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Performance of Tongue Swabs for Tuberculosis Diagnosis in Hospitalized Children Under 5 Years of Age

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BACKGROUND – there is a growing interest in NON-SPUTUM based diagnostics

ca. 30 STUDIES
(last 10-15 years)

Wilbur *et al.* 2012
Rosenbaum *et al.* 2012
Meesawat *et al.* 2023

Nicol *et al.* 2015
Ealand *et al.* 2021
Cox *et al.* 2022
Khambati *et al.*, 2025; **Lala *et al.*, 2025**

Wood *et al.* 2015

Luabeya *et al.* 2019

Mesman *et al.* 2020; Molina-Moya *et al.* 2020
Lima *et al.* 2020

Song *et al.* 2021; Wood *et al.* 2021

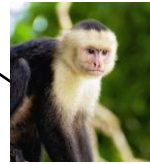
Shapiro *et al.* 2022; Andama *et al.* 2022; LaCourse *et al.* 2022

Ealand *et al.* 2023; Wood *et al.* 2023

Chilambi *et al.* 2024; Ahls *et al.* 2024; Olsen *et al.* 2024

David *et al.*, 2025; Rockman *et al.*, 2025; Olson *et al.*, 2025;
Wang *et al.*, 2025; Chilambi *et al.*, 2025; Bezuidenhout *et al.*,
2025; Ntombela *et al.*, 2025; Mendelson *et al.*, 2025; Wood *et al.*,
2025; Singh *et al.*, 2026

Monkeys



Children



Adults



SUMMARY

Swabs associated with variable sensitivity to detect *Mtb* (13-98%)

Specificity is relatively high (80-100%)

qPCR assays target *IS6110* or *IS1080* insertion elements

TONGUE swabs retrieve best yield of material for testing (relatively)

Swab type doesn't influence capture significantly

Alternative sampling type for adults, children & animals

Testing on GeneXpert – poor yield
Multiple swabs & Time of collection

Oral wash / rinse as an alternative to oral swabs

Studies (in South Africa) show high acceptability amongst patients & healthcare workers

How is TB typically diagnosed in young children?

