# Diagnostic accuracy of Computer-Aided Detection for Tuberculosis® and Stool Xpert for detecting TB in prospectively recruited West African children.



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Introduction

- Tuberculosis (TB) diagnosis in children is challenging due to the difficulty in obtaining sputum and the subjectivity of Chest X-ray interpretation.
- Therefore, most of these cases are clinically diagnosed, resulting in a wide case detection gap. Non-sputum-based TB diagnostic tests remain a priority.
  We evaluated the diagnostic accuracy of CAD4TB software and Stool Xpert for diagnosing TB in prospectively recruited children in three West African countries

# **Preliminary results**

- A total of 186 participants were enrolled, with a median age of 3.7 (IQR, 1.4-8.7) years, and 28/164 (17.1%) were HIV positive.
- Twenty-five (14.8%) had confirmed TB, 17 (10.1%) had unconfirmed TB, and 127 (75.1%) had unlikely TB.

## **CASE DETECTION GAP**

#### % of TB patients that are missed in different age groups



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**Overall 55%** of estimated children with TB (0–14 years) are **not reported** to national TB programmes

**TB can be a cause or co-morbidity of common child illnesses, especially pneumonia and malnutrition.** More specific tests are needed to improve diagnosis. (Oliwa et al., 2015 (14); Patel and Detjen, 2017 (15))

### Methodology

This is an ongoing multi-country study with consecutive recruitment of children aged less than 15 years assessed for presumptive pulmonary TB at study sites in Benin, Gambia, and Ghana. Participants undergo standardized conventional investigations for TB.
In addition, morning stool samples are simultaneously collected for testing with GeneXpert Ultra ('stool Xpert'), while Computer-aided Detection for TB-version 7 ('CAD4TBv7') abnormality scores are derived for digital chest radiographs.
The performance of stool Xpert and CAD4TBv7 were measured against a microbiological reference standard (MRS) and area under the receiver operating characteristic (AUROC) curve, point estimates of sensitivity and specificity were determined.

- Using the MRS, the AUROC, sensitivity, and specificity of CAD4TBv7 were 0.65 (95%CI 0.53-0.76), 33.3% (95%CI 13.3-59.0), and 96.3% (95%CI 90.8-99.0%), respectively.
- The AUROC, sensitivity, and specificity of stool Xpert were 0.82 (95%CI 0.72-0.92), 63.6% (95%CI 40.7-82.8), and 100% (95%CI 97.2-100%) respectively.
- Comparing the AUCROC of CAD4TBv7 to a human reader while using the MRS as the reference, there was no statistical difference (CAD4TBv7: 0.65 (0.53-0.76); human reader: 0.68 (0.56-0.80), DeLong p= 0.558).

Table: Diagnostic Performance of Stool, CAD4TB, and Human Reader against MRS.

Test	AUC	Sensitivity % (95%Cl)	Specificity % (95%Cl)	PPV % (95%CI)	NPV % (95%CI)
Stool Xpert	0.82 (0.72- 0.92)	63.6 (40.7- 82.8)	100 (97.2- 100)	100 (76.8- 100)	94.2 (89.0- 97.5)
CAD Abnormality Score	0.65 (0.53- 0.76)	33.3 (13.3-59)	96.3 (90.8- 99.0)	60.0 (26.2- 87.8)	89.7 (82.6- 94.5)
Human Reader	0.69 (0.60- 0.79)	78.3 (56.3- 92.5)	60.0 (51.2- 68.3)	25.0 (15.5- 36.6)	94.2 (87.0- 98.1)

PPV=Positive Predictive Value NPV = Negative Predictive Value Value (95% CI) AUC= area under receiver operating characteristics

# **Study Flow**



# Conclusion

- While the performance of CAD4TBv7 is comparable to human readers, it does not meet the WHO recommendation as a stand-alone screening test.
- The high specificity of stool Xpert makes it a good add-on as a microbiological test..

# Acknowledgment

- Supervisors and Advisory team
- MRCG Childhood Tb Clinic/field team
- Teams at the partner sites in Ghana and Benin
- Study participants
- WANETAM/TALENT Grant secretariat.





As part of the study, early morning stool sample will be taken for Xpert analysis + pooled digital images deidentified and a TB score assigned via CAD4TB + expert radiologist will provide an independent interpretation of <u>xrays</u>

 CAD4TB box will be installed at MRC Unit The Gambia

 Digital Xray images from the three study sites will be de-identified, transferred electronically to the Gambia site using an encrypted internetbased file transfer software

Using data from the baseline routine clinical and radiological evaluation, and laboratory investigations of the children, TB disease will be defined according to the revised standardized case definitions for the classification of intrathoracic TB in children

 All children diagnosed with TB disease will be referred for treatment according to the national paediatric TB treatment guidelines in each country.

Estimate the diagnostic accuracy of CAD4TBv7 and 'stool Xpert' against mycobacterial culture as primary reference standard.
 >+ accuracy of CAD4TBv7 against independent human radiologist.
 Bayesian Latent Class Analysis (LCA) will be used to fit mathematical models to determine the added-value of the tests in terms of relative increases in sensitivity and specificity by combining the CAD4TBv7 and 'stool Xpert' results to conventional methods.

#### Funding: EDCTP-TALENT PhD Fellowship (Ref: PSIA2020AGDG-3317-TALENT)