

Community-based intervention and health education to scale up TB preventive treatment for children

Promoting adherence to TB preventive treatment (TPT) and TB disease treatment (TDT) is a challenge that all national programmes face, both in low- and high-burden countries. Long-term therapies of at least 6 months' duration were until recently the only therapeutic options for TPT and TDT, and are still those most frequently prescribed.¹ However, although the duration of therapy may be a barrier to the completion of TPT and TDT, this alone does not explain the complex myriad factors that may prevent an individual from completing treatment. Among the many causes of low adherence are factors related to treatment (such as adverse events or pill burden), comorbidities (HIV infection, alcohol or drug use), socio-economic and cultural aspects (e.g., lack of education about TB, catastrophic costs or TB-related stigma) and operational problems (e.g., unprepared, overworked and underpaid health professionals or limited opening hours of health facilities).^{2–5} Despite the difficulties related to TPT and TDT completion, substantial advances have been made globally in the last decades. It is estimated that in 2000–2020, about 66 million TB deaths were averted by TB treatment and provision of antiretroviral therapy for people living with HIV and TB.¹ Such advances in TB treatment have allowed more ambitious goals to be launched, including the recommendation of TPT for priority groups. In 2015, the WHO published the first guidelines on TPT,⁶ which were later updated,^{7,8} with policy guidance on the management of TB infection (TBI), contact screening, TPT initiation and treatment options, integrating previous WHO guidelines specific to people living with HIV⁹ and to child contacts under 5 years of age.¹⁰ Guidelines on the management of TBI was considered by the WHO as a necessary instrument to achieve the goals set out in the End TB Strategy of achieving a 90% reduction in TB incidence and 95% reduction in TB deaths.¹¹

The risk of TB in children younger than 5 who have not received TPT is particularly high in the first 2 years after contact with a patient with pulmonary TB.^{12,13} However, TPT with isoniazid (INH) for 6–9 months reduces the risk of developing TB by around 60%.^{13,14} Despite the high risk of TB in this age group, and the recommendation of TPT in international guidelines,^{6–8,15,16} the completion rate of unsupervised TPT with INH under routine conditions can be as low as 20% in countries with a high TB

burden.¹⁷ WHO data show that despite an increase in the global number of people who were provided with TPT from 1.0 million in 2015 to 3.6 million in 2019, only 29% of the target population of 4 million household contacts under 5 received TPT during the period 2018–2022. The COVID-19 pandemic has also had a negative impact on TPT; between 2019 and 2020, there was a reduction in the number of people on preventive therapy, which fell from 3.6 million to 2.8 million (21%).¹

The availability of new regimens for TPT with proven efficacy has expanded in recent years. Compared to the “classic” 6–9 month INH regimen, shorter regimens with rifampicin for 4 months, or the combination of rifapentine and INH for 1 or 3 months, were equally effective, and have a lower risk of hepatotoxicity in adults^{18,19} and higher rates of treatment completion in adults and children.^{18,20,21} However, although shortened regimens for TPT have improved adherence to therapy in clinical studies, their availability is still limited and INH remains the drug of choice for TPT in most countries.²² In the recent Global TB report,¹ the WHO reinforces the need for intensified efforts to promote TPT, which includes better TB screening at the household level, strengthening follow-up to TB screening (mainly in households and among people living with HIV) and increased access to rifamycin-based regimens of shorter duration, with the combined rifapentine and INH regimen for 1 or 3 months. New studies on TPT for higher risk contacts that promote innovative initiatives and study designs to increase the rate of adherence to TPT should therefore be a priority in high TB burden countries.