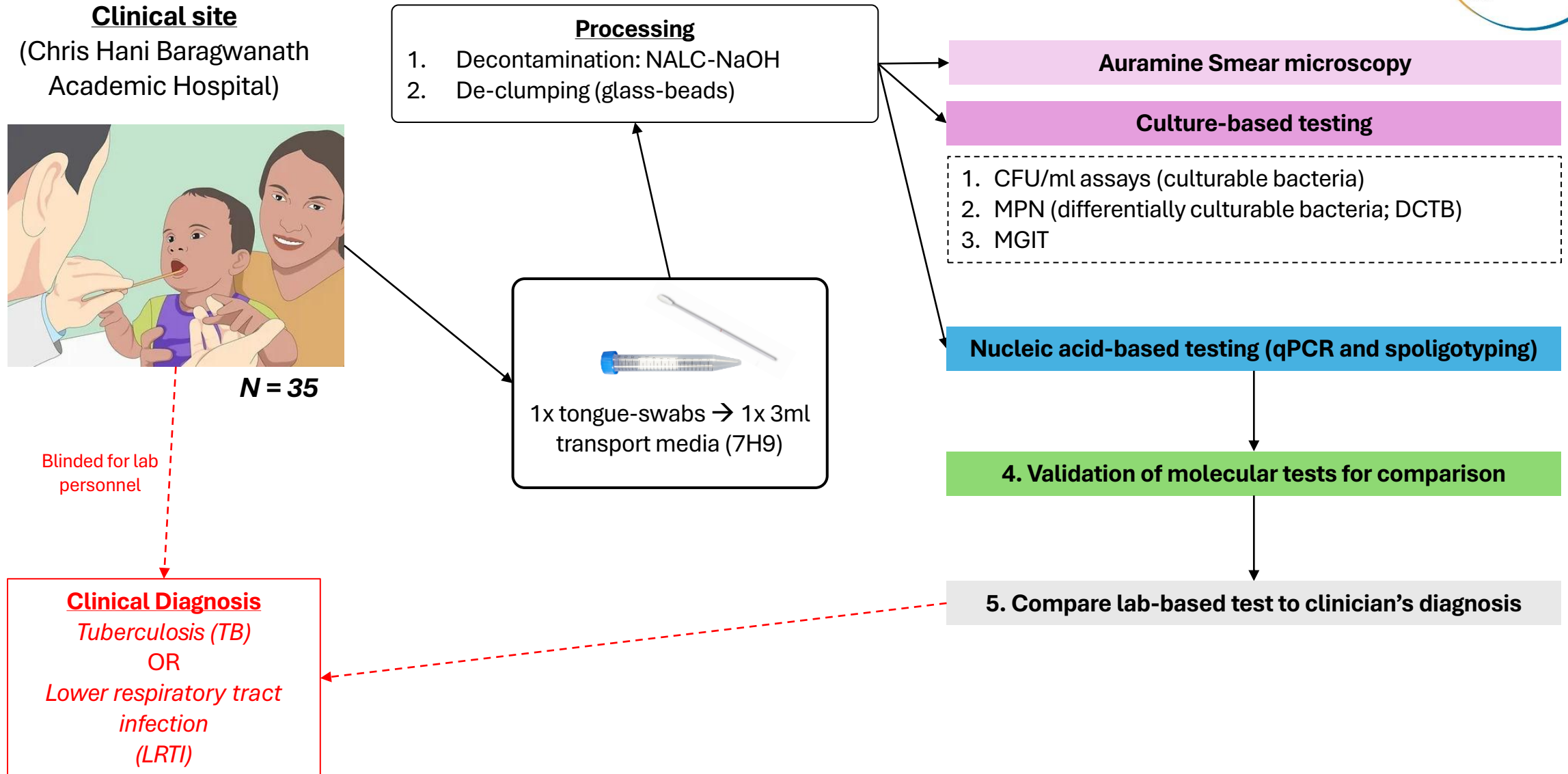
Relies on a "symptom analysis" rather than a single definitive test, as children rarely have enough bacteria in their sputum to test positive.

- Several interconnected diagnostic methods:
 1. **Symptom and Exposure Screening:** History (close contact with anyone who has active TB within the last 5 years); Persistent unexplained fever; Cough lasting more than 2-3 weeks; Weight loss.
 2. **Immune System Tests:** TST or IGRA
 3. **Imaging:** Chest X-ray (characteristic signs of TB in the lungs or enlarged lymph nodes).
 4. **Specimen testing:** Swallow respiratory secretions (instead of coughing up). Gastric wash to obtain stomach fluids for culture/GX or direct stool testing.

Rationale: Diagnosing TB in young children is challenging & extremely invasive. Can we improve this via alternative sampling approaches?



