

Tuberculosis Preventive Therapy

Dr Refiloe Matji
Regional Director - URC

TB Preventive Therapy: Theory

- Treatment of latent infection
- Clinical trials have examined effectiveness of 6 to 12 months regimens designed to sterilise latent infections
- In high TB prevalence settings, preventive therapy may also prevent new infections

TB Preventive Therapy: Risk of Resistance

- In latent infection, <1 million bacilli
- Natural rate of mutation for isoniazid resistance is 1 per million
- In clients with latent infections (no symptoms and no active disease), there are not enough bacilli for resistant mutants to develop and survive
- There has been no documented increase in INH resistance as a result of TBPT in any clinical trial

TB Preventive Therapy: Effectiveness

- Meta-analysis:
isoniazid decreases risk of TB in HIV+
(RR=0.58: 95%CI,0.43-0.80)
- In HIV+ PPD+, RR=0.40 (0.24-0.65)
- In HIV+ PPD-, RR=0.84 (0.54-1.30)
- 6H=2RZ₂=3RZ₂=3HR=3HRZ

(Haiti, Kenya, Mexico, Uganda, United States, Zambia)

Bucher HC 1999

TB Preventive Therapy: Feasibility

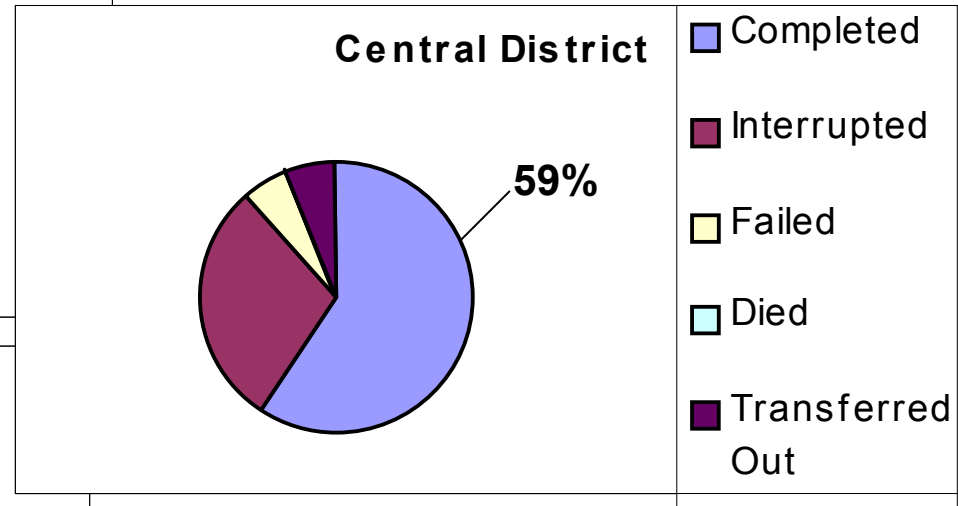
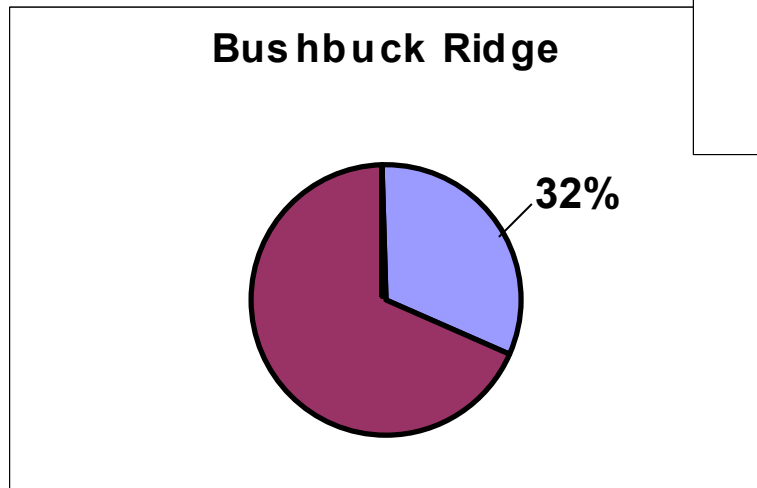
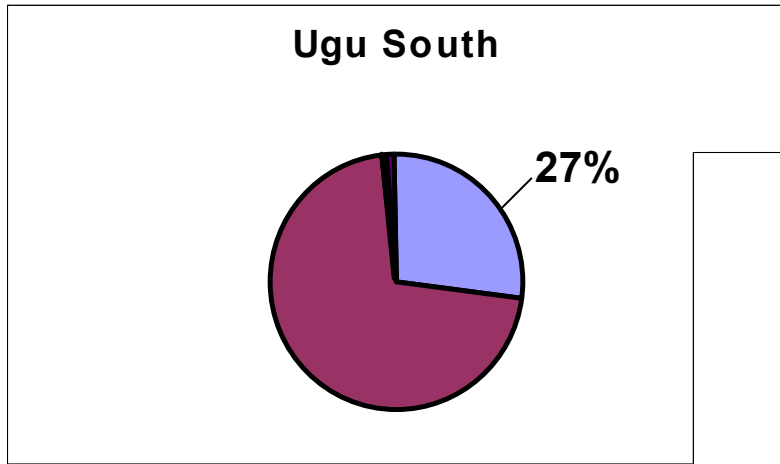
Country	%Screened	%Started	%Adherence
Uganda Aisu T, 1995	15	30	62
Rwanda Anglaret X, 1995	95	12	-
Zambia Godfrey-Faussett P 1995	34	38	-
Thailand Ngamvithayapong J, 1997	100	89	69
Uganda WHO, 1999	51	38	70
Brazil Calvacante S 1999	100	75	61

