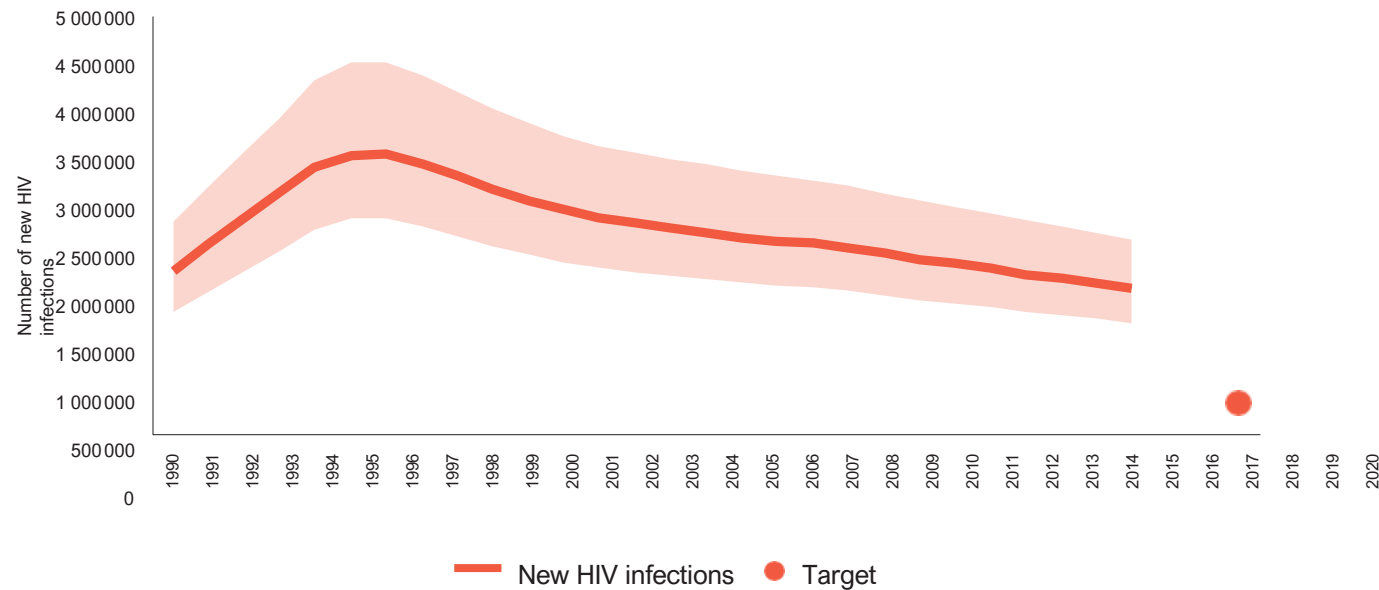# HPTN 071 (PopART)
Population Effects of Antiretroviral Therapy to Reduce HIV Transmission

IMPACT OF UNIVERSAL TESTING AND TREATMENT IN ZAMBIA AND SOUTH AFRICA: RESULTS OF A COMMUNITY-RANDOMIZED TRIAL

IAS SPECIAL SESSION

Insufficient progress on prevention

Number of new HIV infections, global, 1990–2017 and 2020 target

Source: UNAIDS 2018 estimates.

Universal testing and treatment

- All community members should test regularly for HIV and know their status *(Universal testing)*

- All those diagnosed HIV-positive should be offered ART *(Universal treatment)*

- Once established on ART and "virally suppressed", risk of transmission to partners is negligible

   Undetectable = Untransmissible

PopART: What were the questions?

