

Immunologic and Virologic Disease Progression and Response to ART Across Geographic Regions: Outcomes from HPTN 052

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Abstract Authors

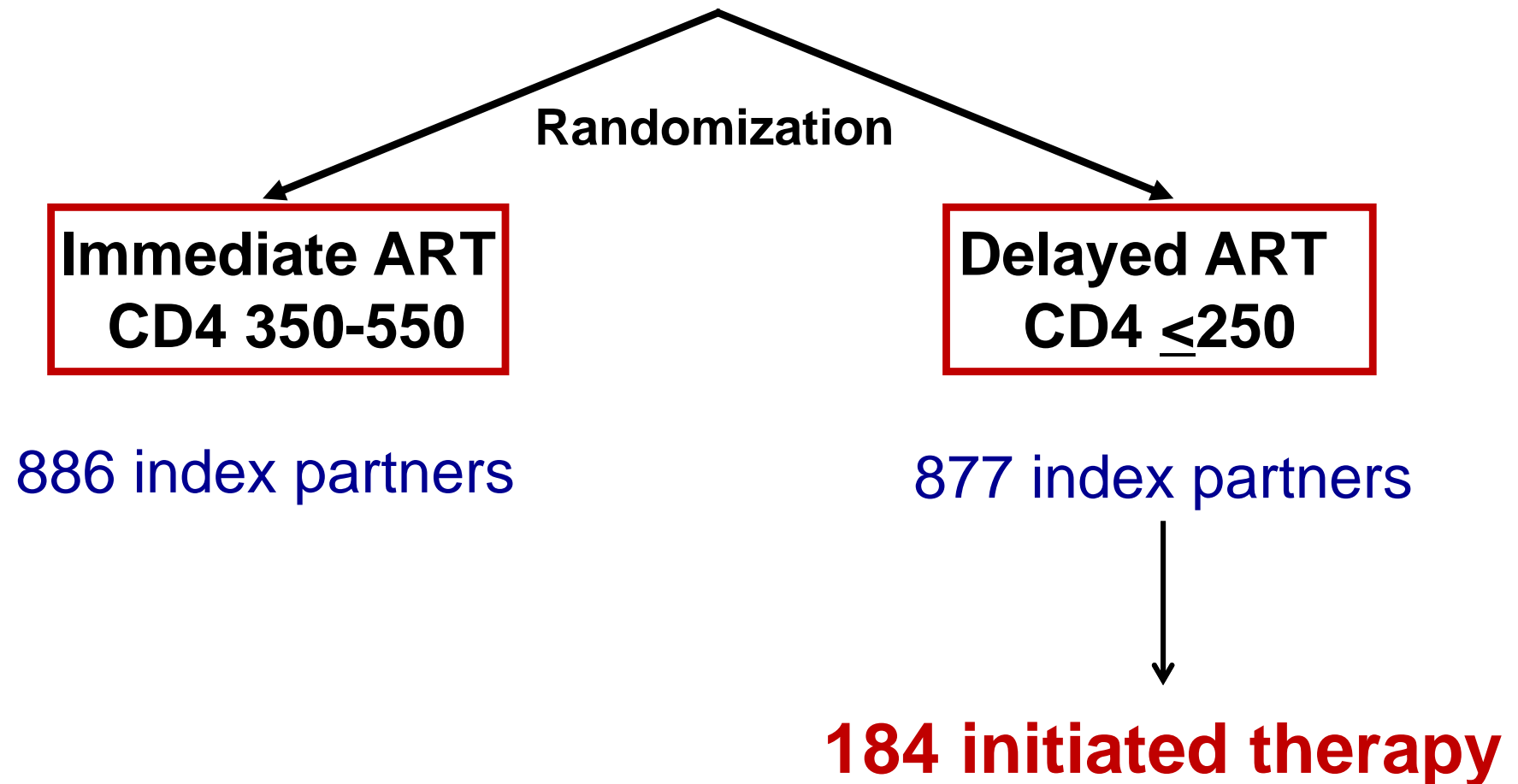
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and the HPTN 052 study team**