Kritski AL, 2000

TB Preventive Therapy: Adherence

- In Thailand of 412, 286 (69.4%) completed 6 month regimen
- Better Adherence: ♀ > ♂ ,
married/widowed > single, self-
employed > employed, symptom'c > asx'c
- Missed appointments: out migration, denial of HIV status, perceived SE's
- Good adherence: acceptance of HIV, desire to care for children, satisfaction with health care providers

TB Preventive Therapy: Adherence (Q2 2000)



- Completed
- Interrupted
- Failed
- Died
- Transferred Out

TB Preventive Therapy: Adherence

- Interviews with 15 HIV+ clients
- Barriers:
 - lack of money for transport and food
 - belief that meds must be taken with food
 - belief that meds should only be taken if ill
 - belief that should not mix meds with trad'l
- Reasons for better adherence:
 - support group
 - acceptance of HIV status Rowe, Makhubele, Pronyk 2001

TB Preventive Therapy: Cost-effectiveness

- Uganda: TBPT saves \$24.16/person (medical&social costs),
\$114-\$275/QALY (provider) Bell JC, 1999
- Zambia: benefit:cost ratio=0.86-1.71
Foster S, 1997
- South Africa: in 100,000 HIV+ over 8 years, TBPT saves \$10 million if 68.5% adherence and \$265,000 if 41%
Masobe P 1995

TB Preventive Therapy: Cost-effectiveness

- Cost per TB case prevented by TBPT in ProTEST TB/HIV pilot district in Cape Town, South Africa
 - \$486 with 44% adherence
 - \$962 with 57% Hausler et al, 2005 (WHO Bulletin in press)
- Screening: CXR not cost-effective, tuberculin skin testing does not affect cost-effectiveness (costs more to screen but TBPT more effective when only given to PPD-positives) Hausler et al, 2005 (WHO Bulletin in press)
- Comparable to the cost of treating a TB case in a previous study in Cape Town (\$823-\$1362) Sinanovic et al, 2003

TB Preventive Therapy: Pros

- If clients take it, it decreases their risk of developing TB by 60% in HIV+ PPD+
- It is inexpensive and cost-effective
- It encourages the screening of HIV+ clients for TB
- It is one of the only effective interventions available to offer people living with HIV in clinical stage 1

TB Preventive Therapy: Cons

- Adherence is low
- If isoniazid is inappropriately used by someone with a cough who has active TB, it could lead to resistance

TB Preventive Therapy: Current Recommendations in SA

- Only consider if:
 - VCT by trained staff available
 - Patients can be effectively screened for active TB before initiating TBPT
 - Patients can be followed monthly to monitor adherence and to exclude active TB & S.E.s
 - Provision of TBPT does not interfere with detection and cure of infectious TB patients
 - Local AIDS programme takes responsibility for implementation in collaboration with TB

Eligibility and exclusion criteria

ELIGIBLE CRITERIA:

- Asymptomatic (exclude active TB)
- Positive Tuberculin result
- Acceptance / commitment of patient

EXCLUSION CRITERIA:

