

Advancing Access through Market Interventions:

Lessons Learned from the GeneXpert Tuberculosis Test Buy-down

By David Branigan

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Introduction

The urgent demand for rapid, accurate, and affordable tests for SARS-CoV-2, the virus that causes COVID-19, is driving forward global action to invest in the development, scale-up, and deployment of new diagnostic tests. The continued lack of equitable and affordable access to COVID-19 testing around the world—more than eight months after COVID-19 first appeared—reflects a lack of global solidarity and a system in which monopolies and high pricing have been allowed to persist despite significant public investment and need.

The diagnostics pillar of the Access to COVID-19 Tools Accelerator (ACT-A)—the global collaboration

to accelerate development, production, and equitable access to COVID-19 tests, treatments, and vaccines—is assessing possible market interventions intended to support the development of new diagnostic tests for COVID-19 and advance access to these tests in low- and middle-income countries.¹ The market interventions under consideration by the ACT-A diagnostics pillar include push incentives, such as direct investments in research and development (R&D), and pull incentives, such as advance market commitments, volume guarantees, and buy-downs. At this critical juncture, it is essential that the ACT-A diagnostics pillar heed the lessons learned from prior market interventions intended to expand global access to diagnostic tests

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for other diseases. The 2012 buy-down of Cepheid’s Xpert MTB/RIF, a rapid molecular test for detecting *Mycobacterium tuberculosis* (MTB) and resistance to rifampicin (RIF), provides both a cautionary tale and helpful lessons learned.

Before Xpert MTB/RIF, countries relied on sputum smear microscopy—a technology from the late 1800s—and mycobacterial culture—a method that takes weeks to yield an accurate result—for diagnosing TB. The endorsement of Xpert MTB/RIF by the World Health Organization (WHO) in 2010 offered the prospect of more rapid and accurate TB testing that could be delivered close to the point of care.² However, even the reduced price of Xpert MTB/RIF was high, at US\$16.86 per test for 145 low- and middle-income countries,³ compared with smear microscopy, which can cost as little as \$0.26 per test.⁴ At the time no other companies were ready to enter the market with a rapid molecular test, so there was no immediate prospect of competition as a lever to lower the price. To catalyze


the rollout of the test, the WHO—with support from Unitaid, the Bill & Melinda Gates Foundation, the U.S. Agency for International Development (USAID), and the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR)—entered into an agreement to pay Cepheid \$11.1 million to buy down the price of Xpert MTB/RIF to \$9.98 for 145 low- and middle-income countries for 10 years.⁵

The buy-down catalyzed the uptake of this game-changing test, but it also contributed to unanticipated, adverse, and—in some cases—lasting effects on the TB diagnostics market. This policy brief reviews the background and unexpected consequences of the Xpert MTB/RIF buy-down; applies lessons learned to the ongoing development of COVID-19 diagnostic tests and efforts to scale up access to these tests; and provides recommendations and pro-access conditions that should be applied to R&D funding, buy-down, and other market intervention agreements for COVID-19 diagnostics.

Public and philanthropic funding for Xpert TB test R&D and evaluation:

In the 1990s and early 2000s, the U.S. Department of Defense granted the diagnostics company Cepheid \$120 million in funding to develop the GeneXpert testing device. The U.S. National Institutes of Health spent about \$45 million from 1994 to 2016, and the Foundation for Innovative New Diagnostics (FIND) has spent nearly \$22 million since 2006 to support the development and evaluation of Xpert TB tests.⁶