Outline

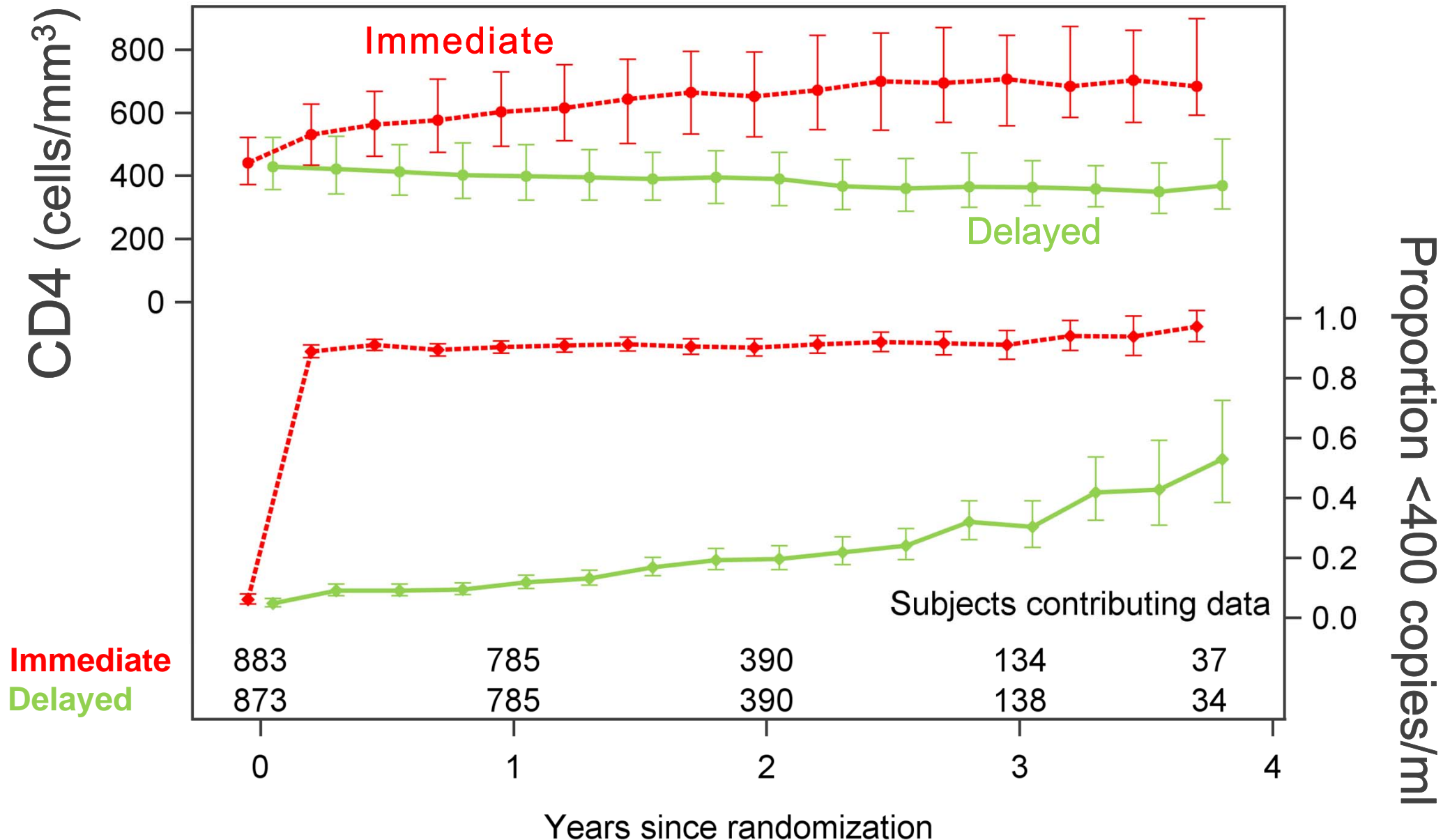
- Review HIV disease progression of the HIV infected index participant
 - HIV-1 RNA and CD4 changes over time
 - ART initiation
 - Treatment response
- Explore differences in baseline, behavioral and disease progression characteristics across regions that may explain observed differences in the number of transmissions between participants enrolled at African versus non-African sites

