The Botswana "Ya Tsie" HIV combination prevention project: what did we learn?

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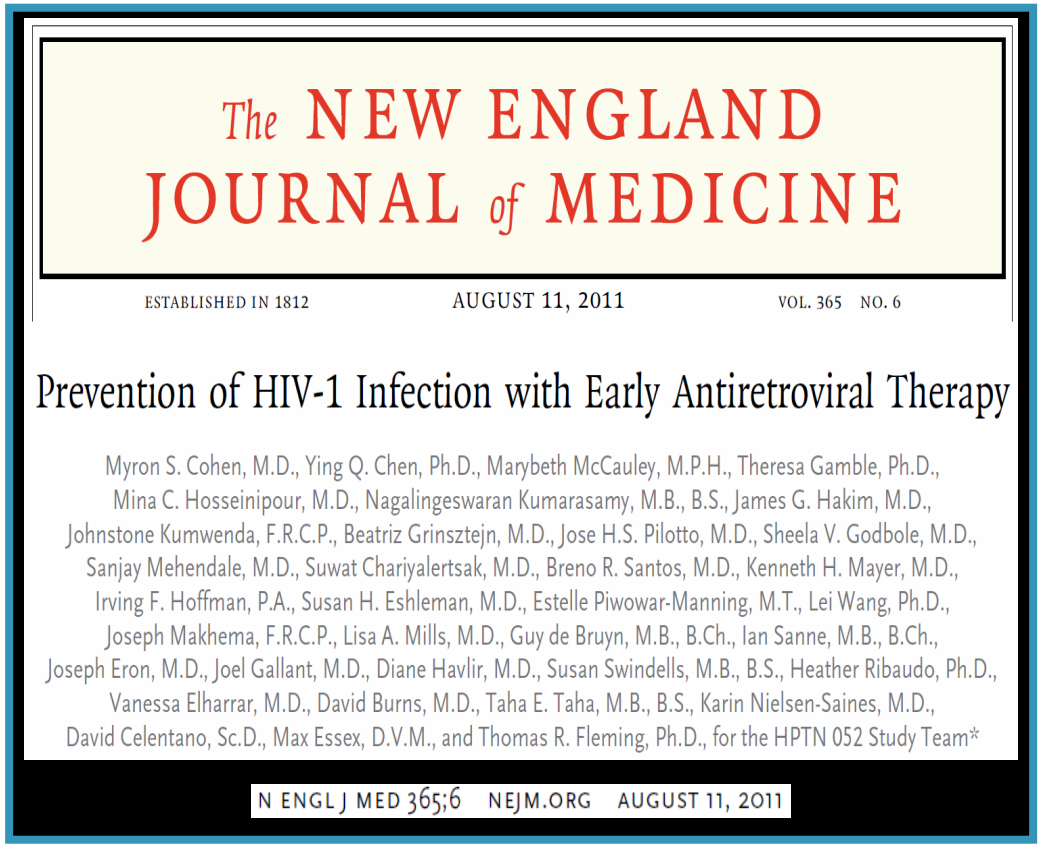

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Prevention of HIV-1 Infection with Early Antiretroviral Therapy

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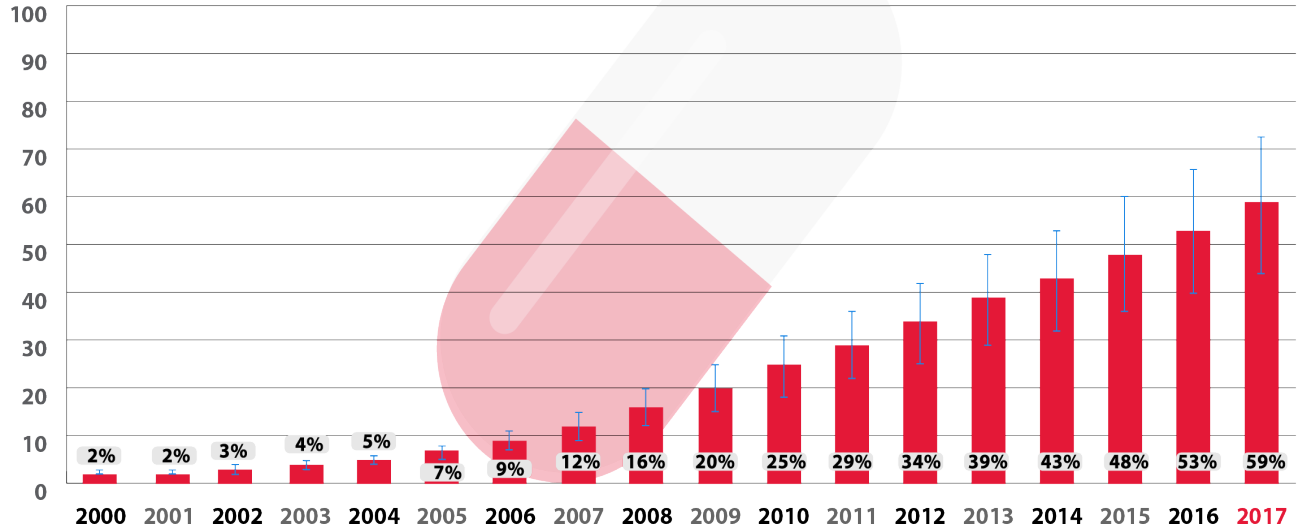
HPTN 052 randomized trial in sero-discordant partners: 96% reduction in risk of HIV transmission if infected partner on antiretroviral treatment

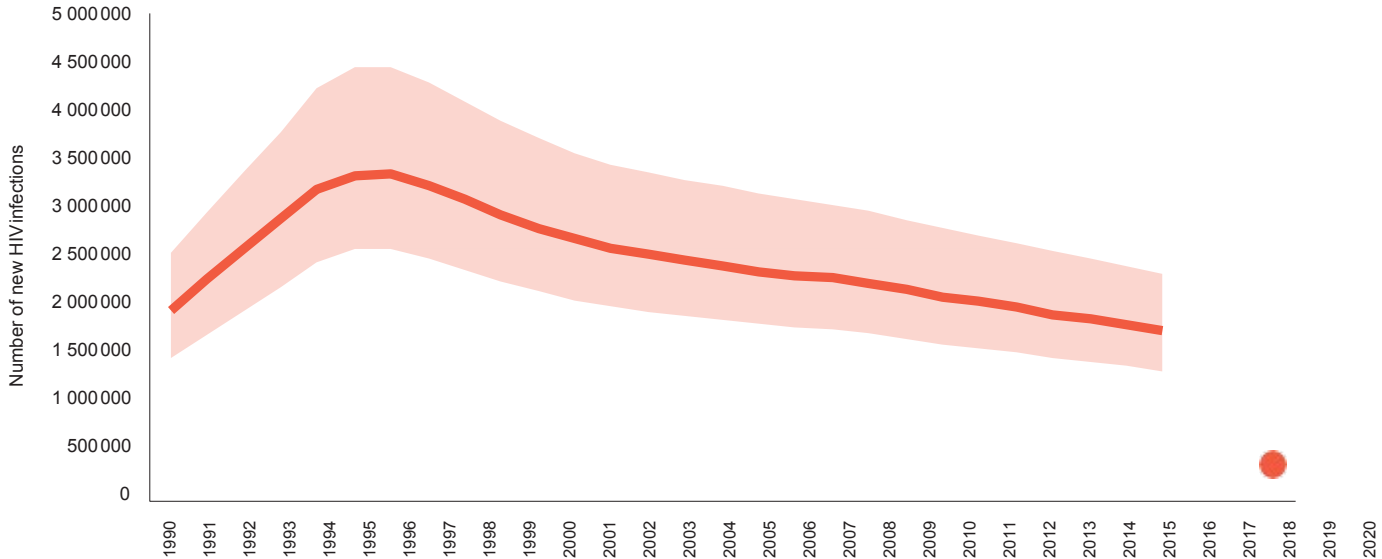
PARTNER 2 study: 972 gay couples and 516 heterosexual couples reported total **76,991 condomless sex acts: zero transmissions** between partners (15 non-phylogenetically-linked) *Rodger IAS Amsterdam 2018*

Despite remarkable increases in the proportion of HIV-positive persons receiving ART…

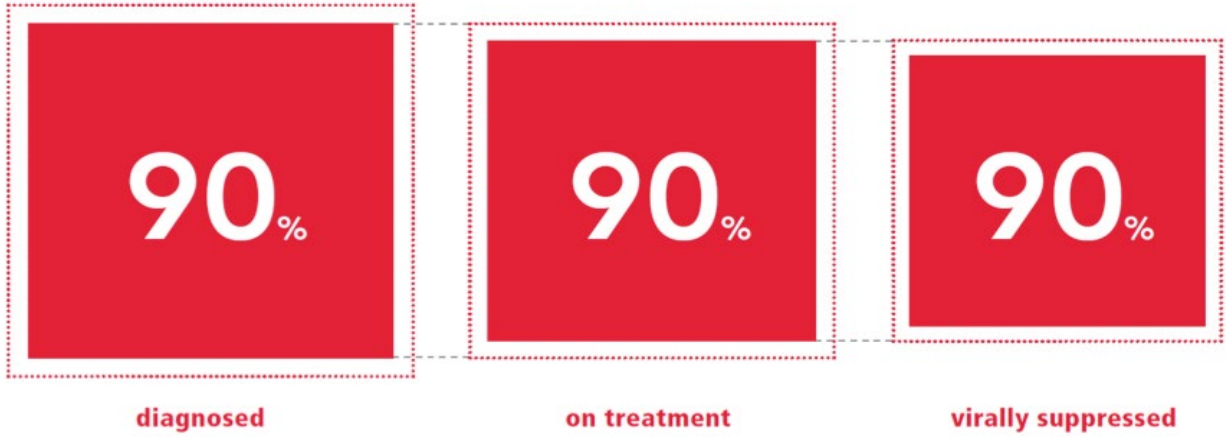


…Insufficient progress on reducing the number of new HIV infections:

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



UNAIDS Targets (2014)

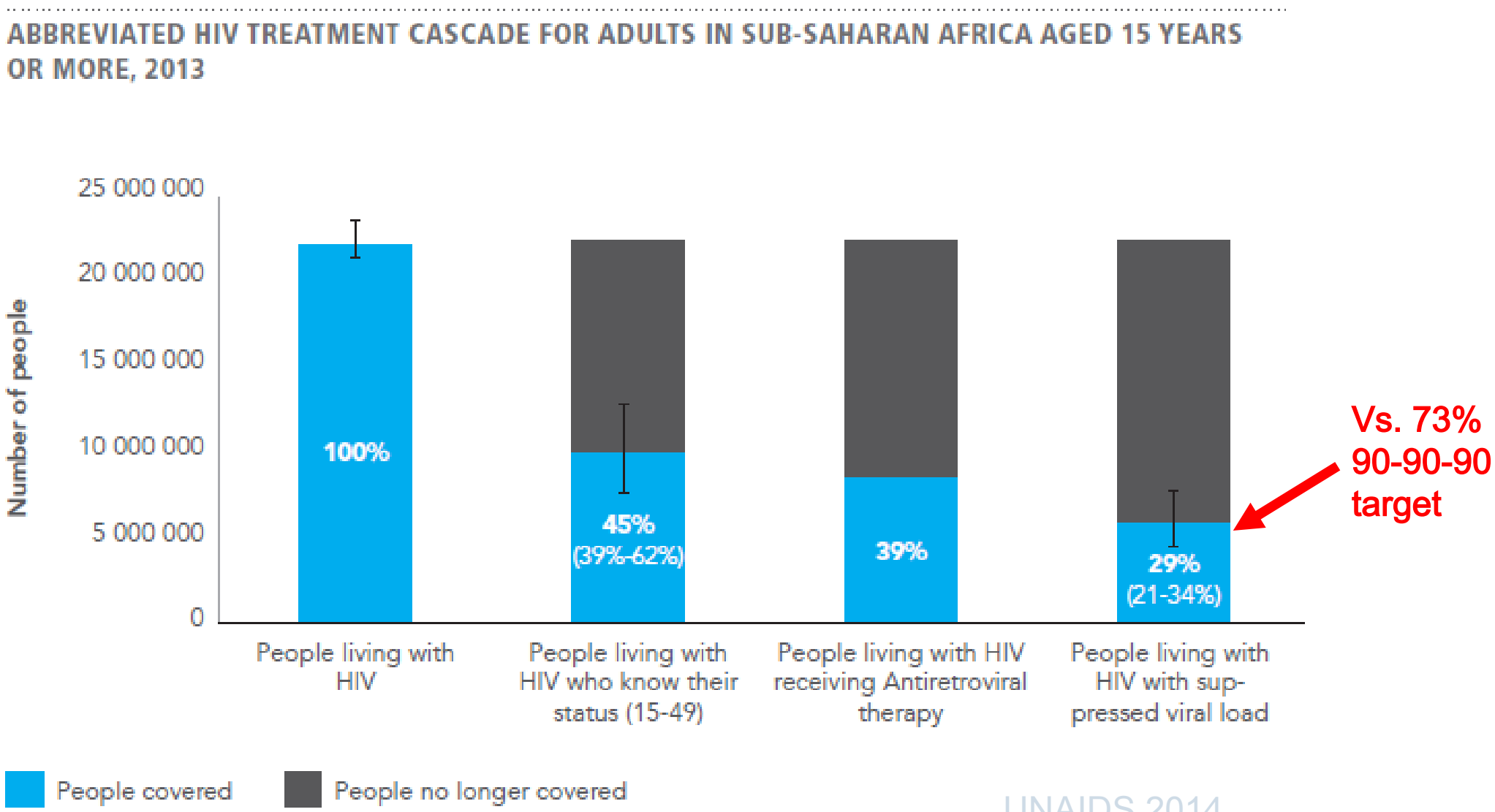


- Mathematical modeling: achieving 90-90-90 targets by 2020 would lead to “end of the HIV epidemic” by 2030 (in combination with PrEP, MC, other?)
  - “Virtual elimination” commonly defined as HIV incidence <0.1%
- Multiple optimistic assumptions; not supported by 6 of 9 other models *(Eaton)*

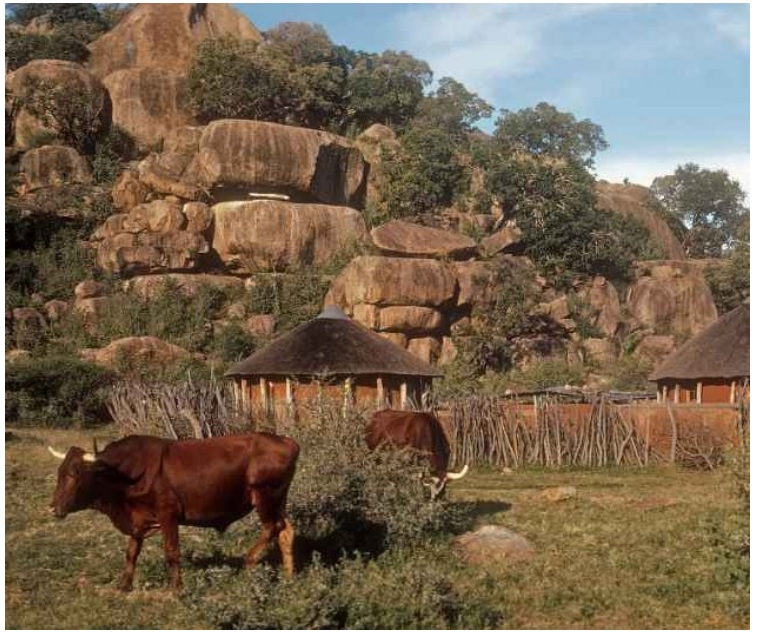
Why even do a trial of universal HIV test - and-treat (UTT)?

