

Intensive case finding – does symptom screening cut it?

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**Guidelines for intensified
tuberculosis case-finding
and isoniazid preventive
therapy for people
living with HIV
in resource-
constrained
settings**



HMTB

Why intensified case finding?

- Undiagnosed TB is common in HIV+
- Earlier treatment reduces transmission
- Earlier treatment reduces morbidity & mortality
- Select people eligible for IPT

All people living with HIV should be regularly screened for TB....at every visit to a health facility or contact with a health worker. Screening for TB is important, regardless of whether they have received or are receiving IPT or ART.

ICF yield in HIV+ in SA

Antenatal clinic 0.7%

← Only women with symptoms cultured

Community 5%

Gold mines 4.9%

VCT 7.4%

Pre-ART 31.5%

Int J Tuberc Lung Dis 2006;10:523

AIDS 2010;24:1323

PLoS Med 2012;9(8):e1001281

Am J Respir Crit Care Med 2007;175:87

Effect of ART on ICF yield

Study	Pre-ART	On ART
Jo'burg	8.4%	4.1%
Cape Town	13%	5.4%

For IPT essential to **rule out** active TB

Ideal test: neg. predictive value $\sim 100\%$

neg. likelihood ratio < 0.1

Development of a Standardized Screening Rule for Tuberculosis in People Living with HIV in Resource-Constrained Settings: Individual Participant Data Meta-analysis of Observational Studies

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N=8,148

From 9 studies

Sputum cultures done

TB screening algorithm

Best symptom screen for TB – any one of:

- Cough – active (**any duration**)
- Fever >2 weeks
- Night sweats
- Weight loss

Overall diagnostic performance

- Sensitivity 78.9%
- Specificity 49.6%
- Likelihood ratio negative (LR-) 0.426

Predictors		Sensitivity (95% CI)	Specificity (95% CI)
Study level			
Setting	Community	1.0	
	Clinical	4.45 (1.02, 19.46) ^a	0.25 (0.06–1.01)
	Miners	0.25 (0.02–2.51)	4.07 (0.44–37.68)
Screening	Prescreened for TB	1.0	
	Not screened for TB	10.82 (2.45–47.78) ^a	0.08 (0.06–0.12) ^a
Culture medium	Solid	1.0	
	Liquid	3.41 (0.57–20.30)	0.33 (0.06–1.97)
Region	Sub-Saharan Africa	1.0	
	Southeast Asia	4.03 (0.65–24.84)	0.20 (0.04–1.00) ^a

TB symptom screen performance in clinic by TB prevalence

TB prevalence	1%	5%	20%
NPV	99.7%	98.3%	92.3%

Effect of ART on WHO symptom screening (clinic regularly does TB screening)

