Increasing Access and Coverage of HIV-1 Early Infant Diagnosis through Use of Point of Care Testing

**COUNTRY:** Mozambique

**IMPLEMENTING PARTNER:** EGPAF, CHASS, ICAP, FGH, ARIEL, Vanderbilt, MoH, CHAI, UNICEF

Mozambique has demonstrated the feasibility and impact of the use of point of care testing (POCT) for early infant diagnosis (EID), resulting in significantly reduced turnaround times and increased rates of antiretroviral therapy (ART) initiation. Strong partnership between the Ministry of Health (MoH) and other stakeholders was key to successful implementation. The success in Mozambique has been replicated in seven additional countries with partial data analysis showing the cost-effectiveness of initiation of infected infants on ART.

**WHAT WAS THE PROBLEM?**

Access to EID by two months of age remains poor at only about 51% of infants having access to this test globally (Essajee, et al, 2017)). HIV infection in infants is aggressive, with the highest morbidity and mortality occurring in the first few months of life for infants not on treatment (Bourne, et al, 2009). Conventional laboratory testing networks requiring specimen referral can limit access to treatment when not optimized. Delays in the lab-clinic interface and systems supporting EID can result in unacceptably long turnaround times (TAT) for the return of results. This in turn contributes to high attrition rates and delays initiation of infants on life-saving ART. Historically, TAT in Mozambique has been lengthy; one study published in 2011 reports that 75% of HIV-exposed infants received EID test results more than two months after the initial visit (Jani, et al, 2014). In Mozambique, as in other low-resource settings, errors in sample collection, transport, storage and processing, and cumbersome result return systems ensure that some families never receive the results of infant HIV diagnostic tests.

**WHAT IS THE SOLUTION?**

In Mozambique, the National Health Institute (NHI) together with UNITAID, Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), Clinton Health Access Initiative (CHAI) and UNICEF implemented a project in 16 primary health facilities. This project compared standard of care (SOC) testing (conventional HIV diagnostic testing practices) to point
of care (POC) EID testing. In 8 of the facilities providing SOC testing, 1876 infants were enrolled, while another 2034 received POC testing. The primary outcome monitored was the proportion of infants initiating ART within 60 days from specimen collection. POC EID sites demonstrated improved access, reduced TAT for release of results and earlier initiation on ART. This evaluation led to a decision by the Mozambican MoH to nationally scale up EID POC with the support of UNITAID and PEPFAR. Immediately below is a stepwise approach to the ongoing national scale up process for EID POC in Mozambique.

**Involvement of Technical Working Group**

The MoH prevention of mother-to-child transmission (PMTCT) technical working group (TWG) led the implementation of POC EID with the goal of coordinating, planning, and monitoring implementation progress. The membership of the TWG included MoH technical staff from both PMTCT and laboratory programs, NHI, and key stakeholders (Centers for Disease Control, UNICEF, EGPAF, CHAI, and Partnership for Supply Management). The TWG, led by the MoH, played several key roles, including:

- Developed an *Implementation Manual for POC EID for HIV in Mozambique*.
- Coordinated and supported the integration of POC EID into the laboratory diagnostic and clinical services network.
- Identified successes and challenges, and leveraged synergies among members to address those challenges.
- Provided tailored mentorship and interventions in order to expedite implementation.
- Gathered and analyzed evidence of best practices and innovations related to POC for EID implementation in order to facilitate knowledge sharing between global, regional and in-country stakeholders.
- Increased visibility of implementation through work plans of key stakeholders to ensure efficiencies and reduce duplications.

**Site Selection**

POC for EID is most impactful when strategically placed within a tiered laboratory network. In order to generate a site selection matrix, performance data for clinical sites was tabulated. Site level data included the volume of pregnant women receiving antenatal care, EID testing volumes, the distance between the conventional testing laboratory and the clinical site, historical TAT to clinical sites, availability of HIV services, and locations of bottlenecks within the sample transport network.
Site selection for EID POC placement was then prioritized based on four weighted criteria:

- Average weekly volume of EID tests performed at the site (50%),
- Number of HIV+ pregnant women seen at site in the past year (20%),
- Long TAT for results delivery in weeks (20%), and
- Limited access to conventional laboratory testing and long distance to laboratory (10%).