In this context, the cluster-randomised trial by Hirsch-Moverman et al.²³ in this issue of the Journal is of interest. The study was carried out in Lesotho, which has the highest TB incidence in the world²² and high rates of TB-HIV co-infection,¹ and offers a new look on how to promote TPT to child contacts through a community-based intervention (CBI). In this CBI model, the authors developed a multi-component approach that involves community health workers based in the health unit (facility-based lead village health worker [LVHW]), as well as in the community (village health worker [VHW]), who provide health education and adherence support for children and their families. Educational activities

focused on the importance of TPT adherence to TB prevention. Adherence to TPT was supervised using SMS messages, weekly phone calls and home visits. The healthcare team was trained before the start of the study, but periodic meetings with the team were also organised to review data and intervention activities, proposing solutions to the problems identified. Another study feature is the use of a mixed-methods approach, including the qualitative analysis of interviews with healthcare providers and caregivers through thematic analyses. The integration of quantitative and qualitative data allowed for the evaluation of the rates of TPT initiation completion, as well as CBI acceptability.

Even with a high TPT initiation rate (88%) in standard-of-care (SOC) facilities, Hirsch-Moverman et al. found a higher TPT initiation rate (98%) at CBI sites ($P < 0.0001$).²³ TPT completion with INH for 6 months was also significantly higher among children at CBI (82%) than in those at SOC sites (59%) ($P = 0.03$); child contacts at CBI sites were almost 40% more likely to complete TPT than those at SOC sites. Interviews with child caregivers revealed an appreciation for VHWs and health unit reminders, and scheduling visits with contacts together with the index case facilitated adherence. Interviews with health professionals revealed the importance of training and mentorship, as well as educational resources to support interventions. Among the proposals made by the healthcare providers to increase adherence to the TPT, the expansion of educational activities on TB to schools and the community as a whole, including the heads of villages, stands out.

The findings of the study by Hirsch-Moverman et al. confirm the impact that health education initiatives and the engagement of community health workers may have on increasing adherence to TPT.²³ Educational activities empower patients and their families, reducing the stigma associated with TB and promoting the self-esteem of those affected by the disease.^{24–26} In the recently published guidelines on the management of TB in children and adolescents,²⁷ the WHO recommends that decentralised models of care be used to provide TB services. This approach may be used along the full cascade of care, with a focus on TB detection and provision of TPT to children and adolescents.

Promotion of health education on TB and treatment adherence, defining the best strategy for TPT uptake and monitoring, use of digital technology such as SMS or video/phone calls, and support to overcome the emotional and economic impact of TB are among the main principles of TB patient-centred care, in line with Pillar 1 of the End TB Strategy.²⁸ The study by Hirsch-Moverman et al. includes these principles and gives us hope that such an approach can provide an important contribution

in pursuit of the goal of ending TB. However, individual- and population-level impact and cost of such approaches in increasing TPT completion among child contacts must be evaluated in other contexts in order to assess the role of shorter, better-tolerated therapeutic regimens with respect to local sociocultural characteristics and resources.

A. C. C. CARVALHO¹

A. L. KRITSKI²

¹Laboratory of Innovations in Therapies, Education and Bioproducts, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, RJ,

²Academic Tuberculosis Program, Faculty of Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

Correspondence to: Anna Cristina C Carvalho, Laboratory of Innovations in Therapies, Education and Bioproducts, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, RJ, Brazil. e-mail: anna.carvalho@ioc.fiocruz.br

