Population-level Viremia Predicts HIV Incidence across the Universal Test and Treat Studies

Maya Petersen, Joseph Larmarange, Kathleen Wirth, Timothy Skalland,
Helen Ayles, Moses Kamya, Shahin Lockman, Collins Iwuji, François Dabis,
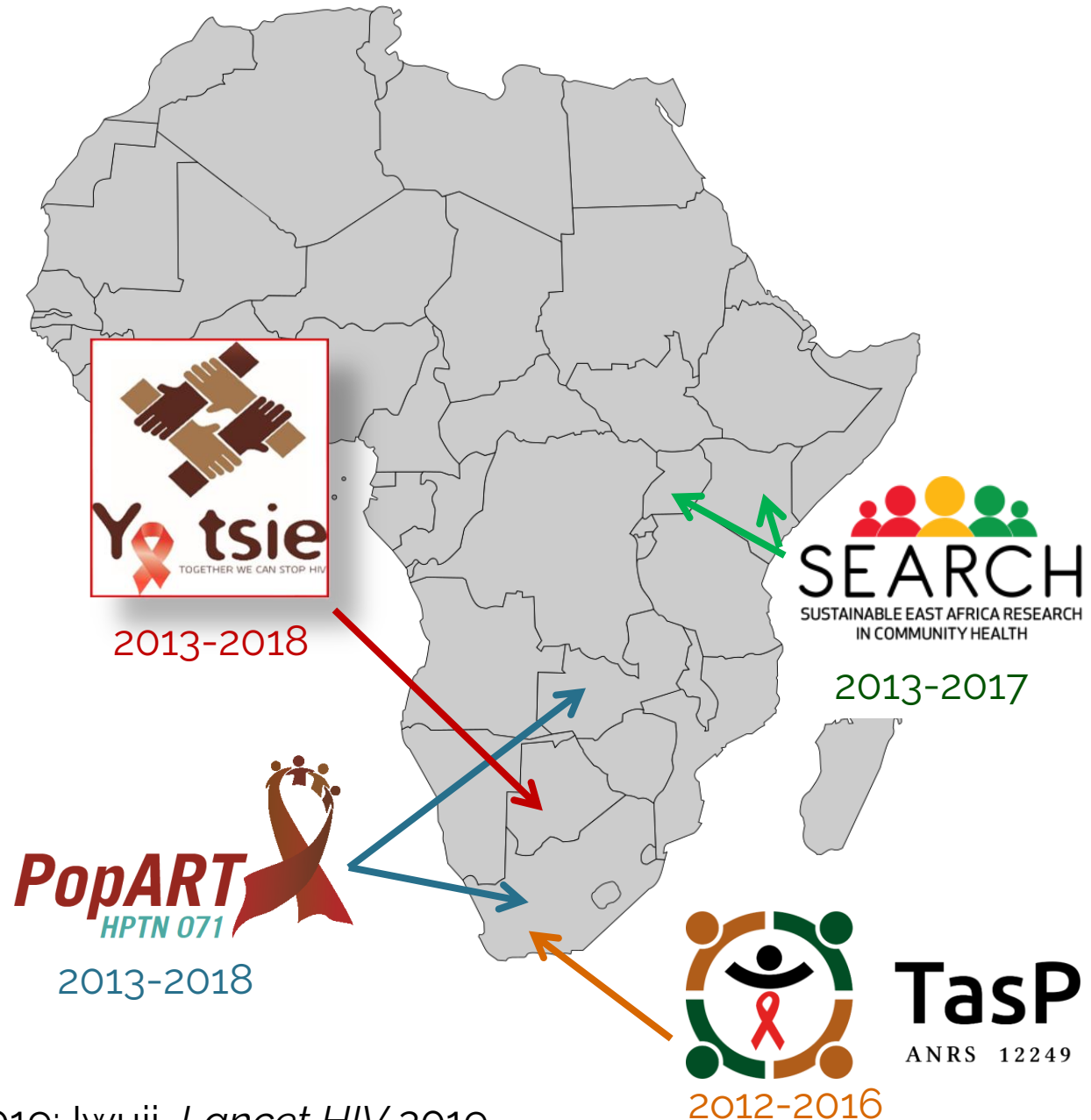Joseph Makhema,   Diane Havlir, Sian Floyd, Richard Hayes
for the
UT³C Consortium

Background and Objectives

› Universal Test and Treat interventions can increase population-level viral suppression rapidly

› Improved understanding of the impact of increased viral suppression on HIV incidence is needed

› Using data from four large cluster randomized Universal Test and Treat Trials, we evaluated:

1. The relationship between **HIV viremia** (among all adults) and **HIV incidence**

2. The relationship between **viral suppression** (among all HIV+ adults) and **HIV incidence**

3. Consistency with the UTT primary trial results

Study Settings

› **Ya Tsie**:
  › 30 communities, ~3,600 adults each
  › HIV prevalence 29%

› **HPTN 071 (PopART)**
  › 21 communities, ~25,000 adults each
  › HIV prevalence 22%

› **SEARCH**
  › 32 communities, ~5,000 adults each
  › HIV prevalence 4-19%

› **ANRS 12249 (TasP)**
  › 22 communities, ~1,300 adults each
  › HIV prevalence 30%

2013-2018

2013-2017

2013-2018

2012-2016

Makhema, *NEJM* 2019; Hayes, *NEJM* 2019; Havlir, *NEJM* 2019; Iwuji, *Lancet HIV* 2019

UTT Trial Designs: Key Features

Trial	Ya Tsie		PopART			SEARCH		TasP	
Arm	C	I	C	I Arm A	I Arm B	C	I	C	I
Universal testing	-	✓ Home, mobile	-	✓ Home + field (men, youth)	✓ Home + field (men, youth)	✓ Multi-dz Fairs/ Home	✓ Multi-dz Fairs/ Home	✓ Home	✓ Home
Testing frequency		Baseline; ongoing targeted		Ongoing ~Annual	Ongoing ~Annual	Baseline	Annual	6 monthly	6 monthly
Universal treatment	✓ (from 2016)	✓ (from 2016)	✓ (from 2016)	✓	✓ (from 2016)	✓ (from 2016)	✓		✓

Measures

› **Population-based**
  › Household census or Google Earth enumeration of community residents
› **HIV prevalence**: Study baseline/midpoint
› **Viral non-suppression**: Plasma HIV RNA > 400-500 cps/ml
  › # HIV+ adults with non-suppression/**# HIV+ adults**
  › Estimated at study midpoint
› **Population viremia:** # HIV+ adults with non-suppression/**# all adults**
  › Estimated at study midpoint based on HIV prevalence and non-suppression
› **HIV incidence rate**: Repeat testing in HIV-negative cohorts
 › Followed for up to 18 to 40 months (depending on study)

Analyses

› Community–level linear regressions to evaluate

1. Relationship between HIV Incidence and Viremia
   › Adjusted for study

2. Relationship between HIV Incidence and Non-suppression
   › Adjusted for study and prevalence

3. Cross-study heterogeneity in
   › *Intercept:* Projected incidence under no viremia/non-suppression
      - Zero in a closed population- no external infections
   › *Slope:* Reduction in expected HIV incidence for a given reduction in viremia/non-suppression

Results (1): Sample characteristics

› N=105 communities

› **HIV prevalence**: **2% to 40%**
  › Measured in 257,929 total persons
    › PopART: 37,006; BCPP: 12,570; TasP: 20,978; SEARCH: 187,375

› **Non-suppression among HIV+**: **3% to 70%**
  › Measured in 39,928 persons
    › PopART: 6,233; BCPP: 2,318; TasP: 6,617; SEARCH: 16,209.

