A SHORT GUIDE ON METHODS

MEASURING THE IMPACT OF NATIONAL PMTCT PROGRAMMES

Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive

JULY 2012

World Health Organization

HIV/AIDS Programme

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CONTENTS

ACKNOWLEDGEMENTS

ABBREVIATIONS AND ACRONYMS

AIDS   acquired immune deficiency syndrome

ANC   antenatal care

ART   antiretroviral therapy

ARV   antiretroviral drug

CDC   Centers for Disease Control and Prevention

DBS   dried blood spot

DHS   Demographic and Health Surveys

DPT   diphtheria, pertussis, tetanus

DSS   demographic surveillance site

EID   early infant diagnosis

ELISA   enzyme-linked immunosorbent assay

EMTCT   elimination of mother-to-child transmission (of HIV)

HEI   HIV-exposed infant

HIV   human immunodeficiency virus

IATT   Interagency Task Team

ICD   International Classification of Diseases

M&E   monitoring and evaluation

MICS   Multiple Indicator Cluster Survey

PCR   polymerase chain reaction

PEPFAR   US President's Emergency Plan for AIDS Relief

PMTCT   prevention of mother-to-child transmission (of HIV)

UNAIDS   Joint United Nations Programme on HIV/AIDS

UNICEF   United Nations Children's Fund

USAID   United States Agency for International Development

WHO   World Health Organization

1. INTRODUCTION

1.1 BACKGROUND

The Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping Their Mothers Alive *(1)* was launched in June 2011. With the goal of virtually eliminating new HIV infections of children by 2015, the plan sets ambitious targets—for example, reducing new paediatric HIV infections by 90%, reducing HIV-associated deaths to women during pregnancy, childbirth and puerperium by 50%, and reducing mother-to-child transmission (MTCT) of HIV to less than 5% at the population level. While progress towards these targets will be modelled at the global level, directly measuring impact at the country level is important. Impact assessment activities should be part of every country's plans for the elimination of mother-to-child-transmission of HIV (EMTCT).

1.2 PURPOSE OF THIS GUIDE

This short guide summarizes the different approaches to assessing specific outcomes of interventions to prevent mother-to-child transmission (PMTCT) of HIV. It can serve as a reference that provides an overview of methods to measure PMTCT impact. It also can be used when planning impact assessment activities because the description may support the selection of activities and estimation of the cost of a particular assessment method.

For most methods described, more detailed guidance or a generic protocol will be developed, which can be adapted for country implementation. These generic protocols will provide more information about each method and the practical steps necessary to implement it.

This guide and the generic protocols, as they become available, will be posted on the WHO web site at http://www.who.int/hiv/pub/me/en/index.html.

1.3 OUTCOME MEASURES OF PMTCT IMPACT

Different metrics can be used to assess the effectiveness and impact of national PMTCT programmes. These include the level of new paediatric HIV infections, the rate of mother-to-child transmission of HIV, maternal survival and health, child survival and health, HIV-free survival, effect on health services, and cost-effectiveness.

National PMTCT programmes seek to measure these metrics at the national level. For example, it is important to assess mother-to-child transmission (MTCT) of HIV at the population level rather than only in a smaller number of mother-baby pairs that were followed over time. Information for the entire population is necessary to assess whether PMTCT programmes have achieved wide enough coverage and sufficient impact that MTCT need no longer be considered a public health problem.

This guide highlights metrics to assess several important outcomes:

- new paediatric HIV infections

- mother-to-child transmission of HIV

- HIV-free child survival

- infant and child health and survival

- maternal health and survival.

In addition to measuring these outcomes, most of the assessment methods discussed in this guide can also assess the coverage of PMTCT interventions, such as ARVs during pregnancy and breastfeeding, to provide another source to validate and improve national PMTCT programme data. Future versions of this guide may expand to focus on other metrics such as the estimation of HIV-associated deaths among women during pregnancy, childbirth and puerperium.

1.4 TIME POINTS FOR ESTIMATION OF MTCT

Various time points have been used in research and programmes for reporting the impact of PMTCT interventions. In order to track changes over time and to compare estimates from different sites, it is recommended that all evaluations monitor outcomes at six weeks and 18 months postpartum. While there may be additional transmission to infants through breastfeeding after the age of 18 months, estimates at six weeks and 18 months will be the most helpful. Additional outcome data at 12, 24, and 36 months could be collected, depending on resources and purpose (Table 1).

TABLE 1. TIME POINTS FOR MONITORING MOTHER-TO-CHILD TRANSMISSION OF HIV

Time point	Justification
Recommended	
6 weeks	Reflects peripartum transmission and therefore impact of antenatal interventions including HIV testing and providing antiretrovirals (ARV) (either lifelong antiretroviral therapy (ART) or prophylaxis). Links with timing for early infant diagnosis (EID).
18 months	Captures the vast majority of HIV transmissions through breastfeeding and, therefore, the impact of interventions to promote HIV-free survival of infants. Links with recommended programmatic testing and use of antibody tests at 18 months. Permits comparison with findings of research that commonly reports final outcomes at 18 months.
Optional	
12 months	Potentially easier to identify HIV-infected infants at this age rather than later. Links with efforts to estimate infant mortality rates. (Reflects HIV transmissions through breastfeeding only until about 11 months.)
24 months	Reflects more final outcomes, including mortality among infants who become infected despite prevention efforts. Captures late transmissions through breastfeeding in populations with prolonged breastfeeding, especially if HIV testing rates are low among pregnant women and coverage of ARV interventions is low.
36 months	Same as for 24 months.

1.5 STRUCTURE OF THIS GUIDE

This guide summarizes the following methods for assessing PMTCT impact:

- modelling
- facility-based survey (and follow-up)
- cohort/follow-up data
- population-based household surveys
- analysis of early infant diagnosis (EID) and child HIV testing data.

The description of each method adheres to the following structure:

- brief description of the method
- questions/outcomes that the method can address
- suitable setting
- strengths and weaknesses
- steps and tips
- budgeting.

In addition to employing these methods, routine health information systems, such as vital registration and HIV case reporting, and triangulation of available data can be strengthened to provide more comprehensive data on new child HIV infections, HIV-associated deaths in women and children, and the effect of PMTCT programmes. Annex 1 provides references and links related to vital registration systems, and Annex 2 provides a summary and example of data triangulation related to PMTCT.

1.6 MONITORING EMTCT

To monitor progress towards global and country EMTCT, baselines need to be established and targets need to be set. Usually, longitudinal data on virtually all mother-child pairs and their outcomes are not readily available to establish a baseline. Therefore, initially, in many countries baselines will likely be modelled. Similarly, overall global progress will likely be modelled because accurate impact data will not be available routinely from all countries every year.

In addition to modelled estimates, it is necessary to use real data to measure PMTCT impact, employing one or more of the methods described in this guide. The resulting data will help triangulate modelled estimates and refine and better interpret the modelled data. In the collection of real data to measure the outcome and impact of PMTCT programmes, inevitably some data are missing and some subjects are lost to follow-up. Therefore, an effort to assess outcomes in the population not captured, in order to derive a more nationally representative measurement, is a common feature of the approaches described in this guide. Whenever possible, real data should always be compared with modelled data to explore any data issues and decide on a best estimate of impact.

Measuring PMTCT impact with real data requires proper planning and budgeting. Table 2 presents an illustrative schedule of the types of PMTCT impact assessments that can be planned and implemented in the period through 2015, the target date for EMTCT.

