomes
- Quality of services provided
- Sustainability
- SA TBCP Mvusi 2005

Diagnosis of Tuberculosis in HIV

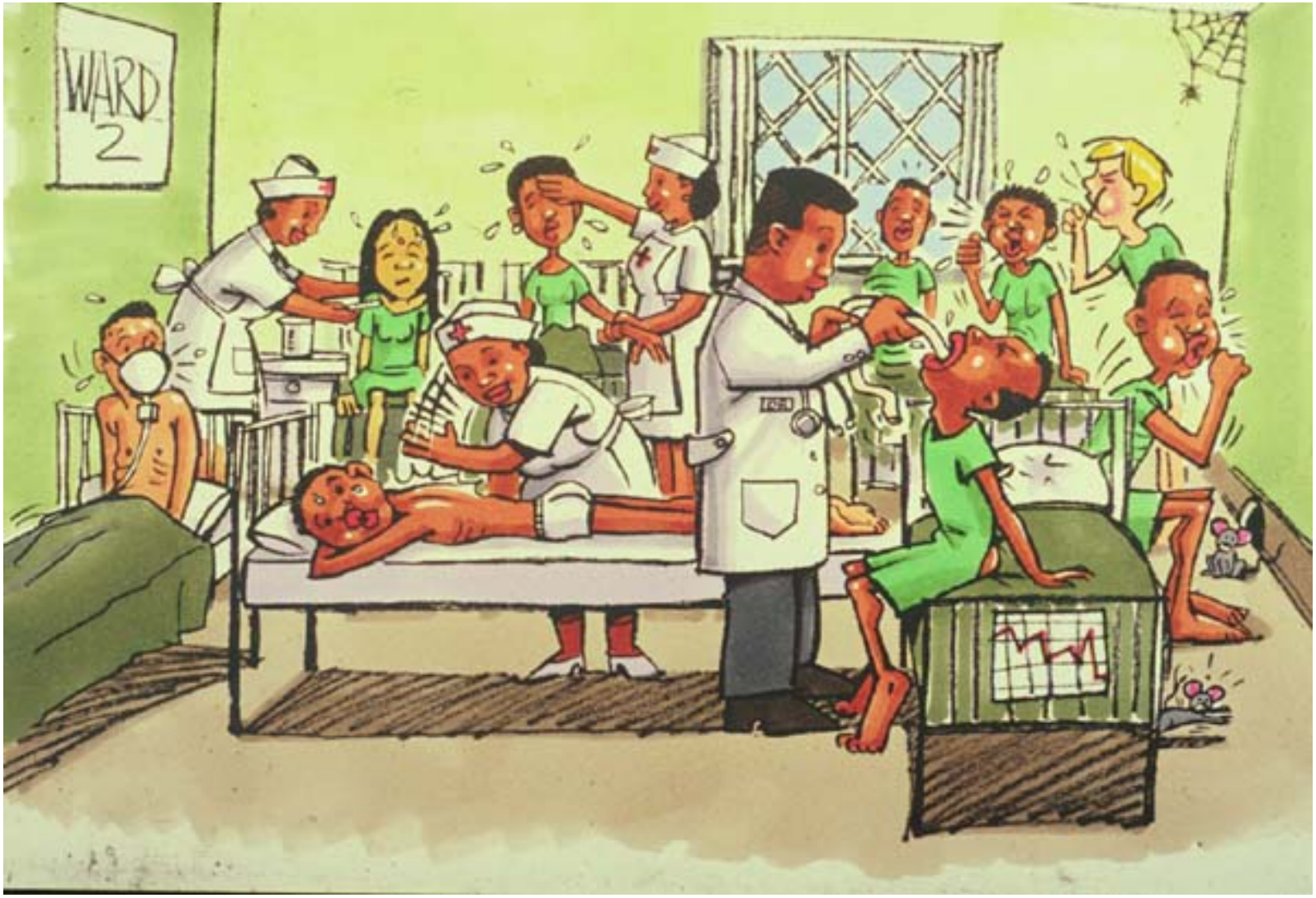
Clinical features

- **Depend on degree of immunodeficiency**
  - In earlier stages of HIV clinical presentation similar to HIV negative individuals
  - As CD4 count drops TB more atypical and increased risk for extra-pulmonary disease
  - Prominent weight loss
  - Prominent night sweats
  - Less massive haemoptysis

