The Tuberculosis Diagnostics Pipeline

By Colleen Daniels

Currently, smear microscopy and mycobacterial culture are the most widely used diagnostic tests, but microscopy, though relatively fast, is too inaccurate—missing over half of cases[1]—while culture is accurate but slow, taking from two to eight weeks to produce a definitive result. These tests are simply not accurate and rapid enough for proper diagnosis of TB, particularly in people living with HIV and in children. Early diagnosis of TB is essential to reducing transmission and mortality.[2] Five key barriers to the detection of TB are the difficulty of diagnosing latent TB infection and active TB disease; the lack of validated, accessible, and rapidly testable biomarkers; long delays before patients seek care; lack of an accurate, lab-free point-of-care (POC) test;[3] and the "widespread unavailability of facilities that can test for drug resistance."[4]

Sputum microscopy, the diagnostic tool developed in the 1880s, and still the most widely used diagnostic for TB despite its low sensitivity, finally has alternatives that are faster and more accurate.[5] The innovations in technology that transformed HIV diagnosis are finally being seen with TB. The price of HIV polymerase chain reaction (PCR) testing has decreased since it was first rolled out. In 2005, the minimum average price was US$31, and by 2012 it was US$21.[6,7,8] The potential for this technology to be developed and used in TB diagnosis is growing. However, current PCR platforms are too complex and technically demanding for community-level or true point-of-care use. Even with recent progress, we still lack a fast, cheap, accurate, and lab-free POC test that does not require sputum and can work at the lowest levels of health-service delivery.

Xpert MTB/RIF, which incorporates a nucleic acid amplification technology, is an automated device that tests for *Mycobacterium tuberculosis* (MTB) and rifampicin resistance. It has shown that new technologies have the potential to make diagnosis faster and more accurate. Since 2008, Treatment Action Group (TAG) has been working to change the diagnostic paradigm and increase resources for appropriate research and development (R&D) for new TB tools. In this and the next two chapters, we will review the pipeline for new TB diagnostics, treatments, and vaccines.

The introduction of Xpert MTB/RIF technology in high-burden settings such as South Africa and moderate-burden settings such as Brazil has encouraged R&D on new molecular diagnostics. Several fast followers are already on the market in some places, and more are in the pipeline. Today more than 50 diagnostic

companies and test developers are working on TB diagnostic technologies.[9] There is increased interest in developing better, broader, faster drug susceptibility testing (DST) approaches to guide rational use of therapies.[10] Most new technologies in the pipeline are dependent on electricity, require placement at reference- or peripheral laboratories, and still rely on sputum samples for detection of TB.

Table 1. 2013 TB Diagnostics Pipeline[11]

Test	Developer(s), Country	Type/Sample	Status
Molecular technologies			
❖Alere Q[12]	Alere, United States	Molecular diagnostic platform to screen MTB and drug resistance	In development; supported by the Bill & Melinda Gates Foundation (BMGF)
❖B-SMART	Laboratory Corporation of America Holdings (LabCorp), United States	Combines nucleic acid amplification and detection with phenotypic DST to detect MTB and determine resistance to anti-TB drugs[13] including pyrazinamide	In development; Sequella licensed technology to LabCorp
❖Genedrive MTB/RIF ID	Epistem, United Kingdom	Real-time PCR for TB and rifampicin resistance	Epistem was awarded CE/IVD accreditation (European Union accreditation for medical devices)[14]
❖GeneXpert XDR cartridge	Cepheid, United States	In-cartridge PCR to detect XDR-TB on GeneXpert platform	In development[15]
GenoType MTBDRs*l* line probe assay (LPA), second-line	Foundation for Innovative New Diagnostics (FIND), Switzerland/Hain Lifescience, Germany	Line probe assay for genetic mutations associated with resistance to fluoroquinolone antibiotics and the second-line injectable drugs amikacin, kanamycin, and capreomycin	On the market; not endorsed by the WHO. Field validation of the MTBDRs*l* assay in smear-negative and smear-positive patients under way in India, Moldova, and South Africa[16]

