

The Role of Point-of-Care testing for Early Infant Diagnosis

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IAS2018 Satellite Session:
Diagnose, treat, innovate: A paradigm shift for ending paediatric AIDS

Monday, July 23rd, 2018



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The World Health Organization recommends early testing of all HIV-exposed infants, rapid return of test results, and prompt initiation of treatment for those who are HIV-positive.



- All HIV-exposed infants should have a **virological test at 4–6 weeks of age** or at the earliest opportunity thereafter (strong recommendation)¹
- The turnaround time from specimen collection to results return to caregiver should **never be longer than four weeks**. (strong recommendation)²
- Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable **prompt initiation of ART** (strong recommendation)¹
- **Point of care can be used** for early infant HIV testing (conditional recommendation)²

¹ World Health Organization (2016). *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Second edition*. Geneva

² World Health Organization (2010). *WHO recommendations on the diagnosis of HIV infection in infants and children*. Geneva.

A decade-long effort to scale-up access to conventional EID testing services has nearly doubled the number of tests conducted.

EARLY INFANT DIAGNOSIS

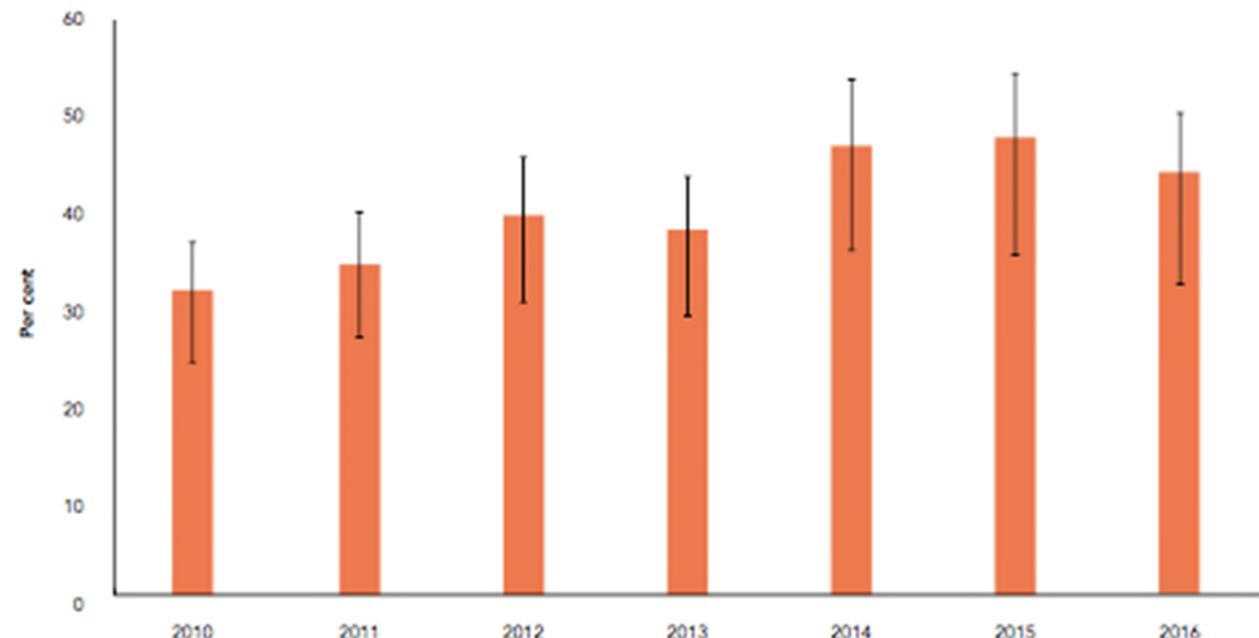


FIGURE 3.12. PERCENTAGE OF HIV-EXPOSED INFANTS WHO HAVE BEEN DIAGNOSED WITHIN TWO MONTHS OF BIRTH, 21 HIGH-BURDEN COUNTRIES, 2013 AND 2016