History of the Xpert TB test buy-down

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- 2006** FIND enters into an agreement with Cepheid to provide funding and assistance for the development and validation of the Xpert MTB/RIF TB test; under the agreement, Cepheid agrees to independent cost-of-goods-sold (COGS) audits (COGS includes costs of materials, labor, and overhead) as well as a COGS+ pricing structure (COGS + intellectual property [IP] royalties + 20 percent profit) and annual volume-based price adjustments.⁷
- 2010** Cepheid markets Xpert MTB/RIF at \$55–82 per test in high-income countries;⁸ the WHO endorses the use of Xpert MTB/RIF for the detection of TB and rifampicin resistance.⁹
- 2011** FIND and Cepheid negotiate a lower price of \$16.86 for Xpert TB tests at annual volumes over 600,000 for 145 low- and middle-income countries;¹⁰ however, there is still public outcry over the high price of the test.
- 2012** The WHO—with funding from Unitaid, the Bill & Melinda Gates Foundation, USAID, and PEPFAR—enters into an agreement to pay Cepheid \$11.1 million to buy down the price of Xpert TB tests for 10 years (2012–2022), establishing a ceiling price of \$9.98—based on projected annual sales volumes just over 4.7 million tests.¹¹
- 2013** The WHO recommends Xpert MTB/RIF as the initial test for TB and rifampicin resistance for all people being evaluated for TB.¹²
- 2014** Xpert TB test annual sales volumes exceed 4.7 million tests,¹³ the projected volumes used to inform the buy-down ceiling price of \$9.98.
- 2018** Annual Xpert TB test sales volumes surpass 11.5 million—nearly triple 2014 volumes¹⁴—but the buy-down ceiling price of \$9.98 is not reduced.
- 2019** An independent COGS analysis commissioned by Médecins Sans Frontières (MSF) Access Campaign estimates that at annual volumes over 10 million tests, it likely costs Cepheid \$2.95–4.64 to manufacture each Xpert TB test (\$2.95 is the estimated cost after royalties on certain test cartridge components expire, and \$4.64 is the cost including ongoing royalty commitments); the COGS analysis also finds that manufacturing efficiencies and cost savings achieved through the sales of TB tests* likely extend across Xpert tests for other diseases;¹⁵ civil society organizations and activists launch the Time for \$5 campaign calling on Cepheid to lower the price of Xpert tests for TB and other diseases to \$5 for low- and middle-income countries in line with estimated COGS and overall volume of sales.¹⁶
- 2020** Cepheid responds to the Time for \$5 campaign by contesting the MSF-commissioned COGS analysis, claiming that COGS are trade secrets, and refusing to transparently provide data on COGS or commit to reducing the price of any Xpert tests;¹⁷ Cepheid releases its Xpert SARS-CoV-2 test for COVID-19 after receiving \$3.7 million in funding from the U.S. Biomedical Advanced Research and Development Authority (BARDA) to develop the test¹⁸ (using open-source genetic targets) and prices it at around \$40 for high-income countries¹⁹ and \$19.80 for 145 low- and middle-income countries.²⁰ Treatment Action Group and the Time for \$5 campaign condemn Cepheid’s pricing given public investments and COGS evidence that suggest Cepheid is charging low- and middle-income countries four to six times what it costs the company to make its Xpert SARS-CoV-2 test.²¹

* The increased volume of sales in low- and middle-income countries along with economies of scale that reduce COGS increase the profit margin on Xpert test sales in high-income countries; this higher profit margin should be accounted for in lowering Xpert test prices for low- and middle-income countries.

Unintended consequences of the Xpert TB test buy-down

In 2012, to help catalyze the uptake and implementation of Xpert MTB/RIF, the WHO—with support from global donors—agreed to pay Cepheid \$11.1 million to buy down the price of the test from \$16.86 to the ceiling price of \$9.98 for 145 low- and middle-income countries for 10 years. Although the buy-down improved access to Xpert TB tests, it failed to promote COGS transparency, eliminated volume-based price adjustments, and may have played a role in reinforcing Cepheid’s monopoly, though the barriers that preempted potential competitors from entering the market have not been well documented. The buy-down agreement:

- did not compel Cepheid to reduce the price of the test as volumes rose and costs fell,^{22, 23} which:
 - effectively decoupled the price of the test from its COGS and sales volumes, leading to profit inflation as economies of scale improved, and
 - allowed the \$9.98 price intended as a price ceiling to instead become a price floor independent of volumes;
- indirectly supported Cepheid’s monopoly on rapid molecular tests for TB—which lasted nearly a decade²⁴—by driving the scale-up of Xpert TB tests amid lack of market competition necessary to apply

