WELCOME TO HABA NA HABA!

This publication provides a dynamic forum for the routine sharing of technical information and promising practices with our fellow colleagues and extended family of partners and like-minded organizations around the world. Each issue of Haba Na Haba highlights a topic of particular importance to the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF). The topic highlighted in this issue is point-of-care innovations in identifying and treating HIV.

The name of the bulletin, Haba Na Haba (“little by little”), is borrowed from the Swahili proverb haba na haba, hujaza kibaba (“little by little fills the pot”) and was chosen to reflect the often incremental nature of progress in our field. As the experiences described on the following pages demonstrate, the smaller efforts of every one of us are the essential “ingredients” for mounting a strong and united global response to HIV and AIDS.

Feedback is welcomed from all readers, and contributions are accepted from all EGPAF staff. Please send your questions, comments, or content submissions to publications@pedaids.org.
INNOVATIONS ARE TURNING THE TIDE ON CONTROL OF THE HIV EPIDEMIC

Undeniably, the face of the HIV epidemic has changed. At the beginning, there was no treatment and for far too many, that meant progressive illness and death. As antiretroviral treatment (ART) became available, the conversation changed. The global community’s commitment to end AIDS has cut new infections in half. However, the elimination of HIV has yet to be achieved, and as we limit the spread of HIV, those who are unidentified and untreated have become harder and harder to reach. A population particularly difficult to reach with early testing and treatment services: HIV-exposed infants and young children, of whom nearly 500 are infected with HIV each day, around the world. In the last year alone, over 100,000 children lost their lives from AIDS-related illnesses.

In 2018, 1.7 million children were living with HIV, 90% of whom were infected by their HIV-positive mothers through pregnancy, delivery, or breastfeeding. In high-income countries, mother-to-child HIV transmission has been all but eradicated. Unfortunately, a rising tide does
not lift all boats, and global inequalities mean that economic and market forces that improve the HIV epidemic in one part of the globe, leave other populations behind. Children in high HIV burden, low-income regions remain vulnerable, facing daunting and complex obstacles en route to treatment and care.

While the World Health Organization (WHO) recommends that all HIV-exposed infants receive a virological test for HIV within two months of birth, only half had access to early infant HIV diagnostic (EID) screening in 2015, and almost 50% of infants who were tested never received the results. Fifty percent of children perinatally infected with HIV will die by their second birthday. Peak mortality risk among among HIV-infected infants infected in-utero occurs at just six to eight weeks of life.

Caregivers who pursue testing and treatment for their infants assume the logistic and economic challenges of taking them to often-distant service centers for tests, waiting for results to be returned, and returning for results and again for treatment, if it was not initiated on the day the result was received. Centralized laboratory testing requires training of laboratory staff and strong infrastructure (particularly transport and communication mechanisms) to ensure efficiency. But this is not the reality in many high HIV burden settings that leave a mother and child waiting often for several months for a result and access to treatment.

Once within the treatment cascade, another host of barriers present themselves, including drug supply stock-outs and poor interpretation or implementation of national treatment guidelines which recommend more advanced and efficacious regimens for children. In fact, studies suggest, the factor most associated with lack of viral suppression is administration of less efficacious, nevirapine-based pediatric treatment formulations, and yet nevirapine-based regimes are still very much in use among HIV-positive pediatric populations in high HIV-burden settings. Beyond this, caregivers experience psychosocial challenges, and practical difficulties of administering treatment to a child.

In light of the unique constraints, it is unsurprising that children are lagging behind adults in progress toward the United Nations International Programme on HIV/AIDS 95-95-95 targets, or that many suffer from advanced HIV disease. This makes the need for innovative, tailored approaches all the more urgent.

**Point-of-Care Early Infant HIV Diagnostics**

The WHO’s official recommendation is that all HIV-exposed infants receive a virological test four to six weeks post-delivery or as soon as possible thereafter. The turnaround time (TAT) from collecting the specimen to returning the results to the caregiver should never be longer than four weeks, and positive test results should be fast-tracked to enable prompt initiation of ART.

Although the reach of centralized laboratory-based EID screening has improved, integrating point-of-care (POC) testing into, national EID laboratory networks can do even more to support effective diagnoses. New-to-market, POC EID technology can help address the aforementioned challenges by ensuring HIV-exposed infants are tested on-site or in close proximity
to where a child presents for care. The 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 returns a greater number of test results to caregivers and allows infants diagnosed as HIV-positive to be rapidly enrolled on ART, in most cases on the same day they were tested.

Importantly, POC technologies may be used to test for more than EID. Both the Abbott m-PIMA and Cepheid GeneXpert machines can also be used for measuring the HIV viral load in adults and children for routine monitoring of patients and documenting treatment effectiveness. The U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) already supports using POC technologies for monitoring the viral load in pregnant and breastfeeding women, and some countries are beginning to adopt this approach. The Cepheid GeneXpert platform can also test for many other diseases, such as TB and human papillomavirus (HPV) (the causative agent of cervical cancer). Development of additional diagnostic products to test for a wider range of diseases with POC technologies is ongoing, but it has already become clear that these machines are solving many issues that commonly slow diagnostics and access to treatment among many in resource-constrained settings.
Implementing POC EID

Since 2015, through funding and support from Unitaid, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF), the Clinton Health Access Initiative (CHAI), and the United Nations Children's Fund (UNICEF) have accelerated ART initiation and treatment for HIV-infected children by integrating POC EID into national EID systems. EGPAF led this integration in Cameroon, Côte d'Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Eswatini, Zambia, and Zimbabwe. In collaboration with the Ministries of Health (MOHs) in these nine high-prevalence countries, along with key stakeholders, the project took a phased implementation approach at both the global and country levels.

LEVERAGING PROCUREMENT TO IMPROVE THE MARKET FOR POC TECHNOLOGIES

Along with Unitaid, the Global Fund to Fight AIDS, Tuberculosis and Malaria, the U.S. Agency for International Development (USAID), and the U.S. Centers for Disease Control and Prevention (CDC), EGPAF worked to improve the value for money of POC EID and viral load testing and advocated for manufacturers to ensure uninterrupted provision of timely, high-quality EID and viral load testing in countries most in need. This consortium, conceived in 2015, aimed to catalyze demand for and uptake of POC technologies and to ensure sustainability of the market by pooling test volumes across purchasers, sharing market intelligence, providing advanced procurement forecasts to manufacturers, agreeing on procurement principles and negotiation targets, jointly negotiating prices and service and maintenance terms, and coordinating the placement of orders.

