

# Point-of-Care EID and VL Products: What's in the Pipeline?

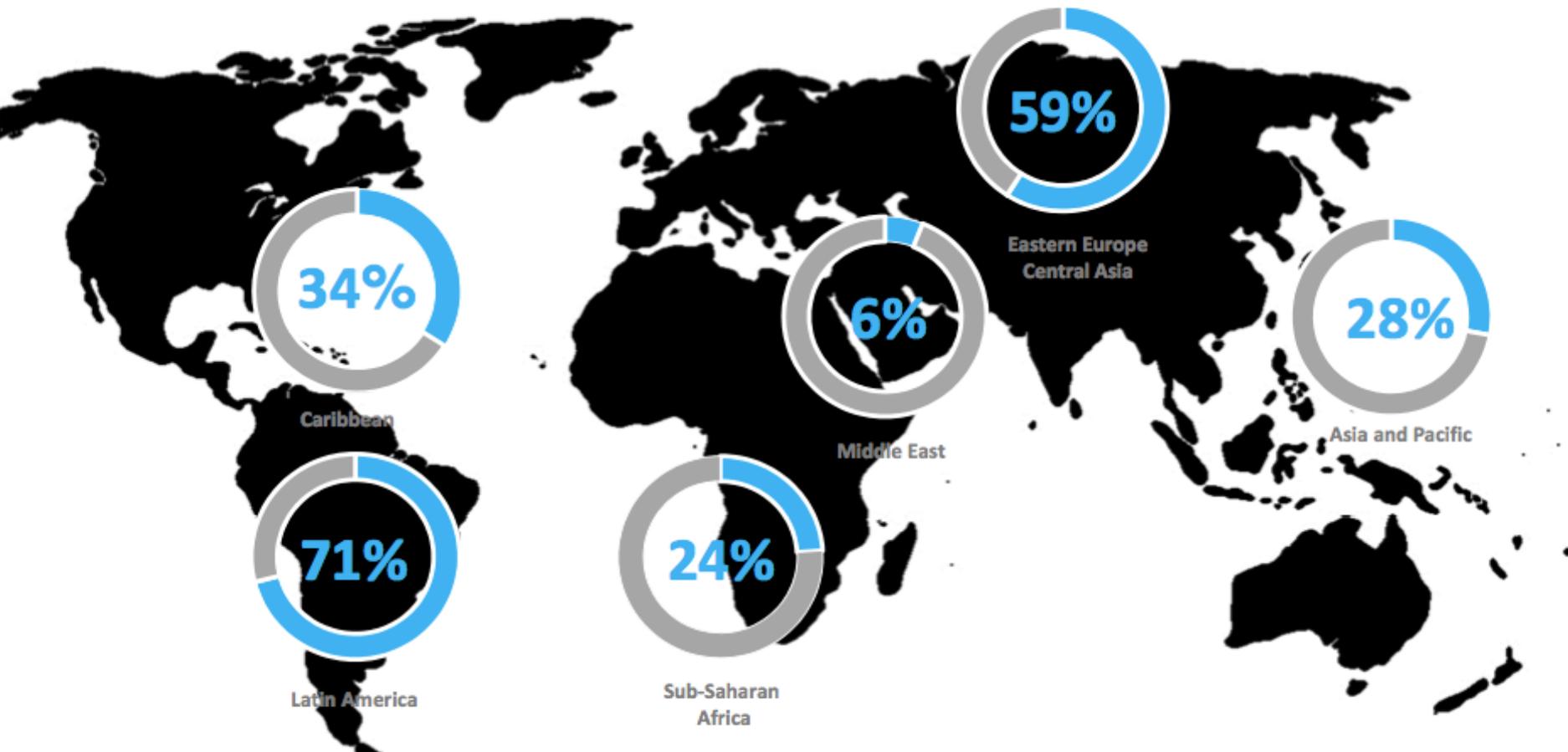
June 2016



# Point-of-Care EID and VL Products

- **Background**
- POC EID and VL product pipeline
- Preliminary evidence
- Regulatory approval
- EID Consortium for technical evaluations
- Patient impact of POC EID technologies – pilot indications

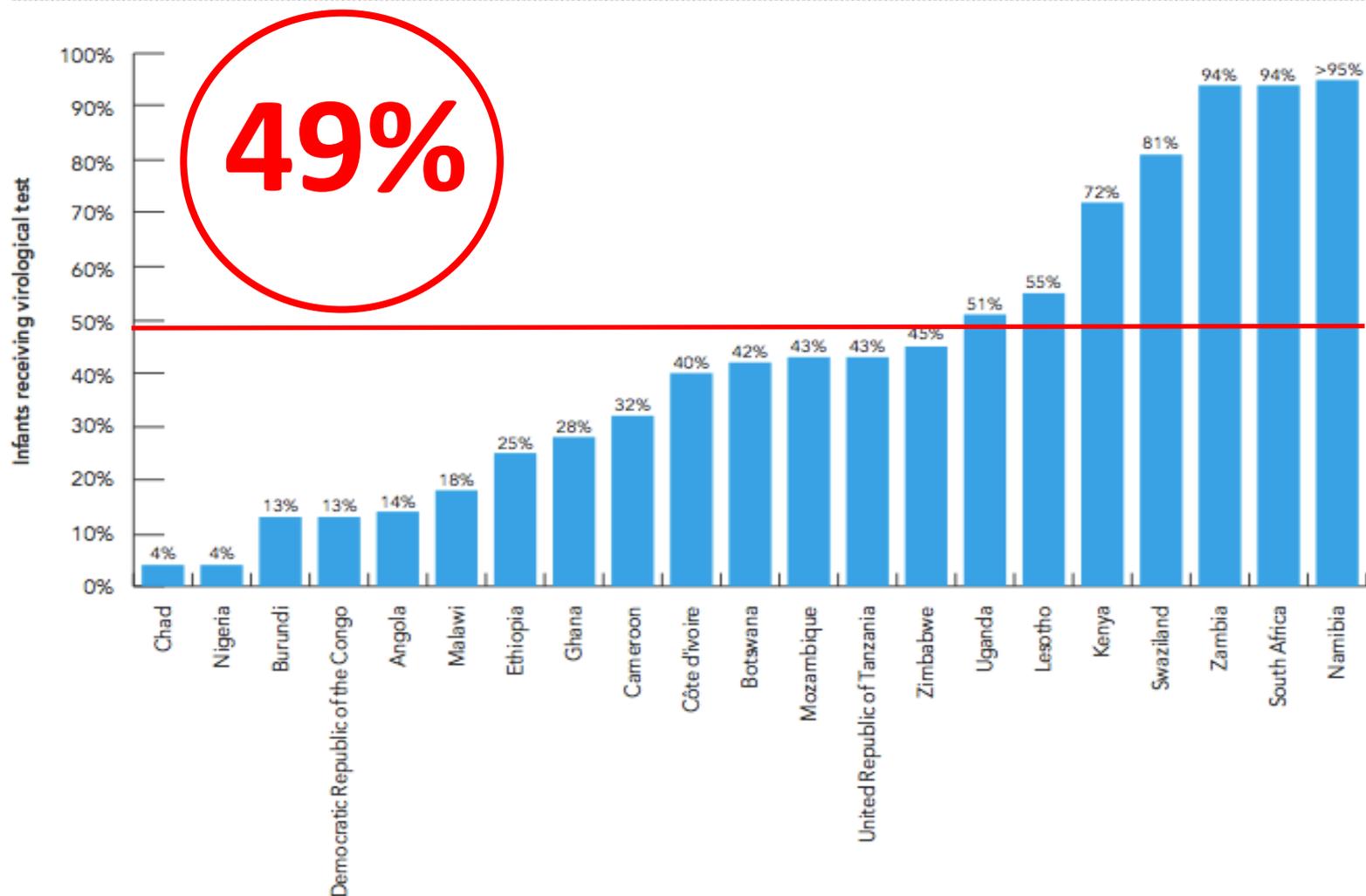
# Pediatric ART coverage rates by region



