

TB diagnostics: from R&D to policy to practice and the impact of COVID-19

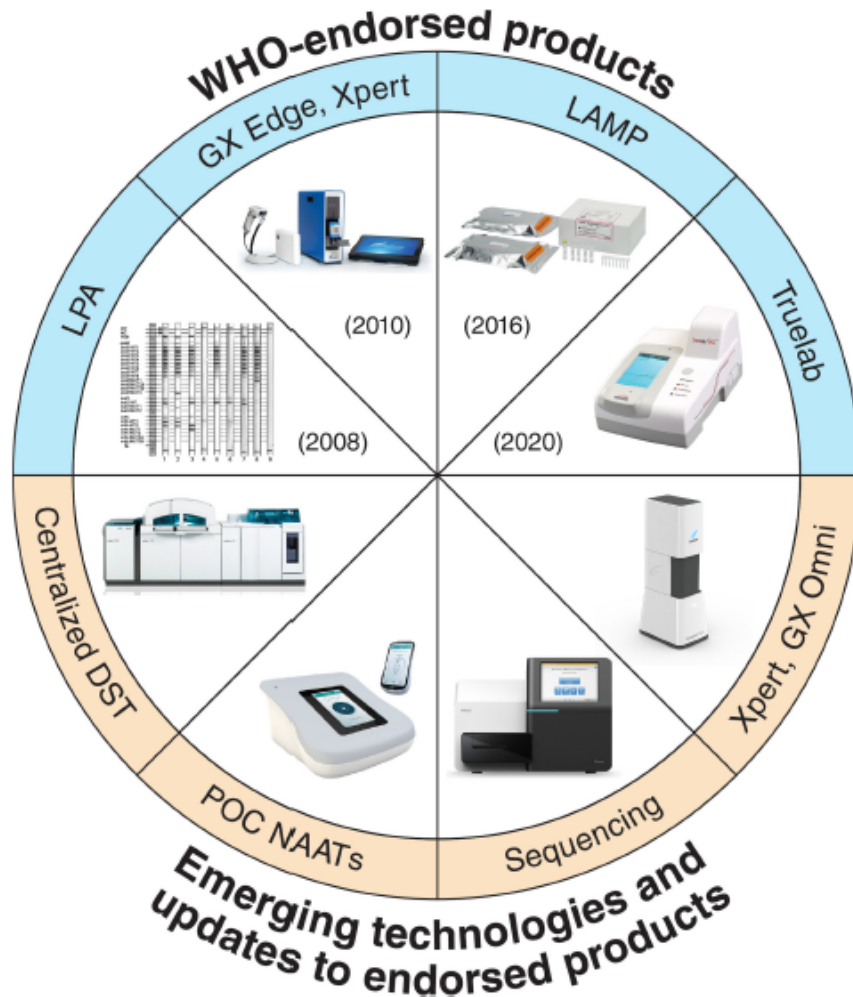
TBEC webinar – 2 October

STIJN DEBORGGRAEVE
MSF Access campaign



TB diagnostics

Central to district



MacLean et al. 2020 J Clin Microbiol 58: e01582-19

Point of care

MSF Access Campaign Technical Brief

June 2019
(Updated March 2020)



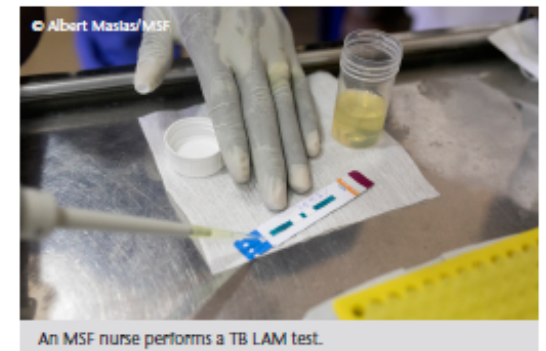
A RAPID TB TEST FOR PEOPLE LIVING WITH HIV

TB LAM can help close the deadly TB testing gap

INTRODUCTION

Médecins Sans Frontières (MSF) has been treating tuberculosis (TB) for more than 30 years and HIV for nearly 20. Our teams currently support treatment for more than 250,000 people living with HIV (PLHIV) in 19 countries, primarily in sub-Saharan Africa. We have many projects in these countries to address TB/HIV co-infection.

