TB-Speed

Emerging experiences with diagnostic approaches in children with HIV, severe pneumonia and malnutrition

Feasibility of NPA, stool collection, and Ultra testing for microbiological diagnosis

Dr. Chishala Chabala, University of Zambia

Annual meeting of the Child and Adolescent TB working group
16 October 2020

Child & Adolescent TB Working Group

université de BORDEAUX | Inserm | BORDEAUX POPULATION HEALTH Centre de Recherche - U1219 | IDLIC / Infectious diseases in lower-income countries | anrs France REcherche Nord & sud Sida-hiv Hépatites Agence autonome de l'Inserm | INITIATIVE 5% SIDA, TUBERCULOSE, PALUDISME | Unitaid

TB-Speed project

- Goal (impact)
  - Contribute to the reduction in childhood mortality from TB
- Outcome
  - Feasible and cost-effective strategy using innovative diagnosis tools and decentralized approaches improving childhood TB diagnosis in high TB-burden settings
- Research project implemented in 7 countries
  - Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, Uganda, Zambia

ANRS France REcherche Nord & sud Sida-hiv Hépatites
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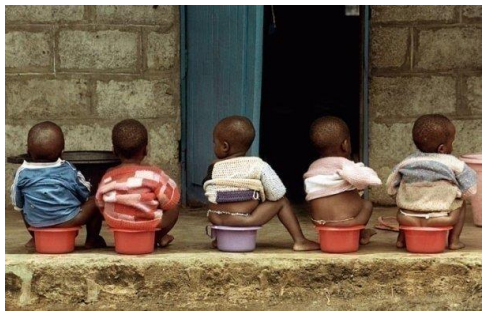
Microbiological diagnosis approach

Nasopharyngeal aspirates (NPA)

& Stool samples

High feasibility and good Dx performance with Xpert MTB/RIF

Now recommended by WHO (2020)



Molecular testing using Xpert MTB/RIF Ultra

GeneXpert G4

Battery-operated G1 Edge

TB lab

Wards or PHCs

Highly vulnerable children in TB speed

- Children with HIV-infection, severe acute malnutrition (SAM), severe pneumonia
  - High risk of TB disease
  - High risk of death
  - High risk of under-diagnosis

- 3 studies targeting specifically these 3 groups in TB-Speed
  - TB-Speed **Pneumonia**: children <5 years hospitalized with WHO-defined severe pneumonia
  - TB-Speed **SAM**: children <5 years hospitalized for severe acute malnutrition
  - TB-Speed **HIV**: HIV-infected children <15 years with presumptive TB

Preliminary results focusing on the feasibility of NPA and stool sample collection and Xpert Ultra testing for TB diagnosis in vulnerable children

TB-Speed Pneumonia: study design

- **Primary objective**: to evaluate the **impact on all-cause mortality at 12 weeks** of adding the systematic early detection of TB with Xpert Ultra, performed on one NPA and one stool sample (followed by immediate TB Tx if positive, to the WHO SOC in young children with severe pneumonia, as compared to the SOC alone.
- **Cluster-randomized trial, stepped wedge design**
- **15 tertiary level hospitals, 6 high TB incidence countries** (CI, CM, MZ, UG, ZM, and KH)
- **3780 children**
  - Aged 2 to 59 months
  - Newly hospitalized for severe pneumonia defined using WHO criteria
- **Control arm**: the WHO standard of care (SOC)
- **Intervention:** in addition to the SOC,
  - → Xpert Ultra performed immediately upon admission on 1 NPA and 1 stool sample
  - → Immediate TB treatment initiation if Ultra positive

