Lebele Mathato with her daughter, Nyakallo, and lay counsellor, Sefoli Mabafokeng at a 6-week check-up in Lesotho. [EGPAF Lesotho]

Elizabeth Glaser Pediatric AIDS Foundation / **Unitaid** Innovation in Global Health

Issue Brief
Point-of-Care Early Infant HIV Diagnosis

Doing more, faster: Results from the routine use of innovative point-of-care technologies for early infant diagnosis in eight sub-Saharan African countries

"Even if they follow PMTCT protocols, mothers still worry about the HIV status of the baby, so to wait a long time for the mother to get the results is really hard," said Sefoli Mabafokeng, a lay counselor in Lesotho. "The machine is doing a fantastic job. It fills the gaps in early infant diagnosis."

In 2015, more than 1.2 million babies were born to mothers living with HIV in 21 countries.[1] While the World Health Organization (WHO) recommends that all HIV-exposed infants receive a virologic test for HIV within two months of birth, only 51% were tested and, of those, only 50% received results, with weeks or months passing before caregivers knew the test outcome. Of those infants who received their results and were dignosed with HIV, only half were placed on treatment (Figure 1).[2,3,4] Without treatment, up to 50% of HIV-infected children will die by their second birthday, with a peak mortality at two to three months of age.[5,6,7]

To improve health and save lives, HIV-infected infants must be diagnosed early and immediately initiated on treatment. Yet, current early infant diagnosis (EID) systems in resource limited countries are challenged at multiple levels of the cascade.
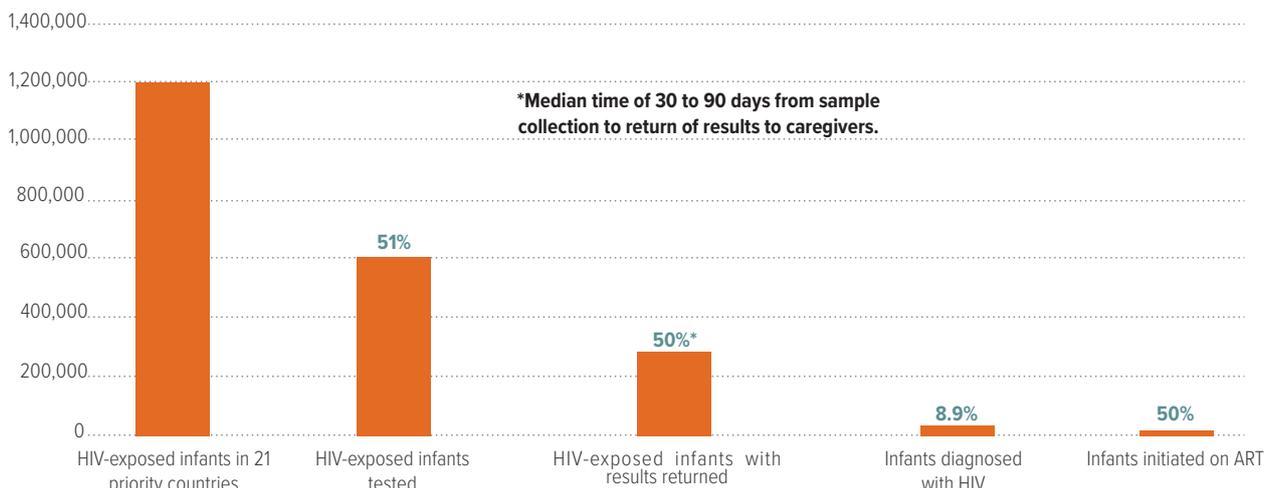

Figure 1. Cascade of EID through initiation of treatment, across 21 priority countries, 2016[1]

New-to-market, point-of-care (POC) EID technology can help address these challenges and ensure HIV-exposed infants are tested on-site, or at nearby sites. POC testing platforms are easy to use in a variety of service delivery settings, and do not require specialized laboratory technicians to operate. This technology allows for a greater number of HIV-infected infants to be rapidly enrolled on lifesaving antiretroviral treatment (ART).

Since 2015, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), through funding and support from Unitaid, has been working to initiate more HIV-infected infants on life-saving treatment earlier and faster by integrating POC EID into the current EID system in nine high-prevalence countries: Cameroon, Côte d'Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Swaziland, Zambia, and Zimbabwe.