Sputum collection

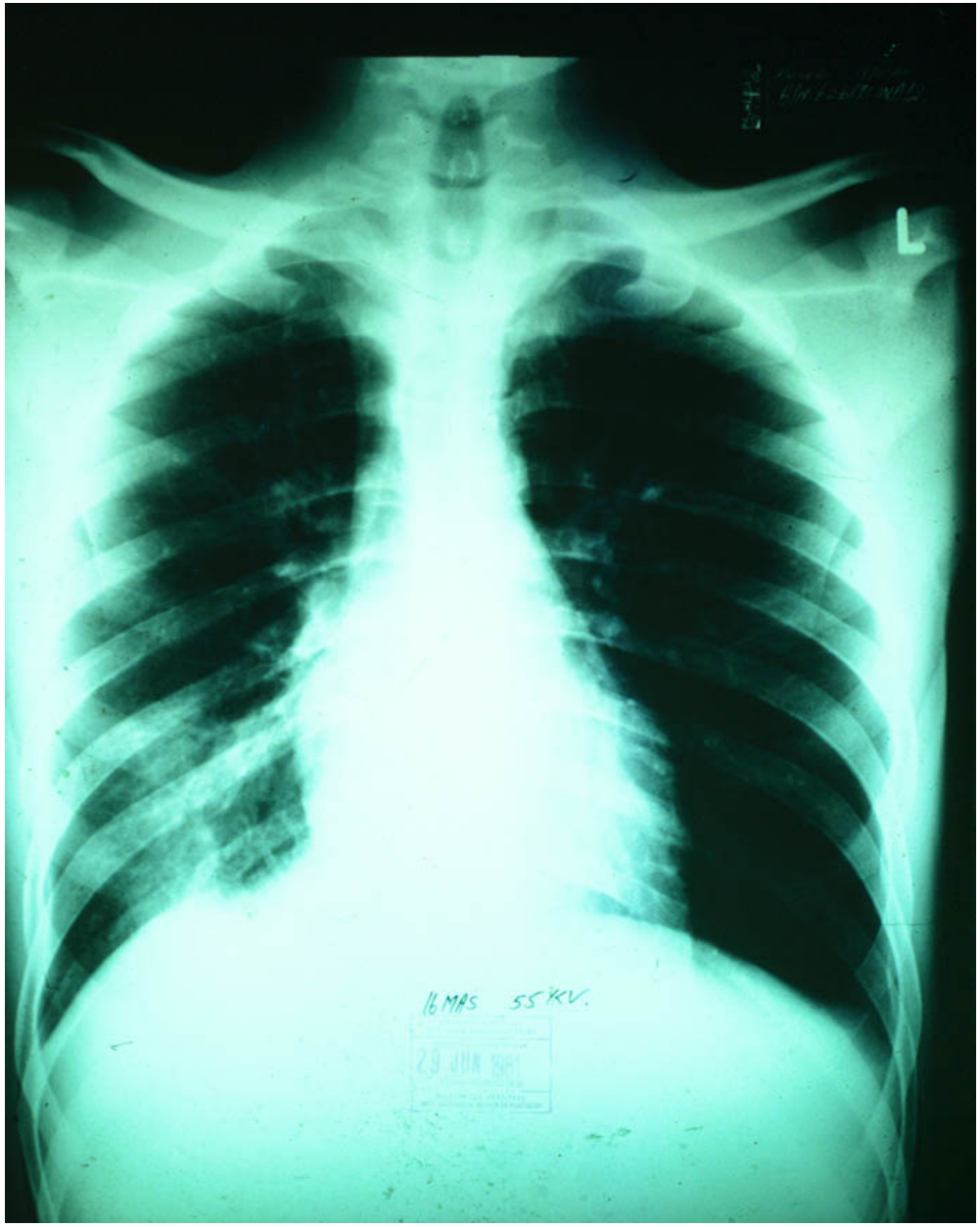
- **Sensitivity of microscopy depends on:**
  - **quality of sputum**
  - **quality of laboratory processing and**
  - **Quality of staining and microscopy**

- **If a patient is unable to produce adequate sputum, nebulisation with sterile 5% saline may be indicated and the service of a physiotherapist may be helpful**


WARD
2

Microscopy

- Cornerstone of TB diagnosis
- Detects the most infectious cases of pulmonary TB responsible for spreading the epidemic
- Feasible in resource poor areas
- Inexpensive
- Rapid



