# CONSULTATIVE MEETING ON

# EVALUATING THE IMPACT OF PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV (PMTCT) SERVICES IN LOW- AND MIDDLE-INCOME COUNTRIES IN AVERTING NEW HIV INFECTIONS IN CHILDREN AND IMPROVING CHILD SURVIVAL

12-13 February, 2009
Vanderbilt University School of Medicine
Nashville, Tennessee, USA

unicef
World Health Organization
UNAIDS
VANDERBILT School of Medicine

# CONSULTATIVE MEETING ON EVALUATING THE IMPACT OF PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV (PMTCT) SERVICES IN LOW- AND MIDDLE-INCOME COUNTRIES IN AVERTING NEW HIV INFECTIONS IN CHILDREN AND IMPROVING CHILD SURVIVAL

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## ABBREVIATIONS

| | |
|---|---|
| **AIDS** | Acquired Immunodeficiency Syndrome |
| **AIS** | AIDS Indicator Survey |
| **ANRS** | Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (France) |
| **ART** | Antiretroviral Therapy |
| **ARV** | Antiretroviral |
| **CDC** | Centers for Disease Control and Prevention (USA) |
| **CIFF** | Children's Investment Fund Foundation |
| **CTX** | Cotrimoxazole |
| **DHS** | Demographic and Health Survey |
| **EGPAF** | Elizabeth Glaser Pediatric AIDS Foundation |
| **EPI** | Expanded Programme on Immunization |
| **FHI** | Family Health International |
| **HAART** | Highly Active Antiretroviral Therapy |
| **HIV** | Human Immunodeficiency Virus |
| **HPLC** | High-Performance Liquid Chromatography |
| **IATT** | Inter-Agency Task Team |
| **MCH** | Maternal and Child Health |
| **MICS** | Multiple Indicator Cluster Survey |
| **MTCT** | Mother-to-Child Transmission |
| **NIH** | National Institutes of Health (USA) |
| **NVP** | Nevirapine (a non-nucleoside reverse transcription inhibitor antiretroviral drug) |
| **PCR** | Polymerase Chain Reaction |
| **PEARL** | PMTCT Effectiveness in Africa: Research and Linkages to Care and Treatment |
| **PEPFAR** | United States President's Emergency Plan for AIDS Relief |
| **PMTCT** | Prevention of Mother-to-Child Transmission of HIV |
| **QI** | Quality Improvement |
| **TLC** | Thin-Layer Chromatography |
| **UNAIDS** | Joint United Nations Programme on HIV/AIDS |
| **UNICEF** | United Nations Children's Fund |
| **USAID** | United States Agency for International Development |
| **VIGH** | Vanderbilt University Institute for Global Health, Nashville, Tennessee, USA |
| **WHO** | World Health Organization |

# Executive Summary

The United Nations Children's Fund (UNICEF), the World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS), in collaboration with the Vanderbilt University Institute for Global Health (VIGH), hosted a consultation to review the most commonly used methods for assessing the impact of programmes for the prevention of mother-to-child transmission of HIV (PMTCT) in low- and middle-income countries. To date, UNICEF, WHO and UNAIDS have been reporting global progress on PMTCT implementation using globally agreed-upon indicators that include: HIV testing in pregnant women and receipt of antiretroviral (ARV) drugs in HIV-positive pregnant women. The data indicates that much progress has been achieved. However, translating these data into impact using existing models is limiting; the consultation sought to build a consensus on the most robust and feasible approaches for assessing PMTCT programme impact in averting new paediatric HIV infections and improving HIV-free child survival.

A desk review of existing methodologies for measuring PMTCT impact was conducted prior to the meeting. Presented and discussed during the meeting were major PMTCT impact studies (both published and unpublished) as well as country examples, assessing various methodologies applied in different epidemiological contexts and settings; issues related to how infant feeding practices impact on child HIV outcomes; the use of laboratory measurements; and statistical modelling of PMTCT impact. Group discussions focused on three thematic areas: 1) Routine programme monitoring data; 2) Health facility-based surveys; and 3) Population-based surveys to draw recommendations.

## *Meeting Conclusions*

Participants concluded that:

a) To the extent possible, it would be ideal to assess impact through the measurement of new child infections averted, mortality rates among HIV-exposed but uninfected children and HIV exposed and infected children, and HIV-positive mothers. However, there are various challenges in measuring these in different settings.

b) Indicators to be considered when doing such studies may include:
   - Percentage of HIV-exposed children that are HIV-free at 12 and 18-24 months (accounting for breastfeeding transmission, replacement feeding risks and other mortality factors).
   - Percentage of HIV-exposed children with HIV-infection at the 6 weeks immunization visit.
   - Percentage of HIV infections averted in children at 6 weeks
   - HIV prevalence in children 6-8 weeks of age
   - HIV prevalence in children under age 2
   - Percent of HIV-infected children born to an HIV-infected mother
   - Percent of pregnant women who are HIV-infected
   - Infant and child mortality in HIV-exposed but uninfected children at 12 and 18-24 months
   - Infant and child mortality in HIV-infected children at 12 and 18-24 months

   Some indicators, although ideal, are difficult to measure at the national level. In addition, some of the measurement methodologies may only be practical in settings with certain epidemiological and health-system characteristics. The appropriate indicator(s) and methodology will depend on the context of the country.

c) The meeting also identified other proxy indicators for PMTCT impact in high HIV prevalence settings (See Appendix 4 on group work summaries):

- Infant and child mortality from all causes
- Maternal mortality, given that maternal deaths are related to poor outcomes (deaths) in their infants, irrespective of the infant's HIV status.

d) Some PMTCT process indicators, many identified from the PMTCT and paediatric HIV Inter-Agency Task Team (IATT) summary of core national programme monitoring and evaluation indicators were also discussed and are still relevant.

- Percentage of HIV-positive pregnant women who receive ARVs for PMTCT, disaggregated by regimen categories
- Percentage of HIV-positive pregnant women assessed for ART eligibility either clinically or using CD4
- Percentage of HIV positive pregnant women receiving ART for their own health.
- Percentage of HIV-exposed infants initiated on cotrimoxazole (CTx) prophylaxis within 2 months of birth
- Percentage of HIV-exposed infants who received an HIV test within 2 months of birth
- Percentage distribution of breastfeeding practices (exclusive breastfeeding, replacement feeding, mixed feeding) of HIV-exposed infants at the DPT3 immunization visit
- Percentage of women 15–49 years old attended at least once during pregnancy by skilled health personnel (doctors, nurses or midwives)
- Percentage of births attended by skilled health personnel (doctors, nurses or midwives) in the past year (or two years) according to the woman's HIV sero-status

General consideration was given to potential unintended negative effects of PMTCT on the delivery of other health services to mothers and their children, such as antenatal care and infant feeding practices in the general population.

d) Discussions on methodological approaches

These discussions were based on the study population (facility-based versus population-based) and the actual study design (cohort or case-control versus survey approach).

Key agreement on methodological approaches to be considered include:

- Facility-based surveillance targeting infants attending immunisation clinics: The most feasible approach is to set up a surveillance system that tests infants at 6-8 weeks at the 6 week immunisation visit in countries with good immunisation coverage.
- Household population-based surveys: Population-based surveys have better external validity and generalizability and they allow for measurement of other important outcomes at population-level. However, they require high response rates, large sample sizes, and are resource intensive; they are also subject to significant bias due to incomplete identification of the exposed population or losses over time (e.g. deaths of children before 12 months).
- Follow-up of cohorts of HIV exposed infants and children: This approach was found to have high internal validity to allow for direct measurement of mother-to-child transmission (MTCT) rates and related-mortality. However, this methodology is complex, time-consuming, not widely applicable, subject to the Hawthorne effect (when participants or patients have a better experience because of the quality of follow-up or care received) and is subject to potential bias due to the rate of loss to follow-up over time.
- Combined approaches of the above

## *Background and Rationale*

HIV continues to have a significant impact on children. In 2008, an estimated 2.1 million children were living with HIV worldwide, there were 4300,000 new HIV infections in children, and 280,000 HIV-related deaths among children.[13] Children, according to these estimates, constitute about 6% of all people living with HIV, 16% of new infections, and 14% of all AIDS-related mortality.[1] The majority of children living with HIV are in Sub-Saharan Africa.[13] HIV is also resulting in the stalling or reversal of gains in child survival in some countries in this region.

UNICEF and WHO, on behalf of the Inter-Agency Task Team (IATT) on PMTCT, currently facilitate global data collection of process indicators to monitor global trends in provision of PMTCT and paediatric HIV services. While these data provide essential information regarding progress,[2] they do not measure the impact of these services or interventions on HIV infections averted among children or HIV-free child survival. Increasingly, the international community is looking for clear, standardized and simple approaches to assess the impact of PMTCT services which take into account the typology of the local epidemic and the context-specific epidemiology of child morbidity and mortality. A number of studies have been conducted in low- and middle-income countries to measure the impact of programmes to prevent mother-to-child transmission of HIV, but with variable reliability.[5-12] These studies have differed in their methodological approaches and in the outcomes selected for assessment.

