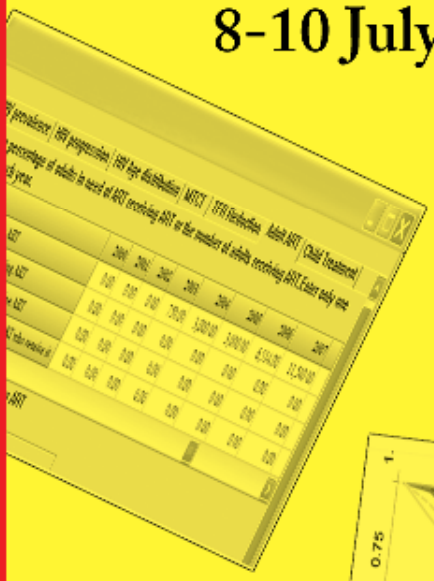
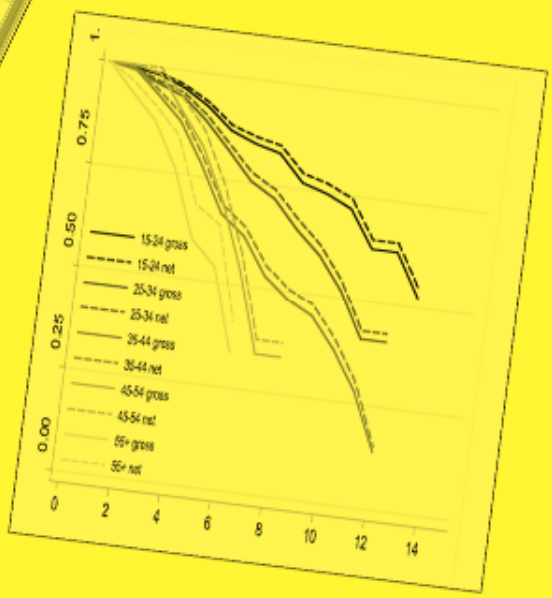
Consultative Meeting on
Data Collection and Estimation Methods *Related to* HIV Infection in Infants and Children

8-10 July 2008, New York





UNAIDS unicef World Health Organization

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Acronyms

AIDS	Acquired immune deficiency syndrome
ARV	Antiretroviral drug
ART	Antiretroviral therapy
CDC	United States Centers for Disease Control and Prevention
CHERG	Child Health Epidemiology Reference Group (World Health Organization)
CPV	Conjugate pneumococcal vaccine
CTX	Co-trimoxazole
DHS	Demographic and Health Surveys
EPP	Estimation and Projection Package
FHI	Family Heath International
FXB	François-Xavier Bagnoud Center
GAVI	Global Alliance for Vaccines and Immunization
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human immunodeficiency virus
IATT	Interagency Task Team
INH	Isoniazid
LINCs	Lower-income countries
MICS	Multiple Indicator Cluster Surveys
MTCT	Mother-to-child transmission of HIV
M&E	Monitoring and evaluation
sdNVP	Single dose nevirapine
PCP	*Pneumocystis jiroveci* pneumonia (formerly *Pneumocystis carinii* pneumonia)
PMTCT	Prevention of mother-to-child transmission of HIV
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNGASS	United Nations General Assembly Special Session
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Executive Summary

Accurate data describing the impact of HIV on children, disease progression — including HIV-related morbidity and mortality and need for treatment — are crucial for advocacy, accountability, fundraising, and programme planning at regional and country levels. On 8-10 July 2008, UNICEF, WHO and the UNAIDS Reference Group on Estimates, Modelling and Projections hosted the Consultative Meeting on Data Collection and Estimation Methods Related to HIV Infection in Infants and Children to review data collection and estimation methods, and to address the need for improving the HIV estimation methods and process as well as the availability of direct data on children.

The tools currently in use for HIV and AIDS estimation in children are based on the recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections and include the Estimation and Projection Package (EPP), Workbook, and Spectrum. The meeting recommended changes to the current methods and parameter estimates, key recommended changes include the following:

- Track separately (in the model) children infected perinatally versus those infected through breastfeeding
- Calculate directly the reduction in mother-to-child transmission (MTCT) due to antiretroviral therapy (ART)
- Update default MTCT rates according to infant feeding practices and ARV prophylaxis
- Update default annual survival probabilities for children on ART and on co-trimoxazole
- Update the method used to calculate the number of children in need of ART, as per the recently revised WHO paediatric treatment guidelines

The meeting made recommendations for improved data collection and research:

- Support the strengthening of countries' monitoring and evaluation systems through mechanisms that include the Interagency Task Team (IATT), the IATT Monitoring and Evaluation (M&E) Working Group, and during Joint Technical Missions
- Expand information reported related to child diagnosis and treatment: age at initiation of ART and of those on ART, CD4 level at initiation, overlap of ART and co-trimoxazole use, second line ART
- Encourage and support research in the following areas: the effect of ART on fertility, the effect of maternal HIV-related mortality and disease on the survival of their HIV-negative children, the effect of ART on MTCT rates, the effect of ART on child survival, the effect of co-trimoxazole on child survival, and child HIV infection not explained by MTCT
- Conduct an analysis of the proportion of child mortality directly caused by HIV

Finally, the meeting made recommendations to strengthen national estimation processes and international monitoring and evaluation reporting:

- Include government counterparts knowledgeable about monitoring and evaluation data for PMTCT and child care and treatment programmes, as well as UN and other IATT partners in training for EPP and Spectrum
- Strengthen the quality and ownership of child HIV and AIDS estimates by promoting an in-country consensus process convened by the UNAIDS monitoring and evaluation advisors and supported by all stakeholder organizations; and by building the capacity of regional institutions

Introduction

HIV continues to have a significant impact on children. The UNAIDS 2008 Report on the Global AIDS Epidemic estimates that the number of children (0 through 14) living with HIV was just over 2,000,000 in 2007, nearly 90% of these children (1.8 million [1.7 – 2 million]) lived in sub-Saharan Africa. Even though HIV prevalence in children continues to increase, the number of new HIV infections appears to have peaked in 2000–2002. In 2007 there were 370,000 [330,000-410,000] new infections in children compared to 460,000 [420,000-510,000] in 2001. Interestingly, the percentage of children living with HIV out of all people living with HIV increased from 5.4% in 2001 to 6.1% in 2007.

The estimated number of child deaths due to AIDS peaked in 2003 and declined to about 290,000 for 2007 — more than 90% of them in sub-Saharan Africa. This is believed to be due mainly to the stabilization of HIV prevalence among women overall, and to increasing coverage of programmes for preventing mother-to-child transmission of HIV.

Table 1: Children (0–14) living with HIV by region, 2007.

Region	Number[1]	% of global total[2]
Caribbean	11,000 [9,400 – 12,000]	0.5% [0.4-0.6%]
East Asia	7,800 [5,300 – 11,000]	0.4% [0.2-0.6%]
Eastern Europe & Central Asia	12,000 [9,100 – 15,000]	0.6% [0.4-0.8%]
Latin America	44,000 [37,000 – 58,000]	2.2% [1.6-3.1%]
Middle East & North Africa	26,000 [18,000 – 34,000]	1.3% [0.8-1.8%]
North America	4,400 [2,600 – 7,300]	0.2% [0.1-0.4%]
Oceania	1,100 [1,200]	0.1% [<0.1%]
South & South East Asia	140,000 [110,000 – 180,000]	6.9% [4.8-9.5%]
Sub-Saharan Africa	1,800,000 [1,700,000 – 2,000,000]	87.8% [74-100%]
Western and Central Europe	1,300 [<1,000 – 1,800]	0.1% [<0.1%]
Global	2,000,000 [1,900,000 – 2,300,000]	100%

Reasonably accurate data regarding the impact of HIV on children, including mother-to-child transmission (MTCT), disease progression including HIV-related morbidity and mortality and need for treatment is crucial for advocacy, accountability, fundraising, and programme planning at regional and country levels.

Currently there is a lack of direct data on HIV in children. Sentinel surveillance among children is currently not recommended. Case reporting for AIDS and HIV infection is believed to be grossly underestimating the actual burden of disease and infection. Only

1 UNAIDS. 2008 Report on the global AIDS epidemic, Annex 1. Available at: http://www.unaids.org/en/KnowledgeCentre/HIVData/GlobalReport/2008/

2 Ghys, Peter. "Latest child estimates and trends through 2007 (UNAIDS)." Unpublished presentation July 2008

four countries have so far included children below the age of 15 years in national surveys with HIV prevalence measurement. HIV estimates for children are currently presented for the 0 through 14 year age group, while the international definition of children includes those up to the age of 17 years.

UNICEF, WHO and the UNAIDS Reference Group on Estimates, Modelling and Projections hosted the Consultative Meeting on Data Collection and Estimation Methods Related to HIV Infection in Infants and Children to review data collection and estimation methods to address the need for improving the HIV estimation methods and process as well as the availability of direct data on children.

Consultation Participants

The meeting included 41 leading experts in data collection and estimation methods related to HIV in children. Participants represented UNAIDS, UNICEF, WHO, CHERG; others attended as experts in modelling, epidemiology, clinical health or research. The meeting included representatives from countries with a general HIV epidemic (Kenya and Uganda) and countries/regions with concentrated HIV epidemics (Brazil, Central and Eastern Europe, and Cambodia), as well as other stakeholders and experts in the field. The list of participants is included as Appendix 1.

Consultation Goal, Objectives and Expected Outcomes

Goal

- To review the current methods, inputs and assumptions used for the generation of paediatric HIV estimates as well as the data available and data collection methods with the aim to improve the quality of paediatric HIV estimates.

Objectives of the consultation

- To review the current UNAIDS/WHO methods, inputs and assumptions used for the generation of PMTCT and paediatric HIV estimates including the number of children living with HIV, new infections, deaths due to AIDS, the need for PMTCT, ART and co-trimoxazole.
- Review new scientific and programmatic data that may result in improvements of the estimation methods and assumptions.
- Review current and proposed data collection methods on HIV among children.
- Review current and potential mechanisms to improve the quality of countries' national paediatric HIV estimates.

Expected outcomes of the meeting

- A summary of the current modelling processes, including assumptions and inputs used to generate the estimates.
- A summary of all new scientific and programme data relevant to estimations of HIV in children, including MTCT rates, and disease progression and response to care and treatment in children.
- Recommendations for UNAIDS/WHO and UNICEF on how to improve the estimation methods for estimates of children living with HIV, new infections among children, AIDS deaths among children, children in need of ART, children in need of co-trimoxazole, women needing PMTCT, etc.
- Recommendations to UNAIDS/WHO and UNICEF on data collection strategies with a specific focus on surveillance and surveys.
- Recommendations for UNAIDS/WHO and UNICEF on how to strengthen national processes and data inputs that underpin national and international estimations.

Workshop Methodology

The workshop included presentations, time for question and discussion, and group work. The workshop agenda is in Appendix 2.

- Presentations: each day's proceedings included presentations on topics covering current methods, processes and results; new data, including survival with treatment and prophylaxis; and non-MTCT transmission. Presentations were provided as background or as updates.
- Group work: there were 3 group sessions — one per day — during which participants divided into two smaller groups based on area of interest. The group sessions provided opportunity for participating experts to discuss key issues. The groups presented their findings in plenary sessions that followed the group meeting.
- Question and discussion: followed both the presentations and group work presentations. The question and discussion sessions were limited to approximately 10 to 30 minutes and moderated by the session chair.

