

Study shows children with multidrug-resistant tuberculosis can be treated

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This photomicrograph reveals *Mycobacterium tuberculosis* bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains that are carbolfuchsin methods specific for *M. tuberculosis*. Credit: public domain

The results of a large, international systematic review published in the journal *PLOS Medicine* show that tuberculosis treatment is successful in children with multidrug-resistant tuberculosis (MDR-TB). The study was

used to inform the World Health Organization guidelines on treatment of MDR-TB in children.

The study, which involved a collaborative group of international researchers, included a systematic review and patient data meta-analysis on the clinical characteristics and treatment outcomes of 975 children from 18 countries. The results show that 78% (764 of 975) of these children had successful treatment outcomes when treated with second-line MDR-TB drugs.

"An estimated 32 000 children develop multidrug-resistant tuberculosis (resistant to the two main TB drugs, namely isoniazid and rifampicin), each year. Treatment for MDR-TB is of a longer duration and requires drugs that are more toxic. These regimens are frequently hard to tolerate, particularly in children, due to the length of treatment, drug toxicity and the lack of child-friendly formulations," said one of the authors Prof. Anneke Hesselning from the Desmond Tutu TB Centre, Faculty of Medicine and Health Sciences, Stellenbosch University. "To date, little has been known about the optimal treatment for these children. This review therefore gives vitally important information as to potential outcomes and some very good news for the TB field."

"There are too few examples where researchers share their data for the public good, and this is impressively what this global team of researchers did—this helped to ensure that we could capture all published and unpublished evidence for treating children with MDR-TB. The search yielded 2772 reports and, ultimately, 33 studies were eligible for inclusion," said Dr. Tamara Kredo, co-author and Senior Specialist at Cochrane South Africa, an intramural research unit of the South African Medical Research Council.

Need for HIV treatment

The review also showed the urgent need for HIV treatment in children with HIV and TB co-infection. TB treatment was less successful in children who were HIV positive but not receiving antiretroviral therapy (ART).

"Treatment was successful in only 56% of children with bacteriologically confirmed TB who were infected with HIV who did not receive any antiretroviral treatment during MDR-TB therapy," said Hesseling, "compared to 82% in children infected with HIV who received ART during MDR-TB therapy."

"This highlights the urgent need for ART in these children, which should be a priority in our setting, where rates of HIV/TB coinfection are so high," she added.

Malnutrition was shown as another factor that affected [treatment outcome](#) and highlights the need for aggressive solutions.

Second-line injectable agents and high-dose isoniazid were associated with treatment success. However, a high proportion of children with non-severe disease who received no second-line injectable agents still did well.

"This means children with non-severe disease may be able to be spared from these more toxic medications," said Hesseling.

"Further work is still needed on individual drug effects on treatment outcome," added Kredo. "Although these results were used to update the WHO guidelines, further rigorously collected evidence is needed to help guide the management of MDR-TB treatment in children globally. This work gives us more understanding of the potential success of treatment, the potential for certain [children](#) to receive less-intensive, less-toxic regimens, and an understanding of risk factors for poor outcomes across

settings, which is important for designing future [treatment](#) regimens."

More information: Elizabeth P. Harausz et al, Treatment and outcomes in children with multidrug-resistant tuberculosis: A systematic review and individual patient data meta-analysis, *PLOS Medicine* (2018). [DOI: 10.1371/journal.pmed.1002591](https://doi.org/10.1371/journal.pmed.1002591)

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