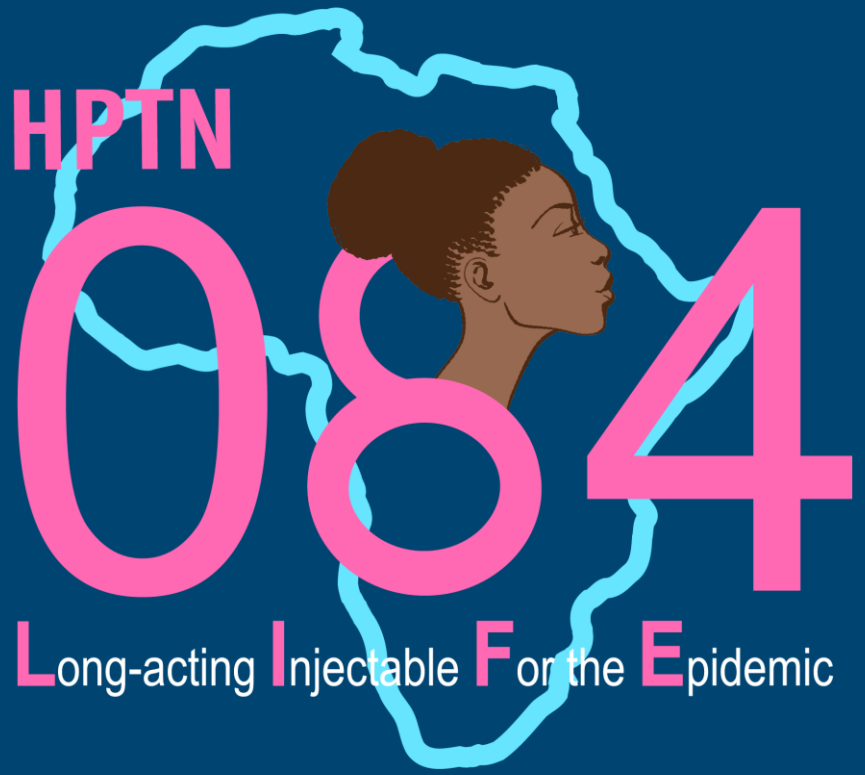


Performance of HIV RNA screening in the context of long-acting injectable cabotegravir in HPTN 084

S Delany-Moretlwe, M Holt, B Hanscom, E Piwowar-Manning, A Asmelash, N Mgodi, P Nahirya Ntege, J Farrior, L Soto-Torres, J Rooney, A Rinehart, M Cohen, M Hosseinipour, S Eshleman **on behalf of the HPTN 084 study team**

CROI 2025, San Francisco

HPTN HIV Prevention Trials Network

Background

- HPTN 084 demonstrated the effectiveness of long-acting injectable cabotegravir (CAB-LA) compared to daily oral TDF/FTC for PrEP in individuals born female.
- CAB-LA may delay the detection of early HIV infection using conventional diagnostics, leading to the emergence of resistance
- In retrospective analyses in HPTN 083, HIV RNA testing detected HIV infection prior to the emergence of resistance
- HIV RNA testing may not be feasible in many settings
- We evaluated the performance of HIV RNA screening in the HPTN 084 open-label extension (OLE)

