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Correspondence

A human rights-based approach to tuberculosis diagnosis

To the Editor,

We read with concern the piece by van Deun et al. who have emphasized the importance of smear-microscopy for tuberculosis (TB) diagnosis.[1] Despite recent high-level meetings on TB elimination,[2] low expectations are common in the field of TB care. Much of this defeatism is cloaked in the mantle of public health responsibility. Shortcomings of the 'public health approach' underpinning the global response to TB in the past half century are readily apparent: TB is the leading infectious killer in adults, and a serious infection that has contributed to the growing crisis created by antimicrobial resistance.[3]

It is therefore worrisome that van Deun et al. open their opinion piece by stating that the first priority of a TB diagnostic should be an epidemiologic one '[that] identifies transmitters'. They only mention 'identifying patients suffering from any form of TB' as a secondary priority. Prioritizing the identification of people who are transmitting TB (preferable to the derogatory term 'transmitters') has not had a significant impact on the TB pandemic, but has led to the exclusion of vulnerable populations from TB services—including children and people living with human immunodeficiency virus infection—and may be responsible for the limited funding for research and programs that is a feature of TB management today.[4] This approach stands in direct opposition to patient-centered care and a human rights-based approach to TB, where every person affected by TB is offered the highest standard of care.[5]

Proponents of the public health approach rely on continued acceptance of double standards in TB care.[6] The claim that 'it is likely that most African countries are currently unable to replace even 50% of their microscopes with GeneXpert® (Cepheid, Sunnyvale, CA, USA) machines' is unsubstantiated. A more useful solution than advocating for the continued use of smear microscopy would be to mobilize political will and necessary resources, both to ensure universal access to Xpert testing for TB diagnosis and to develop better tools for treatment monitoring. International human rights laws make it clear that any references to the progressive improvement of health care should be accompanied by the setting of timebound goals, and not simply presented as statements of immutable fact. Instead, van Deun et al. perpetuate the idea that some countries can never achieve a higher standard of TB care, which only reinforces the 'subtle bigotry'[7] of their low expectations against people who live in resource-poor settings.

The challenges we face in tackling TB are serious and can seem intractable. Overcoming poverty, weak health systems, and the resistance to change that plagues national TB programs and results in poor-quality services that further deepen the inequities that drive the TB epidemic will require courage and a can-do attitude that takes us beyond what is currently deemed practical into the realm of the ambitious. The TB community needs to act as a progressive coalition of forces that confront challenges, instead of falling back on strategies that may feel familiar, but leave the standard of care in stasis. Clinging to smear microscopy will not end TB.

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In reply: A human rights-based approach to tuberculosis diagnosis

We thank Mr Frick and Drs McKenna and Furin for their comment. Unfortunately, they seem to have

missed the true message of our reflective piece that is not, 'only microscopy, only transmitters of tubercle bacilli'. We certainly agree with them that the Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA) has revolutionized the rapid detection of resistance to the most important anti-TB drugs; however, we are also convinced that disinvesting in quality-assured microscopy networks will hurt TB patients. Rather than repeating here the extensive and balanced argumentation of our article, we invite the correspondents to scrutinize the content again carefully.

The so-called 'unsubstantiated claim' regarding the current prospects for Xpert coverage in Africa is in fact supported by our two African co-authors. Both are directors of their national TB laboratory networks, as well as directors of the only two supranational TB laboratories (SRLs) between the Sahara and South Africa, with significant experience, including in the building of Xpert-based networks. Three are SRL directors or senior staff, including one who is employed at the coordinating SRL in Antwerp (Belgium), with decades of experience supporting TB laboratory services in Africa and a multitude of low- and middle-income countries all over the world.

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Causal inference in tuberculosis treatment studies: bias considerations and data needs

A letter by the Editor-in-Chief, G Marks, published in the December 2018 issue of the *IJTLD*, drew attention to a recent publication recommending strategies to strengthen the ability to draw causal inferences from epidemiological data.[1] Recommendations included careful consideration of confounding factors, de-emphasizing *P* values, and transparent reporting.[2] We are in full agreement, and would like to highlight selection and misclassification biases that pose important threats to the validity of analyses of tuberculosis (TB) treatment cohorts. These biases require careful consideration.

Selection bias can occur when patients excluded from a study are at higher or lower risk than those included. Consider the example of sputum culture conversion as an indicator of treatment response. Complete monthly culture results are rarely available from all patients, and patients who are missing culture results may be more or less likely to experience conversion due to, for example, death, loss to follow-up, or inability to produce a sputum sample. We provide below an extreme example for illustrative purposes. Among 100 patients, 75 have complete follow-up culture results, all of which are negative; the remaining 25 patients have no culture results because they were lost to follow-up. Unbeknownst to the investigators, the 25 patients without culture results died of TB with a positive sputum culture. Restricting conversion analyses to patients with complete follow-up would dramatically overestimate the percentage of patients who experience culture conversion (100% vs. 75%), resulting in a clearly biased estimate. Methods, such as inverse probability weighting, can be used to mitigate selection bias by taking into account the ways in which included and excluded patients differ.[3]

Misclassification bias may occur in analyses of drug-resistant TB regimens, when available data do not reflect the dynamic nature of treatment. For example, the absence of detailed longitudinal data may lead to the classification of a patient's regimen according to initial composition or to drugs 'ever' received, so that patients who receive a drug for 1 month or 12 months are considered similarly exposed. It is also possible that the analysis fails to take into consideration the effect of drug additions,