POINT OF CARE HIV DIAGNOSTICS: BRINGING FASTER RESULTS FOR EARLY AND MORE EFFECTIVE TREATMENT

Accelerating Access and Integration of Innovative Point of Care Diagnostics for HIV in National Diagnostics Programmes

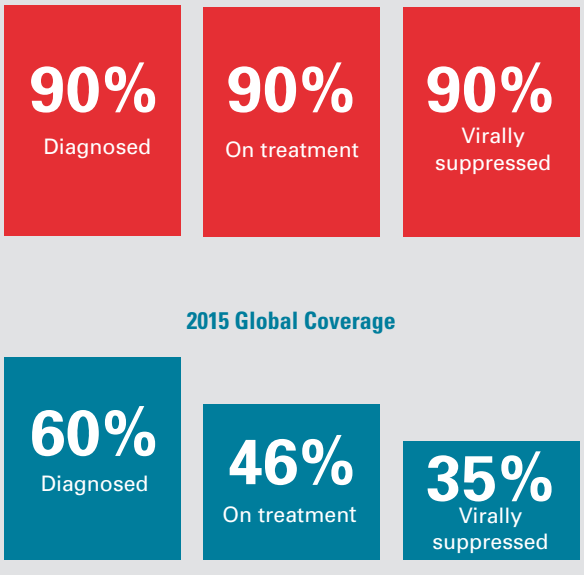
A partnership amongst Unitaid, the Clinton Health Access Initiative, the United Nations Children's Fund, and the African Society for Laboratory Medicine

Background

Over the last decade, access to antiretroviral therapy (ART) has improved dramatically, with 46% people living with HIV on treatment in 2015 compared to only 7% in 2005.[1] Moreover, since 2010, advances in the prevention of mother-to-child transmission (PMTCT) and the scale-up of PMTCT programmes have contributed to a 50% decline in the number of new HIV infections among children.[2] To build on these gains and further expand treatment coverage, UNAIDS launched ambitious new targets in 2014. The UNAIDS 90-90-90 Fast Track targets call for 90% of all people living with HIV to know their status, 90% of HIV-diagnosed people to be on ART, and 90% of people on ART virally suppressed by 2020.

Despite the remarkable progress over the past 10 years, gaps in diagnostic and treatment coverage still persist. In 2015, only 60% of people living with HIV knew their status, 46% of people in need were receiving ART and 35% of people living with HIV were virally suppressed (see Box 1).[1] In order to reach the 90-90-90 Fast Track targets and realize the 2016 World Health Organization (WHO) recommendation for universal treatment coverage, there is an urgent need to expand testing and treatment services.

Box 1 Progress Toward UNAIDS Fast Track Targets



Source: UNAIDS, 2016

Early Infant Diagnosis

Testing and treatment coverage remain low for children under 15 years old, and closing this gap is one of the most persistent challenges facing the global HIV response. In 2015, 1.8 million children were living with HIV, the majority in sub-Saharan Africa.[2] Yet, only half of infants born to mothers with a known HIV status received a virological test for early infant diagnosis (EID) within the first two months of life, and only half of children diagnosed with HIV received lifesaving treatment.[2] For the majority of countries, the current standard of care for HIV-exposed infants is to perform polymerase chain reaction (PCR) testing using dried blood spots (DBS) at 4-6 weeks of age. Detecting infection as early as possible is critical to reducing mortality among HIV-positive infants – without treatment 30% of HIV-positive infants die before their first birthday, and 50% by their second birthday, with mortality peaking at 2-3 months of age among untreated, HIV-positive infants.[3,4] Yet approximately 43% of conventional EID test results are never received by patients.[5] Even in situations where results are returned, long turnaround times, e.g., those averaging more than 30 days[6], contribute to delays in ART initiation and high loss to follow up (LTFU).

Viral Load Monitoring

Once an individual living with HIV is on treatment, routine viral load (VL) monitoring is used as an indicator of treatment efficacy, adherence and potential drug resistance. VL monitoring preserves the efficacy of first-line treatment regimens by identifying patients in need of adherence counselling prior to the development of HIV drug resistance, and helps identify those with treatment failure, facilitating transition to more effective second-line treatment regimens. It is estimated that with access to VL testing, approximately 1.1 million people living with HIV/AIDS in low and middle-income countries who have an elevated VL would be able to stay on first-line treatment, while 220,000 people living with HIV/AIDS could be appropriately switched to second-line treatment.[7]

Innovative point of care HIV diagnostic technologies: A promising approach for faster test results and earlier treatment

Reaching the 90-90-90 targets by 2020 will require enhanced testing capacity that facilitates timely treatment initiation of HIV positive infants and access to support services, including adherence counselling. Although conventional, laboratory-based technologies have formed the backbone for national HIV testing programs over many years, their ability to reach more people has been limited by various systemic challenges. These include (amongst others)

- limited infrastructure
- insufficient human resource capacity, and
- weak supply chains for laboratory commodities.