Less than 35% of HIV-positive infants are on ART globally

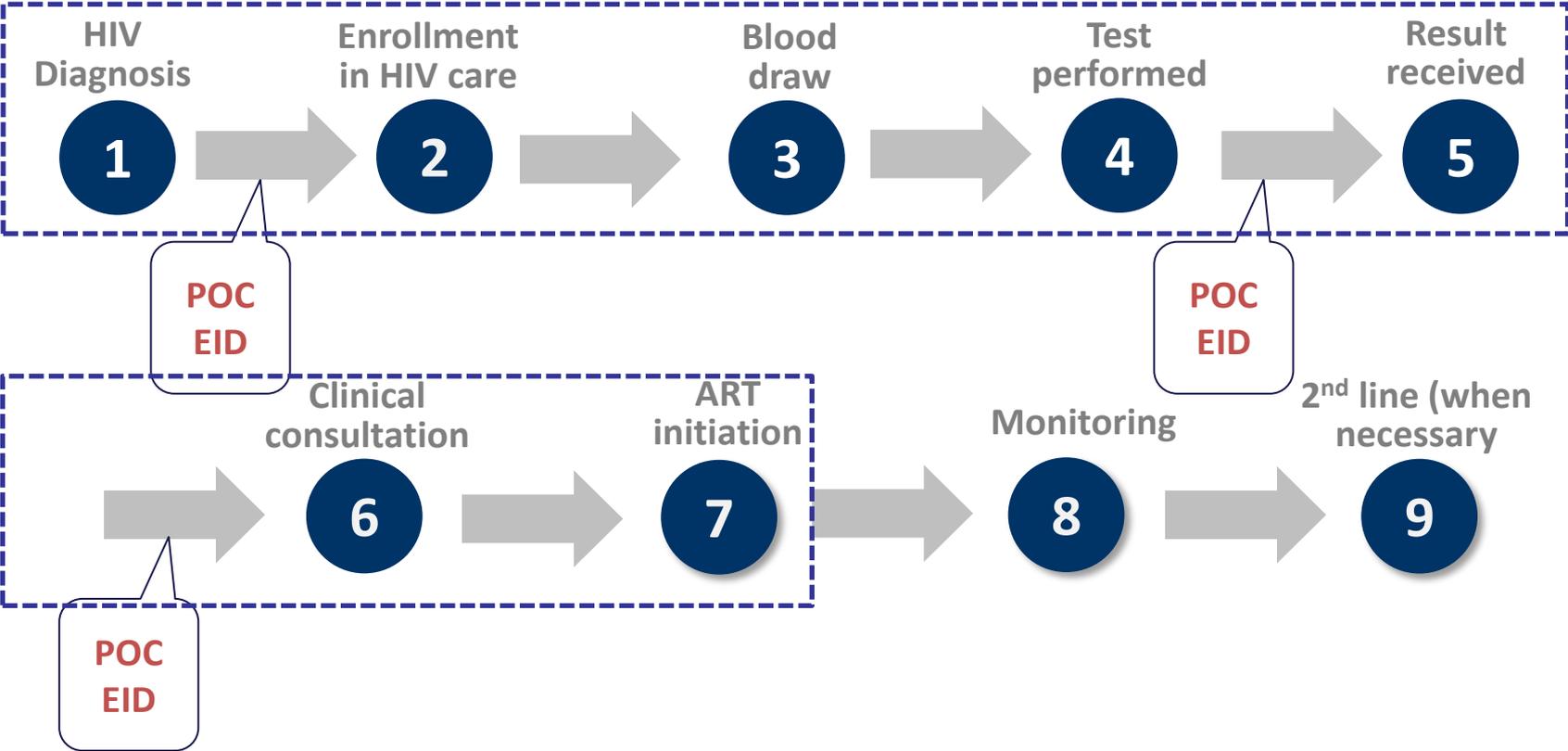
# Infant HIV diagnosis: Access to early infant diagnosis and ART for infants remain low

Percentage of infants born to women living with HIV receiving a virological test within the first two months of life in 21 Global Plan priority countries, 2014



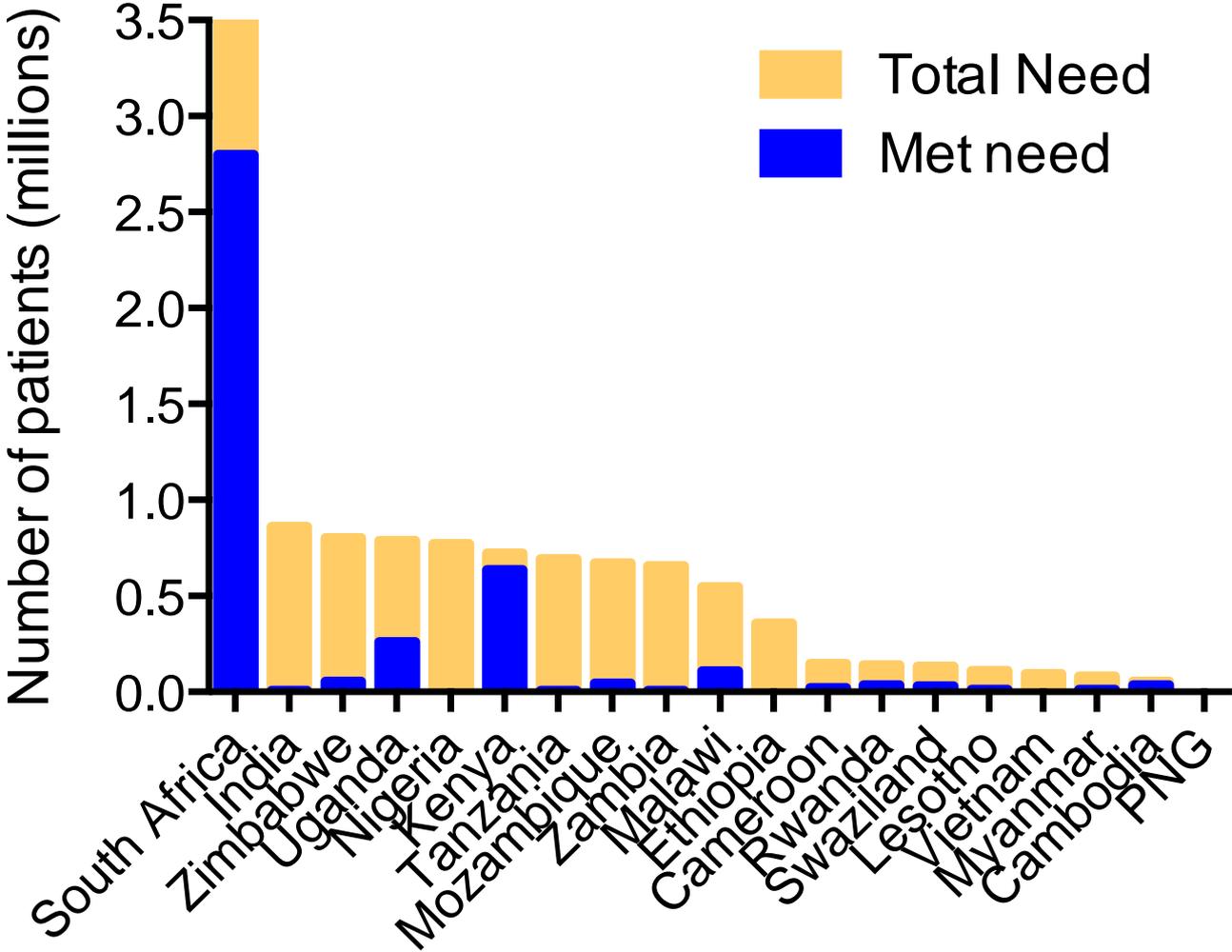
# POC will transform the way that HIV care and treatment are provided

## Continuum of Care *Same day EID to ART initiation*



Point of care will expand access to actionable results, reduce loss and improve patient outcomes.