- Universal testing and treatment (UTT) proposed as strategy to achieve steep reductions in HIV incidence

- Can UTT be delivered in practice in generalized epidemics in sub-Saharan Africa?
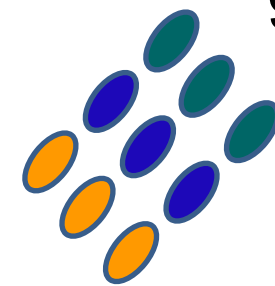
- What impact on HIV incidence can actually be achieved?
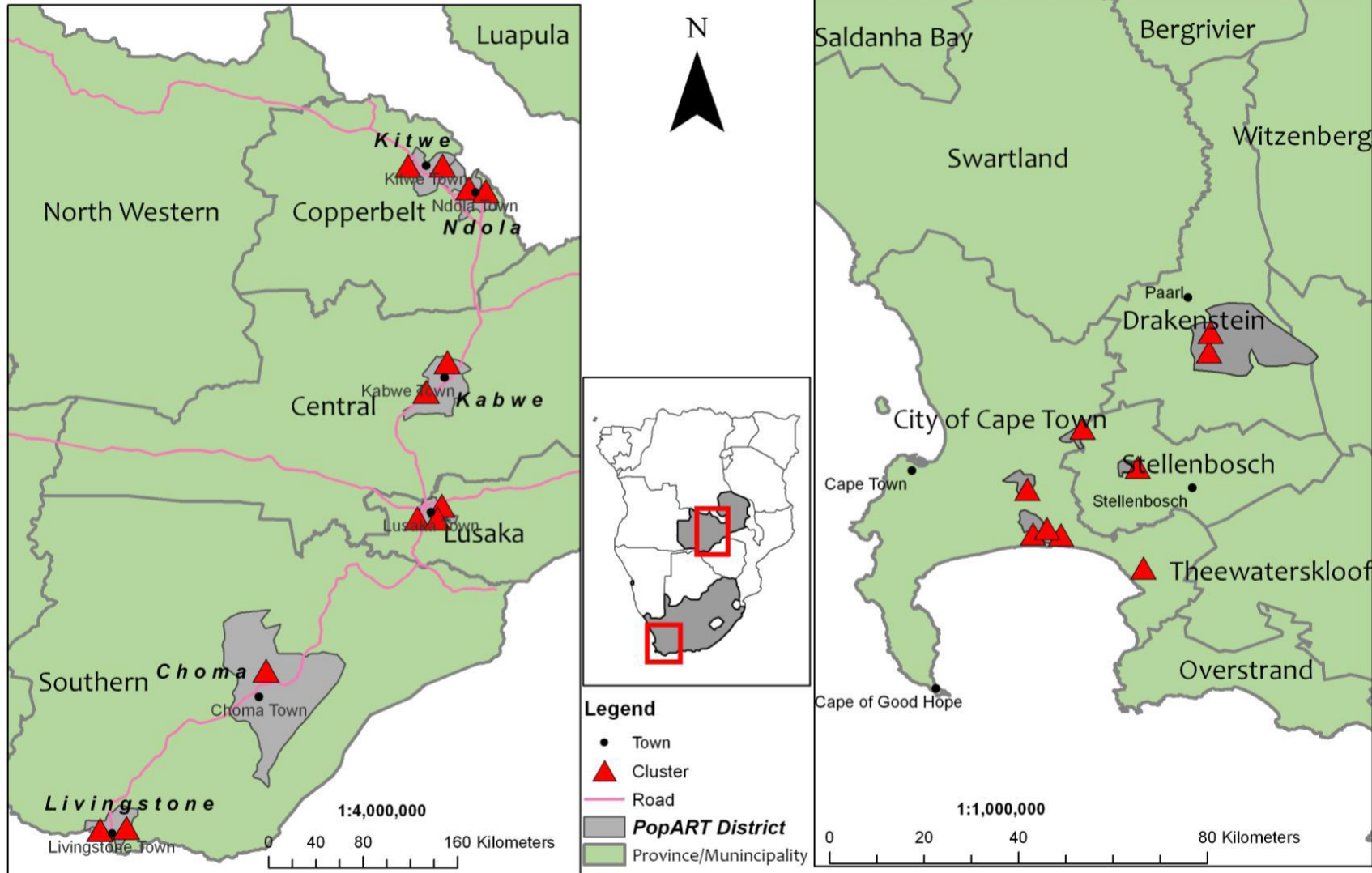
21 Communities
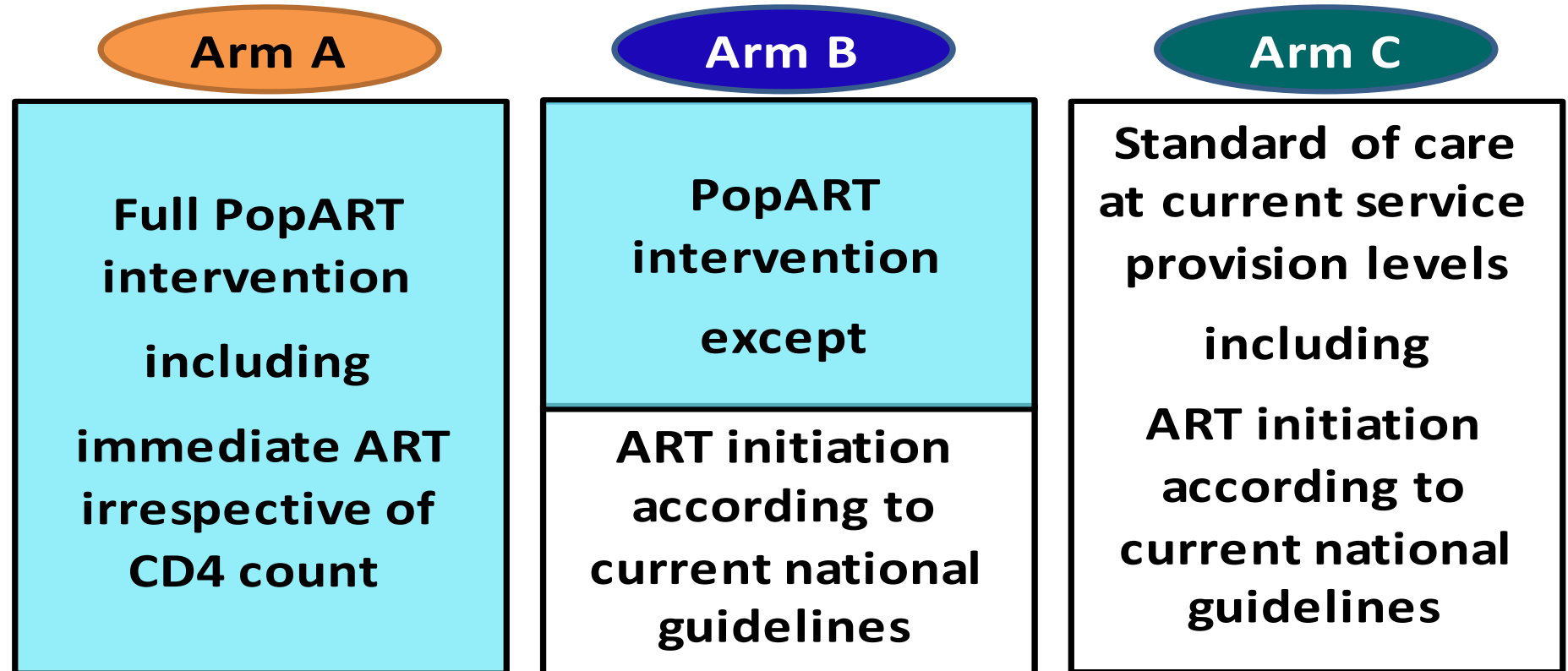7 per arm (A, B & C)

