

HPTN 071 (PopART)

Population Effects of Antiretroviral Therapy to Reduce HIV Transmission

**IMPACT OF UNIVERSAL TESTING AND TREATMENT IN ZAMBIA AND SOUTH AFRICA:
RESULTS OF A COMMUNITY-RANDOMIZED TRIAL
PANGEA WEBINAIR
APRIL 2019**

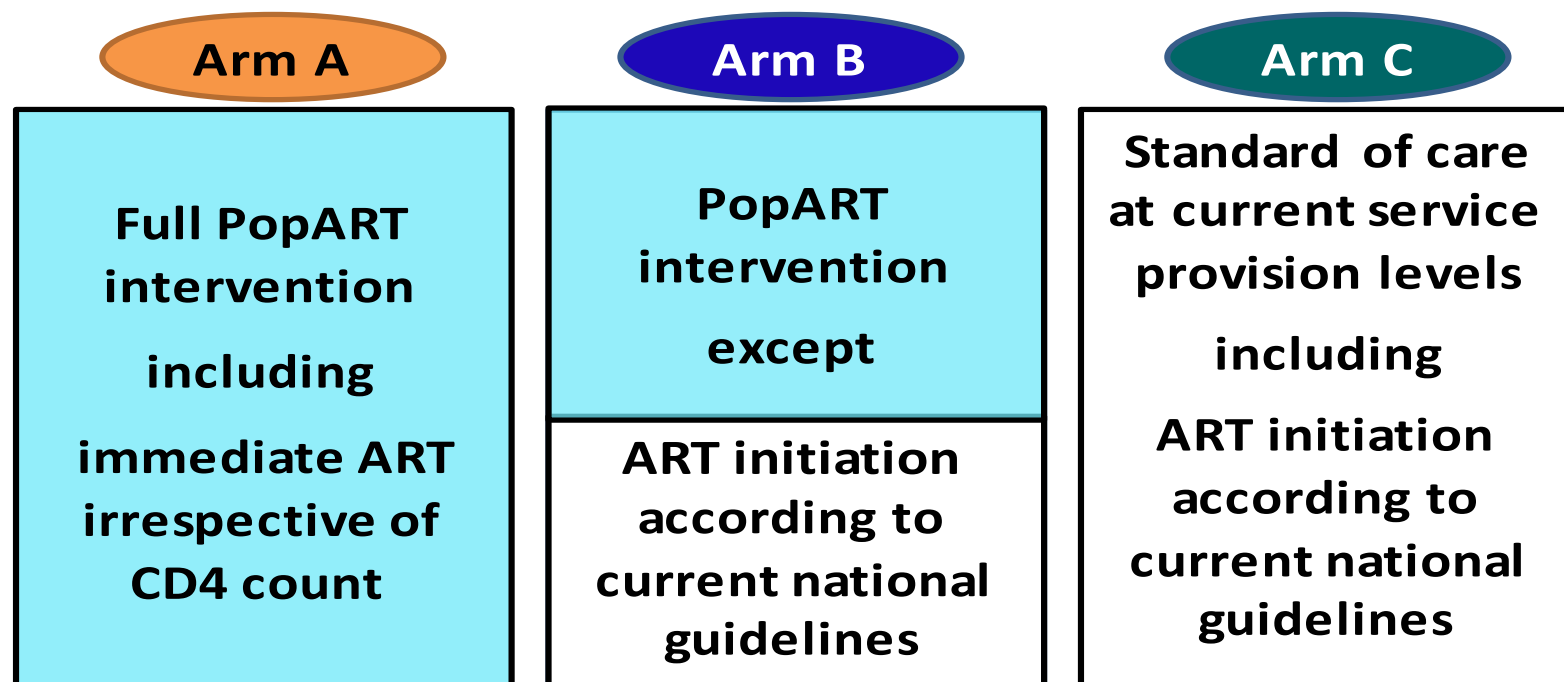
Background

- Undetectable HIV viral load reduces the risk of HIV transmission to zero (U=U)
- Universal testing and treatment (UTT) proposed as strategy to achieve steep reductions in HIV incidence
- Previous UTT trials have shown inconclusive results
 - SEARCH & TasP trials found no impact of UTT intervention vs standard care
 - BCPP found 30% reduction (borderline significance)

Research question

- Can UTT be delivered in practice in generalized epidemics in sub-Saharan Africa?
- What impact on HIV incidence can be achieved?