Presentation Summaries and Recommendations from Sessions

1. Current approaches to estimations and projections

1.1. Summary of Presentations

The global community relies on UNAIDS/WHO for HIV-related estimates, both for adults (age 15 and above) and children (age 0 through 14). The tools that have been developed to support estimation methodology are based on the recommendations of the UNAIDS Reference Group on Estimates, Modelling and Projections (hereafter referred to as the "UNAIDS Reference Group") and include the EPP, Workbook, and Spectrum.[3] The EPP is used to estimate and project adult HIV prevalence from surveillance data. While EPP can be used in all countries with sufficient surveillance data, it is currently specifically recommended for countries with generalized epidemics. The input to EPP in countries with generalized epidemics is surveillance data from various sites and years showing HIV prevalence among pregnant women, as well as data from national population-based surveys. EPP is used to fit a simple epidemic model to data from urban and rural sites.

For countries with low level or concentrated epidemics surveillance data collected from populations at high risk (commercial sex workers, men who have sex with men, injecting drug users) and at lower risk, is combined with estimates of the size of these populations in a simple spreadsheet model (the Workbook Method)[4] or EPP to find the best fitting curve that describes the evolution of adult HIV prevalence over time. For both generalized and low/concentrated epidemics, adult prevalence estimates — along with national population estimates and epidemiological assumptions — are entered into the Spectrum software program to calculate the number of people living with HIV, new HIV infections, deaths due to AIDS, orphans due to AIDS, adults and children in need of antiretroviral therapy (ART), children in need of co-trimoxazole, and pregnant women in need of PMTCT.

UNAIDS, in collaboration with the UNAIDS Reference Group, WHO, UNICEF, World Bank (2007), CDC, GFATM (2007), Futures Institute, East-West Center, FHI and United States Census Bureau — hosted Regional Estimation Training Workshops in all regions in 2003, 2005 and 2007 and provided in-country assistance to support countries to undertake their own estimates. Workshop participants use the software and country data

[3] UNAIDS. "AIDS epidemic update: December 2007". Available at: http://data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en.pdf. See also: http://www.unaids.org/en/KnowledgeCentre/HIVData/Epidemiology/episoftware.asp

[4] See http://www.unaids.org/en/KnowledgeCentre/HIVData/Epidemiology/epi_software2007.asp

to produce analyses and estimates for their country. These draft estimates are then discussed in country before being finalized. This year's estimates included reconciliation with ART numbers for adults and children as well as PMTCT coverage.

Although the process has the advantage of improved methodology, software tools and training materials as well as greater in-country capacity, there are still a number of challenges:

- Timing of available coverage data, both PMTCT and ART, may not coincide with timing of estimates.
- There are multiple data sources that need to be collated and reconciled.
- In-country PMTCT and paediatric ART experts are typically not present at regional training workshops.
- Although agencies are given deadlines to collate numbers, delays in receipt of data can lead to delayed report submission.[5]

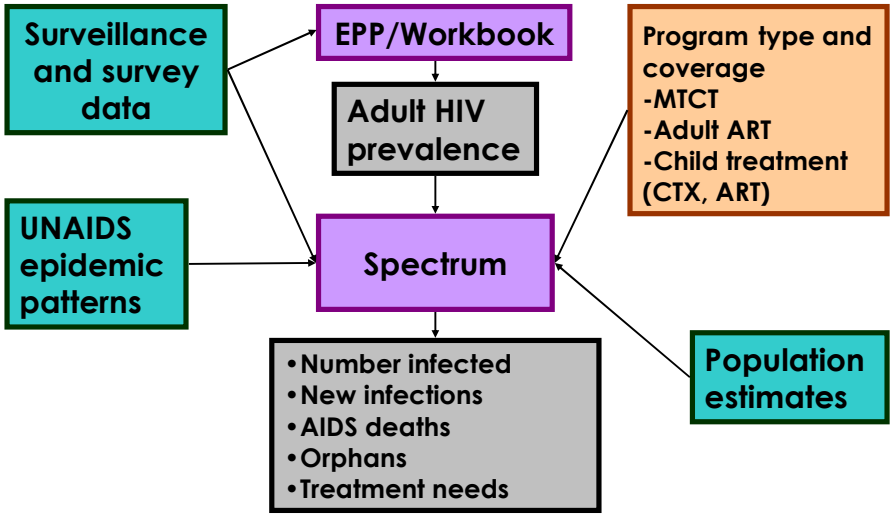
The current model calculates estimates and projections of children with HIV and child deaths from HIV disease by using the Spectrum software package in which the following information is input:

- Demographic (obtained from United Nations Population Division)
    - Population by sex and age over time
    - Births to HIV-positive women — derived from total fertility rates and age distribution of fertility for the general population and adjusted based on the assumption that women with HIV who are young (age 15 through 19 years) have a 50% increase in fertility and women age 20 through 49 have a 30% decrease in fertility (in comparison to HIV-negative women) due to HIV and previous sexually transmitted infections.
    - Mortality rate
- Epidemiological
    - HIV prevalence over time
    - Sex ratio of HIV prevalence
    - Number of HIV-positive pregnant women covered by PMTCT programmes including antiretroviral (ARV) prophylaxis and infant feeding
    - Number of HIV-positive women receiving ART
    - Probability of infection from mother to child
    - Survival distribution from infection with HIV to death among children
    - Number of HIV-positive children receiving ART treatment and co-trimoxazole prophylaxis

Figure 1 summarizes the inputs into the Spectrum software package.[6]

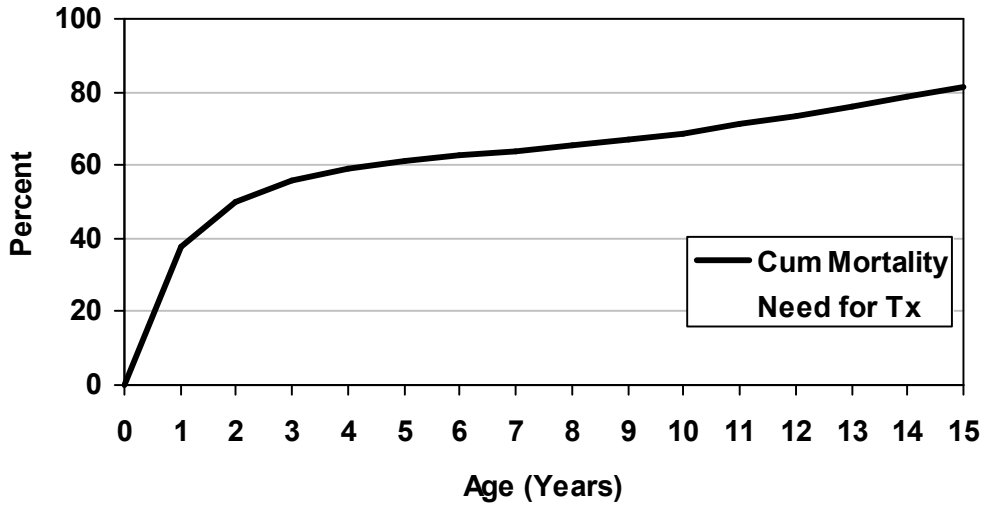
[5] Stanecki, Karen for the UNAIDS/WHO Working Group on Global HIV/AIDS & STI Surveillance. "HIV and AIDS Estimates: Country Process and Dissemination." Unpublished presentation July 2008

Figure 1: Approach to estimates and projections



The double Weibull curve that is currently used in Spectrum represents the net survival (HIV only) of HIV-infected children from birth and takes into account that there are fast and slow progressors (see the curve in Figure 2, below).[7]

Figure 2: Progression from New Infection to AIDS Death



6 Stover, John. "Current Assumptions and Data Sources Within Spectrum to Model PMTCT Needs and Child HIV Estimates." Unpublished presentation July 2008.

7 Marston, Milly. "Child mortality: development of a functional representation for net mortality due to HIV." Unpublished presentation July 2008.

1.2. Recommendations

1.2.1. Recommendations to improve methods for estimates and projections

- Consider changing the age-specific effect of HIV on fertility in Spectrum. It is likely that the impact of HIV on fertility increases with time since infection and/or age. The assumption that HIV-infected women aged 20 through 49 have a 30% decrease in fertility, probably overestimates infertility in women in their 20s and overestimates fertility for those in their 40s. To investigate this, an analysis of birth histories will be undertaken of those with and without HIV — disaggregated by age and reported contraceptive use — from demographic and health surveys (DHS). As it is not possible to know when an HIV-positive woman was infected, it is necessary to use information from her most recent pregnancy. Populations with lower reported use of contraception will provide a truer picture of the effect of HIV. The review should also consider assessing fertility rates by CD4 (a surrogate marker for number of years infected and probability of MTCT).
- Implement in Spectrum the possibility to modify the number of births to HIV-positive pregnant women, by inputting information about termination of pregnancy (in some populations pregnant women with HIV are more likely to terminate their pregnancy).
- Separate in Spectrum inter-partum/in utero acquired HIV from that acquired postpartum, and apply two separate net survival curves to these two separate categories of HIV-positive children. Currently it is assumed in Spectrum that all children are infected at age 0; for children infected through breastfeeding it should be changed to a non-zero age.
- Implement in Spectrum a changing proportion over time of diagnoses using virological testing instead of the current all or nothing assumption.
- Encourage countries that have undertaken an evaluation of PMTCT effectiveness to enter their own estimates of vertical transmission in Spectrum (rather than using the Spectrum default settings).
- In Spectrum, specify the number of pregnant women receiving ART for their health using data from the PMTCT programme rather than that from the HIV care clinics (at present Spectrum applies the treatments rates of the general female population to pregnant women). However, studies have suggested that pregnant women are *less* likely to be on ART due to both recency of diagnosis and failure of PMTCT programmes to refer them for HIV-related care. Although ART coverage in Spectrum increases with age — meaning that younger women, who are generally more likely to be pregnant, are assumed to be less likely to be on ART — the participants in the Consultative Meeting agreed that Spectrum should discontinue applying general population ART coverage rates to pregnant women to estimate MTCT.

1.2.2. Recommendations on data collection and research

- Track children's age at diagnosis to provide a better understanding of the timing of infection via breastfeeding and the proportion of infant/child infections acquired

postpartum, including during ARV prophylaxis scale-up. Tracking age at diagnosis during the scale-up of the revised WHO guidelines, will allow monitoring of the effect of the new guidelines on the fast versus slow progressors to test the hypothesis that early treatment could blur the effect of timing of infection.

- Review data on the impact of ARVs on fertility: some reports suggest that women on ART also experience an increase in fertility, but it is unclear how universal and large this effect is.
- Collect and analyse data on mortality of HIV-negative children of HIV-positive mothers, which is known to be higher than mortality of the children who have HIV-negative mothers. In some countries HIV-infected children may have higher rates of non-HIV deaths because they are born into socially disadvantaged settings.
- Review and update estimates of the proportion of child mortality directly caused by HIV.

2. MTCT transmission rates by ARV prophylaxis regimens and by breastfeeding patterns

2.1. Summary of Presentations[8,9]

Breastfeeding continues to be an important source of MTCT, increasing risk of transmission from mother-to-child by 3% (for women who breastfeed exclusively) to 10.5% for infants who are mixed fed. Estimations of postpartum HIV transmission rely on the prevalence of exclusive breastfeeding, replacement feeding and mixed feeding.

