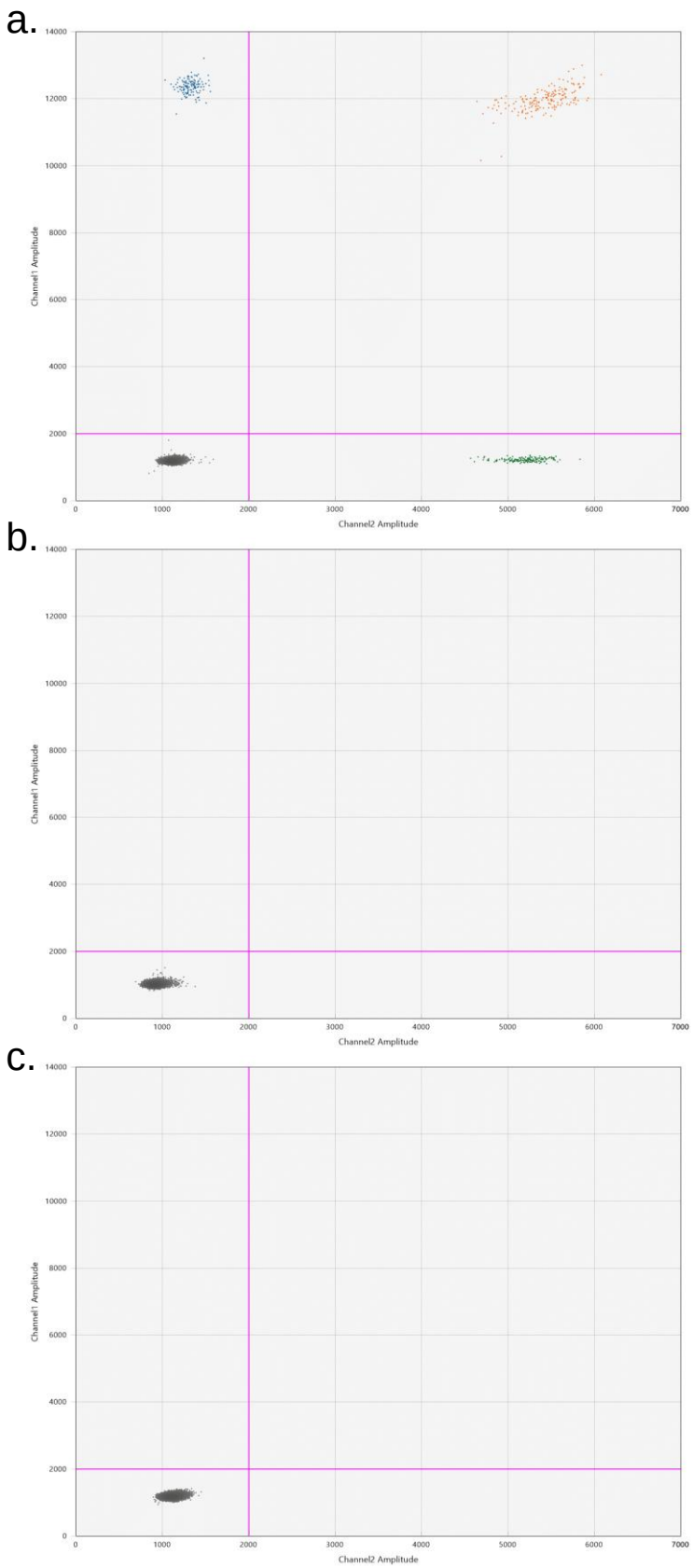


Figure S1. Representative results for IPDA controls. To monitor to performance of the IPDA, three control materials are analyzed in parallel with HIV-1 infected subject samples: (**a**) JLat full-length clone 6.3 cells, (**b**) CD4+ T cells from uninfected donors processed in parallel with subject samples, and (**c**) buffer only. Representative 2D ddPCR plots are shown for the IPDA HIV-1 Proviral Discrimination Reaction.

