The CEPAC-Pediatric Model User's Guide

(United States and International)

Updated January 8, 2014

Senior Programmer: Taige Hou

CEPAC-Pediatric Model: User's Guide

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A. Introduction

The Cost Effectiveness of Preventing AIDS Complications (CEPAC)-Pediatric model is a computer-based, state-transition, Monte Carlo simulation model of the progression and outcomes of HIV disease. Disease progression of each simulated patient is characterized by a sequence of monthly transitions from one logical "health state" to another. Important determinants of a patient's state at any given point in time include age, gender, current and past CD4% or absolute CD4 count, current HIV RNA (HIV viral load, abbreviated HVL) levels, history of opportunistic infections (OIs), and currently administered therapies (including both OI prophylaxes and ART).

In the Monte Carlo approach to simulation, solutions are approximated by repeated statistical sampling from probability distribution functions. In contrast, a more conventional approach to numerical solution may involve solving a system of closed form equations describing the problem. Multiple experiments (or "trials") are done, and observations are averaged to arrive at an expected solution.

The CEPAC team has developed an AIDS treatment model for adults, as well as several other models of HIV testing and HIV transmission. Full details of the adult model can be found in the CEPAC-International Model User's guide, available at: http://web2.research.partners.org/cepac/model.html. The current document focuses on the CEPAC-Pediatric model, describing elements that are shared between the CEPAC-Adult and CEPAC-Pediatric models, as well as those specific to the CEPAC-Pediatric model (Section C.7).

A1. Major Changes in CEPAC Models over Time

In the early years of the CEPAC-Adult program, there were two executable versions representing two different CEPAC models: one tailored for the U.S. (and other developed countries like France) and one focused to less developed countries (initially referred to as the LDC model, or at times the Africa model or the GAP model, but now called CEPAC-International model). With version 3.0 of the CEPAC program, these two versions have been merged into a single model, based primarily on the LDC model.

The key changes in version 3.0 of the program from the prior U.S. version included:

1. Elimination of the post-acute OI state – After an acute OI, patients had transitioned to a post-acute state, which implicitly incorporated maintenance therapy of the OI(s) and increased resource utilization. In version 3.0, secondary prophylaxes are explicitly specified for those patients with a history of OI(s).
2. Explicit modeling of clinic visits – Version 3.0 of the program makes explicit the notion that patients must make clinic visits to receive care. At a clinic visit, disease progression is monitored and treatment is administered as specified.
3. Allow increased heterogeneity of patients in cohort – New patient variables have been introduced, including parameters to specify patterns of clinic visits and propensity to initiate prophylaxis, ART, or no treatment at all.
4. Revamped ART regimen efficacy mechanism – At the initiation of an ART regimen, patients are now assigned to one of two predestined states: virologic suppression and failure. After an initial regimen-specific time period, suppressed patients incur a monthly probability of transitioning to the failure state. Each of the two states induces different immunologic and virologic responses in patients.

Version 4 of the model was a complete rewrite of the CEPAC adult model. All major functionality was maintained and there were no changes to the inputs and outputs of the model. The key changes that occurred in this rewrite were:

1. Object oriented C++ design – The code base was rewritten in C++ with a modular, object oriented approach for the model inputs, patient state, run time statistics, and functional units. This makes it much easier to read and understand the code, diagnose and fix errors, and add new functionality.

2. New and improved GUI – A new graphical user interface was written using a simpler, platform independent package. This allows for new features to be quickly implemented and the possibility of using the graphical interface on non-Windows platforms.
3. Functionality reordering – The functional units of the model were reordered to provide a clean separation between patient disease/health updates and clinical/treatment changes. This improves the logical flow of the model and eliminates unintended side effects that were present in the old version.
4. HIV testing module integration – The HIV testing module has now been integrated into the main CEPAC model. HIV negative patients go through the main simulation loop but skip all unnecessary modules. This eliminates substantial redundant and error prone code, while allowing for the possibility of developing new functionality that effects both HIV-infected and HIV-uninfected patients.