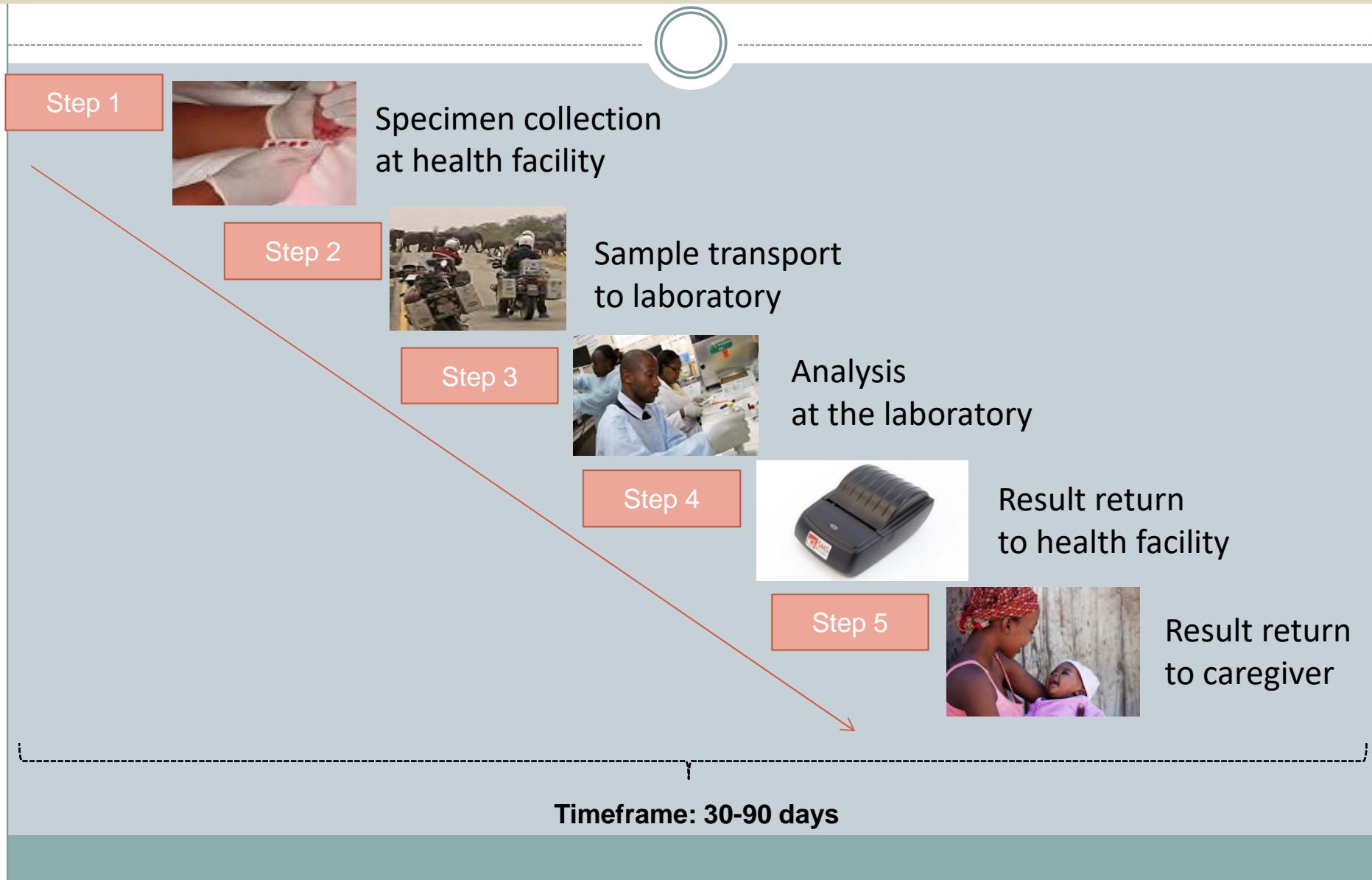
Source: Global AIDS Monitoring, 2017; UNAIDS 2017 estimates.

The proportion of HIV-exposed infants receiving a timely virological test for HIV by 2-months of age remained below 50% from 2010-2016.

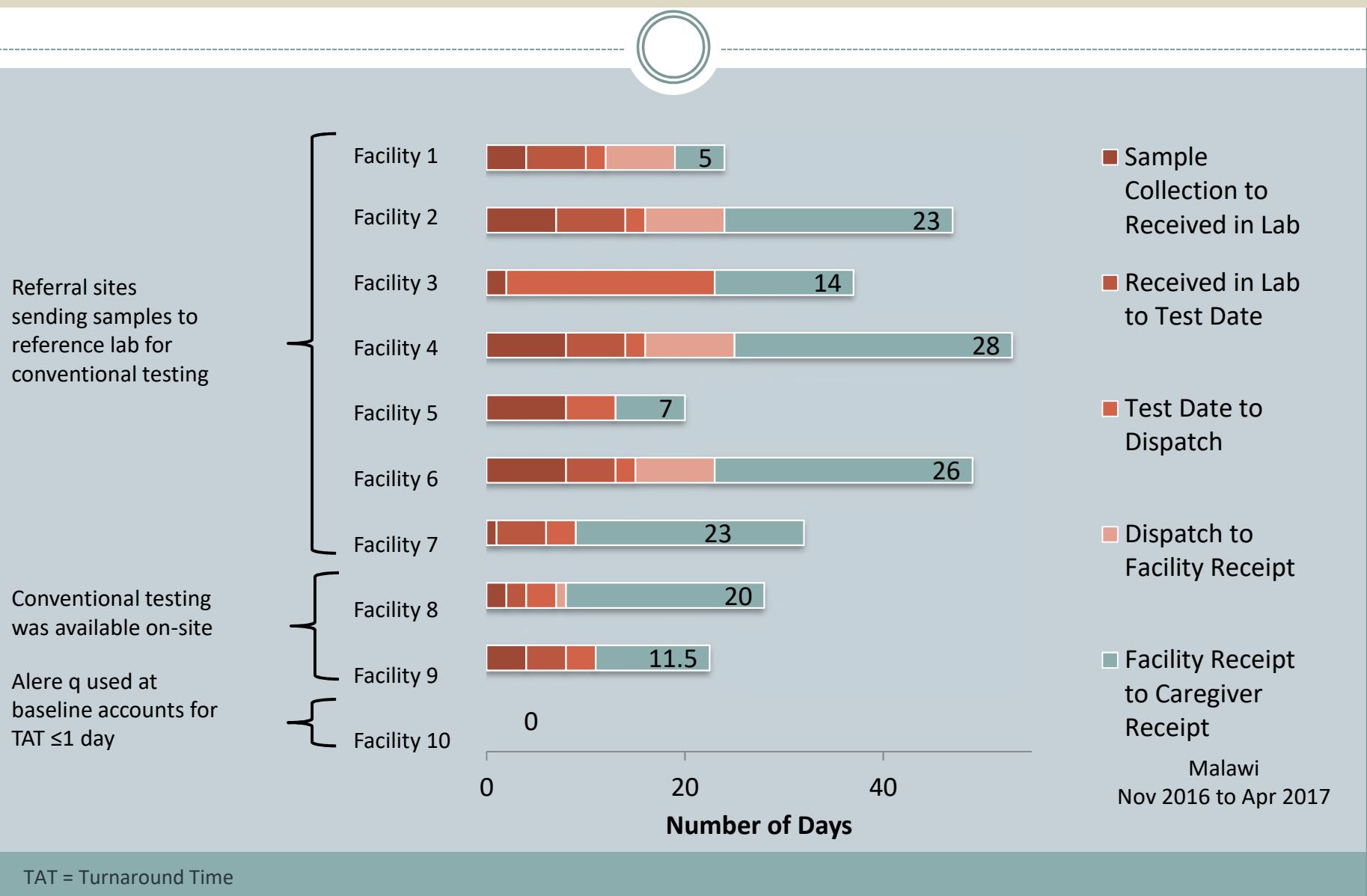
During the same period the number of EID tests nearly doubled. However long turnaround time and a high proportion of results not returned have remained problems.

