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BACKGROUND

- Initiation of antiretrovirals (ART) during acute HIV infection reduces viral reservoirs and improves long term virologic control. There is, however, limited data in youth.
- Youth are likely to have a better response to ART than adults as they still have a functioning thymus.
- Early treatment initiation decreases viral reservoir size. The earlier the treatment, less likely the virus is to seed HIV reservoirs, enabling improved immune reconstitution and potentially favoring future strategies for viral control/ eradication.
- ATN 147 Hypothesis:** HIV reservoir decay is greater in youth initiating ART during acute infection (A) as compared to youth initiating treatment during non-acute infection (NA).
- ATN 147 was a longitudinal cohort study which identified ART naïve youth living with HIV between 12-24 years of age at the time of diagnosis, initiating ART at study enrollment with follow-up for 24 months.

METHODS

- Youth at risk for HIV were screened using point of care assays such as GeneXpert, antigen/antibody rapid assays and RNA PCR in Los Angeles (LA) and New Orleans (NO).
- Upon HIV diagnosis, youth were offered study enrollment. Standard of care ART were initiated usually with an INTSI and 2 backbone ARTs. Patients were followed at close intervals in the first 2 months and at 4, 8, 12, 18, 24 months with HIV RNA in plasma measured, and quantification of cell-associated HIV DNA in 10⁶ PBMC assayed by quantitative ddPCR at baseline (BL), 4, 12, 24 months. WB was performed at BL, 12, 24 mos.
- Acute infection (A) was defined as a Fiebig Stage I-V on HIV Western Blot (WB) at baseline. A Fiebig Stage of VI (p31 band present) defined non-acute (NA) infection.



Fiebig stage	Cumulative duration (days)	HIV RNA	p24 antigen	Immunoassay	Western blot
1	5	+	-	-	-
2	10	+	+	-	-
3	14	+	+	+	-
4	19	+	+/-	+	Indeterminate
5	88	+	+/-	+	+ (p31 band negative)
6	Open-ended	+	+/-	+	+ (p31 band positive)

ART-naïve youth with either Acute (A) or Non-acute (NA) HIV at the time of ART initiation, who subsequently achieved HIV VS, similarly attained significant reduction in HIV DNA levels by ddPCR from BL to 4, 12, and 24 mo. By 2 years of ART initiation, 34% had waning HIV ab, predominantly seen in A youth, OR = 15.

RESULTS

- 103 youth enrolled between 7/2017 to 7/2021 (Fig 1), with mean age of 20.8 years (range 16-24).
- 51 participants enrolled in LA/ 52 in NO; 90% identified as cis-male & MSM or bisexual; 31 (30%) were recruited from a high-risk HIV seronegative cohort partner study (ATN 149) upon HIV diagnosis.
- 35% of participants (n=36) had Acute infection (A) and 65% (n=67) NA infection at BL. HIV RNA levels were significantly higher in A than NA infections at BL (Fig 2).

