Manual for Use of
A Cost-Effectiveness Tool for Evaluating Antiretroviral Drug
and
Substitute Feeding Interventions to Prevent Mother-to-Child Transmission of HIV

Photo credit: Childhood Health Unit, University of Capetown, South Africa

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Introduction

In 1999, an estimated 570 000 children aged 14 or younger became infected with HIV. Over 90% were babies born to HIV-positive women, who acquired the virus at birth or through their mother's breastmilk. the vast majority of these cases occurred in sub-Saharan Africa and other low-income countries (UNAIDS, 1999). In this context it is imperative that mother-to-child HIV transmission (MTCT) prevention funds be used as efficiently as possible. The purpose of this MTCT "Cost-Effectiveness Tool" (CET) is to aid in achieving that goal by allowing decision makers to compare the cost-effectiveness of a range of MTCT prevention strategies.

This introduction provides an overview of the manual and of the CET itself. It outlines the purpose of the CET, its basic organization, and its analytic methods. It also will orient you to this manual so that use of the CET is as easy and productive as possible. The introduction consists of the following five sections:

- Please do this first
- Excel versions of the CET and "Macros"
- Why this manual?
- Overview of manual
- Documenting estimates
- Analytic features of the CET

The remainder of the manual is organized in sections that correspond to the worksheets of the CET that they explain.

Please do this first

The cost-effectiveness calculations are carried out by means of an Excel workbook called "MTCTCET4.xls." It requires about 740 kilobytes of memory, about half the capacity of an ordinary floppy disk. We suggest that you make a copy of this file using a different file name and work with that copy. This precaution ensures that you can always return to the original workbook if necessary. We also recommend that you backup both the original file and your work file on an external storage medium such as a floppy or zip disk.

Excel versions of the CET and "Macros"

The CET runs on Excel for Windows in Office 97 and Office 2000. It will also work in Excel in Microsoft Office 98 and 2000 running in the Macintosh operating system. The CET uses "macros" to reveal and mask portions of the screen according to decisions that the user makes and to generate tables and graphs in the "Sensitivity Analysis" worksheet. Although the program will generally work in Excel version 5 for Windows 95, the macros do not run properly, so we do not recommend its use in this version of Excel. If you must run the model in Excel 5/95, we can

instruct regarding which macros will run and which won't. The workbook will be revised and updated as enhancements are added, bugs are detected and fixed, and new trial results demonstrate the efficacy of additional MTCT interventions. (See http://www.*** for updated versions of the CET and other information).

Why this manual?

This manual is a guide for using the CET. It is intended to calculate the health outcomes, cost, and cost-effectiveness of MTCT control programs in specific settings. With this program you will be able to estimate the cost and health outcomes of five different ARV-based interventions, with or without substitute feeding interventions to reduce the risk of HIV transmission via breast milk. The ARV interventions are ACTG 076 (long-course AZT); HIVNET 012 (ultra short-course nevirapine); Thai-CDC (short course AZT); Petra-A (short-course AZT/3TC) and PETRA-B (same as PETRA-A without the prepartum treatment). The period of breast milk feeding and other characteristics of the substitute feeding intervention is specified by the user.

An important secondary objective of the CET is to provide insights that could lead to greater program efficiency. By guiding the user through the details of program design and cost, and by clarifying which elements contribute the most to cost and cost-effectiveness, administrators may be able to identify areas where higher output or lower cost can be leveraged.

We estimate, based on pilot tests, that it will take **-** hours to complete this analysis using the CET. Although we have tried to make the CET and this manual as complete and self-explanatory as possible, we know that questions may arise as you conduct the analysis. Please contact Dr. Elliot Marseille with questions. He can be reached at:

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Overview of Manual

This manual is designed to provide practical guidance in the use of the computer-based CET model. Its purpose is to clarify the use of terms and to guide the user through the process of identifying what data are needed for the evaluation of the cost-effectiveness of a vertical transmission program. We recommend that the manual and the Excel workbook be open at the same time and that the user follow the instructions presented in the manual while viewing the relevant areas of the computer screen.

The Excel-based CET workbook consists of 12 worksheets. Each worksheet is a 'module' that addresses a particular component of the analysis (e.g., **"VCT"** or **"ARVs"**). You can access each worksheet by clicking on the corresponding tabs at the bottom of the Excel screen. Due to space limitations, the 12 tabs may not all show on the screen at the same time. To access the hidden ones, click on the left or right arrow buttons on the bottom left-hand corner of the Excel screen.

The worksheets are arranged from left to right on the tabs at the bottom of the MTCTCET4.xls workbook as follows:

CET Excel Worksheet	Page in manual
Title – Contact information and CET version number	10
Summary – Overview of important inputs and outcomes	10
Setting – Description of the population to be served	13
Interventions – Selection of ARVs and substitute feeding	20
Voluntary Counseling and Testing (VCT) – Calculation of cost per client; and of the number of women completing VCT.	22
Anti-Retroviral Drugs (ARVs) – Calculation of costs and efficacy of the ARV regimens	38
Substitute Feeding – Calculation of costs and efficacy of the substitute feeding regimen	47
Cost of HIV/AIDS – Calculation of medical costs to the public sector for each case of pediatric HIV/AIDS	58
Results – Cost, health outcomes, and cost-effectiveness outcomes	61
Sensitivity Analyses (SAs) – Tables and graphs showing how outcomes vary with the value of key inputs	70
DALY Calculation – Calculation of the number of disability-adjusted life years (DALY) associated with each case of HIV/AIDS averted	75

Working with the CET

The 12 worksheets in the CET are organized into "Tables" that handle a particular type of input, such as the "Variable cost of VCT" in the **"VCT"** worksheet or "Gestational age at start of ARV treatment" in the **"ARV"** worksheet.

The color of the cell indicates whether data need to be entered. Yellow is for data entry, blue indicates a calculated value or a value provided by the authors. Every yellow data entry cell and most blue cells are discussed in this manual. You can locate the instructions for any cell by

turning to the section on that worksheet in the manual, and finding the relevant table. Cell numbers are bolded for easy identification.

Cell protection and locking

To make sure that no errors are inadvertently introduced, we have locked all cells except the yellow ones. We suggest that you keep them locked. However, if you decide to alter other cells in the workbook, you can do so by pulling down "Protection" in the "Tools" menu and entering the word "HIVFREE" in the password space.

Cell Colors and Error Messages

- Yellow cells indicate that data needs to be entered.
- Blue cells contain the results of a calculation or values that the authors of the CET have entered.
- Messages to the right of data entry cells can alert you to having entered incorrect values.

Error messages

We have included error messages to the right of many of the data entry cells. These read "OK" if there is no problem detected. Error messages appear if the user enters a value outside the range of possible values for that input, or if the value entered is logically inconsistent with the values in other cells. For example, where "low", "base case" and "high" estimates are needed, an error message will appear if the low estimate exceeds the base case or high estimate.

Data entry tips

The data entry process will make the most sense if you do each worksheet in the order listed above. Start at the top left corner of each worksheet (Cell A1) and work your way down row by row. Although you do not have to alter the blue cells, they are helpful in clarifying the logic of the analysis and providing intermediate results. They can be a good "reality check". If a value calculated in a blue cell does not look correct, it may indicate an error in data entry elsewhere.

Note that the "**Title**", **"Summary"**, "**Sensitivity Analyses**" and **"DALY Calculation"** worksheets do not require any data entry.

Selecting summary versus detailed estimates

In two sheets, **"VCT"** and **"Cost of HIV/AIDS"**, you can select either a "detailed" or a "summary" method for entering data. The detailed format requires a little more time. We strongly encourage you to use it because it will yield a more accurate and better documented result. However, if you wish to do a "quick and dirty" analysis you will find it easier to use the summary method. When you select the summary method, the cells pertaining to the detailed method are masked (via an Excel macro). When you select the detailed method, the summary cells are masked.

Background and sources for each item

In the manual, background information is provided for each major input or set of inputs. This includes an explanation of terms and the relevance for the cost-effectiveness calculation. Wherever possible, the manual also provides suggestions for sources of needed information and for data collection methods. Because the situation in each country, region and program is different, these recommendations are suggestive only

Documenting estimates

It is very important to document how you arrived at the estimated value for the major input variables, since you may be making program decisions based on the results of the analysis. This will allow you to reconstruct and explain how those estimates were derived, which will be helpful to others users of the CET, both in your project and, as we share experiences with the CET, elsewhere. For these reasons Appendix A contains a table for your convenience in documenting your work. As a possible alternative or addition to using this table, you may want to enter documentation using the Comments" feature of Excel. Comments may be accessed in the "Insert" menu. To print "comments":

1. Click the worksheet.
2. On the File menu, click "Page Setup", and then click the Sheet tab.
3. To print the comments at the end of the sheet, click "At end of sheet" in the Comments box. To print the comments where they are displayed on the worksheet, click "As displayed" on sheet in the Comments box.
4. **Note:** If you click "As displayed on sheet", Excel prints only the comments that are displayed. To display all comments, click "Comments" on the View menu. To display an individual comment, right-click the cell that contains the comment, and then click "Show Comment" on the shortcut menu.

Sources of data for CET inputs

See section "Published Studies and Other Resources" for a bibliography of materials that will help you to identify information needed to identify CET inputs. This bibliography lists citations for published studies as well as web sites and other sources. Its organization parallels the headings of the CET worksheets such as ("VCT", "ARVs"). Review articles which may be particularly helpful in summarizing the state of the science in a given area are listed in bold font. We would welcome suggestions for additions to this bibliography to be included in future versions of this manual.

Analytic features of the CET

Cost-effectiveness analyses may be conducted using different analytic approaches and different types of comparisons. We intended the CET to be as useful as possible to program decision makers contemplating a range of MTCT prevention options. This section describes three important aspects of the approach incorporated in the CET

- Analytic perspective – the point of view from which health benefits and financial costs (or savings) are tabulated.
- Incremental cost-effectiveness analyses – comparing the costs and benefits of different interventions with each other as well as with the *status quo.*
- Sensitivity analyses – measuring the effects of uncertainty and variation in input values.

Analytic perspective

Cost-effectiveness analyses in health care are concerned with health benefits and costs. The latter typically include both program costs and the costs or savings in future health care outlays resulting from the program. A question which must be answered implicitly or explicitly in all cost-effectiveness analysis is, whose perspective is assumed in the accounting of these costs and potential savings? Among the possible perspectives are those of the patients and their immediate family; the budget of the clinic or hospital that provides program services; the national health care payer; or society as a whole. The CET takes the perspective of a public sector health care payer: It tabulates financial costs and savings to a national entity such as the Ministry of Health. This entity is responsible for the budgets of both the HIV prevention programs that sponsor the intervention and for the budget of the cure facilities such as hospitals that treat pediatric HIV. This perspective excludes costs and savings that accrue only to households or to society at large. For example, it does not take into account families' contributes toward MTCT program fees or toward pharmacy costs for treating HIV-infected children. It also excludes foregone future earnings of HIV-infected children and the lost productivity of adults who must care for sick or orphaned children.

Incremental cost-effectiveness

Cost-effectiveness in health programs implies a comparison of the new or "incremental" costs and health outcomes associated with a program against either, (1) no intervention (the *status quo*) or (2) other possible programs. Both types of comparisons can be useful. The UFM focuses the analyses on a comparison with no intervention, that is, the current status quo in the service area. In then allows the user to perform incremental cost-effectiveness analyses in which the additional costs and benefits incurred in moving from one intervention to another are analyzed. This is an important extension. Intervention "A" may be cost-effective compared with no intervention. But the incremental cost-effectiveness associated with moving from "A" to "B" may be favorable, even if "B" is less cost-effective than "A" when both are compared with no intervention.

Incremental Analysis

The cost-effectiveness analysis is concerned with **incremental** (new or additional) costs, savings and health benefits. Only those costs, savings and benefits that result from the new intervention should be included in the analysis.

Sensitivity Analyses

Sensitivity analysis is a technique for determining how much variation in outcomes is caused by variation in the value of one or more inputs. This is important when the true values of the inputs are uncertain or when you want to explore how outcomes differ in different settings. For example, if an intervention is cost-effective where HIV prevalence is 20%, sensitivity analysis can indicate whether it will still be cost-effective in an area where prevalence is 10%. The CET has a worksheet that displays both graphs and charts that show how cost-effectiveness changes across a range of possible values for a set of important inputs. The ranges for these inputs are provided by the user in each of the worksheets. For example, in **"Setting"** cells **C38 – E38**, the user is asked to provide a low estimate, a "base case" estimate, and a high estimate for HIV prevalence.

In each case, the CET incorporates the inputs provided by the user as the low and high ends of the range over which the sensitivity analyses are performed. A more detailed discussion of sensitivity analyses is in the "Sensitivity Analysis" section of the manual starting on page 70.

"Title" worksheet

This worksheet provides contact information for assistance, and the current version number of the CET. We believe it is self-explanatory.

No data entry is required on this worksheet.

"Summary" worksheet

This worksheet provides a brief overview of the model structure and displays the values of key variables, both inputs and outcomes used elsewhere in the model The first table of this worksheet shows the inputs and outcomes for the cost-effectiveness estimates comparing each intervention with no new intervention. The second table shows the results of the incremental cost-effectiveness analysis.

No data entry is required on this sheet.

Summary Table -1: Selected Inputs

Background

Inputs displayed here include variables pertaining to:

- Program setting and scale
- Mother-to-child transmission
- Voluntary Counseling and Testing (VCT)
- Interventions to be evaluated
- Antiretroviral (ARV) interventions
- Substitute feeding interventions
- Lifetime cost of treating pediatric HIV/AIDS

B2 – C35. Each variable is listed here with a reference to the worksheet and cell where it can be found and to the page in the manual containing its explanation. (THIS TABLE TO BE COMPLETED BASED ON REVISIONS FOLLOWING FIELD TEST)

Selected Inputs	Location on Summary Sheet	Location elsewhere in CET	Page in manual
Program setting and scale			
Annual births in service area	C5	**"Setting"** C19	**
HIV prevalence			
Proportion of women who obtain prenatal care in health facilities capable of delivering MTCT interventions			
Births reachable by any MTCT intervention			
Mother-to-child transmission			
Percent of children of HIV+ mothers who are born HIV-infected			
HIV risk from breast-feeding (with current feeding pattern)			
Voluntary Counseling and Testing (VCT)			
Cost per HIV+ woman who completes VCT (Total costs / HIV+ who complete VCT and register for intervention; public sector share only)			
Cost per woman who completes VCT (Total costs / all women (both HIV+ and HIV-) who complete VCT and register for intervention; public sector share only)			
Attrition			
Portion of VCT (both public and private) costs assumed to be associated with non-MTCT benefits			
Interventions to be evaluated			
Antiretroviral drug (ARV) therapy?			
Substitute feeding?			
Antiretroviral (ARV) interventions			
Efficacy (unadjusted): Relative % reduction in transmission			
Efficacy adjusted for late arrival and imperfect adherence			
Cost of ARV drugs per mother/child pair			
Substitute feeding interventions			
Proportion of HIV- women who ever breast feed			
Non-HIV mortality by age 12 months			
Relative risk non-HIV mortality of SF versus breast feeding			
Cost of infant formula			
Lifetime cost of treating pediatric HIV/AIDS			
Discounted lifetime cost (public sector share only)			

Summary Table -2: Selected health, cost and cost-effectiveness outcomes

Background

Inputs displayed here include variables pertaining to:

Health outcomes

- HIV cases averted by ARV component
- Net fatal events averted by substitute feeding
- Net fatal events averted through intervention
- DALYs generated by program

Cost outcomes

- Program cost
- Net medical cost savings
- Net program costs [Prog. cost minus medical costs savings]

Cost-Effectiveness

- Cost per case averted by program
- Cost per DALY

B38 – G54. Each variable is listed in the table below with a reference to the worksheet and cell where it can be found and to the page in the manual containing its explanation. (THIS TABLE TO BE COMPLETED BASED ON REVISIONS FOLLOWING FIELD TEST)

Selected Health, Cost and Cost-Effectiveness Outcomes	Location on Summary Sheet	Location elsewhere in CET	Page in manual
Health Outcomes			
HIV cases averted by ARVs			**
Net fatal events averted by substitute feeding			
Net fatal events averted through intervention			
DALYs generated by program			
Cost Outcomes			
Program cost			
Net medical cost savings			
Net program costs [Prog. cost minus medical costs savings]			
Cost-Effectiveness			
Cost per case averted by program			
Cost per DALY			

Summary Table 3: Incremental Cost-Effectiveness Analysis

Background

This table presents selected portions of the incremental cost-effectiveness analysis. The full version is shown in **"Results"** rows 70 through 130. The table below lists only the variables used in the Summary sheet.

B66 – E82. **Selected Inputs and Outputs**

Selected Inputs and Outputs	Location on Summary Sheet	Original location elsewhere in CET	Page in manual
Cost-effectiveness threshold (CE ratio above which interventions are deemed not cost-effective)			
Interventions currently being compared:			
More effective but more costly intervention			
Incremental cost per DALY			
Incremental cost per case averted			
Policy implication			

“Setting” worksheet

In the Excel worksheet called **“Setting”** you will describe key features of the area served by the planned intervention. This includes population parameters such as birth rates and life expectancies, and health services parameters such as the percentage of pregnant women who reach clinics for antenatal care. The variables presented here will also determine the size of the cohort that will receive each of the MTCT interventions that you will be asked to specify in subsequent sections.

Table Setting-1: Annual births in service area

Background

“Service area” refers to the geographical territory in which the majority of your clients live. The more closely tied your information is to this specific area the better. For example, if 90% of your clients come from one district, use information from this district if possible, rather than information that pertains to the Province or to the country as a whole.

There are three methods by which annual births can be estimated. Review each of these methods (A – C) below. You will then select one. Since each of them can provide a good estimate, it is reasonable to choose the method which requires the most readily-available information.

> **Method A.** Enter a figure for the overall population (both male and female, adults and children) and the births per 1,000 population. **Data sources:** These data are available from a wide range of publications including national census reports, the Demographic and Health Surveys produced by Macro International Inc., the World Bank’s World Development Report and a range of UN publications.
>
> **Method B.** Enter information on the number of women aged 15-45 and the 'General Fertility Rate' (GFR). The GFR is defined as the number of live births per 1,000 women ages 15-44 or 15-49 years in a given year. **Data sources:** This statistic is available for most countries from the Population Reference Bureau in Washington DC, USA. They can be contacted at (http://www.prb.org/ or phone in the USA: (202) 483-1100). The “Population Data Sheet” available from PRB provides GFR and a wide range of other country-specific demographic data.
>
> **Method C.** Enter a figure directly for the annual number of births in your service area derived from some other source. **Data sources:** Possible sources include census report or other population study conduced by universities, national NGOs or international NGOs.

Influence on cost-effectiveness: Low. The number of annual births affects potential program size and therefore costs but it does not affect cost-effectiveness. The latter depends on costs and outcomes per child and is unaffected by the number of children

Expected effort of data collection: Medium. Because it is important for estimating public health impact and program cost it is worth while getting a good estimate for this input.

C9. Select a method. Select which of the three methods you wish to use by entering "A", "B" or "C". When a method is selected the program automatically shades out the cells that are not needed for this method, leaving only the relevant cells visible.

C11, C12, C14, C15, C17. Enter data corresponding to the method selected. Enter the correct information in cells **C11** and **C12** if you selected "A"; in **C14** and **C15** if you selected "B" and in **C17** if you selected "C".

C19. Result: Estimated annual births in service area. Review the number in this cell. Does this seem about right based on your knowledge of your service area? If not, re-check the values entered above.

Table Setting-2: Births reachable by interventions

Background

"Births reachable by intervention" is the percentage of women who give birth at clinics capable of delivering MTCT interventions. Many women in lower-income countries give birth at home or in the care of traditional birth attendants who do not have access to the MTCT interventions considered in this analysis. The potential population of women available for services must therefore be adjusted to reflect only <u>that portion which can and do use clinics capable of delivering ARVs or breast milk substitutes as part of an MTCT prevention program.</u>

Influence on cost-effectiveness: Low. The number of women reachable by the intervention has no direct effect on <u>cost-effectiveness</u>: women not treated by the intervention contribute to neither program costs nor benefits. However, this input is extremely important in determining the program's overall public health <u>impact</u>. Also, since it determines the size of the annual treatment cohort, it is also likely to be the most important single determinant of the program's <u>cost</u>.

