METHODS

For the HIV-positive children, flow cytometry was performed at 4 central laboratories (3 in Thailand and 1 in Cambodia) by dual-platform flow cytometry with FACS Calibur (Becton Dickinson, San Jose, Calif) at 3 sites and Coulter (Beckman Coulter, Miami, Fla) at 1 site. For the healthy controls, cytometry was performed at 1 site in Thailand using FACS Calibur. Flow analysis was performed with a standardized 3-color analysis protocol that gated on cells stained with 1 fluorochrome (generally peridinin chlorophyll protein or CyChrome conjugated to CD45, CD4, or CD8), followed by 2-color analysis of cells stained with the prescribed remaining fluorochromes (fluorescein isothiocyanate and phycoerythrin). The relative proportions of each subset were expressed as the percentage of the anchor gated population. For both groups, the following subsets were performed: $CD45^+/3^+/19^-$ (total T cells), $CD45^+/3^+/4^+$ (T_H cells), $CD4^+/45RA^+/62L^+$ (naive T_H cells), $CD3^+/4^+/45RO^+$ (memory T_H cells), $CD4^+/DR^+/38^+$ (activated T_H cells), $CD45^+/3^+/8^+$ (cytotoxic T cells), $CD8^+/45RA^+/62L^+$ (naive cytotoxic T cells), $CD3^+/4^-/45RO^+$ (memory cytotoxic T cells), $CD8^+/DR^+/38^+$ (activated cytotoxic T cells), $CD45^+/3^-/19^+$ (B cells), $CD45^+/3^-/16^+/56^+$ (NK cells), $CD14^+/16^+/DR^+$ (activated monocytes), and $CD14^+/16^+/163^+$ (perivascular monocytes believed to be precursors of brain perivascular macrophages).[E1]

Statistical analysis

Histograms were plotted and examined, and the Shapiro-Wilk test was performed to test normality and to select the best transformation method to be used in each regression. Most of cell subset counts and percentages were transformed by Box-Cox power transformation except for activated T_H-cell percentage, activated monocyte percentage, and activated cytotoxic T-cell counts, for which distributions were better with a $\log_{10}$ transformation. Untransformed data were used in regressions for activated cytotoxic T-cell percentage and memory T_H-cell percentage.

We first categorized the cell subset counts and percentages into 4 groups by their quartiles. After examining the distribution by LTNP status in contingency tables together with their ORs, we collapsed adjacent quartiles if this was supported by the distribution. Covariates that were assessed to predict LTNP included sex, CDC classification, baseline log HIV RNA, and cell subsets. In the logistic regression models, covariates with $P \leq .1$ in univariate models were adjusted for in the multivariate models. For example, the distribution by cytotoxic T-cell percentage quartiles was 59, 29, 6, 6 for LTNPs and 14, 24, 32, 30 for non-LTNPs, which corresponded to OR (95% CI) for LTNP of 1 (reference), 3.4 (0.8-14.2), 22.8 (2.4-214.6), and 22.4 (2.3-201.9), respectively. Quartiles 3 and 4 were therefore combined.

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E1. Kim WK, Alvarez X, Fisher J, et al. CD163 identifies perivascular macrophages in normal and viral encephalitic brains and potential precursors to perivascular macrophages in blood. Am J Pathol 2006;168:822-34.