This technical brief analyses gaps in the diagnosis of TB for people living with HIV, describes the critical role TB LAM testing can play in saving lives, and provides recommendations for governments to implement and rapidly scale up access to testing.



An MSF nurse performs a TB LAM test.

3.5\$

<https://msfaccess.org/rapid-tb-test-people-living-hiv>

TB diagnostics R&D

R&D PIPELINE



Catalyse Development

Concept	Feasibility	Development
Pathogen-specific typhoid RDT (typhus, leptos)	LAM sputum monitoring (Otsuka)	Centralized use: Fluorotype XDR (Hain/Bruker)
High-priority malaria RDT	Triage POC test	GeneXpert OMNI (Cepheid)
Gonorrhoea DR test	Centralized use: NGS	eHealth solutions: DX in a BX
Near-POC MDx for VHF detection (incl. Lassa)	POC molecular test (BLINK DX)	Multiplexed immunoassay (Chembio)
	2 nd Gen LAM for broad use cases	Highly sensitive combo RDTs (SD/Abbott)
	Host & pathogen marker screening	Buruli: LAMP (DITM, NMIMR)
	<i>P. vivax</i> serology (WEHI, Mologic)	Buruli: Ag capture (SD/Abbott, Swiss TPH)
	Bacterial/non-bacterial triage test	HAT: malaria combo RDT (SD/Abbott)
	Schistosoma: RDT (Mologic)	cAg RDT format (DCN, Mologic)
	Buruli: mycolactone RDT (DOTD)	
	HCV self-test (Orasure, Access Bio)	
	Xpert Carba-R v2 (Cepheid)	
	RDT reader for connected Dx	
	Gonorrhoea Dx (CT/NG detection)	
	Substandard & falsified medicine screening	
	Semi-open molecular platform for Lassa (aitona, Cepheid)	
	POC multi-analyte, polyvalent (BLINK DX)	
	Zika-dengue-chikungunya flex assay	

Guide Use and Policy

Evaluation	Demonstration
TrueNAT (Molbio)	hsRDT in maternal & child health
Centralized DST (Roche, Abbott, BD, Hain/Bruker)	CRP + malaria test (SD BIOSENSOR)
Host biomarker and phenotypic ID tool landscaping	HAT: 2nd Gen RDT (SD/Abbott)
Paediatric TB stool kit (Rutgers)	Xpert HCV VL Fingerstick test (Cepheid)
Radiology: CAD4TB (Delft), Qure.ai	Multiplexed fever panel (BioFire)
Breath test (Enose, RBS)	
1 st Gen LAM (Fujifilm)	
Decentralized use: Xpert XDR (Cepheid)	
Biomarker-based product validation	
CRP + malaria test (SD BIOSENSOR)	
Buruli: iTLC (Harvard, WHO)	
Leishmania: Rk28 RDT for WHO (CTK Biotech)	
RNA (genedrive)	
Serology RDTs for WHO PQ	
RNA DBS for WHO	
cAg test of cure (Abbott)	
RDA Truenat (Molbio)	
Lassa RealStar 2.0 ERPD for WHO (aitona)	



Pipeline Report

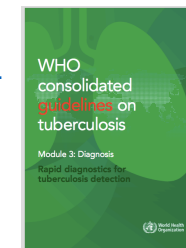
Overview of Innovations for Diagnosing, Preventing, Treating, and Curing HIV, HCV, and TB

<https://www.treatmentactiongroup.org/resources/pipeline-report/2020-pipeline-report/>

<https://www.finddx.org/tb/>

WHO recommendations (2020)

WHO consolidated guidelines on TB: Module 3



**Xpert MTB/RIF
Xpert MTB/RIF Ultra**

Should be used
Initial test for all
Signs of TB and EPTB

9.98\$
*



**Truenat MTB (Plus)
Truenat MTB/RIF Dx**

May be used
Initial test for all
Signs of TB

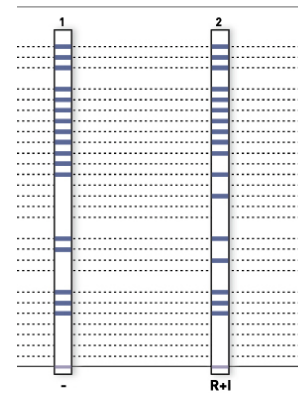
9.0\$



LAMP

May be used
Replace microscopy
Signs of TB

6\$



LPA

May be used
**Initial test to replace
phenotypic DST**
First line: RIF and INH
resistance
Second line: FLQ & SLIDs

