Scaling up tuberculosis preventive therapy for contacts in high transmission settings

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Tuberculosis is the world's deadliest infectious disease, with 1·5 million deaths globally in 2018.[1] Airborne epidemic spread, particularly of drug-resistant tuberculosis, is a threat to global health security because of the human and economic impact, which is most pronounced in low-income and middle-income countries. The target of elimination of tuberculosis by 2030 cannot be achieved without a strategy to address latent infection that is subclinical or quiescent.[2] Effective treatment of latent tuberculosis infection to prevent active disease, known as tuberculosis preventive treatment, is a critical component of the WHO End TB Strategy.[2]

Around 1·7 billion people—a quarter of the world's population—is estimated to have latent tuberculosis infection, although only 5–10% of these individuals will develop active disease.[1] There is no gold standard test for detection of infection or those at highest risk of progression to active disease. Limitations of the available tests for infection are well recognised, including major logistical challenges for scaling up implementation in most high transmission settings. Guidelines are needed to maximise the effect on the epidemic and the benefit and safety for individuals, which are also relevant when health-care system capacity is constrained.

In *The Lancet Global Health*, Courtney Yuen and colleagues[3] use a decision-tree model to compare the effect of providing tuberculosis preventive treatment for all household contacts on tuberculosis incidence and severe adverse events among selected age groups and different preventive treatment regimens, with a test-and-treat approach.[3] A treat-all approach in household contacts was predicted to lead to 13 fewer incident tuberculosis cases (IQR –5 to –18) and four additional severe adverse events (2 to 6) compared with using an approach whereby only contacts with a positive tuberculin skin test were treated. The authors suggest that serious adverse effects could be minimised by using non-isoniazid containing tuberculosis preventive treatment regimens in adult contacts. The findings are not surprising given that the model was informed by clinical trials and natural history studies. In fact, the study might underestimate the benefit of tuberculosis preventive treatment in high transmission settings. The risk of disease progression was based on a study in a low transmission setting and the study did not consider the potential benefit of preventive treatment on further transmission by reducing incident tuberculosis in contacts. Compared with young child contacts, preventing tuberculosis in adolescents and adults is likely to have a far greater effect on community transmission.

This study provides original and important age-related data, which are timely and could be applied to specific settings to guide policy and practice. In March, 2020, WHO published updated tuberculosis preventive treatment guidelines, along with an operational guide to support programmatic implementation.[4] A range of preventive treatment options, including rifamycin-based regimens, are recommended for high-risk groups in which benefit outweighs risks. The tuberculosis preventive treatment recommendation for HIV-negative contacts aged 5 years and older is conditional, with a preference for confirmation of latent tuberculosis infection with a test, but an option of proceeding to preventive treatment if a test is unavailable, as is typically the case.

There are many other major challenges for the scale-up of programmatic management of tuberculosis preventive treatment for older children, adolescents, and adult contacts in high transmission settings, in which the risk-benefit balance will be context specific. These include optimising screening approaches that effectively and efficiently detect or rule out active tuberculosis, using tools such as computer-assisted X-ray, molecular diagnostics, and telemedicine for decision support; models of care that deliver early contact screening with high coverage, high uptake, adherence, and completion of preventive treatment through patient support;[5,6] integration with community-based case finding and other interventions; application of guidance to specific at-risk communities or geographic locales that might benefit from population-wide tuberculosis preventive treatment as part of a comprehensive intervention;[7] and preventive treatment options for those living in a community with a high prevalence of drug-resistant tuberculosis, irrespective of known drug susceptibility of the index case.[8]

At the first UN high-level meeting on tuberculosis in 2018, member states committed to provide tuberculosis

preventive treatment to at least 30 million people in 2018–20, including 20 million household contacts. This target is now beyond reach, especially given the massive impact of the coronavirus disease 2019 (COVID-19) pandemic on health-care systems and services in high tuberculosis transmission settings. However, the public health response to COVID-19 similarly relies on community-based case detection, contact screening, management, and effective community engagement, thereby providing an opportunity not to neglect the response to the pandemic of tuberculosis. Research in high tuberculosis transmission settings will remain critical to evaluate novel tools and strategies for implementation of preventive treatment at scale and inform responses to local epidemics.

We declare no competing interests. SSM is a recipient of a National Health and Medical Research Council (NHMRC) Postgraduate Scholarship and the Royal Australasian College of Physicians NHMRC Woolcock Scholarship. The Burnet Institute receives support from the Victorian Government Operational Infrastructure Fund. The views expressed in this publication are those of the authors and not necessarily those of the Australian Government.

*Suman S Majumdar, Rina Triasih, Stephen M Graham
suman.majumdar@burnet.edu.au

Burnet Institute, Melbourne, VIC 3004, Australia (SSM, SMG); Centre for International Child Health, Department of Paediatrics University of Melbourne and Murdoch Children's Research Institute, Royal Children's Hospital, Melbourne, VIC, Australia (SSM, SMG); and Department of Paediatrics, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia (RT)

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