Fig 1 ATN 147: Enrollments over time

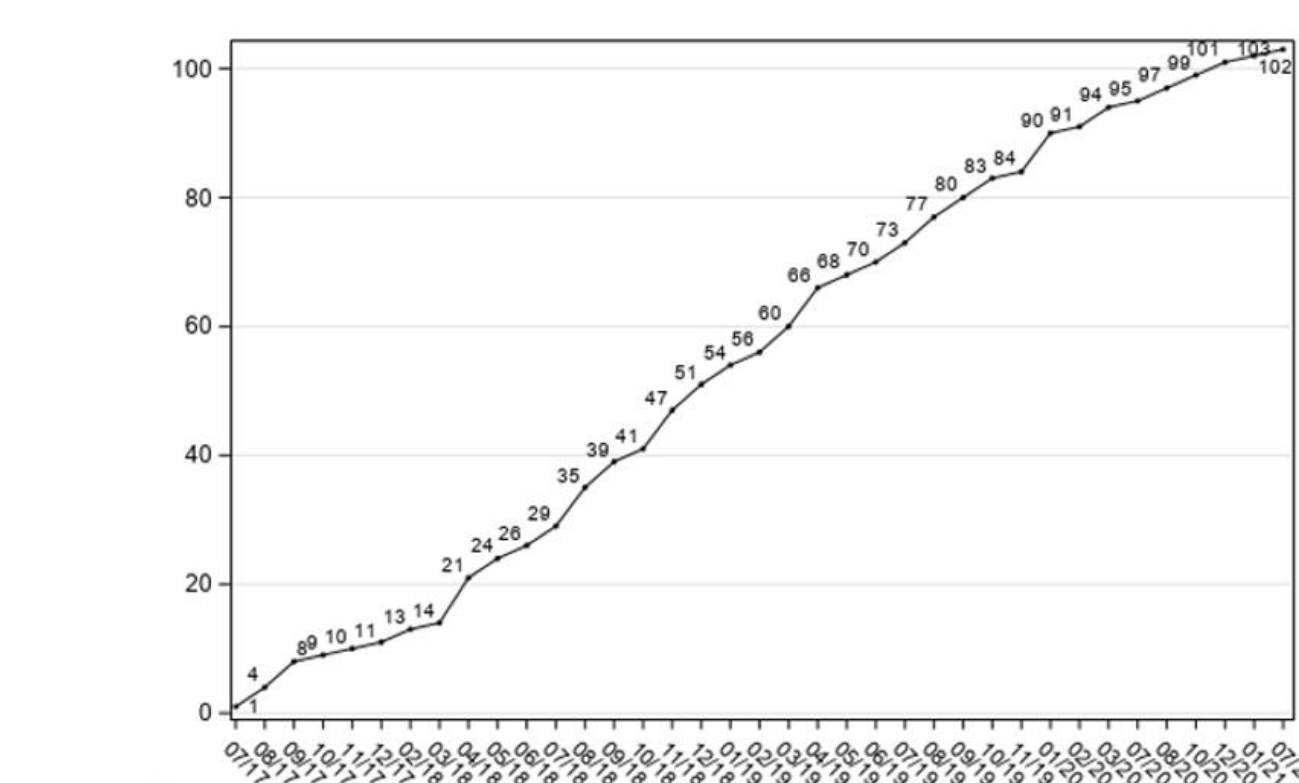
