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Table S1. Monoclonal antibodies used to distinguish T cell subsets by immunophenotyping.

T cell subsets	Monoclonal antibody panel
Naïve, Central and Effector Memory, and Effector	CD3-PerCP, CD4 or CD8-APC, CD45RA-FITC, CCR7-PE
Activated	CD3-PerCP, CD4 or CD8-APC, HLA-DR-FITC, CD38-PE
Long-lived memory capacity	CD3-PerCP, CD4 or CD8-APC, IL7R α -PE

FITC = fluorescein isothiocyanate, PE = phycoerythrin, PerCP = peridinin chlorophyll-A protein, APC = allophycocyanin.

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Table S2a. Mean CD4⁺ T cell percentages (95% CI) of cell subsets estimated from linear mixed models, adjusting for age and sex. [†] $p < 0.05$ comparing control vs. HIV-infected children at 0 months post-HAART. $*p < 0.05$ comparing HIV-infected children at 0 months post-HAART vs. subsequent post-HAART time points. *N* displayed in last row reflect number of samples evaluated for activated CD4⁺ T cells; otherwise, *N* is equivalent to the number of samples evaluated for total CD4⁺ T cells.

	Control children	HIV-infected children, months since HAART initiation						
		0	3	6	9	12	15	18
Total CD4 ⁺	33.4	11.4 [†]	21.8*	24.8*	27.5*	27.8*	28.4*	27.6*
	(29.5, 37.6)	(9.9, 13.1)	(19.5, 24.3)	(22.3, 24.9)	(25.2, 30.5)	(25.8, 31.2)	(24.6, 30.7)	(26.9, 33.3)
	N=34	157	107	97	79	71	60	39
Naïve	33.8	19.4 [†]	24.2	26.9*	27.7*	32.6*	25.4	25.9
	(25.1, 43.7)	(15.7, 23.6)	(19.5, 29.5)	(21.9, 32.5)	(22.2, 33.7)	(26.4, 39.4)	(19.8, 31.7)	(19.2, 33.6)
Effector	25.0	27.4	23.7	24.2	21.1*	25.0	28.1	22.9
	(19.6, 31.0)	(23.8, 31.2)	(20.1, 27.7)	(20.3, 28.4)	(17.3, 25.2)	(20.7, 29.7)	(23.3, 33.3)	(17.8, 28.7)
Effector Memory	24.3	37.2 [†]	34.3	32.1*	34.3	28.4*	28.9*	30.5
	(18.3, 31.1)	(31.3, 41.4)	(30.1, 38.8)	(27.9, 36.7)	(29.7, 39.3)	(24.2, 33.0)	(24.5, 33.8)	(25.3, 36.1)
Central Memory	5.7	4.6	6.2*	5.7*	6.1*	6.3*	5.1	6.4*
	(4.3, 7.3)	(3.9, 5.4)	(5.2, 7.2)	(4.7, 6.8)	(5.1, 7.2)	(5.2, 7.5)	(3.9, 6.5)	(4.9, 8.1)
Activated	3.1	10.8 [†]	6.0*	4.5*	3.7*	3.6*	4.0*	3.6*
	(2.5, 4.0)	(9.2, 12.6)	(5.0, 7.1)	(3.8, 5.4)	(3.0, 4.4)	(3.0, 4.3)	(3.3, 4.9)	(2.9, 4.5)
		N=150		98	76		59	37
		HIV-infected children, months since HAART initiation						
		21	24	27	30			
Total CD4 ⁺	30.0*	26.0*	26.4*	25.4*				
	(26.9, 33.3)	(22.9, 29.3)	(23.1, 30.0)	(21.2, 29.9)				
	33	26	25	11				
Naïve	30.1*	35.4*	28.2*	34.3				
	(22.5, 38.9)	(26.1, 46.1)	(19.8, 38.1)	(21.2, 50.6)				
Effector	17.1*	20.2*	28.3	23.7				
	(12.5, 22.5)	(14.5, 26.8)	(21.3, 36.3)	(14.8, 34.7)				
Effector Memory	31.2	29.8*	29.9*	26.0				
	(25.6, 37.4)	(23.7, 36.6)	(23.8, 36.7)	(18.0, 35.6)				
Central Memory	6.5*	7.0*	6.3*	8.5*				
	(4.9, 8.3)	(5.2, 9.0)	(4.0, 9.1)	(8.5, 8.5)				
Activated	3.2*	4.1*	4.8*	3.7*				
	(2.5, 4.1)	(3.1, 5.3)	(3.7, 6.2)	(2.5, 5.3)				

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Table S2b. Mean CD8⁺ T cell percentages (95% CI) of cell subsets estimated from linear mixed models adjusting for age and sex. [†]*p*<0.05 comparing control vs. HIV-infected children at 0 months post-HAART. **p*<0.05 comparing HIV-infected children at 0 months post-HAART vs. subsequent post-HAART time points. *N* displayed in rows below Activated and IL7Rα⁺ reflect number of samples evaluated for activated and IL-7Rα⁺ CD8⁺ T cells; otherwise, *N* is equivalent to the number of samples evaluated for total CD8⁺ T cells.

	Control children	HIV-infected children, months since HAART initiation						
		0	3	6	9	12	15	18
Total CD8 ⁺	23.6 (19.1, 28.1) N=34	43.5 [†] (40.8, 46.2) 155	41.1* (38.2, 44.0) 108	35.8* (32.9, 38.7) 98	34.8* (31.9, 37.7) 78	33.6* (30.7, 36.5) 72	33.8* (30.9, 36.7) 60	31.5* (28.2, 34.8) 39
Naïve	24.2 (19.3, 29.7)	3.6 [†] (2.3, 5.2)	9.3* (7.0, 12.0)	10.4* (7.8, 13.4)	13.5* (10.4, 17.0)	14.4* (11.2, 18.1)	10.9* (8.0, 14.2)	14.1* (10.2, 18.5)
Effector	50.7 (40.6, 61.9)	46.6 (42.2, 51.3)	51.3 (46.1, 56.7)	54.2* (48.6, 60.1)	50.4 (44.7, 56.4)	54.0* (47.9, 60.5)	52.7 (46.4, 59.5)	48.0 (40.7, 55.9)
Effector Memory	16.2 (11.3, 22.1)	39.8 [†] (35.3, 44.7)	29.8* (25.5, 34.5)	26.2* (22.2, 30.6)	27.8* (23.4, 32.5)	25.2* (20.9, 29.9)	25.8* (21.4, 30.6)	26.4* (21.3, 32.1)
Central Memory	2.5 x10 ⁻³ (1.4, 4.4)	0.9 x10 ^{-3†} (0.7, 1.2)	1.5* x10 ⁻³ (1.1, 2.0)	1.4* x10 ⁻³ (1.0, 2.0)	1.6* x10 ⁻³ (1.1, 2.2)	2.2* x10 ⁻³ (1.5, 3.1)	1.5* x10 ⁻³ (1.1, 2.1)	2.1* x10 ⁻³ (1.4, 3.2)
Activated	14.4 (10.2, 19.4)	31.8 [†] (28.4, 35.4)	21.8* (18.6, 25.2) N=107	18.5* (15.6, 21.6) 99	16.9* (14.0, 20.1) 76	16.9* (13.8, 20.3) 71	17.5* (14.3, 20.9)	17.4* (13.7, 21.5) 38
IL7Rα ⁺	37.9 (30.2, 46.6)	10.7 [†] (8.2, 13.6) N=154	23.5* (19.4, 28.1) 107	24.8* (20.3, 29.7) 97	28.0* (23.0, 33.4) 77	32.0* (26.7, 37.8)	23.6* (18.9, 28.8)	28.8* (22.9, 35.5)
HIV-infected children, months since HAART initiation								
		21	24	27	30			
Total CD8 ⁺		33.9* (30.4, 37.4) 33	36.4* (32.7, 40.1) 26	35.6* (31.9, 39.3) 25	32.9* (27.8, 38.0) 11			
Naïve		13.9* (9.9, 18.6)	12.9* (8.7, 18.0)	10.8* (6.9, 15.7)	13.8* (7.7, 21.6)			
Effector		47.5 (39.7, 55.9)	54.3 (45.2, 64.3)	58.5* (48.8, 69.2)	55.5 (41.9, 71.1)			
Effector Memory		27.6* (21.9, 33.9)	26.0* (20.0, 32.8)	25.2* (19.3, 31.9)	24.4* (16.3, 34.1)			
Central Memory		2.0 x10 ⁻³ (1.3, 3.2)	1.1 x10 ⁻³ (0.7, 1.9)	1.2 x10 ⁻³ (0.7, 2.1)	1.6 x10 ⁻³ (0.7, 3.4)			
Activated		16.1* (12.4, 20.3)	22.2* (17.5, 27.4)	21.8* (17.0, 27.2)	20.8* (14.3, 28.6)			

