

# Positive Predictive Value of HIV Serological Tests in HPTN 084 Trial

Session title: HIV prevention: novel approaches and promising findings

IAS 2023, Brisbane Australia, Abstract 5788

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- What is your main question?
  - What is the positive predictive value of the HPTN on-site HIV testing algorithm?
- What did you find?
  - Two reactive HIV serology tests had high positive predictive value. The Ag/Ab test resulted in a high number of false positive results and had low positive predictive value, particularly for those on Cabotegravir LA.
- Why is it important?
  - As programs roll-out CAB LA, interpreting HIV status based on currently available serology testing will require strategies for confirmatory testing, counselling and transition planning to ART or resumption of PrEP.

- HPTN 084 showed that injectable cabotegravir (CAB) is effective for PrEP in women and superior to oral TDF/FTC <sup>1</sup>.
- HIV diagnosis in the context of PrEP use may be complicated by both false negative and false positive tests results.
  - False positive due to non-biologic reasons
  - False positive due to biologic causes (cross-reacting pathogens)
  - “LEVI” syndrome<sup>2</sup>- Delayed Detection of Antibodies or Viral suppression secondary to Long Acting antiretrovirals
- False Negative- Delayed ART initiation, Emergence of Resistance
- False Positives- Incorrect Initiation of ART, Implication for PrEP gaps, and Complex Counseling

<sup>1</sup> Delaney Moretlwe, Lancet 2022,

<sup>2</sup> Eshleman, CROI 2023

# WHO Recommended 3-Stage Algorithm for Settings with National HIV testing Strategy < 5%

## Serial Testing

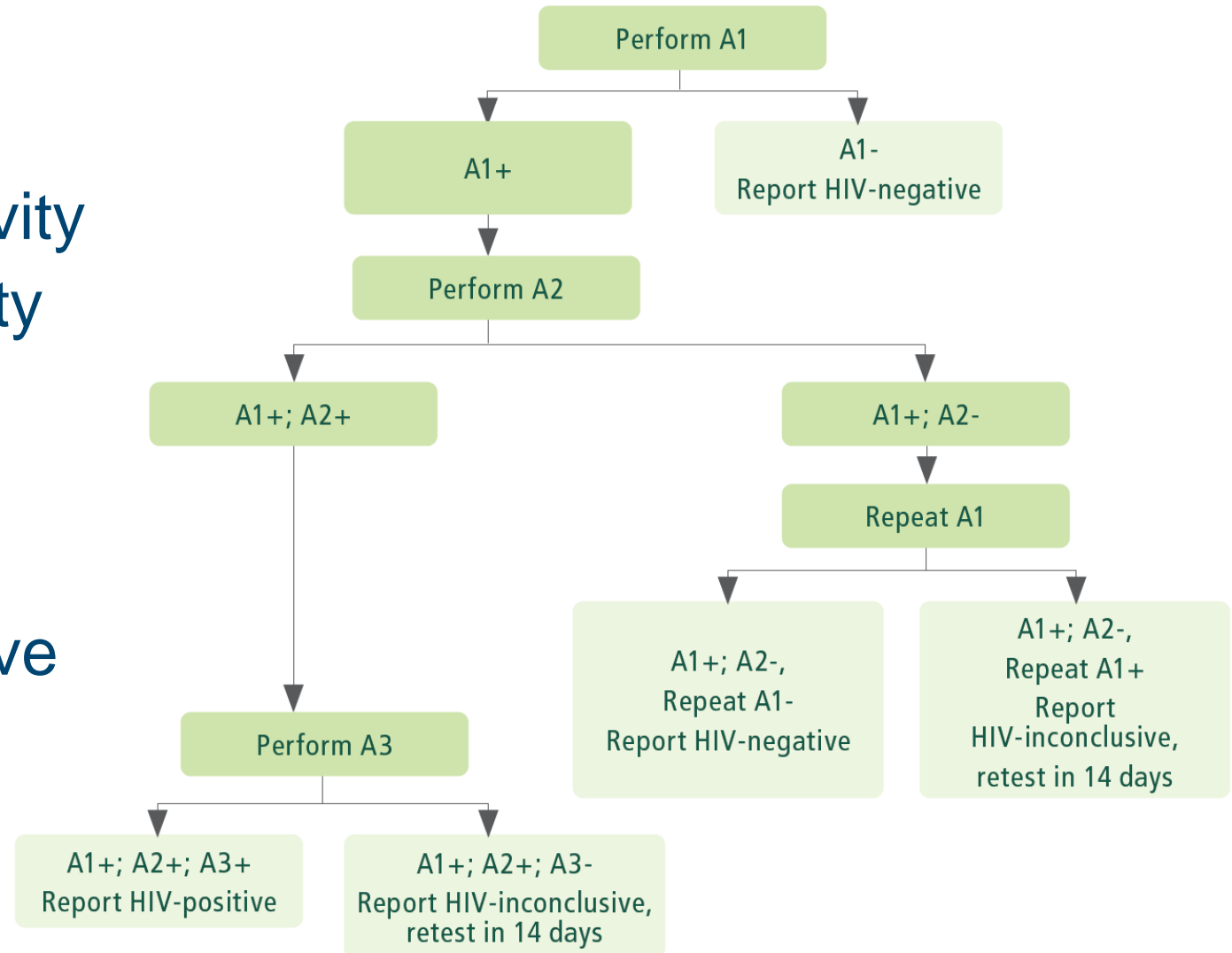
- First Test- High Sensitivity
- Second- High Specificity
- Third- High Specificity

