

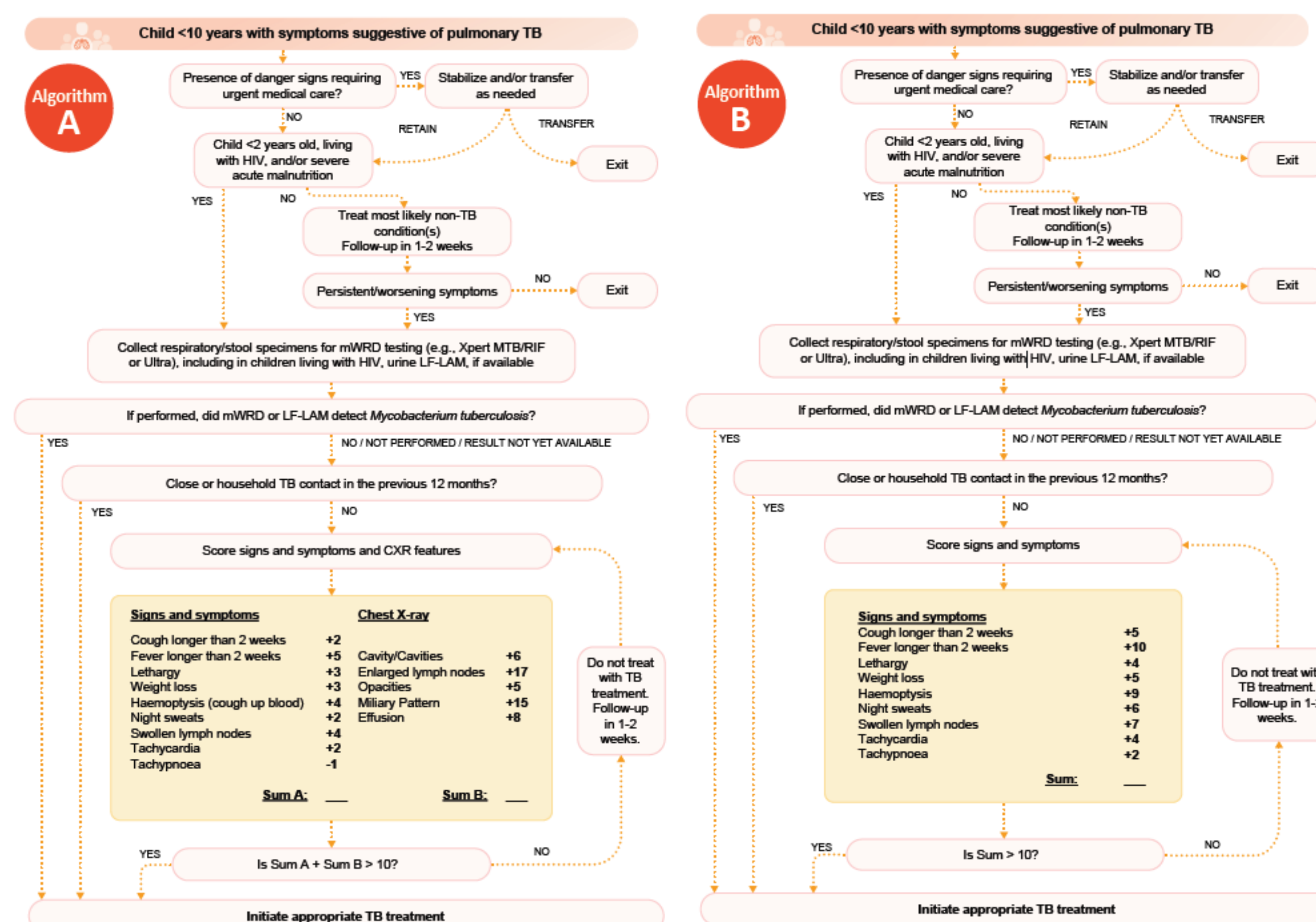
# DIAGNOSTIC PERFORMANCE AND FEASIBILITY OF TWO NEW TREATMENT DECISION ALGORITHMS FOR PULMONARY TUBERCULOSIS IN CHILDREN: A DIAGNOSTIC AND MIXED-METHODS MULTI-COUNTRY STUDY

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## BACKGROUND AND OBJECTIVES

- It is estimated that at least 1 million children become ill with tuberculosis (TB) each year
- Under-diagnosis and subsequent under-treatment of TB in children** remain a major public health issue
  - 60% of children with TB are not diagnosed and 96% of children who die with TB were not on treatment
  - Several contributing factors, including non-specific clinical presentation, difficult collection of respiratory specimens, paucibacillary nature of TB in children leading to less frequent bacteriological confirmation.
- In **2022**, the **World Health Organization (WHO)** introduced **new treatment decision algorithms for pulmonary TB in children**, incorporating clinical and laboratory features, and where available, radiography.
- WHO called for generation of evidence on the diagnostic performance and the feasibility of implementing these algorithms in real conditions.
- Objective:** We initiated a study to prospectively evaluate the diagnostic performance, describe the diagnostic cascade, and assess the feasibility of implementing these new algorithms for pulmonary TB in children under 10 years old under programmatic conditions in five sub-Saharan African countries with high TB burden.
- Here, we present interim results describing steps of the diagnostic cascade observed using the TB treatment decision algorithms in Niger, Nigeria, South Sudan and Uganda.**



Child investigated for TB in Mbarara, Uganda (Picture taken with the consents of the nurses and the child's mother)

