Elizabeth Glaser
Pediatric AIDS Foundation
Fighting for an AIDS-free generation

Welcome to EGPAF's Evidence to Action Webinar: Point-of-Care Diagnostics

February 19, 2020

Agenda

- Point-of-Care (POC) Molecular Testing for Priority Populations: Early Infant Diagnosis (EID) and Beyond (Rebecca Bailey, Associate Director, Innovations, EGPAF)
- Health System Investment for POC EID (Sushant Mukherjee, Associate Director, Program Cost Analysis, and Rantimi Adetunji, Sr. Program Officer, Economic Evaluations, EGPAF)
- POC for Birth Testing, Eswatini (Philisiwe Khumalo, Research Associate)
- Getting Us to The Next 95 (Judith Kose, Regional Senior Technical Advisor - Pediatric HIV)
- Discussion

Webinar Engagement

- Every participant joining remotely is automatically muted to avoid feedback, but we are happy to hear all of your questions and comments! Here's how to engage:
  - **Joining on your computer: a Q&A box should appear at the bottom of your screen** – open it up to ask a question at any time during this webinar. Questions for our presenters will be brought to our moderator's attention during the discussion portion. Questions on connectivity/sound quality will be handled immediately.
  - **Joining on the phone: press *9 to "raise your hand"** this will notify a host to unmute your line. We will unmute calls one at a time, so wait until you hear the "unmuted" announcement to begin speaking.
  - If you have any questions or concerns regarding the Zoom technology you can ***chat* with the host, Sarah Denison-Johnston**, privately. For any issues rejoining, send a note to publicatons@pedaids.org.

Point-of-Care Molecular Testing for Priority Populations: Early Infant Diagnosis and Beyond

Rebecca Bailey

Time is of the Essence: Viremia in Pregnant and Breastfeeding Women (PBFW) and HIV Infection in Infants

Infant Virologic Testing (IVT)

- Peak mortality among HIV-infected infants infected in-utero at 8-10 weeks
- The World Health Organization (WHO) recommends return of IVT results no later than four weeks following sample collection
- Due to the need for rapid intervention, WHO recommends POC for IVT
- Recommended in PEPFAR COP

PBFW

- Risk of viremia during pregnancy and breastfeeding appears higher than pre-pregnancy (1.8 and 2.0 times higher)
- 22% of pregnant women who achieved viral load suppression (VLS) will become viremic
- 20% of pregnant women are viremic at time of delivery
- Viremia, particularly in third trimester and while breastfeeding → negative impact for woman, increased risk of mother-to-child transmission (MTCT)

Laboratory-based IVT and VL: The Current Situation

Step 1

Specimen collection at health facility

Step 2

Sample transport to laboratory

Step 3

Analysis at the laboratory

Step 4

Result return to health facility

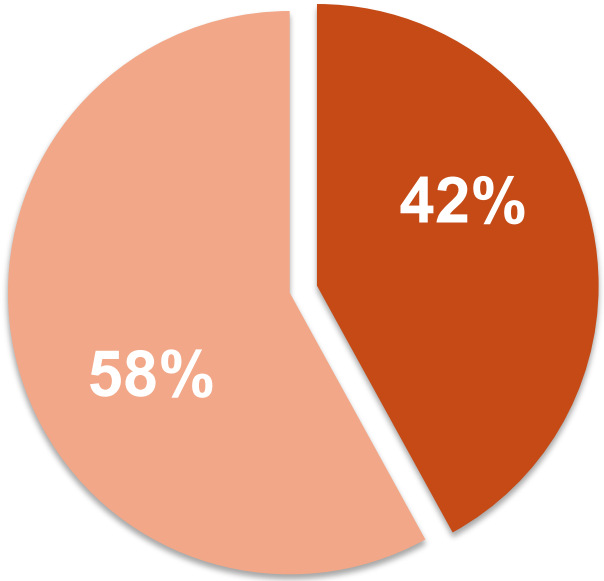
Step 5

Result return to caregiver/patient

Timeframe: 30-90 days

With Centralized, Laboratory-based EID Testing Many Infants Never Get Results

Based on a weighted average of nine studies, as well as monitoring and evaluation (M&E) data, 42% of **EID** test results are <u>not</u> received by the patient



- Wasted reagents
- Wasted human resource (HR) time
- Unnecessary repeat testing
- Infants lost to follow-up (LTFU) before receiving results
- Poor linkage between testing and care and treatment
- High infant mortality

Opportunity: POC NAT Diagnostics with WHO Prequalification Status

Opportunity

- Point-of-care and near point-of-care
- Largely automated and simple to operate
- Run times 52-92 minutes
- Battery power-operated
- Accurate

Challenge

- More expensive per test (but not per result)
- Issues with breakdowns and service
- Supply chain (cartridge short shelf life)
- Quality assurance (QA)

Need for complementarity with current system

- Integration considering existing resources
- Optimize access
- Build scalable model

Abbott M-PIMA

Cepheid GeneXpert

Strategy: Integration with Existing System

Step 1: Determine EID access goal: Turnaround time (TAT) to caregiver, percent results returned, percent HIV-infected infants initiated on antiretroviral therapy (ART) etc…

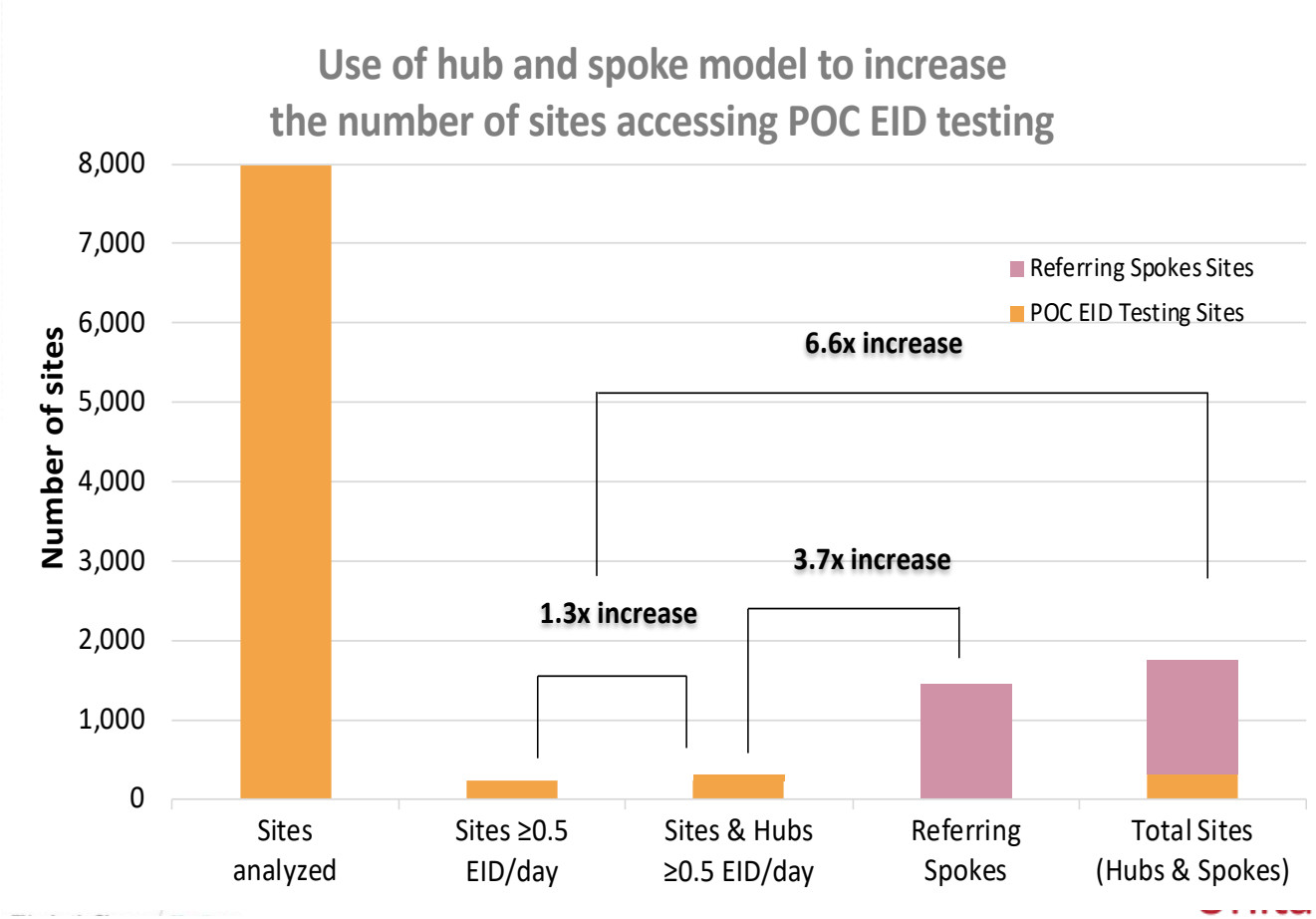
Step 2: Assess current EID landscape

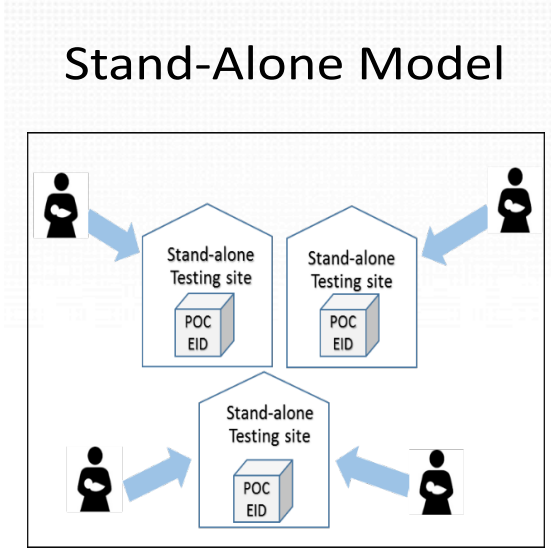
- Include both central lab-based and POC products
- Include key indicators: distance to currently-available testing, TAT to caregiver, percent results returned, demand, other testing demand at a given site
- Software such as Lab EQIP can help during this stage