> *"Everyone knows that the problem here is the period of time that elapses between collecting and transferring blood samples to laboratories, but also the time it takes to send the test results back to health centers." Key Stakeholder, Cameroon (2016)*

POC EID placement

Working side-by-side with each country's ministry of health and key stakeholders, the project is employing multiple approaches and models to optimize national EID networks according to unique needs, implementation context, and priorities. POC EID placement models aim to increase access to EID testing in underserved areas, and to decrease turnaround time in high-volume and/or decentralized facilities. In eight of the nine project countries, a hub-and-spoke model has been applied to increase both access to EID and decrease turnaround time. The hub-and-spoke model (see Figure 2) places POC platforms in a centrally located facility "hub", with smaller health outpost "spokes" delivering samples for faster diagnoses to these hubs. Countries are also using stand-alone sites, such as high-volume facilities, that only process samples collected at their own facility (see Figure 3).
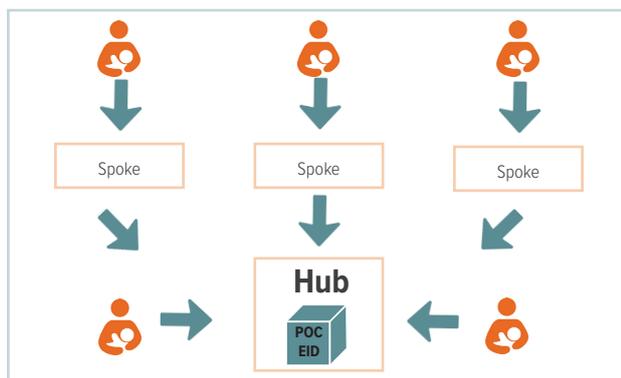

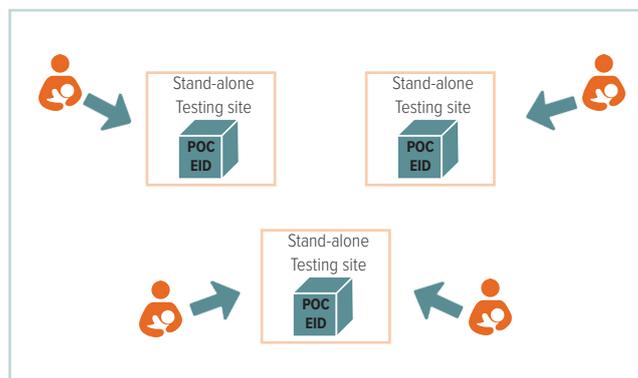Figure 2. Testing samples collected at spoke sites; processing samples at hubs

Figure 3. Stand-alone testing sites (without spokes): process tests collected from clients directly

Evaluating the effect of POC EID: Preliminary results from eight countries

To understand the effect of POC EID, EGPAF is conducting a pre- and post-intervention evaluation comparing data on key service delivery indicators. Pre-intervention, baseline data on infants tested using conventional, laboratory-based EID were collected in 2016 and 2017 from a sub-set of intervention sites, prior to introducing POC technology. Baseline data were compared with data collected during the early implementation of POC EID. Findings from eight intervention countries are summarized below.

Comparison of pre- and post-intervention data

Pre-intervention data on conventional EID testing were collected from patient registers in 92 health facilities, representing a sub-set of project intervention sites across Cameroon, Côte d'Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Swaziland, and Zimbabwe. In each facility, data were collected for a sample of 30 consecutive conventional EID tests on infants born to mothers living with HIV.

To collect post-intervention data, a POC EID test request form was introduced in all but one project country as part of routine service delivery. All key data on POC performance, including the time and date of blood sample collection, specimen processing, return of results to caregiver, and initiation of treatment are collected in one form. Post-intervention data were analyzed and compared to pre-intervention data, stratifying by testing sites and spoke sites.

Cost and cost-effectiveness analyses

The price of diagnostic technologies for EID – both conventional and POC – is a key consideration for national programs, other implementers, and funders. Currently, the individual test price is higher for POC EID than for conventional EID. However, it is important to not only consider the price of the test itself, but also other costs, such as service and maintenance costs, and to factor in the proportion of test results received. The cost per test result received is a closer measure of the true value of a diagnostic, as any results not received by a caregiver cannot impact clinical decision-making, which can be considered a waste of scarce human, financial, and material resources that are used to collect and analyze a blood sample but not deliver a test result.

Cost per result received estimates were derived from The Global Fund to Fight AIDS, Tuberculosis and Malaria's (The Global Fund) total cost of ownership (TCO) calculations for both POC and conventional EID.[8] Additionally, preliminary cost-effectiveness analysis was undertaken utilizing a previously-validated computer modeling tool called Cost Effectiveness of Pediatric AIDS Complications (CEPAC)[9] which is informed by data from Zimbabwe. An incremental cost-effectiveness ratio was calculated for the POC EID testing strategy as compared to conventional EID, and the resulting cost per Year of Life Saved was compared to available benchmarks in the published literature to assess cost-effectiveness.

