# Spectrum: Methods for Estimating HIV among Children

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New HIV infections among children due to vertical transmission are calculated on the basis of the proportion of HIV+ mothers and children receiving prophylaxis and the effectiveness of each prophylaxis regimen as described in a companion document to this one: “Spectrum: Methods for Estimating Mother-to-Child Transmission.”

## Progression from infection to AIDS death

In the absence of ART and cotrimoxazole prophylaxis, children infected through vertical transmission progress over time to AIDS death according to a Weibull pattern. Different progression patterns are used for children infected perinatally and those infected 0-6 months, 7-12 months and >12 months postpartum through breastfeeding. Analysis of data from sub-Saharan Africa shows distinct survival patterns for these four groups[[1]](#footnote-1),[[2]](#footnote-2). The patterns used in Spectrum are shown in Figure 1.

Figure 1. Percent of Children Survival by Years Since Infection



## Eligibility for ART

[Note: This discussion is taken from the previous methods paper on ART parameters[[3]](#footnote-3).]

Eligibility for treatment can be defined in terms of three criteria: (1) a specific age below which all HIV+ children are eligible for treatment, (2) CD4 percent, and (3) CD4 count. The default settings in Spectrum reflect the timing and criteria of the WHO guidelines as they have been implemented. From 2000 until 2006 eligibility for ART among children was based on a graduated CD4 cell count or percent depending on age (see Table 1). From 2007-2009 the guidelines included as eligible that all children identified as HIV-positive under 12 months of age. In 2010 the WHO published guidelines recommending that all children under 24 months be provided with ART and children ages 24 - 59 months were eligible for ART if their CD4 count was less than 750[[4]](#footnote-4).

Table 1. ART eligibility criteria for children in Spectrum

|  |  |  |  |
| --- | --- | --- | --- |
|  | 2000-2006 | 2007-2009 | 2010-2015 |
| Age below which all HIV+ children receive treatment (months) | 0 | 12 | 24 |
| **CD4 count threshold for eligibility** | |  |  |
| Age < 11 months | 1,500 | 1,500 | 750 |
| Age 12-35 months | 750 | 750 | 750 |
| Age 35-59 months | 350 | 350 | 750 |
| Age >= 5 years | 200 | 200 | 350 |
| **CD4 percent threshold for eligibility** | |  |  |
| Age < 11 months | 25 | 25 | 25 |
| Age 12-35 months | 25 | 25 | 25 |
| Age 35-59 months | 25 | 25 | 25 |
| Age >= 5 years | 15 | 15 | 15 |

Spectrum estimates the proportion of HIV-infected children eligible for treatment by using patterns of the distribution of HIV-infected children by CD4 count or CD4 percent. These patterns were derived from the HIV Paediatric Prognostic Markers Collaborative Study (HPPMCS) which took place in western countries before ART was available. The study included a meta-analysis of individual longitudinal data on 3,941 HIV-1 infected children enrolled in cohort studies and randomized control trials in the USA and Europe. Care was taken to avoid using the same children in multiple studies[[5]](#footnote-5).

The distribution of CD4 count and percentage CD4+ from HPPMCS provide a basis by which to progress children from birth to need for treatment in the Spectrum model. All HIV-infected children less than one year old are assigned the CD4 distributions from the HPPMCS. The patterns in Figure 2 were used to calculate the proportion of HIV-infected children at each age and CD4 category that remain in the same CD4 category the following year or drop down to a lower CD4 category. Thus, Spectrum reproduces these patterns in the absence of ART and the number of children eligible for ART at any age can be easily determined based on the country-specific eligibility criteria. As ART coverage increases children are drawn from the eligible categories leaving an altered distribution of HIV-infected children who are not on ART.

Figure 2a. Distribution of HIV+ Children by CD4 Percent and Age



Figure 2b. Distribution of HIV+ Children by CD4 Count and Age



**Survival on ART**

In 2008, Dabis and colleagues conducted a literature review on child survival on ART in lower-income countries on behalf of UNICEF. Articles were selected after screening of PubMed/MEDLINE and Scopus up to March 2008 and abstracts of 2007-2008 international conferences. Observational cohorts, clinical trials and programme reports were eligible as long as they took place in lower income countries and included children on ART or on ART and cotrimoxazole. Only studies with death as the outcome were included in this pediatric ART review update. The extracted data included patients demographic characteristics, baseline CD4 count, survival estimates and factors associated with mortality of children receiving cotrimoxazole and/or ART. A total of 14 prospective studies were eligible for the analysis[[6]](#footnote-6).