HPTN 052 Study Design

HIV-infected subjects with CD4 350 to 550 cells/mm³
Serodiscordant couples

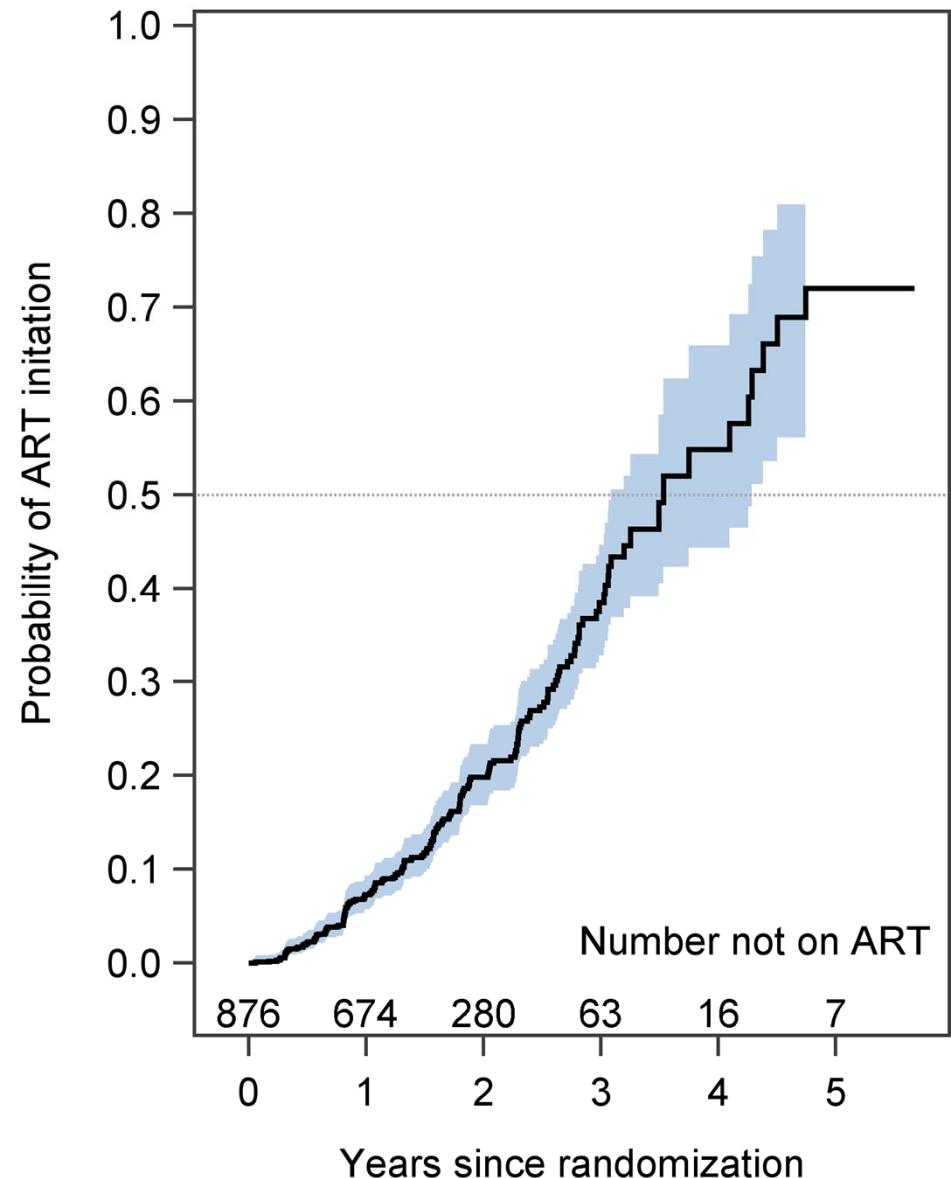


HIV-1 RNA and CD4 Over Time (ITT)