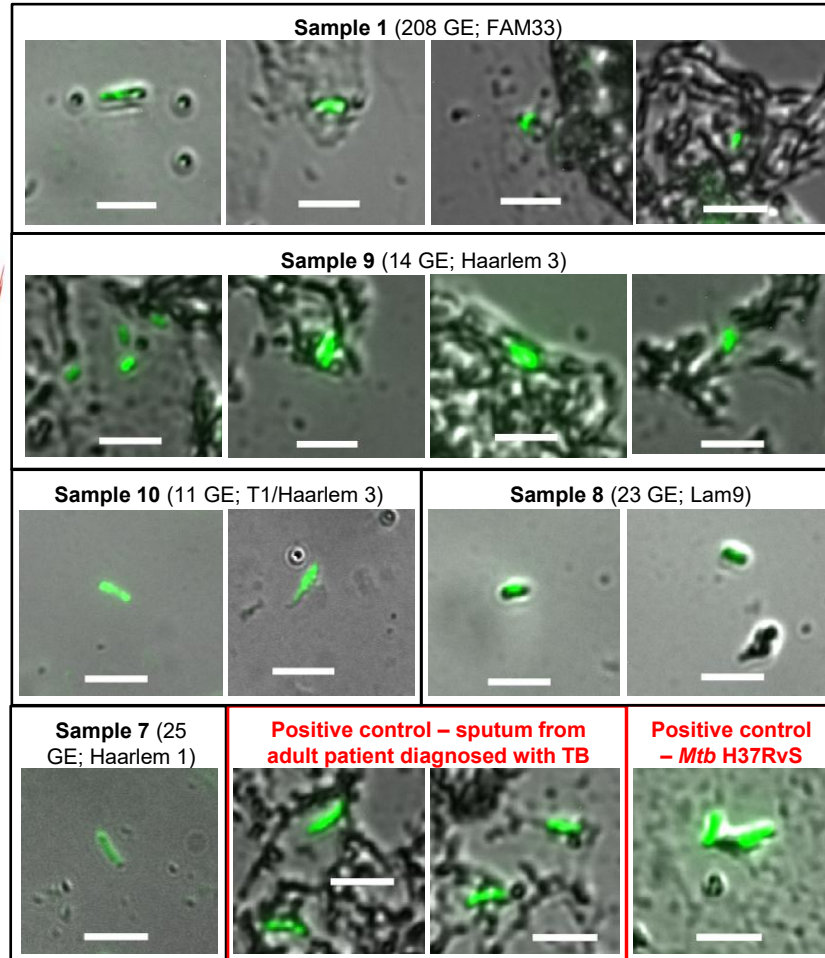
PILOT - The utility of oral swabs to detect TB in hospitalized babies (under 5 years of age)



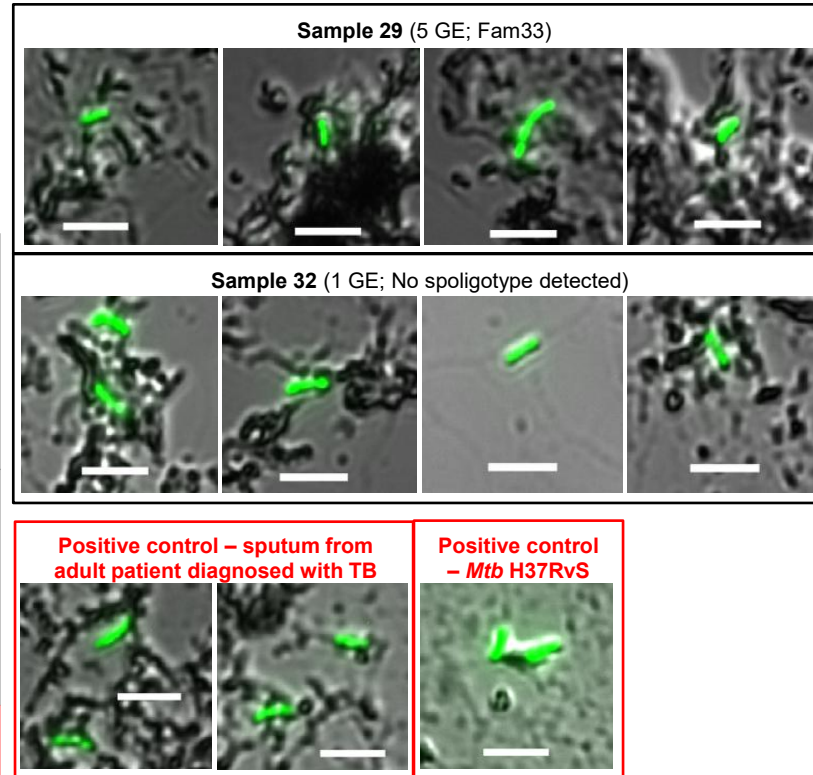
PILOT - The utility of oral swabs to detect TB in hospitalized babies (under 5 years of age)

Examples of smear positivity (using Auramine staining)