Establishing reliable sample transportation networks, returning test results to patients, and optimizing laboratory workflows are also enduring challenges, and often result in long turnaround times for test results, high rates of patient LTFU, and delayed treatment decisions.[8]

Point of care (POC) diagnostic technologies provide an innovative and unique opportunity to address these challenges and increase access and utilization of high-quality EID and VL testing.

Figure 1 Project Countries, Point of Care Diagnostics Project

Catalysing change through partnership

In November 2012, Unitaid in partnership with the Clinton Health Access Initiative, Inc. (CHAI) and UNICEF launched the Point of Care diagnostics project "Accelerating Access and Integration of Innovative Point of Care Diagnostics for HIV in National Diagnostics Programmes" in seven sub-Saharan African countries: Ethiopia, Kenya, Malawi, Mozambique, Tanzania, Uganda and Zimbabwe. This tripartite initiative supported the introduction and implementation of POC HIV diagnostics for CD4 staging and monitoring, EID, and VL testing. In October 2016, the initiative extended its geographical reach to include three additional countries in West and Central Africa (Cameroon, Democratic Republic of Congo and Senegal), and also added a fourth partner, the African Society for Laboratory Medicine (ASLM). Figure 1 highlights all ten project countries.

Phases 1 and 2a: Enhancing Systems and Preparing the Market

This project has evolved over multiple phases (Phases 1, 2a, and 2b), adjusting with POC technology advancements and changing WHO guidelines and recommendations, which shifted in 2016 from recommending CD4 testing to determine treatment eligibility to a "Treat All" approach. Phases 1 and 2a of the project (2012-2016) focused primarily on developing national systems and capacity to scale-up POC CD4 testing, as well as prepare the market for emerging EID and VL POC technologies. Key achievements from early implementation are detailed in Table 1.

Building on the lessons learned from POC CD4 implementation, the current phase of the project (Phase 2b) aims to optimize national EID and VL programmes for improved patient outcomes. Given the changing role of CD4 as a marker for treatment initiation and the growing evidence to support the use of POC diagnosis for EID, Phase 2b (2016-2020) places stronger emphasis on: improving service delivery of national EID and VL programmes by supporting expansion of POC testing; strengthening the evidence base through impact studies and operational research; demonstrating cost-effectiveness; and promoting sustainable POC programmes.

Table 1 Key achievements from Phases 1 and 2a

Increased Access to CD4 testing (across the seven original project countries)	Increased the number of sites with on-site access to CD4 testing by 630 sites
	Increased patient access to on-site CD4 testing from 50% to 71%
POC EID Implementation Pilots	Showed that same-day return of POC EID results and same-day ART initiation for infants can significantly improve ART initiation rates in Mozambique and Malawi (see Box 2)
POC EID Consortium	Contributed to the establishment of the POC EID consortium, a collaborative effort among researchers and partners to evaluate and accelerate the adoption of POC EID and minimize the need for in-country evaluations
Market Shaping and Procurement	Negotiated a service and maintenance agreement in Zimbabwe for incremental pricing on Alere's PIMA at a cost of US$0.35 per test
	Negotiated BD Presto price reductions, with all in price reduced from US$10.90 to US$7.50 for five project countries, with further reductions expected in late 2017
	Contributed to the formation of the EID and VL Procurement Consortium comprised of the Global Fund, Unitaid, CHAI, Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), Médecins sans Frontières (MSF) and UNICEF to pool negotiation power and harmonize contract terms with manufacturers

Phase 2b: Strengthening National EID and VL Programs for Improved Patient Outcomes

The strategic direction of Phase 2b builds on the lessons learned from early implementation, which show that POC devices can be successfully operated by non-laboratory technicians and that same-day results can accelerate ART initiation in infants (see Box 2). The goal of Phase 2b is to increase access to EID and VL testing in order to speed clinical decision making. This would enable:

- Earlier initiation of treatment for HIV-positive infants;
- Earlier adherence counselling for patients with poor treatment adherence;
- Timelier switching of patients failing first-line treatment onto more effective second-line regimens.

Specifically, the project aims to reduce the time between EID and VL sample collection and return of results to zero days on POC platforms. It is expected that this will accelerate progress towards quality of care and treatment targets for HIV-exposed and HIV-positive infants (EID) as well as children and adults on treatment (VL).

Box 2 POC EID Implementation Pilots: Results from Malawi and Mozambique

- Both the Malawi and Mozambique implementation pilots found that POC EID can reduce test turnaround time between sample collection to ART initiation to 0 days. The median turnaround time decreased from 122 days with conventional testing to the same day in Mozambique with 98.2% of patients receiving results the same day.
- ART initiation rates increased by 99% in Malawi and 570% in Mozambique.
- In Malawi, 91% of infants diagnosed as HIV-positive on a POC device (approximately 800 POC EID tests were performed) were initiated on ART, compared with 45.8% using a conventional device.
- In Mozambique, 87.4% of infants with a positive test result started ART within 60 days of sample collection at POC EID sites, compared to 12.8% at facilities that refer samples to conventional laboratories.