Following up on the recommendations of the Consultative Meeting on Data Collection and Estimation Methods Related to HIV Infections in Infants and Children, held July 8-10 2008 in New York,[14], UNICEF, WHO and UNAIDS, in collaboration with Vanderbilt University Institute of Global Health, hosted a consultation to review approaches to assess the impact of PMTCT programmes. A primary aim of the consultation was to build consensus on approaches which could be considered for wider implementation in a number of resource-limited countries (see Appendices 1 and 2: Concept Note and Meeting Agenda).

**Meeting Goal**

- To gather and share country experiences in PMTCT impact assessment and discuss methodologies used in past and present research studies and evaluations, with the aim of reaching consensus on the most effective way to develop and design approaches to assess the effectiveness of national PMTCT programmes on HIV-free survival among children that can be implemented widely in a number of countries.

**Meeting Objectives**

1. To review the most commonly used methodological approaches for assessing the impact of PMTCT programmes on essential child health outcomes in low- and middle-income countries (including their strengths and limitations), taking into account the different HIV epidemic contexts (high and low prevalence).
2. To build consensus on the most robust and feasible approaches for assessing impact of national PMTCT programmes in averting new paediatric HIV infections and improving child survival.
3. To agree on a PMTCT Impact Assessment Framework for assessing the impact of PMTCT programmes on essential child health outcomes that can be implemented widely in a

number of resource-limited countries. The Framework will highlight various methodological approaches to glean more definitive data on HIV-free child survival, and will cite requirements for applying these methodologies in different settings, including data availability, additional data needed, operational considerations for data collection and varying approaches appropriate for different epidemic types.

**Meeting participants**

The consultation included 51 experts in PMTCT and paediatric HIV service delivery, epidemiology, monitoring and evaluation, survey data collection and interpretation, laboratory assessment, and mathematical modelling. Participants represented United Nations agencies (UNICEF, WHO and UNAIDS); United States Government agencies – the United States President's Emergency Plan for AIDS Relief (PEPFAR), United States Agency for International Development (USAID) and Centers for Disease Control and Prevention (CDC); international NGOs and foundations - Family Health International (FHI), Elizabeth Glaser Pediatric AIDS Foundations (EGPAF), Children's Investment Fund Foundation (CIFF); Research Institutions - Agence Nationale de Recherches sur le SIDA et les Hépatites Virales (ANRS), National Institutes of Health (NIH), epidemiologists, monitoring and evaluation,statistical modelling, and laboratory experts from Universities; and representatives from countries with generalized HIV epidemics (Zambia and South Africa) and from countries with low level or concentrated HIV epidemics (Brazil, Thailand and India), (see Appendix 3).

**Consultation Methodology**

On Day 1, the meeting format included plenary presentations and discussions. Presentations covered topics related to current methods for evaluating PMTCT, effects of breastfeeding on transmission, laboratory requirements for infant diagnosis and updates on current PMTCT monitoring systems, among others (see Appendix 2).

Participants were divided into three working groups on Day 2 to discuss strengths and limitations of different methodological approaches for evaluating PMTCT impact, with a focus on routine programme monitoring data, health facility-based surveys and studies and population-based surveys. The group rapporteurs presented their findings in plenary sessions that followed the group meetings. An initial proposal for a framework for assessing PMTCT impact was presented in the final session (see Annex 5).

## *SUMMARY OF PLENARY PRESENTATION SESSIONS*[1]

### 1. Measuring Impact of PMTCT Interventions

Impact studies are used to determine: whether an implemented intervention has made a difference, the magnitude of change observed and how the programme can be improved. The UNAIDS MERG has defined impact evaluation as an assessment of "the long-term, cumulative effect of programmes or interventions over time on what they ultimately aim to change, such as a change in HIV infection and AIDS-related morbidity and mortality"[15]. Impacts at the population-level are rarely attributable to a single programme/intervention, but to the collective effects of related programmes/interventions.

The impact or effectiveness of PMTCT interventions are a function both of how much the prescribed regimen reduces the risk of mother-to-child transmission (MTCT) (efficacy) and the proportion of the at-risk population that accesses and correctly uses the intervention (effective coverage). Coverage is diminished when PMTCT services are not accessible to women who need them, when service delivery failures occur, or when women do not accept or adhere to the interventions. The "PMTCT cascade" has multiple steps that must be negotiated successfully (see Table 1 below).

**TABLE 1: PMTCT CASCADE STEPS** (adapted from E. M. Stringer et al.[4])

| **PMTCT STEPS**<br><br>**All pregnant women should:** | **Causes of reduced coverage** |
|---|---|
| A. Attend institutional antenatal care | No or only partial antenatal care available |
| B. Be offered HIV test and counselling | -High cost of testing or accessing antenatal care for the expecting mother<br>-Lack of counselling and testing services or supplies |
| C. Accept taking the HIV test | -Fear of stigma or lack of interest<br>-Cultural, family and social barriers |
| D. Obtain test results | -Non-retrieval of results by mother<br>-Results lost or not provided by health facility |

**HIV-positive women should then receive the PMTCT intervention.**

| **PMTCT STEPS** | **Causes of reduced coverage** |
|---|---|
| E. Agree to antiretroviral prophylaxis | -Fear of stigma<br>-Sub-optimal quality of counselling |
| F. Access effective antiretroviral regimen* | -Unavailability/high cost of ART<br>- Low capacity of health personnel to prescribe appropriate regimens. |
| G. Adhere to antiretroviral prophylaxis | -Failure to self-administer ART<br>-Home delivery<br>-Loss to follow-up |

[1] Copies of the specific presentations are available upon request.

| | |
|---|---|
| H. Adhere to infant ART doses | -Low capacity of health personnel to prescribe appropriate regimen<br>-Unavailability of paediatric treatment<br>-Loss to follow-up |
| I. Receive counselling on infant feeding | -Suboptimal quality of infant feeding counselling |
| J. Apply minimum risk infant feeding practices | -Lack of safe, acceptable, affordable alternatives to breastfeeding<br>- Cultural barriers and norms |
| K. Infant is tested for HIV for diagnosis/treatment | -No testing for infants available<br>-Loss to follow-up |
| L. Confirmatory testing at 18-24 months | -No testing for infants available<br>-Loss to follow-up<br>- Death of child |
| M. ART for children testing HIV positive | -Loss to follow-up<br>-Death of child<br>-Social barriers |

**ART will differ based on programme capacities and funding, drug availability, staffing level, and national policies.*

When considering conducting an impact evaluation, the methodology should take into account the infrastructural capacity, outcome measures to be assessed, and the epidemiological and operational setting.

### Process indicators

Currently, a series of process indicators are used to monitor provision of PMTCT services. These data indicate progress in scale-up of services by monitoring the successful migration of women down the "PMTCT cascade" (see Table 1).

Measuring the proportion of women who move successfully through each step of this cascade is important to evaluate successful implementation of any programme, as each stage has unique programmatic elements and challenges, requiring tailored solutions. Process indicators are especially good at identifying poorly functioning PMTCT programmes, but they are not surrogates of a definitive outcome, such as HIV-free survival. Currently reported PMTCT indicators can have a limited role in assessing impact of PMTCT interventions on *in utero* or intrapartum transmission. However, they provide very little information on longer term effects of different infant feeding practices, or combination ARV regimens given to the mother on HIV transmission rates or child survival, for example.

Where breastfeeding is the norm and prevention and care capacities are typically the least developed, HIV-free child survival would be ideal to measure or estimate at ages 18 to 24 months, but this is not possible at the national level. Thus, other indicators of PMTCT interventions can be used to try and model HIV-free child survival at 18-24 months.

## Methodological approaches

Different methodologies for impact studies were discussed with particular attention to the effects of the fertility rate and the type of HIV epidemic on the feasibility of a particular methodology. These included the potential use of process indicators, but more importantly, cohort studies, cross-sectional health facility surveys of children 6-8 weeks old and population-based surveys. Modelling was also discussed.