❖iCubate System	iCubate, United States	Multiplexed assay that detects TB and nontuberculous mycobacteria, and rifampicin-, isoniazid-, ethambutol-, and streptomycin-resistance in a single cartridge[17]	For research use only
❖INFINITI MTB Assay	AutoGenomics, United States	Multiplex PCR amplification/ microarray detection assay to detect MTB, common rifampicin (RIF) and isoniazid (INH) resistance mutations (i.e., MDR-TB) and Mycobacterium bovis[18]	Product is available for research use only
❖LATE-PCR with Lights-On/Lights-Off Probes and PrimeSafe technology	Stellenbosch University, South Africa; developed by Brandeis University, United States	PCR for simultaneous detection of MTB and resistance to INH, RIF, ethambutol, and injectables	In development; will be testing against clinical samples in South Africa[19]
Loopamp TB Detection[20]	FIND, Switzerland/ Eiken, Japan	Loop-mediated isothermal amplification (LAMP) for TB	On the market; CE-marked and registered in Japan; not endorsed by the WHO; evaluation studies completed in Brazil, Peru, South Africa, and Vietnam;[21] demonstration studies under way in Cambodia, Cameroon, Ethiopia, Gambia, India, Ivory Coast, Madagascar, Malawi, Mongolia, Romania, South Africa, Tanzania, Uganda, and Vietnam[22]

GenoType MTBDR*plus* 2.0	Hain Lifescience, Germany/Global Consortium for Drug-resistant TB Diagnostics, United States	Line probe assay (PCR)	On the market; version 1.0 endorsed by the WHO; version 2.0 not endorsed by the WHO; field validation of the assay in smear-negative and smear-positive patients in India, Moldova, and South Africa under way[23]
❖NATeasy TB Diagnostic Kit[24]	Ustar Biotechnologies, China	Isothermal nucleic acid amplification and lateral flow detection cartridge	On the market; not endorsed by the WHO. Regulatory submissions under way in China
❖TruArray MDR-TB	Akkoni, United States	Microarray-based NAAT	In development[25]
Truelab/Truenat MTB	Molbio/bigtec Diagnostics, India	Chip-based NAAT for MTB; runs on a portable battery-operated device	On the market in India. Independent studies incomplete[26]
Nonmolecular technologies			
Alere Determine TB-LAM Ag lipoarabinomannan (LAM) lateral flow test	Alere, United States	Lateral flow urine test detects TB protein in adults with HIV	On the market; field studies conducted and under way[27]
TB Rapid Screen[28]	Global BioDiagnostics, United States, with support from FIND, Switzerland	Reporter Enzyme Fluorescence (REF) to detect β-lactamase produced by live bacteria in sputum samples (1st generation substrate)	In development; expected to use simple, low-cost fluorescence reader
TBDx	Signature Mapping Medical Sciences, United States	Automated slide-loading and -reading system for smear microscopy[29]	In development; field studies ongoing[30]
Culture-based technologies			
❖BNP Middlebrook	NanoLogix, United States[31]	Culture	In development
MDR-XDR TB Color Test	FIND, Switzerland/ Imperial College, United Kingdom	Rapid colorimetric drug susceptibility test (DST)	In development; feasibility study to commence[32]

TREK Sensititre MYCOTB MIC plate	Trek Diagnostic Systems/Thermo Fisher Scientific, United States	A dry microdilution plate containing lyophilized antibiotics for determination of minimum inhibitory concentrations to first- and second-line TB drugs (except pyrazinamide)	In development; in field studies[33]
Volatile organic compounds			
BreathLink	Menssana Research, United States	Volatile organic compound	In development; in feasibility studies, but has received CE mark[34]
❖Prototype breathalyzer device[35]	Next Dimensions Technology, United States	To identify active TB and MDR-TB	In development; received continued funding from the BMGF to further develop

❖ Indicates no published data available.

The current pipeline for TB diagnostics is relatively robust for nucleic acid amplification-based technologies. Most of these technologies are targeted at levels of the health system that most people cannot easily access. A true POC diagnostic for TB will remain elusive if it is not specifically delivered at the peripheral health service-level or to communities and households for active case-finding—ideally with an electricity- and cold-chain-free, small, cheap, simple, and portable instrument.