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IL7R α ⁺	21.1* (15.7, 27.2)	26.8* (20.2, 34.4)	25.0* (18.6, 32.3)	32.6* (22.4, 44.8)
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Table S3. Mean (95% CI) differences in the percentage of a) CD4+ and b) CD8+ T cell subsets by age category and sex at baseline. Estimates in bold are statistically significantly different from zero ($p < 0.05$). Estimates are from multivariable linear regression models of baseline data with an ordinal covariate for age (<12, 12-23, 24-35, 36-47, and 48+ months) and an indicator of female sex. Estimates are interpreted as the change in cell subset percentage with each 1-unit increase in age category (*e.g.*, <12 months vs. 12-23 months) or the difference in each cell subset percentage for females relative to males. Models were performed separately for HIV-infected and control children.

CD4+ T Cell Subset	Age		Female Sex	
	Controls	HIV+	Controls	HIV+
Total	0.02 (-0.001, 0.12)	-0.02 (-0.001, -0.06)	0.25 (0.01, 0.84)	0.08 (-0.01, 0.35)
Naive	-0.14 (-0.15, 1.31)	-0.07 (-0.001, -0.25)	0.64 (-0.92, 6.53)	-0.53 (-1.85, -0.01)
Effector	-0.005 (-0.37, 0.22)	-0.02 (-0.13, 0.003)	0.03 (-1.15, 1.93)	-0.10 (-0.77, 0.06)
Effector Memory	0.29 (0.02, 0.89)	0.20 (0.06, 0.43)	-0.90 (-3.48, -0.001)	0.44 (0.01, 1.47)
Central Memory	0.003 (-0.002, 0.02)	0.002 (-0.04, 0.09)	-0.04 (-0.63, 0.14)	-0.09 (-0.32, -0.001)
Activated	-0.32 (-0.84, 0.21)	1.18 (-0.001, 2.35)	-0.05 (-1.25, 1.15)	-1.80 (-4.96, 1.35)

CD8+ T Cell Subset	Age		Female Sex	
	Controls	HIV+	Controls	HIV+
Total	0.51 (-0.100, 2.022)	0.92 (-0.58, 2.42)	-2.64 (-6.09, 0.81)	0.26 (-3.75, 4.27)
Naive	-0.14 (-0.85, 0.03)	-0.001 (-0.03, 0.013)	2.75 (0.16, 8.51)	0.03 (-0.30, 0.05)
Effector	-0.06 (-0.57, 0.06)	0.01 (-0.02, 0.10)	-0.12 (-2.27, 0.65)	-0.53 (-1.83, -0.01)
Effector Memory	0.32 (0.01, 1.02)	0.00004 (-0.04, 0.05)	-0.72 (-3.51, 0.03)	0.17 (-0.02, 0.095)
Central Memory	0.02 (-0.07, 0.10)	0.15 (-0.87, 1.18)	-0.10 (-0.30, 0.09)	1.37 (-1.38, 4.13)
Activated	-0.10 (-0.44, 0.001)	0.0005 (-0.04, 0.04)	-0.08 (-1.17, 0.27)	-0.21 (-0.97, 0.01)

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Table S4a. Mean CD4⁺ T cell counts in cells/μL (95% CI) of cell subsets estimated from linear mixed models adjusting for age and sex.

	Control children	HIV-infected children, months since HAART initiation						
		0	3	6	9	12	15	18
Total CD4 ⁺	1789 (1503, 2100) N=28	666 [†] (542, 801) 123	1211* (1031, 1405) 85	1289* (1101, 1492) 83	1552* (1336, 1784) 63	1498* (1283, 1729) 53	1340* (1119, 1581) 37	1505* (1254, 1780) 30
Naïve	2034 (1409, 2774)	1156 [†] (878, 1472)	1391 (1054, 1776)	1576* (1211, 1989)	1624* (1227, 2077)	1989* (1531, 2507)	1296 (885, 1785)	1537 (1047, 2120)
Effector	1303 (858, 1841)	1592 [†] (1310, 1901)	1282* (1006, 1590)	1246* (971, 1555)	1096* (823, 1407)	1197* (903, 1533)	1310* (964, 1710)	967* (649, 1349)
Effector Memory	1211 (816, 1684)	2034 [†] (1730, 2363)	1849 (1532, 2196)	1584* (1289, 1910)	1901 (1553, 2284)	1459* (1147, 1809)	1498* (1140, 1904)	1467* (1083, 1909)
Central Memory	257 (174, 381)	206 (160, 266)	242 (184, 319)	242 (184, 319)	268 (200, 359)	311* (227, 426)	167 (118, 238)	302 (204, 447)
Activated	164 (122, 220) N=172	561 [†] (461, 683) 70	290* (234, 360) 125	230* (186, 286) 137	172* (136, 218) 151	171* (135, 216) 159	176* (136, 227) 142	148* (113, 195) 135
		HIV-infected children, months since HAART initiation						
		21	24	27	30			
Total CD4 ⁺		1429* (1176, 1706) 27	1267* (1005, 1560) 20	1089* (797, 1426) 12	1475 (985, 2063) 5			
Naïve		2043* (1447, 2741)	1840* (1207, 2606)	1798 (1031, 2776)	2683 (1310, 4543)			
Effector		795* (498, 1161)	818* (481, 1244)	801* (397, 1345)	888* (296, 1798)			
Effector Memory		1246* (881, 1675)	1399* (960, 1919)	1136* (657, 1745)	1096 (437, 2051)			
Central Memory		321* (212, 484)	330* (206, 529)	281 (156, 507)	498 (202, 1226)			
Activated		161* (120, 216)	171* (125, 234)	172* (117, 255)	161* (89, 289)			

[†]*p* < 0.05 comparing control vs. HIV-infected children at 0 months post-HAART.

**p* < 0.05 comparing HIV-infected children at 0 months post-HAART vs. subsequent post-HAART time points.

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Table S4b. Mean CD8⁺ T cell counts in cells/μL (95% CI) of cell subsets estimated from linear mixed models adjusting for age and sex.