Time to ART Initiation (Delayed Arm)

- 21% initiated therapy
 - Mostly (75%) triggered by a decline in CD4 count
- Median time to initiation was 3.5 years
- Median CD4 at initiation was 225 cells/mm³
 - Q1–Q3: 199 – 247



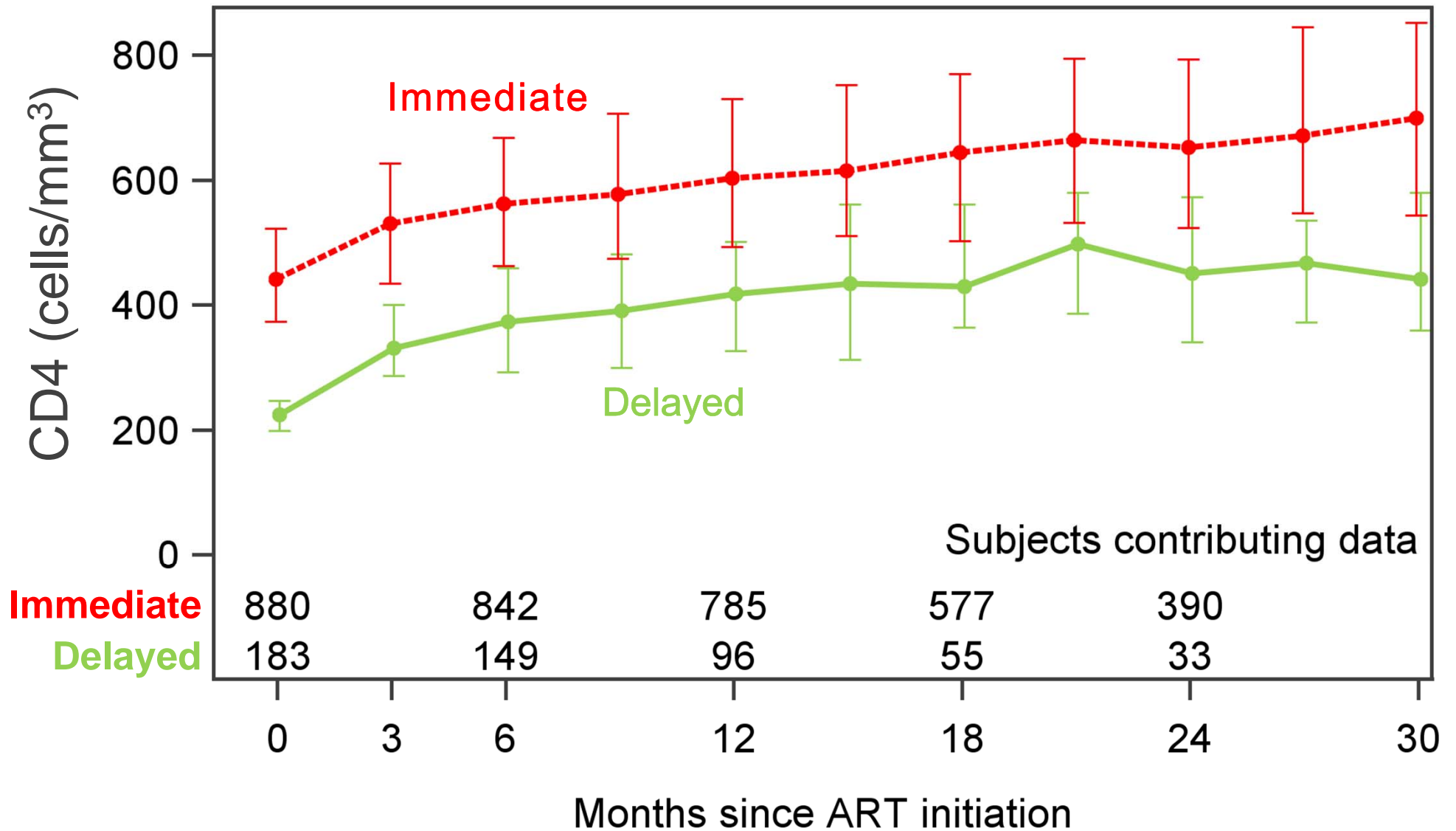
Factors Associated with ART Initiation (Delayed Arm)

