

Estimated long-acting PrEP effectiveness in the HPTN 084 cohort using a model based counterfactual

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HPTN 084 Background

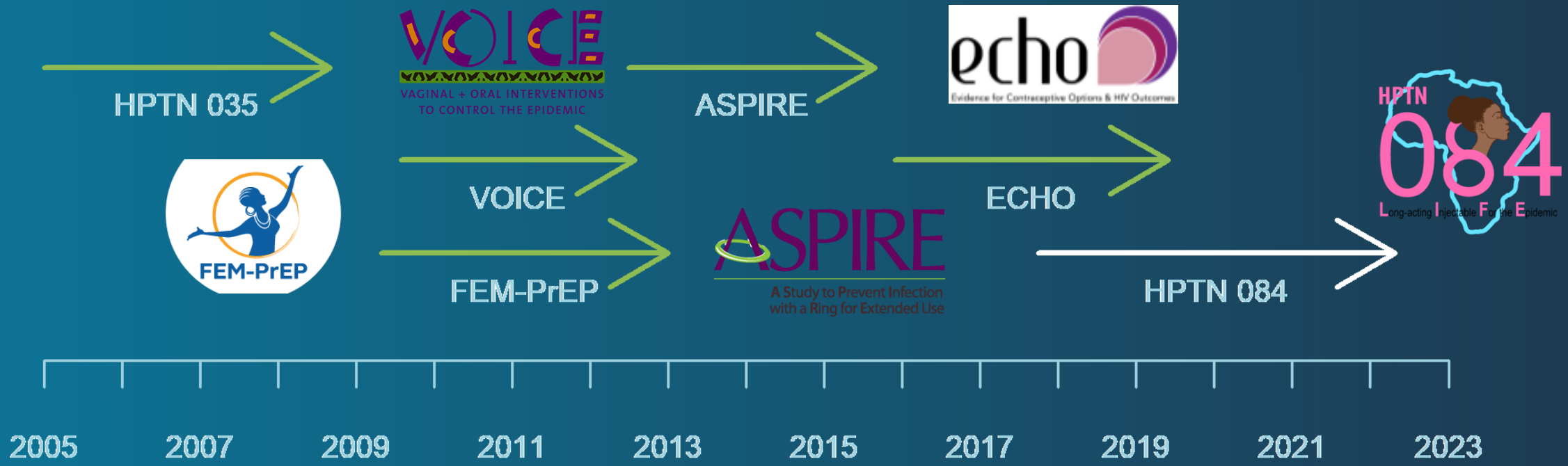
- HPTN 084 is a phase III study to evaluate the effectiveness long-acting pre-exposure prophylaxis (LA PrEP) with cabotegravir in young women in sub-Saharan Africa
- The study uses an active control arm consisting of daily oral PrEP via tenofovir and emtricitabine (TDF/FTC)
- The effectiveness of TDF/FTC depends on product adherence which is highly variable
- The goal of this study is to provide a counterfactual estimate of placebo incidence by making use of data from previous HIV prevention studies.
- This counterfactual is just one of several that will be used to evaluate LA PrEP effectiveness.

