Need-based approach for cost-effective tuberculosis control in India

Vassall A, Siapka M, Foster N, Cunnama L, Ramma L, Fielding K, McCarthy K, Churchyard G, Grant A, Sinanovic E. (TB Centre and Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, UK; Health Economics Unit, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; Aurum Institute, Johannesburg, South Africa; School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; Division of Public Health, Surveillance and Response, National Institute for Communicable Disease of the National Health Laboratory Service, Johannesburg, South Africa; Advancing Treatment and Care for TB/HIV, South African Medical Research Council, Johannesburg, South Africa; Africa Health Research Institute, School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa.) Cost-effectiveness of Xpert MTB/RIF for tuberculosis diagnosis in South Africa: A real-world cost analysis and economic evaluation. *Lancet Glob Health* 2017;**5:**e710–19.

SUMMARY

Vassall *et al*. conducted a real-world cost analysis and economic evaluation, embedded in a cluster randomized controlled trial (RCT). In South Africa, the National Department of Health, following the recommendation by the WHO, rolled out Xpert MTB/RIF in 2012. The authors conducted a cluster RCT, the XTEND (Xpert for Tuberculosis: Evaluating a New Diagnostic trial) study, during the rollout. The objective was to study the effect of Xpert MTB/RIF on mortality and cost-effectiveness compared to sputum smear microscopy as an initial diagnostic test for tuberculosis (TB) among adults suspected to be suffering from the disease. The XTEND study concluded that Xpert introduction did not reduce the 6-month mortality risk. For cost estimation at the laboratory and above-laboratory level, cost data from all 20 XTEND peripheral laboratories and 1 central reference laboratory were used. Costing data of drug-sensitive TB treatment were collected from 10 purposively selected XTEND study clinics using bottom-up methods. Multidrug-resistant TB (MDR-TB) treatment cost was retrospectively collected from 5 non-XTEND study health facilities. From a systematic review by Siapka *et al*., HIV treatment cost was retrieved.[1] Direct and indirect costs incurred by the study participants were also collected by interview and from a study by Ramma *et al*.[2] There was no significant difference in the total costs incurred by the Xpert MTB/RIF (US$ 312.58; 95% CI 252.46–372.70) and sputum smear microscopy groups (US$ 298.58; 95% CI 246.35–350.82). In the upper left quadrant of the cost-effectiveness plane, both mean incremental costs and mean incremental effect of Xpert MTB/RIF fell, compared with sputum smear microscopy. By applying the willingness to pay thresholds, there was <3% probability that Xpert MTB/RIF was cost-effective.

COMMENT

The study concluded that Xpert roll-out in South Africa for the initial diagnosis of presumptive drug-susceptible TB was cost neutral. The time-frame for this economic analysis was within the

trial period of 6 months, potentially underestimating the benefits of Xpert MTB/RIF as an initial diagnostic test among the presumptive drug-susceptible TB individuals. A large study by Sachdeva *et al*. among 115 340 individuals with presumptive pulmonary TB found that Xpert MTB/RIF as an initial diagnostic test increased the bacteriologically confirmed TB cases by 39% compared to sputum smear microscopy as an initial diagnostic test.[3] It also found that there was a 5-fold increase in case notification and rifampicin-resistant TB cases. This evidence from India suggests that Xpert MTB/RIF can reduce the lead time for both drug-sensitive and drug-resistant detection of TB and can increase its cost-effectiveness. Compared to South Africa, India has different epidemiological characteristics and health systems for the prevention and control of TB and AIDS. Raizada *et al*. conducted a study covering 8.8 million people in 18 subdistrict level TB units.[4] It compared the efficiency of Xpert MTB/RIF and sputum smear microscopy as an initial diagnostic test for HIV-infected patients with suspected TB. It was found that 27.6% of presumptive TB cases were positive by Xpert MTB/RIF, compared to 12.9% with sputum smear microscopy. Increased sensitivity of Xpert MTB/RIF in diagnosing presumptive TB among HIV-positive patients reduces the transmission of TB and helps in the control of AIDS. Not considering the above benefits of Xpert MTB/RIF may reduce its cost-effectiveness. The costs of false-positive and false-negative TB diagnosis were not taken into consideration. False-positive diagnosis leads to morbidity and mortality for which treatment is deferred. It may also lead to overuse of TB drugs leading to acquired drug resistance. False-negative diagnosis may further increase the transmission of TB. Disregarding these effects may overestimate the cost-effectiveness of Xpert MTB/RIF.