PTB in Advanced HIV

- Atypical CXR
- **Increase in smear-negative TB**
- Marker of advanced immunosuppression
- Infectivity unchanged
- Higher mortality

Karstaedt, IJTLD 1998

Indications for CXR

- Sputum results are negative but strong clinical suspicion of TB remains after course of antibiotic
- When only one of the required pre-treatment smears is positive
- In children suspected to have TB
- Suspected pleural effusion or pneumothorax

Case definition for smear negative PTB

- 3x negative smears sputa
- No response to antibiotics
- Compatible CXR

Hargreaves 2001

Culture

- Gold standard to identify viable TB bacilli
- TB is slow growing → delayed results limit impact on patient management
- High sensitivity: increases case finding 20-40%
- Expensive
- Resources and skills needed
- Contamination issues

Press Release

- **December 15, 2004**

  ## FIND and BD Combine International Efforts to Improve Rapid Tuberculosis Diagnosis for HIV-positive Patients in Developing Countries

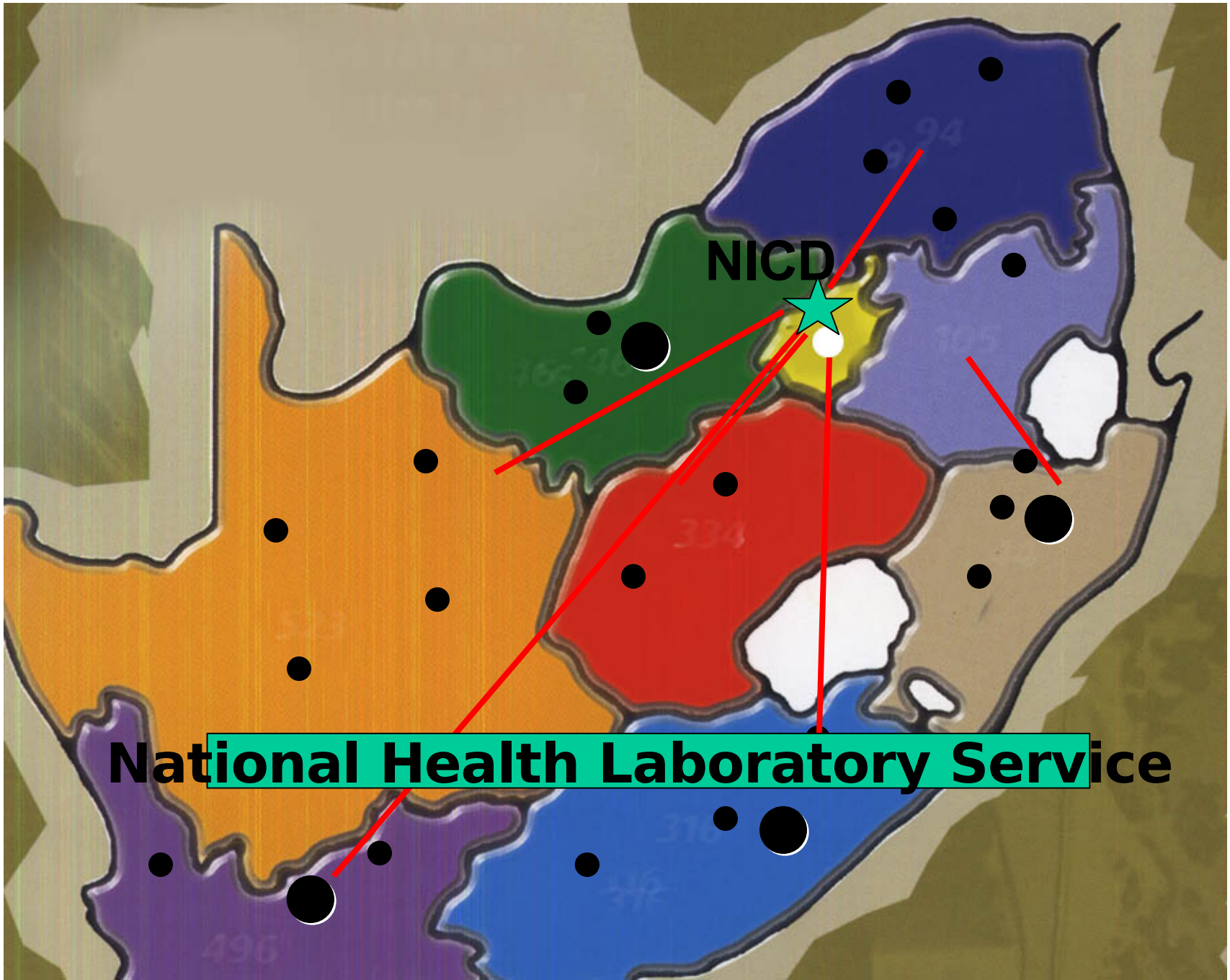
  Related Press Tuberculosis and the expanding role of the laboratory
  TB continues to dominate infectious diseases globally by its ability to infect, become quiescent, and then reactivate later. Find out how new tests are moving us out of the TB-diagnostics "stone age."
  By L. Masae Kawamura, MD, and Edward Desmond, PhD
  details in article from MLO website [pdf 376kb]