Reference Studies



HIV Reference Studies

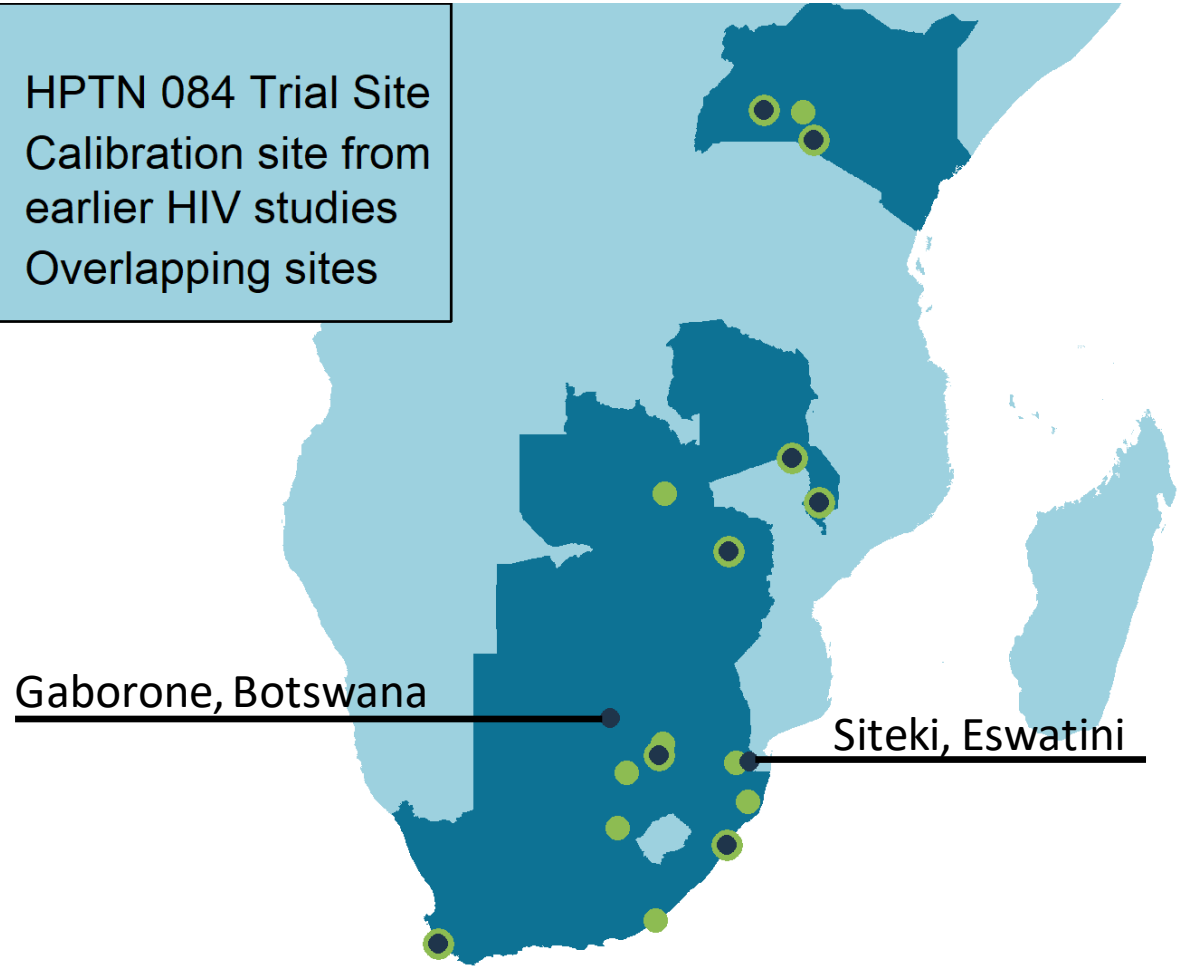
The reference studies and their followup periods relative to the study of interest: HPTN 084



Trial Site Locations

- All but two communities with HPTN 084 trial sites have hosted previous HIV studies
- The remaining communities: Gaborone, Botswana and Siteki, Eswatini are close geographically to the prior set of sites.

- HPTN 084 Trial Site
- Calibration site from earlier HIV studies
- Overlapping sites



