Better detection of tuberculosis in children with decentralized diagnosis

Press release | Marseille, March 22, 2024

Copyright TB-Speed

Tuberculosis (TB) affects more than 1 million children each year but less than half are diagnosed and treated for the disease. Underdiagnosis leads to more than 200,000 child deaths due to TB each year. TB diagnosis is complex in children, requiring specialized sample collection procedures for testing, clinical expertise, and good chest radiography interpretation. Often this capacity is lacking at lower levels of healthcare in resource-limited settings, where most children with TB seek care. In 2022, the World Health Organization recommended the decentralisation of childhood TB services to increase access in peripheral healthcare settings.

Two articles from one study focusing on decentralising the diagnosis of childhood TB to district hospitals (DH) and primary health centres (PHC) in high tuberculosis incidence countries have just been published in *eClinicalMedicine*. The study was carried out in six countries with a high incidence of tuberculosis (Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone, and Uganda) as part of the TB-Speed project implemented by the Institut Pasteur (Cambodia), French National Research Institute for Sustainable Development (IRD) (Cameroon), PACCI (Côte d'Ivoire), Instituto Nacional de Saude (Mozambique), Soltis (Sierra Leone), MU-JHU (Uganda), and coordinated by the University of Bordeaux (France).

The first publication, led by the Ugandan research institution MU-JHU (Makerere University John Hopkins University collaboration), IRD and the University of Bordeaux, focuses on the effect of decentralising the diagnosis of childhood tuberculosis to district hospitals and primary health centres. The second publication, led by the University of Sheffield (UK) and the University of Bordeaux, focuses on the cost-effectiveness and budgetary impact of decentralising childhood TB diagnostic services to these peripheral healthcare settings.

Low detection of tuberculosis in children is largely due to the difficulty of collecting sputum in young children and the low yield of current tuberculosis microbiological tests, due to the paucibacillary nature of tuberculosis in children. Another important factor explaining low

detection of TB in children is the design of health systems. Childhood tuberculosis services are mostly centralised at high levels of care, inaccessible to most children living in high incidence and resource-limited countries. Child-adapted respiratory specimen collection methods and rapid molecular testing are often lacking at lower levels of healthcare. Chest X-ray, a useful tool for diagnosis of non-microbiologically confirmed tuberculosis, is often only available at referral hospitals and hampered by poor quality of X-rays and lack of training on interpretation for children who may have TB. In addition, there is often low awareness of childhood TB and lack of confidence in making a clinical diagnosis among healthcare workers at low health system levels. There is, so far, little evidence on what, how, and where to decentralise childhood TB diagnostic capacity.

Recent advances in diagnostic approaches could contribute to improved childhood TB diagnosis at low levels of care. Training and clinical mentoring could build confidence in healthcare workers to initiate treatment without microbiological confirmation.

Operational evaluation

The first publication[1] report results of an operational research study using a pre-post intervention cross-sectional design that assessed the effect of decentralising a diagnostic package for childhood TB in 12 district hospitals (DHs) and 47 primary health centres (PHCs) of 12 districts across Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone and Uganda.

The intervention included:

- a comprehensive diagnosis package at patient-level with TB symptom-based screening for all sick children and young adolescents <15 years, and clinical evaluation, Xpert Ultra-testing on nasopharyngeal aspirate and stool samples, and digitalized chest radiography for children with presumptive TB;

- two decentralisation approaches, one strengthening diagnostic capacity at DH level with children with presumptive TB at PHC level after screening, referred to DH (DH-focused), and one strengthening diagnostic capacity at PHC level (PHC-focused). In each country, two districts were randomly allocated to one of the decentralisation approaches. New diagnostic equipment was installed in health facilities; healthcare workers were trained and engaged in adopting new practices; support supervision and clinical mentoring were implemented as a mechanism for helping healthcare workers deal with some of the challenges met by frontline staff, practicing in rural and remote settings.

We compared the proportion of TB detection in children and young adolescents <15 years pre-intervention (August 2018 to November 2019) versus during intervention (March 2020 to September 2021), overall and by decentralisation approach.

Economic evaluation

The second publication[2] focused on assessing the cost-effectiveness and budget impact of decentralising a comprehensive diagnosis package for childhood tuberculosis to DH or PHC compared to the standard of care in Cambodia, Cameroon, Côte d'Ivoire, Mozambique, Sierra Leone and Uganda.

A decision analytic mathematical model was developed to assess the benefits, cost-effectiveness, and budget impact of the intervention from a health system perspective. Estimated outcomes included the number of children treated for tuberculosis, number of deaths averted, number of disability adjusted life-years averted, costs and the incremental cost-effectiveness ratios for both interventions in each country. The budget impact of nationwide implementation of these interventions over a 5-year period (2022-2026) was also calculated using cost functions and decision analytic model outputs.

Main results

The delivery of the comprehensive diagnosis package at DH and PHC nearly tripled the detection of children with TB as compared to pre-intervention data. The DH-focused approach had a larger effect on the detection of children with TB than the PHC-focused approach. The effect was variable between countries with larger effect of the intervention in countries with no or limited prior decentralisation of childhood TB services. The high uptake of the different components of the diagnostic package at DH and PHC levels illustrates the high feasibility of the intervention.

