

Диагностика: от исследований и разработок к политике и практике, влияние COVID-19

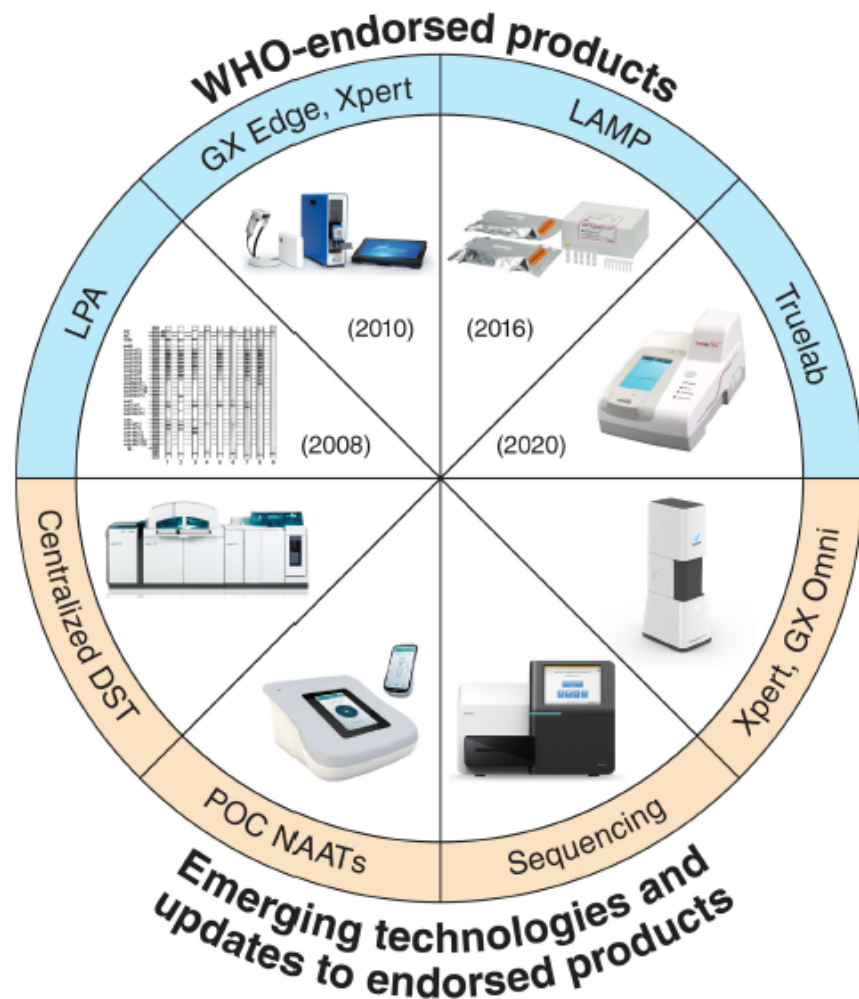
Вебинар ЕКТБ – 2 октября

СТЕЙН ДЕБОРГГРАВЕ
Кампания MSF Access campaign



Диагностика

От центрального – к районному уровню



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

По месту предоставления услуг

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.



3.5\$

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

Исследования и разработки в сфере диагностики ТБ

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

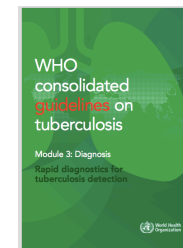
Overview of Innovations for Diagnosing, Preventing, Treating, and Curing HIV, HCV, and TB

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

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

Рекомендации ВОЗ (2020)

Консолидированное руководство ВОЗ по ТБ: Модуль 3



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

Должен использоваться как **начальный тест** при любых признаках ТБ или внелегочного ТБ

9.98\$

*



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

Может использоваться как **начальный тест** при любых признаках ТБ

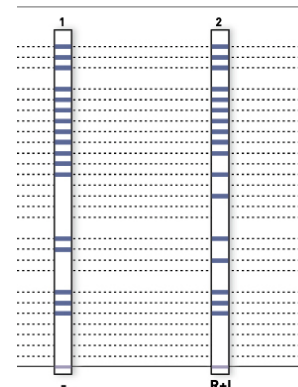
9.0\$



LAMP

Может использоваться как замена микроскопического исследования при признаках ТБ

6\$



LPA

Может использоваться как **начальный тест** для замены **фенотипического ТЛЧ**
Первый ряд: устойчивость к RIF и INH
Второй ряд: FLQ и SLIDs