Only 51% of HIV-infected children are on life-saving ART.

With laboratory-based EID testing, the number of steps from sample collection to return of results to caregiver and clinical action lead to persistent delays and a high proportion of lost results.

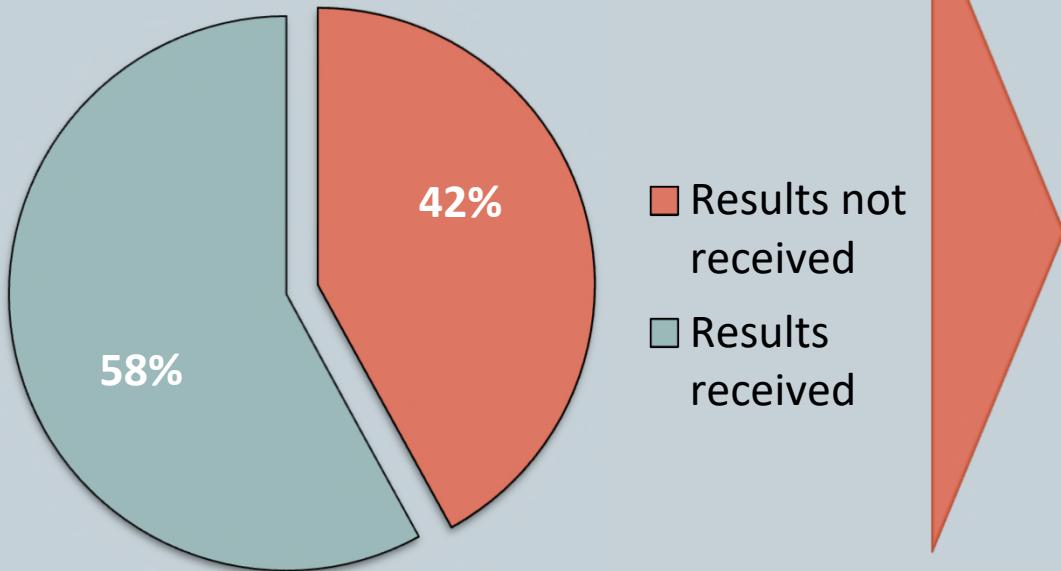


Long turnaround times from specimen collection to result receipt at the clinic, and an even longer time for results return to caregivers, contributes to high loss-to-follow-up.



With centralized lab-based testing, many test results are never received by the patient.