› **HIV incidence**: **0.03 to 3.4 per 100PY**
  › Measured over 345,844 person-years,
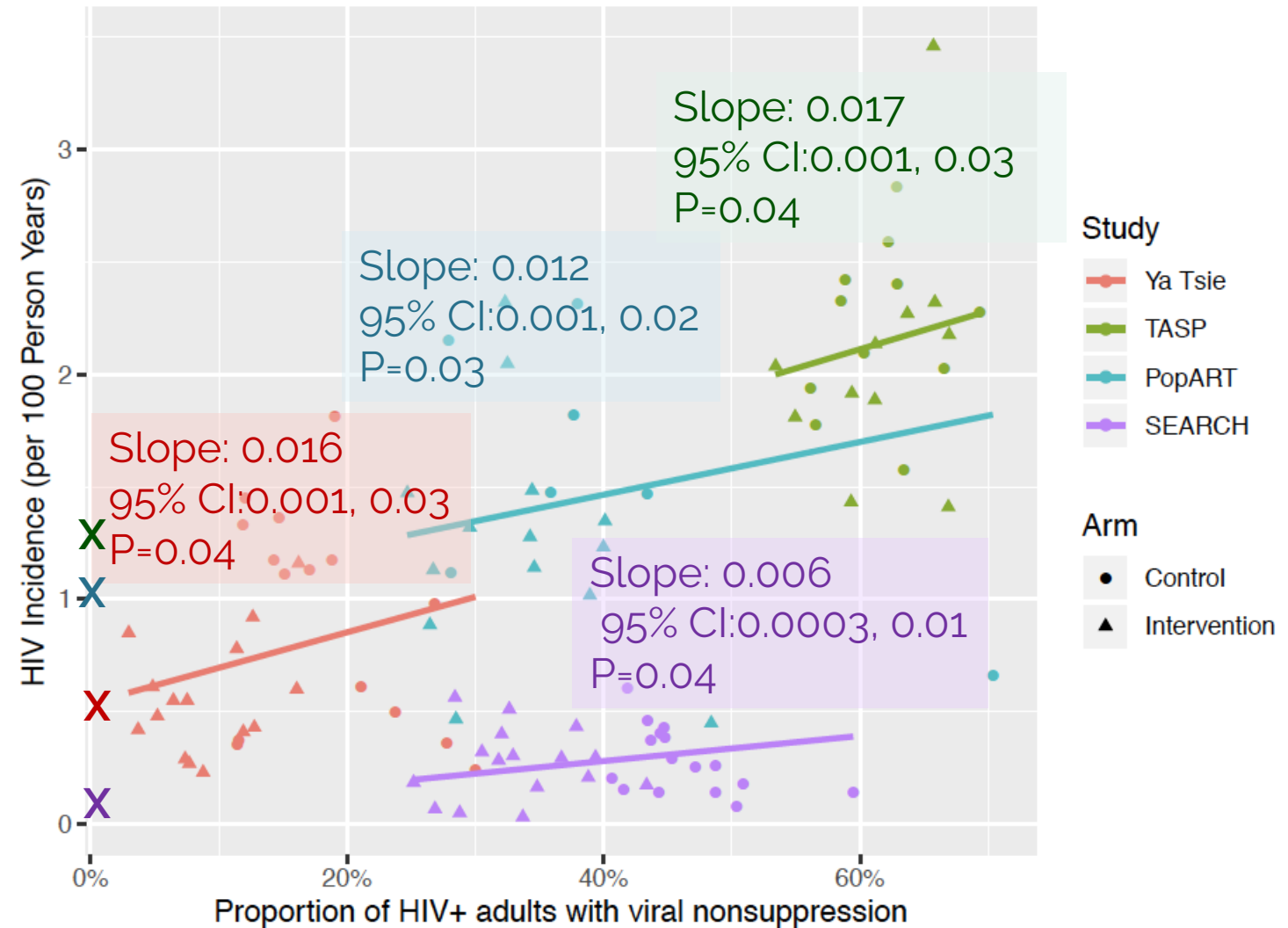   › PopART: 39,702; BCPP: 8,551; TasP: 26,832; SEARCH: 270,759

