

The Iniciativa PrEx Study: Safety, Efficacy, Behavior, and Biology

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Fundación
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Iniciativa PrEx (The Andean PrEP Trial)

- 1400 High Risk MSM
- Randomized 1:1 FTC/TDF vs Placebo
- Followed on Drug for 72 Weeks For:
 - HIV seroconversion
 - Adverse Events (especially renal & liver)
 - HBV Flares among HBsAg+
 - Risk Behavior & STIs
 - Bone Mineral Density and Fat Composition
 - Adherence
 - Immune responses
 - If infected
 - Drug Resistance
 - Viral load
 - Immune responses & CD4 Count

HIV Infection Status

- Antibody tests to screen
 - The gold standard for HIV diagnostics
 - More feasible than RNA tests
 - Testing used for decision making in trial would become part of recommended use
 - Timepoints
 - Screen and Baseline
 - Every 4 wks on Drug
 - Every 4 wks for 12 wks After Drug
- RNA testing
 - At Enrollment if seroconverts in 3 mos
 - per FDA
 - Last Seronegative Visit

Adherence Assessments

- Pill Counts
- Computer Assisted Structured Interview
- Drug levels
 - Among seroconverters
 - A sample of high risk seronegatives

Site Selection

Based on Capacity to:

- High Retention and High Incidence
 - High Prevalence in young men (all)
 - High Incidence by BED (Lima, Guayaquil)
 - High Incidence in Cohorts (Lima, Iquitos)
- Experience with GCP Compliance
- Engender Robust Public Discourse
- Range of Service Settings
 - Medical Clinics
 - Community Based Organizations

Why Peru / Ecuador?

- Proven Track Record for On-time Recruitment of Large Numbers of High Incidence MSM
- A mixed research & education model
 - Educational activities routinely draw thousands of participants at a time
 - The Puentes Program linked to Impacta

HIV incidence by LS-EIA

*sites selected for the trial

	<i>2000</i> <i>N=4,304</i>	<i>2002</i> <i>N=2876</i>	<i>2006</i> <i>N=550</i>
Arequipa	4.72	4.29	
Chiclayo	1.92		
Ica	2.07		
Iquitos*	7.09	6.83	
Lima*	12.03	8.33	
Pucallpa	4.55	1.78	
Sullana/Piura	1.00	1.57	
Tacna	2.41		
Trujillo	1.44		
Peru	5.59	5.12	
Guayaquil*			7.82%