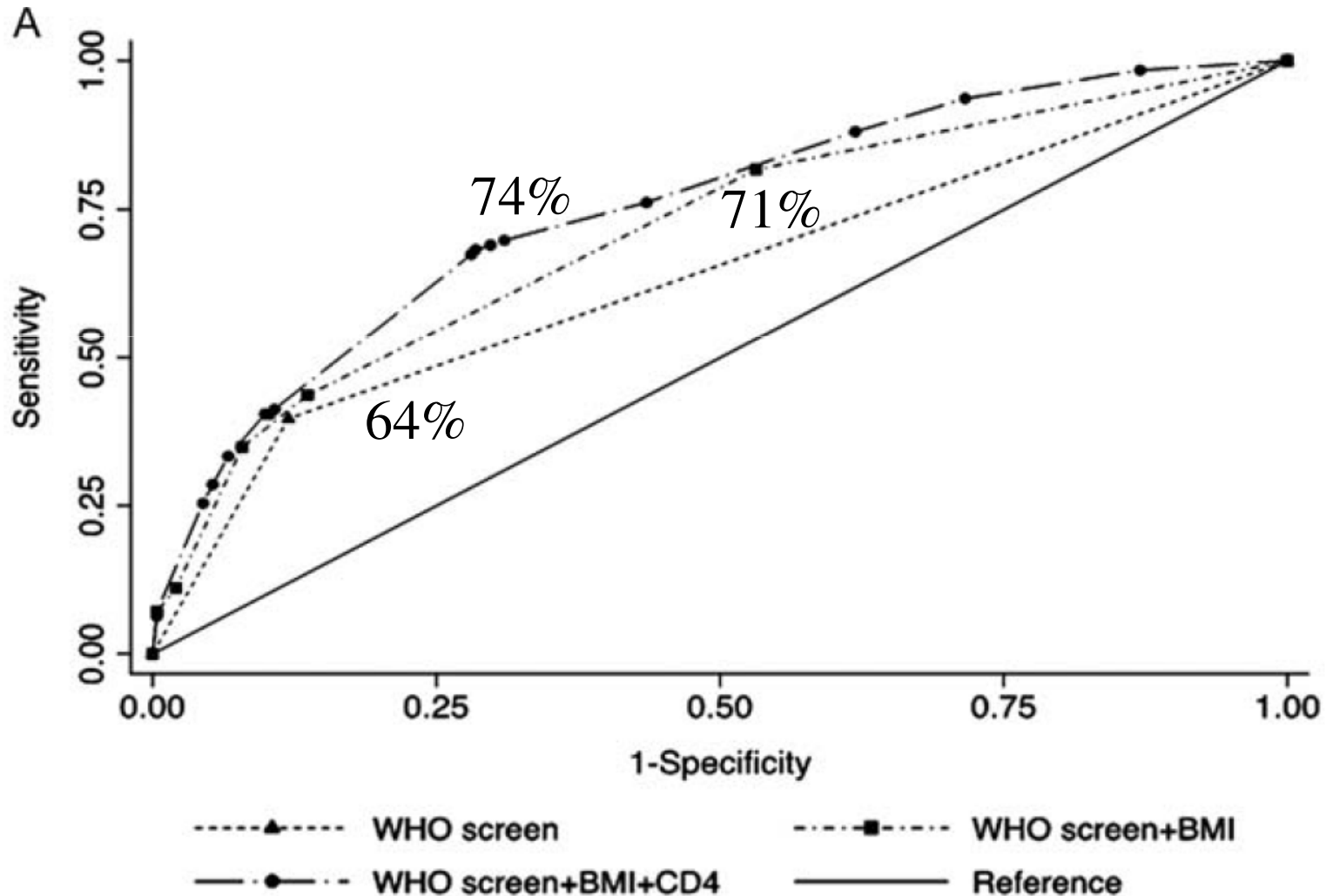
ART status	Sensitivity	Specificity	NPV	LR-
Pre ART (n=657)	47.6%	79.8%	91.2%	0.66
On ART (n=772)	23.8%	94.4%	95.6%	0.81

Pre ART
On ART

prior prob. 13%
prior prob. 5%

post. prob. 9%
post prob. 4%

BMI <18.5 & CD4 count <200 contribute to screening for TB



What about CXR? - WHO

Abnormal CXR increased sensitivity of symptoms
by 11.7%, but reduced specificity by 10.7%

What about CXR? - BOTUSA

‘Symptom+CXR’ vs ‘Symptoms only’: 98 excess cases of TB, 15 excess deaths.

‘Symptom+CXR’ policy reduced deaths only if attrition were close to zero, but the cost would be US\$2.8 million per death averted.

Does tuberculin skin test help?

- TST+ benefit from IPT (Tom Boyles)
- TST+ group have more TB in ICF studies
 - aOR 3.5 (95%CI 1.9-6.7)
 - aOR 4.8 (95%CI 1.6-14.4)

Microbiological screening

- Xpert MTB/RIF had sensitivity of 73.3% in an ICF study in a Cape Town pre-ART clinic – similar to passive case finding

CRP screening?

- Passive case finding study in Pietermaritzburg
 - Sensitivity 98%
 - Likelihood ratio negative 0.04
- No data in ICF
- Point of care CRP test available

Conclusions

- There is a lot of HIV-associated TB when you look
- Symptom screening reasonable yield if no prior screening & done in a clinic pre-ART
- Need better rule out tests in other settings
- High prevalence argues for routine culture or PCR in some settings, especially pre-ART