7.5\$

*



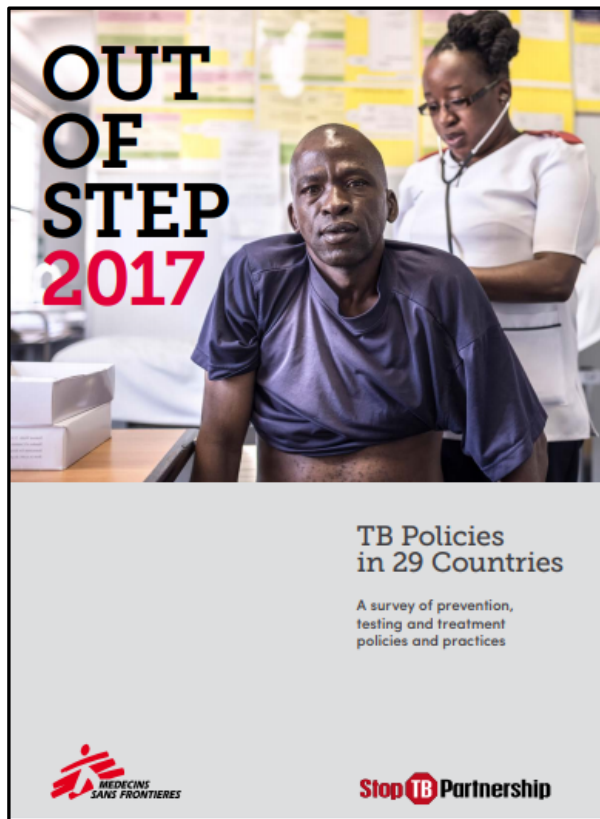
TB LAM

Рекомендовано **ЛЖВ**
Стационар
- признаки ТБ/ВЛТБ
- AHD
- CD4 <200
Амбулаторно
- признаки ТБ/ВЛТБ
- CD4 <100

3.5\$

* Информация о ценах: <https://www.finddx.org/pricing/>

Диагностика ТБ: национальная политика



- Кампания **STEP UP FOR TB 2020**
- Политики по борьбе с ТБ в 37 странах
- *Скоро ожидается выход*

KEY POLICIES DASHBOARD

COUNTRY	DIAGNOSIS				MODELS OF CARE				
	Expert RTB/HR in the initial TB diagnostic test for adults and children having investigated for TB	TB-LAM used to diagnose TB in PLHIV with CD4 < 100 µL or seriously ill	Fast-flow TBST (chromogenic and isoniazid) in place for all DR-TB cases or for people at risk of DR-TB	Second-line DR-TB (fluoroquinolones & second-line injectable agents) in place for all DR-TB cases	DS-TB treatment is started at the primary health care level ¹	DR-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 ³	ART treatment is offered to all PLHIV (Test and start) ⁴
Afghanistan	●	●	●	●	●	●	●	●	●
Armenia	● ⁵	●	●	●	● ⁵	● ⁵	●	● ⁵	●
Bangladesh	●	●	●	●	●	●	●	●	●
Belarus	● ⁵	●	●	●	●	●	● ⁵	● ⁵	●
Brazil	●	●	●	●	●	●	●	●	●
Cameroon	●	●	●	● ⁵	●	●	●	●	● ⁵
CAR	●	● ⁵	●	●	●	●	●	●	●
China	●	●	●	●	●	●	●	●	●
DRC	●	●	●	● ⁵	●	●	●	●	●
Ethiopia	●	●	●	●	●	●	●	●	●
Georgia	●	●	●	●	● ⁵	● ⁵	●	●	●
India	●	●	●	●	●	●	●	●	●
Indonesia	●	●	●	●	●	●	●	●	●
Kazakhstan	●	●	●	●	●	●	●	●	●
Kenya	●	●	●	●	●	●	●	●	●
Kyrgyzstan	● ⁵	●	●	●	●	●	●	●	●
Mozambique	●	●	●	● ⁵	●	●	●	●	●
Myanmar	●	●	● ⁵	● ⁵	●	●	●	●	●
Nigeria	●	●	●	● ⁵	●	●	●	●	●
Pakistan	●	●	●	●	●	●	●	●	●
PHG	●	●	●	●	●	●	●	●	●
Philippines	●	●	●	●	●	●	●	●	●
Russian Fed.	● ⁵	●	●	●	●	●	●	●	●
South Africa	●	●	●	●	●	●	●	●	●
Sweden	●	●	●	●	●	●	●	●	●
Tajikistan	●	●	●	●	●	●	●	●	●
Ukraine	●	●	●	●	●	●	●	●	●
Viet Nam	●	●	●	●	●	●	●	●	● ⁵
Zimbabwe	●	● ⁵	●	●	●	●	●	●	●