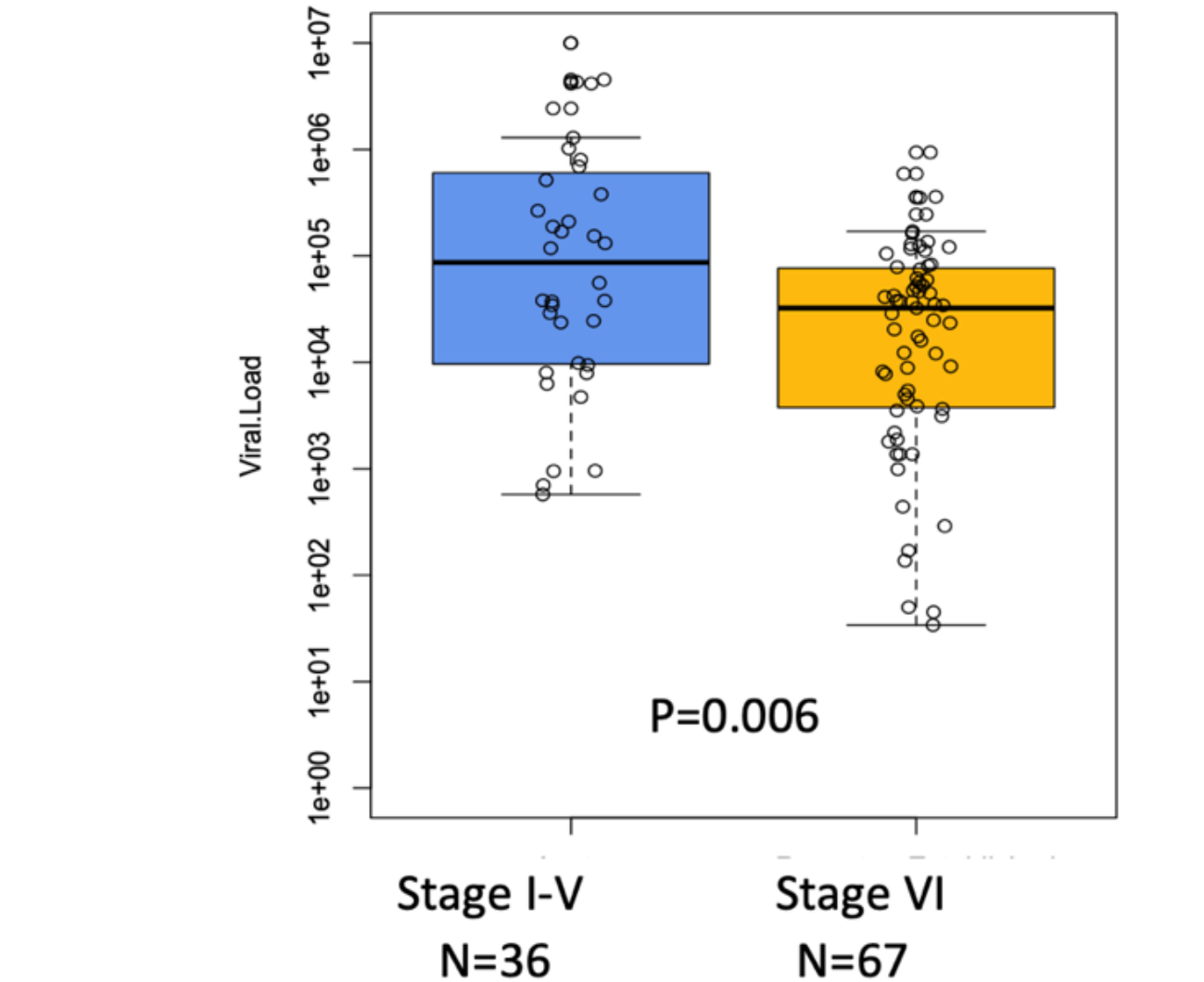