Infant feeding practices: Key sources of information on infant feeding method in high prevalence countries are contradictory. UNICEF's 2007 Report Card found that 64% (12,100/19,000) of HIV-exposed infants in 47 countries (18 of which were in sub-Saharan Africa) were exclusively breastfed in 2007. Thirty-nine per cent (7,400) of the 19,000 infants received replacement feeding and less than 1% (<50) reported being mixed fed in 2007. This low percentage of mixed fed infants is not supported by population-based surveys and likely to be grossly underreported due to country definitions of mixed feeding. Population-based surveys from 35 countries, accounting for 94% of HIV-positive pregnant women in low- and middle-income countries, found that rates of exclusive breastfeeding till 6 months and exclusive replacement feeding is quite low and most women practice mixed feeding (see Appendix 3). The population based surveys are assumed to provide a more accurate picture than the Report Card.

The risk of HIV transmission through breast milk is associated with duration, infant feeding practices and with maternal HIV disease. The prevention of HIV transmission

[8] Dabis, François DABIS, MD, PhD. "Long-term effectiveness of interventions to prevent mother-to-child transmission of HIV." Unpublished presentation July 2008.

[9] Chatterjee, Anirban and Doughty, Patricia. "Country data on infant feeding distribution, and on PMTCT regimens distributions." Unpublished presentation July 2008.

through breast milk is still an unresolved issue in Africa where breastfeeding provides protection against infant mortality, particularly in first 6 months of life. To date, postpartum ARV interventions have targeted either the breastfeeding woman or the neonate for short periods of time with partial efficacy and at the expense of acquisition of viral resistance.

Although some countries provide commercial infant formula to women with HIV for whom it is acceptable, feasible, affordable, sustainable and safe (AFASS) and encourage early cessation of breastfeeding (at one point in time even referred to as "abrupt weaning") at or around six months if AFASS, both strategies raise programmatic concerns in settings where there are risks of malnutrition, morbidity and mortality from unsafe preparation of alternatives.

Rates of HIV transmission: Tables 2.1 through 2.3 summarize the probability of transmission by mode of feeding and PMTCT prophylaxis, currently used in Spectrum, for different background duration of breastfeeding. The data is based on information from clinical trials for which results were available up to around 2006, and extrapolations where no direct data was available.

Table 2.1. Probability of transmission for breastfeeding duration of <= 6 months

Treatment	Mixed Feeding	Replacement Feeding	Exclusive Breastfeeding
1. None*	**26%**	**20%**	**23%**
2. SD NVP	17%	11%	14%
3. Dual prevention ARV	10%	4%	7%
4. Triple prevention ARV	4%	2%	3%
* Includes general population of women as well as women who do not know their HIV status.			

Table 2.2. Probability of transmission for breastfeeding duration of 6-18 months

Treatment	Mixed Feeding	Replacement Feeding	Exclusive Breastfeeding
1. None*	**30.5%**	**20%**	**23%**
2. SD NVP	21.5%	11%	14%
3. Dual prevention ARV	14.5%	4%	7%
4. Triple prevention ARV‡	5%	2%	3%
* Includes general population of women as well as women who do not know their HIV status.			

Table 2.3. Probability of transmission for breastfeeding duration of > 18 months

Treatment	Mixed Feeding	Replacement Feeding	Exclusive Breastfeeding
1. None*	**35%**	**20%**	**23%**
2. SD NVP	26%	11%	14%
3. Dual prevention ARV	19%	4%	7%
4. Triple prevention ARV‡	6%	2%	3%
* Includes general population of women as well as women who do not know their HIV status.			

In the absence of intervention, the 18 month MTCT rate ranges from 22.2% (Petra Study Team 2002) to 30.2% (Leroy 2002), in populations that breastfeed from 6.5 to 13 months.

Short course ARV prophylaxis regimens for PMTCT are simple and cost effective and have the advantage of preventing some mother-to-child transmission. However these ARV prophylaxis regimens are only partially efficacious, provided at the expense of acquisition of viral resistance, insufficiently used (single-dose nevirapine most often), and do not cover the breastfeeding period.

Both maternal ART and the administration of infant post-exposure prophylaxis (PEP) have been considered to reduce postpartum transmission of HIV. Given the clear reduction in HIV transmission, ART is now promoted not only for the mother's health but also for PMTCT (see Appendix 4, a pooled analysis postpartum transmission in the absence of maternal ARVs in comparison to the MTCT risk for breastfeeding women on ART as summarized in Appendix 5). Preliminary results shed some light on the limits of the maternal-only approach of MTCT prevention, which has only in part been addressed by the administration of ARV drugs to breastfed infants as post-exposure prophylaxis (PEP) (see Appendix 6). Given the persistent risk of HIV as long as the infant is breastfeeding, PEP will probably need to be maintained throughout the breastfeeding period — an intervention which may be difficult to implement.

2.2. Recommendations

2.2.1. Recommendations to improve methods for estimates and projections

- The MTCT rates in Tables 2.1 – 2.3 (above) need to be reviewed and possibly revised based on any new relevant information that has become available since 2006. New data are available from ZEBS (NEJM 2008), ZVITAMBO (AIDS 2005), VTS (Vertical Transmission Study, Lancet 2007). Proposed changes will be circulated to the New York meeting Working Group for consensus.
- In Tables 2.1 – 2.3 (above) an additional row should be added to reflect the transmission rate of women on ART (different from triple prevention ARV). Until more specific data are available, the transmission probabilities should be considered the same as those for triple prevention ARV. The number of women already on ART (as therapy, not prophylaxis) will have to be collected or calculated. Pregnant women on ART should be recorded on an ART register in the HIV care clinic (rather than the PMTCT register) or it may be calculated based on general population surveys but adjusted down by a set factor — as the proportion of pregnant women on ART is likely to be lower than the proportion of the general population on ART.
- Apply MTCT probabilities for women with no treatment (Table 2.1, Table 2.2 and Table 2.3, row 1) to ***women who do not use PMTCT services*** (either because they decline, services are unavailable, or they do not know their HIV status). For these women the following information should inform probability of transmission, all of which can usually be derived from DHS data:

  - Distribution of women by feeding modality (mixed feeding, replacement feeding or exclusive breastfeeding). This information is available from the UNICEF review of DHS/multiple indicator cluster surveys (MICS) (see Appendix 3).
  - Average duration of breastfeeding for general population (currently assumed to be somewhere between 7 and 17 months). Note that the DHS/MICS data from an additional UNICEF review following the meeting shows that for all countries where the information is available, the median duration of breastfeeding is in fact 18 months or more, ranging from 18.6 months in Namibia and 18.8 months in Haiti and Zimbabwe to 24.4 months in India and 25.2 months in Rwanda (see Appendix 3).
  - The available data on the duration and type of breastfeeding (see Appendix 3) should be made available as background information in estimation software manuals.
- Apply MTCT probabilities (Table 2.1, Table 2.2 and Table 2.3, rows 2, 3, and 4) to ***women who use PMTCT services***.
  - Distribution of these women by feeding modality should be based on PMTCT programme data rather than DHS findings as these women have access to HIV-related infant feeding counselling and support advising them to exclusively breastfeed for 6 months unless replacement feeding is AFASS.
  - When available, adjust the probability of transmission on the basis of data from the country's own research.

2.2.2. Recommendations on data collection and research

- UNICEF should add information about the average duration of breastfeeding to its review of the distribution of infant feeding practices in DHS/MICS surveys.
- Improve data collection strategies focusing on the key high burden countries in sub-Saharan Africa.
- Support further research about the number of children who die prior to contact with the healthcare system.
- Support countries to collect data on the number of women already on ART (as therapy, not prophylaxis). Pregnant women on ART should be recorded on an ART register in the HIV care clinic rather than the PMTCT register.
- Support research to estimate the mother-to-child transmission rates of mothers on ART.
- Support countries to collect relevant data when implementing the latest care and treatment guidelines.
- Support stronger linkages between HIV care centres and PMTCT programmes.

2.2.3. Recommendations to strengthen national estimation processes and international monitoring and evaluation reporting

- Continue to focus on building capacity for the monitoring and evaluation components when scaling up the implementation of WHO's HIV care and treatment guidelines for infants, children, adolescents/young people, in support of high quality reporting.
- Include government counterparts knowledgeable about PMTCT, and UN and other IATT partners in training for EPP and Spectrum.

3. Survival of children on ART

3.1. Summary of Presentations

The data from UNICEF's 2007 Annual Report Card on PMTCT and Paediatric HIV Care and Treatment — which is facilitated jointly by UNICEF and WHO on behalf of the IATT on PMTCT — represents 109 countries (93% of all pregnant women and 98% of all HIV-infected pregnant women from countries included in the Report Card) for most indicators and 128 countries for children receiving ART. The Report Card found a 78% increase in the number of children receiving ART from 2005 to 2006 and a 55% increase from 2006-2007. But despite increases in coverage, median age of initiation is still quite old, ranging from 4.4 years in Kenya to 9.2 in Uganda.

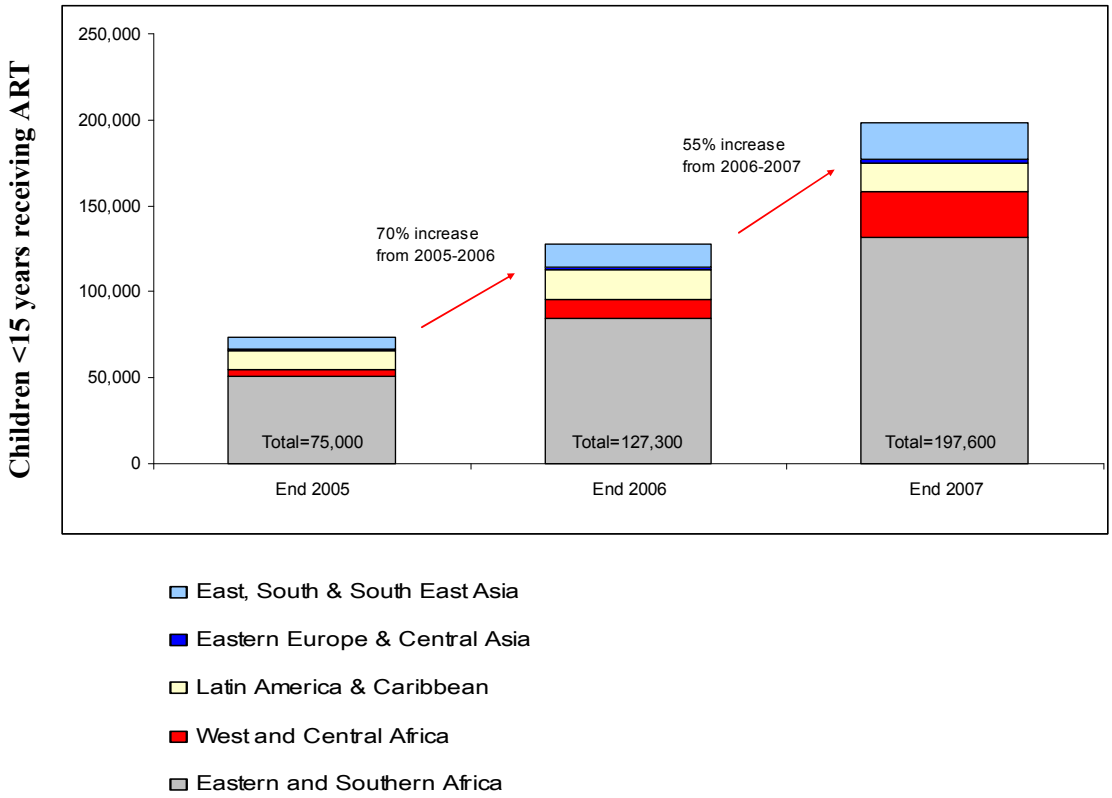
Definition of "Need for Treatment"

Until this year "need" for treatment was based on the estimated proportion progressing to Moderate-to-Severe Disease. As of 2009 the definition of need for treatment will need revision in line with the new WHO recommendations:

Age	Recommendation[10]	Updated definition of "need"
For children under 12 months of age:	Start ART as soon as HIV infection is confirmed	All children with confirmed HIV infection
For children over one year of age:	Start ART on the basis of immunological and clinical criteria, operationalized in model on basis of progression to death	Based on the estimated proportion progressing to Moderate-to-Severe Disease

[10] Gilks, Charlie. "New ART eligibility criteria for infants, April 2008 Revisions" Unpublished presentation July 2008. The April 2008 meeting report, which summarizes these recommendations is available at: http://www.who.int/hiv/pub/paediatric/WHO_Paediatric_ART_guideline_rev_mreport_2008.pdf

Figure 3: Number of Children Receiving ART: 2005 - 2007[11]



A scarcity of data on the benefits of child ART is, in part, explained by the fact that child ART services have been very recently scaled up. In preparation for this Consultative Meeting, Dr. François Dabis led an analysis of 14 prospective studies (observational cohorts, cross-sectional studies or clinical trials) of paediatric ART in lower income countries (LINCs). Appendix 7 summarizes probability of survival, survival probabilities adjusted for baseline %CD4, first line ART and for WHO stage. The analysis found that the following baseline factors were associated with increased mortality:

- In initial and current reviews: older age (≥5 years), WHO stage 4, low %CD4
- Additional factors in the review update include:
    - Younger age <18 months
    - Weight-for-age z-scores <-3
    - Weight-for-age z-scores <5th percentile
    - Adherence to ART <90%
    - Anaemia (haemoglobin <8 g/dl)
    - HIV disease conditions (chronic gastro-enteritis)

[11] Gass, Robert and Doughty, Patricia Doughty. "Programmatic Data on Children: Antiretroviral Therapy, Cotrimoxazole Preventive Therapy, and Early Infant Diagnosis." Unpublished presentation July 2008.

The analysis indicated that children with HIV experience mortality from all causes, not just HIV, and that nutrition is clearly a factor affecting mortality. In general, the studies analysed did not include younger (less than 6 months) infants. In some studies the young children who were included were very sick, so given this selection bias their survival was poorer. In general, the results of the studies analysed is encouraging, particularly in light of the fact that many of these children did not have the advantage of paediatric formulations; results from future studies are likely to be even more optimistic, especially as countries scale up the April 2008 WHO Paediatric Guidelines.

Documentation of study findings is still lacking in clarity, particularly around mortality and program retention, given that caveat, ***the most plausible estimates of one-year and 24-month survival on ART are: 0.93-0.95 and 0.91-0.92, respectively.*** There is no meaningful report on survival of children beyond 2 years after initiating ART.[12] These estimates can be refined in the future — studies addressing survival of children on ART have more than doubled since December 2006. Sample sizes for some of the studies are large (>1000 children) therefore better quality (e.g. Arrive in press, O'Brien 2006 & 2007, Bolton-Moore 2007) and at least one study is analysing a wider range of factors associated with mortality (Arrive in press).

3.2. Recommendations

3.2.1. Recommendations to improve methods for estimates and projections

- Participants in the consultative meeting divided into two groups to discuss current assumption about effectiveness of ART (annual survival is currently estimated differently for <1 year [0.8] versus >1 year [0.9 during first year and 0.95 during following years]. The outcomes of the discussions from both groups and the consensus after the plenary discussion follow:

Table 3: Consensus of Working Groups on effectiveness of ART

Question	Group 1	Group 2	Consensus
Should there be changes in Spectrum about effectiveness of ART?	• First year: Assume **15%** mortality • 2nd year: **5%** • After 2nd year: 2%. (98% survival is based on the adult studies)	• First year: **83%** inclusive of 5% loss/mortality[13] • 2nd year **89%** survival (inclusive of 5% loss/mortality) • After 2nd year: **93%** survival (inclusive 5% loss/mortality)	CHER data suggested 4% mortality/year but gave co-trimoxazole and CPV. • First year: 85% (factor in 33% increased survival for those of co-trimoxazole and the survival rates for ART plus co-trimoxazole are 90%) • 2nd year: 93%* • After 2nd year: 93%*

[12] Dabis, François and Namale, Leticia. "Mortality after antiretroviral therapy (ART) initiation in children in lower-income countries (LINCs)" Unpublished presentation July 2008.

[13] This figure is calculated as follows: 93-95% of infants survive first year of treatment (Dabis). **Correction for the first year of age** (because first year of treatment is not usually first year of life), multiply risk of death by 1.8 to 2.0 (Dabis et al, "Survival of HIV-infected children on co-trimoxazole and ART in LINCs, Long-term

3.2.2. Recommendations on data collection and research

- Support countries to collect data on the age at initiation of ART, e.g. <1, 1 through 4, 5 through 14.
- Support countries to collect data on CD4 level at start of ART.
- Support countries to collect data on the number of children on second line treatment.
- Encourage additional cohort research, including well-documented study findings (need to enforce the 2007 STROBE guidelines) designed to inform regional survival estimates. These studies should address:
    - Survival of children beyond 2 years after initiating ART
    - Survival of children initiating ART in the first six months of life
    - Survival of children on second-line ART
- Collect and analyse data to further quantify the effect of non-HIV-related child survival initiatives that will affect the mortality rates of children with HIV. These programmes may include (depending on status of specific country adaptation) but are not limited to Isoniazid (INH) prophylaxis, conjugate pneumococcal vaccine (CPV), and insecticide-treated bednetting (ITN).
- Regularly collect and meta-analyse research data on survival on ART, with special attention for the 2nd and onwards year on ART, for children on second line treatment, for CD4 level at initiation, and for the percentage of patients lost to follow-up and their outcome (mortality rate).

3.2.3. Recommendations to strengthen national estimation processes and international monitoring and evaluation reporting

- Continue to support countries (through the IATT M&E Working Group, PMTCT monitoring and evaluation guide, and continued focus on monitoring and evaluation during Joint Technical Missions) to strengthen national monitoring and evaluation systems, reduce double counting where a child is provided care in more than one clinic, develop appropriate data collection tools (e.g., registers, health cards), support adoption of new indicators, and build capacity for reporting on all relevant indicators (e.g., co-trimaxozole preventive therapy, early infant diagnosis, and others recommended in this report) in national monitoring and evaluation systems.
- Report the number of children initiating ART by age bands, i.e. <1, 1 through 4, 5 through 14, and by CD4% category.
- Report number of children on second line ART.
- Country monitoring and evaluation systems should continue to review pharmacy data to correct underreporting of children on treatment at programmatic level.

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effectiveness of interventions to prevent MTCT." Table 18), i.e., 88% survival. **Correction for death/loss to follow up**: The studies that Dabis looked at experienced approximately 10%; if half of the loss to follow up was attributable to death (see Dalal et al, J Acquir Immune Defic Syndr 2008; 47: 101–107), then it can be assumed that an additional 5% died. 88%-5 = **83% survival in 1st year as a provisional figure**. Calculations for the other age groups was similar.

- Include government counterparts knowledgeable about child ART programmes, and UN and other IATT partners in training for EPP and Spectrum.

4. Mortality after co-trimoxazole initiation

4.1. Summary of Presentations

It is currently assumed that co-trimoxazole reduces mortality by 33% in the first four years, 17% in year 5, and 0% after year 5. These figures are based on one study: Chintu et al 2004 — Zambia (the "CHAP" study) and expert opinion. Despite its proven efficacy, the 2007 Report Card found that only 4% of infants born to HIV-infected mothers are initiated on co-trimoxazole preventive therapy within 2 months of birth.

Definition of need

The definition of "need" for co-trimoxazole: all HIV-exposed infants until HIV is definitively ruled out (and breastfeeding has stopped for at least 6 weeks). All HIV-infected infants and children until clinical and immunological indicators confirm restoration of immune system.

In preparation for this Consultative Meeting, Dr. François Dabis lead an analysis of 7 papers deemed meaningful and useful (3 are from the CHAP study) describing prospective studies (observational cohorts, cross-sectional studies or clinical trials) of paediatric co-trimoxazole in lower- and middle-income countries. The aim of the review was to document more evidence from countries and regions to further strengthen the public health policy of routine co-trimoxazole prophylaxis in children.

In general, the review reinforced the scarcity of data regarding the benefits of paediatric co-trimoxazole despite seven years of WHO guidelines (global guidelines are based primarily on the findings of studies that were undertaken in the United States and Western Europe, as well as the CHAP study). Not only did the studies in the analysis deal with relatively older children (≥ 4 years), but the accuracy of some of the findings (e.g. according to age or CD4 percentage) must be interpreted with caution due to limited sample size and follow-up, which did not exceed 24 months. An overview of the findings from the analysis is included as Appendix 8. In general the analysis found:

- There is a consistent and significant benefit in using co-trimoxazole to reduce child mortality.
- Co-trimoxazole had a protective effect even among HIV-infected children who later acquired *Pneumocystis jiroveci* pneumonia (formerly *Pneumocystis carinii* pneumonia) (PCP): the hazard ratio was 0.57 (in comparison to placebo) across age groups and CD4 strata.
- The CHAP trial still captures the majority of the relevant information.

- The ARV studies did not include discussion of co-trimoxazole, even though they do state that co-trimoxazole was systematically prescribed. Studying the effect of co-trimoxazole in the context of ART is challenging. As an example, although the CHER study — which looked at early initiation of co-trimoxazole — found a 75% reduction in mortality, study participants also received ART and conjugate pneumococcal vaccine. It is unclear if health policy should prioritize scale up of ART or co-trimaxazole, based on projected public health benefits.
- Low CD4 and poor nutrition were risk factors for death.
- Co-trimoxazole, given its anti-malarial effect, may have benefits for HIV-negative children
- The effect of co-trimoxazole wanes after 6 to 12 months in children; mirroring the waning of effect seen in adults.[14]

4.2. Recommendations

4.2.1. Recommendations to improve methods for estimates and projections

- Participants in the consultative meeting divided into two groups to discuss possible changes to the current assumptions about effectiveness of co-trimoxazole [reduction of mortality by 0.33 in years 1 through 4, by 0.17 in year 5, and no effect beyond year 5]. Should interaction of co-trimoxazole with ART be modified? How should ART needs and co-trimoxazole needs be estimated, in the light of previous methods and new recommendations regarding early diagnosis and ART eligibility? The outcomes of the discussions from both groups and the consensus after the plenary discussion follow:

[14] Dabis, François and Namale, Leticia. "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Unpublished presentation July 2008.

Table 4: Consensus of Working Groups on effectiveness of co-trimoxazole

Question	Group 1	Group 2	Consensus
Should current assumptions about effectiveness of co-trimoxazole be changed?	.57 relative risk of mortality for 14-16 months of use. Assume this goes down: • Year 1 40% • Year 2 20% • Year 3 10% • Year 4 5%	• Year 1 33% • Year 2 33% • Year 3 33% • Year 4 33% • Year 5 33% Assume no effect after 5 years[15]	For those not on ART: • Year 1 33% • Year 2 33% • Year 3 33% • Year 4 33% • Year 5 33% Assume no effect after 5 years For those on ART: • Year 1 32% • Year 2 16% • Year 3 8% • Year 4 4% • Year 5 2%
Should interaction of co-trimoxazole with ART be modified?	Assume the same	Multiplied effect in year one only; after year 1 no additive/multiplicative effect.	Apply multiplier to the mortality rate (as in above rates for those on ART).
Estimation of ART and co-trimoxazole need	ARVs: All those on treatment All new infection under 12 months Greater than 1 year reflecting progression and criteria co-trimoxazole: • All HIV-exposed less than 18 months • All children over 12 months • 1-4: less than 20% CD4 or stage 3, 4 • Age 5+ less than 15% CD4	ARVs • All children under the age of 1 • All children already on treatment • All children over the age of 12 months who are eligible for treatment	ARVs Same in both groups Co-trimoxazole: • All HIV-exposed less than 18 months • All HIV-positive children over 18 months

4.2.2. Recommendations on data collection and research

- Continue to collect data on co-trimoxazole preventive therapy through the Report Card.
- Support countries to collect data on the overlap of ART and co-trimoxazole (i.e. the number of children who are on both ART and co-trimoxazole).
- Support research with large cohort studies to better document the additional effect of co-trimoxazole among children on ART, on the effect of co-trimoxazole use in young infants, and on the long term effects of co-trimoxazole (i.e. beyond 2 years of use).