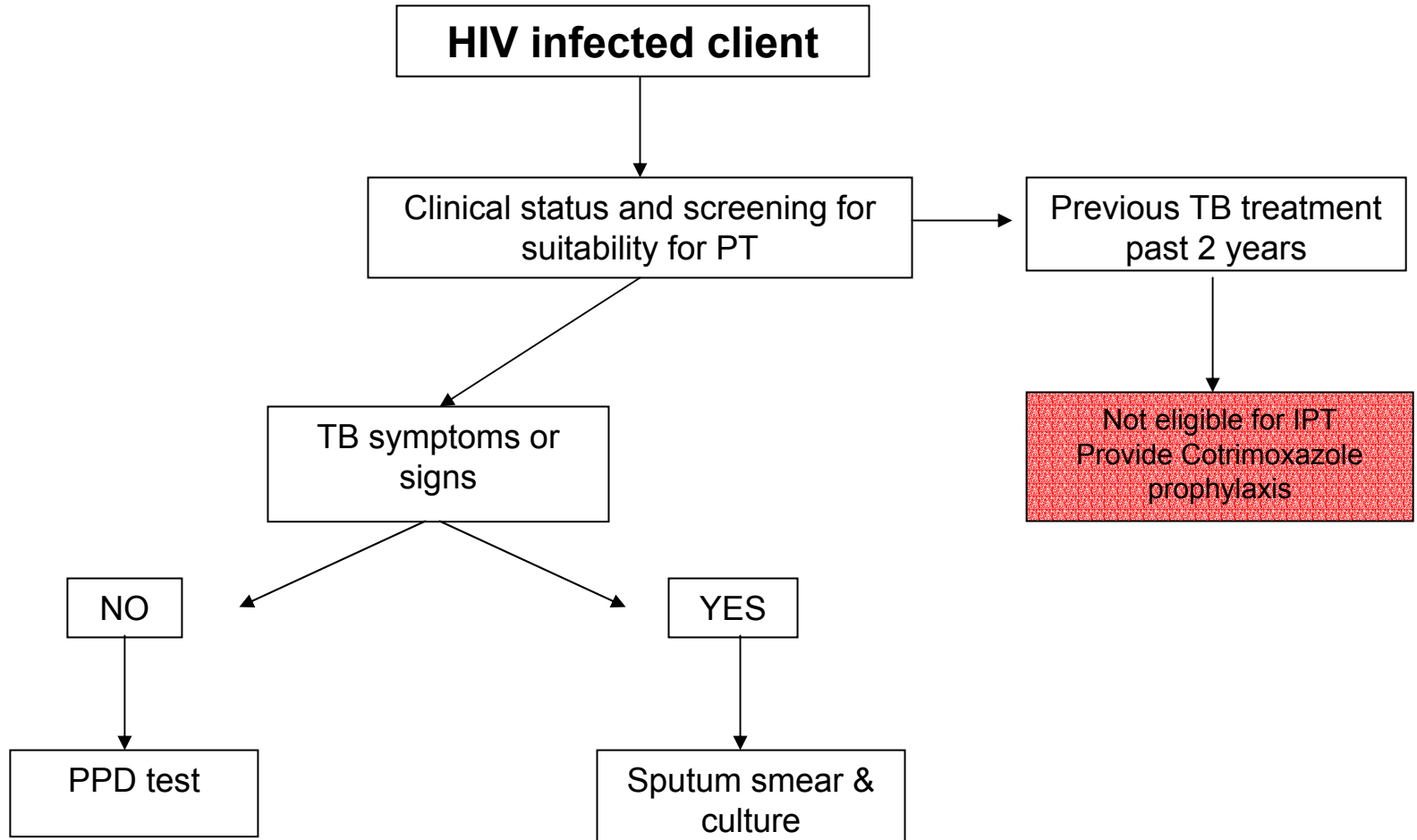
- Exclude in case of active TB disease OR TB treatment in past 2 years
- Exclude in case of active liver disease

Tuberculin Test

- Intradermal injection of PPD
- Measure INDURATION 48-72 hrs later
- A positive results means infection (not necessarily disease)