Study Design



Total estimated Population of all 21 study communities 1 million people

Primary Outcome measurement

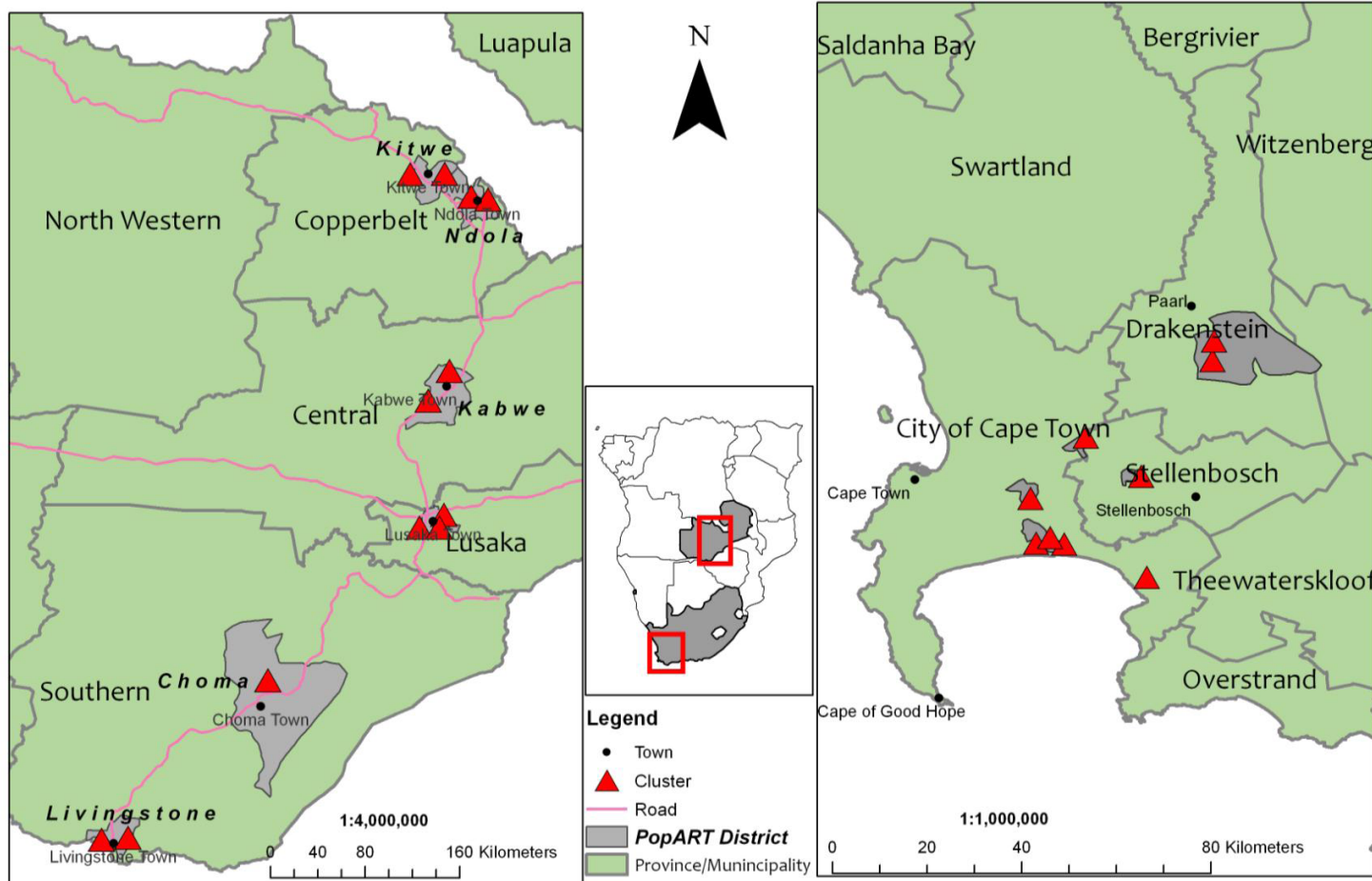
**2,500 random sample from each community
(aged 18-44)**