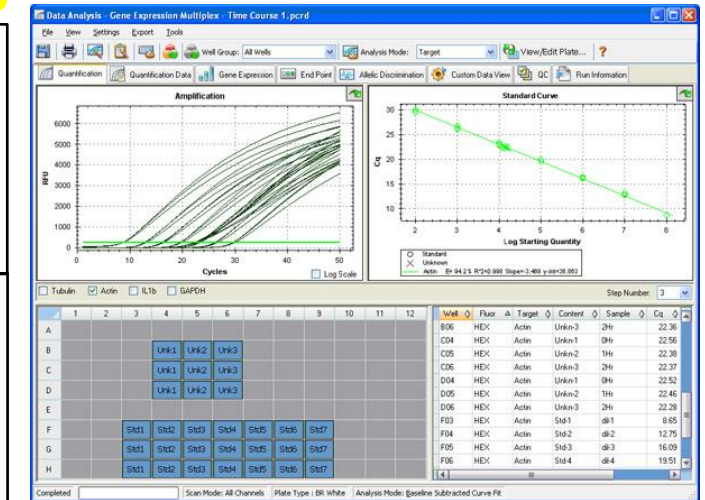
(A) Tuberculosis



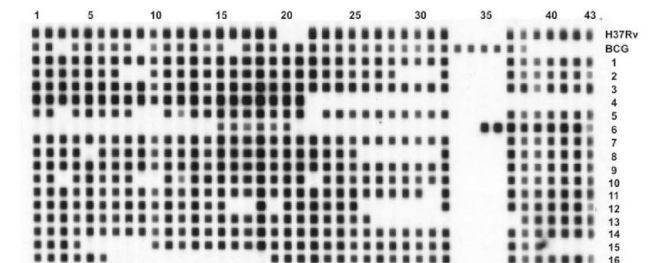
(B) Lower Respiratory Tract Infection



qPCR positive

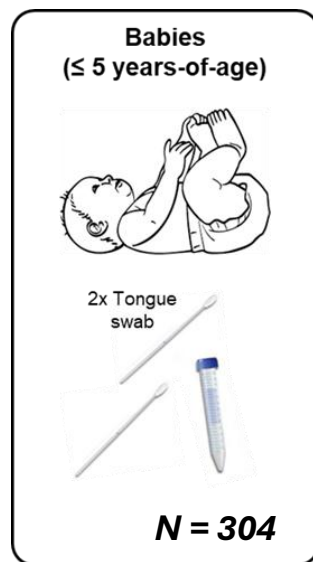


Genotyping = MTBC



Whole *Mtb* bacilli present in the mouth – found by using a tongue swab (42% concordance with clinical TB diagnosis)