¹DS including smear- and/or culture individuals. In some countries exceptions are made for people who are smear- and/or culture-negative and on second-line therapy. ²DR-TB including smear- and/or culture individuals. In some countries exceptions are made for people who are smear- and/or culture-negative and on second-line therapy. ³DR-TB including smear- and/or culture individuals. In some countries exceptions are made for people who are smear- and/or culture-negative and on second-line therapy. ⁴DR-TB including smear- and/or culture individuals. In some countries exceptions are made for people who are smear- and/or culture-negative and on second-line therapy.

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



52% стран рекомендуют проведение Xpert MTB/RIF как начального теста для всех пациентов

40% стран, реализующих политику Xpert для всех, обеспечили широкую доступность теста

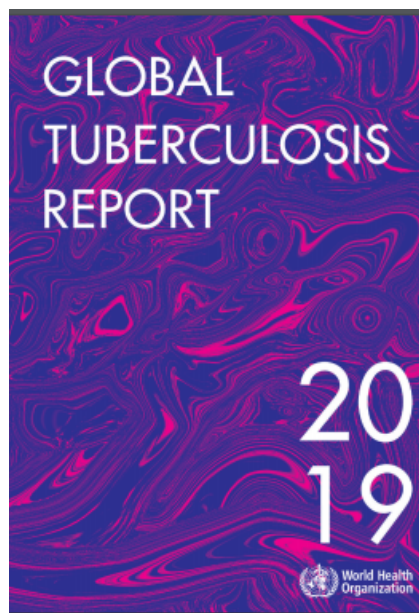
7% стран рекомендуют проведение теста TB LAM для ЛЖВС

0% обеспечили доступность теста

Singhroy et al. 2020

46% рекомендуют проведение теста TB LAM для ЛЖВС

Меньше половины обеспечили доступность теста



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

TB GeneXpert: пришло время для теста за \$5



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.