- Determine whether it is feasible and acceptable to scale up the interventions to a level that will have impact
  - Need high coverage; “last 20%” often harder to reach than “first 80%”
  - HIV-positive persons who feel well may not want to take ART
  - Acute infection and sexual networks could undermine effectiveness of treatment as prevention
- Assess the magnitude of impact on HIV incidence
- Understand the most effective approaches to implementation
- Evaluate cost-effectiveness
- Understand and quantify potential negative effects (e.g., sexual risk dis-inhibition, stigma, drug resistance)

The HIV "treatment cascade" in Africa ~6 years ago (when TasP trials started)



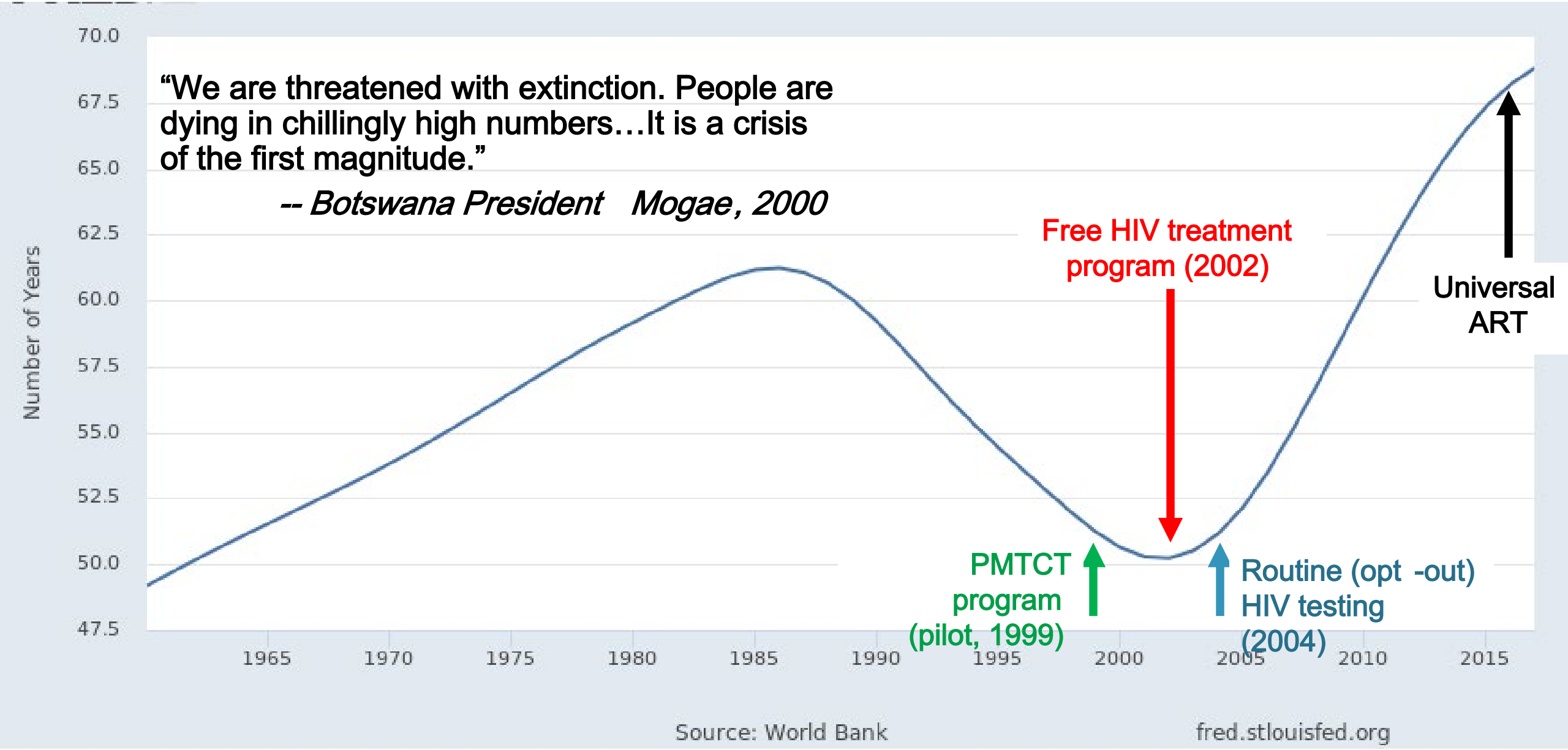
UNAIDS 2014



Botswana

- Stable democracy since 1966
- Population ~2.2 million, upper middle income
- Free health care and education for citizens
  - ~20% unemployment
  - 3rd highest Gini (inequality) index globally *(2009)*
- HIV prevalence = 20% in adults *(2018)*

Botswana: life expectancy at birth



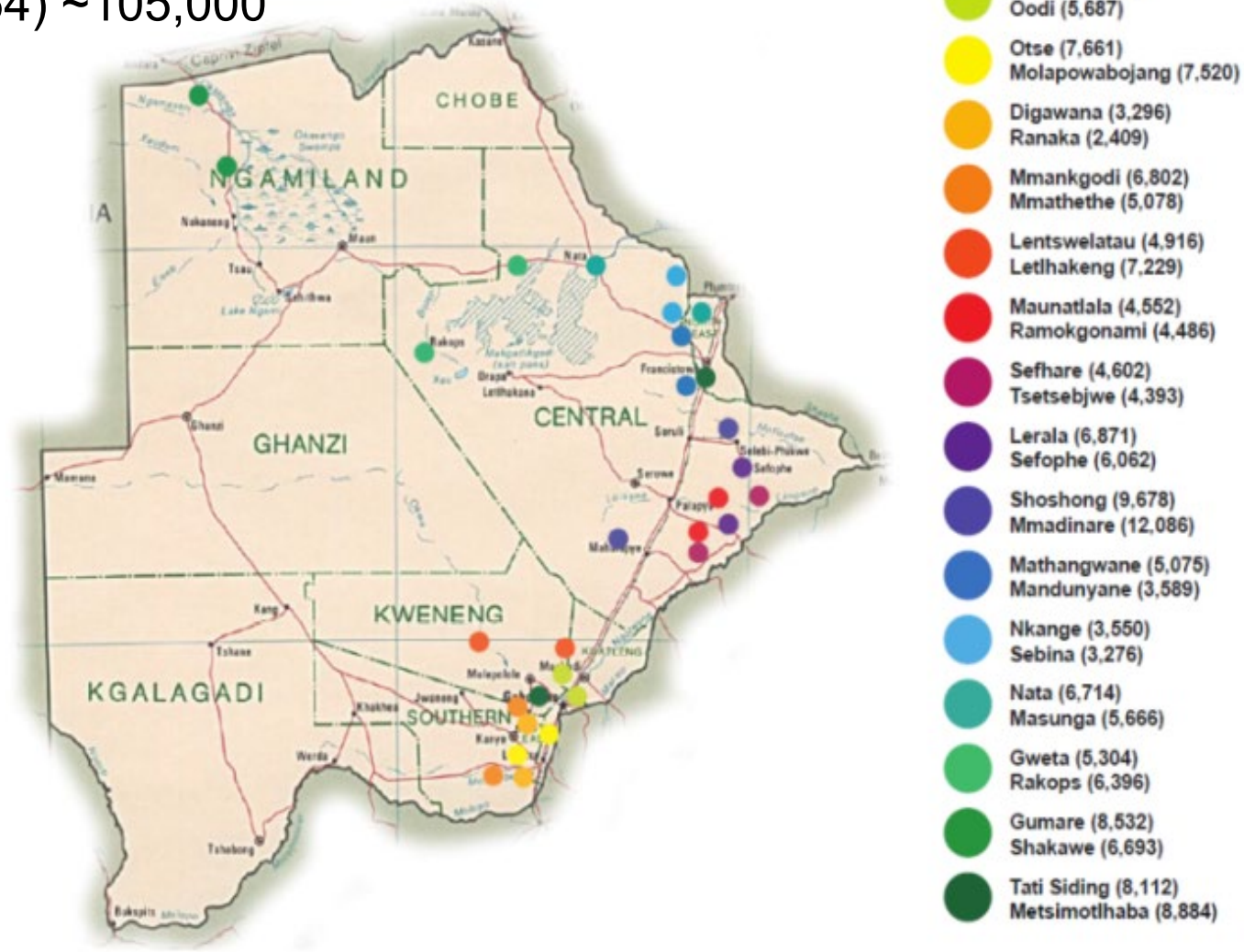
Primary aims of the Ya Tsie (BCPP) study

Cluster-randomized trial designed to:

- Determine whether a package of interventions (primarily universal test and treat) significantly reduces population-level, cumulative HIV incidence in adults in 30 Botswana communities
- Estimate population-level uptake of the intervention
- Evaluate cost-effectiveness of the intervention
- Also: explore viral transmission patterns using viral phylogenetic methods

Ya Tsie Study Population

- 30 communities, each with average population 6,000
- Total population ~180,800 (nearly 10% of entire Botswana population)
- Age-eligible (16-64) ~105,000



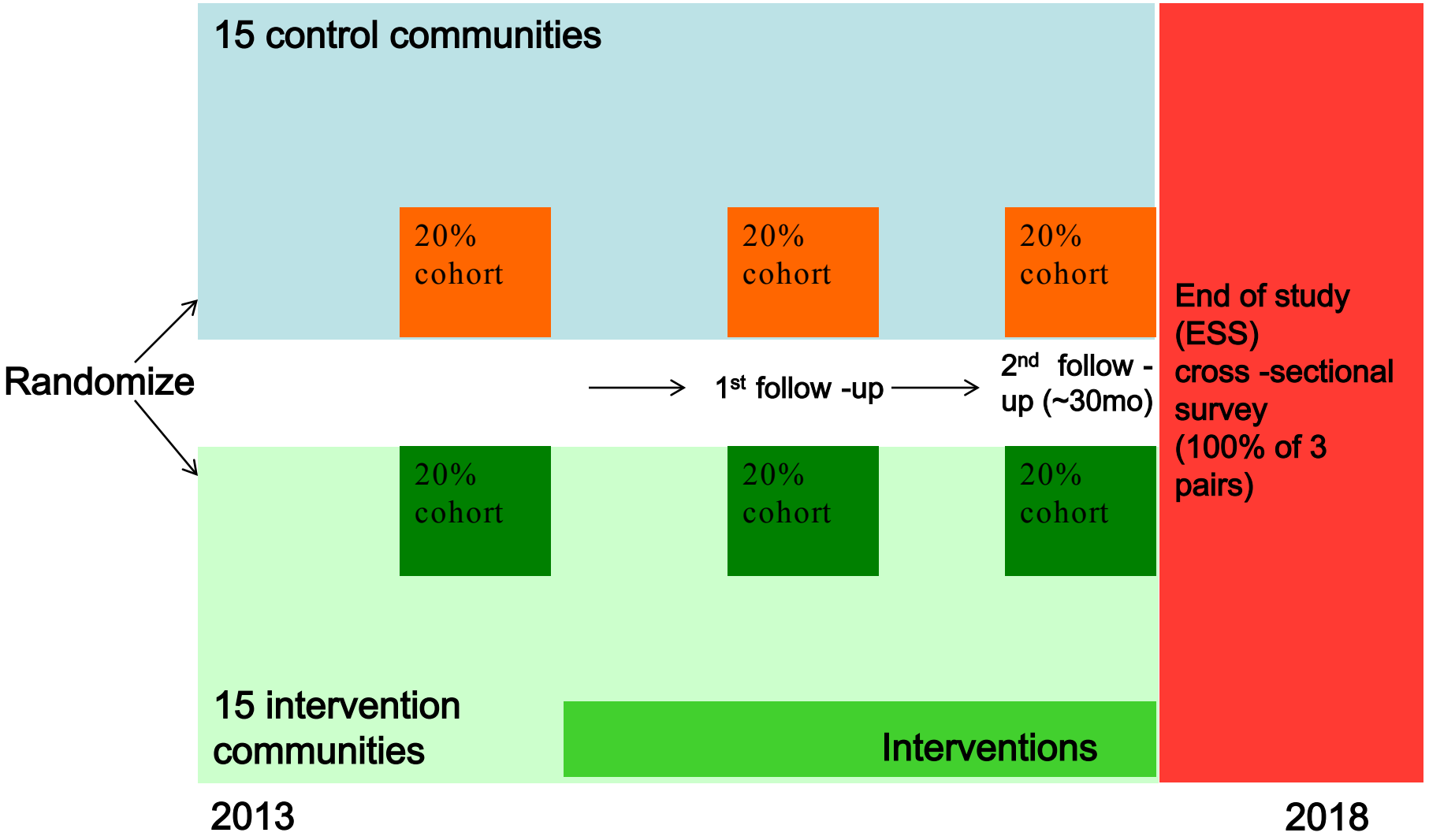
Ya Tsie Study Interventions

- **Interventions in combination prevention communities**
  - Community mobilization
  - Universal HIV testing (aim: test all residents 16-64 years)
  - Linkage to care support
  - Universal ART as of June 2016 *(previously, expanded ART for residents with HIV-1 RNA≥10,000 depending on CD4)*
    - Also as of June 2016: same-day ART start
  - Enhanced male circumcision (MC) services
- **In standard of care communities:**
  - ART for persons with CD4≤350 or WHO III/IV (or pregnant) until June 2016, when moved to universal ART

Ya Tsie Main Study Endpoints/Outcomes

- **HIV incidence** measured via longitudinal follow-up of community-based **HIV Incidence Cohort**
  - >9,000 HIV-negative adult residents of **random ~20% sample** of community plots/households, all 30 communities
  - **Primary study endpoint =** cumulative HIV incidence over ~30 months (baseline + 2 follow-up surveys)
- **"Coverage" parameters (intervention uptake)** and behavior measured in annual household surveys, end of study survey, and program monitoring data (HIV+ and HIV-)
- **Viral phylogenetics** in all HIV-infected survey participants and all consenting HIV+ persons attending clinics in intervention communities

Ya Tsie Study Design Schematic

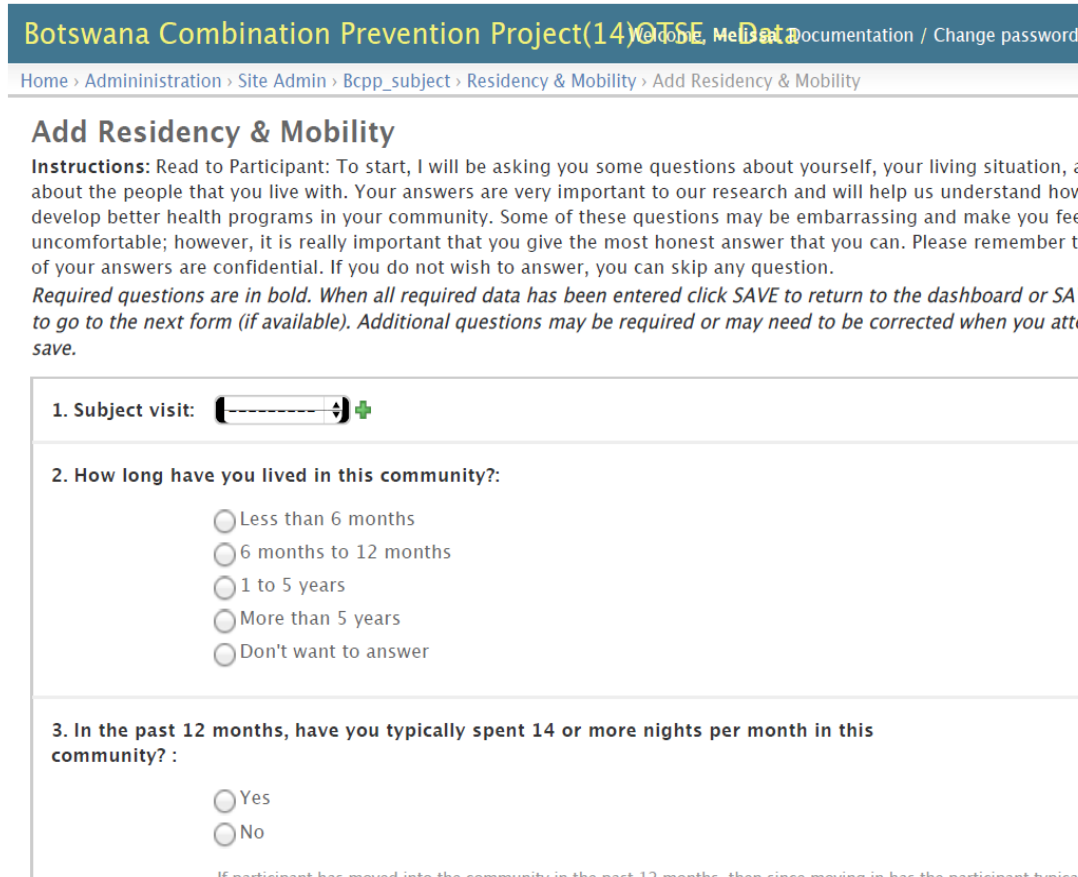


Ya Tsie: Started With Community Engagement

Ya Tsie Plot Mapping and Electronic Data Capture

- GPS coordinates to map and confirm each plot in all 30 communities
- Household/individual data linked to plot
- 73,700 plots mapped in 30 communities
  - Random 20% sample selected for household survey / incidence cohort
  - Maps also used by HTC campaigns

Screen shot of an electronic data capture survey



Field teams visited households

Mobile project van (and lab)

Findings from Baseline (pre-intervention) household survey

In 20% cohort, all 30 communities

How close was Botswana to achieving UNAIDS "90 90 90" targets at study baseline?