	Univariate		Multivariate	
	HR (95% CI)	p	HR (95% CI)	p
Baseline CD4 (per 100 cells/mm ³)	0.6 (0.5, 0.7)	<.0001	0.6 (0.5, 0.7)	<.0001
Baseline HIV-1 RNA (per log ₁₀ copies/ml)	1.7 (1.4, 2.1)	<.0001	1.5 (1.2,1.8)	0.0003
Index gender (male vs. female)	1.3 (0.9,1.8)	0.63	1.2 (0.8,1.5)	0.6

ART Regimens

	Immediate Arm	Delayed Arm
N initiating ART	886	184
(AZT/3TC)/EFV	72%	70%
(AZT/3TC)/ATV	10%	7%
(FTC/TDF)/EFV	9%	11%
(AZT/3TC)/(LPV/RTV)	7%	2%
Other	2%	10%

CD4 Trends Post ART Initiation



Virologic Failure and Second Line ART

	Immediate Arm	Delayed Arm
Enrolled	886	877
Initiated primary regimen	886	184
Experienced virologic failure	5.1%	2.7%
Initiated secondary regimen	67%	60%

Brief Summary So Far

- ART response in the immediate arm was rapid and robust
- In the delayed arm ART was initiated in a minority of participants and was significantly associated with baseline CD4 and viral load
- Virologic failure was uncommon in either arm
- The magnitude of CD4 responses were similar but the absolute CD4 levels achieved were lower in the delayed arm

