Characterisation of South Africa's XPERT MTB/RIF Ultra "trace" Laboratory Results

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BACKGROUND

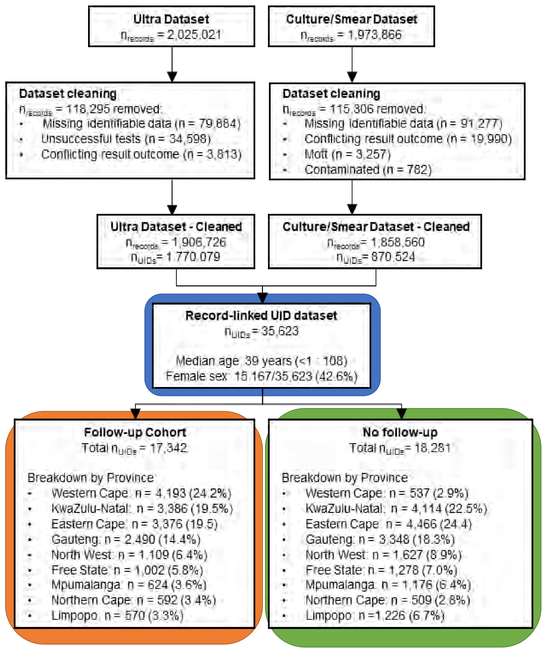
- South Africa transitioned to the Xpert-MTB/RIF Ultra (Ultra) assay in their national TB program in October 2017 across 200 public sector testing sites and perform ~2.27million tests/an.
- Increased sensitivity of the Ultra over the previous Xpert MTB/RIF assay is attributed to the inclusion of IS*6110*/IS*1081*, improved chemistry, and larger PCR reaction volume. The lower limit of detection of Ultra is 15.6cfu/ml, and a new semi-quantitative category "trace" identifies paucibacillary specimens that are IS*6110*/IS*1081* positive but *rpoB* negative. The complexities of "trace" was explored.

METHODS

Extracted laboratory test results from the central data warehouse between Oct'17 – Nov'18 in two datasets:

- Ultra records [n=2,025,021]
- Smear & MGIT records [n=1,973,866]

Performed exact matching between the datasets (to identify unique individuals) and their laboratory results over time. Key matching fields: province, patient first name, patient surname, sex and date of birth.



Ultra "trace" contributes an **additional 2% TB detected** (~39,000 results/an)

Up to **39% individuals with "trace" cultured *M.tb*** from their sputum indicating TB disease

These **would have remained undiagnosed by Xpert** and not available for confirmation of Rifampicin susceptibility testing

RESULTS AND FINDINGS

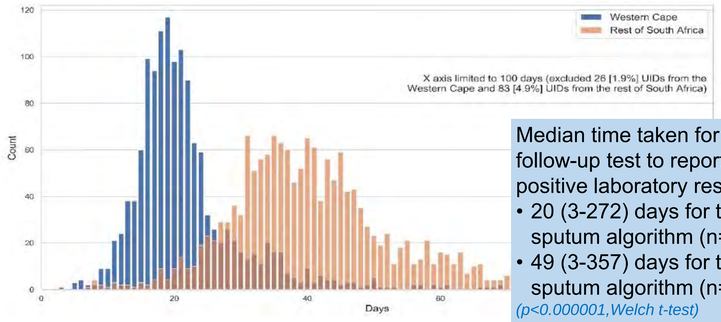
Record-linked UID dataset (35,623): median age 39 years and 42.6% were female

Factor investigated for UIDs	National Results (n=17,342)	1-sputum algorithm (8 provinces) Variability among provinces (n=13,149)	2 sputum algorithm (Western Cape) (n=4,193)
Follow-up testing within:			
5 days	62% (10,798)	53% (6,902)	93% (3,896)
14 days	82% (14,208)	77% (10,155)	97% (4,053)
Follow-up test requested:	50% (8,648)	51% (6,646)	48% (2,002)
Ultra	58% (10,022)	48% (6,305)	89% (3,717)
MGIT	64% (11,475)	69% (9,090)	57% (2,385)
Smear			
Follow up tests detecting MTBC:			
Ultra positive	53% (4,575)	52% (3,450)	56% (1,125)
MGIT positive	34% (3,364)	31% (1,926)	39% (1,438)
Smear positive^	7% (750)	7% (588)	7% (162)