The objective of this real-world cost and economic evaluation was to provide better evidence on the cost-effectiveness of Xpert MTB/RIF using primary data from the XTEND study, a cluster RCT. Costing for the diagnostic test in the laboratory and above-laboratory level was done only in the first and last 2 months of the XTEND study. Costing for the drug-sensitive TB treatment was done by conveniently selecting 10 XTEND study clinics. Five non-XTEND study clinics selected retrospectively were used for costing the MDR-TB. A systematic review by Siapka *et al.* was used in the costing of HIV.[1] The sample was not adequate to capture the cost incurred by the patients. The above methods used in the costing of the trial could have introduced bias and affected the cost-effectiveness of the XTEND study. Even though the study aimed to provide a real-world economic evaluation, the use of a single RCT is inadequate for arriving at a decision. Sculpher *et al*. argued that economic evaluation from an RCT should be viewed as one of the sources of evidence and must be placed in a broader framework of evidence synthesis and decision analysis.[5]

Compared to sputum smear microscopy, Xpert MTB/RIF gives results within 2 hours and detects rifampicin resistance, which is a marker for drug-resistant TB.[6] Xpert MTB/RIF has sensitivity and specificity of 88% and 98%, respectively.[7] Currently, under Revised National Tuberculosis Control Programme (RNTCP), Xpert MTB/RIF is used to diagnose presumptive MDR-TB patients, pulmonary TB in children and HIV-positive patients.[8] Chadha *et al*. conducted a cost analysis of various diagnostic algorithms for pulmonary TB varying in the placement of Xpert MTB/RIF, sputum smear microscopy and chest radiography.[9] Diagnostic algorithms which used Xpert MTB/RIF after having done sputum smear microscopy and chest radiography had the lowest total cost per case compared to the RNTCP guidelines (sputum smear examination followed by antibiotic trial in smear-negative patients, repeat smear examination if symptoms continue and chest radiography if repeat smear examination was negative) for presumptive pulmonary TB diagnosis. Even total cost of the direct introduction of Xpert MTB/RIF as an initial diagnostic test for presumptive pulmonary TB was found to be 39.5% less than the cost mentioned in the RNTCP guidelines. Kelly *et al*. showed in a cost utility study that light-emitting diode fluorescence microscopy is a cost-effective intervention for detecting TB in high-workload settings.[10] More than 46% of TB patients in India seek care from the unregulated private sector.[11] In the private sector, TB care practices may not adhere to the programme guidelines, and the high price of Xpert MTB/RIF may limit its availability. Suen *et al*. studied the cost-effectiveness of Xpert MTB/RIF and public–private mix (PPM)/partnership delivered alone or in combination with drug sensitivity testing from 2015 to 2025.[12] The authors used a previously published dynamic transmission microsimulation model of TB calibrated to Indian demography and TB epidemiology.[13] The authors concluded that public–private mix (PPM)/partnership is more cost-effective than Xpert MTB/RIF alone. They also found that, in situations where resources are readily available, both PPM and Xpert MTB/RIF implementation should be considered than either alone.

For more than 5 decades, India has been fighting to control TB. Yet, it continues to be among the top 10 causes of mortality along with HIV/AIDS in India.[14] The National Strategic Plan (NSP) for tuberculosis elimination 2017–25 visions a TB-free India with 0 deaths, disease and poverty due to TB.[15] The goal of eliminating TB a decade before the set target of 2035 by the WHO 'End TB Strategy' may seem overambitious. Nevertheless, the increased understanding of the epidemiology of TB and the availability of newer drugs, diagnostics and newer strategies for treatment and control may achieve the goal of NSP. The aim of universal access to accurate diagnosis in India could be achieved by adopting the diagnostic algorithm based on the prevalence of TB and the profile of patients at the district level rather than having a single diagnostic algorithm countrywide. By adapting to local needs, newer diagnostic tests such as Xpert MTB/RIF may be utilized cost-effectively.

Conflicts of interest. None declared

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