Expected effort of data collection: Medium-high. Obtaining a reasonable estimate is worth considerable effort. If only a small portion of women are likely to benefit from the intervention, it may be worth putting more resources into outreach and possibly patient transportation. A highly cost-effective program that helps only a few women may be less desirable than a less cost-effective one that helps many.

C22. Proportion of women who obtain prenatal care in health facilities capable of delivering MTCT interventions. Enter the best estimate for the area or population served by the MTCT prevention project you are analyzing. This input represents the potential pool of clients your project will serve. **Data Sources:** The best way to estimate it is by examining the caseload records of the facilities that will be referring pregnant women to your project. Be sure to take possible seasonal variation into account in estimating the annual total. If it is possible to arrive at an estimate directly, adjust the percentage entered in **"Setting" C22** until the number in **C23** equals that estimate. Although less useful than an estimate based on actual data from your service area, nation-wide and some regional and city-specific figures are available for selected countries from the Demographic and Health Surveys (DHS). We assume that the clinics referred to in the DHS are capable of delivering MTCT services. However this may not always be true. If not, enter an estimate of the proportion of women that can be reached by an MTCT intervention that reflects your area.

To get a general idea of the proportion of women who receive antenatal care in selected countries please refer to "Table 1: Percentage of Births Taking Place in a Health Facility" compiled by The Futures Group International (TFGI) from Demographic and Health Survey data published by Macro International. It is presented in the TFGI document entitled "Mother-To-Child Transmission Module". This is available for download from http://www. *****. In Southern Africa this statistic ranges from a low of 15.4% in Niger to 69.1% in Zimbabwe. In Latin America the range is from 42.2% in Bolivia to 92.0% in the Dominican Republic. Other large countries covered in this table include India with 25.5% and Indonesia with 17.5%.

Table Setting-3: Percent arriving at clinic in each gestational age interval.

Background

This input reflects the gestational age in weeks when women arrive for antenatal care. Since women will arrive at different times, the model requires a figure for the percentage of women who arrive in each of eight defined intervals. If a woman arrives too late to receive the full intended prepartum portion of the regimen, efficacy may be reduced. For example, suppose a project intends to provide a 'short' course of ARVs defined as beginning at week 36 of pregnancy. If only 75% of women who receive antenatal care at all reach a clinic by week 36, the remaining 25% will be ineligible for treatment or (more likely) will receive an even shorter regimen. The worksheet uses the information on arrival time by gestational age to adjust efficacy, assuming that those who do not receive the full prepartum regimen experience higher rates of transmission than those who receive all medications.

Influence on cost-effectiveness: Medium – high. Since late arrival for prepartum treatment affects regimen efficacy, these estimates can have a significant impact on cost-effectiveness. This

is particularly true if ACTG 076 is being evaluated since it has the longest prepartum treatment period.

Expected effort of data collection: Medium-high. Gestational age at arrival is a routine piece of information that we assume most projects will be obtaining in any case. The extra effort need to compile this information for the CET should be minimal.

C27. By week 28. Enter value representing the women who arrive by week 28 or earlier as a percent of all pregnant women who come to the clinic. **Data sources**: Many clinics keep a log of mothers' arrival that notes the estimated gestational age. If these data do not already exist, it may be worthwhile recording it for 100-200 women.

C28 – C33. By weeks 29 – week 40+. Continue entering the corresponding values for each of the other gestational week intervals specified.

D27 – D34. Cumulative total percent of women arriving at the clinic by gestational age. If these figures don't seem correct, check to make sure that the values entered in cells C27 – C33 are correct. Note that the total of all age intervals must equal 100%.

Table Setting-4: HIV prevalence rate in pregnant women

Background

The prevalence rate is the number of people with a particular attribute (such as HIV) at a particular point in time, divided by the population who have that attribute at that same point in time. The higher the prevalence the greater a program's cost-effectiveness (all else equal). This is because fewer counseling and testing resources are "wasted" on HIV-negative women.

Influence on cost-effectiveness: Medium-high. HIV prevalence has a major effect on the cost per HIV+ women identified through VCT. This is because in low prevalence settings more VCT services must be provided to identify the same number of positive women as in high prevalence settings. Because drug costs are low in interventions such as HIVNET 012 and PETRA-B, these regimens are very sensitive to the costs of the other key cost component, VCT, and thus also to HIV prevalence. Conversely, ARV-intensive regimens such as PETRA-A and ACTG –076, are less sensitive to HIV prevalence.

Expected effort of data collection: Medium-high. It is worth putting particular care into refining prevalence estimates if your analysis centers on HIVNET-012 or PETRA-B

C38 - E38. HIV prevalence in pregnant women attending antenatal care clinics – base case. Enter the best single estimate in this cell in **D38. In C38** and **E38**, enter low and high estimates. The full range of values should encompass the likely random errors in estimation so that this range includes the true value with very high certainty. Some studies

provide a 95% confidence interval and this would be a reasonable range to adopt. In a sensitivity analysis graph (starting at "**SAs" M20**), cost-effectiveness will be calculated for the range of HIV prevalence you specify. We recommend that you use a wide range in order to understand how cost-effectiveness changes as the HIV epidemic subsides or intensifies and how the same intervention. **Data sources:** Fortunately, reasonably good estimates of HIV prevalence among pregnant women (ideal) or among women attending STD or family planning clinics (O.K.) are available for most locales. Clearly, the more specific to your geographical setting the study is, the better. Surveys conducted by the Ministry of Health (MOH), and by NGOs and private agencies that deliver STD and FP services often present this information.

Failing more service area-specific data, there is an extensive compilation of HIV prevalence estimates from around the world in the HIV/AIDS Surveillance Data Base administered by the US Bureau of the Census. This database is freely available for download from: www.census.gov/ipc/www/hivaidsn.html. It is also available on CD-ROM by inquiry at ipc-hiv@census.gov. The UNAIDS web site at http://www.unaids.org/ also has useful country-specific data on HIV prevalence and incidence.

Table Setting-5: Rate of perinatal mother-to-child HIV transmission

Background

This input is the probability that a child born to an HIV-infected mother will be HIV infected via in-utero or intrapartum transmission in the absence of therapy. Your estimate should be based on a published finding from a setting that is most similar to yours in terms of women's health status.

C41. Rate of mother-to-child transmission (perinatal). Enter the best estimate for your setting of the percent of children of HIV infected mothers who are born HIV infected. **Data sources:** Clinic and hospital-based studies and placebo-controlled clinical trials are the major sources of this information. The ATCG 076 found a transmission rate of 25.5% in the industrialized world setting of this trial. In the CDC-Thai in Thailand and in the HIVNET 012 nevirapine trial in Uganda, transmission rates in the control groups were very similar, about 25%. The PETRA trials found the average transmission rate for the placebo groups of the three sites in Tanzania, Uganda and South Africa to be considerably lower, 17.2%.

Influence on cost-effectiveness: Medium. This parameter can have substantial effect on the final cost-effectiveness estimates. All else equal, the higher the rate of transmission, the more cost-effective the intervention will be because there are more potential cases to prevent.

Expected effort of data collection: Medium. Estimates from settings similar to yours are probably easy to obtain. It is probably not worth the extra precision to undertake a study on your own if you weren't otherwise planning to do one.

Table Setting–6: Discount rate

Background

This is the rate at which future financial costs and health benefits are reduced when converted to their equivalent value in the present. This adjustment is made to reflect the greater societal preference for money and health benefits in the present compared with the same quantum of money or health benefits at a future date. The rate of 3% is a well-accepted rate for developing countries and is recommended by the World Bank. Changing the discount rate can have a large effect on health outcome as measured in DALYs. ***We therefore recommend that you not alter this value unless you have a strong rationale for doing so.***

Influence on cost-effectiveness: High. The choice of discount rate can have a strong effect on the economic appraisal of MTCT programs. For example, 50 life-years discounted at 3% are equivalent to 25.7 net present life years. At a 5% discount rate, those same 50 years have a net present value of only 18.3 life-years, a decrease of 1/3.

Expected effort of data collection: Low. Although the choice of discount rate can be important, it is difficult to select the objectively correct rate in a given situation. For ease of comparison with other studies, we recommend that you use the 3% default.

C44. Discount rate. The default value is 3%. You may enter a different value here. Numbers below 0% or above 15% compute but yield an error message in the adjacent cell (**D44**) since values outside the range are likely to be in error. **Data Sources**: See Appendix B in the World Bank's 1993 World Development Report for an explanation of the recommended 3% discount rate.

Table Setting-8: Life expectancy

Background

This input refers to the life expectancy at birth. The health benefits of MTCT interventions are measured in both HIV infections averted and in Disability-Adjusted Life Years (DALYs). The latter measure requires an estimate of the number of years the infected child would have lived had she or he not been infected. Life expectancy is the average number of years of life at birth.

C47 and C48. Life expectancy for males and for females. Enter the best estimate for your setting of the average life expectancy at birth. If your data source provides separate figures for males and females, enter each in the corresponding cell (C47 for females and C48 for males). If it

provides only one figure, enter this single number in both cells. **Data sources:** Life expectancy at birth is a common health statistic found, among other places, in UNICEF, UNDP and World Bank reports, and in the World Population data Sheets published by the Population Reference Bureau. Some sources give separate figures for males and females. Others provide one figure which is the average for both males and females.

“Interventions” worksheet

The purpose of this worksheet is to select the types of interventions you wish to evaluate: ARVs, Substitute Feeding or both.

Table Intervention - 1: Specifying Interventions

Background

You have the option of evaluating ARVs alone; substitute feeding alone or both interventions in tandem.

ARVs: Selection of this intervention activates the evaluation of five ARV regimens that have been proven to be effective in clinical trials. As shown in cells **C15 – C19** these are ACTG 076; HIVNET 012; CDC-Thai; PETRA-A and PETRA-B. Details of each regimen are portrayed in the ARVs sheet and on page 39 of this manual.

Substitute feeding: Substitute feeding eliminates HIV transmission through breast milk, but increases the risk of non-HIV infant mortality. The model examines both of these health effects for each month of age. Substitute feeding program managers must decide between no breastfeeding, or short term exclusive breastfeeding followed by a switch to substitute feeding. You will need to specify either a predetermined number of months of breast feeding (0 to 6) or “Optimal” – in which case the program determines the duration of breast feeding that minimizes the total of HIV infections plus non-HIV deaths (“fatal events”).

Both ARVs and Substitute Feeding: If both types of interventions are selected the CET calculates the impact of ARVs and the incremental impact of substitute feeding when combined with ARVs. The cost and health outcomes attributable to ARVs and to substitute feeding are shown separately in the **Results** sheet.

C11 and C12. Specifying interventions. Type in either “Yes” or “No” to select the types of interventions you wish to evaluate.

C13. Specifying breast feeding duration. Type in a value from 0 to 6 for the duration of breast feeding you wish to evaluate; or type the word “Optimal” if you prefer that the model calculate the duration of breast feeding that will minimize fatal events.

Substitute Feeding Intervention Cell C13: Specifying Breast-Feeding Duration

- Enter a value from 1 – 6 months, or
- Enter "Optimal” for the CET to calculate the duration of breast-feeding that minimizes “fatal events” (combined HIV infections and non-HIV mortality).

"VCT" worksheet

This worksheet calculates the cost of voluntary counseling and testing (VCT). It does so by accepting data on each cost element (e.g., test kits, personnel, and rent) and on the percent of women who drop out at various stages during the VCT process. It provides two methods for calculating costs: (1) a detailed method likely to yield a more accurate result but requiring more time to complete, and (2) a summary approach that can be useful for generating a "quick and dirty" estimate. We strongly recommend the detailed approach for costing VCT because VCT can represent a large portion (up to 75% or more) of total program costs.[1] The added accuracy and flexibility of detailed VCT costing compared with the summary approach is worth the added effort. **Data sources:** The needed information should be obtained from the setting in which the intervention is to be implemented or a similar setting. It is unlikely to be available in published or even unpublished reports. Instead you will probably have to generate your own estimates. You may find that pages 5-43 of the book *Cost analysis in primary health care* edited by Andrew Creese and David Parker and published by WHO in 1994 provides useful additional guidance. A companion volume to this book entitled *Costing Guidelines for HIV/AIDS Prevention Strategies* is another very useful reference. It can be downloaded from the Internet at http://www.unaids.org/unaids/document/economics/costguid.

VCT typically includes:

- Registration and pre-test counseling
- Initial HIV test
- Post-test counseling
- Confirmatory test for these who initially test positive for HIV
- Ancillary services such as client transportation that may be needed to maintain the agency's caseload of VCT clients for MTCT prevention.

In low prevalence areas it may also include an initial screening by interview to eliminate women at low risk of HIV. For purposes of this analysis, VCT does *not* include other activities such as research projects or maternal health services not directly tied to MTCT-related VCT.

Fixed vs. Variable costs. Many costing approaches distinguish *variable costs* such as expendable supplies that change as the level of output changes, from *fixed costs* such as administrative activities that remain constant over a wide range of output levels. Other approaches, such as *Cost Analysis in Primary Health Care*, distinguish between "recurrent" costs such as personnel compensation, and "capital" costs which occur only once or at long intervals (e.g., buildings, vehicles and other major equipment). We wish to be able to document how costs vary for each step of the VCT process as the number of clients remaining in the sequence varies. We therefore take the approach of distinguishing between fixed costs and variable costs.

[1] In fact, the reported costs are so high for some types of VCT that it may make sense in some programs to attempt to reduce costs (e.g., by offering pre-test counseling in larger groups) if this can be done without seriously compromising quality.

Only the cost of services to women should be counted. The cost of services to male partners such as STD testing should not be included as these are not part of the activities needed to prepare mothers to receive the ARV or substitute feeding intervention.

If VCT for MTCT is to be added on to an existing program such as a maternal health program or to an STD clinic, only the *incremental* resources needed to provide this VCT should be included in the cost assessment.[2] Here are three related issues that may enter into the cost assessment:

> *Sharing of joint resources.* Certain resources such as equipment, space, and overhead costs may be used both for VCT for the MTCT intervention and for other purposes such as STD testing or services to male partners. In evaluating VCT costs, estimate the percentage of the cost of these resources that should be assigned specifically to the MTCT intervention. Base this estimate on the number of full time equivalent staff members assigned to each type of service.
>
> *Patient fees*. Revenues generated for the project by registration or other fees paid by clients should be separately noted and subtracted from costs, so that costs represent the net cost to the program. Space is provided to do this on the VCT spreadsheet.
>
> *Start-up and seasonal effects.* Low attendance and relative inefficiency during the start-up period are likely to increase costs during the initial months but will not represent typical project operations. Similarly, during certain seasons of the year the caseload may be much higher or lower than average. Your analysis should be based on a period of time that reflects the average operations of the project.

Table VCT-1: Per-Client cost of VCT

Background

This table presents one of the key results of the VCT analysis, the total cost per client who completes VCT and registers for the ARV/substitute feeding interventions. It is presented both for HIV+ clients and for all clients. These are the most important summary statistics for measuring the efficiency of the VCT program. They are determined by variable supply and personnel costs, plus capital and other fixed costs. They also depend on the attrition rate since the denominator is the number of clients who *complete* VCT. Cost per HIV+ client is extremely sensitive to HIV prevalence (**C9)**. As a measure of VCT operational efficiency, cost for all clients (both HIV+ and HIV-) may therefore be the more meaningful statistic **(D9)**.
No data entry required.

[2] *Incremental* simply means additional. For example, incremental costs are the new costs entailed by a program and excludes costs which would have been incurred had there been no new program. Incremental cost-effectiveness analyses compare the additional costs and the additional benefits of one program with another.

C9. VCT cost per HIV+ client only. Total annual expenditures for VCT divided by the number of HIV+ clients who complete VCT and register for the MTCT intervention itself.

D9. VCT cost per client (both HIV+ and HIV-). Total annual expenditures for VCT divided by the total number of clients who complete VCT and register for the MTCT intervention itself.

Table VCT-2: "External" cost of VCT

Background

External cost of VCT refers to the portion of the cost that could be attributed to non-MTCT health benefits. VCT for vertical transmission prevention may also reduce horizontal (adult-adult) transmission. This reduction in horizontal transmission is not captured by the model in its calculation of health benefits to children and is referred to as *external*. One way to capture or "*internalize"* the potential horizontal transmission reduction benefits is to reduce the cost of VCT attributable to MTCT. If, for example, we believed that 30% of the total health benefits of VCT take the form of horizontal transmission reduction, we could reduce the cost of VCT by 30%. However, because this "external" benefit of VCT has not been documented, we have set the default value of this parameter to zero.[3] This is likely to introduce a conservative bias to the cost-effectiveness results (tending to make results appear less favorable than they really are). The consequences of non-zero values for this external benefit can be assessed by entering other values in cell "**VCT" C5**.

Influence on cost-effectiveness: High. The portion of the cost of VCT that is "billed" to horizontal transmission benefits has a major influence on the effective cost of VCT attributed to MTCT and therefore on overall program costs. This is especially true for the less drug intensive regimens such as HIVNET-012 and PETRA-B. VCT's importance is also greater if substitute feeding interventions are not implemented.

Expected effort of data collection: Low. Estimating VCT's benefits for horizontal transmission would be a major research undertaking in its own right. We suggest that for the "base case" analysis you use the default value of 0%.

C14. Specifying external cost of VCT. Enter numbers from 0% to 100% to evaluate changes in the value of this parameter. Note that the table in cells **"VCT" I18 – "VCT" P29** show the current values of the various cost components of VCT. The left-hand side shows these values assuming no external benefits of VCT and the right-hand side shows these same values assuming the external benefit entered in **C5** (and displayed also in **P29**).

[3] Interested readers can refer to (Wolitski, et al., 1997), and (Zoysa, et al., 1995) for a review of recent studies regarding sexual risk behavioral change following VCT. Studies vary in their findings from significant increase in condom use (Kamenga, et al., 1991) to no benefit from one session (Temmerman, et al., 1990).

Table VCT-3: Summary VCT information

Background

This table provides a quick method for estimating VCT costs. It can be unmasked via a macro if you opt to use the summary method of evaluating VCT costs. Enter "S" for **"**Summary**"** in cell **"VCT" C18**. If "D" for "Detailed" in cell **"VCT" C18** is selected this table is masked and you may proceed to Table VCT – 3 to enter more detailed information. In that case you may skip this section of the manual and proceed to page 27. This summary method is most appropriate if data are available from projects that focus on VCT for HIV or for projects in which the finances of the non-VCT activities are easily separable from the VCT services.

By dividing total monthly operating expenditures (including capital costs converted to a recurring cost basis), into the number of clients who complete VCT and register for the MTCT intervention, one can directly derive a per-client operating cost. The issues mentioned above such as how to treat research and other adjunct activities; start-up and seasonal effects; patient fees; and the sharing of joint resources apply to this summary costing approach as well. A shortcoming of this approach is that it does not permit differential accounting for the cost of HIV-negative versus HIV-positive clients. This could be useful for predicting cost changes if prevalence in the caseloads changed, or if the VCT program were transferred to an area with a different HIV prevalence. Another disadvantage of the summary costing approach is that, since one cannot document the cost of the various steps in the VCT sequence, it is far less useful for cost control purposes.

In cells **D23** through **F28** of Table VCT-2 you are asked to enter "low", "best" and "high" estimates for each of six variables that determine total net annual costs of providing VCT to pregnant women in your service area.

Influence on cost-effectiveness: High. VCT costs can constitute up to 75% of total program. costs.

Expected effort of data collection: Medium. You have chosen to enter summary estimates in order to reduce the effort of estimating VCT costs in detail. Some loss of accuracy is inevitable. Because VCT costs have such a strong influence on cost-effectiveness, it makes sense to review budget and expenditure documents and to interview relevant project personnel in order to arrive a reasonable data-based estimate.

D23-F23. Number of HIV-positive clients who complete VCT and register for MTCT intervention per year. Enter a low, best and high estimate for the number of HIV positive women you expect will complete VCT and register to receive an MTCT intervention, either ARVs or substitute feeding. **Data sources:** One way to obtain a quick estimate is to use last year's figures and adjust them upward or downward to reflect the factors that might make future reality differ from past experience.

