Evaluation of Signature Mapping TBDx for fluorescent microscopy

- interim analysis -

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Conflict of interest

- No conflicts of interest to declare
- Signature Mapping TBDx loaned from manufacturer

What is it?

- Computer-aided fluorescence smear microscopy with algorithms to identify bacilli using an automated slide management system.
- Microscope (conventional FM)
- Engine for autofocus
- Camera
- Slide loader (4-200)
- Software to capture and read smears
- https://www.youtube.com/watch?v=DH9fKEjYSkE

What do we know?

- Evaluated in South Africa in concentrated sputum
- 80% sensitivity and 79% specificity
- Manufacturer suggests using with Xpert to exclude false+
- No studies on direct sputum



Study design

- Cross sectional survey
- Consecutive adults attending 5 district hospitals in Abuja.
- 2 sputum specimens. On the spot, 1 hour apart.
- Specimens transported to a research lab (ZMC)
- Diagnostics assessed in tandem (Genedrive, Mycolic acids, Fluorotype, TBDx)
- Laboratory staff blind to experimental tests.

Laboratory tests

Adults >18 years with cough for > 2 weeks New and re-treatment cases

Whole Blood

Spot sputum 1

Spot sputum 2

Serum

LED-FM

LED-FM

RAP-TB

TBDx

Genedrive

Genedrive

Culture x 2

Xpert

Re-stained

Positive

Negative

DST

Geno and Spolygoryftyping

Report to clinic

Not reported

Participants

- Recruited 1650 patients by September 2014
- This analysis
  - 703 patients
  - Positive/negative Culture
  - LED-FM (x2)
  - TBDx (x1)
  - Sub-analysis by HIV

- Definitions:
  - Positive smear microscopy: > 1 AFB in ≥1 LED-FM
  - TBDx: > 1 object in ≥1 field
  - Final analysis will include ROC curves

Participants

- Culture: 199 (28%) pos, 504 (72%) neg
- HIV: 277 (39%) pos, 292 (42%) neg, NK 134 (19%)
- LED-FM :
  - Negative 554 (78.8%)
  - Scanty 16 (2.3%)
  - Positive (+/++/+++) 133 (18.9%)

} 21.2%

- TBDx
  - Negative 555 (78.9%)
  - Scanty 45 (6.4%)
  - Positive (+/++/+++) 103 (15%)

} 21.4%

Combined:

Sens: 68% (95CI 61-75)
Spec: 97% (95CI 94-98)

LED-FM

- HIV negative

	Culture pos	Culture neg	Total
Negative	18 (20.9)	198 (96.1)	216
Scanty	3 (3.5)	3 (1.5)	6
Positive	65 (75.6)	5 (2.4)	70
TOTAL	86	206	292

- Sens: 79.1% (95CI 69-86)
- Spec: 96.1% (95CI 91-97)

- HIV positive

	Culture pos	Culture neg	Total
Negative	35 (43.8)	193 (97.8)	228
Scanty	7 (8.8)	1 (0.5)	8
Positive	38 (47.5)	3 (1.5)	41
TOTAL	80	197	277

- Sens: 56% (95CI 45-80)
- Spec: 98% (95CI 95-99)

Combined:

Sens: 56% (95CI 49-64)

Spec: 92% (95CI 90-95)

TBDx

- HIV negative

	Culture pos	Culture neg	Total
Negative	30 (34.9)	187 (90.8)	217 (74.3)
Scanty	5 (5.8)	17 (8.3)	22 (7.5)
TB P+	11 (12.8)	0 (0)	11 (3.8)
TB P++	16 (18.6)	2 (1)	18 (6.2)
TB P+++	24 (27.9)	0 (0)	24 (8.2)
TOTAL	86	206	292

- Sens: 65% (95CI 55-74)
- Spec: 91% (95CI 86-94)