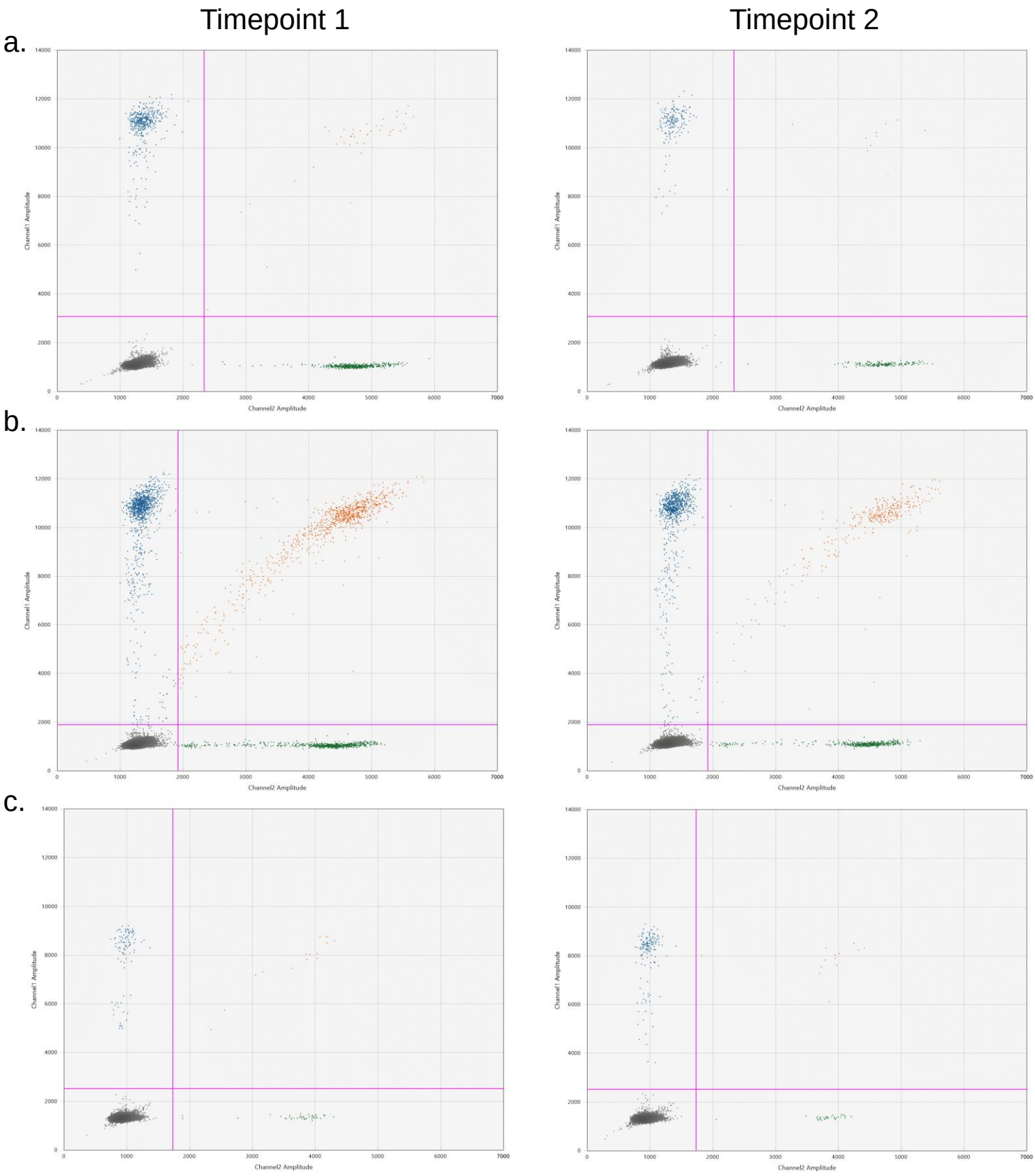
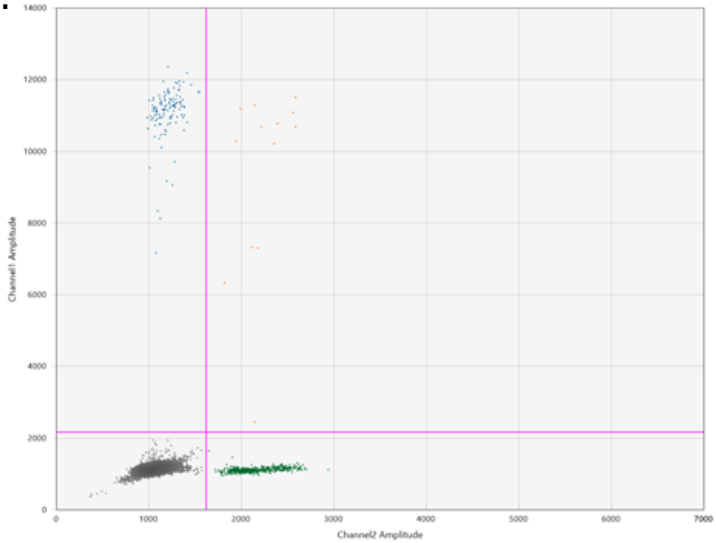


Figure S2. Typical IPDA results for HIV-1 infected subjects. Typical IPDA results are shown for three HIV-1 infected subjects from this study (a, b, c) for each of the two timepoints analyzed. 2D ddPCR plots are shown for the IPDA HIV-1 Proviral Discrimination Reaction for each subject at each timepoint. As shown, identical gates were applied for each subject across timepoints to ensure consistent interpretation of results.

a.



b.