- Mike Meehan (BD) and Giorgio Roscigno (FIND) **Geneva, Switzerland and Franklin Lakes, NJ, USA – December 15, 2004** – FIND (Foundation for Innovative New Diagnostics) and BD (Becton, Dickinson and Company) (NYSE: BDX) today announced **an international collaboration aimed at improving diagnosis of pulmonary tuberculosis (TB) in HIV-infected patients in developing countries.**

- Today, TB is the leading cause of death in AIDS patients in high-burdened countries, mainly in sub-Saharan Africa. TB is particularly difficult to diagnose in AIDS patients because they often have few or no TB bacteria in their sputum; thus, the standard diagnostic procedure using microscopy is insensitive. Classical culture methods for TB are more sensitive, but notoriously slow, typically requiring 21 to 42 days. BD has developed an improved culture method, the BD MGITTM (Mycobacteria Growth Indicator Tube) system, which provides results within 10 to 14 days.

South African National TB Control Programme

- Standardised, free good quality combination drugs
- Standardised laboratory programme for diagnosis and monitoring through a network of laboratories


NICD
National Health Laboratory Service

ART in patients with TB

- Very common situation as TB is the **commonest cause** of morbidity and mortality in HIV-infected patients
- Complex **drug-drug interactions**
- Shared **toxicity**
- Paradoxical **deterioration** of TB due to immune reconstitution

TB & ARV's

- TB treatment always comes first!
- If already on ART, change to **regimen that is compatible with Rifampicin**
- **CD4^{+} > 200** – commence ART **after TB treatment** has been **completed**.
- **CD4^{+} < 50** – initiate ART as soon as TB medication is tolerated
- **CD4^{+} 50 - 200** – delay ART until **after intensive phase** of TB

ARVs in HIV patients with TB

Situation	Recommendations
PTB and CD4 > 200 /	Treat TB, monitor CD4 count 3–6 monthly
PTB and CD4 50-200 / μl	Start TB Rx and repeat CD4 count after 2/12. Initiate HAART ✓ Efavirenz (EFV) ✓ d4T/3TC (or AZT/3TC or AZT/ddI) ✓ For second line treatment ritonavir / lopinavir
PTB and CD4 < 50 / μl or EPTB	Start TB Rx and HAART as soon as TB Rx tolerated (2 weeks)