- HIV positive

	Culture pos	Culture neg	Total
Negative	42 (52.5)	187 (94.9)	229 (82.7%)
Scanty	6 (7.5)	9	15
TB P+	10 (12.5)	1 (0.5)	11 (4)
TB P++	10 (12.5)	0 (0)	10 (3.6)
TB P+++	12 (15)	0 (0)	12 (4.3)
TOTAL	80	197	277

- Sens: 48% (95CI 37-58)
- Spec: 95% (95CI 91-97)

Difference between TBDx and LED-FM not significant

Discrepancies

	TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	521 (93.9)	31 (68.9)	2 (1.9)	554
Scanty	12 (2.2)	4 (8.9)	0 (0)	16
Positive	22 (3.4)	10 (22.2)	101 (98.1)	133
Total	555	45	103	703

	Culture Pos TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	60 (69.8)	1 (8)	2 (2)	63
Scanty	8 (9.3)	3 (23.1)	0 (0)	11
Positive	18 (21)	9 (69.2)	98 (98)	125
TOTAL	86	13	100	199

- 60 missed by both
- 3 missed by LED-FM, TBDx +
- 26 missed by TBDx, LED-FM +
- 109 found by both

Discrepancies

	TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	521 (93.9)	31 (68.9)	2 (1.9)	554
Scanty	12 (2.2)	4 (8.9)	0 (0)	16
Positive	22 (3.4)	10 (22.2)	101 (98.1)	133
Total	555	45	103	703

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Scanty	8 (9.3)	3 (23.1)	0 (0)	11
Positive	18 (21)	9 (69.2)	98 (98)	125
TOTAL	86	13	100	199

	Culture Neg TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	461 (98.3)	30 (93.4)	0 (0)	491
Scanty	4 (1)	1 (3)	0 (0)	5
Positive	4 (1)	1 (3)	3 (100)	8
TOTAL	469	32	3	504

Discrepancies

	TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	521 (93.9)	31 (68.9)	2 (1.9)	554
Scanty	12 (2.2)	4 (8.9)	0 (0)	16
Positive	22 (3.4)	10 (22.2)	101 (98.1)	133
Total	555	45	103	703

- 461 correctly negative by both
- 30 LED-FM -, TBDx +
- 8 TBDx - , LED-FM +
- 5 positive by both

	Culture Neg TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	461 (98.3)	30 (93.4)	0 (0)	491
Scanty	4 (1)	1 (3)	0 (0)	5
Positive	4 (1)	1 (3)	3 (100)	8
TOTAL	469	32	3	504

“Come in Xpert MTB/RIF”

	Culture		
Xpert	Pos	Neg	Total
Neg	49 (24)	469 (95)	518
Pos	150 (76)	25 (5)	175
TOTAL	199	494	693

- 25 culture neg/Xpert pos and 49 culture pos/Xpert neg
- TBDx/LED-FM results among these?

Xpert in culture-neg, TBDx/LED-FM pos patients

	Culture Neg TBDx			
LED-FM	Neg	Scanty	Pos	Total
Negative	461	30	0	491
Scanty	4	1	0	5
Positive	4	1	3	8
TOTAL	469	32	3	504

- 5/8 TBDx Neg, LED-FM Pos, Xpert pos
- 0/30 TBDx Pos, LED-FM Neg, Xpert neg
- 4/5 TBDx Pos, LED-FM Pos, Xpert pos

Sensitivity/specificity

- Against culture:
  - Sensitivity = 61% (95% 53 - 68)
  - Specificity = 93%, (95CI 90 – 95%)

- If Xpert used in culture-negative/AFB+ patients
  - Sensitivity = 62% (95CI 54 – 69%)
  - Specificity = 94% (95CI 91 – 96%)

No statistical difference to 2 manual LED-FM

Conclusion

- Preliminary analysis
- Sensitivity of 1 x TBDx = 2 x LED-FM
- Sensitivity decreases with HIV (as in LED-FM)
- Specificity of TBDx =LED-FM (but trend to lower spec)
- These parameters may change once
  - All patients are included
  - Reference standard is a composite of culture and Xpert
  - Culture results typed in Barcelona
  - ROC curves are constructed to select different cut off points

Many thanks

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