D24-F24. Variable costs. Enter a low, best and high estimate for the annual expenditures on items that vary with the number of patients seen. This includes both supply items such as test kits; and personnel items such as wages and benefits for counselors and lab personnel. Since test kits are likely to be a large part of total costs it makes sense to obtain a good estimate of these costs. **Data sources:** Project expenditure documents.

D25-F25. Fixed costs. Enter a low, best and high estimate for items that tend to remain the same over relatively large changes in program scale. These include administrative costs and rent. Some personnel may have both administrative and direct service duties. If so, divide their compensation expenses appropriately between variable and fixed costs. **Data sources:** Project expenditure documents.

D26-F26. Capital goods. Enter a low, best and high estimate for annual expenditures on durable items (those lasting over a year) such as furniture and office equipment that are being used for the MTCT-VCT activities. **Data sources:** Project expenditure documents.

D27-F27. Average life of capital goods. Enter a low, best and high estimate for the average length in years of the useful life of these capital goods. **Data sources:** None. Use your best judgment based on the current condition of the items and how intensively they will be used.

D28-F28. Patient revenues. Enter a low, best and high estimate for the annual revenues that you expect to receive from VCT clients. This could be in the form of registration and other fees or from voluntary donations. **Data sources:** Project financial documents.

I18 – P29. Result of VCT cost calculation using the summary approach. If **C18** = "S", this table displays the results of the summary calculation; if **C18** = "D" it displays the results of the detailed calculation. In both cases it gives the low, best and high estimates for:

- Variable costs
- Patient revenues
- Net variable costs (variable costs minus patient revenues)
- Fixed costs
- Capital costs
- Total annual costs
- Cost per HIV-positive patient who completes VCT

The left half of the table shows these results assuming that there are no external benefits of VCT. The right side shows the results with whatever the current value in cell C5 is (external benefit of VCT). *The figures on the right-hand side are operative in the cost-effectiveness calculation. If you wish to run the analysis assuming no external benefit of VCT, make sure 0% is entered in cell **C5**.*

Table VCT-4: Detailed VCT information (Variable costs)

Background

"Variable costs" are costs that vary with the volume of service. These are primarily the cost of personnel and disposable supplies. Variable costs are likely to constitute at least 50% of total VCT cost. Using the detailed costing approach, resource consumption is determined by identifying, measuring and valuing all cost elements of the variable cost portion of VCT.

Personnel. This is the amount of staff time required per client for each task. The costing of personnel resources entails calculating the average length of time spent on each VCT activity. This time estimate is then multiplied by the wages of the personnel needed to provide the specified activity. For services provided to groups, such as most pre-test counseling, the personnel costs are divided over the average size of the group. Activities to be costed include: seeking consent for pre-test counseling for the HIV test; entering client's name and demographic information into project records; administration of the HIV test; pre- and post-test counseling; and laboratory work. Remember, even if the client drops out of the process before the intervention itself, the time staff spends on that client is a real cost. The CET performs the arithmetic entailed in these calculations. The user's task is to enter reliable information on parameters such as the wage rates, length of time required for each task, and on the proportion of women who drop out of the VCT cohort at each stage of the process.

Supplies. The HIV test kit is usually the most important item in this category. This includes the kit for the initial test (e.g., ELISA) and the kits for confirmatory tests, which may be more expensive (e.g., Western blot). These should be costed according to the price the agency actually pays. In most cases this will be a bulk purchase price available through a non-profit agency, not the local retail price for this item. To the bulk price should be added the cost of transporting it to the point of use.

This table provides space for entering detailed information on the items needed to calculate the variable costs. It includes information on each significant cost item and the number of women who receive each item. Several of the information items ask for very specific figures on the percentage of women who drop out of the treatment group at various points in the VCT process. Column E provides figures that convert the percents that you enter into actual numbers of women. In this way you can match the percentages entered in the CET with the actual numbers of women observed in your program.

Double-check cell C5: External benefits of VCT

Remember to check the value in cell **C5** for external benefit of VCT. This number adjusts the cost of VCT used to calculate cost-effectiveness. We recommend that you use the conservative default value of 0% for the base-case analysis.

Influence on cost-effectiveness: High. Variable costs are likely to be 50% or more of total VCT costs.

Expected effort of data collection: High. Since variable cost estimates have an important influence on cost-effectiveness and because relevant data should be readily available from project documents and personnel this should be considered a high priority.

C35. Prior testing. In cell **C35** enter information on the percentage of women who register for VCT who are known to be HIV-positive from previous testing. Only those women who do not require further counseling and testing should be included. **Data sources:** Document indicating prior positive test results.

C36 and **C37. Test characteristics.** Enter the false positive rate for the initial and confirmatory tests you plan to use. The false positive rate is 1- specificity. The ELISA test has a specificity of 99.5% (Phillips, 1994). We have entered 0.5% in both **C36** and **C37** as the default values. Mislabeling of test results and other errors of clerical or lab technician are probably a greater source of error than the technical limits of the tests. this is hard to quantify and will vary from setting to setting. Program managers should in any case conduct periodic assessments to ensure that the error rate is very low.

C40 – C42. Wages per hour including benefits. Enter the average hourly compensation rates for clerical staff, counselors and lab staff. This should include both wages and benefits calculated on an hourly basis. Since pay is usually provided on a monthly basis, the hourly rate can be derived by dividing the average monthly wage by the number of days worked per month multiplied by the average number of hours per day. Other benefits such as health insurance and paid holidays should be added to the monthly wage. The formula for calculating the hourly wage would then be:

(Monthly financial compensation + monthly value of benefits)
divided by
(Average days worked per month x average hours worked per day).

"Clerical" staff here refers to those who assist with managing the paperwork involved in processing the daily caseload. This would be primarily registration and other patient record management and perhaps collecting patient fees, issuing receipts, etc. It would not include higher-level financial, administrative, or supervisory activities. **Data sources:** Project financial documents.

C45 – C48. Test kits and other cost items. Enter the per-unit cost of the initial test kit; the confirmatory test kit; and blood-draw tubes in cells **C45, C46** and **C47** respectively. In **C48,** enter the cost per woman of ancillary service such as transportation and meals if these services are needed to maintain the VCT caseload. **Data sources:** Project expenditure documents.

C50 – C51. Cost sharing. Enter average per-patient revenues from registration fees or other sources (if any). This figure can be obtained by dividing the monthly cost-sharing revenue by the number of women who register for VCT. **Data sources:** Project expenditure documents.

C58 – C61. Screening to identify high-risk women. Rather than counsel and test all women some programs may conduct an initial screening to identify high-risk women. The purpose of this screening is to reduce the resources used for pre-test counseling and testing of those who are HIV-negative. This strategy is most sensible in areas with very low prevalence of HIV. Since it inevitably means that some HIV-infected women will be inadvertently screened out, careful planning is required to hold these occurrences to a minimum. If this program does conduct an initial screening enter "Yes" in cell **C55**. Entering "Yes" unmasks cells **C58** through **C61**.

NOTE: Data entry for cells C58 through C61 is only required if this program conducts an initial screening to identify women at high risk of HIV. This is only indicated if "Yes" is entered in **C55.** If this program dies not conduct an initial screening enter "No" in **C55** and proceed to cell **C64**.

C58. Percent who decline initial high-risk screening and therefore drop out of VCT cohort. This is the attrition ("drop-out" rate) of women who refuse the high-risk screening and are therefore no longer in the counseling and testing cohort. **Data sources:** By examining patient records, project staff can tabulate the number of women who reported for antenatal services and received a referral for the initial high-risk screening for MTCT. The percent who decline the screening is then calculated by comparing this figure (number of women available) with the number who actually registered for the screening. This comparison should be carried out over five randomly selected days in order to ensure an adequately precise estimate.

C59. Minutes per woman needed to conduct the initial screening. If the screening is conducted in a group, this would be the length of time required to process each group divided by the average number of women per group. **Data sources:** Direct observation on three randomly-selected days.

C60. Percentage of women who were in fact found to be at high risk. This is the portion of women of all women screened who are determined by the screening criteria to be high risk. Only these women would then proceed to VCT. Estimates should be based on staff observation of the average number of minutes required for each high-risk screening session

and the average number of women in each session. **Data sources:** Direct observation on three randomly-selected days.

C61. Number of women who were in fact HIV-infected but were excluded by the initial screening. The proportion of undetected positives inadvertently screened out of treatment in each program can be determined by periodic sampling of those screened out and offering to test them. In general, as the value in cell **C60** goes down (screening criteria more stringent and higher proportion of positives in cohort screened in for services), the value in cell **C61** goes up (more undetected positives screened out of services). Apart from its value in calculating cost-effectiveness, this figure is very important in ensuring that the screening process is not screening out an unacceptably large number of HIV-infected women. **Data sources:** Estimating this input requires periodic random sampling of those screened out and offering to test them to determine how many are in fact HIV-infected. Since this is an important parameter for reasons additional to the cost-effectiveness analysis, we recommend that this check should be carried out on an ongoing basis on one randomly selected day each month. Ten women should be randomly chosen on each of these days.

Cell C64 – C67. Registering for VCT. What appears in these cell range varies according to whether initial screening (**C55**) is offered or not. Please follow the instructions that correspond with your situation. Use the instructions in the first box "Registering for VCT-I" (below) if no initial screening for high-risk women is offered and the second box "Registering for VCT-II" on page 32 if initial screening is provided.

Registering for VCT - I

Complete only if no initial screening is offered (If C55 = "No")

C64. Percent of those known to be HIV-infected but who decline to register. Another point of possible attrition, this is the proportion of women known to be positive from previous testing who arrived at the clinic for the MTCT intervention but who then declined to register. We expect that this number would be very small, particularly since, being already documented as HIV-infected, they would not have to be tested again. Using patient registry data, calculate the percentage of women referred for VCT who (1) are known from previous tests to be HIV-infected, but who (2) decline, for whatever reason, to register for VCT. **Data sources:** This information is probably available from client registry data. Since the number of women with known HIV+ status is likely to be small, a sample of 50 known HIV-infected women who received antenatal services should be adequate. If possible, this sample should be dawn from two or more time periods separated by 1-2 months.

C65. Percent of those of unknown HIV status who decline to register. Another point of possible attrition. **Data sources:** See "Percent of those known to be HIV+ who

decline to register" (above) but considering only women of unknown HIV status. Because there are far more women with unknown HIV status, 100 should be a reasonable sample.

C66. Time in minutes required to register women of known HIV+ status for the MTCT intervention. **Data sources:** Observe patient flow directly to record the time required for each woman to register. A sample of 10-15 women of known HIV-positive status is adequate.

C67. Time in minutes required to register women of unknown HIV status for VCT. **Data sources:** As in **C66**, observe patient flow directly. A sample of 15-20 women is adequate.

Registering for VCT - II
Complete only if initial screening is offered (C55 = "Yes")

C64. Masked.

C65. Percent of those who complete initial screening for high risk who decline to register for VCT. Another point of possible attrition. **Data sources:** Over 5 randomly-selected days, record the number of clients who complete the screening for high-risk and are found to be at "high risk" but who then do not register for VCT. Divide the average figure for these five days this into the total found to be "high risk". The recording of this information should be as unobtrusive as possible, so that women's decisions are not affected by their awareness of being monitored.

C66. Masked.

C67. Minutes required to register each 'high risk' woman for VCT. Data sources: Time the actual length of time required to register "high risk" women on three randomly selected days and take the average of all three days.

C70. Percent of women receiving ancillary services. Percent of women who register for VCT who received ancillary services. If no ancillary services are provided, set this to 0%. This is the default value. **Data sources:** Review project records of the number of clients who receive ancillary services in a month. If family members of a client receive ancillary services such as transportation this should also be counted as services to that client. Calculate the percentage of all clients seen during that month that this constitutes. Since ancillary services may vary by time of year, collect this information during different seasons if possible. Average the results over the number of months that you collected data. A total sample of 100 clients should be adequate.

Cell C73 – C79. Pre-test counseling.

C73. Percent registered for VCT but who do not accept pre-test counseling. Data sources: Requires direct observation of the number of clients who drop out before pre-test counseling. Compare the number of registrations in a given day with a count of those who complete pre-test counseling. Completing this count over five randomly selected days would give a reasonable estimate. In most cases this number will be quite small and zero is the default.

C74. The number of women who receive pre-test counseling in one session. For individual counseling this will of course be "1"; but usually group counseling will

be employed and the number should reflect the average size of the pre-test counseling group. In most cases we expect that a maximum number is set by policy. However, if patient flow is lower than expected, sessions may be conducted with less than this maximum. **Data sources:** Counting the actual number in each session over five randomly-selected days would provide an adequate basis on which to take an average. This may be an input that is sensitive to seasonal fluctuations. If possible, repeat this exercise during normal, low and high caseload seasons.

C75. Minutes required for pre-test counseling session. **Data sources:** Whether it is individual or group, time the actual length of the counseling sessions on five randomly selected days and take the average of all sessions.

C76. Percent of women who completed pre-test counseling but do not accept blood draw for initial HIV test. Another point of possible attrition. **Data sources:** This input can be calculated by asking staff to count the women who accept blood draw over the course of a randomly selected day and comparing this with the number who completed pre-test counseling on that day. Repeating this exercise over five randomly selected days should be an adequate basis on which to take an average percentage.

C77. Minutes required for blood draw. Data sources: Direct observation of 10-15 clients who are having their blood drawn on two randomly selected days should give an adequate estimate.

C78. Number of initial tests processed in a batch. There may be a maximum determined by the type of equipment in the lab, but depending on patient flow the number actually processed in a batch could be lower. **Data sources:** The lab staff can count the number per batch over five randomly selected days. If seasonal variation in patient flow is an issue, the sampled days should include days in different seasons.

C79. Minutes of lab technicians' time for each batch of initial tests. **Data sources:** Project staff should time the number of person-minutes needed to process each batch of initial tests. This should include the time between delivery of samples to the lab and delivery of the results to the counselors. Observations should cover a full day on two randomly-selected days.

Cell C82 – C85. Confirmatory test

C83. Percent of women who test positive on initial test who do not take the confirmatory test. If no confirmatory tests are provided, enter "No". The remaining data entry cells in this section are then masked. In the vast majority of cases however, VCT programs will provide confirmatory tests to those who tested positive on the first test. **Data sources:** Over five randomly-selected days, staff

should compare the number of women who test positive with the number who take the confirmatory test. Because women may return for the confirmatory test either before or after they are asked to return, staff should keep track of those who return by name or ID number over a two week**(?) period. This will ensure that results include all who return, not only those who return at the appointed time.

C84. Number of confirmatory tests processed in a batch. See explanation for **C78** above.

C85. Number of minutes of lab technicians' time for each batch of confirmatory tests. See explanation for **C79** above.

C89 – C92. Post-test counseling. Different lengths of time for post-test counseling and different sized groups can be entered for HIV-negative versus HIV-positive women. The default assumption is that HIV-negative women will be counseled in the same sized groups at post-test as at pre-test but that HIV-positive women will be counseled on an individual basis at post-test.

C89. Number of women HIV-negative women who receive post-test counseling in one session. For individual counseling this will of course be "1". **Data sources:** If the number per session is variable, counting the actual number over five randomly-selected days would be provide an adequate basis on which to take an average. This may be an input that is sensitive to seasonal fluctuations. If possible, repeat this exercise during normal, low and high caseload seasons.

C90. Minutes required for post-test counseling session for HIV-negative women. See explanation for **C75** above.

C91. Number of women HIV-infected women who receive post-test counseling in one session. See explanation for **C89** above

C92. Minutes required for post-test counseling session for HIV+ women. See explanation for **C75** above.

C95 – C96. Registration for MTCT intervention. These cells record the number who may drop out at the final point of possible attrition, namely at the time of registration for the MTCT intervention itself. We assume that registration for MTCT is part of post-test counseling in the case of those women with previously unknown HIV status.

Registration for MTCT Intervention - I

If initial screening *is not* provided (C55 = "No")

C95. Percent of women of previously *unknown* HIV status who completed post-test counseling who do NOT register for MTCT intervention. Final point of attrition. **Data sources:** This can be calculated by comparing the number of women who complete VCT and are referred to the MTCT intervention(s), with the number who actually register. This input, which determines the uptake rate for the interventions, can have an important effect on cost-effectiveness. We suggest you take the average percentage over 10-15 randomly selected days. Care needs to be taken only to include women who were not known to be positive from previous testing. This could perhaps be done by designating a space in the registration books and forms that record whether each client arrived at the facility with known HIV+ status from a previous test.

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C96. Percent of women of previously *known* HIV-positive status who completed post-test counseling who do NOT register for MTCT intervention. See explanation for **C95** above.

Registration for MTCT Intervention - II

If initial screening *is* provided (C55 = "Yes")

C95. Percent of women who complete post-test counseling who do NOT register for MTCT intervention. The final point of attrition. The sheet is now set to reflect the provision of an initial screening to identify high-risk women (C55= "Yes"). All women who register for MTCT therefore completed this initial screening. We assume that in the low prevalence settings where initial screening for high risk make sense, very few women will have known HIV-positive status, and we do not track them separately.

C96. Masked.

D101 - F102. Total annual variable costs: Result and ranges. The blue cells **E101** and **E102** contain the results of the calculation of variable costs based on the data you have provided. (For more detail on how these results were derived, see the calculations in cells **I45 – V62**). In cells **D101** and **D102** you are asked to enter low-end estimates for supply and for personnel costs respectively. Cells **F101** and **F102** require high-end estimates for these same variable. These ranges will be used to define the lower and upper end of the ranges used in the sensitivity analyses to examine how cost-effectiveness varies with the cost of VCT.

C107 – F107. Annual number of women who complete VCT. Given the number of women who give birth in this service area; the portion of these women reachable by the program; HIV prevalence; and the number of women who drop out of the VCT process at various stages, cells **C107, D107** and **E107** display the number of HIV+, HIV-, and combined HIV+/HIV- women who complete VCT and register for the ARV/substitute feeding intervention. **F107** shows the percentage of all women who register for VCT who do not complete the VCT sequence and register for the MTCT intervention itself.

Table VCT- 5: Detailed VCT information: (Fixed costs excluding capital costs)

Background

Fixed costs are expenditure items that do not vary with short-term changes in the caseload. Good examples of fixed costs include rent, telecommunications and administrative expenses. They do not include the wages of personnel who provide direct services. This table provides a template for entering detailed information on the fixed cost expenditures required by the VCT program.

Influence on cost-effectiveness: Medium. Fixed costs can constitute over half the cost of running a VCT program, and VCT can be the dominant cost of an MTCT program.

Expected effort of data collection: Low-medium. This may be an area in which it possible to get a reasonable estimate fairly quickly by focusing on the large expenditure items which are likely to include rent, administrative costs and possibly vehicle fuel and maintenance. The increased precision obtained by tracking down the exact cost of low-cost items may be small.

C117 – C137. Monthly expenditures for fixed cost items. For each cost item, you are asked to enter a monthly expenditure figure and the percentage of that amount spent on the MTCT program. In the first few lines some typical cost items are supplied such as "accounting", and "telecommunications". You may alter these as you wish and can enter up to 11 additional items that are not currently listed. Finally, in cells **C137** and **D137** you may record the combined expenditures for all other items not specifically listed in the rows above. **Data sources:** Project expenditure reports are the best sources of information on fixed costs. If these are not available, budget documents can also be used though they are less desirable since they reflect planned rather than actual outlays.

D117 – D137. Percent of fixed costs expenditures that are for MTCT-related VCT. Throughout this cost analysis we seek to separate items that are strictly for VCT associated with MTCT prevention from other costs. In some cases this may be challenging. For example, consider the case in which VCT for MTCT is carried out at a clinic that also provides VCT in conjunction with STD services for men. It is likely that these services will be housed in the same building and share administrative staff and other fixed expenses. The problem then is to make a reasonable allocation of costs to these two distinct activities. **Data sources:** Project managers may have a good sense of how staff

time and other resources are allocated among activities and in some cases the information that they are able to provide will be sufficient. In other cases it will be worthwhile to undertake a more formal accounting either by observing how staff and equipment is used (time and motion studies) or by interviewing key staff members to learn how they allocate their time.

D143 – F143. Total annual fixed costs: Result and ranges. The blue cell **E143** contains the results of the calculation of fixed costs based on the data you have provided. In cells **D143** and **F143** please enter low-end and high-end estimates for fixed costs. As was the case with variable costs, these ranges will be used to define the lower and upper end of the ranges used in the sensitivity analyses to examine how cost-effectiveness varies with the cost of VCT.