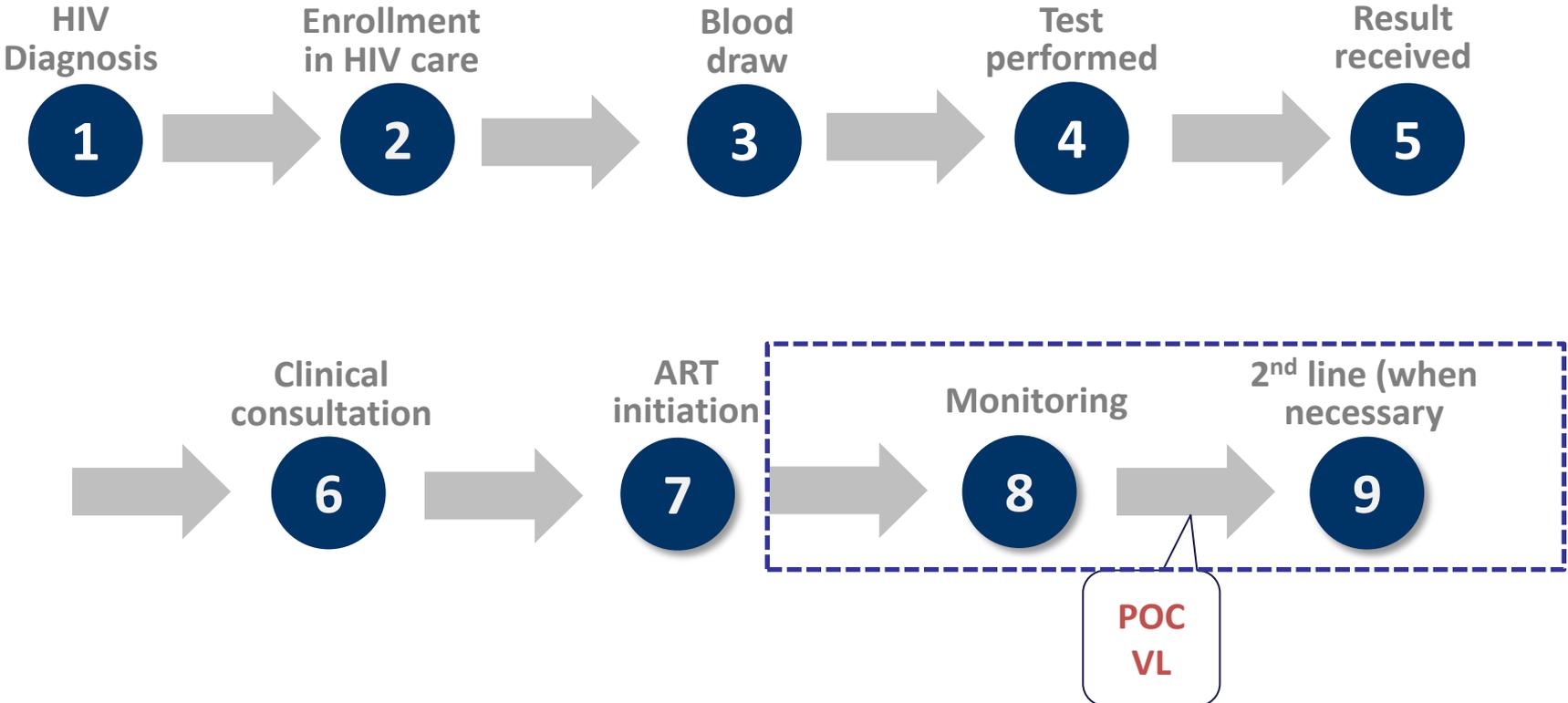
# Viral load testing is expanding quickly, but significant need remains



# POC will transform the way that HIV care and treatment are provided

## Continuum of Care

*Same day viral load results for faster clinical decision-making*

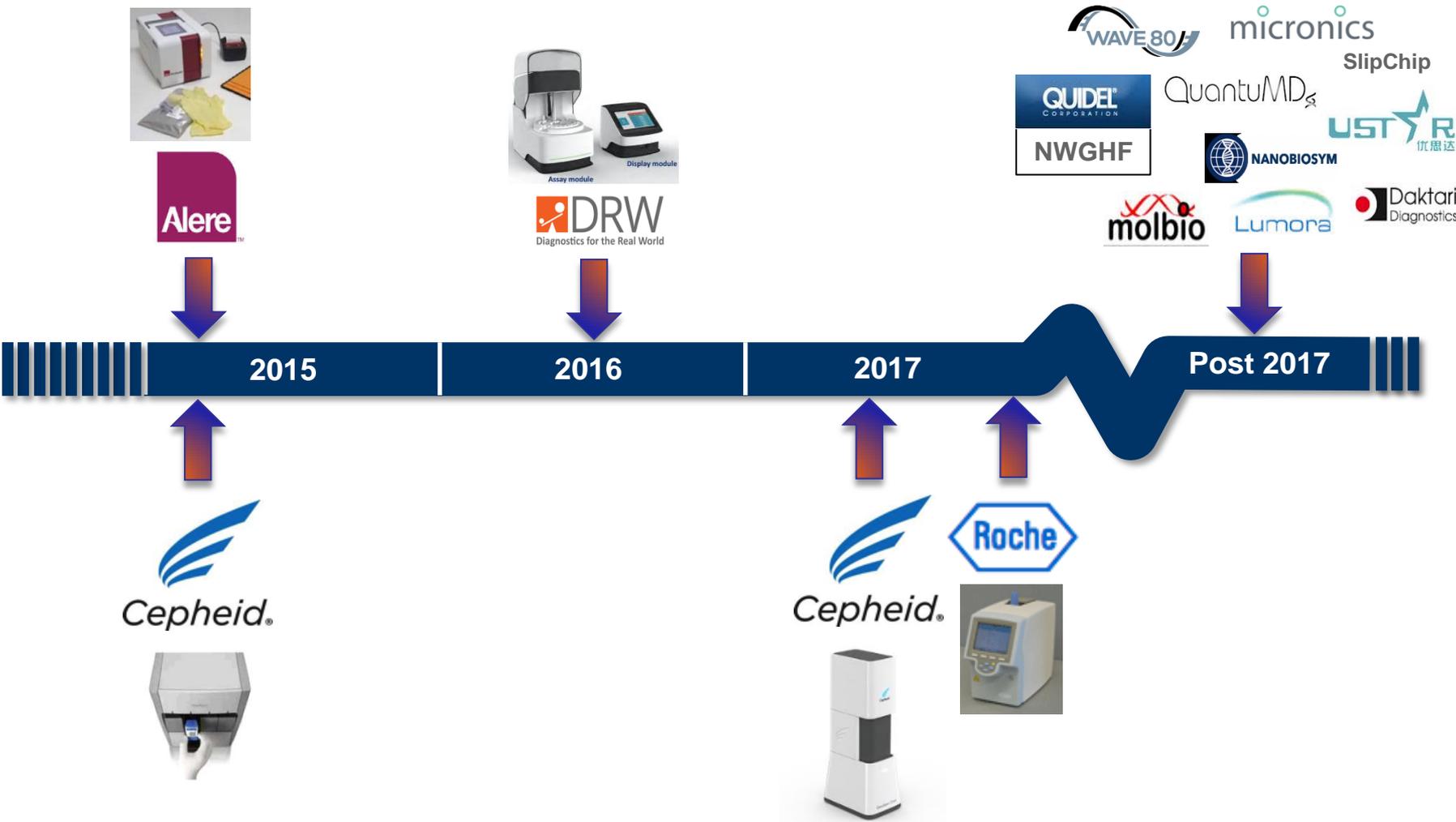


Point of care will expand access to actionable results, reduce loss and improve patient outcomes.

