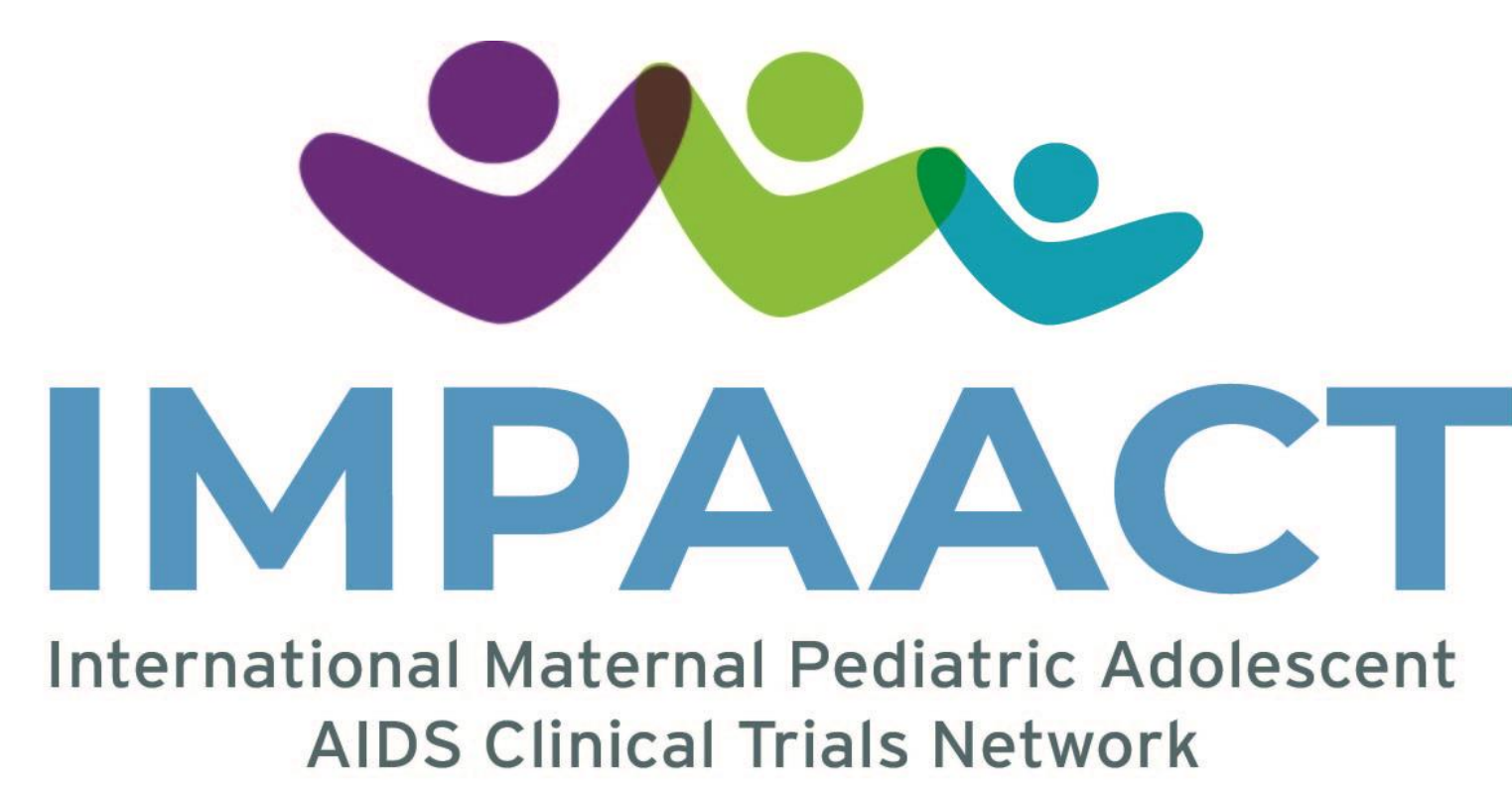


Is Routine PCP Prophylaxis Needed in Very Early-Treated Infants with HIV?



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BACKGROUND

- Global guidelines recommend routine cotrimoxazole (CTX) prophylaxis for the first year of life to prevent *Pneumocystis jirovecii* pneumonia (PCP) in infants with HIV.
- Infants with HIV are increasingly diagnosed and given antiretroviral therapy (ART) shortly after birth, preserving CD4 cell counts and likely reducing risk of PCP.

