Commentary

Gene Xpert MTB/RIF assay confirms its value in the first multicentre, randomised, controlled trial conducted in primary-care settings in Africa

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Invited Commentary on 'Feasibility, accuracy and clinical effects of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial' by Theron et al.

WHO proposed the achievement of ending the global TB epidemic through the reduction of TB deaths and TB incidence rates within 2025. Part of this strategy is to improve the diagnostic ability at point-of-care, especially in high-burden countries, in order to facilitate and accelerate the beginning of an appropriate anti-tuberculosis treatment. Indeed, the 2014 focus of TB day, promoted by STOP TB, is to 'reach three million', which is to ameliorate the diagnostic procedure in three million cases, which are still unrecognized and consequently untreated.

Theron *et al.*¹ recently published an article, conducted in several primary care settings in Africa, which evaluates feasibility, accuracy, and clinical effects of the Xpert MTB/RIF assay. This test is able to detect both *Mycobacterium tuberculosis* (MTB) complex DNA and rifampicin (RIF) resistance (as a proxy of MDR resistance) within 2 hours. This study is the first multicentre, randomised controlled clinical trial which evaluated the real impact of this technology in a primary care setting in an area of hyper-endemic tuberculosis such as Sub-Saharan Africa. The study was conducted between 12 April 2011 and 30 March 2012 and involved 1502 eligible patients, which were randomly assigned: 758 to smear microscopy (91 culture positive) and 744 to Xpert MTB/RIF (154 culture positive). The setting of the study is the primary health-care facilities in South Africa, Zimbabwe, Zambia, and Tanzania.

The study showed that point-of-care MTB/RIF Xpert had higher sensitivity and similar specificity than microscopy and had similar sensitivity than laboratory-based MTB/RIF. More patients started the same day treatment, more culture positive started

therapy and experienced a shorter time to cure. In addition, this test can accurately be administered by a nurse working in primary care clinic with a similar sensibility, a better specificity, and a similar failure rate compared with that done by a technical laboratory.

Nevertheless, this randomised controlled trial failed to achieve the primary outcome, since the Xpert MTB/RIF technology did not reduce tuberculosis morbidity, evaluated by TB score and Karnofsky performance score.

In agreement with these results, Churchyard² recently reported at the CROI meeting (Boston, 3–6 March, 2014) the results of the study conducted in South Africa, which indicate that Xpert technology did not reduce rates of loss to follow-up and there were no differences in rates of treatment initiation between patients who underwent smear microscopy versus those diagnosed with Xpert MTB/RIF. Overall, about 71% of those who tested TB positive in either arm had their TB results microbiologically confirmed. Xpert yielded significantly more confirmations.

These trials confirm that this technology is simple, can be administered by a nurse, is rapid, fully-automated and, for these reasons, it can be used in low-resource settings. The treatment can be offered immediately since the test becomes positive in less than 2 hours.

Although the study of Theron failed to reach its primary endpoint, i.e. to reduce tuberculosis related morbidity, probably because of the high levels of empirical evidence based treatment in smear-negative patients, it is possible that implementing this technology in a larger number of individuals this empirical treatment could be reduced in the future in favour of an expert-driven therapy. In conclusion, this controlled, randomised clinical trial provides strong support to the WHO recommendation³ to a broader usage of Xpert MTB/RIF test in order to revolutionize and transform tuberculosis case management and control in forthcoming years.

References

- 1 Theron G, Zijenah L, Chanda D, Clowes P, Rachow A, Lesosky M, *et al.* Feasibility, accuracy and clinical effects of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial. *Lancet*. 2014;383:424–35.
- 2 Churchyard G, McCarthy K, Fielding KL, Stevens W, Chihota V, Nicol M, *et al.* Effect of Xpert MTB/RIF on early mortality in adults with suspected TB: a pragmatic randomized trial. In: Proceedings of the 21st Conference on Retroviruses and Opportunistic Infections (CROI 2014); 3–6 March 2014; Boston, MA, USA. Abstract 95.
- 3 WHO. Implementation and roll-out of Xpert MTB/RIF May 2013. Update from the STOP TB Department. Geneva: World Health Organization; 2013.

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