Beginning in 2009, an initial version of the CEPAC-Pediatric model was developed, using a similar structure to the adult model, but with key changes to reflect HIV disease in infants and young children aged 0-5. This document describes the initial CEPAC-Pediatric model. Substantial changes to the model have been proposed, focusing on early infant diagnosis; ART adherence, retention in care, and drug resistance; and laboratory monitoring of patients on ART and ART switching strategies.

A2. Note on Terminology and Conventions

For purposes of clarification, it is important to note terminology and conventions used within this document. **CD4** generally refers to patient CD4 T-cell count; distinction will be made between the numerical count of CD4 cells and the various CD4 strata as necessary. **HVL** is the abbreviation for the HIV RNA viral load count of HIV-infected patients. The actual numerical count of patients' HVL is not modeled; only a patient's current HVL stratum is tracked. Each simulated patient has **actual** CD4 and HVL levels in any given month. These counts may not be reflected in the patient's **observed** CD4 and HVL readings until the time of the respective CD4 and HVL tests.

Opportunistic infections (**OI**s) are broken out by specific categories, with the sole exception being the *OTHER OI* category, which includes all infections not covered by the other explicitly defined types. Ten unique OIs are included for children <5 years of age, and 10 unique OIs for children and adults ≥5 years of age; these OIs can be specified by the user to be the same or to differ between children and adults. A distinction is made between the actual occurrence of OIs and the observation of those OIs in the patients' histories by the care providers.

ART, also known as HAART in the literature, refers to antiretroviral therapy.

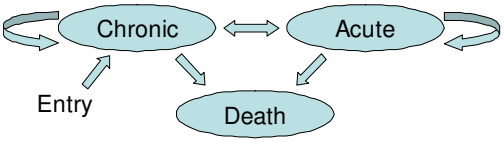
In this document, the term **model** encompasses CEPAC's assumptions, conception, and operation. In practice, the model is often broken down by the **data** elements – as represented by the input tables of the MS Excel spreadsheet – and the executable **program,** which performs the **simulation** of the hypothetical cohort. Human users of the program will be frequently referred to as operators or simply users in this document.

Operators of the model specify all desired values as **inputs** to the program, which in turn produces **output** files containing results of the simulation(s). Each input file corresponds to one simulation **run**. Each run can optionally be grouped into a **set**. At program invocation, all accessible input files are grouped as a **batch**, and processed sequentially. In general, output files contain only summary results of the simulated cohort. The program can also produce **traces** of each patient, detailing state and event information of each patient's clinical course. Each run involves a **cohort** – typically very large in size – of individual patients, simulated sequentially. At the completion of each batch, the program writes **summary** information to a separate file (currently named `popstats.out`).

B. Basic Model Structure and Usage

Each simulated patient's clinical course is tracked from the time of entry into the model until death. The fundamental unit of time in the simulation is a month. Upon the patient's death, summary statistics are recorded and a new patient enters the model. The simulation run completes when the last patient in the cohort has passed through the model. The program maintains tallies of clinical events, duration spent in each health state, monthly life and quality-adjusted life expectancies, and costs.

The model defines three general categories of health states as depicted in the following diagram: chronic, acute, and death. Normally, patients reside in one of the chronic states, where progression of disease and immune system deterioration occur. Patients who develop an acute complication, such as an OI, temporarily move in that month to an acute health state, where quality of life is lower and both resource consumption levels and mortality rates are higher. Deaths can occur from either a chronic or an acute state, and can be attributed to a particular OI, chronic AIDS (e.g. wasting), or non-AIDS-related causes.



Immunologic function is assessed by infected patients' CD4 percent (CD4%, for patients aged <5) or CD4 count (patients aged ≥5); virologic function is assessed using HIV RNA viral load (HVL) count. In the model, HVL drives immune function only to the extent that it determines the rate of CD4 decline for patients age ≥5 years. HIV disease progression is interrupted through clinical care, such as prophylaxis against OIs and ART, which are described in their own sections below.

Patients who enter the model at < 5 years of age are assigned (based on a user-defined distribution of CD4%) to one of 8 CD4% strata: 0-5%, 5-10%, 10-15%, 15-20%, 20-25%, 25-30%, and >35% CD4. The 6 CD4 strata used in the model for patients who enter at ≥ 5 years of age are generally defined as *VHI* (>500 cells/μL), *HI* (301-500 cells/μL), *MHI* (201-300 cells/μL), *MLO* (101-200 cells/μL), *LO* (51-100 cells/μL), and *VLO* (0-50 cells/μL). The user may redefine the strata boundaries in the run inputs.