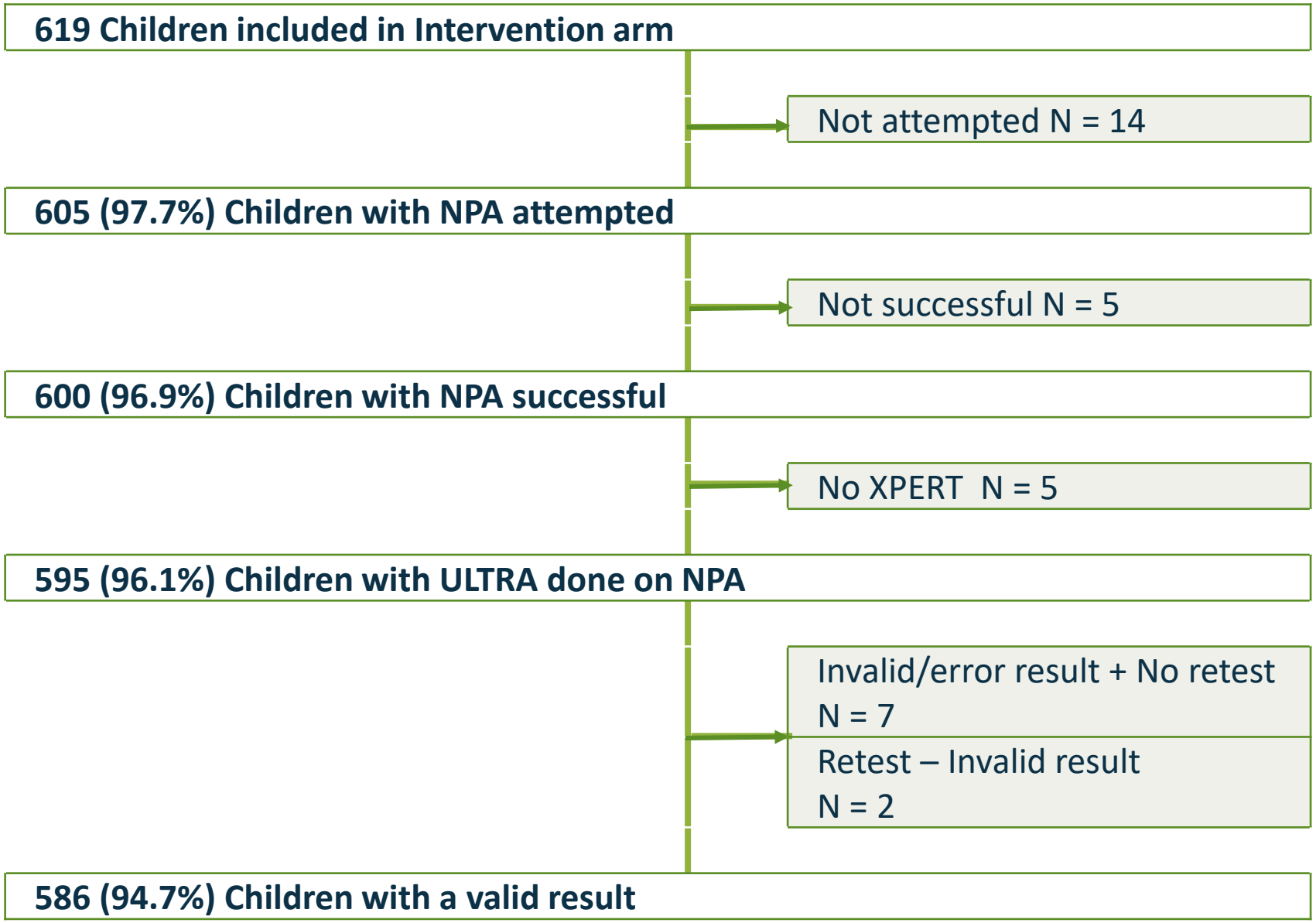
TB-Speed Pneumonia: Baseline characteristics – Comorbidities

	Overall (N = 1940)
	n(%) or median [IQR]
Gender (F)	830 (42.8%)
Age (months)	11 [5, 20]
Tachypnea*	1068 (55.1%)
Respiratory rate	48 [38, 58]
Peripheral O_2 saturation	93 [88, 97]
Positive HIV test	103 (5.3%)
Malaria test	158 (8.1%)
Severe Acute Malnutrition**	383 (19.7%)