Fig 2

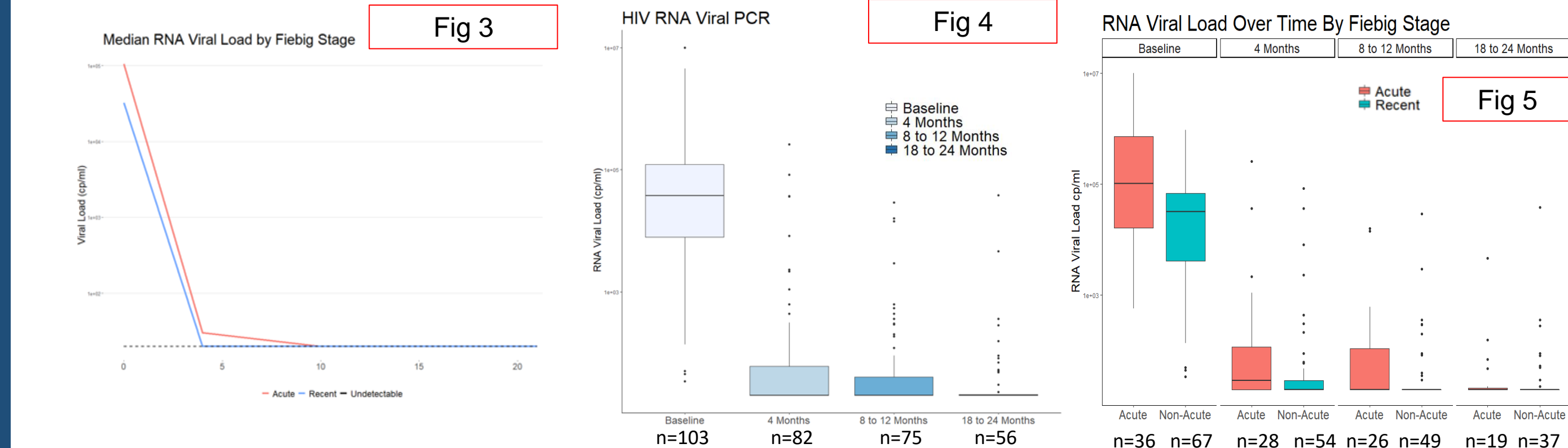


- 63% of the cohort had a concurrent STI at enrollment.
- Nearly ¼ of the cohort (n=25) reported ever being homeless. (Table 1)
- 40% of youth reported symptoms consistent with acute HIV infection; 27% had acute retroviral symptoms at enrollment. (Table 1)
- 75% of the cohort qualified for some type of government-assisted insurance. (Table 1)
- ART were started within a week of enrollment in 88% of the cohort; 78% within 48 hours. (Table 1)

	median	IQR
RNA Viral Load (copies/ml)	37313	(5849-126162)
CD4 count (N=100)	445.5	(357-613)
Age	N	%
Average (sd)	20.8	2.3
16-18 years	21	20.4%
19-21 years	39	37.9%
22-24 years	43	41.7%
Co-infection STI at baseline		
Yes	56	54.3%
RACE/Ethnicity		
Black or African American	62	60.2%
Asian/Native American/Alaska Native/Pacific Islander	7	6.8%
Latino	26	25.2%
White	8	7.8%
Gender Identifying		
Cis-male	93	90.3%
Cis-female	2	1.9%
Trans-Female	5	4.9%
Gender nonconforming	3	2.9%
Sexual Orientation		
Gay/Same gender	74	71.8%
Bisexual	5	4.9%
Other	19	18.4%
Other	5	4.9%
Housing		
Recently Homeless	11	10.7%
Ever Homeless	25	24.3%
Relationship		
Monogamous	12	11.7%
Single or One of more Casual Relationships	86	83.5%
Other/ Did not Answer	5	4.9%
Employment		
Student	30	29.1%
Full/Part/Self employed	51	49.5%
Unemployed	18	17.5%
Did not answer	4	3.9%
Education		
Below high school	17	16.5%
High school diploma/Equivalent	26	25.2%
Some higher education	54	52.4%
Completed higher education	4	3.9%
Missing	2	1.9%
Site		
Los Angeles	51	49.5%
New Orleans	52	50.5%
Symptoms at Enrollment		
Before	13	12.6%
At Enrollment	28	27.2%
None reported	62	60.2%
Insurance		
Private	18	17.5%
Medical, Medicare, ADAP or other assistance	77	74.8%
Other or Unknown	8	7.8%
ART start date		
within 24 hours of enrollment	70	68.0%
within 48 hours of enrollment	10	9.7%
within one week of enrollment	10	9.7%
more than one week unknown	13	12.6%