7.5\$
*



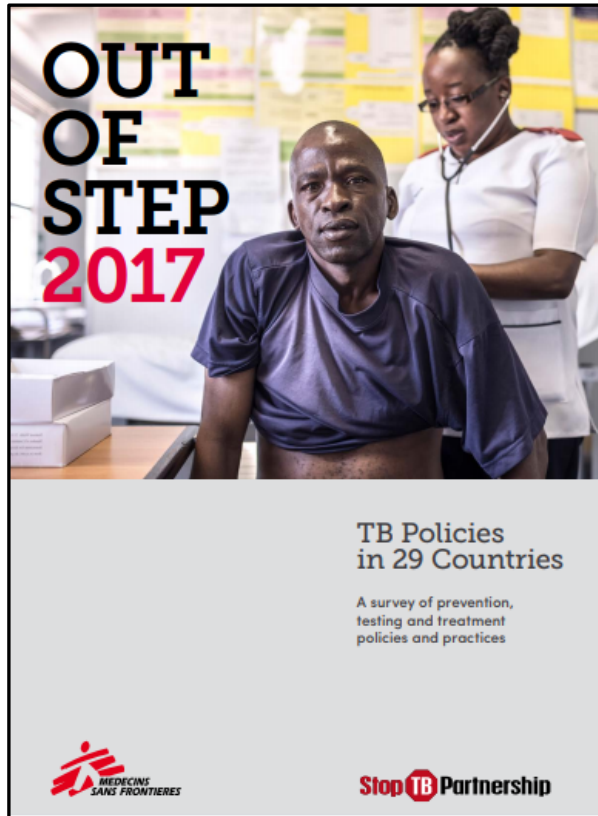
TB LAM

Recommended
**PLWHA
Inpatients**
- Signs of TB/EPTB
- AHD
- CD4 <200
&
Outpatients
- Signs of TB/EPTB
- CD4 <100

3.5\$

* FIND negotiated prices: <https://www.finddx.org/pricing/>

TB diagnostics: national policy adoption



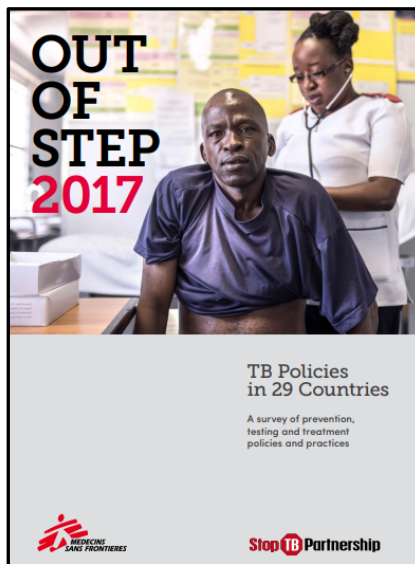
- STEP UP FOR TB 2020
- TB Policies in 37 countries
- *Will be released soon*