Goal: 99% PPV

Optimal Tests should have

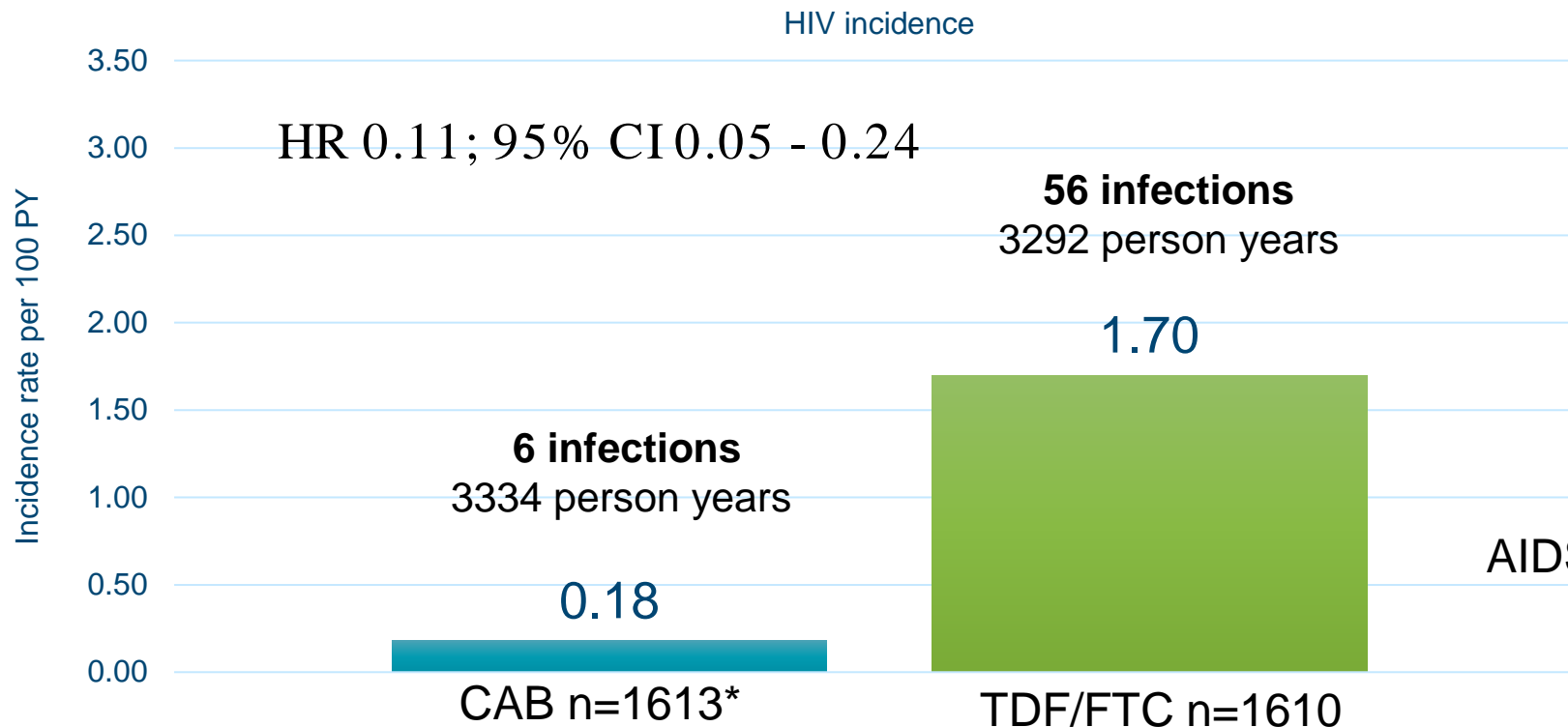
≥99% sensitivity

≥98% specificity

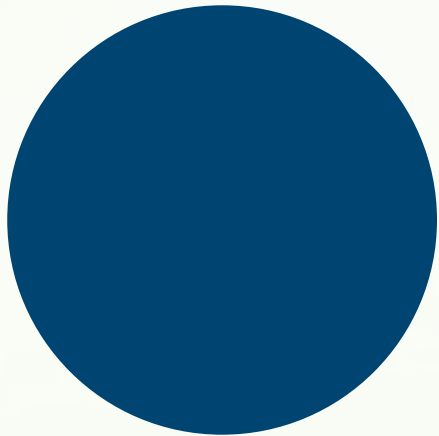


A1: Assay 1 (first test); A2: Assay 2 (second test); A3: Assay 3 (third test).