**Population-based surveys**

Population-based surveys allow the assessment to have better external validity and hence to be more generalizable to the wider population. Surveys also have the advantage of collecting other population measures of important programme outputs (e.g. proportion breastfeeding). However, a high response rate is needed for the survey to adequately measure PMTCT programme effectiveness. In addition, it has been problematic to collect sensitive personal information about HIV status, treatment and other related data from respondents through population-based surveys.‘

When discussing population-based survey approaches, many of the participants felt that some data collection for impact evaluations could be incorporated into existing Demographic and Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS), and other nationally representative surveys conducted in-country. Population-based surveys can be used to capture some information related to PMTCT interventions such as women completing the testing and counselling process, women receiving counselling on infant feeding at first follow-up visit and infant feeding practices. Of particular interest is the potential to capture HIV-infected infants born to HIV-infected mothers in some settings, enabling a survey to estimate population-based prevalence rates. A DHS survey that collected this information was conducted in Uganda in 2004-2005. While this provided a useful estimate of HIV prevalence among children under 5, this estimate could be misleading because it does not take into account differences in mortality of HIV-infected children among all children in the survey, and fails to report on children who have died prior to the survey.

There are also other limitations of population-based survey estimates of transmission rates. First, to establish vertical transmission rates, HIV status of both mother and infant must be known. This can be difficult to ascertain if either mother or child has died. Without that information, mother-infant pairs cannot be used in population-based estimates. There are also concerns about how to accurately determine time of sero-conversion for the mother since her sero-status at the time of survey does not necessarily reflect her HIV status during pregnancy and might overestimate this proportion. This information is particularly relevant if older children are included in the survey, as was the case in Uganda. However, typical sampling strategies used for these surveys would not be large enough to provide accurate power to estimate prevalence rates in infants, except in countries with very high HIV prevalence. Finally, there is always the concern about the cost of such surveys, although that is less of a consideration when a child component is added to an adult survey that is already funded.

**Health Facility-based Surveys**

In South Africa, a facility-based study was used to assess the impact of PMTCT in seven sites in three districts. Expanded Programme on Immunizations (EPI) clinics were used as a venue for HIV testing of all infants reporting for six-week immunization visits, whether or not the mother was known to be HIV-positive or a PMTCT programme participant. The transmission rate at six weeks was calculated using detection of antibodies in the infant (indicating maternal status and therefore exposure = denominator) and Polymerase Chain Reaction (PCR) in the infant (=numerator); other information, including infant mortality (using modified previous birth technique), and related to programme uptake and possible barriers to service were also collected. Most women (89%) consented to a heel prick for their infants. A disaggregation of transmission rates resulted in a robust description of which pregnant women were most likely to transmit the virus to their children. The study demonstrated that a large number of women were infected with HIV after their initial negative antenatal HIV tests, resulting in a higher transmission

rate from these unrecognized HIV-infected women to their babies. The survey also tracked how infant mortality has changed over time, though it was not clear how much of that increase was a result of HIV. A principal advantage of this survey method was its representativeness; given that a large proportion of infants in South Africa attend six-week EPI visits, this study methodology can be used for a country-level evaluation of PMTCT impact. In countries where EPI is not well attended, the survey may not be representative. This methodology is also robust and relatively straightforward to manage and implement. However, logistical issues could be significant if implemented at scale nationally, with dried blood spot (DBS) collected for all children attending immunization clinics. Local community health workers were trained and dried blood spot samples were transported to the lab every 1-2 weeks. Given its relative simplicity (though cost is not insignificant), it is a process that can be repeated every 2-3 years to provide trend data. Considerations of HIV prevalence should be taken into account when implementing this approach at the national level. Retrospective process indicators can also be determined, though this method did not explain why women and their infants failed to progress successfully through all the steps of the PMTCT cascade.

**Combined facility and population-based surveys**

The PMTCT Effectiveness in Africa: Research and Linkages to Care and Treatment (PEARL) study, has combined both population-based survey data with facility-based data to provide a more comprehensive and robust impact assessment method. This study was conducted in 43 randomly selected sites in 4 countries: Zambia (11 sites); Cote d'Ivoire (10 sites); RSA (14 sites in Free State and Western Cape); and Cameroon (8 sites in English-speaking provinces).

PEARL consists of facility-based process data and cord blood surveillance plus a structured evaluation and a population-based survey.[4]

This combination of methodologies provides PMTCT coverage data, process indicators for progression through the PMTCT cascade, socioeconomic and demographic information and HIV-free child survival estimates for women stratified by PMTCT usage. A cost-effectiveness analysis is also being conducted. The advantage of this combination approach is that not only are robust process/output indicators collected (NVP uptake coverage is determined by unlinked cord blood surveillance) to inform why coverage might be low among women accessing PMTCT services, but it also provides a longer-term outcome indicator for PMTCT, namely HIV-free child survival at two years. At present, PEARL methodologies (including use of the High-Performance Liquid Chromatography [HPLC]-dependent cord blood NVP tests, for example) might be too costly for widespread implementation, but new technologies may make some of the evaluation elements more affordable over time.[20, 21] It is also a large and complex evaluation that would be difficult to replicate in multiple sites and repeatedly over time.

**Cohort studies**

Cohort studies can directly measure MTCT rates and mortality and also have high internal validity. However, they are complex, time consuming, and not always generalizable at country level due to the representativeness of the cohort, bias due to loss to follow-up and the "Hawthorne" effect.[182]

[2] The Hawthorne effect is the notion that study participants improve an aspect of their behavior because they know they are being studied. For example, if participants in a smoking cessation study are called monthly about smoking cessation, then this may affect their smoking habits.

The *Good Start* study in South Africa is one example of how a cohort study can be used for PMTCT impact evaluations. Women from three PMTCT sites in South Africa were recruited antenatally or post-delivery and were followed up with home visits 36 weeks after delivery. HIV-free child survival was calculated at 36 weeks along with socioeconomic and demographic variables. Loss to follow-up was about 20% for HIV-infected and uninfected mothers. This cohort design allowed for rich analysis of a woman's ability to transition through the PMTCT cascade, as well as providing robust estimates of longer-term outcome measures in infant and mother alike. Using this methodology, *Good Start* was able to estimate that 33% of the difference in HIV transmission and/or death across sites could be explained by socio-demographic factors and health-systems failures. This type of analysis not only yields findings about the effectiveness of the programme, but also provides insights into how the programme can be improved, which will ultimately result in more robust and effective PMTCT interventions. However, given the cost and logistical support necessary for this evaluation, scale-up to an entire province or country would be difficult in resource-limited settings without external funding support. In addition, this type of assessment can only capture impact in the areas where the cohort study is conducted (e.g. the area serviced by the selected clinics with PMTCT programmes) and will fail to capture the more limited impact in areas with limited or no PMTCT programmes.

In Thailand, a perinatal HIV outcome monitoring system (PHOMS) is used to follow-up with infants in 14 provinces; the CHILD reporting system is used to follow-up with children born to HIV-infected mothers nationwide, while CHILDPLUS is used to follow-up with children born to HIV-infected mothers and their families in 11 provinces. The Thai Ministry of Health conducted a five-month study including chart reviews, interviews and focus group discussions to assess the impact of the PMTCT programme in 11 provinces in 2008. The data provided information regarding transmission rates, PMTCT knowledge and uptake, infant feeding practice and uptake of infant HIV testing. This information is supplemented with data gathered from a national surveillance programme. The advantage of this survey methodology over a cohort study is that a more representative sample is collected and survey costs are lower than cohort study costs. The extent to which combining survey results with national surveillance data will create a comprehensive evaluation of PMTCT impact is not yet known.

**Considerations for assessing impact of breastfeeding patterns**

To assess PMTCT impact fully, breastfeeding transmission and also mortality due to non-breastfeeding must be considered. More complex evaluations that determine HIV-free child survival at age 18-24 months are needed to determine if a comprehensive PMTCT programme has had an impact on breastfeeding practices and hence transmission via this route, and also increased morbidity and mortality from non-HIV infectious diseases or malnutrition not associated with breastfeeding. Breastfeeding increases an infant's risk for HIV infection typically by 10% to 20%,[22] such that it must be considered. Not breastfeeding increases the risk of death from diarrhoea or pneumonia by up to 6 times in the first six months of life. Evaluation of infant feeding practices provides process indicators such as proportion of children that are exclusively formula feeding, exclusive breastfeeding or mixed feeding. The fewest HIV transmissions are expected from replacement feeding, but non-HIV-related mortality is also associated with this practice, particularly if food is prepared in unsanitary conditions. Process indicators such as types of breastfeeding practices can enable a comparison of HIV transmission and mortality rates by group.[24]

Capturing breastfeeding information during impact evaluations poses some problems. There is a substantial social desirability bias, such that breastfeeding is favoured in more traditional

societies. In fact, failure to breastfeed is so aberrant that a mother may be labelled as HIV-infected, selfish or incompetent if she chooses replacement feeding for her infant. Without some prospective component to the evaluation, or at least serial surveys, independent verification of feeding practices following the initial survey may be difficult.

