

# HPTN 052

**Myron S. Cohen, MD**  
**Protocol Chair**  
6<sup>th</sup> IAS Conference, Rome, Italy  
July 18, 2011



# Antiviral Treatment as Prevention

- Extensive biological plausibility
  - The concentration of HIV-1 in blood and genital tract correlates with sexual transmission
  - Antiretroviral agents that concentrate in the genital tract reduce HIV-1 viral load
- Most observational reports indicate ART reduces transmission of HIV-1 in couples

# A Randomized Controlled Trial

---

- To determine if ART reduces HIV-1 transmission
  - magnitude?
  - durability of benefit?
- To determine if ART is used “earlier” to reduce HIV-1 transmission
  - personal health benefit(s)?

# **HPTN 052 Presentations**

---


- **HIV Prevention: RCT (Cohen)**
- **Linkage Analysis (Eshleman)**
- **HIV-1 Virology and Immunology (Hosseinipour)**
- **When to Start ART (Grinsztejn)**
- **Summary (Cohen)**
- **Questions and Answers**



# **Prevention of Transmission of HIV with ART**

---

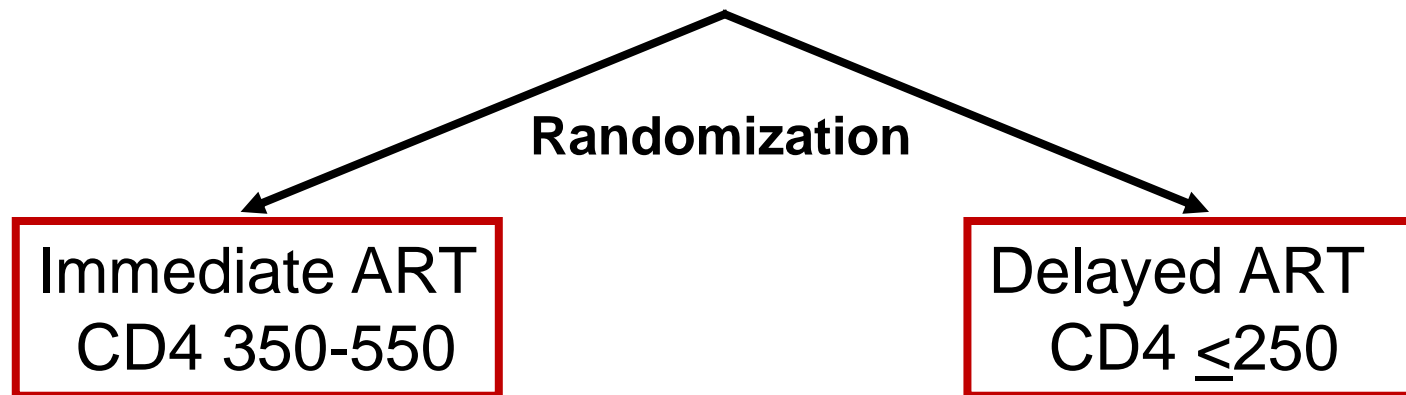
**M Cohen, Y Chen, M McCauley, T Gamble, R Bollinger,  
Y Bryson, D Burns, D Celentano, S Chariyalertsak,  
F Conradie, L Cottle, G De Bruyn, V Elharrar, S Eshleman,  
M Essex, E Filho, S Godbole, B Grinsztejn, J Hakim,  
I Hoffman, M Hosseinipour, N Kumarasamy, J Kumwenda,  
J Makhema, A Martinez, K Mayer, S Mehendale, L Mills,  
K Nielsen, J Pilotto, E Piwowar-Manning, I Sanne, B Santos,  
T Taha, L Wang, S Safren, T Fleming,  
and the HPTN 052 Protocol Team**



# HPTN 052 Study Design

---

Stable, healthy, serodiscordant couples, sexually active  
CD4 count: 350 to 550 cells/mm<sup>3</sup>