Table VCT-6: Detailed VCT information: Capital costs

Background

Capital goods refer to physical goods with a useful life longer than the annual budget cycle. Examples include furniture, lab equipment and computer hardware and software. Expenditure documents supported by receipts are the best sources of information on capital costs. Capital costs require special accounting methods because they can vary greatly from year to year. Typically a program must make a large capital goods outlay during its start-up period. These expenses then drop dramatically as additional outlays are only made to replace worn-out equipment. There are a number of accounting methods, some of them quite sophisticated, for depreciating capital goods over their expected lives so that the "lumpy" capital costs can be smoothed out and put on the same annual basis as other costs. We have adopted a simple "straight-line" approach that amortizes the cost of an item evenly over its expected life.

As is true for every cost estimate in the CET, only consider the additional (or "incremental") costs needed for this intervention. If, for example, a desk is purchased for use by the project administrator, and only 50% of her time is devoted to VCT, only 50% of the cost of that desk should be attributed to the program. Column "F" cells **F151 – F168** labeled "% of use for VCT" allows you to make the appropriate allocation of cost.

Influence on cost-effectiveness: Depends. VCT is not a capital-intensive activity in general. However, capital costs could be important in some projects, (e.g., if the project purchased new computers for record keeping, particularly in countries that place high import duties on such items).

Expected effort of data collection: Depends. The level of precision to seek depends upon how large overall capital expediters are likely to be.

C151- F168. Capital goods. For each capital item this range of cells requires estimates of the quantity, cost, months of expected useful life and percent of use devoted to VCT for MTCT prevention. These data are then used to calculate the total monthly cost of that item to the VCT activity. As with fixed costs, some suggested items with hypothetical cost figures are provided to help get you started. **Data sources:** Project financial documents.

D170 – F170. All remaining items. Here you may enter combined cost data on any capital items not included in the list above. It may make sense to use these cells if you have numerous small items that would be tedious to itemize and which constitute only a small portion of total capital goods. We suggest that you limit the use of these cells because combining cost items and estimating an average useful life for all of them is likely to introduce inaccuracy into the calculation. **Data sources:** Project financial documents.

D175 – F175. Total annual capital costs: Result and ranges. E175 displays the "Best estimate" of total annual capital costs. Enter a low and high estimate in cells **D175** and **F175** respectively.

Table VCT-7: Variable cost of VCT by task

Background

This table shows the personnel and supply costs entailed in each step of the VCT process and may be particularly useful for cost analysis purposes. The percent that each task constitutes of total variable costs shown in column **M** shows where the most money is spent and where, therefore, the greatest potential for improved economy may lie. Notice that the large number of women who receive services at early stages in the process such as registration and testing itself, may drive costs more than services provided in later stages such as post-test counseling which involves relatively few women.

B180 – M197. VCT cost analysis. All values in this table are derived from data entered elsewhere. Based on the attrition data entered in Table VCT-3, column **C** shows the number of women remaining in the VCT cohort at various stages of the process. Columns **E** through **G** detail personnel costs for each task. These are calculated by multiplying wage rates by minutes spent per client per task. Columns **H** through **K** treat supply costs and show unit costs, number of units used based on the number of clients receiving each item, and unit costs. Column **L** sums personnel and supply costs for each task and totals the annual costs net of revenues in **"VCT" L197.** Column **M** shows the percent that each task constitutes of the total.

"ARV" worksheet

In this section, you will be presented with a description of the ARV regimens you wish to evaluate including their efficacies and dose patterns. The corresponding Excel spreadsheet is called **"ARVs"**.

The choice of ARVs, doses, timing of doses and estimated efficacy of these regimens are derived from clinical trials and are given by the model (blue cells). The trial-derived efficacy figures can then be adjusted to reflect imperfect adherence (relevant if you believe that adherence in your setting will be different from adherence in the trials); and late arrival for treatment (relevant for the three regimens with a prepartum component – ACTG 076; CDC-Thai; and PETRA-A). In addition, the user enters the cost of each dose to mother and to infant. Based on this cost data, the intended number of doses in the regimen, and the number of mothers who receive each component of the regimen, the model then calculates the drug costs per woman and annual drug costs for the expected number of women to be treated in the service area.

Table ARV-1: Regimen components

Background

The spreadsheet permits the analysis of five different ARV regimens that are based on clinical trials that were able to demonstrate clinical and statistical significance:

- ACTG 076 -- Zidovudine prepartum treatment starting at week 28 of gestation, plus intrapartum, and postpartum (mother and child) treatment.
- HIVNET 012 – One 200 mg NVP to mother at outset of labor; 2 mg/kg to infant once within 72 hours of birth.
- CDC-Thai -- 300 mg dose AZT twice daily from 36 weeks' gestation and every 3 hours during labor through delivery..
- PETRA-A -- 300 mg AZT and 150 mg 3TC twice daily from 38 week's gestation through labor and 300 mg AZT every three hours of labor through delivery; 300 mg AZT and 150 mg 3TC twice daily for a week postpartum; 5 mg/kg AZT and 2 mg/kg 3TC for infant every 12 hours for week postpartum
- PETRA-B -- Equivalent to PETRA-A without prepartum therapy.

C4 – G9. Table ARV-1: Regimen components. This table provides a summary of which component (prepartum, intrapartum and postpartum) is included in each regimen. **C5** indicates that those who arrive too late for the full prepartum portion of ACTG 076 will receive a shorter prepartum course as a substitute. Since it may be hard to justify providing no treatment to those who arrive too late for the full treatment, we have set this to "yes". **D5 – G5** read "NA" to indicate that since the other three regimens do not include a long

prepartum component, there is no substitute for a long prepartum component. No data entry is require for this table.

Table ARV-2: Gestational age at start of treatment

Background

In the "Settings" sheet you entered information about the percentage of women who were available for VCT and treatment by gestational age. Table ARV-2 uses this information combined with an estimate of the latest prepartum treatment arrival time consistent with receiving the full efficacy of the prepartum portion of the regimen; and the latest arrival time consistent with receiving partial efficacy from the prepartum component. Unfortunately, there are no definitive data bearing on the relationship between length of prepartum treatment and efficacy. We therefore provided numbers based on reasonable guesses as follows:

Relationship between length of prepartum treatment and efficacy

Regimen	Treatment start time (gestational age)	Efficacy
ACTG076	34 weeks or earlier	67.5% (full efficacy)
ACTG076	> 34 weeks through 38 weeks	55% (reduced efficacy)
ACTG076	> 38 weeks	40% (reduced efficacy)
CDC-Thai	38 weeks or earlier	51% (full efficacy)
CDC-Thai	> 38 weeks	30% (reduced efficacy)
PETRA-A	38 weeks or earlier	50% (full efficacy)
PETRA-A	> 38 weeks	37% (reduced efficacy)

If you wish to explore the effect of a different set of efficacy adjustments, you may do so by altering the values in the table located in cells **"ARVs" X99 – AE107**. (You must first unlock the worksheet using the password as explained on page 6). Using the information provided in the table above)on arrival times and efficacy, combined with the data on the cumulative percent of women who arrive at various gestational ages, we calculated a weighted average efficacy adjusted for late arrival. This is shown in row **63** of **"ARVs"** and is discussed further in the section of the manual pertaining to "Table ARVs-5".

Influence on cost-effectiveness: Medium. Since late arrival for prepartum treatment affects regimen efficacy, these estimates can have a significant impact on cost-effectiveness. This is particularly true if ACTG 076 is being evaluated since it has the longest prepartum treatment period, and relative to other regimens, the greatest portion of its benefit is presumed to occur during the prepartum period.

Expected effort of data collection: Medium. See explanation for **"Setting" C27 –C34.**

Adjusting for late arrival

Enter for ACTG-076 only

C13. Latest gestational age in weeks that a woman can arrive at clinic and still receive *full* efficacy for ACTG 076. The default is set at 34 weeks.

C14. % of women who receive any prenatal care who arrive in time for 'long' course of ARV. This figure is derived from estimated cumulative arrival time from cells "**Setting" C27** through **C34.**

C16. Latest gestational age in weeks that a woman can arrive at clinic and still receive *partial* efficacy from the prepartum portion of ACTG 076. The default is set at 38 weeks.

C17. % of women who receive any prenatal care who arrive in time for 'short' course of ARV. This figure is derived from estimated cumulative arrival time from cells **"Setting" C27** through **C34.**

Adjusting for late arrival

Enter for CDC-Thai and PETRA-A only

C19. Latest gestational age in weeks that a woman can arrive at clinic and still receive *full* efficacy for CDC-Thai and PETRA-A. The default is set at 38 weeks.

C20. % of women who receive any prenatal care who arrive in time for 'short' course of ARV. This figure is derived from estimated cumulative arrival time from cells **"Setting" C27** through **C34.**

Table ARV-3: Mothers and children receiving various service components

Background

This table shows the number of women receiving each of the components of each ARV intervention. We assume no mother is denied treatment because she is not available for the full intended course; but rather all mothers who are tested and agree to ARV therapy receive some treatment. As shown in the table, all mothers receive intrapartum treatment even if they do not arrive in time for the prepartum component.

No Data entry is required.

C24 – G31 Table ARV-3. The figures in this table are derived from the estimates entered on the number of women completing VCT and the gestational age at start of treatment as shown in Table ARV-2.

Table ARV-4: Doses, drugs and drug costs.

Background

This table displays information needed to estimate the cost of each regimen. It requires data from the user on the cost per dose and, in the case of ACTG 076, the average number of weeks between the start of therapy and delivery. The CET then calculates the ARV costs for each intervention given their dosing schedules and amounts.

Influence on cost-effectiveness: Medium – High. The importance of these variables in determining cost-effectiveness varies a lot from regimen to regimen. As shown in the sensitivity analysis graph Figure 1c starting at cell "**SAs" B20,** the ARV-intensive interventions such as ACTG-076 and PETRA-A are more sensitive to drug costs than the less drug intensive regimens such as PETRA-B and especially HIVNET-012. If substitute feeding is also being evaluated, the drug cost inputs also assumes less importance because they represents a smaller portion of total program costs.

Expected effort of data collection: High. These data are both easy to obtain and important.

Estimating the cost of ARV doses to mother and to infant. The cost of ARVs to the public sector provider can vary depending upon agreements reached between the government and pharmaceutical companies or other third-party suppliers. The inputs required here are figures for the amount paid by the public sector provider for each dose of the relevant ARV agent. Since price information may be available in various forms (e.g., per bottle or per case), arriving at a per-dose price may require a calculation to be made outsides of the worksheet. If transportation

and distribution costs are entailed that are additional to the price paid for the ARVs themselves, this too should be included in the per-dose cost estimate.

The default costs per dose currently used in the CET are shown below.

Default values of cost per dose of ARVs

Regimen	Mothers	Infants
ACTG-076	$0.78 per 300 mg dose AZT	$0.04/ml of Retrovir
HIVNET 012	$3.87 per 200mg NVP	$0.13 per 4 mg/kg NVP
CDC-Thai	$0.78 per 300 mg dose AZT	NA
PETRA-A	$2.22 per dose Combivir (combination of AZT/3TC)	$0.07/ml of Epivir (3TC); $0.04/ml of Retrovir (AZT)
PETRA-B	$2.22 per dose Combivir (combination of AZT/3TC)	$0.07/ml of Epivir (3TC); $0.04/ml of Retrovir (AZT)

Sources: Nevirapine - Johns Hopkins University Hospital Pharmacy, 1999; Combivir, Epivir. Retrovir – Personal communication, Joseph Saba, UNAIDS, 1999; AZT - Associated Press, Drug Company Cuts Cost of Aids Treatment, in New York Times. 1998: New York City. p. 87.

Cells ARV-C37 through ARV-I37. **Cost per dose for mother.** For each regimen, enter the cost per dose for mother for each ARV involved. For the Thai regimen, this is AZT (zidovudine) only, whereas the two PETRA regimens include both AZT and 3TC (lamivudine). **Data sources:** Project expenditure documents.

Cells ARV-C38 through ARV-I39; and ARV-D40. Cost per dose for infant. For each regimen, enter the cost per milliliter and number of milliliters of each postpartum dose to the infant. Since the HIVNET 012 regimen includes just one dose to the infant it is probably easier to enter this cost directly. Cell **D40** is therefore a data entry (yellow) cell. Since the Thai regimen includes no postpartum treatment of infants, these cells read "NA". As was the case with mothers, postpartum treatment of infants includes both AZT and 3TC for infants in the PETRA regimens. **Data sources:** Project expenditure documents.

Estimating the cost of the prepartum regimen. The number of doses and therefore the overall cost of prepartum treatment depends upon the average number of days of prepartum treatment and the number of doses per day. This period begins on the first day of treatment and ends on the day of delivery just prior to any change to a different intrapartum dosing pattern. The worksheet requires an estimate of the average number of days in this period for all women receiving each type of prepartum treatment. It then multiplies this number by the doses per day to calculate the total number of doses needed during the prepartum period. This product is in turn multiplied by the

cost per dose in order to arrive at the overall cost for prepartum treatment. Because the possible start time for the ACTG 076 regimen can be so variable, the user is asked to enter figures for the actual number of weeks between the start of therapy and onset of labor. For each ARV agent used the prepartum treatment cost is simply: (Number of days of treatment) x (doses per day) x (cost per dose).

Cell ARV-C44. Average number of days for "long course" (only applies to ACTG-076). Enter figure for the average number of weeks of prepartum therapy experienced by mothers receiving ACTG 076 for women arriving in time for the long pre-partum course of treatment. **Data sources:** Project patient records.

Cell ARV-C49. Average weeks between therapy start and delivery for those receiving "short course" (only applies to ACTG-076). Enter figure for the average number of weeks of prepartum therapy experienced by mothers receiving ACTG 076 for women arriving too late for the full intended long prepartum course but in time for a shorter prepartum course of treatment. **Data sources:** Project patient records.

Low and high range of ARV drug costs. ARV prices tend to be fairly stable, and when they move, they usually move in a downward direction. Nevertheless, since they can be a major determinant of overall program costs we ask you to enter a percentage range above and below the base case estimate. Ideally the range would be based on knowledge of actual market conditions for the drugs or the state of negotiations with suppliers. However, in the absence of such knowledge, defining a range of 20% above and below the default prices will probably capture most of the potential short-term price variation. This will be used in the sensitivity analysis to show how cost-effectiveness varies with different estimates of drug costs.

C80 - G80. Enter the a figure for each regimen that represents the percent above and below the current drug cost estimate that you wish to examine in the sensitivity analyses. While it is possible to enter different figures for each regimen, the results of the sensitivity analyses will be easier to interpret if you use the same estimate across all five regimens. The default value is 20%.

C84 - Q85. Cost summary. The table in the blue cells **"ARV" C84 through "ARV" Q85** provides summary information on the cost of ARVs for each of the regimens under consideration. The table includes both the cost of the entire cohort of women who complete the VCT sequence each year and the cost for each woman.

Table ARV-5: Effectiveness estimates

Background

ARV effectiveness refers to the percentage reduction in transmission in a treatment group compared with an untreated comparison group and is one of the most important determinant of overall cost-effectiveness. The model takes the relative percentage reduction in transmission as an input. Since effectiveness is sometimes expressed in absolute and sometimes in relative percentage terms it is necessary to understand the difference between the two and to be able to convert from one to another.

Relative efficacy: Relative percent is the more common way we think about applying percents. Multiplying the probability of transmission without treatment by the relative percent reduction would yield the efficacy. For example, if the intervention is 50% effective and the probability of transmission without treatment is 25%, the relative efficacy is 12.5%.

Absolute efficacy: The amount of reduction expressed directly as percentage points of transmission. For example, if an intervention has an absolute efficacy of 9%, the probability of transmission is reduced from 25% (to use the same background transmission rate as in the previous example) to 16%.

Influence on cost-effectiveness: High. ARV efficacy will have a large effect on program benefits and therefore on cost-effectiveness.

Expected effort of data collection: Low. Published efficacy estimates from the clinical trials are the accepted standard for these inputs. These estimates may be revised as the results from additional trials become available. We cannot foresee any circumstances under which it would be sensible to alter these estimates outside the context of the trials.

C91 - Q91. Relative efficacy. In the blue cells **C91** through **Q91** the relative reduction in HIV transmission for the ACTG 076, HIVNET 012, Thai, Petra-A and Petra-B regimens are shown as 67.5%, 47%, 51%, 50% and 37% respectively. These figures are based on the reported results of the respective clinical trials with the high and low estimates representing the limits of the 95% confidence interval around the point estimate. (See the ARV section of "Published studies and other resources" on page 76). These cells are locked to prevent casual changes in these values. Unless you have very good reasons to change them, such as new data from trials in your setting, we suggest that you not alter the default values given.

Background Transmission Rates and Efficacy

Only the relative efficacy from the trials are being applied not the absolute values.

A difference in background transmission rates between your setting and that of the clinical trials does not mean that the estimated efficacies from the treatment will be different in the two settings. For example, in absence of specific knowledge to the contrary, it is reasonable to suppose that a regimen which is 50% effective where transmission rates are 30% will also be 50% effective where transmission rates are only 20%.

As new trials are completed their results will be incorporated into subsequent versions of this model. Please visit the UNAIDS web site at http://www.UNAIDS/MTCT/*** for information about what additional regimens are being considered for inclusion.

Table ARV-6: ARV effectiveness – Adjustments for imperfect adherence

Background

"Imperfect adherence" refers to the difference between the intended number and timing of doses in a regimen and the number and timing actually experienced by patients. The efficacy estimates incorporated into this model are based on the results of well-funded clinical trials. It is possible that patient adherence outside the trial setting will be lower than in the trials. The actual efficacy experienced in your client population may therefore also differ once adherence rates are taken into account. While lower adherence is undoubtedly associated with lower efficacy in general, the specific relation between the two have not been documented for the regimens under analysis. The default value of adjustments to reflect imperfect adherence is 0%. This means that adherence is expected to be the same as was attained in the trials. Depending on the setting, this may not be realistic. For example the infrastructure present in the industrialized countries where ACTG 076 was conducted may not be available in lower income countries. Adherence to this regimen may therefore be lower.

Treatment Adherence Rates

Country	Rates	Source
Northern Thailand	90% adherence	Thaineua et al., 1998
NTPHPT (Thailand)	99% of the women took at least 90% of the antenatal ZDV doses and 99% took at least 1 dose during labor	Weekly Epidemiological Record, 1998
UNAIDS PETRA trials (Uganda, Tanzania, South Africa)	7.7% of women did not take any of the prescribed medication	Marseille et al., 1998

Source: Adapted from John Stover, TFGI, 1999.

As shown in the table above, adherence can be variable even in the context of well funded clinical trials. The very sparse data that is available suggest that adherence may be more of a problem in sub-Saharan Africa than in Thailand. It is also possible that adherence will increase as people understand that they are taking a proven effective drug rather than a possible placebo or a drug which may or may not be effective. The adherence adjustment cells (**ARVs-C98 – G98**) can accept negative values. This would indicate that adherence in your project is better than that experienced in the trials and that this greater a adherence is associated with greater efficacy.

Unless good adherence data is available from your project we suggest you retain the default value of 0%. This makes for consistent comparisons with results generated by other users of this model. However, if you have reason to believe that adherence may be significantly above or below the levels experienced in the trials, cells **C98** through **G98** allow one to explore the consequences of different assumptions about adherence and its bearing on effectiveness.

Influence on cost-effectiveness: Potentially high. Adherence directly affects efficacy.

Expected effort of data collection: High. Since low adherence will render any intervention ineffective, most projects will find it worthwhile to monitor adherence independent of a cost-effectiveness analysis.

C98 - G98. Imperfect adherence. After reading the cautionary notes in the preceding paragraphs, enter changes in the adjustment for efficacy to reflect imperfect adherence if you believe they are warranted. **Data sources:** Project patient records.

"Substitute Feeding" Worksheet

This spreadsheet calculates the costs and benefits of a substitute feeding program to reduce HIV transmission via breast milk. The benefit calculation requires information on current feeding patterns, the risk of HIV transmission via breast milk, non-HIV mortality, and compliance with recommended feeding strategies.

These inputs are combined with data provided elsewhere in the CET to arrive at a month-by-month estimate of non-HIV mortality and HIV infections – together referred to as "fatal events" – for a specified substitute feeding strategy. Interested readers may refer to the area to the right of column K in the "**Substitute Feeding"** spreadsheet to see how these estimates were implemented.