Results (2): Viremia associated with higher HIV incidence

› HIV incidence increased by 0.07/100PY for each 1% absolute increase in viremia.
  › 95% CI: 0.05,0.10, p<0.001
› Cross-Study heterogeneity
  › Slope and Intercept (**X**)
› Increased viremia associated with increased incidence in each study
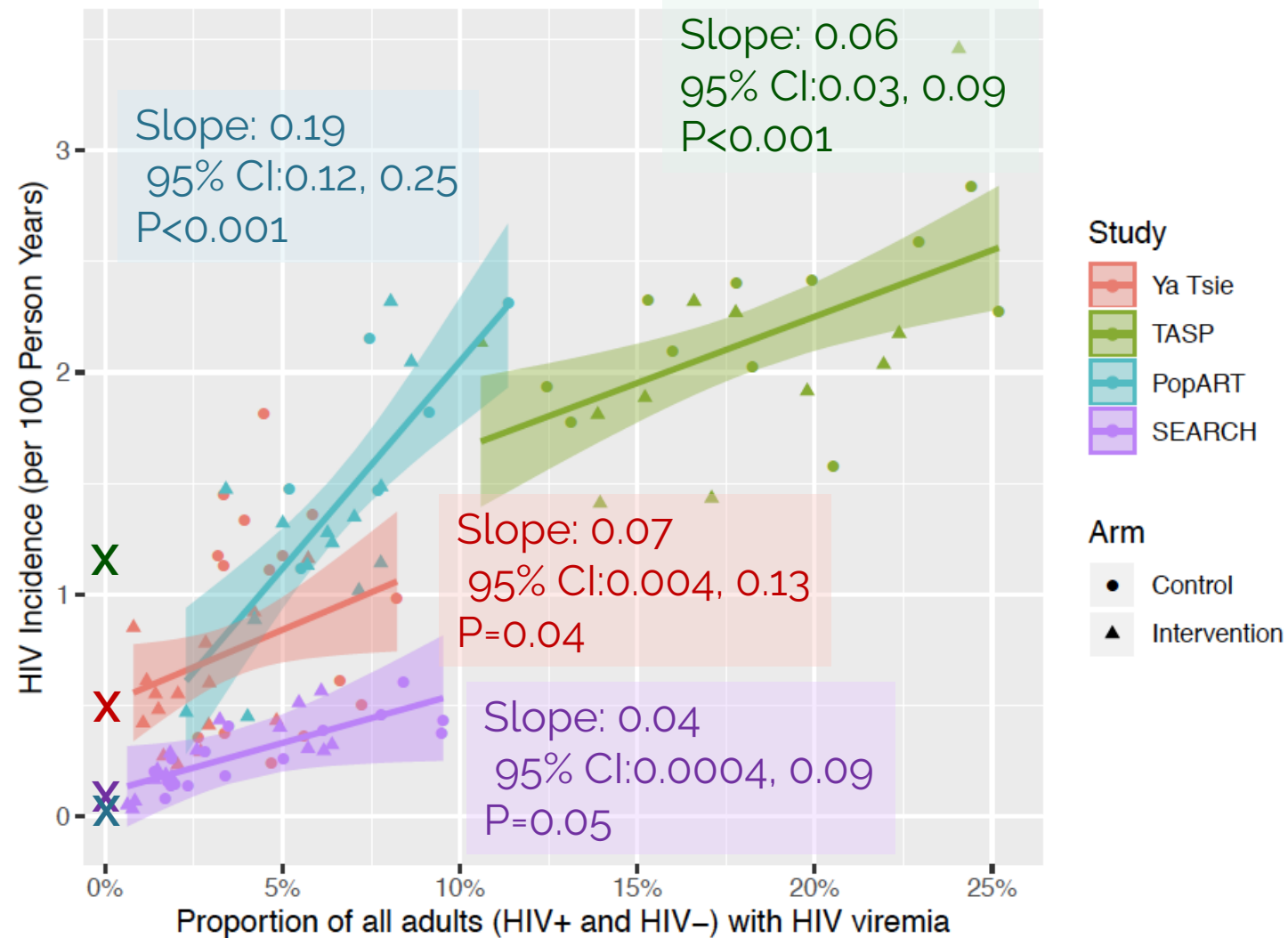
Results (3): Non-suppression among HIV+ associated with higher HIV incidence

› HIV incidence increased by 0.12/100PY for each 10% absolute increase in viral non-suppression

  › 95% CI: 0.01, 0.23, p=0.03

› Cross-study heterogeneity

  › Intercept (**X**) highest in TasP

› Incidence associated with non-suppression in each study

Adjusted for study and HIV prevalence

Slope: 0.017
95% CI:0.001, 0.03
P=0.04

Slope: 0.012
95% CI:0.001, 0.02
P=0.03

Slope: 0.016
95% CI:0.001, 0.03
P=0.04

Slope: 0.006
95% CI:0.0003, 0.01
P=0.04

HIV Incidence (per 100 Person Years)