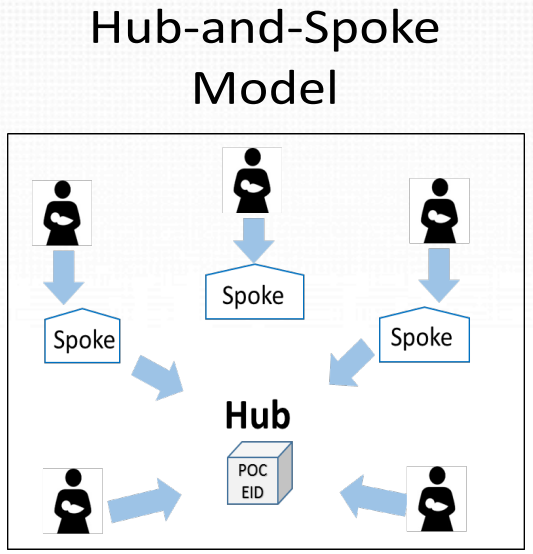
Step 3: Make a plan to close the gap between your goal (*Step 1*) and your mapping of the current landscape (*Step 2*)

- Use POC if current conventional system is not meeting goals
- First, access existing POC sites (consider: capacity of platform, HR, distance and sample transport needs, waste management)
- Next, place new POC NAT if necessary (consider: demand, ability to refer additional samples from nearby sites, site infrastructure and HR—tools like the modified SPI POCT check list can help)

Strategy: Optimizing Access







Strategy: Building a Sustainable Model

Pre-implementation site assessment

- Identify staff who will be involved in POC EID
- Identify site upgrade needs
- Patient flow considerations
- Sample transport

Use existing HR when possible and task shift

- Nurses and even nurse assistants may help run samples

Pragmatic trainings

- Ensure staff from all entry points attend to increase use

Integrate site-monitoring into existing systems

- Recommend at least quarterly
- Can help with QA by including operator observations

The Evidence for POC IVT (Infant Virologic Testing): Results from Implementation Study in 9 Countries

(Cameroon, Cote d'Ivoire, Eswatini, Kenya, Lesotho, Mozambique, Rwanda, Zambia, Zimbabwe)

	Conventional EID (N=102 sites, n=3,082 tests)	POC EID (N=1574 sites, n=126,789 tests)	p value
Median TAT from blood sample collection to result returned to caregiver (IQR)	50 days (31-71)	0 days (0-1)	p<0.001
Results received by caregiver within 30 days	19.2 %	96.9%	p<0.001
HIV-infected infants started on ART within 60 days of sample collection	41.5% (44/106)	92.2% (3,990/4,327)	p<0.001
Median TAT from blood sample collection to ART initiation for HIV-infected infants (IQR)	50 days (30-68)	0 days (0-1)	p<0.001

But is it Affordable? Cost per Test Result Returned

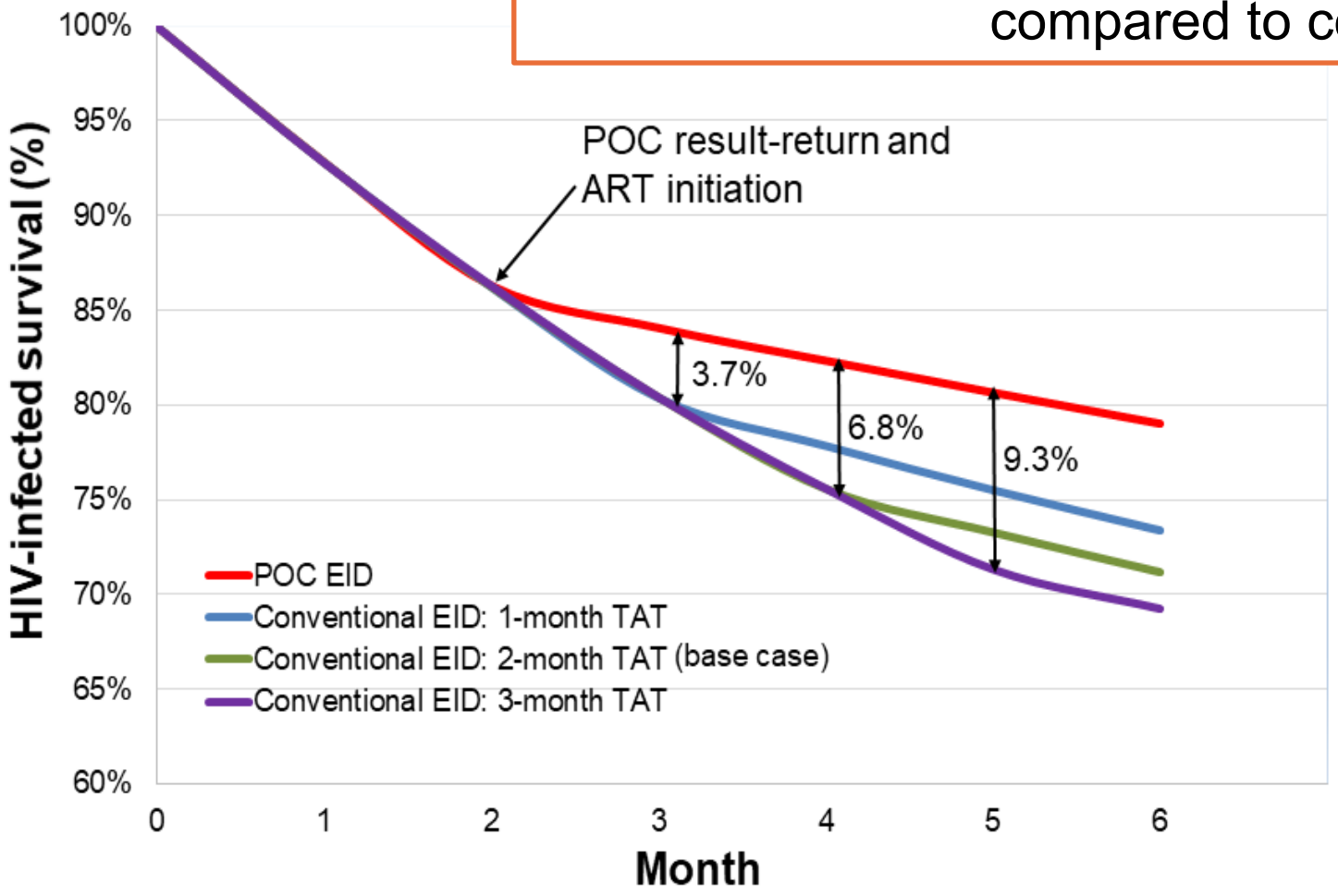
- Current conventional reagents are approximately $10, while the price of POC EID cartridges range from $14.90 to $25.

- ***BUT*** what truly matters is **cost per test result returned**, so clinical action can be taken (and time and resources are not wasted).

	Conventional	POC (current throughput)	POC (optimal throughput)	Cepheid ($0.96 S&M surcharge)	M-PIMA ($20 reagent rental)
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)	$21.66	$21.64
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)	$21.31	$21.29

Cost-Effectiveness

Cost-effectiveness 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.



Incremental cost-effectiveness ratio (ICER) vs conventional for year of life saved: $630 USD

Is It Acceptable to Frontline Health Care Workers?

Indicator	Post-intervention (175 health care workers)
Occupation	35.9% nurses 4.8% midwives 29.5% lab technicians 5.8% nurse assistants 5.1% doctors 19.2% other
Compared to conventional EID, how complicated do you consider drawing blood into specimen container for POC EID machine?	12.8% More complicated 11.7% no difference 71.3% less complicated 4.2% other
How complicated do you consider running the POC EID machine?	1.75% very complicated 10.6% somewhat complicated 5.3% neither easy nor hard 8.8% somewhat simple 73.7% very simple
Compared to conventional EID, how does POC EID affect your ability to care for HIV-exposed infants?	93% improves ability to care 6.3% no difference 0% decreases ability to care 0.7% other
Compared to conventional EID, how has patient flow changed as a result of POC EID?	3.8% more difficult flow 48.7% no difference 44.2% easier flow 3.2% other
Based on what you know about POC EID, do you recommend country increase use of POC EID?	100% yes 0% no 0% other