TABLE 2. SUGGESTED COUNTRY SCHEDULE FOR PMTCT IMPACT ASSESSMENTS

Year	Planning	Implementing
In very high HIV prevalence countries		
2011 (or Year 1 of planning)	• Develop measurement strategy and workplan through 2015–2016 • Develop protocol and prepare for facility-based (e.g. immunization-clinic) survey	• Establish baseline (e.g. number of new child HIV infections and MTCT rate) • Set 2015 and intermediate annual targets (model) • Identify any issues with programme data (which also are used as input for modelling)—e.g. the need to collect ARV coverage data during the breastfeeding period, collecting data on adherence, double-counting issues, data quality issues
2012	• Population-based survey (follow country schedule): Only the highest prevalence countries should consider whether and at what sample size it is feasible to incorporate PMTCT impact questions .	• Start immunization clinic survey I • Implement solutions to improve programme data • Model
2013	• Prepare follow-up component of facility-based survey (e.g. training, sensitization, supplies, etc.) • Review programme data quality, propose improvements	• Follow up immunization clinic survey I • Model • Population-based survey, if appropriate: collect data in field
2014	• Prepare for facility-based survey II (if suitable) • Prepare for cohort data extraction/collection	• Analyse EID and child HIV testing data • Collect cohort data • Model and triangulate with other data • Population-based survey, if appropriate: clean and analyse data
2015	• Prepare follow-up component of facility-based survey II • Review quality of M&E system and programme data	• Start facility-based survey II • Collect cohort data • Model
2016	• Plan for next five years as relevant	• Follow up facility-based survey II • Model • Conduct stakeholders' workshop to agree on estimates of impact on, for example, MTCT rate and reduction in new child HIV infections, and to validate EMTCT
In low prevalence/concentrated epidemic countries		
2011 (or Year 1 of planning)	• Develop measurement strategy and workplan through 2015–2016, including hard-to-reach populations • Discuss methods to estimate the number of HIV-positive pregnant women and identify any improvements that can be made	• Establish baseline (e.g. number of new child HIV infections and MTCT rate) • Set 2015 and intermediate annual targets (model) • Identify any issues with programme data (which also are used as input for model)—e.g. the need to collect ARV coverage for a longer duration and during the breastfeeding period if relevant, collecting data on adherence, data quality issues
2011–2014	• Plan to improve availability of cohort data on mother-infant pairs, infant and child testing data, case reporting • Develop protocol to estimate outcomes in populations that are hard to reach or not attending facilities	• Collect data and measure impact • Develop assumptions and assess outcomes in populations not covered by available data • Model • Review and triangulate programme data and any models
2015–2016	• Plan for next five years as relevant	• Directly measure new infections AND estimate for populations with no data • Model • Conduct stakeholders' workshop to agree on impact estimates on, for example, MTCT rate and reduction in new child HIV infections, and to validate EMTCT

Proper planning requires proper budgeting. Realistically estimating the funding needed to implement PMTCT impact evaluations and securing the funds in advance should be a step in the national monitoring and evaluation (M&E) plan. For some countries potential funding sources may be the US President's Emergency Plan for AIDS Relief (PEPFAR) (http://www.pepfar.gov) and the Global Fund to Fight AIDS, Tuberculosis and Malaria (theglobalfund.org).

The Global Fund Proposal Guidelines describe the requirements for monitoring and evaluation of programmes supported by the Global Fund. Measurement of the impact of PMTCT programmes should be seen as an essential part of programme implementation and addressed by applicants in their proposals. The Global Fund generally recommends allocating between 5% and 10% of the proposal budget to M&E. The M&E budget should be apportioned among three M&E service delivery areas:
1. M&E stewardship, governance and coordination
2. routine programmatic data collection and reporting
3. evaluation, surveys, surveillance, and special studies.

The Global Fund guidelines describe specific functional areas within each of these three service delivery areas.[1]

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1 http://www.theglobalfund.org/documents/core/guidelines/Core_BudgetingInGlobalFundGrants_Guideline_en/

2. SUMMARY OF METHODOLOGIES TO MEASURE THE IMPACT OF PMTCT PROGRAMMES

Method	How it is done	What it can measure	Pros and cons	Sustainability, cost
Modelling				
1. Models	• Use HIV sentinel and population-based surveillance data and programme data in a demographic model to estimate results.	**National-level estimates** • Mother-to-child transmission rate • Number of children living with HIV • Number of new HIV infections in children • HIV-related adult and child deaths Sub-national models can be developed, as well.	• Relatively easily implemented • To obtain good results, many data are required. Results are only as valid as the data and assumptions that go into the models. • Does not help the child or mother get services or know their HIV status.	• Spectrum modelling software is available free of charge to everyone. Country teams are trained on its use every two years.
Surveys and surveillance				
2. Immunization Clinic Survey	• Test all children attending clinics for DPT 1 immunization to assess HIV exposure (antibody test) and early (around 6 weeks) infection/ transmission (PCR test). • Questionnaire can collect information on intervention uptake to allow for further analysis, interpretation. • Later follow-up of identified HIV-exposed children can provide data on later or final infection/transmission status.	• National or sub-national population-level • Early transmission rate • Number of HIV-exposed and HIV-positive children • Later or final transmission rate and survival can be assessed, but validity will depend on percentage of all children who can be tracked at later scheduled immunization visits or followed up from the initial entry point of the study.	• In settings with high immunization coverage, can capture real data on population-level transmission and early infant HIV infection. DPT 1 coverage is usually quite high. • Relatively quick to undertake and can be repeated to provide trend data, especially if a modest amount of additional data is collected at same time. • Also provides results for children whose mothers did not attend antenatal clinic or receive PMTCT care. • Misses children who have died before immunization. • Effort needed to minimize loss to follow-up when assessing later/final transmission.	• Can be expensive, depending on scope and whether many extra staff must be employed.
3. Household surveys (nationally representative)	• Test children in nationally representative household surveys • Survey can ask questions about PMTCT-related service uptake (Currently, DHS do not permit questions related to ARVs; however, other population-based surveys have covered them.)	**National-level** • Estimated MTCT rate (if mother also tested) • Number and percentage of children who are HIV-positive, by age and sex • HIV-free survival, if mother's HIV status also ascertained Data can be further interpreted if additional questions are included.	• Can be conducted as part of periodic population-based surveys usually conducted every 3—5 years (e.g. DHS, MICS) • Adult HIV prevalence must be high (2% or more) or sample size must be large. • Surveys every 3—5 years are not frequent enough to suffice but can provide valuable information to triangulate other assessments in high-prevalence countries. • Need to address ethics and means of providing test results to people who want to know their status and of linking to care and treatment services.	• Expensive to undertake surveys large enough to estimate HIV prevalence among children. Practical only in high prevalence countries.

Method	How it is done	What it can measure	Pros and cons	Sustainability, cost
4. Demographic surveillance site (DSS)	• Household survey asking behavioural and other questions of interest • Test children born to HIV-positive women when conducting routine periodic interviews (e.g. every 6 months or 1 year). • Can also collect data on uptake of PMTCT interventions	• Sub-regional, smaller populations (limited geographical coverage) • Transmission rate • Number of HIV-positive children • Estimation of new HIV infections in DSS population.	• Some DSS already exist.	• Not necessarily sustainable over time • Inexpensive if added to existing surveillance sites. • More appropriate for research than for routine periodic assessment of national impact
Programme data				
5. Analysis of EID data	• Analyse routinely collected early infant diagnosis (EID) data. Postnatal transmission can then be estimated to predict final transmission rate. • Questions can be added in lab requisition forms to collect additional data.	• National EID-positive rate in settings with almost universal EID coverage. • In settings with suboptimal EID coverage, combine with estimates of population lost to follow-up and their outcomes to get a more nationally representative estimate.	• EID lab registers usually consolidate these data from patient-specific registers. • Where EID coverage is low, results should be interpreted cautiously.	• Should be systematically analysed as part of EID database.
6. Collection of cohort data	• Retrospective or prospective construction of cohort data, e.g. identify women from ANC files, follow up and try to link with child records; test children as necessary • Routine linking and reporting of PMTCT intervention data and outcomes by ANC or birth cohort • Prospective cohort data collected at selected facilities or from a representative sample • Effort needed to minimize loss to follow-up and to trace those lost to follow-up.	National or sub-national: • Transmission rate • Number of HIV-positive children by age • survival of mother and child • HIV-free survival of child	• Collection of outcome data should be part of routine programme monitoring • Requires names and addresses of all clinic attendees; may need mobile staff to locate women. • Loss to follow-up can be large especially if >3 years. • When various PMTCT interventions (for mother and child) are provided in multiple service delivery points, linking records can be time-consuming, especially without unique patient ID numbers that can be linked.	• Can be expensive to find all women and children lost to follow-up. • Special technology can be used, but may be costly—e.g. an electronic system storing all patient histories and test results.
7. Case reporting	• Confirmed cases of HIV infection are reported – both prevalence and incidence cases.	National: • Number of new HIV infections by age and sex and location of residence	• Numbers will be underreported if testing coverage is poor. • Currently, no HIV case reporting system in sub-Saharan Africa.	• Sustainable and inexpensive if built into routine monitoring system.
Other useful assessment: Triangulation of existing data				
8. Triangulation of various data sources	• Trend data on PMTCT/HIV interventions (e.g. PMTCT ARV coverage, EID coverage, ART coverage) and other health statistics (maternal and child health programme indicators, vital registration statistics, hospital admissions data, other major health events) are reviewed together to hypothesize trends and impact of various HIV services on other health outcomes and mortality.	• Review of trends in HIV intervention coverage vis-à-vis other health intervention coverage and outcome. For example, child mortality rates can be reviewed alongside PMTCT ARV coverage trend.	• Good way to use various data collected from multiple data sources and make inferences • Data quality not always ideal	• Cost to extract data if not readily available. Once a foundation is established, similar exercise can be repeated periodically.