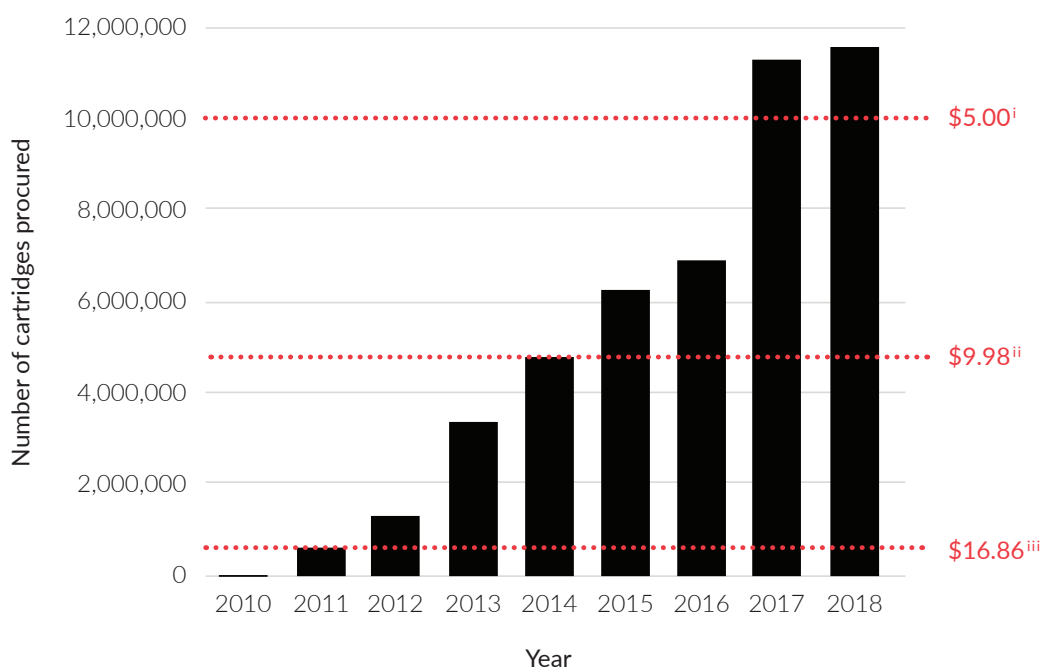
pressure for lower prices (despite efforts of the Bill & Melinda Gates Foundation to fund and fast-track potential competitors), leading countries to become tied to the GeneXpert testing device because of sunk equipment and staff training costs;

- established a \$10 precedent (irrespective of COGS) for other diagnostics manufacturers, entrenching an unaffordable target price for future TB diagnostic tests and distorting R&D priorities because of misalignment with the WHO’s target product profile price of <\$4 to <\$6 for smear microscopy replacement tests;²⁵
- contributed to the false expectation among manufacturers that buy-downs are the norm for achieving lower prices, rather than COGS+ and volume-based pricing models along with healthy market competition; and
- promoted price opacity instead of transparency, undermining public accountability over the use of public money to fund TB diagnostics research and access.

After the buy-down, country procurement of Xpert TB tests did increase, but despite rising sales volumes (see Figure 1)—and evidence of lower manufacturing costs²⁶—Cepheid did not reduce the price from \$9.98. Instead, the \$9.98 price remains a barrier preventing many countries from fully scaling up use of Xpert TB tests in line with WHO recommendations.²⁷

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Figure 1: Annual volumes and estimated volume-based prices of Xpert TB test cartridges procured by high-burden countries, 2010–2018^{28, 29, 30}



i \$5 is the Time for \$5 target price based on estimated COGS and annual volumes over 10 million

ii \$9.98 is the buy-down price for volumes over 4.7 million

iii \$16.86 is the FIND-negotiated price for volumes over 600,000

Unhealthy dynamics of the current global market for COVID-19 diagnostics

The global demand for COVID-19 diagnostic tests far outstrips the supply of available tests, making it a seller’s market and limiting the leverage and influence global institutions and donors hold over test pricing. Estimates show that 500 million tests will be needed for low- and middle-income countries in the first year of the COVID-19 response;³¹ yet, in the first three months of the response, less than 15 million tests were delivered to low- and middle-income countries.³² As the world awaits the development, scale-up, and deployment of accurate and affordable rapid antigen tests capable of detecting the SARS-CoV-2 virus, molecular tests such as Cepheid’s Xpert SARS-CoV-2 test are the only option for rapidly and accurately detecting the virus. Many

low- and middle-income countries, in particular, depend heavily on the Xpert SARS-CoV-2 test, because of their less-developed laboratory capacity and extensive GeneXpert testing infrastructure that is already in place. However, because of high demand in high-income countries and limited manufacturing materials and capacity to rapidly scale up production of tests, molecular tests for SARS-CoV-2 are in short supply and are overpriced.³³

