

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

**Mia Moore** 

**Fred Hutchinson Cancer Research Center** 





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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 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.







#### **Adjusting Participant Risk**

Risk		Trial Population (% with factor)			Odds Ratio of HIV Infection
Factor	Description	VOICE	ASPIRE	HPTN 084	[VOICE]
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**

Predict Risk

Simulate Infections

Estimate Efficacy

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







#### **Model Validation**

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

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).





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#### **HPTN 084 Counter factual**

		Adult Male Commu	Counter Factual		
		HIV Incidence	HIV Prevalence	Viral Suppression	Incidence 🕈
Country	Community	(per 100 py)	(%)	(%)	(Female per 100 py)
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)



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#### 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!

Mia Moore PhD (She/Her) Vaccine and Infectious Disease Division Fred Hutch Cancer Research Center Seattle, WA, USA

jrmoore@fredhutch.org







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