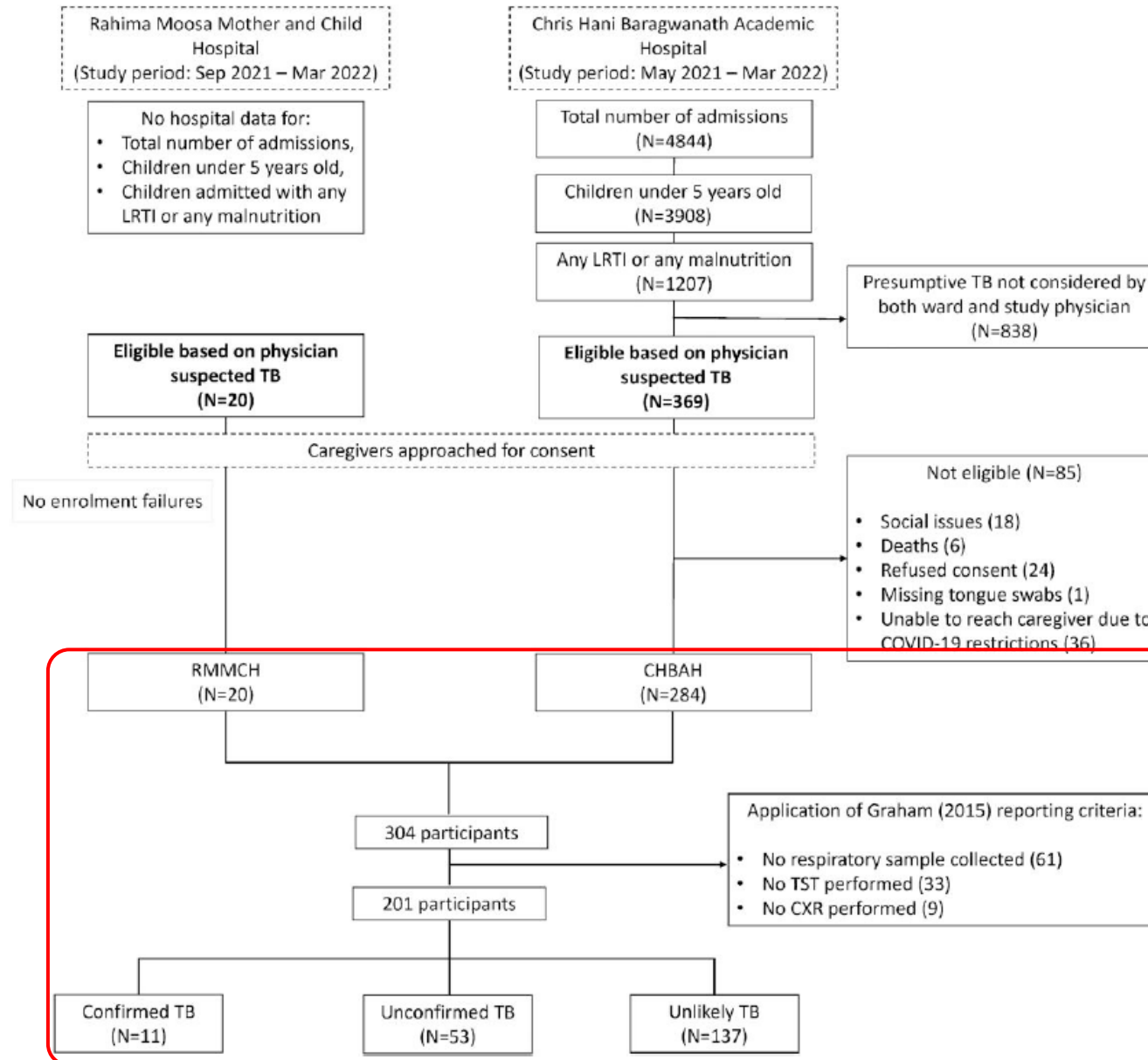
The utility of oral swabs to detect TB in hospitalized babies (under 5 years of age)



Culture-based testing

Auramine Smears

Nucleic acid-based testing (qPCR and GX)



Baseline (no follow ups)

All would have been started on antibiotics (hospitalized for a respiratory infection)

