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A test of infection should not be a "standard" for guiding TB preventive therapy in at-risk populations

Dear Editor,

We read with interest the article "Clinical standards for the diagnosis, treatment and prevention of TB infection" (TBI) by Migliori and colleagues.[1] Although there are many aspects that we feel are forward-thinking, particularly the inclusion of patient counseling, we are concerned by the emphasis on TBI testing in Standard 1. This article advocates that all individuals belonging to at-risk groups for TB should undergo TBI testing.[1] These at-risk groups, as defined by the WHO, include people living with HIV (PLHIV) and all household contacts of people with pulmonary TB, regardless of age, i.e., individuals who are most likely to benefit from TB preventive treatment (TPT).[2] However, testing for TBI is fraught with challenges, many of which relate to the poor performance of the currently available tests.[3] Both the tuberculin skin test (TST) and interferon-gamma releasing assays (IGRAs) require a functioning immune system to test positive.[4] Ironically, they perform most poorly in populations at highest risk for developing TB disease, including PLHIV, young children, and people who are malnourished,[5] which the authors of this paper acknowledge. The administration of a TBI test also introduces logistical and socioeconomic challenges, both for health systems and for people at risk of TB disease. These range from obtaining a blood sample to needing to make multiple trips to health facilities for testing.[6] Other barriers include the global shortages of quality-assured purified protein derivative and the laboratory and financial resources required to perform IGRAs. These are some of the reasons why the WHO guidelines state that TBI testing is not essential prior to providing TPT for individuals at high risk. Indeed, several high TB burden countries (including South Africa) no longer include TBI testing in their national TPT guidance.[7] Requiring TBI testing will add pressure to already constrained health systems, currently trying to implement their TB recovery plans.[8]

It should be noted that there is a lack of clarity between Standard 1 and Standard 4, which states that TB disease should be excluded prior to initiating TPT. The included algorithm for exclusion of disease suggests that PLHIV and household contacts <5 years old do not require TBI testing, and that a simple four-symptom screen is adequate for excluding TB. Other risk groups, including older household contacts, are suggested to require TBI testing in the algorithm. This seeming contradiction has the potential to introduce further confusion and delays into what is already a complicated care cascade for TB prevention.[9] Testing for TBI may be warranted in some populations, to identify those who would benefit most from TPT (i.e., people with diabetes, or those without close household contact) and in settings with greater resources. However, we argue that the disadvantages of requiring a positive TBI test before initiating TPT in at-risk groups may outweigh any advantage. Instead, in most high TB burden settings, particularly those with high HIV prevalence, a greater emphasis on excluding TB disease is likely warranted. In South Africa, a 'TB test & treat' approach, where individuals are either offered TB treatment for active TB disease or TPT is in the process of becoming policy.[7]

The roll out of TPT has been a global failure, with only 29% of people in need (including children and household TB contacts) receiving it.[10] The article by Migliori and colleagues aims to provide both clinical and public health standards that can be used by program managers; however, in its current form, Standard 1 could introduce yet another barrier to improving access to TB prevention. We believe that this is not in keeping with WHO recommendations, or with the global commitment to "end TB."

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Reply to Furin et al.: Clinical standards that are appropriate for all settings

Dear Editor,

We thank Furin and colleagues for their Correspondence[1] on our article "Clinical standards for the diagnosis, treatment and prevention of TB infection",[2] and we also commend their efforts in rolling out TB preventive treatment (TPT) policies in South Africa. But let us now address the points they raise.

First, clinical standards are widely accepted levels of diagnosis and care for the management of patients with a particular infection or disease. Although these are universal principles, we recognise the need to adapt the standards for TB infection (TBI) to specific settings for organisational, or economic reasons. The standards were derived using a consensus Delphi process with co-authors who have extensive experience of resource-limited settings, and a considerable number were involved in creating the WHO operational handbook on TB.[3] In this, Module 1: Prevention; TB preventive treatment[3] states that testing for TBI is one of the key steps in the cascade of care for TB case-finding and preventive treatment (as featured in Figure 1.1).[3] For people living with HIV (PLHIV) and household contacts less than 5 years old, testing for TBI is not mandatory, but based on operational and economic constraints. Furin et al. propose that "a test for TB infection should not be a "standard" for guiding TB preventive therapy in many at-risk populations".[1] They interpreted the algorithm on excluding TB as simply performing a 4-symptom screen for TB disease for PLHIV and children less than 5 years old. However, we would like to draw their attention to the figure legend, which states that it is ideal to include both chest radiography and TBI testing (but the absence should not be a barrier to initiating TPT), which is in keeping with WHO recommendations. Second, we would also like to highlight the aim of Standard 1, which is "Identifying the population groups that need to be tested", as stated in our aims. We acknowledge that TBI testing may not be available in resource-limited settings, and emphasised in Standard 4 that this should not be a barrier to initiating TPT. Finally, although global efforts at TPT are yet to be scaled up, we feel it is premature to deem this a "failure".[1] There is certainly huge room for improvement, but as we move to shorter regimens for TPT,[4,5] there is also renewed hope.

In conclusion, we believe that the series of IJTLD Clinical Standards for Lung Health, provide universal guiding principles for the care of patients.[6–8] They are designed to be flexible and recognise the needs of different settings. The fight against TB is a laborious, drawn-out, and often frustrating process, but by constructively and collaboratively working together we can achieve the common goal to end TB.

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