[15] Assumptions based on Walker, Sara. CHAP Study

4.2.3. Recommendations to strengthen national estimation processes and international monitoring and evaluation reporting

- Compare the number of children on co-trimoxazole with the number of women enrolled in PMTCT programmes, to validate completeness of co-trimoxazole data.
- Continue to support countries (through the IATT M&E Working Group, PMTCT monitoring and evaluation guide, and continued focus on monitoring and evaluation during Joint Technical Missions) to strengthen national monitoring and evaluation systems, reduce double counting where a child is provided care in more than one clinic, develop data collection tools (e.g., registers, health cards), build capacity for reporting on newest indicators, and support adoption of certain indicators (e.g., co-trimoxazole preventive therapy) in national monitoring and evaluation systems.
- Include government counterparts knowledgeable about child treatment and care programmes, and UN and other IATT partners in training for EPP and Spectrum.
- Country monitoring and evaluation systems should continue to review pharmacy data to correct underreporting of children on treatment at programmatic level.

5. Reporting categories

5.1. Summary of Presentations

Age categories: The following are currently used in different settings by different institutions:

- UNAIDS/WHO HIV and AIDS estimates: children are 0 through 14 years; adults are 15+
- Convention on the Rights of the Child: “For the purposes of the present Convention, a child means every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier”
- Child mortality = Under-5-mortality
- Infant: <12 months (IMR)
- Young people: 15 through 24 year olds
- Adolescents: 10 through 18 yrs

Current methods do not allow for age-stratification of incidence among children; finer age bands on age at infection would provide information about mode of transmission, which would help in targeting HIV prevention initiatives. Also, as PMTCT and ART programmes are starting to be scaled up — particularly in light of the new guidelines recommending diagnosis and treatment in the first months of life — it may be desirable to align HIV and AIDS estimates with the usual definitions used in child health. If this is

the case, then the "infant" age categories could be adjusted to reflect early diagnosis and ART, keeping in mind age range of paediatric dosing of ART.

With more success in treating children, it will be important for the monitoring of paediatric treatment to anticipate aging of the HIV-infected paediatric population. The validity of age-specific estimates will depend on availability of age-specific data on ART age distribution. The current convention for age banding is simple, easy to understand and conveniently separates out perinatally acquired HIV — which make up the great majority of those in the 0 through 14 year age band.[16] The disadvantage of finer age banding is the risk of being confusing if there are too many categories. There continues to be a need to balance what is wanted versus validity given available data and credibility of reporting entities.

Case reporting: Case reporting — although the basis for estimates in the United States — is believed to grossly underestimate the actual burden of disease and infection in low- and middle-income countries where it has been implemented. Where HIV case reporting is a source of reliable and valid information, it is an important source of information to estimate the total number of children with HIV and to compare this figure with the number of children in care. Low and concentrated epidemics with well developed health systems and HIV case reporting in particular, may be usefully informed by case reports. In most high burden countries, case reporting is not a priority.[17]

Sentinel surveillance: Currently there is a lack of direct data on HIV in children. Sentinel surveillance among children is currently not recommended.

National surveys (including demographic and health surveys): Only four countries have so far included children below the age of 15 years in national surveys with HIV prevalence measurement. Potential limitations of measuring HIV prevalence in population based surveys include the following:

- Non-response (refusal to participate or absence from household)
- Measurement error
- Sensitivity and specificity of laboratory tests — WHO estimates that most HIV antibody tests currently used for surveillance have specificity of 98% or higher, but the actual sensitivity and specificity of the tests when conducted in the field may vary

Where population-based surveys have included HIV, the prevalence results for children age 0 through 14 follows the same pattern as the prevalence estimates from Spectrum, but are generally slightly higher. It is not clear if the differences in HIV estimates are related

[16] Ghys, Peter and Luo, Chewe. "Advantages and disadvantages of reporting HIV and AIDS estimates for children by additional age categories" Unpublished presentation July 2008.

[17] Consensus of Working Group 1 (July 10, 2008): What additional data collection among children should be conducted? Consultative Meeting on Data collection and Estimation methods related to HIV Infection in Infants and Children.

to survey test specificity, non-response, or other potential risk factors (e.g. breastfeeding by non-biological mother has been identified as a risk factor in South-Africa).[18]

During the planning phase of population-based surveys, the following practical as well as ethical questions must be considered: which age groups should be tested, how to deal with informed consent, and access to HIV test results. In reference to minimum age for HIV testing in population-based surveys, South Africa measured HIV prevalence in those over the age of two years, so that the HIV antibody test could be utilized. Studies using two years as a cut off have to add the caveat that HIV burden estimates derived from these studies overlook HIV infection in children below the age of 2 years.

The use of population-based surveys to measure HIV prevalence in children is feasible only in countries whose HIV prevalence is high — probably at least 10% in adults, possibly higher — due to sample size requirements[19]. Likewise, measurement of HIV prevalence of children attending immunization clinics may be biased toward well children and children living in urban areas, as such may not be a good reflection of national HIV prevalence; where these surveys populations are compared to the population as a whole, findings may help validate estimates of child HIV infection.

5.2. Recommendations

5.2.1. Recommendations to improve methods for estimates and projections

- Keep the 0 through 14 years age band for the purpose of reporting the number of people living with HIV because it is convenient, easy to comprehend and the current convention. The UNGASS indicators and other well defined demographic indicators, including those used for many population-based surveys, are based on this cut-off. Changing this age banding would potentially necessitate changes to the other data collection systems. In summary the Consultative Meeting consensus was to use the following age bands:
    - Population 15+ 15+ years
    - Infants <1 (Under one).
    - Children 0-14 0 through 14 years
- The consensus of the consultation meeting working group on age reporting for the number of new infections:
    - Under 1
    - Children 0 through 14.
- Create supplementary age bands for ***programmatic*** purposes. The consensus of the consultation meeting was to band ages as follows for collection of information about the number of people living with HIV, the number of children needing ART, and the number of children needing co-trimoxazole:

[18] Gouws, Eleanor. "HIV infection among children in Southern Africa." Unpublished presentation July 2008.

[19] Consensus of Working Group 1 (July 10, 2008): What additional data collection among children should be conducted? Consultative Meeting on Data collection and Estimation methods related to HIV Infection in Infants and Children.

Age category	Comment
▪ Under 1 year	Supports the monitoring of new treatment guidelines that recommend early diagnosis and treatment
▪ 1 through 4	Under 5 is an important universal indicator of the performance of healthcare systems and of development
▪ 5 through 9	Enables programmes to tease out the need for paediatric versus adult formulations: most of the 5 through 9s will need paediatric formulations, the 10 through 14s will be growing into the adult formulations
▪ 10 through 14	
▪ 15 through 17	Corresponds to the Convention on the Rights of the Child's definition of a child
Each of the above age bands should also be broken down by sex.	

- The consensus of the consultation meeting working group on age reporting for ***mortality***:
    - Children less than 1 year (even though these figures might be less reliable than under 5)
    - Children 0 through 4 years (to allow comparison with total under 5 mortality figures)
    - All children 0 through 15 years
    - Population 15+

5.2.2. Recommendations on data collection and research

- Continue to release country-specific data every two years. The release of reports according to a flexible or inconsistent timeline, not only has internal resource implications, but also has the disadvantage of affecting public confidence in data and potentially causing confusion amongst stakeholders, national decision makers, and the public. Non-routine updates can give the appearance that the figures are arbitrary and makes the process seem disorganized because the non-routine updates to country estimates, in turn affects the regional and global estimates. Countries understand that estimates are dated as per an agreed timeline and that new data is integrated into the next cycle. A transparent process can help overcome any accusations that the timing of routine reports is not flexible to country processes.
- Where important data affecting a country estimate is released outside of the schedule, consider releasing real time updates to country figures with the caveat that country figures no longer add up to the previously released regional and global figures.

5.2.3. Recommendations to strengthen national estimation processes and international monitoring and evaluation reporting

- Recommendation of the consultation meeting working group to build consensus within country
    - Invite paediatric, PMTCT and ART experts to trainings and workshops
    - Build on experience of countries with existing consensus-building processes

- Use UNAIDS monitoring and evaluation advisors to strengthen consensus building in country; consider using this individual to coordinate the consensus building process
- Use regional institutions (e.g., academic institutions) to support training follow up

6. Non-MTCT transmission

6.1. Summary of Presentations

The South Africa HSRC study of "HIV Risk Exposure in Children Aged 2-9 years Served by Public Health Facilities in the Free State — 2005" reviewed evidence to further an understanding of the vulnerability of children to HIV infection. The study, which focused on non-MTCT transmission included 3,530 mother-child (children age 2 through 9 years) pairs from 88 public healthcare facilities. 29.1% of the mothers (which is consistent with national HIV prevalence at that time) and 14.8% of the children were HIV-positive (i.e. about half of the infants of women with HIV were infected). 92.3% of HIV-positive mothers breastfed their babies, 60% for longer than a year. The overwhelming majority of children who were HIV-positive had HIV-positive mothers, confirming that the majority of infection comes from MTCT. Breastfeeding by an HIV-infected non-biological caregiver is the single most important factor besides MTCT. Other risk factors for non-MTCT infection include the following:

- Hospital error: Banked breast milk bottles were labelled by the mother's cot number rather than by name. If the mother was moved to a different cot there was the possibility that the infant might receive the wrong banked breast milk
- Dental instruments: 24.6% of dental instruments had traces of blood
- Maternity/paediatric instruments: 24% of maternity and paediatric instruments were contaminated with invisible blood and 17.5% with visible blood
- Possible sex abuse

The study authors recognized that because the BED Capture has not been validated for use in children, it may have overestimated HIV in the study group, but data was not available to support or refute this assumption.[20]

6.2. Recommendations

- Link data on children with that of their mothers in the DHS analysis.

[20] Ngongo, Ngashi. "Report from the March 2008 UNICEF/HSRC consultation on non-MTCT transmission" Unpublished presentation July 2008.

- Develop appropriate tools to measure the incidence of non-vertical HIV infections in children: the WHO Working Group on BED assays should validate the method for use in children and provide guidance to countries.
- Support and undertake further studies on non-MTCT transmission in children, including longitudinal studies to understand when infection occurs, cross-sectional studies to understand the risk factors, and studies of biomarkers (e.g. hepatitis B) along with risk factors associated with them.
- Although scarification, traditional circumcision and use of traditional medicines were not found to be significant factors for transmission, include these factors in future research of non-MTCT transmission, particularly in studies that include older children, up to age 14 years.

Next Steps

This Consultative Meeting report includes more than fifty recommendations to improve estimation methods and parameters, data collection and to strengthen national estimation processes and data inputs. The vast majority of recommendations were focused on improving estimates, the next steps for which are generally in the domain of the UNAIDS Reference Group, including further data synthesis to inform parameters estimates, and implementation of several changes to the model in Spectrum, in time for the next round of regional estimation training which is expected to take place during the first half of 2009.