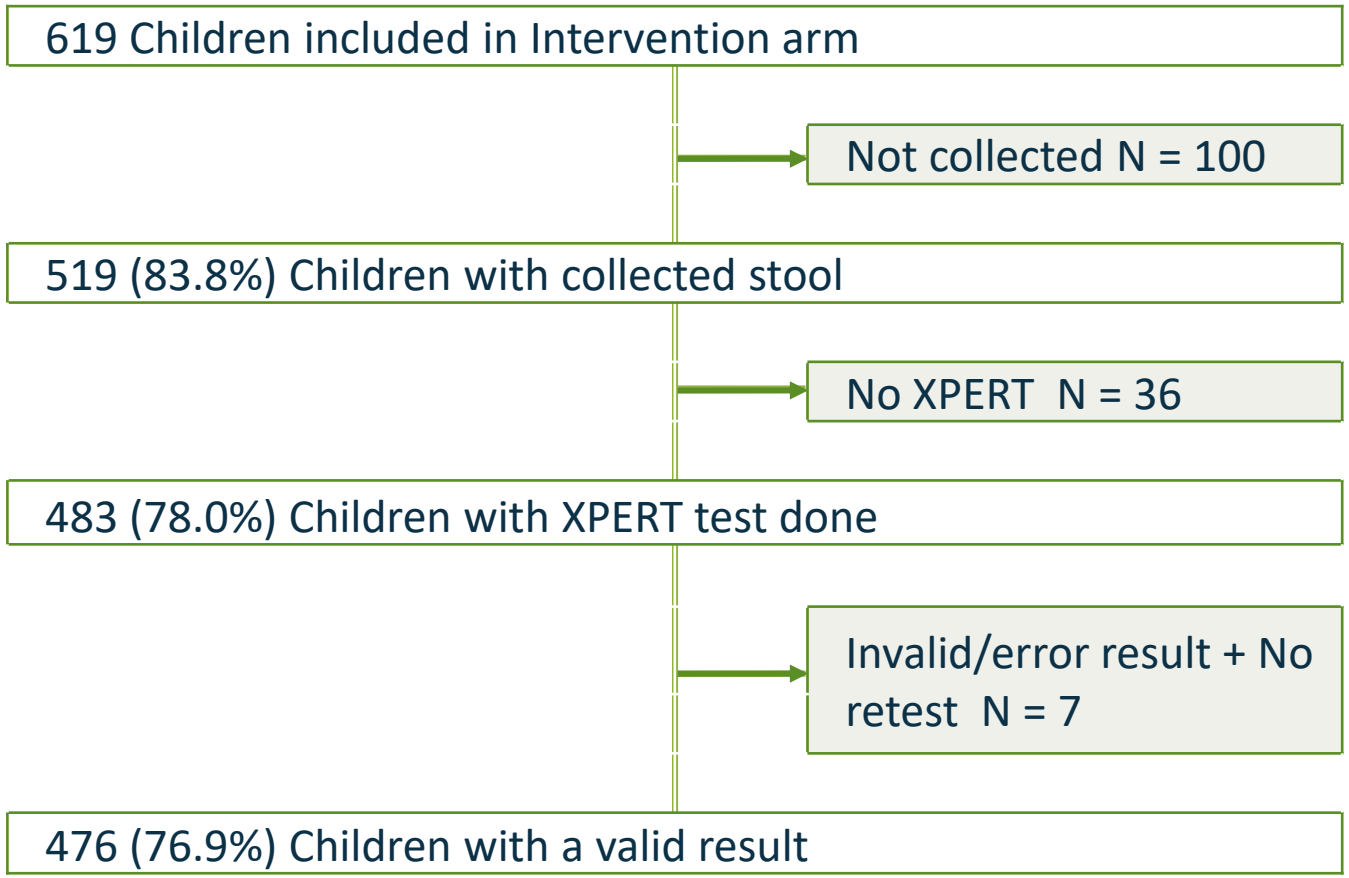
* Defined by children aged 0-11 with RR > 50 ; children aged 12-35 with RR > 40 ; children aged 36-60 with RR > 30

* WHZ < -3SD and/or MUAC < 115 and/or Presence of edema

NPA – collection and Xpert testing feasibility



Stool – collection and Xpert testing feasibility



TB-Speed HIV: study design

- **Primary objective**: To evaluate the **proportion of missed TB cases** (i.e. false negative) in HIV-infected children with presumptive TB not initiated on treatment as per the PAANTHER TB treatment decision algorithm

- **External validation study:** prospective, multicenter management study evaluating the safety and feasibility of the **PAANTHER TB treatment decision algorithm** for HIV-infected children with presumptive TB