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# Viral load and early infant diagnosis POC technology pipeline



# Alere q Qual/Quant



- Tests: EID, VL
- Limit of detection: 1,000 copies/ml
- Sample types: plasma, whole blood
- Input sample volume for plasma: 25ul or 500ul
- Input sample volume for whole blood: 25ul
- HIV-1 Group M, N, O; HIV-2
- 50 minutes per test
- 8-hour throughput of 8 tests
- Automated/semi-automated
- Requires consistent electricity
- Regulatory approval (device and EID cartridge): CE-IVD, WHO-PQ
- Regulatory approval (VL cartridge): still in development

# Diagnostics for the Real World SAMBA II



- Tests: EID, VL
- Limit of detection: 1,000 copies/ml
- VL is semi-quantitative
- Sample types: plasma, whole blood
- Input sample volume for plasma: 200 ul
- Input sample volume for whole blood: 120 ul
- 60-90 minutes per test
- 8-hour throughput of 4-8 tests
- Semi-automated
- Requires constant electricity
- Regulatory approval (device and EID cartridge): CE-IVD

# Cepheid GeneXpert Qual/Quant



- Tests: EID, VL
- Limit of detection: 40 copies/ml
- Sample types (VL): plasma
- Sample types (EID): whole blood, DBS
- Input volume for plasma (VL): 1 ml
- Input volume for DBS (EID): 1 spot
- Input volume for WB (EID): 100 ul
- HIV-1 Group M, N, O
- 95 minutes per test
- 8-hour throughput for 4-module: 20 tests
- Requires computer skills, constant electricity, AC
- Semi-automated: plasma separation (VL) or DBS sample preparation (EID, if DBS is used)
- Regulatory status (VL plasma): CE-IVD
- Regulatory status (EID): CE-IVD, WHO-PQ

# Cepheid Omni



- Tests: TB, EID, VL, HCV, MTB (2017)
- Limit of detection: 20 copies/ml
- Sample types (VL): plasma
- Sample types (EID): whole blood, DBS
- Input volume for plasma (VL): 1 ml
- Input volume for DBS (EID): 1 spot
- Input volume for WB (EID): 100 ul
- HIV-1 Group M, N, O
- 95 minutes per test
- 8-hour throughput: 6 tests
- Semi-automated: plasma separation (VL) or DBS sample preparation (EID, if DBS is used)
- Regulatory status (VL plasma): CE-IVD
- Regulatory status (EID): CE-IVD
- Regulatory status (device): none
- Price: \$2,895/device

# Cepheid HIV quant plasma assay sample preparation



Collect 5 mL whole blood in an ACD-A or EDTA plasma tube.



Centrifugation at 800-1600 x g for 20 minutes



Transfer 1 mL plasma to chamber 3 via transfer pipette



Scan cartridge barcode



Load cartridge

# Cepheid HIV qual assay whole blood sample preparation



OR

Collect  $\geq 100 \mu\text{l}$  whole blood and transfer to EDTA microtainer tube or lavender tube



Use the 1mL pipette to transfer 0.75 mL sample reagent into chamber 3



Use the transfer pipette to transfer  $100 \mu\text{l}$  whole blood into chamber 3



Scan cartridge barcode



Load into GX and close door

# Cepheid HIV qual assay dried blood spot sample preparation

1



Collect DBS with 60-70  $\mu$ l whole blood per spot

2



Transfer one DBS into the sample reagent bottle and mix. Incubate in Thermomixer at 56°C, 500 rpm for 15 min

3



Transfer all liquid into chamber 3 with the 1 mL transfer pipette

4



Scan cartridge barcode

5



Load into GX and close door



# **HIV/AIDS Diagnostics Technology Landscape**

**5<sup>th</sup> edition**

**October 2015**

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# Alere q HIV-1/2 Detect preliminary test performance

## Accurate Early Infant HIV Diagnosis in Primary Health Clinics Using a Point-of-Care Nucleic Acid Test

*Ilesh V. Jani, MD, PhD,\* Bindiya Meggi, MSc,\* Nédio Mabunda, MSc,\* Adolfo Vubil, MSc,\* Nadia E. Siteo, MSc,\* Ocean Tobaiwa, MPhil,† Jorge I. Quevedo, BA,† Jonathan D. Lehe, BA,† Osvaldo Loquiha, PhD,‡ Lara Vojnov, PhD,† and Trevor F. Peter, PhD, MPH†*

AIDS 2016

**Sensitivity: 98.5% (91.7 – 99.9)**

**Specificity: 99.9% (99.3 – 100)**

RESEARCH ARTICLE

## Laboratory Evaluation of the Alere q Point-of-Care System for Early Infant HIV Diagnosis

Nei-yuan Hsiao<sup>1\*</sup>, Lorna Dunning<sup>2</sup>, Max Kroon<sup>3</sup>, Landon Myer<sup>2</sup>

<sup>1</sup> Division of Medical Virology, University of Cape Town, Cape Town, South Africa, <sup>2</sup> Division of Epidemiology & Biostatistics, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa, <sup>3</sup> Department of Neonatal Medicine, University of Cape Town, Cape Town, South Africa

PLoS One 2016

**Sensitivity: 95.5% (91.7 – 97.9)**

**Specificity: 99.8% (99.1 – 100)**

# Cepheid GeneXpert qual assay preliminary test performance

## Evaluation of Xpert HIV-1 Qual assay for resolution of HIV-1 infection in samples with negative or indeterminate Geenius HIV-1/2 results

Michal Michaeli<sup>a,1</sup>, Marina Wax<sup>a,1</sup>, Yael Gozlan<sup>a</sup>, Aviya Rakovsky<sup>a</sup>, Ella Mendelson<sup>a,b</sup>, Orna Mor<sup>a,\*</sup>

JCV 2016

**Sensitivity: 100% (92.7 – 100)**

**Specificity: 100% (92.6 – 100)**

## Diagnostic Accuracy of Cepheid GeneXpert HIV-1 Qual for Early Infant Diagnosis

Sekesai Mtapuri-Zinyowera<sup>1</sup>, Zibusiso Ndlovu<sup>2,3</sup>, Emmanuel Farjardo<sup>3</sup>, Carol Metcalf<sup>3</sup>, Kekeletso Kao<sup>4</sup>, Maryam bibi Rumaney<sup>3</sup>, Elton Mbofana<sup>2</sup>, Daniel Orozco<sup>4</sup>, Helen Bygrave<sup>3</sup>

CROI 2016

**Sensitivity: 97.0% (93.2 – 99.0)**

**Specificity: 100% (98.6 – 100)**

# Cepheid GeneXpert quant assay preliminary test performance

## Diagnostic Accuracy of the Point-of-Care Xpert HIV-1 Viral Load Assay in a South African HIV Clinic

**Performance Evaluation of the new HIV-1 quantification assay, Xpert® HIV-1 Viral Load, on a wide panel of HIV-1 variants**

Marie Gueudin<sup>1,2</sup>\$, Adeline Baron<sup>1</sup>\$, Elodie Alessandri-Gradt<sup>1,2</sup>, Véronique Lemée<sup>1</sup>, Thomas Mourez<sup>1,2</sup>, Manuel Etienne<sup>2,3</sup>, Jean Christophe Plantier<sup>1,2\*</sup>

## Multi-site clinical evaluation of the Xpert® HIV-1 viral load assay

J.A. Jordan<sup>a,\*</sup>, J.C. Plantier<sup>b</sup>, K. Templeton<sup>c</sup>, A.H.B. Wu<sup>d</sup>

<sup>a</sup> Department of Epidemiology and Biostatistics, George Washington University, School of Public Health, Washington, DC, USA

<sup>b</sup> Laboratoire de Virologie associé au Centre National de Référence du VIH, Institut de Biologie Clinique, Hôpital C. Nicolle, CHU Rouen, Rouen cedex, France

<sup>c</sup> Department of Medical Microbiology, NHS Lothian, Royal Infirmary of Edinburgh, Edinburgh, UK

<sup>d</sup> San Francisco General Hospital, UCSF, San Francisco, CA, USA

## Evaluation of the RealTime HIV-1, Xpert HIV-1, and Aptima HIV-1 Quant Dx Assays in Comparison to the NucliSens EasyQ HIV-1 v2.0 Assay for Quantification of HIV-1 Viral Load

Orna Mor,<sup>a</sup> Yael Gozlan,<sup>a</sup> Marina Wax,<sup>a</sup> Fernando Mileguir,<sup>a</sup> Avia Rakovsky,<sup>a</sup> Bina Noy,<sup>b</sup> Ella Mendelson,<sup>a,c</sup> Itzhak Levy<sup>d</sup>

National HIV Reference Laboratory, Central Virology Laboratory, Ministry of Health, Sheba Medical Center, Ramat-Gan, Israel<sup>b</sup>; Ilex Medical, Petach Tikva, Israel<sup>b</sup>; School of Public Health, Tel Aviv University, Tel Aviv, Israel<sup>f</sup>; Infectious Diseases Unit, Sheba Medical Center, Ramat-Gan, Israel<sup>d</sup>

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# International Stringent Regulatory Pathways