### Laboratory considerations and limitations

There are also numerous laboratory issues to consider in the implementation of impact evaluations. Regardless of the process, output or outcome measures chosen (e.g., NVP levels in cord blood, HIV transmission rates at 6-8 weeks or HIV-free child survival at 9, 18, or 24 months) all require a laboratory test for the infant, mother or both.

In developing countries, access to necessary laboratory equipment with trained personnel can be difficult, especially when high-level skills are required for PCR tests and HPLC to measure NVP. To assess infant HIV status, PCR to measure viral DNA is the current standard since infants born to HIV-infected mothers can test positive for antibodies for up to 18 months due to passive placental transfer of maternal antibodies. The availability and expense of PCR limits its use even when dried blood spots are used.

Ultra-sensitive p24 antigen is a promising diagnostic tool for infants aged 2-6 months, although it is not yet commercially available. There are also promising point-of-care PCR diagnostic tools being developed that could be available in a few years.[30] However, each infant HIV diagnostic tool has serious limitations related to quality assurance and inability to efficiently test the volume of samples being sent. High throughput screening that is low in cost and technology-friendly for more rural and resource-limited settings is not yet available. When assessing NVP-levels in cord blood, concerns about cost and feasibility arise. The gold standard for measuring NVP levels in cord blood is to test for its presence using HPLC. However, HPLC is prohibitively expensive, costing US$75-100 per sample. Thin Layer Chromatography (TLC) has been used as a less costly alternative, but sensitivity is too low at present. An immunochromatographic test strip has been deployed at US$4/test with high sensitivity and specificity.[20, 21] This appears to be a cost-effective alternative for NVP detection that could be used for routine cord blood surveillance. However, extensive field testing has not been done with multiple viral subtypes, nor is this test available commercially. Regardless of the outcome measure chosen, issues related to cost, quality of testing, and ability to accommodate high throughput screening must be considered.

### Role of mathematical modelling

While impact studies are necessary to measure the success and limitations of PMTCT programmes, mathematical and statistical modelling can also play an important role in predicting the effects of the programme on a variety of indicators and outcomes. Modelling can depict differing scenarios of programme impact based on changes in the programmatic inputs that might be expected to affect HIV transmission and both HIV-related and unrelated mortality. Modelling can help estimate the answers to key questions such as: What is the impact on HIV-free child survival if maternal prevalence declines due to programmatic inputs? What is the estimated impact of improved PMTCT coverage or more efficacious prevention regimens? For modelling to examine alternative scenarios and predict effects of PMTCT programmes, key parameters must be measured such that accurate modelling assumptions can be built into the models. Parameters based on excellent epidemiologic and clinical trial studies are valuable, but too often, data are limited. Impact of ART on breastfeeding transmission and mortality is one example, with only a few studies to cite. This risks the use of parameters that do not accurately represent true transmission dynamics in real world settings.

More robust and accurate estimates are needed that are representative of a variety of populations and types of epidemics. Studies are needed that examine data gaps systematically to enable more valid models to be developed to assess the effects of breastfeeding choices and patterns on HIV transmission rates and mortality, for example. Models are often created to examine certain scenarios on a national or even regional/global scale. Such models may not guide local programme officials because they are often based on national level data and estimates. Models that can be created with accurate district or even provincial level parameters would be especially beneficial to local programmes. The lack of age-specific data on important parameters such as proportion of infants on ART or proportion on cotrimoxazole is a further limitation in the modelling arena. Mathematical models help to predict effects of a programme and can determine impact of programmes, given varying scenarios. However, without high quality inputs, valid outputs cannot be anticipated.

## *Summary of Working Group Discussions*

Participants broke up into three groups to examine different PMTCT impact evaluation methods and correspondingly appropriate outcome measures for measuring impact:

- Group 1 examined how **routine PMTCT monitoring information** could be used to evaluate programme impact;
- Group 2 examined the feasibility of **health facility-based surveys/studies for PMTCT impact evaluations**; and
- Group 3 discussed the feasibility of using **population-based surveys** for PMTCT evaluation.

Each group discussions were guided by the following questions:

1. What are the most robust and feasible measures for assessing impact of PMTCT and the best way to use them in resource-limited settings? Consider: process issues of testing, uptake, adherence, baby dosing, infant follow-up, breastfeeding; outputs necessary for impact; outcomes that are more definitive, including infant HIV-free survival.
2. What existing data are available and what additional data may be needed in resource-limited settings to enhance measurement of PMTCT programme impact? Consider programme data available at facilities and data available from surveys.
3. What is the operational feasibility of introducing these approaches, and what key action steps are needed for implementation of these methodologies in different epidemic settings?

A worksheet was developed to guide and provide focus for group discussions (see Appendix 4).

The main outputs of the group discussions are summarised in Table 2 below, followed by more detailed discussions on each of the methodologies considered during the meeting.

**TABLE 2: Summary of strengths and limitations of the proposed main outcome measures and impact assessment methodologies**

| | ASSESSMENT | STRENGTHS | LIMITATIONS |
|---|---|---|---|
| **Outcome/impact measures** | Infant HIV transmission at 6 weeks | ▪ Directly measures the effect of the ARV (and C section where applicable) components of the PMTCT programme<br>▪ Can be incorporated into immunization (EPI) visits | ▪ Does not measure programme effectiveness to minimize breastfeeding transmission<br>▪ Requires HIV PCR testing<br>▪ If EPI infrastructure is used, then can only be carried out in populations with good immunization coverage at 6 weeks<br>▪ Must use neonatal mortality data to ensure that transmission rates account for children born 6 weeks prior and not those that survive |
| | HIV-free child | ▪ Directly measures programme | ▪ Low child attendance reduces feasibility of |
| | survival at 18-24 months of age | ▪ effectiveness<br>▪ | ▪ facility-based methods in most resource-limited settings |

| | | | |
|---|---|---|---|
| | | | ▪ Determination of mortality requires active follow up<br>▪ Difficult to link outcome to PMTCT intervention in population studies because of confidentiality issues related to revealing HIV status<br>▪ Methodologies for verbal autopsy to account for cause of deaths problematic |
| | Intervention coverage (e.g., NVP uptake) | ▪ Relatively easy to measure<br>▪ Provides useful information regarding programme coverage along the cascade of PMTCT interventions | ▪ Not a direct outcome measure of programme effectiveness<br>▪ Very difficult if Maternal and Child Health (MCH) is not occurring within a health facility<br>▪ High Performance Liquid Chromatography (HPLC) measurement of NVP is costly |
| **Other outcome measures** | • Infant and child mortality in HIV-exposed but uninfected children at 12 and 18-24 months<br>• Infant and child mortality in HIV-infected children at 12 and 18-24 months<br>• Percent of children under age 2 who are HIV-infected<br>• Percent of HIV-infected children born to an HIV-infected mother<br>• Percent of women who delivered their most recent birth in the past year in a health facility according to woman's HIV sero-status<br>• Percent of pregnant women who are HIV-infected | | |
| **Study Population** | Facility-based | ▪ Convenient to sample<br>▪ Could link between patient and interventions received | ▪ Not representative of population<br>▪ Poor access to older children (e.g., 18-24 months) who are not receiving routine EPI or other care |
| | Population-based | ▪ More representative of entire population<br>▪ May enable more complete determination of indirect benefits | ▪ Requires large sample size to ensure accurate estimate of outcome measure<br>▪ |
| **Methods** | Cohort | ▪ High internal validity<br>▪ More complete "cascade" assessment<br>▪ Direct measure of MTCT rates and mortality | ▪ Complex, expensive and time consuming<br>▪ Concern of "Hawthorne" effect, namely biased ascertainment due the impact of the interactions related to the observational cohort itself<br>▪ Bias due to loss of follow-up |
| | Survey | ▪ Good external validity and generalizability<br>▪ Allows population measure of other outcomes (e.g., antiretroviral therapy coverage) | ▪ Needs high response rate<br>▪ Many need to correct for underreporting due to deaths of children or their mothers<br>▪ |

**Group 1: Routine PMTCT monitoring to evaluate programme impact**

Group 1 discussed using vital statistics as a way to measure impact of PMTCT. Participants advocated using birth and death data and to supplement data on HIV prevalence among infants to examine impact. These methodologies require accurate and near-complete reporting of births and deaths. While reasonably feasible and already collected in some countries, many countries are unable to collect this information accurately due to a lack of infrastructure. When this is the case, the group agreed that, in high HIV prevalence countries, measuring trends in child mortality in the general population and trends of children started on ART would be proxy indicators that would be easier to collect in resource-limited settings. This methodology also requires collecting both HIV status and additional information about infants to ensure that

change in infant HIV prevalence is likely due to PMTCT programmes and not other factors. Additional data that would need to be collected includes HIV-free survival, survival of HIV-infected infants, and survival of HIV-infected mothers. Survival of HIV-uninfected infants born to HIV-infected mothers should also be considered for inclusion in endpoints, though may serve as an indicator of adult access to therapy rather than a PMTCT indicator per se. The group presented a variety of outcome measures and proxy indicators that were very similar to group 2 and are summarized in Appendix 4, Group 1.

