

# Point-of-Care Diagnostics for HIV and Tuberculosis: Landscape, Pipeline, and Unmet Needs

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**Abstract:** Early diagnosis and rapid initiation of treatment remains a key strategy to control both HIV and tuberculosis (TB). However, HIV and TB control programs have had completely contrasting successes, especially with the development and deployment of point-of-care (POC) diagnostics. Clinicians, researchers, and public health staff who work at the frontlines of HIV care and control have had access to an outstanding array of POC diagnostics at their disposal, including those used for screening, initial diagnosis, staging, treatment monitoring, and early infant diagnosis. The field has also advanced to consider over-the-counter, self-testing options for HIV and the use of multiplexed platforms that allow for simultaneous detection of infections associated with HIV. In sharp contrast to HIV, suboptimal and delayed diagnosis of TB has perpetuated the epidemic in many high-burden countries. Although the TB diagnostics pipeline is substantially better today than it was even five years ago, absence of a simple POC test continues to be a gaping hole in the pipeline. In this review, we compare the POC diagnostics landscape and pipelines for these two important infectious diseases, and highlight gaps and unmet needs. [*Discovery Medicine* 13(68):35-45, January 2012]

Low-cost, point-of-care (POC) tests have completely transformed the management of several major infectious diseases (e.g., malaria and HIV) (Yager *et al.*, 2008), especially in resource-limited settings where healthcare infrastructure is weak, and access to quality and timely medical care is a challenge. These tests offer rapid results at the point-of-care, allowing for rapid initiation of appropriate therapy, and/or establishment of linkages to care (Peeling and Mabey, 2010). Most importantly, POC tests can be simple enough to be used at the primary care level and in remote settings with no laboratory infrastructure. POC tests are often more cost-effective for the healthcare delivery system (Peeling and Mabey, 2010), and can potentially empower patients to self-test in the privacy of their homes and make informed decisions.

The synergistic epidemics of HIV and tuberculosis (TB) have had a huge adverse impact on many populations, especially in high prevalence, resource-limited settings such as sub-Saharan Africa and Asia (Lawn and Churchyard, 2009). Early diagnosis and rapid initiation of treatment remains a key strategy to control both infections. However, HIV and TB control programs have had completely contrasting successes, especially with the development and deployment of POC diagnostics (Denkinger and Pai, 2011). Indeed, there are many lessons to be learnt by comparing the POC diagnostics landscapes and pipelines for these two important infectious diseases.

## HIV Diagnostics: Current Landscape and Pipeline

Clinicians, researchers, and public health staff who work at the frontlines of HIV care and control have had access to an outstanding array of POC diagnostics at their disposal (Table 1), although uptake of these tests has varied across countries. POC tests for HIV include those used for screening, initial diagnosis, disease stag-

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ing, treatment monitoring, and early infant diagnosis. The field has also advanced with the development of over-the-counter (OTC) self-testing options for HIV, and multiplexed platforms that allow for simultaneous detection of infections associated with HIV, such as hepatitis B and C, and syphilis (e.g., Multiplo®, MedMira Inc., Nova Scotia, Canada). An excellent survey of the current HIV diagnostics landscape has been published recently (Murtagh, 2011).

For initial screening and diagnosis, simple, accurate, whole-blood, finger-stick, and oral mucosal fluid-based rapid tests are widely popular and have been successfully scaled-up via voluntary counseling and testing (VCT) programs in many countries, supported by agencies such as PEPFAR, UNITAID, and the Global Fund to Fight AIDS, TB, and Malaria. Dozens of inexpensive POC HIV tests are available commercially, and quality-assured kits can be procured via the WHO prequalification program for diagnostics (World Health Organization, 2011f).

A recent evaluation of all FDA-approved rapid HIV tests on finger stick specimens documented their high accuracy (sensitivity and specificity exceed 99%) in controlled laboratory settings (Delaney *et al.*, 2011). Rapid oral mucosal fluid tests have comparable accuracy to blood tests (Pai *et al.*, 2012). While the vast majority of rapid HIV tests are based on antibody detection, the most recent fourth generation immunoassays simultaneously detect HIV p24 antigen as well as antibodies to HIV-1

and HIV-2 in serum, plasma, and whole blood.

Although confirmatory testing is required for all first line screening tests, even oral fluid rapid HIV tests have been found to have high accuracy in high risk populations such as sexually transmitted disease (STD) clinic attendees, and unregistered pregnant women that present at the time of delivery (Pai *et al.*, 2007; Pant Pai *et al.*, 2007). In addition to high diagnostic accuracy, these POC tests have also been shown to have clinical impact in resource-limited settings (Pai *et al.*, 2008; Pai and Klein, 2009). For example, use of a simple oral-fluid test in a labor ward was successful in reducing mother-to-child HIV transmission in a rural hospital in India (Pai *et al.*, 2008; Pai and Klein, 2009). In fact, oral fluid based HIV rapid tests may be simple enough to be potentially useful for home-based HIV self-testing (Pai and Klein, 2008), as shown in a recent study in Africa (Choko *et al.*, 2011).