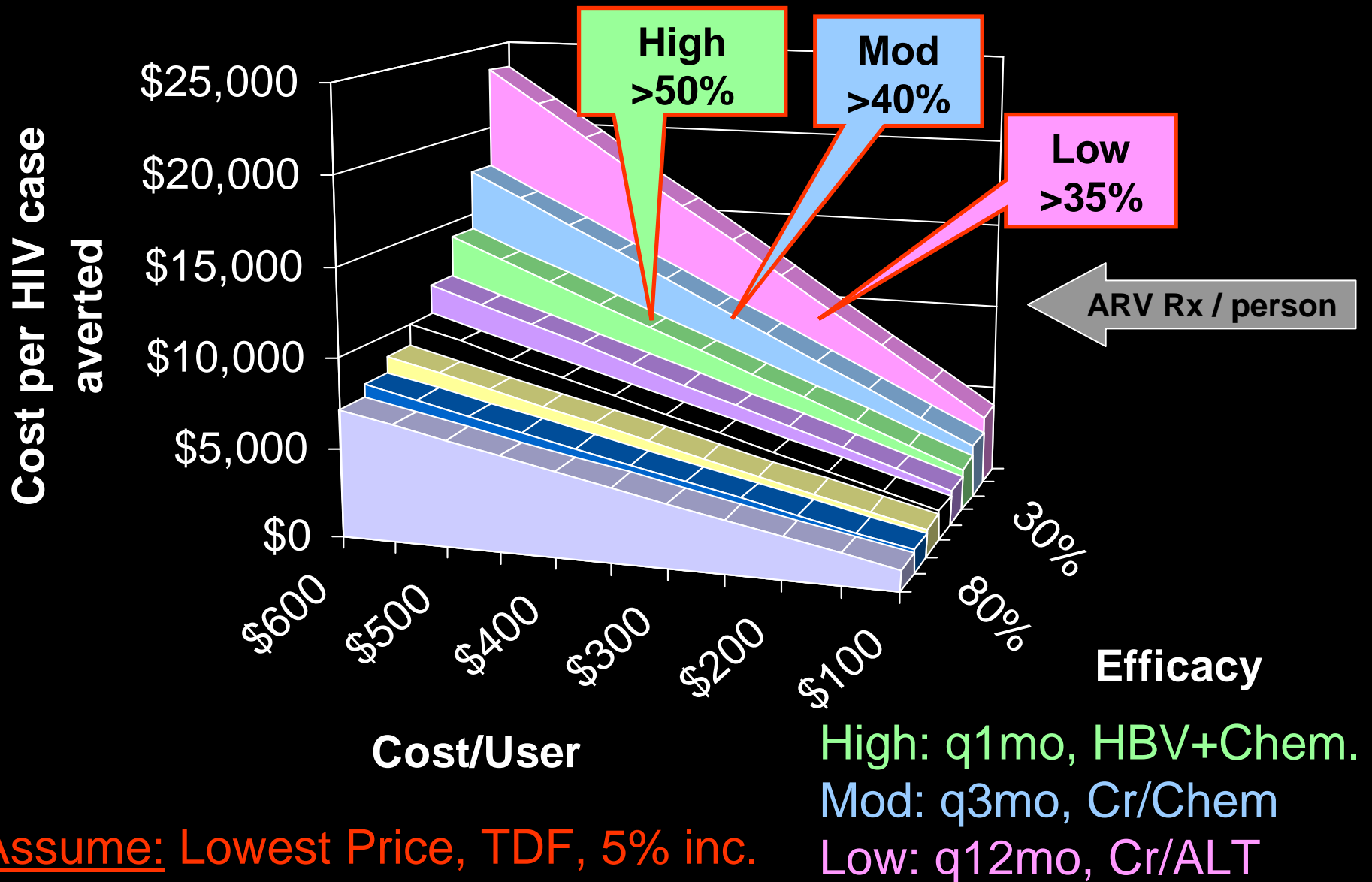
Incidence Estimates

- Seronegative Cohort Incidence
 - HPTN 036 cohort in Lima, Peru
 - N=254 participants enrolled in 5 months, ahead of schedule
 - At 12 Months:
 - 96% retention
 - 6.15/100 py incidence
- Recent Prevention Trial Incidence
 - HPTN 039
 - 2.8/100 py in Lima

Enrollment Plans

- Not defined by the Protocol
- Current Plans
 - Lima North N=400
 - Lima Central N=400
 - Iquitos N=300
 - Guayaquil N=300
- Dynamic Reallocation of Enrollment

Minimum Efficacy for Cost Effectiveness By Lab Monitoring Required for Safety



Sample Size

Proof of Concept

- 1400 total subjects (700/arm)
- Fixed 72 week follow-up
- 4% per yr incidence in placebo group
- 60% reduction from FTC/TDF
- 52 HIV infections
 - placebo: 37 expected events
 - FTC/TDF: 15 expected events

Iniciativa PrEx **Proof of Concept**

Yearly Incidence of Infection (Placebo Group)	Risk Reduction in FTC/TDF Group	Study Power
5%	50%	0.79
	60%	0.93
	75%	1.00
4%	50%	0.68
	60%	0.86
	75%	0.98
3%	50%	0.59
	60%	0.74
	75%	0.95

Goals of Expansion

- Increase sample size
 - To increase power to detect 60% efficacy to above 90%, even if incidence is 3.0%
 - To exclude efficacy of $<30\%$
- Answer the question with the same time frame
- Goal: 85 observed events