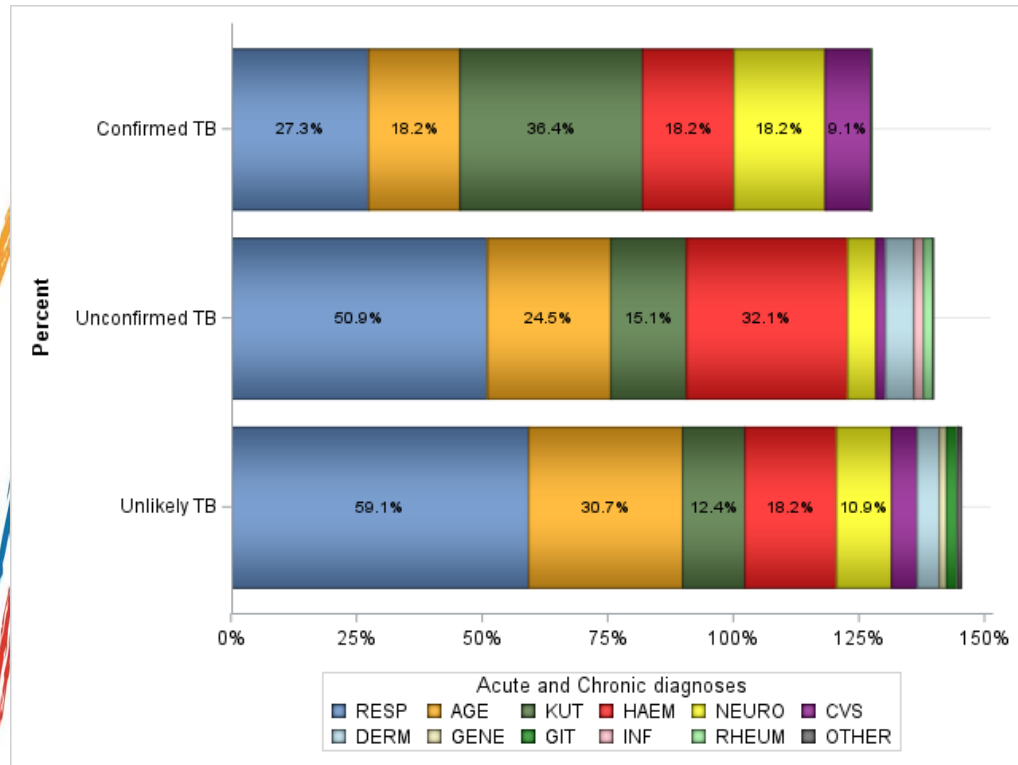
Patient Demographics



	All children (n=201; 100%)	Confirmed TB (n=11; 5.5%)	Unconfirmed TB (n=53; 26.4%)	Unlikely TB (n=137; 68.2%)	P-Value
Male gender (%)	121 (60.2)	5 (45.5)	33 (62.3)	83 (60.6)	0.5767
Median age [months: IQR]	13.1 (7.9-20.0)	11.1 (7.1-22.2)	13.3 (9.5-26.5)	12.8 (7.4-18.3)	0.1994
Hospital Participant enrolled					
CHBAH (%)	185 (92.0)	7 (63.6)	51 (96.2)	127 (92.7)	0.0012
RMMCH (%)	16 (8.0)	4 (36.4)	2 (3.8)	10 (7.3)	
Nutritional status [n, Median (IQR)]					
Weight for Age Z-Score	200, -2.5 (-4.1, -1.0)	11, -3.9 (-5.1, -1.7)	53, -2.1 (-3.6, -1.0)	136, -2.5 (-4.1, -1.0)	0.2585
Length/Height for Age Z-Score	199, -2.2 (-3.8, -1.0)	11, -3.3 (-5.0, -0.5)	53, -2.0 (-3.5, -0.9)	135, -2.2 (-3.9, -1.1)	0.3045
Weight for Height Z-Score	199, -1.6 (-3.3, -0.2)	11, -2.2 (-4.5, 0.4)	53, -1.8 (-3.3, -0.6)	135, -1.4 (-3.2, -0.2)	0.5534
Severe acute malnutrition	94 (46.8)	9 (81.8)	29 (54.7)	56 (40.9)	0.0130^a
HIV status					
Living with HIV (%)	39 (19.4)	4 (36.4)	18 (34.0)	17 (12.4)	0.0017^b
Exposed but negative (%)	56 (27.9)	5 (45.5)	10 (18.9)	41 (29.9)	
Unexposed (%)	106 (52.7)	2 (18.2)	25 (47.2)	79 (57.7)	
Hospital stay (days) [Median (IQR)]:	8.00 (5.00-18)	21.00 (4.00-28)	8.00 (5.00-22)	7.00 (5.00-14)	0.1224
Death in hospital	5 (2.5)	1 (9.1)	1 (1.9)	3 (2.2)	0.3488
Contact with person with TB in past 3 months	8 (4.0)	2 (18.2)	3 (5.7)	3 (2.2)	0.0254^c
Previous TB diagnosis	3/200 (1.5)	0	2 (3.8)	1/136 (0.7)	0.2780
Cough	143 (71.1)	9 (81.8)	38 (71.7)	96 (70.1)	0.7065
Cough duration (days) [n, Median (IQR)]	104, 5.00 (3.00-14)	8, 16.00 (2.50-46.5)	31, 7.00 (4.00-20)	65, 5.00 (3.00-7)	0.1536
Self-reported weight loss	102/199 (50.8)	9 (81.8)	35 (66.0)	58/135 (42.3)	0.0092^d
Visible BCG vaccine scar	132 (65.67)	8 (72.73)	39 (73.58)	85 (62.04)	0.2721
TB treatment (started this admission)	73 (36.3)	11 (100)	53 (100)	9 (6.6)	<.0001^e