UNAIDS co-sponsor organizations, including UNICEF and WHO, and other partner organizations are expected to support the implementation of the recommendations in this report, including:

- Support countries to adapt and implement the newest treatment guidelines for children, and monitor and evaluate their implementation.
- Provide support to countries to monitor and evaluate their PMTCT services, and treatment and care services for HIV-infected children.
- Collect an expanded set of indicators through the Report Card.
- Support data collection and research.
- Strengthen HIV and AIDS child estimates through support for expanded consensus in-country processes.

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Appendix 1: List of Participants

Name	Title and Affiliation
UNAIDS REFERENCE GROUP	
Geoff Garnett	Chair, UNAIDS Reference Group on Estimates & Modelling, Imperial College
Annick Borquez	UNAIDS Reference Group on Estimates & Modelling, Imperial College
UNICEF	
Chewe Luo	Senior Adviser, HIV and AIDS Section, UNICEF
Jimmy Kolker	Chief, Associate Director, HIV and AIDS Section, UNICEF
Rene Ekpini	Senior Advisor, PMTCT, UNICEF
Patricia Doughty	Programme Officer, HIV and Health, Health Section, UNICEF
Robert Gass	Project Officer, Paediatric HIV, Health Section UNICEF
Anirban Chatterjee	Project Officer, HIV, Nutrition Section UNICEF
Priscilla Akwara	Advisor, Statistics & Monitoring Section
Danielle Burke	Project Officer, Statistics & Monitoring Section, UNICEF
Patricia Lim Ah Ken	Project Specialist, HIV and AIDS Section, UNICEF
Behzad Noubary	Consultant, Strategic Information on HIV/AIDS, HIV and AIDS Section, UNICEF
Mariam Jashi	Specialist, HIV/AIDS Partnerships, Health Section, UNICEF
Xiaodong Cai	Project Specialist, Statistics & Monitoring Section, UNICEF
Diane Widdus	Senior Specialist, HIV and AIDS Section, UNICEF
Pierre Robert	Adolescent Development and Participation (ADAP), UNICEF
Ngashi Ngongo	Chief, Health and Nutrition Section, UNICEF, South Africa
UNAIDS	
Paul De Lay	Director of Evidence, Monitoring and Policy, UNAIDS
Peter Ghys	Epidemic Monitoring and Prevention, UNAIDS
Eleanor Gouws	Epidemic and Impact Monitoring, UNAIDS
Karen Stanecki	Epidemic and Impact Monitoring, UNAIDS

Appendix 1: List of Participants *(continued)*

WHO

Kevin De Cock	Director, Department of HIV/AIDS, WHO
Txema Calleja	EIP/ Measuring Health Information, WHO
Charles Gilks	Department of HIV/AIDS, WHO
Ying-Ru Lo	Coordinator Prevention in the Health Sector, Department of HIV/AIDS, WHO

MODELING EXPERTS

John Stover	President, Futures Institute
Peter Johnson	U.S. Census Bureau
Wiwat Peerapatanapokin	Senior Fellow, East-West Center

CHERG

Neff Walker	Professor, Johns Hopkins University, Department of International Health

EPIDEMIOLOGISTS / CLINICAL HEALTH EXPERTS / RESEARCHERS

Lynne Mofenson	Branch Chief, National Institute of Child Health and Human Development
Megan O'Brien	Research Director, Clinton Foundation

COUNTRIES — General Epidemic

Irene N. Mukui	ART programme Officer, National AIDS/STD control programme (NASCOP), MOH, Kenya
Justine Nankinga	National Coordinator ART, STD/AIDS Control Programme, MOH, Uganda

COUNTRIES — Concentrated Epidemic

Gerson Fernando Mendes Pereira	National AIDS Programme, MOH, Brazil
Ruslan Malyuta	Regional Advisor, CEE/CIS, UNICEF
Mean Chi Vun	Director, National Center for HIV / AIDS Dermatology and STD (NCHADS), MOH

AUTHORS OF MEETING PAPERS

Francois Dabis	Bordeaux School of Public Health, France
Milly Marston	Lecturer, London School of Hygiene & Tropical Medicine

Appendix 1: List of Participants *(continued)*

KEY STAKEHOLDERS

Michelle Sherlock	Strategic Information, OGAC
Patrick Gerland	Population Estimates and Projection Section, UN Population Division
Gerhard Heilig	Chief, Population Estimates and Projections Section, UN Population Division

RAPPORTEUR

Virginia Allread	Director, Global Products, François-Xavier Bagnoud Center, UMDNJ

Appendix 2: Consultative Meeting Agenda

Tuesday 8th July

09:00	Welcome, introductions (10 min)	Jimmy Kolker
09:10	Opening Remarks (10 min)	Richard Morgan
09:20	Objectives of meeting (10 min)	Geoff Garnett
09:30-11:10	**Session 1: Current methods, process and results** • Latest child estimates and trends through 2007 (UNAIDS) (10 min) • Experience from last training workshop round, and from recent country estimation round (15 min) • Current Assumptions and data sources within Spectrum to model PMTCT needs and child HIV estimates (30 min) • Summary of available data on population-based estimates of HIV prevalence and incidence among children, and comparison with Spectrum. (15 min) • Discussion (30 min)	**Chair: Kevin de Cock** Peter Ghys Karen Stanecki John Stover & Peter Johnson Eleanor Gouws
11:10-11:40	***Coffee Break***	
11:40-12:55	**Session 2: New data: PMTCT rates, intervention coverage, infant feeding distribution, survival without treatment or prophylaxis** • MTCT rates by breastfeeding patterns, and efficacy and effectiveness of PMTCT regimens, and of infant feeding interventions (15 min) • Country data on infant feeding distribution, and on PMTCT regimens distributions (15 min) • Survival of children to death in the absence of treatment, including "net survival" and differential survival of children infected perinatally versus through breastfeeding (15 min) • Discussion (30 min)	**Chair: Paul de Lay** Francois Dabis Arniban Chatterjee & Patricia Doughty Milly Marston

Appendix 2: Consultative Meeting Agenda *(continued)*

Tuesday 8th of July (continued)

Lunch

13:55-16.10	**Working Groups** **Group 1: overall approach including child survival** Can the overall modelling approach in Spectrum be improved? i.e. approach to deal with age-specific fertility related to HIV and ART, MTC transmission, survival of children • What could be modified? • What can be added? • What can be left out? • For each of the areas, consider data availability (in countries or in literature) • Should different child survival be considered for children infected 1) perinatally, 2) through breastfeeding? • How should this be implemented in Spectrum? • What future research could further inform this issue? • Mother's survival impact on child's survival **Group 2: MTCT rates, including influence of infant feeding patterns and interventions, and antiretroviral drug interventions** 2.1 Should current data on the prevalence of breastfeeding (e.g. from national surveys) and infant feeding distribution (from programme data) be used to inform default values for these distributions in Spectrum? • If so, how, and based on which data (and how will it become available? • Should country data on these two issues be used differently in Spectrum (compared to the current use)? 2.2. Should default MTCT rates in Spectrum be modified, including for interventions (drug prophylaxis for PMTCT)? • Should additional interventions be considered? (consider data availability in countries) • Should country data on these two interventions be used differently in Spectrum (compared to the current use)? • Should we include ART coverage in adults by gender?	All

Appendix 2: Consultative Meeting Agenda *(continued)*

Wednesday 9th of July

09:00-10:00	Plenary from 1st day's working groups: **Recommendations of the working groups and discussion**	**Chair: Geoff Garnett**
10:00-11:00	**Session 3: Survival with treatment and prophylaxis, the uses and availability of programmatic data and the new ART eligibility criteria**	**Chair: Jimmy Kolker**
	• Survival of children on ART, by age and by duration of ART, overall and by CD4 level, for first and second line regimens (15 min)	François Dabis
	• Survival of children on co-trimoxazole, by age and by duration of ART, overall and by CD4 level, and interaction with effect of ART on survival (15 min)	François Dabis
	• Discussion (30 min)	
11:00-11:30	***Coffee Break***	
11:30-12:30	• Programmatic data on the age distribution of children on ART and co-trimoxazole (at ART initiation and overall), on the availability of early diagnosis technology and frequency of early diagnosis (15 min)	Robert Gass Charles Gilks
	• Report on new ART eligibility criteria for low- and middle-income countries (15 min)	
	• Discussion (30 min)	
12:30-13:30	***Lunch***	
13:30-16:00	**Working Group questions**	All
	• Should the current assumption about effectiveness of ART be changed (annual survival is currently estimated differently for <1 year [0.8] versus >1 year [0.9 during first year and 0.95 during following years]. Also should annual survival be modified by CD4 level (based on what country data?) and/or by first versus second line?	
	• Should the current assumption about effectiveness of co-trimoxazole be changed [reduction of mortality by 0.33 in years 1-4 and by 0.17 in year 5]? Should interaction of co-trimoxazole with ART be modified?	
	• In absence of programme data on age distributions, what should be assumed regarding age distribution of ART in Spectrum? What data could inform this in future?	
	• How should ART needs and co-trimoxazole needs be estimated, in the light of previous methods and new recommendations regarding early diagnosis and ART eligibility?	
16:00-17:00		**Chair: Geoff Garnett**
18:00-19:30	**Recommendations of the working groups and discussion**	
	Reception (Danny Kaye Visitor's Center)	

Appendix 2: Consultative Meeting Agenda *(continued)*

Thursday 10th July

09:00-10:00	**Session 4: Non-MTCT transmission, data collection, and reporting** • Position paper on advantages and disadvantages of reporting categories 0-14 years and 0-17 years (15 min) • Report from the March 2008 UNICEF/HSRC consultation on non-MTCT transmission (15 min) • Discussion (30 min)	**Chair: John Stover** Peter Ghys & Chewe Luo Ngashi Ngongo
10:00-11:00	**Working Group questions:** **Group 1** 1. What additional data collection among children should be conducted? Consider: • HIV case reporting. If need to reinforce this, should it be on a national basis or on a sentinel basis? Should be collected status of mothers (alive or death, HIV status)? • Age and sex distribution of children on ART? • National surveys. If recommended, at which levels of expected HIV prevalence (consider required sample size)? Which age groups (e.g. 0-14, >18 months, others)? How to deal with ethical issues: informed consent, access to HIV results, access to ART? • Prevalence measurement at immunization clinics (see Rollins, AIDS 2007)? 2. How to further investigate non-MTCT transmission? **Group 2** 3. Reporting by additional age categories • Prevalence, PLHIV: Should we routinely (e.g. in Global Report and AIDS Epidemic Update) report on different age groups than 0-14, or should this continue as present and be supplemented by special publications with additional age breakdowns (e.g. UNICEF reports, scientific papers)? Which age categories should be considered? • Incidence: should we report for different age groups than 0-14? • Mortality: should we report for different age groups than 0-14? Should analyses of AIDS-specific under-5-mortality be done and disseminated? Should AIDS-specific analyses of infant mortality be done and disseminated? • ART need: should it be presented for 0-14 or for other age categories? 4. How to strengthen future training and consensus workshops on HIV and AIDS estimates?	All
11:00-11:30	***Coffee Break***	
11:30-12:30	**Recommendations of the working groups and discussion**	**Chair: Geoff Garnett**
12:30-13:00	**Final comments**	Jimmy Kolker

Appendix 3: Breastfeeding Status of Children under 6 Months and Median Duration of Breastfeeding: 35 Countries Accounting for 94% of HIV-Infected Pregnant Women in Low- and Middle-Income Countries[21]