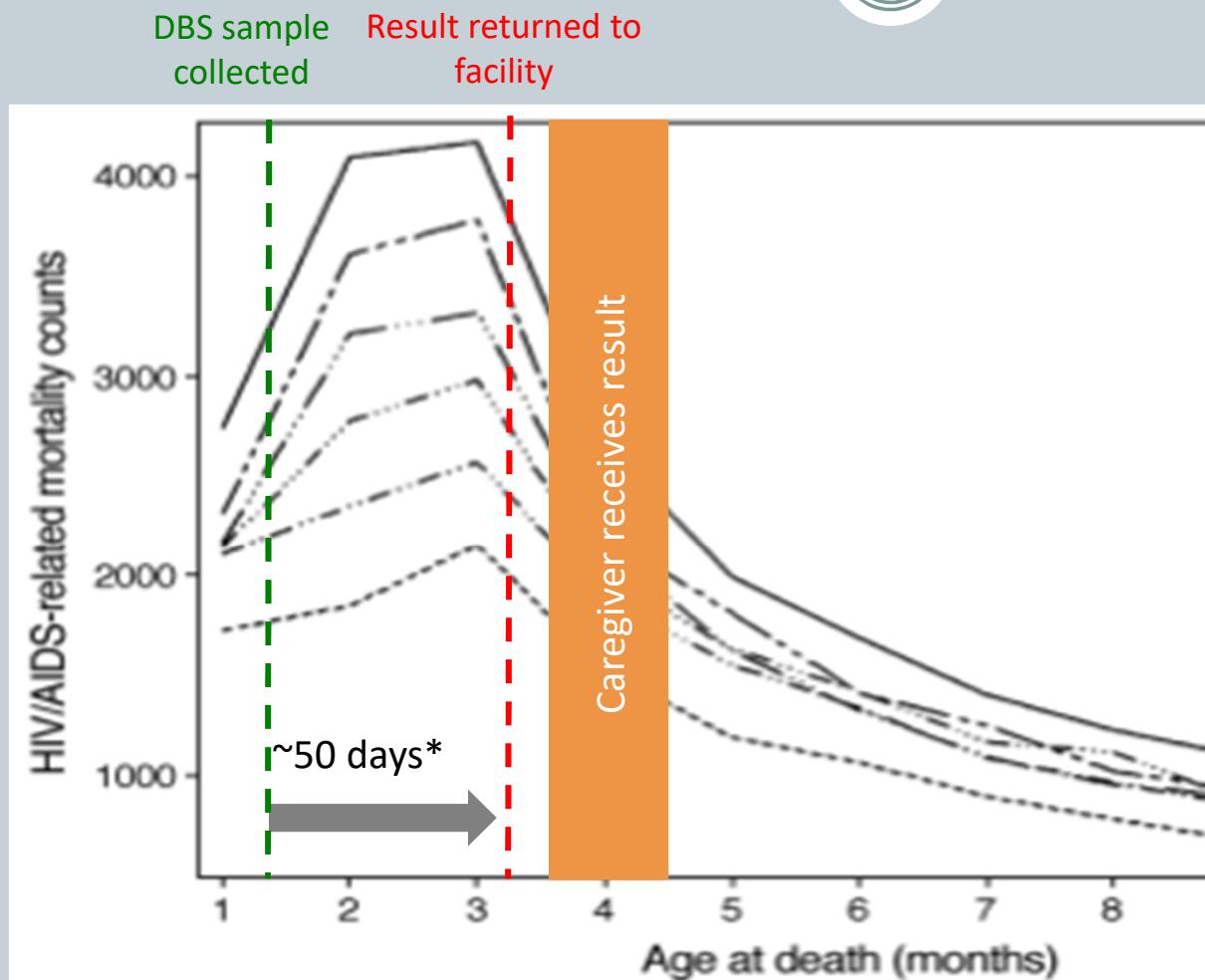
Based on a weighted average of nine studies and monitoring and evaluation (M&E) data, 42% of **EID** test results are not received by the patient¹



- Wasted reagents
- Wasted HR time
- Unnecessary repeat testing
- Infants LTFU before receiving results
- Poor linkage between testing and care and treatment
- High infant mortality

¹ See final slide for list of references

If untreated, infants infected with HIV in-utero or perinatally experience high mortality, which peaks from 2 to 3 months of age. Most conventional EID test results are returned to patients after peak mortality.



Without treatment:

- 30% of HIV-positive children will die by their first birthday (with a peak mortality at 2 to 3 months of age)
- 50% by age 2
- 80% by age 5

Source: Bourne AIDS 2009

* Vojnov L et al JAIDS 2017

Published studies and routine M&E data demonstrate that POC testing can diagnose more HIV-positive infants faster, and can significantly reduce the turnaround time from specimen collection to initiation of treatment for HIV-positive infants.

Study Use

Country	Setting	Device/ Sample	# of sites	n (infants)	% result return to caregiver		TAT result return	% ART initiation		TAT ART Initiation
					≤ 30 [#] days	Same day		≤ 60 days	Same day	
Mozambique (Maputo, Sofala)	Randomized controlled trial (cRCT)	Alere q/ Whole blood	SOC - 8	1,876	0.32%	0%	125	12.8%	NA	127
			POC - 8	2,034	98.7%	98.2%	0	89.7%		0
Malawi	Observational pre/post	Alere q/ Whole blood	7 pre POC	963	18.1%	0%	56	41.9%	43.8%	38
			7 post POC	789	100%	99.5%	0	91.1%	70.7%	0

M&E – Routine Use

Nine countries (Dec 2016 – March 2018)*	M&E	Alere q/ Whole blood & Xpert/ Whole blood	SOC – 102	2,867	19.7%	0%	55	41.3%	0%	50
			POC – 339	25,102	98.3%	67%	0	91.7%	65%	0