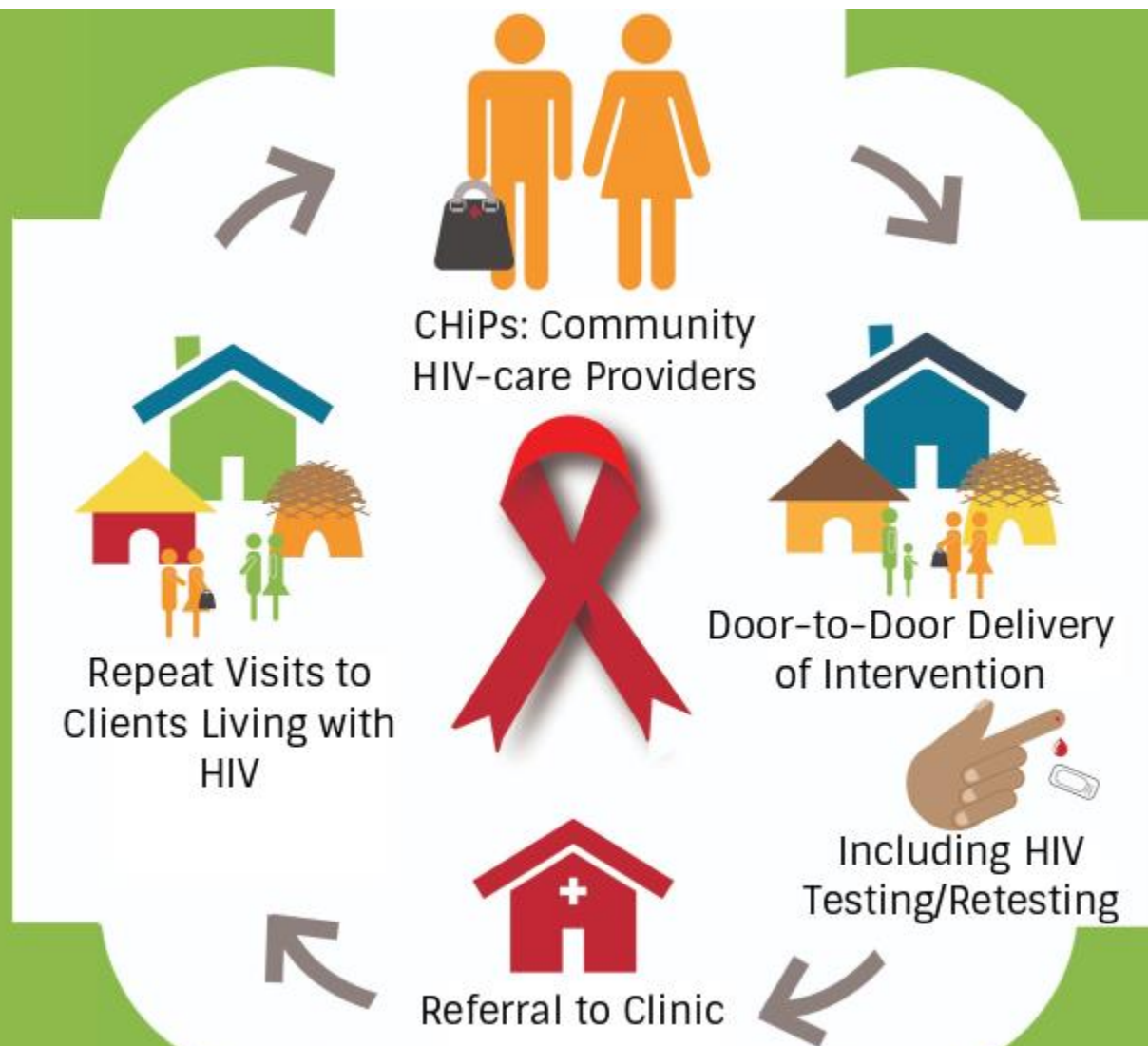**12 in Zambia**

9 in S Africa

Total population ~1M

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

CHiPs Door-To-Door Intervention

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

CHiPs: Community HIV-care Providers

Door-to-Door Delivery of Intervention

