Supplemental File 1. Evaluation of the timing of viral load measurements in the first year after ART initiation.

The HPTN 052 trial opened in 2005 with a pilot phase (2005-2007); the full study enrollment period was from 2007 to 2010. The pilot phase included quarterly viral load testing. In November 2006, when the study was still in the pilot phase, an additional study visit with viral load testing was added 1 month after ART initiation. A window of 14 days (+/-) was permitted for visit scheduling. Throughout the trial, site investigators were permitted to order additional testing that they felt was important for patient care.

In this report, viral suppression was defined as occurring on the first of two successive viral loads <400 copies/mL after ART initiation. Time to viral suppression was analyzed in three participant groups: (1) participants in the early ART arm; (2) participants in the delayed ART arm who initiated ART before May 2011; and (3) participants in the delayed ART arm who initiated ART after May 2011. These data are shown in Figure 2A. This plot shows that participants achieved viral suppression ~2 months after ART initiation (between the scheduled 1- and 3-month study visits). Furthermore, the portion of participants who achieved viral suppression between 1 and 3 months after ART initiation appeared to differ in the three participant groups. Additional statistical analyses were performed to assess whether the timing of viral load measurements was significantly different in these three groups, and whether this could have introduced bias in the analysis of time to viral suppression.

To address this issue, we first compared the mean number of viral load measurements obtained during different time periods after ART initiation in the three participant groups (Table S1).

Table S1. Frequency of viral load testing

	Mean # viral load tests performed following ART initiation*		
Group (timing of ART initiation)	0-1 month after ART initiation	0-3 months after ART initiation	0-6 months after ART initiation
Early arm	1.74	2.77	3.75
Delayed arm, before May 2011	1.85	2.80	3.78
Delayed ART arm, after May 2011	1.86	2.81	3.83

*For this analysis, months after ART initiation were rounded to the nearest whole month.

These data show that participants in the three groups had similar mean numbers of viral load tests performed in each time interval. There was a slightly higher mean number of viral load tests completed by 1 month in the delayed arm groups (1.85, 1.86 vs. 1.74).

We next compared the number of participants in the three groups who achieved viral suppression during each 1-month interval after ART initiation (Table S2).

Table S2. Number of participants in each study group who achieved viral suppression during each month of follow-up after ART initiation.

	Months after ART initiation												
Group (timing of ART initiation)	0-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12+
Early arm	280	234	107	79	0	18	16	0	8	2	0	4	30
Delayed arm, before May 2011	38	56	40	21	15	15	1	2	3	0	1	2	4
Delayed ART arm, after May 2011	157	171	54	48	18	7	9	1	8	8	3	1	15

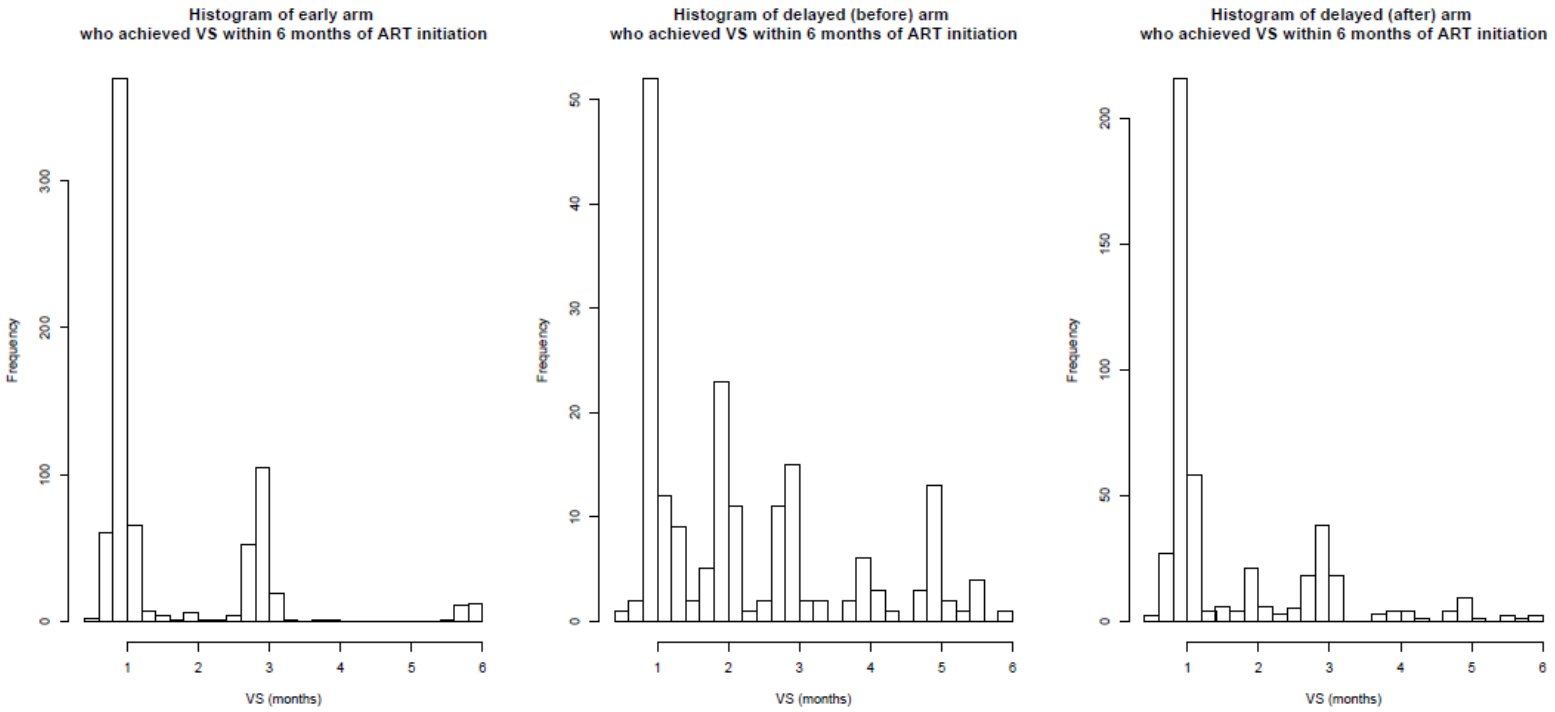
[1]The numbers indicate the range of months included in each category (e.g., 0-1 indicates ≥ 1 month and < 2 months).