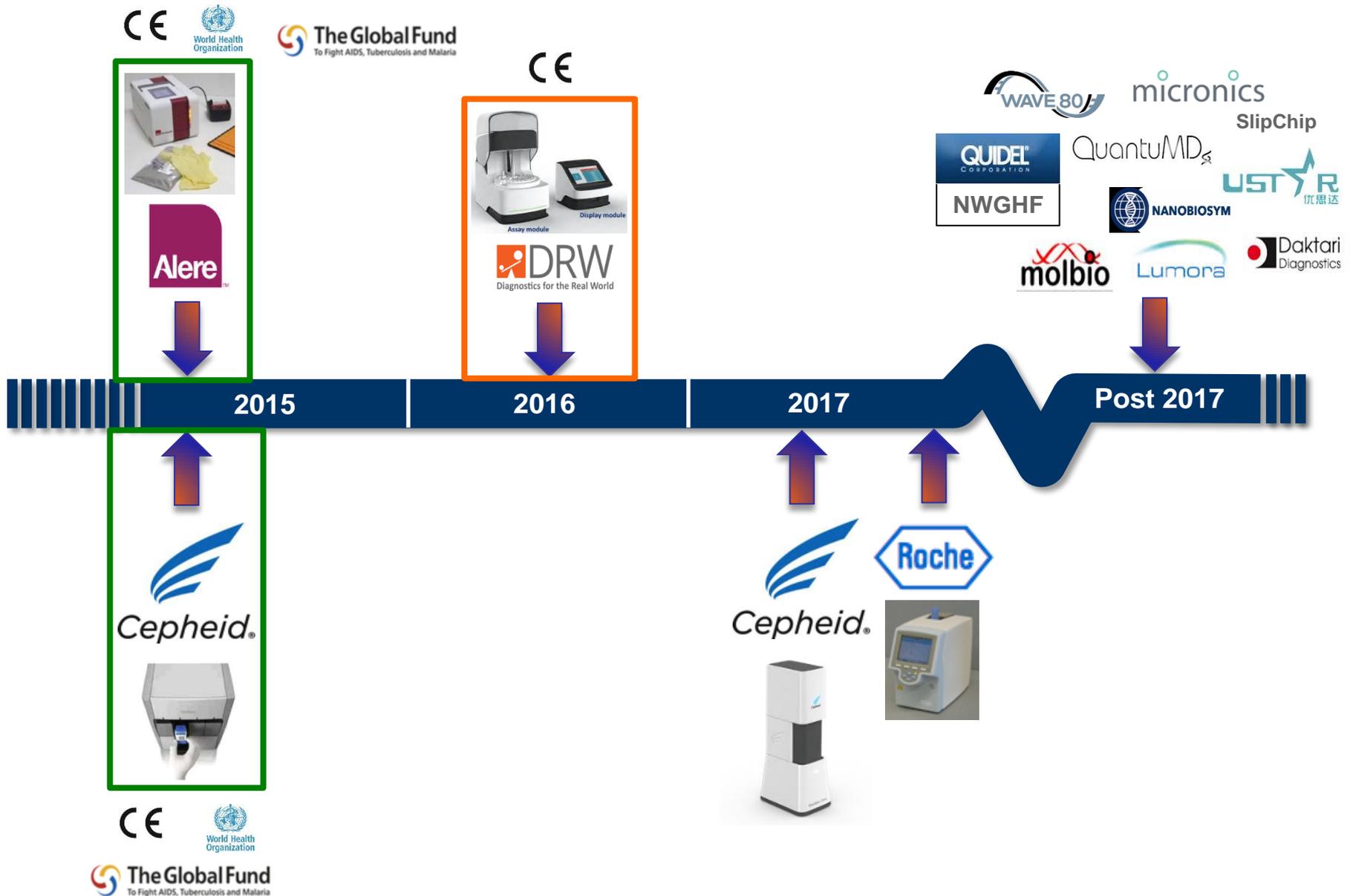
- HIV viral load and early infant diagnosis (molecular diagnostic assays) are typically considered high risk and thus go through a stringent evaluation process.
- **CE-IVD:** European Union regulatory approval body; several notifying bodies across Europe of various quality. Primarily dossier review.
- **WHO-PQ:** [http://who.int/diagnostics\\_laboratory/en/](http://who.int/diagnostics_laboratory/en/)
  - Dossier review
  - Laboratory evaluation: in collaboration with CDC and NHLS South Africa
  - Site inspection
- **Expert Review Panel for Diagnostics (ERPD):** panel of experts to assess the potential risks/benefits associated with diagnostic products lacking WHO-PQ or other stringent regulatory approval. Primarily dossier review.

<http://www.theglobalfund.org/en/healthproducts/qualityassurance/diagnostic/>

# Global Fund Quality Policy for HIV virological assays (EID and viral load)

- Manufactured at a site compliant with ISO 13485:2003 or an equivalent Quality Management System recognized by the Founding Members of GHTF;
- AND
- Recommended by WHO for use in HIV (**WHO prequalification**); OR
- Authorized for use by one of the Regulatory Authorities of the Founding Member of **GHTF** (such as CE-IVD, US-FDA, etc.); OR
- Acceptable for procurement based on the advice of an **Expert Review Panel (ERPD)** due to a public health need yet lacking WHO-prequalification of regulatory approval by a Founding Member of GHTF.

# Viral load and early infant diagnosis POC technology pipeline



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# Once a technology is ready, significant barriers and delays remain

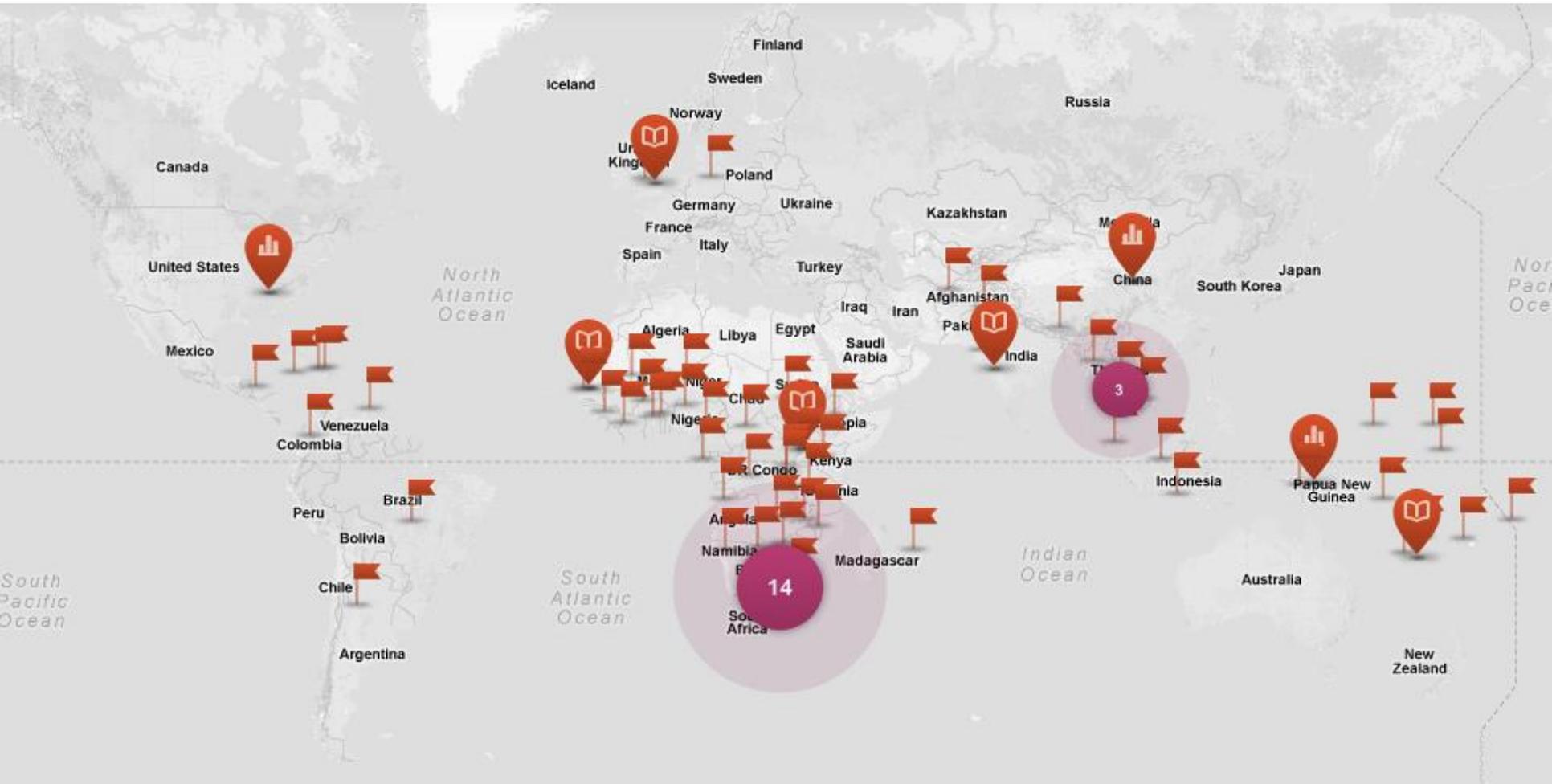


**Result in significant delays in uptake**



**Duplication of international regulatory processes**

# The Alere Pima Product Evaluation Story



# The Alere Pima Product Evaluation Story

Glencross et al. *Journal of the International AIDS Society* 2012, 15:3  
<http://www.jiasociety.org/content/15/1/3>