Delany-Moretlwe, Lancet 2022; Landovitz, NEJM 2024; Eshleman, JID 2022

Attributes of a good screening test

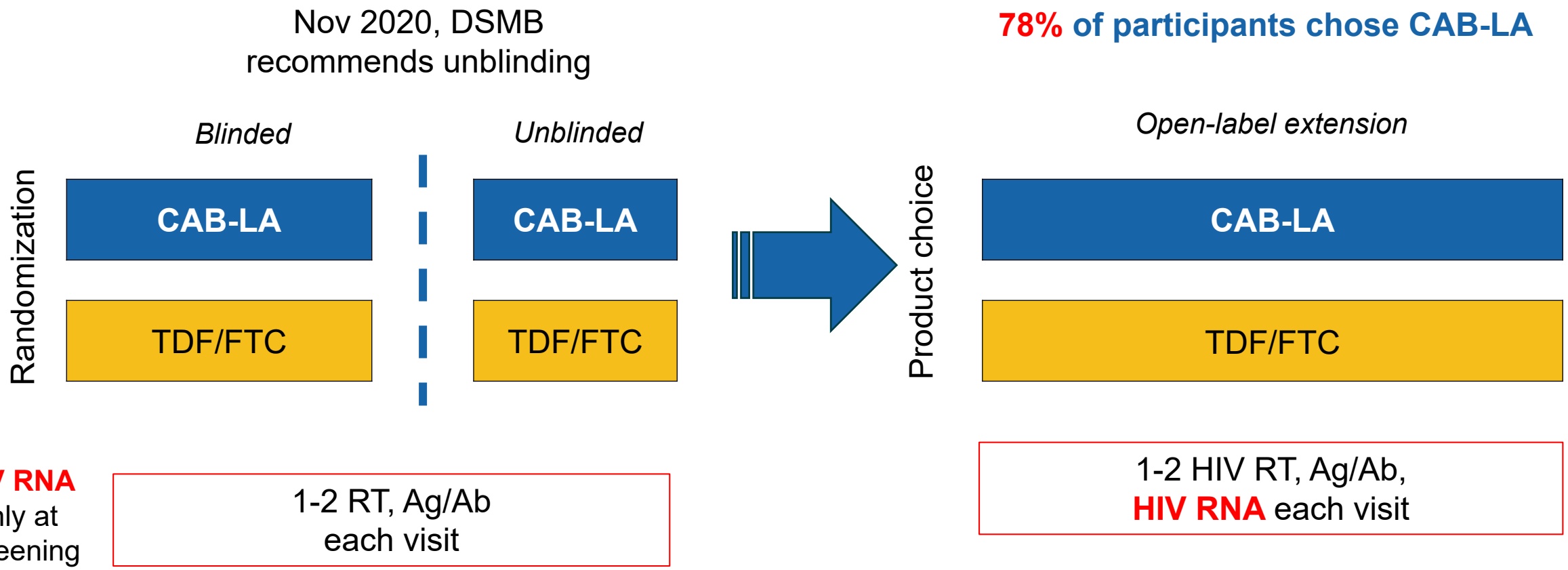
When selecting a screening test, there is a need to balance
the benefits of early treatment for those with undetected infection
vs **the harm to those that do not need treatment**

Ideally a screening test should

- Should be capable of detecting infection at an early stage
- accurately identify those with disease i.e. high sensitivity
- Have a high positive predictive value i.e. it accurately predicts the presence of infection
- Results should be easy to interpret with clear cut-off for what constitutes a positive test
- Should be reasonably priced
- Should be widely available