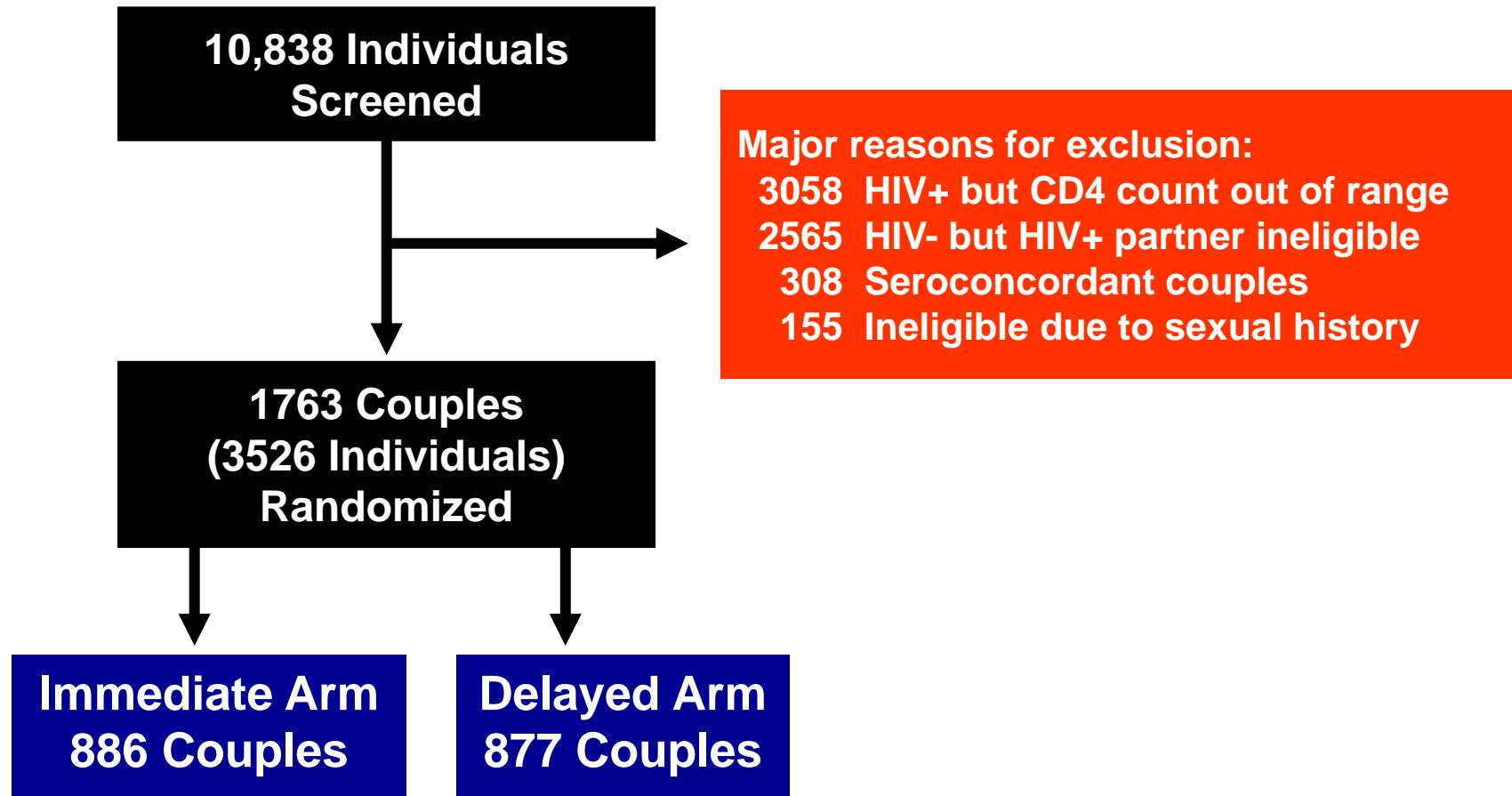


**Primary Transmission Endpoint**  
Virologically-linked transmission events

**Primary Clinical Endpoint**  
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

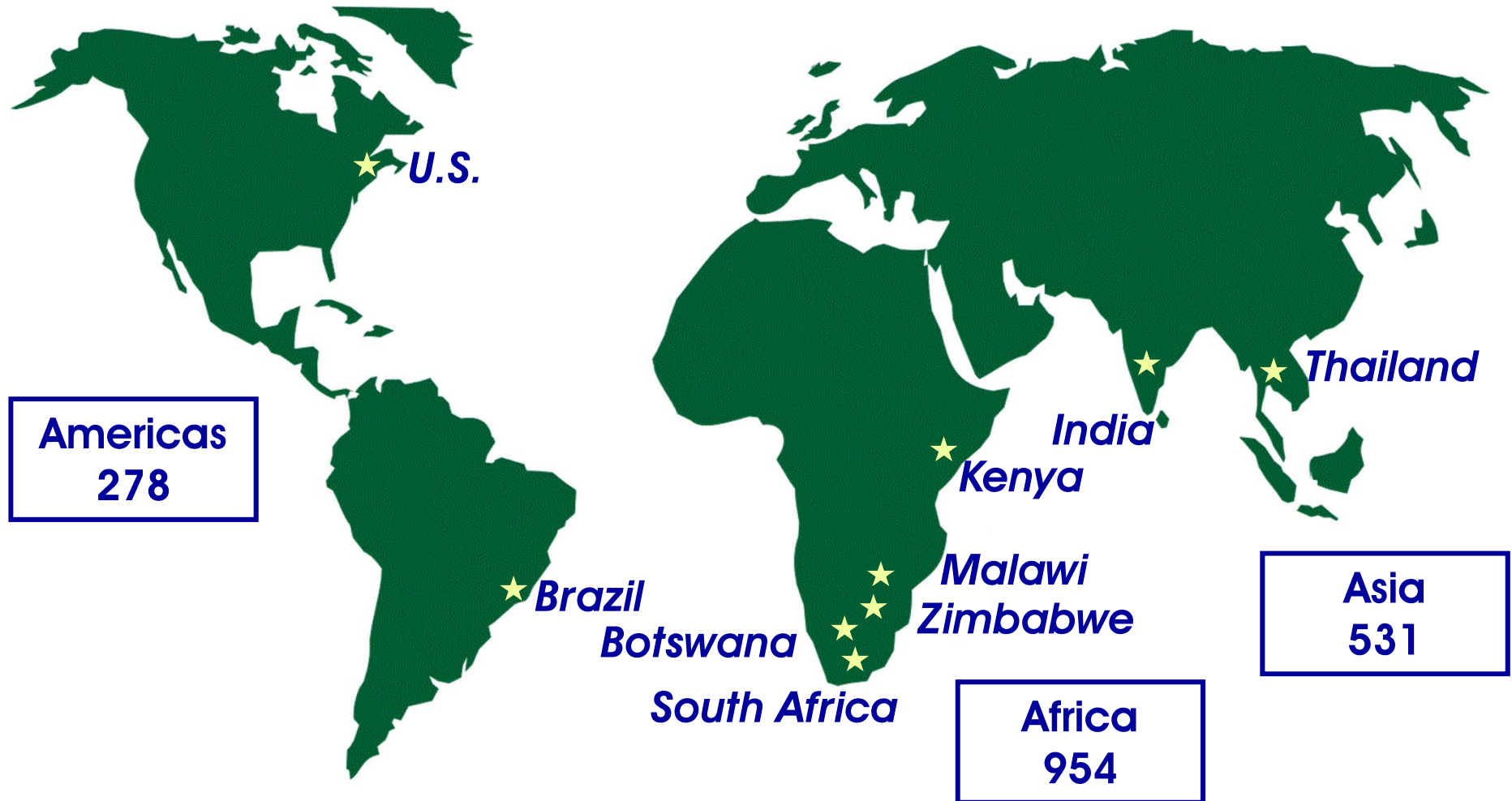
# HPTN 052 Enrollment

---



# HPTN 052 Enrollment

(Total Enrollment: 1763 couples)





# HPTN 052 Enrollment

Region	Site	Couples
Americas (278)	Porto Alegre, Brazil	90
	Rio de Janeiro, Brazil	186
	Boston, United States	2
Asia (531)	Chennai, India	250
	Pune, India	175
	Chiang Mai, Thailand	106
Africa (954)	Gaborone, Botswana	77
	Kisumu, Kenya	60
	Blantyre, Malawi	230
	Lilongwe, Malawi	251
	Johannesburg, South Africa	46
	Soweto, South Africa	50
	Harare, Zimbabwe	240
	Total	1763

# HPTN 052: Baseline Characteristics

	Index		Partner	
	Immediate N = 886	Delayed N = 877	Immediate N = 893	Delayed N = 882
<b>Female</b>	49%	50%	49%	47%
<b>Age (median)</b>	33	32	32	32
<b>Married</b>	94%	95%	93%	94%
<b>Any unprotected sex</b>	6%	8%	8%	8%
<b>CD4 (median [IQR])</b>	442 [373-522]	428 [357-522]	---	---
<b>HIV RNA log<sub>10</sub> (median [IQR])</b>	4.4 [3.8-4.9]	4.4 [3.9-4.9]	---	---

# HPTN 052: Baseline Characteristics

	Index		Partner	
	Immediate N = 886	Delayed N = 877	Immediate N = 893	Delayed N = 882
<b>Female</b>	49%	50%	49%	47%
<b>Age (median)</b>	33	32	32	32
<b>Married</b>	94%	95%	93%	94%
<b>Any unprotected sex</b>	6%	8%	8%	8%
<b>CD4 (median [IQR])</b>	442 [373-522]	428 [357-522]	---	---
<b>HIV RNA log<sub>10</sub> (median [IQR])</b>	4.4 [3.8-4.9]	4.4 [3.9-4.9]	---	---