HIV-positive who know their status	Currently on ART (among HIV+ who know status)	Virologically suppressed (among persons on ART)	Virologically suppressed (among all HIV-positive)

UNAIDS targets:

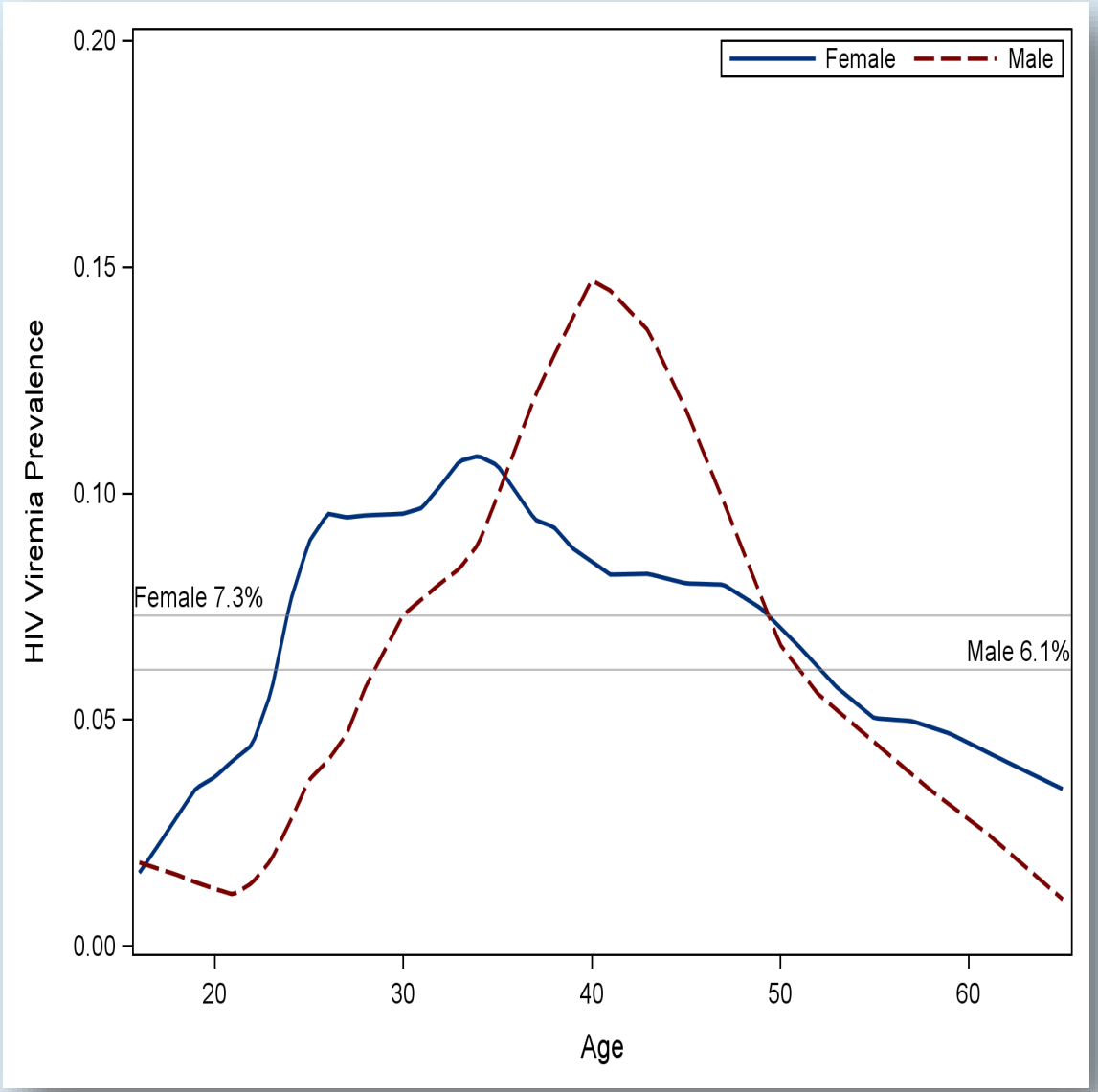
90% x 90% x 90% =73%

At study baseline in Botswana communities:

83% x 87% x 96% = 70%

Measured in 12,610 participants of the 20% cohort (8,974 HIV-negative, 3,596 [29%] HIV-positive)

High prevalence of detectable HIV viremia *in general adult population* at baseline, despite high coverage



Slide from Scott Dryden-Peterson

Ya Tsie: HIV testing, linkage to care, and antiretroviral treatment (ART) interventions and their uptake in the intervention arm

Based on programmatic/intervention data; many slidesin this section shared by Drs. Jan Moore, Pam Bachanas , Lisa Block and others (CDC)

HIV testing intervention: universal HTC

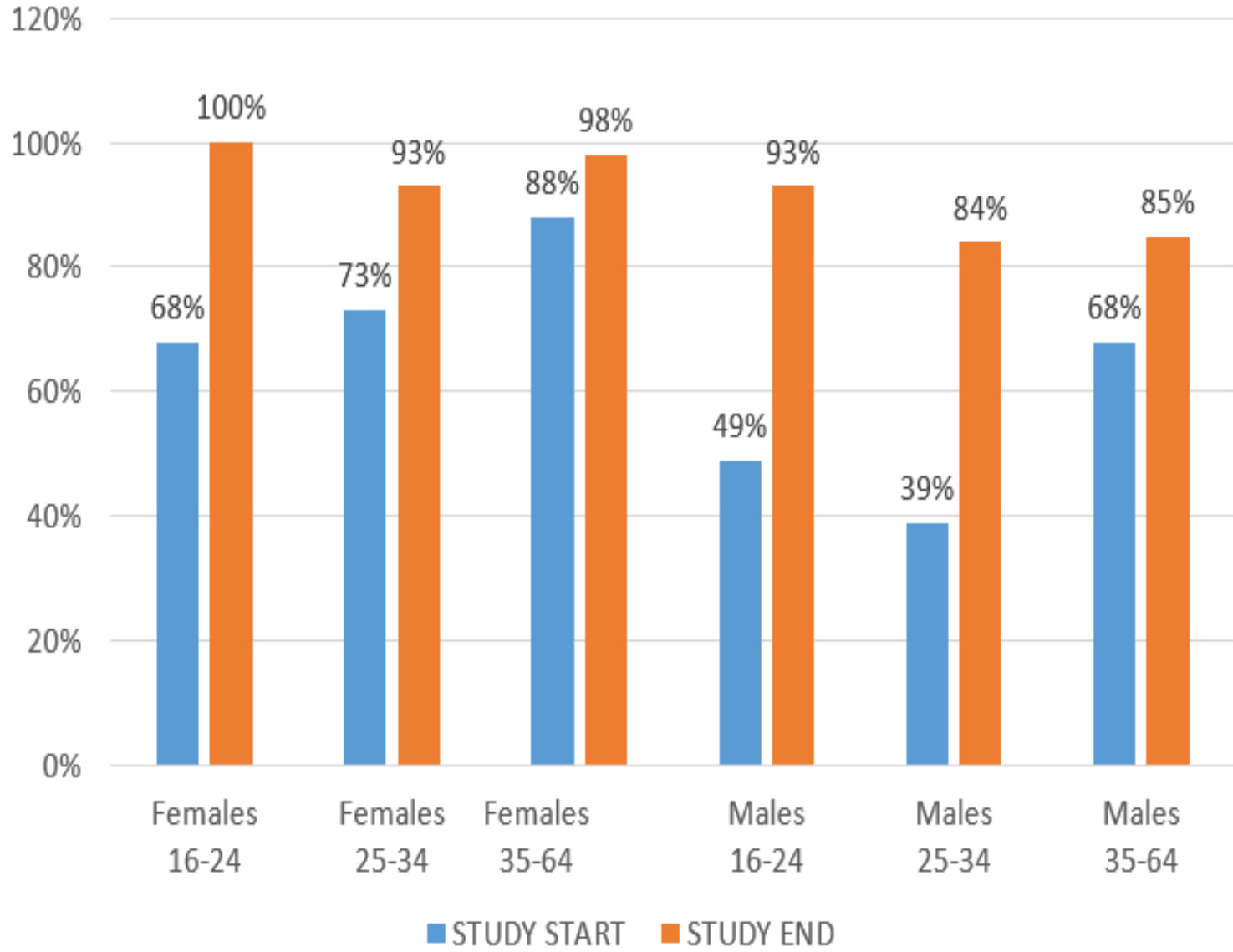
- Initial (one-time) campaign (~2 months per community) to test all adult residents not documented to be living with HIV (PLHIV)
  - Home-based testing: every community household visited and enumerated
  - Mobile testing: tents in areas with high traffic, e.g. markets, transport hubs, and adjacent to ongoing home-based testing
  - Nights, weekends, holidays, multiple visits to reach all eligible
- After initial universal testing round, employed testing targeted at reaching primarily men and youth
  - In places where men and youth gathered or worked, e.g. workplaces, markets, shebeens/bars, cattle posts/farms
  - Provided HIV testing at community events and multi-disease health fairs

Percentage of Newly -Identified HIV -Positive Persons Among all Persons Tested by Sex, Age & Testing Venue

	Total Females	Total Males	Females 16-24	Females 25-34	Females 35-64	Males 16-24	Males 25-34	Males 35-64
Tested in Home N=22,613	13,275	9,338	4,317	3,550	5,408	3,443	2,659	3,236
HIV+ in Home N=1,105 (4.9%)	608 (4.6%)	497 (5.3%)	122 (2.8%)	190 (5.4%)	296 (5.5%)	48 (1.4%)	157 (5.9%)	292 (9.0%)
Tested in Mobile N=26,235	11,767	14,468	5,131	3,703	2,933	5,111	5,171	4,186
HIV+ in Mobile N=935 (3.6%)	455 (3.9%)	480 (3.3%)	155 (3.0%)	162 (4.4%)	138 (4.7%)	51 (1.0%)	196 (3.8%)	233 (5.6%)

- Tested fewer people in homes but identified more new HIV+
- Cost of home-based testing: $53 per test, $758 per positive test
- Cost of mobile testing: $34 per test, $572 per positive test

Increases in Population-Level Knowledge of HIV-Positive Status from Study Start to Study End by Sex and Age



Key take-home points from Ya Tsie HIV testing intervention

- Of the 61,655 eligible adults assessed, 13,328 HIV-positive individual were identified through Ya Tsie (93% of the estimated 14,270 PLHIV in the communities)
- Knowledge of HIV status increased by 25% during study
  - **Greater increases in men** (37%) than women (19%), and in **youth** aged16-24 (77%) than older age groups (21%)
- Although more men tested through mobile/outreach, **higher** rates of **newly-diagnosed** HIV-positive **men** were found with **home-based testing** (included nights, weekends, mult. visits)
- Over 40% of PWLH referred to start ART already knew their positive HIV status but were not yet on ART
- **Even when HIV testing coverage is already high, additional gains can be made using a multi-modality, accessible HIV testing strategy to reach different sub-populations who are being missed by non-targeted program activities**

Ya Tsie Linkage Interventions

- Persons referred to start ART were given **appointments** at local HIV clinics
- **SMS appointment reminders**
- Persons not attending clinic appointment were **traced** by community linkage to care manager (telephone calls, home visits)
  - Individuals traced through cascade using **national unique identifier (Omang)**
- Those not linking within 90 days were sought in the national electronic medical records system to **determine if linked to HIV clinic in different community**

Ya Tsie: linkage to care/ART initiation among PLHIV referred to local clinics, by age and gender

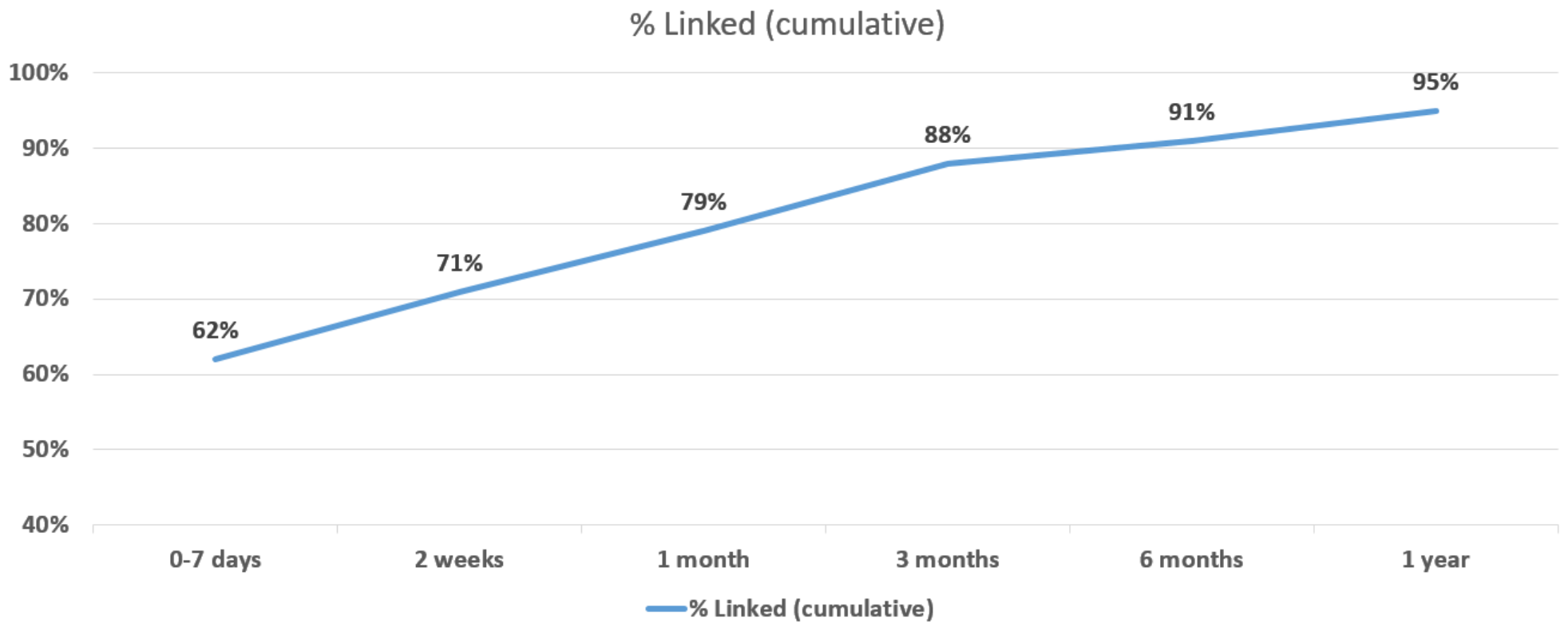
	TOTAL		Women > 25	Men > 25	Youth (16-24)
HIV+ Not on ART Referred to Treatment	3,629		1,781	1,310	538
Linked to care and started ART	3,356 (93%)		1,696 (95%)	1,177 (90%)	483 (90%)

- 93% of PLWH who were referred linked to care and started ART
- Men > 25 and youth had lower rates of linkage than women >25, but still at 90%

Detail on linkage to care/ART

Linkage Outcome	Result	Intervention
Kept 1st appointment at community clinic	1,764 linked (49%)	1. Clinic appointment given 2. SMS reminder
Linked later to community clinic	995 linked (27%)	1. Traced individuals by telephone or home visit 2. Tracked individuals in EMR system
Linked to clinic outside community	608 (17%)	1. Traced individuals by telephone or home visit; verified attendance/treatment status in outside clinics 2. Tracked individuals in EMR system
Never Linked	268 (7%) LTFU; no evidence of clinic activity after intake	1. Traced individuals by telephone or home visit 2. Tracked individuals in EMR system