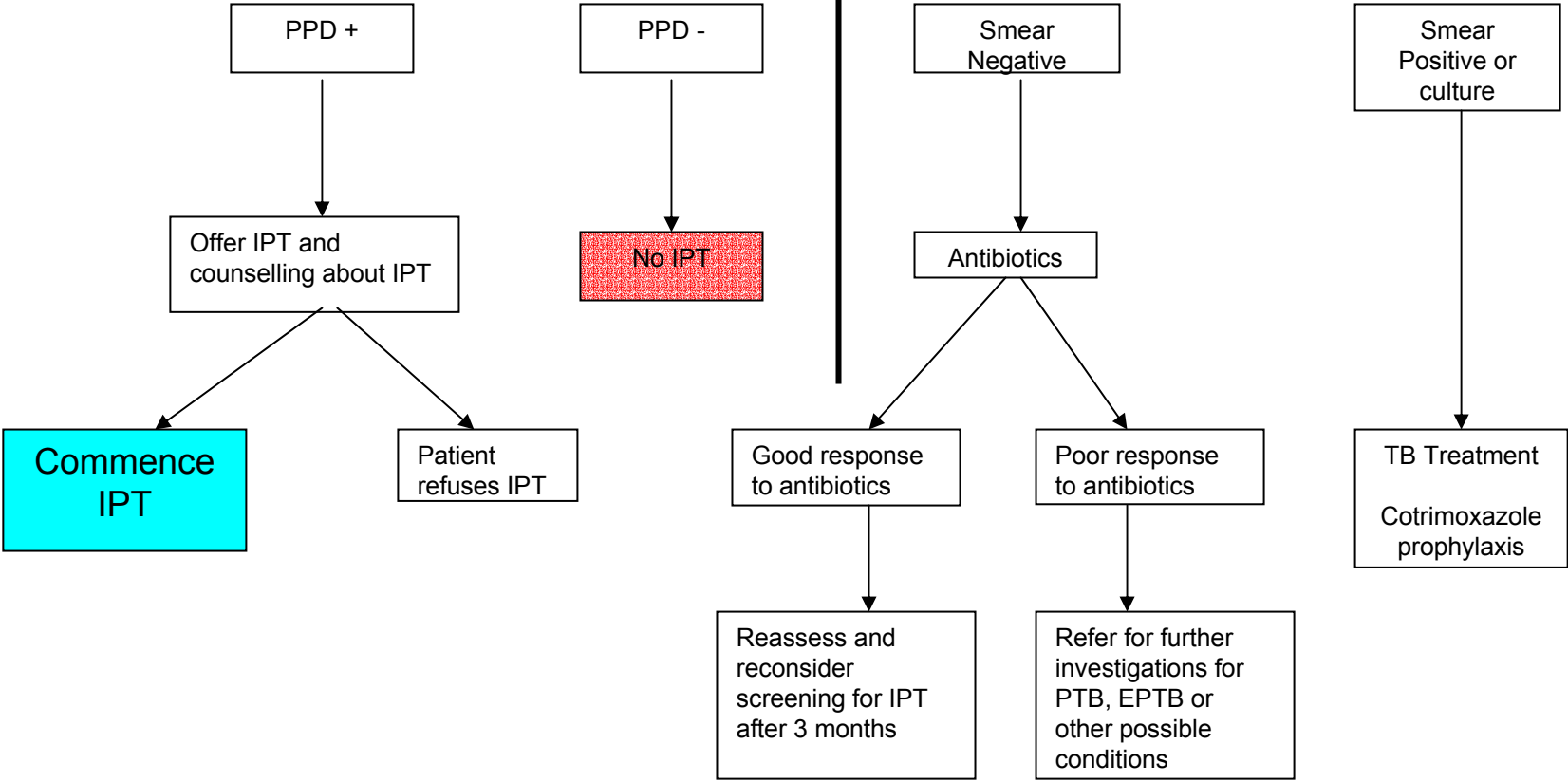
Tuberculin Test	Previous BCG	No previous BCG	HIV infected
Mantoux	≥ 15	≥ 10	≥ 5

FLOW CHART TB PREVENTIVE THERAPY



No symptoms
PPD test

Symptoms
Smear / culture



Regimen

- ISONIAZID tablets
- The dose is: 5 mg/kg/day
(maximum **300 mg per day**)
- The recommended duration is: **6 months**

Monitoring

- Identification of side effects
 - minor: peripheral neuropathy
 - Major: jaundice, vomiting and confusion due to hepatitis
- In case of peripheral neuropathy: 100 mg pyridoxine (vit B6) daily
- If the patient develops active TB, stop the preventive therapy and start the full TB treatment regimen.
- If the patient develops signs and symptoms suggestive of hepatitis, stop INH preventive therapy immediately and refer to a medical officer.
- If the patient interrupts therapy, enquire about the possible reasons for interrupting and counsel on the importance of adherence appropriately. Restart the therapy after ensuring that obstacles to adherence have been addressed.
- Ensure that the 6 months therapy is taken within a 9 months period. If the patient interrupts for the second time, consider stopping the therapy.

Research questions on TBPT

- Does PMTCT provide a suitable structure for INH preventive therapy in HIV-positive persons in Stage I or II?
- Does the addition of INH to ART further reduce the incidence of new TB and recurrent TB in HIV-positive patients in Stage III and IV?