# **DSMB Recommendation**

**April 28, 2011**

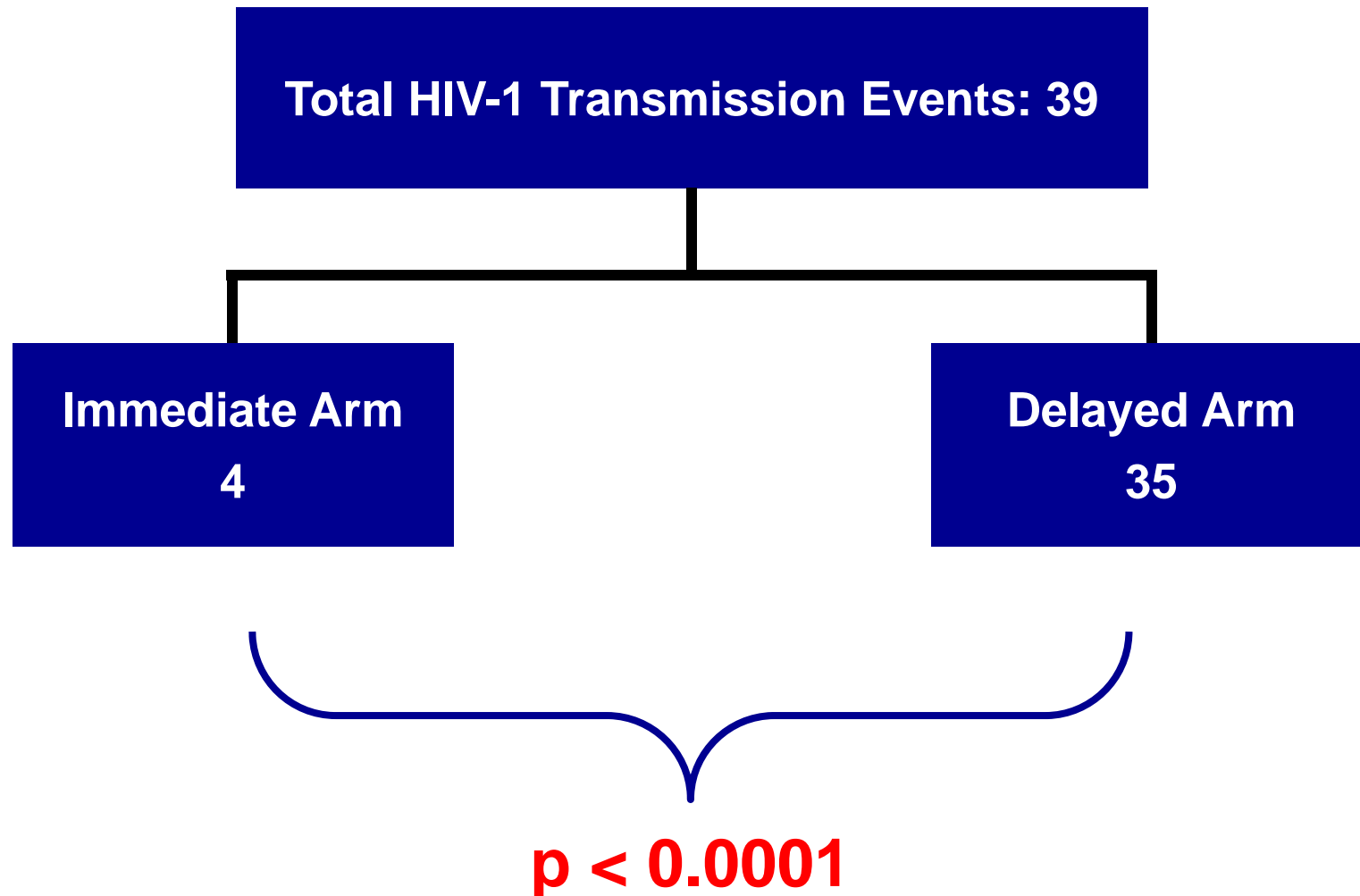
---

**“The Board recommends that the results of the trial be announced as soon as possible”**

**HPTN 052 continues to follow couples, but all HIV-infected participants are being offered ART**

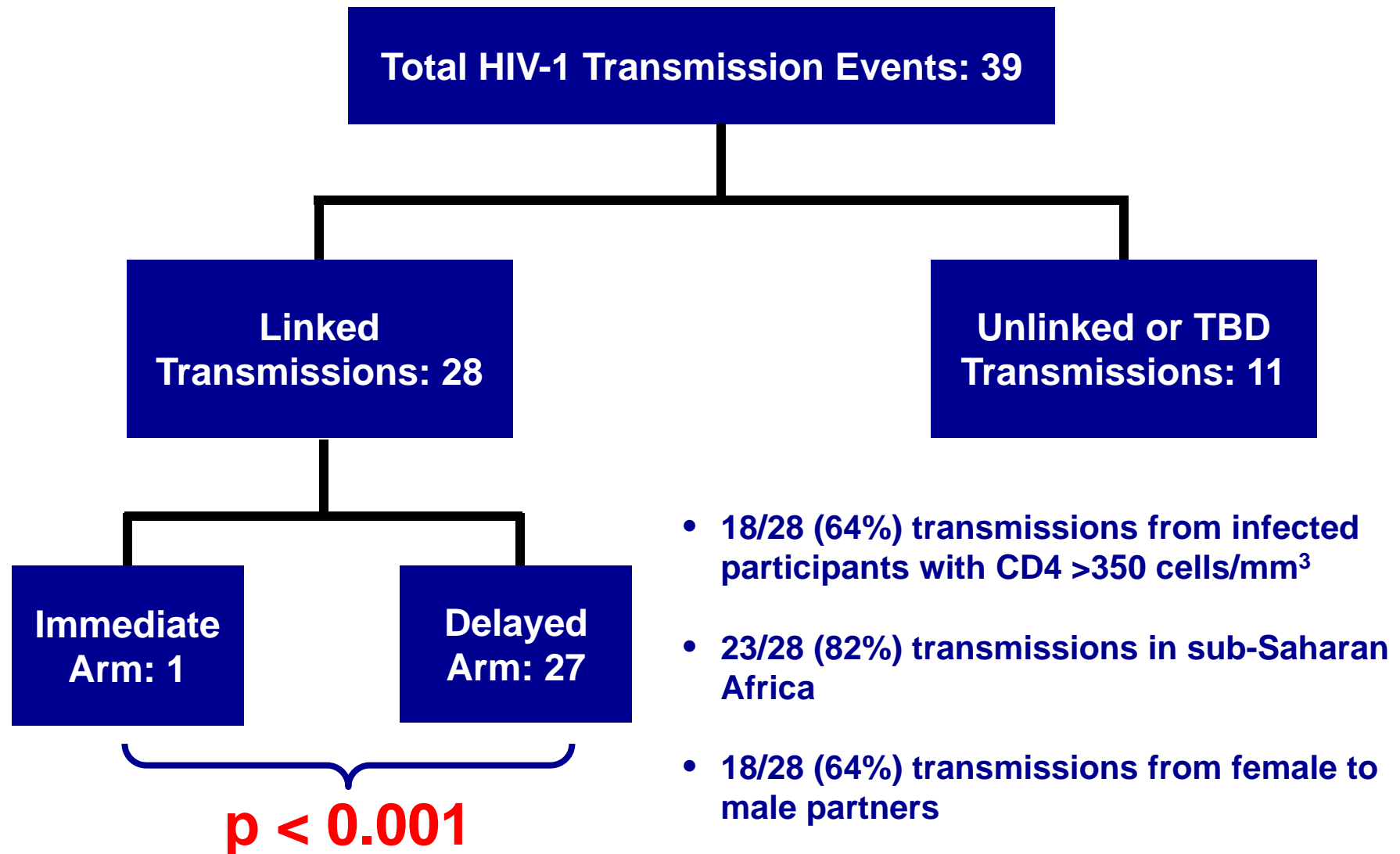