Clinical

ORIGINAL ARTICLE

RESEARCH

## Evaluation of PIMA point-of-care CD4 testing in Performance evaluation of the Pima a large UK HIV service care CD4 analyser using capillary blood in field tests in South Africa

Sophie Herbert,<sup>1</sup> Simon Edwards,<sup>1</sup> Gina Carrick,<sup>1</sup> Andrew Copas,<sup>2</sup> Christopher Sandford,<sup>1</sup> Marc Amphlett,<sup>3</sup> Paul Benn<sup>1</sup>

Deborah K Glencross<sup>1,3\*</sup>, Lindi M Coetzee<sup>1,3</sup>, Mamsallah Faal<sup>2</sup>, Martin M...<sup>4</sup>, W...<sup>1,3</sup>  
WD Francois Venter<sup>2</sup> and Regina Osih<sup>2</sup>

OPEN ACCESS Freely available online

PLoS one

## Accurate CD4 T-cell enumeration drug toxicity monitoring in clinics using point-of-care Evaluation of Portable Point-of-Care CD4 Counter with High Sensitivity for Detecting Patients Eligible for Antiretroviral Therapy

Yukari C. Manabe<sup>1,2,3\*</sup>, Yaping Wang<sup>2</sup>, Ali Elbireer<sup>3,4</sup>, Brandon Auerbach<sup>1</sup>, Barbara Castelnovo<sup>1</sup>

Thakar et al. *AIDS Research and Therapy* 2012, 9:26  
<http://www.aidsrestherapy.com/content/9/1/26>



RESEARCH

Open Access

## Utility of the point of care CD4 analyzer, PIMA, to enumerate CD4 counts in the field settings in India

Madhuri Thakar<sup>1\*</sup>, Bharati Mahajan<sup>1</sup>, Nawaj Shaikh<sup>1</sup>, Salman Bagwan<sup>1</sup>, Suvarna Sane<sup>1</sup>, Sandhya Kabra<sup>2</sup>, Bharat Rewari<sup>2</sup>, Mohamad Shaukat<sup>2</sup>, Namita Singh<sup>3</sup>, Peter Trevor<sup>3</sup> and Ramesh Paranjape<sup>1</sup>

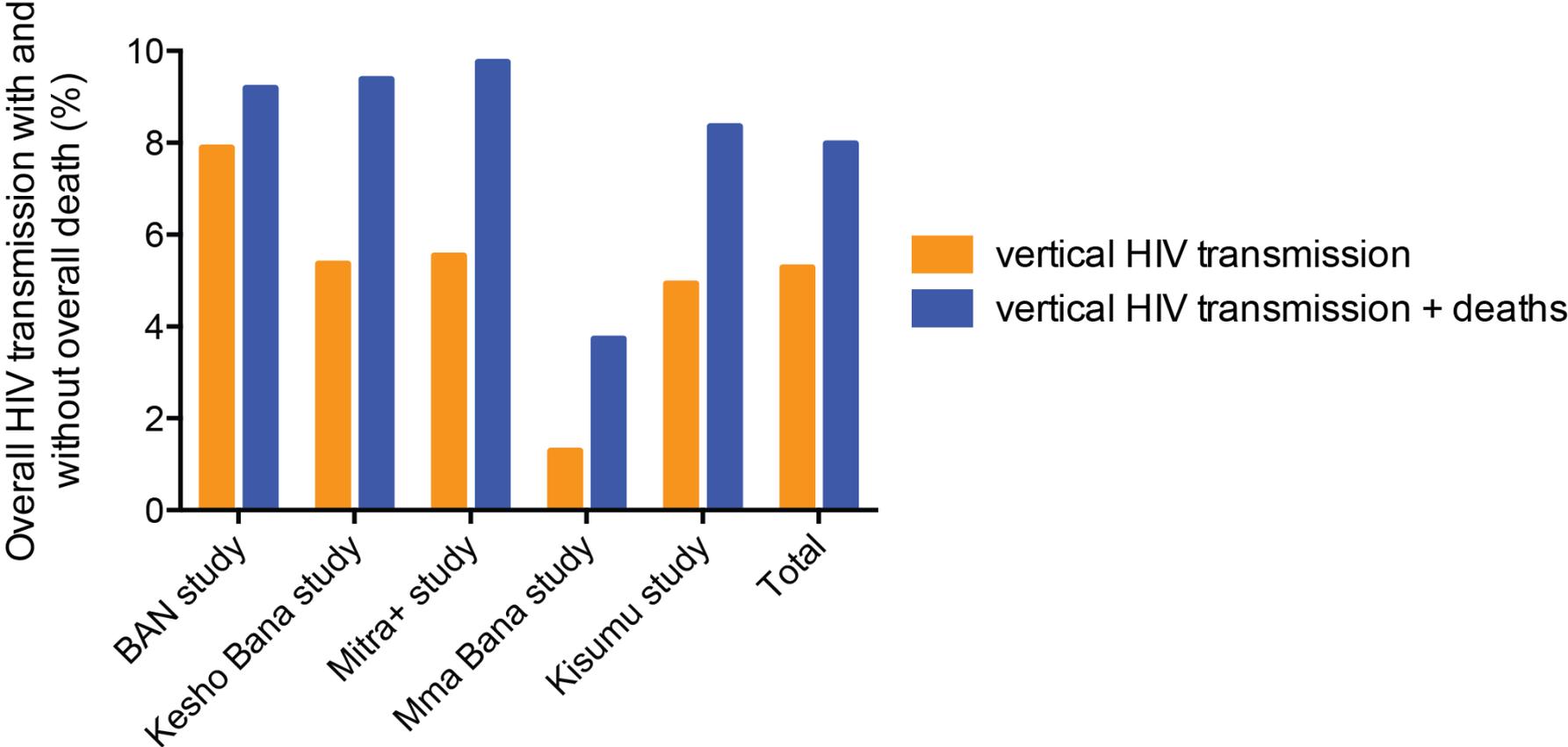
able online

PLoS one

## Estimate the Cost of Point-of-Care CD4 Testing in Settings: An Example Using the Alere Pima™ in South Africa

Maryn Schnippel<sup>2</sup>, Buyiswa Ndibongo<sup>2</sup>, Lawrence Long<sup>2</sup>, Matthew P. Fox<sup>1,2,3</sup>, Sydney Rosen<sup>1,2</sup>