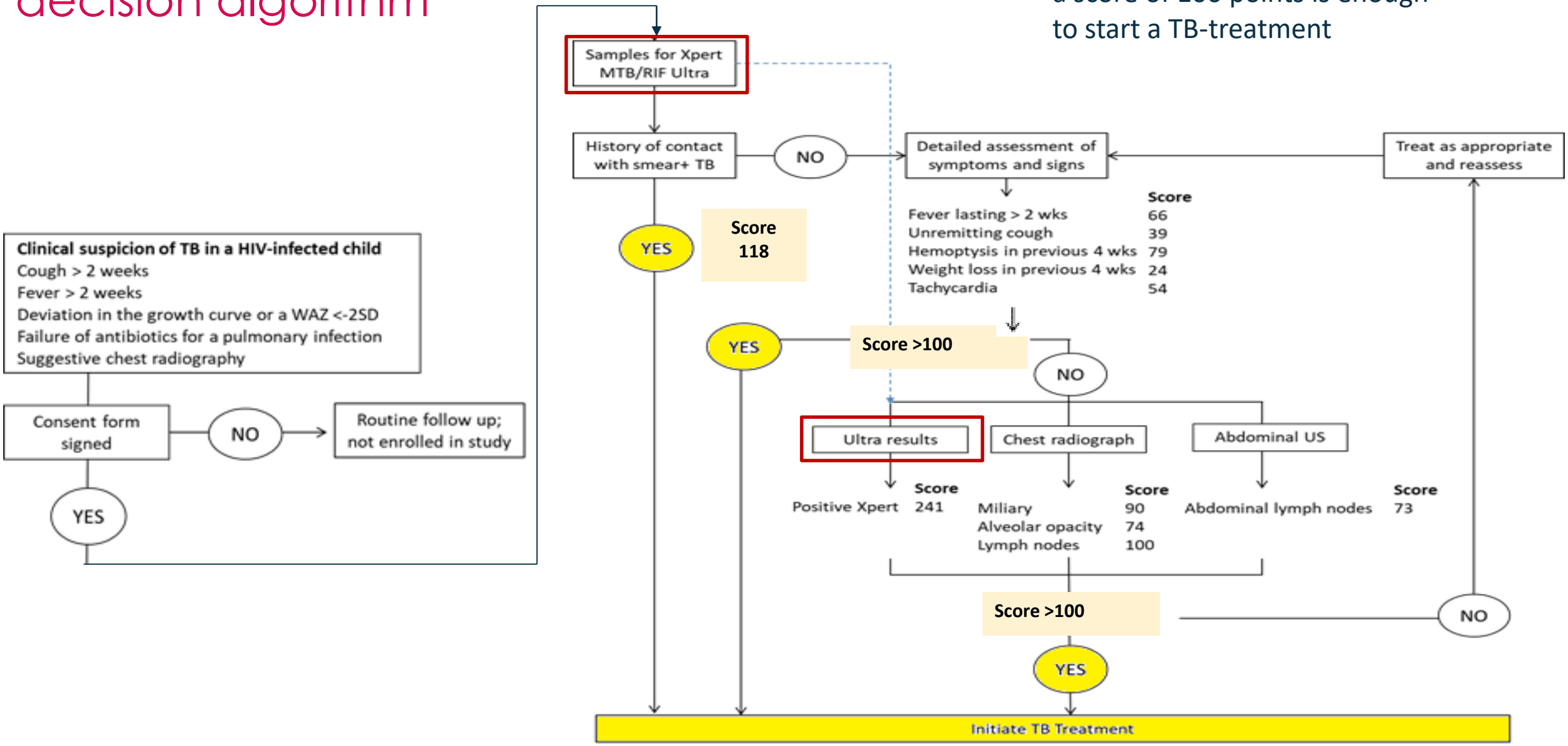
- **7 hospitals, 4 countries** (CI, UG, MZ, ZM) that did not participate in the PAANTHER study

- **550 HIV-infected children**
  - Aged 1 month to 14 years
  - With presumptive TB based on the PAANTHER inclusion criteria

Marcy O et al. A treatment decision score for HIV-infected children with suspected tuberculosis. Pediatrics 2019