Paradoxical worsening of TB

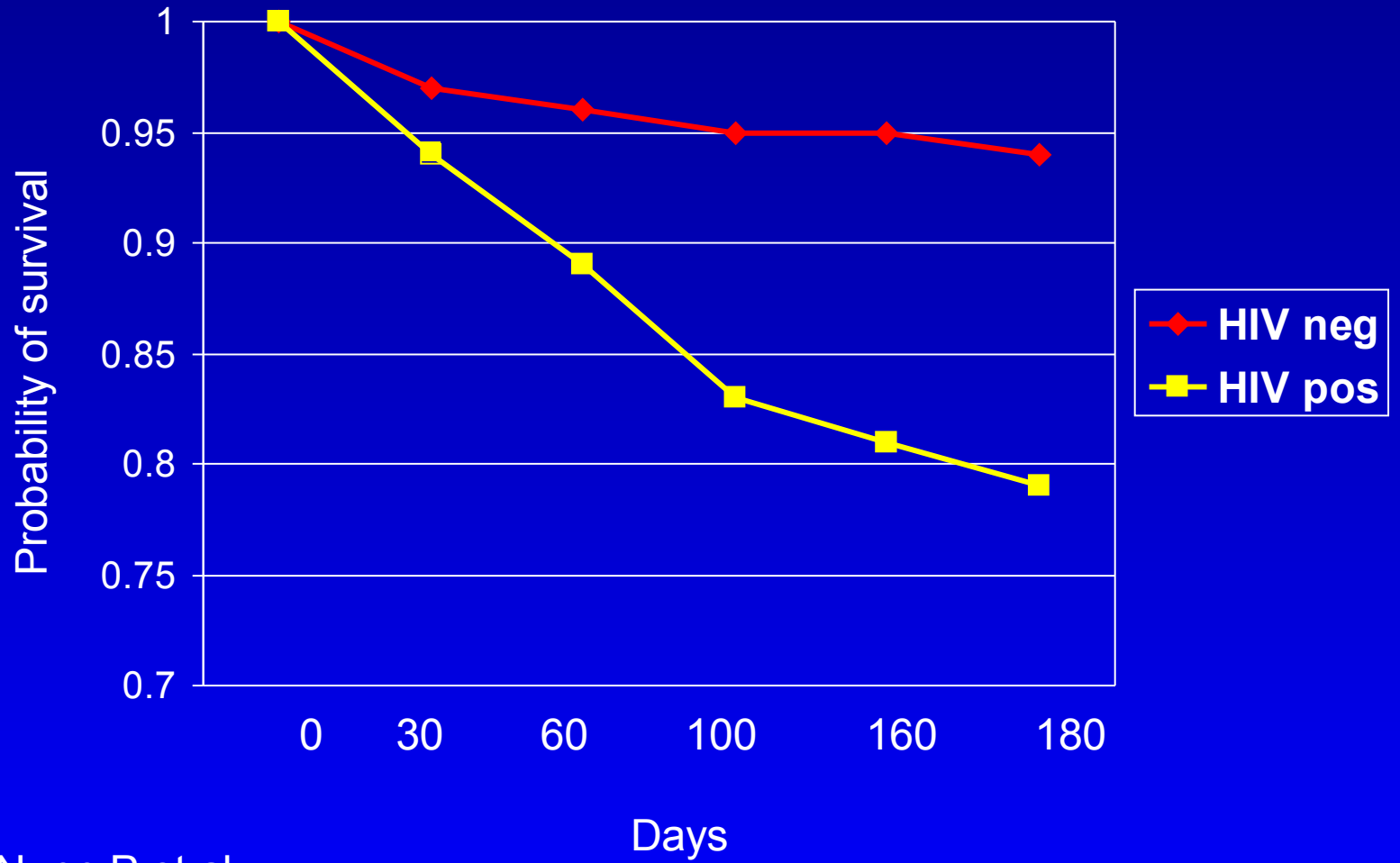
- Well documented
- More **common** in HIV-infected patients
- Typical in large **lymph nodes** or **tuberculomas**
- Temporally **related to initiation of ART**, especially if commenced within intensive phase of TB treatment

Immune reconstitution

- Effects up to 25% patients starting ART
- First weeks sees a worsening of conditions

