Evaluation of WHO 4-symptom tool to rule out TB: data from the XPHACTOR study

Yasmeen Hanifa[1], Katherine Fielding[1], Violet Chihota[2], Nontobeko Ndlovu[2], Alan Karstaedt[3], Faieza Sahid[3], Lungiswa Adonis[4], Linda Erasmus[5], Mark Nicol[5], Gavin Churchyard[2], Alison Grant[1]

Yasmeen.Hanifa@lshtm.ac.uk

[1]London School of Hygiene & Tropical Medicine, London, UK; [2]Aurum Institute for Health Research, Johannesburg, South Africa; [3]Department of Medicine, Chris Hani Baragwanath Hospital, Johannesburg, South Africa; [4]Mamelodi Hospital, Pretoria, South Africa; [5]National Health Laboratory Service, Johannesburg, South Africa.

Introduction

Background

- WHO recommends screening HIV+ individuals for TB using tool comprising any cough, weight loss, fever or night sweats ("WHO tool")
- Tool developed from meta analysis of individual participant data, largely not on ART; designed to maximise sensitivity and negative predictive value (NPV) to exclude TB so IPT and ART can be initiated
- XPHACTOR is an interventional cohort study evaluating a risk-based algorithm to prioritise testing with Xpert MTB/RIF amongst adults attending for HIV care in South Africa

Aim

- To evaluate performance of the WHO tool as a test to rule out TB among patients in the XPHACTOR study

Methods

Population

- Systematic sample of adults attending 4 HIV clinics in Gauteng were screened for TB, Sept 2012 – Feb 2014
- Enrolled in three groups, on ART vs. pre-ART vs. newly diagnosed HIV + from HIV Counselling and Testing (HCT)
- Excluded if any TB treatment in last 3 months

Procedures

- Structured questionnaire incorporating WHO tool
- Xpert MTB/RIF requested if high priority for TB investigation according to XPHACTOR algorithm (any of: cough, BMI<18.5, CD4<100, weight loss ≥10%) and from all HCT
- Monthly review with reinvestigation if indicated, to 3 months, when sputum and blood were taken for TB culture
- Clinic file review to identify additional TB diagnoses

Definitions

- Definite TB: Xpert+ or culture+ for *M. tuberculosis*
- Clinical TB: Started on TB treatment by health care provider
- Not TB: No positive microbiology for *M. tuberculosis* (at least one specimen)

Excluded from analysis

- On isoniazid preventive therapy (IPT) at enrolment
- Died within 3 months of enrolment without TB diagnosis
- TB diagnosed >6m from enrolment
- Did not meet criteria for TB or Not TB based on definitions

Results

Table 1: Characteristics of study population at enrolment (N=3229)

Characteristic	On ART: N=2439	Pre-ART: N=693	New HIV + HCT: N=97
Age, yrs	41 (35-48)	35 (29-43)	36 (30-41)
Female	70.5 (1719)	67.2 (466)	50.5 (49)
House owner	47.3 (1154)	33.5 (232)	20.6 (20)
Previous TB treatment	39.7 (967)	9.0 (62)	7.2 (7)
Previous IPT	2.5 (61)	22.5 (156)	N/A
History of CPT	78.2 (1906)	47.6 (330)	N/A
BMI, kg/m^2 (N=3225)	25.0 (21.6-29.4)	24.5 (20.8-29.0)	23.2 (20.1-28.4)
Duration since HIV diagnosis, months (N=3107)	67 (39-100)	9 (1-33)	N/A
Duration on ART, months (N=2429)	49 (28-79)	N/A	N/A
CD4, cells/mm^3	439 (283-621)	360 (184-528)	248 (106-412)
Positive WHO symptom screen	30.2 (736)	42.6 (295)	62.9 (61)

Data are median (IQR) or % (n); IPT=Isoniazid preventive therapy; CPT=Cotrimoxazole preventive therapy
HCT=HIV counselling and testing

Figure 1: Prevalence of TB and basis for diagnosis % (95% CI)

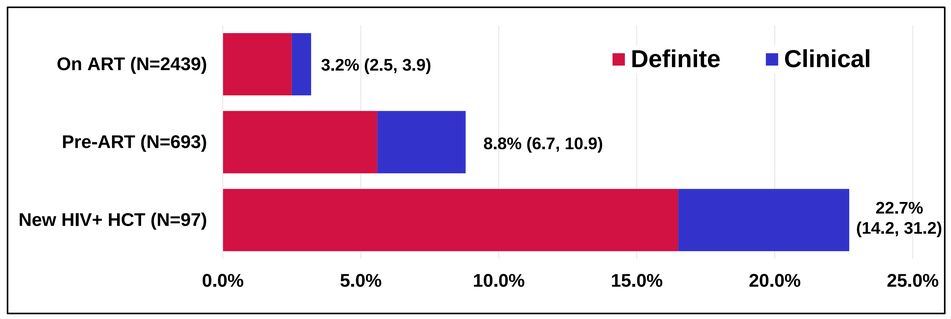


Table 2: Performance of WHO tool

	Sensitivity n/N % (95% CI)	Specificity n/N % (95% CI)	NPV n/N % (95% CI)	PPV n/N % (95% CI)
All TB[1]: On ART (79/2439)	53/79 67.1% (55.6,77.3)	1677/2360 71.1% (69.2,72.9)	1677/1703 98.5% (97.8,99)	53/736 7.2% (5.4,9.3)
All TB[1]: Pre-ART (61/693)	58/61 95.1% (86.3,99)	395/632 62.5% (58.6,66.3)	395/398 99.2% (97.8,99.8)	58/295 19.7% (15.3,24.7)
All TB[1]: New HIV+ HCT (22/97)	20/22 90.9% (70.8,98.9)	34/75 45.3% (33.8,57.3)	34/36 94.4% (81.3,99.3)	20/61 32.8% (21.3,46)
Definite TB[2]: On ART (61/2421)	37/61 60.7% (47.3,72.9)	1677/2360 71.1% (69.2,72.9)	1677/1701 98.6% (97.9,99.1)	37/720 5.1% (3.6,7.0)
Definite TB[2]: Pre-ART (39/671)	37/39 94.9% (82.7,99.4)	395/632 62.5% (58.6,66.3)	395/397 99.5% (98.2,99.9)	37/274 13.5% (9.7,18.1)
Definite TB[2]: New HIV+ HCT (16/91)	14/16 87.5% (61.7,98.4)	34/75 45.3% (33.8,57.3)	34/36 94.4% (81.3,99.3)	14/55 25.5% (14.7,39.0)

[1] Gold standard=definite and clinical TB combined; [2] Gold standard=definite TB (clinical TB excluded from analysis)
NPV=Negative predictive value; PPV=Positive predictive value

Results

Prevalence of TB is high, particularly among those not on ART (figure 1)

Performance of WHO tool (table 2):

- NPV (proportion without TB of those WHO -ve)
  - >98% in pre-ART and on ART groups
  - Lower in new HIV+ HCT among whom TB prevalence is very high (23%)
- PPV (proportion with TB of those WHO +ve) is low, particularly among those on ART (7.2%)

Conclusions

- NPV of WHO 4-symptom tool is very high among on ART and pre-ART groups
  – supporting use of WHO tool to rule out TB in people established in HIV care
- NPV lower in HCT attendees newly testing HIV+ where TB prevalence very high
  – this group requires systematic investigation rather than screening
- Relatively low PPV among on-ART and pre-ART groups necessitates guidance on prioritisation of further investigation to avoid burdening health care systems in resource-limited settings

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