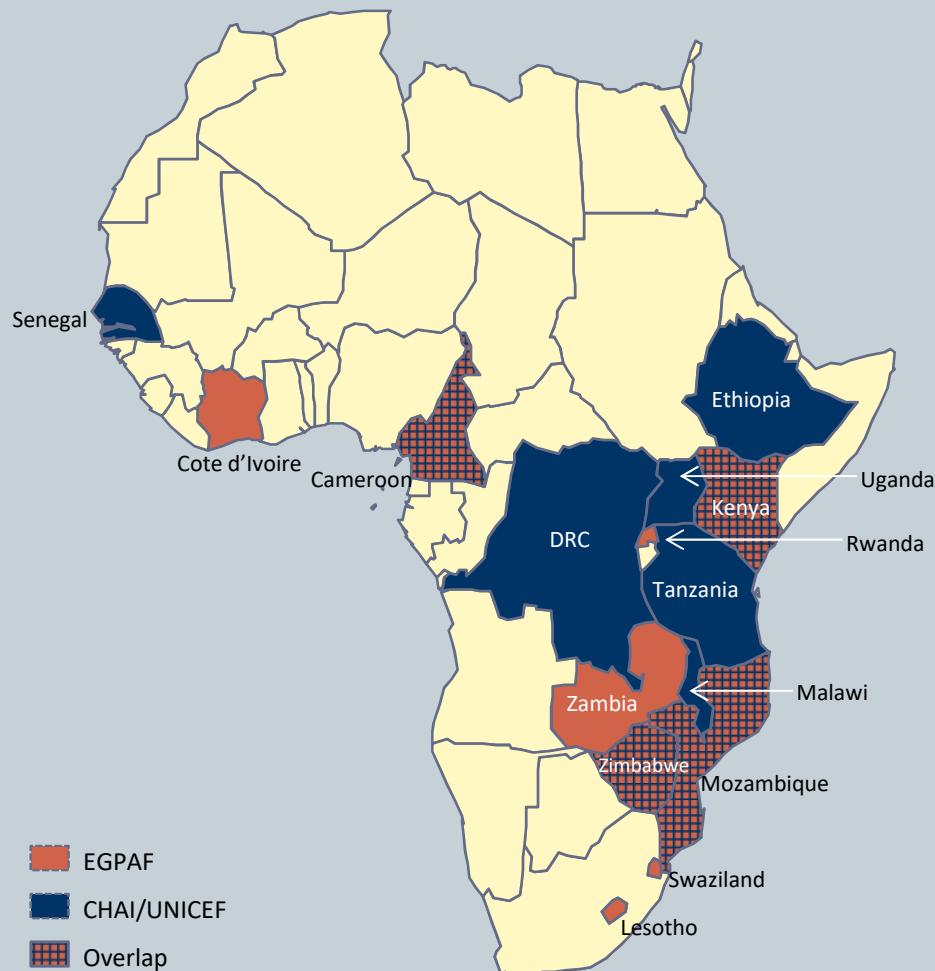
[#]Mozambique SOC: 7.2% within 60 days; Malawi pre: 41% within 60 days

NA = not available

*Cameroon, Côte D'Ivoire, Kenya, Lesotho, Mozambique, Rwanda, Swaziland, Zambia, Zimbabwe (EGPAF)

SOC = Standard of Care (Conventional, lab-based testing) POC = Point-of-Care testing

The goals of the Unitaid-supported CHAI/UNICEF and EGPAF projects are to speed clinical decision making, increase the number of HIV-exposed infants whose HIV status is known and facilitate early initiation on treatment.



Goal: Speed clinical decision making, increase the number of **HIV-exposed infants with known HIV status** and facilitate early treatment initiation

Purpose: Ensure that at-risk infants have **timely access to HIV testing, diagnosis and treatment** through the incorporation of POC testing into national EID networks

Scale:

- 15 countries – 4 overlapping
- 5 years
 - EGPAF 2015-2019
 - CHAI/UNICEF 2016 – 2020
- \$157 million

Cost per result returned to caregiver is the same or lower for POC EID compared to conventional EID, despite higher individual test price.

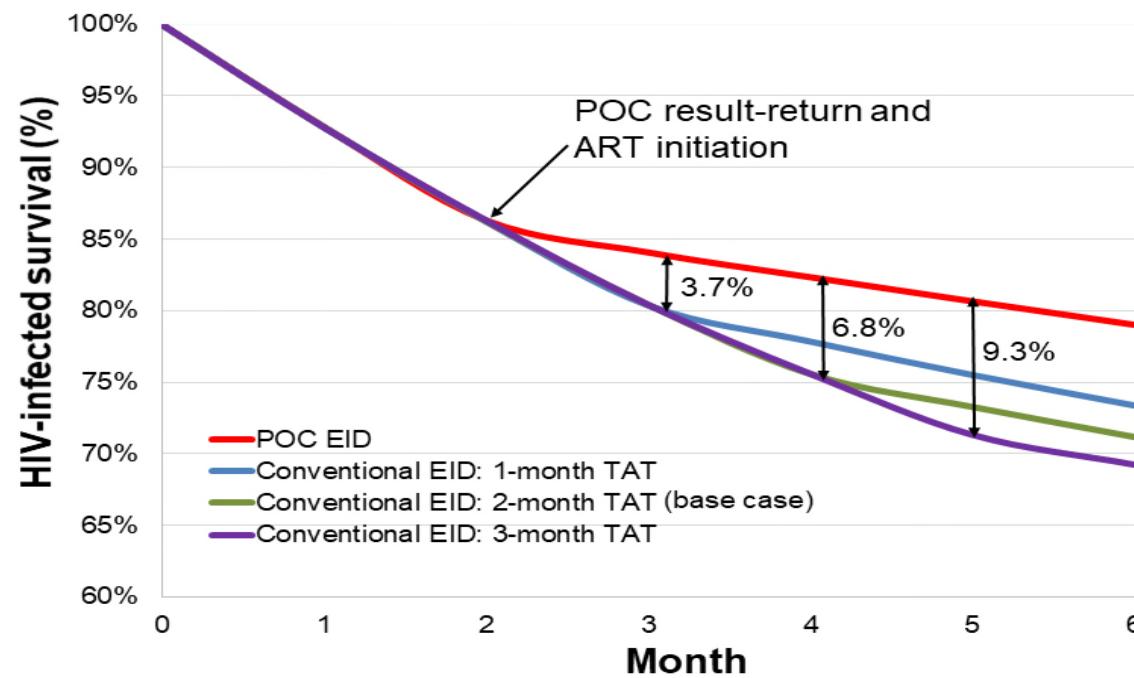
- Price of diagnostic technologies is a key consideration for national programs, implementers, and funders.
- Total cost of ownership includes: reagents, controls and other consumables, costs of equipment, logistics, basic training, and service and maintenance costs.