The Cochrane Infectious Diseases Group, in its Diagnostic Test Accuracy (DTA) review of Xpert MTB/RIF,[36] and Dr. Madhukar Pai of McGill University have both noted that the effective rollout of Xpert MTB/RIF is not without challenges;[37] the system is still expensive and not available in peripheral centers. Last year, a consortium including UNITAID, the U.S. President's Emergency Plan for AIDS Relief (PEPFAR), the U.S. Agency for International Development (USAID), and the Bill & Melinda Gates Foundation (BMGF) concluded a pooled purchase agreement with Cepheid to bring the price of Xpert cartridges down to US$9.98 for the public sector in high-burden countries.[38] Several projects are under way to roll out Xpert MTB/RIF over the next few years, including EXPANDx TB and TBXpert. The TBXpert project, a collaboration between the WHO and the Stop TB Partnership, is funded by UNITAID. Between 2013 and 2015, the project will provide 1.4 million Xpert MTB/RIF cartridges and 220 GeneXpert instruments in 21 countries.[39]

Stable Supply of Xpert MTB/RIF Cartridges

The lack of a stable supply of cartridges is a huge concern for those implementing Xpert MTB/RIF. In 2012, the Xpert MTB/RIF manufacturer, Cepheid, experienced difficulties in keeping up with the cartridge orders that were placed by countries, particularly after the price was lowered. In a press release dated January 8, 2013, then-CEO John Bishop said, "the underlying causes of our 2012 second half challenges have been resolved."[40] In a more recent web update, Cepheid now claims that they "expect to have considerably reduced—or even eliminated—any product allocations by the end of June [2013]."[41]

However, at the Xpert MTB/RIF Implementers Meeting held in Annecy, France, on April 16, 2013, new Cepheid executive vice president of emerging markets, Philippe Jacon (formerly CEO of FIND), indicated that the company would not be able to meet current back orders and demand until the third quarter of this year. Xpert MTB/RIF cartridges remain on allocation, which means that the company determines how much of an order to fulfill, and prioritizes orders. As professor Wendy Stevens of the National Health Laboratory Service in South Africa (the largest purchaser of Xpert MTB/RIF machines and cartridges) rightly pointed out, having only one global supplier of cartridges is far from ideal,[42] and Cepheid benefited from the pooled purchase agreement.

The lack of Xpert MTB/RIF cartridges is yet another of the ongoing drug- and diagnostic stock-outs. An inconsistent supply of Xpert MTB/RIF cartridges means that there will be fewer people who are accurately diagnosed and treated in a timely manner.

An adequate and consistent supply of diagnostic systems and assays must be guaranteed, and all stakeholders must be involved in ensuring the broadest possible access to useful new technologies where they are needed. The investment in the development and rollout of Xpert MTB/RIF must not be wasted.

Rather than rolling out TB-only laboratories, we need diagnostic tools and platforms that can be used in any laboratory (though tools at facility-level are optimal), and integration of tools such as Xpert MTB/RIF into HIV-, maternal and child–, and other health care services as soon as possible. This will facilitate more active case-finding instead of waiting for people to come to TB clinics.

The reactive nature of many TB control programs slows the development of aggressive national strategies to introduce new diagnostic tests.[43] Some countries implementing Xpert MTB/RIF are currently developing a strategy specifically for this one tool; a TB CARE project implementing Xpert outlined 37 steps necessary to roll it out—the first of which is to establish a working group.[44] Sometimes global agencies develop lengthy, overly complex diagnostic algorithms[45] that may be more confusing than useful to countries that may be deterred from trying the newer tests without FDA- or WHO guidance. Countries must work to develop national strategies that permit the introduction of any new tool or regimen whenever it is needed and available. As complex as the current system is, countries like South Africa, which rolled out GenoType MTBDR*plus* and then Xpert MTB/RIF, should be applauded for implementing these tests as quickly as they did.

Some countries have been slow to implement Xpert MTB/RIF as they wait for more data from fast followers such as Molbio's Truelab Real Time micro PCR System and Truenat MTB test for quantitative detection of MTB in sputum samples, which was launched this year in India. The system works on microchips with TB-specific genetic sequences and preloaded reagents for conducting a real-time PCR. Nikam et al. analyzed Molbio's Truenat MTB in a sample of 226 patients: the "Truenat MTB test was found to have sensitivity and specificity of 91.1% and 100% respectively, in comparison with 90.58% and 91.43% respectively for the in-house nested PCR protocol."[46] These data are hard, if not impossible, to interpret since no one else has an in-house nested PCR protocol, and the researchers did not compare Truenat with something more clearly validated, such as Xpert. While this product is available on the Indian market, there are few data about it. Efforts are now under way to evaluate this technology in the Indian public sector to inform the national TB policy.