The cost calculation requires data on the cost of the substitute food itself as well as staff training and monitoring costs to deliver a high-quality substitute feeding intervention. It also includes the cost of the increased medical services required by children consuming breast milk substitutes.

What are "fatal events"?

Substitute feeding can affect mortality in two ways:

- Good: Decrease HIV infections (future mortality).
- Bad: Increase non-HIV mortality.

The sum of these effects are referred to as "fatal events". The CET can calculate an "optimal" breast feeding duration chosen to minimize fatal events.

Table SF - 1: Duration of Breastfeeding and Substitute Feeding

Background

A substitute feeding program should use one of two recommendations for mothers: no breastfeeding, or a short duration of exclusive breast feeding followed by a switch to substitute feeding. Mixed feeding appears to increase both HIV and non-HIV risk as compared with breast feeding, and so should be strongly discouraged.

This table displays the CET's current settings regarding breast feeding durations, in months. These settings were selected in the **"Interventions"** worksheet. If "Optimal" was selected in **"Interventions" C13**, the CET calculates the breast feeding duration that minimizes fatal events. If instead of "Optimal" the user entered a particular number of months in **"Interventions" C13**, the CET calculates costs and cost-effectiveness based on that breast feeding duration. In either case, the calculations take into consideration compliance with feeding recommendations as specified in this table. (See below).

D7 – H7. Months of breast feeding or "Optimal". Reminds the user whether "Optimal" or a set number of months (0-6) was specified for length of breast feeding in "**Interventions"**.

D8 – H8. Number of months of breast feeding with optimal feeding strategy. If "Optimal" was selected in **"Interventions"**, these cells show the number of months of breast feeding found to be optimal by the CET. Notice that this number can vary among the five ARV interventions. These cells are blank if a specific number of months of breast feeding was chosen in **"Interventions"** in which case this duration is displayed in the previous row.

D9 – H9. Months of substitute feeding in program. These numbers represent simply the months of breast feeding subtracted from 12 months. It is assumed that a substitute feeding program will provide formula up to 12 months, by which age children will be consuming a significant portion of their diet from solid foods.

Table SF - 2: Breastfeeding, HIV Risk, and Non-HIV Mortality

Background

This table accepts data about current feeding patterns as well as non-HIV mortality and HIV risk via breast feeding in the local setting. This information is used to predict health outcomes for the local setting if feeding patterns are changed by an intervention program.

Influence on cost-effectiveness: High. These data are extremely important for calculating cost-effectiveness. Together they determine if substitute feeding is better than breast feeding, and if so by how much.

Expected effort of data collection: Medium-high. It is best to use local data, some of which should be available from standard sources. For some measures, such as HIV risk via breastfeeding, data from other settings may be all that is available.

D15 – D20. Current breast feeding. Enter the relevant information pertaining to the percent of mothers in the anticipated client population who *exclusively* breast feed at 1, 3, and 6

months; who ever breast feed; and who provide any breast feeding at 6 months and 24 months. "Exclusive" breast feeding means no tea or other liquids or alternative foods of any kind. "Any" breast feeding includes both exclusive breast feeding and breast feeding in combination with other liquid and/or solids foods. **Data sources:** Ideally, survey information for your specific client population is available to accurately portray feeding patterns. If not, the Demographic and Health Surveys published by Macro International (http://www.macroint.com/dhs/) contain infant feeding data for a wide range of countries, and regions/cities within those countries.

NOTE: Please don't enter a zero in cells D15 - D20, even if current feeding practices might suggest, for example, that 0% of infants exclusively breast feed at 6 months. A zero creates problems in some formulas in the model. Instead, put a very low value (e.g., 0.0001). This approach may also help if you find that zeros create problems in other parts of the model..

D23 – F23. HIV risk from breast feeding. Enter in **E23** the overall HIV risk associated with breast feeding. This is the difference in mother-to-child HIV transmission between women who don't breastfeed (e.g., 25%) and those who do (e.g., 40%); here, the difference is 15% = 40% - 25%. If the value is uncertain – due to conflicting studies or statistical uncertainty in a single study, use **D23** and **F23** to specify the lowest and highest likely values, respectively. **Data sources:** If a local study has been done, use that estimate. Otherwise, you can use estimates from other studies. The mean risk associated with any breastfeeding, including short duration, has been estimated at 14% (Dunn 92).

D25. Non-HIV mortality at 1 month (28 days) Enter the percent of babies who die by age one month. **Data sources:** This data is often available in the Demographic and Health Survey conducted by Macro International for many countries, including regions and cities within those countries.

D28 – F28. Non-HIV mortality at 12 months (1 year) Enter the percent of babies who die by age one year in **E28**. If the value is uncertain – due to conflicting studies or statistical uncertainty, use **D23** and **F23** to specify the lowest and highest likely values. **Data sources:** Same as 28-day mortality.

D30. Relative risk of non-HIV mortality, SF versus breast feeding. This number indicates how much higher 12-month mortality is in full substitute feeders than in exclusive breast feeders. Enter **3** if the treatment setting is primarily urban, and **4** if it is primarily rural. These estimates are based on multiple past studies. (Other values won't work as the model is currently set up. If you have a good estimate for your local setting from a research study, let us know and we will help you incorporate it.) **Data sources:** Use our default values unless a local study is available.

D33, D34. Compliance with the feeding recommendation. Mixed feeding (breast feeding supplemented by other foods) appears to be the worst feeding strategy – combining high

risk of HIV with minimal protection against non-HIV deaths. That is why the feeding recommendation should be either pure substitute feeding or exclusive breast feeding with a rapid switch to substitute feeding. However, women may not be able to perfectly comply, and these two cells quantify the imperfect compliance.

D33. Compliance with exclusive breast feeding. This cell specifies the proportion of women who exclusively breast feed when they have accepted the recommendation to do so. A value of 1.0 is perfect compliance (no mixed feeding), and a value of 0.5 means 50% mixed feeding. **Data sources:** Compliance can be estimated from studies of feeding practices when recommendations of exclusive feeding are made, if such studies exist. Unfortunately, compliance cannot be derived from current feeding patterns, because the recommendation of exclusive feeding is intended to change feeding practices, which is difficult to do and thus has uncertain compliance. We have not found any studies of this compliance, but continue to consult with experts. In the meantime, we assume 75% compliance.

D34. Compliance with substitute feeding. This cell specifies the proportion of women who use only substitute feeding (formula and later other foods), when they have accepted the recommendation to do so. A value of 1.0 is perfect compliance, and a value of 0.5 means 50% do some breastfeeding. **Data sources:** Compliance can be estimated from studies of feeding practices when recommendations of substitute feeding are made, if such studies exist. We have not found studies of this compliance, but continue to consult with experts. In the meantime, we use a value of 75%.

D37- H39. Proportion HIV-negative at birth. Using data on the background rate of HIV transmission ("**Setting"** C41) and ARV efficacy ("**ARVs"** row 93), this section of the table shows the percentage of HIV-negative births to HIV-infected mothers.

Row 37 includes both those that would have been HIV-negative in any case and those that were negative as a result of the ARV intervention.

Row 38 shows just the percentage that were negative due to the intervention. (The difference between rows 37 and 38 is those who would have been HIV-negative even without the ARV intervention; this is the same for all ARV strategies.)

Row 39 shows the relative risk of HIV infection via breast feeding for those whose infections were averted due to ARVs. While it is plausible that these babies are at higher risk during lactation (sometimes referred to as a "rebound effect"), recent clinical trials strongly suggest no increased risk. We therefore set this parameter equal to 1.

D41 – H42. Postnatal efficacy of perinatal ARVs regimens. Some ARV regimens include up to a week of therapy for the newborn child, and evidence from clinical trials and drug metabolism studies suggests that some regimens (e.g., Nevirapine) may have effects for a week or more even after the medicine is stopped. Thus, we assume some benefit after birth

in reducing the risk of transmission via lactation. **Row 41** shows the duration of benefit and **Row 42** shows the relative reduction in benefit; these have been set equal to the respective perinatal ARV efficacies.

Table SF - 3: Health outcomes (per 100 children of HIV+ mothers)

Background

The health outcome this model calculates is called *fatal events*. This equals the total of deaths due to non-HIV causes such as diarrhea and pneumonia ("non-HIV mortality") plus new HIV infections occurring via breastfeeding (excluding infections that occurred *in utero* or *intra partum*). Table SF-3 tabulates the number of fatal events estimated for women who follow the current feeding pattern (**Rows 47 - 49**) and for women who participate in the substitute feeding intervention (**Rows 51 - 52**). The fatal events are calculated by dividing overall non-HIV mortality and HIV infection risk into month-by-month risks. (These calculations are performed in **column M** through **column AN**. This part of the spreadsheet was not set up for user interaction and has very little documentation, so if you have questions please contact Jim Kahn.)

The difference between fatal events with current feeding and with the substitute feeding intervention is displayed in **Row 54**. The numbers in this row represent the net health benefit of the substitute feeding intervention.

D47 – H47. Fatal events with current feeding. The sum of non-HIV deaths and HIV infections assuming continuation of current feeding patterns as described in cells **D19-D24**.

D48 – H48. Non-HIV deaths. Anticipated non-HIV deaths with current feeding.

D49 – H49. HIV infections. Anticipated HIV infections with current feeding.

D50 – H50. Fatal events with substitute feeding program. The sum of non-HIV deaths and HIV infections assuming the duration of breast feeding associated with the substitute feeding program (entered by the user in "**Interventions" C17** and shown in **"Interventions" D19-D23** and **"Substitute Feeding" D11 – H11**).

D51 – H51. Non-HIV deaths. Anticipated non-HIV deaths assuming the substitute feeding intervention.

D52 – H52. HIV infections. Anticipated HIV infections assuming the substitute feeding intervention.

D54 – H54. Fatal events averted with SF program. The combined HIV infections and non-HIV mortality averted thorough the substitute feeding intervention. These are the values in **Row 47** minus the values in **Row 50.**

Table SF - 4: Program Costs - Counseling, Training and Substitute Food

Background

This table calculates the cost of the substitute feeding program. Costs include counseling about the intervention, as well as infant formula and other supplemental foods. (Changes in health care costs are considered in table SF-5.) Inputs such as the cost of infant formula and wage rates for counselors may be determined by local economic conditions, whereas inputs such as the length of counseling sessions will reflect program design decisions.

We assume that the costs of infant formula and other foods are borne by the public sector only if a substitute feeding option is offered and taken up by mothers. Substitute feeding costs are *not* attributed to the public sector under the "current feeding" option, but are instead assumed to be paid by families. In **Rows 74, 85** and **86**, only enter cost information for new costs of formula, micronutrients and other foodstuffs that are incremental to whatever the public sector might be supplying currently, that is, prior to the initiation of a new MTCT prevention program.

Influence on cost-effectiveness: High. These data are extremely important in calculating cost-effectiveness. Together they determine the cost of a substitute feeding program

Expected effort of data collection: Medium-high. It is best to use local data. Most should be available from standard sources or with manageable data collection. Other data represent program design decisions.

D60 – H60. Hourly wage/benefit counselor. See the discussion of hourly wages on page 29.

D61 – H61. Counseling/training to discuss feeding strategy (minutes per session). The average number of minutes of each session of counseling that women receive for substitute feeding education that is beyond what they would have received if they were to breast-feed. **Data sources:** This estimate can be obtained several ways. First, it can reflect program policy. If the program is operating, a better option is to time counseling sessions on 2-3 randomly selected days, including time the counselor spends between sessions on paperwork and waiting. Finally, if a counselor works only on this task, his or her hours per week can be divided by the number of sessions completed in that week.

D62 – H62. Number of training sessions beyond breast feeding norm. The number of additional training sessions the staff provide to mothers adopting the substitute feeding intervention beyond what they would ordinarily receive if breast-feeding. **Data sources:** This estimate should reflect program design, and if the program is operating can verified by interviewing counselors and reviewing records.

D63 – H63. Cost of additional training sessions. This equals the number of training or counseling sessions multiplied by the duration of the training sessions and the hourly wage/benefit rate. No data entry is required.

D64 – H64. Duration of monitoring visits (minutes). Amount of time staff spends monitoring mothers' adherence to substitute feeding, and solving miscellaneous problems arising from their participation in the program. This estimate should include transportation time for the counselor, if any. It should exclude time spent on other health care matters. **Data sources:** Similar to cells **D61 – H61**. This estimate reflects program decisions and, if the program is operating, can be verified with record review and interviews with staff.

D65 – H65. Number of monitoring visits. Average number of monitoring visits per participant over the full time of their participation in the program. Currently the value is set at 6 visits per 12 months, divided by the duration of substitute feeding. **Data sources:** Same as above.

D66 – H66. Cost of monitoring visits. The number of monitoring sessions multiplied by the average duration of monitoring visits. No data entry is required.

D68 – H68. Subtotal for counseling/monitoring. Calculated as the sum of the above costs. This is the cost to the public sector payer of the extra counseling and monitoring required by the substitute feeding intervention. No data entry is required.

D73 – F73. Formula cost per kilogram (including distribution). This is the net cost to the public sector payer of formula purchase (including any discounts obtained), plus added costs for storage, delivery, and distribution. If clients pay a portion of costs, this should be deducted. Since formula cost has a large effect on cost-effectiveness, please include low and high estimates. **Data sources:** For the formula itself: price in local markets, past bulk purchase prices, or promised prices from manufacturers or donor agencies. For other costs, best estimates from other health supply programs (e.g., vaccinations) or, preferably, program experience with formula.

E73. Best estimate. (See explanation in paragraph above).

D73. Low estimate. This could reflect a possible bulk purchasing agreement or other efficiencies of large scale; or perhaps a client contribution option.

F73. High estimate. This might reflect the price if an agreed-upon discount or client contribution falls through, or if distribution costs are higher than expected.

D76 – H78. Infant formula use: 0-6 months. This section calculates the use and total cost of infant formula for each child through age six months. It uses information already provided on the duration of breast feeding and the cost per kilogram of formula. It assumes that the average child consumes 20 kilos of formula in these six months. No data entry is required.

D80 – H82. Infant formula use: 7-12 months. Similar to above. If the program does not provide formula after 6 months, the quantities in row 77 can be set to zero.

D84 – H85. Supplemental food costs -public sector share only. Some programs may provide micronutrient supplements such as vitamins and iron folate; or supplemental food such as cows milk to infants during the weaning period and beyond. If so, the cost of these materials should be entered here. If clients pay a portion of the cost out of pocket, as always, enter only the net cost to the public payer. Estimate this input by multiplying the amount spent for each item for each child by the quantity of each item provided.

D87 – H87. Subtotal: Cost of replacement foods. The cost of infant formula and other supplemental foods. Calculated, so no data entry required.

D88 – H88. TOTAL PROGRAM COSTS, per HIV+ mother who chooses substitute feeding. This is the sum of the costs of infant formula, other supplemental foods, and added counseling and monitoring costs. No data entry is required.

D89 – H89. TOTAL PROGRAM COSTS, per 100 HIV+ mothers who choose substitute feeding. The values in the previous row multiplied by 100. No data entry required.

Table SF - 5: HIV and Non-HIV Medical Costs

Background

Substitute feeding is likely to produce two effects on health costs. The *intended* reduction in HIV transmission generates savings in HIV treatment costs. The *unintended* effect of increased non-HIV disease (both mortality and morbidity) increases medical costs. This table estimates both effects.

Influence on cost-effectiveness: High. These data are important to calculate cost-effectiveness. They help determine the net costs of substitute feeding

Expected effort of data collection: Medium-high. Much data may be available locally (e.g., outpatient and inpatient utilization and costs).

D95 – H96. HIV medical costs averted. Based on the discounted lifetime cost of treating pediatric HIV/AIDS as calculated in the **"Cost of HIV/AIDS"** sheet and the number of HIV cases averted through substitute feeding, this section estimates savings in HIV-related medical costs associated with substitute feeding. No data entry is required.

D99 – H99. Ratio of non-HIV medical costs with substitute feeding program vs. current non-HIV medical costs. This equals the ratio of non-HIV deaths if women observe current feeding practices to non-HIV deaths if women choose the substitute feeding option.

Thus, the model assumes that non-HIV medical costs are proportional to non-HIV mortality. No data entry is required.

D101 – H101. Usual number of outpatient sick visits in 12 months. Be sure to *exclude* well-baby visits and visits due to HIV. Include the net cost to the public sector payor only. **Data sources:** This data may be available from children's health cards, possibly records at a local hospital or clinic, or special studies that may have been done. If not, it can be derived less formally (and less accurately) by interviewing doctors or auxiliary health professionals who treat infants in your area.

D102 – H102. Cost/outpatient visit (including medications; public sector share). This is the unit cost of a sick visit. **Data sources:** This information may be available in documents produced by particular hospitals or by the Ministry of Health. If not, a reasonable estimate can be obtained by multiplying the average time per outpatient visit and multiplying this by the medical staff's compensation rate including benefits. To this should be added the average cost of medications provided net of the patients' share of medication costs.

D103 – H103. Added number of outpatient sick visits due to substitute feeding. This estimate is based on the ratio of non-HIV mortality in the children of women following current feeding versus substitute feeding (**D99 – H99**). The CET applies this ratio to the usual number of outpatient visits (**D101 – H101**). No data entry is required.

D104 – H104. Cost for added outpatient visits. These figures are the product of the added number of outpatient visits multiplied by the average cost per outpatient visit. No data entry is required.

D106 – H106. Usual number of inpatient stays in 12 months. This is number of hospital stays in the first year of life. **Data sources:** Similar to outpatient visits (**Row 101**).

D107 – H107. Cost per inpatient stay (public sector share only). This is the unit cost of a hospital stay. **Data sources:** This may be available from special studies or published reports. Otherwise, you will need to obtain estimates by interviewing hospital administrators and/or examining a sample of medical records.

D108 – H108. Added number of inpatient stays due to substitute feeding. This estimate is done similarly as the estimate for outpatient visits in row 100. No data entry is required.

D109 – H109. Cost for added inpatient stays. These figures are the product of the added number of inpatient stays multiplied by the average cost per inpatient stay. No data is entry required.

D111 – H111. Cost of contraception per woman (public sector share only). Enter the average cost of contraception that may be provided to women as part of the substitute feeding program. We assume $10 as the default value.

D113 – H113. Non-HIV costs added, per 100 HIV+ mothers who chooses substitute feeding. These estimates are totals of the values above. No data entry is required.

D114 – H114. TOTAL NET MED. COSTS, per 100 HIV+ mothers who choose substitute feeding. These figures represent the savings in HIV medical costs minus the increased medical costs due to elevated non-HIV morbidity and mortality. No data entry is required.

Table SF - 6: Summary of Substitute Feeding Cost Outcomes

Background

For ease of reference, this table presents the key financial subtotals calculated elsewhere in the spreadsheet in one area. No data entry is required in this table.

- **D118 – H118. Total Program Costs, per HIV+ mother who chooses substitute feeding.** (**Row 88**)
- **D119 – H119. Total Program Costs, per 100 HIV+ mothers who choose substitute feeding.** (**Row 89**)
- **D120 – H120. HIV medical costs saved per 100 HIV+ mothers who choose substitute feeding.** (**Row 96**)
- **D121 – H121. Non-HIV med. costs added, per 100 HIV+ mothers who choose substitute feeding.** (**Row 113**)
- **D122 – H122. Net med. costs per 100 HIV+ mothers who choose substitute feeding.** The remainder after HIV medical cost savings are deducted from the increased non-HIV medical costs. (**Row 114 = Row 96 - Row 113**)
- **D123 – H123. Net program costs (program costs minus net savings (or costs) in medical care); per 100 HIV+ mothers who choose substitute feeding.** The remainder when medical cost savings are deducted from program costs (**Row 89 + Row 114**).

"Cost of HIV/AIDS" worksheet

This worksheet provides a template for calculating the savings in medical costs for each case of pediatric HIV/AIDs averted by the interventions.

Cost of treating person with HIV/AIDS: Medical cost to the public sector of treating HIV/AIDS related illnesses and conditions from the onset of HIV disease through AIDS and death.

Medical cost to the public sector: Outpatient, inpatient, pharmacy, and home-care costs borne by publicly funded clinics, hospitals, hospices, and other care agencies. Data from non-profit entities such as NGO-funded clinics should also be included, but private, or for-profit entities are not. Also excluded are out-of-pocket costs paid by patients or their families. Among the most common of these out-of-pocket costs are a portion of pharmacy costs, outpatient registration fees, and the cost of certain expendable supplies.