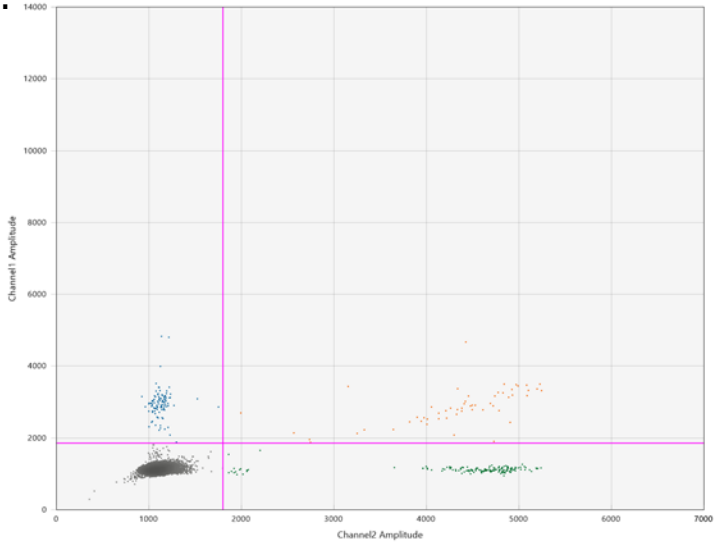
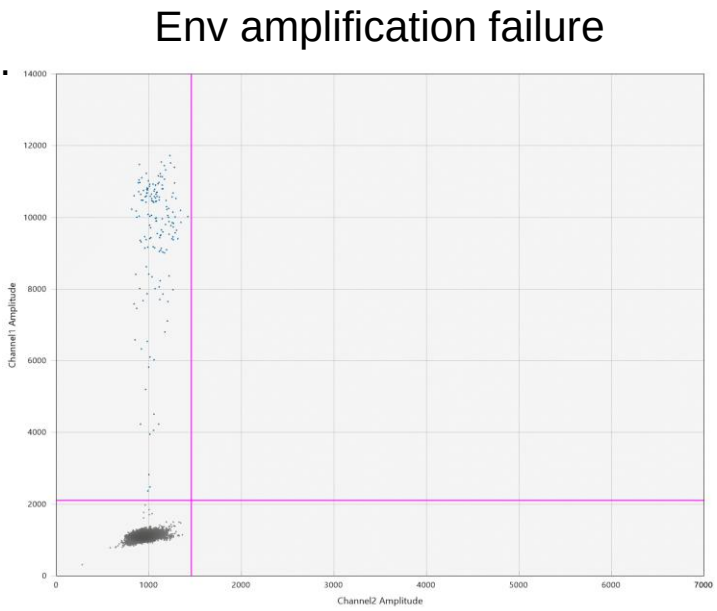


Figure S3. Tolerable variation in droplet amplitude is occasionally observed. In this study, droplet amplitude in the IPDA HIV-1 Proviral Discrimination Reaction was generally quite consistent across subjects. However, variation in droplet amplitude was occasionally observed. Examples of significant variation are shown for 2 subjects from this study (a, b). Such variation is likely a result of polymorphisms at IPDA primer and probe binding sites. Because IPDA results are based upon droplet counting after endpoint amplification, such variation in droplet amplitude is tolerable and is not expected to affect assay results. To ensure consistent interpretation of IPDA results, we apply identical gates for each subject across all samples analyzed.

a.



b.