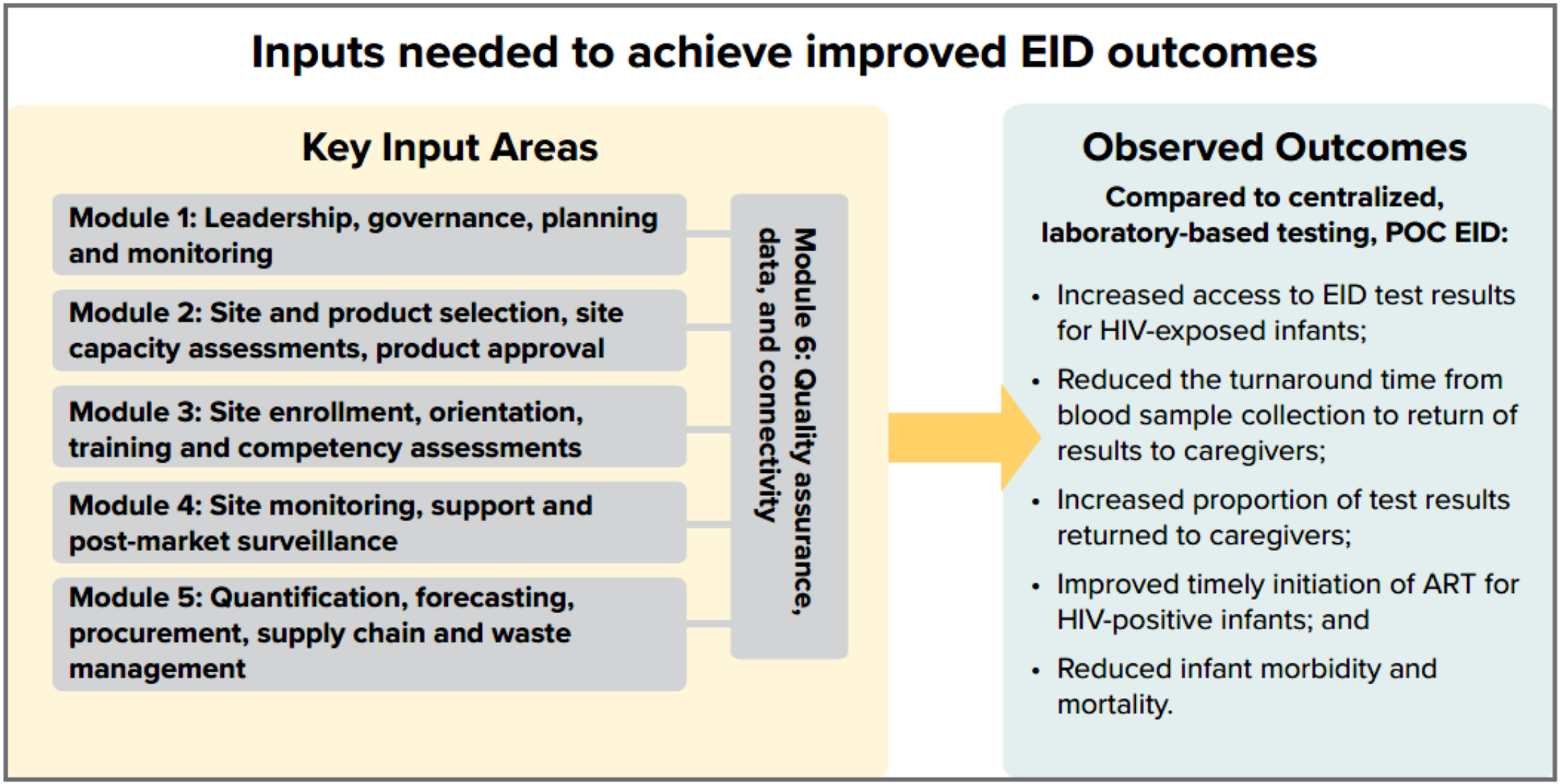
The Future: Other Groups Who May Benefit From POC VL

Group	Rationale
Children	• Lower rates of suppression (62%), and higher rates of resistance • Limited therapeutic options, so making a regimen change before additional drug resistance mutations are accrued is critical • More rapid clinical progression than adults
Patients with advanced HIV disease	• Higher risk for treatment failure • Patients with active opportunistic infections experience improved clinical outcomes, including reduced risk of disease progression and death, with urgent ART and viral suppression
Confirmatory VL after initial detectable VL	• Patients with confirmed virologic failure switch long after initial viral load detection (only 50% made a switch after 2 years in one study) or may not switch at all. • During this time, disease may progress, increasing risk of acquisition of drug resistance mutations. • In draft PEPFAR COP20 guidance

Conclusions: POC NAT Is a Game-Changer

- POC IVT and VL lead to prompt return of test results and rapid initiation of treatment. It may also reduce morbidity and mortality among persons living with HIV (PLHIV) and improve prevention of mother-to-child HIV transmission (PMTCT)
- Modelling demonstrates that POC IVT is cost-effective and saves lives.
- POC NAT testing is feasible and may be integrated into current system to optimize laboratory testing for PLHIV, and beyond.
- Improved prices and all-in pricing models will improve affordability and sustainability, potentially accelerating uptake.
- Governments, implementers and civil society organizations should move toward appropriate coverage of POC NAT for IVT, PBFW and follow-up VL after a detectable VL, using the COP20 process and Global Fund funding cycle to support scale-up
- Diagnostic integration offers the opportunity to provide patient-centered care and also improve platform utilization, thus improving value for money
- **Impactful, scalable, cost-effective – the right ingredients to go to replicate**

POC EID Lessons Learned: Guidance and Tools



Set of six modules with links to guidance and tools on: www.pedaids.org

Health System Investment for POC EID

Sushant Mukherjee and Rantimi Adetunji

Background on Costing and Cost-Effectiveness (C/E) Work

- Conducted detailed cost analysis in Zimbabwe to understand resources required to implement and scale up POC EID
- Implementation costs incorporated into C/E modeling (led by CEPAC group based at Harvard/Mass. General), comparing POC EID to centralized EID
- Initiated time-use study in Zimbabwe to directly observe health workers (HW) operating POC EID to better understand the impact of POC EID on HW workload
- Conducted detailed cost analysis of **strengthened** conventional EID network in Kenya—incorporated into C/E model to assess whether it is more cost-effective to do POC EID or to strengthen existing centralized EID networks

Costing Assumptions and Scenarios

Base Case Assumption on Daily EID Volume

- Volume is a key driver of cost per test.
- We assumed average EID volume of 1.5 tests per day for the base case (based on observed demand from Oct. 2017 to Sept. 2018) and varied for sensitivity analysis.
- Base case estimate is conservative since it does not consider anticipated increased demand for testing at additional ages (e.g. birth and nine months).

Costing Assumptions and Scenarios

Scenario Analysis

We assessed costs for two models: Abbott mPIMA and Cepheid GeneXpert IV

A. For mPIMA, we used two scenarios:

1. Platform is purchased
2. Platform is leased (reagent rental) with a commitment to reaching a minimum volume of tests

B. For GeneXpert IV, we used three scenarios:

1. Platform purchased with gel battery
2. Platform purchased with solar battery
3. No equipment cost for contexts where GeneXpert is already in place for TB diagnosis

Time-Use Study: Human Resource Needs for POC EID

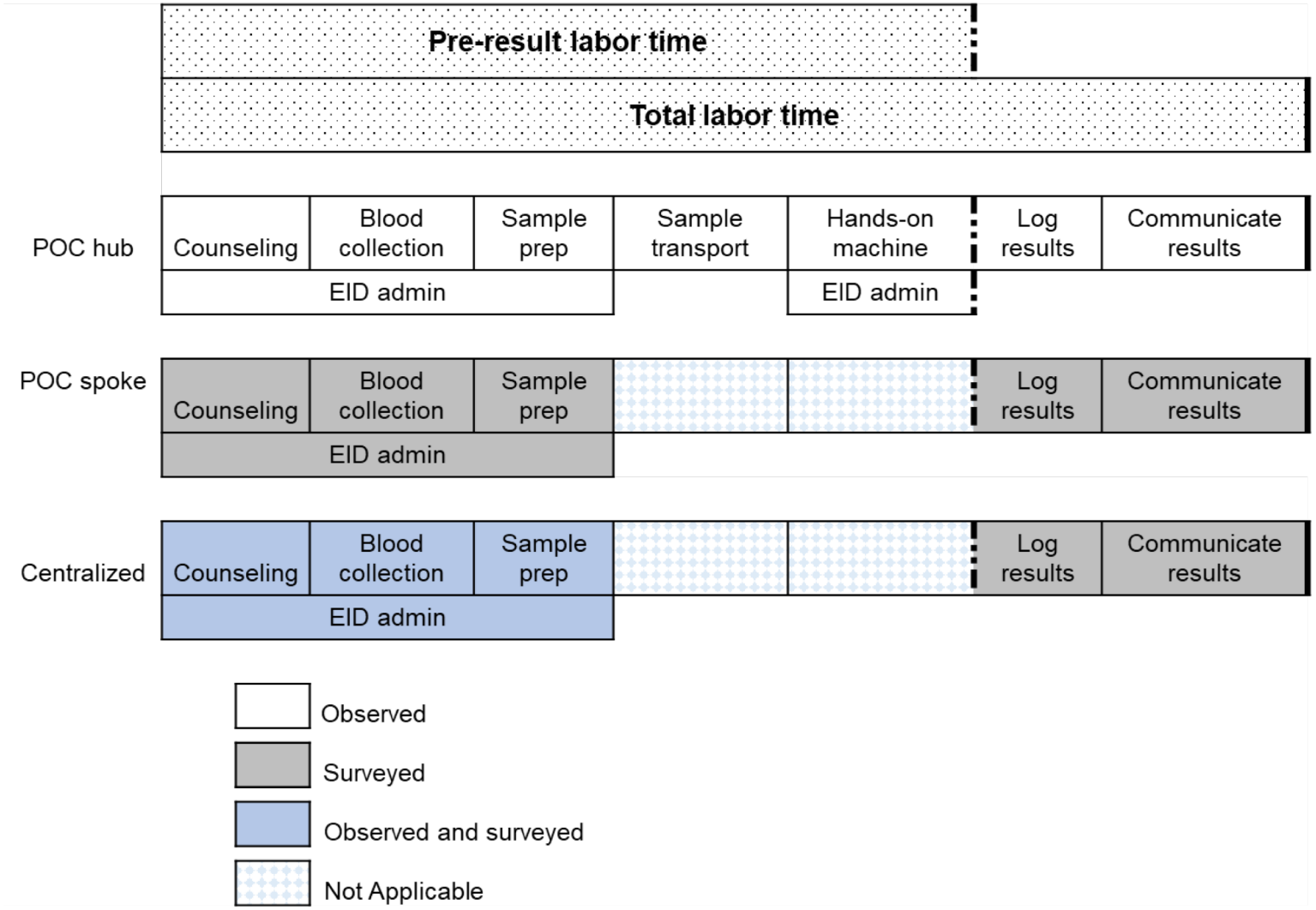
Research question:

What is the human resource labor time associated with the use of EID platforms by front-line health workers?

