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STRENGTHENING POINT-OF-CARE EARLY INFANT DIAGNOSIS TOWARDS THE ELIMINATION OF PAEDIATRIC AIDS

In 2017, an estimated 1.4 million infants were born to mothers living with HIV globally. Although the effective scale up of the prevention of mother-to-child transmission (PMTCT) of HIV services has led to a significant decline in vertical transmission since 2010, there were still 180,000 new childhood HIV infections in 2017.¹ Due to rapid disease progression among untreated infants infected with HIV – with peak mortality at 2-3 months of age² – ensuring that HIV-infected infants have the earliest possible access to life-saving antiretroviral treatment (ART)³ is a global health imperative. Given the critical importance of early diagnosis and treatment, WHO recommends that HIV-exposed infants have a virological test at 4-6 weeks of age; that results are returned to caregivers as quickly as possible (within 30 days after sample collection); and that

infants with a positive test result begin ART immediately.⁴

Yet enduring gaps in paediatric HIV diagnosis and treatment continue to hamper efforts to achieve the Super-Fast-Track targets for paediatric HIV. These targets set out in the Start Free, Stay Free, AIDS Free Framework⁵ call for reaching 95 per cent of all children living with HIV with lifelong treatment by 2020.

In 2017, only 51 per cent of HIV-exposed infants received a virological test within the first two months of life, and only 52 per cent of children (0-14 years) living with HIV received life-saving ART.¹ Without access to treatment, up to 30 per cent of HIV-infected children will die by their first birthday, and 50 per cent will die by their second birthday.⁶ In 2017, 76,000 young children (0-4 years) died from AIDS-related causes.¹

PAEDIATRIC HIV FAST FACTS
In 2017

**1.4 MILLION
BABIES**
WERE BORN TO MOTHERS
LIVING WITH HIV

ONLY 51% OF
**ALL HIV-EXPOSED
INFANTS**
WERE TESTED WITHIN THE
FIRST TWO MONTHS OF AGE

ONLY 52% OF
**CHILDREN
LIVING WITH HIV**
ARE RECEIVING ART

76,000
**AIDS-RELATED
DEATHS**
IN CHILDREN (0-4 YEARS)

Sources: Global AIDS Monitoring 2018 and
UNAIDS 2018 Estimates

Point-of-care early infant diagnosis is a game changer

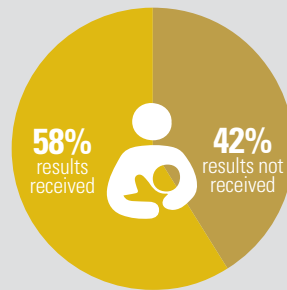
A game changer for paediatric HIV, point-of-care early infant diagnosis (POC EID) is an innovative approach to strengthen EID programs, and improve health outcomes for the youngest and most vulnerable children. POC EID allows test results to be produced at or near the site of patient care. Due to the presence of maternal antibodies in infants and young children up until the age of 18 months, HIV infection in these children can only be conclusively determined through virological testing using nucleic acid testing (NAT) technologies. In many resource-limited settings, NAT technologies are only available in centralized laboratories.

Logistical processes such as transporting samples to laboratories, batching blood samples for testing, and returning results to testing sites often create long delays between the time when the blood sample is collected and when the result is received by the clinic and/or caregiver. Existing data, for example, suggest that over 40 per cent of EID test results are never received by the parent/caregiver,⁷ contributing to high loss to follow-up, poor linkage between testing and treatment, and high infant mortality (see Figure 1). And for those who do receive their test results, the average turnaround time (TAT) between sample collection and the receipt of the results by the caregiver is often lengthy, exceeding 50 days.⁸ Due to long turnaround times for conventional EID, many infants do not receive EID results or get initiated on treatment before peak mortality at 2-3 months of age.

Timely diagnosis of HIV with rapid delivery of results to the caregiver and initiation on treatment is essential for saving the lives of infants living with HIV and ending paediatric AIDS.

Figure 1

Percentage of EID results received and not received by the caregiver



Infants lost to follow-up **before** received results

Poor linkage between testing, treatment, and care

High infant mortality

Source: Based on EGPAF POC EID implementation data from 8 countries and a weighted average of 8 studies: See reference 7.

Diagnosing infants at the point-of-care helps more children access life-saving care

POC EID ensures that infants are tested onsite, and that their caregivers receive their test results quickly – often on the same day or during the same clinic visit. By reducing TAT for test results and speeding up clinical decision making and treatment initiation, POC EID substantially increases ART initiation rates among HIV-positive infants and young children and helps more children access life-saving care.

