



# Asymptomatic pulmonary tuberculosis among HIV-infected adults screened for the Botswana isoniazid preventive therapy clinical trial, 2004 -2006



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## Background

IPT is recommended for PLWH in tuberculosis (TB)-endemic settings. Evidence for the value of CXR as a screening tool to rule out active TB is controversial. Based upon pilot phase observations (2000-2001), the Botswana IPT Program recommends that asymptomatic PLWH receive IPT without a screening CXR. We sought to validate this earlier recommendation among patients enrolled in a two-site clinical trial integrated with the National Program.

## Methods

PLWH referred from counseling & testing centers and local clinics were screened Nov 2004 – Jun2006 for TB symptoms and other National IPT Program exclusion criteria. Asymptomatic individuals received CXRs.

Individuals with abnormal CXRs potentially compatible with TB were evaluated for active TB either retrospectively or for some prospectively. Sputum specimens were examined for acid fast bacilli (AFB) and cultured for TB in those able to produce sputum.

A diagnosis of TB was categorized as 'definite' if there was one positive TB culture; 'probable' if a smear or biopsy was positive for AFB with no positive culture; 'possible' if there was no laboratory evidence but a clinical diagnosis compatible with TB. An individual was categorized as 'Not TB' if s/he developed no illness for a period of 6 months after screening.

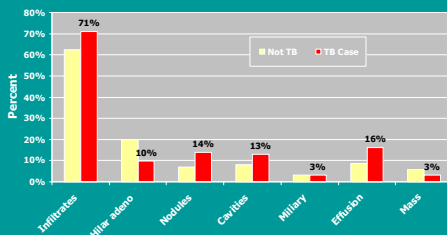
## Results

Comparison of screened asymptomatic PLWH with abnormal (n=305) vs. normal (n=2297) CXR

Characteristic	Abnormal (%)	Normal (%)	RR	95% CI
>35 y age (n=2600)	49%	41%	1.33	1.1-1.6
Male sex (n=2600)	38%	29%	1.43	1.2-1.8
Underweight (n=2129)	27%	18%	1.62	1.2-2.2
CD4 < 200 (n=2600)*	51%	39%	1.58	1.3-2.0
TST ≥5mm (n=2186)*	39%	24%	1.86	1.5-2.4
h/o TB >3 y (n=2136)*	20%	4%	4.61	3.5-6.1

\* Remained significant in multivariable model, h/o TB > 3 y ago being the strongest predictor for abnormal CXR.

### Screening CXR abnormalities in TB cases (n= 31) & non-TB cases (n=159)



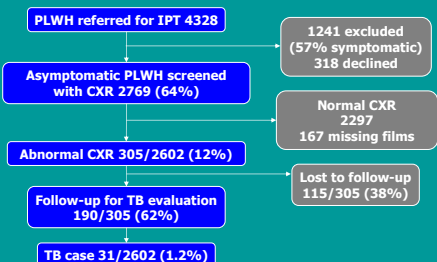
\* No CXR finding was statistically different between TB vs not TB

### Comparison of persons with abnormal CXR that had TB (n=31) vs. not TB (n=125)

Characteristic	TB (%)	Not TB (%)	RR	95% CI
TST ≥5mm (n=120)	67%	38%	2.62	1.1-6.0
≥ 1 symptom* (n=124)	73%	30%	5.21	1.5-18.6
Cough 2 wk (n=124)	45%	10%	5.63	1.9-16.3
Weight loss (n=124)	45%	12%	4.61	1.6-13.6

No significant differences were found for age, gender, CD4 < 200, BCG, h/o TB > 3 years ago, BCG scar, h/o smoking, h/o mine work. None were significant in a multivariable model. \* 'Symptom' refers to symptoms after screening and included fever, cough, hemoptysis, night sweats, weight loss, chest pain or shortness of breath.

## Results Overview



Participants with abnormal CXRs were interviewed a median of 8 months after screening (range 0-22 months). Demographic and CD4 characteristics of persons lost to follow-up were more similar to those determined not to have active TB than those determined to have TB.

### Characteristics of asymptomatic PLWH with abnormal CXR

Characteristic (n, available)	n (%)
Female (n=305)	188 (62%)
Age (median, n=305)	34.0 years, range 18-71
CD4 count (median, n=275)	218 cells/mm <sup>3</sup> , range 4-2839
History of TB >3 y. ago (n=213)	43 (20%)
Body mass index <18.5 (n=305)	173 (57%)
Tuberculin skin test (TST) ≥5mm (n=234)	91 (39%)
BCG scar (n=166)	122 (73%)
On antiretroviral therapy (n=305)	11 (4%)
TB case (n=190)	31 (10%)

Among the 31 cases there were 7 definite, 4 probable and 20 possible cases of TB. Extrapulmonary TB was also diagnosed in 2/31 (6%).

### IPT Exposure

Among the 305 with abnormal CXRs, 72 were known to have initiated a 6-month course of IPT. Four of these developed active TB, one of whom had an INH mono-resistant TB isolate.

### Comparison of IPT Program Pilot vs. Present Study

	Population (n)	Abnormal CXR n (%)	TB cases	P-value
Pilot 2000-01	560	24 (4%)	1* (0.2%)	
Present study	2602	305 (12%)	31 (1.2%)	<0.01

\* Diagnosed based upon the finding of an effusion in a CXR. Mosimaneotsile et al., Lancet 2003.

## Conclusions

Abnormal CXRs were common (12%) among asymptomatic PLWH seeking IPT: of those with abnormal CXR and an interview 20% had active TB; 10% of all those with abnormal CXRs had TB; 1.2% of all asymptomatic persons screened had TB.

Further consideration of public health issues, logistic factors and cost-benefit analyses will help to inform National IPT Program policy.