EMBEDDING POC EID WITHIN THE HEALTH SYSTEM TO ENSURE MAXIMAL RATIONAL ACCESS TO POC EID

In each country, EGPAF worked with the MOH and technical working groups to create a site network plan that considered existing resources, local HIV burden, patient demand, and site and product characteristics. The identification of potential POC sites was based on country-level analyses of historical site-level data, such as testing volume, positivity rates, TAT (from collecting samples to returning results), and geographic proximity. Sites burdened with the highest volume of EID tests were labeled either standalone testing centers or “hubs.” Both were supplied with their own POC machine to broaden access to EID testing in a phased approach (taking lessons learned from a smaller-run pilot phase to apply to full implementation and expansion across these countries). Standalone sites ran samples for their own clients. Hubs processed samples for not only their own clients but also for smaller, nearby health sites and outposts (known as “spokes”), with lower EID test volumes, sending results back to the spokes using SMS printers. The hub-spoke model allowed samples taken from these smaller sites to receive speedy results from the hubs, thereby alleviating congestion in centralized laboratory networks and ultimately giving results to caregivers faster. This hub-and-spoke system increased the number of health facilities accessing POC EID by over 600%.
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STRIVING FOR SUSTAINABLE POC FUNCTIONING
Continuous work with the consortium enabled manufacturer performance to become an integral component in this project. The consortium created key performance indicators (KPIs) and collected routine data around error rates with machines and the median, range, and interquartile range time for the manufacturer to provide replacements or address errors or issues (both within and outside warranty parameters). Routine monitoring of KPIs ensured immediate problem solving in the field and was used to determine whether the agreed practices, including manufacturer contractual commitments, were achieved or whether corrective actions were needed.

DEVELOPING DATA FOR IMPACT
Monitoring and evaluating POC EID was at the forefront of implementation. EGPAF conducted a pre- and post-intervention evaluation comparing data on key service delivery indicators. The baseline data on infants tested using conventional, laboratory-based EID were collected in 2016 and 2017 from a subset of intervention sites in nine project countries prior to introducing POC technology. The baseline data were then compared with the data collected during the implementation of POC EID in eight countries. The routine project data were collected, cleaned, and reported in real-time through a data dashboard.

MOVING TO SUSTAINABLE SCALABILITY
Throughout the project, but particularly during the transition phase in this last and final year, the team worked closely with the MOHs, implementers, and funders to ensure a seamless transition of the project to the national authorities. Supporting sustainability was the development of a six-module toolkit to sustain the procurement, maintenance, and effectiveness of this technology in resource-limited health systems.
POC EID OUTCOMES

The data from the routine use of POC EID show that the introduction of POC technologies into national EID networks is improving patient outcomes. Through POC EID, more caregivers are receiving their infants’ results faster: almost five times more results reached caregivers within 30 days of blood sample collection when tested using POC EID. More specifically, the percentage of results received by caregivers within 30 days rose from 18.3% using the centralized method to 98.8% through the six-month POC EID pilot phase and to 96.7% during its expansion (Figure 1). The percentage of HIV-infected infants initiated on ART within 60 days of blood sample collection rose from 41.5% with the centralized laboratory EID to 93% with the POC EID (Figure 2). Notably, the difference in key service delivery indicators between the testing and spoke sites is minimal, making the hub-and-spoke model a viable option to optimize POC EID.

Figure 1.
Percentage of caregivers who received an early infant diagnosis

Figure 2.
Number of infants initiated on ART within 60 days of testing

EGPAF procured 259 machines and over 244,000 test kits across nine project countries
Scaled up POC EID technology to over 30% of the total EID market in nine project countries and reduced the overall price of POC products or service level agreements

Tested over 132,000 HIV-exposed infants and identified 4,870 HIV-infected infants
Returned over 98% of test results to caregivers
Initiated 4,551 HIV-infected infants on ART
The median TAT from collecting the blood sample to returning the results to caregivers moved from 55 days via the conventional method to zero days through POC EID. The median TAT from collecting the blood sample to initiating ART for HIV-infected infants decreased from 50 days to zero days with POC EID (Figure 3).

**Figure 3.** TAT for a POC EID cascade, comparing conventional testing to POC

Currently, the individual test price for POC EID is higher than laboratory-based EID. However, it is important to consider not only 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 returned to the caregiver. The cost per test result received is a closer measure of the true value of a diagnostic test. Any result not received by a caregiver cannot affect clinical decision making, which can be considered a waste of the scarce human, financial, and material resources used to collect and analyze a blood sample but not deliver a test result.

Assessing the cost per test received by caregivers places POC EID in a more cost-effective category than traditional testing approaches. Estimated expenses per test result returned within 30 days are $131.02 for the centralized method compared to just $37.89 for POC EID at current throughput (and $27.24 at optimal throughput; Figure 4). Meanwhile, estimated costs per result returned in three months are $38.89 for the conventional method versus $37.51 for POC EID at current throughput (and $26.97 at optimal throughput). As demand for POC EID increases, lower prices may be negotiated, and the POC EID cost per result returned may become even more favorable.

**Figure 4.**
Estimated total expenses per test result returned to caregivers within 30 days

When caregivers and clinicians receive test results sooner, they can make patient care decisions faster and save infants’ lives. There are significant clinical and cost-effectiveness benefits of incorporating POC into the existing EID network. National programs, funders, and other implementers should consider introducing or expanding the use of POC EID testing.
Advocacy for Transition and Sustainability

AUTHORS
TAMAR GABELNICK (PPA@PEDAIDS.ORG)

Innovations are often funded for demonstration and small-scale implementation, but sustainable, widespread access and impact require political will and financial support. Significant advocacy secures the latter. Thus, one of the central goals of EGPAF’s POC EID project was to ensure the sustainability of this innovative technology by transitioning its management and financing to the national authorities. In the countries still relying on external funding sources for EID, the transition meant working with both the national authorities and donors to identify new sources of funding by the end of EGPAF’s Unitaid grant (July 2019).

The path to transition was not always smooth, but it has ultimately proven successful in almost all project countries. The process of building support among stakeholders involved hurdles often seen with the introduction of innovative measures that disrupt the status quo. Some were wary of investing in new POC equipment because they have seen previous diagnostic tools that were scaled up to subsequently go underused. Ensuring a successful path to transition requires obtaining critical and detailed data on the impact and cost of POC EID, working with stakeholders to coordinate leadership, advocating for lab systems to be more efficient, and amplifying the voices of those who are most affected—caregivers of HIV-exposed infants and the health care workers who take care of them.

THE DATA COME FIRST
To show donors and other stakeholders that the innovation was effective, feasible, and affordable, it was necessary to present clear, detailed data on patient outcomes, health system and caregiver acceptability, programmatic inputs, and comprehensive costs. The POC EID team at EGPAF worked closely with Unitaid, and fellow implementing partners CHAI and UNICEF, to present strong evidence to countries, donors, and policymakers on POC EID’s public health benefits and cost-effectiveness as well as to advocate for political and financial support. Scientific evidence was also presented at global conferences and in peer-reviewed journals. Still, the data alone were not sufficient to ensure the successful transition and scale of this important technology.

SUSTAINABILITY REQUIRES COUNTRY LEADERSHIP AND COORDINATION
Most national governments were supportive from the outset, and support grew stronger once results became visible. In some cases, however, a lack of alignment and coordination existed between the clinical units and lab units. For example, challenges in identifying a governmental unit to take ownership of the POC EID implementation delayed the development of plans for full integration of POC EID into the national lab network. Coordinating and developing
a system of shared responsibility took time and deliberate planning. The work of governmental units and other key stakeholders is paying off, with many countries developing both a national plan for POC integration into EID systems and a clear system of shared leadership.