Discounted costs: Future costs are not valued the same as costs occurring in the present. To obtain the net present value of a future stream of costs, the stream of costs must be discounted. (See "Discount rate" on page 19). Most HIV cost studies present the discounted costs in their results.

Table Cost of HIV/AIDS - 1: Summary information

Background

This table provides a template for a "quick and dirty" estimate of HIV/AIDs treatment costs. Studies that thoroughly cost out all the resources needed to care for HIV/AIDS patients are fairly rare. More common are efforts to calculate the quantity of care provided, often at just one health facility. For example, some studies tabulate the number of outpatient visits and the number of hospital days for each HIV/AIDS patient or for each episode of HIV/AIDS illness. You may be able to obtain information from other sources such as reports produced by the Ministry of Health or academic institutions on the average cost per outpatient visit or inpatient day. By multiplying each service unit by the cost per unit one can arrive at a total cost estimate. **Data sources:** Among the few published estimates of the lifetime discounted cost of care for pediatric AIDS are $396 based on estimates from Tanzania and Zaire (Mansergh, 1998); $195 for Tanzania (Pallango and Laing, 1990) and $3,300 for Thailand (Walker, 1997).

A critical issue is correctly identifying public sector costs. Here are examples of the concerns you should be aware of:

1. A study performed in a public hospital may not include the cost of services provided by an NGO or a satellite public clinic before the patient came to the hospital. This would result in an underestimate of real public sector costs.

2. Some percentage of AIDS patients may obtain care from private physicians and clinics. Assuming that all AIDS patients are cared for in the public sector would overestimate the public sector share.

3. Some items that may be counted as public sector costs shouldn't be. For example, drug costs may actually be paid by patients or their families.

4. Registration fees and other charges that generate revenues for the service provider should be deducted from costs in order to arrive at the correct *net* public cost.

It may be worthwhile to speak with the Medical Director or Chief Administrator of the large urban hospitals in your country. He or she may know of HIV/AIDS cost studies or may be able to refer you to someone who does. The Office of AIDS in the MOH may also have compiled some information on resources allocated to HIV/AIDS care. The MOH might also have an expert on the mix of public, private insurance, and out-of-pocket spending for health care.

Another approach is based on the observed correlation between per-case HIV expenditures (both private and public sector) and per-capita GNP. Expenditures vary from between 0.6 times per-capita GNP in Tanzania to 3.0 times per-capita GNP in Sao Paulo (Shepard, 1997). Another survey of five developing countries suggests that the average is about 1.5 times per-capita GNP. (Martin, 1996). Since the expenditure data includes both public and private sector, the final figure would have to be adjusted by an estimate of the portion that public sector expenditures constitute of total public/private expenditures. Because this method depends on broad ratios which may not be very precise for your setting, this method should only be used if others are impractical.

C18. Enter "D" or "S". The left portion of this table is unmasked if you opt to use the summary method of evaluating HIV/AIDS costs. (Enter "S" for "Summary" in cell "Cost of **HIV/AIDS" C18**). If "D" ("Detailed") in cell **"HIV/AIDS" C18** is selected the right portion of the table is unmasked. This right-hand portion of Table Cost of HIV/AIDS-1 shows you the results of the detailed analysis performed in Table Cost of HIV/AIDS-2. Table Cost of HIV/AIDS-2 is only unmasked if you select the more detailed approach to the cost analysis by entering "D" in cell **C18**.

F24. Enter a single best estimate for the discounted lifetime cost of treating a case of pediatric HIV/AIDS.

F27. Cells **E24** and **G24** of Table *Cost of HIV/AIDS-1* provide a low and high range around the best estimate. This range is defined by the percentage you enter in **F27**.

Table Cost of HIV/AIDS - 2: Detailed information

Background

This table provides a data entry template for a more detailed and accurate estimation of HIV/AIDS treatment costs. It is divided into four sections: inpatient costs; outpatient cost; drug costs not already included in inpatient or outpatient costs; and home health care costs. Costs will change with the progression of the child's disease. Due to discounting, the timing of the costs affect the final results. The table therefore requires estimated costs for each year of the child's life, from the time of infection through death. The cost calculation is performed based on the information you provide on the units of service received per year, such as the number of outpatient visits and inpatient days, and the cost per unit. You are then asked to enter a number for the percentage of the cost of those services borne by the public sector health care payer. The product of these figures are then summed to yield the total estimated spending for each type of service. These are summarized and totaled in cells **D84 – D89.** In cells **C84 – C89** and **E84 – E89** you are asked to enter low and high estimates respectively for each of the four types of medical care costs. **Data sources:** The detailed method of calculating HIV/AIDS costs requires primary data from a health facility in your area. The information could be obtained from a combination of chart and interviews with key physicians and administrators.

C33 – E43. Outpatient care. Enter information on the average number of outpatient visits for each year of the child's life; the average cost per outpatient visit and the percent of those costs borne by the public sector health payer.

C45 – F55. Inpatient care. Enter information on the average number of inpatient visits for each year of the child's life; the average number of inpatient days per visit; the average cost per inpatient day; and the percent of those costs borne by the public sector health payer.

C57 – E67. Drugs. Enter information on the average number of prescriptions for each year of the child's life; the average cost per prescription; and the percent of those costs borne by the public sector health payer. Make sure there is no double-counting of drug costs that might be included under inpatient or outpatient care.

C69 – E79. Home health care. Enter information on the average number of days of home health care for each year of the child's life; the average cost per day of care and the percent of those costs borne by the public sector health payer.

C85 – C89 and **E85 – E89.** Enter low and high estimates respectively for each of the four cost components. The defaults are set to 20% above and below the best estimates.

"Results" worksheet

This worksheet contains the detailed results of the analysis. It is divided into three tables and a graph. Each of these components is described here briefly. The first, "Table Results - 1: Health, Cost and Cost-Effectiveness Results" contains four sections:

- Program scale
- Health outcomes
- Cost outcomes
- Cost-effectiveness

No data entry is required in this table.

DEFINITION OF "DALY"

DALY = **D**isability **A**djusted **L**ife **Y**ear

= Number of years of life saved by an intervention weighted by:

(1) Quality of life experienced by the person
(2) Social value of that year of life as a function of age

Advantages of using DALYs rather than "cases averted":

(1) Takes duration of benefit (added life-years) into account
(2) Makes comparisons across programs possible by putting different types of outcomes on the same metric

The second table, "Table Results - 2: Exploring the results" allows the user to specify a cost-effectiveness threshold. This is a cost per DALY or cost per case HIV averted below which an intervention is considered cost-effective. The Table then indicates which intervention is:

- Cost-effective given this threshold
- Cost-saving to the public sector heath payer
- Most cost-effective (or cost-saving)

The third table, "Table Results - 3: Incremental Cost-Effectiveness" allows the user to examine the incremental cost-effectiveness of any two interventions specified. It first determines whether the basic condition for an incremental cost-effectiveness analysis is fulfilled. This condition is that one of the interventions is both more effective and more costly than the other. If so, the CET determines which intervention that is. It then gives the following information on the comparison of the more costly but more effective intervention with the less costly but less effective intervention:

- Incremental fatal events averted through more effective/more expensive program
- Incremental DALYs generated through more effective/more expensive program
- Incremental program cost
- Incremental cost per DALY
- Incremental cost per fatal event averted

Finally, starting in cell **C103** a bar graph is provided which shows the cost effectiveness of each of the five interventions and the incremental cost-effectiveness of the two interventions selected for the incremental cost-effectiveness analysis. For comparison purposes, the left-most bar shows the cost effectiveness threshold set in **D52.**

Table Results - 1: Health, Cost and Cost-Effectiveness Results

Background

This table displays the results of calculations based on information provided elsewhere in the CET that pertain to the overall scale (public health impact), costs and health benefits of the interventions being analyzed. The last two rows of this table, 43 and 44 contain the final cost-effectiveness ratios, the cost per case averted and the cost per DALY generated. For most users, these are probably the most important numbers produced by the CET. No data entry is required in this table.

C11 – H15. Program scale. This section re-caps information entered or calculated in the **"Setting"** sheet and elsewhere in the CET.

D11 – H11. Annual births in service area -- Calculated from information on population and birth rates or fertility rates in **"Setting" C19.**

D12 – H12. Annual births to HIV+ women . Annual births multiplied by the prevalence rate as given in **"Setting" D38.**

D13 – H13. HIV-positive women who receive intended intervention. Derived from data on the number of women who complete VCT and register for the intervention **("VCT" M62)**;

clinic arrival time (**"Setting" C27** through **"Setting" C34);** and the latest gestational age a woman can arrive at the clinic and still receive the intended intervention **("ARV" C13)**.

D14 – H14. HIV-positive women who receive shorter course intervention. Derived from data on the number of women who complete VCT and register for the intervention (**"VCT" C107)**; clinic arrival time (**"Setting" C27** through **"Setting" C34)** and the latest gestational age a woman can arrive at the clinic and still receive a shorter substitute for the intended intervention (**"ARV"**: **C16** and **C19)**.

D15 – H15. HIV+ women who receive no intervention. This is simply the difference between the number of HIV+ women who give births and the number who receive an intervention.

Where are the final cost-effectiveness ratios?

Cost per case averted: "Results": D43 – H43.

Cost per DALY: "Results": D44 – H44.

C18-H27. Health outcomes. This section displays information on the number of fatal events that occur; and that are averted in the service area with no intervention, with ARVs, and with substitute feeding.

D18 – H18. Fatal events (HIV cases and non-HIV deaths) with no intervention. For the HIV-infected pregnant women in this population, the combined number of pediatric HIV cases and non-HIV deaths that would occur in children by age 24 months in the absence of any interventions.

D19 – H19. Fatal events with ARV intervention only. The number of fatal events that would occur if the ARV intervention only were provided.

D20 – H20. Fatal events with ARV and SF interventions. The number of fatal events that would occur if both ARV and substitute feeding intervention (if any) were provided.

D22 – H22. Fatal events averted by ARV component. The number of fatal events with no intervention minus the number of fatal events averted that can be attributed to the ARV intervention only (Row 18 - Row 19).

D23 – H23. Fatal events averted by SF component. The number of fatal events with no intervention minus the number of fatal events averted that can be attributed to the substitute feeding intervention only (Row 20 – Row 22).

D24 – H24. Total fatal events averted. The sum of the fatal events averted by the two types of interventions. Row 27 is shaded in gray to draw attention to it as the most important single summary measure of program benefits

D26 – H26. Percent of all fatal events averted for HIV+ mothers in service area. This is the net reduction in fatal events as a portion of all HIV-infected women who give birth in the service area each year. The denominator includes those women who received no services. This is an important reminder of the difference between cost-effectiveness and public health impact. An intervention can be highly cost-effective for the women that it reaches. However, if only a small portion of women in the service area have access to the program, the benefit to the population in the service area as a whole could be very limited. The value in **"Setting" C22**, namely "Proportion of women who obtain prenatal care in health facilities capable of delivering MTCT interventions" is very important in determining the percent of fatal events averted for HIV+ mothers in the service area.

D27 – H27. DALYs generated by program. This is the total benefit generate by the interventions expressed in DALYs. It is simply the number of fatal events averted multiplied by the number of DALYs per fatal event averted. The number of DALYs per fatal event averted, in turn, is to a significant degree determined by average life expectancy for those who do not suffer a fatal event by 24 months. Life expectancy was entered in cells **"Setting" 47 and 48.**

C30 – H40. Cost outcomes.

D30 – H30. Program cost. Cost of VCT plus ARVs plus Substitute Feeding (Row 31 + Row 32 + R0W 33).

D31 – H31. Cost of VCT (minus portion for horizontal transmission). This is the cost of VCT per HIV+ woman who completes VCT multiplied by the number of women who complete VCT each year. This product is then weighted by the portion of the benefits of VCT that are considered attributable to horizontal (adult-adult) transmission reduction benefits. *This is an important point: If you are concerned with the immediate financial outlays required to support VCT for MTCT you should set **"VCT" C5** equal to 0%. Only if you want to take into account the presumed reduction in costs to the health system from reduced adult HIV infection should **"VCT" C5** assume non-zero values.* (See page 24 for a discussion of the external portion of VCT costs to be entered in **C5**.

D32 – H32. Cost of ARVs. This is the cost of ARVs per mother/child pair multiplied by the number of HIV+ women who complete VCT and receive ARV treatment.

D33 – H33. Cost of substitute feeding. This is the cost of substitute feeding per mother/child pair multiplied by the number of HIV+ women who complete VCT and receive a substitute feeding intervention.

D35 – H35. Net medical cost savings. The savings in pediatric HIV care costs due to both ARVs and substitute feeding , minus the medical cost increase due to a higher incidence of non-HIV mortality associated with substitute feeding (Row 36 + Row 37– Row 38).

D36 – H36. HIV medical cost savings due to ARVs. This is the product of the number of HIV cases averted due to ARVs and the discounted lifetime treatment costs per case.

D37 – H37. HIV medical cost savings due to substitute feeding. This is the product of the number of HIV cases averted due to substitute feeding and the discounted lifetime treatment costs per case.

D38 – H38. Non-HIV medical cost increase due to substitute feeding. Children receiving breast milk substitutes are at an elevated risk for non-HIV morbidity and mortality. The associated increase in medical care expenditures are shown here. As shown in rows 101, 106, and 108 of **"Substitute Feeding"** these expenditures include inpatient stays, outpatient visits and contraception provided to mothers to simulate the amennorhea they would have experienced had they been breast-feeding.

D40 – H40. Net program costs [Prog. cost minus medical costs savings]. This is the difference between program costs including VCT, ARVs and substitute feeding and the net medical costs savings accounting for savings due to ARVs, substitute feeding and increased non-HIV medical costs (Row 30 – Row 35).

D43 – H43. Cost per case averted by program. This is the net program cost divided by the number of fatal events (Row 40 / Row 24). The cost-effectiveness ratio of the most cost-effective of the five interventions appears on the screen in blue text.

D44 – H44. Cost per DALY. This is the net program cost divided by the number of DALYs generated by the intervention (Row 40 / Row 27). The cost-effectiveness ratio of the most cost-effective of the five interventions appears on the screen in blue text.

Cost-effectiveness ratios:
Higher is worse, lower is better, negative is best

- The lower the Cost per DALY or cost per case averted, the better. As cost-effectiveness goes up, the cost per DALY goes down.
- Cost-effectiveness ratios can drop below zero. This signifies that the intervention is not only cost-effective, but cost saving. Based strictly on economic criteria, all such programs should be implemented.
- Apart from signifying cost-savings, negative cost-effectiveness ratios are hard to interpret.

Table Results - 2: Exploring the results

Background

This table allows the user to examine some of the further implications of the analysis beyond the cost-effectiveness ratio itself. Since "cost-effective" is a relative term, any cost-effectiveness analysis contains the implied question, "Cost-effective compared to what?" In general terms, the answer is "compared with alternative uses of available health resources." In most cases we anticipate that the CET will be used to compare various MTCT options with one another. However, it can also be used to determine whether any of the MTCT interventions are cost-effective compared with other possible uses of these health care funds. To do so the user must establish a threshold below which the MTCT interventions can be considered cost-effective. This threshold will vary from setting to setting. In sub-Saharan Africa in general, it is about $50 per DALY (World Bank, 1993) (Jamison, 1993). However, in the wealthier countries of the region such as South Africa, and in wealthier regions of the developing world such as South Asia or Latin America it is likely to be higher than this. This is because, broadly speaking, as countries become wealthier, they tend to implement the most cost-effective health interventions (e.g., immunization and basic antibiotics to treat respiratory infections), at least in those areas that can be served most easily. In addition, greater wealth generally means greater resources devoted to health care. Differences in per-capita income can therefore be used as a rough guide to the cost-effectiveness threshold appropriate in various regions.

D52. Cost-effectiveness threshold. Enter an estimate here representing the cost-effectiveness threshold for your setting in dollars per DALY. In cell **D53,** the CET then calculates the equivalent threshold as the cost per case averted .

D55. Are any of these interventions cost-effective? If any of the interventions have a cost-effectiveness ratio below the threshold given the word "Yes!" appears; if not, "No" appears.

D58 – H59. Which interventions are cost-effective? If an interventions has a cost-effectiveness ratio below the threshold its description appears in this section (e.g., "Thai-CDC and 6 months breast feeding"). If the intervention's cost per DALY exceeds the threshold established in cell **D52** the words "Not CE" appears in its column.

D61 – H61. Cost per DALY. For easy reference, the cost per DALY is repeated here. These are the same values that appear in row 44. Again, the cost-effectiveness ratio of the most cost-effective intervention appears in blue text.

D62 – H62. Is intervention both cost effective and cost saving? An intervention would be cost saving if net program costs are negative. This can occur when estimated savings in medical expenditures exceeds the cost of the intervention. Considering economic criteria only, all such programs should be implemented. Because net costs assume a negative value, the cost-effectiveness ratio of these programs are also negative. However, because a negative cost-effectiveness ratio is difficult to interpret, it is more appropriate to report the amount of cost savings than the negative cost-effectiveness ratio.

D63 – D65. Which intervention is most cost-effective? The description of the most cost-effective intervention is repeated here, whether it is cost saving or not.

Table Results - 3: Incremental Cost-Effectiveness

Background

"Incremental cost-effectiveness" refers to the comparison of costs and benefits of one intervention to another. The analysis so far has compared the costs and benefits of each intervention with no intervention. But another important question is whether it is sensible to move from a less effective but less costly intervention to one which may be more effective but more costly. The question is worth considering because the incremental cost per DALY gained as one moves to the more expensive intervention may be below the cost-effectiveness threshold. If so, this suggests that the more expensive intervention should be adopted even though, compared with no intervention it is less cost-effective than the less costly/less effective alternative.

If one intervention is both more effective and less costly than another, it is said to "dominate" the other. No analysis is needed to see that it would be preferred. For this reason incremental cost-effectiveness analyses are only performed when one intervention is both more effective and more costly than another.

E73 and G73. Select interventions for incremental cost-effectiveness analysis. Enter a number from 1 to 5 in each of these cells. These numbers correspond to the interventions you wish to compare as shown in **D57 – H59**. **E74-E75** and **G64-G75** display the respective interventions that have been selected.

C80 – C83. Error detection. An error message appears if any one of these three conditions is met:

- The same numbers are entered in cells **E73** and **G73.**
- Neither of the interventions selected is both more costly and more effective than the other.
- A number outside the range 1-5 was entered in either **E73** or **G73.**

C85 – C87. More effective but more costly intervention. The intervention that is both more effective and more costly is shown here.

F92 – F96. Results of incremental cost-effectiveness analysis. Each of these four items are displayed here:

- Incremental DALYs generated through more effective and costly program.
- Incremental program cost.
- Incremental cost per DALY.
- Incremental cost per fatal event averted.

The "Incremental cost per DALY" is in large, bold type as this is the key result of the incremental analysis.

C99. Policy implication. This cell provides a message saying whether it is or is not advisable to implement the more effective/more costly intervention (**C85 – C87**) based on whether the incremental cost per DALY falls below or exceeds the cost-effectiveness threshold specified in **D52.**

C102 - I130. Cost Effectiveness and Incremental Cost Effectiveness (if relevant). This bar graph shows the user-entered cost-effectiveness threshold; the cost per DALY for all five interventions; and the incremental cost-effectiveness of the two interventions selected for the incremental analysis. Because many people prefer to look at graphs rather than tables of numbers, this graph may be particularly useful in presenting the results of your analysis to others.

When is it appropriate to perform an "Incremental cost-effectiveness analysis?

Definition of incremental CEA: Comparison of the increased benefits and increased costs of one program versus another

"Sensitivity Analyses (SAs)" worksheet

The purpose of this worksheet is to gauge the effect of uncertainty on the results of the analysis. To make this task manageable we selected only eight inputs to include in the formal sensitivity analyses. Bear in mind that you can perform your own sensitivity analysis on any variable or set of variables that are of interest to you. Simply enter the new value for the variable(s) you wish to explore, and record the cost per DALY or other outcomes as given in the **"Results"** worksheet.

The eight inputs included in the formal sensitivity analyses given in **"SAs"** are shown below.