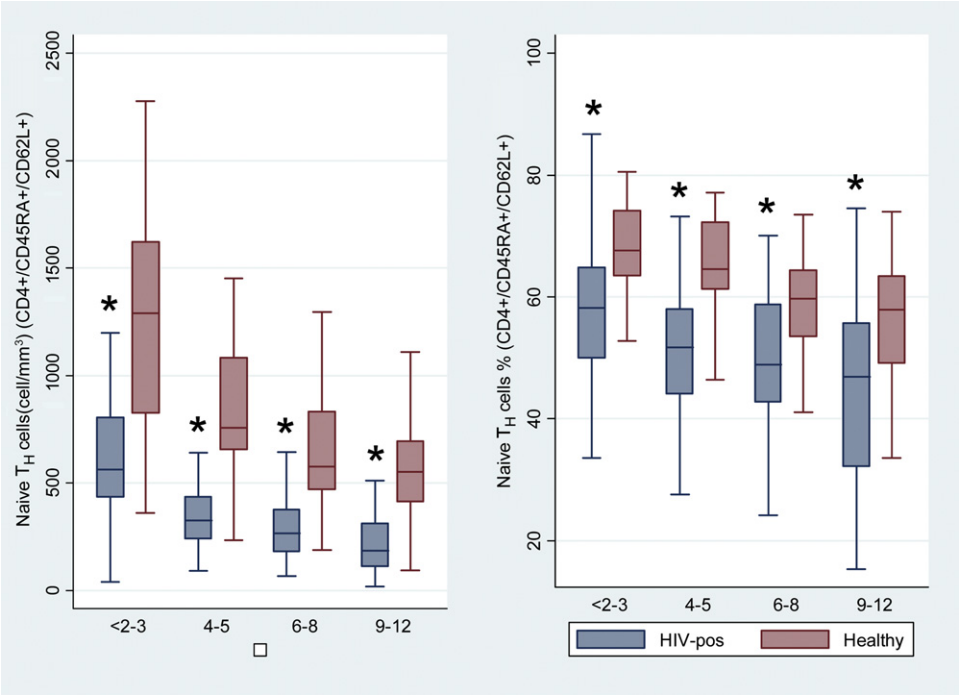

FIG E1. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD4^+/45RA^+/62L^+$ (naive T_H cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

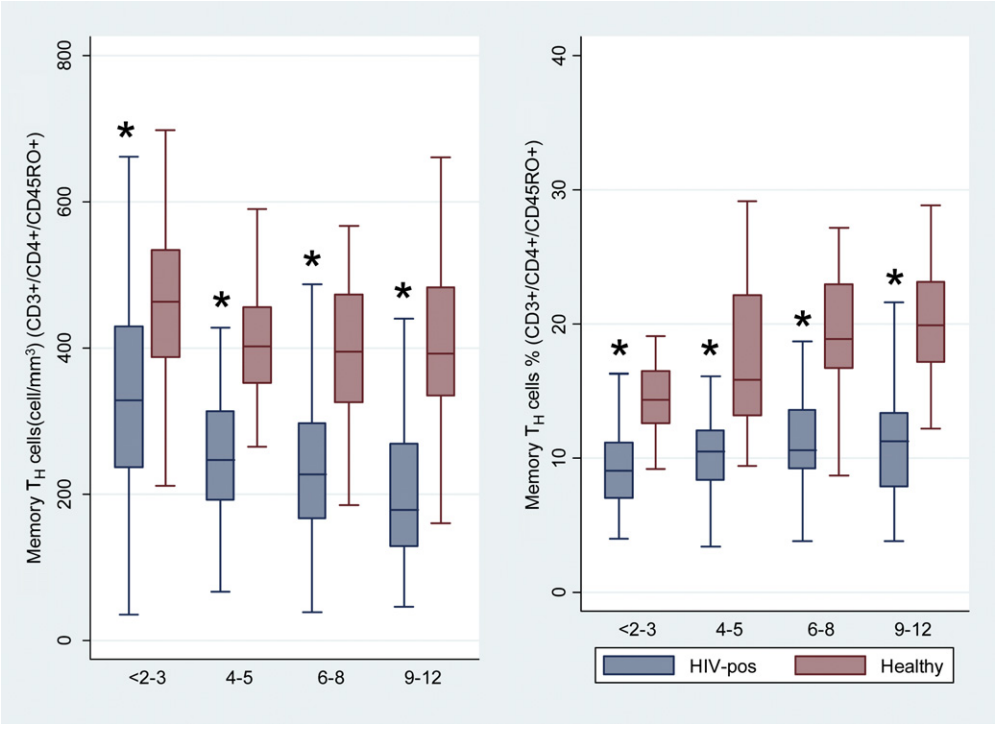

FIG E2. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD3^+/4^+/45RO^+$ (memory T_H cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