**ADVOCATING FOR SYSTEM EFFICIENCIES**

None of the key stakeholders contested that getting HIV test results three to four months earlier than the standard of care could save the lives of HIV-positive infants and bring great psychological relief to the parents of HIV-negative infants. Yet these public health benefits could not be divorced from the reality of the limited budgets of stakeholders. Consequently, our analyses demonstrated the efficiencies that could be gained by using POC EID. For example, the cost of the test results returned for POC EID was lower than that of the conventional method—a more meaningful metric of efficiency than the price tag of the test cartridge itself. In some countries, POC EID platforms were also supported to do more than just EID testing. Where a single platform can perform EID, HIV viral load, and TB testing, improved efficiencies can be realized. In most countries, donors required additional lab network analyses to demonstrate that the maximum use would be made of existing equipment capable of performing POC EID.

**AMPLIFYING THE VOICES OF CAREGIVERS AND HEALTH CARE WORKERS**

Caregivers of HIV-exposed infants and health workers are perhaps the most important stakeholders. The team worked with civil society groups, nationally and globally, to supplement advocacy messages. EGPAF also worked to ensure that the personal testimonies of caregivers and health care workers who benefited from the POC tests were highlighted in global fora.

**SUCCESS AND CONTINUED UNCERTAINTY**

Over time, the positive data have had a transformative effect. The PEPFAR guidance to countries for their 2018 and 2019 operational plans provided increasingly strong support for POC EID; guidelines from the PEPFAR 19 Country Operational Plans (COP) unequivocally stated that “PEPFAR programs should continue to use POC to support EID scale-up.” Widespread support for POC EID was also demonstrated at a high level meeting convened by the Vatican in December 2018, where donors committed to providing support for POC EID, manufacturers committed to staying in the market and working on better pricing systems, and other stakeholders committed to building demand for the system within the country.

**NEXT**

As of June 2019, all but two of the EGPAF POC EID project countries had a clear path to financial transition to the MOHs from EGPAF implementation in place, while national and global stakeholders closely collaborated in the remaining countries to find solutions. Given the enthusiasm of national authorities for POC EID, the parents, health care workers, and others that benefit from this new technology should be able to count on its availability for the foreseeable future.
Opportunities for strategic advocacy continue, to confront key challenges ahead, including

1. The price of POC EID is still greater than conventional EID. With flat-lined funding, every cent counts. We call on the manufacturers of POC EID to further reduce the price of POC EID and for donors to continue funding this critical technology as we move ever closer to a truly sustainable price.

2. More efficiencies can be gained. In particular, where the country policy or practice stands in the way of using POC platforms to test across multiple disease areas, all stakeholders should move to integrate testing.

3. Where the lack of clear coordination among governmental agencies, donors, and implementing partners or MOH-supported EID networks is a barrier to scaling up, relevant governmental bodies should move to agree on, take ownership of, and finalize plans to avoid service disruption. Implementation partners should work together to support this process.

4. There should be no unnecessary and repetitive field studies ahead of implementation. Where products have already gone through the WHO prequalification (PQ) process, further country-by-country field studies may delay access to lifesaving diagnostics and add unnecessary expense. Countries should eliminate the requirement for these types of studies where WHO PQ approval is already in place or robust information already exists from field studies in similar contexts.
Moving to the Second 95:
Identifying Children is Only the First Step

AUTHORS
JENNIFER COHN (JCOHN@PEDIAIDS.ORG)

With Unitaid support, EGPAF has helped to realize success in using POC EID to diagnose infants with HIV and link them to care. However, diagnosis is only the first of the 95-95-95 targets. In order to ensure we give children the best chance of survival, we must provide children and health systems with sustainable access to the best available treatments to ensure viral suppression. Pediatric drug development suffers from a lack of financial incentive for manufacturers. The development of pediatric formulations of important medicines for HIV and TB often lags 8-10 years behind that of adult formulations. Once available, child-friendly formulations are often more expensive and are not adopted quickly.

Currently, for younger HIV-positive children in EGPAF-supported countries, we see a mix of Nevirapine (NVP) and Lopinavir-Ritonavir (LPV/r)-based regimens used as first-line therapies. Neither of these treatments is ideal. Clinical trials have demonstrated that the use of LPV/r and Dolutegravir (DTG)-based regimens save more lives and these regimens are better tolerated in children. Unfortunately, the presently available syrup is extremely unpalatable and requires a cold chain. For these reasons, many countries continue to provide the inferior NVP.

New solid formulations of Lopinavir and Ritonavir, including two-in-one pellets and granules (2-in-1 is Lpv/r), have tentative approval of the U.S. Federal Drug Administration and a four-one granule (Abacavir-Lamivudine-Lpv/r) is expected to be approved in early 2020. Moreover, the WHO now recommends DTG as the preferred first-line therapy where appropriate formulations are available and supports the use of the adult 50mg tablet (already available from generic suppliers) for children weighing at least 20kg. The WHO recommends use of LPV/r as a bridge until the 20kg weight band is reached in a child. By mid-to-late 2020, we expect that a 10mg scored dispersible DTG tablet will be available and approved for use in children.
weighing less than 20kg. The entry of dispersible DTG into the market will offer an affordable, child-friendly treatment option that is demonstrably superior to other first-line HIV treatments in adults and adolescents.

This rapid succession of improved formulations and treatments for children living with HIV offers opportunities to ensure our patients have more effective and more tolerable treatment, in addition to introducing operational and supply risks and complexities. There must be even greater resolve to secure the political will, technical guidance, operational support, and resources to take advantage of these improved treatments.

EGPAF will work alongside partners to improve pediatric drug development and delivery. In order to ensure that children living with HIV have access to the best available products, EGPAF will fast-track patient access to quality pediatric antiretrovirals, ensuring that children living with HIV receive improved medicines as soon as possible. EGPAF has identified a number of potential barriers to the rapid adoption of the new pediatric HIV medicines that the organization and its partners will address.

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<tr>
<th>BARRIER</th>
<th>EGPAF ACTION</th>
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<tr>
<td>Delays in uptake and transition to newer formulations</td>
<td>Work with national technical working groups, quantification groups, and within the PEPFAR COP process to ensure transition plans are in place early and that their implementation is supported. Build improved pharmacovigilance systems to support a more rapid transition with a “safety net.”</td>
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<td>Risk of unstable supply and stock-outs during the transition</td>
<td>Work with countries to create transition plans, identify current stock supplies, and flag countries that may have a slower transition or supply issues requiring a continued supply of older formulations until the supply of newer formulations is adequate. Work at the facility level to ensure a strong “last-mile” supply chain for pediatric antiretroviral medications (ARVs).</td>
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<td>Supply-demand mismatch: As newer formulations enter the market, supply capacity may be lower than the demand</td>
<td>Work as partners with the technical working groups, donors, and manufacturers to create a coordinated transition plan that recognizes supply constraints.</td>
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<td>High prices lead to significant opportunity costs</td>
<td>Advocate for fair and sustainable pricing of pediatric ARVs.</td>
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<td>The complexity of health worker and patient training as demonstrated by the mixed uptake results so far</td>
<td>Create and adapt comprehensive tools for clinicians and patients and introduce these at the facility level with intensive training, monitoring, and mentorship.</td>
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POC EID IN ACTION

Evelyn Nkomo is a 36-year-old mother of two, living in Victoria Falls, Zimbabwe. Every day she is reminded of her HIV-positive status when she takes her ARV medication. In 2010—while pregnant with her oldest—Evelyn discovered her status. She enrolled in the prevention of mother-to-child HIV transmission (PMTCT) program at Victoria Falls Hospital and prayed that her child would be born healthy and free of HIV.