The amount of data on the survival of HIV-infected children on ART in lower and middle income countries more than doubled since a previous review that covered a period ending in December 2006[[7]](#footnote-7). Sample sizes were generally larger, exceeding 400 participants for some of the studies, thereby increasing the accuracy of the findings. Some reports allowed for the production of survival estimates up to 24 months after ART initiation.

The authors concluded that the probability that infants survive the first year of treatment was estimated to be 0.93-0.95 and survival until two years was estimated to be 0.91-0.92. The authors estimated that the provision of cotrimoxazole along with ART additionally reduced mortality of approximately 32% in the first year, 16% in the second year, and 8% in the third year.

**Loss to follow-up on ART**

The above study also compiled available data on loss to follow-up among children. Very little data were available at the time of finalizing the Spectrum model. Rough estimates were thus incorporated in the model. The model assumes that an estimated 10% of children were lost to follow-up and among those, 50% were expected to have died within one year. A recently conducted comparative analysis of loss to follow-up data of children on ART by region of the world indicated that the 18-month crude probability of loss to follow-up was 5.6% in Asia, 17.8% in East Africa, 23.2% in Southern Africa and 24.3% in West Africa (p<0.0001). This study was performed on 15,113 children on ART in the context of the IeDEA initiative[[8]](#footnote-8).

After adjusting for the reduced mortality due to the use of cotrimoxazole, the estimated survival among those children who started on ART was 85% in the first year on ART and 93% for subsequent years.

1. Becquet R and UNAIDS Child Survival Working Group. Survival of Children HIV-infected Perinatally or Through Breastfeeding. A Pooled Analysis of Individual Data from Sub-Saharan Africa. The 17th Conference on Retroviruses and Opportunistic Infections, San Francisco, USA, 2010. Paper # 840 (http://www.retroconference.org/2010/PDFs/840.pdf). [↑](#footnote-ref-1)
2. Marston M, Becquet R, Zaba B, Moulton LH, Gray G, Coovadia H, *et al.* Net survival of perinatallly and postnatally HIV-infected children: a pooled analysis of individual data from sub-Saharan Africa, forthcoming. [↑](#footnote-ref-2)
3. Mahy M, Lewden C, Brinkhof M, Dabis F, Tassie JM, Souteyrand Y, Stover J. Derivation of parameters used in Spectrum for eligibility for antiretroviral therapy and survival on antiretroviral therapy *Sec Trans Infect* 2010 86: ii28-ii34 doi: 10.1136/sti.2010.044255. [↑](#footnote-ref-3)
4. Wold Health Organization. Antiretroviral Therapy of HIV Infection in Infants and Children: Recommendations for a public health approach. Geneva: World Health Organization, 2010. http://www.who.int/hiv/pub/guidelines/paediatric020907.pdf. Accessed on: 16 August 2010 [↑](#footnote-ref-4)
5. Dunn D. Short-term risk of disease progression in HIV-1-infected children receiving no antiretroviral therapy or zidovudine monotherapy: a meta-analysis. Lancet 2003;362(9396):1605-11. [↑](#footnote-ref-5)
6. UNAIDS, World Health Organization, UNICEF. Consultative meeting on Data Collection and Estimation Methods Related to HIV Infection in Infants and Children. New York: UNICEF, 2008. http://www.epidem.org/Publications/UNAIDS\_UNICEF\_Paediatric%20HIV%20Report\_9%20Dec%202008\_Final.pdf. Accessed on: 18 March 2010 [↑](#footnote-ref-6)
7. Coffie P, Moh R, Ekouevi DK, et al. Survival of HIV-infected adults and children on antiretroviral therapy in low and middle-incomes countries. Bordeaux: Institut de Santé Publique, Epidémiologie et Développement (ISPED) Université Victor Segalen 2007. [↑](#footnote-ref-7)
8. Leroy V, Malateste K, Rabie H. 18-Month mortality and loss to follow-up in ARTtreated children in Asia and Africa. XVIIIth International AIDS Conference, Vienna, Austria, 18-23 July, 2010 [↑](#footnote-ref-8)