Time to linkage at local clinic (among PLHIV linking)



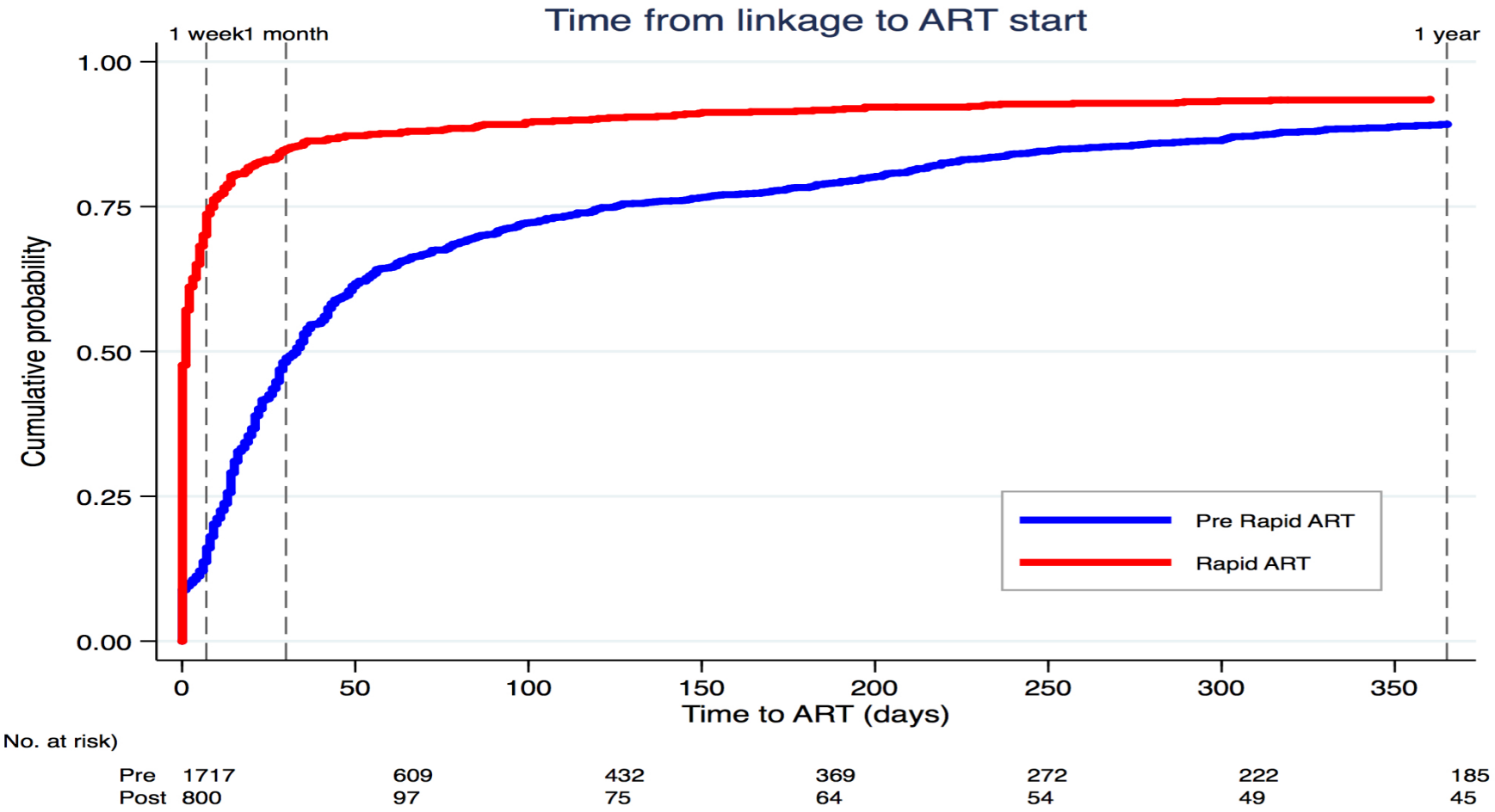
Nearly 90% of those who linked did so by 3 months after referral

Fast-Track/Rapid ART Interventions

When Botswana moved to "Treat All" in June 2016, Ya Tsie moved to "Fast Track ART Initiation" in the intervention arm

- Adherence counseling initiated in community after positive HIV test
- **ART initiated at first clinic** visit for stable patients
- Labs drawn at first clinic visit but ART started before results available
- Persons recalled to clinic if abnormal lab results returned

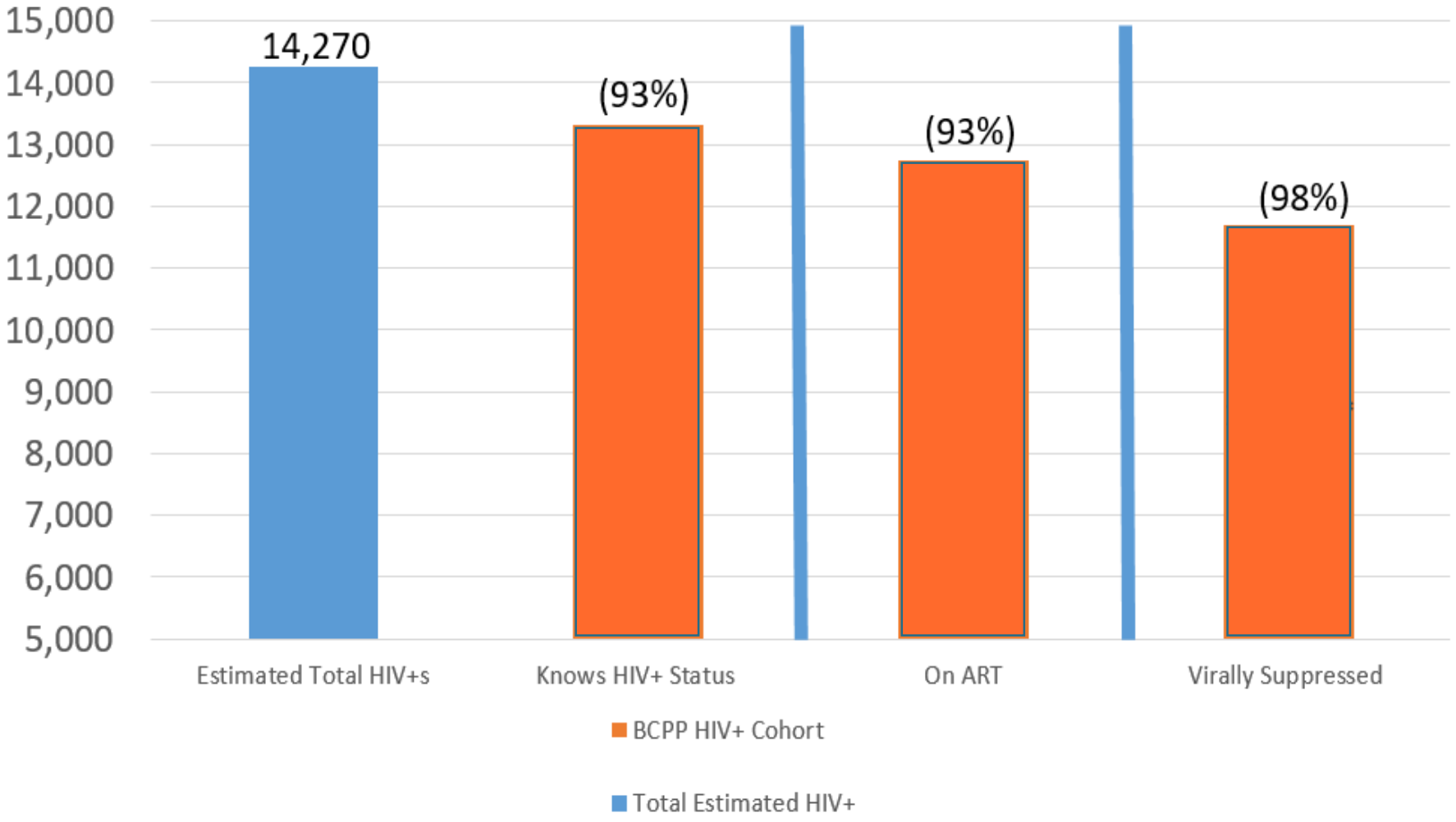
More rapid linkage/ART start, and equally good retention/viral suppression, in era of fast -track ART



Time from linkage	Pre Rapid ART (1717)		Post Rapid ART (800)	
	Number	Cumulative probability of ART initiation (95% CI)	Number	Cumulative probability of ART initiation (95% CI)
1 day	163	9.5% (8.2-11.0)	457	57.1% (53.7-60.6)
1 week	276	16.1% (14.4-17.9)	589	73.7% (70.6-76.7)
2 weeks	499	29.1% (27.0-31.3)	641	80.3% (77.4-83.0)
1 month	839	48.9% (46.5-51.3)	678	84.9% (82.4-87.3)
3 months	1208	70.4% (68.2-72.5)	711	89.2% (86.9-91.2)
1 year	1532	89.2% (87.7-90.6)	744	93.5% (91.6-95.1)

One year after starting ART, 91% of those who linked in the standard ART period were in care and had VL<400 cp/ml, vs. 92% in rapid ART period

HIV Care Cascade Among HIV-Infected Adults in 15 Intervention Communities

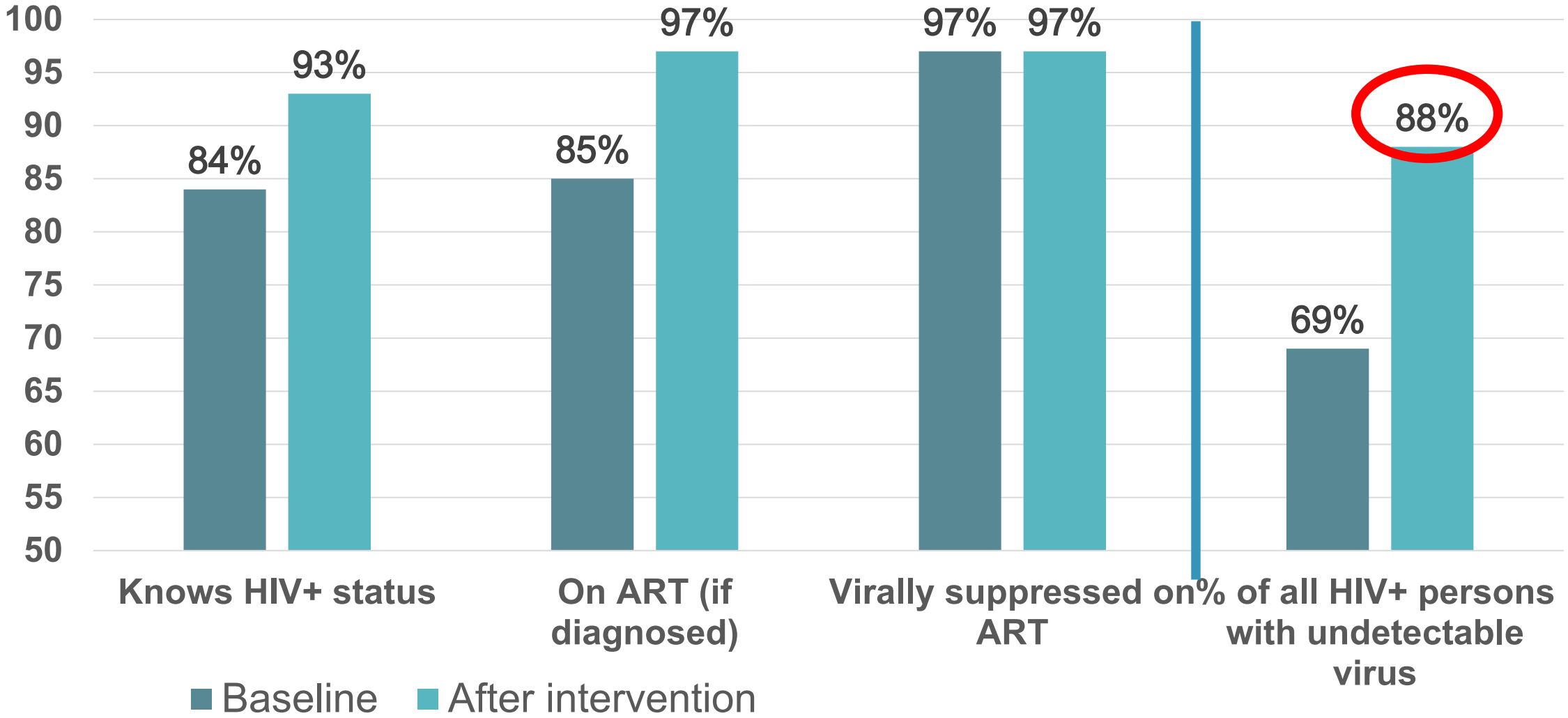


* Denominator (n=13,124) reflects people alive at study end
**Denominator (n=11,954) reflects people retained on ART, alive at study end and have VL result

- If missing VL=failure, then 95% (not 98%) of those on ART had viral suppression
- **Overall, of the total estimated 14,270 PLHIV, ~85% had VL suppression by study end**

Data source: programmatic data

Ya Tsie: change in 90 -90-90 coverage over time, based on data from 20% cohort (baseline) and 80% population (end)



88% viral suppression exceeds “95 -95-95” target of 86% (3 ESS intervention communities)

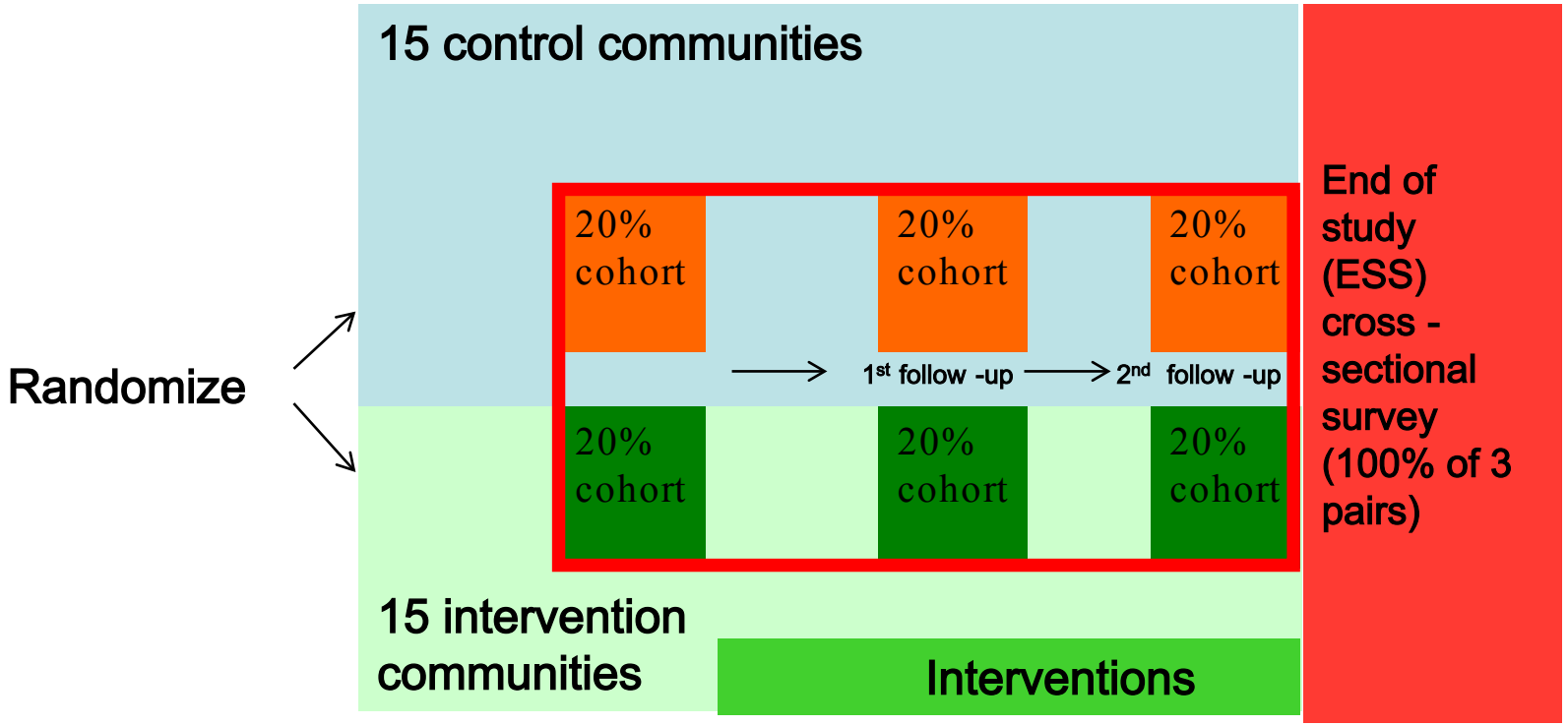
Conclusions

- Universal testing with multi-modal approach effectively reaches important population segments and is essential for UTT
- Tracking & tracing procedures with dedicated staff and data systems can reduce loss to follow-up from 50% to <10%
- Treatment offered on same day as linkage can reduce time to ART start by >50%
- Possible to reach equivalent of 95-95-95 coverage even in high-prevalence, resource-constrained countries