	Conventional	POC (current throughput)	POC (optimal throughput)
Cost per result returned in 30 days (range)	\$131.02 USD (\$96.26-\$165.76)	\$37.89 USD (\$32.54-\$43.25)	\$27.24 USD (\$21.39-\$33.10)
Cost per result returned in 3 months (range)	\$38.89 USD (\$28.57-\$49.21)	\$37.51 USD (\$32.21-\$42.81)	\$26.97 USD (\$21.17-\$32.76)

*Based on The Global Fund's total cost of ownership estimates for both conventional and POC EID testing, reported in the April 2017 *HIV Viral Load and EID Selection and Procurement Information Tool*, and adjusted for the return of test result rates for conventional and point-of-care (pre- and post-intervention).

POC EID was found to improve infant survival by 6.8% and be cost-effective compared to conventional EID.

Cost-effectiveness pre-study modeling for Zimbabwe found POC EID improved survival by 6.8% in the first 3 months of life and was cost-effective compared to conventional EID



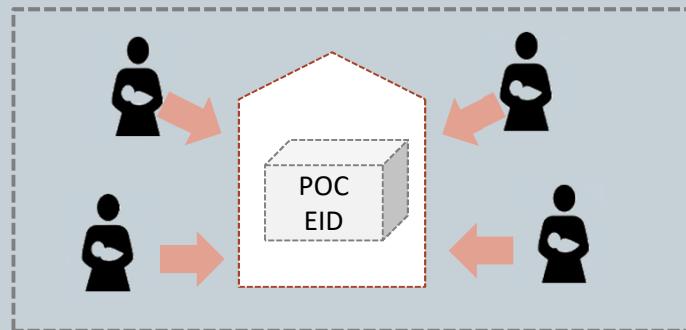
ICER vs conventional
for year of life
saved: \$630 USD

Pre-study model
assumption=83%
result returned (true
result return is 59%)
and ART
initiation=72% (true
ART initiation is
56%)

A combination of POC testing strategies are used to: increase access to testing; expand case finding; decrease result TAT; and optimize platform utilization.

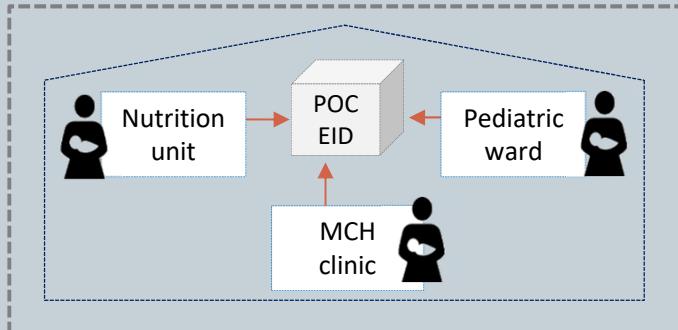
Stand-Alone Sites

Receive samples directly from clients and perform POC EID tests on site



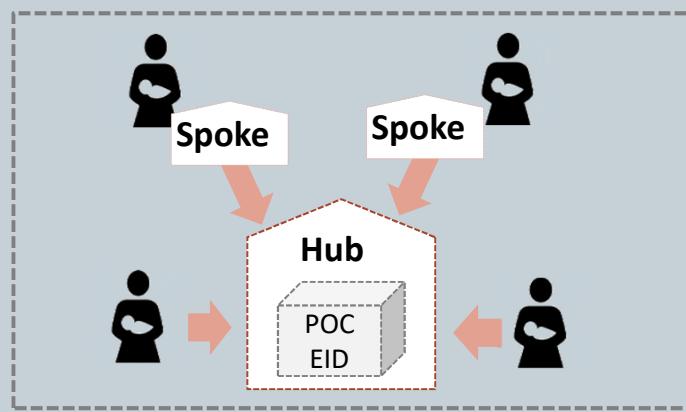
Multiple-Entry-Point Sites

Stand-alone or hub testing sites receive samples from different units or wards within the same health facility