Over-the-counter (OTC) versions of oral mucosal fluid-based tests are now available (e.g., Aware Oral OTC, Calypte Biomedical Corporation, Portland, OR, USA). Although self-testing is a promising approach to expand HIV screening programs, several issues related to self-testing are unresolved, and the ideal public health strategy that can safely and effectively offer this option is yet to be determined. With the impending FDA approval of an OTC oral HIV test, some of these logistical issues may get addressed, although infrastructural and logistical barriers for linking self-testers to

**Table 1. Commercially Available Point-of-Care Tests for HIV/AIDS.**

Purpose/Indication	Illustrative Examples	Strengths	Limitations
Diagnosis of HIV infection using blood, plasma, serum specimens	Determine® HIV-1/2 Ag/Ab Combo (Alere Inc., Waltham, MA, USA)	Rapid, inexpensive, results within minutes, high accuracy, can be performed with minimal training; included in WHO prequalification program	False-positive results; require confirmatory testing
Diagnosis of HIV infection using oral fluid specimens	OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, PA, USA); Calypte Aware™ HIV-1/2 OMT (Calypte Biomedical Corporation, Portland, OR, USA)	Rapid, inexpensive, results within minutes, high accuracy, can be performed with minimal training; non-invasive and convenient	False-positive results; require confirmatory testing
Over-the-counter oral fluid HIV tests	Aware™ Oral OTC (Calypte Biomedical Corporation, Portland, OR, USA)	Designed for OTC use, results within minutes, can be performed with minimal training; useful for self-testing	False-positive results; require confirmatory testing
Simultaneous screening for HIV, hepatitis B/C	Multiplo™ HBV/HIV/HCV (MedMira Inc., NS, Canada); Core Combo HIV-HBsAg-HCV® (Core Diagnostics, UK)	Rapid, inexpensive, results within minutes, can be performed with minimal training	Modest accuracy; Limited published evidence
CD4 counts	PointCare NOW™ (PointCare Technologies Inc., MA, USA); Pima™ CD4 Analyzer (Alere Inc., Waltham, MA, USA); CyFlow™ CD4 miniPOC (Partec GmbH, Germany)	Rapid, provides absolute CD4 counts; can be performed with minimal training	Relatively expensive; limited throughput

follow-up care will require work (Pai and Klein, 2008).

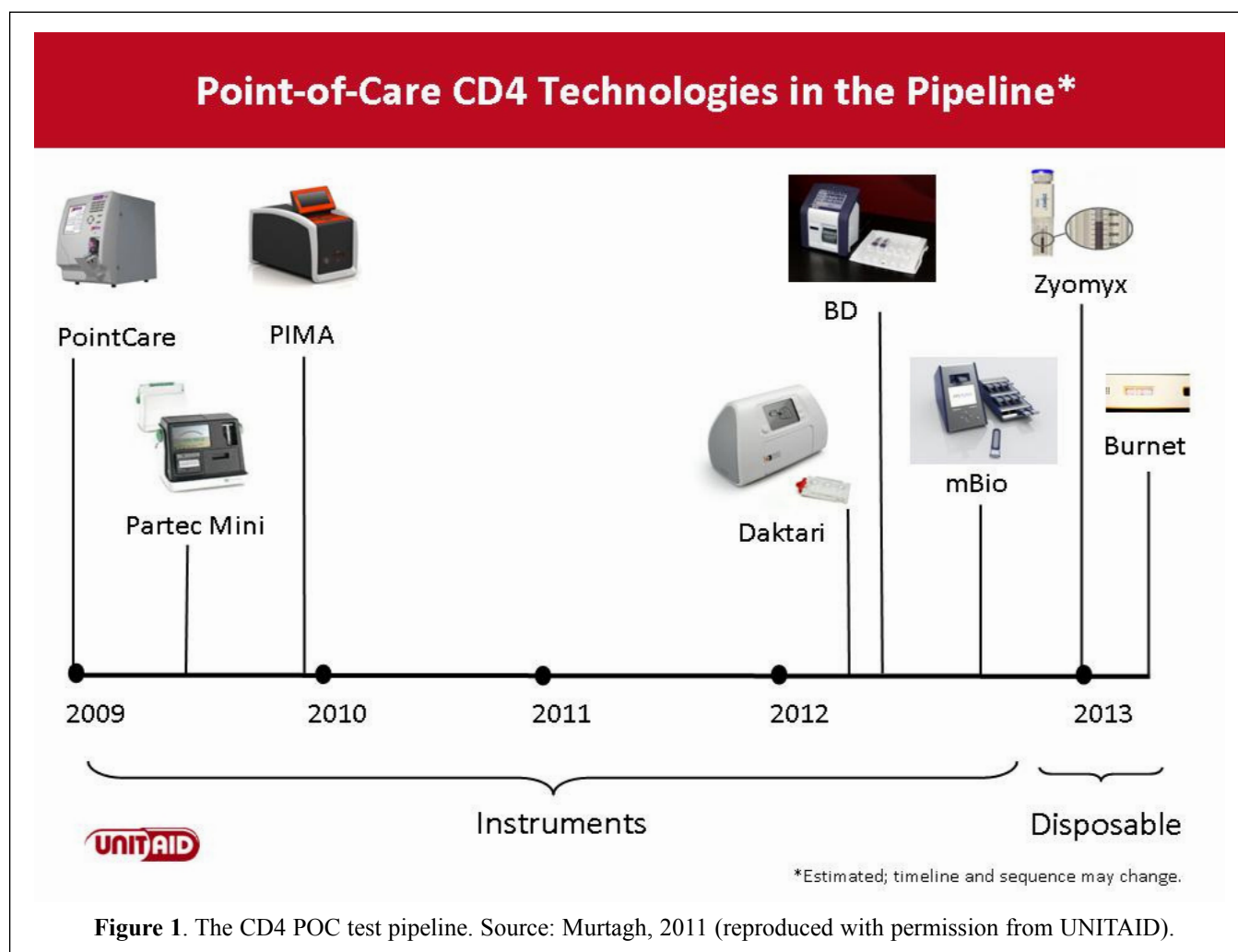
For disease staging and for making decisions about anti-retroviral therapy (ART) initiation or monitoring, there are qualitative and quantitative CD4 POC tests that are now available (Figure 1 shows the pipeline). These are a significant advance over the traditional, expensive, laboratory-based, flow cytometry assays (Boyle *et al.*, 2011; Murtagh, 2011). Efforts are also underway to develop more affordable (and disposable) POC tests for CD4 counts and several such technologies are expected to reach the market within the next few years (Figure 1) (Murtagh, 2011).