## METHODS/STUDY DESIGN

- Prospective observational diagnostic study
- Study population and setting: ambulatory or hospitalized patients age less than 10 years with signs or symptoms suggestive of pulmonary TB
  - with acute malnutrition in Madarounfa, Niger and Maiduguri, Nigeria
  - from a general pediatric population in Malakal, South Sudan and Mbarara, Uganda
- Targeted sample size: at least 2,020; Enrolment started in August 2023 and will continue until December 2024.
- Children assessed according to the treatment decision algorithm, including:
  - Clinical examination
  - Laboratory tests (GeneXpert on respiratory or stool sample; urine TB-LAM for children living with HIV; *Mycobacterium* culture where available)
  - Chest X-ray, where available
  - Scoring and decision to treat for TB according to the WHO treatment algorithms (A: with X-ray; B: without X-ray)
- Data collection at initial assessment, 7 to 14 days later for children not initiated on TB treatment at first visit, and at 2-month follow-up

## RESULTS

Table. Baseline characteristics, medical follow-up and TB treatment initiation

Characteristics at admission	Niger	Nigeria	South Sudan	Uganda	Total
<b>Enrolled patients</b>	<b>n=74</b>	<b>n=107</b>	<b>n=14</b>	<b>n=116</b>	<b>n=311</b>
Female	29 (39%)	44 (41%)	9 (64%)	59 (51%)	141 (45%)
Age (years), median (IQR)	1.4 (0.8 - 1.9)	2 (1 - 4)	3 (1.3 - 5)	2 (0.8 - 5)	1.8 (0.8 - 3.8)
Living with HIV	0	1 (1%)	2 (14%)	12 (10%)	15 (5%)
Severe acute malnutrition	74 (100%)	105 (98%)	12 (86%)	33 (28%)	224 (72%)
Inpatients	70 (95%)	107 (100%)	8 (57%)	27 (23%)	212 (68%)
<b>Medical visits and main reason for starting TB treatment</b>					
Patients scheduled for a second visit	60 (81%)	98 (92%)	6 (43%)	89 (77%)	253 (81%)
of which attended the 2 <sup>nd</sup> visit	38 (63%)	66 (67%)	2 (33%)	70 (79%)	176 (70%)
<b>TB treatment initiation at any time</b>	<b>16 (22%)</b>	<b>20 (19%)</b>	<b>10 (71%)</b>	<b>30 (26%)</b>	<b>76 (24%)</b>
<b>TB treatment initiation at the first visit</b>	<b>14 (19%)</b>	<b>9 (8%)</b>	<b>8 (57%)</b>	<b>27 (23%)</b>	<b>58 (19%)</b>
<b>Main reason for TB treatment initiation (at any time, n=76)</b>					
Positive GeneXpert	2 (13%)	3 (15%)	0	1 (3%)	6 (8%)
Positive TB-LAM (only if living with HIV)	0	0	0	2 (7%)	2 (3%)
Being a contact of a TB patient	2 (13%)	1 (5%)	1 (10%)	7 (23%)	11 (14%)
Algorithm A (with X-ray) score > 10	11 (69%)	7 (35%)	0	11 (37%)	29 (38%)
Algorithm B (without X-ray) score > 10	0	9 (45%)	9 (90%)	9 (30%)	27 (36%)
Clinical suspicion	1 (6%)	0	0	0	1 (1%)

- This **preliminary** analysis covers 311 enrolled patients, 154 of whom had completed their study participation, including 19 deaths (database of the 25<sup>th</sup> of March 2024).
- A **GeneXpert** test was performed on stool for 259 (83%) children, on gastric aspirate for 184 (59%) children, on nasopharyngeal aspirate for 41 (13%) children, and on sputum for 20 (6%) children; 272/311 (88%) children had  $\geq 1$  sample analyzed. The GeneXpert result was positive in 10/272 (3.7%) children with  $\geq 1$  sample, 7/259 (2.7%) with stool, 6/184 (3.3%) with gastric aspirate, 1/41 (2.4%) with nasopharyngeal aspirate, and 0/20 (0.0%) with sputum.
- A **chest X-ray** was taken for 135 (43%) patients, allowing the use of algorithm A. The interpretation of 61/135 (45%) X-rays was highly or possibly suggestive of active TB.
- Most TB treatments were initiated **at the first contact** with the patient (58/76, 76%) based on the algorithm scores (74% of main reasons). Laboratory results accounted for 11% of the main reasons for initiating TB treatment.

## DISCUSSION/CONCLUSION

- The scores of algorithm A and B, based on clinical and radiological observations, triggered the majority of decisions to initiate anti-TB treatment in the study population. The systematic use of the algorithms also strengthened TB screening and enabled a prompt initiation of anti-TB treatment at first contact with patients. These interim results underline the continued importance of a multifaceted approach in diagnosing TB in children, not relying on imaging or lab tests alone. They also suggest the relevance of an enhanced follow-up for children with signs or symptoms suggestive of pulmonary TB in whom TB treatment is not initiated at first contact.
- The study results will be communicated to the involved Ministries of Health and to the WHO, to shape future recommendations. Further results of this prospective observational diagnostic study will also allow assessing the performance of these algorithms.

**ETHICS STATEMENT:** This study has been reviewed and approved by the MSF Ethics Review Board (ERB), the CNERS of Guinea, the CNERS of Niger, the NHREC of Nigeria, the MOH-RERB of South Sudan, the MUST-REC and UNCST of Uganda.