Time-Use Study: Methods

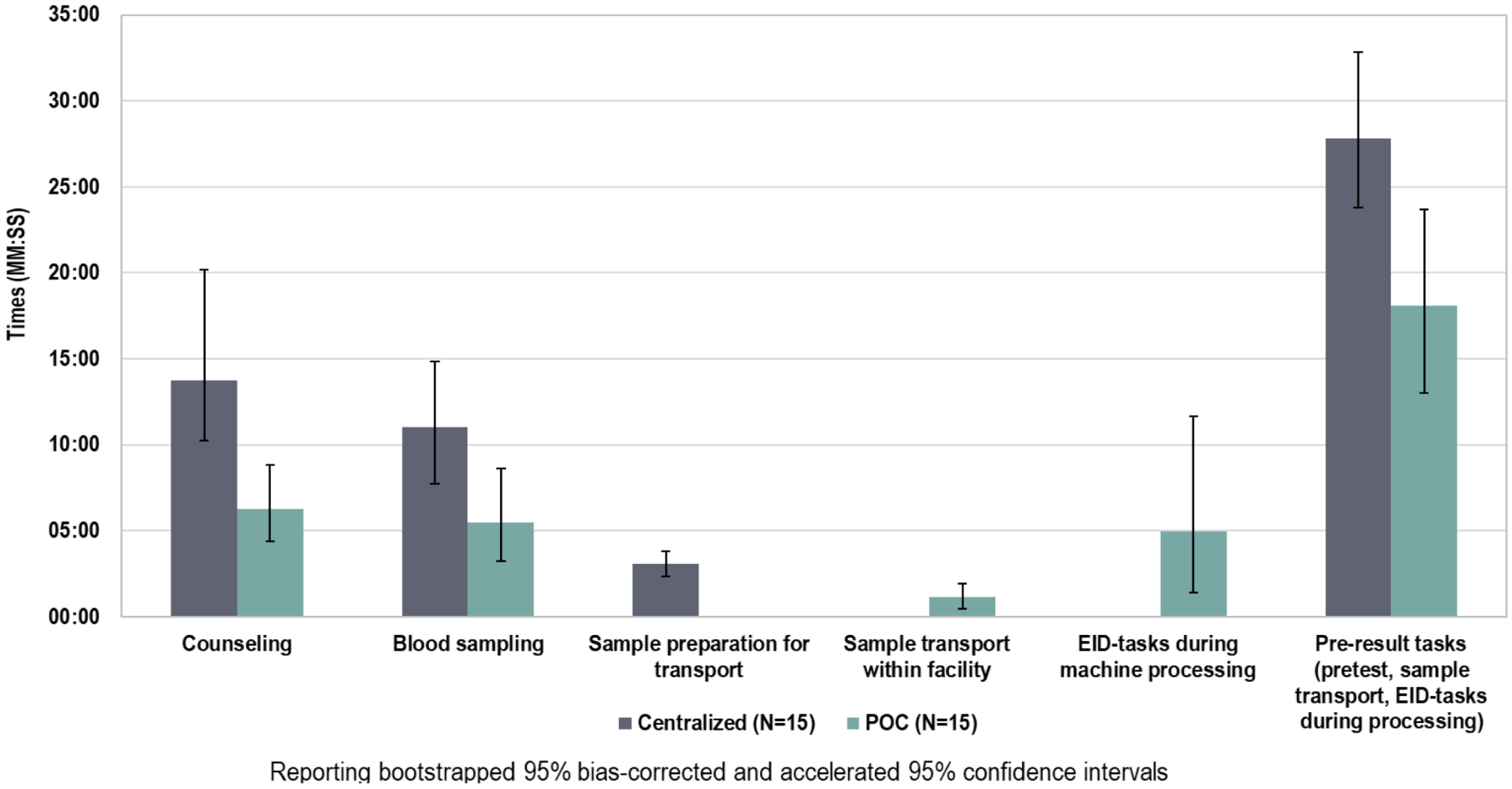
- Observed 30 EID processes at five POC hub and 11 centralized EID health facilities in Zimbabwe
- 30 health workers self-reported time for EID tasks at nine POC spokes and 11 centralized EID health facilities

Time-Use Study: Methods



EID tasks were aggregated into **pre-result** and **total** labor time

Time-Use Study: Observed Times



- Mean time for POC **pre-result** tasks was 9 min, 42 secs lower (statistically significant)
- Self-reported time estimates for non-observed tasks was not different.
- Thus, use of POC likely less time-consuming than centralized EID for frontline HWs.

Results: Total Cost per Test

mPIMA (Platform Purchase)	mPIMA (Reagent Rental)	GeneXpert Solar	GeneXpert GeI	GeneXpert No Equipment
$44.55	$25.89	$27.70	$27.27	$23.85

Cost Categories:

- ✓ Materials and Supplies
- ✓ Training
- ✓ Supervision, Monitoring, and QA
- ✓ Facility Upgrades and Repairs
- ✓ Equipment
- ✓ Labor
- ✓ Freight and Shipping

- Supplies (esp. cost of cartridge) comprised 73-74% of costs and equipment comprised 14-20%.
- Data is important for budgeting and planning for POC EID scale-up.
- Reagent rental scenario for mPIMA shows value in negotiating contracts where manufacturer responsible for providing equipment, service, and maintenance, in exchange for minimum volume commitments.

Cost/Effectiveness Modeling Results

- CEPAC modeling determined that POC EID was **cost-effective** relative to centralized EID.
- Model outcomes included survival, life expectancy, and mean lifetime per-person treatment cost.
- Incremental C/E ratio (ICER) for POC vs. centralized was $680 per year life saved.
- WHO-accepted definition of C/E indicates that an intervention with ICER < GDP per capita is considered very cost effective.
- Zimbabwe's GDP per capita in 2016 was $1,010; thus, POC is seen as very cost effective.
- Model determined that POC would remain C/E even if costs rose to $60 per test, well above even the highest-cost scenario estimated via costing (mPIMA with equipment purchase)

Comparing Strengthened Centralized EID to POC EID

- Donors and other stakeholders have flagged that POC EID may not be necessary if countries can invest in strengthening existing centralized EID to improve result return times and initiation on ART
- Compiled costs of strengthening centralized EID in Kenya (more frequent sample transport, more lab technicians at central labs, better SMS printer coverage)
- Full results to be presented at CROI

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POC for Birth Testing in Eswatini

Philisiwe Khumalo

Background

- Eswatini piloted POC NAT HIV testing at birth in three maternities, since **August 2017**:
  - Mbabane Government Hospital (national referral hospital)
  - Good Shepherd (regional referral hospital)
  - Hlathikhulu Government Hospital (regional referral hospital)
- **All three maternity birth testing sites**
- Provide labour and delivery, caesarean sections, neonatal, postnatal and PMTCT services
- Basic maternity services are free, but additional services may have a fee (Good Shepherd charges a fee for extra inpatient days)
- The POC platform at Hlathikulu was shared with the Public Health Unit (PHU) to also run EID tests as needed (same hospital compound, different building)

