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# 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

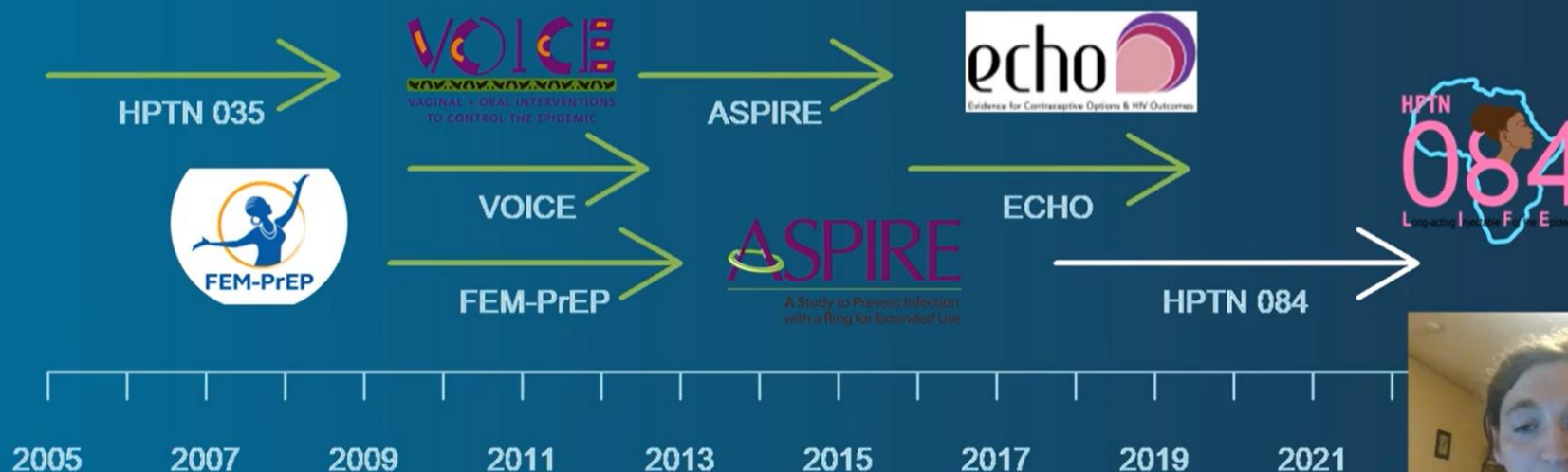
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# HIV Reference Studies

The references 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

Gaborone, Botswana

Siteki



# Adjusting Participant Risk

Risk Factor	Description	Trial Population (% with factor)			Odds Ratio of HIV Infection [VOICE]
		VOICE	ASPIRE	HPTN 084	
<b>MP</b>	Not married/living with main partner	68	58	82	1.8 (1.2-2.8)
<b>FN</b>	No financial support from main partner	17	46	60	1.4 (1.0-1.8)
<b>SE</b>	Main partner may have other partners	75	57	94	1.6 (1.0-2.6)
<b>ST</b>	STI at enrollment	20	21	29	1.5 (1.1-1.9)
<b>DR</b>	Alcohol use past three months	26	12	61	1.4 (1.1-1.9)
<b>AG</b>	Less than 25 years old	51	39	48	1.7 (1.3-2.2)
<b>Mean Risk Score (HPTN 082 Scoring)</b>		<b>4.7</b>	<b>4.1</b>	<b>6.3</b>	



# Counter-factual Model

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# Counterfactual model outline

Predict Risk

Simulate Infections

Estimate Efficacy

- **VOICE risk survey of participants**
- **Local adult male:**
  - HIV incidence
  - HIV prevalence
  - Viral suppression

