# TITLE PAGE

### The need to prioritise childhood tuberculosis case detection

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With 10 years left to the WHO End TB Strategy's interim milestones of 80% reduction in new tuberculosis cases and 90% reduction in tuberculosis deaths by 2030 compared with 2015,<sup>1</sup> little progress has been made. The COVID-19 pandemic has worsened the situation because of its negative impact on tuberculosis case detection and reduced access to tuberculosis treatment and prevention services globally.<sup>2</sup> In a worst-case scenario, COVID-19 might have resulted in up to 400 000 excess tuberculosis deaths in 2020, which would mean the worldwide number was similar to that in 2012.<sup>3</sup> Estimates suggest that the COVID-19 pandemic could cause an additional 6·3 million tuberculosis cases globally between 2020 and 2025, with the most vulnerable populations, especially children, at risk.<sup>4</sup> These extreme outcomes would slow or reverse any progress made towards the tuberculosis treatment and prevention milestones and targets.<sup>5</sup>,6

WHO estimated that children younger than 15 years constituted 12% of the 10 million people who became ill with tuberculosis in 2019.<sup>4</sup> The global annual numbers of tuberculosis cases accounted for by children have been on the rise, increasing from about 1 million in 2017 to 1.2 million in 2019, 4,7 with the highest burden of childhood tuberculosis in China, the Democratic Republic of the Congo, India, Indonesia, and Nigeria.<sup>8</sup> Despite the global efforts to combat tuberculosis, an estimated 192 000 children died from tuberculosis in 2019.<sup>4</sup> The high burden of childhood tuberculosis and poor outcomes are largely because of the difficulties in confirming the diagnosis of tuberculosis in children, arising from the non-specific nature of symptoms and signs of tuberculosis in children, the paucibacillary nature of childhood tuberculosis, the challenge of obtaining good-quality sputum samples, especially in young children, and difficulties in accessing health services.<sup>9</sup> As a result, more than 90% of these children encounter delays in receiving treatment since they are either never diagnosed or are misdiagnosed.<sup>7</sup> An estimated 568000 missing childhood tuberculosis cases in 2019 were neither diagnosed nor adequately treated.<sup>4</sup> A fundamental problem is the absence of large-scale contact screening and provision of tuberculosis preven- tive therapy to eligible children, which is largely due to insufficient health-care resources, workforce, and services in low-income and middle-income countries (LMICs).<sup>4</sup> In 2019, more than 40% of eligible household child contacts were not screened for tuberculosis disease or infection.<sup>4</sup> Therefore, access to and provision of tuberculosis contact screening and preventive treatment needs to be substantially expanded.

Alongside efforts to address multidrug-resistant tuberculosis in children and deliver less toxic and more childfriendly tuberculosis treatments,<sup>7</sup> improving child- hood tuberculosis case detection is crucial. Efforts to prioritise case detection will also benefit from innovative community-based approaches to case finding, such as the need for enhanced screening for tuberculosis in children presenting at general child health services in LMICs. Given that many children with presumptive tuberculosis present to maternal and child health clinics and private care providers in LMICs,<sup>10</sup> a close interaction between tuberculosis programmes and these services is needed. This approach is essential to reach the over 60% of children who acquire the infection outside the household and who would not be reached by household contact-based approaches, even with the most optimistic assumptions for coverage of household contact tracing.<sup>11</sup>

Tuberculosis testing is reliant on sputum, a sample that is not easy to collect, especially in young children. Additionally, WHO-recommended rapid tuberculosis diagnostic tests such as Xpert-Ultra are not easily accessible at the primary care level in LMICs where they are most needed.<sup>7</sup> The development of non-sputum biomarker-based tests for diagnosis of tuberculosis, especially in children who are typically paucibacillary, is now a recognised research priority.<sup>12</sup>

To achieve the WHO End TB Strategy targets and narrow the childhood tuberculosis case detection gap, tuberculosis vaccines are needed that are effective for both pre-exposure and post-exposure prevention and treatment.<sup>13</sup> COVID-19 has shown how several efficacious vaccines can be developed within a short timeframe, given the right motivation and available funding. The BCG vaccine, which was developed 100 years ago, effectively prevents severe forms of the disease but has only moderate benefits for prevention of pulmonary tuberculosis.<sup>14</sup> Having new tuberculosis vaccines would help reduce new tuberculosis cases and deaths. Given the demonstrated ability to develop effective COVID-19 vaccines rapidly, it is no longer justifiable to not equally invest in the development of tuberculosis vaccines.

To accelerate progress toward ending tuberculosis, there is the need for sustained increase in investments in tuberculosis control services that are delivered as part of comprehensive primary health-care services, and for strengthening health workforce capacity and health systems as part of overall efforts toward achieving universal health coverage in LMICs. Therefore, as we mark World Tuberculosis Day on March 24, 2021, the theme— The Clock is Ticking—is aptto convey a sense of urgency. As countries move towards recovery from the setbacks caused by COVID-19, it is a pivotal moment to make tuberculosis case detection in children a priority. The next few years will be crucial in the tuberculosis response, and it will take sustained efforts by many stakeholders to achieve the internationally agreed targets by 2030. Tuberculosis is preventable and treatable and no child with tuberculosis should miss out on the care they need.

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