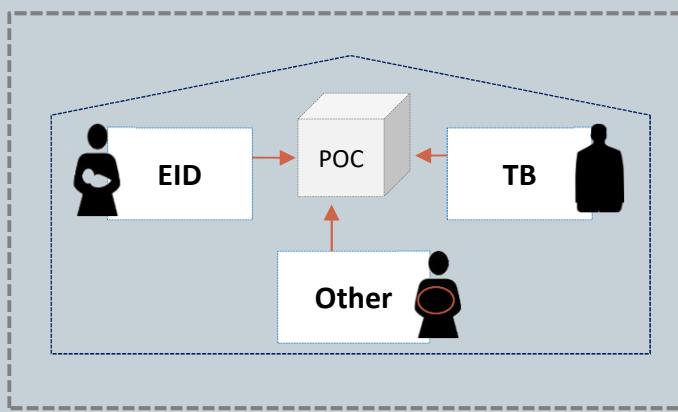
Hub-and-Spoke Networks

Hub sites provide testing for patients at that site and for spoke sites.
Nearby spoke sites send samples to the hub sites for testing



Integrated Testing Sites

Process different types of POC tests
(e.g. EID, TB, other)



Short-haul, hub-and-spoke networks using POC EID show comparable performance for results returned and treatment initiation rates; while spokes experienced slightly slower turnaround times.

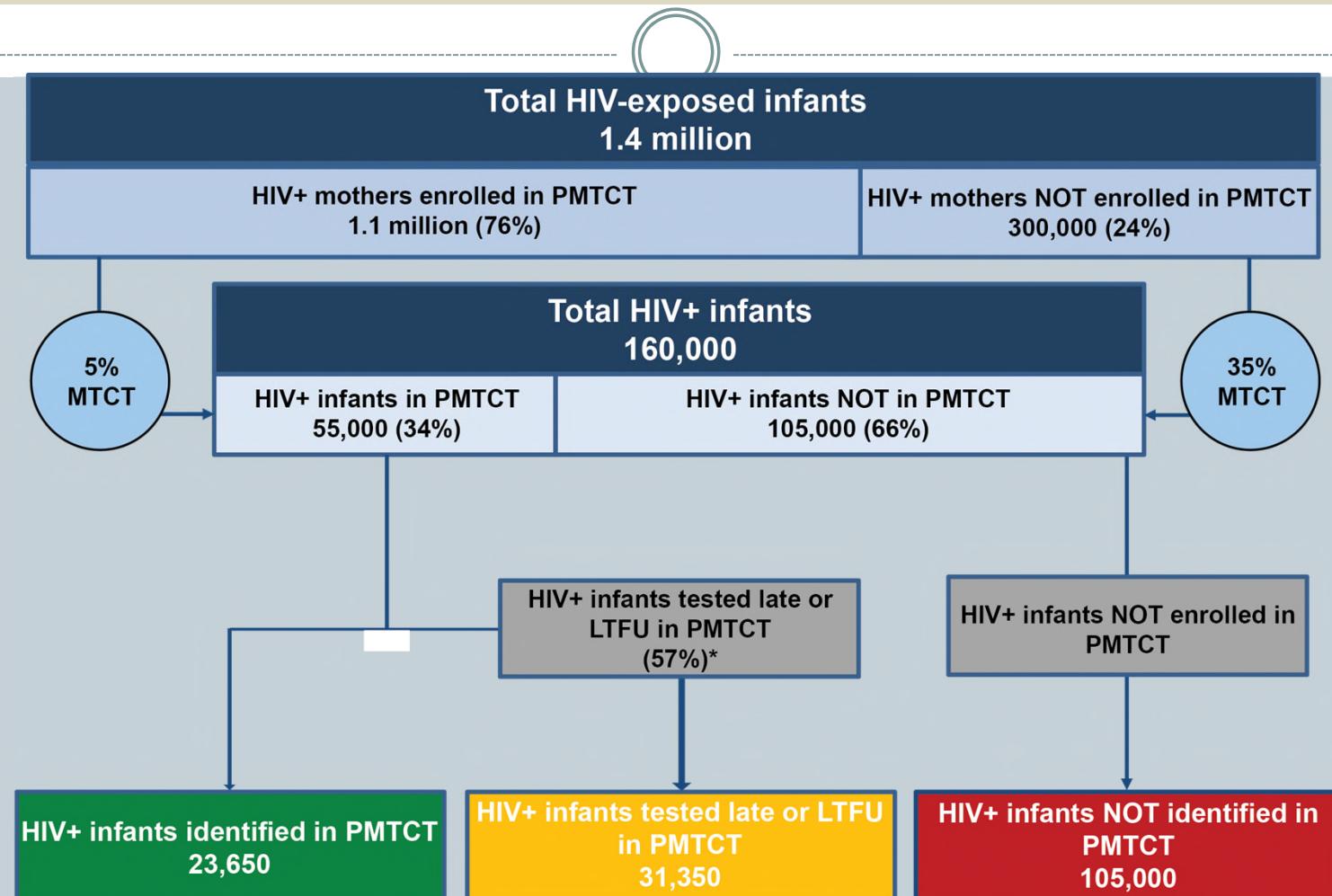
Key Outcomes (Dec 2016 – Dec 2017)	Testing Sites (106 sites, n = 13,070)	Spoke Sites (233 sites, n = 5,155)
Results received by caregiver within 30 days	99.4%	95.5%
Median TAT from blood sample collection to result returned to caregiver	0 days (IQR: 0-0)	2 days (IQR: 1-7)
Percent of HIV-infected infants started on ART within 60 days of blood sample collection	91.9%	94.4%
Median TAT from blood sample collection to initiation of ART for HIV-infected infants	0 days (IQR: 0-1)	3 days (IQR: 1-5)

Integration represents an opportunity to increase access and realize cost-savings, without compromising testing results.