3. METHODS

3.1 MODELLING

Models are mathematical equations that can predict the number of child HIV infections and the population-level MTCT rate and also produce other important estimates based on a number of parameters and data inputs. Modelling can be a useful tool for estimating values that are difficult to measure directly. For example, currently, reliable measures of national-level HIV incidence are not easily available. Instead, models can be used to estimate incidence rates in countries based on available HIV prevalence and antiretroviral therapy (ART) coverage data. Assumptions about the average time from infection to death in people with HIV with and without ART can be used to back-calculate incidence estimates for previous years.

3.1.1   BRIEF DESCRIPTION OF THE SPECTRUM SOFTWARE

The Spectrum computer software package enables countries to model their HIV epidemic, including estimating values related to new paediatric HIV infections and mother-to-child transmission rates. Spectrum is a compartmental, dynamic model that moves individuals through different stages of HIV disease over time (Figure 1). Other models also are available—for example, the Asian Epidemic Model, the Actuarial Society of South Africa (ASSA) AIDS and Demographic Model for South Africa—that estimate the effects of the AIDS epidemic. An Excel-based MTCT rate calculator that facilitates the calculation of MTCT rate under hypothetical scenarios of PMTCT ARV regimen coverage and distribution also is available.

Data required to create a Spectrum model include adult HIV prevalence obtained from sentinel surveillance, programme data on the number of pregnant women receiving ARVs including ART, by regimen, the number of children receiving cotrimoxazole and ART, the number of adults receiving ART, infant feeding practices among HIV-exposed children, and demographic data. For countries the demographic data are already populated in the software. For sub-national estimates the population data must be entered manually.

Spectrum makes assumptions about various mother-to-child transmission rates depending on the PMTCT ARV regimen and infant feeding practice, as well as how long children living with HIV will survive—both those on ART and those not on ART. Other factors such as CD4 cell counts and cotrimoxazole coverage also are taken into consideration.[1] The results from Spectrum include plausibility bounds to reflect the uncertainty around the assumptions and thus also around the estimates.

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1 See www.epidem.org for a working paper on these transmission rates as well as a full description of how Spectrum handles paediatric infections.

FIGURE 1. STRUCTURE OF THE SPECTRUM SOFTWARE

Demographic data	Demographic and epidemic calculations: • **mother-to-child transmission** • **child model** • **adult model**	Results • **number HIV-positive** • **new infections** • **MTCT rate** • **AIDS deaths** • **need for ART** • **need for PMTCT services**
Programme		
Epidemic patterns		
Surveillance and survey data	Prevalence/incidence	
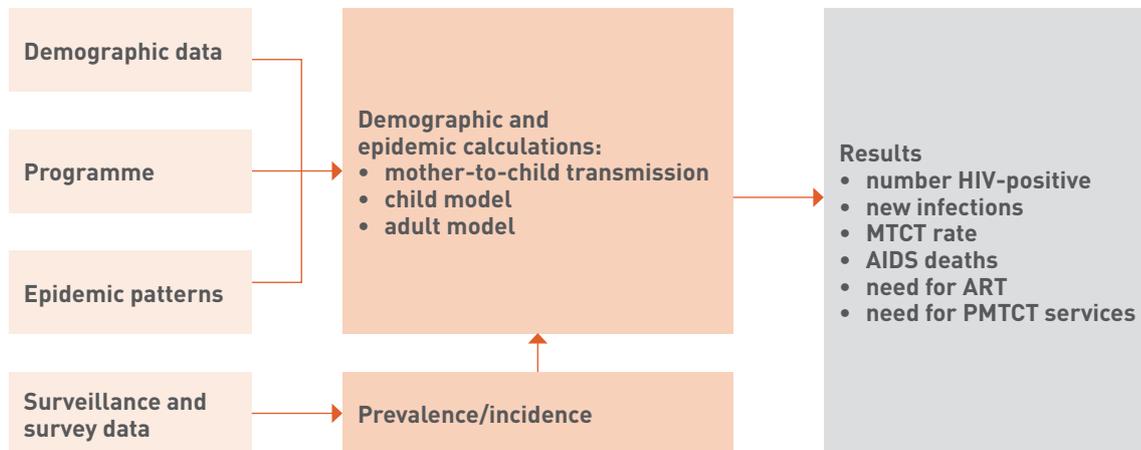
3.1.2 QUESTIONS/OUTCOMES THAT THE SPECTRUM MODEL CAN ADDRESS

Spectrum can estimate numerous variables—for example:

- the number of new child infections at ages 0–14 years
- the mother-to-child transmission rate at six weeks
- the mother-to-child transmission rate after the end of breastfeeding (e.g. after 36 months)
- the number of children living with HIV (for age groups <1, 1–4 and 0–14 years)
- the number of pregnant women in need of PMTCT interventions.

For most countries these estimates will be possible only at the national level. For countries with good sub-national data, sub-national estimates also can be made.

Spectrum can produce annual estimates over time. With hypothetical values for input data, projections for future years are possible.

3.1.3 SUITABLE SETTING

The Spectrum model can be used in all types of epidemic settings. For countries with concentrated epidemics, however, where the majority of HIV infections are a result of sex work, injecting drugs and men having sex with men, there is a large amount of uncertainty in the estimated number of children exposed to HIV. Fertility rates among individuals with these high-risk behaviours are not known. Models can be used to estimate the number of new child infections in concentrated epidemics, but the results should be interpreted with caution and should be triangulated with empirical data.

3.1.4 STRENGTHS AND WEAKNESSES

The model can provide annual values of the indicators listed above, making possible estimates of trends. In fact, models can be updated any time there are new data to inform the model. The software for the models is updated routinely every two years by the UNAIDS Reference Group on Modelling, Estimates and Projections. When countries have new results from sentinel surveillance, programme statistics, or surveys with HIV testing, they should update their models. Since many countries already have a Spectrum file, their models can be updated relatively easily.

The limitation of a model is that it can be only as good as the data and assumptions entered into it. Models rely on data that have been collected in the national HIV surveillance system, such as HIV prevalence from antenatal clinic surveillance or from other biological surveillance systems. In addition, programme data from the national PMTCT and ART services are included in the model. Data on HIV prevalence from sentinel surveillance sites are the core data required to create the model. Collecting data on PMTCT ARV and ART coverage can be challenging, and data quality and completeness are concerns in many settings. If these data are not up-to-date or are biased, the resulting model will be inaccurate.

There are a number of assumptions in Spectrum. For paediatric estimates the most important assumptions are the various transmission rates from mother to child based on ARV regimen and infant feeding practice. These transmission rates are derived from the findings of research on rates of transmission from mother to child according to ARV regimen. These transmission rates are applied to the number of women in the country reported to receive each regimen. Since, currently, countries do not commonly collect national data on adherence to ARVs, the model projects the effect of ARVs on women reported to have started an ARV regimen as if they adhere to the full course of the ARV regimen at the same level as seen in clinical studies; this assumption could result in overestimates of coverage and impact.

The models, and thus country-specific models, are revised periodically as better data become available and when estimation methodologies are improved. This results in better, updated estimates, but estimates that can be difficult to understand because the values of the indicators for all years change.

Although models are convenient and provide a lot of data, they are not a substitute for monitoring systems. Also, models are not linked to processes that inform people of their HIV status or connect them to further assistance or resources.

3.1.5 STEPS AND TIPS

To estimate PMTCT outcomes through Spectrum, a country Spectrum file needs to be produced by inputting country data.

Step 1: Ask members of your country's HIV estimates team to calculate values. Spectrum models already exist in most countries, produced by an estimates team using the latest version of Spectrum. Members of these country teams can help review and produce estimates of the number of

new child infections and of mother-to-child transmission rates; results are available for each year over the course of the epidemic in the country.

Step 2: Check the data input to Spectrum to validate the model. The Spectrum model requires accurate data on the number of woman (and children, where applicable) receiving PMTCT prophylaxis by different ARV regimens (antenatal prophylaxis and postnatal prophylaxis). Individuals with a good understanding of the national PMTCT programme should review the data used in Spectrum to ensure its accuracy. In addition, Spectrum requires data on the proportion of infants breastfeeding at different ages. The more accurate these data are, the more accurate the resulting estimates will be.

Step 3: Hold a stakeholders' consensus meeting to review the estimates and get buy-in.

Step 4: Publish and disseminate the estimates.

3.1.6   BUDGETING

The Spectrum modelling software is free of charge. Costs can include those of the staff member who maintains the model, related training, improving the quality of data inputs, in-country consensus meetings, and publishing and disseminating results.