Population Cohort (N=52,500) PC

Followed up annually for 36 months

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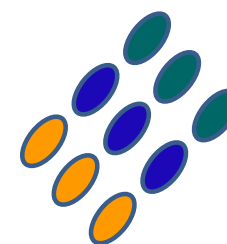


21 Communities

7 per arm (A, B & C)



12 in Zambia



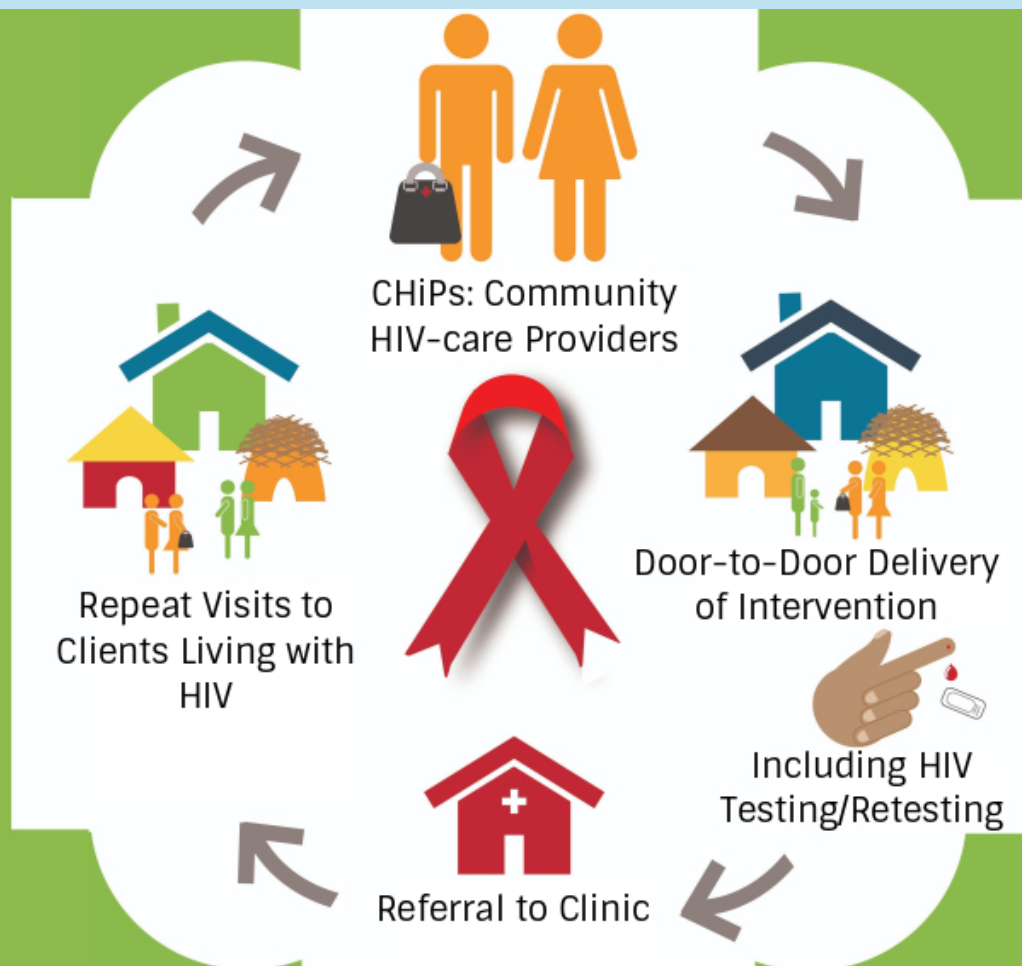
9 in S Africa

Total population ~1M

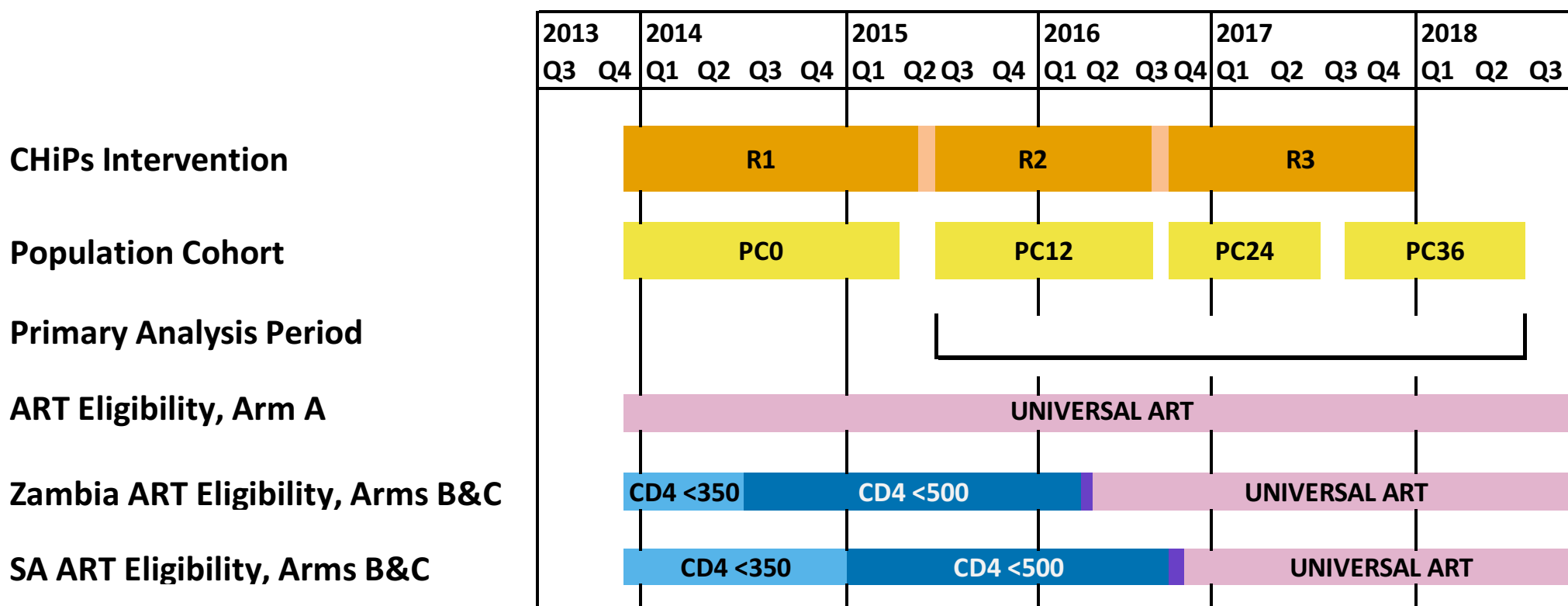


CHiPs Door-To-Door Intervention

- Universal HIV counselling and testing
- VMMC referral
- PMTCT referral
- STI screening
- TB screening
- Condoms



Study Timeline



Research cohort selection (PC)

- Aged between 18-44 years
- Randomly allocated household
- Randomly allocated consented resident individual from within that household within the age range
- **Blood draw** (annually) for HIV, HSV, HIV, viral load, viral sequencing
- **Questionnaire including**; sexual behavior, VMMC, knowledge of HIV status, ART for self reporting HIV+, economics, QoL,

PC enrolment and follow-up

PC0

Enrolled
38,474

PC12

Terminated
5,191 (13%)

Retained
25,289 (66%)

Missed
7,994 (21%)

PC12N
Enrolled
5,014

PC24

Terminated
5,043 (13%)

Retained
25,195 (66%)

Missed
8,059 (21%)