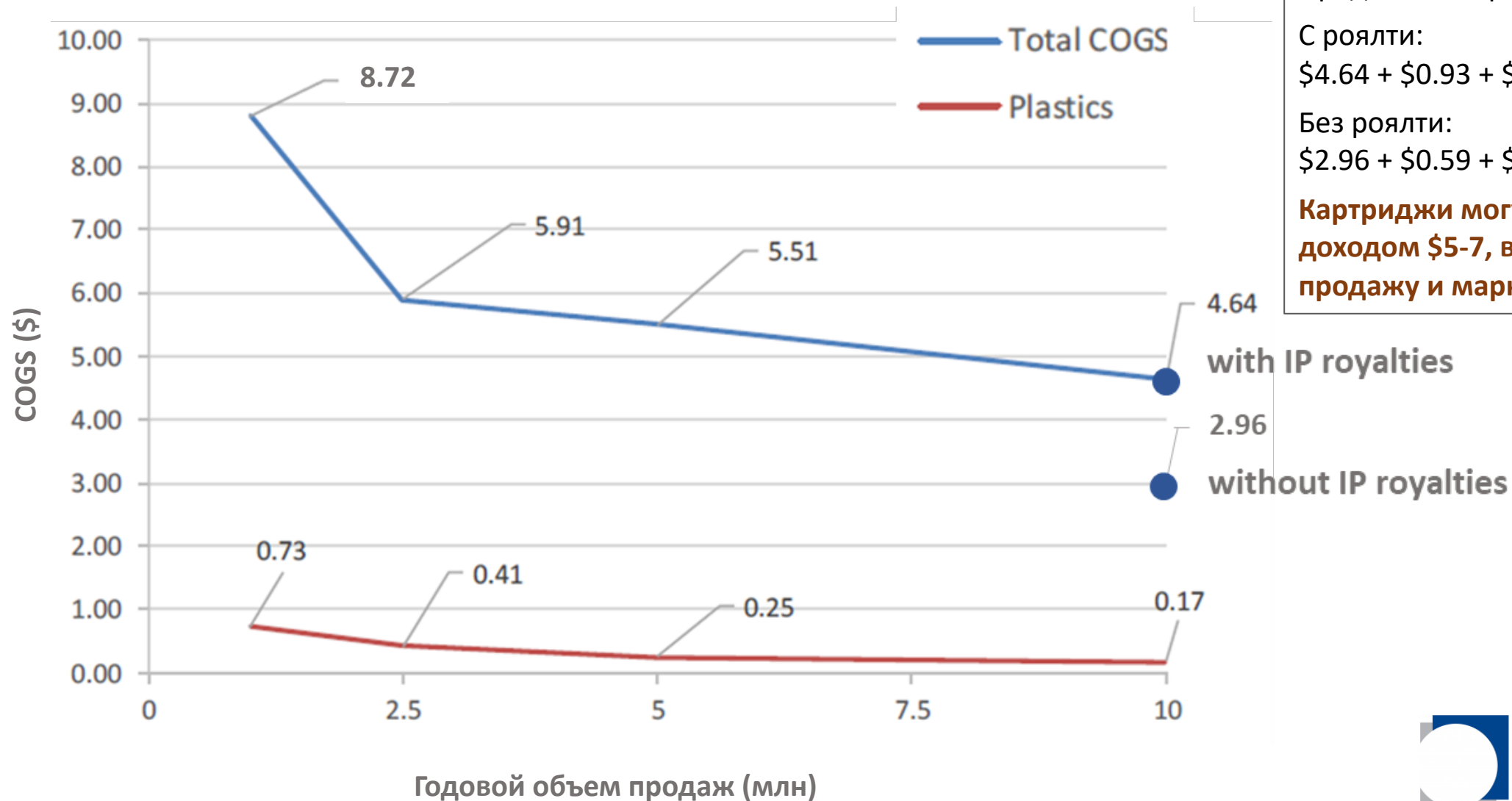
EXECUTIVE SUMMARY

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

TV GeneXpert: Анализ стоимости реализованной продукции (COGS)



COGS за 10 м/г + 20% доход +
Продажи и маркетинг

С роялти:

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

Без роялти:

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

**Картриджи могут продаваться с
доходом \$5-7, включая затраты на
продажу и маркетинг**

Влияние COVID на диагностику ТБ, исследования и разработки



ПОТЕНЦИАЛЬНОЕ ВЛИЯНИЕ МЕР ПО БОРЬБЕ С COVID-19 НА СИТУАЦИЮ С ТУБЕРКУЛЕЗОМ В СТРАНАХ С ВЫСОКИМ БРЕМЕНЕМ ТБ: АНАЛИЗ И МОДЕЛИРОВАНИЕ

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

Влияние COVID на исследования и разработки в сфере диагностики ТБ

- За 3 мес. карантина и 10 мес. восстановления: 6,3 доп. случаев ТБ в 2020-2025 гг.
- COVID-19 может привести к откату в борьбе с ТБ как минимум на 5-8 лет
- Необходима интеграция тестирования на COVID и ТБ
- Двойное тестирование ТБ-COVID: не откладывать тестирование на ТБ
- Необходимо существенно расширить потенциал молекулярной диагностики
- Компании-производители не должны отдавать приоритет в пользу тестов на COVID перед разработкой и производством тестов на ТБ



MTB RIF

9.98\$



SARS-CoV-2

19.8\$

Оптимизация предоставления услуг диагностики ТБ

- Все рекомендации ВОЗ должны быть отражены в нац. политике и на практике
- RMD для всех лиц с подозрением на ТБ и на всех уровнях оказания мед помощи, в т.ч. перенаправление образцов
- TB LAM в стац. и амбул. условиях и на уровне первичной мед. помощи
- Включение TB LAM в политики по ТБ/ВИЧ, заявки в ГФ, PERFAR (при соотв. критериям)
- Профилактика ТБ в тюрьмах: скрининг на входе – массовый – контактных лиц
- Адвокация сообществ с требованием, чтобы правительства обеспечили широкую доступность RMD и TB LAM