KEY POLICIES DASHBOARD

COUNTRY	DIAGNOSIS				MODELS OF CARE				
	Expert RTB/HR in the national TB diagnostic test for adults and children having investigated for TB	TB-LAM is used to diagnose TB in PLHIV with CD4 < 100 µL or seriously ill	Fast-flow TBFT (chromogenic and isoniazid) is done for all DR-TB cases or for people at risk of DR-TB	Second-line DR-TB (fluoroquinolones & second-line injectable agents) is done for all DR-TB cases	DS-TB treatment is started at the primary health care level ¹	DS-TB treatment is started at the district level ²	Hospitalisation is NOT required for DS-TB treatment ³	Hospitalisation is NOT required for DR-TB treatment ⁴	ART treatment is offered to all PLHIV (Test and start)
Afghanistan	●	●	●	●	●	●	●	●	●
Armenia	● ⁵	●	●	●	● ⁵	● ⁵	●	● ⁵	●
Bangladesh	●	●	●	●	●	●	●	●	●
Belarus	● ⁵	●	●	●	●	●	● ⁵	● ⁵	●
Brazil	●	●	●	●	●	●	●	●	●
Cameroon	●	●	●	● ⁵	●	●	●	●	● ⁵
CAR	●	● ⁵	●	● ⁵	●	●	●	●	●
China	●	●	●	●	●	●	●	●	●
DRC	●	●	●	● ⁵	●	●	●	●	●
Ethiopia	●	●	●	●	●	●	●	●	●
Georgia	●	●	●	●	● ⁵	● ⁵	●	●	●
India	●	●	●	●	●	●	●	●	●
Indonesia	●	●	●	●	●	●	●	●	●
Kazakhstan	●	●	●	●	●	●	●	●	●
Kenya	●	●	●	●	●	●	●	●	●
Kyrgyzstan	● ⁵	●	●	●	●	●	●	●	●
Mozambique	●	●	●	● ⁵	●	●	●	●	●
Myanmar	●	●	● ⁵	● ⁵	●	●	●	●	●
Nigeria	●	●	●	● ⁵	●	●	●	●	●
Pakistan	●	●	●	● ⁵	● ⁵	● ⁵	●	●	●
PHG	●	●	●	●	●	●	●	●	●
Philippines	●	●	●	●	●	●	●	●	●
Russian Fed.	● ⁵	●	●	●	●	●	●	●	●
South Africa	●	●	●	●	●	● ⁵	●	●	●
Sweden	●	●	●	●	●	●	●	●	●
Tajikistan	●	●	●	●	●	●	●	●	●
Ukraine	●	●	●	●	●	● ⁵	●	●	●
Viet Nam	●	●	●	●	●	●	●	●	● ⁵
Zimbabwe	●	● ⁵	●	●	●	●	●	●	●

¹Excluding women and/or children. In some countries, exceptions are made for people who are smear-negative and/or on second-line drugs. ²The location of the patient.

https://msfaccess.org/sites/default/files/MSF_assets/TB/Docs/TB_Report_OutOfStep_3rdEd_ENG_2017.pdf



52% countries recommend Xpert MTB/RIF as initial test for all

40% countries with Xpert for all policy have made the test widely available

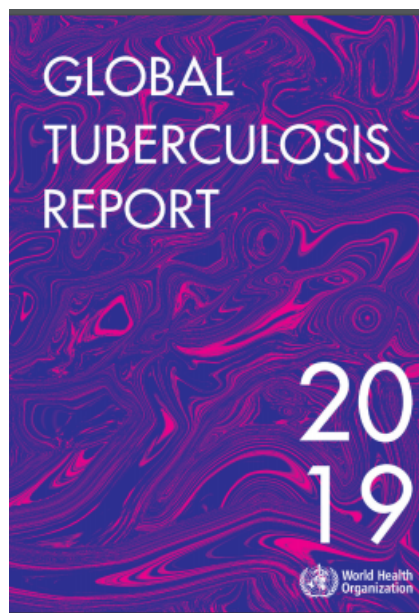
7% countries recommend TB LAM for PLWHA

0% have made the test available

Singhroy et al. 2020

46% recommend TB LAM for PLWHA

less than half make the test available



Percentage of new and relapse^a pulmonary TB cases with bacteriological confirmation, globally and for WHO regions, 2000–2018

TB GeneXpert : time for \$5 per test

TECHNICAL BRIEF | 02 DECEMBER 2019

Time for \$5: GeneXpert diagnostic tests

TUBERCULOSIS

Download



MSF_Access_TechnicalBrief...

Annexes:

Download detailed methodology and findings from the cost analyses conducted for MSF by Cambridge Consultants and referenced in the 'Time for \$5' technical brief.