The 7 HVL strata are defined as *VHI* (>100000 copies/mL), *HI* (30001-100000 copies/mL), *MHI* (10001-30000 copies/mL), *MED* (3001-10000 copies/mL), *MLO* (501-3000 copies/mL), *LO* (0-500 copies/mL), and *VLO* (0-50 copies/mL) – corresponding to roughly half a logarithm range for each stratum. The lowest stratum, *VLO*, is currently just a placeholder for future updated data to reflect the use of more sensitive HVL tests in published reports of ART efficacy. Currently, HVL less than 500 copies/mL is considered below detectable levels. As for CD4, the user may redefine the HVL strata boundaries in the run inputs

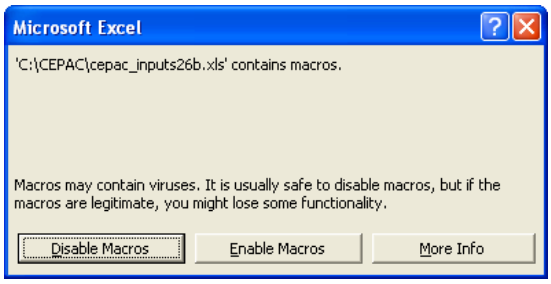
The program currently supports up to 10 categories of OIs with different probabilities of acquiring and then and dying from each OI for children <5, children ≥ 5 and < 13, and adults ≥ 13. Each type of OI may be classified as either mild or severe. The severity associated with each of these OIs affects the attribution effect assessed on the patients' probability of chronic AIDS death. Currently, three broad categories of OI are being modeled in children < 5 years old, based on currently available data: WHO Stage 3, WHO Stage 4, and TB events. These categorizations and the associated OI effects can be redefined by the user.

B1. Instructions for Running the CEPAC Program

All of the inputs to the CEPAC program are contained in the `cepac_inputs4xx.xls` Microsoft Excel workbook. The workbook was developed in Office 2007 and is also compatible with Office 2003. `Cepac4`

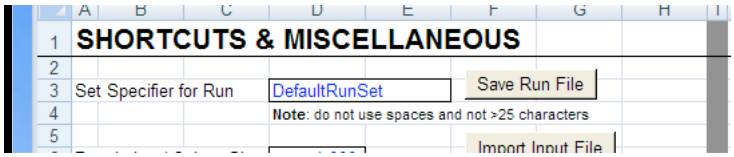
xx.exe is the executable program that actually performs the model simulation. (See Note on Versions on the current naming scheme for both the program executable and input spreadsheet.)

The cepac_inputs.xls workbook is intended to allow the user to manipulate the actual inputs before a run input file is generated. When opening this workbook, you may be prompted by the following security dialog:



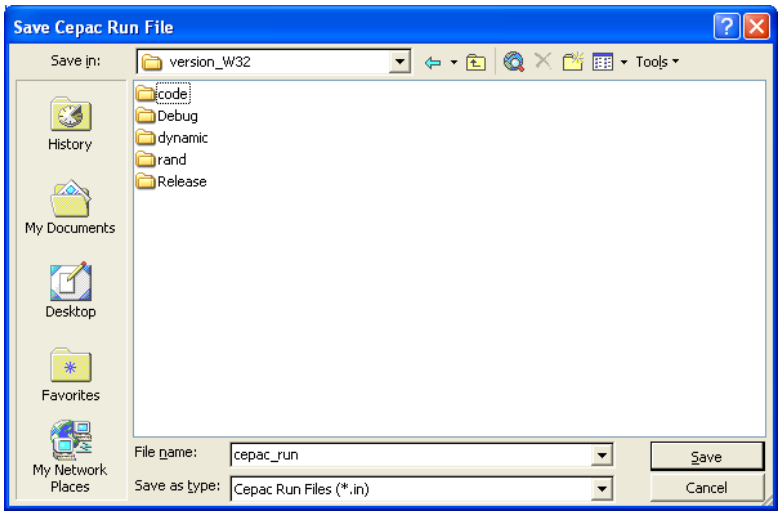
It is important to select "Enable Macros" in this case, as macros are defined for actually generating the run input files required by the program. (The scripts to produce the run input files are implemented in unsigned VBA and embedded within the cepac_inputs4*xx*.xls workbook itself.) Note in that some installations of Excel, the macro security level may be set to high to disable unsigned macros. To allow the necessary macro scripts to run, the security level must be lowered.