- **Low testing volumes** for some disease programs may make it unaffordable to use point-of-care devices for a single test type. However, higher volumes gained through testing of multiple diseases on a single device can improve cost efficiencies in certain areas and expand **access to POC testing to more sites**.
- Integrating testing and using existing infrastructure, when there is spare capacity, will result in **cost savings from a duplicative instrument placement**.
- Preliminary analysis of integrated testing pilots on GeneXpert devices in Malawi and Zimbabwe, using TB and HIV viral load and EID specimens, suggest that:
 - Implementing HIV testing on GeneXpert devices currently used for TB testing **does not increase the TAT to results received for TB patients**
 - HIV testing on devices used for TB testing **is operationally feasible**
 - There **is sufficient capacity** on some installed devices to run TB and HIV testing (perhaps other test types too)

An estimated 66% of HIV-infected infants are born to mothers not enrolled in PMTCT and will not be identified through PMTCT-based EID programs; another 20% of infants are enrolled in PMTCT but are tested late or are lost to follow up.



Ending pediatric AIDS will require expanding testing beyond PMTCT sites to alternative entry points

Published studies and M&E data show high positivity rates at alternative entry points, such as pediatric wards and nutrition units. POC technologies support rapid diagnosis and linkage of infants to treatment before they are discharged and lost to follow up.

“Where have all the children gone?...”

Kiyaga, JIAS, 2018

	EMTCT	Nutrition	Inpatient	Outreach	Outpatient	Immunization
# cases	23	59	21	2	11	1
% cases	3.8	9.8	3.5	0.3	1.8	0.2

Odds ratio

2.75**

0.91

0.08**

0.47*

0.04**

**p<0.01

*p<0.05

EGPAF M&E results from 8 African countries:

Entry Point	# infants tested (% of all infants tested)	HIV-infected infants percent	Percent HIV-infected started on ART
PMCT	15,493 (85.4%)	3.2% (494/15,493)	95.1% (470/494)
Maternity	1,078 (5.9%)	1.1% (12/1,078)	66.7% (8/12)
Pediatric Inpatient	526 (2.9%)	15.2% (80/526)	86.3% (69/80)
Immunization	412 (2.3%)	2.9% (12/412)	83.3% (10/12)
Outpatient	265 (1.5%)	17.7% (47/265)	87.2% (41/47)

Connectivity is the ability to connect a diagnostic instrument to a server, providing a cost-effective way to routinely monitor the performance of a decentralized fleet of POC instruments.



Benefits of connectivity:

- Monitor diagnostic instrument performance (e.g. downtime, IQC failures, warranty)
- Monitor supplies and avoid stock outs (e.g. cartridge consumption)
- Possibility to send testing statistics to LIMS or electronic registers
- Secure, encrypted data transfer with no patient identifiers (only the sample number)
- Password-protected access for different types of users (e.g. MOH, partners, etc.)

Common elements of a connectivity solution:



Connectable instrument that produces electronic data



Means to transmit data from the instrument to a server (LAN, or modem using 3G, Wi-Fi, or SMS)



A secure, cloud-based server



Software platform that receives and displays data



Users who interpret data and take action as needed (e.g. train staff, order supplies, etc.)

Consistent delivery of accurate and reliable test results requires strong supportive systems, including a quality assurance (QA/EQA) system, that address all aspects of testing.



Countries that have successfully implemented POC testing have built or strengthened systems and structures for:

- Criteria-based ***site and product selection***, including site capacity assessments and upgrades
- ***Training and certification*** to ensure the competency of health facility staff and instrument operators
- Frequent ***site monitoring, competency assessments and mentoring*** using standardized tools and checklists
- Provision of standardized ***training materials, testing algorithms, standard operating procedures, and job aids***
- Reliable and accurate ***procurement, supply chain management, and waste disposal***
- ***Connectivity*** for instrument monitoring and results reporting
- ***External quality assurance (EQA)***, such as proficiency testing

Summary

- Early HIV testing, prompt return of test results, and rapid initiation of treatment are critical for reducing morbidity and mortality among HIV-infected infants.
- Studies and early routine use of POC EID have demonstrated that incorporating this innovative technology into laboratory networks significantly improves testing, diagnosis and treatment initiation in infants.
- Cost analyses and cost-effectiveness modeling have shown that the total cost of POC is comparable to lab-based testing; and that POC improves survival and is cost-effective.
- National ministries of health, donors, and other implementers should consider introducing or expanding the use of POC EID testing as a key tool in their efforts to end pediatric AIDS.

Thank you



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References for conventional EID test return rate.

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