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Tuberculosis preventive therapy for children and adolescents: an emergency response to the COVID-19 pandemic



COVID-19, the clinical syndrome caused by SARS-CoV-2, has caused a tremendous burden of global morbidity and mortality. COVID-19 is predicted to have a devastating impact on other global infections, most notably tuberculosis.¹ Steep declines in tuberculosis diagnoses are predicted to lead to an excess six million people becoming ill with tuberculosis in the next 5 years and an additional 400 000 tuberculosis-related deaths in 2020 alone.² Measures taken to control the spread of COVID-19 could have increased tuberculosis transmission in households because people were told to shelter in place at the same time that the most effective infection control measures (ie, rapid diagnosis of tuberculosis and prompt initiation of therapy³) were hampered. Children and adolescents are a vulnerable population that have been overlooked in the COVID-19 and tuberculosis responses worldwide.^{4,5} Given the biology of tuberculosis in these age groups and the well-documented difficulties in diagnosing paediatric tuberculosis,⁶ the effect of COVID-19 on tuberculosis transmission and health-care services for children and adolescents might be especially severe.

However, these dire tuberculosis predictions are not inevitable, especially given that there is an effective means to prevent tuberculosis disease after exposure in the form of tuberculosis preventive therapy.⁷ Often referred to as treatment of tuberculosis infection, WHO has recommended a number of tuberculosis preventive therapy regimens for individuals (including

children and adolescents) at high risk, including those exposed to rifampicin-resistant forms of tuberculosis (RR-TB), and has recently expanded their tuberculosis preventive therapy recommendations to include exposed household contacts.⁸ However, the 2020 global report on tuberculosis shows that only 782 952 eligible household contacts under the age of 5 years received tuberculosis preventive therapy (less than 20% of those estimated to need it by 2022) and only 179 051 eligible household contacts in older age groups received tuberculosis preventive therapy (less than 1% of the 5 year target) after a known tuberculosis exposure in the home in 2018 and 2019.⁹

The provision of tuberculosis preventive therapy for all forms of tuberculosis should be seen as an emergency measure to combat the devastating effect of COVID-19 on tuberculosis, which might not only avert the development of active tuberculosis disease and the ensuing morbidity and mortality in the paediatric population but could also ease the strain of overstretched health-care systems. However, emergency implementation of tuberculosis preventive therapy provision requires adaptation to traditional approaches. We are providing tuberculosis preventive therapy for children and adolescents exposed to RR-TB in households in Khayelitsha, South Africa, as part of a joint emergency response plan implemented by the National, Provincial, and City Departments of Health in Cape Town, South Africa, and the medical humanitarian organisation Médecins

Panel: Responding to tuberculosis exposure during a pandemic

In Khayelitsha, South Africa, post-exposure management services for children and adolescents exposed to rifampicin-resistant forms of tuberculosis in the household were modified to entail home-based screening and tuberculosis preventive therapy initiation, telephone follow-up visits, multimonth medication refills, and provision of nutritional support as well as other social services in conjunction with partner organisations. Potential adaptations for the roll-out of emergency tuberculosis preventive therapy responses in other settings could include the following changes:

- The use of community-based and home-based household contact assessments carried out by paid community health workers or medical teams with adequate protective equipment
- The use of community-based and home-based household contact assessments carried out by paid community health workers or medical teams with adequate protective equipment
- Diagnostic testing for tuberculosis in individuals who have clinical indications
- Community-based and household-based initiation of tuberculosis preventive therapy for individuals who are well
- Community-based and household-based dispensing of multiple months of medication for individuals receiving tuberculosis preventive therapy
- Telephone-based counselling and follow-up for all individuals receiving tuberculosis preventive therapy, with in-person visits only for individuals who have medical concerns or challenges
- Provision of socioeconomic support via partner organisations, to minimise risks of insecurity regarding food and nutrition

Sans Frontières. In this programme, household child and adolescent contacts of newly diagnosed patients with RR-TB who are deemed to be at high risk for COVID-19 are screened and initiated on tuberculosis preventive therapy at home if RR-TB disease is ruled out by a negative tuberculosis symptom screen and a clinical exam. Chest radiographs and microbiological specimens are only requested or collected from individuals with symptoms of tuberculosis or with suspected RR-TB disease. Multimonth medication refills are delivered to homes or given to the index patient at routine clinical encounters. Most follow-up visits for individuals receiving RR-TB treatment of infection are provided telephonically. The families of known individuals living with TB that are identified as having food insecurity are provided with food parcels from partner organisations. These community-based services are provided by a mobile team that consists of a general medical practitioner who is experienced in child and adolescent health, a nurse, and where the need is identified, a social worker, counsellor, and health promoter or peer support worker.