**Group 2: Health facility-based studies for impact evaluation**

Group 2 developed a clinic-based assessment construct to summarize the type of clinic that would be suitable for different HIV epidemic contexts depending on the degree to which the community actually uses this clinic. In circumstances of higher clinic usage rates, the families coming for maternal and child health (MCH) care are excellent sentinels for community PMTCT programmatic impact. In a lower usage setting, other approaches are needed. Similarly, the approaches for a high HIV prevalence region differ from that in a low prevalence region. EPI programmes within well-child or MCH clinics were highlighted as a potentially efficient clinical venue for evaluations in settings of a generalized epidemic whenever the facilities have substantial utilization rates. At lower clinic utilization rates, intensive and periodic population-bases surveys may be the best for high prevalence regions. Low clinic utilization and low background HIV prevalence rates would suggest that evaluations be nested within PMTCT programmes themselves.

**Group 3: Population-based surveys**

Group 3 discussed the feasibility of using population-based surveys for PMTCT impact evaluations. The goal of using this methodology was to create national-level indicators that will easily allow for monitoring changes over time of programme impact. The group discussed benefits and limitations of this methodology, as well as appropriate indicators to monitor given a specific epidemic setting. There was also discussion about what additional questions could be added to periodic surveys (e.g., DHS, AIS, MICS) that would help inform PMTCT impact evaluations.

Using population-based surveys for impact evaluations has the benefit of being able to measure the effects of a programme at the national level and allows for coupling of PMTCT-related data with additional background information (e.g., socioeconomic and demographic data) that can help inform programme improvement. Additionally, they collect other child health data that can help determine the effects of PMTCT on child survival. Table 3 below summarizes the indicators proposed for population-based surveys and considerations for their implementation.

**TABLE 3:** Proposed indicators for population-based surveys, and considerations for their implementation

| Indicators collected through population-based surveys | Methodological approaches | Sampling process/data requirements | Epidemic settings | Operational feasibility |
|---|---|---|---|---|
| **1 Percent of children under age 2 who are HIV-infected** (comment: in high prevalence, good programme, you can have higher prevalence, and that would be good; other confounding associations – should be age specific) | - Population-based surveys (e.g., DHS/AIS; EPI-type)<br>----------<br>Add on to existing (e.g., EPI, malaria surveillance or campaigns) | Survey: Collect sero-status for all kids 0-2 (there is a desire to include data collection for the entire population)<br>----------<br>Add-ons: 6wks, 9m visits; need to assess attendance rates; consider PCR:ELISA ratio | 5% + prevalence (Meade will determine the power calculations)<br><br>For lower-prevalence countries, consider reporting system for case reporting | Pooled sample testing for low-prevalence settings; collecting HIV sero-status for entire population has extremely high costs in terms of $ and HR |
| **2 Percent of HIV-infected children born to an HIV-infected mother** | - Pop-based surveys (e.g., DHS/AIS)<br>- Need to account for mortality of HIV-infected children | Mother & child sero-status, or consider PCR:ELISA ratio | 5% + prevalence (Meade will determine the power calculations) | Possible for infants |
| **3 All-cause infant and child mortality rates (according to maternal sero-status where possible)** | pop-based surveys (e.g., DHS/AIS/MICS/RHS; EPI-type)<br><br>Continuous surveys would be highly advantageous | cluster-based surveys; ensure provincial-level estimates, consider district-level;<br>possible oversampling in certain: (e.g.)<br>-epidemic settings<br>-age groups<br>-rural areas | best for hyperepidemic settings; less useful in settings where HIV-attributable mortality is <20% | Difficult to sort out attributability<br><br>Collecting all-cause mortality because can't attribute HIV from survey data and verbal autopsy data are unreliable |
| **4 Percent of infants who are exclusively breastfeeding, replacement feeding, or mixed feeding at 6 months according to maternal sero-status (also important to assess national level feeding practices regardless of contact with PMTCT services)** | DHS | May need to consider increasing sample size even in hyperendemic countries | Hyperepidemic | |
| **5 Percent of women who delivered their most recent birth in the past year in a health facility according to woman's HIV sero-status** | DHS | | | |
| **6 Percent of pregnant women who are HIV-infected** | DHS | | | Many women sero-convert later in pregnancy |

Using population-based surveys, however, is costly and, typically, data have only been collected every 2-5 years. There is also a delay between the time of programme implementation and when the impact will be measurable within a national survey. There is also a difficulty in determining conclusively that changes in child survival or HIV transmission rates are due to PMTCT programmes and not outside factors. Finally, surveys can only gather information from people who are alive, so care must be taken to ensure that accurate mortality reporting occurs. Without these mortality data, programme impact may look better than it actually is. For example, if a large proportion of all babies who are HIV-positive die before they are 2 years old and mortality of these infants is not fully recorded, PMTCT programme effectiveness will appear better than it is.

Group members also discussed important factors to be considered when determining appropriate impact evaluations, including the level of national HIV prevalence (5% was considered reasonable for population-based surveys); size of the DHS sample; proportion of women aged 15-49 currently pregnant, prevalence of HIV infection among women aged 15-49, and the survey design effects.

The group also discussed whether there would be a role for strengthening Demographic Surveillance Surveys for impact evaluations. Specific impact indicators and proxy measures that the group discussed were presented. While most of the impact indicators discussed are based on data already collected from surveys, discussions ensued about the need to include more detailed questions about HIV sero-status and current drug regimens being taken by individuals. While these questions are currently not asked in surveys, the group felt that there was a need to include this information in future surveys. Need to spell out what the recommendations are for the information that should be collected and is not currently collected, e.g. exposure to ARV from PMTCT programme, exposure to infant feeding counselling, etc.

In particular, group members felt that the IATT should draft a letter to USAID/DHS strongly advocating the inclusion of HIV testing for all children during DHS surveys, in countries where HIV prevalence is 5% and above. It was felt that sero-prevalence estimates for this age group could greatly inform not only PMTCT impact but overall HIV monitoring.

A summary of group discussions on the key recommendations on outcome measures and methodologies for assessing PMTCT impact on averting infections in infants and children and improving HIV-free survival are presented in Annex 4.

Participants also discussed a potential framework (guidelines) for a standardized methodology for the assessment of PMTCT programme impact on averting HIV infection in infants and improving HIV-free survival in children i.e. prong three. The discussion did not address HIV prevention including assessment of activities related to Prongs 1 and 2 or maternal outcomes or child treatment and care (See Annex 5)

## *NEXT STEPS*

In order that robust, feasible and comparable PMTCT impact evaluations can be carried out in a variety of epidemiological settings, the following next steps were recommended:

- Begin discussions with USAID, MACRO and DHS teams to advocate that additional PMTCT indicators be collected during DHS survey, specifically the inclusion of HIV testing in children in settings with HIV prevalence of over 5%.
- Meade Morgan of CDC will conduct power calculations to determine what HIV prevalence level is appropriate for conducting nationally representative population-based PMTCT impact evaluations
- Finalization of the guidelines (framework) for assessing the impact of PMTCT programmes in averting new paediatric HIV infections and improving child survival by Vanderbilt University, UNICEF, WHO and UNAIDS. These guidelines will help guide in-country programme managers in implementing routine impact evaluations, given their particular epidemic settings. The guidelines will reference the PMTCT M&E guide that describes national programme monitoring and evaluation indicators for PMTCT and paediatric HIV care and treatment.
- Support strengthening of national M&E systems to enable measurement of process indicators across the PMTCT cascade.

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## Appendix 1: Concept Note

**1. Background:**

HIV continues to have a significant impact on children. The most recent reports from UNAIDS/WHO include estimates of 2 million children living with HIV worldwide. In 2007, there were an estimated 370,000 new infections in children, and 270,000 deaths.[3] Children, according to these estimates, constitute about 6% of all people living with HIV, 14% of new infections, and 14% of all AIDS-related mortality.[4] The majority of children living with HIV are in Sub-Saharan Africa. HIV is also resulting in the stagnation or reversal of gains in child survival in some countries in this region.

UNICEF and WHO, on behalf of the Interagency Task Team (IATT) on PMTCT, currently facilitate data collection of a series of process indicators used to monitor the provision of PMTCT services and interventions. While these data provide essential information regarding progress being made toward the scale-up of provision of services, they do not provide information on the impact of these services or interventions on HIV infections averted or HIV-free child survival. Increasingly, the international community is looking for clear, standardized and simple approaches to assess the impact of PMTCT services which takes into account the prevalence of HIV in the country and the local epidemiology of child morbidity and mortality. A number of studies have been conducted in low and middle-income countries to measure impact of programmes to prevent mother-to-child transmission of HIV but with variable reliability. These studies have differed in their methodological approaches and in the outcomes selected for assessment.