	Control children	HIV-infected children, months since HAART initiation						
		0	3	6	9	12	15	18
Total CD8 ⁺	1282	2460 [†]	2125*	1849*	1910*	1764*	1739*	1640*
	(909, 1718)	(2163, 2777)	(1829, 2444)	(1572, 2148)	(1617, 2227)	(1477, 2076)	(1423, 2087)	(1312, 2005)
	N=28	123	85	83	63	53	37	30
Naïve	1414	207 [†]	562*	630*	812*	864*	552*	818*
	(1096, 1771)	(121, 317)	(400, 751)	(457, 831)	(602, 1054)	(641, 1121)	(356, 792)	(555, 1131)
Effector	2852	2683	2735	2841	2756	2746	2500	2304
	(2072, 3755)	(2283, 3116)	(2292, 3218)	(2386, 3335)	(2277, 3281)	(2253, 3288)	(1964, 3101)	(1746, 2939)
Effector Memory	773	2247 [†]	1624*	1354*	1544*	1376*	1568*	1318*
	(459, 1168)	(1909, 2612)	(1315, 1966)	(1072, 1669)	(1226, 1900)	(1069, 1723)	(1197, 1989)	(953, 1741)
Central Memory	10.6	2.1 [†]	6.7*	5.8*	6.2*	10.1*	4.5	11.0*
	(3.7, 29.9)	(1.3, 3.4)	(3.9, 11.3)	(3.4, 9.8)	(3.5, 11.2)	(5.5, 18.5)	(2.2, 9.1)	(5.1, 23.7)
Activated	853	1798 [†]	1116*	942*	870*	894*	936*	812*
	(542, 1233)	(1557, 2056)	(908, 1345)	(753, 1153)	(673, 1093)	(690, 1124)	(698, 1209)	(573, 1093)
IL7Rα ⁺	2107	645 [†]	1362*	1391*	1592*	1689*	1149*	1310*
	(1619, 2659)	(468, 850)	(1074, 1684)	(1100, 1717)	(1257, 1967)	(1340, 2078)	(831, 1519)	(942, 1740)
HIV-infected children, months since HAART initiation								
	21	24	27	30				
Total CD8 ⁺	1764*	1714*	1459*	1697*				
	(1410, 2158)	(1327, 2151)	(1028, 1966)	(1031, 2530)				
Naïve	27	20	12	5				
	936*	671*	734*	986				
Effector	(641, 1287)	(398, 1015)	(385, 1195)	(407, 1817)				
	2480	2440	2352	2970				
Effector Memory	(1876, 3168)	(1765, 3225)	(1534, 3344)	(1630, 4710)				
	1136*	1340*	999*	1197*				
Central Memory	(786, 1550)	(913, 1848)	(558, 1566)	(512, 2169)				
	8.0*	4.3	4.5	8.6				
Activated	(3.6, 17.9)	(1.7, 10.8)	(1.4, 14.5)	(1.4, 52.1)				
	835*	967*	888*	1183*				
IL7Rα ⁺	(582, 1135)	(658, 1336)	(525, 1345)	(576, 2008)				
	1218*	1211	1218	1697				
	(849, 1653)	(800, 1706)	(717, 1850)	(843, 2849)				

[†]*p*<0.05 comparing control vs. HIV-infected children at 0 months post-HAART.

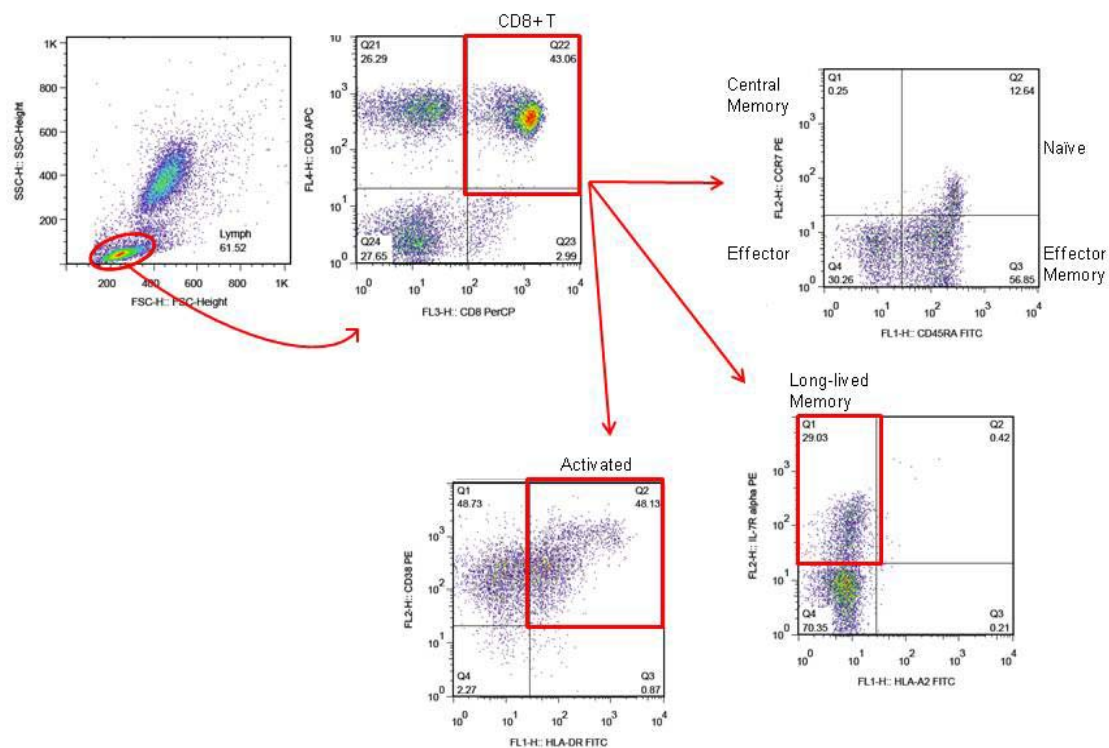
^{*}*p*<0.05 comparing HIV-infected children at 0 months post-HAART vs. subsequent post-HAART time points.

[†]*p*<0.05 comparing control vs. HIV-infected children at 0 months post-HAART.

**p*<0.05 comparing HIV-infected children at 0 months post-HAART vs. subsequent post-HAART time points.

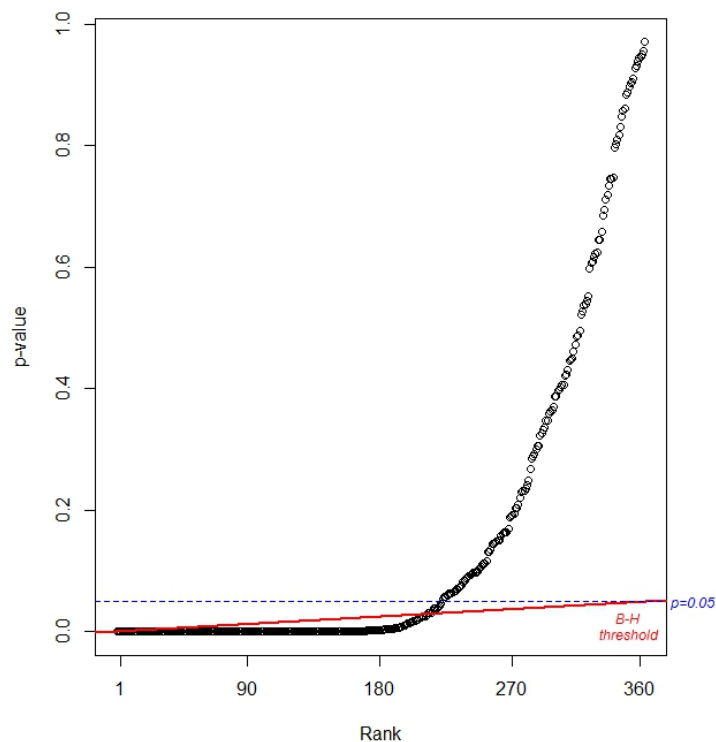
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Figure S1. Gating strategy to identify CD8⁺ T cell subsets. Gating strategy to identify CD4⁺ T cells was similar.