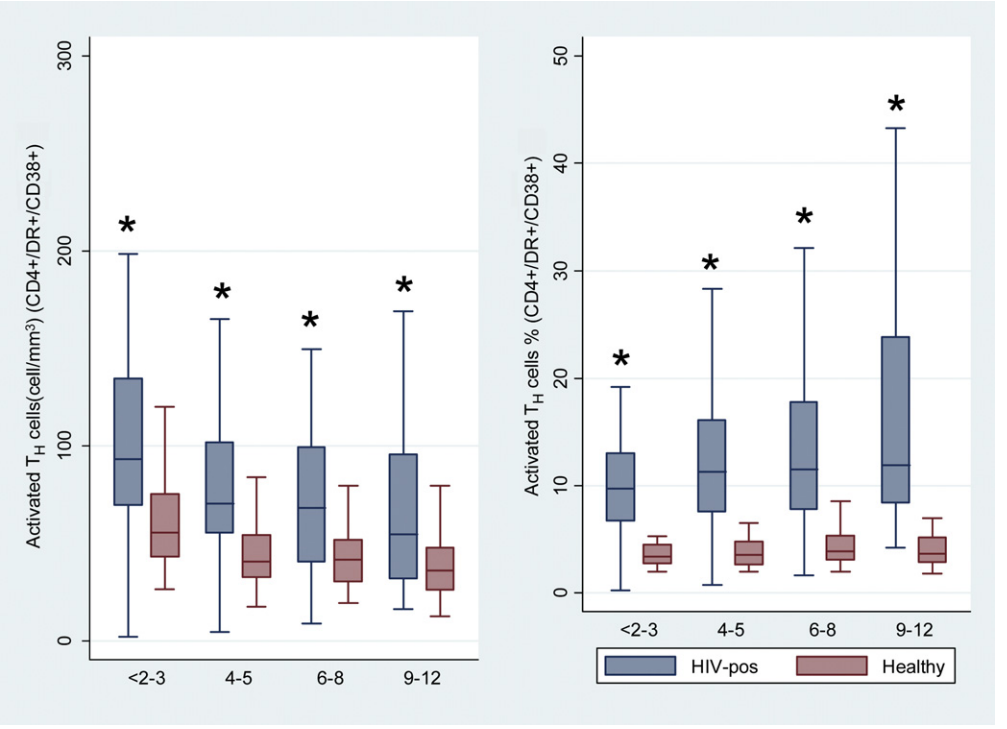

FIG E3. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD4^+/DR^+/38^+$ (activated T_H cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