Given the urgent need to systematically estimate the impact of different PMTCT programmes across countries, UNICEF, WHO, UNAIDS and in collaboration with Vanderbilt University Institute of Global Health, is proposing to host an expert consultation to review approaches used to assess the impact of PMTCT programmes to date and to build consensus on a standardized approach which can be implemented widely in a number of resource-limited countries.

**2. Purpose**

To gather comprehensive information on past and present research on the impact of PMTCT programmes, and the most effective ways to develop and design an approach which can be implemented widely in a number of resource-limited countries.

**3. Expected results**

1. Background paper based on existing studies conducted to date on the impact of PMTCT programmes in low- and middle-income countries, including most commonly used methodological approaches.

2. Identification of strengths and limitations of past and present research on the impact of PMTCT programmes in averting new infections and improving child survival.

3. Consensus on the most effective and feasible approaches to assess the impact of PMTCT programmes which can be implemented widely in a number of resource-limited countries.

4. Draft template/tool for systematic assessment of PMTCT programme impact using a public health approach.

[3] UNAIDS. 2008 Report on the global AIDS epidemic, Geneva, Switzerland: UNAIDS; August 2008.
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## Appendix 2: Meeting Agenda

**Consultative Meeting on evaluating the impact of prevention of mother-to-child transmission of HIV (PMTCT) services in low- and middle-income countries in averting new infections in children and improving child survival**

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**Date** **February 12-13, 2009**

**Venue** **Vanderbilt Institute for Global Health, Nashville, TN, USA**
**Vanderbilt University Student Life Center – Board of Trust Room**
310 25th Avenue South, Nashville, TN 37203
615.343.0371

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**Objectives**

**1**. To review the most commonly used methodologies for assessing the impact of PMTCT programmes in low- and middle-income countries, including their strengths and limitations.

**2.** To build consensus on the most robust and feasible approaches to assess impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival, including proxy and breastfeeding indicators.

**3.** To determine how different PMTCT service and survival indicators could be used in different epidemiological and operational settings e.g. breastfeeding versus non-breastfeeding populations, high- versus low-HIV prevalence countries, different levels of health infrastructure.

**4**. To agree on:
-A framework for assessing the impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival that can be implemented widely in a number of resource-limited countries, including:

- methodological approaches for different epidemic settings
- requirements for implementation in different epidemic settings (e.g. data availability and additional data needed; operational considerations for data collection)
- key steps for systematic assessment of PMTCT programme impact at country level

**Thursday 12th February 2009**

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| **9:00-9:35** | **Session 1: Opening Session**<br>Welcome and introductions (10 min)<br>Opening Remarks (15 min total)<br>• UNICEF (5 min)<br>• WHO (5 min)<br>• UNAIDS (5 min)<br>Objectives of Vanderbilt meeting (10 min) | **Chair: Chewe Luo** Sten Vermund Rene Ekpini |
| **9:35-10:10** | **Session 2: Measuring PMTCT impact**<br>• Definition and overview of current methods, key results and gaps in measuring impact of PMTCT programmes in averting new paediatric HIV infections and improving child survival (20 min)<br>• Q&A for clarification (15 min) | **Chair: Mrudula Phadke** Sten Vermund |

**Expected outcomes**

- Common understanding of different parameters for measuring impact of four-pronged strategy of PMTCT programmes
- Overview of methodological approaches for measuring impact of PMTCT programmes on infant outcomes in terms of averting new paediatric HIV infections and improving HIV-free child survival

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| **10:10-10:55** | **Session 3: Overview of major studies assessing impact of PMTCT programmes in averting new paediatric HIV infections and improving child survival**<br>• Experience from South Africa (15 min)<br>• Experience from Thailand (15 min)<br>• Impact of nutritional and antiretroviral PMTCT interventions on child health: experience from cohort studies in Côte d'Ivoire and South Africa (15 min) | **Co-Chairs: R.J. Simons & Simon Gregson**<br>Mickey Chopra<br>Pornsinee Amonwichet<br>Renaud Becquet |
| **10:55-11:15** | ***Coffee Break*** | |
| **11:15-12:25** | **Session 3: (contd.)**<br>• Measurement of PMTCT impact in PEPFAR supported programmes (15 min)<br>• Current approaches and perspectives on modelling PMTCT impact (15 min)<br>• Discussion (40 min) | Nathan Shaffer<br><br>Peter Ghys |

**Expected outcomes**

- Brief update on approaches to assessing PMTCT impact from different epidemiological/country settings (with focus on definition and measurement of outcomes, including indicators used and assessment of strengths and limitations) and their potential utility for measurement of impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival among breastfeeding and non-breastfeeding populations

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| **12:25 - 13:25** | ***Lunch*** | |
| **13:25 - 14:15** | **Session 4- Using process indicators and clinical outcomes at facility level to measure PMTCT impact in averting new infections in children and improving child survival**<br>• PEARL Study (15 min)<br>• Use of clinical outcomes to determine PMTCT impact (15 min)<br>• Discussion (20 min) | **Chair: Priscilla Akwara & Ying-Ru Lo**<br>Elizabeth Stringer<br>Elizabeth Stringer |

**Expected outcomes**

- Common understanding of methodological approaches, strengths and limitations in using programmatic and clinical outcomes indicators and/or proxies for measuring impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival
- Implications for existing and opportunities for additional data collection at country level in different epidemiological settings

**14:15 - 15:40**

**Session 5- Using surveillance activities, and facility and population-based surveys to measure PMTCT impact in averting new infections in children and improving child survival**

- Using EPI services and population-based surveys for PMTCT impact surveillance and early infant diagnosis (15 min)
- Using surveillance activities to measure the impact of PMTCT programmes (15 min)
- Using population-based surveys to assess the impact of PMTCT programmes (15 min)
- Discussion (40 min)

**Co-chair: Peter Ghys & Nancy Binkin**

Nigel Rollins

Margaret Brewinski

Kiersten Johnson

**Expected outcomes**

- Common understanding of methodological approaches, strengths and limitations in using surveillance and facility/population-based survey data for measuring impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival
- Implications for existing and opportunities for additional data collection at country level

**15:40 - 16:15**

**Session 6: Assessing infant feeding practices in the context of PMTCT programmes and their effect on measurement of PMTCT impact**

- Methods for monitoring infant feeding practices and their implications for different methodological approaches of measuring impact of PMTCT programmes (15)
- Discussion (20 min)

**Chair: Moses Sinkala**

Louise Kuhn

**Expected outcomes**

- Methods for monitoring infant feeding practices in PMTCT programmes
- Common understanding of the implications of infant feeding practices and interventions to reduce postnatal transmission for different methodological approaches for measuring impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival

**16:15- 16:30**

**Break**

**16:30 - 17:15**

**Session 7: Laboratory measurements to assess the impact of PMTCT programmes in averting new paediatric HIV infections and improving child survival**

- Serological and virological tests to measure PMTCT impact (15 min)
- Pharmacokinetics of cord blood/serum NVP (15 min)
- Discussion (15 min)

**Chair:**
**Subbarao Shambavi**

Susan Fiscus
Mark Mirochnick

**Expected outcomes**

- Common understanding regarding the laboratory-related aspects (serological and virological) of methods that have been reviewed for assessing impact of PMTCT programmes in averting new paediatric HIV infections and improving HIV-free child survival

**17:15 -18:15**

**Working Group discussion 1:**
Group 1: Population-based surveys (Rapporteur: Kiersten Johnson)
Group 2: Health facility-based settings (Rapporteur: Jeff Andrews)
Group 3: Routine programme monitoring data (Rapporteur: Louise Kuhn)

Questions to be answered by each group:
**1**. What are the most robust and feasible measures for assessing impact of PMTCT and the best way to use them in resource-limited settings? Consider: process issues of testing, uptake, adherence, baby dosing, infant follow-up, breastfeeding; outputs necessary for impact; outcomes that are more definitive, including infant HIV-free survival.
**2.** What existing data are available and what additional data may be needed in resource-limited settings to enhance measurement of PMTCT programme impact? Consider programme data available at facilities and data available from surveys.
**3.** What is the operational feasibility of introducing these approaches, and what key action steps are needed for implementation of these methodologies in different epidemic settings?