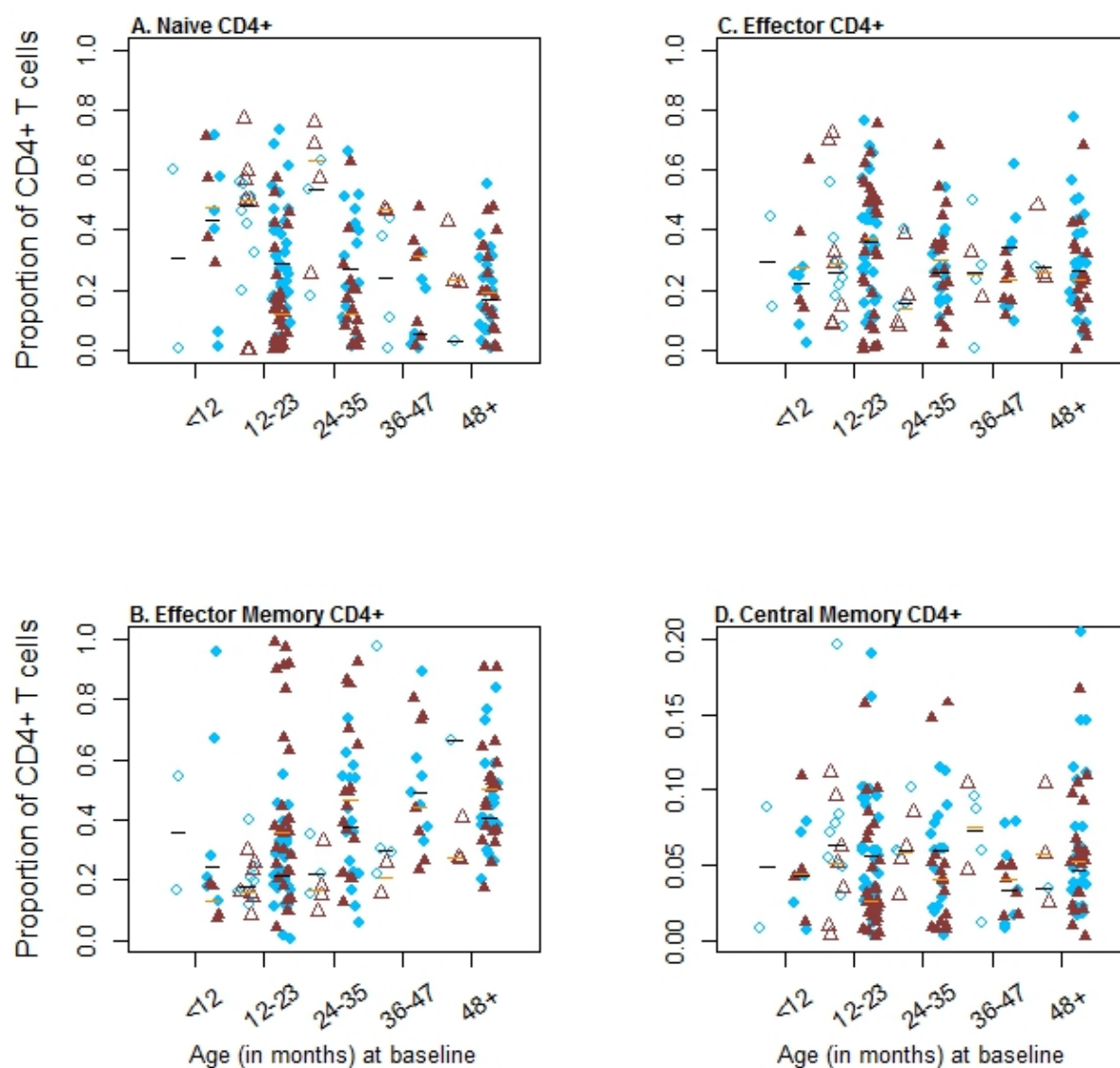
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Figure S2. Unadjusted, original p-values in ascending order by rank to illustrate the false discovery rate observed in this study. The 10 p-values falling between the original Type I error rate ($\alpha < 0.05$; blue dashed line) and the threshold (red solid line) represent potential false discoveries as estimated by the Benjamini and Hochberg method. *Adapted from <http://www.unc.edu/courses/2007spring/biol/145/001/docs/lectures/Nov12.html> .*



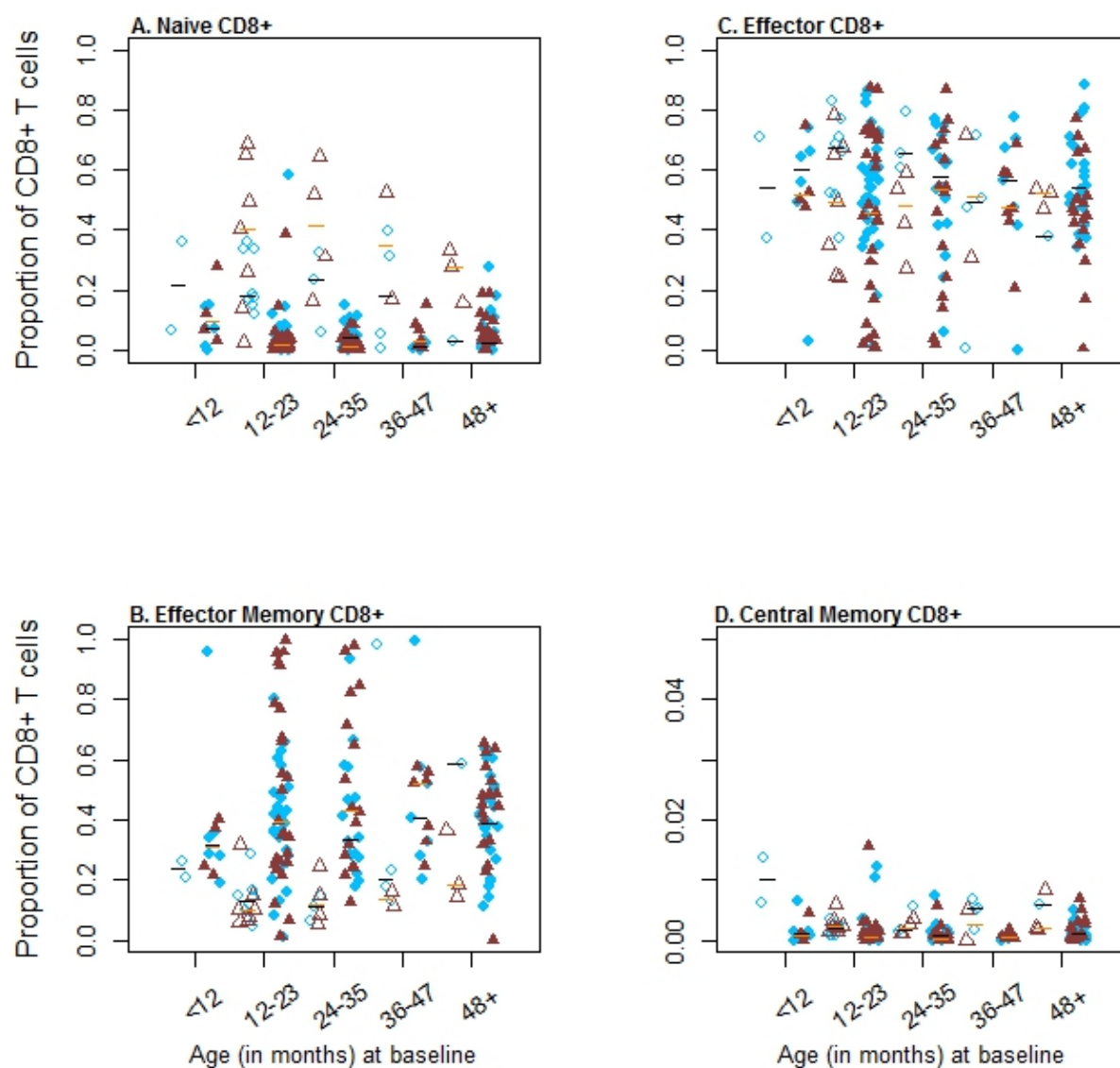
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Figure S3. Unadjusted CD4+ T cell subsets of pre-HAART, HIV-infected (filled symbols) and control (open symbols) children stratified by age at baseline. Unadjusted CD4+ T cell proportions for each study participant represented by circles (males) and triangles (females) and medians represented by black (males) and orange (females) lines.