POC Birth Testing Services Offered at the Three Sites

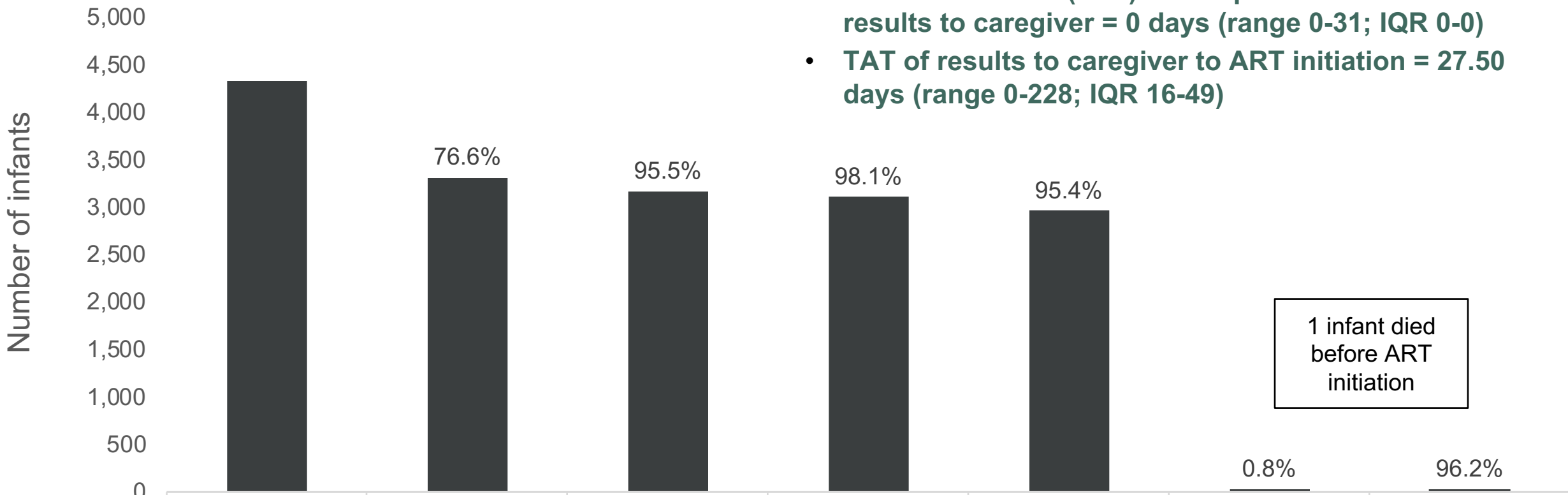
- Tests were offered to HIV exposed infants within 72hrs after delivery
  - All infants born to HIV-positive mothers were eligible for the test
- Tests took approximately 1 hour to run
- Only one test could be run at a time
- In case of an error, the POC platform produced an invalid result;
  - Lead to delays if test needed to be run again
- Phlebotomists were the primary operators of the POC platforms (normal work hours were approx. 8.00am – 16:45pm),
  - Nurses/midwives also performed tests, especially at night and on weekends
- However, maternities are generally understaffed
  - Nurses/midwives prioritized deliveries than testing infants for HIV
- Clinical guidance for infected infants is to initiate children on NVP based regimen as soon as possible and switch to LPV/r based regimen at 14 days

Data Collection

- Prospective data were collected on tests occurring August 1, 2017 through November 30, 2018
- Six-month retention data among infants testing HIV-positive at birth and re-testing at 6-8 weeks among infants testing HIV-negative at birth data were also abstracted from facility-based medical registers and electronic databases including:
  - Laboratory Information System (LIS)
  - Client Management Information System (CMIS)
- A combination of variables including name and surname of infant, birth testing barcode, date of birth, CMIS number, ART number, name of birth testing facility, were used to link records across registers and databases

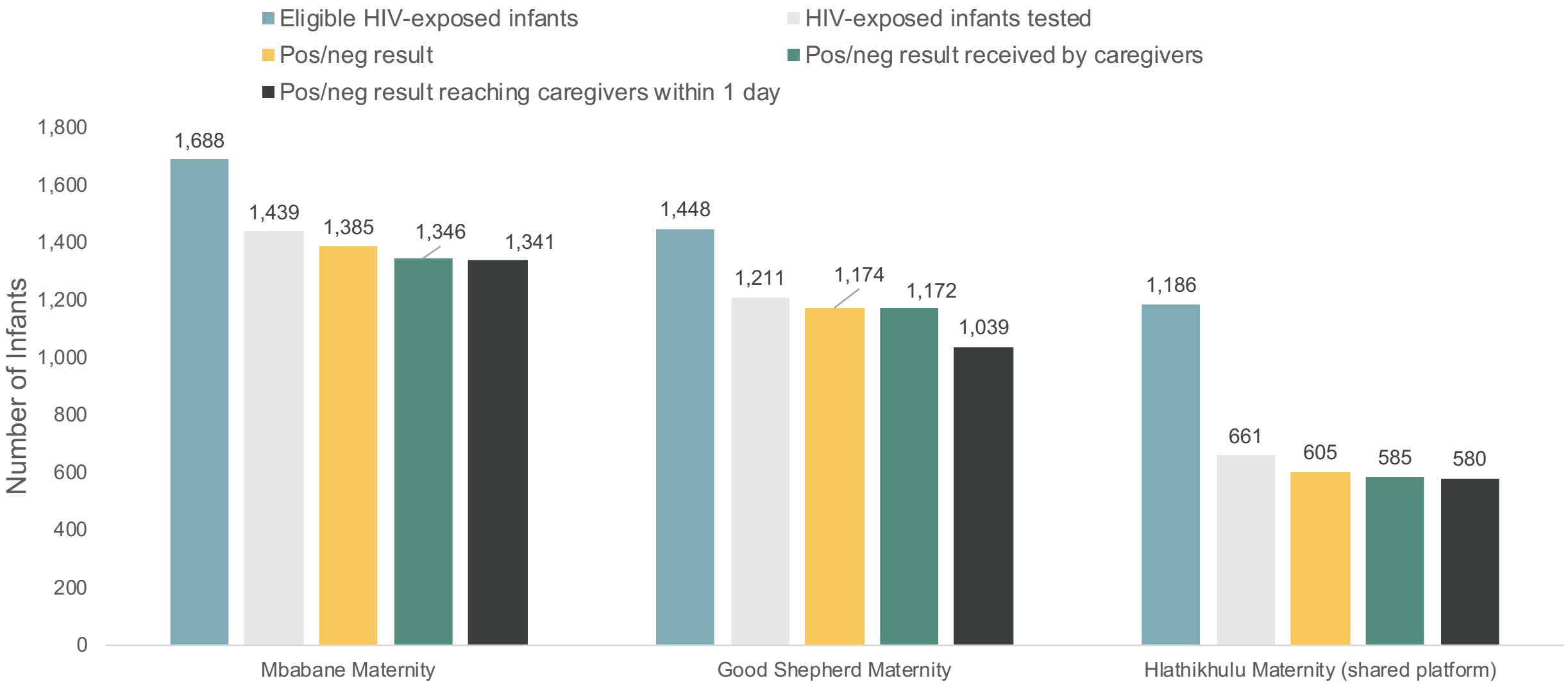
POC Birth Testing Data (August 1, 2017 through November 30, 2018)

- **Turnaround time (TAT) of sample collection to results to caregiver = 0 days (range 0-31; IQR 0-0)**
- **TAT of results to caregiver to ART initiation = 27.50 days (range 0-228; IQR 16-49)**