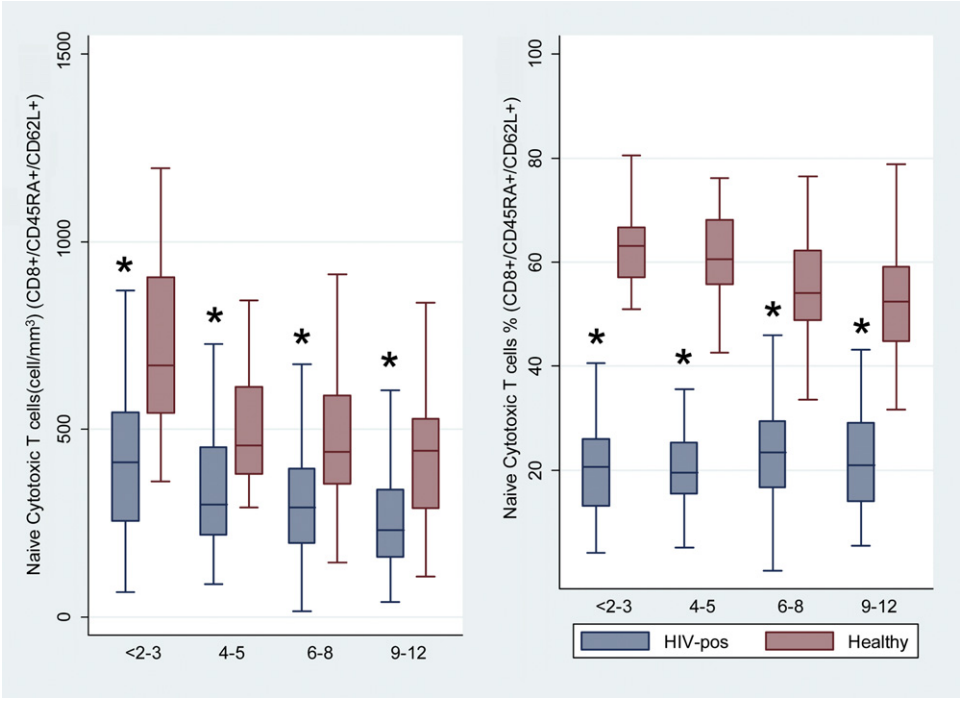

FIG E4. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD8^+/45RA^+/62L^+$ (naive cytotoxic T cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

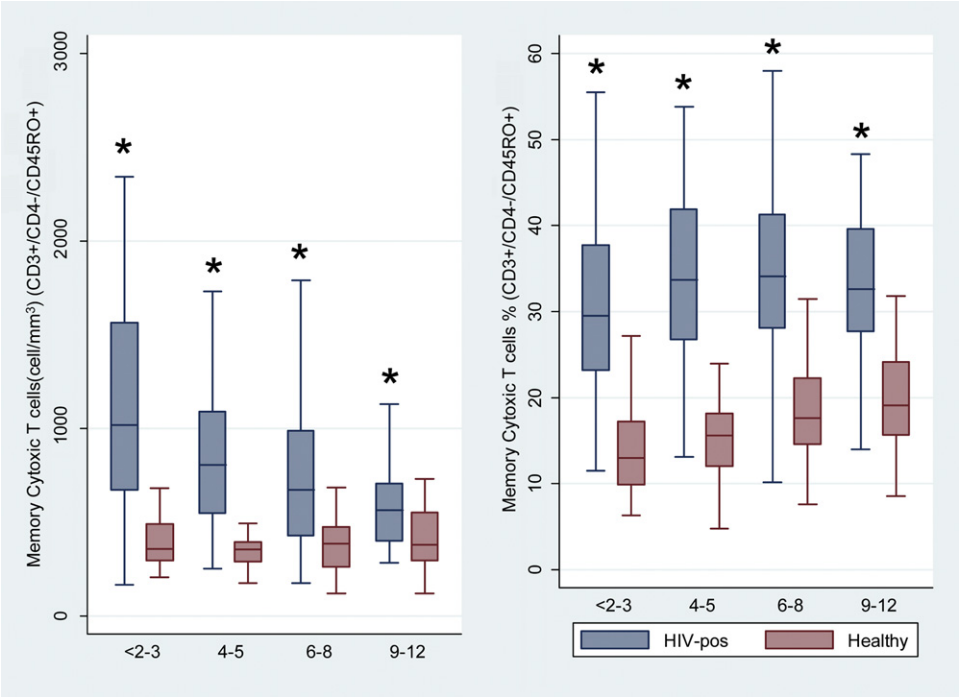

FIG E5. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD3^+/4^-/45RO^+$ (memory cytotoxic T cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

