What To Do with Xpert Negatives?

The Cost of Alternative Diagnostic Algorithms for TB Suspects Who Are Xpert MTB Negative in a High HIV/MDR-TB Burden Setting

Gesine Meyer-Rath[1,2], Kate Schnippel[1], Lawrence Long[1], William MacLeod[1,2], Ian Sanne[1], Wendy Stevens[3,4,5], and Sydney Rosen[1,2]

[1]Health Economics and Epidemiology Research Office, Department of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [2]Boston University Center for Global Health and Development, Boston, USA; [3]National Health Laboratory Service, Johannesburg, South Africa; [4]Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [5]Department of Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, South Africa

BACKGROUND

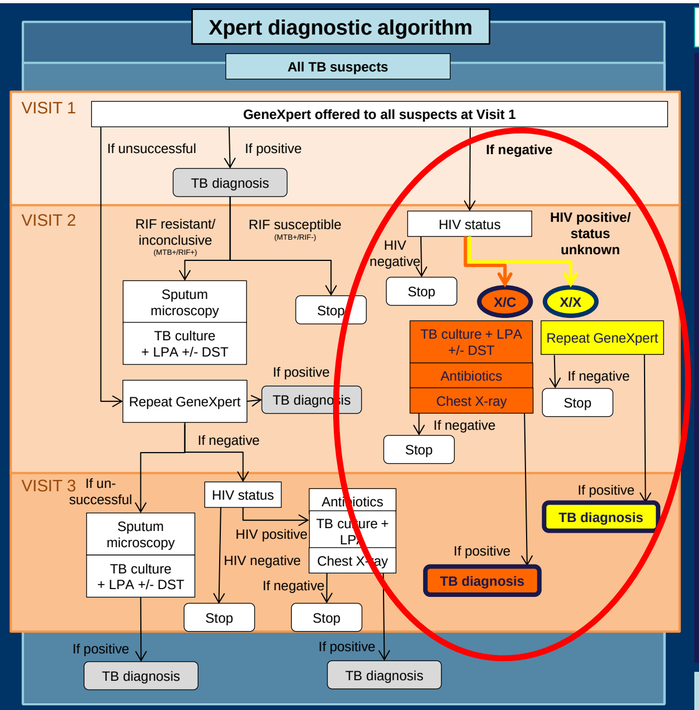
South Africa is rapidly implementing the World Health Organization's recommendation to adopt Xpert MTB/RIF technology (Xpert) for first-line diagnosis of pulmonary tuberculosis (TB). With a high burden of HIV/TB co-infection and a high proportion of patients with smear-negative TB, however, determining the optimal diagnostic algorithm for Xpert negative TB suspects is an important challenge. South Africa's current Xpert algorithm calls for HIV-infected TB suspects with an initial negative Xpert result to provide a consecutive sputum sample for culture.

OBJECTIVE

We estimated the difference in cost and number of TB cases diagnosed and initiated on treatment if the algorithm incorporated a second Xpert test (**X/X**) instead of culture (**X/C**), at full Xpert scale-up in 2014.

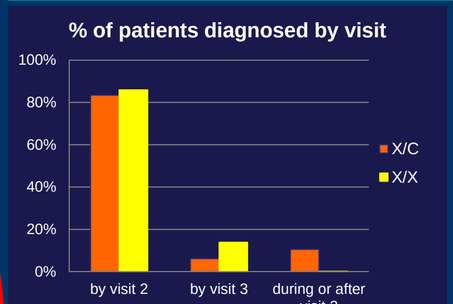
METHODS

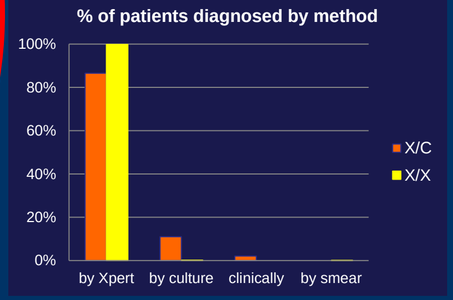
Using a population-level decision model we developed for the South African government, we estimated the incremental cost per TB patient treated of replacing culture with a second Xpert test for known or suspected HIV-positive TB suspects whose first Xpert test was negative. Xpert test costs were calculated using data from a pilot evaluation conducted by the National Health Laboratory Service. Public-sector salaries and drug and laboratory prices from 2011 were used for all other costs. The number of patients requiring diagnostics, TB treatment uptake, and loss to follow-up at each clinic visit were estimated using results from Xpert demonstration studies and TB and HIV positivity rates calculated from the national TB register and public-sector laboratory databases. Costs are reported in 2011 USD.



Diagnostic algorithm for TB in South Africa. The current Xpert algorithm (**X/C**) calls for HIV-infected TB suspects with a negative Xpert result during the first visit to provide a consecutive sputum sample for culture at the second visit and undergo a chest X-ray and an antibiotic trial. We examined the cost consequences of replacing this by a second Xpert text at the second visit (**X/X**).

RESULTS





Replacing culture and clinical diagnosis with a second Xpert test allows almost 100% of patients to be diagnosed by visit 3. Whereas under **X/C** 11% of patients rely on culture for their diagnosis, under **X/X** almost all cases are diagnosed by Xpert.

Outcomes

	Current algorithm (X/C)	Proposed algorithm (X/X)	Difference to X/C
TB cases diagnosed (% of suspects)	447,999 (17.4%)	433,401 (16.8%)	-3% (-3%)
TB cases treated (% of cases diagnosed)	363,318 (81%)	364,443 (84%)	+0.3% (+4%)

Costs in 2011 USD

	Current algorithm (X/C)	Proposed algorithm (X/X)	Difference to X/C
Cost per test	Culture: $13	Xpert: $25	+92%
Cost per suspect	$59	$53	-1%
Cost per case diagnosed	$342	$315	-8%
Annual cost of TB diagnostic programme	$153 million	$136 million	-11%

Because Xpert is less sensitive than culture for smear-negative suspects, the **X/X** algorithm diagnoses 3% fewer TB cases. This may be offset by higher expected treatment uptake under **X/X** due to the faster availability of results, resulting in an estimated 4% more patients initiating treatment under **X/X** than under **X/C**. Although Xpert is almost twice as expensive per test than culture when only laboratory costs are considered, **X/C** requires more non-laboratory resources (clinic visits, chest x-rays and antibiotics). As a result, the full cost of **X/X** is 8% lower than the full cost of **X/C** per case diagnosed, and **X/X** is 11% less expensive at national programme scale, with the potential to save $17 million per year.

CONCLUSIONS

Modifying the diagnostic algorithm to use a second Xpert test for HIV-infected TB suspects who have an initial negative Xpert test could provide rapid results, simplify the diagnostic process, and generate cost savings, without negatively affecting the number of patients initiating TB treatment.

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Center for Global Health and Development
Boston University School of Public Health
801 Mass Ave, Boston, MA 02118 USA
gesine@bu.edu www.bu.edu/cghd