METHODS

- 54 infants with *in utero* HIV infection followed in the IMPAACT P1115 study of very early ART:
 - Cohort 1 (N=34)** born to high-risk (no ART) mothers enrolled and started nevirapine (NVP)-based ART within 48 hours of birth.
 - Cohort 2 (N=20)** enrolled within 10 days of birth, having been diagnosed with HIV and started an NVP-based regimen outside the study within 48 hours of birth.
- Study ART:** Lopinavir (LPV/r) added when age-appropriate. NVP discontinued 12 weeks after confirmed viral load (VL) below the limit of detection (<LOD).
- CTX given per local guidelines.
- Infants not achieving VL <200 c/mL at 24 weeks or with VL ≥200 c/mL after 24 weeks discontinued from follow-up.
- Virologic Suppression:** VL <200 c/mL at 24 weeks and no confirmed detectable VL thereafter.

TABLE 1. Participant Characteristics

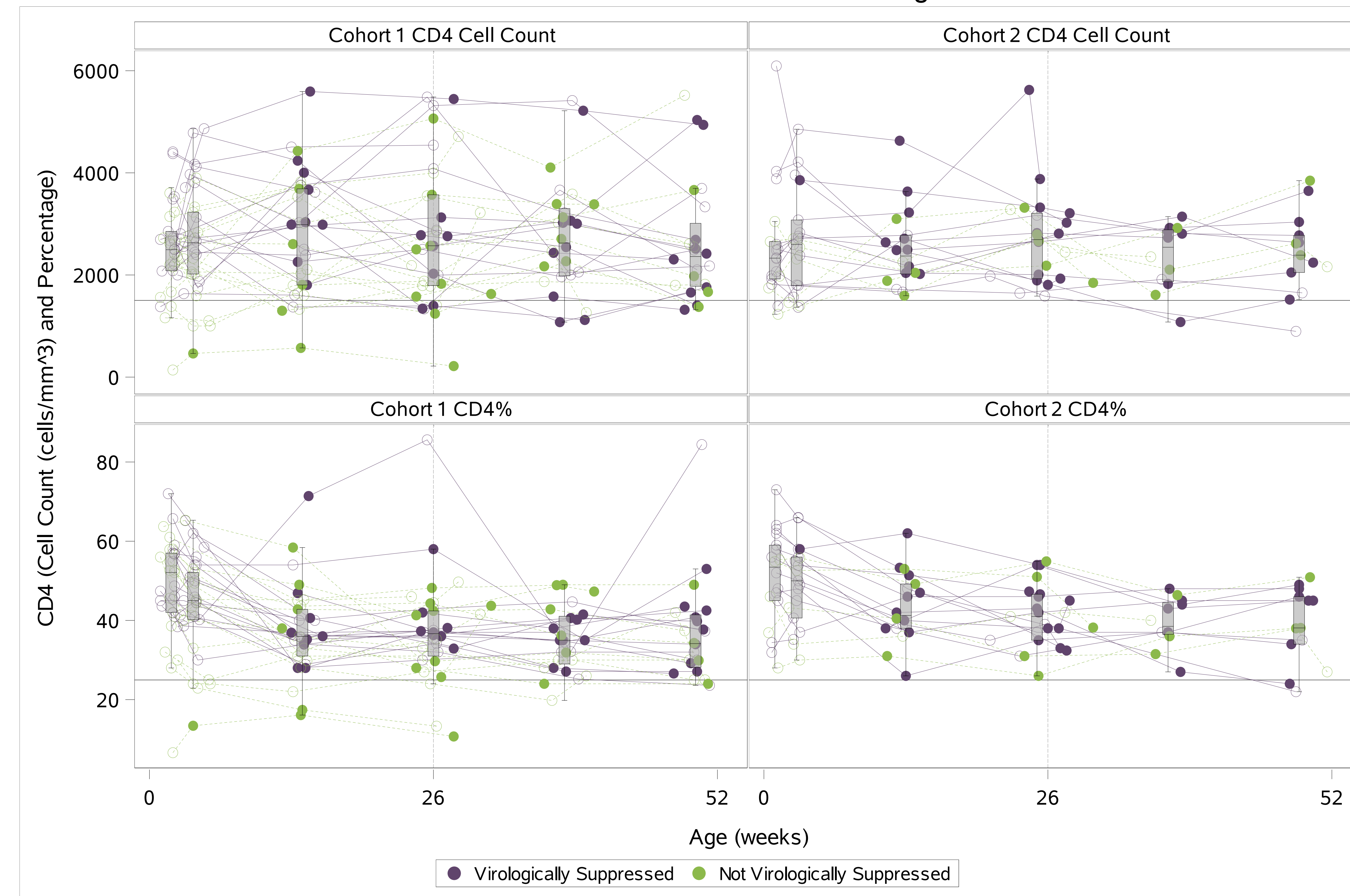
	Cohort 1 (N=34)	Cohort 2 (N=20)
	Median (Q1-Q3) or n (%)	
Female Sex	23 (68%)	10 (50%)
Region		
Africa	33 (97%)	14 (70%)
Asia	1 (3%)	—
North America	—	2 (10%)
South America	—	4 (20%)
Age at Study Entry	22.2 (12.6-32.6) hours	8 (5.5-8) days
Premature (34-<37 weeks Gestational Age)	4 (12%)	2 (11%)
Earliest Weight (kg) ⁽¹⁾	2.7 (2.5-3)	2.7 (2.3-3.3)
Small for Gestational Age ⁽²⁾	9 (27%)	N/A
Earliest VL (log ₁₀ c/mL) ⁽³⁾	4.9 (4-5.3)	4.1 (3.2-5.2)
Earliest CD4 Cell Count (cells/mm ³) ⁽⁴⁾	2458.5 (2080-2789.5)	2330 (1923-2654)
Earliest CD4% ⁽⁴⁾	50.4 (42-57.5)	53.5 (45-59)