Note: uptake of MC was higher in the intervention arm, but low overall (data not shown)

Ya Tsie: HIV incidence by randomized study arm

Ya Tsie: HIV Incidence Cohort



- **8,974** HIV-uninfected individuals in incidence cohort (4,487/arm)
- Median duration of follow-up = **29 months**
- **95-96%** of participants in each arm **re-tested for HIV** during at least 1 follow-up visit

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

Annual HIV incidence: 0.59% in the intervention arm versus 0.92% in the standard of care arm

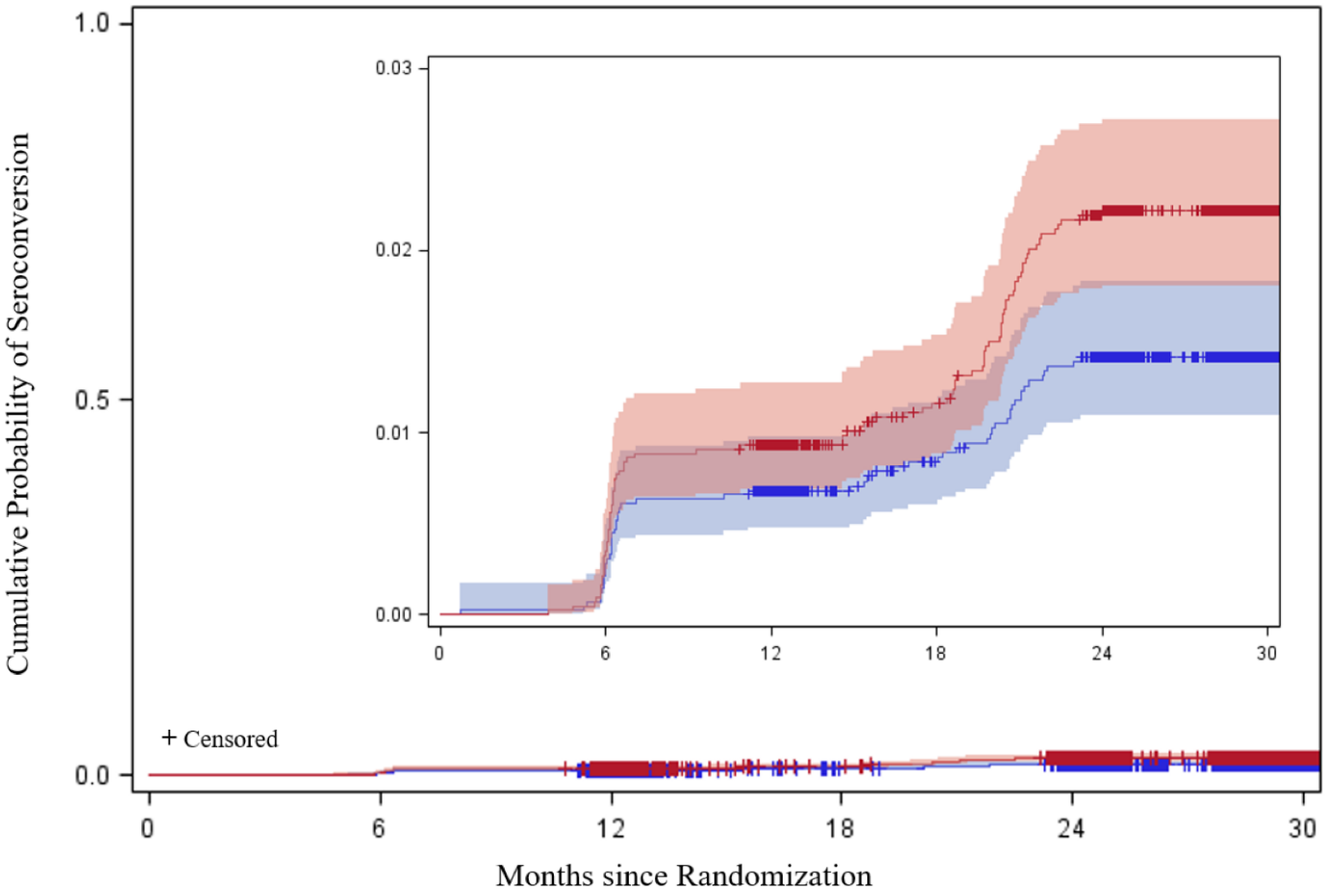
Analysis	Incidence Ratio	95% CI	2-sided p-value
Primary analysis, unadjusted (permutation test, pair-specific Cox PHM)	**0.69**		**0.09**
Analysis to obtain 95%, unadjusted CI (pair-stratified Cox PHM)	0.65	**0.46-0.90**	0.01
Primary analysis, adjusted*	0.63		0.05
Analysis to obtain 95% CI, adjusted*	0.70	0.50-0.98	0.04

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

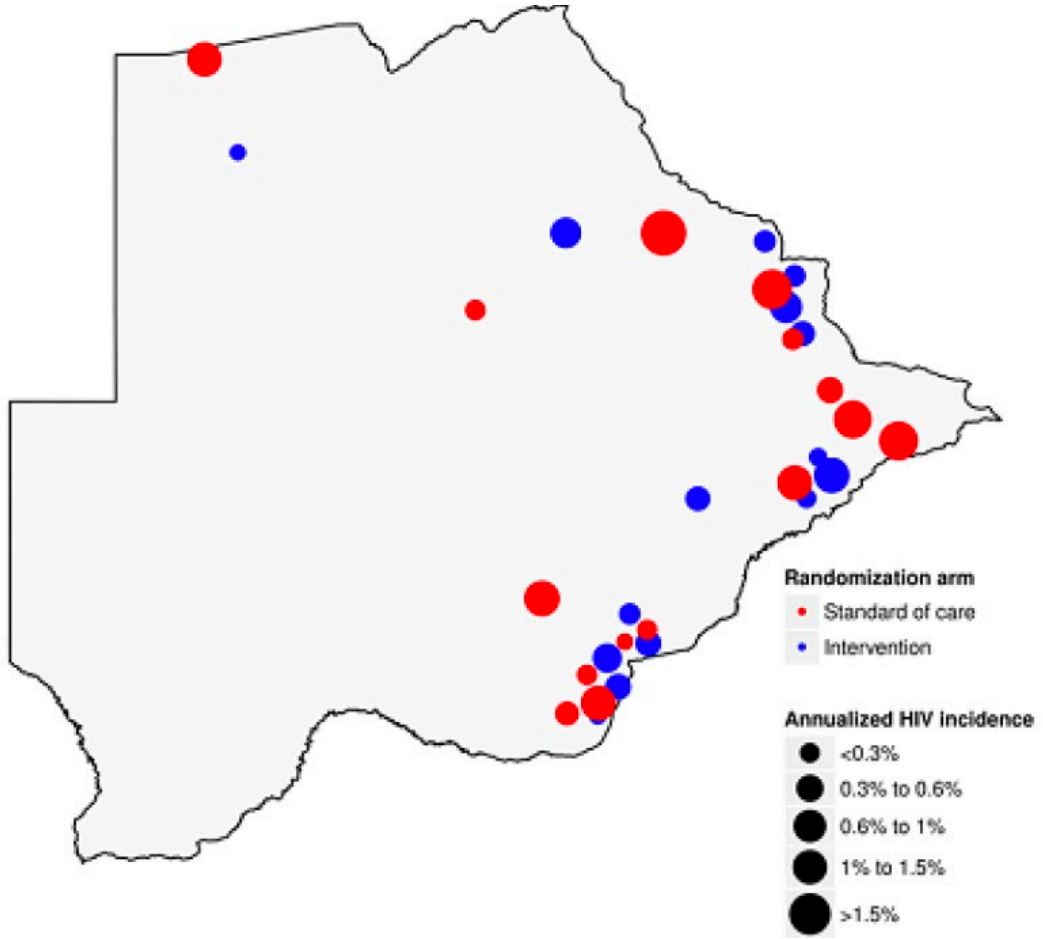
Results of main analyses were consistent, and indicated ≥30% reduction in HIV incidence associated with intervention *(note: impact likely substantially blunted by "mixing" / infection acquired from outside intervention communities)*

Ya Tsie: HIV incidence lower in intervention arm, but quite variable by community

Population HIV incidence in intervention vs. standard of care arms



Map of HIV incidence by community and randomization arm

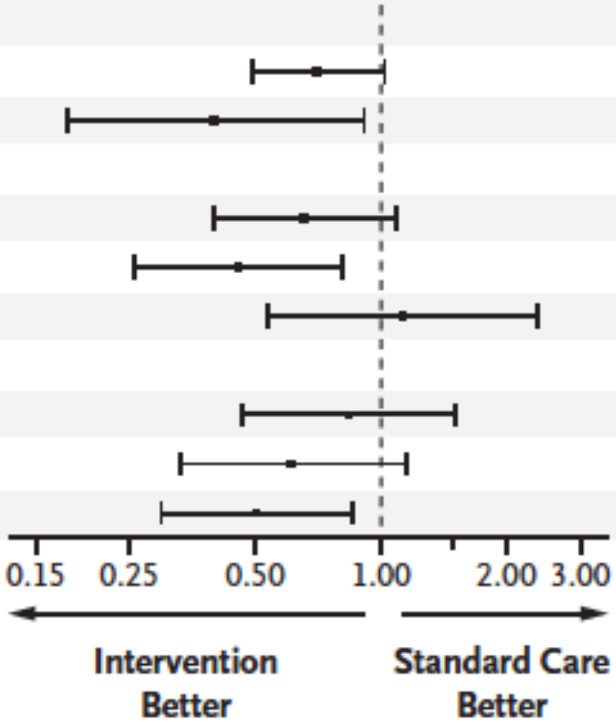


Ya Tsie: impact of intervention varied by group

› Greater apparent impact of intervention on HIV incidence in men (and variable by age, region)

› HIV incidence remained higher in women than in men (and in 16-24 year olds)

Subgroup	Intervention	Standard Care	Incidence Ratio (95% CI)
	no. of events/person-yr of follow-up (event rate/100 person-yr)		
Sex			
Female	49/5911 (0.83)	70/6010 (1.16)	0.71 (0.5–1.0)
Male	8/3757 (0.21)	20/3791 (0.53)	0.40 (0.2–0.9)
Age			
16–24 yr	25/3238 (0.77)	40/3420 (1.17)	0.66 (0.4–1.1)
25–34 yr	17/2818 (0.60)	37/2826 (1.31)	0.46 (0.3–0.8)
35–64 yr	15/3611 (0.42)	13/3556 (0.37)	1.14 (0.5–2.4)
Region			
Southern	19/3368 (0.56)	27/4068 (0.66)	0.84 (0.5–1.5)
Central	16/2384 (0.67)	26/2388 (1.09)	0.62 (0.3–1.2)
Northern	22/3915 (0.56)	37/3345 (1.11)	0.51 (0.3–0.9)



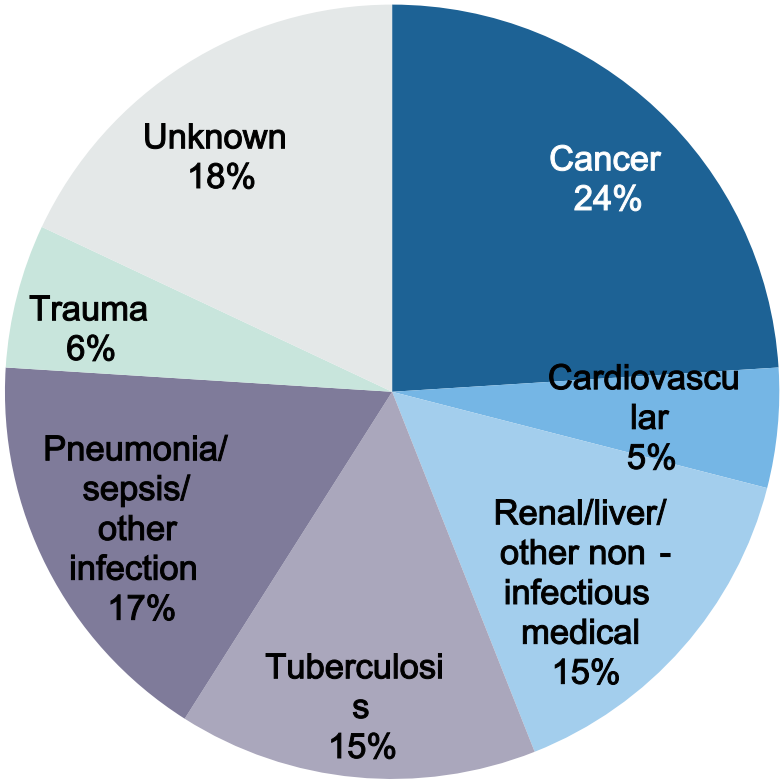
Makhema et al

Lightning rounds: selected additional Ya Tsie results

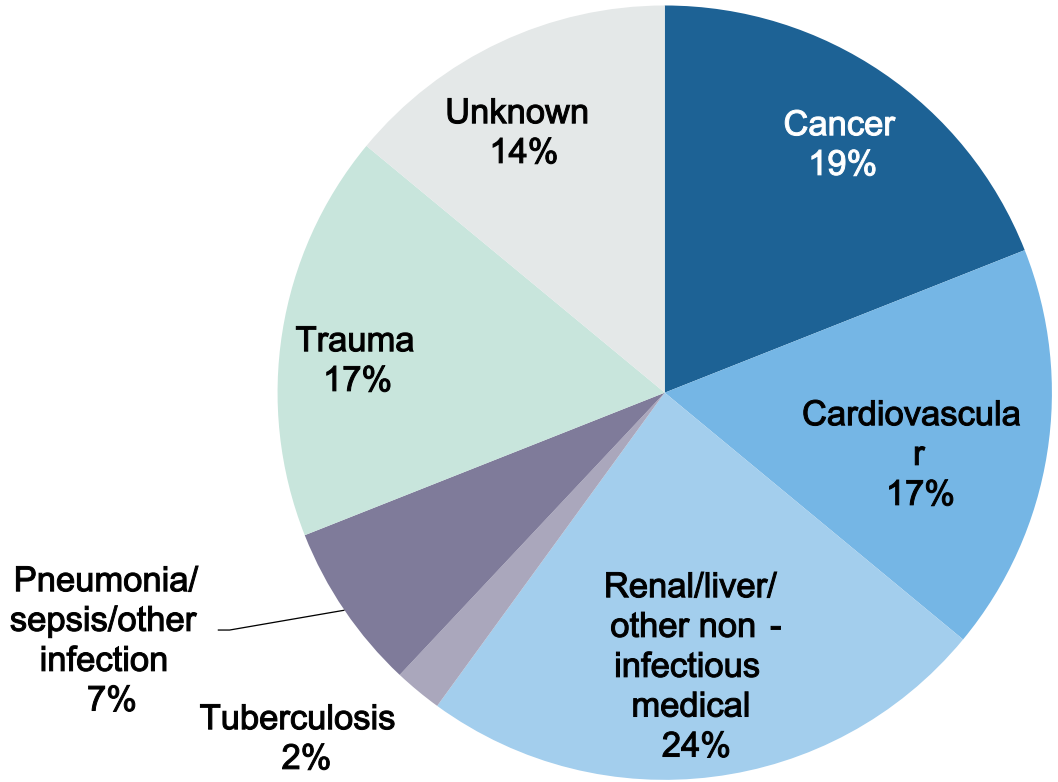
Mortality remains higher in persons with treated HIV

