

Cost-effectiveness of Xpert MTB/RIF and investing in health care in Africa

We welcome the Comment by Keertan Dheda and colleagues (October issue)¹ about our modelling study² that assessed the effects and cost-effectiveness of several new tuberculosis diagnostic algorithms for adult pulmonary tuberculosis in Tanzania. However, we would argue that some key points about the importance of the work have been omitted.

Dheda and colleagues point out that the accuracy of clinical diagnoses for tuberculosis or empirical tuberculosis treatment is highly setting-specific. We agree with this viewpoint; indeed, we would suggest that tuberculosis diagnosis in general is highly setting-specific, which, rather than being a limitation of our study, is precisely why our study is relevant. Variations in test quality, patient pathways, levels of centralisation, and many other factors mean that accurate assessment of the effect of any new diagnostic algorithm needs to take these factors into account. These variations are why the detailed and comprehensive modelling approach of our study is needed at the national level to support national policy decision makers to make decisions in the context of their country's needs. Although each context needs modelling that is fitted to local data, the approach used in our study can be generalised and adapted to model other contexts.

Contrary to the implication in the Comment by Dheda and colleagues that our modelling assumptions result in much lower levels of overtreatment than reported in South Africa, our modelling approach suggested that, on the basis of Tanzania's national data for smear-positive and smear-negative tuberculosis cases, alongside assumptions for the sensitivity and specificity of microscopy and clinical diagnosis,^{3,4} more than 40% of the

smear-negative tuberculosis cases are falsely diagnosed as tuberculosis on clinical grounds. This false diagnosis leads to high levels of overtreatment consistent with that referenced by Dheda and colleagues in South Africa, Uganda, and Kenya.^{5,6} Results of our study suggest that the use of Xpert MTB/RIF as the primary diagnostic method would lead to both a reduction in underdiagnosis in patients with microbiologically defined tuberculosis as a result of the accuracy of the test, and a reduction in overdiagnosis in patients without microbiologically confirmed tuberculosis as a result of a reduction in empirical clinical diagnoses. The net result is not much change in overall numbers of patients placed on tuberculosis treatment. We believe that outcomes would be much the same in countries with a similar prevalence of HIV and smear-negative tuberculosis and with decentralised tuberculosis programmes. Importantly, the patient outcome information reported in our study focuses on true cures, and takes into account the overtreatment of tuberculosis. This proportion of true cures is in contrast to the proportion of tuberculosis cases reported as successfully treated (88% in Tanzania), which will usually include some cases as successfully treated even when tuberculosis treatment was not necessary.

We agree with Dheda and colleagues that the costs incurred by patients are very important and affect whether patients complete diagnosis or not. To this end, we reported the projected effect of different diagnostic algorithms on the number of visits to a diagnostic centre and the diagnostic loss to follow-up. Both these outcomes have the potential to be reduced by implementation of Xpert MTB/RIF. We also detail how the effect of new diagnostics on patients' costs could be projected using our study approach and report our findings in our appendix using data from Malawi.

Dheda and colleagues point out that we did not specifically model the

transmission of multidrug-resistant tuberculosis, mainly because we were modelling a setting with low multidrug-resistant tuberculosis. However, our approach could be used in contexts with a higher prevalence of multidrug-resistant tuberculosis than Tanzania because both the effect on the level of multidrug-resistant tuberculosis diagnosed and the related costs of multidrug-resistant tuberculosis treatment were included with an assumption that the incidence of multidrug-resistant tuberculosis is in proportion to the number of tuberculosis cases. If this assumption is not applicable, further research would be needed to model effect on multidrug-resistant tuberculosis transmission of alternative diagnostic algorithms. We agree wholeheartedly with Dheda and colleagues' comment that the sensitivities of the model should be seen as flags that inform programmatic implementation. Indeed, we ran many simulations testing several of the assumptions, which we described in our appendix.

Finally, an important element of our study is that, rather than focusing on the effect of one diagnostic test, our modelling deliberately models whole diagnostic algorithms and alternative placements of new diagnostic tests within those algorithms. We think that this is an important element of our approach that helps to compare whole algorithms involving microscopy (eg, same-day front-loaded fluorescence light-emitting diode microscopy), targeted use of Xpert MTB/RIF (eg, to HIV-positive or smear-negative patients), empirical clinical diagnosis, and any combination of the above.

We declare no competing interests.

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- 1 Dheda K, Theron G, Welte A. Cost-effectiveness of Xpert MTB/RIF and investing in health care in Africa. *Lancet Glob Health* 2014; **2**: e554–56.
- 2 Langley I, Lin HH, Egwaga S, et al. Assessment of the patient, health system, and population effects of Xpert MTB/RIF and alternative diagnostics for tuberculosis in Tanzania: an integrated modelling approach. *Lancet Glob Health* 2014; **2**: e581–91.
- 3 Boehme CC, Nicol MP, Nabeta P, et al. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resistance: a multicentre implementation study. *Lancet* 2011; **377**: 1495–505.
- 4 Swai HF, Mugusi FM, Mbwambo JK. Sputum smear negative pulmonary tuberculosis: sensitivity and specificity of diagnostic algorithm. *BMC Res Notes* 2011; **4**: 475.
- 5 Huerga H, Varaine F, Okwaro E, et al. Performance of the 2007 WHO algorithm to diagnose smear-negative pulmonary tuberculosis in a HIV prevalent setting. *PLoS One* 2012; **7**: e51336.
- 6 Nakiyingi L, Bwanika JM, Kirenga B, et al. Clinical predictors and accuracy of empiric tuberculosis treatment among sputum smear-negative HIV-infected adult TB suspects in Uganda. *PLoS One* 2013; **8**: e74023.