Once Akash was born, she kept a close eye on her baby boy, continuing to adhere to their PMTCT treatments as she breastfed him. At six weeks, she took him to the hospital. He was tested for HIV using the centralized, laboratory-based dried blood spot (DBS) testing—the only method available at the time. A health worker took Akash’s blood sample and deposited it on a special filter card to dry. A courier service containing the card was subsequently sent to Harare—900 km (559 miles) away. In 2010, the average TAT for a DBS test was 30 to 90 days.

Evelyn waited anxiously for months to hear news about her son’s HIV status. Finally, the results came back: he tested negative. Yet, this relief was short-lived; twice more, she took Akash to have blood collected and sent out to Harare. At 24 months old (breastfeeding cessation), the boy was definitively declared HIV-free.

Seven years later, Evelyn holds her youngest: a wiggly seven-month-old boy named Anold. Through the partnership between Unitaid and EGPAF, POC EID technology was available to Evelyn. When Anold was six weeks old, she took him to be tested for HIV, just as she had with Akash. This time, however, the health care worker could immediately analyze the blood sample through an innovative desktop POC EID machine stationed in the facility itself. Anold was tested at the Victoria Falls Hospital in the morning, and in the afternoon, she received the result: Anold had tested negative for HIV. “I feel very happy because I [learned] the results of my [child’s health] in a short frame of time. I’ve talked to other[s] about this technology, and the people are accepting it.”
Like Evelyn, Nolwazi is an HIV-positive mother with an infant in the same district. She attended the Chinotimba Health Center in Victoria Falls for her antenatal care, delivery, and postnatal care. The health center is smaller than the hospital and does not have its own POC EID machine. The center is a spoke of the Victoria Falls Hospital hub.

A mother of five, Nolwazi has also spent fretful, “scary” months waiting for HIV test results. Thankfully, she received her five-month-old son’s results within a day. “Before, we would wait up to six months,” observes Sister Sheila Rudzuna, the nurse in charge at Chinotimba. “[Now] we give the test results to the mother within 24 hours of collecting the sample. [With] turn-around time being 24 hours, it is easier for us to start children on ARVs right away,” she adds. Rudzuna notes that this has not yet been necessary: “Since September [2017], we have had around 26 samples and all [of] those have come back negative. We are still monitoring those babies for up to two years.”

Today, Evelyn and Nolwazi sleep easier knowing early on that their babies have tested negative for HIV. Furthermore, they can be certain that they will continue to receive speedy test results for future postnatal visits. Evelyn is grateful for the support that she receives at Victoria Falls Hospital. Fittingly, her vision for the future involves things she can impart to her son and things he can, in turn, do for others: “I will teach Anold that there is HIV out there, so that he knows how to conduct himself, [and] so that he will also tell his friends how to conduct themselves … I want him to be a doctor so that he can help mothers and other patients like me.”
IMPLEMENTATION OF POC EID IN CÔTE D’IVOIRE

AUTHORS
PATRICIA FASSINO\U{00A0}(PFASSINOU@PEDAIDS.ORG)

When the POC EID project was launched, Côte d’Ivoire (CDI) was in the midst of a crisis: only 50% of HIV-exposed infants were receiving a virological test within their first two months of life, an issue exacerbated by extended TAT, which only further protracted treatment. The 15- to 90-day TAT—from blood sample collection to the return of results—was mainly due to the limited availability of DBS testing in only seven conventional laboratories, most of which were located in Abidjan.
NATIONAL SCALING UP OF POC EID

LEADERSHIP AND GOVERNANCE
EGPAF implemented POC EID in close collaboration with the leadership from the MOHs. The MOH in each supported country collaborated with EGPAF in all phases of project implementation. Ministry staff members worked with EGPAF on site selection and assessment of readiness for implementation and training of site-level staff to implement this project. The project relied on the national sample transportation systems to move samples from spokes to hubs and back. The POC EID data, achievements, and challenges were shared during programmatic and laboratory technical working group meetings and EGPAF and civil society meetings.

SITE SELECTION
With the MOH, EGPAF considered EID demand and access to timely laboratory-based EID testing and whether a POC product could meet multiple diagnostic needs for each supported facility (e.g., integrating EID testing with TB and HIV viral load testing).

PRODUCT SELECTION
We first examined sites with existing POC technologies to see if the integration of new testing needs with already-existing POC platforms was possible. If no platform existed at a site with a demonstrated need, the site’s infrastructure and human resources capacities, as well as any additional testing needs, were taken into account when determining what product may be the best fit for that site.
CREATION OF AN INTEGRATED POC EID NETWORK

We built a hub-and-spoke network to increase access to POC molecular testing. These hub-and-spoke networks may leverage existing sample transportation (such as riders for health). It proved important to consider the sample stability for storage and transport and the frequency of sample pick up as well as whether good bi-directional communication exists between the hubs and spokes.

SITE CAPACITY ASSESSMENTS

These were important to conduct pre-implementation to identify the infrastructure upgrades and training needs, as well as the health worker cadres who would be using POC technologies.

PROGRESSIVE AND PHASED SITE ENROLLMENT

On-site training is critical to ensure that interventions are used and implemented. A progressive, monitored, and phased enrollment allows for the implementation plan to be adjusted based on the early lessons learned.

REGULAR SITE MONITORING

Frequent site visits were held early in the implementation, with more spaced routine visits occurring throughout the project. These visits allowed staff support and troubleshooting as well as staff retraining when turnover was an issue. Site monitoring and mentorship support sustainable quality implementation and can be integrated into other site-monitoring visits.

ONGOING SUPPLY MONITORING

A supply chain for molecular diagnostic products may need to be built or strengthened to support rolling out the POC molecular technologies.
In CDI, POC EID implementation was launched in 2015 under the sponsorship of the country’s first lady, Dominique Ouattara, Joint United Nations Programme on HIV and AIDS (UNAIDS) special ambassador for PMTCT and the promotion of pediatric HIV treatment. While EGPAF was leading this innovative initiative alongside the Ministry of Public Health and Hygiene (MSHP), four technical implementing partners were involved in the project: 85 sites were managed by EGPAF, while the Ariel Foundation (EGPAF’s affiliate) managed 10 sites, the International Center for AIDS Care and Treatment Programs managed 17, and the Global Fund supported 16.