Including HIV Testing/Retesting

Referral to Clinic

Repeat Visits to Clients Living with HIV

Study Timeline
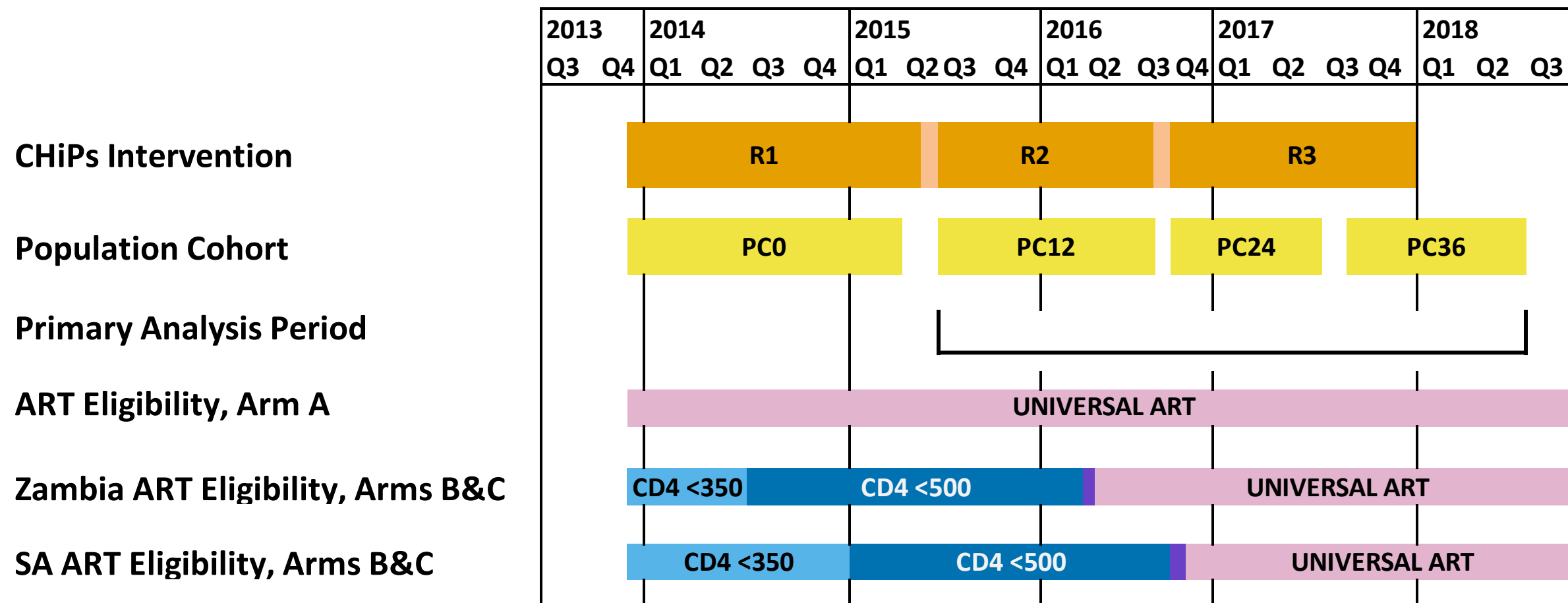
Delivery of intervention: ART coverage in arm A & B communities at end of trial
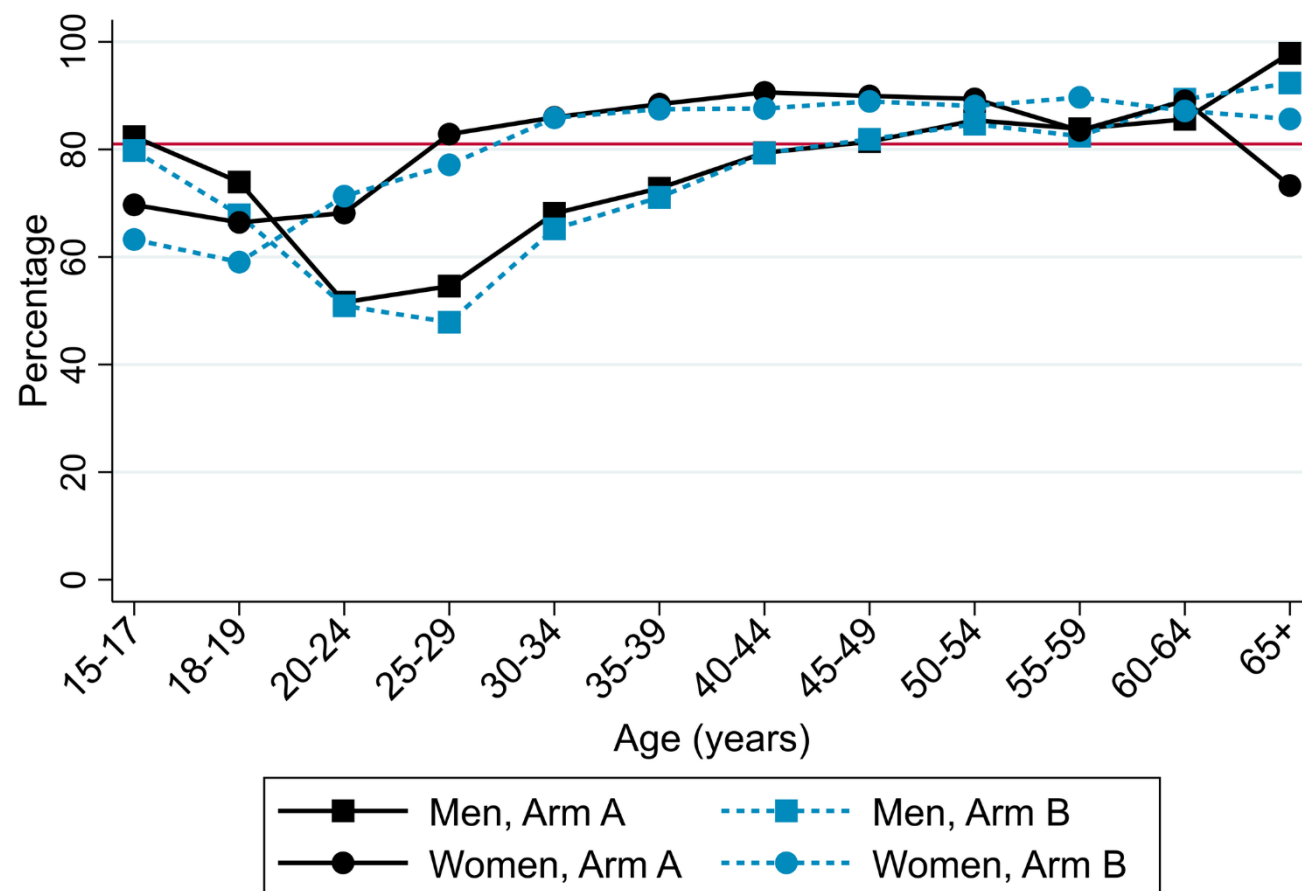
90-90 target = 81%