The data shown in Table S2 show that a significant number of participants (N=461) achieved viral suppression between 1 and 3 calendar months after ART initiation. This reflects variability in the timing of the 1- and 3-month follow-up visits and/or inclusion of ad hoc study visits during this time interval.

We next compared the portion of participants who achieved viral suppression as a function of time during the first 6 months after ART initiation; this analysis included only data from participants who achieved viral suppression within 6 months of ART initiation.

Figure S1. Portion of participants in each study group who achieved viral suppression as a function of time after ART initiation.

Early arm | Delayed arm, before May 2011 | Delayed arm, after May 2011



The histograms in Figure S1 show some differences in the distribution of time to viral suppression in the three groups. The figure also highlights the variability in the timing of viral load measurements. Of note, a higher portion of participants in the two delayed arm groups achieved viral suppression between 1 and 3 months after ART initiation, and between 3 and 6 months after ART initiation, when there were no scheduled viral load measurements.

The variability in the timing of viral load measurements during the 6 months after ART initiation raised the possibility that there may have been ascertainment bias that could have impacted the analysis of time to viral suppression (i.e., variability in the timing of viral load measurements may have impacted the time when viral suppression was detected in different participant groups).

To address this, we analyzed data from two critical contiguous time intervals among participants who achieved viral suppression; these two time intervals cover the entire period from ART initiation to viral suppression.

1) Interval 1 (not suppressed, NS): Time between the study visit when ART was initiated to the last study visit before viral suppression was documented. Participants were not virally suppressed during this time interval.
2) Interval 2 (virally suppressed, VS): Time between the last study visit before viral suppression was achieved to the study visit where viral suppression was documented. Participants achieved viral suppression at some time during this time interval.

Table S3 shows the data, stratified by the three study groups.

Table S3. Mean and median time in each time interval.

Interval 1 (not suppressed):

	Early arm	Delayed arm, before May 2011	Delayed arm, after May 2011
Mean	1.37	1.27	1.37
Median	0	0.89	0

Interval 2 (virally suppressed):

	Early arm	Delayed arm, before May 2011	Delayed arm, after May 2011
Mean	1.41	1.57	1.38
Median	0.99	1.07	0.99

These data show that the mean and median time intervals (NS and VS) are similar for the three participant groups.

Figures S2-S4 show box plots of these data, stratified by the three study groups. Because the data were heavily skewed, both untransformed and log (time + 1) transformed data are shown for time Interval 1.

Figure S2. Untransformed data from individual participants for the time interval prior to viral suppression: Interval 1 (not suppressed)