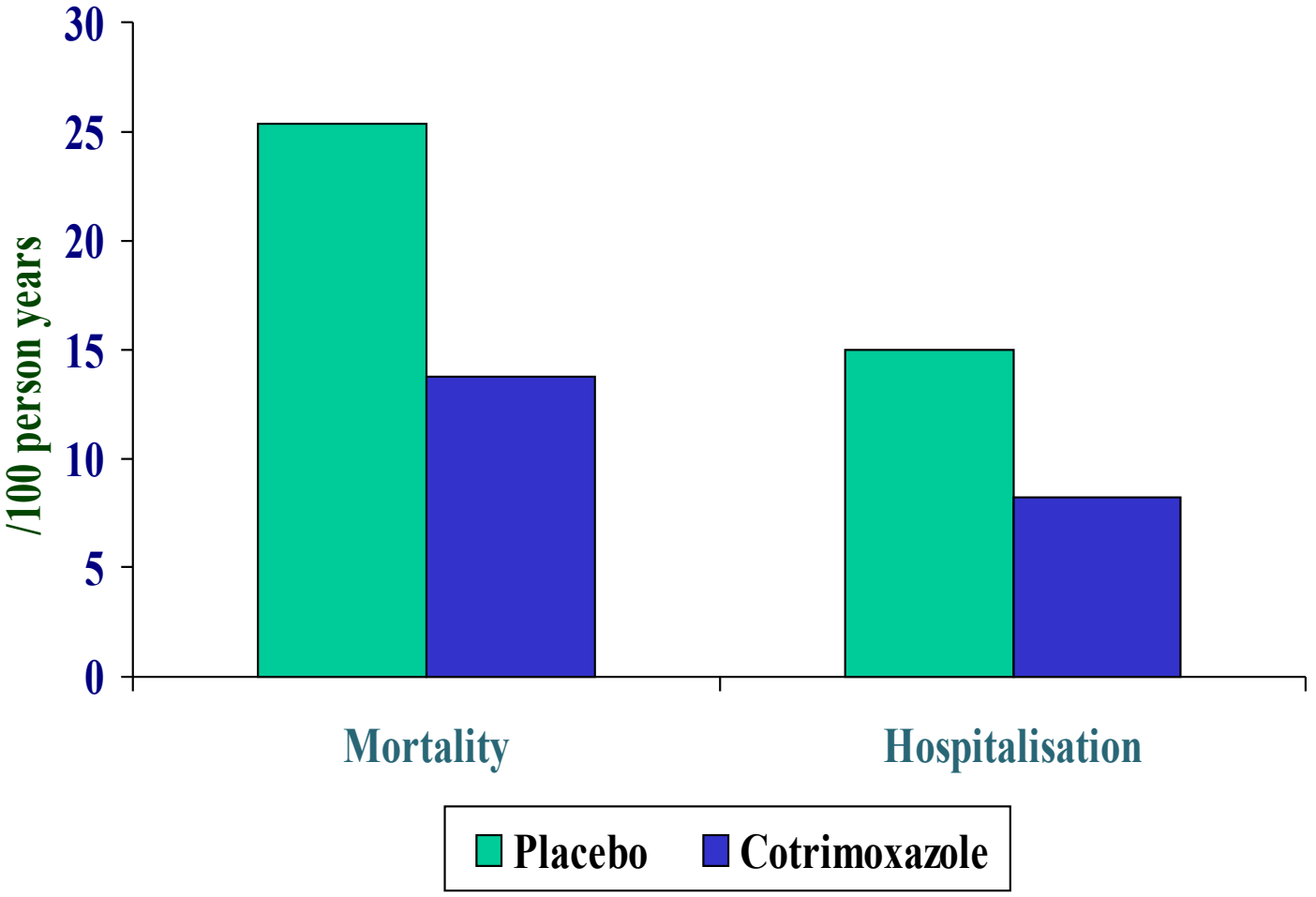
  Pulmonary infiltrates, cough, persistent fever, sweats, lost of weight, decreasing visual acuity
- TB most common reason for IRIS
- Do not stop ART drugs
- Treat with high doses corticosteroids (1 mg/kg) for 2 weeks

Probability of Survival during TB Treatment



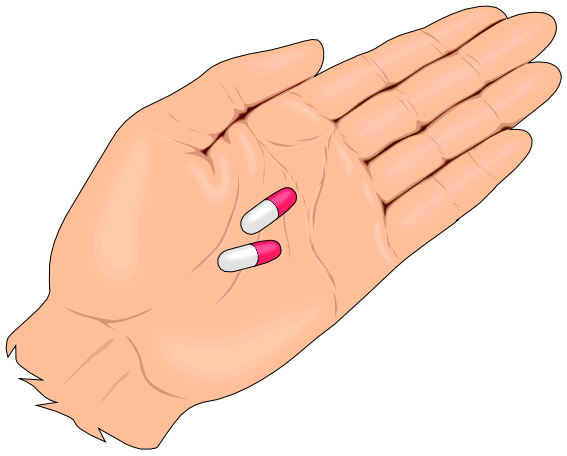
Nunn P et al
Am Rev Respir Dis 1992;146:849-54