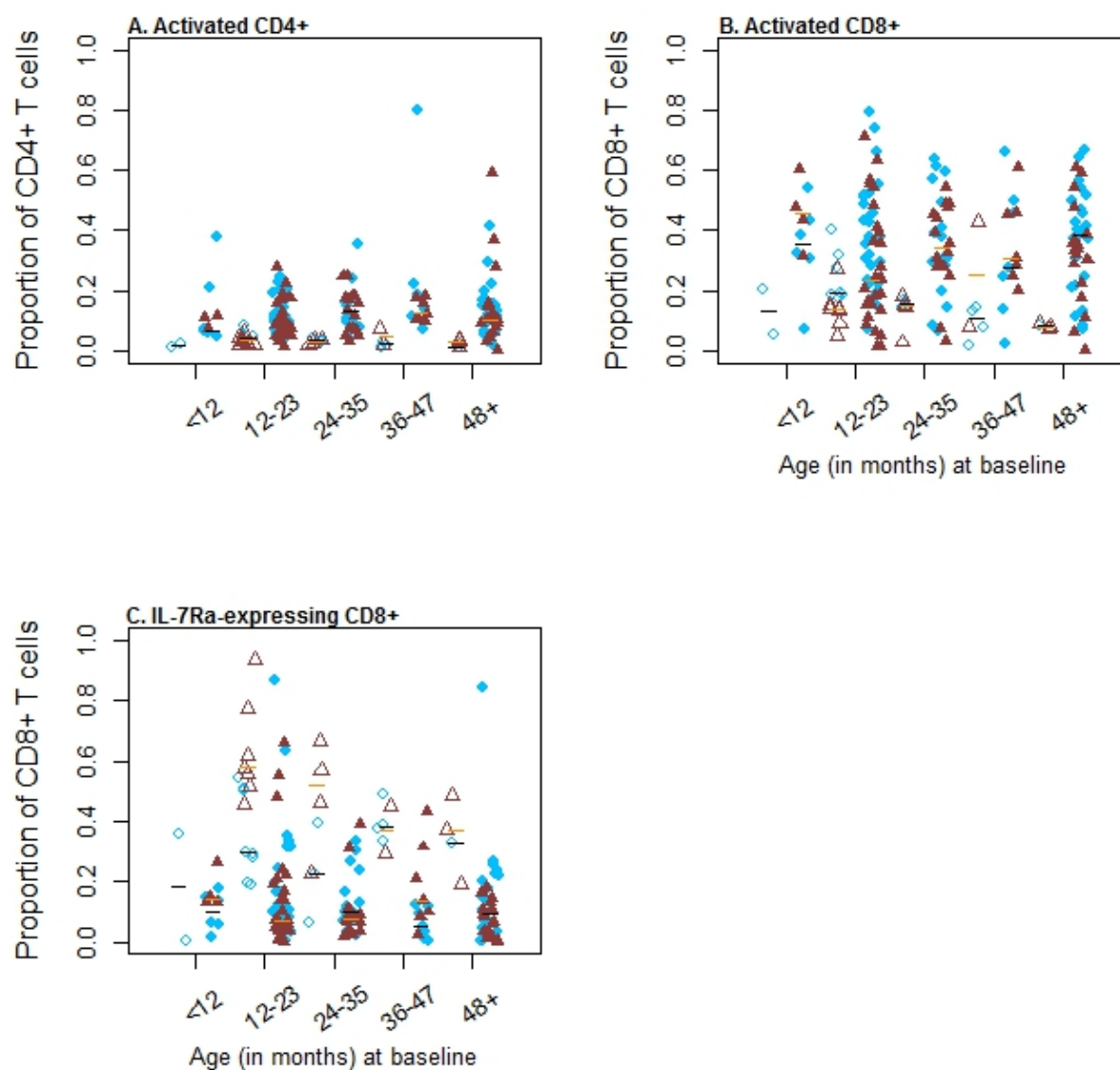
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Figure S4. Unadjusted CD8+ T cell subsets of pre-HAART, HIV-infected (filled symbols) and control (open symbols) children stratified by age at baseline. Unadjusted CD4+ T cell proportions for each study participant represented by circles (males) and triangles (females) and medians represented by black (males) and orange (females) lines.



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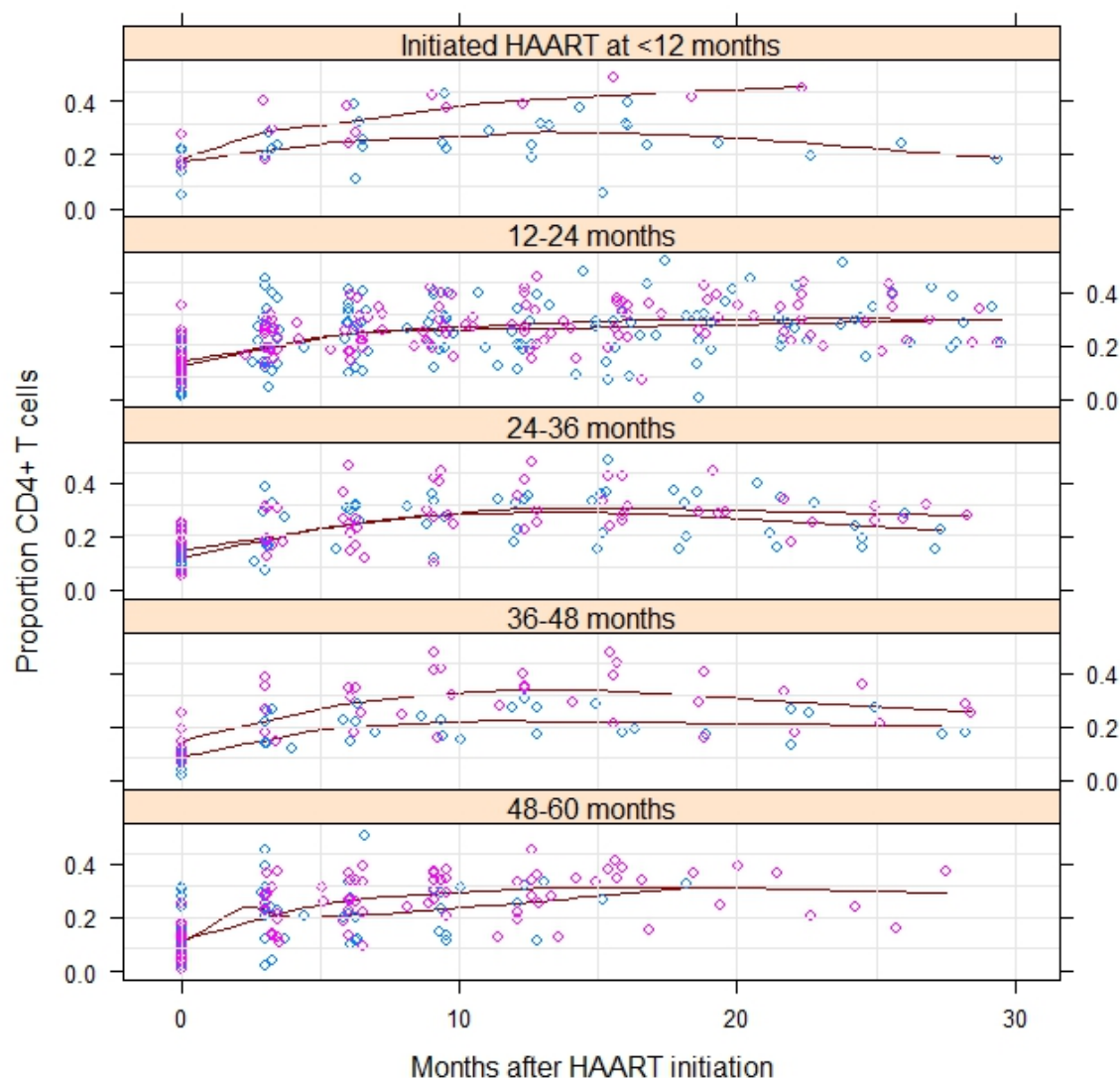
Figure S5. Unadjusted CD4+ and CD8+ T cell subsets of pre-HAART, HIV-infected (filled symbols) and control (open symbols) children stratified by age at baseline. Unadjusted CD4+ T cell proportions for each study participant represented by circles (males) and triangles (females) and medians represented by black (males) and orange (females) lines.