Product Selection and Site Assessment

The product selected for POC EID testing was the Alere q HIV-1/2 Detect, which has been prequalified according to World Health Organization (WHO) standards. The Alere q HIV-1/2 Detect uses whole blood for the test. Some of the factors considered for product selection included staffing for testing and the use of results at site, infrastructure, and access to site, electricity and waste management. The POC instrument were deployed in Child at Risk Clinics in Primary Health Centers (PHC) where maternal child health nurses were trained to use them.

A site assessment tool was developed and used for assessment to ascertain site readiness prior to deployment. This was critical to ensure all the required components needed to provide a complete package of services were available. Some selected sites were refurbished or upgraded for adequate working environment, storage, electricity and water. Standard operating procedures (SOP) and job aids were developed and distributed to sites for instrument operation and performing tests. The work flow in the testing facility was mapped out to ensure a streamlined and efficient output.

Installation of POC and Training

NHI and other stakeholders within the TWG coordinated with site management staff, and agreed on dates for instrument installation and training. The installation and verification of each POC EID testing device was performed by the manufacturer onsite. The nurses at the site were trained via a trainer-of-trainers (TOT) model on the SOPs for operating the device and using it to perform EID. The training covered technology introduction, sample collection, performing tests, testing algorithm, quality control and interpretation of results, biosafety and waste management, and monitoring of the new testing site. The nurses trained were certified competent (i.e. the ability to perform tests unsupervised). After the initial training, the nurses were challenged with diagnosing 10 specimens with the correct corresponding known results. Certificates were issued to nurses who successfully completed the competency training. All certificates are valid for 12 months after training completion.
PEPFAR SOLUTIONS
PLATFORM (BETA)

There were also TOTs at the provincial level to train individuals as Provincial Focal Points. Some of the responsibilities included providing technical support to POC EID sites, ensuring certified operators at sites, refresher trainings, monitoring quality, replacing malfunction POC device with back up, stock management and connectivity of POC sites.

Quality Control and Site Supportive Supervision Monitoring

All the POC sites were routinely monitored through site supportive supervision to ensure accurate test results. The site supportive visits were provided by the Provincial Focal Points. Site supportive visit to PHC were conducted monthly for the first 6 months and quarterly thereafter using a standardize supervision checklist. These visits allowed for review of site performance and documents (Internal quality control logs, inventory logs, instrument logs, adherence to SOPs or Job aids) and mentorship was provided during these visits. Although site visits were scheduled monthly and/or quarterly, additional visits were scheduled if sites notified of problems.

Furthermore, POC EID testing sites are recommended to enroll into external quality assessment (EQA) where they will receive proficiency testing panels to monitor the quality of testing. Additionally, the WHO/CDC Checklist Stepwise Process for Improving the Quality of HIV-related Point-of-Care Testing should be used to routinely assess sites.

Equipment Maintenance

Prior to implementation, NHI had negotiated a contract to support equipment repair for the project. Site staff and partners reported instrument breakdown to NHI, who then notified the manufacturer for repairs. There were backup POC instruments held at the provincial health office. If instrument breakdown was unresolved within 1 to 2 weeks, the backup instrument at the provincial health office was used to substitute the malfunctioning instrument pending its repair.

The solution reported above has also been implemented (with minor adjustments based on country context) in seven 7 additional countries Cameroon, Ethiopia, Kenya, Malawi, Uganda, Tanzania and Zimbabwe.

WHAT WAS THE IMPACT?

In the original evaluation in Mozambique, there were significant advantages associated with POC EID compared to the SOC testing (Jani, et al, 2017). There were 2,034 and 1,876 infants enrolled in the POC and SOC arms, respectively. This information is further summarized in the below Figure 1.
Figure 1: Clinical cascade for POC EID vs. SOC testing

Additionally:

- All POC EID results were available at the PHC sites while 19% of results obtained through SOC were never returned to the sites.
- The median TAT from sample collection to results received (in days) was 1 (0-1) day for POC compared to 125 (84-185) days in the SOC arm.
- 99.5% of results obtained with POC testing were given to infant parents or guardians compared to 65% with the SOC, with only 7.2% and 47.2% of SOC results returned to infant parents or guardians within 2 months and 6 months of testing, respectively.
- 89.7% of infants who tested positive with POC EID were initiated on ART within 2 months of sample collection compared to only 12.8% on ART in the SOC arm.
- The median TAT from sample collection to ART initiation (in days) for identified infected infants was 1 (0-1) day for POC EID and 127 (44-154) days for SOC.
- The proportion of HIV-positive infants' retention rate after 3 months of ART initiation was higher in the POC arm (61.6%) compared to 42.9% in the SOC arm.

