Sequential & Parallel Testing for the Microbiological Diagnosis of TB Disease in Children: A Prospective Diagnostic Accuracy Cohort in Low- and Middle- Income Countries

Zoe Franckling-Smith, Laura Olbrich, Leyla Larsson, Issa Sabi, Nyanda Ntinginya, Celso Khosa, Denise Banze, Marriott Nliwasa, Elizabeth Corbett, Robina Semphere, Valsan Verghese, Joy Michael, Marilyn Ninan, Elmar Saathoff, Timothy McHugh, Alia Razid, Stephen Graham, Rinn Song, Pamela Nabeta, Andre Trollip, Mark Nicol, Michael Hoelscher, Christof Geldmacher, Norbert Heinrich, Heather Zar. On behalf of the RaPaed-AIDA-TB consortium

Background

Microbiological confirmation of TB in children may be challenging, especially in young children, those with malnutrition and those living with HIV. However, microbiological diagnosis may enable rapid initiation of treatment, including for DR-TB.

Objective

To investigate optimal sampling & testing strategies to microbiologically confirm TB in children

Methods

- Prospective study enrolling children (<15yrs) with suspected TB from 5 low-middle income countries; South Africa, Tanzania, Malawi, Mozambique & India
- Samples collected: 2 sputum/gastric lavage
  1 NPA if <5yrs
  Extrapulmonary specimens according to local guidelines
- Confirmed TB if MTB detected on Ultra &/or culture
- Incremental yield calculated in children with samples tested by Ultra & two serial cultures

Results

- 965 participants with valid microbiological results, median age 5.0 years (IQR 1.8–9.0)
- 2299 samples collected, 93.8% (2157) respiratory specimens:
  - 59% (1273/2299) induced sputa
  - 18% (389/2299) spontaneous sputa
  - 15% (332/2299) NPA
  - 7% (151/2,299) GL
- Microbiological confirmation obtained in 36.2% (239/661) of children with TB disease

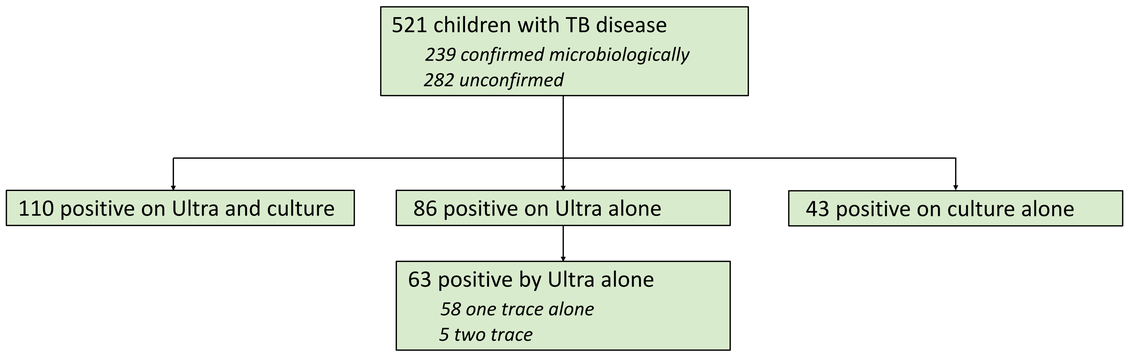
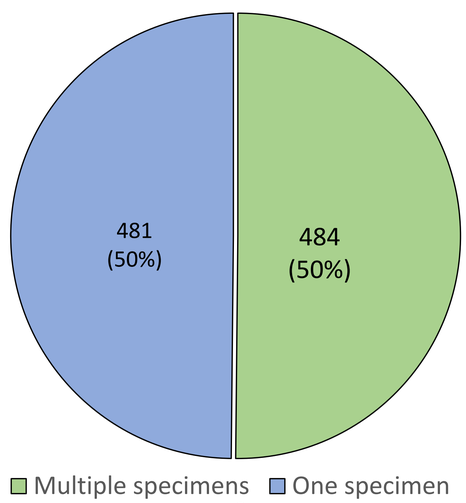


Figure 1: Overview of microbiological confirmation

- Microbiological confirmation in vulnerable subgroups:
  - < 5 years: both Ultra & culture 36/97 (37%), Ultra alone 45 (46%), culture alone 16 (16%)
  - Children with HIV: both 6/24 (25%), Ultra alone 8 (33%), culture alone 10 (42%)
  - SAM: both 21/30 (70%), Ultra alone 6 (20%), culture alone 3 (10%)



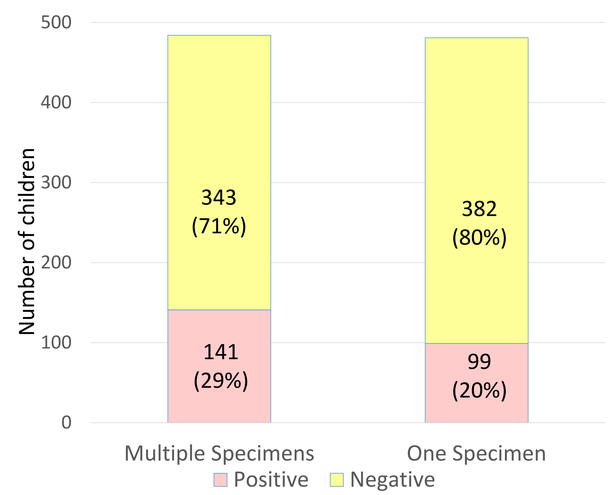


***Figure 2: Mycobacterium tuberculosis* results for the overall cohort by number of specimen types collected**
(A) Distribution of specimen collection count; (B) Proportion of Mycobacterium tuberculosis results by number of specimen types collected

	All children				Children with HIV				Children with SAM			
	Total	Test positive	Add. yield	Cum. yield	Total	Test positive	Add. yield	Cum. yield	Total	Test positive	Add. yield	Cum. yield
All children with PTB disease												
Any respiratory specimen types combined												
First Ultra	447	124	NA	28%	87	11	NA	13%	62	26	NA	42%
First culture	447	94	21	32%	87	12	6	20%	62	19	2	45%
Second culture	447	93	22	37%	87	9	2	22%	62	18	2	48%
Sputum												
First Ultra	420	112	NA	27%	86	10	NA	12%	54	19	NA	35%
First culture	420	79	15	30%	86	12	6	19%	54	12	1	37%
Second culture	420	80	22	36%	86	9	2	21%	54	13	2	41%
Children aged <5 years in the overall cohort												
First Ultra on NPA	129	19	NA	15%	14	3	NA	21%	13	3	NA	23%
First sputum Ultra	129	37	22	32%	14	4	1	29%	13	5	2	39%
First sputum culture	129	23	2	33%	14	3	0	29%	13	4	0	39%
Second sputum culture	129	23	7	39%	14	3	0	29%	13	3	0	39%

Table 1: Incremental yields of Ultra, first & second cultures on serial samples in children PTB disease, and in those <5 years
Incremental yield calculated for children with PTB disease, both confirmed and unconfirmed, & at least one serial Ultra and culture each. Those with EPTB only were excluded. For all with PTB, denominator is number with a result for first Ultra & first culture. For those <5 years, denominator is number with a result for first Ultra on NPA, first sputum Ultra, & first sputum culture

Conclusions

- One of the highest rates of microbiological confirmation reported in children
- Most confirmed via Ultra (most commonly trace), except in those with HIV or SAM
- Parallel sampling & concurrent testing increased detection, even among vulnerable subgroups

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