- [2018 COGS analysis of Xpert MTB/RIF Ultra cartridges](#)
- [2015 COGS analysis of Xpert HIV-1 Viral Load cartridges](#)
- [2012 COGS analysis of Xpert MTB/RIF cartridges](#)

<https://www.msfaccess.org/time-for-5>

MSF Access Campaign
Technical Brief
DECEMBER 2019



TIME FOR \$5: GENEXPERT DIAGNOSTIC TESTS

MSF and others call on Cepheid for \$5 all-inclusive price for Xpert tests for TB and HIV, and price reductions across all assays

KEY MESSAGES:

1. The Xpert MTB/RIF (standard and Ultra) test run on Cepheid's GeneXpert platform is the best test for rapidly diagnosing tuberculosis (TB) and rifampicin-resistant TB in one step.
2. The 2012 donor-negotiated price of US\$9.98 per cartridge helped with uptake in many countries but is still too high for use as the initial TB test for everyone who needs it.
3. Given high sales volumes and public investments for GeneXpert product development and commercialization, further price reductions are feasible and long overdue.
4. Xpert cartridges for other diseases (HIV, hepatitis, sexually transmitted diseases, cervical cancer) use the same technology and, by extension, with pooled upstream manufacturing costs, need price reductions.
5. Cepheid's existing service and maintenance package is too costly and ineffective for most countries. Changes in service provision are needed, with costs either included within an all-inclusive cartridge price (US\$5) or through a reasonable standardised global surcharge per cartridge (US\$1) per any assay.
6. It's time for a single, lower, all-inclusive price of US\$5 for all Xpert MTB/RIF (Ultra) cartridges in all settings for all people who need testing.
7. It's time for Cepheid to include lower pricing options for all assays used for high-burden diseases to maximise the feasibility of introducing other tests on the same platform.



Testing a sample from a person with suspected TB in a GeneXpert machine, Bangassou Hospital, Central African Republic.