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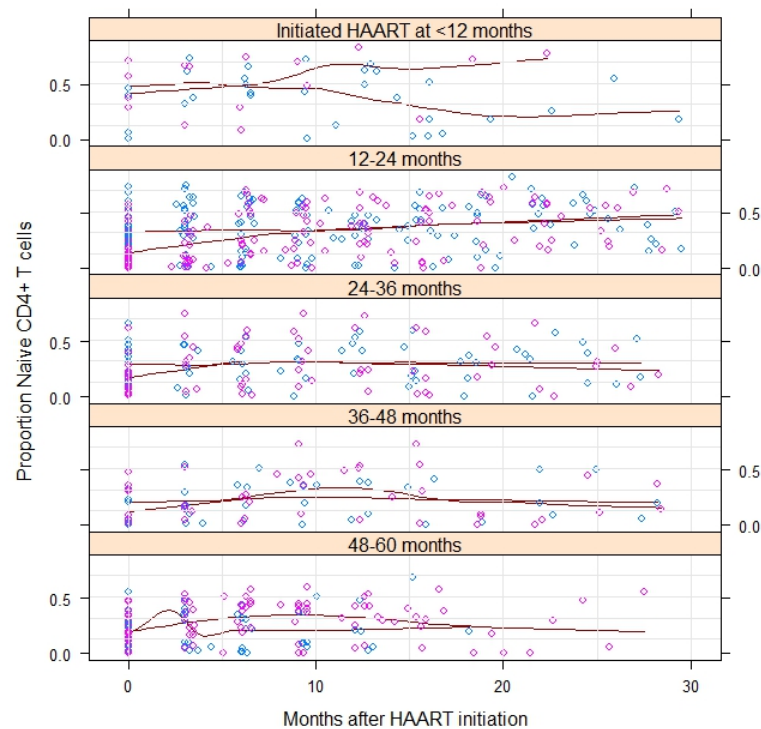
Figure S6. Trajectories of a) Total, b) Naive, c) Central Memory, d) Effector Memory, and e) Effector CD4+ T cells from HIV-infected Zambian children stratified by age at HAART initiation. Red circles represent females; blue circles represent males. Lines represent loess curves stratified by sex. Two outliers were removed for central memory and activated CD4+ T cells.

A. Total CD4+

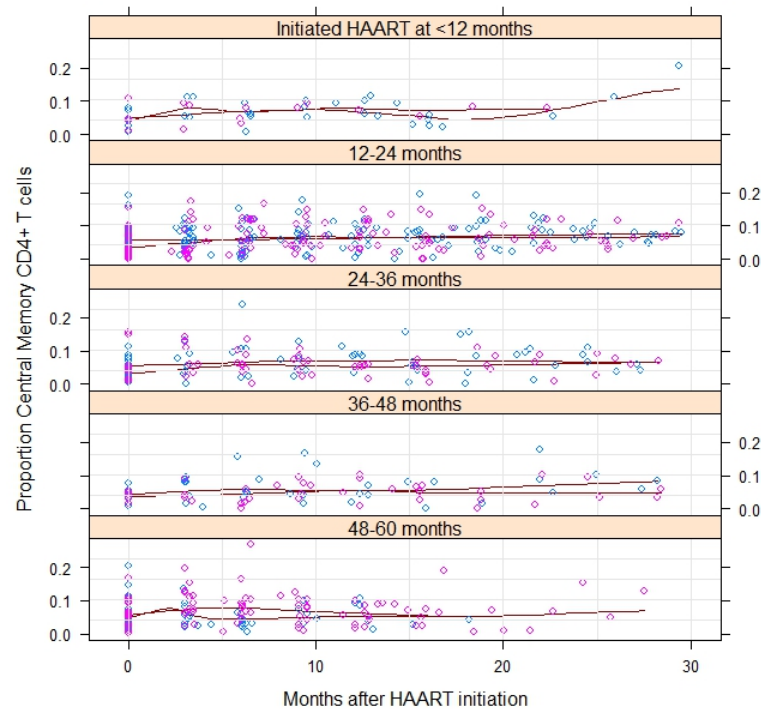


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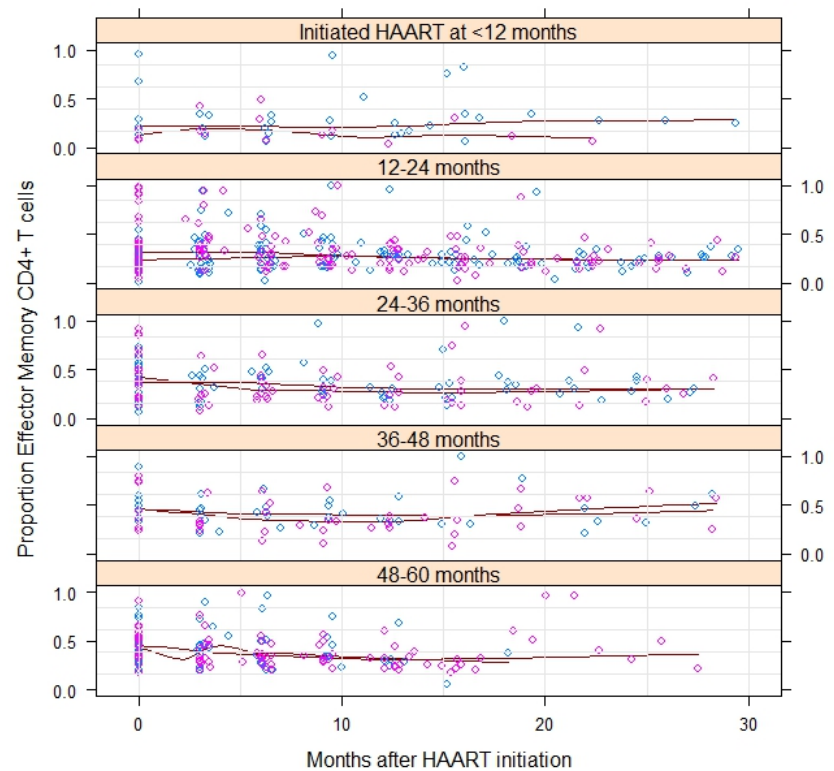
B. Naive CD4+ T cells