Preliminary results from eight countries

Key service delivery indicators: pre- and post-intervention

As of October 31, 2017, data have been analyzed across 191 sites, including 62 testing sites and 129 spoke sites. Just over 9,800 POC EID tests have been run on 9,428 infants. Table 1 below shows the pre- and post-intervention results. POC EID resulted in impressive increases in caregivers who receive EID results within 30 days and percentage of HIV-infected infants initiated on HIV treatment.

Table 1. Pre- and post-intervention data: key findings

	Pre-intervention data (conventional) N=92 sites n=2,701 infants tested	Post-intervention data (POC EID) N=191 sites n=9,428 infants tested
Percent of results returned to caregiver within 30 days	18.6%	99.8%
Median turnaround time from blood sample collection to caregiver receipt of results	55 days (range: 3-451)	0 days (range: 0-168)
Median turnaround time from receipt of results to initiation on treatment	0 days (range: 0-75)	0 days (range: 0- 83)
Percent of newly identified HIV-infected infants initiated on treatment	70%	91.8%
Median turnaround time from blood sample collection to ART initiation for infants identified as HIV-infected	49 days (range: 0- 213)	0 days (range: 0-168)

Table 2 presents post-intervention findings disaggregated between testing and spoke sites. Preliminary results are promising, suggesting that a hub-and-spoke model can effectively expand access to EID testing. Almost 100% of results were received by caregivers across both testing and spoke sites, and the median turnaround time between sample collection and return of results to caregiver was comparable.

Table 2: Comparison of testing and spoke sites

	Testing sites (n=56) Infants tested (n=7,009)	Spoke sites (n=128) Infants tested (n=2,419)
Percentage of results returned to caregiver within 30 days	99.6%	99.5%
Median turnaround time from blood sample collection to caregiver receipt of results	0 days (range: 0- 92 days)	3 days (range: 0-168 days)
Median turnaround time from receipt of results to initiation on treatment	0 days (range: 0- 83 days)	0 days (range: 0-30 days)
Percent of newly identified HIV-infected infants initiated on treatment	92.7%	88%

Cost and cost-effectiveness

Using The Global Fund TCO calculations, and pre- and post-intervention data for the proportion of results returned to caregivers, the cost per test result returned are estimated to be similar under the two approaches - approximately $20-$41 for conventional, and $21-$33 USD for POC. Preliminary cost-effectiveness analysis using the CEPAC model, with Zimbabwe as an example, suggests that POC EID is cost effective compared to conventional EID. This model includes the following assumptions: (1) the probability of conventional result return to caregiver is below 96% and the probability of POC result return is above 96%; (2) linkage to ART following a positive POC test is above 80%; (3) POC assays have a sensitivity of at least 85% and a specificity of at least 92%; and (4) the POC assay cost is below $60. Thus, large improvements in the probability of conventional test return would be needed to offset the slightly lower sensitivity of the POC assay.

Conclusions and recommendations based on early routine use of POC EID

Initial data from routine use of POC EID show that introduction of POC technologies into national EID networks is improving patient outcomes and may reduce HIV-related pediatric mortality. Through POC EID, more infants and their caregivers are receiving their results faster: 80% more results reached caregivers within 30 days of blood sample collection when tested using POC EID; and 20% more infants were initiated on treatment as compared to infants identified as HIV-infected through conventional EID. Furthermore, data from early routine use of POC EID show that there is very little difference in key service delivery indicators between testing and spoke sites, making the hub-and-spoke model a viable option to optimize EID.

Initial cost analyses using The Global Fund's TCO estimates suggest that POC and conventional EID are nearly equivalent for cost per result returned to caregiver. As demand for POC EID increases, lower prices may be negotiated and the POC EID cost per result returned may become even more attractive. In addition, the CEPAC pre-study model showed that POC EID improved survival and life expectancy and was cost-effective in Zimbabwe compared to conventional EID, with an incremental cost-effectiveness ratio (ICER) of $750 per year of life saved.

When caregivers and clinicians get test results sooner, they can make patient care decisions faster and save infants' lives. Early implementation results are very encouraging, suggesting that there are significant benefits to incorporating POC into the existing EID network. National programs, funders, and other implementers should consider introducing or expanding the use of POC EID testing.

Follow POC EID results online, in real time

EGPAF developed an interactive data dashboard, using Microsoft Power BI, to summarize and display key POC EID findings across the nine project countries. Project data is regularly uploaded to the dashboard, allowing for real-time monitoring of key metrics and indicators. View the POC EID data dashboard online at:

http://www.pedaids.org/pocdashboard.

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