Overall Coverage
Arm A: 81%
Arm B: 80%

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%

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

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

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.

Hypotheses for Arm A vs C finding

- Poorer delivery of intervention in Arm A
- Written informed consent initially required to start ART outside local guidelines in Arm A
- Sexual risk disinhibition in Arm A if perceived risk lower
- Higher migration or mobility in Arm A communities leading to "contamination"
- Chance

Post-hoc analysis of (A + B) vs C

- Note: Interventions in Arms A and B were identical for most of the primary analysis period

- Combining arms A and B, and comparing with Arm C;
  - **RR = 0.81 (95% CI: 0.66 – 0.99; p = 0.04)**

Evidence of a ~20% reduction in HIV incidence

PopART and the other UTT trials

UTT trials reported previously:

- TasP (South Africa)

- SEARCH (Uganda and Kenya)

- BCPP (Botswana)

ANRS 12249 TasP: HIV incidence comparison

	Number of HIV-positive DBS tests	Person-years	Incidence for 100 person-years	95% CI
Control	268	11,787	**2.27**	2.00-2.55
Intervention	227	10,646	**2.13**	1.85-2.41
TOTAL	495	22,434	2.21	2.01-2.40

Adjusted risk ratio*

	aRR	95% CI	P-value
Intervention vs control	0.95	0.79-1.14	0.5821

Estimated with Poisson regression, adjusted on sex, age, change in national ART guidelines, baseline cluster HIV prevalence and ART coverage