As the solution has been expanded to seven other countries, we present here the impact in two countries, Malawi and Zimbabwe.

Malawi

Malawi enrolled 963 infants in the SOC and 789 in the POC arm (Mwenda, et al, 2018).

- The median TAT from sample collection to results received (in days) was 1 (0-1) day for POC EID compared to 56 (30-81) days for SOC.
The median TAT from sample collection to ART initiation (in days) was 1 (0-1) day for POC EID and 38 (30-54) days for SOC.

The proportion of infants who tested positive initiating treatment within 2 months was 91.1% in the POC EID compared to 41.9% in the SOC arm.

Zimbabwe

In Zimbabwe, 277 infants were tested using POC for EID with a 4.3% (12) positivity rate (Ndlovu, et al, 2018).

- All the POC EID results were available within 90 minutes.
- The median TAT from specimen collection to ART initiation (in days) was 1.5 (0-3) days.
- 10 (83.3%) of the 12 infants who tested positive initiated ART within 1 (0-1) day.

HOW DOES IT WORK?

INDIVIDUAL LEVEL

The target population is all infants who may have been exposed to HIV. Previously, SOC testing for EID has mostly been carried out in centralized laboratory facilities. This setting requires robust and reliable systems, for example, sample referral and results network for transportation of collected specimens to testing labs and results back to clients. A lack of an optimal and efficient system in place has most often resulted in:

- Limited access to EID in clinical settings outside of ANCs offering PMTCT services.
- Long TAT from specimen collection to receipt of results.
- High attrition rate as infant parents or guardian do not return for results.
- Unacceptable inequitable access of HIV infected infants to timely ART.

POC EID improves access, reduces TAT and allows early initiation on ART, thus preventing infant mortality due to HIV.

SYSTEMS AND SERVICES LEVEL

For SOC testing, a dried blood spot (DBS) sample is collected, prepared and sent to a centralized laboratory for analysis. The sample referral network for transporting DBS specimen to centralized laboratories are suboptimal, and typically it takes more than 2 months to return results (Jani, et al, 2014). Weak laboratory-clinical communications contribute to loss and/or delay in results returned. The use of POC at facilities does not require specimens or results to be transported, thus circumventing the weak specimen referral/result return system. The supply chain for DBS collection materials, packaging and transportation can be challenging with stockouts leading to disruption of services. With POC, whole blood is collected directly into cartridges for testing, bypassing the need for multiple consumables. The availability of POC EID results within an hour
eliminated the need for mothers to return for results, decreasing loss to follow-up and increasing opportunities for successful enrollment into ART care.

LOCAL ENVIRONMENT
Provincial governments have been engaged since the start of planning, and through determination of final allocation of POC EID instruments based on site recommendations. Through the provincial government, Provincial Focal Points were identified, trained and responsible for engaging with the PHC to provide mentorship. Site leadership was also actively involved in site enrolment and training, as well as routine monitoring and evaluation.

NATIONAL ENVIRONMENT
The MoH has been instrumental in the introduction and implementation of POC EID. Through NHI, early evaluations (including field evaluations) were performed. These early evaluation results contributed to both the WHO considerations on POC EID and the evaluations results for WHO pre-qualification. The MoH endorsed the use of the innovative technology, and has facilitated collaboration between the Mozambican NHI, MOH PMTCT TWG and PMTCT program to provide governance for the scale up process, and to oversee procurement. The MoH, with support from PEPFAR, developed a POC Implementation Guideline, following the WHO prequalification.

SCALABILITY
Following the successful evaluation as described above, the Mozambican MoH launched a national scale up of EID POC. PEPFAR Mozambique has invested in the rollout of POC EID to priority sites located in Zambezia Province. Site selection and assessment have already been completed with approval of 30 POC instruments. As mentioned earlier, POC EID scale up is being implemented in 7 other countries (with minor adjustment based on country context) including Cameroon, Ethiopia, Kenya, Malawi, Uganda, Tanzania and Zimbabwe. Most of these implementations are not within PEPFAR supported sites. In COP18, many PEPFAR country programs have included use of POC for EID as an innovative strategy to support accelerated scale up in testing. Thoughtful placement of POC EID technologies within the national system and healthcare facilities will allow increased access to test infants presenting at traditional PMTCT entry points, as well as additional healthcare facility entry points, such as maternity, nutrition, and inpatient wards.