Sources: Jani et al., Effect of Point-of-Care Testing on Antiretroviral Therapy Initiation Rates in Infants. Conference Abstract, CROI, Seattle, February 2017. Mwenda et al., Significantly improved ART initiation rates after the implementation of POC EID. Conference Abstract, ASLM 2016, Cape Town, December 2016.

Figure 2 Phase 2b Project Goals

Public health goal: Speed up clinical decision making

Access goal: Increase access to high-quality EID/VL testing

POC implementation

- New POC product registration
- Rational, transparent product and site selection to maximize impact and meet country priorities
- Establish effective systems and processes to effectively manage programme, and improve linkage to care and retention

Strengthening national laboratory programs

- Generate testing demand to increase access
- Systems strengthening where there are gaps to improve efficiency and effectiveness
- Improve linkage to care and retention

Healthy, sustainable, competitive market

- Increase options that may meet countries' different needs and priorities
- Negotiate for better pricing and service terms
- Explore new models of fleet management
- Harmonize pricing and service terms with the Global Fund and PEPFAR and make them available to others

Advocacy for investment in high quality diagnostic interventions

- Strong WHO recommendation for POC testing
- Secure investment in POC testing from Ministries of Health, the Global Fund, PEPFAR, and other partners
- Partner coordination to leverage synergies, and reduce duplication and fragmentation

As outlined in Figure 2 the project centres on four pillars: POC implementation; strengthening of national laboratory programs; healthy, sustainable and competitive markets; and advocacy for investments in high quality diagnostic interventions. For the project's systems strengthening and public health targets, see Box 3.

Another critical component of Phase 2b is support for the rapid dissemination of evidence and best practices generated through pilots and operational research to inform accelerated context-specific implementation. To address the need for timely uptake of evidence-based approaches to POC testing implementation, the partnership leverages ASLM's leadership, technical expertise and extensive network in laboratory medicine to disseminate the latest science and share the practical experience of frontline workers using POC devices.

Lastly, it is important to emphasize that strong laboratory-based diagnostic programmes are the backbone on which to build POC testing and will maintain an important role in the diagnostics landscape. Effective implementation of both conventional and POC testing will need to address persistent barriers such as inadequate sample referral networks, incomplete data management and poor linkage to treatment. Recognizing this, Phase 2b of the project will extend support to strengthen conventional laboratory programs, while also scaling up POC EID and VL technologies.

Box 3 Expanding Access, Achieving Results

With total EID test volumes expected to double between 2014 and 2019, and VL testing to grow nearly five-fold in the same period[9], there is a pressing need to keep pace with the projected demand for testing. The project is expected to increase the capacity of countries to offer POC EID and VL testing and increase the number of EID and VL tests returned.

By the end of 2020, it is estimated that the project will have:

- **Procured 435,000 POC/near-POC EID tests and 1.1 million POC/near-POC VL tests**
- **Equipped approximately 110 sites with POC/near POC EID and VL testing capacity and 193 sites with POC/near POC VL**

The project is expected to enhance country capacity to implement POC EID and VL and contribute to improved patient outcomes, with the goal of achieving the following targets by 2020:

- **Saving an additional 9,235 lives among people living with HIV**
- **Initiating an additional 18,470 children living with HIV on treatment (through EID testing)**
- **Adding 522,902 patient years on effective treatment**

Conclusion

Early results from the initial phases of the POC project have demonstrated the potential of POC diagnostic technologies to accelerate access to testing and earlier and more effective treatment - ultimately saving more lives. This is paramount for infants living with HIV for whom early identification and treatment can mean the difference between life and death. Furthermore, as countries move to "Test and Treat All," the demand for VL monitoring to assess adherence and treatment failure will grow significantly.

By integrating POC into national programmes, the project is also expected to strengthen national diagnostic capacity and contribute to health systems strengthening. Making POC technologies more affordable and sustainable and disseminating lessons learned from this project can catalyse the scale-up of POC EID and VL technologies in similar settings beyond the focus countries. Taking these elements together, it is hoped this project, through POC EID and VL implementation, will strengthen HIV programmes and more importantly, improve the health and survival of people living with HIV.

References

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[9] CHAI CD4, EID, and VL forecast 2015, updated and presented routinely. Most recent update August 2015. Published in AIDS Medicines and Diagnostics Service, HIV Diagnosis Tests in Low-and Middle-income Countries: Forecasts of Global Demand for 2014-2018. July 2015. http://apps.who.int/iris/bitstream/10665/179864/1/9789241509169_eng.pdf?ua=1

Contact Information

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Resources

POC Webinars Playlist:

https://goo.gl/CuuzBi

Early Infant Diagnosis and Viral Load:

https://childrenandaids.org/d8/point-of-care

For the complete list of prequalified diagnostic products, please refer to:

http://www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/

For further information please visit the WHO Prequalification of Diagnostics programme web site

http://www.who.int/diagnostics_laboratory/evaluations/en/

Knowledge gateway:

HIV Point of Care Diagnostics Community hosted by CHAI and UNICEF
https://knowledge-gateway.org/childrenandaids/poc

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