Lastly, HIV diagnostics have benefited from the growing momentum towards simple, multiplexed tests that can diagnose multiple infectious diseases at the point-of-care. There are now POC options available for multiplexed detection of HIV, hepatitis B and C, and syphilis (Figure 2). Although evidence on their test performance in real world settings is limited, they offer promise of simultaneous detection of several infections,

with greater convenience for patients and providers. The convergence of fields such as nanotechnology, microfluidics, proteomics, and genomics has inspired the development of novel platforms, including POC and nucleic acid amplification tests (NAATs), which enable the detection of multiple biomarkers at the point of care. Also, integration of smartphone technology with such novel platforms might lead to the development of novel testing platforms that can also use mobile telephones for delivering results quickly and efficiently.

### HIV Diagnostics: Gaps and Needs

A key gap has been lack of simple, affordable POC options for early infant diagnosis and for viral load determination (Murtagh, 2011; Usdin *et al.*, 2010). While conventional NAATs are accurate and commercially available for early infant diagnosis and viral load, they are expensive and require sophisticated laboratory infrastructure that is not available in many resource-limited settings. Thus, most ART programs in resource-limited settings have no access to these technologies.



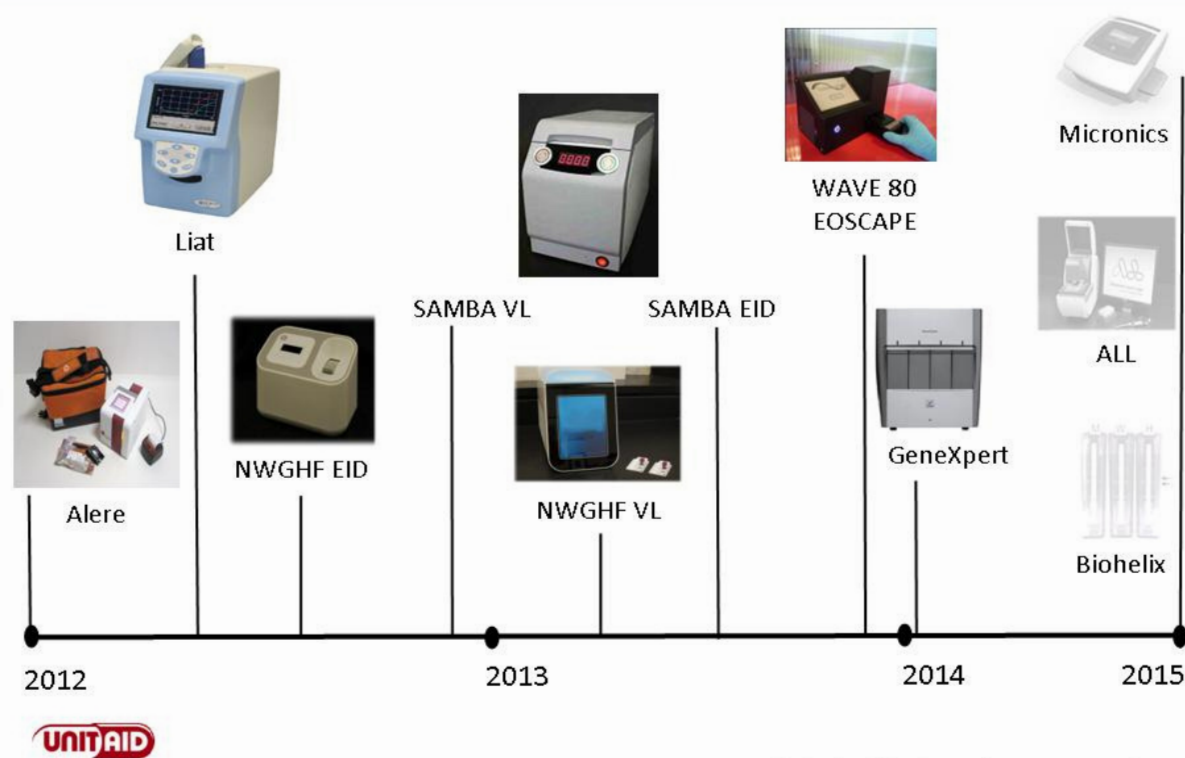


**Figure 2.** Point-of-care tests that can simultaneously detect HIV and hepatitis B and C (Multiplo®, MedMira Inc, NS, Canada). Source: MedMira Inc., NS, Canada (reproduced with permission).