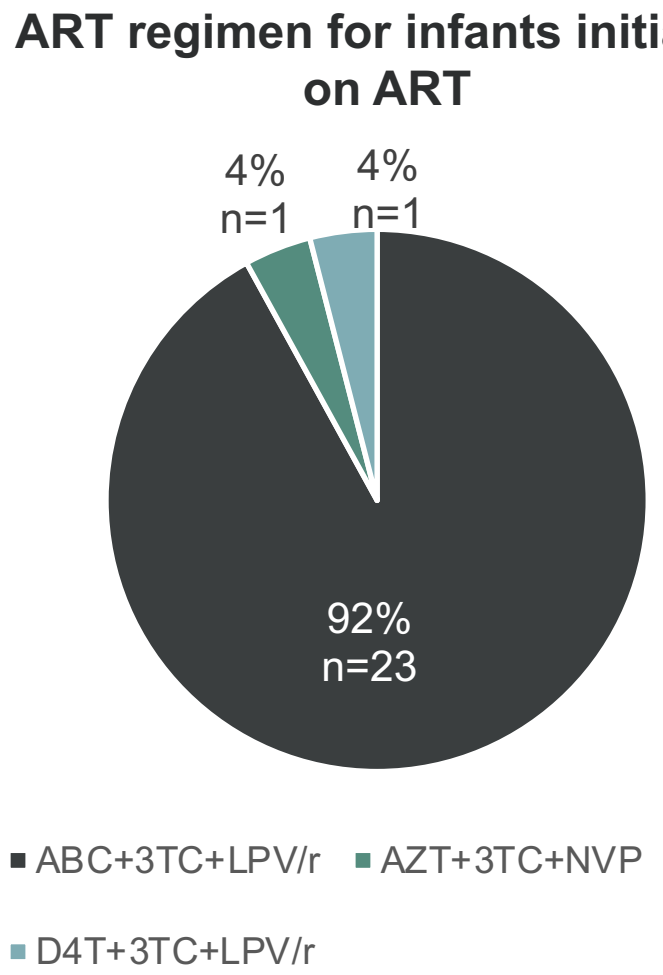


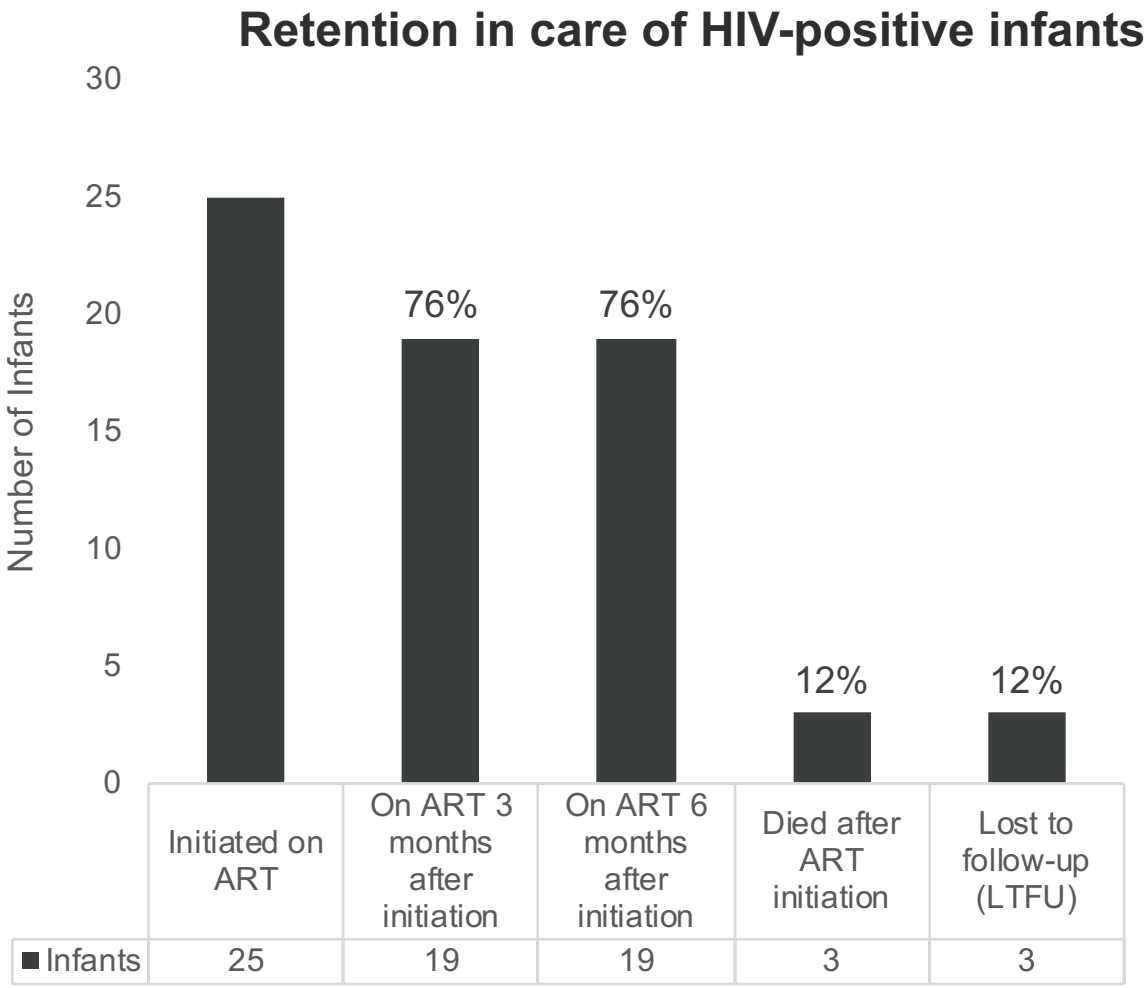
	Eligible HIV-exposed infants	HIV-exposed infants tested	Positive/negative result	Positive/negative result received by caregivers	Positive/negative result reaching caregivers within 1 day	Tested HIV-positive	Initiated on ART
Overall	4,322	3,311	3,164	3,103	2,960	26	25

Testing Data by Site (August 1, 2017 through November 30, 2018)

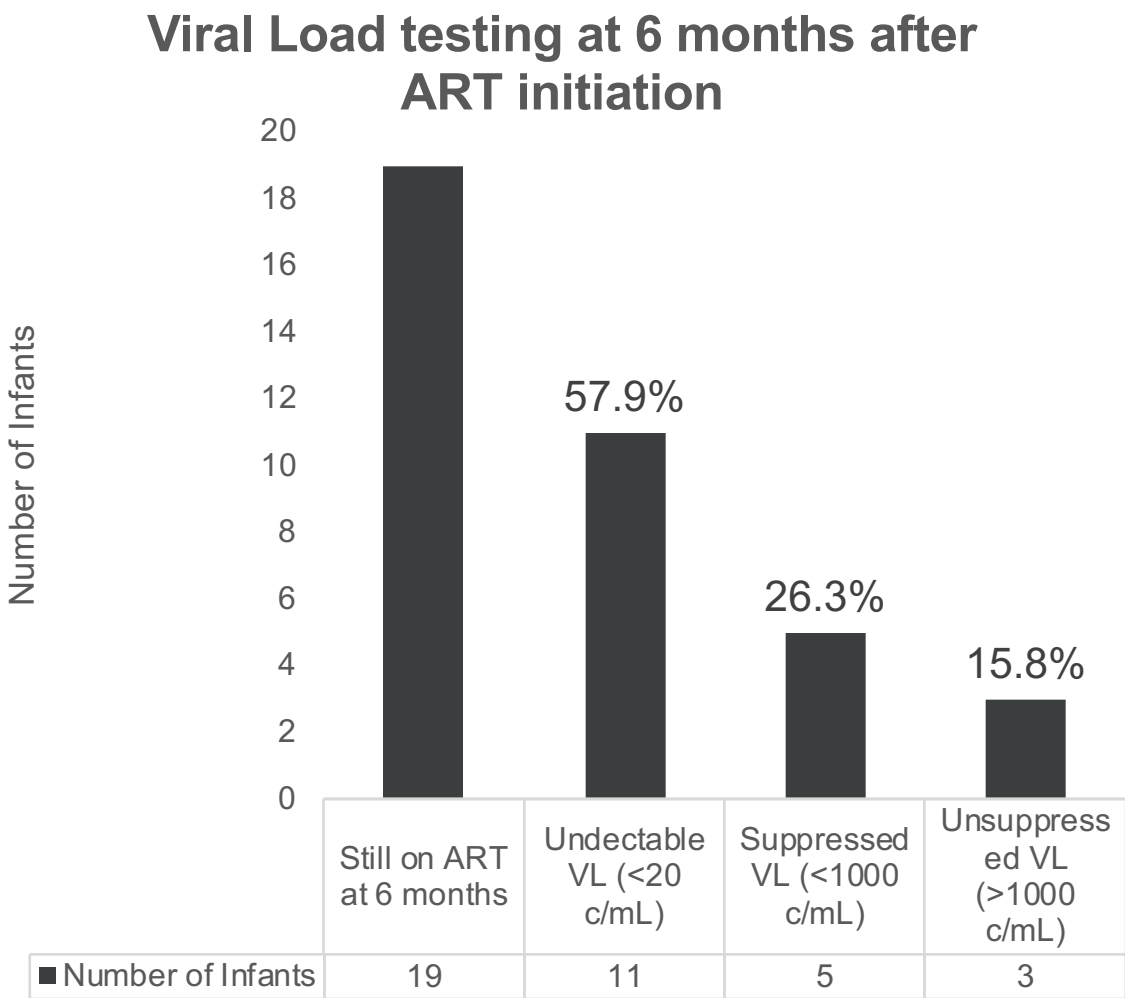


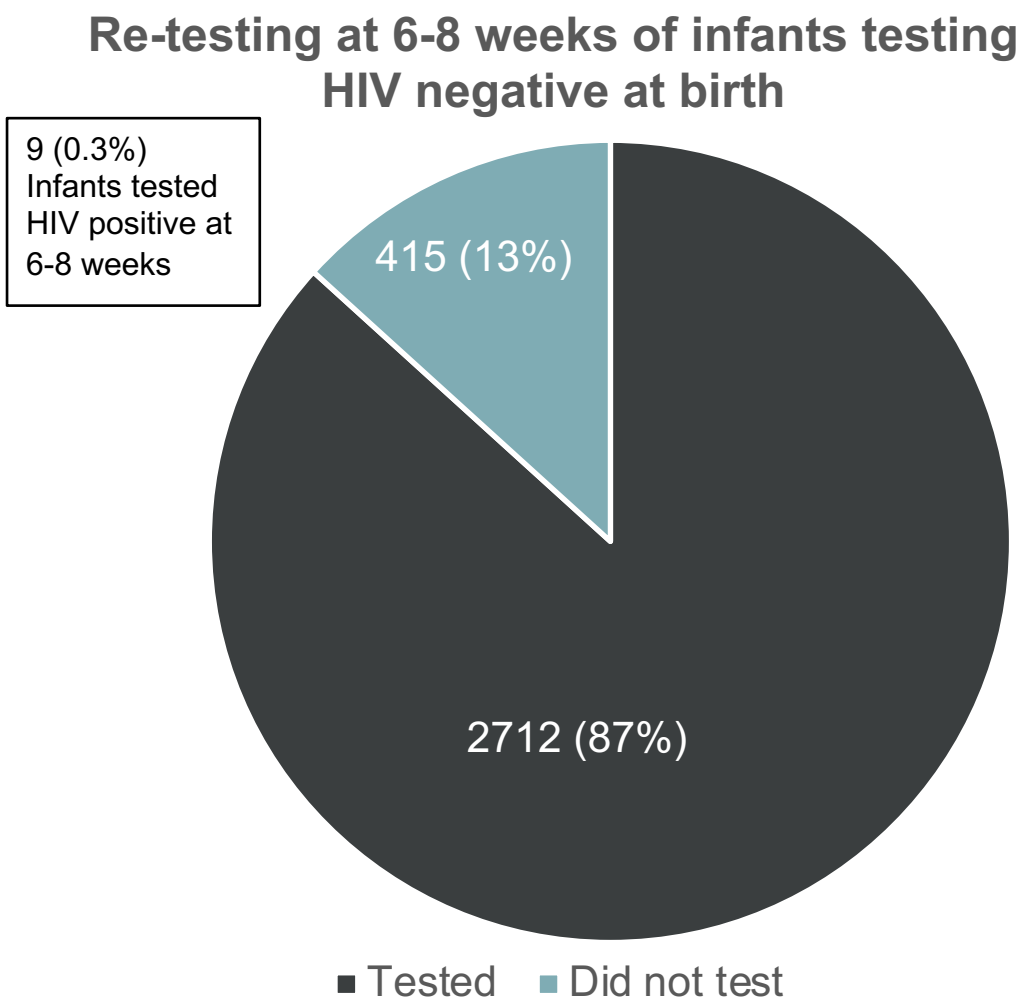
ART Regimen and Retention in Care among Identified HIV-positive Infants