3.2 FACILITY-BASED SURVEY AND FOLLOW-UP

One of the main reasons that programmatic data are not used to assess the impact of national PMTCT programmes is that the cascade of PMTCT interventions makes it difficult to follow virtually every HIV-positive mother and exposed child from first contact with the health care system through to eventual outcomes. For example, the number of HIV-exposed children tested is often fewer than the number of HIV-positive pregnant women. This may be partially due to early fetal losses and stillbirths. In many settings data from early infant diagnosis (EID) cannot be considered nationally representative because coverage is not universal and not representative of all HIV-exposed infants. In addition, where only known HIV-exposed infants are tested, EID data fail to capture outcomes when mothers are unaware of their HIV-positive status, either because they did not test for HIV in the recent pregnancy or they became infected with HIV during pregnancy, after initial testing.

One way to overcome these biases in programmatic data is to test all infants attending immunization clinics and determine their HIV exposure and infection status. In settings with high levels of immunization coverage, these clinics provide access to nearly all children, including those not currently in PMTCT programmes. Other health facility visits (e.g. mother's postpartum visit) that have high coverage could also serve as opportunities to collect data on a representative sample of infants.

3.2.1   BRIEF DESCRIPTION OF METHOD

A cross-sectional, facility-based survey can ascertain the HIV exposure and HIV infection status of infants at ages 4—8 weeks attending clinics for immunization, particularly in settings where the level of DPT1 immunization coverage is high (Figure 2). Surveying older infants will yield data that may be

difficult to interpret, as attendance rates for other immunizations are often lower than for the first, and therefore the sample will be less representative. Also, transmissions due to breastfeeding will be included, making it difficult to distinguish the impacts of antenatal and postnatal interventions.

With informed consent of the mother or other caregiver, dried-blood spots (DBS) are taken from all infants ages 4–8 weeks, and antibody tests are performed to assess HIV exposure. Infants born to a mother with HIV will test antibody-positive due to the presence of maternal antibodies. Thus, these results reflect maternal HIV prevalence or 6-week infant HIV exposure.[1] Samples from infants that were antibody-positive are then tested by polymerase chain reaction (PCR) test to determine HIV infection status. This allows the calculation of rates of HIV exposure, HIV infection, and, thus, MTCT.

Questionnaires collecting data on socio-demographic variables as well as on uptake of antenatal care (ANC) and PMTCT interventions can help assess personal characteristics and service uptake that may be related to transmission outcomes.

While testing for HIV exposure and transmission at 4–8 weeks is useful to assess peripartum transmission, it misses HIV transmission through breastfeeding. Therefore, in breastfeeding populations a follow-up component is strongly recommended to ascertain, at 18 months and possibly other time points, further PMTCT outcomes of the infants identified as HIV-exposed at 4–8 weeks. The method of follow-up will depend on the setting and resources. Throughout, efforts must be made to minimize loss to follow-up.

FIGURE 2. STEPS IN IMMUNIZATION CLINIC SURVEY AND FOLLOW-UP

Screen all infants attending for routine immunization services.

Request participation and obtain informed consent of caregiver of infants of a specific age (e.g. ages 4–8 weeks) attending for immunization.

Complete questionnaires and collect DBS samples from infants.

HIV-exposed

Test infant DBS from heel-prick samples for HIV antibodies to determine exposure status, then PCR-test antibody-positive samples to determine HIV infection status.

Early HIV infection

Follow up to assess postnatal transmission.

HIV infection – final

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1 A variation of this approach is to test mothers first to determine maternal HIV status and thus child HIV exposure and then, for those testing positive, to take a DBS sample from the HIV-exposed child to test for HIV infection.

This method was developed and first evaluated in KwaZulu-Natal *(2)*. Subsequently, South Africa *(3)* and Rwanda *(4)* have adopted a similar approach at the national level.

3.2.2 QUESTIONS/OUTCOMES THAT THE METHOD CAN ADDRESS

Surveys in immunization clinics and similar venues can gauge the following:

- percentage of infants ages 4−8 weeks who are HIV-exposed
- percentage of infants ages 4−8 weeks who are HIV-positive
- rate of early mother-to-child transmission, measured at 4−8 weeks of age
- coverage of PMTCT interventions.

If linked with a follow-up component:

- rate of mother-to-child transmission at age 18 months (and other specified age for follow-up HIV testing in the survey);
- HIV-free survival at age 18 months (and/or other specified age for follow-up in the survey);
- information on mothers and children after 4−8 weeks, including deaths and linkage to HIV care and coverage of PMTCT interventions.

Depending on what data are collected through the questionnaires, additional assessments can be made, such as the rate of mother-to-child transmission by ARV regimen and the coverage of the various PMTCT interventions along the cascade, to identify missed opportunities and areas for programme improvement.

3.2.3 SUITABLE SETTING

This methodology is most appropriate where the level of coverage of DPT1 immunization (or other routine health facility visit) is high, usually above 80%. It may still provide data of value in settings with lower immunization attendance rates, especially if other programmatic or population data are limited.

The goal is to recruit a survey sample of infants age 4−8 weeks that is representative of the country. Therefore, if assessment of mothers' postpartum HIV status is common and EID coverage is high (with the result that most HIV-exposed infants in the country are routinely tested for HIV at 4−8 weeks), then it may be preferable to analyse EID data for 4−8 week outcomes instead of undertaking this survey of immunization clinics.

Calculating the sample size necessary for the outcomes of interest will help determine how large and resource-intensive the survey may be. In general, a low HIV prevalence and low expected MTCT will increase the required sample size.

3.2.4 STRENGTHS AND WEAKNESSES

The facility-based survey (e.g. at immunization clinics) provides information on HIV exposure and HIV infection status and on perinatal mother-to-child transmission regardless of whether the mother

and/or infant received any PMTCT interventions or are known to the PMTCT programme. If they are enrolled in PMTCT services, it is possible for their data to be linked with information on ARVs provided in pregnancy. The immunization clinic survey is especially useful where retention through the PMTCT cascade seems suboptimal but immunization coverage is high. In these circumstances the survey will provide population-level data on mother-to-child transmission outcomes, including outcomes for mother-baby pairs who may not have known of their HIV infection or exposure. The survey also can provide data for projecting the ART needs of HIV-positive infants.

If the survey is well-planned, it can be relatively rapid to undertake. It can be repeated periodically (e.g. every two years) to provide trend data. Sometimes clinic staff can collect basic data. Depending on how the survey is designed, however, it can be resource intensive—for example, if it requires staffing and logistics beyond the current capacity.

Without the follow-up component (i.e. since the baseline immunization clinic survey is limited to the cross-sectional 4–8 week visit), the data collected at 4–8 weeks reflect only early transmission; in breastfeeding populations a final assessment of transmission is necessary to catch transmission during breastfeeding. Loss to follow-up may be a problem when trying to assess post-natal transmission after 4–8 weeks. Additional efforts to assess final transmission outcomes must be planned.

Other weaknesses of the method are that coverage data on ARVs taken during pregnancy or on HIV testing history may be biased if mothers are not willing to share this information with the survey team. Also, any early infant deaths, before the immunization visit, are not captured.

3.2.5 STEPS AND TIPS

Step 1: Define the objective of the survey and any sub-objectives. For example, for a survey including the follow-up component, the primary objective could be to determine the national (final) MTCT rate, as well as to determine the national early MTCT rate at 4–8 weeks and the subsequent late MTCT rate between 4–8 weeks and the time of final assessment. HIV-free survival can also be estimated. Secondary objectives may be to determine MTCT rates and HIV-free survival at the sub-national level as well to assess coverage of PMTCT interventions. With extra effort and resources, other useful information can also be gathered and analysed, such as HIV acquisition during pregnancy and HIV drug resistance among HIV-infected children.

The country study team should discuss, review, and prioritize the various metrics of interest, taking into consideration data and programme priorities, feasibility, and the availability of other measurement methods for certain metrics.

Step 2: Based on the objectives, determine the sample sizes. The primary goal of the sample size calculation is to allow the survey to produce a reliable national estimate of the main outcomes of interest (e.g. early perinatal MTCT rate and overall MTCT rates measured at 4–8 weeks and 18 months, respectively). Once the number of HIV-exposed infants that need to be recruited is determined, the number and location of facilities to survey and the number of samples to be taken per facility is based on the distribution and average number of DPT1 immunizations in the facilities in a time period.

Step 3: Determine the inclusion and exclusion criteria for participants in the survey—e.g. what age range of infants should be included (usually 4–6 weeks but can be 6–8 weeks for the baseline survey) and whether caregivers who are not mothers will be eligible to participate.

Step 4: Draft the questionnaire, consent forms, and other tools necessary to manage the survey.

Step 5: Discuss operational issues in implementation of the survey—e.g. whether and how to integrate the survey into existing services for sustainability and cost-savings, return of results, laboratory considerations, participant flow at the facility, flow of data and data collection responsibilities, quality control, and staffing requirements.

Step 6: Complete the protocol, budget and plan for implementation. Final planning steps include assuring funding, submitting plans to ethical review boards, recruiting any additional staff needed, developing training materials and training staff, pre-testing data collection, planning a quality control strategy, and procuring supplies.