This leads to treatment failure, impacting quality of clinical management. Viral load testing that could be conducted at the POC will reduce the need for laboratory infrastructure and lower the cost for ART programs (Murtagh, 2011). Resistance assays that are currently prohibitively expensive and run only as part of clinical studies will have tremendous potential in expediting linkages to care if offered at POC. Although there are currently no POC viral load assays that are commercially available, there are several technologies in development (Figure 3 shows the pipeline) (Murtagh, 2011).

For epidemiological and surveillance purposes, there is a felt need for an accurate, inexpensive, and easy-to-use kit that can be used to estimate HIV incidence at the population level (Incidence Assay Critical Path Working

## Point-of-Care Viral Load and EID Technologies in the Pipeline\*



\*Estimated; timeline and sequence may change.

**Figure 3.** Pipeline for viral load and early infant diagnosis platforms. Source: Murtagh, 2011 (reproduced with permission from UNITAID).

Group, 2011). A recent report by the Incidence Assay Critical Path Working Group outlines the challenges in developing such an assay, and the work that is ongoing to overcome the challenges (Incidence Assay Critical Path Working Group, 2011).

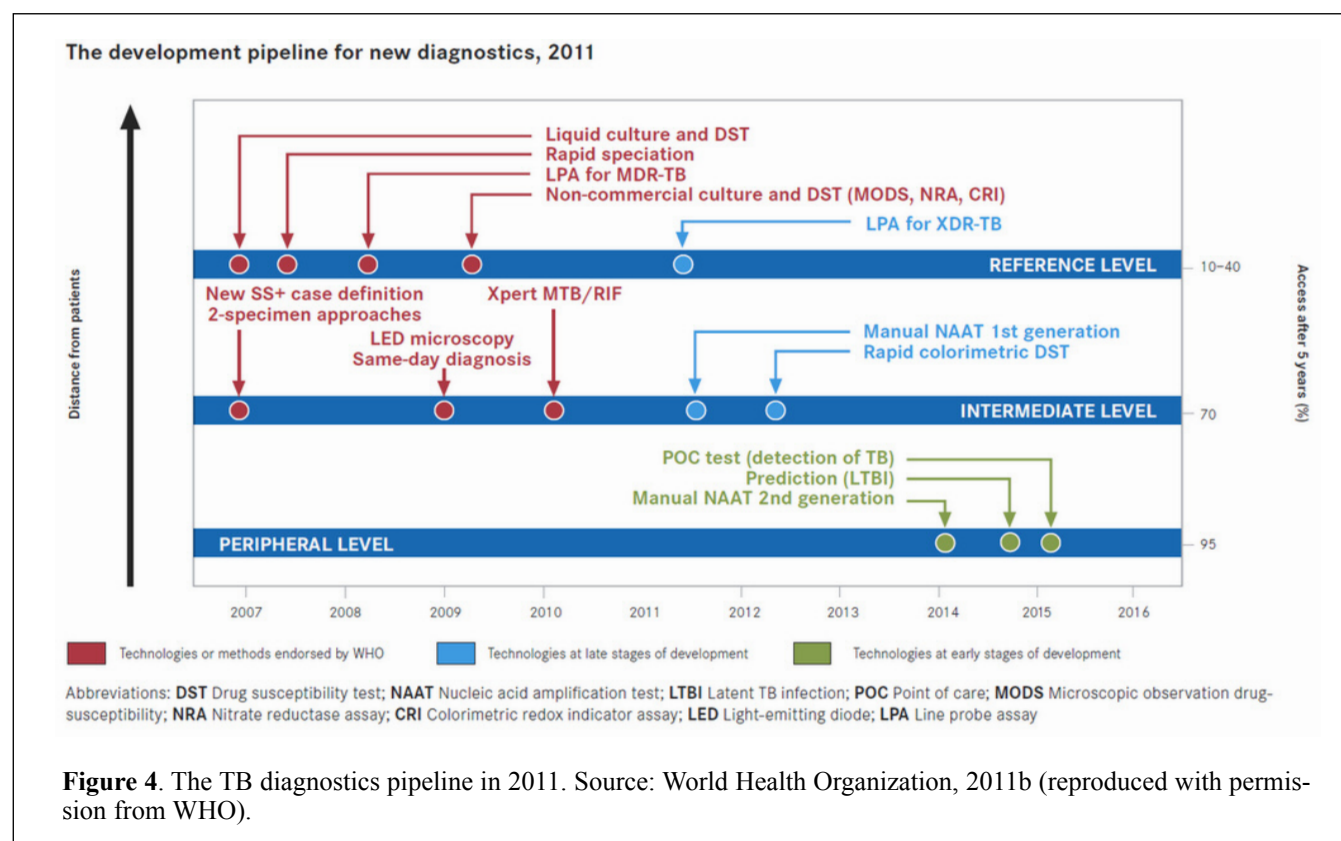
Lastly, although the HIV diagnostics portfolio is impressive, there remains a concern about inadequate uptake of good tests and insufficient scale-up in many settings. An unacceptably large proportion of HIV patients (50-70%) continue to be unaware of their status in developing country settings, posing a problem for timely detection of HIV infection. Early detection and initiation of ART hinges on knowledge of serostatus, which is the key step in bringing people to treatment and care. Thus, efforts that are currently being made to link POC tests with more efficient, decentralized counseling and treatment services may have an impact. For example, research is now ongoing to combine oral fluid OTC HIV tests and mobile-phone based counseling into comprehensive HIV self-testing strategies that can be used to scale-up testing in underserved areas where trained counselors may not be available, and to overcome stigma and logistical challenges associated with conventional voluntary counseling and testing approaches (Pai and Klein, 2008). These approaches if carefully planned may leverage the growing interest in mHealth and mobile telemedicine, and further build on

the phenomenal growth of mobile telephony in many developing countries and emerging economies (Estrin and Sim, 2010).