# HPTN 052: HIV-1 Transmission

---



# HPTN 052: HIV-1 Transmission

---



# HPTN 052: HIV-1 Transmission

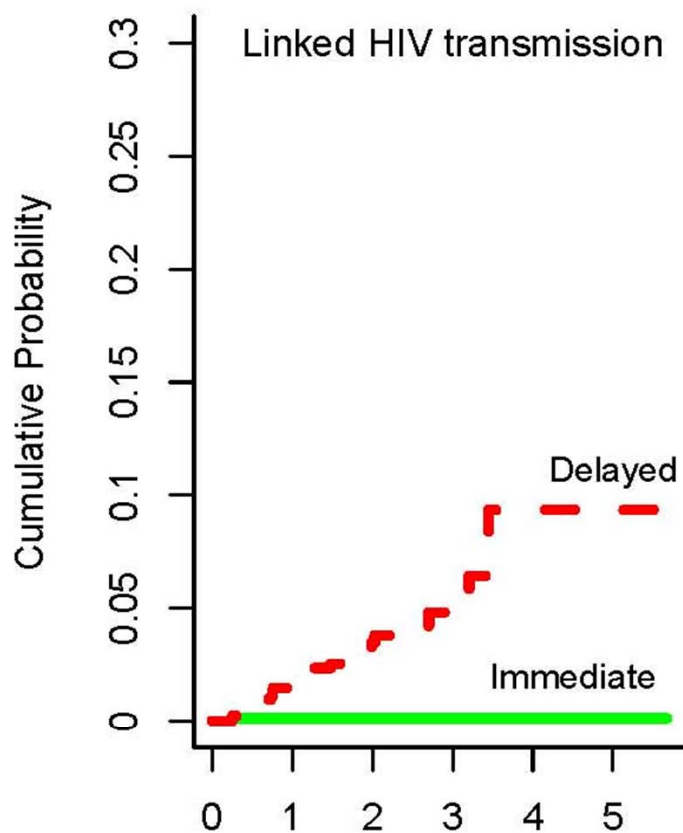
---

Study Arm	Follow-up (PY)*	Incidence/100PY [95% CI]	
		Linked	Overall
Immediate	1585	0.1 [0.0 – 0.4]	0.3 [0.1 – 0.6]
Delayed	1567	1.7 [1.1 – 2.5]	2.2 [1.6 – 3.1]