Countries A	Breastfeeding Status				Mixed Feeding (%) F=D+E	Median duration (months) and frequency of breastfeeding (any breastfeeding) G	Year H	Source I
	Not breast feeding (%) B	Exclusive breastfeeding among infants (%) C	Breastfeeding and plain water (%) D	Breastfeeding and other milk/ liquids/complementary foods (%) E				
Angola[a]	2.8	11.3	29.6	56.4	86.0	-	2001	MICS 2001
Botswana	-	33.7	-	-	-	-	2000	MICS 2000
Brazil	-	-	-	-	-	-	-	-
Burkina Faso	3.0	6.8	64.9	25.2	90.1	-	2006	MICS 2006
Burundi	-	44.7	-	-	-	-	2005	ISTEEBU, Rapport de l'Enquête Nationale de Nutrition de la Population 2005, Table 8, p. 26
Cameroon	3.1	21.2	37.3	38.5	75.8	-	2006	MICS 2006
Central African Republic	2.4	23.1	26.4	48.1	74.5	-	2006	MICS 2006
Chad	0.5	2.1	57.9	39.5	97.4	21.3	2004	DHS 2004: p. 196, Table 12.2; p. 198, 12.3
China	-	50.8	-	-	-	-	2003	Third National Health Services Survey, Ministry of Health, 2003
Côte d'Ivoire	1.7	4.3	62.6	31.3	93.9	-	2006	MICS 2006
Democratic Republic of the Congo	0.4	24.2	24.1	51.3	75.4	-	2001	MICS 2001
Ethiopia	1.3	49.0	14.5	35.2	49.7	25.8	2005	DHS 2005: p. 145, Table 11.2; p. 147, Table 11.3
Ghana	0.4	54.4	21.0	24.2	45.2	-	2006	MICS 2006
Guatemala	5.5	50.6	7.3	36.7	44.0	20.6	2002	Encuesta Nacional de Salud Materno Infantil (ENSMI) 2002: p. 187, Table

[21] Chatterjee, Anirban. Review of breastfeeding and infant feeding practices from DHS/MICS

Countries A	Breastfeeding Status				Mixed Feeding (%) F=D+E	Median duration (months) and frequency of breastfeeding (any breastfeeding) G	Year H	Source I
	Not breast feeding (%) B	Exclusive breastfeeding among infants (%) C	Breastfeeding and plain water (%) D	Breastfeeding and other milk/ liquids/complementary foods (%) E				
								9.3; p. 190, Table 9.5
Guinea	1.5	27.0	53.5	18.0	71.5	22.4	2005	DHS 2005: p. 155, Table 10.2; p. 156, Table 10.3
Haiti	2.2	40.6	9.0	48.1	57.1	18.8	2005-2006	DHS 2005-2006: p. 150, Table 11.2; p. 151, Table 11.3
India	1.8	46.4	22.4	29.4	51.8	24.4	2005-2006	National Family and Health Survey (NFHS) 2005-2006: p. 279, Table 10.6; p. 281, Table 10.7
Kenya	0.2	12.7	13.4	73.7	87.1	20.1	2003	DHS 2003: p. 155, Table 10.2; p. 157, Table 10.3
Lesotho	3.0	36.4	12.3	48.4	60.7	21.3	2004	DHS 2004: p. 159, Table 10.2; p. 161, Table 10.3
Malawi	1.6	56.7	9.7	31.9	41.6	-	2006	MICS 2006
Mali	0.6	37.8	53.4	8.2	61.6	20.9	2006	DHS 2006: p. 160, Table 11.2; p. 161, Table 11.3
Mozambique	0.7	30.0	38.9	30.4	69.3	22.1	2003	DHS 2003: p. 169, Table 10.2; p. 170, Table 10.3
Namibia	5.8	18.6	18.8	56.8	75.6	18.6	2000	DHS 2000: p. 145, Table 10.2; p. 146, Table 10.3
Nigeria	1.7	17.2	44.6	36.5	81.1	18.6	2003	DHS 2003: p. 154, Table 11.2; p. 155, Table 11.3
Russian Federation	-	-	-	-	-	-	-	-
Rwanda	0.3	88.4	1.3	10.0	11.3	25.2	2005	DHS 2005: p. 134, Table 10.2; p. 136, Table 10.3
South Africa	-	7.2	-	-	-	-	2003	DHS 2003, Preliminary report, Table 15, p. 19
Sudan (data for North Sudan)	-	15.6	-	-	-	-	2000	MICS 2000
Swaziland	3.6	23.9	2.3	71.4	73.7	-	2000	MICS 2000

Countries A	Breastfeeding Status				Mixed Feeding (%) F=D+E	Median duration (months) and frequency of breastfeeding (any breastfeeding) G	Year H	Source I
	Not breast feeding (%) B	Exclusive breastfeeding among infants (%) C	Breastfeeding and plain water (%) D	Breastfeeding and other milk/ liquids/complementary foods (%) E				
Thailand	26.6	5.4	19.5	48.5	68.0	-	2005-2006	MICS 2005-2006
Togo	31.4	28.4	15.0	25.3	40.3	-	2006	MICS 2006
Uganda	0.4	60.1	7.3	32.2	39.5	20.4	2006	DHS 2006: p. 159, Table 12.3; p. 161, Table 12.4
Ukraine	20.6	6.0	10.5	62.8	73.3	-	2005	MICS 2005
United Republic of Tanzania	2.1	41.3	18.3	38.4	56.7	21.1	2004-2005	DHS 2004-2005: p. 180, Table 11.2; p. 182, Table 11.3
Zambia	0.6	40.1	26.0	33.3	59.3	21.4	2001-2002	DHS 2001-2002: p. 166, Table 11.2; p. 168, Table 11.3
Zimbabwe	2.0	22.2	15.5	60.4	75.9	18.8	2005-2006	DHS 2005-2006: p. 151, Table 11.2; p. 152, Table 11.3

Countries with disaggregated ARV regimens

Definitions:

Breastfeeding status:
Per cent distribution of living children under 6 months by breastfeeding status (not breastfeeding, exclusively breastfeeding, both breastfeeding and receiving plain water, and both breastfeeding and receiving other milk/liquids/complementary foods). Breastfeeding status refers to 24 hours preceding the survey. Children classified as breastfeeding and plain water only receive no other complementary foods or liquids.

Mixed feeding:
Calculated by adding the percentage of children breastfeeding and receiving plain water and the percentage of children breastfeeding and receiving other milk/liquids/complementary foods
.

Median duration of breastfeeding:
Median duration of any breastfeeding among children born in the three years preceding the survey. Medians are based on current status and durations are in months.

Notes:
a "The survey estimates do not represent Angola as a whole because the sample was restricted to territory that was regarded as secure by the Government. That territory comprised only about 65 per cent of the population. An important point to note is that most of the secured territory in Angola is urban, while most of the unsecured territory is rural. For this reason the sample is disproportionately larger in urban communities. However, since most of the urban community in Angola is secure, the urban part of the sample is a fairly accurate representation of all of urban Angola. By contrast, the rural sample only represents the rural secured territory; since a large proportion of rural Angola was not covered by the survey sample, it is not expected that the rural results would reflect rural Angola as well as the urban results reflect urban Angola. The totals, that is, urban and rural combined, represent what can be described as Angola-Secured Territory but not the nation as a whole. We advise users to keep these points in mind when analyzing the data.

Appendix 4: Eighteen Month Postnatal Transmission of HIV[22]

Eighteen month postnatal transmission of HIV among children diagnosed uninfected at 4 weeks of age stratified by maternal antenatal CD4 count. Pooled analysis of Vertical Transmission Study (VTS) (South Africa) and Ditrame (Côte d'Ivoire) studies. N=1151

Antenatal maternal CD4 count (cells/ml)	N	Number of children HIV-infected through breastfeeding	HIV postnatal transmission (%)	95% confidence interval
< 200 (10% mothers)	119	15	15.3	9.5-24.2
≥ 200	1032	57	6.2	4.9-8.0
< 250	181	20	11.0	5.3-16.2
≥ 250	970	52	5.4	3.5-6.5
< 350	353	38	12.6	9.3-16.9
≥ 350	798	34	4.8	3.4-6.6
< 200	119	15	15.3	9.5-24.2
200-349	234	23	11.3	7.6-16.5
350-500	320	18	6.3	4.9-9.1
≥ 500 (41% mothers)	478	16	3.7	2.3-6.0

- Median duration of breastfeeding: 5 months overall (different patterns by country)
- 18-month postnatal transmission: 9.0% in Côte d'Ivoire and 5.0% in South Africa
- 9.0 transmissions per 100 child-years of breastfeeding (95% CI: 6.2 - 11.7)

[22] Dabis, François DABIS, MD, PhD. "Long-term effectiveness of interventions to prevent mother-to-child transmission of HIV" Slide 11. Unpublished presentation July 2008.

Appendix 5: MTCT Risk for Breastfeeding Women on ART[23]

Summary of studies of mother-to-child transmission of HIV risk for breastfeeding women on ART stratified by antiretroviral intervention:

Study	Antiretroviral intervention		MTCT risk according to baseline maternal CD4 count (95% confidence interval)
	Maternal regimen Infant regimen	Duration	
Kisumu, Kenya	ZDV/3TC+NVP* NVP single dose for infants	from 34 weeks of gestation until 6 Mo post-partum but continued if WHO treatment criteria were met	Among women with CD4 <250: 4.3% at 1 Mo (1.8-10.0) 5.2% at 6 Mo (2.4-11.2) 6.7% at 12 Mo (3.2-13.9) Among women with CD4 ≥250: 3.8% at 1 Mo (2.2-6.3) 4.9% at 6 Mo (3.1-7.7) 5.5% at 12 Mo (3.6-8.4)
Kesho-Bora, Burkina Faso - Kenya	ZDV/3TC+NVP NVP single dose for infants	from 18-36 weeks of gestation	Among women with CD4 <200: 6.4% at 12 Mo (0.3-12.4)
MTCT-Plus, Côte d'Ivoire	ZDV/3TC+NVP NVP single dose + 1 week of ZDV for infants	from 20 weeks of gestation	Among women eligible for ART: 1.0% at 1 Mo (0.0-3.1) 3.3% at 12 Mo (0.0-6.9)
Dream cohort, Mozambique	ZDV/3TC+NVP NVP single dose for infants	from 15 weeks of gestation	Among women eligible for ART: 1.2% at 1 Mo 2.2% at 6 Mo 2.8% at 12 Mo
AMATA cohort, Rwanda	ART eligible (CD4<350 or stage IV): d4T+3TC+NVP Non eligible ZDV+3TC+EFZ NVP single-dose + 1 week of ZDV for infants in both strata	Non eligible: from 28 weeks of gestation until 7 Mo post-partum Stop breastfeeding at 6 Mo	1.1% at Day 1 1.5% at 7 Mo
MITRA-Plus cohort, Tanzania	ZDV+3TC+NVP† 1 week ZDV+3TC for infants	from 34 weeks of gestation until 6 Mo post-partum	4.1% at 1.5 Mo (2.1 – 6.0) 5.0% at 6 Mo (3.2 – 7.0)

[23] Dabis, François DABIS, MD, PhD. "Long-term effectiveness of interventions to prevent mother-to-child transmission of HIV" Slides 12-14. Unpublished presentation July 2008.