Collecting 2 sputum specimens at initial clinic visit increased the turn around time to confirm active TB infection by 2 fold (20days vs 40days)

A repeat Ultra is requested >50% UIDs (>50% positive for TB DNA, of which 63% report trace)

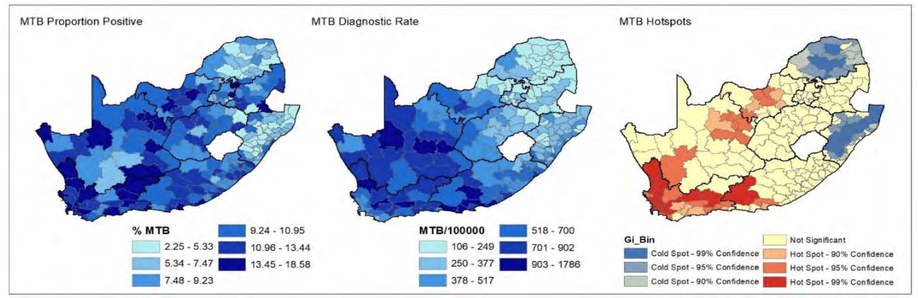
^Acid Fast Bacilli present

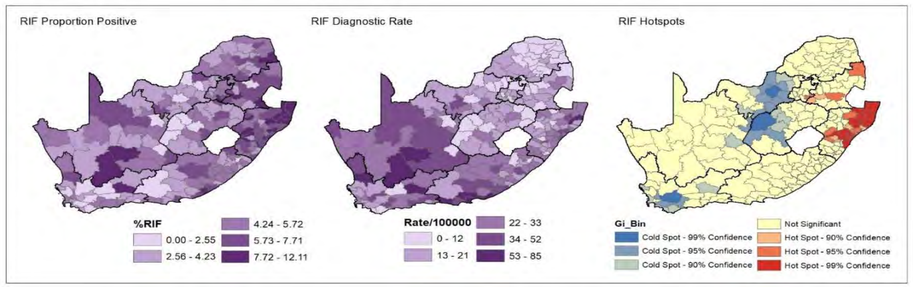


Median time taken for a follow-up test to report a positive laboratory result was:

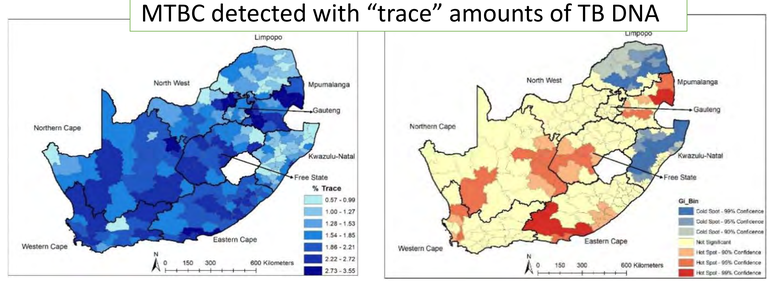
- 20 (3-272) days for the two sputum algorithm (n=1395)
- 49 (3-357) days for the 1 sputum algorithm (n=1709)

(p<0.000001,Welch t-test)





MTBC detected with "trace" amounts of TB DNA



CONCLUSIONS

- South Africa reports **9.56% MTBC detected**, and **5.3% Rifampicin** resistant using Ultra
- The TB epidemic is dynamic with geographic variability
- Algorithms for managing individuals with "trace" results are not well adhered as only 49% of individuals with "trace" are microbiologically followed up
- Collecting 2 sputa at first visit reduces turnaround time to confirm active TB infection
- Laboratory diagnostic algorithms can be refined to reduce costs and increase turn around time to improve linkage to care and patient management.
- Clinical cohort studies are suggested to further explore the "trace" category result for patient management