PC24N
Enrolled
4,813

PC36

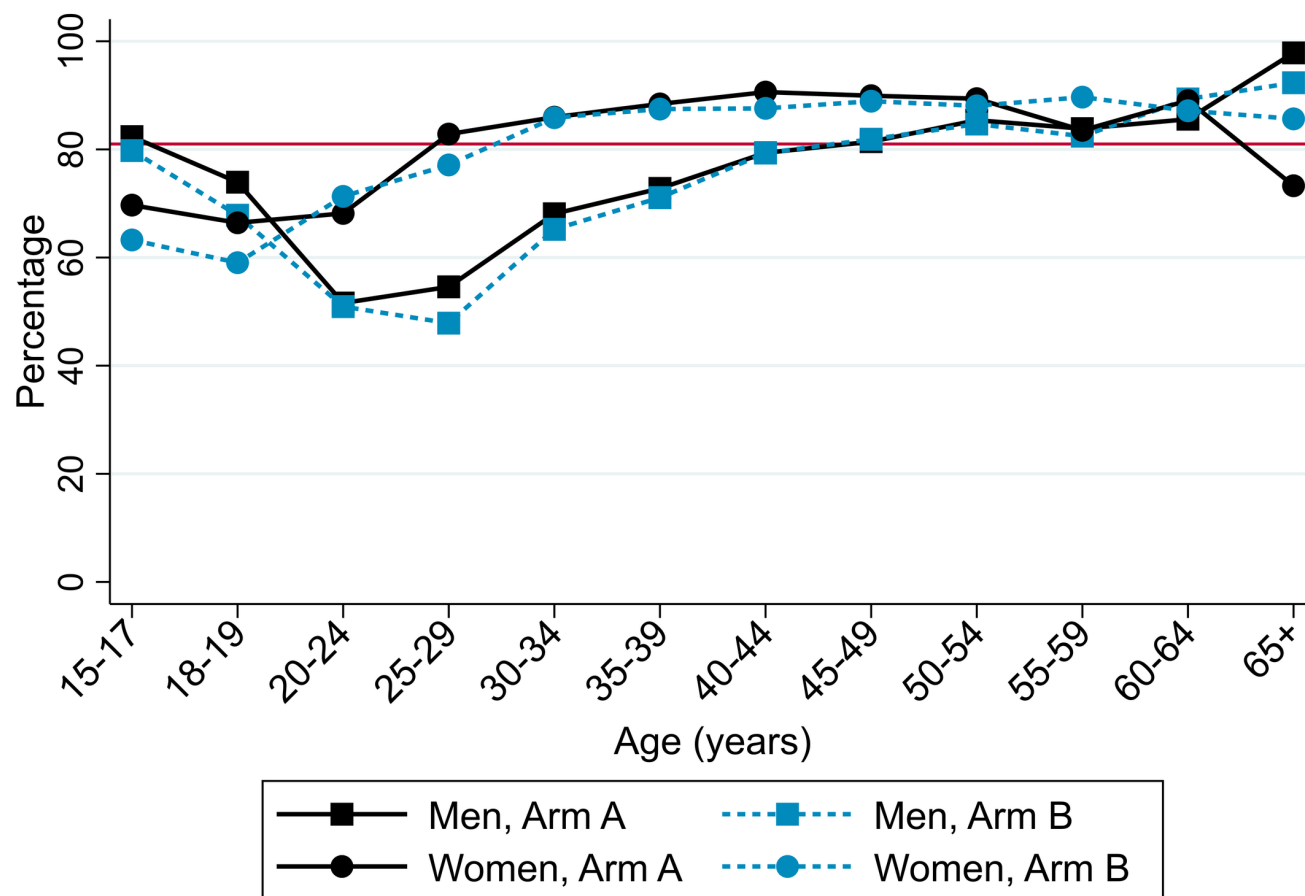
Terminated
10,566 (28%)

Retained
27,501 (72%)

Baseline characteristics of Population Cohort (PC0)

	Arm A N = 12,671	Arm B N = 13,404	Arm C N = 12,399
Male	28%	29%	30%
Age: 18 – 24	40%	39%	40%
25 – 34	39%	39%	38%
35 – 44	21%	23%	22%
HIV Prevalence: Overall	21%	21%	22%
Men	12%	11%	12%
Women	25%	25%	27%
HSV2 Prevalence: Overall	44%	43%	46%
ART (self-reported coverage in HIV+)	33%	41%	35%
Viral suppression (HIV+; 75/community)	56%	57%	54%
Medical Male Circumcision	17%	16%	19%

Delivery of intervention: ART coverage in arm A & B communities at end of trial (CHiPs data)