Appendix 6: MTCT Risk for Infants Given PEP[24]

Studies that administered post-exposure prophylaxis (PEP) to breastfed infants assumed not to have contracted HIV during gestation/birth:

Study	Antiretroviral intervention		MTCT risk according to baseline maternal CD4 count (95% confidence interval) [duration of breastfeeding]
	Maternal regimen	Infant regimen	
SIMBA, Rwanda	ZDV+ddI from 36 weeks of gestation to 1 week post-partum	daily NVP or 3TC * from birth for up to 6 months	6.9% at 1 Mo 7.7% at 6 Mo (independent of ARV infant regimen [14 weeks]
MASHI, Botswana	ZDV+sdNVP from 36 weeks of gestation to 1 week post-partum	daily ZDV from birth for up to 6 months	4.6% at 1 Mo 9.0% at 7 Mo 9.5% at 18 Mo [unknown – mothers instructed to wean at 5 Mo]
MITRA, Tanzania	ZDV+3TC from 36 weeks of gestation to 1 week post-partum	daily 3TC from birth for up to 6 months	3.8% at 1.5 Mo (2.0-5.6) 4.9% at 6 Mo (2.7-7.1) [18 Mo]
Extended Infant Post-Exposure Prophylaxis study (PEPI), Malawi	sdNVP	daily NVP or NVP/ZDV from birth for up to 14 weeks	Among infants who were HIV-uninfected at birth Infant NVP prophylaxis 5.9% at 9 Mo (3.9-7.0) Infant NVP/ZDV prophylaxis 6.4% at 9 Mo (4.9-8.3) [unknown – most infants weaned between 6 and 9 Mo]
SWEN, Ethiopia, Uganda, India	sdNVP	daily NVP from birth for up to 6 weeks	Among infants who were HIV-uninfected at birth 2.5% at 1.5 Mo 6.9% at 6 Mo [unknown – most infants weaned between 14 weeks and 6 Mo]

[24] Dabis, François DABIS, MD, PhD. "Long-term effectiveness of interventions to prevent mother-to-child transmission of HIV" Slides 15-16. Unpublished presentation July 2008.

Appendix 7: Probability of Survival of Infants/Children on ART

The following tables summarize the findings of 14 prospective studies (observational cohorts, cross-sectional studies or clinical trials) that reviewed mortality after ART initiation in children in LINCs.

Survival probabilities[25]

Study	Probability of survival (%) [95 CI]					
	6 mths	12 mths	18 mths	24 mths	36 mths	42 mths
Eley 2006	NM	0.84 [0.80-0.87]	NM	NM	NM	NM
O'Brien 2006	NM	0.95 [0.93-0.97	NM	NM	NM	NM
Fassinou 2004	0.92 [0.84-0.97]	0.91 [0.82-0.96]	0.88 [0.78-0.94]	0.88 [0.78-0.94]	0.88 [0.78-0.94]	0.86 [0.77-0.92]
Arrive in press	0.95 [0.93-0.96]	0.93 [0.92-0.95]	-	0.92 [0.90-0.94]	-	-
Bolton-Moore 2007	0.95 [NM]	0.94 [NM]	0.92 [NM]	0.91 [NM]	0.90 [NM]	NM
Janssens 2007	NM	0.92 [NM]	NM	0.91 [NM]	NM	NM
O'Brien 2007	0.92 [0.90 – 0.94]	0.89 [0.86 – 0.92]	NM	0.82 [0.78 – 0.86]	NM	NM
Reddi 2007	NM	0.91 [0.85-0.95]	0.91 [0.85-0.95]	0.91 [0.85-0.95]	NM	NM

Survival probabilities adjusted for baseline %CD4[26]

Study		Probability of survival (%) [95% CI] (P=0.15)		
		<5%	[5%-15%[	≥15%
O'Brien 2007	6 mths	0.85 [0.76 - 0.91]	0.94 [0.91 - 0.96]	0.92 [0.86 - 0.96]
	12 mths	0.83 [0.74 - 0.90]	0.91 [0.87 - 0.93]	0.90 [0.83 - 0.94]
	24 mths	0.80 [0.69 - 0.87]	0.82 [0.75 - 0.87]	0.86 [0.76 - 0.92]

[25] Dabis, François and Namale, Leticia "Mortality after antiretroviral therapy (ART) initiation in children in lower-income countries (LINCs)" Slides 7-8. Unpublished presentation July 2008.

[26] Dabis, François and Namale, Leticia "Mortality after antiretroviral therapy (ART) initiation in children in lower-income countries (LINCs)" Slide 9. Unpublished presentation July 2008.

Appendix 7: Probability of Survival of Infants/Children on ART *(continued)*

Survival probabilities adjusted for first line ART[27]

	Probability of survival at 12 mths (%) [95% CI]				
	AZT+3TC+NFV	**AZT+3TC+EFV**	**d4T+3TC+EFV**	**d4T+3TC+NFV**	**Others**
Wemin 2006	0.95 [NM]	0.94 [NM]	0.85 [NM]	0.81 [NM]	0.85 [NM]

Survival probabilities adjusted by WHO stage[28]

	Probability of survival at 12 months (%) [95% CI]		
	WHO stage 2 (n=3)	**WHO stage 3 (n=149)**	**WHO stage 4 (n=255)**
Eley 2006	1.0 [NM]	0.96 [0.91-0.98]	0.77 [0.71-0.82]

[27] Dabis, François and Namale, Leticia "Mortality after antiretroviral therapy (ART) initiation in children in lower-income countries (LINCs)" Slide 10. Unpublished presentation July 2008.

[28] Dabis, François and Namale, Leticia "Mortality after antiretroviral therapy (ART) initiation in children in lower-income countries (LINCs)" Slide 11. Unpublished presentation July 2008.

Appendix 8: Overview of Co-trimoxazole Studies

Overview of the analysis of 7 papers deemed meaningful and useful (3 are from the same study) describing prospective studies (observational cohorts, cross-sectional studies or clinical trials) of paediatric co-trimoxazole in lower- and middle-income countries.

Overview of the studies[29]

Reference	Location	Type of study	Number receiving CTX (placebo) n [%]	Median age years [IQR]	Median CD4 percentage [IQR]	Median follow-up months [IQR]	Death n [%] CTX group (no CTX)
Chokephaibulkit 2000	Thailand	Cohort	53	4-8 (in weeks)	NM	6 [NM]	3 (5.7)
Madhi 2002	South Africa	Cohort	91	NC	NM	NM	NC
Chintu 2004	Zambia	RCT	265 (No CTX 269)	4.2 [2.1-8.3] (4.5 [2.1-8.2])	11 [7-17] (10 [5-16])	19.4 [14.7 - 24.1] (17.7) [12.9-23.9]	74 [28%] (112) [42%]
Harambat 2008	Cote d'Ivoire	2 comparative cohorts	98	5.7 [1.8-16.5] 6.6 [0.7-14.6] (in weeks)	18 [6 - 37]	8.7 [0.4-18.0] 12.1 [0.7-18.0]	34 (64.1) 23 (51.1)
Mulenga 2007	Zambia	RCT	265	4.4 [0.7-15.2]	7.5 [2.1-11.1]	36 [30-42]	74 (28)
Theophil 2007	Tanzania	Cross-sectional	78 [65]	79 [6-165] (in months)	NM	NM	1 (7.7)
Walker 2007	Zambia	RCT	278	7.9 [6.0 – 11.7]	19 [13-27]	546 CY	40 (14.2)

Mortality comparison — overall and by time period[30]

Reference (CHAP trial)	Death n (%) CTX group	Death n (%) Placebo / control group	HR [CI]	P value
Chintu 2004	74 (28)	112 (42)	0.57 [0.43 – 0.77]	P = 0.0002
Mulenga 2007	74 (28)	112 (42)	0.57 [0.43 – 0.77]	P <0.001

Reference	≤6 months		6 – 12 months	
	HR [CI]	P value	HR [CI]	P value
Chintu 2004	0.56 [0.36 – 0.87]	P = 0.002	0.70 [0.41 – 1.23]	NM

[29] Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 8. Unpublished presentation July 2008.

[30] Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 9. Unpublished presentation July 2008.

Appendix 8: Overview of Co-trimoxazole Studies
(continued)

Mortality comparison by age groups[31]

Reference	Age group (years)	CTX Deaths (%)	Placebo Deaths (%)	HR (CI)	P-value
Chintu 2004	<1	8 (73)	8 (89)	0.68 [0.25 – 1.83]	
	1-2	25 (29)	42 (50)	0.43 [0.26 – 0.72]	P = 0.82 (test for heterogeneity)
	2-5	16 (24)	26 (32)	0.68 [0.36 -1.26]	
	6-9	15 (25)	21 (40)	0.54 [0.28 – 1.05]	
	≥10	10 (26)	15 (35)	0.63 [0.28 – 1.41]	

Mortality comparison by CD4 percentages[32]

Reference	%CD4 range	CTX Deaths (%)	Placebo Deaths (%)	HR (CI)	P-value
Chintu 2004	0 – 4	14(52)	20 (53)	0.87 [0.44 – 1.72]	
	5 - 9	16 (27)	24 (44)	0.53 [0.28 – 0.99]	P = 0.36 (test for heterogeneity)
	10 – 14	7 (15)	20 (42)	0.29 [0.12 -0.69]	
	15 - 19	4 (14)	8 (26)	0.51 [0.15 – 1.70]	
	≥20	5 (14)	4 (15)	0.87 [0.23 – 3.24]	

Before-after mortality comparisons[33]

	Mortality rates – deaths per 100 child-years [CI]	
	Before CTX prophylaxis	After CTX prophylaxis
Walker 2007	23 [16 – 34]	15 [8 – 26]

Risk factors of mortality by confirmed PCP[34]

		Children who died n = 20	Children who survived n = 80	P value
	Age in years [range]	3.0 [2.2 – 14.2]	5.1 [1.7 – 27.3]	P = 0.003
Madhi 2002	Number (%) on CTX prophylaxis	2 (10)	31 (38.8)	P = 0.03

Co-trimoxazole had a protective effect even among HIV-infected children who later on acquired PCP (age as a possible confounder)

31 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 10. Unpublished presentation July 2008.

32 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 11. Unpublished presentation July 2008.

33 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 12. Unpublished presentation July 2008.

34 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 13. Unpublished presentation July 2008.

Appendix 8: Overview of Co-trimoxazole Studies
(continued)

Risk factors of all-cause mortality with co-trimoxazole use[35]

	Cut-off	Mortality rates Deaths per 100 CY [95% CI]	Relative Risk [95% CI]	P value
a. Weight-for-age z-scores				
Walker 2007	<–3 SD	15 [10 – 24]	5.25 [2.50 – 11.01]	NM
b. CD4 percentage				
Walker 2007	<15%	7 [5 – 12]	4.08 [1.38 – 11.80]	NM

Causes of death according to co-trimoxazole use[36]

	CTX group n = 35 Number	**Placebo group n = 56 Number**	**P-value (test for heterogeneity)**
Mulenga 2007			P = 0.96
Septicemia	03	02	
Meningitis	04	04	
Pneumonia/ empyema	10	22	
Serious bacterial infections	17	28	
Other infections	01	02	
Tuberculosis	01	03	
Diarrhea and/ or dehydration	04	08	
Malnutrition	03	04	
Malaria	01	01	
Anaemia	02	01	
Other	05	06	
Not known	01	03	
Harambat 2008 ♣	n=98		
Pneumonia	18		
Diarrhea	16		
Neurological disorders	06		
Failure-to-thrive	11		
Indeterminate	06		

35 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 14. Unpublished presentation July 2008.

36 Dabis, François and Namale, Leticia "Mortality after cotrimoxazole (CTX) initiation in children in lower-income countries (LINCs)" Slide 15. Unpublished presentation July 2008.