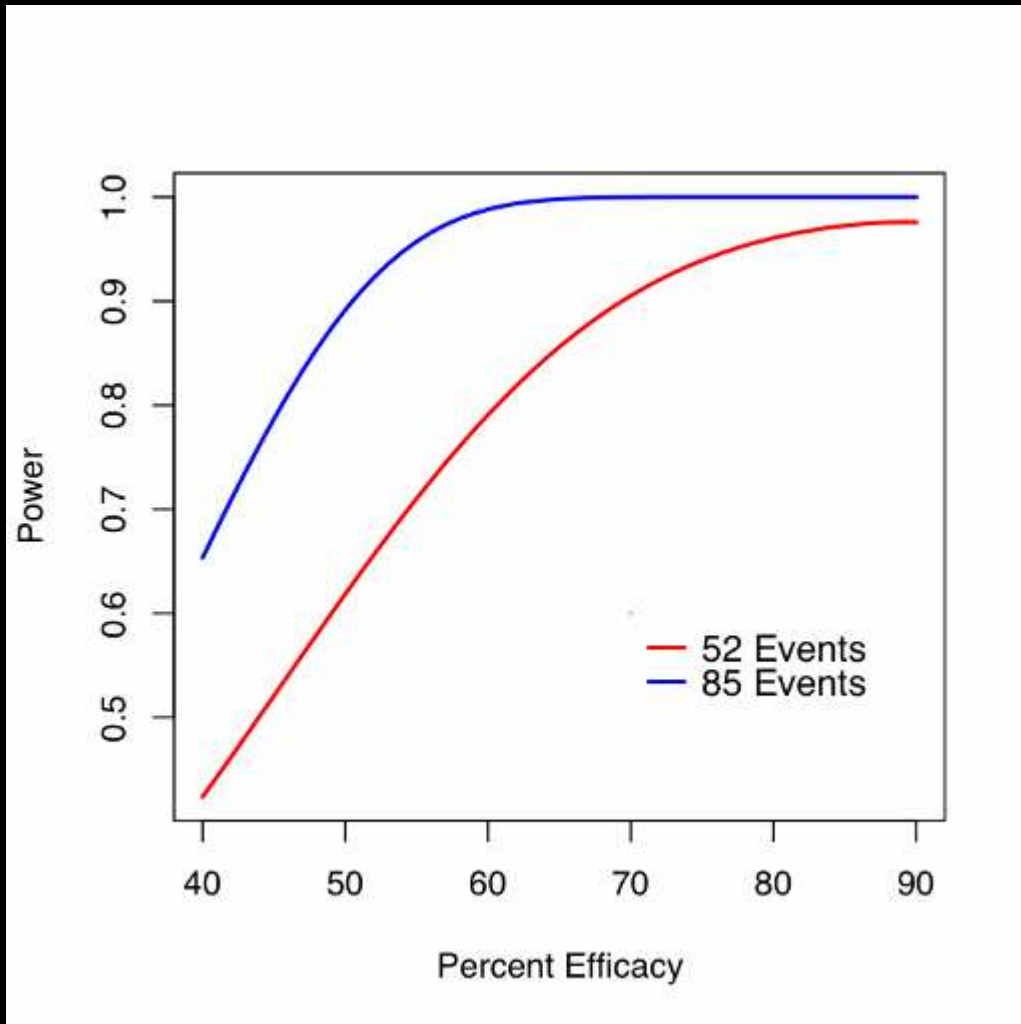
Increased Power for Efficacy

85 Events

Efficacy	Power
50%	0.89
60%	0.99
70%	1.00

52 Events

Efficacy	Power
50%	0.57
60%	0.74
70%	0.87



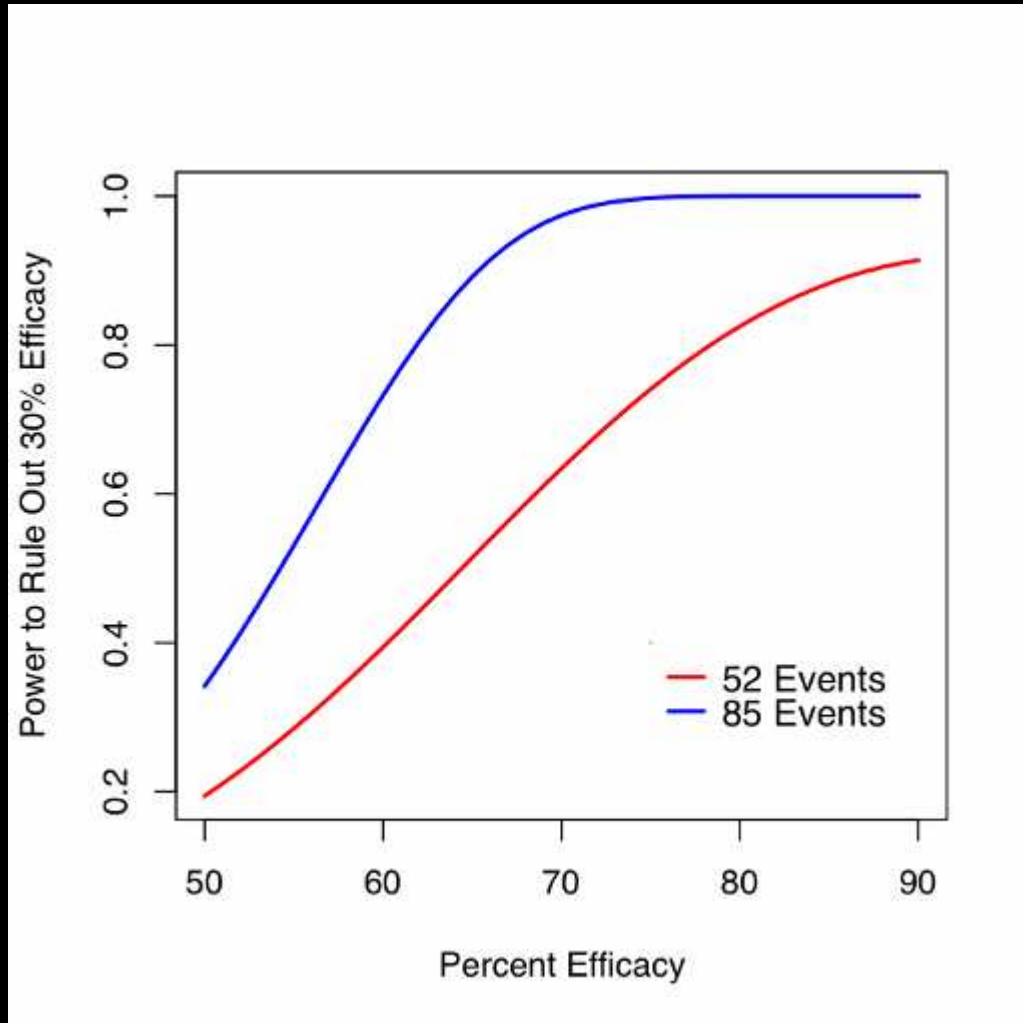
Power to Exclude 30% Efficacy

85 Events

Efficacy	Power
60%	0.73
70%	0.97
80%	1.00

52 Events

Efficacy	Power
60%	0.36
70%	0.58
80%	0.78



Interim Analysis Plan

- Monitored by DAIDS Intl DSMB
- Efficacy: Lan-Demet O'Brien-Fleming use
- Futility: Conditional power calculated at 1/3, 2/3 events
- Administrative monitoring: 2-3 per year

Sample Size Adjustments

- Conservative sample size assumptions
- Collect data on all screened subjects
- Willing to expand
 - sites, sample size, inclusion criteria
- No plans to resize based on rx difference
- Conditional power also useful

Analytic Challenges

- Subjects lost to follow-up
 - FDA: “Impute based on placebo incidence”
- Analysis of compliance/efficacy
- Secondary analyses in HIV+
 - VL
 - Mutations
- Mix of treatment and subj selection
- Difficult causal inference problems