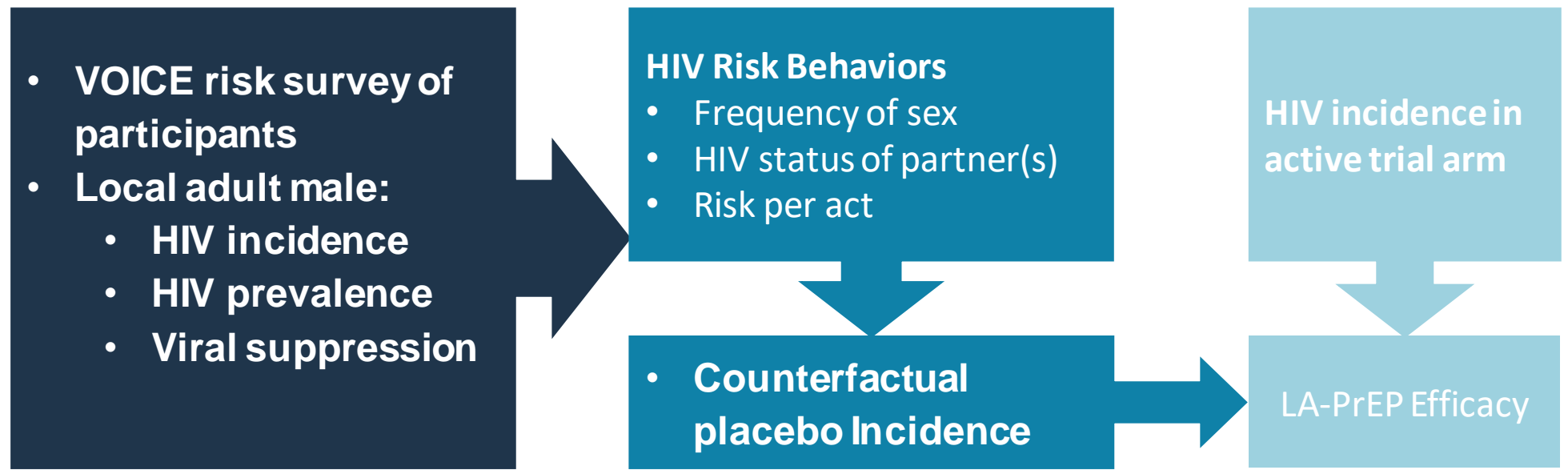
Adjusting Participant Risk

Risk Factor	Description	Trial Population (% with factor)			Odds Ratio of HIV Infection [VOICE]
		VOICE	ASPIRE	HPTN 084	
MP	Not married/living with main partner	68	58	82	1.8 (1.2-2.8)
FN	No financial support from main partner	17	46	60	1.4 (1.0-1.8)
SE	Main partner may have other partners	75	57	94	1.6 (1.0-2.6)
ST	STI at enrollment	20	21	29	1.5 (1.1-1.9)
DR	Alcohol use past three months	26	12	61	1.4 (1.1-1.9)
AG	Less than 25 years old	51	39	48	1.7 (1.3-2.3)
	Mean Risk Score (HPTN 082 Scoring)	4.7	4.1	6.3	

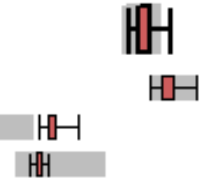

















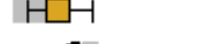
Counter-factual Model



Counterfactual model outline





Model Validation

	Observed	Simulated	
1) VOICE Trial (Calibration)	6.0 (5.3 - 6.7)	6.1 (5.6 - 6.9)	
South African Sites	7.3 (6.5 - 8.3)	7.1 (6.5 - 8.0)	
Harare, ZW	0.5 (0.1 - 1.5)	2.2 (1.9 - 3.2)	
Kampala, UG	2.1 (0.8 - 4.4)	1.7 (1.5 - 2.0)	
2) HPTN035 (Validation)	3.4 (2.7 - 4.1)	4.3 (3.4 - 5.6)	
Malawian Sites	2.3 (1.7 - 3.1)	3.5 (2.9 - 4.7)	
South African Sites	6.1 (5.1 - 7.3)	5.4 (4.0 - 7.3)	
Harare, ZW	2.5 (1.4 - 3.9)	4.0 (2.9 - 5.5)	
Lusaka, ZM	4.1 (2.4 - 6.4)	3.4 (2.5 - 4.8)	
3) FEM-PrEP (Validation)	4.8 (3.7 - 6.1)	4.8 (3.5 - 6.1)	
Bondo, KE	4.5 (3.0 - 6.5)	4.4 (3.0 - 6.2)	
Manguang, ZA	3.0 (1.2 - 6.0)	4.0 (2.7 - 6.0)	
Tshwane, ZA	6.0 (4.2 - 8.3)	5.8 (3.9 - 8.2)	
4) ASPIRE Trial (Validation)	3.7 (3.0 - 4.5)	3.2 (2.6 - 4.1)	
Malawian Sites	2.6 (1.0 - 5.2)	2.3 (1.7 - 3.1)	
South African Sites	5.2 (4.1 - 6.5)	3.9 (3.2 - 5.2)	
Kampala, UG	1.6 (0.4 - 4.0)	1.3 (1.0 - 1.8)	
Harare, ZW	1.5 (0.7 - 2.7)	2.5 (1.4 - 3.7)	
5) ECHO Trial (Validation)	3.8 (3.5 - 4.2)	3.2 (2.6 - 4.1)	

Observed HIV incidence from the first year of follow-up of each study (gray bar = 95% confidence interval)