References

- 1 World Health Organization. Global tuberculosis control: WHO report 2021. Geneva, Switzerland: WHO, 2021. <https://www.who.int/publications/i/item/9789240037021>
- 2 Wingfield T, et al. Beyond pills and tests: addressing the social determinants of tuberculosis. *Clin Med* 2016; 16(Suppl 6): s79–s91.
- 3 Szkwarko D, et al. Child contact management in high tuberculosis burden countries: A mixed-methods systematic review. *PLoS One* 2017; 12(8): e0182185.
- 4 Duarte R, et al. Tuberculosis, social determinants and comorbidities (including HIV). *Pulmonology* 2018; 24(2): 115–119.
- 5 de Aguiar RM, et al. Factors associated with non-completion of latent tuberculosis infection treatment in Rio de Janeiro, Brazil: a non-matched case control study. *Pulmonology* 2020; doi: 10.1016/j.pulmoe.2020.04.004 [Online ahead of print]
- 6 World Health Organization. Guidelines on the management of latent tuberculosis infection. Geneva, Switzerland: WHO, 2015. <https://www.who.int/publications/i/item/9789241548908>
- 7 World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva, Switzerland: WHO, 2018. <https://apps.who.int/iris/handle/10665/260233>.
- 8 World Health Organization. WHO consolidated guidelines on tuberculosis: module 1: prevention: tuberculosis preventive treatment. Geneva, Switzerland: WHO, 2020. <https://apps.who.int/iris/handle/10665/331170>.
- 9 World Health Organization. Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, Switzerland: WHO, 2011. https://apps.who.int/iris/bitstream/handle/10665/44472/9789241500708_eng.pdf?sequence=1
- 10 World Health Organization. Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries. Geneva, Switzerland: WHO, 2012. <https://apps.who.int/iris/handle/10665/77741>
- 11 Uplekar M, et al. WHO's new end TB strategy. *Lancet* 2015; 385(9979): 1799–1801.
- 12 Marais BJ, et al. The natural history of childhood intra-thoracic

- tuberculosis: a critical review of literature from the pre-chemotherapy era. *Int J Tuberc Lung Dis* 2004; 8: 392–402.
- 13 Martinez L, et al. The risk of tuberculosis in children after close exposure: a systematic review and individual-participant meta-analysis. *Lancet* 2020; 395(10228): 973–984.
 - 14 Ayieko J, et al. Efficacy of isoniazid prophylactic therapy in prevention of tuberculosis in children: a meta-analysis. *BMC Infect Dis* 2014; 14: 91.
 - 15 Sulis G, et al. Policies and practices on the programmatic management of LTBI: a survey in the African Region. *Int J Tuberc Lung Dis* 2018; 2: 158–164.
 - 16 Migliori GB, et al. Clinical standards for the diagnosis, treatment and prevention of TB infection. *Int J Tuberc Lung Dis* 2022; 26: 190–205.
 - 17 Marais BJ, et al. Adherence to isoniazid preventive chemotherapy: a prospective community based study. *Arch Dis Child* 2006; 91(9): 762–765.
 - 18 Menzies D, et al. Four months of rifampin or nine months of isoniazid for latent tuberculosis in adults. *N Engl J Med* 2018; 379(5): 440–453.
 - 19 Sterling TR, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. *N Engl J Med* 2011; 365(23): 2155–2166.
 - 20 Cruz AT, Starke JR. Safety and completion of a 4-month course of rifampicin for latent tuberculosis infection in children. *Int J Tuberc Lung Dis* 2014; 18: 1057–1061.
 - 21 Diallo T, et al. Safety and side effects of rifampin versus isoniazid in children. *N Engl J Med* 2018; 379(5): 454–463.
 - 22 World Health Organization. Global tuberculosis control: WHO report 2020. Geneva, Switzerland: WHO, 2020. <https://www.who.int/publications/i/item/9789240013131>
 - 23 Hirsch-Moverman Y, et al. Effectiveness of a community-based intervention to prevent childhood TB in Lesotho. *Int J Tuberc Lung Dis* 2022; 26: 612–622.
 - 24 Volmink J, Garner P. Withdrawn: interventions for promoting adherence to tuberculosis management. *Cochrane Database Syst Rev* 2007; (4): CD000010.
 - 25 M'imunya JM, Kredo T, Volmink J. Patient education and counselling for promoting adherence to treatment for tuberculosis. *Cochrane Database Syst Rev* 2012; 2012(5): CD006591.
 - 26 Toczek A, et al. Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2013; 17(3): 299–307.
 - 27 World Health Organization. WHO consolidated guidelines on tuberculosis. Module 5: management of tuberculosis in children and adolescents. Geneva, Switzerland: WHO, 2022. <https://www.who.int/publications/i/item/9789240046764>
 - 28 World Health Organization. A patient-centred approach to TB care. Geneva, Switzerland: WHO, 2018. <https://apps.who.int/iris/bitstream/handle/10665/272467/WHO-CDS-TB-2018.13-eng.pdf>