The PAANTHER TB treatment decision algorithm

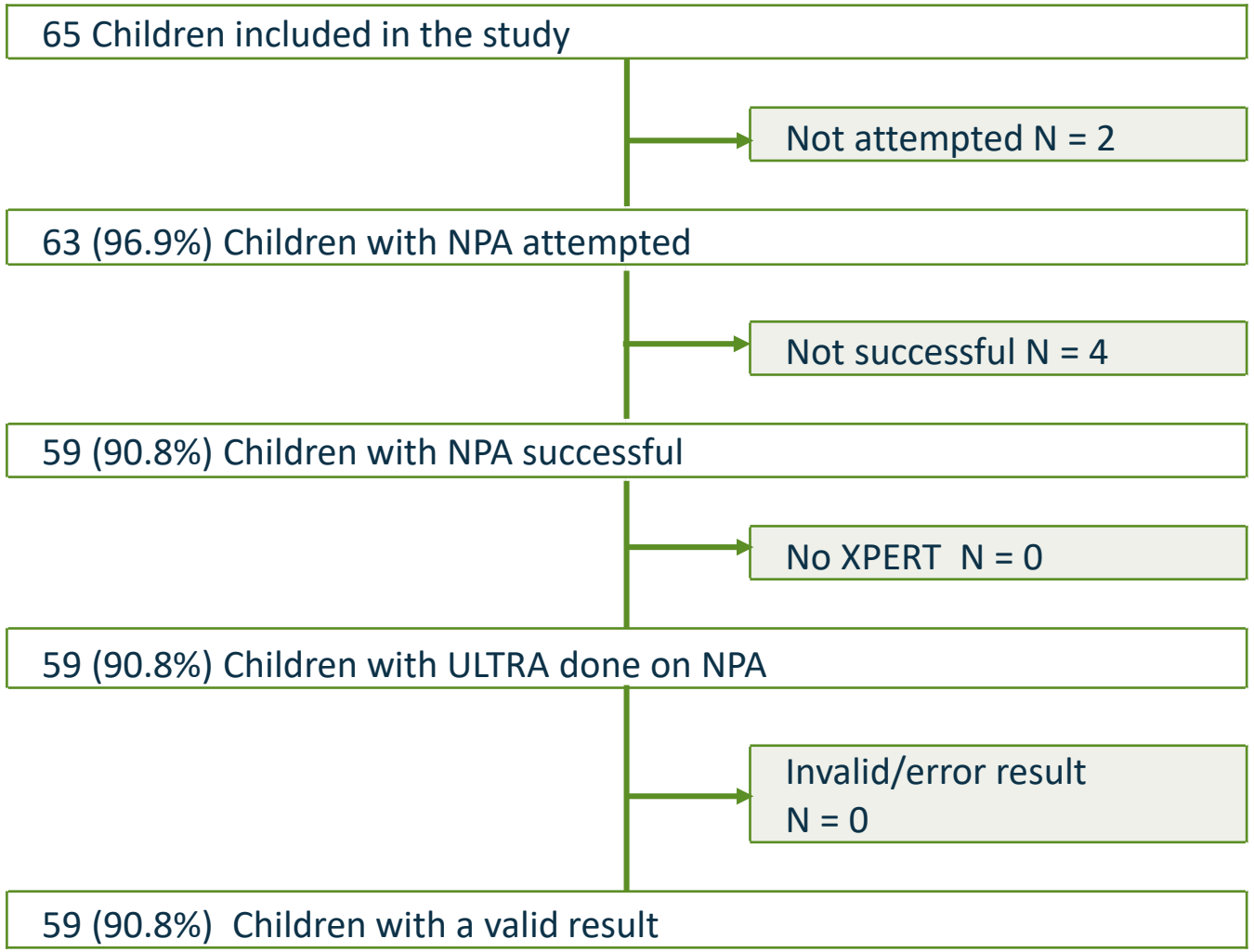
At any level of the decision algorithm a score of 100 points is enough to start a TB-treatment