- Persons with viral suppression on treatment for ≥10 years were still >3 times more likely to die than persons without HIV *(BCPP study cohort, adjusted analyses)*
- Much of this mortality due to non-communicable diseases

Cause of Death in Persons with HIV



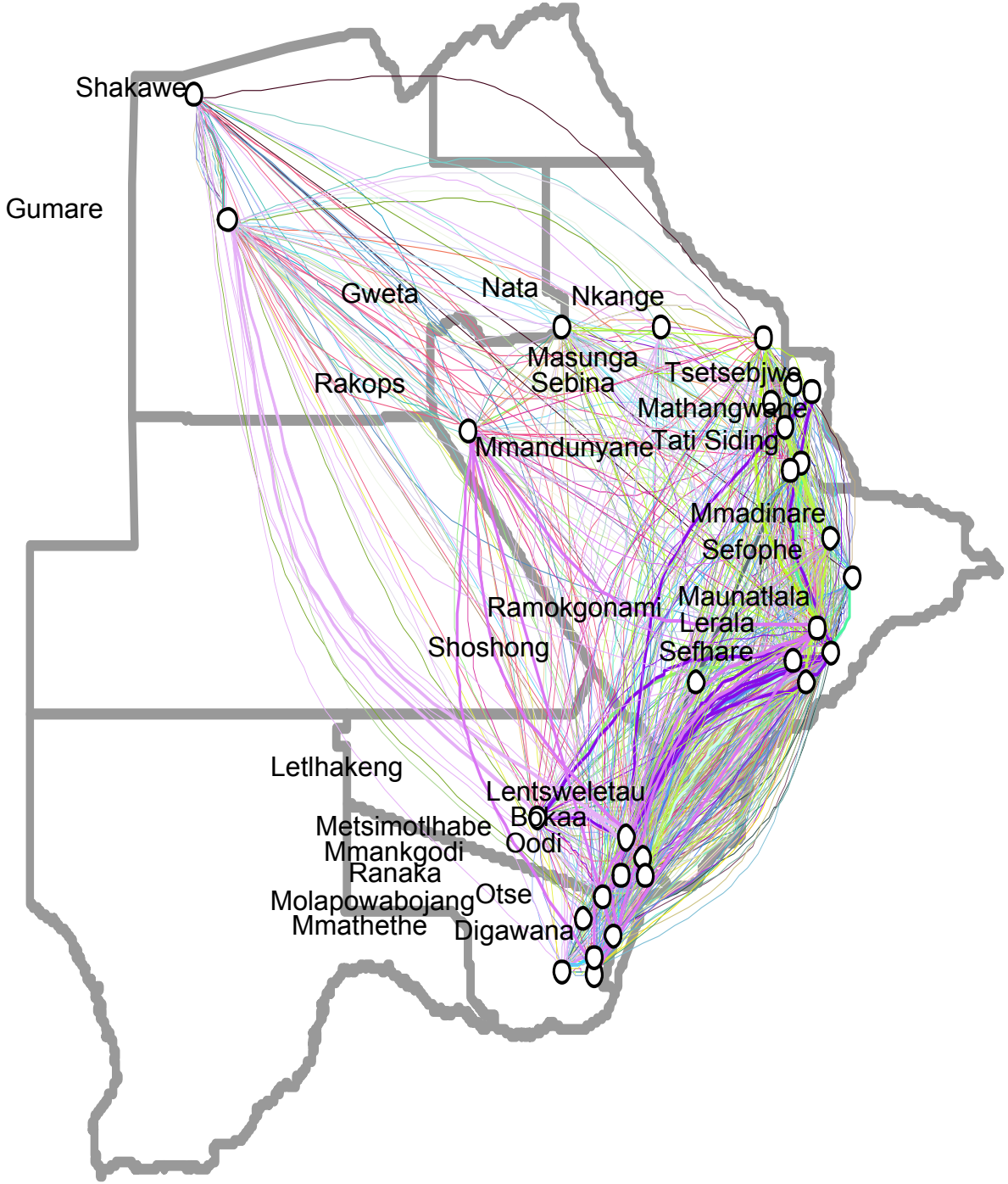
Cause of Death in HIV-Negative Individuals



Phylogenetic analyses :HIV -1 transmission networks

Near full-length HIV-1 genome sequences from ~6,000 Ya Tsie participants

Cluster-specific coloring: n=939 clusters with Botswana sequences



Advanced HIV and the Care Cascade

- Twenty percent of HIV-infected individuals not on ART had advanced HIV-disease (CD4 <200)
- Those with advanced disease had lower rates of linkage/ART initiation and retention and higher mortality (2.3% vs 1.1%; p=0.05) compared to healthier PLHIV.
- Highlight the need to <u>focus efforts on earlier identification of HIV-infected persons</u>

Lebelonyane CROI 2018 #887

Association Between Being More Mobile, and Having Detectable HIV -1 RNA

- More mobile HIV-infected individuals were significantly more likely to be viremic
  - Lower proportions of more mobile PLHIV knew their HIV status (P=0.001) or were on ART (P=0.02) compared with non-mobile
- Health systems needs to better accommodate more mobile populations, to achieve high ART/viral suppression targets

Mmalane CROI 2018 #883

High Prevalence of Multiple Concurrent Sexual Partnerships (MCP)

- Despite efforts to reduce MCP behaviors, MCPs were still common (reported by 31% of sexually active individuals), esp. men
- After adjusting for age and gender, reporting MCP was significantly associated with being employed, transactional sex, intergenerational sex, and high alcohol consumption

Kadima CROI 2018 #1294

Self-Reported Risky Sexual Practices Among Adolescents and Young Adults

- Females were more likely to report inconsistent condom use, intergenerational sex, and transactional sex
- Males more likely to report early sexual debut and alcohol use with sex
- Economic stress was strongly associated with increased sexual risk behavior in females
- Programs targeting episodic risk, particularly around alcohol, could be more effective in young males

Chakalisa CROI 2018 #1030

High Prevalence of Hypertension in HIV-Infected and –Uninfected Adults

- Nearly one in three adults (out of 2,441 assessed in population-based cohort) had hypertension (previously diagnosed or current)
  - HIV-infected individuals were less likely to meet the definition of hypertension than HIV-uninfected
- While 90% of individuals with previously-diagnosed hypertension were receiving antihypertensive medications, one-half of those with hypertension had not previously been diagnosed

Mosepele CROI 2018 #2000

Prevalence of NRTI, NNRTI, PI, INSTI Drug Resistance Mutations, 2013 -2015

- Using long-range genotyping, found low prevalence of NRTI- (2.9%), NNRTI- (3.2%) and PI (1.2%) drug resistance mutations in 2,343 participants
  - 68% of those tested were on ART, & 96% of those on ART had VL<400
- Prevalence of DRM to any of these 3 drug classes = 5.8%
- Individuals on ART with detectable virus (n=63) had higher prevalence of NRTI (22%) and NNRTI (24%) mutations
- Only 47 (2%) of 2,241 participants had INSTI DRM

Moyo CROI 2018 #1680

Gaseitsiwe CROI 2018 #2012

Undisclosed Antiretroviral Drug Use

- Among 134 participants with HIV-1 RNA < 400 copies/mL but who reported not being on ART, undisclosed ART use (detectable antiretroviral levels) was found in 52 (39%)
  - Most commonly EFV, NVP, FTC, TDF

Moyo CROI 2018 #1255

Four Universal Test & Treat trials: What they tell us about HIV epidemic control in 2019

Yo tsie
TOGETHER WE CAN STOP HIV

SEARCH
SUSTAINABLE EAST AFRICA RESEARCH IN COMMUNITY HEALTH

PopART
HPTN 071

TasP
ANRS 12249

The following slides shared courtesy of:

BCPP (Ya Tsie)

Kathleen Wirth, Molly Pretorius Holme, Joseph Makhema, Kara Bennett, Jean Leidner, Max Essex, Jan Moore, and the BCPP team

Sponsors: PEPFAR, US CDC, Botswana Ministry of Health and Wellness

PopART

Richard Hayes, Helen Ayles, Sara Fidler, and the PopART team

Sponsors: PEPFAR, Bill and Melinda Gates Foundation, NIH

SEARCH

Diane Havlir, Maya Petersen, Moses Kamya, Laura Balzer, Gabe Chamie and the SEARCH team

Sponsors: NIAID, PEPFAR, Gilead Sciences, Ministers of Health in Uganda and Kenya

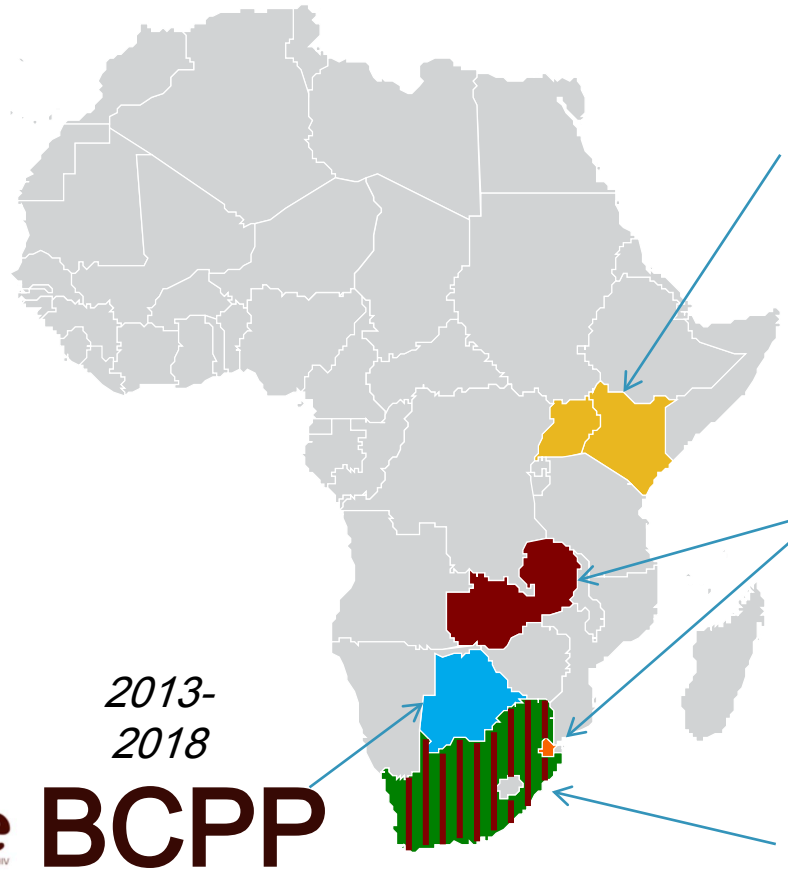
TasP

Collins Iwuji, Joseph Larmarange, Deenan Pillay, François Dabis and the TasP team

Sponsors: ANRS, GIZ, 3ie

Four Major Universal Test and Treat (UTT) Trials

Community -randomized studies with HIV incidence endpoint



2013-2020

SEARCH

SUSTAINABLE EAST AFRICA RESEARCH IN COMMUNITY HEALTH

2013-2018

PopART

HPTN 071

2013-2018

Ya tsie

TOGETHER WE CAN STOP HIV

BCPP

Botswana Combination Prevention Project

2012-2016

TasP

Antiretroviral Treatment as Prevention • ANRS 12249

Ukuphila kwami, ukuphila kwethu (my health for our health)

Four-UTT study slides courtesy of J Orne-Gliemann

Overall Design of the Four UTT Trials

- Community randomized trials, 2 arms (3 arms in PopART)
- Primary outcome: cumulative HIV incidence
- Average 30-36 months follow-up

	Ya Tsie *Botswana*	PopART *Zambia + South Africa*	SEARCH Uganda + Kenya	ANRS TasP *South Africa*
Number of clusters	30	SA: 9 Z: 12	U: 20 K: 12	22
Population of trial communities*	~105,000	~1,000,000	~334,500	~28,000
Population of primary outcome evaluation	~9,000	~33,000	~118,000	~17,600

** Eligible for trial interventions, both control and intervention arm*

Main Interventions in the Four UTT Trials

	Intervention		Control
Ya Tsie	Universal testing (home-based, mobile and targeted); expanded/universal ART; enhanced MC		Per evolving national guidelines
PopART	Annual home-based HIV testing universal ART	Annual home-based HIV testing, ART per national guidelines	Per evolving national guidelines
SEARCH	Baseline and annual multi-disease campaign and home-based testing universal ART Streamlined HIV and NCD care		Baseline home-based HTC; rest per evolving national guidelines
TasP	Home-based HIV testing universal ART		Home-based HIV testing ART per national guidelines

ART was delivered in Government/public facilities in all trials except TasP

Baseline HIV / ART Characteristics in the Four UTT Trial Populations

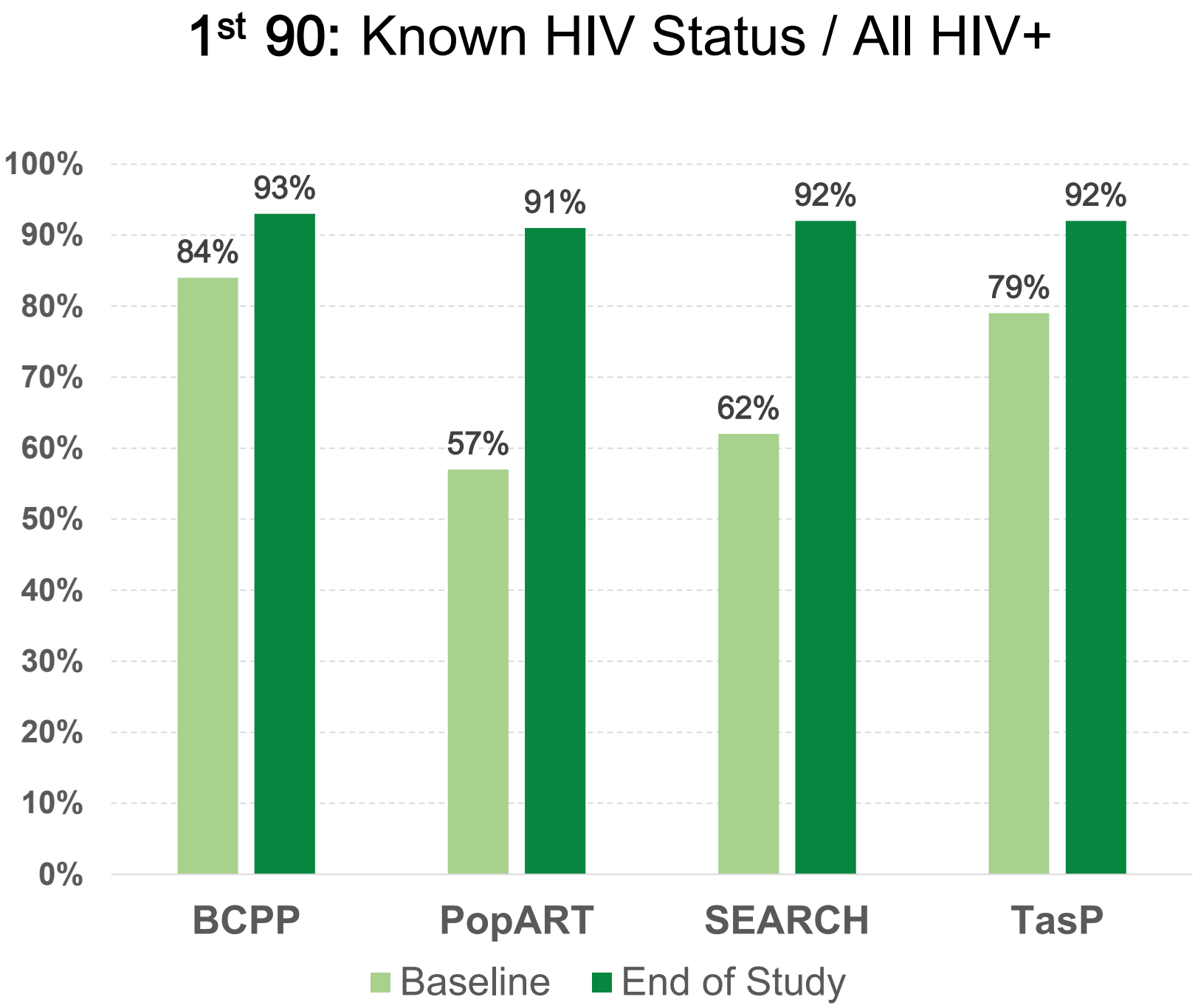
Age eligibility criteria	*16-64y*	*18-44y*	*⩾15y*	*⩾15y*
	Ya Tsie *Botswana*	**PopART** *Zambia + South Africa*	**SEARCH** Uganda + Kenya	**ANRS TasP** *South Africa*
HIV prevalence at baseline	29%	SA: 22% Z: 21%	U: 3-7% K: 20%	30%
ART coverage at baseline (% of *all* HIV+ on ART)	70%	SA: 29% Z: 38%	57%	38%