Viral Load Testing at 6 Months after ART Initiation





Lessons Learned

- **Need for strong leadership and governance**
  - Have the MOH take leadership and ownership to advocate for the program, collaborate with implementing partners and communicate with health facilities
- **Provide consistent and structured supervision and mentorship for sites**
  - Training and refresher training for nurses to identify HIV-exposed infants, sensitize mothers on birth test, perform tests (particularly on weekends)
  - Institute continuous quality improvement activities
  - Conduct feedback meetings with health workers to discuss performance of site on birth testing
  - Monitor the use of platforms to run tests; platforms used by multiple people tend to produce high rate of errors
- **Strengthen M&E systems to track eligible infants throughout the EID cascade, through subsequent tests, in different or multiple health facilities**
  - Track and document reasons for not testing & receiving results
  - Sensitize and orient other health facilities about M&E systems

Opportunities

- Providing testing where it would also be possible to initiate ART for infants
- Provide a well-structured counselling package for women
- Engage male partners; women struggled deciding on testing infants without consent of the father
- Provide additional personnel/phlebotomists: maternity units are the busiest in the health facilities, and generally understaffed

Conclusion

- Birth testing can reduce turnaround times for testing, results reception by caregivers and initiation on ART
- Birth testing implementation underscored needed improvements in the EID cascade, particularly:
  - Identification and testing of all eligible HIV-exposed infants
  - More rapid ART initiation of those found to be HIV-positive
  - Stronger follow-up strategies of HIV-negative infants at birth for subsequent EID services
- Given high risks of AIDS-related infant mortality, soonest possible linkage to ART among HIV-infected infants is critical


Undetected
Undetected
Undetected

Getting to the Second “95” Pediatric ARV Initiation

Dr. Judith Kose | February 19, 2020

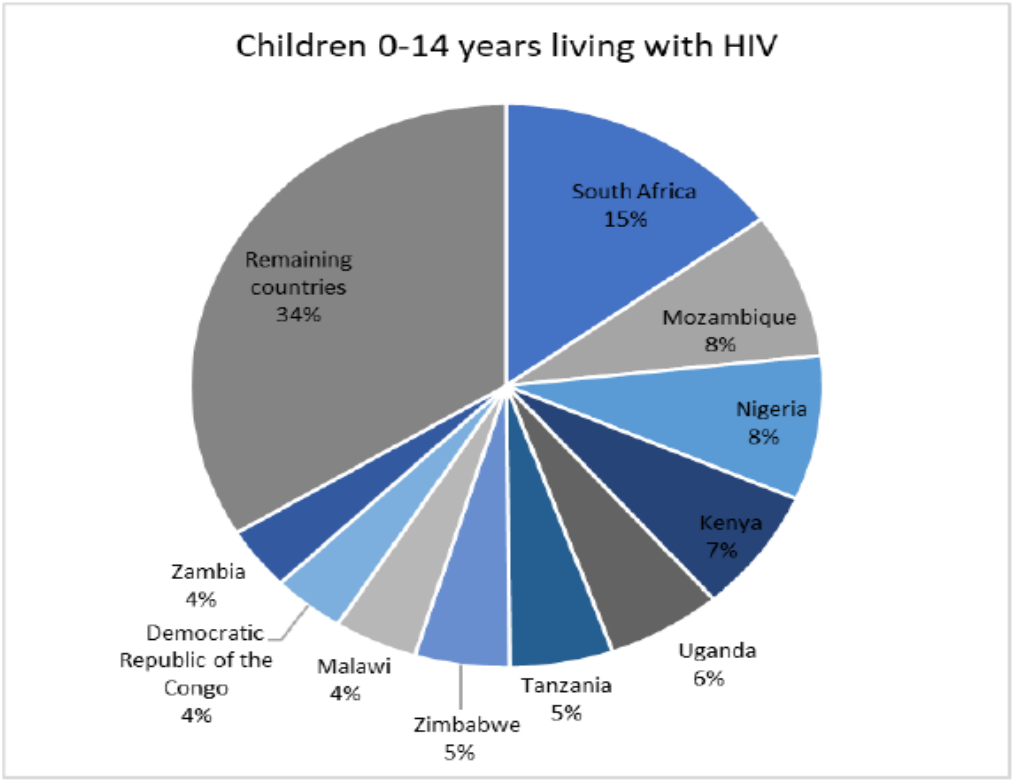
State of the Epidemic

- Two out of three CLHIV (age 0–14) are in East and Southern Africa
- 50% are in just six countries

Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
Total	37.9 million [32.7 million – 44.0 million]	1.7 million [1.4 million – 2.3 million]	770 000 [570 000 – 1.1 million]
Adults	36.2 million [31.3 million – 42.0 million]	1.6 million [1.2 million – 2.1 million]	670 000 [500 000 – 920 000]
Women	18.8 million [16.4 million – 21.7 million]	–	–
Men	17.4 million [14.8 million – 20.5 million]	–	–
Children (<15 years)	1.7 million [1.3 million – 2.2 million]	160 000 [110 000 – 260 000]	100 000 [64 000 – 160 000]