Complexity of detecting TB in young children

Co-existing acute and chronic diseases



Tongue swab Ultra results



	Negative (n=85)	Trace (n=90)	Very low (n=21)	Low/Medium* (n=5)	Positivity rate
Confirmed TB (n=11)	4 (4.7%)	4 (4.4%)	0	3* (60)	7/11 (63.6%)
Unconfirmed TB (n=53)	22 (25.9%)	23 (25.6%)	8 (38.1)	0	31/53 (58.5%)
Unlikely TB (n=137)	59 (69.4%)	63 (70%)	13 (61.9)	2 (40)	78/137 (56.9%)
Air swab controls (n=8)	7 (87.5%)	1 (12.5%)	0	0	1/8 (12.5%)

*One under-five had a 'medium' result; the rest were 'low'

Tongue swab Ultra results in hospitalised under-fives with confirmed TB, unconfirmed/unlikely TB, and no TB



Trace regarded as **positive**

	Confirmed + Unconfirmed TB	Unlikely TB	
Positive	38	78	116
Negative	26	59	85
	64	137	301

Trace regarded as **negative**

	Confirmed + Unconfirmed TB	Unlikely TB	
Positive	11	15	26
Negative	53	122	175
	64	137	201

P value (χ^2):	0.7442	0.2195
Sensitivity:	59.4% (95% CI: 47.3 – 71.4)	17.2% (95% CI: 7.9 to 26.4)
Specificity:	43.1% (95% CI: 34.8 to 51.4)	89.1% (95% CI: 83.8 to 94.3)
PPV:	32.8% (95% CI: 24.2 to 41.3)	42.3% (95% CI: 23.6 to 61.3)
NPV:	69.4% (95% CI: 59.6 to 79.2)	69.7% (95% CI: 62.9 to 76.5)

As an additional diagnostic test, tongue swabs tested on Xpert increased TB detection rates in under-fives with unconfirmed and unlikely TB

***Caveat: Gold standard (gastric aspirate + culture = low sensitivity)**

Lala et al. (2025) Performance of Tongue Swabs for Tuberculosis Diagnosis in Hospitalized Children Under 5 Years of Age. Open Forum Infect Dis. 2025 Aug 20;12(9):ofaf474. DOI: 10.1093/ofid/ofaf474 (**EDICT-2**)

What does this mean for TB testing in children (clinical implications)?



- Accurate diagnosis of TB is essential for appropriate management of TB disease
- Diagnosis of TB disease is difficult in **children under 5** years of age OR in **PLWH** – sputum is difficult sample to obtain (but remains gold standard)
 - **Gold standard (gastric aspirate + culture = low sensitivity)**
- Tongue **swabs retrieve less bacteria** (than sputum) – ROUTINE CLINICAL TESTS will be adversely impacted
- **Swabs** could have utility for **active case finding** where large numbers of people are **screened**
- **Complementary sample** instead of sputum replacement
- Tongue swab detected TB in children where **routine tests missed them** (increased confirmed TB in 12% of children)

What does this mean for TB testing in children (clinical implications)?



- In under 5's, any increase is **very significant**
 - When they do get TB, it tends to be severe
 - Paucibacilliary
 - TB in adults and children are not the same
 - New tests are developed/tested on adults
- **Easy to collect** (oral rinse on young children would be challenging)
 - Cost issue in resource-limited settings
- Issue of **TRACE**
 - Adults = previous TB or sub-clinical disease
 - Children = tough to interpret (wards or lab processing)
 - **No follow up** in this cohort
- Requires further optimization (**larger studies; multiple swabs; time of sampling**) before integration into standard diagnostic platforms

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