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Commentary on Evidence Summaries

The accuracy of the Xpert[®] MTB/RIF assay compared to smear microscopy and culture for detecting pulmonary tuberculosis and rifampicin resistance in adults

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1. Importance of the Cochrane Review to tuberculosis (TB) control in low-and middle-income countries (LMICs)

The evidence summary¹ of the Cochrane Review² is timely, as the questions addressed are important in the light of the fact that in December 2010 the World Health Organization (WHO) endorsed the use of the Xpert[®] MTB/RIF assay after reviewing available evidence through a wider consultation process. The WHO came out with a strong recommendation to use this as an initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB, and a conditional recommendation to use Xpert[®] as a follow-on test to microscopy in settings where MDR-TB and/or HIV are of lesser concern, especially in smear-negative specimens.^{3,4}

The review has tried to summarise the evidence for the diagnostic accuracy of this rapid molecular assay, which when applied at the point of clinical care has clear advantages, such

as requirement of minimal technical expertise, and the ability to diagnose TB as well as simultaneously assess rifampicin resistance generally within two hours.

In the present scenario where TB control in LMICs is challenged by increasing drug resistance to TB, and given the difficulties inherent in testing for drug resistance due to issues such as operational feasibility and access to drug testing centres,⁵ the review definitely addresses a crucial public health issue.

2. Applicability of the results to LMICs with a high TB burden

The evidence summary has presented the findings of the review on the diagnostic accuracy of the Xpert[®] assay, taking into consideration the effects of differing TB prevalence for both detection of TB as well as rifampicin drug resistance. When detecting TB, the evidence for using Xpert[®] as the initial

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test replacing sputum microscopy, and as an add-on test following a negative smear result have been presented. The accuracy of Xpert® when applied to sub-groups such as those who are smear-positive and culture positive; smear-negative but culture positive have also been presented, as have the results in those with TB who are HIV-positive, and HIV-negative.

While the pooled specificity for TB detection and rifampicin resistance detection ranges from 97% to 99% in all categories, except smear-positive and culture positive subgroup where it could not be estimated, the pooled sensitivity is overall relatively low for TB detection.

Against this backdrop, the dual advantage of both TB detection and rifampicin resistance detection within hours at the peripheral health facility level with minimal bio-safety requirement, and technical expertise, holds promise for LMICs. However, the LMICs need to have the facility to further confirm rifampicin-resistant isolates identified by Xpert®, by drug susceptibility testing (DST); and have systems in place for treating all diagnosed cases of MDR-TB.

The merits of this evidence for the diagnostic accuracy of Xpert® have to be weighed against the need for more evidence that will throw light on the costs involved with implementation. In addition to capital costs, the operational costs will also need to be considered, as well as the savings that will be incurred by dispensing with the need for bio-safety equipment. The impact of detecting false-positive rifampicin resistance will also affect cost estimates. There are likely to be difficulties associated with annual calibration, especially in remote settings that may be dealt with by developing web-based systems, for which there will be additional costs involved that will also need to be considered. Finally, there are likely to be practical difficulties related to ensuring regular electricity, supply of assay cartridges, and quality control, and widespread training associated with the scaled-up use of this assay in rural health care settings. These are the concerns related to implementing the Xpert® MTB/RIF assay for detecting pulmonary tuberculosis and rifampicin resistance for health systems in LMICs.

3. Conclusions

While the cost issues pose a problem for LMICs, summary estimates of the diagnostic accuracy indicate a dual advantage in simultaneous detection of TB and rifampicin drug resistance. However, caution will be needed in interpretation of rifampicin resistance in the given community. Further evidence is also needed regarding the usability of the Xpert® MTB/RIF assay in rural settings in LMICs with less developed health systems.

Conflicts of interest

The author has none to declare.

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