⁽¹⁾1 (0-1) days in Cohort 1 and 8 (5.5-8) days in Cohort 2. ⁽²⁾below INTERGROWTH 10th %ile for sex and gest age (N/A in Cohort 2 due to entry age). ⁽³⁾1 (0-1) days in Cohort 1 and 6.5 (2-8) days in Cohort 2. ⁽⁴⁾15 (13-16) days in Cohort 1 [N=32] and 8 (5-8) days in Cohort 2 [N=18].

Most infants with HIV receiving very early ART and achieving viral suppression maintained high CD4 cell count and CD4% through age 1 year.

Guidelines for routine PCP prophylaxis through 1 year of life where malaria or severe bacterial infections are not prevalent warrant re-evaluation.

FIGURE 1. Infant Profile Plots of CD4 Cell Counts and CD4 Percentages



The dashed vertical line corresponds to the week 24 visit, at which point only infants with HIV plasma viral load <200 c/mL continue to be followed. Horizontal lines at 1500 cells/mm³ and 25%. Filled circles indicate participant was on CTX at the time of CD4 measurement. Virologically Suppressed = HIV plasma viral load <200 c/mL at 24 weeks and no confirmed detectable viral load thereafter.

TABLE 2. Proportion of Infants at Each Study Visit with both CD4 Cell Count ≥1500 cells/mm³ and CD4% ≥ 25%

	Cohort 1 (N=34)	Cohort 2 (N=20)
Entry	29 / 33 (88%)	16 / 18 (89%)
Week 2	26 / 29 (90%)	16 / 19 (84%)
Week 12	27 / 33 (82%)	18 / 18 (100%)
Week 24	24 / 32 (75%, 95%CI* 57%-89%)	18 / 18 (100%, 95%CI* 81%-100%)
Week 36**	22 / 26 (85%)	11 / 12 (92%)
Week 48**	18 / 23 (78%, 95%CI* 56%-93%)	10 / 12 (83%, 95%CI* 52%-98%)

*Clopper-Pearson Exact Confidence Interval (CI).

**Only infants maintaining VL<200 c/mL remained on study after week 24.

RESULTS

- The 10th percentile for CD4 cell count (CD4%) ranged from 1340 to 1592 cells/mm³ (24% to 32%) in Cohort 1 and 1390 to 1665 cells/mm³ (24% to 34%) in Cohort 2 over the first year of life (**Figure 1**).
- At weeks 24 and 48, ≥75% in Cohort 1 and ≥83% in Cohort 2 had both CD4 cell count ≥1500 cells/mm³ and CD4% ≥25% (**Table 2**).
- 71% in Cohort 1 and 80% in Cohort 2 initiated CTX and continued for a median of 29.1 and 40.7 weeks.
- There were no cases of PCP.
- 91% in Cohort 1 and 80% in Cohort 2 had ≥1 adverse event on study: primarily infections, anemia or neutropenia; 15% in Cohort 1 and 55% in Cohort 2 had hospitalizations; and 1 death occurred in Cohort 1 due to probable bacterial pneumonia (last CD4 cell count (CD4%) was 3621 cells/mm³ (40%) and last VL was undetectable).

CONCLUSIONS

- Most infants with HIV receiving very early ART and achieving viral suppression maintained high CD4 cell count and CD4% through age 1 year.
- Guidelines for routine PCP prophylaxis through 1 year of life for infants with consistently high CD4 cell count and CD4% in settings where malaria or severe bacterial infections are not prevalent warrant re-evaluation.

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