Regional Analysis

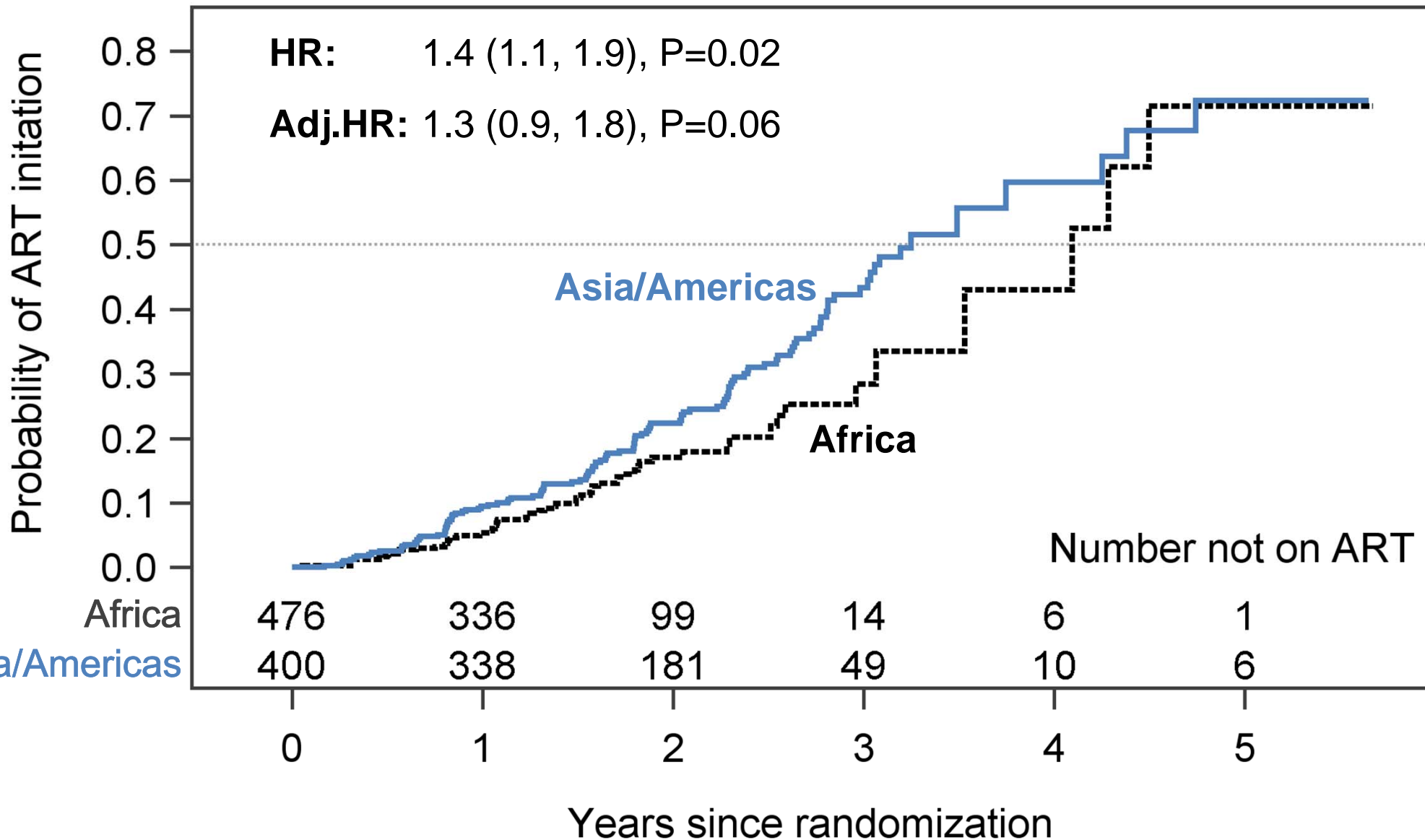
- Regional variance in transmission was apparent
 - 23/28 (82%) linked and 32/39 (82%) unlinked transmissions in sub-Saharan Africa
 - 54% enrollment at African sites
- Differences in baseline HIV RNA and CD4, HIV subtype, adherence and response to ART, sexual behavior on study and/or differential timing of ART initiation in the delayed arm may contribute to these differences
 - Baseline characteristics compared using Wilcoxon rank sum and chi-square tests
 - Time to event outcomes compared using Cox proportional hazards

Baseline Characteristics by Region

	Africa (N=954)	Asia/Americas (N=807)	P
Demographic			
Female sex	58%	40%	<0.0001
Age group			
18-25	20%	15%	0.003
26-40	59%	67%	
>40	21%	19%	
Clinical			
CD4 cell count (/mm ³)	436 (361, 526)*	448 (370, 518)*	0.95
HIV-1 RNA (log ₁₀ copies/ml)	4.4 (3.8, 4.9)*	4.5 (3.9, 5.0)*	0.006
Behavioral			
Unprotected sex last week	9%	4%	0.0007
3+ sex acts last week	29%	18%	<0.0001

*Median (Q1 – Q3)

Time to ART Initiation by Region



Viral Suppression

- Immediate arm: After one year, 90% of total had viral suppression
 - 90% non-Africa
 - 91% Africa
- Delayed arm: After one year, 93% of total had viral suppression.
 - 96% from non-Africa region
 - 85% from Africa

Adherence According to Region

	Africa	Non-Africa
N on ART	615	533
N with evaluable adherence	582	517
Adherence \geq 75%	95%	96%
Adherence $>$ 95%	74%	82%
Mean (SD) adherence (%)	95 (12)	95 (15)
Median adherence (%)	99	99

Conclusions

- **High rates of virologic suppression and CD4 increase for persons on ART (both arms)**
- **Lower absolute CD4 one year post-ART initiation in subjects with delayed ART (ongoing clinical risk)**
- **Regional differences seen in baseline characteristics, sexual behavior, and progression to ART initiation (may help explain regional variation in HIV transmission)**

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