

Older children with HIV may need to start treatment sooner to normalize future CD4 count

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Although younger children with HIV are at high risk of disease progression if not treated, new research published this week in *PLOS Medicine* indicates that they have good potential for achieving high CD4 counts (a measure of a type of white blood cell that correlates with immune function) in later life provided antiretroviral therapy (ART) is initiated according to current treatment guidelines. However, the research also suggests that the recommended CD4 count thresholds for ART initiation are unlikely to maximize immunological health in children who have never received ART before the age of ten years.

For [children](#) aged 2-3 years, ART initiation is currently recommended once their CD4 count drops below 750 cells/microliter of blood, whereas for older children the threshold for ART initiation is 350 CD4 cells/microliter. Because of improved ART coverage, many more HIV-infected children now survive into adulthood than in the past. It is therefore important to know how the timing of ART initiation in childhood affects long-term immune reconstitution.

The research led by Joanna Lewis from University College London, UK, was an international collaboration and used data collected during the ARROW trial, a study designed to investigate monitoring strategies during first-line HIV treatment in 1,206 HIV-positive children in Uganda and Zimbabwe. In this study the researchers used children's CD4 counts that were collected every 12 weeks for approximately 4 years to analyze how the long-term CD4 count outcomes changed after ART initiation.

In three-quarters of the children, CD4 counts increased rapidly immediately after ART initiation, then slowed before eventually reaching a constant level of about 80% of the CD4 count expected in

an HIV-uninfected child of the same age. Using this data the researchers were able to predict CD4 trajectories for children starting ART at different ages and with different CD4 counts. Higher long-term counts were predicted for children starting ART earlier and with higher CD4 counts. However, using current recommended CD4 thresholds for starting ART in children older than 5 years, lower CD4 counts were predicted when they become adults, such that children who have been infected from childbirth and who remain untreated beyond 10 years of age are unlikely ever to normalize CD4 count, regardless of CD4 count at ART initiation.

The authors conclude, "[o]ur results indicate that although younger ART-naive children are at high risk of [disease progression](#), provided they start ART following current WHO/Paediatric European Network for Treatment of AIDS/US Centers for Disease Control and Prevention guidelines, they have good potential for achieving high CD4 levels in later life. However, to attain maximum immune reconstitution in older children, particularly those >10 y, ART may need to be initiated regardless of CD4 cell count."

More information: Picat M-Q, Lewis J, Musiime V, Prendergast A, Nathoo K, et al. (2013) Predicting Patterns of Long-Term CD4 Reconstitution in HIV-Infected Children Starting Antiretroviral Therapy in Sub-Saharan Africa: A Cohort-Based Modelling Study. *PLoS Med* 10(10): e1001542. [DOI: 10.1371/journal.pmed.1001542](https://doi.org/10.1371/journal.pmed.1001542)

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