90-90 target = 81%

Overall Coverage

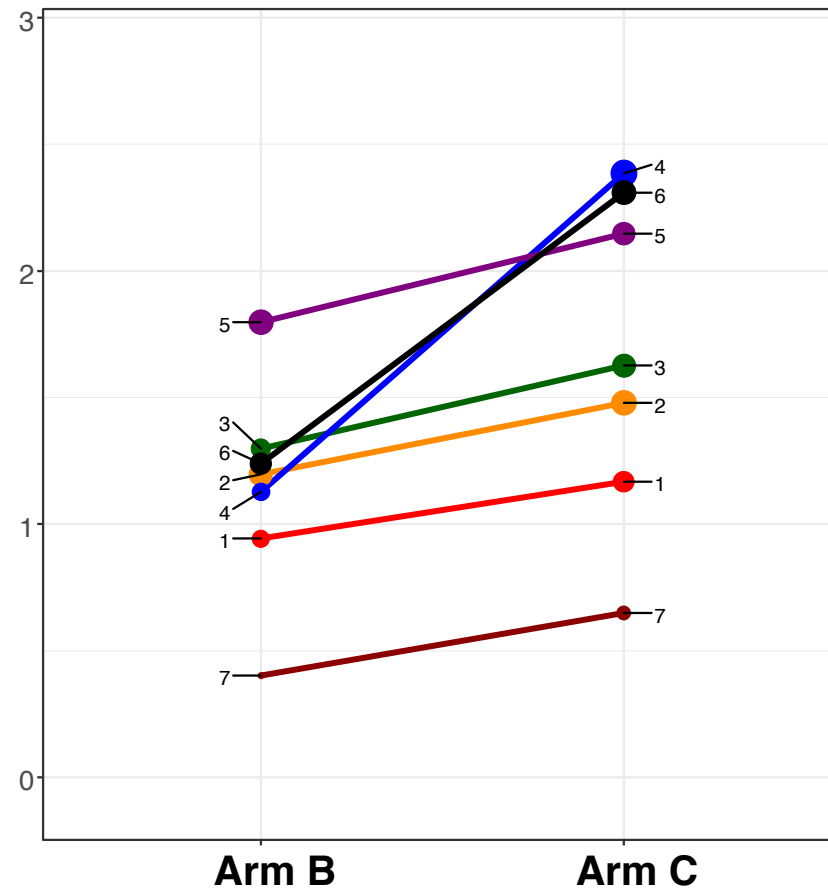
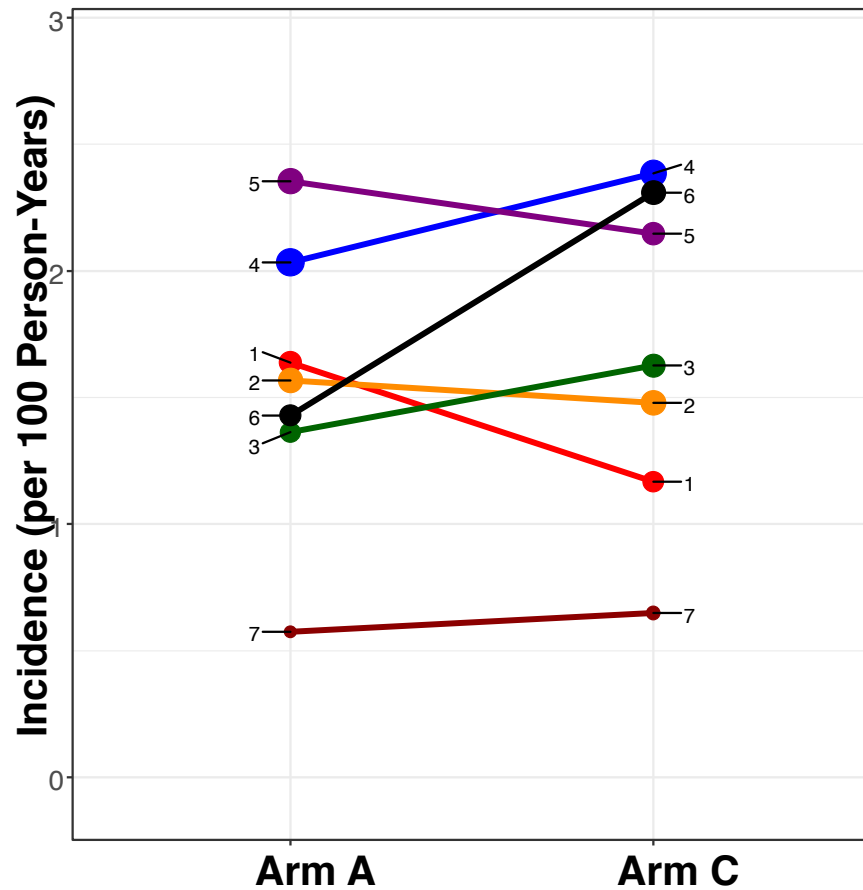
Arm A: 81%