### TB Diagnostics: Current Landscape and Pipeline

In sharp contrast to HIV, suboptimal and delayed diagnosis of TB continues to perpetuate the epidemic in many high-burden countries, especially those with a high prevalence of HIV infection (Wallis *et al.*, 2010). The need for an instrument-free, laboratory-free, POC test for TB has been articulated by many groups, including patient advocates and civil society (Batz *et al.*, 2011; Lemaire and Casenghi, 2010; Weyer *et al.*, 2011). Although the TB diagnostics pipeline is substantially better in 2011 than it was even 5-10 years ago, absence of a dipstick type of POC test continues to be a gaping hole in the pipeline (Figure 4 shows the current pipeline) (World Health Organization, 2011b). Table 2 summarizes the diagnostic options for TB that can potentially be used at the point-of-care.

Sputum smear microscopy, in principle, can be done at the point-of-care in a primary care setting, provided a basic microscopy facility and a trained technician are available (Steingart *et al.*, 2007). Unfortunately, smear microscopy is an insensitive technique and misses nearly half of all TB cases. To compensate for this, at





least two sputum smears need to be stained and read, and this makes the test difficult to implement as a genuine POC test. On the positive side, smear microscopy is inexpensive, and a trained microscopist can identify several disease conditions (e.g., malaria, filariasis, urinary tract infections). Conventional, direct Ziehl-Neelsen microscopy can be optimized using LED fluorescence microscopy, and by using two spot sputum smears to ensure same-day diagnosis. Indeed, these approaches are now endorsed by the World Health Organization (WHO) (World Health Organization, 2011a; World Health Organization, 2011e).

The recent WHO endorsement of Xpert MTB/RIF (Cepheid Inc., Sunnyvale, CA, USA), an automated, cartridge-based nucleic acid amplification test (NAAT), has greatly stimulated resurgent interest in using molecular tests for rapid diagnosis of active TB and drug-resistance (World Health Organization, 2011c). While the Xpert MTB/RIF assay is accurate and can potentially be used outside of a laboratory setting by a minimally trained health worker, it falls short of meeting the ideal POC requirements on two important grounds: at current prices, it is expensive and unaffordable in many settings, and it requires sophisticated equipment that cannot be deployed at the community level (Pai, 2011b). Also, the pricing of Xpert MTB/RIF assay in the private sector in developing countries is substantially higher than the pricing for the public sector, imposing additional barriers for scale-up.

For decades, researchers and the industry had pinned their hopes on serological antibody-detection methods for POC test development. Indeed, dozens of serological

rapid (lateral flow assays) and ELISA tests got commercialized, even though no international guideline recommended their use. Today, these tests are on the market in at least 17 of the 22 highest tuberculosis burden countries, and millions of patients in the private sector undergo serological testing (Grenier *et al.*, 2012). Unfortunately, TB serological tests are neither accurate nor cost-effective (Dowdy *et al.*, 2011; Steingart *et al.*, 2011), prompting the WHO to issue a strong negative recommendation against their use (World Health Organization, 2011d). The WHO policy, announced on July 20, 2011, states that, since the “the harms/risks [of commercial serodiagnostic tests] far outweigh any potential benefits (strong recommendation) ... these tests should not be used in individuals suspected of active pulmonary or extra-pulmonary TB, irrespective of their HIV status” (World Health Organization, 2011d).

It is important to clarify three points regarding this WHO recommendation. Firstly, the WHO policy encourages research to develop new serological tests for TB based on antigen/antibody biomarkers. The negative recommendation only applies to existing commercial tests. Secondly, the WHO policy does not include commercially available blood-based tests (interferon-gamma release assays) for latent TB infection. It only applies to antibody-based (serological) tests for active TB. Thirdly, the WHO policy does not call for a ban on the technology platforms used for antibody or antigen detection (ELISA or rapid immunochromatography). They are excellent for many diseases, just not currently for TB.

The failure of antibody-based approaches spurred interest in antigen-detection methods (Flores *et al.*, 2011).

**Table 2. Point-of-Care Tests for TB.**

Purpose/Indication	Illustrative Examples	Strengths	Limitations
<i>Sputum smear microscopy</i>	Direct and concentrated Ziehl-Neelsen and fluorescence staining	Inexpensive, rapid, results can be obtained the same day; most infectious patients are identified; microscopy can be used for several disease conditions	Requires laboratory infrastructure and a trained technician; sensitivity is poor; not very useful in extra-pulmonary TB
<i>Diagnosis of active TB using serological antibody detection platforms</i>	MycoDot® (Mossman Associates, Blackstone, MA, USA), ICT TB® (ICT Diagnostics, Sydney, Australia), and many others	Rapid, inexpensive, results within minutes, can be performed with minimal training	Inaccurate and highly inconsistent; WHO has recommended against their clinical use
<i>Automated, cartridge-based nucleic acid amplification test</i>	Xpert MTB/RIF® (Cepheid Inc., Sunnyvale, CA, USA)	High accuracy, can be performed with minimal training; results within 90 minutes; can detect MTB and drug resistance	Expensive, requires investment in equipment; not deployable in the community
<i>Urine LAM test</i>	Determine® TB-LAM (Alere Inc., Waltham, MA, USA)	Rapid, inexpensive, results within minutes, can be performed with minimal training; uses urine specimens	Poor sensitivity overall; higher sensitivity in HIV-infected patients with low CD4 counts; will require CD4 testing to integrate into algorithms; limited evidence on clinical utility and impact