# HPTN 084 Timeline & Primary Result



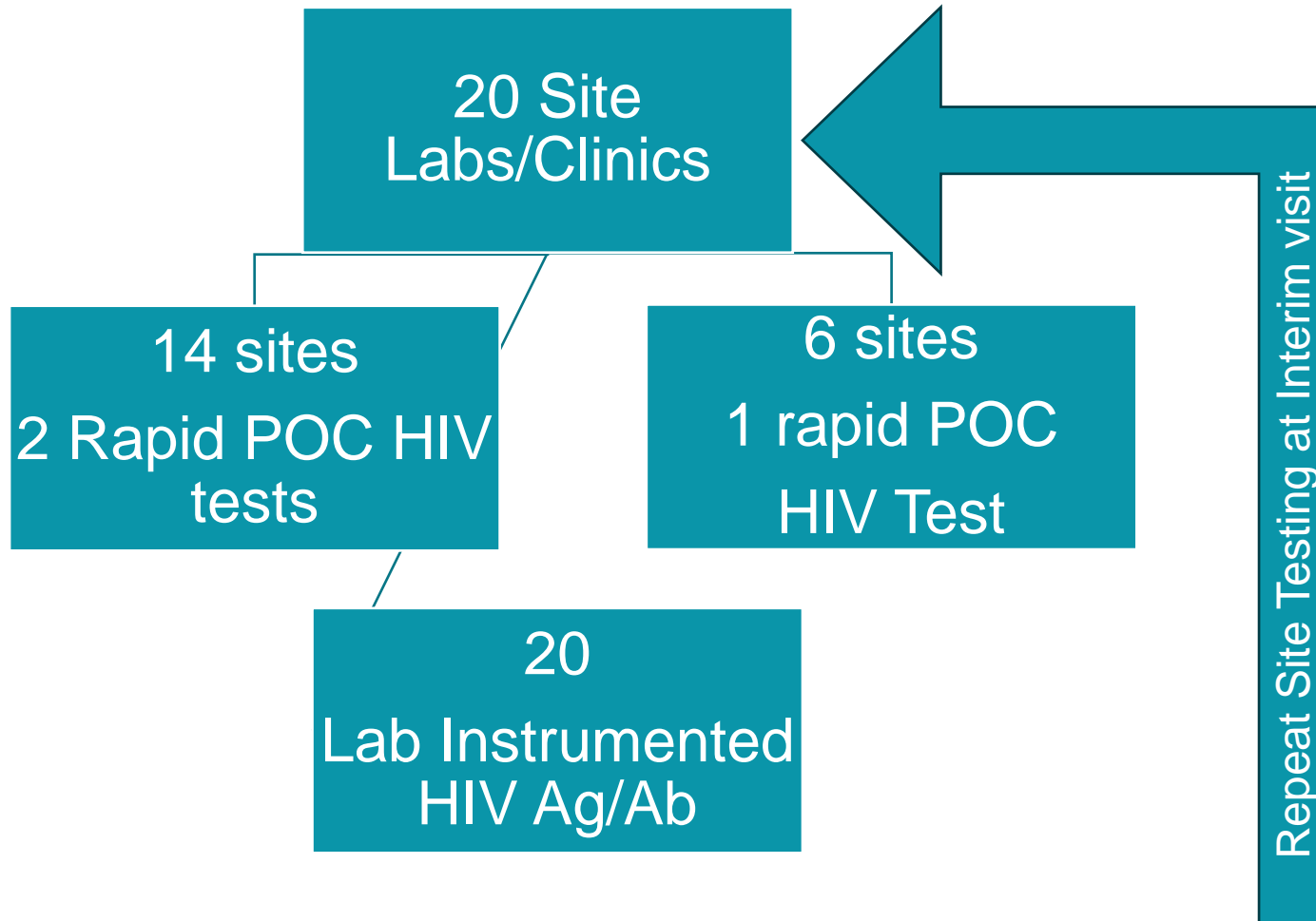
AIDS 2022, Montreal, abstract #OALBX0108



# Objective

We evaluated the positive predictive value (PPV) of the HPTN 084 Site testing algorithm to guide HIV treatment initiation decisions in women on PrEP.

# HIV testing algorithm



Further testing was conducted by the HPTN Laboratory Center

- Back Testing of Previous Visits
- Additional Ag/Ab testing (Architect HIV Ag/Ab Combo test)
- Additional Ab testing (Geenius HIV 1/2 Confirmatory Assay)
- Additional qualitative RNA testing (Aptima HIV RNA Qualitative assay; LOD 30 copies/ml)
- Viral load testing (RealTime HIV Viral Load Assay; LOQ 400 copies/ml)
- Single copy RNA testing (as needed) (University of Pittsburgh)

Any Reactive Test Prompts Product Hold and Site Confirmatory Testing and Central Lab assessment