Proportion of HIV+ adults with viral nonsuppression

Study
Ya Tsie
TASP
PopART
SEARCH

Arm
● Control
▲ Intervention
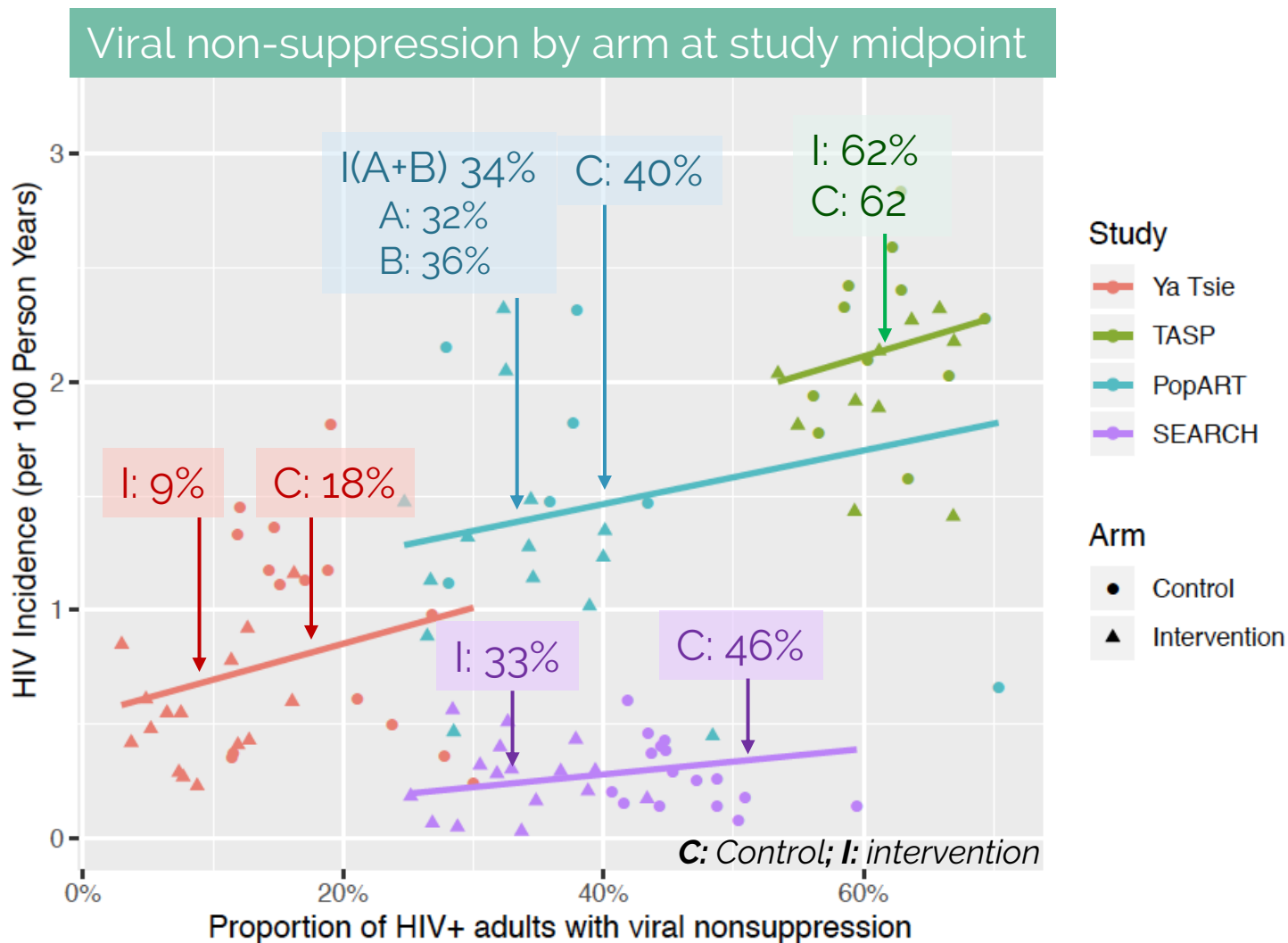
UTT Trial Results: Between Arm Differences

Viral Suppression

› <u>All trials</u>: Large increases in suppression *over time*

› Expanded ART eligibility during trials reduced *between arm differences*

› <u>Between arm difference further reduced in SEARCH, TasP:</u>
  › Due to universal testing at baseline in *both* arms

HIV incidence

› <u>Ya Tsie, PopART</u>:

Lower HIV incidence in Intervention vs. Control arms

› <u>SEARCH, TaSP</u>:

 No (detectable) incidence difference between arms
  › SEARCH: incidence declined 32% over 3 years

Do observed differences in viral suppression between arms help explain incidence findings?

Viral non-suppression by arm at study midpoint

I(A+B) 34%
A: 32%
B: 36%

C: 40%

I: 62%
C: 62

I: 9%   C: 18%

I: 33%   C: 46%

HIV Incidence (per 100 Person Years)

Proportion of HIV+ adults with viral nonsuppression

Study: Ya Tsie, TASP, PopART, SEARCH

Arm: Control, Intervention

C: Control; I: intervention

Relative reduction in HIV incidence	Observed (95% CI)	Predicted
TasP	1.01 (0.87, 1.17)	1.00
Ya Tsie	0.7 (0.50, 0.98)	0.82
SEARCH	0.95 (0.77, 1.17)	0.77
PopART Arm A+B	0.81 (0.66, 0.99)	0.95
Arm A	0.93 (0.74, 1.18)	0.94
Arm B	0.70 (0.55, 0.88)	0.96

Summary/Discussion

› Both population-level HIV viremia and non-suppression among PLWH were associated with HIV incidence
  › Across wide range of epidemic settings in sub-Saharan Africa

› Between arm differences in incidence largely explained by between arm differences in non-suppression
  › Residual differences may be due to
    › Measurement (using estimated midpoint suppression vs. viremic person time)
    › Additional intervention effects

› Consistent support across UTT Trials: Increasing population-level viral suppression reduces incidence
  › Trials further provide a model for achieving such reductions at a population level quickly (<3 years)

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ANRS 12249
TasP trial