Like Truenat, GeneDrive (Epistem) is a portable device developers say is targeted for use in low-resource settings. Unfortunately, although Truenat is CE-marked, there are no data about the product available at this time. A press release from August 2012 announced a partnership between Epistem and Becton Dickinson to supply and distribute the platform.[47]

These two molecular technologies, similar to Xpert MTB/RIF, aim to be cheaper. Independent studies are forthcoming. TAG believes that the evidentiary standards for the introduction of new diagnostic tests are far from rigorous. In fact, many

diagnostic companies make claims, which if they were made regarding new and untested drugs would likely result in the companies' facing civil or criminal sanctions for unjustified promotion of unvalidated medical commodities. However, in most parts of the world, diagnostics are not regulated as rigorously as drugs are.

The World Health Organization (WHO) approved the use of Xpert MTB/RIF in 2010[48] and, together with partners, has helped some countries roll out the technology by issuing documents such as the *WHO Policy Framework for Implementing New Tuberculosis Diagnostics 2010*[49] and *Prerequisites to Country Implementation of Xpert MTB/RIF and Key Action Points at Country Level: Checklist*,[50] as well as by sending rotating teams of technical experts from Geneva and other well-resourced centers to high–TB burden implementing countries.

In 2013, the WHO emphasized that the Hain GenoType MDRTBs*l* assay "cannot be used as a replacement test for conventional phenotypic drug susceptibility testing," due to lack of supporting evidence.[51,52] This was also the case with LAMP. Countries may use the tests, however, if they believe there is a role for them in their settings. A study (NIAID U01AI082229) currently being conducted by the Global Consortium for Drug-resistant TB Diagnostics, a group funded by the U.S. National Institutes of Health (NIH), is assessing the MTBDRs*l* assay in smear-negative and smear-positive patients in India, Moldova, and South Africa. Data should be available by fall 2013 and published in 2014.[53]

Based on the results of studies on the Alere Determine TB-LAM Ag, a urine-based TB LAM test, in HIV-infected adults with TB symptoms,[54] many authors concluded that the test holds promise for diagnosing TB faster in HIV-positive persons with CD4 counts under 100 cells/mm^3, who tend to have more extrapulmonary and smear-negative disease.[55] In most studies published to date, sensitivity is approximately 50 percent in patients with advanced immune suppression (CD4 count <100 cells/mm^3).[56]

Where should we be going?

Lawn and colleagues discuss the challenges related to cost-effectiveness as well as the clinical and programmatic effects of implementing GeneXpert.[57] They conclude that a rapid, accurate, affordable POC diagnostic test that can be "readily implemented is urgently needed."

The optimal point-of-care TB test would be affordable, patient- and user-friendly, accurate in people with any form of TB, and would result in TB treatment decisions in one visit or encounter. There is nothing in the pipeline that looks like it has even remote potential to fulfill these criteria. Médecins Sans Frontières, TAG, and

partners developed detailed specifications for such a test as long ago as 2008 (see http://www.msfaccess.org/sites/default/files/MSF_assets/TB/Docs/TB_event_POC_meetingoutcomes_full_ENG_2008.pdf).

Despite the improvements being made in TB diagnostics, we still cannot quickly and accurately detect TB in those with suspected extrapulmonary disease, children, and people living with HIV.[58]

Funding

Funding for research and development for TB diagnostics is hugely inadequate. TAG's *Tuberculosis Research and Development: 2012 Report on Tuberculosis Research Funding Trends, 2005–2011*[59] indicates that funding for TB diagnostics in 2011 was US$55,043,541. *The Global Plan to Stop TB: 2011-2015* calls for annual funding for new TB diagnostics to be US$340 million. The largest funders of TB diagnostics remain the BMGF, the U.S. National Institute of Allergy and Infectious Diseases (NIAID) at the NIH, and USAID.

According to David Walwyn's modeling study, spending on TB R&D in countries such as South Africa is disproportionately small relative to disease burden.[60] The cost of treating TB in South Africa for example, is over US$588 million per year. Walwyn's calculation, based on return on investment, indicates that South Africa should be spending at least US$92 million annually on TB R&D. It is crucial that the BRICS countries, (Brazil, Russia, India, China, and South Africa) now increase their investment in TB R&D. This investment should not only be for the search for new tools, but also for the infrastructure to evaluate and demonstrate their field effectiveness.[61]

Increased and sustainable investment in the TB diagnostics pipeline must remain a priority for funders and researchers. In a 2006 report, the World Health Organization estimated that US$1 billion is spent worldwide on TB diagnostics. This is a potentially huge market, and diagnostic developers must use this as an opportunity to invest in accelerating TB diagnosis, enabling rational use of therapies, and reducing TB mortality.[62] Since the TB diagnostics landscape has changed in the past few years, updated market estimates are required to guide test developers (see www.tbfaqs.org, a new website developed to address key questions by test developers).