K: Kenya; SA: South Africa; U: Uganda; Z: Zambia

With UTT, >90% of all PLHIV were diagnosed (1 st 90)

- Achieved within 1-2 of years in some studies
- In a variety settings- urban and remote rural

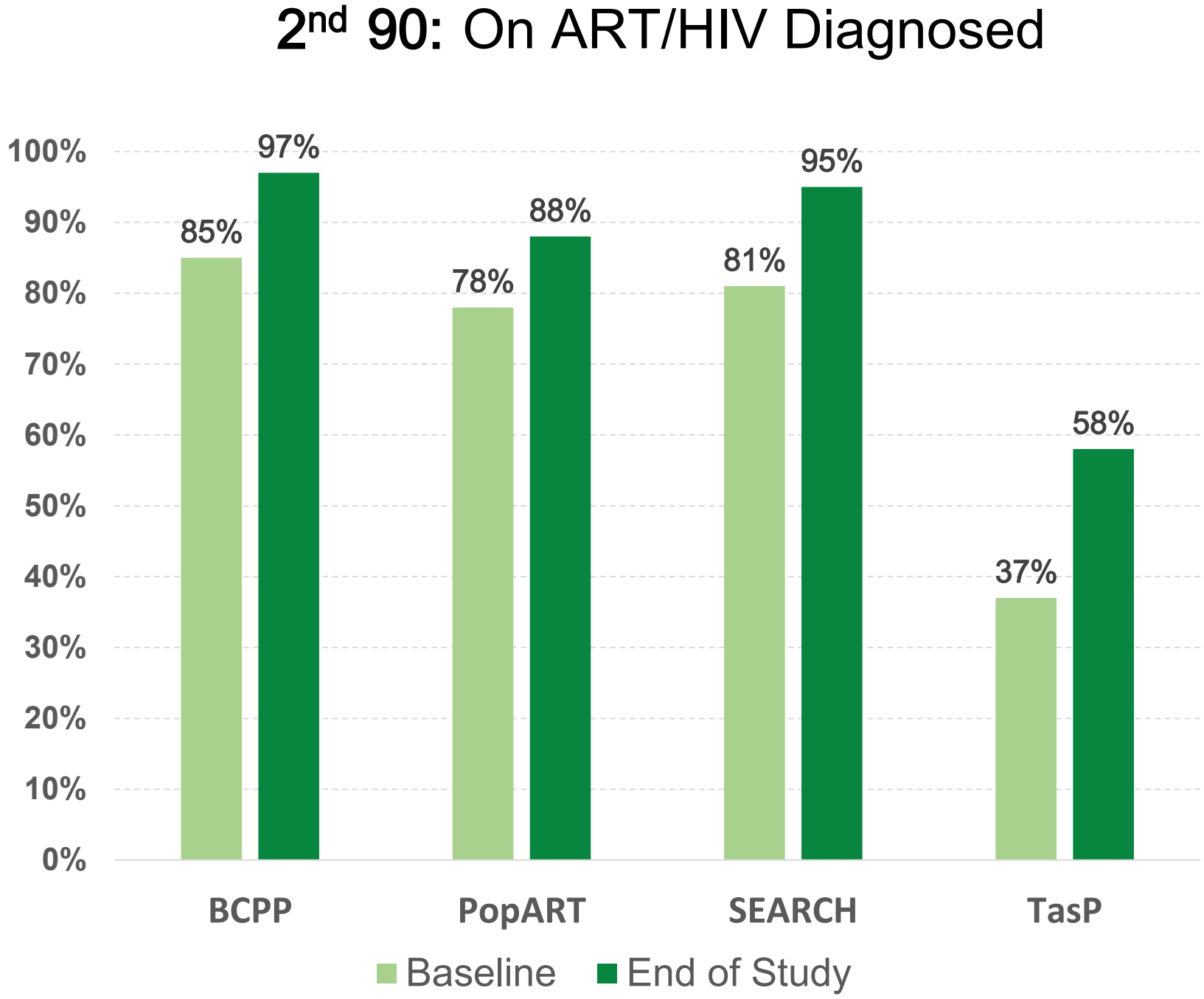
*Intervention arms only.
PopART Intervention arms combined



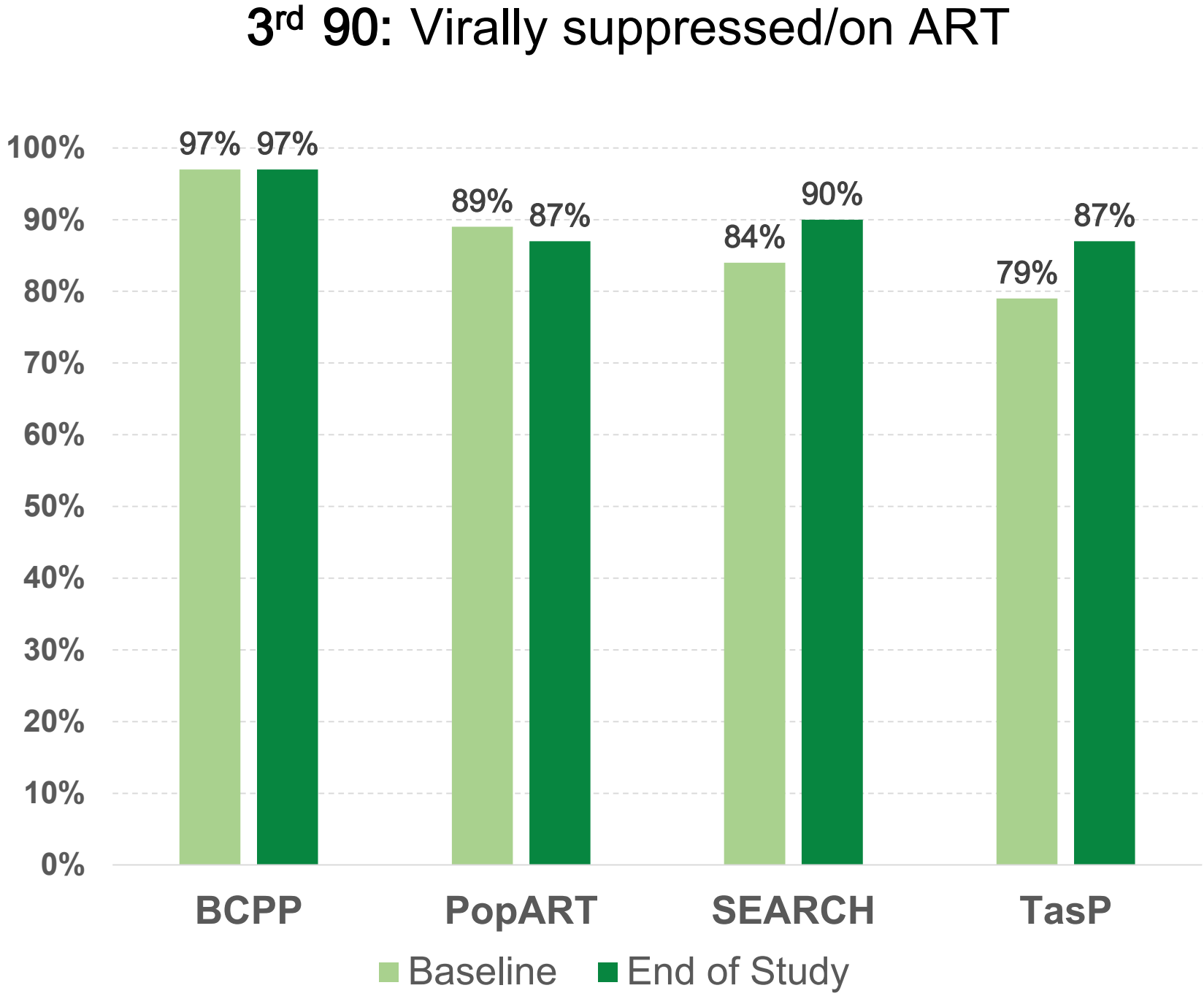
With UTT, 3 of 4 studies started ART in ~90-97% (2nd 90)

- Rapid linkage and much faster ART start in intervention arms
- Low linkage in TasP, but ART initiation high once linked to clinics

*Intervention arms only.
PopART Intervention arms combined



With UTT, all studies reached viral suppression ~90% if on ART (3rd 90)

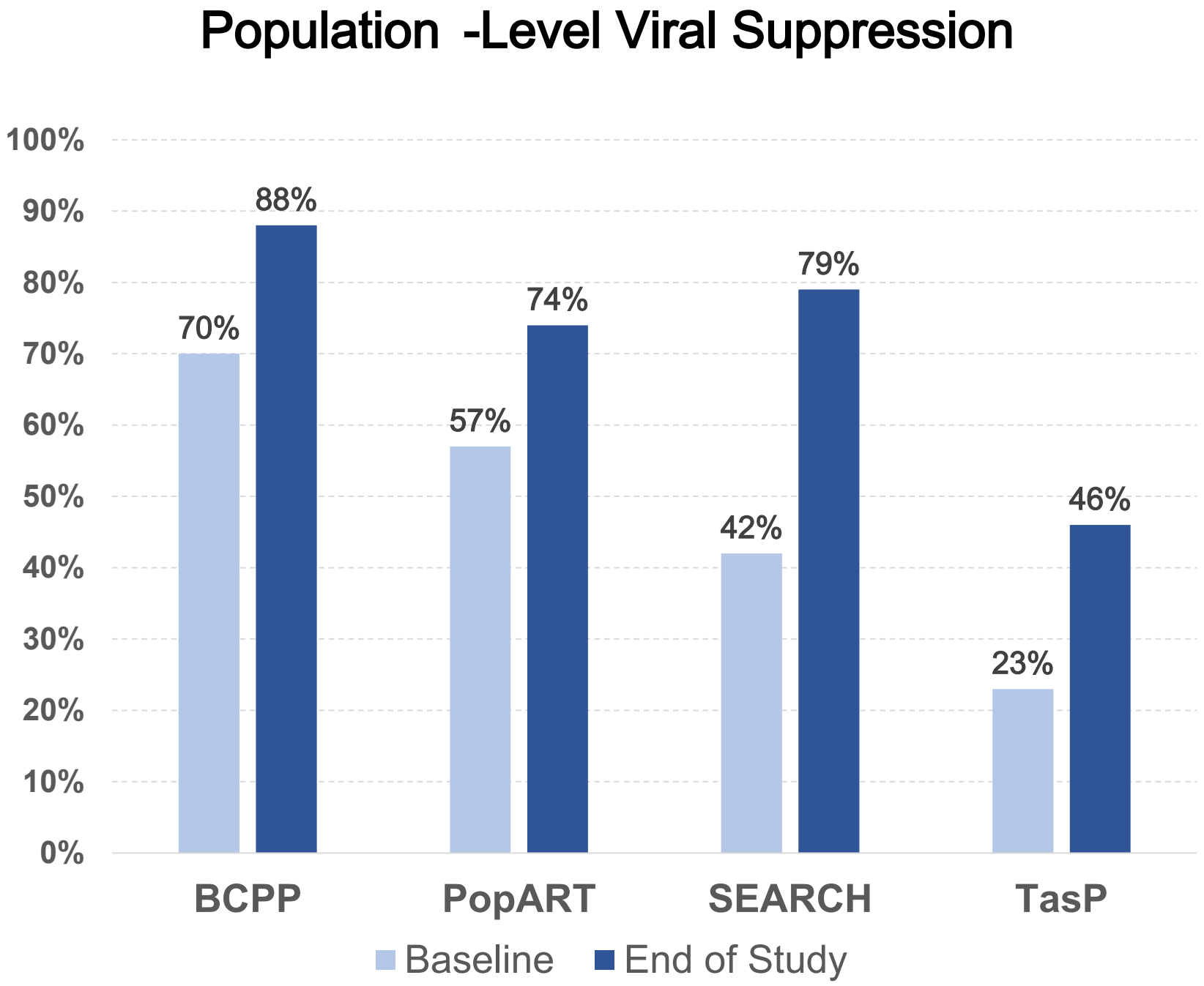


*Intervention arms only.
PopART Intervention arms combined

With UTT, 3 studies reached Population -level viral suppression >73%

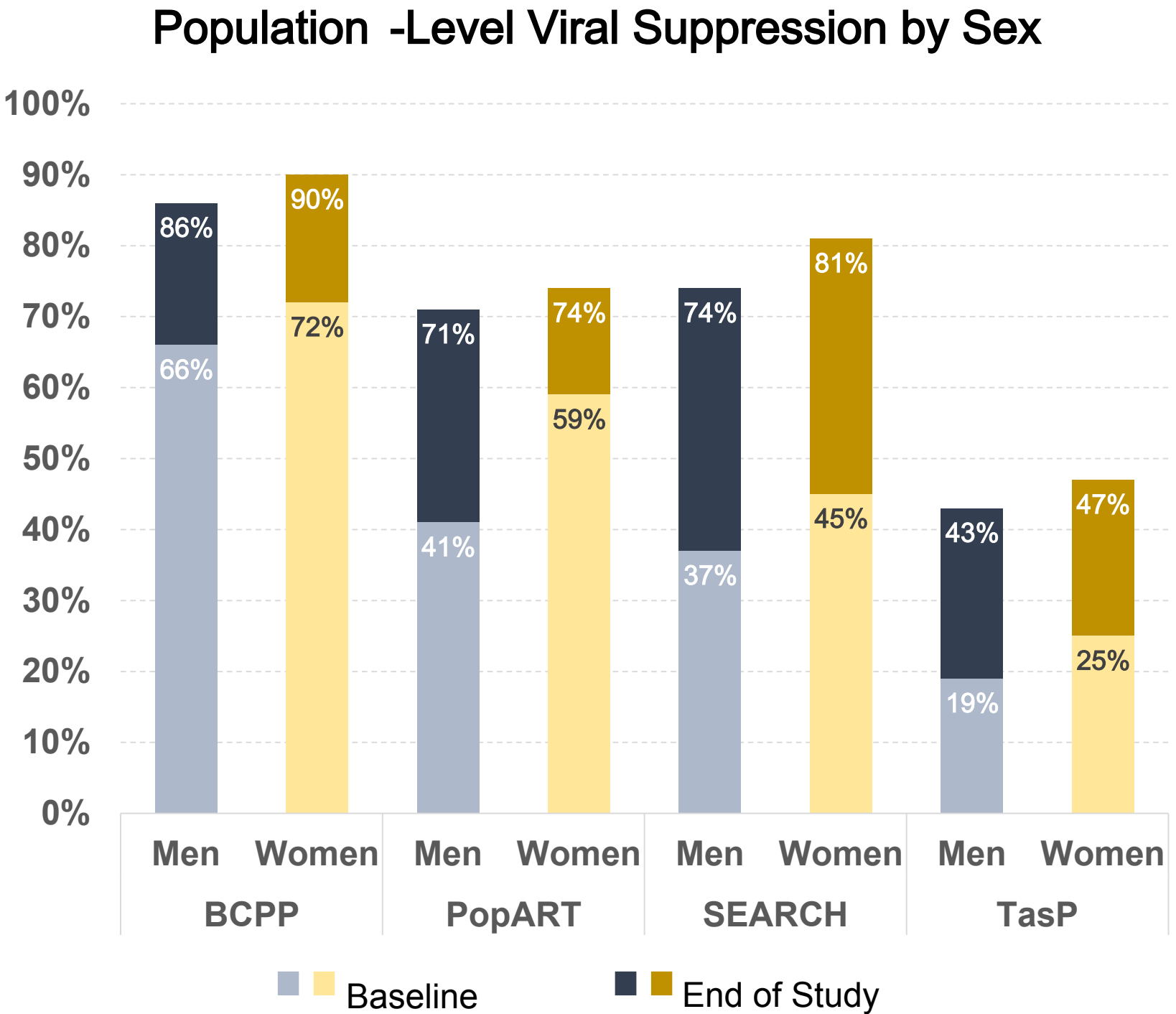
- Dramatic increases in population viral suppression over short period of time
- From low (23%) or high (70%) starting point