While many candidate antigens have been evaluated, urine lipoarabinomannan (LAM) detection assay was the first and, to date, the only antigen detection test to be commercialized, based on promising results from early studies (Boehme *et al.*, 2005). Unfortunately, subsequent research showed that the urine LAM ELISA assay had suboptimal accuracy for routine clinical use in unsolicited patients (Minion *et al.*, 2011; Peter *et al.*, 2010).

Two recent studies have evaluated the Determine® TB-LAM (Alere Inc., Waltham, MA, USA), a low-cost, POC version of the urine LAM test (Figure 5), in HIV-infected persons in South Africa (Lawn *et al.*, 2011; Peter *et al.*, 2011). Consistent with previous studies, the overall sensitivity of Determine® TB-LAM was low in patients with culture-confirmed TB. However, these studies showed that a combination of POC LAM test and sputum smears may offer value in screening for TB among severely immune-compromised HIV-infected patients (e.g., CD4 counts <50), a subgroup of high-risk patients for whom diagnostic delays can be fatal (Lawn *et al.*, 2011; Peter *et al.*, 2011). Further research is necessary to assess the clinical impact of using this POC LAM test and its role in improving case management (Denkinger and Pai, 2011). Because the Determine® TB-LAM test may have value only in those with low CD4 counts, the test must be evaluated as part of an algorithm which includes, ideally, HIV and CD4 testing at the point-of-care.

### TB Diagnostics: Gaps and Needs

Tests such as Xpert MTB/RIF and Determine® TB-LAM are not the ideal POC tests that are desperately needed for TB control. But they have shown us a glimpse of what the future holds, and give us hope that an ideal POC TB test may be within reach. Clearly, if we want to replicate the successes achieved in HIV diagnostics, renewed efforts must be made to develop laboratory-free, POC tests for all forms of active TB, regardless of HIV status or CD4 counts. Mathematical models suggest that such POC tests can have a huge impact on TB case detection rates as well as TB incidence (Abu-Raddad *et al.*, 2009; Dowdy *et al.*, 2008; Keeler *et al.*, 2006).

The target product profile for such an ideal TB POC test has been recently published (Table 3) (Batz *et al.*, 2011). However, because of insufficient progress in biomarker research and because of lack of strong industry interest in TB, progress has been much slower than anticipated. In fact, efforts are being made to devel-

op incentive prize models for successful POC tests for TB (Wilson and Palriwala, 2011). Incentive prizes are large cash rewards for achievement of specified objectives, and can be an approach to spur development of novel health technologies (e.g., diagnostics) for diseases of poverty and neglected diseases (Wilson and Palriwala, 2011). While two prizes have been proposed for POC TB tests, neither has been successfully launched (Wilson and Palriwala, 2011).

While a simple, dipstick type of POC test for TB might not be ready in the near future, the landscape is looking more promising for a more decentralized, field-friendly, affordable molecular test, which can be used at the point-of-care to reduce diagnostic delays (Figure 6) (Niemz *et al.*, 2011). These include hand-held or portable platforms, based on DNA chips and/or disposable cartridges (Figure 7). Many of the technologies under development are capable of detecting many different infectious diseases, and that makes them very attractive for scale-up. For example, a platform that can detect TB, drug-resistant TB, as well as HIV viral loads could be very helpful in a clinic setting.

### Bridging the Chasm Between HIV and TB Control

While TB is an ancient disease, the HIV epidemic has been a problem for only 30 years. Yet, a comparison of the HIV and TB diagnostics landscapes clearly suggests that research & development (R&D) in TB has greatly lagged behind HIV, and there may be several explanations for this big gap (Harrington, 2010). Patients, providers, and activists have played a major role in pushing for innovations in HIV diagnosis and treatment



**Figure 5.** Point-of-care strip test for TB using LAM antigen detection. Source: Alere Inc., Waltham, MA, USA (reproduced with permission).

and in lobbying for price reductions and generic products. Funders, researchers, industry, and governments have responded to this pressure by supporting R&D efforts on all fronts (drugs, diagnostics, and vaccines). Because the HIV epidemic historically began as a disease of the developed world, much of activism generated in the West helped translate the R&D into products

that ultimately benefited the developing world. Private pharmaceutical industry has played a big role in developing products in part because HIV is now a chronic disease that requires lifelong management and this ensures a large market. These factors partly explain the interest of pharma and biotech industries in enhancing and expanding on the ever growing HIV diagnostics