IMPLEMENTATION

The POC EID project took a progressive implementation approach in CDI that consisted of four phases: preparation, pilot, implementation, and transition. The preparation phase involved stakeholder identification and engagement. During this time, a site-needs assessment was conducted with enrollment preference given to spaces that demonstrated high and unmet PMTCT service needs (the antenatal care visits and volume of activities were taken into account), appropriate infrastructure (particularly the space available to display a platform), and human resources capacity to handle POC EID services. Site selection (designating higher-volume facilities as standalone facilities or hubs and mapping smaller nearby spokes) was followed by a baseline assessment to evaluate the readiness for POC EID platform placement. The preparation phase also involved planning for the implementation stage by developing tools and systems for POC EID data collection. Platforms, accessories, and other consumables were procured and delivered during this time, while facilities were upgraded to be ready for service initiation.

During the pilot phase, 13 health facilities implemented the POC EID testing platforms to evaluate the operationalization of systems and procedures and to troubleshoot and address problems, as necessary. This was followed by the implementation phase, during which the project was scaled up and the implementation was extended to all 128 sites within 10 health districts. Finally, the transition phase involved a seamless handover of project activities to the MSHP to ensure sustainability.
RESULTS
Ultimately, a total of 373 health care providers were trained on POC EID, and 70 among them are also platform users. There were 300 monitoring site visits conducted by EGPAF staff, in addition to the provision of remote, web-based coaching and support using the POC EID database. In total, 18 POC EID platforms were deployed to serve 128 health facilities in seven health regions and 10 districts. Of the 18 platforms at hub sites, 14 are operated by non-lab technicians in consultation rooms. At the spokes, a total of 110 SMS printers generate instant test results via SMS technology.

In the project’s final, transitional phase, the activities were handed over to key stakeholders. As such, EGPAF has worked to maintain collaborative ties with the MSHP, national technical working groups, and relevant stakeholders throughout all implementation phases to ensure a smooth transition of POC EID activities and their integration and expansion into the global national system.

The POC EID project led to increased uptake of EID services and positively affected health providers and beneficiaries.

- Before the intervention, only 70% of EID test results were returned to caregivers, whereas, post-intervention, 97% of caregivers received EID test results.
- The median TAT from collecting the blood sample to returning the results to the caregivers decreased from 89 to 0 days.
- The percentage of newly identified HIV-infected infants initiated on treatment dropped from 100% pre-intervention, to 94% post-intervention, but it must be noted that the number of infected infants identified saw a 300% increase, from 5 (pre-intervention) to 200 (post-intervention).
- The median TAT from collecting the blood sample to initiating ART for HIV-infected infants went from an average of 61 days to an average of 0 days.
LINKING MORE WOMEN TO CERVICAL CANCER DIAGNOSES AND TREATMENT:

POC Diagnostics are Addressing Needed HIV Identification and Early Linkage of Treatment Among Children and Prevention of Cervical Cancer Among Women.

AUTHORS
MAFUSI MOKONE (MMOKONE@PEDIAIDS.ORG) AND OLUWASANMI AKINTADE

Lesotho has the second-highest HIV prevalence in the world at 25.6%. At 28%, the prevalence among pregnant women is even higher than the average. In the absence of PMTCT interventions, there would be an estimated 5,882 new pediatric infections each year. The survival of HIV-infected infants depends on early HIV testing, prompt test-result return, and urgent initiation of ART. But like other countries, Lesotho faces challenges in identifying HIV-exposed infants early and swiftly initiating ART among those in need.
Lesotho is also home to one of the highest estimated cervical cancer incidence rates in the world at 52.1/100,000 in 2018. Cervical cancer is the most common cancer in the country and is a leading cause of death among women. This cancer is often caused by a sexually transmitted infection called human papillomavirus (HPV). More than 75% of women living with HIV are estimated to be infected with HPV, which is diagnosed via nucleic acid testing, commonly from a tissue sample collected via pap smear. In Lesotho, these diagnoses are made at centralized laboratories with TAT to clients at around five months.

IMPLEMENTING POC TECHNOLOGY IN LESOTHO

In 2015, EGPAF launched the POC EID project in Lesotho. The project was implemented through a phased approach, scaling up from five platforms in the pilot phase to 29 platforms serving the needs of 160 health facilities by project end in 2019. The MOH and EGPAF jointly determined machine placement and trained health workers on their use in Lesotho health facilities in 2015.

Lesotho also invested in diversifying the use of POC platforms. Makoanyane Military Hospital already had an underused Cepheid platform for TB with technical support and consumables already available. This platform could be and was also used for POC EID. Improved use of underused POC platforms is a win-win for both TB and HIV programs because it improves the value for money of the use of POC testing while delivering patient-centered care to clients.

In December 2018, EGPAF-Lesotho promoted the use of two GeneXpert machines procured for POC EID to run samples for HPV tests at two high-volume sites, Sankatana National Center of Health and Mafeteng Hospital. The POC HPV test is more accurate and sensitive than nucleic acid testing. Sankatana is an EGPAF-supported site, which was deemed by the MOH to be a “center of excellence” for its comprehensive reproductive health services. This center provides a full complement of cervical cancer screening and treatment services, with a large volume of clients. Mafeteng is a regional hospital, which is being supported to provide cervical cancer screening and treatment services (including the loop electrosurgical excision procedure [LEEP], which removes abnormal cells from the cervix thereby preventing cervical cancer).

RESULTS

Currently, Lesotho is looking into ensuring each POC machine is also used to monitor viral loads in pregnant and breastfeeding women, allowing health care workers and clients same-day access to viral load measurement and earlier treatment adherence counseling or shifts to second- or third-line treatment, if needed. These are versatile machines that allow users to address a host of issues affecting those living with HIV, including identification and treatment success as well as the linkage to the treatment of reproductive cancers. The POC platforms have not just improved EID TAT and increased the number of HIV-positive children initiated on ART. They have also given almost 3,000 women the opportunity to test for HPV, linking over 800 to treatment and thereby reducing their risk of cervical cancer and associated mortality risks. This technology is creating access to laboratory functions for sites previously left without and for those with minimal HR capacity.
Using POC to expand access to HPV testing has resulted in a greater number of women tested and linked to cervical cancer prevention and treatment.

As of July 31, 2019, EGPAF-Lesotho has supported HPV testing for 2,975 women using POC technologies, 55% of whom were HIV-infected and thus at a high risk of developing cervical cancer.

Nearly 83% of the women tested using POC received their results in about one month. Further reduction in TAT is expected as the backlog clears out of the centralized lab system with the help of POC.

Those found HPV-positive (nearly 800 women) were treated at these facilities.
BRINGING A MOTHER RELIEF IN LESOTHO

Today, Lebele Mathato has brought her daughter, Nyakallo, for her six-week check-up at the Maputsoe Clinic in Leribè, Lesotho. Nyakallo is alert and growing well. But as a woman living with HIV, Lebele has a lingering concern. Has she transmitted the virus to her daughter during pregnancy or childbirth?
Lebele well remembers her anxiety of several years back when she brought her infant son, Tuma, to the clinic to determine his HIV status. When he was six weeks old, a health worker took blood samples from Tuma’s heel and applied them to a special card. Once the blood spots had dried, the card was shipped to a laboratory in Maseru for analysis to see if he had been infected with HIV. Lebele had to wait more than a month for the results.