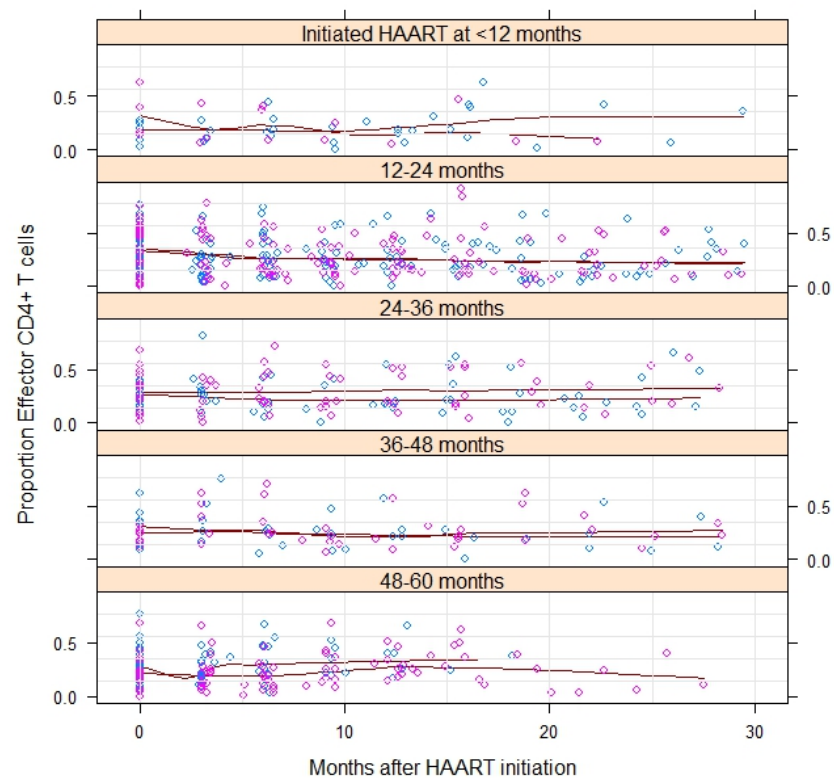
C. Central Memory CD4+ T cells



D. Effector Memory CD4+



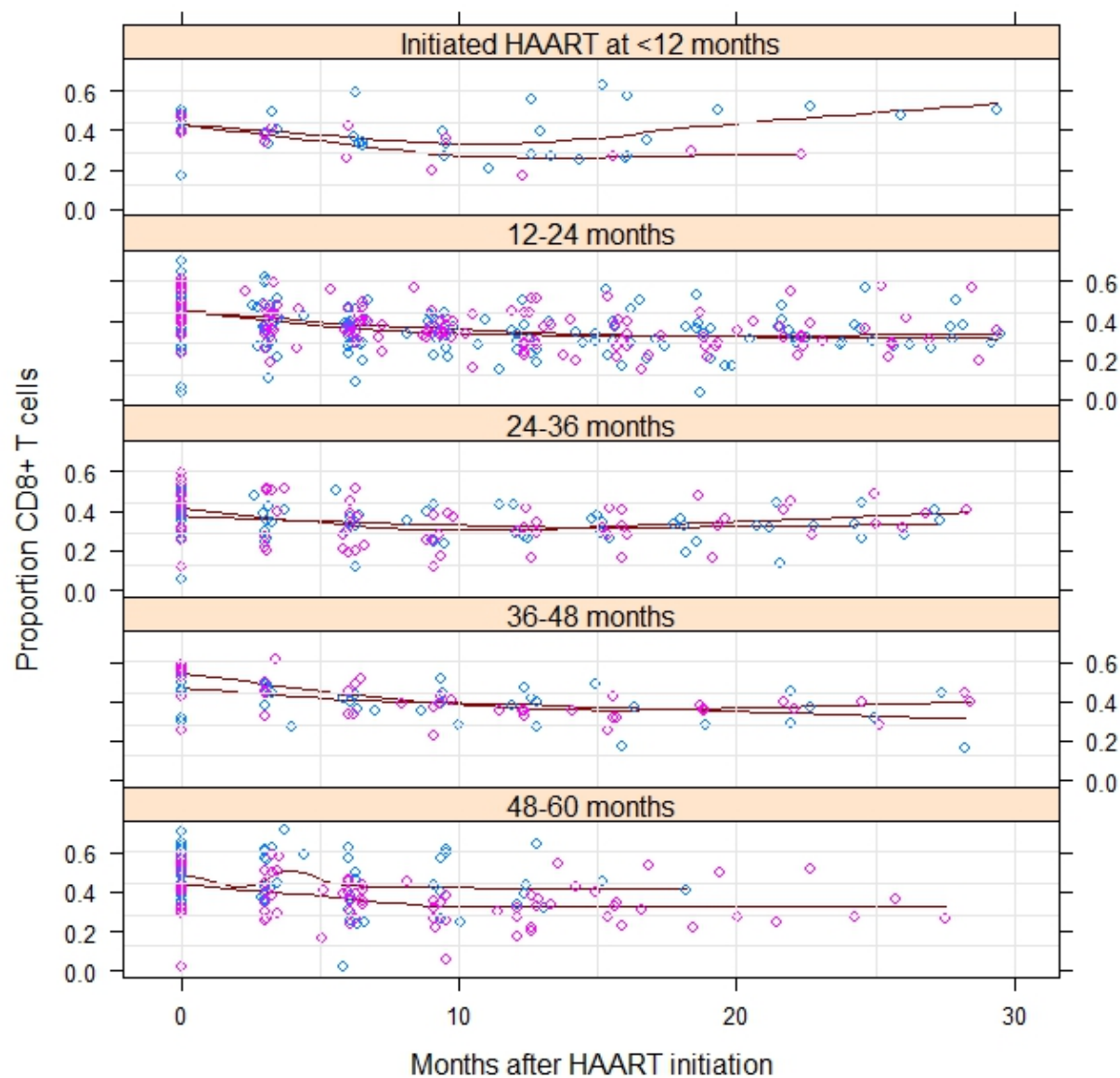
E. Effector CD4+



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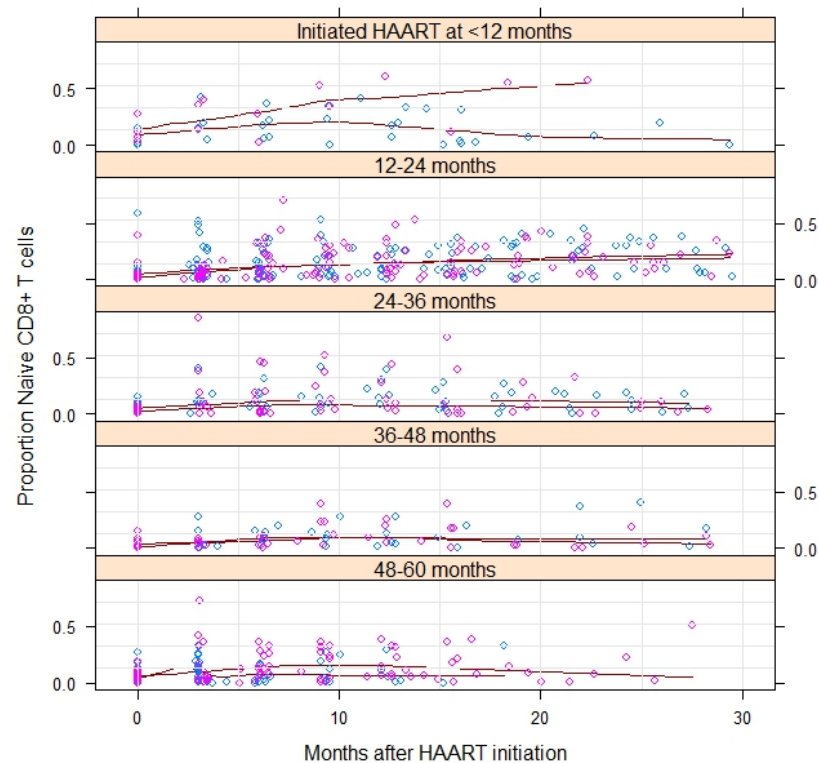
Figure S7. Trajectories of a) Total, b) Naive, c) Central Memory, d) Effector Memory, and e) Effector CD8⁺ T cells from HIV-infected Zambian children stratified by age at HAART initiation. Red circles represent females; blue circles represent males. Lines represent loess curves stratified by sex. Eleven outliers were removed for central memory CD8⁺ T cells to more clearly illustrate most data.