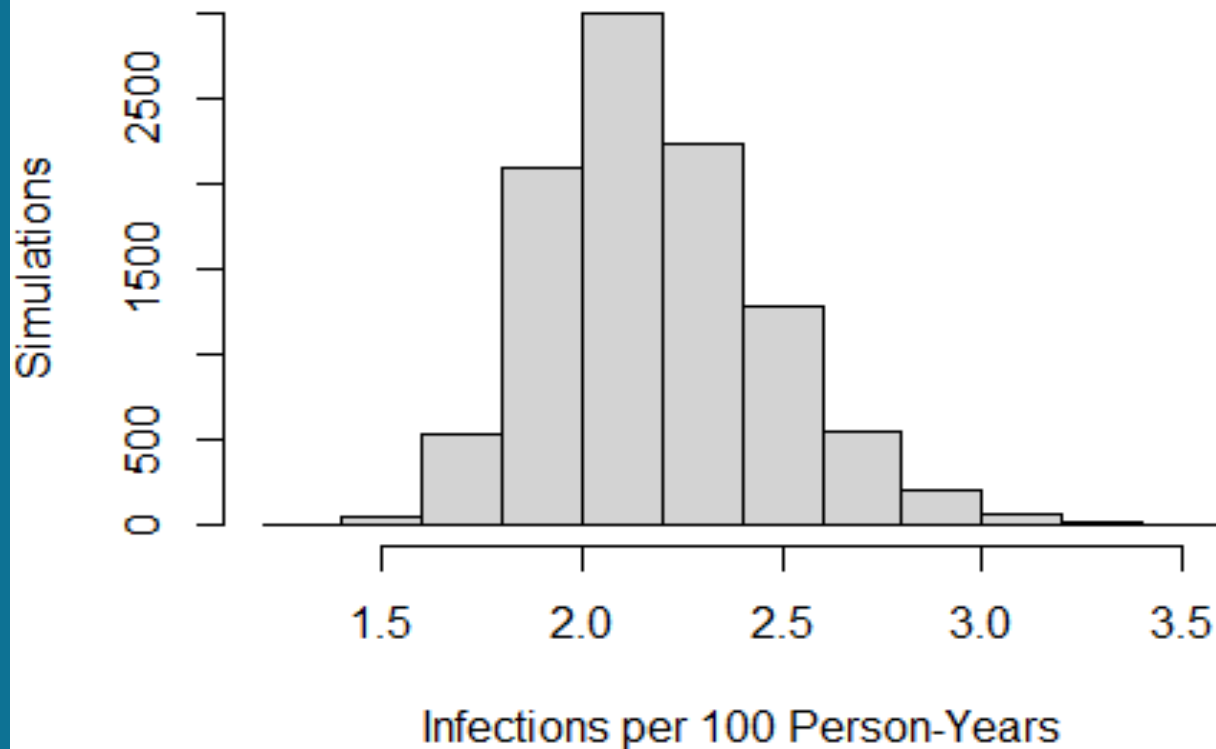
Simulated HIV incidence using our methodology (whisker = 95% credible interval, box = interquartile range).

HPTN 084 Counter factual

Country	Community	Adult Male Community Characteristics 			Counter Factual Incidence (Female per 100 py) 
		HIV Incidence (per 100 py)	HIV Prevalence (%)	Viral Suppression (%)	
Botswana	Gaborone	0.55 (0.46-0.66)	20.4 (18.5-22.5)	67.8 (61.0-74.0)	3.0(1.9-4.5)
Eswatini	Siteki	0.70 (0.51-0.94)	20.3 (17.0-24.1)	90.6(79.2-96.0)	0.9(0.5-1.7)
Kenya	Kisumu	0.51 (0.31-0.82)	14.2 (11.6-17.4)	77.3(63.5-87.0)	1.3(0.7-2.8)
Malawi	Blantyre	0.28 (0.06-1.21)	11.4 (9.3-13.9)	52.3(43.6-60.7)	3.2(2.1-4.6)
	Lilongwe	0.17 (0.04-0.73)	7.1 (5.7-8.9)	58.0(49.2-66.4)	1.6(1.0-2.5)
South Africa	Cape Town	0.43 (0.28-0.66)	10.0 (4.9-19.4)	49.0 (42.6-55.5)	3.1(1.6-6.1)
	Durban-Botha's Hill-Isipengo	0.60 (0.33-1.09)	16.6 (11.0-24.2)	62.3 (56.1-68.2)	3.2(2.0-5.4)
	Johannesburg-Soweto	0.29 (0.16-0.52)	9.1 (5.1-15.8)	51.3 (44.8-57.7)	2.6(2.0-5.4)
Uganda	Kampala-Entebbe	0.20 (0.14-0.28)	4.3 (3.4-5.5)	66.0 (53.0-77.0)	0.7(0.4-1.3)
Zimbabwe	Harare-Chitungwiza	0.36 (0.23-0.55)	9.9 (7.5-12.9)	68.2(55.1-79.0)	1.4(0.7-2.8)

Overall study incidence

Counterfactual HIV incidence



- Posterior Distribution of HIV Incidence in HPTN 084
- Median is 2.2 infections per 100 person years
- 95% Credible Interval (1.7-2.8)
- Incidence in the active (Cabotegravir) arm was 0.2 infections per 100 person years (0.06 – 0.52)

91% (76-97)

Efficacy of Long Active PrEP vs Placebo (Intention to Treat)

Conclusions

- We used data from previous HIV studies to project incidence in a counterfactual placebo arm of HPTN 084
- Our model-based approach allows for the adjustment of risk due to changes in time, place, and participant risk behaviors
- Using our model, we estimate that Long acting PrEP is roughly 90% effective for reducing HIV infection in women in sub-Saharan Africa
- This is only the first of several counterfactual incidence estimates that we will use to refine this estimate

Thank you!

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Acknowledgments

- Overall support for the HIV Prevention Trials Network (HPTN) is provided by the National Institute of Allergy and Infectious Diseases (NIAID), Office of the Director (OD), National Institutes of Health (NIH), National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) under Award Numbers UM1AI068619-15 (HPTN Leadership and Operations Center), UM1AI068617-15 (HPTN Statistical and Data Management Center), and UM1AI068613-15 (HPTN Laboratory Center).
- The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.