Efforts are under way to quantify the current TB diagnostics market, accounting for the ongoing rollout of Xpert MTB/RIF and other changes in the landscape. This effort involves the BMGF, the McGill International TB Centre, UNITAID, FIND, the Stop TB Partnership's New Diagnostics Working Group, country partners, and national TB programs. The proposed project will conduct a rapid assessment of

the served available market (SAM) for TB diagnostics (i.e., current algorithms; regulatory and policy landscape; testing volumes/sales; total dollar-value spending on diagnostics; and market segmentation) in four high-burden countries: India, China, Brazil, and South Africa. This market analysis will cover 2012–13, providing a snapshot of the current market in these emerging economies, and is expected to be completed by early 2014.

In 2013, the BMGF granted Alere US$21.6 million and debt financing of up to US$20.6 million to develop a cartridge-based point-of-care molecular diagnostic platform. Called Alere Q, it is meant to rapidly and affordably screen TB patients. There are plans for a second cartridge, which will be used in people found to have active TB, to determine drug resistance; validation is expected in two years.[63] The Keck Graduate Institute of Applied Life Sciences and Claremont BioSolutions, LLC, received a US$3.6 million research grant from the NIH to develop a POC assay and device to diagnose MDR-TB. They aim to develop a handheld device that can be built for less than US$100.[64,65] This type of innovation must be nourished and fueled with more funding and by more partners.

Biomarkers for TB

There is still no accurate, validated TB biomarker, despite some progress in the past 10 years.[66] Research has been focused on curing active TB disease, reactivation of latent TB, and the induction of protective immune responses through vaccination. In order to address the main challenge—quantifying biomarkers as surrogate clinical endpoints for clinical trials of new drugs, regimens, or vaccines—there must be increased investment in basic science. In 2012, the BMGF invested US$7.7 million in a portfolio of 10 grants focused on TB diagnostic biomarkers that can result in a simple TB test like that for pregnancy.[67] Additional efforts are needed to accelerate progress.

Drug susceptibility testing

Another key area that lacks funding or priority by donors and sponsors is decentralized DST for fluoroquinolones, pyrazinamide, and other drugs, particularly second-line drugs. With the approval of bedaquiline and the potential for new drugs to enter the market soon, this must become more of a priority for funders and researchers.[68] The *WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis – 2011 Update* recommends "rapid drug susceptibility testing of isoniazid and rifampicin or of rifampicin alone…over conventional testing or no testing at the time of diagnosis of TB, subject to available resources."[69] It is essential that we move to implement this recommendation in all settings.

Specimen bank

Diagnostics developers need more information and access to specimens to validate their technology platforms. The WHO TDR TB Specimen Bank, in jeopardy of closing last year due to lack of funding, is now being managed through FIND (as of March 2013). Its specimens, as well as FIND's, are freely available to qualified investigators on application. FIND has funding to manage the two banks only until October 2014; it does not have funding for new collections.

The Tuberculosis Trials Consortium (TBTC) of the U.S. Centers for Disease Control and Prevention, the AIDS Clinical Trials Group (ACTG) of NIAID, and the Global Alliance for TB Drug Development (TB Alliance) have partnered to establish the Consortium for Tuberculosis Biomarkers (CTB2). The Consortium aims to develop agreed-upon standards for collection, processing, and storage of a core set of relevant samples and a high-quality biobank to facilitate discovery and qualification of biomarkers of TB drug effects. It will be made available to the broader scientific community through a peer-review system.[70]

It is crucial to diagnostics research that useful, viable specimen samples be available openly and freely; these resources need more and sustainable investments.

Policies and Strategies

Without adequately addressing the rollout of new tools, we will not change the number of people who die from preventable, curable TB. For example, if programs implementing Xpert MTB/RIF allow for starting TB therapy on the same day as diagnosis, this will result in quicker treatment initiation and reduced loss to follow-up and transmission.