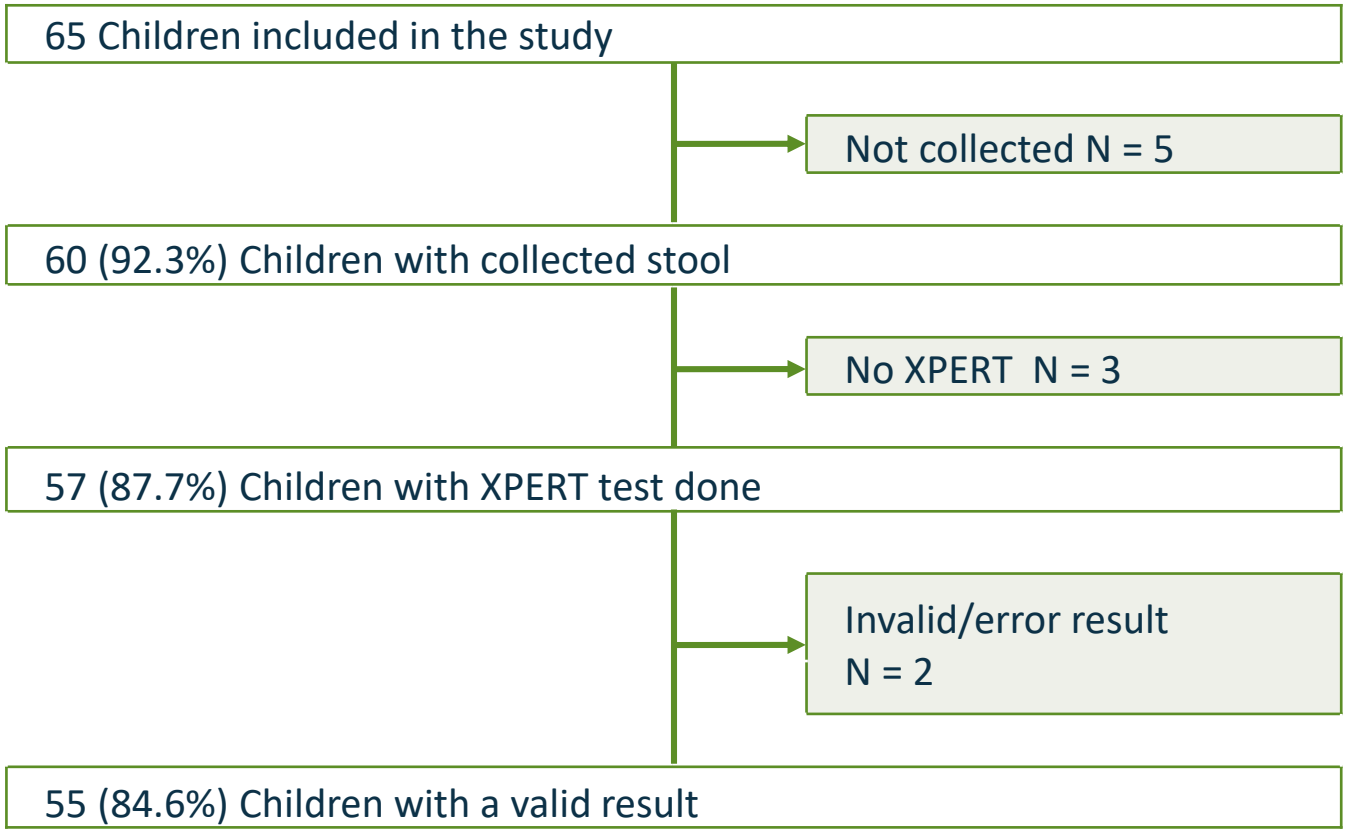
TB-Speed HIV: Baseline characteristics

	Overall (N = 65)
	n(%) or median [IQR]
Gender (F)	28 (43.1%)
Age (y)	5 [2, 10]
Previous TB treatment	6 (9.2%)
Severe Acute Malnutrition	26 (40.0%)
Hemoglobin (g/dl)	9.8 [8.1, 12]
On ART at inclusion	38 (58.5%)
CD4 percentage	23 [10, 30]
Persistent cough for more than 2 weeks	49 (75.4%)
Persistent fever for more than 2 weeks	18 (27.7%)
History of contact with TB case and any symptom duration	11 (16.9%)

