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http://dx.doi.org/10.1016/j.cegh.2013.05.003

Evidence Summaries

The accuracy of the Xpert®MTB/RIF assay for detecting pulmonary tuberculosis and rifampicin resistance in adults: Summary of the evidence and implications for public health programmes

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ARTICLE INFO

Article history:
Received 9 July 2013
Accepted 10 July 2013
Available online 6 June 2013

Keywords:
Tuberculosis
Xpert
Diagnosis
Evidence update
Policy

ABSTRACT

This review demonstrates that Xpert® is accurate in diagnosing pulmonary TB as well as detecting rifampicin resistance. None of the studies were done in the primary health care setting where the public health benefits are likely to be maximum. The studies used the older generations of Xpert®. It is that the performance of current Xpert G4, will be different. Caution has to be exercised in interpreting the results of rifampicin resistance, as this is influenced by baseline risk of MDR TB in that community & patient's individual risk. Cost will have a bearing on adoption of this test into control programmes.

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1. The evidence

A Cochrane diagnostic test accuracy systematic review and meta-analysis identified 18 studies where the Xpert MTB/RIF® (hereafter referred to as Xpert®), an automated, rapid, polymerase chain reaction (PCR) assay, was used as an initial test replacing smear microscopy (15 studies with 7517 participants) or as an add-on test following negative smear microscopy (14 studies with 5719 participants). The reference standard for pulmonary TB detection was culture; the reference standard for rifampicin resistance detection was phenotypic culture-based drug susceptibility testing. The majority of studies (56%) were performed in low- and middle-income countries, and trained technicians performed the test in reference laboratories in 17 studies.

When Xpert® was used as an initial test replacing smear microscopy, the pooled sensitivity was 88% (95% credible interval (CrI) 83%–92%), and pooled specificity was 98% (95% CrI 97%–99%). As an add-on test following a negative smear microscopy result, Xpert® had a pooled sensitivity of 67% (95% CrI 58%–74%) and pooled specificity of 98% (95% CrI 97%–99%).

In subgroup analyses, the pooled sensitivity was higher in 15 studies for adults with smear-positive, culture-positive TB (98%; 95% CrI 97%–99%) than for smear-negative, culture-positive TB (68%; 95% CrI 59%–75%). Among patients living with HIV infection in four studies, the pooled sensitivity was 80% (95% CrI 67%–88%), while sensitivity was 89% (95% CrI 81%–94%) in those without HIV infection. For rifampicin resistance detection (11 studies, 2340 participants), Xpert® achieved a pooled sensitivity of 94% (95% CrI 87%–97%), and specificity of 98% (97%–99%). Xpert® accurately differentiated TB from non-tuberculous mycobacteria (only 1/139 specimens misidentified). The number of people wrongly diagnosed by Xpert® to have rifampicin resistance would depend on the prevalence of rifampicin resistance and would be lower when this prevalence is high. At levels of accuracy in the studies reviewed, the wrong diagnosis of rifampicin resistance would increase by >40% if the prevalence of rifampicin resistance in the population tested decreased from 30% to 2%.

This review concluded that, "Xpert used as an initial diagnostic test for TB detection and rifampicin resistance detection in patients suspected of having TB, MDR-TB, or HIV-associated TB is sensitive and specific. Xpert may also be valuable as an add-on test following microscopy for patients who have previously been found to be smear-negative. An Xpert result that is positive for rifampicin resistance should be carefully interpreted and take into consideration the risk of MDR-TB in a given patient and the expected prevalence of MDR-TB in a given setting". The review suggested that the increased use of the Xpert® test in routine programmatic and peripheral health care settings, and at the point of care in high TB burden countries, could provide evidence on the actual clinical impact of the test in detecting TB and rifampicin resistance.

2. Why is this question important?

- Tuberculosis (TB) is among the commonest infectious diseases in the world and contributes to a large amount of morbidity and mortality. Pulmonary TB is its common form of presentation. Early and accurate diagnosis is vital for both the patient's well-being, and for the community as undiagnosed patients spread the disease. Early diagnosis of resistance is also vital to choose the correct treatment regimen. Sputum smears are known to have poor sensitivity and culture based resistance testing is cumbersome and time consuming. Rapid diagnostic tests that can both diagnose TB as well as confirm resistance are a potential answer to this problem.
- The Xpert® MTB/RIF assay uses an automated molecular technique (nucleic acid amplification using polymerase chain reaction (PCR)) to detect both *Mycobacterium tuberculosis* complex and rifampicin resistance in a single test generally within 2 h; the assay's reagent, used to liquefy sputum, has the ability to kill TB bacteria, and therefore permits the test to be taken out of a reference laboratory and used nearer to the patient without bio-safety concerns.
- Xpert®, if accurate, would help in earlier diagnosis and the opportunity to begin earlier, appropriate treatment; and provide opportunities to interrupt TB transmission, especially in developing countries.

Review on which this evidence summary is based:

Steingart KR, Sohn H, Schiller I, Kloda LA, Boehme CC, Pai M, Dendukuri N. Xpert® MTB/RIF assay for pulmonary tuberculosis and rifampicin resistance in adults. Cochrane Database of Systematic Reviews 2013, Issue 1. Art No 1: CD 009593. http://dx.doi.org/10.1002/14651858.CD009593.pub2. This summary presents an overview of the findings and the implications for low and middle income countries. For further details, please read the full review that can be downloaded, free of charge (through various funded provisions) in most parts of the world, from *The Cochrane Library* (www.thecochranelibrary.com).

What did the systematic review seek and what did they find?

Review objectives:

To determine summary estimates of the diagnostic accuracy of Xpert for the diagnosis of pulmonary TB and for detecting rifampicin resistance in adults.