Step 7: Implement the survey and analyse the data.

Step 8: Publish, disseminate, and discuss results.

Time required: The study may take several months to plan and several more months to implement, and additional time for the length of the follow-up component if included.

3.2.6 BUDGETING

The cost of an immunization clinic survey, including the follow-up component, depends on several factors specific to the setting, including:
- sample size
- cost of tests
- cost of DBS transport
- need for additional staff to collect data, manage logistics, and analyse data.

The study in KwaZulu-Natal, conducted in six health districts with a total sample size of 8000 dried blood spots from infants ages 4–8 weeks, cost about US$1.2 million. This included interviews with about 35 000 women as well as recruitment of study teams to manage the survey.

The study in South Africa used mobile telephone technology to facilitate data transmission. The cost of this element would need to be budgeted.

A study planned in Swaziland has hired a project manager but will use current health care staff. This approach costs less because the survey is implemented within the existing health service delivery system.

The document *Generic protocol for measuring the effectiveness and impact of national programmes for the prevention of mother-to-child transmission of HIV (PMTCT) at population level using a facility-based survey approach* provides a generic protocol and guidance to support country adaptation and implementation.

3.3 COHORT/FOLLOW-UP DATA

Routinely collected PMTCT programme data often reveal attrition along the cascade of interventions. Although many PMTCT programmes have scaled up significantly over the past few years, some national programme data still show a large gap between the number of identified HIV-positive women and the number of HIV-exposed infants tested, on one hand, and the number who subsequently are on ART, on the other. Postpartum follow-up of mother-child pairs and final HIV testing to confirm the final HIV status of the exposed child are especially weak. Programmes should apply strategies that improve access to care and rates of retention. Such efforts will lead not only to better care but also to more complete outcome data on mother-baby pairs.

FIGURE 3. DIMINISHING NUMBERS THROUGH THE PMTCT CASCADE OF INTERVENTIONS
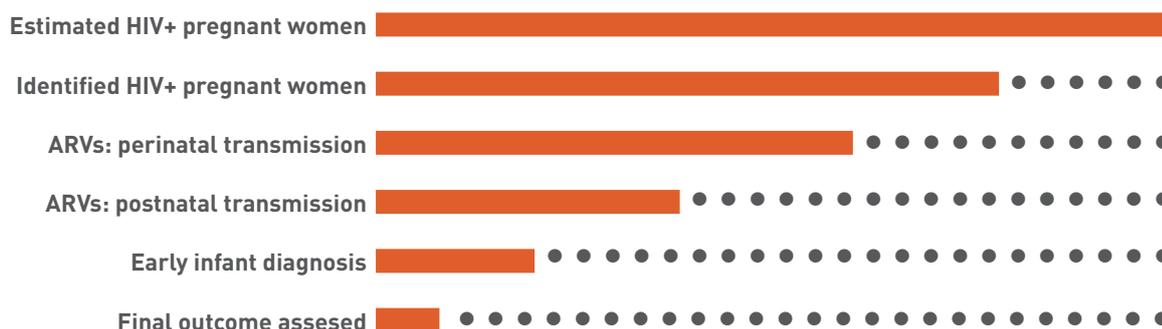
Figure 3 illustrates how more and more outcome data (dots) go missing from programme statistics between the start (top bar) of the PMTCT cascade of interventions and its end (bottom bar). This figure was developed for illustrative purposes only; the relative sizes of the bars, and thus of the data missing, varies by setting.

For several reasons it is difficult to ascertain outcomes through passive monitoring and interpretation of programme data: The time from pregnancy to the cessation of breastfeeding is lengthy; PMTCT interventions may be provided through various service delivery points (e.g. different facilities providing antenatal care, labour and delivery, child health services, and HIV care); programme data are usually summarized and reported cross-sectionally rather than as a cohort; and mother-child follow-up is often suboptimal and records are not linked. Due to these many obstacles, longitudinal follow-up data, particularly information on final transmission and survival outcomes, are often lacking. Still, efforts can be made to ascertain outcomes of cohorts of mother-baby pairs.

3.3.1 BRIEF DESCRIPTION OF METHOD

Efforts to ascertain PMTCT outcomes by following up a cohort of mother-child pairs can be conducted either prospectively or retrospectively. The main aim is to identify the HIV status of pregnant women and find out the outcomes of all mother-child pairs—by linking records, where they are not linked, and, if there is significant attrition, by actively trying to find out the status of those initially lost to follow-up, rather than relying only on available data on facility clients. The value of the cohort approach depends on the capacity to minimize the proportion lost to follow-up and on the ability to estimate outcomes among those who, inevitably, are lost to follow up.

The following methods can be used to construct cohort data:

1. **Active HIV case reporting and outcome monitoring.** Countries can set up a routine active HIV case reporting and outcome monitoring system. For PMTCT all pregnant women diagnosed as HIV-positive would be reported as cases; their HIV-exposed infants would be suspect cases and followed up through an established mechanism until HIV infection is confirmed or ruled out. Routine reporting of cohort data can be institutionalized as part of the standard PMTCT monitoring system and summarized by ANC or birth cohort. Having an electronic data system and unique identifier numbers will greatly facilitate such a system, as demonstrated in countries that already have case reporting systems or outcome monitoring systems.

2. **Prospective cohort data collected at selected facilities** or from a representative sample, with intensive follow-up and efforts to ascertain outcomes. A prospective cohort approach, making special efforts to follow patients and record data as part of a routine programme, is ideal, but it requires close and frequent monitoring and extra resources not ordinarily available in the usual health care settings. A simple, effective, contextually appropriate system to follow up HIV-positive mothers and their children needs to be set up as part of the routine programme. This can be challenging when mother-child pairs do not receive all PMTCT-related interventions in the same facility; the various facilities would have to adopt a standard mechanism to link and coordinate with each other. Where strategies to improve retention may not be optimal, special efforts can be made during a specified period to reinforce follow-up and ascertain outcomes. While a national system would be ideal, one option may be to select representative sentinel sites to collect improved outcome data.

3. **Linking unlinked records.** In settings where certain PMTCT interventions (e.g. provision of ARVs) are offered in ANC facilities while post-delivery PMTCT interventions (e.g. EID) are provided elsewhere (e.g. immunization sites or HIV care sites), effort can be made to link records. For example, HIV-positive women can be identified from ANC records and linked to records in child health centres if the same unique patient ID number appears in both records. If health facility records are missing for some mother-baby pairs, efforts can be made to find them with the help of community health workers.

4. **Retrospective reporting of PMTCT intervention data and outcomes by ANC or birth cohort.** Where PMTCT interventions are well-documented on hand-held patient cards (e.g. maternal health card, under-five card), it may be possible to obtain retrospectively and all at once the history of the

mother-child pair, including PMTCT interventions received and outcomes. For example, if there is a routine two-year-old visit with very high attendance or a community event with large participation, information on PMTCT interventions and health outcomes, such as HIV status or any deaths, can be transcribed from the record cards, and efforts can be made to find out the status of those lost to follow-up These data can be summarized by ANC cohort (that is, for example, women starting ANC in the same month) or by birth cohorts. Limitations and biases of the data collected need to be understood.

Construction of complete cohort data requires intense efforts to minimize loss to follow-up and to trace those lost to follow-up. Although data on the PMTCT cascade can be constructed in this way, obtaining data on outcomes requires keeping mother-child pairs in care.

It is inevitable that some cases will be lost to follow-up. With all approaches, outcomes must be estimated for those lost to follow-up, since those who have been followed do not present the full picture. Assumptions will need to be made about the population lost to follow-up. Also, sensitivity analyses will need to be conducted on potential outcomes for those lost to follow-up. Reviewing available data on those followed up, examining potential scenarios for those lost to follow-up, and combining the two will paint a better picture of the possible population-level outcomes and the uncertainties around them.

Furthermore, where ANC attendance is low and many pregnant women with HIV are not identified through the routine health care system, an estimate must be made for those who do not use health facilities and thus are not entered in health facility records. These estimated outcomes will need to be combined with the available cohort data and the estimates for facility attendees lost to follow-up to produce nationally representative estimates.

3.3.2 QUESTIONS/OUTCOMES THAT THE METHOD CAN ADDRESS

Cohort analysis can provide information on the following indicators:

- mother-to-child transmission rate of HIV in the cohort followed up
- with some assumptions and extrapolations, estimated mother-to-child transmission at the population level
- estimated number of new child HIV infections (from the cohort)
- estimated survival of mothers and children
- estimated HIV-free survival of children.

3.3.3 SUITABLE SETTINGS

Ideally, improving retention of mother-child pairs and ascertaining their outcomes should be part of routine programmes. All countries should try to establish a routine monitoring system that follows and collects PMTCT outcome data.