In the end, she was relieved to learn that Tuma was HIV-negative. But the long wait was hard—especially because, like many Basotho women, she lives in a village far from the town center and must walk for several hours to reach the clinic. The longer an HIV-positive infant goes undiagnosed, the more likely they are to fall ill or die.

In contrast, today, Lebele will receive the results of her daughter’s test by the time that she leaves the clinic. At the beginning of their clinic visit today, Lebele and Nyakallo met with Sefoli Mabafokeng, a lay counselor. Sefoli took a simple heel-prick blood sample from baby Nyakallo and sent the mother-baby pair to meet with other clinicians for a six-week check-up and to get vaccinations. Meanwhile, the POC machine quietly analyzed the sample in the HIV testing and counseling room. Fifty minutes later, Lebele and Nyakallo returned for the test result.

Sefoli immediately told the anxious mother that she could relax. Nyakallo is HIV-negative. “I was worried, but now I am happy because she is not HIV-positive,” says Lebele, visibly relieved. “I just like a good life for her. I don’t want my baby to be sick.”

Lebele says that, with both of her children, she has carefully followed the guidance of her health workers. She came to the clinic for antenatal care. She followed her PMTCT drug regimen. She administered NVP, an antiretroviral drug, to her infant children. But she could not sleep well at night until she received the official word that they were HIV-negative.

“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 for them,” says Sefoli. “The machine is doing a fantastic job. It fills the gaps in early infant diagnosis.”
CATALYZING PEDIATRIC TB INNOVATIONS

AUTHORS
MIKAEL DE SOUZA (MDESOUZA@PEDAIDS.ORG); FOR MORE INFORMATION ON THE CAP TB PROJECT, CLICK HERE.

The global response to TB has made advancements in recent years. Despite some welcome gains, work remains. Estimates state that 36% of TB patients (approximately 3.6 million individuals) remain undiagnosed. Many children with TB are missed. Without timely diagnosis and treatment, children with TB have even higher rates of illness and death than adults.

Because the treatment of children and adolescents is marked by nuances and complexities, with Unitaid support, EGPAF has pioneered the Catalyzing Pediatric TB Innovations (the Cap TB project), an initiative to employ innovative TB care models, diagnostic tools, and drugs. Using lessons learned from the POC EID project, CaP TB will be active in nine sub-Saharan African countries (Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Kenya, Lesotho, Malawi, Tanzania, Uganda, and Zimbabwe) and India from October 2017 to September 2021.

GOALS
EGPAF supports changes to dismantle barriers that constrain access to TB treatment. At the national level, there are efforts to revise guidelines and policies, to ensure adequate training materials for health workers, and to build momentum among stakeholders. In supported clinics, EGPAF focuses on two key activities: 1) case finding, diagnosis, and treatment of children with active TB and 2) the provision of access to preventive therapy among eligible children.

EGPAF supports changes to dismantle barriers that constrain access to TB treatment.

EGPAF aims to double the number of children diagnosed with active TB and the number of children initiated on first-line treatment and to treat more than 16,000 children with active TB and ensure that 90% of them achieve treatment success.

EGPAF seeks to increase the proportion of eligible children initiated on latent tuberculosis infection (LTBI) treatment from 13% of those eligible to 80%.}

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INTERVENTIONS
The enhanced methodology of CaP TB involves integrating screening and diagnosis into various child health entry points (i.e., maternal, newborn, and child health; pediatric inpatient and outpatient facilities; nutrition and HIV care and treatment). Community health workers or other lay community cadres will be trained in the areas of tracing household contacts, screening identified pediatric contacts of TB index cases, counseling patients and caregivers, and monitoring treatment adherence. To complement these efforts, EGPAF will support the use of innovative diagnostic assays. Due to its improved sensitivity, the new GeneXpert Ultra cartridge is expected to improve detection yield in children, and EGPAF will support product transition. Fortunately, the GeneXpert Ultra cartridge is compatible with all existing Cepheid GeneXpert instruments, such as those rolled out by EGPAF under the POC EID project.

EGPAF will also support the use of advanced sample collection techniques. Because the traditional sample used in TB diagnosis (sputum) may be difficult to obtain in children, EGPAF will invest in equipment and training for sample collection techniques that better suit children (such as stool samples).

The CaP TB project will also support the introduction and use of novel drugs and treatment options for childhood TB, such as dispersible fixed-dose combinations for drug-sensitive TB (Rifampicin, Isoniazid, and Pyrazinamide [RHZ] and Rifampicin and Isoniazid [RH]). These fixed-dose formulations are appropriately dosed for children and dispersible in water, and they come in palatable fruit flavors to improve adherence. Notably, novel and shorter drug regimens also exist for LTBI (three months of RH) and the same dispersible fixed-dose combination of RH may be used for younger children on this regimen.

WAY FORWARD
In 2018, EGPAF conducted an analysis of existing policies in all the CaP TB implementation countries. The assessment demonstrated that while all surveyed countries have the basic elements needed to improve pediatric TB prevention, diagnosis, and treatment, most do not have an enabling policy and a regulatory and financial environment conducive to introducing and scaling up innovative diagnostics and treatment. Insufficient health worker training programs for childhood TB is a testament to this gap. Earmarked funding for priority interventions is insufficient in most countries, which may create opportunities for these interventions to be overlooked (though the lack of available information hinders full analysis).

Currently, all countries have started enrolling CaP TB intervention sites, with approximately 20 enrolled in each of the 10 CaP TB countries. Clinicians and lay and non-lay health workers in all countries have been trained to recognize the symptoms of pediatric TB and to diagnose and employ the available treatments for active and latent TB infection. Already we see an important impact of our intervention, and improvements to the diagnostic and care of children with TB. Over 200,000 children have been screened for TB. The overall monthly rate at which CaP TB is diagnosing children is 30% higher today than the monthly rate at project start. Consequently, the number of diagnosed patients initiated on treatment increased by more than 70%.

To measure and evaluate the effects of this project, two significant and exhaustive research initiatives began in Cameroon, Kenya, and Uganda. The INPUT study considers the additional yield of integrating TB screening in non-TB entry points (such as women and children’s clinics or vaccination centers). The CONTACT study analyzes the feasibility and yield of enhancing contact tracing and preventive treatment in the home communities of contact patients (as opposed to waiting for them to be brought for screening in facilities). With these evaluation opportunities, CaP TB aims for rapid adoption of improved practices in identification and diagnosis of TB in children by national health authorities.
CAP TB AT WORK IN DRC

Yangambi is an active six-year-old living in Kinshasa, The Democratic Republic of Congo (DRC). Not long ago, she had become listless and lost interest in playing. She stopped eating and quickly lost weight, which concerned her grandmother and caretaker, Gabrielle Bunzeki. Gabrielle began to worry that her granddaughter had become re-infected with TB—for which she had been diagnosed and treated as a toddler.