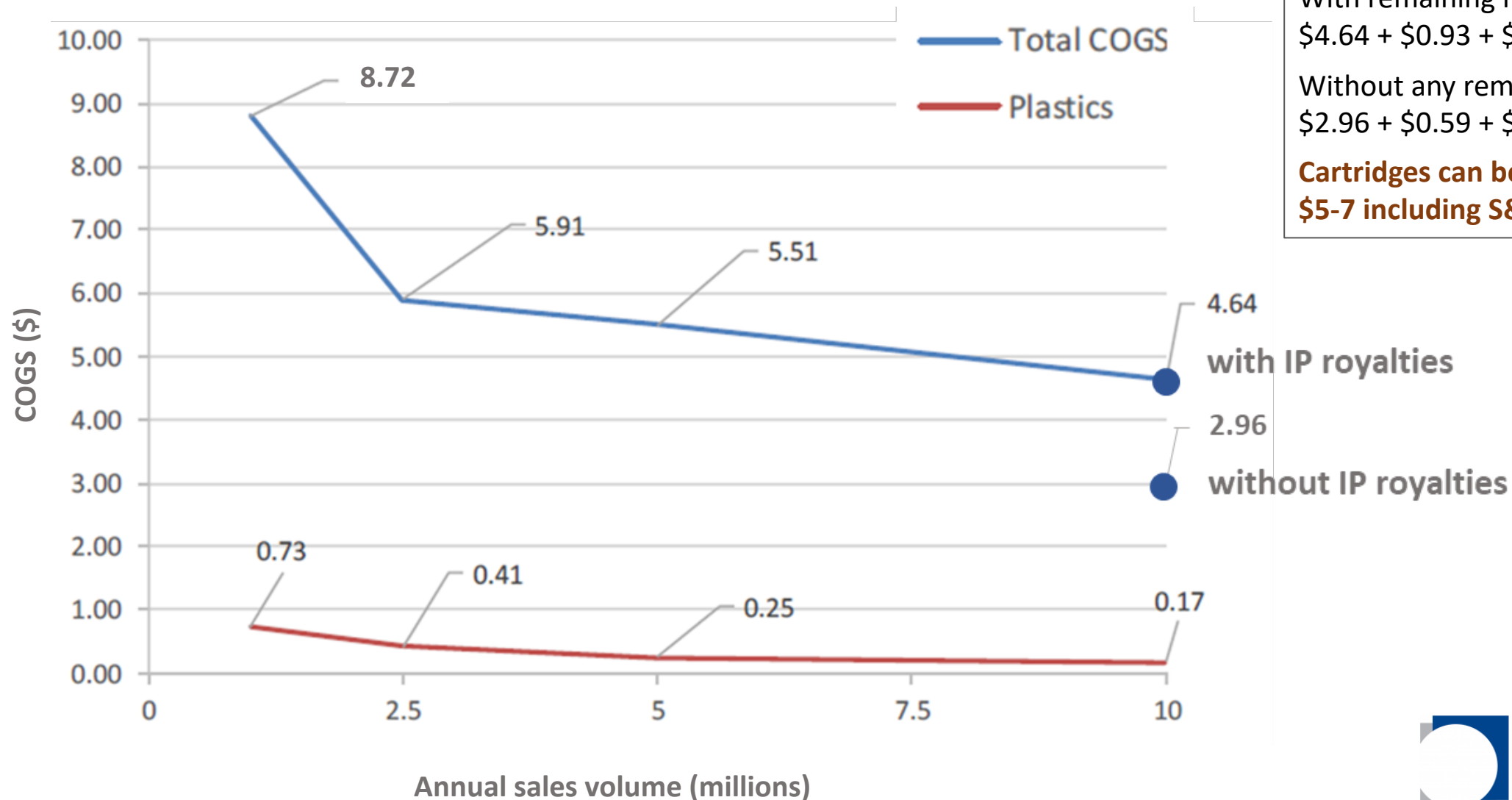
EXECUTIVE SUMMARY

The GeneXpert diagnostic testing technology has revolutionised rapid, accurate diagnosis of tuberculosis (TB) since entering the market in 2010. The World Health Organization (WHO) recommends the Xpert MTB/RIF assays (standard and Ultra) as the initial test for all people with signs and symptoms of TB. Yet, due to the high cost of the GeneXpert instrument and its assays, most high TB-burden countries are not able to scale up testing for all people who need diagnosis.^{1,2} Instead, TB care providers continue to rely on cheaper, less accurate sputum smear microscopy.

To scale up testing and close the gap in diagnosis for people with TB, Médecins Sans Frontières (MSF) calls on Cepheid to reduce the price of Xpert MTB/RIF (Ultra) cartridges to US\$5, inclusive of service and maintenance.³

In addition to TB, several other Xpert assays have been developed to tackle other challenging diseases, which have been added to Cepheid's concessional pricing program for high burden developing countries (HBDC). These diseases

TB GeneXpert : Cost of goods sold (COGS) analysis



COGS at 10 M/y + 20% profit + S&M

With remaining royalties:

$\$4.64 + \$0.93 + \$1 = \6.57

Without any remaining royalties:

$\$2.96 + \$0.59 + \$1 = \4.55

Cartridges can be sold with profit at \$5-7 including S&M

Impact of COVID on TB diagnosis and R&D



THE POTENTIAL IMPACT OF THE COVID-19 RESPONSE ON TUBERCULOSIS IN HIGH-BURDEN COUNTRIES: A MODELLING ANALYSIS

Country	Excess TB cases from 2020 - 2025		Excess TB deaths from 2020 - 2025	
	For every month of lockdown	For every month of restoration	For every month of lockdown	For every month of restoration
India	232,665	144,795	71,290	40,685
Kenya	3,980	3,133	1,747	1,157
Ukraine	1,058	625	270	137
Global	608,400	420,400	126,100	83,200

Table 2. Estimates for incremental impact on TB burden by each additional month of lockdown or restoration

http://stoptb.org/assets/documents/news/Modeling%20Report_1%20May%202020_FINAL.pdf

Impact of COVID on TB diagnosis and R&D

- Per 3-month lockdown and 10-month restoration: 6.3 additional TB cases 2020-2025
- COVID-19 could setback the fight against TB at least 5 to 8 years
- Integration of COVID and TB testing needed
- Bi-directional TB-COVID testing: do not delay TB testing
- Significant expansion of molecular testing capacity needed
- Diagnostic companies should not de-prioritize TB test production nor R&D over COVID



9.98\$

MTB RIF



19.8\$

SARS-CoV-2

Optimal TB diagnostic service delivery

- **Adopt all WHO recommendations in national policies and translate into practice**
- **RMD for all TB suspects and at all health care levels, including specimen referral**
- **TB LAM in both inpatient and outpatient settings, and a PHC level**
- **TB LAM adoption in TB & HIV policies, GF & PEPFAR proposals when eligible**
- **Prevent TB in prisons: screening for TB on entry - mass screening - contact screening**
- **Community advocacy to demand governments to scale up RMD and TB LAM**