Arm B: 80%

Primary outcome

- HIV incidence in Population Cohort
- Between PC12 and PC36 (pre-specified)
- Time of infection imputed for seroconverters who were not seen at PC12 and/or PC24
- Impact comparing Arm A vs C, and Arm B vs C
- Using methods for matched cluster-randomized trials

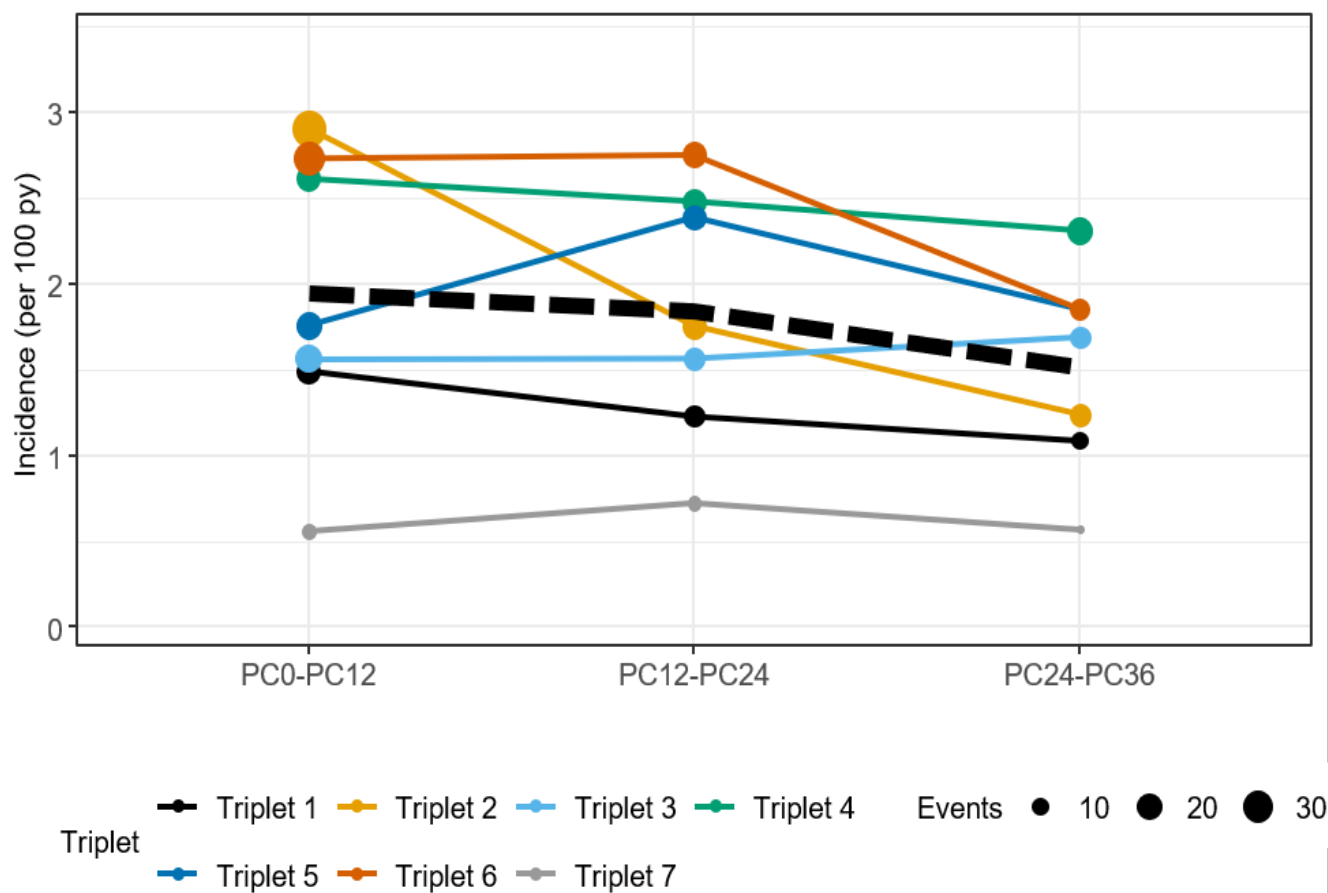
HIV Incidence by community (PC12-PC36)