Cotrimoxazole in TB/HIV



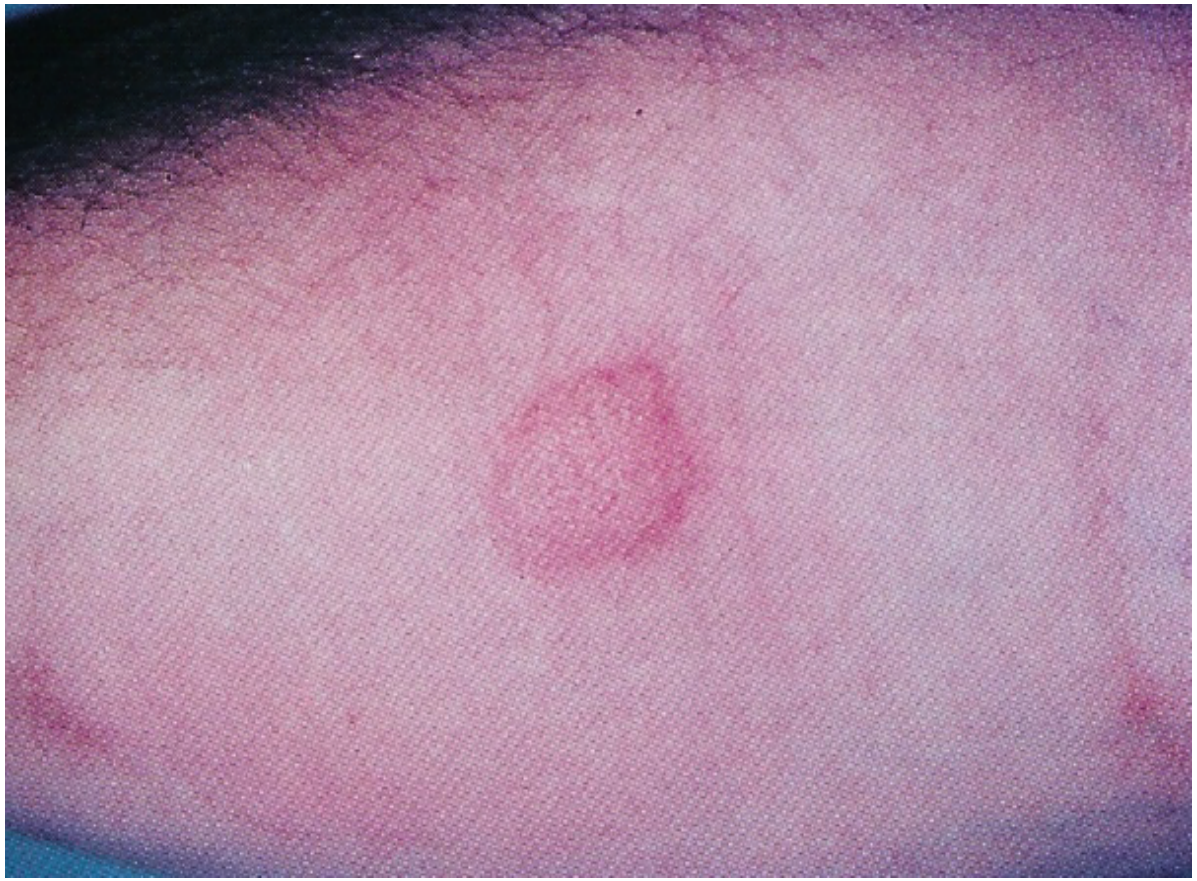
Lancet 1999;353:1469

Indication for Cotrimoxazole preventive therapy



- **CD4 count < 200**
- **Co-existent TB**
- **Any AIDS defining illness (irrespective of CD4 count)**
- **Unexplained weight loss (>10% BW)**
- **Chronic diarrhoea**
- **Oral hairy leukoplakia**
- **Oral thrush**

Tuberculin testing in HIV



Diagnostic value limited in countries where:

