



EDITORIAL: TB-SPEED TOWARDS THE END OF THE PROJECT

In 4 years, TB-Speed has carried out several studies aiming at reducing childhood mortality due to tuberculosis (TB) by developing, testing, and eventually delivering an innovative, decentralized, cost-effective, and feasible childhood TB diagnostic strategy to increase case finding in children.

First results of the TB-Speed testing approach are already available. The results of the TB-Speed Pneumonia study were presented at TBScience Late Breaker Session 2021 during the 52nd Union World Conference on Lung Health. TB-Speed actively contributed to the WHO 2021 consolidated Guidelines and Operational Handbook on the management of tuberculosis in Children and Adolescents. Project will be completed in September 2022.

Country teams are currently actively following up children in the TB-Speed Decentralization, TB-Speed HIV and TB-Speed SAM studies. The international teams based at University of Bordeaux, MU-JHU and IRD are actively coordinating final data management and monitoring.

All results will be presented at an International Restitution Symposium to be held on June 9th & 10th, 2022 in Maputo, Mozambique followed by National Restitution Symposia in countries.

This last year of the project is crucial to inform international and national stakeholders about the project findings, to support countries in their transition plan to scale up the project's findings and strengthen the engagement with civil society to increase the public awareness about childhood tuberculosis.

More than ever, after this unprecedented pandemic and its negative impact on TB control, there are urgent needs to invest to End TB and Save Lives but still keeping children on a frontline of the agenda.

Dr Olivier Marcy

Project Director & Coordinating Investigator

Dr Maryline Bonnet

Coordinating Investigator

Dr Eric Wobudeya

Coordinating Investigator

FOCUS: CONTRIBUTION TO WHO GDL & OPERATIONAL HANDBOOK

TB-Speed contributed with data and expertise to the Module 5 of the WHO consolidated Guidelines and Operational Handbook on tuberculosis on the management of tuberculosis in Children and Adolescents that has been released on March 21st, 2022.

WHO Guidelines on management of tuberculosis in Children and Adolescents

TB-Speed contributed to two PICO questions:

Diagnostic accuracy of Xpert Ultra on stools and gastric aspirate

- Sharing of data from the TB-Speed HIV and SAM studies for the meta-analysis on the diagnostic accuracy of Xpert Ultra on gastric aspirate and stool.
- Presentation of data on the feasibility and the acceptability of stools and nasopharyngeal aspirate (NPA) and interim results from the pooled data analysis from the FIND and TB-Speed head-to-head comparison of three different stool processing methods prior Xpert Ultra testing. These are important data for future implementation of NPA and stool.

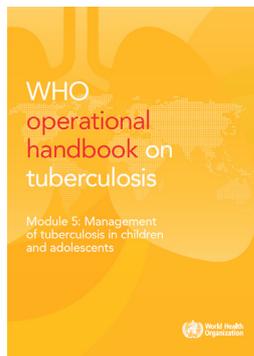
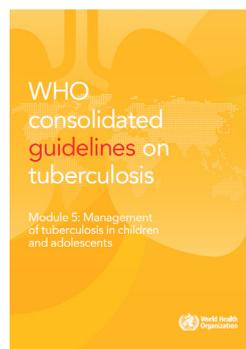
Models of care for childhood TB management

Presentation of preliminary data on feasibility, acceptability, and yield of the decentralized diagnostic approaches implemented in the TB-Decentralization study.

WHO Operational Handbook

TB-Speed shared:

- Results of the TB-Speed Pneumonia study
- Description of the decentralization models of care assessed in the TB-Speed Decentralization study
- NPA & Stool operating procedures
- Brochure describing the course of chest X-ray interpretation in children
- Results of the market screening for battery operated mucus aspirators for NPA



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WRITING TEAM

Project director
Olivier Marcy

Output lead communication
Maryline Bonnet

Output 6 communication manager
Nicolas Koskas

Université de Bordeaux
146 rue Léo Saignat
33076 BORDEAUX - FRANCE

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PARTNERSHIPS



● TB-Speed Pneumonia was the first major TB-Speed study that was completed. Results were presented at the late breaker session of the TBScience side-conference to the 52nd Union World Conference on Lung Health in October 2021.