Compared to the standard of care, incremental cost-effectiveness ratios ranged between $263 (Cambodia) and $342 (Côte d'Ivoire) per disability-adjusted life-year averted for the DH-focused strategy, and ranged between $477 (Cambodia) and $599 (Côte d'Ivoire) for the PHC-focused strategy. The additional costs of implementing the DH-focused strategy ranged between $12·8M (range 10·8 to 16·4) (Cambodia) and $50·4M (36·5 to 74·4) (Mozambique), and between $13·9M (12·6 to 15·6) (Sierra Leone) and $134·6M (127·1 to 143·0) (Uganda) for the PHC-focused strategy.

Decentralising childhood TB diagnosis is likely to reduce the gap between the number of children estimated to develop TB and the number of children notified to the WHO, but the implementation of decentralised services needs to take into account the relatively low frequency of childhood TB and limited resources available in peripheral settings. Sensitivity analysis suggests that decentralisation targeted to geographical areas with high tuberculosis prevalence would likely be cost-effective in all countries. Decentralisation of childhood TB diagnosis services would require substantial financial investment for national implementation, largely due to the initial purchase of machines for X-ray and Xpert Ultra-testing, particularly for the PHC-focused intervention.

References

[1]*Effect of decentralizing childhood tuberculosis diagnosis to primary health center and district hospital level on disease detection in children from high tuberculosis incidence countries – An operational research with a pre-post study design*

[2]*Cost-effectiveness and budget impact of decentralising childhood tuberculosis diagnosis in six high tuberculosis incidence countries: a mathematical modelling study*

More about the TB-Speed project

TB-Speed is a research program funded by Unitaid aiming at reducing childhood mortality due to TB by developing, testing, and delivering an innovative, decentralised, 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. TB-Speed is coordinated by the University of Bordeaux.
https://www.tb-speed.com/

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.
https://unitaid.org/#en

About IRD

IRD is a multidisciplinary French public research organization committed to equitable partnerships with countries in the Global South and in the French overseas territories for nearly 80 years. As a contributor to the achievement of the international development agenda, the IRD aligns its priorities with the implementation of the Sustainable Development Goals (SDGs). Together, scientists and the Institute's partners propose concrete solutions to the global challenges facing societies and the planet. This win-win relationship makes science and innovation major levers for development.
https://en.ird.fr

About university of Sheffield

USFD is a member of the Russell Group of leading UK research universities and ranked within the top 100 in the QS World University rankings. The School of Health and Related Research (ScHARR) has particular strengths in health economic evaluation, modelling to inform policy decisions, and systematic reviewing. The department employs over 300 multi-disciplinary staff, attracts over £10 million a year in research awards and ranked 2nd for 'Impact' and 4th for 'Power' for its Health Research in the 2014 Research Excellence Framework. Previous collaborations include TB-Speed (UBx) and other paediatric TB projects (SU), and the EDCTP-funded TREATS consortium.
https://www.sheffield.ac.uk/

About MU-JHU

MU-JHU Care LTD is an HIV research, prevention, care, and training facility located on Upper Mulago Hill in the city of Kampala (Uganda), in operation since 1988. MU-JHU embodies a collaboration between Makerere University and Johns Hopkins University in Baltimore, USA initially operated under the name MU-JHU Research Collaboration, but in 2006, re-registered as a not-for-profit entity called 'MU-JHU Care Limited'. MU-JHU remains a Clinical Research Site in close collaboration with Johns Hopkins University. Over the last decade, MU-JHU has progressively expanded its clinical and implementation science-research portfolio to include primary HIV prevention, tuberculosis diagnosis and management, paediatric neuro-development assessment and interventions, birth-defects surveillance, women's health (including bone health and reproductive health) and the development of a maternal vaccine platform to assess Group-B Streptococcus and other promising vaccines.
www.mujhu.org

About University of Bordeaux

With more 54,000 students, 3,200 researchers and teachers, and 2,800 staff members, the University of Bordeaux is one of the leading French public research and higher education institutions, located in a dynamic and culturally rich, fast-developing region.

Ranked among the top universities in France, the University of Bordeaux is renowned for the quality of its academic courses and research. It is a multi-disciplinary, research-focused institution with a strong ambition to develop as a leading, international campus. The University of Bordeaux is leading an ambitious, competitive development program in partnership with local higher education institutes and national research organizations, in order to promote Bordeaux as a "Campus of Excellence".
https://www.u-bordeaux.fr/en

Press contacts
- **IRD :** Charlotte Gabet - presse@ird.fr - + 33 6 07 36 84 06
- **University of Sheffield** : Amy Huxtable - a.l.huxtable@sheffield.ac.uk - +44 (0)114 222 9859
- **MU-JHU Care Ltd** : Romana Nabbosa - rnabbosa@mujhu.org - +256 75 23 07 101
- **TB-Speed** : Nicolas Koskas - nicolas.koskas@u-bordeaux.fr