**Facilitators**
Chika Hayashi
Nathan Shaffer
Peter Ghys

## Friday 13th February 2009

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| **8:30-8:45** | **Recap of Day 1** | **Rosalind Carter** |
| **8:45-11:15** | **Working Group discussion (stay in your working groups from Day 1)** | |
| **11:15-11:30** | ***Break*** | |
| **11:30-12:30** | **Feedback from working groups and discussion – GROUP 1**<br>• **Presentations (20 min)**<br>• **Discussion (40 min)** | **Chair: Justin Mandala** |
| **12:30-13:30** | ***Lunch*** | |
| **13:30-14:30** | **Feedback from working groups and discussion – GROUP 2**<br>• **Presentations (20 min)**<br>• **Discussion (40 min)** | **Chair: Laura Guay** |
| **14:30-15:30** | **Feedback from working groups and discussion – GROUP 3**<br>• **Presentations (20 min)**<br>• **Discussion (40 min)** | **Chair: Elizabeth Brown** |
| **15:30-15:45** | ***Break*** | |
| **15:45-17:00** | **Discussion of a proposed Framework for assessing PMTCT programme impact in averting paediatric HIV infections and improving HIV-free child survival in different epidemiological settings** | **Chair: Sten Vermund** |
| **18:00-20:00** | **Reception hosted by the Chancellor of Vanderbilt University, Nick Zeppos, JD**<br>Venue: Chancellor's House<br>211 Deer Park Drive<br>** Buses will depart Embassy Suites at 18:10 ** | |

## Appendix 3: Meeting participants

**VANDERBILT UNIVERSITY**

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| Sten Vermund | Amos Christie Chair and Professor of Pediatrics, Director, Institute for Global Health, Vanderbilt University, USA |
| Katherine Allen | Research Assistant, Institute for Global Health, Vanderbilt University |

**UNICEF**

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|---|---|
| Chewe Luo | Senior Adviser, HIV and AIDS Section, UNICEF Headquarters, USA |
| René Ekpini | Senior Advisor, PMTCT, UNICEF Headquarters, USA |
| Robert Gass | Project Officer, Paediatric HIV, Health Section, UNICEF Headquarters, USA |
| Anirban Chatterjee | Project Officer, HIV, Nutrition Section, UNICEF Headquarters, USA |
| Priscilla Akwara | Advisor, Statistics & Monitoring Section, UNICEF Headquarters, USA |
| Nancy Binkin | Chief, Policy & Evidence Unit, UNICEF Headquarters, USA |
| Ruslan Malyuta | Regional Advisor, UNICEF Regional Office for CEE/CIS, Switzerland |
| Sam Bickel | Senior Advisor, Research & Evaluation, UNICEF Headquarters, USA |
| Ngashi Ngongo | Chief, Health and Nutrition Section, UNICEF, South Africa |

**UNAIDS**

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| Peter Ghys | Chief, Epidemic Monitoring and Prevention, UNAIDS, Switzerland |

**WHO**

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| Bryan Shepherd | Assistant Professor, Biostatistics, Vanderbilt University, USA |
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| Elizabeth Stringer | Associate Professor, Centre for Infectious Disease Research in Zambia |
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**KEY STAKEHOLDERS**

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| Dianna Edgil | Strategic Information Officer, Office of the U.S. Global AIDS Coordinator, USA |
| Kiersten Johnson | Demographer, Macro International, USA |
| Jonathan Levine | Global Portfolio Manager, Children's Investment Fund Foundation (CIFF), UK |
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| Christopher Murrill | Epidemiologist, CDC Global AIDS Programme, USA |
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## Appendix 4: Working Group Guidance and Summaries of Group Discussions

Participants were divided into three working groups and asked to examine key robust and feasible process and outcome indicators that can be used to demonstrate PMTCT impact at the national level. They were asked to specifically consider the sampling method to be used, the sampling process, frequency of sampling, and the effect of epidemic setting on the ability to utilize certain indicators and methodologies for assessment. Group 1 was asked to examine these issues if routine PMTCT programme monitoring was used as the methodology for assessment; group 2 was to examine intermittent facility-based assessments; group 3 was asked to examine population-based surveys as a possible assessment methodology (i.e. DHS, MICS, AIS). Each group was given the following worksheet to help guide the discussion.

| | **Methodological approaches** | **Sampling process** | **Frequency and time points** | **Epidemic settings** | **Level of programme coverage** | **Operational feasibility** |
|---|---|---|---|---|---|---|
| **Question 1: What are the 3-5 top priority impact indicators that could be used to demonstrate impact of PMTCT programmes at national level?** | | | | | | |
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| **Question2: In the absence of the above (e.g. because of resource limitations) what would be valuable proxies, other than process indicators, for evaluating impact e.g. existing clinical or laboratory data?** | | | | | | |
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| **Question 3: What are the priority 3-5 process indicators to inform PMTCT impact evaluation?** | | | | | | |
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## Summary of Group Discussions - Group 1

| Measure/indicator | **Methodological approaches** | **Frequency and time points** | **Epidemic settings** | **Level of programme coverage** | **Operational feasibility** |
|---|---|---|---|---|---|
| 1<br>HIV-free survival to 24 mo | Longitudinal records within services<br><br>Integrated registers<br><br>Linkage of birth and death records<br><br>Improve reporting of deaths<br><br>Difficulty of identify cause of death<br><br>Importance of linking information of HIV status on clinical records and surveillance systems | Declining coverage with longer time<br><br>Immunization time points:<br>6,14wks 9 mo 18 mo | Relevant in all settings<br><br>Informed by health service visits and health profile of community | Relevant all settings<br><br>May be highly biased if coverage low | weak |
| Births<br>HIV prevalence how many exposed babies are there (denominator) | Sentinel surveillance<br><br>Modelling<br><br>Birth registration<br><br>Testing positive rates in programs | | | | |
| 2 transmission rates (how many infected babies) | Follow-up in PMTCT program<br><br>Routine testing in immunization clinics<br><br>Information from central laboratories | 6-8 weeks<br>18 months | Relevant in all | Relevant in all | Biased because of low follow-up & low coverage |
| 3 uninfected exposed child mortality | Follow-up in PMTCT program<br><br>Linkage death records with maternal and child HIV status | 12 months<br>24 months | | | |
| 4 Mortality among infected children | Follow up of children tested<br><br>Pediatric treatment programs data<br><br>Birth and death records | 12 & 24 months | Relevant all | Most relevant where pediatric treatment exists | Easier |

| Measure/indicator | **Methodological approaches** | **Frequency and time points** | **Epidemic settings** | **Level of programme coverage** | **Operational feasibility** |
|---|---|---|---|---|---|
| 5. HIV-infected mothers/women mortality to 24 mo | PMTCT records<br><br>Adult mortality stats<br><br>Foster care/social services stats | 24 months | Relevant all | Relevant all | Weak<br><br>Interpretation difficult due to biases |
| 1 Mortality | Vital statistics<br><br>Hospital based | 12 & 24 months | Most important in settings with high HIV prevalence | | Some data available in most settings |
| 2<br>Children started on ARVs | Treatment programs | | | | |
| 1 Infant feeding interventions | | | | | |
| 2 ARV for PMTCT | | | | | |
| 3 ARV for maternal health | PMTCT records<br><br>Linkage to treatment programs | During pregnancy | Relevant to all | Relevant in all settings | Difficulty because of lack of coordination between PMTCT and treatment programs |
| 4 Cotrimox | Follow-up of PMTCT | | All | All | |
| **5. Infant diagnosis** | **Follow-up of PMTCT**<br><br>**Laboratories** | | **All** | **All** | **Caution with denominators not those who** |

## Summary of Group Discussions - Group 2

| Suggested key measures/indicators | Methodological approaches | Sampling process | Frequency and time points | Epidemic settings | Level of programme coverage | Operational feasibility |
|---|---|---|---|---|---|---|
| 1 HIV-free survival | May use Prev. Birth Technique<br><br>Should not use BRASS technique | Longitudinal study – need continuity of data about a mother-baby couplet<br><br>PEARL methodology<br><br>Cross-sectional subsample during a child health annual EPI testing day (ex-facility) | 24 months (discussion of 9 vs 12 vs 18 vs 24; discussion of interest in all-cause mortality and need to capture confounders) Facility may be practically limited to 9mo-12mo due to program ending | | | Audacious – hard to measure outside of research settings<br><br>Idea of incentives to capture cohorts and have high follow-up<br><br>Need community-based sampling capabilities |
| 2<br>Infection rates – vertical transmission rates | -PMTCT program<br>-EPI/ early (ID linked)<br>-Periodic surveillance (community)<br>-Population-based studies (anonymous)<br>-Combination | Sentinel site survey (select facilities)<br>vs<br>Sampling cross-sectional (top XX% of representative clinics)<br>vs<br>Annual day/week for all facilities | 6 weeks √<br>36 weeks<br>52 weeks<br>18 mo<br><br>(qualifiers: antibody not present yet; loss of data due to death before testing; loss to follow-up; impact of feeding practices; late transmission)<br>Think about combining EPI + imm. campaign days | Community Epidemic may be Generalized High or Low or concentrated | Facility utilization (access and coverage) may be High, Mid, Low<br><br>Choice of site depends on immunization coverage and HIV prevalence rates<br>(see table 1) | Feasible<br><br>Idea of incentives to capture cohorts and have high follow-up |
| 3<br>Maternal mortality (and cause) | Use of audit data | | | | | Challenging |
| **Other Measures** | | | | | | |