“Yangambi developed a high fever, started breathing heavily, and broke out in rashes. I suspected that she might [once again] be ill with TB, so I brought her to St. Pierre Health Center. For a second time, she tested positive for TB and received treatment on the same day of testing,” says Gabrielle. For her previous treatment, Yangambi had to swallow bitter pills, which she hated. The medicine was effective, but it was not as fast-acting as a new formulation available since the beginning of 2018. Gabrielle notes that the sweet flavor is more palatable to young TB patients, which encourages faster recovery. “My granddaughter took the new treatment at 8 a.m., and she was playing at 5 p.m. With the old treatment, we waited for more than 24 hours to see the child [Yangambi] start playing. Now she’s eating food and drinking juice around the clock.”

“To improve adherence to treatment, we use dispersible tablets in fruit flavors,” says Aimé Loando, M.D. “The tablets are dissolved in the water and given to children to drink.” Dr. Loando is the DRC lead of the CaP TB project. “A key difference between CaP-TB and other TB programs is the engagement of the community,” says Dr. Loando. At St. Pierre, the Club des Amis Damien has established a committee of volunteers that works closely with the facility and with EGPAF’s CaP TB project. Dr. Loando notes that free TB treatment is necessary to stem the spread of the disease in low-income countries like DRC. This makes it all the more crucial that governments invest in child-friendly diagnostics, she says, so that health workers
can quickly diagnose TB in children and provide child-friendly medicines. This way, treatment can reach and cure even the youngest TB patients.

“Members of this club are all former and healed TB patients,” says Godet Ilumbe, one of the volunteers. “Every member is based in the facility where they received TB diagnosis and treatment ... For Yangambi's case, we visited the home of her caretaker and completed TB screenings on the spot, [among all] her contacts older than age 5. Because TB symptoms in children are not always easily recognized, we referred the children younger than age 5 to St. Pierre for diagnosis,” says Ilumbe. Notably, TB treatment at this clinic is free, a vital detail in DRC—one of the 10 poorest countries in the world.

“As TB volunteers, we conduct visits at the homes of known cases,” adds Bibi Marie-Jeanne, another club member. This is known as index tracing.

“It is painful—very painful—to hear that your son or your daughter has a TB infection and fear that [they] might die or be disabled by the disease ... I just want Yangambi to recover quickly and forever,” says Gabrielle.
POC EID PROJECT EXPERIENCE IN ZIMBABWE

AUTHORS
ADDMORE CHADAMBUKA (ACHADAMBUKA@PEDAIDS.ORG)

Zimbabwe has an adult HIV prevalence of 16.7%, with an estimated mother-to-child transmission rate of 8.9%. The limited capacity to diagnose HIV in exposed infants resulted in just 63% receiving an HIV test within the first two months of life in 2015 with a result to caregiver wait-time of 30 to 90 days. Only half of those tested ultimately received the results, and only 51% of the infants found to be HIV-infected were actually placed on treatment.

PROJECT SCALE-UP
The project’s initial phase in Zimbabwe involved a review of the national policy landscape to determine the extent to which it supported the adoption of POC EID, which was deemed conducive to project implementation and scale-up, particularly since the country had already begun to use the POC diagnostics for TB and malaria. It was, of course, necessary to ensure that other conditions were primed for the project’s success. As in other settings, the project’s first phase required POC EID platform selection, procurement, and delivery. This was followed by site selection, during which EGPAF analyzed the conventional EID testing data across 1,560 facilities and subsequently performed capacity assessments on promising locations. High-volume sites that conducted an average of (or only slightly below) 0.5 HIV tests per day were categorized as “standalone sites.” Sites with an average that was slightly lower than 0.5 tests each day were designated as hubs with nearby spoke sending samples to hubs for processing.

A training of trainers was held for provincial laboratory managers. These managers held an orientation for program managers and provided classroom training for end users. Mentoring
and post-training support were also made available by provincial lab managers, program managers, and EGPAF—both in-person and virtually. Where necessary, retraining and/or targeted intensive mentorship provided alternative options. Supportive supervision was offered every few weeks early in the implementation, but by year two, these visits were offered quarterly. Implementation then followed a phased approach, with a 10-site pilot assessed over a 6-month period by December 2016. By December 2018, there were 51 platforms and 281 sites with a cartridge consumption of 11,810.

TASK SHIFTING FOR POC EID ENSURES QUALITY AND ACCESS

Both laboratory and non-laboratory personnel conducted testing. To determine whether the efficiencies differed between the two, a comparison assessment was conducted between the two types, testing internal quality control failures with data taken from 1,847 tests. There was no significant difference in performance between the two groups, suggesting that the test could easily be performed by any trained cadre. Task shifting to non-laboratory trained personnel was evidently possible.

RESULTS

Ultimately, POC EID resulted in a significant reduction in TAT from collecting blood samples to returning the results to the caregivers in zero days. A significant increase in early ART initiation among HIV-positive infants has been realized.

By December 2018, 2,911 tests were conducted.

The number of tests increased as new testing sites were enrolled.

Between quarter one of 2017 and quarter four of 2018, 429 infants were identified as HIV-positive, and 393 were initiated on lifesaving ART.

Between January 2017 and June 2018, the median TAT for results returned to caregivers was 0 days with an interquartile range of 0–2.
The TAT and key program outcomes for exclusive EID testing sites were compared to those of five integrated TB-EID testing sites that used GeneXpert platforms in Zimbabwe. The results indicated that using POC platforms for EID in addition to using machines for diagnosis of TB is effective without increasing the machine or operator workload capacity.

**WAY FORWARD**

Transition planning was a core component of the project from its inception. To ensure that the benefits of POC EID would continue beyond the project’s lifespan, EGPAF advocated that the method be included in the national laboratory policy and strategy and that POC EID guidelines be adopted by the MOHCC. The involvement of multiple stakeholders in planning and implementation also ensured that more than one organization was involved and invested in POC EID. This collaborative approach was exemplified through the joint site support and supervision of EGPAF and the MOHCC. The quantification of POC EID commodities was integrated into the national HIV and TB commodity management system. The training of trainers course conducted for the MOHCC created the institutional capacity to train end users when the project life ends. POC EID was determined that platforms can be used with equal efficacy by laboratory and non-laboratory personnel. POC EID is a feasible intervention with evident benefits and should be rolled out widely for the benefit of HIV-exposed infants everywhere.

**INTEGRATION OF EID AND TB TESTING IN ZIMBABWE: FEASIBLE AND EFFICIENT**

Site assessments made certain opportunities salient. The pre-existing Ministry of Health and Child Care (MOHCC) GeneXpert machines were reportedly being underused, allowing for EID capacity to be added to an existing pool of technical resources. Although the MOHCC used the instruments in its TB department, the machines only required a simple software upgrade to perform EID testing as well. A total of 10 GeneXpert platforms were used for this purpose. In the end, EGPAF procured 45 machines for the Zimbabwe implementation.
ADVANCED HIV DISEASE: INNOVATIONS ARE NEEDED AND IN DEVELOPMENT

Despite expanded access to ART and the adoption of globally recommended policies ensuring anyone with a positive HIV test is linked to treatment, AIDS-related deaths have plateaued in recent years. Those facing the greatest risk of death are the individuals living with advanced HIV disease. Advanced HIV disease is defined by the WHO as having a CD4 cell count below 200 cells/mL, people with stage III or IV disease, or any child under 5 years of age with HIV. Those living with advanced disease are more prone to opportunistic infections (e.g., TB, severe bacterial infections, and cryptococcal meningitis) that can result in an increased risk of morbidity and mortality.