## HIV Risk Behaviors

- Frequency of sex
- HIV status of partner(s)
- Risk per act

• **Counterfactual placebo Incidence**




















HIV incidence in  
active trial arm

LA-PrEP Efficacy





# Model Validation




	Observed	Simulated	
<b>1) VOICE Trial (Calibration)</b>	<b>6.0 (5.3 - 6.7)</b>	<b>6.1 (5.6 - 6.9)</b>	
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)	
<b>2) HPTN035 (Validation)</b>	<b>3.4 (2.7 - 4.1)</b>	<b>4.3 (3.4 - 5.6)</b>	
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)	
<b>3) FEM-PrEP (Validation)</b>	<b>4.8 (3.7 - 6.1)</b>	<b>4.8 (3.5 - 6.1)</b>	
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)	
<b>4) ASPIRE Trial (Validation)</b>	<b>3.7 (3.0 - 4.5)</b>	<b>3.2 (2.6 - 4.1)</b>	
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)	
<b>5) ECHO Trial (Validation)</b>	<b>3.8 (3.5 - 4.2)</b>	<b>3.2 (2.6 - 4.1)</b>	

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).

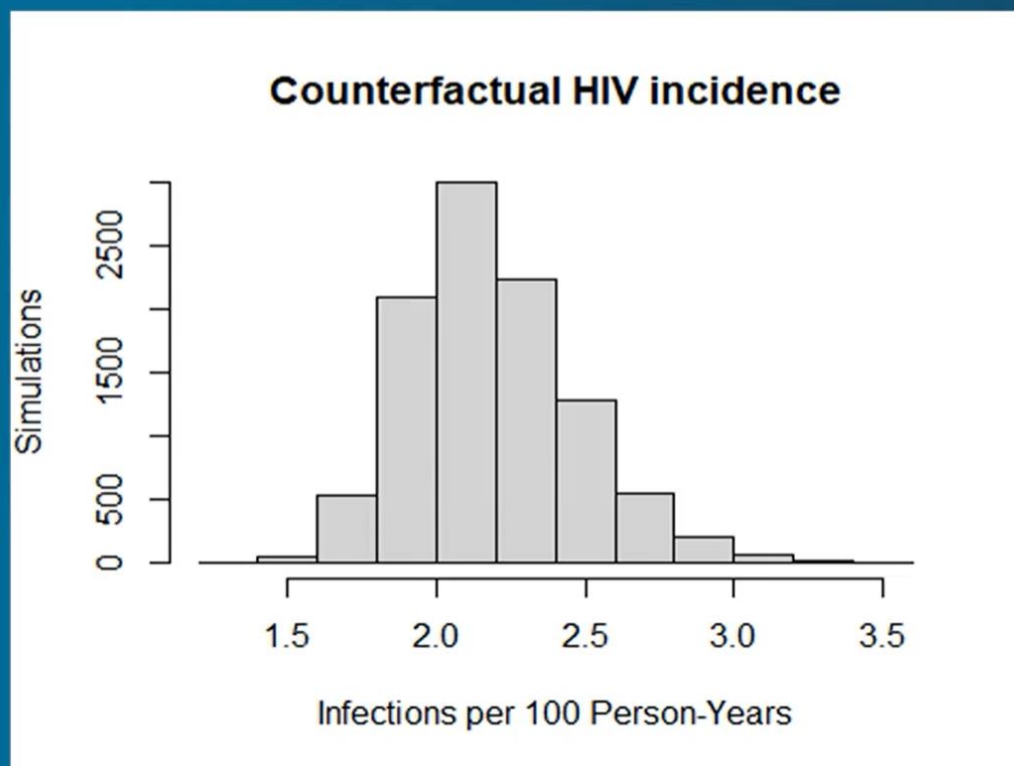


# HPTN 084 Counterfactual

Country	Community	Adult Male Community Characteristics 			Counter Factual  Incidence 
		HIV Incidence (per 100 py)	HIV Prevalence (%)	Viral Suppression (%)	(Female per 100 py)
<b>Botswana</b>	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)
<b>Eswatini</b>	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)
<b>Kenya</b>	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)
<b>Malawi</b>	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)
<b>South Africa</b>	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(
	Johannesburg-Soweto	0.29 (0.16-0.52)	9.1 (5.1-15.8)	51.3 (44.8-57.7)	2.6(
<b>Uganda</b>	Kampala-Entebbe	0.20 (0.14-0.28)	4.3 (3.4-5.5)	66.0 (53.0-77.0)	0.7(
<b>Zimbabwe</b>	Harare-Chitungwiza	0.36 (0.23-0.55)	9.9 (7.5-12.9)	68.2(55.1-79.0)	1.4(



# Overall study 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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