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| Newborn/childMortality (all-cause and HIV, separated by HIV-status)<br>(and audits) | May use Prev. Birth Technique<br><br>Should not use BRASS technique | PEARL methodology<br><br>Cross-sectional subsample during a child health annual EPI testing day (ex-facility)<br>Audit | 24 months<br>(discussion of 9 vs 12 vs 18 vs 24; discussion of interest in all-cause mortality and need to capture confounders)<br>Facility may be practically limited to 9mo-12mo due to program ending | | | Feasible |
| 2<br>Cord blood testing (NVP levels and other) | | | | | | Problems: programs moving away from NVP; newer drugs may have shorter half-life making this technique nonapplicable – will fall back on infection rates; consider a tracer |
| 3<br>Feeding practices (What is actually being done) | Add to PMTCT program | Ask: What was done?<br>(breast-feeding Yes/No and then exclusive Yes/No (limited by recollection) | 6 wks<br>6mo, 9mo<br>(9mo may be too late to collect accurate info about what happened at 3mo, 6mo) | | | Very feasible<br><br>Being careful not to overload the facility efforts<br><br>There's no value in measuring intent |
| 4<br>Clinical proxies such as malnutrition, growth %ile (MUAC), | Clinical assessments | | Child health visits | | | Very feasible |
| 5 Hospitalization for pneumonia, diarrhea, malnutrition, severe morbidity | | | | | | |
| 6 prophylaxis drug | | | 6 wks | | | |

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| regimen % of eligible | | | 9 mo | | | |
| 7 Women below CD4 threshold - % eligible who are on (lifelong) ART | | | | | | Choose CD4 threshold<br><br>Can we also capture the breakdown of factors for this gap (capacity, resources, cost, adherence, access, transportation) |
| 8 Women admitted in labor with unknown HIV status | | | At time of admission in labor | | | Probably collected now – could be combined with other data<br>Missing home deliveries |
| 9 Children % who should be on cotrimoxazole | | | 6 wk | | | Opportunity to do rapid test |
| **Other process indicators** | | | | | | |
| 1 HIV counseling and testing | | | | | | |
| 2 is the facility providing PMTCT care<br>Eligible women receiving intervention<br>Exposed infants receiving | | | | | | |
| 3 intervention<br>ANC effective coverage and access | | | | | | |
| 4 Breast-feeding counseling | | | | | | |
| 5 Quality of services delivered audit | | | | | | |
| 6 Why don't women access services? | | | | | | |

**Summary of Group Discussions - Group 3**

| Indicators collected through population-based surveys | Methodological approaches | Sampling process/data reqs | Epidemic settings | Operational feasibility |
|---|---|---|---|---|
| **1 Percent of children under age 2 who are HIV-infected**<br>(comment: in high prev, good program, you can have higher prevalence, and that would be good; other confounding assoc.s – should be age specific) | - Pop-based surveys (e.g., DHS/AIS; EPI-type)<br>----------Add on to existing (e.g., EPI, malaria surveillance or campaigns) | Survey: Collect serostat for all kids 0-2 (there is a desire to include data collection for the entire pop)<br>----------<br>Add-ons: 6wks, 9m visits; need to assess attendance rates; consider PCR:ELISA ratio | 5% + prevalence (Meade will determine the power calcs)<br><br>For lower-prev countries, consider reporting system for case reporting | Pooled sample testing for low-prevalence settings; collecting HIV serostat for entire pop has extremely high costs in terms of $ and HR |
| **2 Percent of HIV-infected children born to an HIV-infected mother** | - Pop-based surveys (e.g., DHS/AIS)<br>- Need to account for mortality of HIV-infected children | Mother & child serostat, or consider PCR:ELISA ratio | 5% + prevalence (Meade will determine the power calcs) | Possible for infants |
| **3 All-cause infant and child mortality rates (according to maternal serostatus where possible)** | pop-based surveys (e.g., DHS/AIS/MICS/RHS; EPI-type)<br><br>Continuous surveys would be highly advantageous | cluster-based surveys; ensure provincial-level estimates, consider district-level; possible oversampling in certain (e.g.)<br>-epidemic settings<br>-age groups<br>-rural areas | best for hyperepidemic settings; less useful in settings where HIV-attributable mortality is <20% | Difficult to sort out attributability<br><br>Collecting all-cause mortality because can't attribute HIV from survey data and verbal autopsy data are unreliable |
| **4 Percent of infants who are exclusively breastfeeding, replacement feeding, or mixed feeding at 6 months according to maternal** | DHS | May need to consider increasing sample size even in hyperendemic countries | Hyperepidemic | |

| | | | | |
|---|---|---|---|---|
| **serostatus (also important to assess national level feeding practices regardless of contact with PMTCT services)** | | | | |
| **5 Percent of women who delivered their most recent birth in the past year in a health facility according to woman's HIV serostatus** | DHS | | | |
| **6 Percent of pregnant women who are HIV-infected** | DHS | | | Many women seroconvert later in pregnancy |

**Benefits and limitations to using population-based survey methods to measure impact of PMTCT programs at national level**

- Benefits:
  - Measure effects at the national population level, looking at everything going on in the country with additional background info, including geographic information system (GIS)
  - DHS also collects data on other elements of PMTCT (primary prevention of HIV, unmet need for family planning)
  - Major surveys already collect proxy indicators for child survival (anthropometry, nutrition, etc.)
  - Can adjust clinic-based data using survey data (for future integration with other approaches)
- Limitations
  - Cost is a limitation
  - Frequency of data collection can only be within 2-5 years
  - Delay between program implementation and impact measurable with a national survey
  - Must be careful about how we separate out the effects of the programs themselves.
  - Can only survey those people who are alive
    - Could account for this using mortality data
    - Correlation between maternal infection and mortality, and infant infection and mortality – what is the extent of this kind of bias? Can we apply some correction factors? Extent of the bias can change over time, modified by the extent of coverage/quality of PMTCT services
- Considerations:
  - How much difference do you have to see in each lower-level element of PMTCT in order to see impact at pop level?

- Depends on the impact indicator – with mortality, it is difficult to sort out, but with transmission there should be a clearer association
- The value of this is to link back to determinants of outcomes – what is the impact of various interventions?
- Is there a role for Demographic Surveillance Systems?

## Appendix 5: Proposed guidelines (framework) for standardized Methodology for Assessment of PMTCT Programme Impact on child health outcomes

*i.e. prong three (does not address HIV prevention including assessment of activities related to Prongs 1 and 2 or maternal outcomes or child treatment and care)*

A potential framework or guidelines for standardized methodology for a systematic assessment of PMTCT programme impact was presented and discussed. The framework could be used as a guide for key implementing partners, countries and donors to identify impact assessment approaches which can be implemented widely in a number of resource-limited countries. The proposed draft outline is as follows:

- **Background**
    - PMTCT
        - Burden including by region, HIV prevalence and concentrated or generalised epidemic
        - Strategic approach
        - Global commitments
        - Achievements and challenges
    - Programme evaluation: overview and context
        - PMTCT impact:
            - Evaluation gaps – focus on goal standards and other measures
        - Overview of the context:
            - Epidemic settings; level of PMTCT programme coverage; actual utilization of MCH services; operational feasibility including ethical considerations; resources (infrastructure; human and financial resources), functional coordination between relevant health departments e.g. MCH, RH, HIV, Nutrition
        - Make sure quality improvement (QI) included, terminology clarity and synergy with WHO
- **Purpose and focus of the Framework**
- **Target audience**

- **Conceptual approaches to PMTCT impact evaluation for assessing child health outcomes**
  - Routine PMTCT programme monitoring
  - Other facility-based assessments and surveys
  - Population-based surveys
- **Suggested Key impact indicators for assessing child health outcomes**
  - Impact indicator
    - Definition
    - How and where:
      - Methodological approaches (including strengths and limitations) and sampling processes
      - Context: epidemic settings; level of programme coverage; operational feasibility including ethical considerations; resources (i.e. infrastructure; human resource)
    - When: frequency and time points
- **Key proxy indicators (Same set of questions as impact indicators)**
- **Key process indicators (Same as impact indicators)**