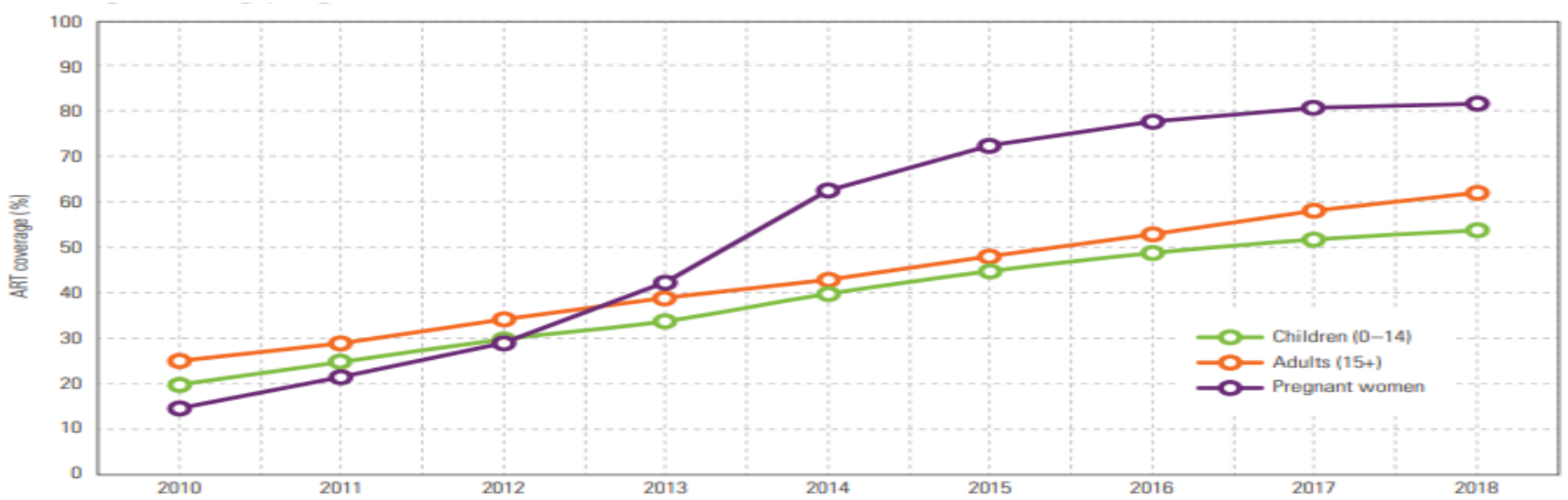
Source: UNAIDS/WHO estimates



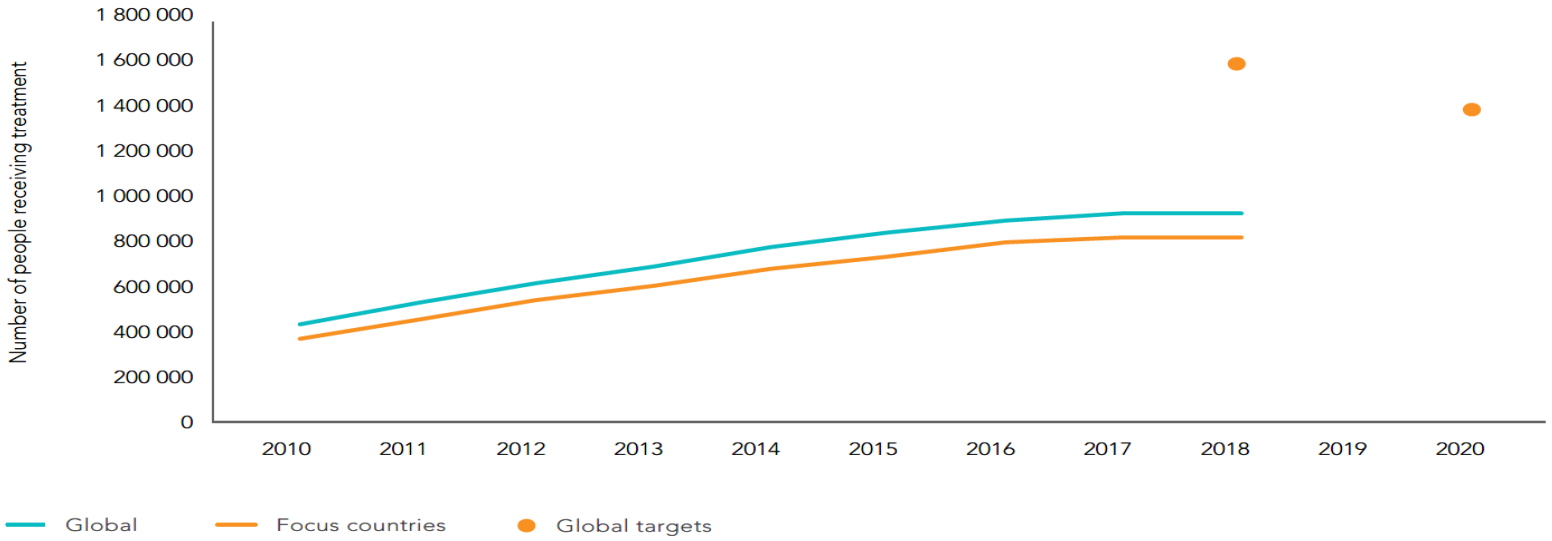
Slow Progress on Coverage for CLHIV

- ART coverage levels have not increased in the last two years despite understanding what works.
- In 2018, about 940,000 children age <15 years were receiving ART globally, an increase from about 430,000 in 2010 (54% [37-73] of CLHIV are receiving ART).
- In 2018, regionally, coverage of ART for children ranged from 28% in West and Central Africa to 91% in South Asia.
- Early diagnosis and treatment are particularly critical to infant survival:
  - The *"Children with HIV Early Antiretroviral Therapy"* study from South Africa demonstrated a 76% reduction in mortality when treatment is initiated in the first 12 weeks of life.
  - Countries have made progress in expanding access to early infant HIV-testing services, but testing rates are still low.

ART Coverage Among Children (0–14 Years) and Adults (>15 Years), and Lifelong ART Coverage Among Pregnant Women, 2010–2018



Number of CLHIV (Aged 0–14 Years) Receiving ART Globally and in 23 Focus Countries, 2010–2018



UNAIDS estimates 2019

Barriers to Pediatric ART Initiation

- Diversity and complexity of regimens across ages
  - Dolutegravir (DTG) approved as first-line and formulation available for those ≥20 kg
  - Awaiting DTG 10 mg dispersible tablet formulation
  - Often review of guidelines are not rapid or straight-forward and transition may cause delay
  - DTG dosing for initiation at two years of age currently under FDA review
- Capacity of programs/facilities/staff where the diagnosis is made (including point-of-care [POC] testing sites), and staff readiness to start treatment in children
- Delay in initiation due to presumptive TB and advanced disease cases
- Quantification of recommended regimens/formulations
  - Need to procure separately DTG 50mg and FDC for NRTIs for younger children and TB co-infected clients
- Neonatal ARV treatment regimen
  - Limited availability/access
  - Hesitance to move to raltegravir granules while waiting for DTG dispersible tablets
  - Lopinavir/ritonavir granules and ‘four in one’ data on use in neonates are not yet available

Effectively Getting to the Second "95": *Three Pillars of Recommendations*

1. Diagnostics

- Use of point-of-care (POC) EID increases linkage to care and shortens time to treatment initiation
- Expand differentiated HIV testing services—consider targeting specific age groups
- Refocus our case-finding and treatment efforts on school-aged children and adolescents
- Optimal mix of testing strategies to maximize identification of newly-infected children
- Operationalizing mother-infant linkage to improve case finding

2. Drugs (effective and palatable treatment options)

- Use of optimal ARVs will:
  - Reduce toxicity
  - Improve palatability/pill burden
  - Increase resistance barrier
  - Reduce drug interactions
- Safe use across different age groups and populations
- Reduce cost

Solution: New Pediatric Formulations

Table 1. Child-Friendly ARV Formulations by Age Group or Weight Band as Recommended in the WHO 2019 Guidelines

	Neonates 0 to 4 weeks	Children < 20kg	Children ≥20kg
Preferred	AZT and 3TC liquids plus RAL granules[1]	ABC/3TC ^{DT} plus LPV/r solid formulations[2]	$ABC/3TC_{DT}$ plus DTG_{AT}
Alternatives	AZT, 3TC and NVP liquid	$ABC/3TC_{DT}$ plus RAL_{CT}[3]	$ABC/3TC_{DT}$ plus LPV/r^{PT} or RAL_{CT} **or** TAF/FTC + DTG[4]
Special circumstances[5]	AZT, 3TC and LPV/r liquids	$ABC/3TC_{DT}$ or $AZT/3TC_{DT}$ plus EFV_{PT}[6] **or** $ABC/3TC_{DT}$ **or** $AZT/3TC_{DT}$ plus RAL_{CT} **or** $AZT/3TC/NVP_{DT}$	$ABC/3TC_{DT}$ or $AZT/3TC_{DT}$ plus EFV_{PT}[6] **or** $AZT/3TC_{DT}$ plus LPV/r_{PT} **or** $ABC/3TC_{DT}$ or $AZT/3TC_{DT}$ plus RAL_{CT} **or** $AZT/3TC/NVP_{DT}$

DT dispersible tablets; CT chewable tablets; PT paediatric tablets; AT adult tablets; : ABC abacavir, AZT zidovudine; DTG dolutegravir; EFV efavirenz; FTC emtricitabine; LPV/r lopinavir/ritonavir; NVP nevirapine; PI/r boosted protease inhibitor; RAL raltegravir; TAF tenofovir alfenamide; TDF tenofovir; 3TC lamivudine

[1] To be used until a solid formulation of RAL, LPV/r or DTG can be used

[2] LPV/r granules are approved for use from 2 weeks. LPV/r pellets can be used from 3 months. Children should be transitioned to LPV/r tablets from 10kg as soon as able to swallow them.

[3] RAL_{CT} above 4 weeks of age

[4] TAF/FTC only for use above 25kg

[5] In cases where no other alternatives are available

[6] EFV should not be used in children younger than 3 years of age

See dosing guidance at https://www.who.int/hiv/pub/guidelines/ARV2018update/en/ (Annex : Interim WHO ARV guidelines)
For guidance on formulation selection(see https://www.who.int/hiv/pub/paediatric/optimal-paediatric-arv-formulary/en/)

Solution: New Pediatric Formulations

Figure 2. Timeline for the expected approval of additional child-friendly ARVs [1]

2020				2021				2022
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
	LPV/r 4-in-1 granules (Cipla) DTG 5mg dispersible (ViiV) [2]		DTG 10mg dispersible[2]		LPV/r 4-in-1 granules (Mylan)		Abacavir-lamivudine-dolutegravir (ALD) 60/30/5 dispersible	

[1] Age/weight bands and appropriate dosing still to be determined.

[2] DTG 5mg and 10mg formulations must be administered together with a dispersible NRTI backbone.

Solution: New Pediatric Formulations

Consideration	LPV/r 2-in-1 (pellets and granules)	LPV/r 4-in-1 formulation	DTG Dispersible Tablet
Predicted date of approval	Approved	April 2020	June 2020 (originator) Sept/Oct 2020 (generic)
WHO guidelines	Accepted as alternative 1st line until DTG formulation/dosing available	Accepted as alternative 1st line until DTG formulation/dosing available	Recommended as WHO-first line when formulation/dosing available
Efficacy (with respect to VL suppression)	Superior (in children) to NVP	Superior (in children) to NVP	Superior (in adults) to other PIs (DRV/r)
Toxicity	Diarrhea	Diarrhea	Good
Palatability	Moderate (pellets are taste masked, but difficult to administer, granules have bitter after-taste)	Good (Cipla), moderate (Mylan – still a bit bitter)	Good
Resistance barrier	High	High	High
Use across age bands	Pellets from 3 months; granules from 2 weeks; LPV/r not recommended as first line in adults and adolescents	Expected that use can be from age 2 weeks (pending approval); LPV/r not recommended as first-line in adults and adolescents	Expected approval will be from 4 weeks (data already presented for >6kg and >6 months); 50 mg tab DTG is recommended first line in children, adolescents, and adults
Cost	$230 (pellets) per patient per year for 3-5.9 kg weight band $218 (granules) per patient per year for 3-5.9 kg weight band	Pending	Expected to be significantly lower than Lpv/r formulations
Administration considerations	Pellet capsules may be difficult to open Not a complete regimen – must be administered with a dispersible NRTI backbone.	Complete regimen	Dispersible tabs are recommended as a preferred formulation by the Child Survival Working Group. Not in FDC formulation – must be administered with a dispersible NRTI backbone. An FDC for ABC/3TC/DTG is expected in late 2021/early 2022

Effectively Getting to the Second “95”: *Three Pillars of Recommendations*

3. Service Delivery

- Operationalizing complex treatment guidelines: creating tools to help TWGs work through the motions of how to roll out new drugs and revise treatment management
- Strong supply chain for pediatric ARVs – stock out, supply monitoring
- Training for health care providers to provide appropriate counseling and education
- Task-shifting for treatment initiation and follow-up
- Implement good differentiated practices for linkage services – intense post-test counselling for mothers/caregivers, SMS services, peer support, linkage case management
- Caregiver support: Patient education materials and peer navigation opportunities
- Decentralized and differentiated age-sensitive HIV treatment (e.g., family- and pediatric-friendly clinics)
- Assisted age-appropriate disclosure
- Address stigma and discrimination

Elizabeth Glaser
Pediatric AIDS Foundation
Fighting for an AIDS-free generation

Questions?

If you have a question or comments, you can either:

- type it in the Q&A box of your screen in Zoom
- Click “Raise Hand” to ask it verbally (if you are calling in on a phone, you can dial *9 to raise your hand)
  - You will be notified when we have un-muted you
    - Once un-muted, please begin by introducing yourself (your name & organization)

Additional References

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Thank you!