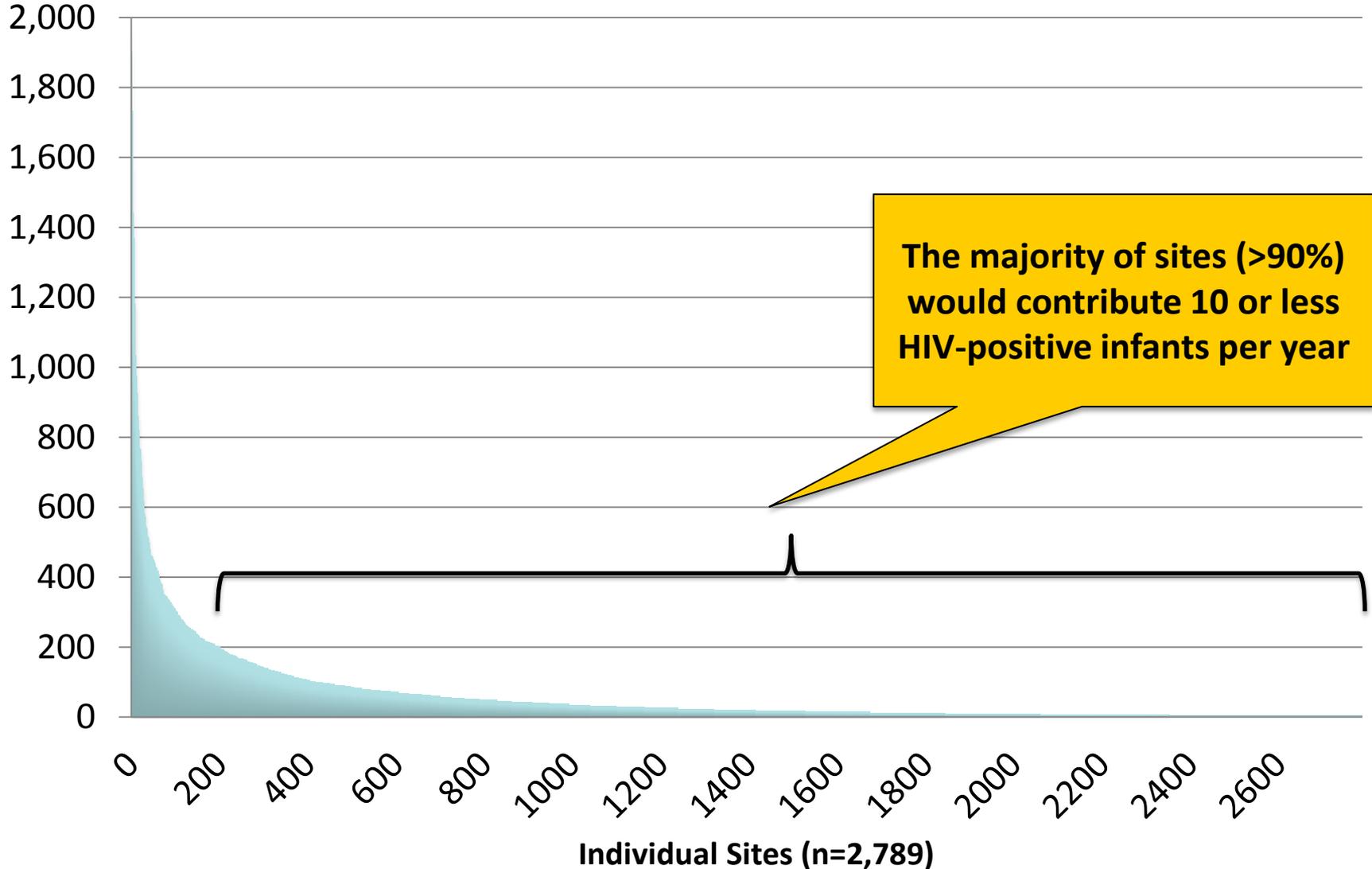
# Option B+/ART for pregnant and breastfeeding women leads to low transmission rates



# Performing EID evaluations or studies independently will significantly slow implementation

Number of Tests per Site per year

## Example Country: EID Testing Need



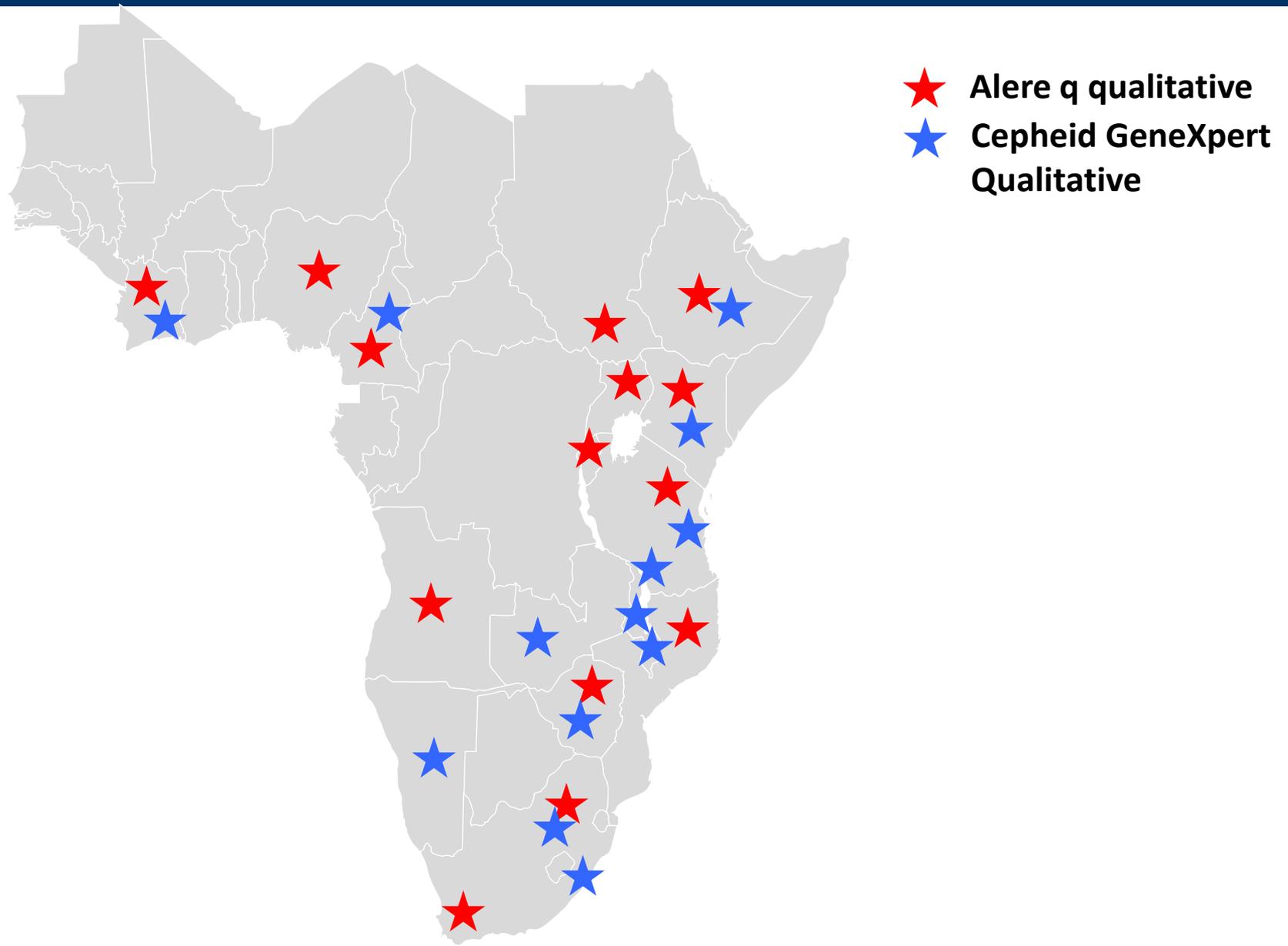
# Regulation and adoption of *in vitro* diagnostics through harmonization

**Goal:** To hasten market entry while ensuring the safety, quality, and effectiveness of new diagnostic technologies.

## Challenges:

1. Regulatory landscape is **highly variable**.
2. Path to approval is **not transparent** in many countries.
3. Excessive **duplication** in clinical trials and inspection of manufacturing sites.
4. Approval process is often **costly** and **lengthy**, especially for imported tests.
5. Regulatory frameworks have not kept up with technological advances and have become a disincentive to innovation

# National regulatory approval often requires technical evaluations



# EID Consortium

Led by Principal Investigators across East and Southern Africa, including ASLM Collaborating Centres of Excellence

**Objective:** Strengthen collaboration and form a consortium for multi-site technical evaluations and impact studies to hasten in-country regulatory approval

**Initial focus:** POC EID testing at 6 weeks (standard of care) and at birth testing

**Key components:**

- Common protocols
- High quality of comparator testing
- Site monitoring visits
- Willingness to share/consolidate interim and final data

**Current status:** Initial analysis of data from nine studies covering six countries has been completed and will be presented at AIDS 2016 in Durban. Additional data review, publication, and report to be completed in the coming months.