**Table 3. Minimum Specifications for a Point-of-Care Test for TB.**

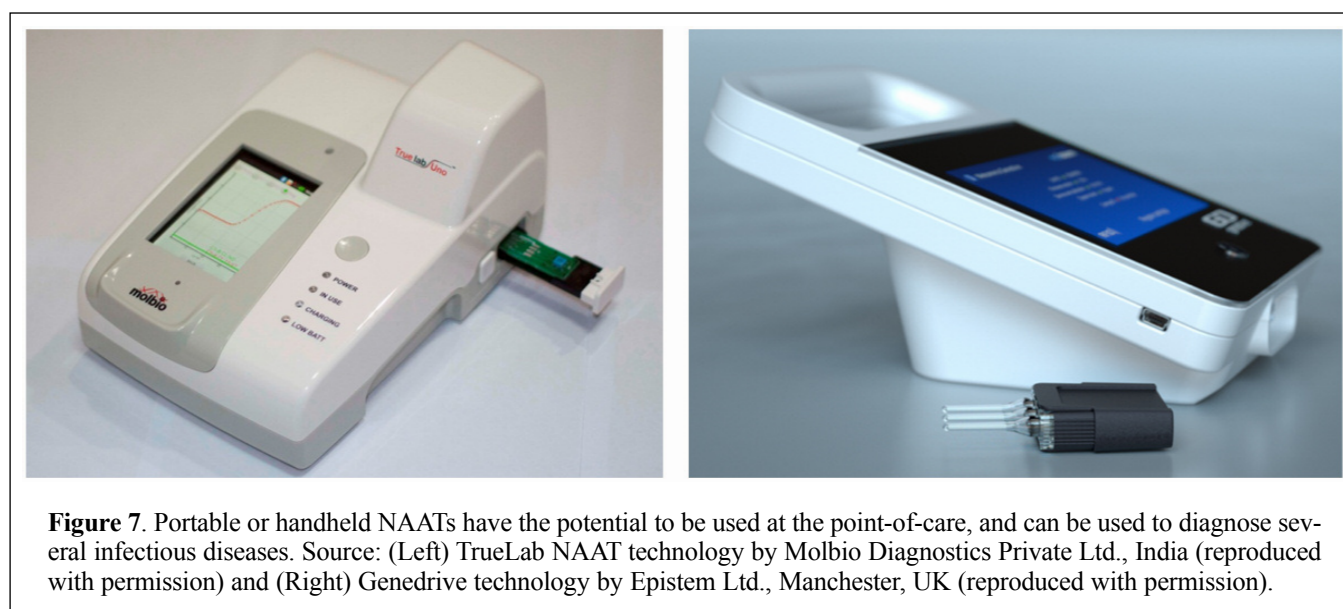
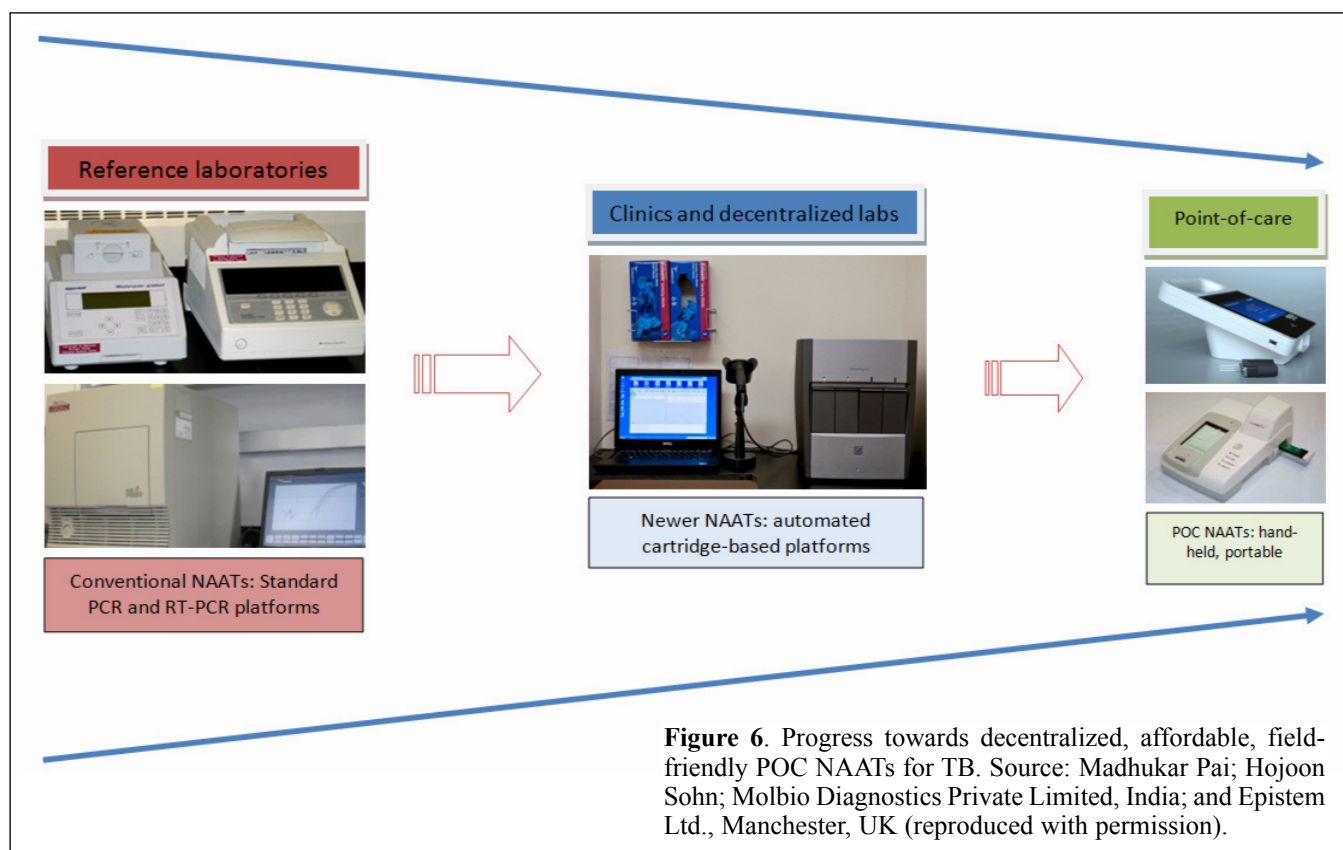
Test Specification	Minimum Required Value
Medical decision	Treatment initiation
Sensitivity - adults [for pulmonary TB only; regardless of HIV status]	Pulmonary TB: - 95% for smear positive, culture positive - 60%-80% for smear negative, culture positive [Detection of extrapulmonary TB being a preferred but not minimal requirement]
Sensitivity - children [including extrapulmonary TB; regardless of HIV status]	- 80% compared to culture of any specimen and - 60% of probable TB (noting problem of lack of a gold standard)
Specificity - adults	- 95% compared to culture
Specificity - children	- 90% for culture-negative probable TB (noting problem of lack of a gold standard) - 95% compared to culture
Time to results	3 hours max (patient must receive results the same day) [Desirable would be <15min]
Throughput	20 tests/day minimum, by 1 laboratory technician
Specimen type	Adults: urine, oral, breath, venous blood, sputum [Desired: NON sputum-based sample type and use of finger prick instead of venous blood] Children: urine, oral, capillary blood (finger/heel prick)
Sample preparation	- 3 steps maximum - Safe: biosafety level 1 - Ability to use approximate volumes (i.e., no need for precise pipetting) - Preparation that is not highly time sensitive
Number of samples	One sample per test
Readout	- Easy-to-read, unambiguous, simple "yes", "no", or "invalid" answer - Readable for at least 1 hour
Waste disposal	- Simple burning or sharps disposal; no glass component - Environmentally acceptable disposal
Controls	- Positive control included in test kit - Quality control simpler and easier than with sputum smear microscopy
Reagents	- All reagents in self-contained kit - Kit contains sample collection device and water (if needed)
Storage/stability required	- Shelf life of 24 months, including reagents - Stable at 30°C, and at higher temperatures for shorter time periods - Stable in high humidity environments
Instrumentation	- If instrument needed, no maintenance required - Instrument works in tropical conditions - Acceptable replacement cost - Fits in backpack - Shock resistant
Power requirement	Can work on battery
Training	- 1 day maximum training time - Can be performed by any health worker
Cost	<US\$10 per test after scale-up
Source: Batz <i>et al.</i> , 2011; reproduced with permission.	