Due to COVID-19, there has been a decrease in the use of health-care services in South Africa, and

this programme has enrolled 58 child or adolescent household contacts over 8 months (between March and October, 2020); 56 (97%) of whom were started on treatment of infection for RR-TB and two (3%) of whom were diagnosed with, and started on treatment for, active RR-TB disease. An internal programme review of observations and feedback from participants suggests five outcomes: (1), there is increased acceptance of tuberculosis preventive therapy compared with before the pandemic, possibly due to changed risk perceptions; (2), there is increased ability to assess the target populations due to lockdown and school closures; (3), there is increased access to health and social care services as a result of the ability to provide home visits (fewer visits to the clinic have been required, thus saving time and money for families); (4), interactions are increased between providers and contacts or guardians at the home visits compared with those that took place solely at the health centres, allowing them to build rapport; and (5), the time spent in facilities has decreased, potentially leading to lower COVID-19 transmission risk. The provision of home-based care also allowed the Médecins Sans Frontières clinical team to observe and address the complex social challenges faced by the families affected by RR-TB, including setting up referral pathways to the Department of Social Development (Khayelitsha, South Africa) for the children and adolescents in extremely vulnerable households. The provision of food parcels over the 8-month period assisted in addressing some of the families' social challenges, potentially making it easier for them to remain engaged in care. Programme challenges have included trouble reaching families via telephone, which has been addressed by undergoing home visits before arranging appointments, and the stigma of both tuberculosis and COVID-19 reducing the acceptability of community household assessments for some families.

The COVID-19 pandemic has been devastating, but its collateral consequences might be felt for decades in the context of tuberculosis.¹⁰ Fortunately, tuberculosis preventive therapy could mitigate the effect of COVID-19 on tuberculosis if implemented urgently, and the experience from Khayelitsha, South Africa, shows one potential model for how this can be done (panel). A major reset is called for on the risk-benefit

assessment for tuberculosis preventive therapy. The provision of tuberculosis preventative therapy must now be viewed as a core and emergency response to COVID-19 for households in which someone has been diagnosed with tuberculosis. Desultory discussions on tuberculosis catch-up plans must be reframed as emergency response interventions, with provision of tuberculosis preventive therapy to all household contacts of persons newly diagnosed with tuberculosis at the core of the mission.

We declare no competing interests.

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Making human milk matter: the need for EU regulation

One in ten infants is born preterm worldwide, with an average preterm birth incidence of 8.7% in Europe.¹ Together with sick and low-birthweight infants, preterm babies belong to the most vulnerable group of patients and require special care, including nutrition. The mother's own milk is without doubt the preferred choice for infant feeding,² and exclusive breastfeeding during the first 6 months of life is recommended. However, when the mother's own milk is not available, donor milk from a human milk bank is the next best option, because of the undisputed health benefits of human milk.^{2,3} Furthermore, donor milk acts as a bridge to breastfeeding, with positive psychological and emotional effects for both mother and child.^{2,4}

In Europe, an increasing number of human milk banks provide this urgently needed nutrition.⁵ The process of human milk donation is complex, entailing (among other processes) screening and blood testing of donors and processing, preservation, storage, and distribution of donated human milk (appendix p 2). Furthermore, the European Directorate for the Quality of Medicines & HealthCare provides evidence-based

recommendations for the establishment and operation of human milk banks.⁶

In view of the unique role and importance of human milk in infant nutrition, it is surprising and problematic that donor human milk (a substance of human origin) and human milk banking are currently unregulated not only at the EU level but also often on a national level.

Legal uncertainty regarding the status and handling of donor human milk provides a disincentive to adopt evidence-based practices about human milk-based nutrition. This uncertainty leads to scant access, concerns about safety, questions about funding and reimbursement, an increased administrative burden, and underutilisation of donor human milk in many neonatal units. These consequences are especially pronounced in countries where human milk bank services are not well established.⁷ The current challenges caused by the COVID-19 pandemic make issues related to human milk banking services even more pressing.⁸

The Human Tissues and Cells Directive (2004/23/EC), which currently does not include donor human milk, was



EFCNI/Christian Klant Photography

See Online for appendix