## Approach

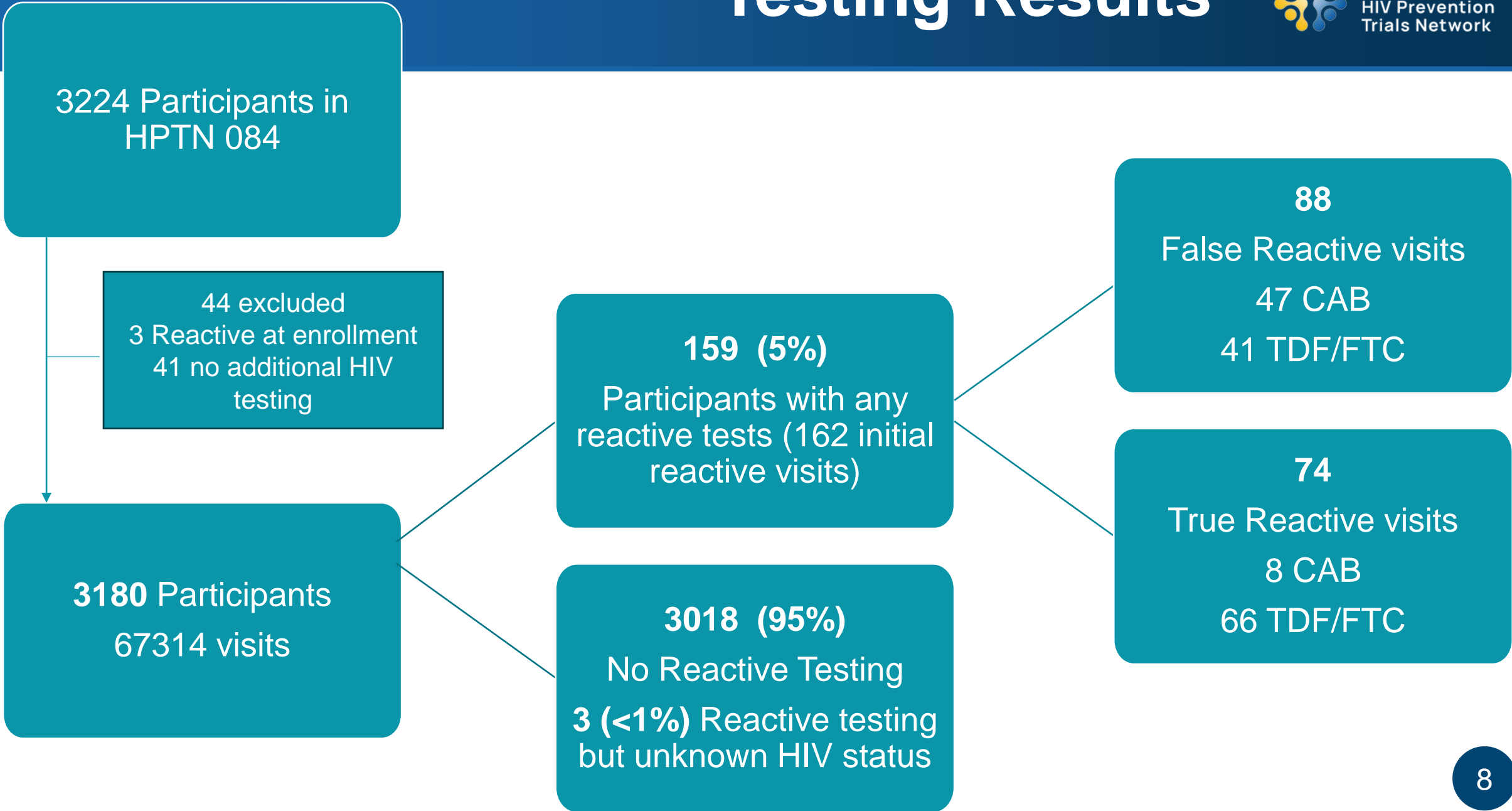
- Testing Records for all visits from the blinded and unblinded periods through May 2022 with adjudication through Nov 2022 (Additional Testing data since last report)
  - Excludes the Open Label Extension
  - Excludes Screening and Enrollment visit
  - Excludes those with no Testing records after Enrollment
- Focused on 1<sup>st</sup> reactive testing visit

## Outcomes

- Positive Predictive Value (95% CI)= Centrally Adjudicated result (True Positive) vs. Initial Site based reactive (Test Positive)
- Difference in PPV by arm (CAB-LA vs TDF/FTC)



# Testing Results



# Results: Testing Patterns

Site Testing Algorithm	Rapid Test 1	Rapid Test 2	Antigen/Antibody	Number of initial reactive visits with this pattern
2 rapid tests per visit	Nonreactive	Nonreactive	Nonreactive	N/A
	Nonreactive	Nonreactive	<b>Reactive</b>	52
	<b>Reactive</b>	Nonreactive	<b>Reactive</b>	4
	<b>Reactive</b>	Nonreactive	Nonreactive	21
	<b>Reactive</b>	<b>Reactive</b>	<b>Reactive</b>	39
	<b>Reactive</b>	<b>Reactive</b>	Nonreactive	0
1 rapid test per visit	Nonreactive	N/A	Nonreactive	N/A
	Nonreactive	N/A	<b>Reactive</b>	36
	<b>Reactive</b>	N/A	Nonreactive	3
	<b>Reactive</b>	N/A	<b>Reactive</b>	5