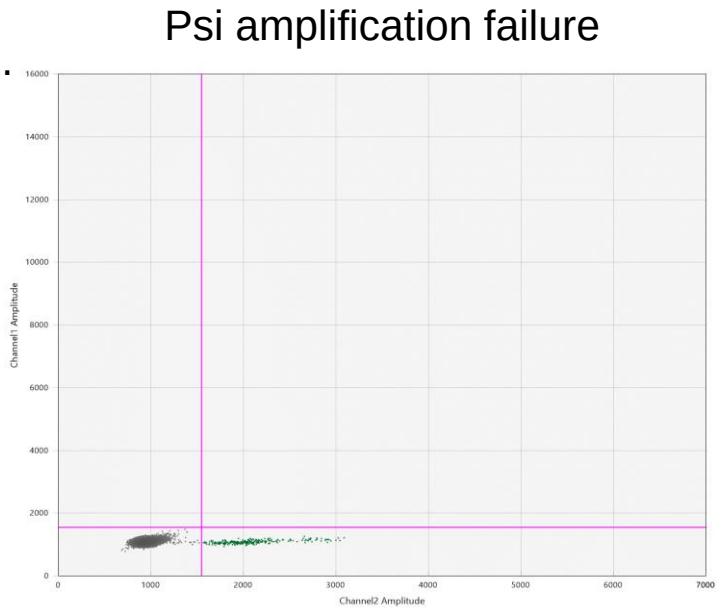


Figure S4. Amplification failure was not observed in this study but does occasionally occur and is readily discernable. We did not encounter an individual for whom amplification consistently failed for either the Psi or Env reaction across all timepoints tested in this study. However, such amplification failures are occasionally observed and are readily discernable. In an unrelated cross-sectional analysis of HIV-1 infected subjects on ART, both Env amplification failure (**a**) and Psi amplification failure (b) were encountered (JHMI-722 and JHMI-324, respectively). As can be seen in the HIV-1 Proviral Discrimination Reaction 2D ddPCR plots, amplification failure results in the detection of only one class of defective provirus. In such cases, IPDA results are flagged and intact proviral frequencies cannot be reported without the use of alternative primers or probes.

Per 100 cells/mm^3 increase	-5.4 (-7.8, -2.8)	<0.0001	-1.7 (-3.0, -0.4)	0.013
Proximal CD4				
Per two-fold increase	-2.2 (-3.8, -0.6)	0.0091	-1.3 (-2.6, -0.1)	0.034
Per 100 cells/mm^3 increase	-2.9 (-4.6, -1.1)	0.0017	-0.7 (-1.7, 0.3)	0.15
Proximal CD8				
Per two-fold increase	-1.7 (-3.3, -0.1)	0.034	-0.9 (-2.2, 0.3)	0.13
Per 100 cells/mm^3 increase	-0.8 (-2.0, 0.4)	0.19	-0.1 (-0.7, 0.5)	0.71
CD4/CD8 Ratio				
Per two-fold increase	-4.1 (-10.3, 2.5)	0.21	-1.6 (-4.4, 1.2)	0.25
Per ratio increase of 1	-11.9 (-19.7, -3.3)	0.0086	-5.6 (-9.7, -1.2)	0.013

Table S1. Estimated effects of covariates on the rate of decline per year in intact virus during the first 7 years of suppression. Note: these effects are from models that do not include the effect of the covariate on the level of intact virus at the initial study timepoint. Abbreviations: MTF, male-to-female; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; INSTI, integrase strand transfer inhibitor.

Models incorporating two covariates	% Estimate	Lower CI	Upper CI	p-value
Per 100 cells/mm^3 increase in CD4 nadir	-4.0	-6.8	-1.2	0.0066
Per 100 cells/mm^3 increase in proximal CD4	-2.1	-4.0	-0.2	0.030
Per 100 cells/mm^3 increase in CD4 nadir	-4.8	-7.3	-2.3	0.0004
Per doubling of proximal CD4	-2.0	-3.5	-0.5	0.010
Per 100 cells/mm^3 increase in CD4 nadir	-4.5	-7.5	-1.4	0.0053
Per CD4/CD8 ratio increase of 1	-6.4	-15.6	3.7	0.20
Per 100 cells/mm^3 increase in CD4 nadir	-5.3	-7.8	-2.8	0.0001
Per two-fold increase in proximal CD8	-1.9	-3.3	-0.4	0.012
Models incorporating three covariates	**% Estimate**	**Lower CI**	**Upper CI**	**p-value**
Per 100 cells/mm^3 increase in CD4 nadir	-5.4	-8.5	-2.1	0.0019
Per two-fold increase in proximal CD4	0.2	-7.5	8.5	0.96
Per two-fold increase in proximal CD8	-2.0	-9.1	5.5	0.58
Per 100 cells/mm^3 increase in CD4 nadir	-5.1	-8.4	-1.8	0.0035
Per 100 cells/mm^3 increase in proximal CD4	-0.3	-3.5	3.0	0.86
Per 100 cells/mm^3 increase in proximal CD8	-1.7	-4.0	0.7	0.15

Table S2. Models of the effect on intact provirus rate of decline per year incorporating immunologic covariates.