The burden of advanced HIV is significant. Those living with advanced disease represent one-third of all HIV-positive patients in active care. A number of factors are leading to advanced HIV disease in children over five years of age and in adults: a large percentage of patients—more than half in some studies—have started ART in the past, had their care interrupted, and are returning to care after a drop in their CD4 count and the presentation of symptoms.

Current national strategies and funding priorities do not adequately address the complex issue of advanced HIV disease. Country-specific efforts to curb mortality cannot succeed without appropriate guideline adoption, financial resource mobilization, and key diagnostic and treatment access. Moreover, care models are needed that fit the needs of those presenting (and re-presenting) with advanced HIV disease, ensuring that health care workers have the capacity to carry
out diagnostics, treatment, and care protocols to manage the complex needs and challenges of these individuals living with advanced HIV.

The WHO released its first advanced HIV disease guidelines in July 2017, which outlines priority evidence-based actions to help reduce morbidity and mortality from advanced HIV disease. These guidelines could be adopted in high-burden settings along with investment in products and tools to diagnose and treat advanced disease. Affordable, user-friendly, and rapid diagnostic tests to measure CD4 and diagnose cryptococcal meningitis and TB disease in patients with advanced disease are now available.

There are also promising drugs that are critical for treating patients living with advanced HIV disease and/or those diagnosed with opportunistic infections. For example, the second leading cause of death for HIV-infected individuals in sub-Saharan Africa is cryptococcal meningitis. Until recently, even with treatment, mortality rates for this disease have been up to 70%. Now, WHO-recommended treatments offer a better chance of survival and are becoming more readily available for patients who desperately need them. One such drug, Flucytosine, has new generic manufacturers that have already or will soon commercialize a quality-assured product, which would offer a sustainable supply of treatment for cryptococcal meningitis in resource-limited settings. Another treatment for cryptococcal meningitis, Liposomal amphotericin B, has far fewer side effects than traditional Amphotericin, and its manufacturer, Gilead, has recently announced price reductions for this important drug as part of a Unitaid-led negotiation effort.

Finally, there are easier preventive treatments for TB, the leading cause of death for people living with HIV. The WHO now supports a three-month regimen of weekly Isoniazid and Rifapentine to prevent TB, a regimen that is easier to complete than traditional six-month daily INH TB preventive therapy.

What is EGPAF doing?

EGPAF is working in several countries to roll out differentiated models of care that work for people living with advanced HIV disease. In addition, EGPAF is decentralizing care, including screening, treatment, and prevention, to lower-level health facilities where patients most often access care. EGPAF has also developed a training package and adopted a package of tools to assist health care workers in identifying advanced disease and meeting the special needs of patients who are presenting or re-engaging in care with the advanced disease. These tools ensure health workers can effectively use new drugs and diagnostics.

EGPAF is also advocating at national and international levels to strengthen adequate funding for diagnostics, treatments, and programs that can reduce mortality and morbidity due to advanced HIV disease. EGPAF is documenting the effect of these efforts to successfully provide the right care to people living with advanced HIV disease.

In addition, EGPAF believes the successful implementation of innovative diagnostics and drugs can be leveraged (such as what has been done for EID and TB) to address the needs of those with the greatest risk of morbidity and mortality in HIV-positive populations.
LESSONS LEARNED FROM POC EID IMPLEMENTATION ACROSS COUNTRIES

THE DATA SUPPORTING USE OF POC EID IS STRONG:

- POC EID testing has been shown to significantly reduce TAT and increase the percentage of caregivers receiving results and the percentage of HIV-infected infants started on ART as compared to centralized laboratory based EID.
- POC EID has been shown to be cost-effective compared to conventional EID and POC EID is expected to become more cost-effective as the price for POC EID continues to come down with increased order volume.
- POC EID is feasible and well-accepted across a wide range of “real-world” contexts in sub-Saharan Africa.

EACH COUNTRY’S POC EID NEEDS ARE DIFFERENT and as such each country must develop its own POC network according to its current lab infrastructure and performance, clinical need for POC testing (including testing for TB, VL and HPV depending on the country context) and testing prioritization, existing POC platforms, and consideration of other requirements such as sample transport.

KEY FINDINGS TO TAKE INTO CONSIDERATION WHEN DESIGNING A PLAN TO INTEGRATE POC INTO THE COUNTRY LAB NETWORK INCLUDE:

- Integrating POC EID into existing platforms use for TB is feasible and well accepted. Early data suggests that integrated testing for EID use, such as platforms used for TB, and HPV is also feasible and well accepted.
- Using a short-haul, hub-and-spoke system increases POC EID coverage without compromising patient outcomes.
- EGPAF’s data demonstrate that facilities using centralized laboratory testing have long TATs and low percentage of results received regardless of distance to the centralized testing site. Thus, POC EID may be beneficial for sites located close to centralized laboratory testing facilities, including urban sites.

IN-COUNTRY, EARLY BUY-IN AND SUPPORTIVE LEADERSHIP ARE INSTRUMENTAL in implementing innovations.
ENGAGING STAKEHOLDERS AND IMPLEMENTERS (nurses and lab personnel), providing necessary training, and defining a precise role for the lab and clinical personnel were also instrumental to the success of this work.

DESIGNING A SCALABLE AND FACILITY-BASED TRAINING MODEL, WITH STRONG SITE SUPPORT IS CRITICAL:

- A training of trainers model can be an effective strategy to scale up these types of training.
- Staff turnover was among the greatest challenges experienced throughout the implementing countries. At locations with POC EID machines, the relocation of trained staff often took place before replacements received the necessary training. Designing a system to ensure that at least one staff member per site is always trained in POC will help ensure sustainability.

PROACTIVE STOCK AND PRODUCT MANAGEMENT IS KEY TO BUILDING A SUSTAINABLE POC SYSTEM:

- Sharing early forecasts with manufacturers and constant, transparent communication with the manufacturers is helpful to reduce lead times and ensure sufficient product is available from manufacturers.
- Short shelf life of current POC products adds to the need for strong supply chains. Strengthening diagnostic supply chains and ensuring meticulous stock management at site level, such as by including stock management in the core POC training and by including stock management indicators during site supervisions visits, will help to reduce the risk of stock-outs.
- Maintaining comprehensive service level agreements and including key performance indicators in these service level agreements will help to ensure that platform breakdowns or other technical issues are rapidly addressed.

BUDGETING MUST INCLUDE NOT ONLY PRODUCT COSTS, BUT ALSO OTHER COSTS such as those for infrastructure upgrades, additional sample transport as needed, training and site monitoring.

IN THE FUTURE, INNOVATIVE PRICE OFFERINGS SUCH AS ALL-IN PRICING FOR POC TESTING, including the costs of the cartridge, platform, service level agreement, data and connectivity and even delivery of cartridges to site level will make the implementation of POC significantly more efficient and simple.
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