ORAL SWAB ANALYSIS (TB-OSA) FOR NON-SPUTUM BASED TB DIAGNOSIS IN KENYA

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Background

- Despite advances in rapid TB diagnostics, sample collection remains challenging, especially in those unable to produce sputum.
- In proof-of-concept data, oral swab analysis (OSA) detected *M. tuberculosis* in HIV-negative Xpert+ TB cases in South Africa (Figure 1) [1].
- A larger, follow-on evaluation in the same South African population found 92% sensitivity, 92% specificity relative to sputum Xpert [2].

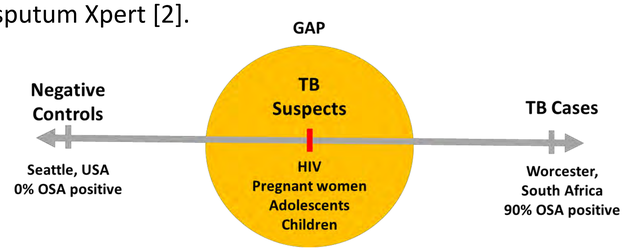


Fig 1. Key populations a non-sputum collection method of TB diagnosis such as OSA could address.

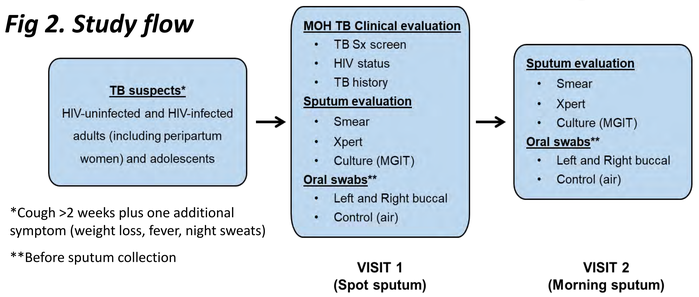
Objective

To evaluate OSA performance to detect TB in HIV-infected and HIV-uninfected TB suspects in Kenya.

Methods

- Observational study of TB suspects ≥13 years enrolled at Ministry of Health (MOH) TB Clinics in Kisumu, Kenya
- Oral swabs and sputum for Xpert, smear, and culture collected at enrollment and consecutive morning visit

Fig 2. Study flow



- Cryopreserved oral swabs underwent Mtb DNA extraction and qPCR analysis targeting IS6110 insertion sequence
- Predetermined threshold quantitation cycle (Cq) <38 considered positive (lower Cq indicating higher copies and stronger/more positive signal)
- OSA performance was compared to reference of sputum Xpert or culture. OSA mean Cq values compared using t-tests.

Results

Participant characteristics

	Total N=100	TB[a] N=20	No TB[b] N=80
	n or median (% or IQR)	n or median (% or IQR)	n or median (% or IQR)
Female	48 (48.0)	4 (20.0)	44 (55.0)
Age	38 (30-44)	32 (28-37)	39 (30-47)
Smoker (any)	6 (6.0)	1 (5.0)	5 (6.3)
Etoh (any)	21 (21.0)	7 (35.0)	14 (17.5)
HIV-infected	54 (54.0)	6 (30.0)	48 (60.0)
Current ARVs	47 (87.0)	3 (50.0)	44 (91.7)
IPT (ever)	10 (18.5)	0 (0.0)	10 (20.8)
Co-trimoxazole	47 (87.0)	4 (66.7)	43 (89.6)
TB symptoms			
Cough	100 (100.0)	20 (100.0)	80 (100.0)
Weight loss	21 (21.0)	3 (15.0)	18 (22.5)
Fever	85 (85.0)	18 (90.0)	67 (83.8)
Night sweats	82 (82.0)	18 (90.0)	64 (80.0)
History of TB	20 (20.0)	3 (15.0)	17 (21.3)

[a]Either culture or Xpert positive for M. tuberculosis
[b]Both culture and Xpert negative for M. tuberculosis