● OBJECTIVES

TB-Speed Pneumonia is a cluster-randomized trial with a stepped wedge design, conducted in 15 tertiary level hospitals in 6 high TB incidence countries, that assessed the impact on 12-week mortality of adding systematic TB detection using Xpert MTB/RIF Ultra on NPA and stools to the WHO standard of care for children <5 years with severe pneumonia. Among secondary objectives, the trial assessed the feasibility and TB detection yield of the Xpert Ultra on NPA and stool samples.

● RESULTS

The study enrolled 2570 children (1401 in the control arm and 1169 in the intervention arm) between March 2019 and March 2021, with 5 months interruption of enrolments in 2020 due to the Covid-19 pandemic. In total, 87 (7.4%) and 71 (5.1%) of children were initiated on TB treatment in the control and intervention arms, respectively. In the intervention arm, 97.4% and 82.2% of children had NPA and stool collected, respectively, and 2.1% had a positive Xpert Ultra results. At 12 weeks, 7.7% of children had died in the intervention arm vs 7.9% in the control arm. The intervention was not associated with decreased mortality.

● CONCLUSION

The TB-Speed Pneumonia study showed that TB screening at the time of admission was feasible and could result in an

increase in children diagnosed and treated for TB however, it did not contribute to reducing TB deaths among children. The TB-Speed Pneumonia trial also brings additional evidence on the acceptability, feasibility and safety of collecting NPA and stool samples to test for TB in highly vulnerable children.

PUBLICATION

Publication in *Pathogens* on March 23rd introducing key research questions and ongoing efforts by TB-Speed on microbiological diagnosis in childhood TB.

Diagnostic Advances in Childhood Tuberculosis: Improving Specimen Collection and Yield of Microbiological Diagnosis for Intrathoracic Tuberculosis



NEWS ON THE PROJECT

TB-Speed Decentralisation, HIV, SAM and Stool processing studies have completed their inclusion during last quarter of 2021.

TB-SPEED DECENTRALIZATION STUDY Massive screening efforts by the study teams!

TB-Speed Decentralization study ended its inclusions on September 30th, 2021.

A total of 168 416 children 0-14 years old were screened for TB in 12 district hospitals, 24 primary health care centers across 6 countries (Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone and Uganda).

3106 children benefitted from TB diagnostic approaches in the study and 584 are followed in the prospective cohort that will bring additional data on the diagnostic accuracy of the approaches and TB treatment outcomes.

Data cleaning of the main study is completed and the primary results are being analysed. Follow up of children enrolled in the nested cohort will last until March 2022.



Kampong Cham Closure Visit Meeting, Cambodia

TB-SPEED HIV & SAM STUDIES

Enrolment in the TB-Speed HIV and SAM studies ended on December 30th, 2021. 278 children living with HIV and 603 children hospitalized with severe acute malnutrition (SAM) were enrolled in these 2 important studies that aim at:

- 1) performing an external validation of the PAANTHER tuberculosis treatment decision algorithm for HIV-positive children with presumptive TB in Côte d'Ivoire, Uganda and Zambia,

2) developing and evaluating a diagnostic prediction score for TB in hospitalized children with SAM in Uganda and Zambia. Both studies will provide important data on alternative approaches specific to these vulnerable populations to the now recommended WHO algorithm.

The nested TB-Speed TB-PK study will bring also important data on TB drugs dose adjustments for children with SAM and HIV. Follow up will end in June 2022. Interim results will be presented in Maputo in June.

TB-SPEED STOOL PROCESSING STUDY

The TB-Speed Stool processing study ended its inclusions on December 30th, 2021. Children will be followed up until the end of March 2022. The study conducted in Uganda and Zambia will compare diagnostic accuracy and feasibility of three centrifuge free stool processing methods prior Xpert Ultra testing.

TB-SPEED FINAL RESTITUTION

TB-Speed will organize its final International Restitution Symposium on June 9th and 10th, 2022, in Maputo, Mozambique inviting more than 100 guests:

- Members of the TB-Speed teams as well as representatives of the National TB Programs of Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone and Uganda
- Representatives of our funders (Unitaid & L'Initiative-Expertise France), sponsor & support (INSERM & ANRS)
- TB-Speed Scientific Advisory Board members & TB Experts

The symposium will be followed by a writing workshop with junior and senior research fellows from the different countries.

It will be followed by National Restitution Symposia in our participating countries.



NEWS ON THE FIELD

ANRS SCIENTIFIC DAYS

The TB-Speed Cambodia and Cameroon teams participated in the ANRS Scientific Days in their respective countries.