A. Total CD8⁺

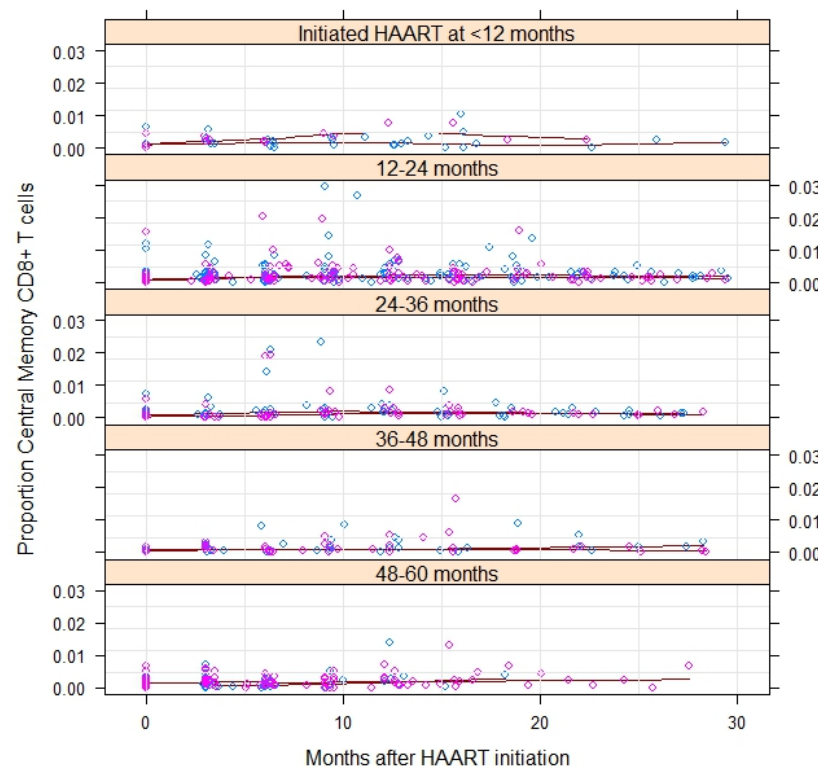


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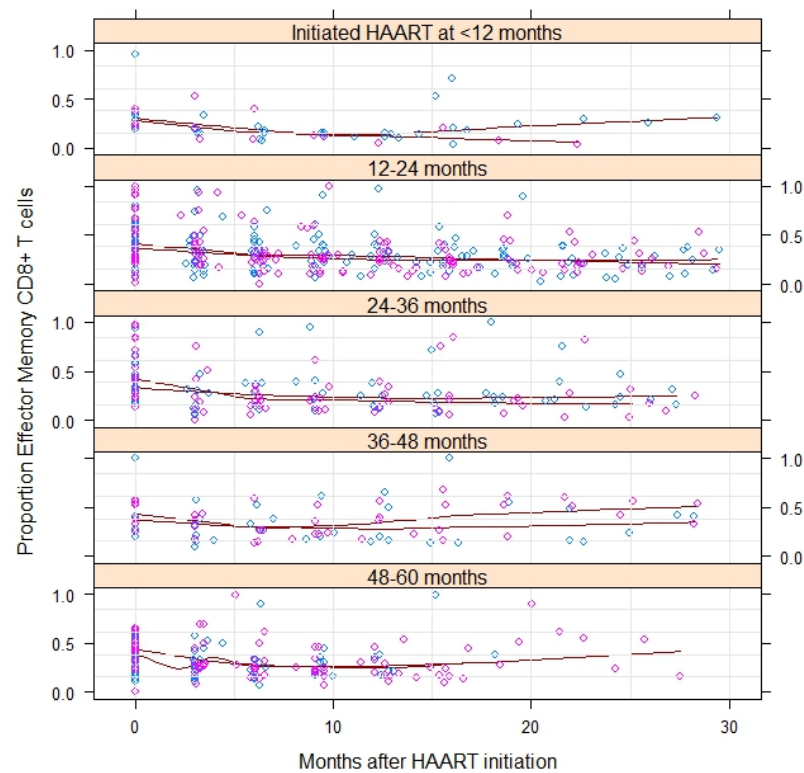
B. Naive CD8+



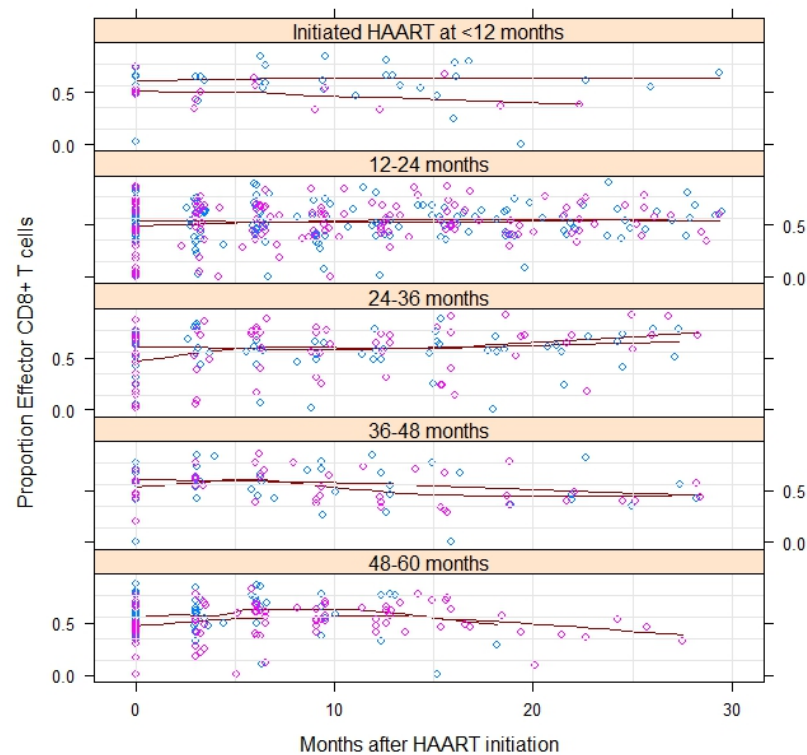
C. Central Memory CD8+



D. Effector Memory CD8+



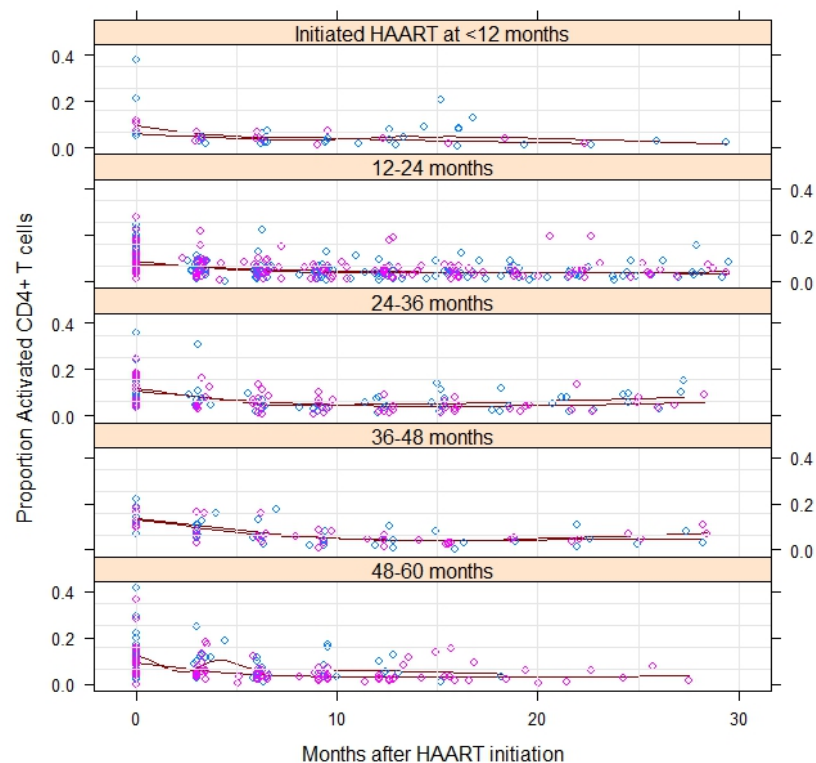
E. Effector CD8+



Supplemental Digital Content

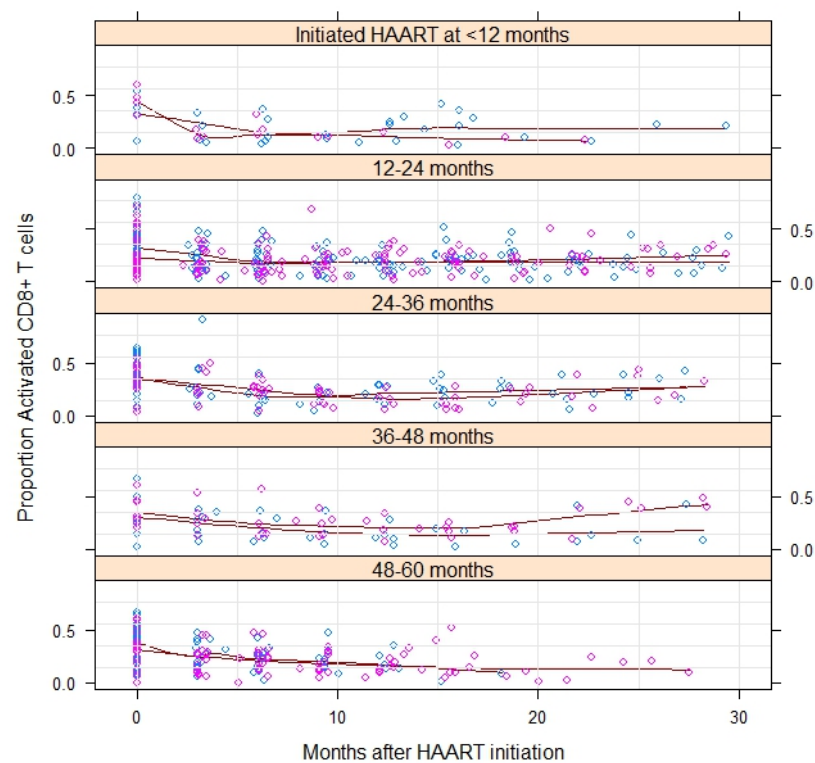
Figure S8. Trajectories of a) Activated CD4+, b) Activated CD8+, and c) IL-7R α -expressing CD8+ T cells from HIV-infected Zambian children stratified by age at HAART initiation. Red circles represent females; blue circles represent males. Lines represent loess curves stratified by sex.

A. Activated CD4+



Supplemental Digital Content

B. Activated CD8+



C. Long-lived memory CD8+