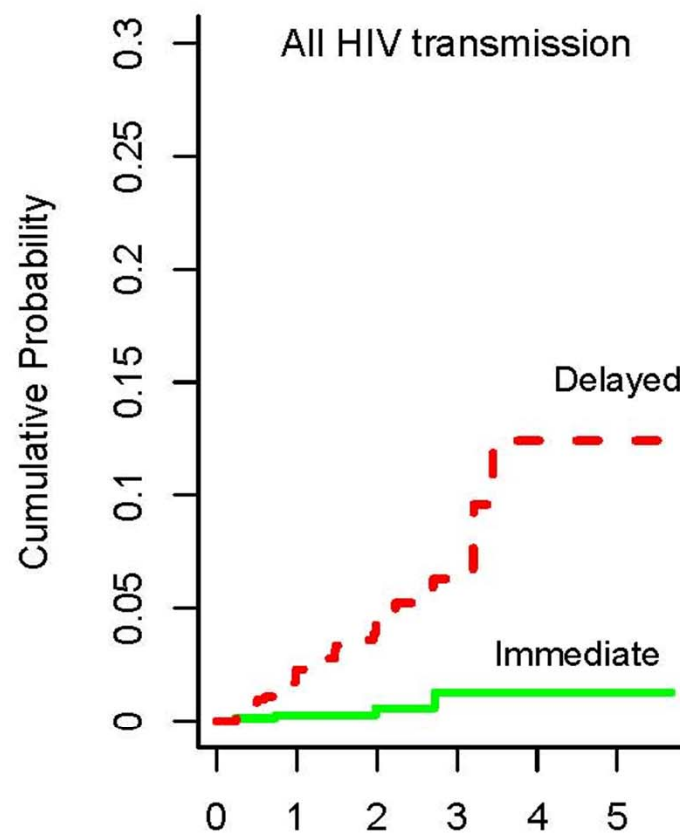
\*Person-years specific for transmission events

Median follow-up: 1.7 years

# HPTN052: HIV-1 Transmissions



No. at Risk		Years since Randomization					
		0	1	2	3	4	5
Immediate	893	658	298	79	31	24	
Delayed	882	655	297	80	26	22	



No. at Risk		Years since Randomization					
		0	1	2	3	4	5
Immediate	893	658	298	79	31	24	
Delayed	882	655	297	80	26	22	



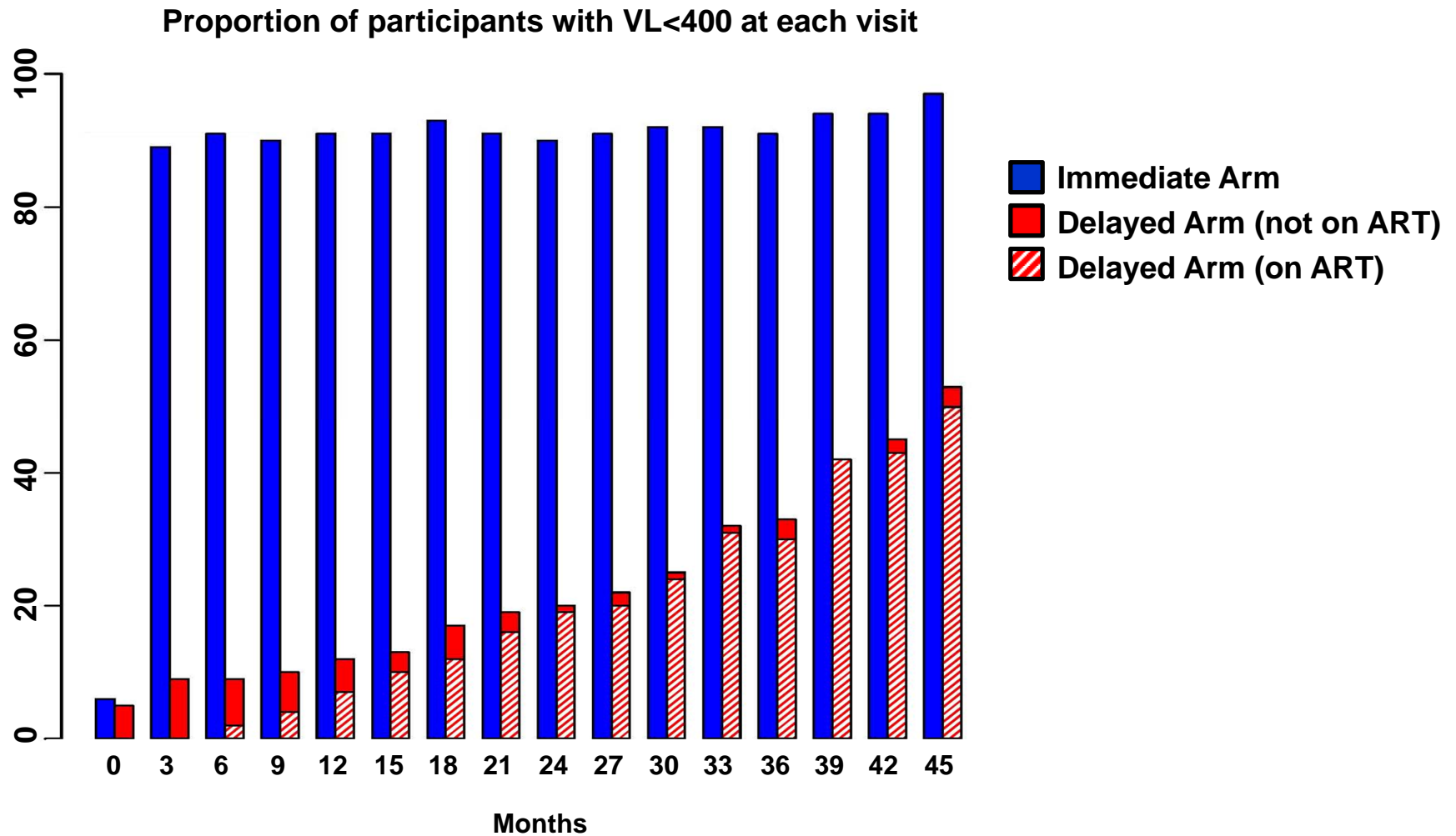
# Sexual Behaviors: Baseline and Follow-up