Based on Wilson and Junger, 1968

HPTN 084 study design



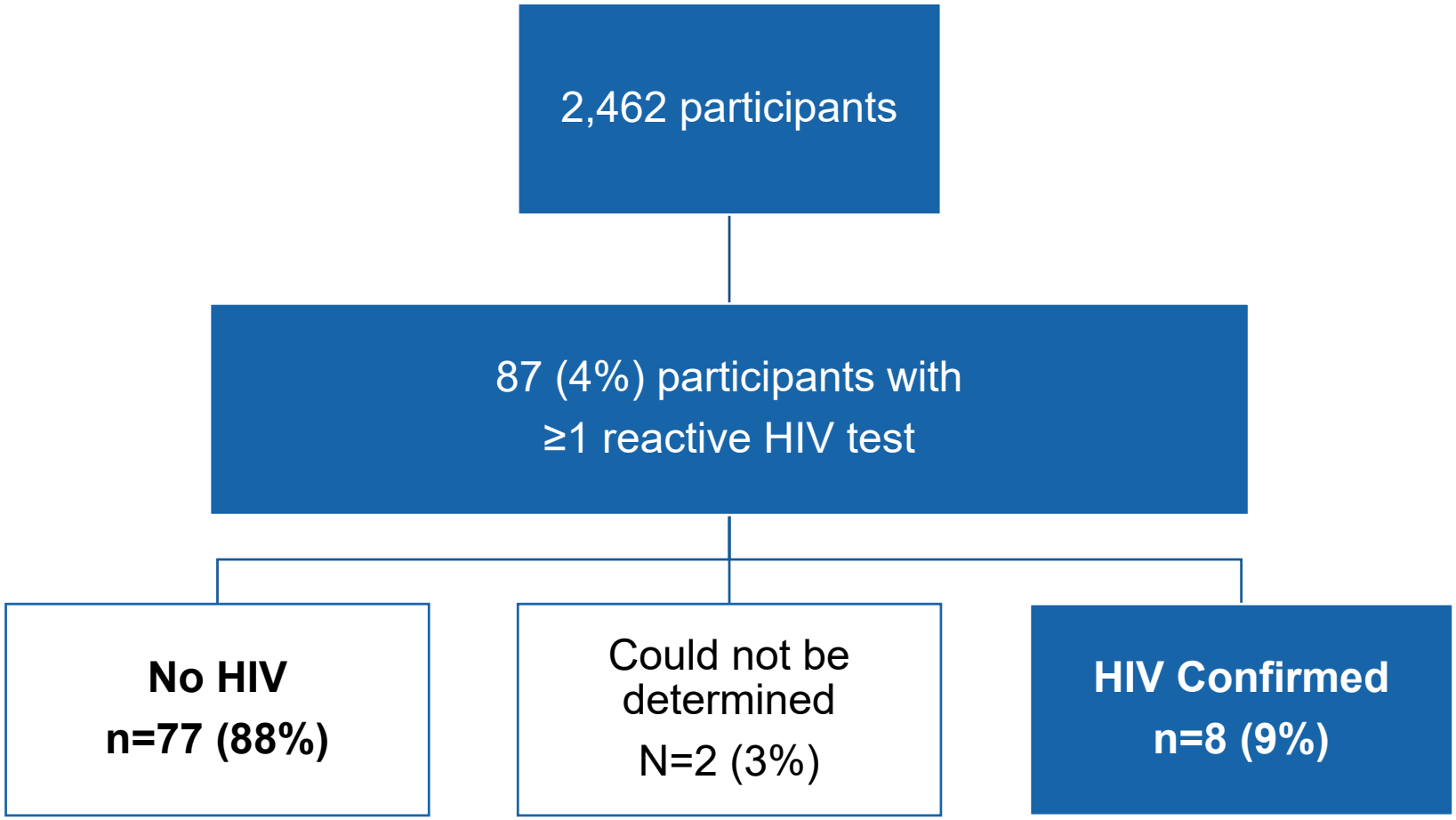
Methods

- Site based testing in OLE (all visits)
  - 1-2 HIV rapid tests (RT), antigen/antibody testing (Ag/Ab)
  - Added HIV RNA testing (LLOQ 50 copies/ml)
- Retrospective testing at central laboratory
- Final HIV status adjudicated by external committee
  - Site testing data AND retrospective testing results
- All tests included from OLE entry through Nov 30, 2023
  - Entry into OLE varied by site, starting Jan, 2022
- Estimated the positive predictive value (PPV) and false positive rate (FPR) of isolated positive HIV RNA, and sensitivity of HIV RNA screening with other tests