MANAGEMENT & OVERSIGHT
PEPFAR TEAM INVOLVEMENT:
PEPFAR Mozambique has been actively involved in the TWG, and working together with UNITAID and partners in developing SOPs, logs and guiding implementation of POC for EID. Furthermore, PEPFAR HQ CDC ILB has collaborated with the Mozambique country team, MoH, and stakeholders to provide quality oversight through providing and
building capacity to support and monitor the quality of POC EID testing sites. The USAID PSM team has been providing support in supply chain management, and developing key performance indicator to monitor instrument performance. With the different parties (manufacturers and stakeholders) involved in setting up POC EID sites, proposed indicators to monitor the various phases of implementation are summarized in Table 1.

IMPLEMENTING PARTNER:
UNITAID provided the POC instruments, cartridges and other consumables through their CHAI and EGPAF partners. This also included funding support for personnel and other needs. Nurses at selected sites were trained on operating the instrument, collecting specimens, performing and interpreting test results, and providing results to infant guardians. NHI provided oversight and support to clinic sites with the POC instruments. Tester and instrument performance, site volume, and consumption rate of cartridges were centrally monitored. The POC results were returned the same day for follow up initiation of infected babies on ART. PEPFAR clinical IP’s provided support for site preparedness prior to EID POC placement, and supported provincial health teams in EID POC deployment.

MONITORING:
USAID oversees PSM in procurement. The CDC lab and PMTCT teams lead PEPFAR engagement within the TWG.

COMMUNICATIONS AND FEED-BACK LOOPS:
Regular TWG meetings involving the different stakeholders served as a forum for discussing challenges that were not immediately resolved. The Provincial Focal Point worked closely with the different sites and implementing partners to resolve challenges either remotely or via site support. The site staff and implementing partners communicated problems to the Provincial Focal Point who in turn informed NHI and the TWG.

BUDGET
COST OF INNOVATIVE SOLUTION:
A full cost-effectiveness analysis is underway. However, preliminary analysis of the Mozambique and Malawi implementation indicated POC EID was less expensive compared to conventional laboratory testing. The cost per test results received by caregiver for conventional laboratory test for EID ranged from USD $24-$43 compared to $21-$33 for POC EID. Per COP18 guidance, countries are encouraged to pursue reagent rental for POC EID instruments to avoid incurring costs on procurement. Also the use of existing POC CD4 systems and expertise for training minimized costs of POC EID implementation.
EFFICIENCY MEASURES

Monitoring quality of testing and reagent consumption in real time allowed measures to be taken to resolve gaps and avoid disruption of services.

RESOURCES

- Key Considerations for Introducing New HIV Point-of-Care Diagnostic Technologies in National Health Systems
- HIV Point-of-Care Diagnostics Toolkit
- Improving the Quality of HIV-Related Point of Care Testing: Ensuring the Reliability and Accuracy of Test Results.
  [http://apps.who.int/iris/bitstream/handle/10665/199799/9789241508179_eng.pdf?sequence=1](http://apps.who.int/iris/bitstream/handle/10665/199799/9789241508179_eng.pdf?sequence=1)

REFERENCES


**Table 1**: Proposed Indicators to Monitor the various Phases of Implementation of POC EID

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<th>Product</th>
<th>Programme</th>
<th>Programme Impact</th>
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| Product and supplier performance based on contractual obligations, including:  
• Percentage of time instrument was broken  
• Percentage of out-of-specification test performances during pre- and post-delivery testing  
• Number of on-time deliveries; order lead time | Programme scale-up, including:  
• Number of sites with connectivity  
• Number of sites successfully passing external quality assessment  
• Number of sites with routine supportive supervision or mentoring visits that address POC testing  
• Number of sites with error rates >5%  
• Number of POC devices in use  
• Total number of POC EID tests performed  
• Number of sites trained to perform testing  
• Number of POC EID devices connected  
• Number of health-care workers trained and certified to perform POC testing  
• Number of trained healthcare workers performing POC testing | • Number of patients receiving a POC EID test  
• Number of patients initiated on ART  
• Percent of patients receiving POC EID results and returning for follow-up  
• Average turnaround time between sample collections to results received by patients |