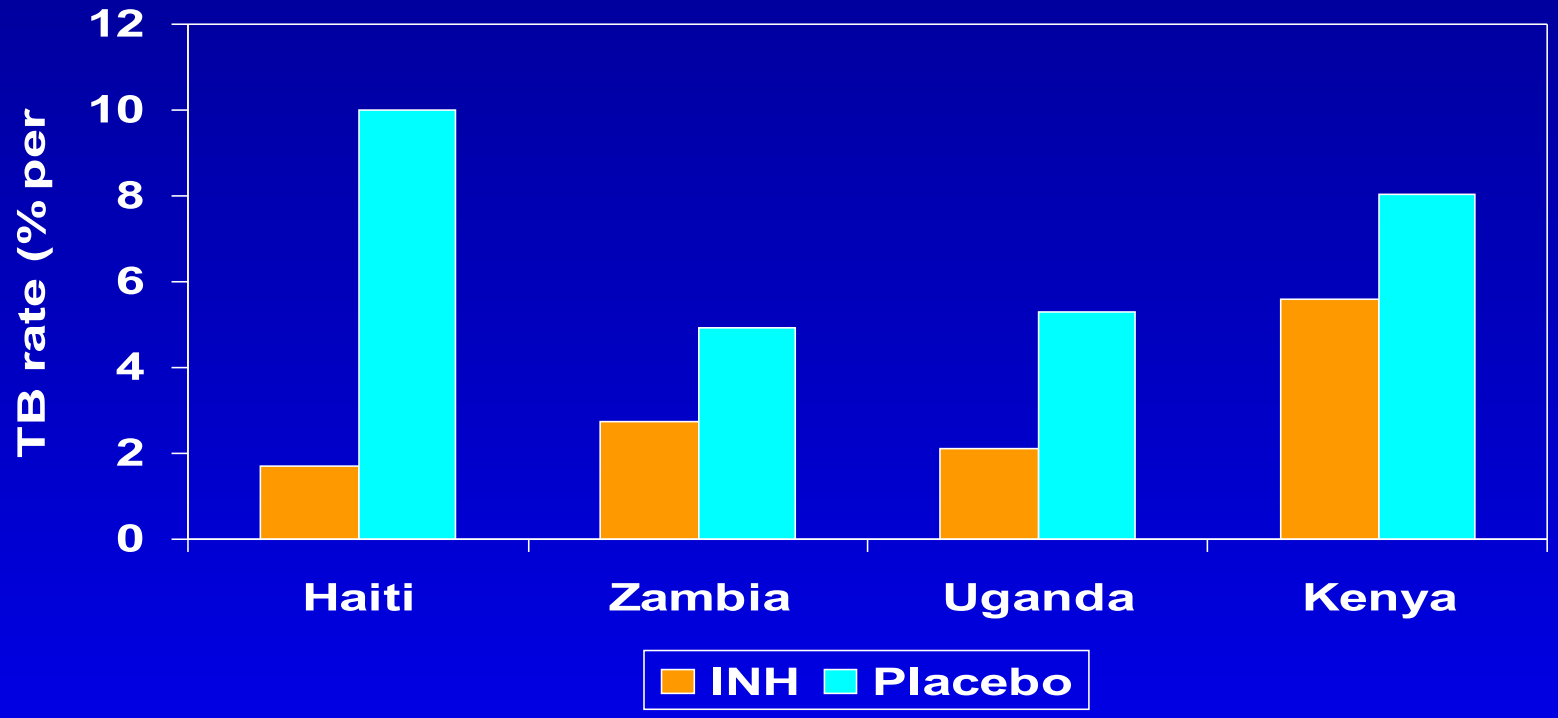
- Incidence of TB is high
  - BCG is used

Significance of TST

- Mantoux test recommended technique
- Injecting a known amount of PPD intradermally
- Reaction is measured 48-72 hours later
- Induration (not erythema) must be measured
- Diameter at widest points of the raised area (mm)
- Positive tuberculin skin test results:

Tuberculin test	Previous BCG	NO previous BCG	HIV+
Mantoux	≥ 15 mm	≥ 10 mm	> 4 mm

Efficacy of INH Preventive Therapy among HIV-positive, TST-positive(≥5mm) Persons



Isoniazid (INH) reduces active TB rate by 60% (but only among TST-positive persons)

TB preventive therapy

- Benefits HIV infected individuals
- Does not aim to control TB on a public health scale
- Is not an alternative to the DOTS strategy for controlling TB
- Very effective intervention for HIV infected individuals prior to starting ARV

Eligibility for TB prophylaxis

- Benefit of TB preventive therapy is greater in HIV+ people with positive TST (> 4 mm)
- TST should be offered to all HIV infected individuals (using the Mantoux technique)
- All HIV+ people with positive TST and no features of active TB are eligible
- Patients with signs and symptoms suggestive of TB must first be investigated for TB (culture)
- HIV+ patients with negative TST should not be offered TB preventive therapy

WHAT ABOUT ART AND TB PREVENTIVE THERAPY?

- In patients on ART there is currently no evidence of added benefit
- Patients who receive TB preventive therapy and who require to start ART can complete their TB preventive therapy even if the ARV treatment is started

To cure sometimes, to relieve often, to comfort always

Hippocrates