TB-Speed

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Research project to strenghen paediatric tuberculosis services for enhanced early detection

PRESS RELEASE

TB-SPEED Pneumonia

Results of an international cluster randomized trial on systematic tuberculosis detection in children with severe pneumonia

A trial investigating systematic tuberculosis (TB) testing for children with severe pneumonia in countries with a high incidence of TB 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 nasopharyngeal (NPA) and stool samples to test for TB in highly vulnerable children. Despite its low detection yield in children, in high TB incidence countries, microbiological TB diagnosis remains important in children with severe pneumonia because it can simplify the diagnostic pathway and allow rapid initiation of appropriate TB treatment, detect rifampicin resistance and build clinicians confidence in their clinical diagnosis.

There is growing evidence that TB is common in children with severe pneumonia and can contribute to mortality, with often acute clinical presentations. However, in those children, TB is usually considered only in case of prolonged symptoms, failure of antibiotics, or history of household contact, thus leading to missed or delayed TB diagnosis. In this context, testing young children with severe pneumonia for TB and starting those who test positive on anti-TB treatment on the day of presentation, could reduce child death from TB.

The TB-Speed pneumonia is one of the very few large outcome driven randomized control trials in the field of paediatric TB. It is an international pragmatic cluster-randomised diagnostic trial conducted in 15 tertiary hospitals across six countries with high TB incidence (Cote d'Ivoire, Cameroon, Uganda, Mozambique, Zambia and Cambodia). It aimed to assess the impact on mortality of adding systematic molecular TB detection using the Xpert MTB/RIF Ultra (Ultra) assay performed on one NPA and one stool sample to the standard of care recommended by the WHO (WHO SOC) for children with severe pneumonia. The trial also assessed the feasibility and TB detection yield of the Xpert Ultra on NPA and stool samples.

In both arms, all young children (< 5 years old) newly hospitalised with WHO-defined severe pneumonia, received care and treatment planned per routine WHO SOC for young children with severe pneumonia that includes large spectrum antibiotic course, oxygen when indicated and treatment of comorbidities, such as HIV infection and severe malnutrition. In the intervention arm, in addition to the WHO SOC children had NPA and stool samples - two samples recently recommended by the WHO for testing with Ultra in children with presumptive TB - performed on the day of hospital admission and tested with Ultra. The sample flow was organised in order to reduce time to results to 3 hours. All children with Ultra positive results were immediately started on treatment. Children were followed for 12 weeks after enrolment (day 3, hospital discharge, 2 weeks post-discharge, and week 12).

Overall, 2570 children were enrolled in the study (1401 in the control arm and 1169 in the intervention arm) between March 2019 and March 2021, with 6-month interruption of enrolments in 2020 due to the Covid-19 pandemic. Median age was 11 months in both arms and 5% of children were HIV-positive. Severe acute malnutrition was more frequent in the intervention arms (25.8%), as compared to the control arm (17.1%), and pneumonia was slightly more severe in the control arm with lower median oxygen saturation at inclusion (92%) compared to the intervention arm (94%). Overall, 87 (7.4%) and 71 (5.1%) of children were initiated on TB treatment in the control and intervention arms, respectively (p=0.012). In the intervention arm, 97.4% and 82.2% of children had NPA and stool collected, respectively, and 2.1% had a positive Ultra results. At 12 weeks, 90 (7.7%) children had died in the intervention arm vs 100 (7.9%) in the control arm. The statistical analysis showed that the intervention was not associated with decreased mortality [adjusted odds ratio 0.95 (95% confidence interval 0.58 – 1.58)].

*More details about the TB-Speed Project: TB-Speed is a Unitaid & Expertise France funded research program aiming at reducing childhood mortality due to tuberculosis (TB) by developing, testing, and delivering an innovative, decentralized, cost-effective, and feasible childhood TB diagnostic strategy to increase case finding in children. This research project is implemented in seven countries in sub-Saharan Africa and South-East Asia. It includes several studies testing different diagnostic approaches in specific paediatric populations at risk of tuberculosis or settings.

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About Unitaid

Unitaid is a global health agency engaged in finding innovative solutions to prevent, diagnose, and treat diseases more quickly, cheaply, and effectively, in low- and middle-income countries. Its work includes funding initiatives to address major diseases such as HIV/AIDS, malaria, and tuberculosis, as well as HIV co-infections and co-morbidities such as cervical cancer and hepatitis C, and cross-cutting areas, such as fever management. Unitaid is now applying its expertise to address challenges in advancing new therapies and diagnostics for the COVID-19 pandemic, serving as a key member of the Access to COVID-19 Tools (ACT) Accelerator. Unitaid is hosted by the World Health Organization.

About L'Initiative

Launched at the end of 2011, L'Initiative is a project implemented by Expertise France that complements the Global Fund's work. It provides technical assistance and support for innovation to Global Fund recipient countries to improve the effectiveness of grants and strengthen the health impact of the programs funded. As such, it contributes to ensuring the effectiveness of the response to pandemics. Among the countries eligible for support from L'Initiative are the 19 priority countries for official development assistance from France and member countries of La Francophonie. L'Initiative's recent work has demonstrated its catalytic effect through building the capacity of health and civil society actors, improving institutional, political and social frameworks, and supporting innovative approaches to respond to pandemics.

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