Dabis et al, AIDS 2016, Durban

ANRS 12249 TasP - Estimated cascade of care

UNAIDS target

	diagnosed	on treatment	virally suppressed	
	90.0%	90.0%	90.0%	= 72.9%

TasP trial (1st January 2016)

Control

93.4%	46.0%	93.6%	= 40.2%

Intervention

92.3%	49.2%	93.4%	= 42.4%
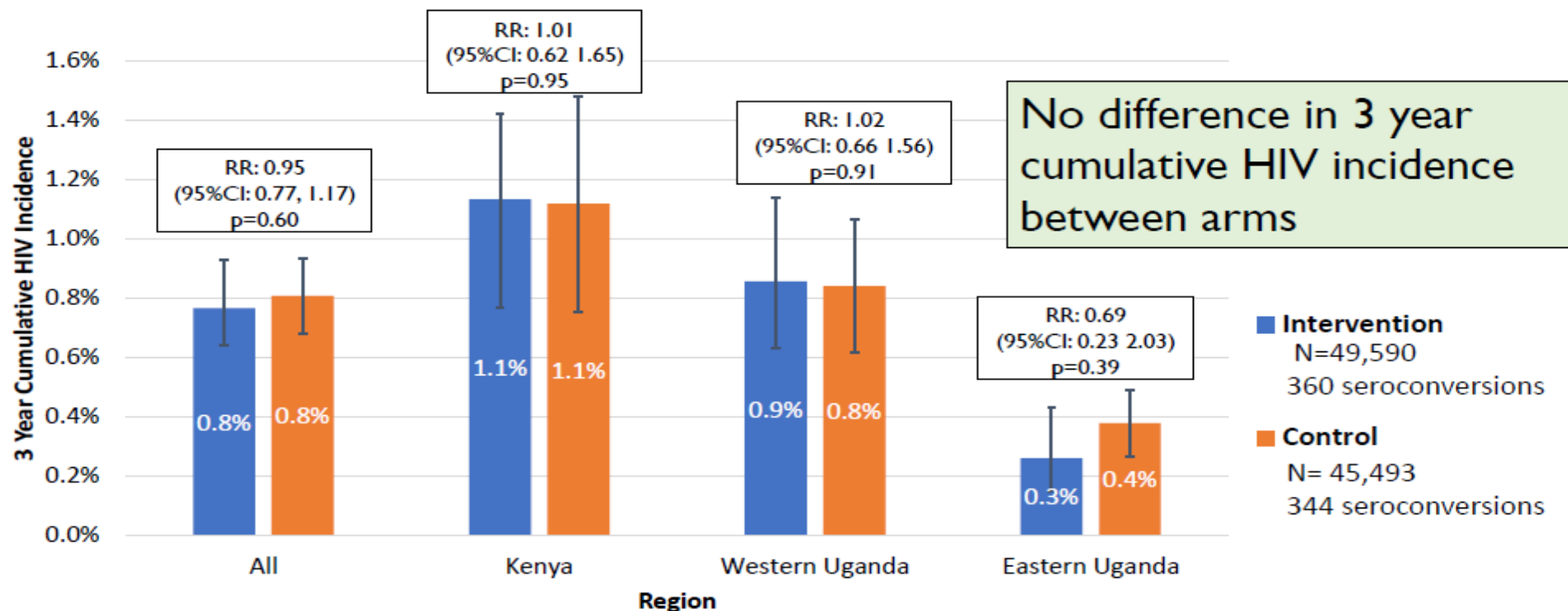
Havlir et al, AIDS 2018, Amsterdam

Primary Results: HIV Incidence in the Intervention vs. Standard of Care Arms

57 participants in the intervention arm (annualized HIV incidence: 0.59%) and 90 in the standard of care arm (annualized HIV incidence: 0.92%) acquired HIV.

