Pragmatic tuberculosis prevention policies for primary care in low- and middle-income countries

To the Editor:

Despite being a curable and preventable disease, tuberculosis is the leading cause of death from infection worldwide and is one of the top 10 causes of death from any cause, including in children [1]. Incidence is at best barely declining, increasing in some countries, and some prevalence surveys in high-burden countries have demonstrated a significantly higher tuberculosis burden than estimated [1]. Between a quarter and a third of the world's population is estimated to be infected with tuberculosis, representing a vast reservoir from which new cases arise [1]. Many of these people are never identified or tested, and even among those who are, only a small proportion receive preventive treatment [2]. Interventions that aim to increase preventive treatment uptake and completion are likely to have a greater impact on tuberculosis control and elimination than those focussing on improving completion of treatment by patients [3].

In their recent article in the *European Respiratory Journal*, Acuña-Villaorduña *et al.* [4] demonstrate once again that contacts of patients with tuberculosis are at increased risk of tuberculosis infection and disease. In this study of contacts of any age from a setting with low tuberculosis incidence (38 per 100 000) and HIV prevalence (<1% of the general population), 507 (71%) out of 710 contacts had tuberculosis infection (defined by a positive tuberculin skin test (TST) or interferon-γ release assay (IGRA)). Over 5 years of follow-up, 36 (4.1%) out of 894 had co-prevalent or incident tuberculosis disease, equating to an overall incidence of 541 per 100 000 person-years: at least 14 times that of the general population. Despite this markedly elevated risk, only a minority (16%) of contacts received preventive treatment, reflecting the low rates of uptake seen globally [2]. Whilst guidelines for preventive treatment in low- and middle-income countries (LMICs) focus principally on children aged <5 years due to the high risk of primary progressive disease and death in this age group, it should be highlighted that in this study 21 (91%) out of 23 of the incident tuberculosis cases occurred in contacts aged ⩾15 years, of whom only 10% received preventive treatment [4].

In LMICs, the great majority of patients with tuberculosis and their contacts are managed in primary care. Healthcare workers consistently face the triple challenges of insufficient human resources, scarce or inadequate material resources, and a large, heterogeneous population presenting with complex medical and social syndromes. Acuña-Villaorduña *et al.* [4] describe how the absence of clear definitions of contacts at highest risk of tuberculosis prohibits effective implementation of contact investigation and preventive treatment in these settings. As a potential solution, they used an adapted Mandalakas score to predict tuberculosis infection and disease [5]. Although higher scores, reflecting increased exposure to potentially more infectious index cases, were associated with an increased risk of both infection and disease in contacts, the overall performance of the score for predicting infection was poor. Notably, the score's performance for predicting tuberculosis disease, the rarer but more important outcome, was substantially improved. In their discussion and conclusion, the authors suggest that a laboratory biomarker with moderate accuracy to predict tuberculosis disease is urgently needed to guide targeted preventive treatment for contacts at highest risk. Although such a biomarker would evidently be welcome, we believe that rather than better, expensive, commercial laboratory tests, more pragmatic and simple healthcare policies for contact investigation and preventive treatment are needed that reflect the realities of the primary care centres in LMICs where they are implemented.

Our research group, Innovation For Health And Development (IFHAD; www.ifhad.org), recently derived and validated a score to predict tuberculosis disease among contacts aged ⩾15 years of patients with laboratory-confirmed tuberculosis, including sputum-smear negative tuberculosis [6]. The IFHAD score incorporates readily collectable data at the time of contact investigation on index case, household and contact factors, including exposure intensity. A preliminary online version is freely available (https://jscalc. io/calc/qoLectXm5TiopbbD). Through the derivation of this score, we have shown that tuberculosis disease in adult contacts may be predicted without any laboratory or invasive testing. Importantly, inclusion of TST results in the score provided no additional predictive value. In children, most cases of tuberculosis occur after missed opportunities for prevention. Although the reasons for this are complex, a key barrier is the perceived necessity to base diagnostic and preventive treatment decisions on TST results. A recent study of 1718 child contacts aged <16 years demonstrated that a single TST result does not provide any additional predictive value for tuberculosis disease following documented household exposure [7]. Indeed, the technical and operational limitations of testing for tuberculosis infection in LMICs are well described [8] and further demonstrated in the study by ACUÑA-VILLAORDUÑA et al. [4]: 20% of recruited contacts had incomplete information on TST/IGRA results, and, of those with complete results, 19% had discordance between the two tests.

As part of the PREVENT TB study [9, 10], our research group is evaluating a policy of risk-based preventive treatment for contacts in Peru, whereby all children aged <15 years are recommended to take preventive treatment, irrespective of TST results, and adults are informed of their risk using the IFHAD score. We aim to substantially increase uptake of preventive treatment among contacts and, through doing so, demonstrate that simple policies can be effectively delivered in primary care to prevent tuberculosis in people at high risk.

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