In the meantime, when a routine cohort monitoring system does not exist, special studies and efforts to collect and construct cohort and follow-up data can be most useful where HIV prevalence is not

high enough to make immunization clinic surveys and population-based surveys cost-effective, as well as where levels of ANC coverage and HIV testing coverage during pregnancy are high and either loss to follow-up of mother-baby pairs is minimal or they can easily be traced.

3.3.4 STRENGTHS AND WEAKNESSES

In all settings PMTCT programmes should be trying to increase retention in care and to better follow up mother-baby pairs. The availability of complete longitudinal data would be ideal, and a cohort study also is an opportunity to assess what happened to those lost to follow-up. Setting up or improving a routine PMTCT outcome monitoring system will strengthen a country's ability to monitor PMTCT outcomes.

Tracking cases can require substantial resources. Even with intensive efforts, however, probably not all cases can be traced. It is difficult to estimate outcomes for those lost to follow-up. The larger the loss to follow-up, the more caution should be taken in interpreting the results.

3.3.5 STEPS AND TIPS

Step 1: Define the outcome measures of interest.

Step 2: Discuss how best to construct cohort data, taking into account the country's context and resources.

Step 3: Determine strategy to increase retention, to minimize loss to follow-up, and to trace missing outcomes.

Step 4: Determine the strategy to assess or estimate outcomes for those lost to follow-up.

Step 5: Discuss operational issues in implementing the strategy.

Step 6: Complete the protocol, budget and plan for implementation.

Step 7: Implement the study and analyse findings.

Step 8: Publish, disseminate and discuss results.

3.3.6 BUDGETING

The size of the budget needed will depend mainly on the method chosen to follow up lost cases and on the availability of already-linked data.

Further guidance on the cohort approach is forthcoming.

3.4 POPULATION-BASED HOUSEHOLD SURVEYS

Since 2001 a number of countries have conducted national population-based surveys that have included anonymous, informed and voluntary HIV testing of male and female respondents. These surveys also include questions on counselling for HIV and testing of pregnant women in ANC. Recently, some countries have included HIV testing of children in their surveys. To date, the Demographic and Health Surveys (DHS), in South Africa the Human Sciences Research Council (HSRC) Survey, and in a few countries the Multiple Indicator Cluster Surveys (MICS) have supported a total of more than 40 surveys with HIV testing, providing standardized data that can be compared across countries and over time. Questions are also available or can be included to capture background characteristics of mother and child, use of ANC services, infant feeding practices, and sexual behaviour.

Population surveys with child HIV testing capture the HIV status of all children, including those whose mothers never attended an antenatal clinic and those who were not taken for HIV testing after breastfeeding had ended. Because the data come from representative samples of the general population, they avoid the biases associated with health facility-based data. However, large sample sizes are required to accurately estimate HIV prevalence in children of narrow age bands (e.g. 1–2 years old). In most countries it is not possible to measure very precisely the HIV prevalence and the MTCT rate in young children using the sample sizes currently employed in population-based surveys.

3.4.1 BRIEF DESCRIPTION OF THE METHOD

Detailed instructions on how to conduct population-based surveys are available from various sources, such as the Measure DHS+ training manuals for interviewers, supervisors and editors and the guidelines for interviewer training,[1] the guidelines for measuring national HIV prevalence in population-based surveys from UNAIDS/WHO,[2] and the 2005 UNICEF manual on Multiple Indicator Cluster Surveys (MICS).[3]

Deciding whether to include HIV testing of young children in population-based surveys would involve several considerations, including revisiting sample sizes to ensure a reasonably precise measurement of the outcome(s) of interest; special ethics, and laboratory logistics for blood collection and HIV testing in children; potential refusal rates and increase in non-response rates for the survey; and the additional cost of more staff, training, quality control, and supplies.

After informed and voluntary consent from the respondent and the child's caretaker, the HIV testing involves collecting blood—either dried blood spots (DBS) on filter paper from a finger or heel prick or else venous blood—and transporting the samples to a testing laboratory. The national HIV testing protocol and quality control procedures should determine the type of HIV tests and protocol to be followed for the different age groups of children.

1 ICF Macro. DHS manuals [web site]. Calverton, Maryland, U.S.A., ICF Macro; http://www.measuredhs.com/What-We-Do/Survey-Types/DHS-Manuals.cfm, accessed March 2012.
2 UNAIDS/WHO working group on global HIV/AIDS and STI surveillance. *Guidelines for measuring national HIV prevalence in population-based surveys*. Geneva, World Health Organization, 2005. http://www.who.int/hiv/pub/surveillance/measuring/en/index.html.
3 *Multiple indicator cluster survey manual 2005: Monitoring the situation of children and women*. New York, United Nations Children's Fund (UNICEF) Division of Policy and Planning, 2006. http://www.childinfo.org/mics3_manual.html, accessed March 2012.

3.4.2 QUESTIONS/OUTCOMES THAT THE METHOD CAN ADDRESS

Population-based surveys can measure the following:

- HIV prevalence among children ages 1–23 months (and, if possible, disaggregation by age groups 1–11 months and 12–23 months)
- HIV prevalence among HIV-exposed children ages 11–23 months (i.e. born to an HIV-positive mother)
- proportion of HIV-negative children ages 12–23 months born to women who are currently HIV-positive (proxy for HIV-free survival)
- infant mortality rate among children born to HIV-positive mothers (deaths due to any cause).

However, even in countries with high HIV prevalence, current sample sizes for population-based surveys still generate large confidence intervals for most of the suggested indicators. Very large sample sizes would be required to provide more precise estimates.

The four indicators listed above were examined using existing data sets of population-based surveys that included child HIV testing—Mozambique AIS 2009, Uganda AIS 2004–2005, Malawi DHS 2010, and Rwanda DHS 2010. (These surveys were not intended to measure these four indicators.) Given the existing sample sizes, confidence intervals around the estimates were large and often not narrow enough to provide a precise estimate.

3.4.3 SUITABLE SETTING

The use of population-based household surveys to measure PMTCT impact makes sense only if the sample size is large enough to provide a reasonably precise estimate of the PMTCT outcomes of interest. Measuring changes overtime would be ideal but would require an even larger sample size and likely is not practical when changes in PMTCT outcomes are small. If HIV testing of young children is included, careful consideration should be given to the large sample size required to get a reliable estimate and the cost implication of such a large sample size.

Population-based surveys are not the appropriate means for collecting PMTCT impact indicators based on HIV testing of children ages 1–23 months in countries with low HIV prevalence among pregnant women or in countries with low expected MTCT of HIV.

3.4.4 STRENGTHS AND WEAKNESSES

Benefits of using population-based surveys to measure PMTCT impact include:

- Estimates are population-based and nationally representative.
- Since other data are collected as part of the survey, if the sample size is large enough, estimates can be broken down by various socioeconomic, health, and background characteristics such as age, sex, residence, mother's education, and household wealth.

Limitations of population-based surveys that test children include the following:

- The very large sample sizes required to make reliable estimates substantially increase survey cost and burden survey logistics.
- Results from a number of population-based surveys show that the refusal rate for HIV testing of children ages 1–23 months (and especially 1–5 months) is higher than that for the general population, biasing the estimates.
- HIV testing of children 1–18 months old requires confirmation of positive cases with PCR, a costly test; laboratory staffs need additional training.
- The prevalence among HIV-exposed children is suggested as a proxy for the MTCT rate but needs to be interpreted with caution because:
- The HIV status of the mother at the time of the survey may not reflect her HIV status during the pregnancy with the child that is tested;
- Transmission of HIV is affected by the mortality of HIV-positive mothers and children. Crucial information on dead children and mothers is not available to these surveys.

3.4.5 STEPS AND TIPS

Successfully planning, designing and carrying out a population-based survey requires considerable expertise; it is important to engage the support of those who have this experience.[1]

Step 1: Identify when the next population-based survey is planned in your country.

Step 2: Decide on the PMTCT outcomes of interest and the sample size required. The sample size is important when measuring HIV prevalence among children and other indicators. The sample size is best decided with the advice of a sampling expert familiar with national surveys and specifically with HIV-related population-based surveys. The sample size will depend on a number of variables and the objectives of the survey. These variables could include the number of children in households, HIV prevalence and distribution in the general population and among pregnant women, expected MTCT rate, total fertility rate, the desired precision for an indicator, and the design effect for the survey, which affects the number of samples needed.

Step 3: Determine the additional resources required to add child testing to the next survey, with the larger sample size required. Take into account additional staff and related training, longer field work and associated costs, increased supplies, testing and laboratory costs, and quality control and other necessary expenses. Consider whether the extra cost is reasonable for the results that will be obtained.