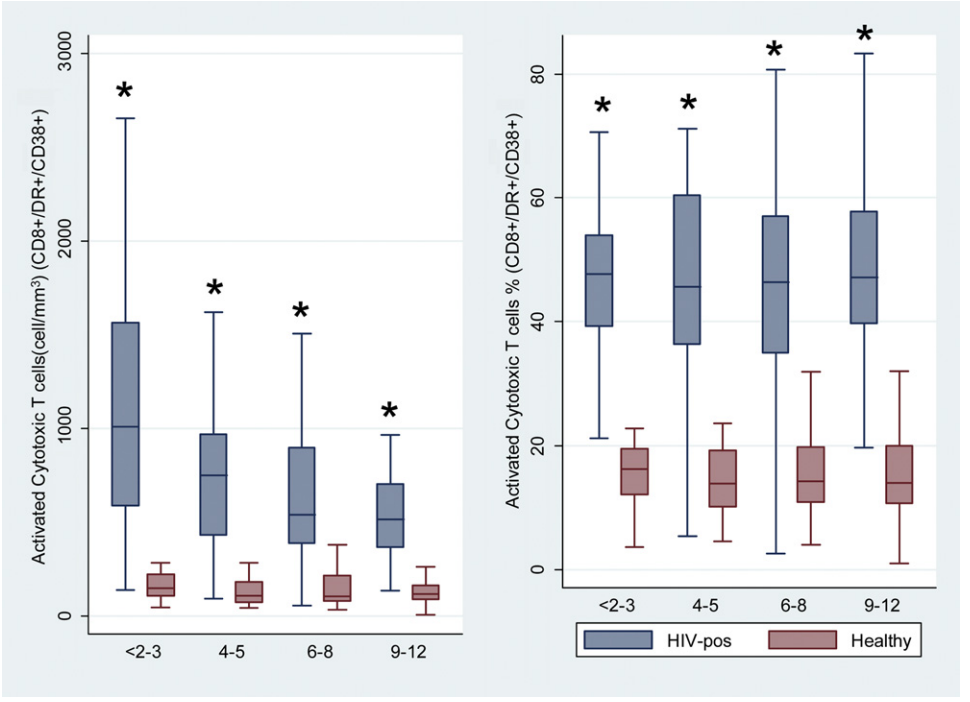

FIG E6. Comparison of cell subsets between HIV-positive and healthy children for 4 age groups. $CD8^+/DR^+/38^+$ (activated cytotoxic T cells). *$P < .05$. No. of children: <2 to 3 years (n = 79), 4 to 5 years (n = 74), 6 to 8 years (n = 135), 9 to 12 years (n = 76). *Pos,* Positive.

TABLE E1. Demographics of LTNPs, non-LTNPs, and healthy controls

Characteristic	LTNPs (n = 50)	Non-LTNPs (n = 17)	Healthy controls (n = 53)
Mean age (y) (SD)	9.7 (1.5)	9.9 (1.1)	10.1 (1.4)
Median age (y) (IQR)	9.0 (8.4-11.0)	9.8 (9.0-10.3)	10.0 (8.8-11.1)
Sex M:F, n (%)	19:31 (38:62)	2:15 (11.8:88.2)	20:33 (37.7:62.3)
Nationality, n (%)			
Thai	42 (84.0)	11 (64.7)	53 (100.0)
Cambodian	8 (16.0)	6 (35.3)	0 (0.0)
CDC class N:A:B (%)	4:66:30	0:71:29	—
Median HIV RNA $\log_{10}$copies/mL (IQR)	4.4 (3.9-4.7)	4.7 (4.4-4.9)	—

F, Female; *M,* male; —, not applicable.

LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 ≥350 cells/mm^3. Non-LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 <350 cells/mm^3. Healthy controls are defined as healthy children age ≥8 years.