- ARV drug efficacy
- VCT cost per HIV+ mother
- ARV drug cost
- HIV prevalence
- HIV/AIDS treatment cost
- Infant formula cost
- HIV risk from breast feeding
- Non-HIV infant mortality rate (at 12 months)

The values for all of the inputs used in the sensitivity analyses have been entered elsewhere in the CET. **There are no data entry requirements on this worksheet.**

Sensitivity analysis on what inputs?

The CET provides built-in sensitivity analyses on eight inputs.

You can perform your own sensitivity analysis on any input or set of inputs that are of interest to you. Simply enter the new value for the variable(s) you wish to explore, and record the cost per DALY or other outcomes as given in the **"Results"** worksheet.

Sensitivity Analysis Graphs: Cost per DALY as a function of four key variables

Background

These graphs show the relationship between the value of inputs and cost-effectiveness for four key inputs -- HIV prevalence; ARV drug efficacy; VCT cost per HIV+ mother; and ARV drug cost. The graphs and tables are not recalculated automatically. Each time you change any input value in the CET you must press the "button" in cell **"SAs" I7** in order to update the graphs and tables.

C10. Figure 1a: Sensitivity analysis by ARV efficacy. For each of the five ARV interventions, this graph shows the relationship between cost/DALY and efficacy for relative reductions in transmission (efficacy) ranging from 25% to 70%. Note that no lines appear on this graph if ARV interventions are not being evaluated (**"Interventions" C11** = "No"). Note also that if substitute feeding duration is set to "Optimal" (**"Interventions" C13** = "Optimal") there is a precipitous decline in the cost/DALY as displayed on the graph. This occurs when the optimal breast feeding duration changes by a one month increment as efficacy crosses a critical threshold.

M10. Figure 1b: Sensitivity analysis by VCT cost. For each of the five ARV interventions, this graph shows the relationship between cost/DALY and the cost of VCT per HIV positive woman identified. To see how this figure was derived, go to **"VCT" 028.** *It is important to note that this figure takes into account the portion of VCT costs considered external to MTCT – that is, the portion of the costs that can be "billed" to horizontal (adult-adult) transmission. The value for this parameter is entered in* ***"VCT" C5****.*

C20. Figure 1c: Sensitivity analysis by ARV cost. For each of the five ARV interventions, this graph shows the relationship between cost/DALY and the cost of ARV drugs per woman-infant pair. Because the drug costs for each of the five ARV regimens evaluated in the CET is different, the horizontal scale represents the percentage of the base case cost, rather than an absolute amount. The point corresponding with 100% of the costs is the base case value as shown on row 85 of the **ARVs** spreadsheet. Other values on the horizontal axis represent the percent above or below this value.

M20. Figure 1d: Sensitivity analysis by HIV seroprevalence. For each of the five ARV interventions, this graph shows the relationship between cost/DALY and HIV seroprevalence in pregnant women. The base case seroprevalence was entered in **"Setting" D38.**

Updating sensitivity analysis graphs and tables

Push the button on **I7** to recalculate the sensitivity analysis tables and graphs. They do not update themselves automatically. To show the current results, you must recalculate each time you have changed the value of one or more inputs.

Table SA-1: Uni-Variable Sensitivity Analyses

Background

This table is termed uni-variable (sometimes also called "univariate') to indicate that the effect of changes in only one variable at a time is being considered. For example, in cells **AF16 – AH16** the cost per DALY that corresponds with a high estimate of saved HIV/AIDS medial costs is calculated leaving the value of all other inputs at their base case values. Table SA-2, discussed later in this section explores the effect of changes in the values of several variables at once.

This table consists of four columns:

- Variables and interventions
- Range of input values
- Cost per DALY
- Cost per case averted

X10 – Y59. Variables and interventions. This area is divided into five sections headed by a designation for each of the five interventions under evaluation. These headings appear in cells **X11, X21, X31, X41** and **X51.** Under each intervention designation are eight rows devoted to the eight inputs subject to sensitivity analysis. Column **Y** reminds the user of the direction of the relationship between the input and cost-effectiveness. For example, as HIV prevalence increases cost-effectiveness also increases (all else equal). Bear in mind that the cost per DALY goes down as interventions become more cost effective.

Z10 – AB59. Range of input values. This area shows the value of "Worse cost-effectiveness estimate", "Base case cost-effectiveness estimate" and "Better cost-effectiveness estimate"

for each of the eight input variables. We use the term "Worse" and "Better" rather than "Lower" and "Higher" because lower values do not necessarily correspond with lower cost-effectiveness. For example, lower drug costs mean higher cost-effectiveness (lower cost per DALY). The three values for each input have already been defined elsewhere in the spreadsheet. By placing your cursor on an input cell, one can see the location in the CET from which it was drawn. For example, the base case for "ARV drug costs" for Intervention 1 in cell **AA15** reflects the value in "ARV": **D85**.

AC10 – AE59. Cost per DALY. This area shows the "Worse cost-effectiveness estimate", "Base case cost-effectiveness estimate" and "Better cost-effectiveness estimate" expressed in dollars per DALY that correspond to the "Worse", "Base case" and "Better" estimates for each of the eight input variables.

AF10 – AH59. Cost per case averted. This area is identical in structure to the previous section "Cost per DALY" except that the results are expressed as cost per case averted. The CET uses both forms of the cost-effectiveness outcome so that the user can compare its results with other analyses that may use just one or the other expression. Bear in mind however, that pediatric HIV cases will usually have more DALYs per case averted than adult cases because more expected life-years are saved in the pediatric cases.[4]

Table SA-2: Multi-Variable Sensitivity Analyses

Background

"Multi-variable sensitivity analyses" examine the effects of changes in two or more variables at once. The uni-variable sensitivity analysis table and graphs help the user understand how variations in the estimated value of *one input at a time* can affect the final cost-effectiveness results. But what if the true values of *two or more inputs at a time* depart significantly from their estimated values? In that case the final cost-effectiveness estimate could deviate much further from the true value than would be indicated in the sensitivity analysis of any one variable. This table explores the combined effect of simultaneous "worse" and simultaneous "better" estimates for five key variables. These variables are:

- HIV prevalence
- VCT cost per HIV+ mother
- HIV/AIDS treatment cost

[4] The difference, however, is less than one might expect because the age weights attached to adult life-years are greater than those attached to childhood years. In pediatric cases, the more highly-valued adult years occur several years in the future and are therefore more heavily discounted than the adult years saved in the case of adult HIV cases averted.

- Non-HIV infant mortality rate at 12 months
- Infant formula cost per kg

As in the case of the uni-variable sensitivity analysis (Table SA-1), the range of each input indicated by the values in "Worse CE scenario" through "Base Case Scenario" to "Better CE Scenario" were determined by the user elsewhere in the CET. The difference is that the values in "Cost per DALY" and "Cost per case averted" reflect the cost-effectiveness results obtained if all five variables simultaneously assumed the values shown in "Worse CE scenario", "Base Case Scenario", or "Better CE Scenario".

While very helpful in determining what the extreme outcomes of the analysis could be, this type of multi-variable sensitivity analysis has a severe limitation – it does nothing to inform the user of the likelihood that the "Worse CE" or "Better CE" scenarios will actually occur. In fact the probability of the simultaneous occurrence of extreme values in five variables could be very small. If an intervention's "Worse CE scenario" is still below $50 per DALY (or other cost-effectiveness threshold) one can have a high degree of confidence that the intervention will be cost-effective. On the other hand, if an intervention's "Worse CE scenario" is not cost-effective, one must assess the probability of this scenario actually occurring. One might wish to isolate the inputs that have the greatest influence on the results and re-assess whether the low or high end estimates are in fact plausible for these inputs. The point is not to force any particular result, but rather to explore contingencies that have a reasonable likelihood of occurring.

AL12 – AN16. Range of input values. This area shows the value of "Worse cost-effectiveness scenario", "Base case cost-effectiveness scenario" and "Better cost-effectiveness scenario" for each of the five inputs.

AR12 – AT16. Cost per DALY. This area shows the "Worse cost-effectiveness scenario", "Base case cost-effectiveness scenario" and "Better cost-effectiveness scenario" expressed in dollars per DALY that correspond to the "Worse", "Base case" and "Better" scenarios defined in **AL12 – AN16**.

AU12 – AW16. Cost per case averted. This area is identical in structure to the previous section "Cost per DALY" except that the results are expressed as cost per case averted.

"DALY Calculation" worksheet

The purpose of this worksheet is to calculate the number of DALYs saved per case of HIV averted. It is based on methods of DALY calculation described by Murray (1996), a disease progression scenario described by (Chin, 1989) and (Chin & Sonnenberg, 1991), and a figure for average life expectancy entered by the user in **"Setting" C46 – C48**. A graph showing disability weights as a function of age is displayed starting in cell **J20.** The disease progression scenario can be altered by entering different values in cells **L9 – L18**. However, unless you have good data suggesting pediatric HIV disease progression in your setting is substantially different from what is given here, we suggest that you leave these numbers as they are. In any case, results are fairly insensitive to changes in the disease progression inputs.

Published Studies and Other Resources

This section contains a bibliography of materials that you may wish to refer to in the process of carrying out the cost-effectiveness evaluation. It is organized into sections that correspond with the following worksheet of the CET:

- Setting
- VCT
- ARVs
- Substitute Feeding
- Cost of HIV/AIDs
- Sensitivity Analysis
- DALY calculations

Review articles, which may be particularly helpful appear in **bold** type.

Setting

General background

UNAIDS. Report on the global HIV/AIDS epidemic. Geneva: UNAIDS, December 1997.

World Bank, Confronting AIDS: Public Priorities in a Global Epidemic. New York, N.Y.: Oxford University Press; 1997.

UNAIDS website: http:///www.unaids.org

Demographic and Health Statistics

Coetzee, N. Implementing a MTCT pilot program in Cape Town, Dept of Community Health, University of Cape Town for the Cape Town MTCT Group, 1999. Power Point presentation available from Dr. Nicol Coetzee at email: **nc@anat.uct.ac.za.**

Haub C, Cornelius D. World Population Data Sheet. Washington, DC: Population Reference Bureau; 1998.

Macro International, Central Statistical Office, and Ministry of Health Zambia. Zambia Demographic and Health Survey, 1996. Calverton, Maryland USA: Macro International Inc; 1997. NOTE: Demographic and Health Surveys can be ordered free of charge for a wide range of countries from Macro International, 11785 Beltsville Drive, Suite 300, Calverton, MD 20705, Tel: 301-572-0200; Fax: 301-572-0999

UNICEF. 1998. The State of the World's Children. Oxford University Press: New York, 1998.

U.S. Bureau of the Census, 1998. *Recent HIV Seroprevalence Levels by Country: July 1998.* Washington, DC: Health Studies Branch, International Programs Center, Population Division, U.S. Bureau of the Census, Research Note No. 25, July 1998.

U.S. Bureau of the Census. HIV/AIDS Surveillance Data Base. NOTE: This HIV prevalence database is available for download from: www.census.gov/ipc/www/hivaidsn.html. It is also available on CD-ROM by inquiry at ipc-hiv@census.gov

Voluntary Counseling and Testing (VCT)

Organization, Cost and Cost-Effectiveness

Aisu T, Raviglione, MC, van Praag E, Eriki P, Narain JP, Barugahare L, et al. Preventive chemotherapy for HIV-associated tuberculosis in Uganda: an operational assessment at a voluntary counselling and testing centre. *AIDS* 1995. 9(3): 267-73.

Alwano-Edyegu M, Marum E. Knowledge is Power: Voluntary HIV counselling and testing in Uganda. Geneva :UNAIDS; 1999.

Creese A, Parker D. editors, *Cost analysis in primary health care*, 1994, Geneva: World Health Organization. NOTE: This is a general guide to the costing of primary health services. it does not focus on VCT.

Kumaranayake L, Pepperall J, Goodman H, Mills, A. Costing Guidelines for HIV/AIDS Prevention Strategies" A companion volume to "Cost Analysis in Primary Health Care: A Training Manual for Programme Managers," Health Economics and Financing Programme, London School of Hygiene & Tropical Medicine. *World Health Organization*, 1998. Download: http://www.unaids.org/unaids/document/economics/costguid

Lovvorn, AE, SC Quinn, DH Jolly. 1997. HIV testing of pregnant women: a policy analysis. J Public Health Policy 1997;18(4):401-32.

McKenna, SL, GK Muyinda, D Roth, M Mwali, N Ng'andu, A Myrick, C Luo, FH Priddy, VM Hall, AA von Lieven, JR Sabatino, K Mark, SA Allen. 1997. Rapid HIV testing and counseling for voluntary testing centers in Africa. *AIDS;* 1997 Sep; 11 Suppl 1:S103-10.

Minkoff, H, MJ O'Sullivan. 1998. The Case for Rapid HIV Testing During Labor. *JAMA*; 279(21):1743.

Phillips KA, Lowe RA, Kahn JG, et al. The cost-effectiveness of HIV testing of physicians and dentists in the United States. JAMA 271:851-858, 1994.

Sweat, M, D Balmer, G Sangiwa. 1998. Cost to clients and willingness to pay for HIV counseling and testing in Kenya and Tanzania: Results from the voluntary HIV counseling and testing study. *Int Conf AIDS*. 1998;12:467-8 (abstract no. 24135).

Wilkinson D, Wilkinson NF, Lombard C, Martin D, Smith A, Floyd K, Ballard R. On-site HIV testing in resource-poor settings: is one rapid test enough? *AIDS* 1997; **11**: 377-381.

Acceptability

Cartoux, M, N Meda, P Van de Perre, M L Newell, I de Vincenzi, F Dabis, and the Ghent International Working Group on Mother-to-Child Transmission of HIV. 1998. Acceptability of voluntary HIV testing by pregnant women in developing countries: an international survey. *AIDS* 1998, 12:2489-2493.

Cartoux, M, P Msellati, N Meda, C Welffens-Ekra, L Mandelbrot, V Leroy, P Van de Perre and F Dabis for the DITRAME Study Group (ANRS 049 Clinical Trial). 1998. Attitude of pregnant women towards HIV testing in Abidjan, Cote d'Ivoire and Bobo-Dioulasso, Burkina Faso. *AIDS* 1998, 12:2337-2344.

Carusi, D, LA Learman, SF Posner. 1998. HIV Test Refusal in Pregnancy. *Obstet Gynecol* 1998; 91:540-545.

Kiarie, J, R Nduati, G John, C Gakuru, J Musia, J Bwayo, K Rogo, K Kamau, J Kreiss. 1996. Acceptability of antenatal HIV-1 screening. *Int Conf AIDS* 1996 Jul 7-12; 11(1):32 (abstract no. Mo.C.211).

Killewo, JZ, G Kwesigabo, C Comoro, J Lugalla, FS Mhalu, G Biberfeld, S Wall, A Sandstrom. 1998. Acceptability of voluntary HIV testing with counselling in a rural village in Kagera, Tanzania. *AIDS Care* 1998 Aug; 10(4):431-9.

Ladner, J, V Leroy, P Msellati, M Nyiraziraje, A De Clercq, P Van de Perre and F Dabis for the Pregnancy and HIV Study Group (EGE). 1996. A cohort study of factors associated with failure to return for HIV post-test counselling in pregnant women: Kigali, Rwanda, 1992-93. *AIDS* 1996, 10:69-75.

Ramon, R, G La Ruche, F Sylla-Koko, A Boka-Yao, D Bonard, IM Coulibaly, C Welffens-Ekra, F Dabis. 1998. HIV counseling and testing: behavior and practices of women of childbearing age in Abidjan, Cote d'Ivoire. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998 Apr 15;17(5)470-6.

Estimating horizontal transmission benefits

Allen S, Tice J, Van de Perre P, Serufilira A, HUD's E, Nsengumuremyi F, et al. Effect of serotesting with counselling on condom use and seroconversion among HIV discordant couples in Africa. *BMJ* 1992; 304(6842):1605-9.

Allen, S, A Serufilira, J Bogaerts, P Van de Perre, F Nsengumuremyi, C Lindan, M Carael, W Wolf, T Coates, S Hulley. 1992. Confidential HIV testing and condom promotion in Africa. Impact on HIV and gonorrhea rates. *JAMA* 1992 Dec 16; 268(23):3338-43.

Bentley ME, Spratt K, Shepherd K, Gangakhedkar RR, Thilikavathi S, Bollinger RC, Mehendale SM. HIV testing and counseling among men attending sexually transmitted disease clinics in Pune, India: changes in condom use and sexual behavior over time. *AIDS*, 1998. 12(14):1869-77.

De Zoysa I, Phillips K A, Kamenga MC, O. Reilly KR, Sweat M D, White RA, Grinstead OA, Coates T J. Role of HIV counseling and testing in changing risk behavior in developing countries. *AIDS*, 1995; (9 Suppl A): S95-101.

Heyward, WL, VL Batter, M Malulu, N Mbuyi, L Mbu, ME St Louis, M Kamenga, RW Ryder. 1993. Impact of HIV counseling and testing among child-bearing women in Kinshasa, Zaire. *AIDS* 1993 Dec; 7(12):1633-7.

Higgins, DL, C Galavotti, KR O'Reilly, DJ Schnell, M Moore, DL Rugg, R Johnson. 1991. Evidence for the Effects of HIV Antibody Counseling and Testing on Risk Behaviors. *JAMA*; 266(17):2419-2429.

Kamenga M, Ryder RW, Jingo M, Mbuyi N, Mbu L, Behets M. et al. Evidence of marked sexual behavior change associated with low HIV-1 seroconversion in 149 married couples with discordant HIV-1 serostatus: experience at an HIV counselling center in Zaire. *AIDS* 1991; 5(1): 61-7.

Pickering, H, M Quigley, J Pepin, J Todd, A Wilkins. 1993. The effects of post-test counselling on condom use among prostitutes in The Gambia. *AIDS* 1993; 7(2):271-3.

Sweat M, Sangiwa G, Balmer D. HIV counseling and testing in Tanzania and Kenya is cost-effective: results from the voluntary HIV counseling and testing study. *Int Conf AIDS*. 1998: 12:648 (abstract no. 580/33277).

Temmerman, M, S Moses, D Kiragu, S Fusallah, IA Wamola, P Piot. 1990. Impact of single session post-partum counselling of HIV infected women on their subsequent reproductive behaviour. *AIDS Care* 1990; 2(3):247-52.

Wolitski, RJ, RJ MacGowan, DL Higgins, and CM Jorgensen. 1997. The Effects of HIV Counseling and Testing on Risk-Related Practices and Help-Seeking Behavior. *AIDS Educ and Prev* 1997; 9 (suppl B):52-67.

ARVs

Clinical trials and HIV transmission rates

Centers for Disease Control and Prevention. 1998. Administration of zidovudine during late pregnancy to prevent perinatal HIV transmission – Thailand 1996-98. *Morb Mortal Wkly Rep.* 1998;47:151-153.

Connor EM, Sperling RS, Gelber R, *et al.* Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Paediatric AIDS Clinical Trials Group Protocol 076 Study Group. *New Engl J Med* 1994; **331**: 1173-80.

Dabis F, Msellati P, Meda N, Welffens-Ekra C, You B, Olivier M et al. 6-month efficacy, tolerance, and acceptability of a short regimen of oral zidovidine to reduce vertical transmission of HIV in breastfed children in Cote d'Ivoire and Burkino Faso: a double-blind placebo-controlled multicentre trial. *The Lancet* 1999;353:786-792.

Dabis F, Msellati P, Dunn D, et al. Estimating the rate of mother-to-child transmission of HIV. Report of a workshop on methodological issues Ghent (Belgium), 17-120 February 1992. *AIDS*. 1993;7:1139-1148.

Guay LA, Musoke, P, Fleming T, Bagenda, D, Allen M, Nakabiito C, Sherman J, Bakaki P, Ducar C, Deseyve, M, Emel L, Mirochnick M, Fowler MG, Mofenson L, Miotti P, Dransfield K, Bray D, Mmiro F, Jackson JB. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prevention of mother-to-child transmission of HIV-1 in Kampala, Uganda. *The Lancet*, 1999; 354 (9181):795-802.

Shaffer N, Chuachoowong R, Mock PA, Bhadrakom C, Siriwasin W, Young NL et al. Short-course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. *Lancet* 1999;353:773-780.