Triplets Z Triplet 1 Z Triplet 2 Z Triplet 3 Z Triplet 4
 SA Triplet 5 SA Triplet 6 SA Triplet 7

Events • 10 • 20
 • 30 • 40

HIV incidence over study years in Arm C communities



Primary analysis: Incidence in PC12-PC36

	Arm A	Arm B	Arm C
HIV Incidence (geometric mean of community incidence rates)	198/12,990 (1.45%)	157/14,149 (1.06%)	198/12,563 (1.55%)
Adjusted Rate Ratio (95% CI)	0.93 (0.74, 1.18)	0.70 (0.55, 0.88)	1
Incidence compared to Arm C	7% reduction	30% reduction	
P value	0.51	0.006	

Adjusted for age category, sex and baseline community HIV prevalence.
Reported numbers include imputation for PC12 and PC24 missed visits

What were the differences between arms A & B communities?

- CHiPs teams
 - Offered ART start from 2014 irrespective of CD4 count
 - Needed written informed consent to start ART outside of guidelines until 2016 if wanting to start ART at clinic
- CHiPs teams
 - Offered ART according to CD4 threshold until Q2 2016 (Zambia) and Q4 2016 South Africa
 - No requirement for informed consent to start ART at clinic

Viral suppression at PC24

	Arm A	Arm B	Arm C
Viral suppression (Geometric mean of community %)	1531/2159 (72%)	1318/1891 (68%)	1480/2183 (60%)
Adjusted prevalence ratio (95% CI)	1.16 (0.99, 1.36)	1.08 (0.92, 1.27)	1
VS compared to Arm C	16% increase	8% increase	
P value	0.07	0.30	

Adjusted for age category, sex.

Viral suppression in HIV-positive PC participants at each study year.

	Arm A	Arm B	Arm C
	# suppressed/no. HIV-positive (Overall Prevalence ¹)		
PC0	294/522 (56.0%)	300/525 (56.6%)	266/492 (50.4%)
PC12	379/529 (71.3%)	364/528 (68.4%)	313/491 (60.9%)
PC24	1467/1989 (74.8%)	1256/1725 (70.6%)	1421/2011 (63.8%)
PC36	371/490 (75.8%)	359/478 (74.3%)	332/450 (68.0%)

Viral suppression and incidence

- Using data from PC24, in the middle of the primary analysis period,
- overall viral suppression in Arms A and B was 72.7%, and in Arm C was 63.8%.
- The corresponding proportions *virally unsuppressed* were 27.3% and 36.2%, which would imply a reduction in HIV transmission of around 25%.
- Post-hoc analysis of arms A+B vs C showed a significant reduction in HIV incidence of approximately 20%

Key observations

- It is **feasible and acceptable** to deliver community-wide HIV services in large urban communities in Southern Africa through a system of community HIV-care providers (CHiPs), so that *every community resident* is visited and provided with services each year.
- The trial results on HIV incidence together with the data on viral suppression show convincingly that the CHiP intervention can be implemented and is expected to reduce HIV incidence each year by around 20-25%, and will build up each year
- Coverage of the CHiP intervention is lower in some subgroups, including men and young people. Continued efforts will be needed to fill these gaps and achieve the highest possible coverage in every subgroup of the population.

HPTN 071 (PopART) Summary

- PopART achieved the first two UNAIDS 90-90 targets in arms A and B
- High rates of viral suppression achieved
- PopART with ART according to local guidelines (Arm B) reduced HIV incidence by 30% in these high burden settings (from 1.6% to 1.1%).
- Lack of an effect in the full intervention arm (Arm A), where universal treatment was delivered ahead of change in guidelines, was surprising and not explained by lower rates of viral suppression.
- Further analysis of quantitative, qualitative and phylogenetic data in progress to explore and explain this dissonant finding.
- **Community-based services for *universal* HIV testing and linkage are a key component of combination prevention in the global effort to achieve effective HIV control.**

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HIV Incidence by community (PC12-PC36)