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## EID algorithm and linkage to proceed per standard of care and national guidelines

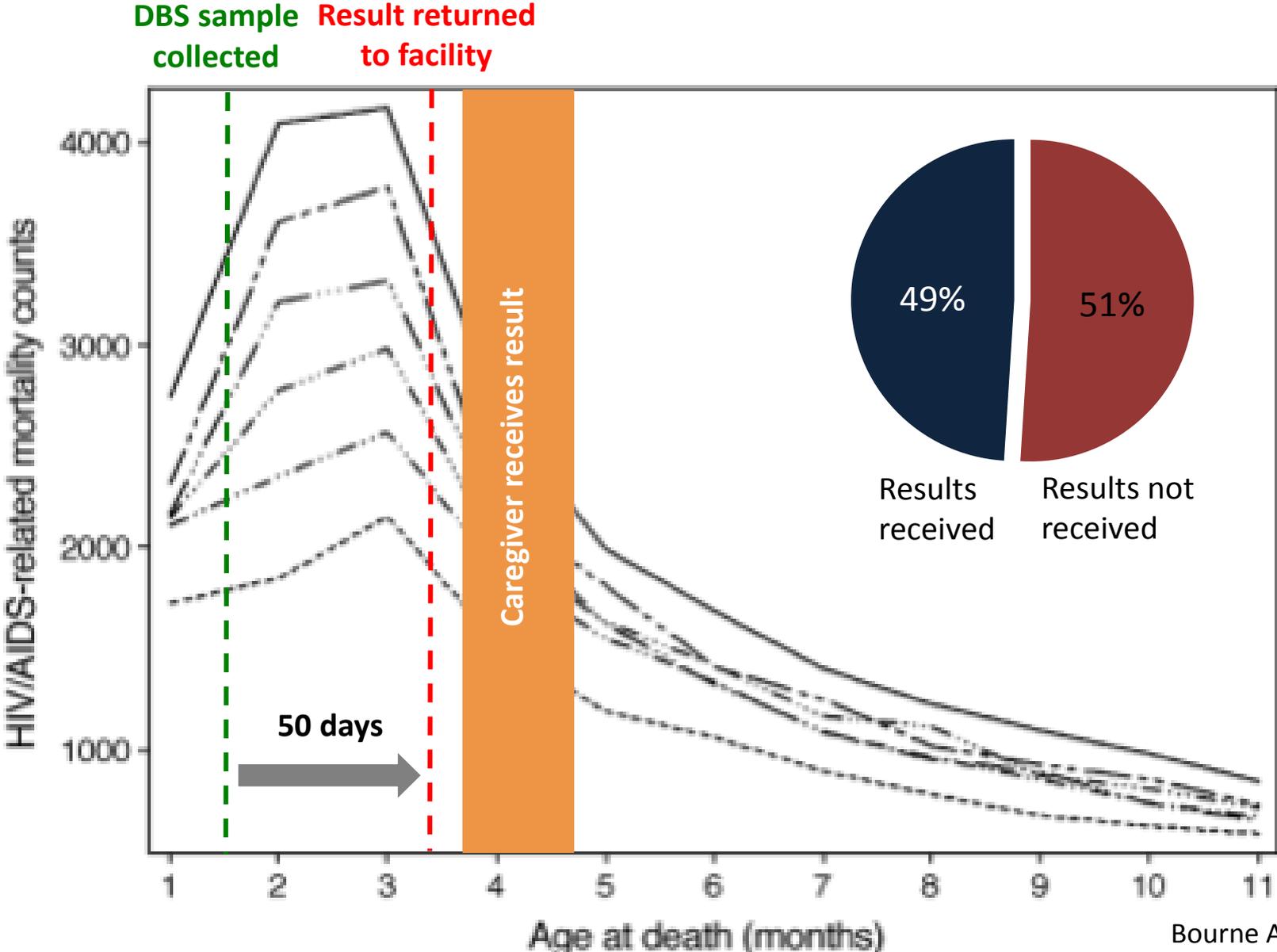
### Primary Objectives

- Turnaround time across the cascade
- LTFU/retention across the cascade
- LTFU/retention three months post-ART initiation

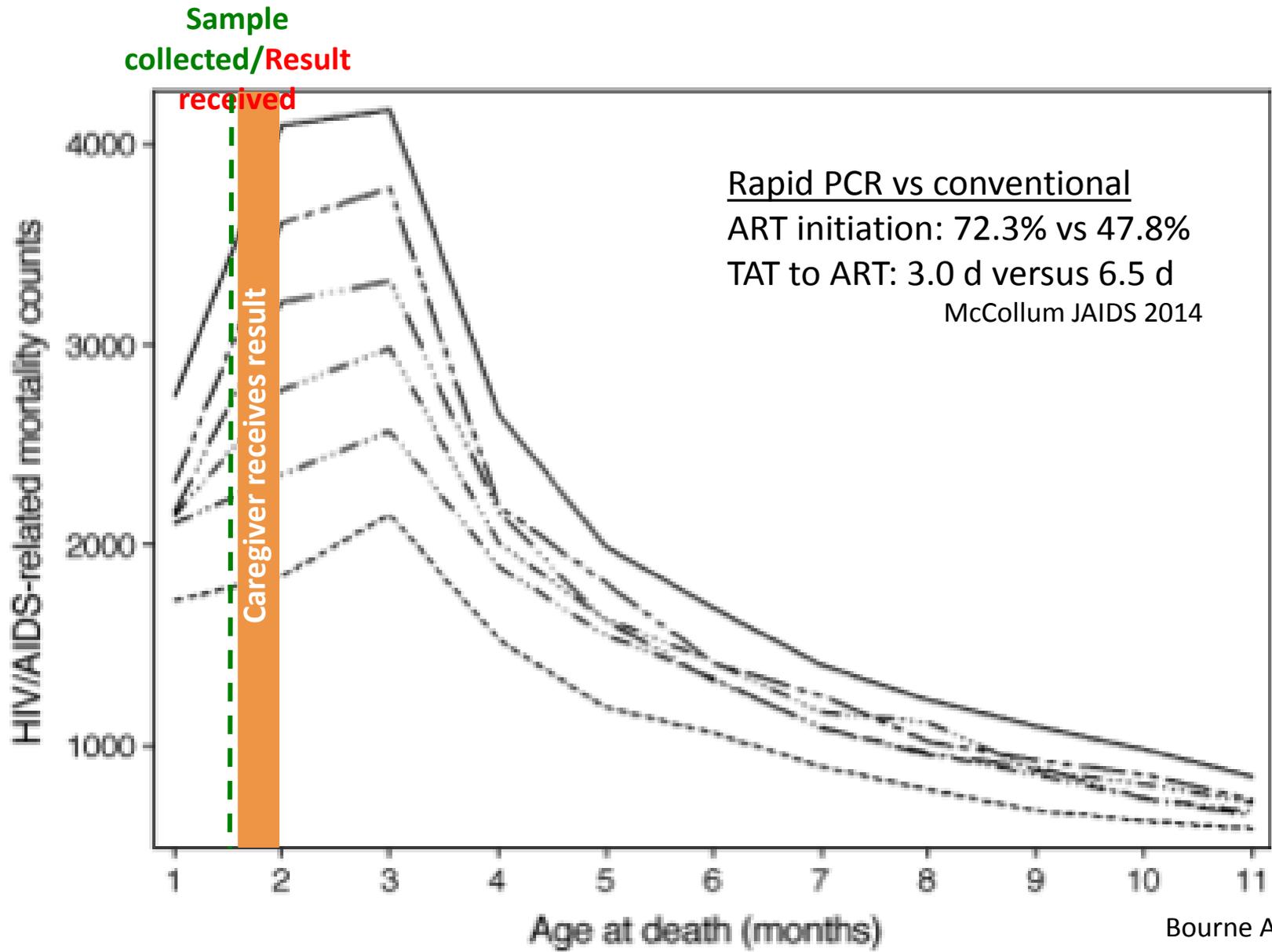
### Secondary Objectives

- Operational considerations for national scale-up
- Cost-effectiveness
- Optimal site selection and deployment
- Proposed training, certification, and QA model
- Health care worker and patient acceptability

# Significant peak of early infant mortality precedes current testing algorithm timing



# POC EID technologies can reduce the time to result receipt



Thank you!

**Questions?**