# Results (Overall)

**PPV for any reactive test: 74/162 (46%, CI:38%, 54%)**

Test	# Reactive Tests	Confirmed Positive	PPV (95% CI)
Rapid Tests (all types)*	114	89/114	78% (69%,85%)
Alere Determine	56	40/56	71% (58%, 83%)
Oraquick Advance	49	44/49	90% (78%, 97%)
2 Rapid Tests Reactive	40	40/40	100%(91%, 100%)
Ag/Ab Test (All types)	136	73/136	54% (45%, 62%)
Any Rapid Reactive and Ag/Ab Reactive	48	48/48	100% (93%, 100%)

\*Some rapid tests were used too infrequently to calculate an accurate PPV

# Results(by ARM)

	HIV-positive/ total reactive (CAB)	HIV-positive/ total reactive (TDF/FTC)	PPV (95% CI) (CAB)	PPV (95% CI) (TDF/FTC)
Rapid test <sup>1</sup> (all types)	8/20	81/94	40% (19%,64%)	86% (78%, 92%)
Alere Determine <sup>2</sup>	4/12	36/44	33% (10%,65%)	82% (67%, 92%)
OraQuick ADVANCE	4/5	40/44	Insufficient sample size	91% (78%, 97%)
Two reactive rapid tests	4/4	36/36	Insufficient sample size	100% (90%, 100%)
Ag/Ab test <sup>3</sup>	7/42	66/94	17% (7%,31%)	70% (60%, 79%)
Any reactive rapid or Ag/Ab test <sup>4</sup>	8/55	66/107	15% (6%, 27%)	62% (52%, 71%)

Difference in PPV (CAB vs. TDF/FTC): <sup>1</sup>-46%(-72%, -21%), <sup>2</sup>-48% (-83%, -14%), <sup>3</sup>-54% (-70%, -37%), <sup>4</sup>-47% (-62%, -33%)

# Conclusions

Two positive serological tests had High PPV in this study

HIV Ag/Ab was frequently falsely positive but detected all infections

Two reactive Rapid Tests correctly confirmed HIV diagnosis to recommend treatment initiation in this study.

PPV is lower when using CAB-LA due to its High Prevention efficacy resulting in Lower HIV incidence.

With a single reactive HIV test and high frequency of false positive testing, PrEP programs should anticipate the need for further testing, counseling about false positivity, and plans to resume PrEP after excluding HIV.

More data is needed to determine if additional testing may be required in the setting of CAB.

# Next Steps

HIV Testing Algorithms will be evaluated further in the Open Label Extensions of HPTN 083 and HPTN 084

HPTN 083 and HPTN 084 studies added HIV-RNA testing in their Open Label Extensions to explore the role of HIV-RNA for diagnosis as programs consider their testing strategies to minimize false negatives and interpret on site serological testing.

## **Sponsor**

U.S. National Institute of Allergy and Infectious Diseases (NIAID), all components of the U.S. National Institutes of Health (NIH)

## **Additional funding support**

ViiV Healthcare  
Bill & Melinda Gates Foundation  
National Institutes of Mental Health

## **Pharmaceutical support**

Gilead Sciences  
ViiV Healthcare

- **HIV Prevention Trials Network**  
Leadership and Operations Centre, FHI360  
Laboratory Centre (Johns Hopkins)  
Statistical Center for HIV/AIDS Research and Prevention, Fred Hutchison Cancer Research Center  
HPTN Leadership

### **HPTN 084 Study team**

20 sites in 7 countries in sub-Saharan Africa  
Community advisory boards and partners

... and our study participants!



Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-17 (HPTN Leadership and Operations Center), UM1AI068617-17 (HPTN Statistical and Data Management Center), and UM1AI068613-17 (HPTN Laboratory Center).

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