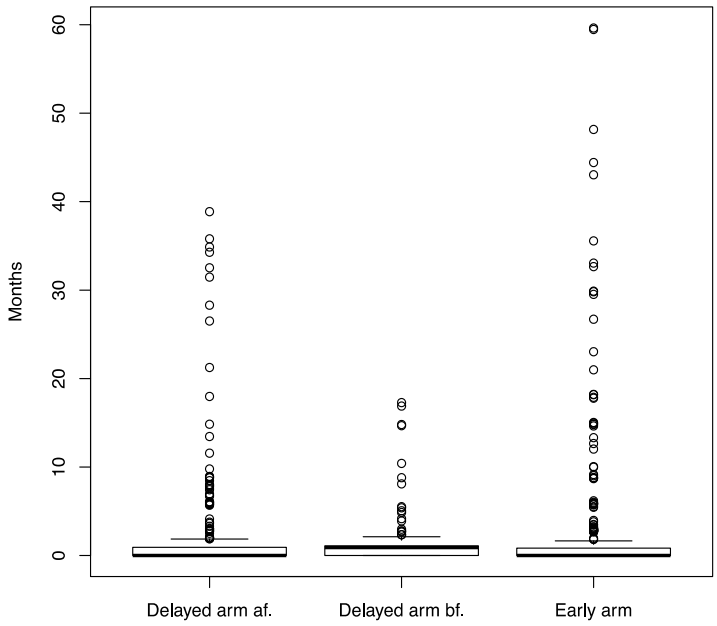


Figure S3. Log transformed data from individual participants for the time interval prior to viral suppression: Interval 1 (not suppressed)

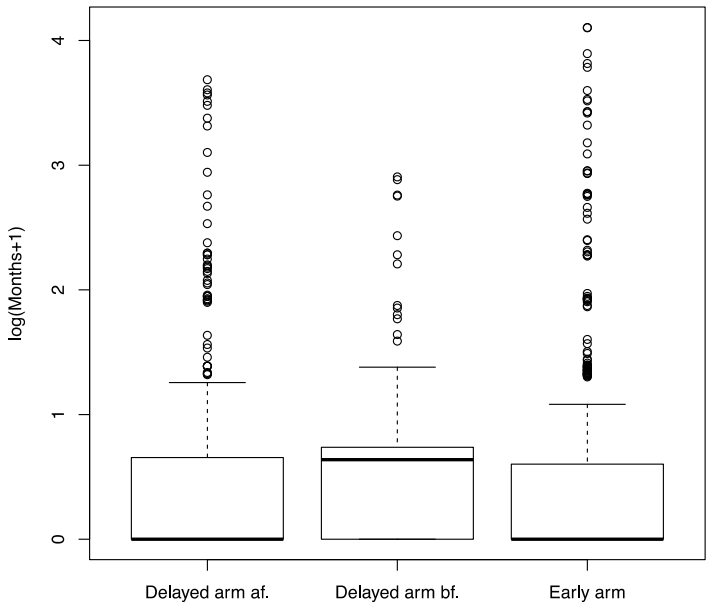
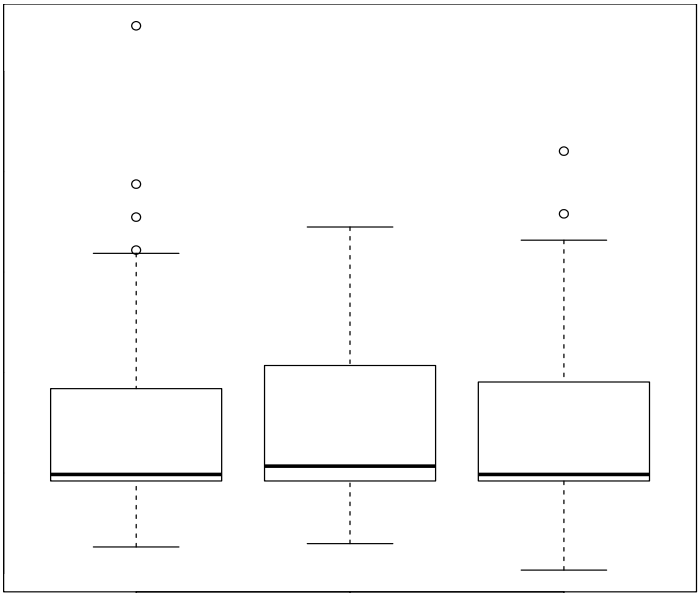


Figure S4. Untransformed data from individual participants for the time interval during which viral suppression was achieved: Interval 2 (virally suppressed)



The box plots in Figures S2-S4 show that the central tendencies of the three groups appear to be more equivalent in Interval 2 than Interval 1.

The two-sample Kolmogorov Smirnoff test was used to verify whether or not the distributions of intervals 1 and 2 were the same for each pair of groups (Table S4). Statistically significant differences were found in all comparisons for interval 1; no statistically significant differences were found in the comparisons for interval 2. This indicates that if there were any ascertainment bias, this bias was relatively small and was not big enough to change the findings in the comparison of the overall time to viral suppression (data shown in Figure 2A). Specifically, the major difference in the overall time from ART initiation to viral suppression reflects a bigger difference in the first time interval (interval 1; time between ART initiation and the last visit without viral suppression), with less of a difference in the second time interval (interval 2, the time interval when viral suppression occurred).

Table S4. Kolmogorov Smirnoff two-sample test

Comparison	Interval 1 p-value	Interval 2 p-value
Delayed ART arm with ART initiation before vs. after May 2011	<0.001	0.083
Early ART arm vs. Delayed ART arm with ART initiation before May 2011	<0.001	0.050
Early ART arm vs. Delayed ART arm with ART initiation after May 2011	0.041	0.495