TB-Speed HIV - NPA collection and Xpert testing feasibility



TB-Speed HIV - Stool collection and Xpert testing feasibility



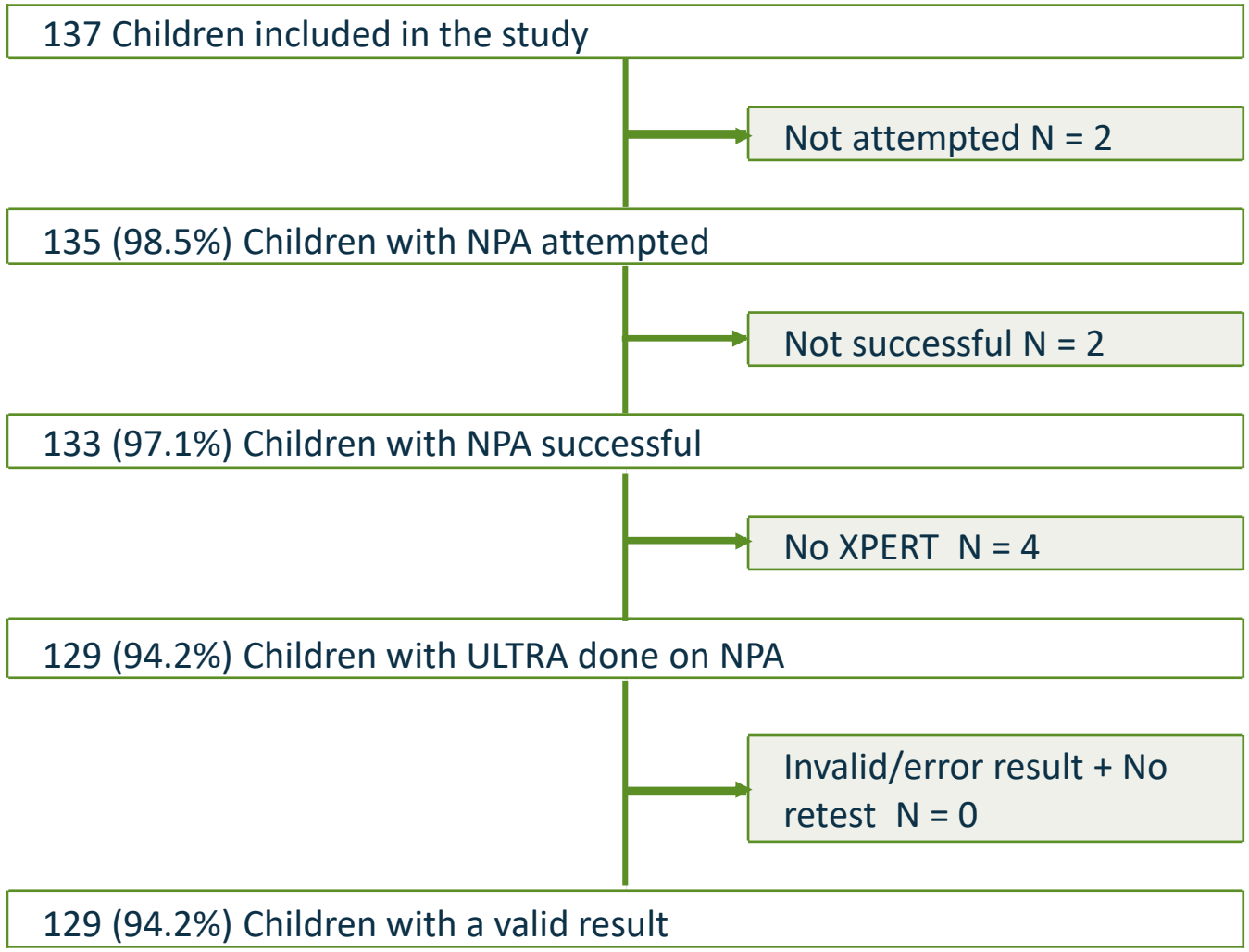
TB-Speed SAM: study design

- **Primary objective**: To develop a diagnostic prediction score for TB in hospitalized children with SAM
- Prospective diagnostic cohort study
- **3 hospitals, 2 countries** (Uganda, and Zambia)
- **720 children with SAM**
  - Aged 2-59 months
  - Hospitalized per clinician's decision (medical complication, danger sign)
- **TB diagnosis made according to existing National guidelines.**
- At the end of the study, children will be **retrospectively classified** as confirmed, unconfirmed, or unlikely TB, using the updated Clinical Case Definitions