Cepheid’s Xpert SARS-CoV-2 test is priced at around \$40 for high-income countries and \$19.80 for 145 low- and middle-income countries—more than four times what the MSF-commissioned COGS analysis estimated that it costs Cepheid to manufacture each Xpert test.³⁴ Because of higher prices and profit margins in rich countries, there is growing evidence that Cepheid is preferentially serving those markets instead of reserving adequate supplies for low- and middle-income countries.³⁵ There are also concerns that Cepheid is

diverting its limited test manufacturing capacity from its less lucrative TB tests (where the bulk of its sales are to low- and middle-income countries) to its COVID-19 tests (where the bulk of its sales are in high-markup rich countries),³⁶ in spite of the urgent need to maintain routine TB testing.³⁷ Moreover, Cepheid developed the Xpert SARS-CoV-2 test using open-source genetic targets and \$3.7 million in funding from the U.S. government.³⁸

Because the global market for COVID-19 diagnostics is currently a seller's market, the ACT-A diagnostics pillar and country governments have been willing to pay the high prices imposed by suppliers in order to compete for minimum quantities of the diagnostic tests they urgently need. Within this market there is a lack of transparency extending to several key areas, including pricing structures and COGS of diagnostic tests, R&D costs and public investments, and volumes and prices of tests sold. This lack of transparency contributes to the risk that the public may be significantly overpaying for these essential diagnostic tests. Overpayment leaves fewer resources for public health systems to make more tests available to everyone who needs them, which in turn lets disease go undetected, contributes to transmission, and delays initiation of care.

Catalyzing uptake, advancing access: setting pro-access precedents for diagnostics market interventions

Grants, loans, licensing agreements, advance market commitments, volume guarantees, buy-downs, and other market interventions are important tools for catalyzing the development and introduction of new and vitally needed diagnostic tools; however—as we've learned from the Xpert MTB/RIF example—to be effective, they must be accompanied by pro-access conditions set in the terms of agreements. The following recommendations and pro-access conditions should be applied to all funding and other market intervention agreements advanced by the ACT-A diagnostics pillar.

Recommendations:

- For reasons of historical public investment and present public health crises, COGS should be public information, not trade secrets, and the methodology used to determine COGS should be standardized and published by a normative body to ensure fairness and reproducibility.
- Funding agreements; test pricing structures; COGS analyses; volumes of tests manufactured, allocated, and delivered to countries; and public and philanthropic funding that contributed to the development of COVID-19 diagnostic tests and testing devices should be transparent and in the public domain, thereby helping to address the ongoing and pressing challenges of price opacity, inequitable allocation, and lack of public accountability.
- Market intervention investments in one company should be complemented by similar investments in other companies with the ultimate goal of creating competition.
- The entry point for considering a buy-down or other subsidy for a new test should be based upon the criteria that: (1) it is the best and only test available; (2) nothing similar is likely to be available any time soon; (3) it is crucial for reducing disease burden and saving lives; and (4) there is no other preferable mechanism of reducing the price within the same time frame.
- Civil society, affected communities, and countries must be meaningfully engaged at the decision-making table—including through consultative discussions before making decisions—and have full oversight and involvement in all stages of developing and finalizing market intervention agreements that use public funding.

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Pro-access conditions:

- Diagnostic tests should be priced according to COGS+ with annual COGS audits and rational price reductions based on increasing volumes (preferably with bundled pricing across the test menu). Royalty payments and profit margin markups should be kept to a minimum.
- Agreements should be flexible and adaptable to changing market dynamics, with time commitments of no more than one to three years in order to incentivize continued innovation and lower barriers for competition and competitive pricing.
- Companies should commit to fast-tracking WHO prequalification and country registration/approval as required for marketing new tests in low- and middle-income countries.
- While scaling up production of COVID-19 tests, companies should agree to maintain production capacity for vitally needed tests for other diseases such as TB.
- Agreements should promote non-exclusive licensing of new tests identified or developed through public funding, especially where price and supply constraints limit access in low- and middle-income countries, and should include a time-bound requirement of technology transfer for test manufacturing of no more than five years (which will also allow for the possibility of generic test manufacturing).
- Companies should be required to commit to equitable allocation of tests between high-income countries and low- and middle-income countries, especially in the context of supplying a pandemic emergency response.

When buy-down and other market intervention agreements do not apply these recommendations and pro-access conditions, they risk undermining equitable access to essential diagnostics by reinforcing monopolies, divorcing price from COGS and volumes, disincentivizing continued innovation, and creating other market inefficiencies and distortions. The ACT-A diagnostics pillar must heed lessons learned from past experience and develop market interventions capable of boldly promoting access and public health in the short and long terms.

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