Step 4: Include procedures for child HIV testing in the survey protocol or guide that outlines each of the key elements of the survey in detail.

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1 Guidance on conducting population surveys that include HIV testing can be found at: http://data.unaids.org/pub/manual/2005/20050101_gs_guidemeasuringpopulation_en.pdf.

Ensure that the survey protocol includes the following elements important for testing children:

- adequate sample size;
- variables of interest are in the survey
- HIV testing strategy and logistics for children (including the required forms and procedure for maintaining the anonymity of respondents)
- the additional budget for testing children
- ethical approvals required and informed consent procedures.

Step 5: Conduct the survey, analyse the data, and write the report.

Step 6: Publish the report and disseminate results.

3.4.6 BUDGETING

The cost of population surveys varies widely, depending largely on the size of the country and the costs of labour and transport. The cost also will depend greatly on the sample size (both of the sample to be tested and of the overall sample). The large sample size requirements of population-based surveys have serious cost implications. They also put an additional burden on survey logistics, such as training, fieldwork, and supervision.

The forthcoming document *Considerations for measuring the impact of PMTCT programmes using population-based surveys in selected high HIV prevalence countries* will provide more details.

3.5 ANALYSIS OF EARLY INFANT DIAGNOSIS AND CHILD HIV TESTING DATA

Early infant diagnosis (EID) is a centralized laboratory and facility-based programme that uses dried blood spot (DBS) specimens, processed at a limited number of national and regional reference laboratories, to determine the HIV status of exposed infants at a young age—ideally, by eight weeks. The objective of identifying HIV-infected infants is to start them on antiretroviral treatment, which substantially reduces HIV-related mortality. EID test results and patient demographics are typically available in electronic format in centralized laboratory-based databases. HIV tests in children older than 8 weeks can also be managed like EID.

3.5.1 BRIEF DESCRIPTION OF THE METHOD

Routinely collected EID and child HIV testing data can be analysed to provide estimates of PMTCT outcomes. To calculate the MTCT rate, the number of infants with DNA-PCR-positive test results (numerator) is divided by the total number of HIV-exposed infants (denominator)—either all those tested during a specified time period or else a number modelled using a national estimate of HIV-exposed infants. Stratification of EID data by age group (less than eight weeks versus older ages) is important to differentiate between early prenatal transmission and later postnatal transmission and interpret the data accordingly.

Since the development of PCR testing on dried blood spots, there has been a dramatic uptake of EID testing and significant resources invested in DBS training, sample transportation and laboratory services. DBS samples collected at the facility level are sent to laboratories accompanied by a laboratory requisition form with patient identifying information, including age. Where the PCR lab form has been modified to include information on maternal and infant ARV prophylactic regimens and breastfeeding exposure, it is possible to calculate MTCT rates by PMTCT regimen.

3.5.2 QUESTIONS/OUTCOMES THAT THE METHOD CAN ADDRESS

Analysis of EID and child HIV testing data can generate:
- the HIV seropositivity rate among the infants and children tested;
- a proxy estimate of the population-level MTCT rate at six weeks and later ages if population-level EID and child HIV testing coverage are high or a mechanism exists to identify those who were not tested and to estimate their outcomes;
- an estimate of the number of new child HIV infections if population-level EID and child HIV testing coverage are high or a mechanism exists to identify those who were not tested and to estimate their outcomes.
- the percentage of all estimate HIV-exposed infants tested and other PMTCT-related information on the requisition form can be collected and analysed, such as PMTCT ARV regimen coverage and the proportion of infants tested within the recommended age range,

Because DNA-PCR testing is ideally first performed on HIV-exposed infants before eight weeks of age, in accordance with WHO guidelines *(5)*, EID data are best suited to provide estimates of early peripartum MTCT rates among the population who had an EID test. Child HIV testing data from later ages, if coverage is very high, could support estimating the final MTCT rate, with careful interpretation of the data and necessary adjustments to estimate a population-level MTCT rate.

To interpret EID and child HIV testing programme data, the following should be taken into consideration:
- Coverage must be high for the estimates to be representative.
- The national infant HIV diagnostic testing algorithms, particularly the recommended ages for first PCR test and for additional PCR and antibody testing at older ages to determine final HIV status;
- PMTCT and EID/child HIV testing service coverage (e.g. what proportion of infants are identified as HIV-exposed and what proportion of HIV-exposed infants obtain DNA-PCR testing before the age of eight weeks.
- Whether the sample of children accessing testing services is representative of the total population of HIV-exposed infants in the country. In settings with universal EID coverage, EID databases can provide reasonable estimates of national seropositivity rates among newborns (within two months of age).

Where EID and child HIV testing coverage is not universal and EID data may not be representative, conclusions about PMTCT efficacy may be biased, either overestimating or underestimating transmission. In such situations data analysis needs to employ methods for handling bias—i.e. developing a model that

accounts for the source and extent of bias in order to provide appropriate confidence intervals around the EID data—or for adjusting the data to estimate population-level outcomes. Bias can be introduced in EID programme data in a number of ways:

- Child HIV testing data excludes infants who die before being tested and infants who are lost to follow-up for other reasons. If an HIV-exposed infant is more likely to die than the average infant, the rate of PCR seropositivity may underestimate the true transmission rate.

- EID and child HIV testing serve as entry points into health care that would be likely to see children with HIV who are seeking care because they are ill. Children who are symptomatic are more likely to return to paediatric programmes and to receive PCR testing than children who are asymptomatic, and these children are also more likely to have a positive test result.

- Positivity rates may also be artificially inflated if the EID programme does not use a system of unique identifiers. Many EID programmes have a policy of retesting infants whose first tests are positive. If the infant does not have a unique identifier, it may appear that there are two HIV-positive infants rather than one HIV-positive infant with two tests.

For these reasons positivity rates from EID and child HIV tests are not an accurate proxy for PMTCT programme effectiveness in many settings. However, they provide useful information for child HIV testing programmes and can be improved to provide a source of routinely collected data to review PMTCT outcomes.

3.5.3 SUITABLE SETTING

If the EID/child HIV testing and case-reporting systems are strong and capture most HIV-exposed infants, positivity rates contribute useful information to a country's paediatric surveillance programme and to the evaluation of PMTCT programme performance.

The ideal setting is a country with an EID/child HIV testing programme that centralizes child HIV testing data in an electronic database, consistently uses a standardized EID/child HIV test requisition form, can analyse data by individual infants (usually by means of a unique identifier) rather than by reviewing tests run, and has the ability to stratify data by age at first PCR test.

3.5.4 STRENGTHS AND WEAKNESSES

One of the primary advantages of this methodology is that in some contexts the data are already routinely available centrally in EID/child HIV testing databases, thus avoiding the expense and burden of additional data collection. In such instances the analysis can be conducted quickly and repeatedly, making possible routine, systematic review and assessment of trends. Conducting such analyses requires only limited technical assistance; computer programmes for routine evaluation can be built into the databases. Therefore, where EID/child HIV testing uptake is virtually universal,[1] this is likely to be an efficient means of gauging PMTCT programme impact.

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1   For the purposes of this guide, we have defined "virtually universal" as greater than 90% EID coverage. This value is arbitrary and has no scientific basis.

Regimen-specific transmission rates can be estimated by stratifying mother-infant pairs by regimen if this information is collected on the requisition forms.

Some of the advantage in cost and convenience is lost where EID/child HIV testing uptake is low. In such contexts strategies to increase uptake are needed, and additional validation is required to ensure that the EID data are representative.

Another limitation of this approach is that in many settings, attrition in EID follow-up after the first PCR test impedes the use of EID databases for estimating MTCT during breastfeeding after age 8 weeks.

3.5.5 STEPS AND TIPS

1. **Assess EID/child HIV testing coverage.** The critical first step involves determining the appropriateness of using this methodology. The primary question to ask is whether infants included in the EID and child HIV testing database are representative of all HIV-exposed infants in the region (or nation). If coverage is less than the virtually universal coverage necessary to apply this methodology without further validation, design a protocol for validating the EID/child HIV testing data. Validation findings must be presented along with the results of any analysis of EID/child HIV testing data to assess PMTCT impact.

2. **Review EID/child HIV testing data system structure.** Look at the requisition forms. Determine if it is possible to identify infants tested or if the data available are only tests run. In the latter case, if the requisition form differentiates between first and repeat tests, this can help minimize bias due to double-counting of tests.

3. **Determine how to calculate the numerator and denominator for the MTCT rate.** The numerator for the early perinatal MTCT rate is the number of infants less than eight weeks of age with a positive PCR test result during the time interval chosen for the study. It is important to define the time period of interest consistently for both the numerator and the denominator. There are two methods for calculating the denominator:

   - Service-based denominator. This is the number of infants age less than eight weeks who received a PCR test during the time interval.
   - Combined service- and population-based denominator. If there is concern about the representativeness of the infants tested, then use a modelled denominator based on the total number of HIV-positive pregnant women delivered during the time interval to gauge the representativeness of the sample and to try to estimate the population-level outcome.