Wiktor SZ, Ekpini E, Karon JM, Nkengasong J, Maurice C, Severin ST et al. Short-course oral zidovudine for prevention of mother-to-child transmission of HIV-1 in Abidjan, Cote d'Ivoire: a randomised trial. *Lancet* 1999;353:781-785.

The Working Group on mother-to-child transmission of HIV. Rates of mother-to-child transmission of HIV-1 in Africa, America, and Europe: results from 13 perinatal studies. *J AIDS Hum Retrovirology* 1995; 8: 506-10.

Economic appraisal

Kinghorn AW. Projections of the costs of anti-retroviral interventions to reduce mother-to-child transmission of HIV in the South African Public Sector. Johannesburg: HIV Management Services Technical Report, 1998.

Lutter C. Mother-to-Child Transmission of HIV in the Dominican Republic: Estimated Population Attributable Risk and Cost of the Integrated Preventive Package. Washington, D.C.: PAHO; 1998.

Mansergh G, Haddix AC, Steketee RW, Nieburg PI, Hu DJ, Simonds RJ et al. Cost-effectiveness of short-course zidovudine to prevent perinatal HIV type 1 infection in a sub-saharan African developing country setting. *JAMA* 1996;276:139-145.

Mansergh G, Haddix AC, Steketee RW, Simonds RJ. Cost-effectiveness of zidovudine to prevent mother-to-child transmission of HIV in sub-Saharan Africa. *JAMA* 1998; **280**; 30-31.

Marseille E, Kahn JG, Saba J. Cost-effectiveness of anti-retroviral drug therapy to reduce mother-to-child HIV transmission in sub-Saharan Africa. *AIDS* 1998; 12: 939-948.

Marseille E, Kahn JG, Mmiro F, Guay L, Musoke P, Fowler MG, Jackson JB. Cost effectiveness of single-dose nevirapine regimen for mothers and babies to decrease vertical HIV-1 transmission in sub-Saharan Africa, in *The Lancet*, 1999; 354 (9191) 803-809.

Mauskopf, JA, JE Paul, DS Wichman, AD White, HH Tilson. 1996. Economic Impact of Treatment of HIV-Positive Pregnant Women and Their Newborns with Zidovidine. *JAMA* 1996;276:132-138.

Newell, M-L, F Dabis, K Tolley, D Whynes for the Ghent International Working Group on Mother-to-Child Transmission of HIV. 1998. Cost-effectiveness and cost-benefit in the prevention of mother-to-child transmission of HIV in developing countries. *AIDS* 1998, 12:1571-1580.

Ratcliffe J, Ades AE, Gibb D, Sculpher MJ, Briggs AH. Prevention of mother to-child transmission of HIV-1 infection: alternative strategies and their cost-effectiveness. *AIDS* 1998;12:1381-1388.

Soderlund, N., et al., Prevention of vertical transmission of HIV: analysis of cost effectiveness of options available in South Africa. *BMJ*, 1999. 318(7199): p. 1650-6.

Wilkinson D, Floyd K, Gilks CF. Antiretroviral drugs as a public health intervention for pregnant HIV-infected women in rural South Africa: an issue of cost-effectiveness and capacity. *AIDS* 1998 (in press).

Implementation issues

Thaineua, V, P Sirinirand, A Tanbanjong, M Lallemant, A Soucat, and J-L Lamboray. 1998. From efficacy to effectiveness: routine prevention of mother-to-child HIV transmission by a short course of zidovudine in Northern Thailand. South East Asian J of Trop Med and Pub Health. September 1998. NOTE: This study contains data on adherence to regimen.

UNAIDS 1998b. Mother-to-child transmission of HIV. UNAIDS Technical update. UNAIDS Best Practice Collection, October 1998.

UNAIDS. 1998. Prevention of HIV Transmission from Mother-to-Child: Meeting on Planning for Programme Implementation (Meeting Statement, Geneva, 23-24 March 1998). http://www.unaids.org/highband/document/statement/mtcstat.html.

UNAIDS. Prevention of HIV transmission from mother to child. Planning for programme implementation. Geneva: UNAIDS, 1998.

UNAIDS and Wold Health Organization. Guidance Modules on Antiretroviral Treatments – Module 2. Introducing Antiretroviral Treatments into Health Systems: Economic Considerations. Geneva: UNAIDS & WHO, 1998.

UNAIDS and Wold Health Organization. Guidance Modules on Anti-retroviral Treatments – Module 6. The Use of Antiretroviral drugs to Reduce Mother to Child Transmission of HIV. Geneva: UNAIDS & WHO, 1998

World Health Organization. 1998. Recommendations on the safe and effective use of short-course ZDV for prevention of mother-to-child transmission of HIV. *Weekly Epidemiological Record* 1998, 73, 313-320.

Acceptance of ARVs

Seals, BF, M Hennessey, R Sowell. 1996. Factors influencing acceptance and adherence to zidovudine treatment to prevent vertical transmission of HIV. *Int Conf AIDS*. 1996 Jul 7-12;11(1):368(abstract no. Tu.C.2594).

Substitute Feeding

General

Cunningham AS, Jeliffe DB, Patrice Jeliffe EF. Breast-feeding and health in the 1980s: A global epidemiologic review. *J Pediatr* 1991;118:659-66.

Heymann, SJ. 1995. HIV Transmission Through Breastfeeding: Perspectives on Prevention. In Harvard AIDS Institute, International Symposium on Pediatric AIDS in Thailand: A Public Health and Social Dilemma. Cambridge, MA: Harvard AIDS Institute, 1995.

UNAIDS/UNICEF/WHO. HIV and Infant Feeding: A Review of HIV Transmission through Breastfeeding, 1998; WHO/FRH/NUT/CHD/98.3.

Economic appraisal

Soderlund, N, GE Gray, KJ Zwi. 1998. Breast or bottle? A cost-effectiveness evaluation of formula feeding for the prevention of postnatal transmission of HIV in an urban South African setting. *Int Conf AIDS* 1998;12:465(abstract no. 316/24124).

Magnitude and timing of vertical transmission

Becquart P, Garin B, Sepou A, et al. High incidence of early postnatal transmission of human immunodeficiency virus type 1 in Bangui, Central African Republic. *J Infec Dis.* 1998:177:1770-1771.

Bertolli J, St Louis ME, Simonds RJ, Nieburg P, Kamenga M, Brown C. et al. Estimating the timing of mother-to-child transmission of human immunodeficiency virus in a breastfeeding population in Kinshasa, Zaire. *J Infect Dis* 1996;174:722-726.

Bobat, R, D Moodley, A Coutsoudis, H Coovadia. 1997. Breastfeeding by HIV-1-infected women and outcome in their infants: a cohort study from Durban, South Africa. *AIDS* 1997; 11(13):1627-33.

Bultery, M, A Chao, A Dushimimana, and A Saah. 1995. HIV-1 seroconversion after 20 months of age in a cohort of breastfed children born to HIV-1-infected women in Rwanda. *AIDS* 1995: 93-94.

Dunn DT, Newell ML, Ades, A, Peckham C. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. Lancet, 1992. 340: p. 585-588.

Gray GE, McIntyre JA, Lyons SF. The effect of breastfeeding on vertical transmission of HIV-1 in Soweto, South Africa. *Int Conf AIDS*. 1996 Jul 7-12;11(2):237 (abstract no. Th.C.415).

Kreiss J. Breast-feeding and vertical transmission of HIV-1. *Acta Paediatrica Suppl* 1997; 421: 113-7.

Leroy V, Newell ML, Dabis F, Peckham C, Van de Perre P, Bulterys M, et al., International multicentre pooled analysis of late postnatal mother-to-child transmission of HIV-1 infection. *The Lancet* 1998; 352:597-600.

Mofenson LM. Interaction between timing of potential human immunodeficiency virus infection and the design of preventive and therapeutic interventions. *Acta Paediatr Suppl* 1997; 421:1-9.

Nicoll A, Newell ML, Von Praag E, Van de Perre P, Peckham C. Infant feeding policy and practice in the presence of HIV-1 infection. *AIDS* 1995; 9:107-119.

Nieburg, P, DJ Hu, S Moses, and N Nagelkerke. 1995. Contribution of breastfeeding to the reported variation in rates of mother-to-child HIV transmission. AIDS 1995:396-7.

Tess BH, Rodrigues LC, Newell ML, Dunn DT, Lago TD. Infant feeding and risk of mother-to-child transmission of HIV in Sao Paulo State, Brazil. Sao Paulo Collaborative Study for Vertical Transmission of HIV-1. J *Acquir Immune Defic Syndr Hum Retrovirol* 1998;19:189-194.

HIV and Non-HIV mortality

Del Fante P, Jenniskens F, Lush L, et al. HIV, breast-feeding and under-5 mortality: modelling the impact of policy decisions for or against breast-feeding. *J Trop Med Hyg.* 1993;96:203-211.

Feachem, RG, MA Koblinsky. 1984. Interventions for the control of diarrhoeal diseases among young children: promotion of breastfeeding. Bull WHO 1984, 62:271-91.

Gray, GE, JA McIntyre, SF Lyons. 1996. The effect of breastfeeding on vertical transmission of HIV-1 in Soweto, South Africa. *Int Conf AIDS*. 1996 Jul7-12;11(2):237 (abstract no. Th.C.415).

Habicht, J-P, J DaVanzo, WP Butz. 1986. Does breastfeeding really save lives, or are apparent benefits due to biases? *Am J Epidemiol* 1986, 123:279-90.

Hobcraft, JN, JW McDonald, SO Rutstein. 1985. Demographic determinants of infant and early child mortality: a comparative analysis. *Popul Stud* 1985, 39:363-385.

Hu DJ, Heyward WL, Byers RH, et al. HIV infection and breast-feeding: policy implications through a decision analysis model. *AIDS*. 1992;6:1505-1513.

Jason JM, Nieburg P, Marks JS. Mortality and infectious disease associated with infant-feeding practices in developing countries. *Pediatrics*. 1984; Supplement Task Force on Infant-Feeding Practicesî:702-727.

Kahn, J., E. Marseille, and J. Saba, Feeding Strategies of HIV-Infected Mothers: Modeling the Trade-Off Between HIV Infection and non-HIV Mortality, in *Quantitative Analysis of HIV Policy*, B.R. Kaplan E , Editor. 1999, Yale Press: New Haven.

Kennedy KI, Fortney JA, Bonhomme MG, Potts M, Lamptey P, Carswell W. Do the benefits of breastfeeding outweigh the risk of postnatal transmission of HIV via breast milk? *Trop Doc*. 1990;20:25-29.

Kreiss, J. 1997. Breastfeeding and vertical transmission of HIV-1. *Acta Paediatr* Suppl 1997 Jun; 421:113-7.

Kuhn, L. and Z. Stein. 1997. Infant survival, HIV infection, and feeding alternatives in less-developed countries. *Am J Public Health* 1997, 87:926-931.

Lederman SA. Estimating infant mortality from human immunodeficiency virus and other causes in breast-feeding and bottle-feeding populations. *Pediatrics.* 1992;89:290-296.

Nadelkerke NJ, Moses S, Embree JE, Jenniskens F, Plummer F. The duration of breastfeeding by HIV-1-infected mothers in developing countries: balancing benefits and risks. *JAIDS*. 1995;8:176-181.

Preble E, Piwoz EG. HIV and Infant Feeding: A Chronology of Research and Policy Advances and their Implications for Programs. The LINKAGES Project, 1998.

Tess BH, Rodrigues LC, Newell ML, et al. Infant feeding and risk of mother-to-child transmission of HIV-1 in Sao Paulo State, Brazil. *JAIDS*. 1998;19:189-194.

Victora, CG, PG Smith, JP Vaughan, et al. 1987. Evidence for protection by breast-feeding against infant diseases in Brazil. *The Lancet* 1987, ii:319-22.

Feeding patterns

Chimere-Dan O. Household Survey 1994, Transkei, Eastern Cape Province. Transkei Department of Welfare and Pensions, Central Statistical Service, Department of Health, and Population Centre Wits University. 1996.

Macro International, Central Statistical Office, and Ministry of Health Zambia. Zambia Demographic and Health Survey, 1996. Calverton, Maryland USA: Macro International Inc; 1997. NOTE: Demographic and Health Surveys can be ordered free of charge for a wide range of

countries from Macro International, 11785 Beltsville Drive, Suite 300, Calverton, MD 20705, Tel: 301-572-0200; Fax: 301-572-0999

Nicoll, A, M-L Newell, E Van Praag, P Van de Perre, and C Peckham. 1995. Infant feeding policy and practice in the presence of HIV-1 infection. *AIDS* 1995, 9:107-19.

Population Reference Bureau. Breastfeeding patterns in the developing world. Washington DC., 1999 Website : www.prb.org. email: popref@prb.org

Ross SM, van Middelkoop A, Khoza NC. Breast feeding practices in a black community. *S Afr Med J* 1983;63:23-25.

Cost of HIV/AIDS

Davachi F. et al, The economic impact on families of children with AIDS in Kinshasa, Zaire, *The Global Impact of AIDS*, Alan Fleming et al Editors, 1988, pp. 167-169.

Martin A. The cost of HIV/AIDS care. In: Mann J, Tarantola D, eds. *AIDS in the World II*. Cambridge, Massachusetts: Harvard University Press, 1996.

Over, M, S Bertozzi, J Chin, et al. 1988. The direct and indirect cost of HIV infection in developing countries: the cases of Zaire and Tanzania. In: Fleming, AF, Carballo M, FitzSimons DW, et al., eds. *Global Impact of AIDS.* New York, NY: Alan R Liss Inc; 1988:123-135.

Pallango K and Laing R. 1990. Background study on alternative approaches to managing the opportunistic illnesses of HIV-infected persons: costs and burdens on the Tanzanian health care system. Prepared for World Bank Tanzania AIDS Assessment and Planning Study.

Sculpher MJ, Gibb D, Ades AE, Ratcliffe J, Duong T. Modelling the costs of paediatric HIV infection and AIDS: comparison of infected children born to screened and unscreened mothers. *AIDS* 1998;12:1371-1380.

Shepard DS. *Expenditures on HIV/AIDS: Levels and Determinants: Lessons from Five Countries.* Presented at AIDS and Development: the Role of Government, sponsored by the World Bank, the European Commission and the Joint United Nations Programme on HIV/AIDS, 17-19 June 1997, Lemelette, Belgium.

Söderlund, N. Likely costs of hospital care benefits to be covered by a Social Health Insurance fund - a report to the National Department of Health. Johannesburg: Centre for Health Policy, 1997.

Söderlund, N. and Peprah, E. An essential hospital package for South Africa - selection criteria, costs and affordability - Monograph no 52. Johannesburg: Centre for Health Policy, 1998.

Sensitivity Analysis

Briggs, A. and Sculpher, M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics*, 1998;13:397-409.

Gold, M., *Cost-Effectiveness in Health and Medicine*, ed. S.J. Gold M, Russell LB, Weinstein MC. 1996, New York: Oxford University Press. NOTE: Excellent general reference on cost-effectiveness analysis methods

DALY Calculations

Chin J. The Epidemiology and projected mortality of AIDS, In Feachem RG, Jamison DT, editors. *Disease and Mortality in Sub-Saharan Africa.* Washington D.C.: Oxford University Press; 1989

Chin J, Sonnenberg F. The Epidemiology and Projected Mortality of AIDS in the Republic of Tanzania. Washington, D.C.: World Bank; 1991.

Jamison, D. T., et al. (1993) *Disease Control Priorities in Developing Countries*, Oxford University Press, New York

Murray, C. and Lopez, A. (Eds.) (1996) *The Global Burden of Disease*, Harvard University Press, Cambridge, Mass.

Murray CLJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years, *Bulletin of the World Health Organization*, 1994, 72(3):429-445.

Owens, D. K., Cardinalli, A. B., et al. (1997) Physicians' assessments of the utility of health states associated with human immunodeficiency virus (HIV) and hepatitis B virus (HBV) infection. *Quality of Life Research*, 6, 77-86.

Pliner, Vadim, J. Weedon and P. Thomas. 1006. “Estimation of Long-Term Survival to AIDS in Perinatally Infected Children.” *11th International Conference on AIDS*, abstract no. We.C.3473.

World Bank. *World Development Report 1993 – Investing in Health.* New York: Oxford University Press, 1993.

Appendix A: Data inputs documentation table

NOTE TO FIELD TESTERS: THIS IS A PROPOSED FORMAT FOR A TABLE TO ASSIST WITH DOCUMENTATION. IT HAS A COUPLE OF HYPOTHETICAL EXAMPLES IN THE "METHODS AND SOURCES" COLUMN. THE TABLE IS NOT COMPLETE PENDING YOUR COMMENTS ON IT. DI YOU THINK IT IS USEFUL AS IS? SUGGESTIONS FOR REVISIONS?

Cell	Input	Base case estimate (and range if relevant)	Methods and sources
Setting			
C11, C12, C14, C15, C17	Annual births in service area		
C22	Proportion of women who obtain prenatal care in health facilities capable of delivering MTCT interventions		
C27 – C34	Percent arriving at clinic in each gestational age interval		Project intake logs: March 1 – April 15, 1999; and August 18 – October 1, 1999
C38 – E38	HIV prevalence in pregnant women attending antenatal care clinics.		HIV prevalence from 1996 multi-site urban perinatal clinic study, from Mrs. Rebtusi in health ministry
C41	Rate of mother-to-child transmission (perinatal)		
C44	Discount rate		Discount rate of 5% requested by Health Minister 7/8/00 to be consistent with govt policy. Will do analysis with both 5% and 3%.
C47 – C48	Life expectancy		
VCT			
C5	"External" cost of VCT		
C35	Percent of women registering for VCT who know they are HIV+ from earlier test		
C36	False positive rate of initial test, (e.g., ELISA)		
C37	False positive rate of confirmatory test, (e.g.,		

	Western Blot)	
C40	Wages: Clerical	
C41	Wages: Counselors	Counselor wages determined from prenatal clinic manager.
C42	Wages: Lab technicians	
C45	Cost of test kit for initial test (e.g., ELISA or PCR)	ELISA cost from purchasing logs 5/2/00 purchase
C46	Cost of test kit for confirmatory test (e.g., ELISA, Western Blot, PCR)	
C47	Cost of one blood draw tube	
C48	Average cost of ancillary services per woman who receives them, including services for accompanying male partners	
C51	Average registration or other fee collected for each client who registers?	
C52	Other client income (per client who registers)	
C55	Does this program provide initial screening to identify high-risk women?	
C58	Percent who decline initial high-risk screening and therefore drop out of VCT cohort	
C59	Minutes required for high-risk screening per woman	
C60	Percent of women screened who are considered high risk (therefore eligible for VCT)	
C61	Percent of women not	

	considered high risk who were in fact HIV+ (HIV prevalence in women screened out)	
C64	Percent of those known to be HIV-infected who decline to register	
C65	Percent of those of unknown HIV status who decline to register for VCT	
C66	Minutes required to register each woman of known HIV+ status for MTCT	
C67	Minutes required to register each woman of unknown HIV status for VCT	
C70	Percent of clients (including family members) registered for VCT who receive ancillary services (e.g., meals, transport)	
C73	Percent registered for VCT but who **do not accept** pre-test counseling	
C64	Number of women who receive pre-test counseling in one session	
C75	Minutes required for pre-test counseling session	
C76	Percent of women who completed pre-test counseling but **do not accept** blood draw for initial test	
C77	Minutes required for blood draw	
C78	Number of initial tests processed in a batch	

C79	Number of minutes of lab technicians' time for each batch of initial tests.	
	Does this program provide confirmatory tests for those who test positive on the initial test?	
	Percent of women who test positive on initial test **who do not take** the confirmatory test	
	Number of confirmatory tests processed in a batch	
	Number of minutes of lab technicians' time for each batch of confirmatory tests.	
	Number of women HIV- women who receive post-test counseling at a time (in one session)	
	Minutes required for post-test counseling session for HIV- women	
	Number of women HIV+ women who receive post-test counseling at a time (in one session)	
	Minutes required for post-test counseling session for HIV+ women	
	Percent of women of previously unknown HIV status who completed post-test counseling who do NOT register for MTCT intervention	

	Percent of women of previously known HIV-positive status who completed post-test counseling but who do NOT register for MTCT intervention	
	Total supplies: Low-high estimates	
	Total personnel: Low-high estimates	
C117 – C137	Fixed costs (excluding capital costs)	
D143 F143	Fixed costs: Low-high estimates	