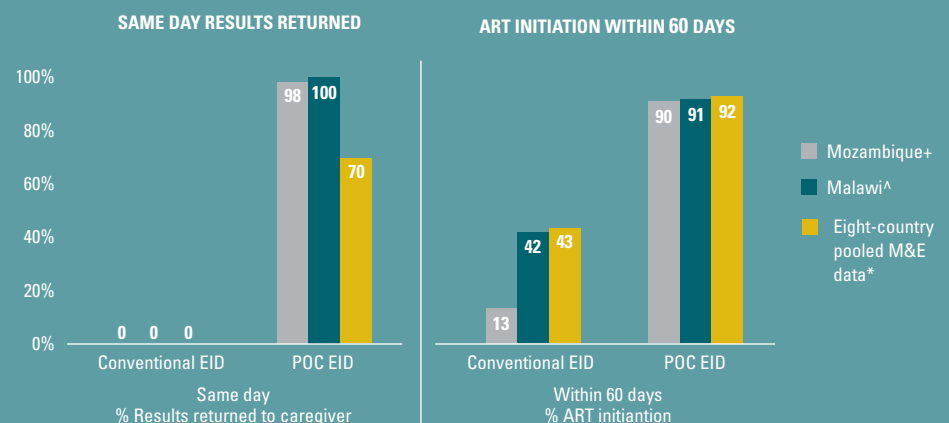
Since 2015, Unitaid has committed over US \$150 million to catalyse the introduction and integration of affordable POC EID technologies into national diagnostic programmes. In collaboration with implementing partners – African Society for Laboratory Medicine (ASLM), Clinton Health Access

Initiative (CHAI), Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), and United Nations Children's Fund (UNICEF) – POC EID is being introduced and scaled up across 15 early adopter countries.⁹

Early pilots and implementation research have already demonstrated striking results. As illustrated in Figure 2 below, in both study settings and as part of routine use across multiple countries, POC EID has been shown to dramatically reduce TAT for test results to a median of zero days and significantly improve ART initiation rates. In Mozambique, POC EID increased the proportion of infants initiating ART within two months by seven-fold.¹⁰ POC EID allows for same day TAT for results returned to caregiver and ART initiation, a game changer for ending paediatric AIDS.

Figure 2

Percentage of HIV test results returned to caregiver and percentage of infants newly diagnosed with HIV initiated on ART, by conventional EID and POC EID (three data sources)



+ Jani, Illesh et al., 'Effect of Point-of-Care Early Infant Diagnosis on Antiretroviral Therapy Initiation and Retention of Patients: A cluster-randomised trial', *AIDS*, May 8, 2018.
 ^ Mwenda, Rauben et al., 'Significant Patient Impact Observed upon Implementation of Point-of-Care Early Infant Diagnosis Technologies in an Observational Study in Malawi', *Clinical Infectious Diseases*, 27 February 2018.
 * EGPAF POC EID implementation data from 8 countries (Cameroon, Côte d'Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Eswatini, Zimbabwe), March 2018.

The technology is ready for scale

POC testing, when integrated into a national laboratory network, is a useful complement to existing centralized laboratory testing, particularly for populations such as infants needing their test results returned quickly.

Over the past two years, the quality of new POC EID technologies has been widely assessed by authorities through technical evaluations. Four POC EID technologies have received CE-IVD (Conformité Européenne in Vitro Diagnostics) marking and two of these have received WHO Prequalification (WHO PQ).¹¹ See Table 1 for additional information.

In addition, the EID Consortium has conducted pooled analyses of the field performance of two POC assays (Aleré™ q HIV-1/2 Detect¹² and Cepheid Xpert® HIV-1 Qual) for early infant diagnosis across 6 countries: Kenya, Malawi, Mozambique, Tanzania, South Africa and Zimbabwe. Both technologies, when operated by a range of health professionals from nurses and laboratory technicians to medical doctors, performed well in the field with high sensitivity and specificity and low internal quality control (IQC) failure rates (4-7 per cent).¹³

In 2016, the WHO conditionally recommended the use of POC EID,⁴ and more recently affirmed the use of POC EID for the confirmation of initial positive results.¹⁴ POC EID diagnostic technologies provide accurate results, are easy to use, and can be operated by non-laboratory personnel across a variety of health settings. The technology is being introduced in fifteen early adopter countries and is ready for scale.

POC EID is cost-competitive

POC EID not only makes sense from a public health and child rights perspective, it also makes sense financially. When comprehensive operational costs are taken into account, POC EID is cost-competitive when compared to conventional EID, due to a high result return rate. Comprehensive costs not only include the cost of delivering EID or the rate of results returned to the caregiver, they also include device service and maintenance as well as efforts to monitor and improve quality.