Results of unadjusted and adjusted analyses of treatment effect

Analysis	Incidence Ratio	95% CI	2-sided p-value
Primary analysis (permutation test, pair-specific Cox PHM), unadjusted	0.69		0.09
Analysis to obtain 95% CI (standard pair-stratified Cox PHM), unadjusted	0.65	0.46-0.90	0.01
Primary analysis, adjusted*	0.62		0.04
Analysis to obtain 95% CI, adjusted*	0.70	0.50-0.99	0.04

* Covariates in adjusted analyses were: sex, age, education, marital status, concurrent sexual partners, and alcohol during last sex

Results of main analyses are consistent, and indicate at least 30% reduction in HIV incidence associated with the intervention

HPTN 071 (PopART): What have we shown?

- Feasible and acceptable to deliver community-wide HIV services in urban communities with severe HIV epidemics

- PopART achieved the UNAIDS 90-90-90 targets with overall Viral Suppression of around 70% - increased from ~55% at start of trial

- Over 3 years, *population-level* HIV incidence was around *20% lower* in Arms A and B than in Arm C

- Proportions with *detectable* viral load (at 24m) were ~30% in Arms A/B and ~40% in Arm C –consistent with an expected effect on HIV transmission of ~20-25%

HPTN 071 (PopART) and UTT trials

- Results of all four UTT trials are aligned with this paradigm:
- Effect on HIV transmission is consistent with the reduction in unsuppressed viral load comparing intervention and control arms
- This means that the product of the three 90s is a valuable marker for delivery of *treatment as prevention*
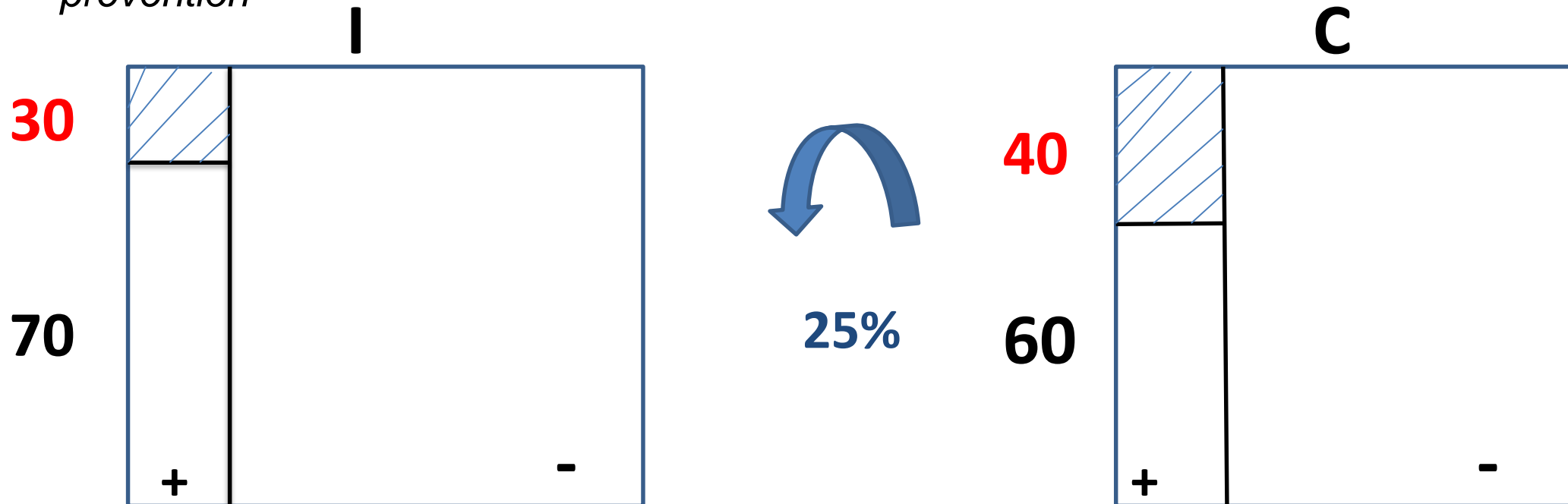
HPTN 071 (PopART): What have we shown?

- A sustained annual reduction in incidence of 20% would have a profound impact on the incidence curve and move us towards the UNAIDS "ending AIDS" targets

- **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.**

ACKNOWLEDGEMENTS

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Dr. Helen Ayles
Dr. Nulda Beyers
Dr. Peter Bock

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