- ***20% of TB suspects with Xpert or culture confirmed TB***

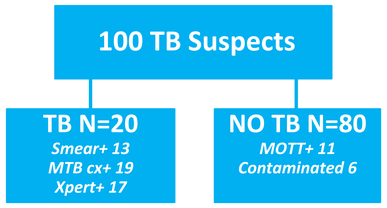


Fig 3. Sputum sample results

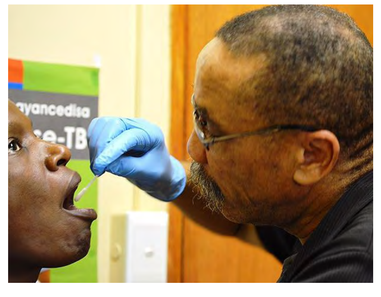


Fig 4. OSA collection
(Source: Kelvin Vollenhoven, South African Tuberculosis Vaccine Initiative)

Mean Cq of OSA swabs by OSA/TB status and visit

	n	Visit 1 mean Cq ± SD	Visit 2 mean Cq ± SD	*p*
OSA+/TB+	13	34.9 ± 2.4	32.5 ± 2.6	0.0008
OSA+/TB-	15	36.3 ± 2.1	35.9 ± 1.3	0.98
OSA-/TB+	7	40.1 ± n/a	41.8 ± n/a	n/a
OSA-/TB-	65	42.0 ± 2.9	40.8 ± 1.8	0.98

- ***Mean OSA Cq lower (stronger signal) among TB cases and at subsequent morning visit***

Mean Cq of OSA swabs by Xpert signal

Xpert result	Visit 1 mean Cq ± SD	Visit 2 mean Cq ± SD
Very low	-	34.8 ± 2.6
Low	38.4 ± n/a	34.4 ± 1.7
Medium	34.8 ± 3.0	32.8 ± 4.4
High	34.6 ± 2.4	29.6 ± 1.9

- ***Mean OSA Cq lower (stronger signal) with higher sputum Xpert signals***

OSA Diagnostic performance by visit

	Sensitivity % (95% CI)	Specificity % (95% CI)
	OSA vs Xpert or Culture	
OSA (any pos)	65.0 (40.8-84.6)	81.3 (71.0-89.1)
Visit 1	50.0 (27.2-72.8)	86.3 (76.7-92.9)
Visit 2	60.0 (36.1-80.9)	92.3 (84.0-97.1)
	OSA vs Xpert alone	
OSA (any pos)	76.5 (50.1-93.2)	81.9 (72.0-89.5)
Visit 1	58.8 (32.9-81.6)	86.7 (77.5-93.2)
Visit 2	70.6 (44.0-89.7)	92.6 (84.6-97.2)

- ***OSA performance appears improved compared to Xpert alone, and on subsequent morning visits vs. enrollment***

OSA Diagnostic performance by HIV status

OSA	Sensitivity % (95% CI)	Specificity % (95% CI)
	OSA vs Xpert or Culture	
HIV+	83.3 (35.9-99.6)	77.1 (62.7-88.0)
HIV-	57.1 (28.9-82.3)	87.5 (71.0-96.5)
	OSA vs Xpert alone	
HIV+	100.0 (47.8-100.0)	77.6 (63.4-88.2)
HIV-	66.7 (34.9-90.1)	88.2 (72.5-96.7)

- ***OSA performance appears improved in HIV+ vs. HIV-, especially compared to Xpert alone***

Limitations

- Limited sample size
- Concurrent South African evaluation showed increased yield with tongue (vs. buccal) swabs
- Limited follow-up: unable to investigate if OSA+ but Xpert/Cx-TB suspects later developed TB

Conclusions

- Detection of Mtb DNA in TB suspects using oral swabs was possible in a high HIV burden setting.
- TB OSA performance appeared improved in HIV+ individuals, and during early morning sampling.
- Despite the lower performance compared to sputum-testing methods, OSA provides a promising means of TB detection for populations that are unable to produce adequate sputum.

References

1. Wood RC, Lubeya AK, Weigel KM, et al. Detection of M. tuberculosis DNA on the oral mucosa of TB patients. *Sci Rep* 2015 Mar 2.
2. Luabeya AK, Wood RC, Shenje J, et al. Non-invasive detection of TB by oral swab analysis. *J Clin Micro* 2018 Dec 12.

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