*Intervention arms only.
PopART Intervention arms combined



Interventions effectively increased population level suppression in both men and women

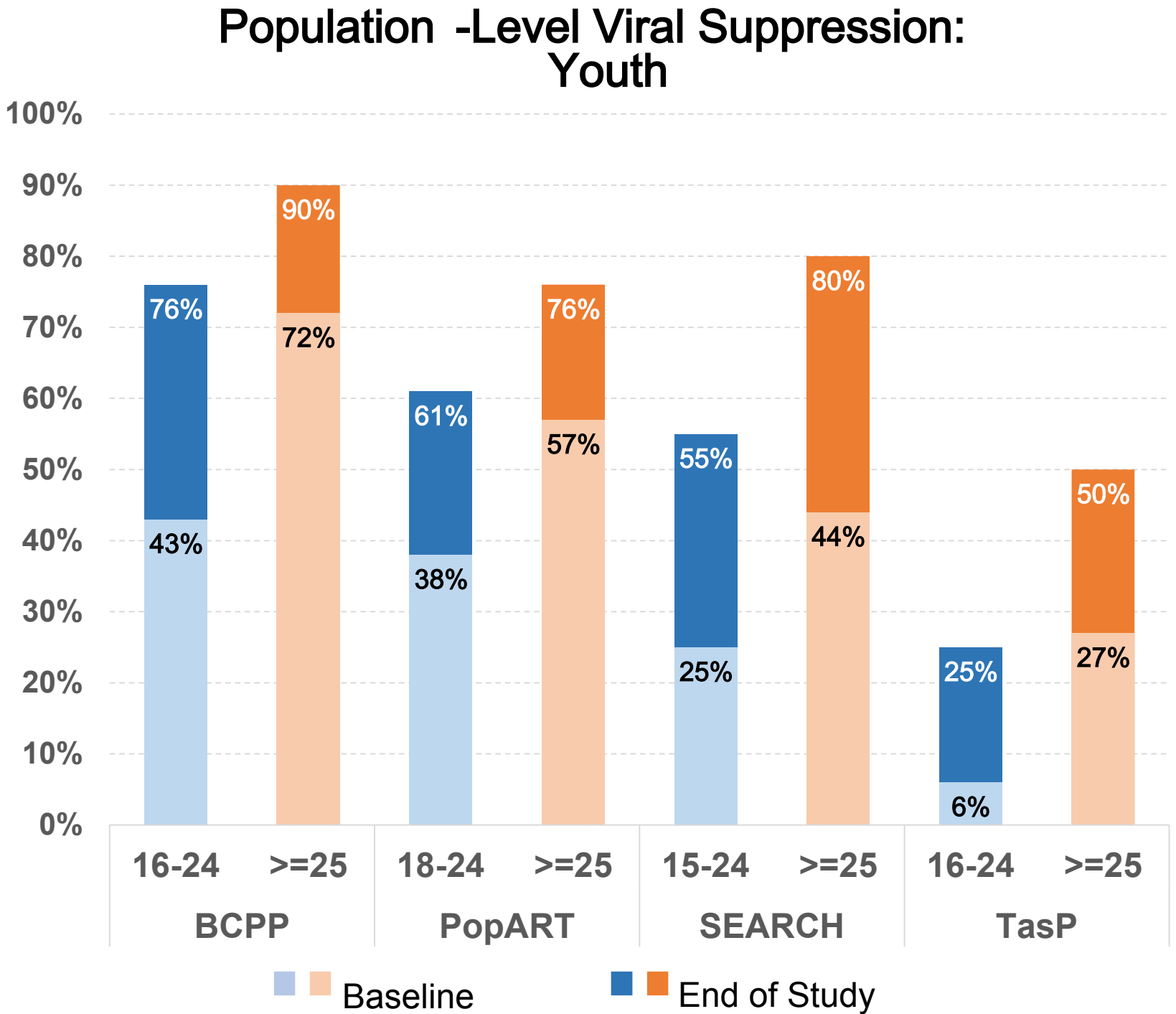
*Intervention arms only.
PopART Intervention arms combined



Interventions showed variable gains in youth

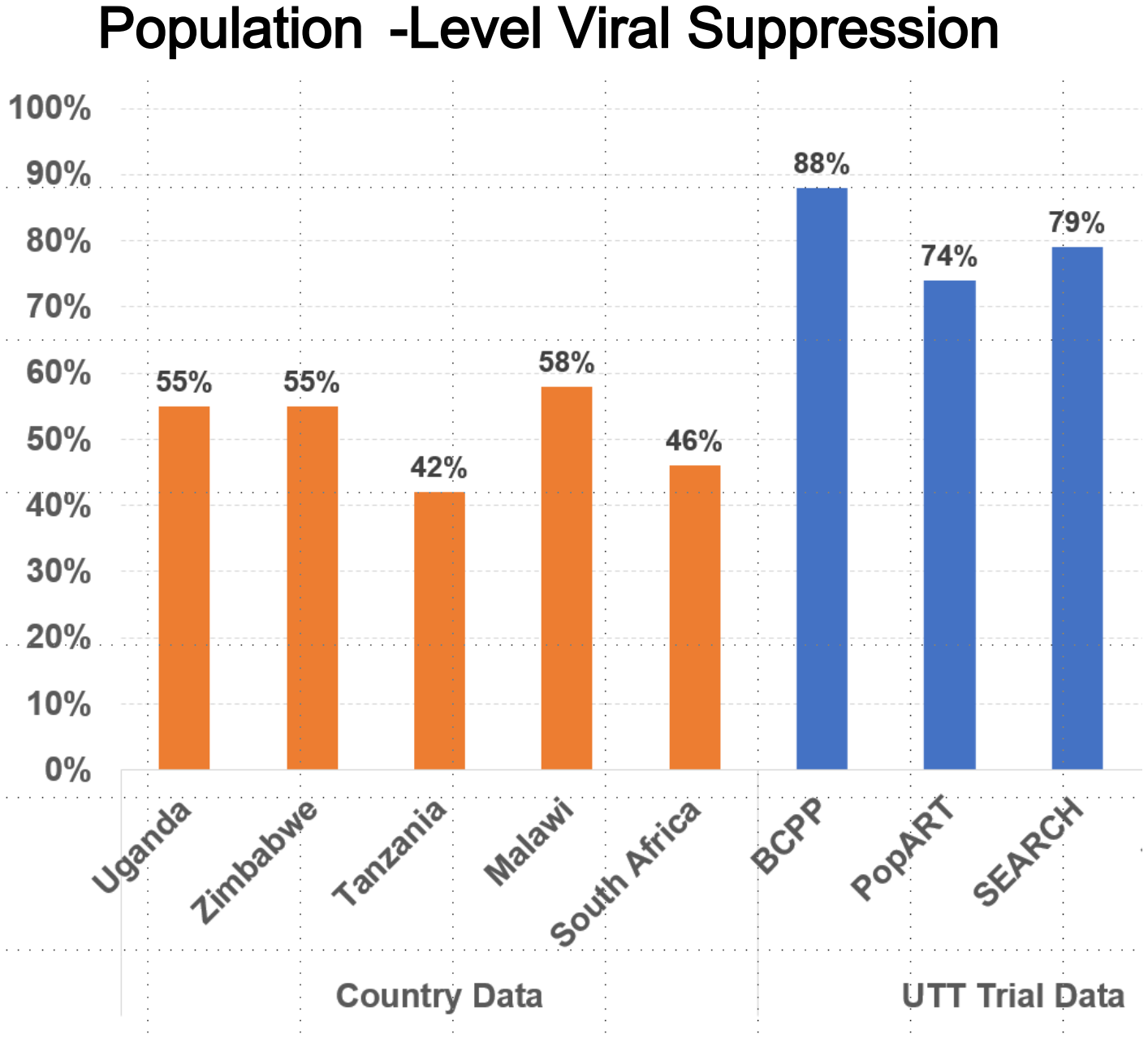
- Suppression among youth still remains low in all studies
- Due to new infections and worse ART uptake / outcomes

*Intervention arms only.
PopART Intervention arms combined



1. UTT rapidly achieved population -level viral suppression higher than current “Standard of Care” in most African countries

2. Achieved substantial increases in suppression among men and youth



Country VS Ref: El-Sadr, NEJM, 2019, and UNAIDS Report
UTT: Makhema, NEJM, 2019;Hayes, NEJM, 2019; Havlir, NEJM, 2019

Did implementation of UTT reduce HIV incidence in the four trials?

HIV Incidence findings

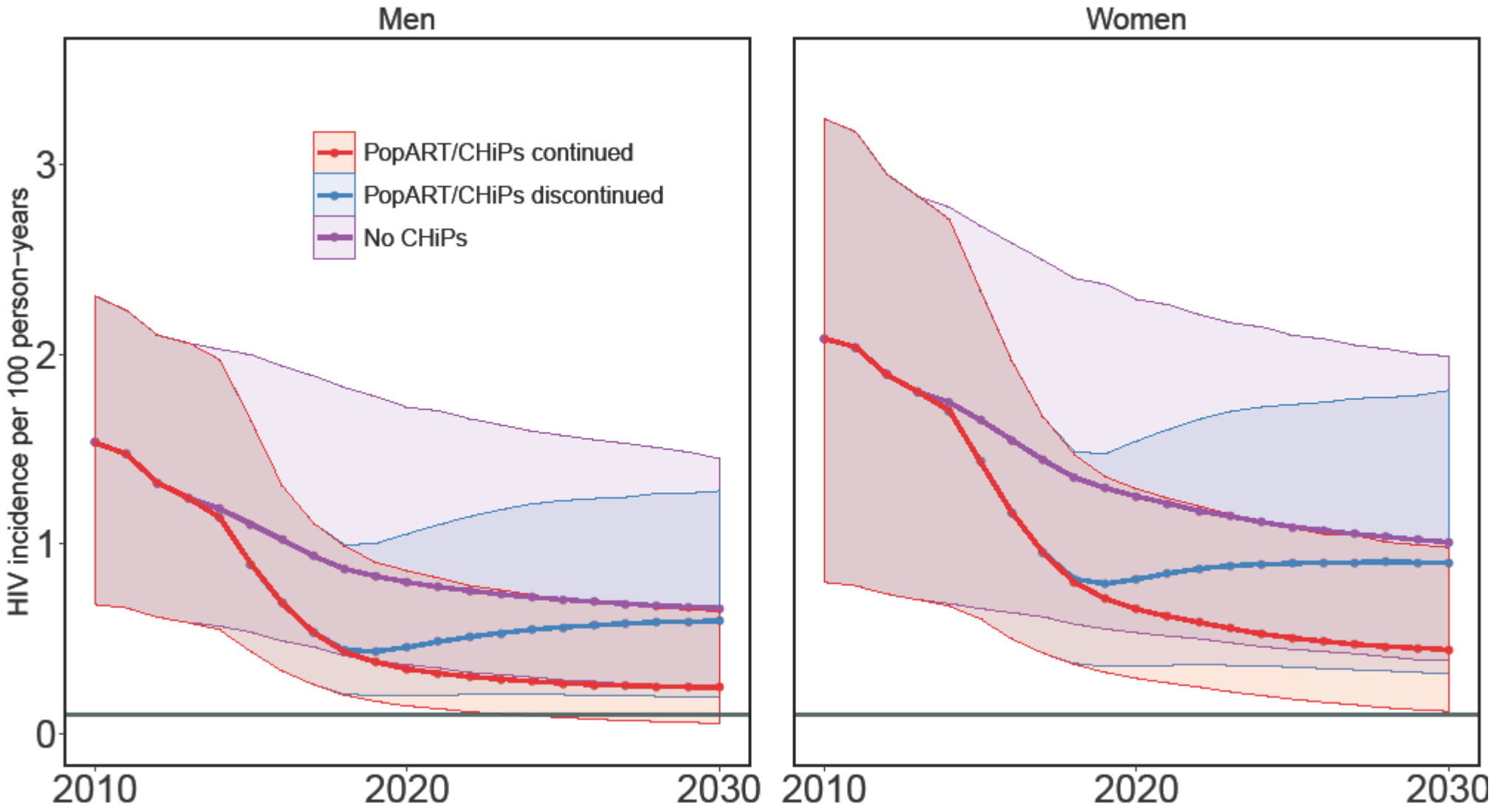
- Population-level outcome
- Reflect very short time frame of these trials (~3 years)

1. **HIV incidence effect (~20 -30% reduction) observed when UTT compared to a control *without* universal testing (BCPP & PopART)**

2. **HIV incidence reduced (~30%) in *both arms* when control arm had universal testing (SEARCH)**
   - 32% reduction observed between years 1 and 3 (SEARCH intervention arm)

Note: Impact of UTT intervention in trials setting (vs national -scale up) was almost certainly underestimated, due to mixing outside of intervention communities

Greater projected impact on HIV incidence if PopART intervention sustained over longer time (modeling)



PopART intervention was cost -effective – projections to 2030

- Cost of CHiPs intervention per capita $5.10-$8.20 per year

Country	Intervention scenario	Outcome averted	ICER range (US$)
Zambia	PopART continued 2014-30	Infections	1,427 - 2,673
		DALYs	465 - 847
	PopART 2014-17	Infections	835 - 1,811
		DALYs	196 - 392
South Africa	PopART continued 2014-30	Infections	2,324 - 4,712
		DALYs	503 - 922
	PopART 2014-17	Infections	1,493 - 3,700
		DALYs	233 - 513

Should we do UTT? UTT teams' conclusion:

- **Yes**
  - UTT with Universal testing and linkage/rapid ART start represents an evidence-based means to rapidly and efficiently reduce incidence and mortality and puts *"Communities at the Center"*
  - Decline in incidence and mortality in UTT trials seen over a short time period → carried forward could have a large, long-term impact
  - The point of controversy for global health policy is universal testing, not universal treatment with rapid ART start
- **But**
  - Appropriate scale for Universal Testing (national, sub-national, local) may vary depending on epidemic setting
  - Repeat testing is important and can to be tailored (many options)
- **And**
  - UTT alone, as done in these 1st generation studies, cannot achieve HIV epidemic control fast enough. However optimized UTT + additional prevention should speed epidemic control.
  - UTT may enhance delivery and serve as a platform for new prevention strategies & other public health priorities

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BOTSWANA HARVARD AIDS INSTITUTE PARTNERSHIP FOR HIV RESEARCH AND EDUCATION

CDC CENTERS FOR DISEASE CONTROL AND PREVENTION

MINISTRY of HEALTH REPUBLIC OF BOTSWANA


Thank you!

HIV incidence outcomes

Trial	BCPP		PopART		SEARCH		TasP	
Country	Botswana		South Africa / Zambia		Kenya / Uganda		South Africa	
Arm	C	I	C	I	C	I	C	I
Universal testing	-	✓	-	✓	✓	✓	✓	✓
Universal treatment	-	✓	-/✓	-/✓	-/✓	✓	-	✓
Population viral suppression								
- at start	75%	70%	52%	57%	42%	42%	26%	24%
- at end	83%	88%	68%	74%	68%	79%	45%	46%
- difference	+8	+18	+16	+17	+26	+37	+19	+23
HIV incidence								
Annual incidence for 100 person-years	0.92	0.59	1.55	1.24	0.27	0.25	2.27	2.11
Reduction (I vs C)	31% reduction		20% reduction		not significant, but 32% reduction in intervention arm between years 1 & 3		not significant	

Note:
both intervention arms were pooled for PopART.