		Immediate (N=886)		Delayed (N=876)	
		Enrollment	Follow-up	Enrollment	Follow-up
Index pregnancy		63	47	59	79
STDs*	Index	1% - 5%	0% - 3%	1% - 5%	0% - 3%
	Partner	1% - 3%	0% - 2%	1% - 2%	0% - 4%
Sexual activity**	Index	72%	62% - 74%	74%	53% - 70%
	Partner	72%	67% - 81%	73%	62% - 76%
Condom use**	Index	94%	92% - 97%	92%	92% - 100%
	Partner	92%	90% - 100%	92%	92% - 100%

\*STDs include hepatitis B, syphilis, gonorrhea, and *C. trachomatis*

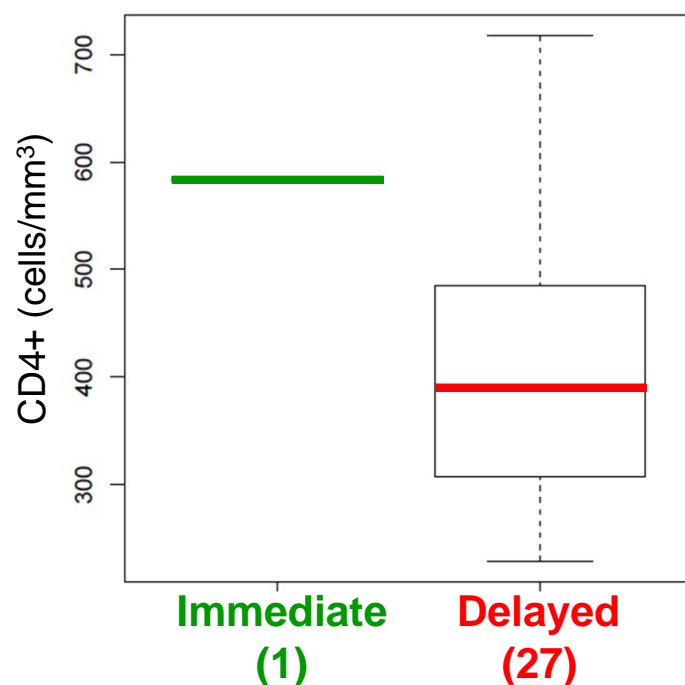
\*\*Self-reported data

# HPTN 052: Effect of ART

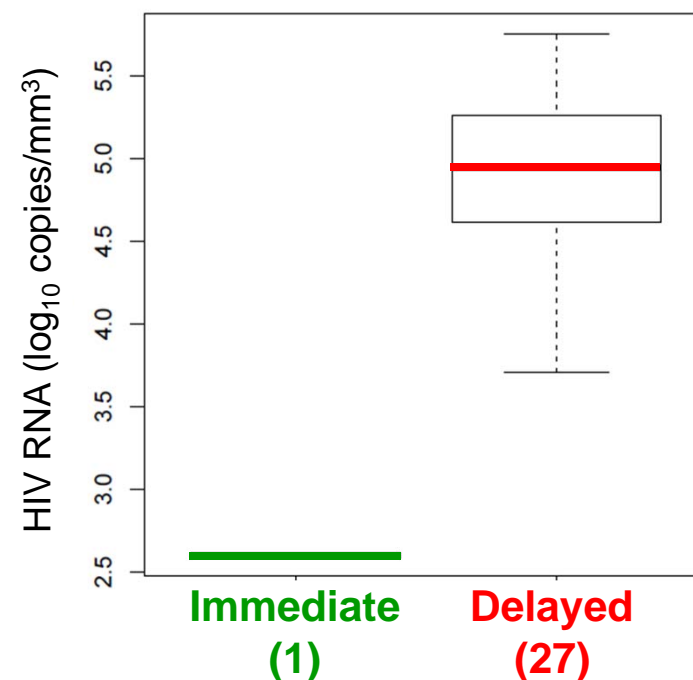


# HIV Transmission: CD4 Count and HIV-1 RNA

## 28 Linked Transmissions

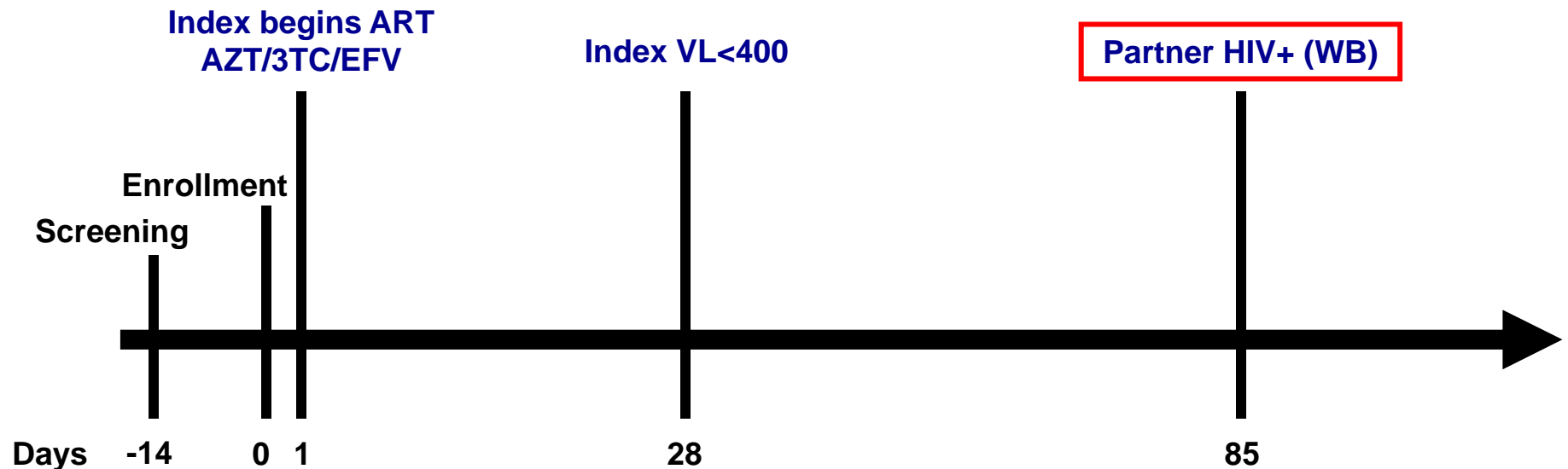


Median proximal CD4 (range): 400 (229-858)  
Immediate arm: 584 (584-584)  
Delayed arm: 391 (229-858)



Median proximal log<sub>10</sub> VL (range): 4.9 (2.6-5.8)  
Immediate arm: 2.6 (2.6-2.6)  
Delayed arm: 4.9 (2.6-5.8)

# One Transmission Event on ART



Partner VL < 400  
Index CD4 = 482  
Index VL = 87,202

Single Genome Analysis: 1-2 viruses transmitted

Analysis of Transmission: >50 days earlier (84 – 190 days)

# Multivariate Analysis – Linked Transmission

---

Variable	Hazard Ratio	95% Confidence Interval
<b>Treatment</b> (immediate vs. delayed)	0.04	[0.01 - 0.28]
<b>Baseline CD4</b> (per 100 CD4 Increment)	1.24	[1.00 - 1.54]
<b>Baseline VL</b> (per unit log increment)	2.84	[1.51 - 5.41]
<b>Baseline condom use</b> (100% vs. <100%)	0.33	[0.12 - 0.91]
<b>Gender (HIV +)</b> (male vs. female)	0.73	[0.33 - 1.65]



## **HPTN 052 Prevention Conclusion**

---

**Early ART that suppresses viral replication led  
to 96% reduction of sexual transmission of  
HIV-1 in serodiscordant couples**

***THANK YOU!***