and antiretroviral drugs portfolio.

In contrast, advocacy for R&D in TB has been weak, and private industry and donor interest has been low (Harrington, 2010). The revised Global Plan to Stop TB 2011-2015 estimates that at least US\$9.8 billion is needed in TB R&D over the next 5 years to reach the targets of 50% reduction in TB prevalence and mortality

by 2015 (World Health Organization, 2010). But according to analyses by Treatment Action Group (TAG) and Stop TB Partnership (STP), TB research globally remains grossly underfunded -- the total funding gap for the next five years (2011-2015) is estimated at US\$6.4 billion (64%). A 2011 funding analysis report by TAG and STP showed significant funding declines in basic science research on TB, which dropped 27%



and 29% to \$126.6 million and \$78 million, respectively (Treatment Action Group & Stop TB Partnership, 2011). This is worrisome because progress in the area of POC test development will require major investments in biomarker and basic research.

Given the flat-lined funding trends and lack of strong industry interest in TB, the attention is now shifting to Brazil, Russia, India, China, and South Africa (BRICS) and the leadership they can provide in the context of the global economic slowdown. There is a lot of excitement over the potential of BRICS in the development of affordable health-care technologies (Frew *et al.*, 2008). This is especially true for diseases of poverty, such as TB, that may not be of great interest to rich countries or to industry, which do not see a market to justify investments (Engel *et al.*, 2012). Although these countries have a large TB burden, they also have the technical resources and intellectual capital to invest in solutions and are capable of addressing the funding gap by infusing more resources into R&D for diseases such as TB (Small and Pai, 2010). Countries like China and India have a strong and growing biotechnology industry, and these countries may support the next wave of innovations in drugs, vaccines, and diagnostics (Frew *et al.*, 2008). There is also potential for philanthropic initiatives from high-net-worth individuals and companies in these growing economies. A recent conference in India highlighted its potential in taking the lead on TB diagnostics innovations (Engel *et al.*, 2012; Pai, 2011a).

The Stop TB Partnership and WHO have set 2015 as the deadline for developing a simple POC test for TB (World Health Organization, 2011b). Clearly, this goal will not be met without the greater engagement of industry, funders, governments, and researchers. Most importantly, the lessons from the response to the HIV epidemic must be used to step up the intensity of advocacy efforts to demand better tools for TB care and control, and to raise the level of ambition. The battle against TB cannot be won with century-old, antiquated tools.

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## Disclosures

The authors report no conflicts of interest.

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