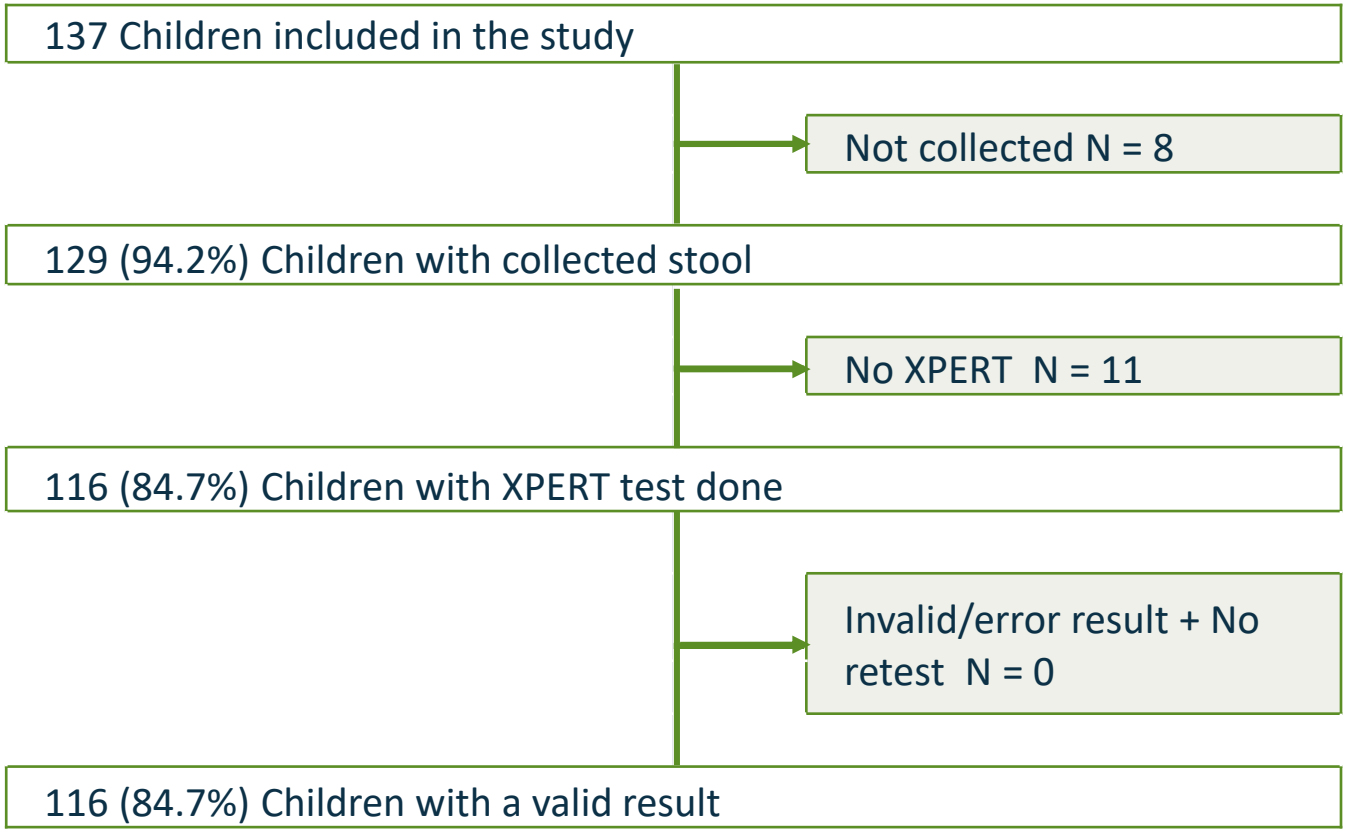
TB-Speed SAM: Baseline characteristics

	Overall (N = 137)
	n(%) or median [IQR]
Gender (F)	54 (39.4%)
Age (M)	14 [10, 19]
Weight for height Z score (WHZ) < -3SD	104 (75.9%)
Mid upper arm circumference (MUAC) < 115mm	89 (65.0%)
Clinical signs of bilateral pitting edema	67 (48.9%)
Previous TB treatment	1 (<0.1%)
Hemoglobin	8.5 [6.9, 9.7]
Positive HIV test	20 (14.6%)

TB-Speed SAM - NPA collection and Xpert testing feasibility



TB-Speed SAM - Stool collection and Xpert testing feasibility



Conclusion

- High feasibility of NPA sample collection confirmed in highly vulnerable children
  - > 90% of children with valid Ultra result from NPA
- High feasibility of stool sample in HIV infected children with presumptive TB and hospitalized children with SAM
  - Slightly more challenging in children hospitalized with severe pneumonia
- Feasibility of approaches at lower level of care (District Hospital and PHC)
  - Currently assessed in TB-Speed Decentralizations
- Qualitative assessment on feasibility and acceptability starting
  - Interviews with parents and healthcare workers in the Pneumonia study
- Final study results
  - TB-Speed Pneumonia: Q4 2021
  - TB-Speed HIV: Q1 2022
  - TB-Speed SAM: Q3 2021

Role and contribution of algorithm and score for diagnosis of paediatric TB. 23 OCT 12:30 13:50 B1.

- TB-Speed symposium: ***Role and contribution of algorithm and score for diagnosis of paediatric TB.*** 23 OCT 12:30 13:50 B1.
  - Overview of challenges in diagnosing TB in children and shortcomings of existing diagnostic algorithms and scores
  - Methodological challenges and alternatives in the evaluation of TB diagnostic algorithms in children
  - ***New TB diagnostic algorithm/score for vulnerable children: children with HIV infection and children with severe acute malnutrition***
  - Performance of new screening and diagnostic tests in potential paediatric TB diagnostic algorithms: interim results from the RaPaed study
  - Contribution of chest X-ray in the paediatric diagnostic algorithm?

TB-Speed

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Chishala CHABALA
Country Principal Investigator

FUNDERS

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