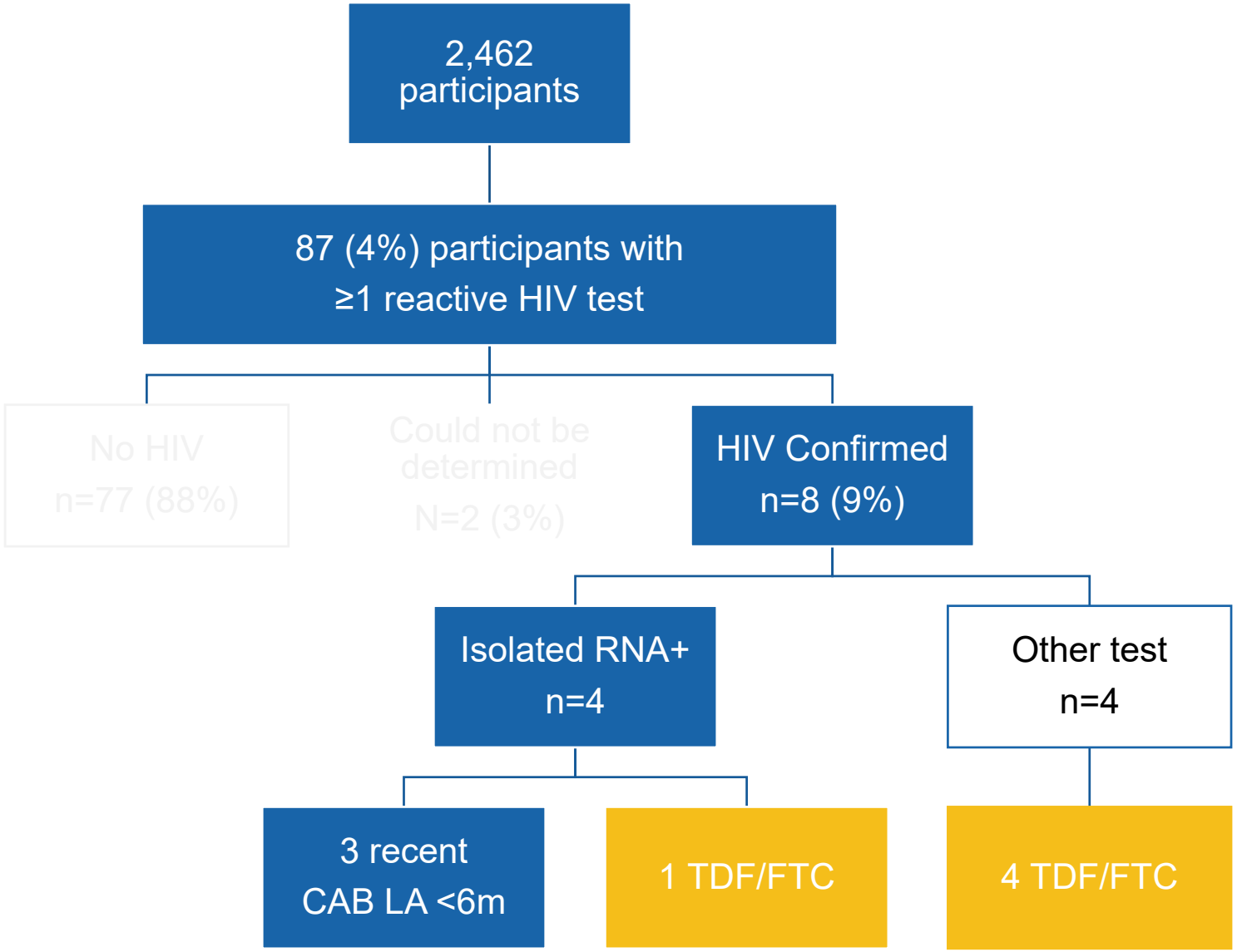
Participant characteristics

	Participants	No. of visits with RNA screening	Person-years
Overall	2,462	24,244	3,229
Country			
Botswana	71	810	108
Kenya	63	733	96
Malawi	157	1,517	200
South Africa	997	9,641	1,329
Eswatini	118	1,155	164
Uganda	419	3,881	509
Zimbabwe	637	6,507	823
PrEP choice			
CAB	1,927	20,262	2,697
TDF/FTC	535	3,982	532