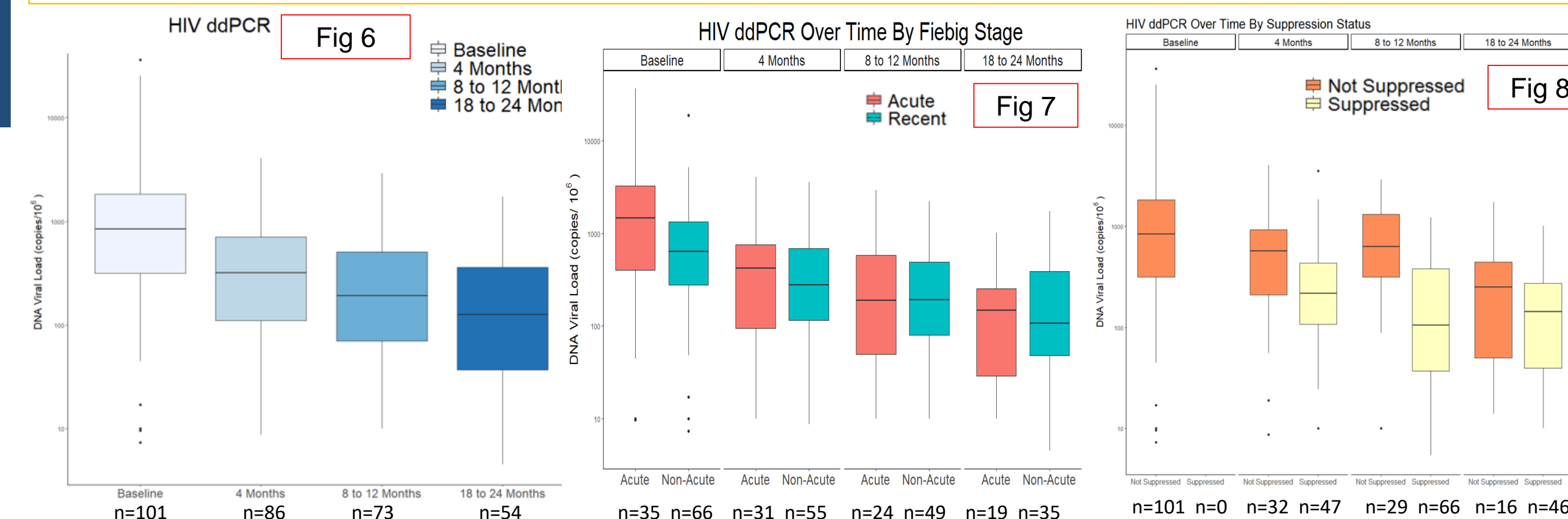
HIV RNA:

- Median BL RNA VL was 104,650 cps/ml (A) vs. 32,334 cps/ml (NA), p < 0.01 (Fig. 2).
- At 4 months of F/up, median VL was 30 cps/ml (A) vs. 20 cps/ml (NA), p = 0.815. (Fig. 3)
- By 12 & 24 mo., both A and NA had median VL of 20 cps/ml.
- At 4, 8 to 12, and 18 to 24 months of F/up, 61%, 68%, and 72% of youth achieved virologic suppression (VS). (Fig 4, 5)



HIV DNA:

- Median ddPCR copies/million PBMCs for the cohort at BL, 4, 12, and 24 mo. were 844, 320,192, 127, p < 0.001. (Fig 6)
- A vs. NA youth: BL, 4, 12, 24 mo. ddPCR values were 1448 vs. 633, 422 vs. 227, 188 vs. 192, 148 vs. 106, p=0.66. (Fig 7)
- VS vs. non-VS youth: Median dd PCR at 12 mo. was 115 in VS vs. 485 in non-VS youth, p<0.001; at 24 mo. 107 (VS) vs. 202 (non-VS), p < 0.001. (Fig 8)



CD4 cell counts: Median increase in CD4 cell count from BL (447 cells) to 24 months (653 cells) was significant, p = 0.0157 (Fig 9). Differences in median CD4 counts between A vs. NA and VS vs. NVS were not significant

Negative/indeterminate WB: was associated with A status at 12 & 24 mo: **OR 14.8; 95% CI: 4.76-45.93, p < 0.001** and was not associated with VL suppression at 12 & 24 mo. **OR 3.13; 95% CI: 0.94-10.37, p = 0.062**

	B/L (n=103)	12mo (n=72)	24mo (n=45)
Positive	84 81%	49 68%	38 67%
Indeterminate	14 14%	19 26%	14 25%
Negative	5 5%	4 6%	5 9%

CONCLUSIONS

- Early ART induced sustained VS in 72% of youth by 24 months.
- HIV RNA & DNA decline was not associated with A vs NA status.
- HIV RNA VS was associated w/ DNA reservoir decline over time.
- A youth were more likely than NA youth to lose HIV AB on WB.

