GeneXpert MTB/RIF Assay

The GeneXpert MTB/RIF assay (Xpert) for the diagnosis of tuberculosis in children

PREVENTION/TREATMENT

PREVENTION DIAGNOSTIC TREATMENT

Condition

In areas of high to moderate transmission, *Mycobacterium tuberculosis (Mtb)* is often difficult to diagnose in children, and those infected frequently do not receive timely or adequate treatment. In addition, children in low-income settings are particularly susceptible to developing tuberculosis disease (TB) due to the pervasiveness of risk factors that can compound immunodeficiency, such as malnutrition, HIV infection, or other opportunistic infections. Timely diagnosis for all TB patients is critical to reduce transmission and improve treatment outcomes, but is often difficult to achieve consistently. This challenge is especially true for children, who produce less sputum and often have fewer TB bacteria in their sputum than adults (paucibacillary). This makes successful diagnosis via sputum smear microscopy, the most common test for TB diagnosis globally, more challenging. However, Xpert can simultaneously detect *Mtb* and resistance to rifampin (RIF) in sputum samples within 2 hours, which helps to accelerate time to diagnosis and treatment initiation, both of which are frequent causes of loss to follow-up.

(Image provided by the TB Alliance.)

GLOBAL ANNUAL DEATHS ASSOCIATED WITH PEDIATRIC TB:

	NUMBER
Children who acquire TB	at least 1,000,000
Children who die of TB	210,000

Mechanism of Action

Xpert is a nucleic acid amplification test (NAAT) that uses a disposable cartridge with the GeneXpert Instrument System. A sputum sample is mixed with the reagent provided with the assay, and the mixture is placed in the GeneXpert platform. Once the cartridge is placed into the machine, all processing is fully automated. Major advantages in the utilization of Xpert are that results are available more quickly than with other tests, minimal technical training is required to run the test, multiple tests can be run at the same time, and it can also quickly identify multidrug-resistant TB (MDR-TB). Rapid diagnosis of drug resistant TB is key in shortening time to treatment initiation, which is a challenge with many other currently available methods of drug susceptibility testing (DST).

The World Health Organization's (WHO's) current policy guidance recommends that Xpert be used as an initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB. This recommendation generalizes data on adults to include use of Xpert in children.

Current Use in Low TB Burden Settings

Currently, WHO guidance provides a conditional recommendation that Xpert be used as a follow-on test to smear microscopy in low-burden settings where MDR-TB or HIV are of lesser concern. Testing everyone who presents with symptoms of TB would cost almost US $470 million per year globally, far exceeding the cost of current, conventional diagnostics. However, in many European counties, that cost would represent less than 10% of current funding for TB programs, and by comparison, using Xpert would be considered highly cost effective in such settings.

Application in High TB Burden Settings

WHO initially recommended Xpert in December 2010, and within 5-6 years, more than 120 high burden and low-/middle-income countries have procured over 4,600 GeneXpert Instruments and close to 16 million Xpert cartridges. When tested against other methods of diagnosis such as sputum smear microscopy, Xpert increased TB detection among culture-confirmed cases by 23%. Additionally, detection of drug resistance and TB disease in HIV-infected individuals also increased. On a global level, use of Xpert to diagnose TB and RIF resistance is cost effective for all individuals suspected of having TB, including those suspected of being co-infected with HIV, when compared to current practices.

REPRESENTATIVE PRODUCTS

WHO Prequalified Manufacturers

MODEL	PROCUREMENT PRICE	TECH	STATUS	NOTES
GeneXpert Instrument	4-module desktop unit: $17,000* 4-module laptop unit: $17,500*	Diagnostic	Marketed and manufactured exclusively by Cepheid	Instrument can test 12-16 samples daily or 3,000-4,000 annually; WHO referenced price 2014
GeneXpert Cartridges	Cartridges and calibration kit: $450.00 Cartridges: $9.96 each*	Diagnostic	Marketed and manufactured exclusively by Cepheid	WHO referenced price 2014

** Indicates preferential pricing available for the public sector and eligible low and middle income countries.*

CHARACTERISTICS OF REPRESENTATIVE PRODUCT

	TECHNOLOGY CHARACTERISTICS	OPERATIONAL PARAMETERS	POTENTIAL OPPORTUNITIES FOR IMPROVEMENT
SKILLS REQUIRED	Intended end user	Pediatric clinician, child	
	Training required	Hours	
	Time required per use	Minutes	
ENVIRONMENT/ INFRASTRUCTURE	Power required	Stable power supply	
	Waste collection	None	
	GeneXpert Platform	GeneXpert Instrument	A single GeneXpert instrument can test 64 samples daily. Busier sites will need larger capacity or a greater number of instruments.
		Cartridges	Cartridges have a shelf life of 18 months. Inventory will need to be managed carefully.
	Temperature and storage	Maximum of 30^{0}C for GeneXpert instrument	
		Maximum of 28^{0}C for cartridges	
	Maintenance	Annual calibration of GeneXpert instrument	
	Adequate storage space	About one square foot	
COST	Total health care costs per patient	US$ 2,728*	
OTHER	Customer support plan	A detailed sales contract and customer support plan should be negotiated with the supplier	
	Treatment capacity	Sufficient capacity to treat patients with TB should be available.	

** Adjusted cost per use in US. This would be considerably less for low-income, high-burden countries.*

Sources:
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World Health Organization (WHO). Xpert MTB/RIF Implementation Manual. 2014. Available from: http://apps.who.int/iris/bitstream/10665/112469/1/9789241506700_eng.pdf.
World Health Organization (WHO). Guideline Development Group (GDG) Webinar to Update Policy Guidance on the Use of Xpert MTB/RIF. Available from: http://www.who.int/tb/areas-of-work/laboratory/gdg_xpert_aug2016.pdf

RTI INTERNATIONAL