If this is a methodology that a country is interested in using, it is important to consider revisiting laboratory requisition forms and the EID/child HIV testing data system and management to improve the usefulness of the data. Depending on a country's infant HIV testing algorithm, it may be appropriate to analyse EID testing of infants older than two months.

3.5.6 BUDGETING

The cost of these analyses depends on the format and quality of the EID and child HIV testing data. Where electronic EID and child HIV testing databases exist, the cost of analysis would be primarily for staff to perform data management and analysis. Where multiple regional laboratories provide laboratory services and the information extracted from requisition forms is not standardized, there may be costs associated with merging data sets. Where PMTCT-specific information is not abstracted from lab requisition forms to the EID/child HIV testing database, expenses for entering these data would be incurred. Where the EID/child HIV testing database contains test results and demographic information, but PMTCT-specific information would have to be gathered from sites using registers and patient files, the resources needed to measure PMTCT impact by this method would be considerable.

Further guidance on the management, analysis and interpretation of EID and child HIV testing data is forthcoming.

ANNEXES: IMPROVING ROUTINE DATA COLLECTION SYSTEMS TO ASSESS PMTCT IMPACT

ANNEX 1. REFERENCES AND LINKS RELATED TO VITAL REGISTRATION SYSTEMS

1. COMMISSION ON INFORMATION AND ACCOUNTABILITY FOR WOMEN'S AND CHILDREN'S HEALTH

Ten recommendations have been agreed by all commissioners. They focus on ambitious but practical actions that all countries and partners can take. Wherever possible, the recommendations build on and strengthen existing mechanisms. More information is available at: http://www.who.int/topics/millennium_development_goals/accountability_commission/en/. The first recommendation consists of the following goal:

> Vital events: By 2015 all countries have taken significant steps to establish a system for registration of births, deaths and causes of death and have well-functioning health information systems that combine data from facilities, administrative sources and surveys. Major efforts are required to move towards a single, sound country system that meets all data needs for women's and children's health; information and communication technologies provide new opportunities to do so.[1]

Health Metrics Network and the MOVE-IT initiative: http://www.who.int/healthmetrics/en/

Going beyond child and maternal health, as it is crucial to have a comprehensive health information system, the Health Metrics Network offers a number of tools that focus on strengthening the health information system. This information is available at: http://www.who.int/healthmetrics/tools/en/

The MOVE-IT initiative focuses on monitoring vital events using information technology: "The Health Metrics Network (HMN) priority strategic initiative, called MOVE-IT, aims to improve monitoring of vital events—births, deaths and causes of death—through innovation and the use of information technologies." MOVE-IT offers useful information at: http://www.who.int/healthmetrics/move_it/en/index.html. Standards and tools can be found at: http://www.who.int/healthmetrics/move_it/en/index3.html.

"Civil registration: why counting births and deaths is important. Fact sheet", available at: http://www.who.int/mediacentre/factsheets/fs324/en/index.html

The 2007 *Lancet* series on vital statistics, entitled "Who Counts?", available at:
http://www.who.int/healthinfo/statistics/WhoCounts1.pdf
http://www.who.int/healthinfo/statistics/WhoCounts2.pdf

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1 See pages 9 and 10 of the Commission's report, available at: http://www.who.int/topics/millennium_development_goals/accountability_commission/Commission_Report_advance_copy.pdf.

http://www.who.int/healthinfo/statistics/WhoCounts3.pdf
http://www.who.int/healthinfo/statistics/WhoCounts4.pdf

International Classification of Diseases (ICD) training tool, available at: http://apps.who.int/classifications/apps/icd/icd10training/

This site also offers specific training on an important aspect of vital statistics systems that needs strengthening, cause of death recording; available at: http://apps.who.int/classifications/apps/icd/icd10training/ICD-10%20Death%20Certificate/html/index.html.

Handbooks, guidelines and training manuals from the UN Statistics Division, available at: http://unstats.un.org/unsd/demographic/standmeth/handbooks/#civilreg

ANNEX 2. DATA TRIANGULATION AND PMTCT IMPACT EVALUATION

The term "triangulation" was originally coined to describe a method used in geographic surveying—the use of two known points to determine the location of a third point. In the social sciences "triangulation" is often used to indicate the use of more than one method or more than one source of data in a study or analysis, as a way to verify results.

Applied to strategic information for health, "triangulation" refers to the synthesis and integrated analysis of data from multiple sources for programme and policy decision-making. Triangulation differs from conventional analysis in four fundamental ways:

1. its reliance on primarily non-statistical analysis;
2. the use of data from multiple sources and of multiple types, both quantitative and qualitative;
3. its principal focus on external validity; and
4. the potential for rapid turnaround from data collection to the presentation of the analysis and results.

Implicit in this application of triangulation is that a lower threshold of proof is acceptable within a data set, as external sources of relevant data are concurrently examined and the results of the multiple viewpoints are integrated.

The advantages of triangulation are a reduction in the likelihood of bias and the ability to rapidly collect and analyse data for policy or programme decision-making. With triangulation the emphasis is on making the best of what data are available. The challenge of triangulation is that it is more dependent than statistical analysis on what social scientists describe as the researchers' "capacity to organize materials within a plausible framework".

Botswana offers an example of data triangulation for evaluation of PMTCT interventions. PMTCT and ART uptake indicators are compared with trends in child mortality and under-five deaths from diarrhoea reported through communicable disease surveillance systems. As Figure 4 shows, over the years 1994 to 2009 infant mortality declined as expected as PMTCT intervention coverage increased, except in 2005. Comparison of data from three sources suggests that an epidemic of diarrhoeal disease explains this one-year reversal of the trend. One can make this reasonable causal inference on the basis of readily available health surveillance and programme data.

A thorough discussion of data triangulation for measuring the impact of HIV programmes is presented in the following article: Rutherford GW et al. Public health triangulation: approach and application to synthesizing data to understand national and local HIV epidemics: *BMC Public Health*, 2010, 10:447, available in full at: http://www.biomedcentral.com/1471-2458/10/447.

FIGURE 4. TRENDS IN CHILD MORTALITY AND PMTCT/ART PROGRAMME INDICATORS, BOTSWANA, 1994–2009
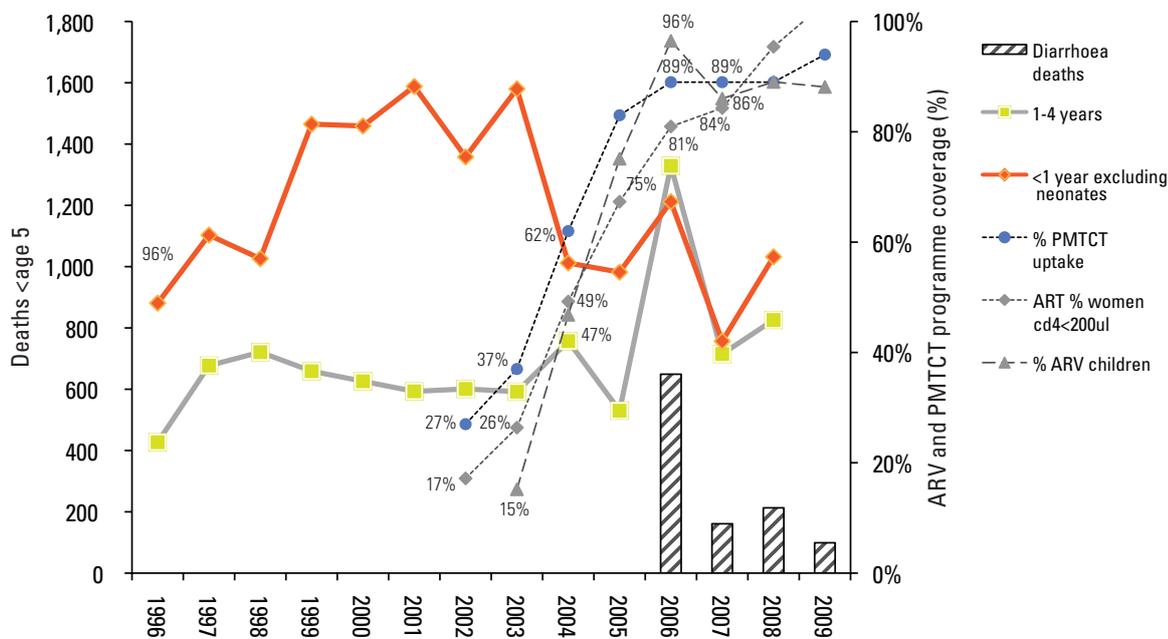
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