The reduced, negotiated prices for Xpert MTB/RIF are not available to the private sector in the highest–TB burden countries like India, even though the private sector is the dominant health care provider. Even poor TB patients seek initial health care in the private sector in countries like Pakistan, Bangladesh, Cambodia, Nigeria, and Indonesia, and it is important that good tests are made available for such patients. This will require innovative business models. In Pakistan, Bangladesh, and Indonesia, a social-enterprise model is being launched to scale up implementation of Xpert MTB/RIF and improve quality of TB care.[71]

In India, the 2012 ban on inaccurate TB serological tests has resulted in a chaotic private market, since WHO-approved TB tests were costly. Some private labs continue to offer serology, while others have switched to blood PCR and QuantiFERON-TB Gold, tests that cannot accurately distinguish latent TB infection from active TB disease.[72]

The Initiative for Promoting Affordable, Quality TB tests (IPAQT), a coalition of accredited private labs in India supported by industry and nonprofit groups (e.g., Clinton Health Access Initiative), has made three WHO-approved tests (Xpert MTB/RIF, Genotype MTBDR*plus*, and BACTEC MGIT 960 TB System) available at affordable prices to patients in the private sector in India. Labs in IPAQT have access to lower, FIND-negotiated prices for the quality tests in exchange for their commitment to pass on the benefits to patients.

Such private-sector efforts need greater support from national TB programs and the public sector. It is insufficient to ban or eliminate inaccurate tests. Efforts must also be made to make good tests more affordable to all sectors, public and private.[73]

Recommendations

Funding

1. Donors must increase funding and work to bring more scientists and innovators into the field to develop an optimal point-of-care TB test that is affordable, patient- and user-friendly, accurate in people with any form of TB, and will result in TB treatment decisions in one visit or encounter.
2. The private sector and middle-income countries need to increase investment in TB diagnostics development. The BRICS countries (Brazil, Russia, India, China, and South Africa) must increase their investment in TB R&D for new tools as well as the infrastructure to evaluate and demonstrate their field-effectiveness.

Biomarkers

1. Donors must prioritize increased investment in basic science to quantify biomarkers as surrogate clinical endpoints for clinical trials of new drugs, regimens, and vaccines.

DST

1. Donors must fund and prioritize decentralized DST for fluoroquinolones, pyrazinamide, and other drugs, particularly second-line drugs.
2. Country programs and donors must implement the recommendation to do rapid DST of isoniazid and rifampicin, or of rifampicin alone, over conventional testing or no testing at the time of diagnosis of TB.

3. Donors and industry must work to develop universal DST and newer DST methods to rapidly identify regimens to which every patient's bacterial organism is susceptible.

Specimen bank

1. Donors need to fund repositories of useful, viable specimen samples that are available openly and freely.

Policies and strategies

1. Donors, national programs, and implementers must develop policies and strategies that move toward active case-finding and integrate TB services across the health system.
2. Donors and national programs must integrate new TB diagnostic tools such as Xpert MTB/RIF into HIV-, maternal and child–, and other health care services wherever possible.
3. Programs must work to develop national strategies that allow the flexibility to introduce any new tool or regimen whenever available and needed.
4. Regulatory agencies must develop stringent evidentiary standards for the introduction of new diagnostic tests to ensure that people have access to good, accurate tools without delay.
5. Programs in countries with high HIV burdens should assess the usefulness of tests that have not yet been endorsed by international agencies, in their own settings, particularly where TB kills many people before they are even diagnosed.
6. National programs should not wait for the WHO to make recommendations regarding the use of tools if they have the resources to do so themselves. However, programs should beware of promotional marketing by diagnostics developers that lacks supporting data.
7. Donors, in particular BRICS and other middle-income countries, must conduct operational research to determine at how low a level of the health system Xpert could be implemented.
8. Donors, industry, and national programs must develop policies that make good tests more affordable to all sectors, public and private.
9. UNITAID, the BMGF, PEPFAR, USAID, and the WHO must ensure that Cepheid identifies the causes of Xpert cartridge shortages and fixes them quickly.

Conclusion

TB diagnostics have the potential to revolutionize the way we diagnose TB and treat and cure people. After decades of neglect of TB R&D, we have now built the architecture to develop new drugs, vaccines, and diagnostics that together would eliminate TB. A simple, affordable, universally accurate point-of-care test is still attainable if diagnostics developers, funders, and patients make it a priority by increasing and sustaining higher levels of funding for new research and development.

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