A preliminary analysis of cost per test result returned within three months shows an estimated cost of USD \$28 to \$49 per conventional EID result returned, and USD \$21 to \$33 per POC EID result returned.¹⁵ Cost per test result is a sound measure of the true value of a diagnostic, as any result not returned cannot impact clinical decision-making. Results not received also contribute to wasted reagents, lost time for clinical staff and caregivers, and unnecessary repeat testing.

Table 2

Cost per test result returned to caregiver within three months

Conventional EID	Point-of-Care EID
USD \$28.00 – 49.00	USD \$21.00 – 33.00

In addition, multi-country costing analysis indicates that POC EID is less expensive than conventional EID testing per HIV-positive infant identified and placed on treatment. For POC EID, the cost per infant initiated on ART was USD \$1,060 compared with USD \$1,205 using conventional EID.¹⁶



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Table 1

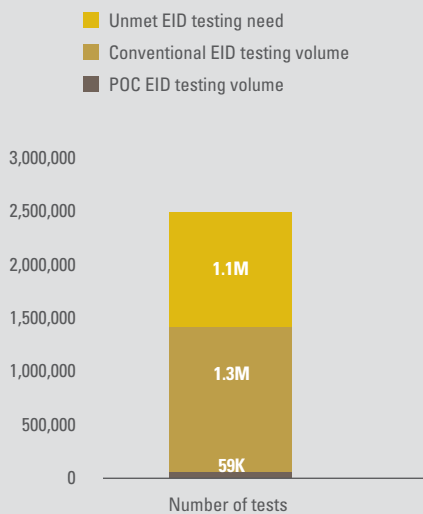
POC EID technologies: Regulatory approval and technical evaluations

Assay	CE-IVD Marking	WHO PQ
Aleré™ q HIV-1/2 Detect	✓	✓
Cepheid Xpert® HIV-1 Qual	✓	✓
Diagnostics for the Real World SAMBA I HIV-1 Qual Test	✓	
Diagnostics for the Real World SAMBA II HIV-1 Qual Whole Blood Test	✓	



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Figure 3
EID testing volumes, 2017



Source: CHAI market intelligence, 2018

Scaling up access to POC EID

Strengthening early infant diagnosis by expanding access to POC EID technologies is a critical strategy for closing the testing and treatment gap for children and ending paediatric AIDS. Less than 5 per cent of EID demand is currently met through POC technologies. In 2017, POC EID testing volumes accounted for only 2.4 per cent of total EID testing need and 4.4 per cent of the total EID tests conducted (Figure 3).¹⁷ Too few HIV-exposed infants have access to POC EID.

To date, the considerable investments made in strengthening conventional EID have not been able to reduce turnaround time to meet the WHO recommendation of results returned within 30 days after sample collection. POC EID technologies address many of the challenges with conventional EID by speeding up result turnaround time, mitigating loss-to-follow up, and expediting treatment initiation for infants in need.

To effectively expand access to testing and to maximize impact, it is crucial that POC EID technologies are strategically placed to complement the existing laboratory network. In addition, as assays for other diseases (e.g., tuberculosis, Hepatitis C virus, and sexually transmitted infections) become available, the same POC platforms can be used to address broader public health needs. Both testing sites and POC technologies should be selected vis-a-vis the specific needs, capacities, and limitations of selected sites, as well as the laboratory-clinic network as a whole.

We can eliminate paediatric AIDS

Bold new approaches and a paradigm shift, such as POC EID, are needed to produce game-changing results and the Super-Fast-Track targets for children. While fewer children are acquiring HIV due to scaled up PMTCT efforts, new infections still occur. For these children, implementation research has clearly demonstrated that POC EID technologies can help children access life-saving care by rapidly identifying HIV-positive infants

and accelerating treatment initiation at an earlier age.

Cost-competitive with conventional EID, POC EID is key to the paradigm shift we need to end paediatric AIDS.

To reduce the mortality associated with paediatric AIDS, EID must be provided to all HIV-exposed infants in a timely manner and be linked to swift treatment initiation for HIV-positive infants. In those instances, where conventional EID is not able to meet the unique and urgent diagnostic needs of HIV-exposed infants, POC EID, an

innovation ready for scale up, must be part of the solution.

We have the evidence. We have the technology. We have the practical “know-how” from implementation experience across more than 15 countries. The time to invest and scale up is now.

With increased investment, accelerated scale-up, and the strategic integration of POC EID technologies into national diagnostics systems, we can achieve an AIDS-free generation.

For every child, we can end AIDS.

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- The Alera™ q HIV-1/2 Detect will be rebranded as the Abbott m-Pima™ q HIV-1/2 Detect beginning in late 2018. Future editions of this brief will be updated to reflect the new product name once the rebranding is complete.
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