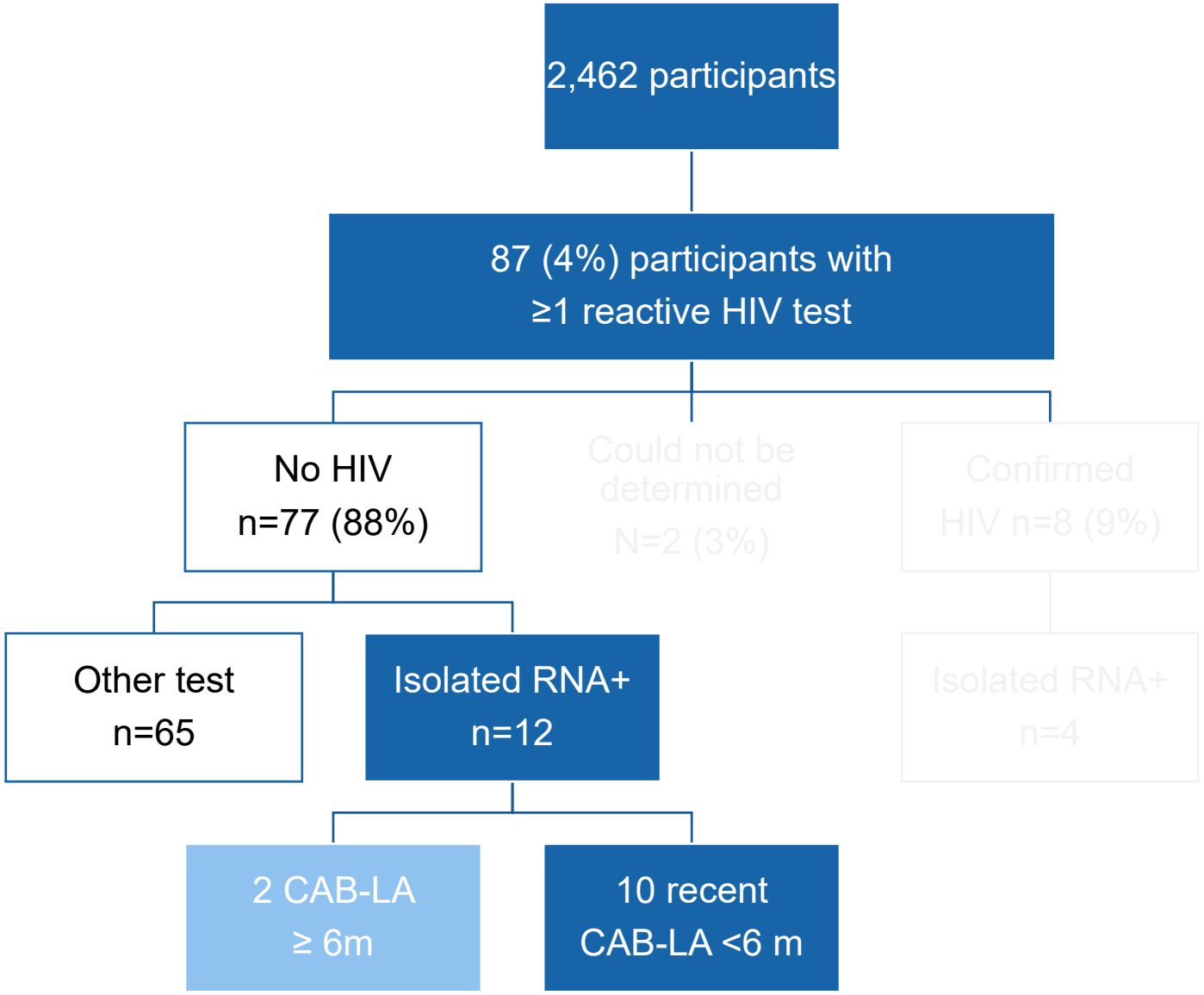
Results – HIV final adjudicated status



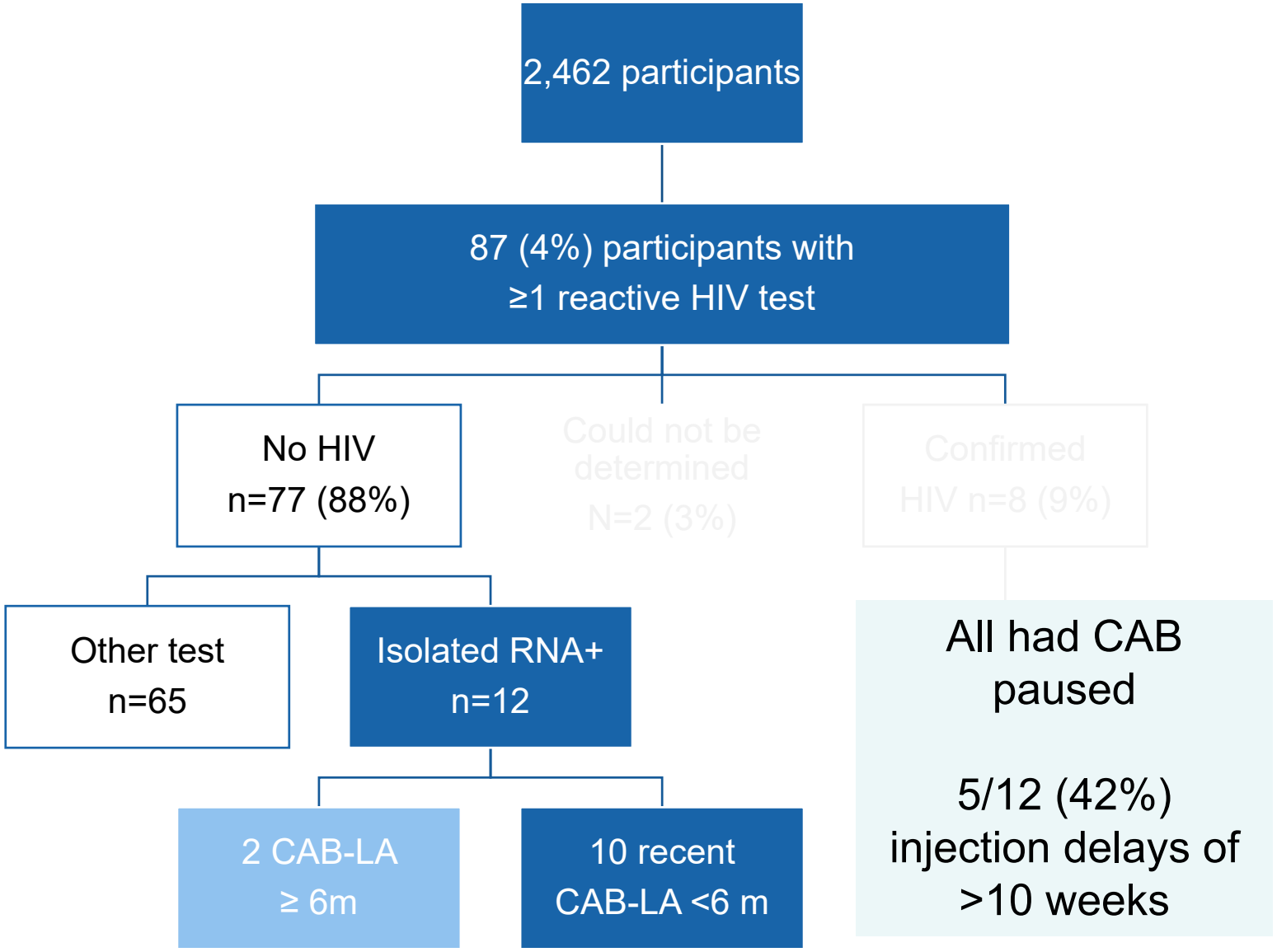
Results – true positive



Results – false positive



Results – false positive

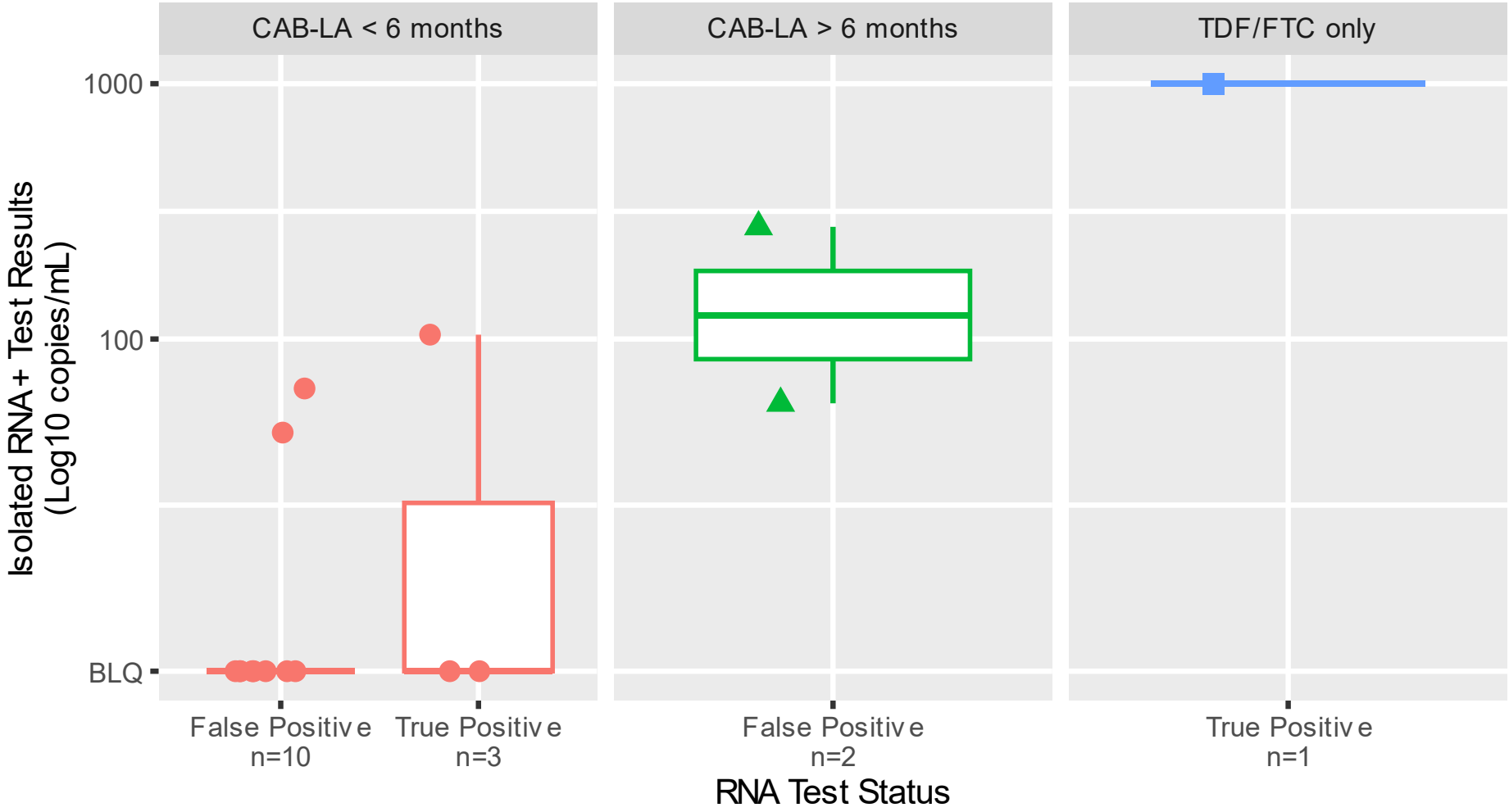


HIV RNA performance characteristics

	FPR (95% CI)	PPV (95%)	Sensitivity* (95% CI)
Overall	75% (47.6%, 92.7%)	25% (7.3%, 52.4%)	62.5% (24.5%, 91,5%)
CAB-LA use < 6 m	76.9% (46.2%, 95.0%)	23.1% (5.0%, 53.8%)	100.0% (29.2%, 100.0%)
CAB-LA use ≥ 6m	100% (15.8%, 100.0%)	0% (0%, 84.2%)	0%

**Sensitivity is based on HIV RNA with other screening tests*

HIV viral load at isolated HIV RNA positive cases



Note: Actual TDF/FTC VL was 93,873

Conclusions

- Single isolated HIV RNA tests performed poorly for detecting HIV infections in the context of CAB-LA PrEP use.
  - Able to detect early infection,
  - But insufficient accuracy (low sensitivity and specificity)
  - Difficult to distinguish true from false positives based on viral load
- Although infrequent, 75% of isolated positive HIV RNA tests were false positive
  - potential for negative clinical consequences, including prolonged PrEP interruptions.
  - High CAB-LA effectiveness in this population and subsequent low prevalence of true infection may explain the low PPV for HIV RNA screening.
- Future HIV testing algorithm guidelines should carefully consider the costs and risks in addition to any benefits of HIV RNA screening, particularly in resource-constrained settings.

Acknowledgments

Co-authors: M Holt, B Hanscom, E Piwowar-Manning, A Asmelash, N Mgodi, P Nahirya Ntege, J Farrior, L Soto-Torres, J Rooney, A Rinehart, M Cohen, M Hosseinipour, S Eshleman on behalf of the HPTN 084 study team

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