TABLE E2. Comparison of cell subset counts among LTNPs, non-LTNPs, and healthy controls

Cell subset	LTNPs (n = 50) (cells/mm^3), median (IQR)	Non-LTNPs (n = 17) (cells/mm^3), median (IQR)	Healthy controls (n = 53) (cells/mm^3), median (IQR)	*P* value (3 gr.)	*P* value (LTNPs vs non-LTNPs)	*P* value (LTNPs vs healthy controls)
Total T cells	2032 (1663-2597)	1186 (1094-1360)	1986 (1616-2367)	<.001	<.001	.4208
T_H cells	575 (417-757)	244 (223-312)	970 (800-1301)	<.001	<.001	<.001
Naive T_H cells	266 (189-417)	107 (70-128)	553 (438-726)	<.001	<.001	<.001
Memory T_H cells	245 (177-290)	129 (90-146)	401 (336-459)	<.001	<.001	<.001
Activated T_H cells	76 (41-115)	36 (26-44)	36 (27-48)	<.001	.0002	<.001
Cytotoxic T cells	1283 (1151-1759)	901 (736-997)	767 (588-1006)	<.001	<.001	<.001
Naive cytotoxic T cells	306 (212-408)	158 (91-192)	419 (290-506)	<.001	.0005	.0063
Memory cytotoxic T cells	734 (543-988)	411 (350-558)	363 (238-530)	<.001	.0004	<.001
Activated cytotoxic T cells	577 (441-895)	416 (362-558)	114 (81-168)	<.001	.0228	<.001
B cells	326 (256-441)	166 (146-231)	432 (363-534)	<.001	<.001	.0005
NK cells	224 (137-411)	137 (95-181)	337 (227-481)	<.001	.0074	.0045
Activated monocytes	33 (15-66) (n = 24)	49 (26-137) (n = 12)	31 (21-50)	.140	.1001	.8863
Perivascular monocytes	16 (6-46) (n = 24)	25 (13-73) (n = 12)	16 (12-23)	.239	.3305	.7167

3 gr., The *P* value signifies any difference between the 3 groups (LTNP, non LTNP and healthy controls). LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 ≥350 cells/mm^3. Non-LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 <350 cells/mm^3. Healthy controls are defined as healthy children age ≥8 years.

TABLE E3. Comparison of cell subset percentages among LTNPs, non-LTNPs, and healthy controls

Cell subset	LTNPs (n = 50) (%), Median (IQR)	Non-LTNPs (n = 17) (%), Median (IQR)	Healthy controls (n = 53) (%), Median (IQR)	*P* value (3 gr.)	*P* value (LTNPs vs non-LTNPs)	*P* value (LTNP vs healthy controls)
Total T cells	74 (68-82)	76 (71-80)	68 (65-72)	<.001	.7458	.0002
T_H cells	20 (17-24)	15 (14-17)	34 (30-39)	<.001	.0002	<.001
Naive T_H cells	49 (40-56)	47 (29-55)	58 (50-63)	<.001	.0751	.0003
Memory T_H cells	12 (9-14)	10 (7-12)	20 (17-23)	<.001	.0705	<.001
Activated T_H cells	12 (7-17)	13 (11-20)	3 (3-5)	<.001	.1710	<.001
Cytotoxic T cells	50 (42-55)	53 (50-56)	27 (23-30)	<.001	.1537	<.001
Naive cytotoxic T cells	24 (15-29)	18 (13-22)	53 (46-60)	<.001	.1622	<.001
Memory cytotoxic T cells	34 (30-40)	32 (26-44)	19 (15-23)	<.001	.6396	<.001
Activated cytotoxic T cells	46 (37-54)	56 (40-69)	14 (11-21)	<.001	.0851	<.001
B cells	12 (9-17)	10 (9-16)	15 (13-17)	<.001	.4322	.0012
NK cells	7 (5-12)	9 (5-10)	12 (9-15)	.005	.9483	.0026
Activated monocytes	7 (5-11) (n=24)	11 (9-18) (n=12)	8 (6-13)	.026	.0149	.1263
Perivascular monocytes	4 (2-8) (n = 24)	6 (3-12) (n = 12)	4 (3-6)	.408	.2021	.9737

3 gr., The *P* value signifies any difference between the 3 groups (LTNP, non LTNP and healthy controls). LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 ≥350 cells/mm^3. Non-LTNPs are defined as antiretroviral-naive, HIV-positive children age ≥8 years with CD4 <350 cells/mm^3. Healthy controls are defined as healthy children age ≥8 years.