Under the "RunSpecs" worksheet in the cepac_inputs4*xx*.xls workbook, the "Save Run File" button is used to save specified inputs relating to a single **analysis**, or **run**:



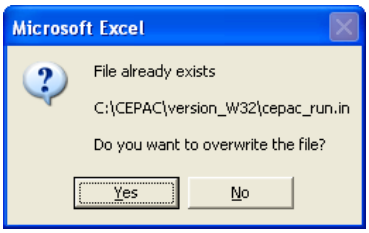
Typically you may want to save multiple analyses at one time before running the cepac.exe program. A set of analyses will be referred to as a batch of runs. The cepac4*xx*.exe program will locate all analyses in the batch at the start of execution, and then process each run individually.

For individual runs, define your analysis set and change the data inputs according to your needs. When the inputs for each run are completely specified, clicking on the "Save Run File" button results in a dialog like the following:



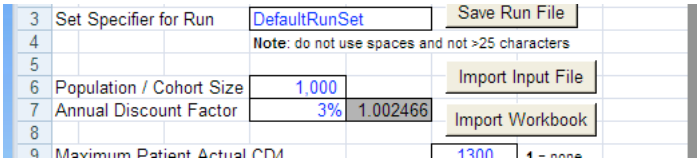
The "Save Cepac Run File" dialog should act like any other file-save dialog: choose a directory in which to save the run input file and then assign a name for the file. In the example dialog, the default run input filename of "cepac_run" is shown.

After clicking "Save" on the dialog, the Excel macro will attempt to generate a run file (with a file extension of "`in`") with the data inputs specified in the spreadsheet. If a run input file with the same name already exists, the following prompt will appear:

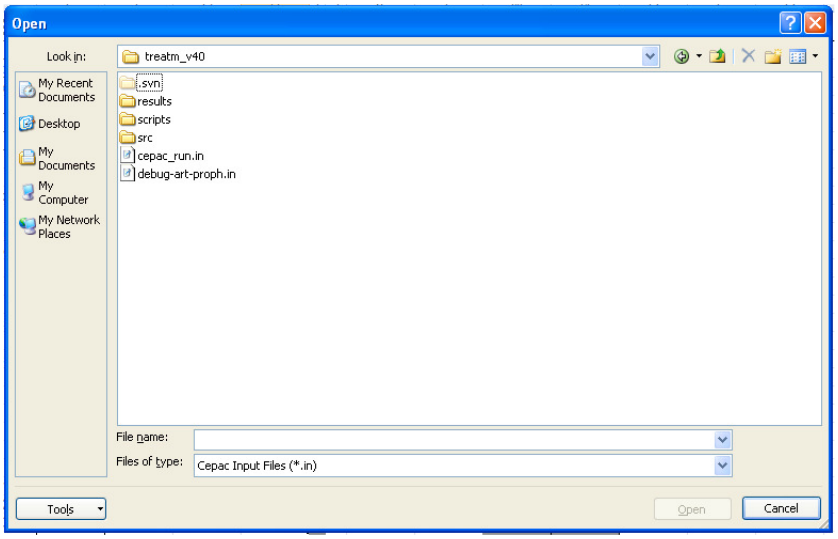


Clicking "Yes" on this dialog results in the previous file being overwritten with the data inputs currently specified in the `cepac_inputs4xx.xls` workbook. Clicking "No" on this dialog leads to the previous "Save Cepac Run File" dialog, which would allow a different filename to be specified.

Due to the large number of model inputs that need to be specified, it is often useful to start an analysis with a default set of inputs. A repository of baseline input files for various countries of interest and standards of care is being developed to serve as the starting point for future analysis. Below the "Save Run File" button in the "RunSpecs" tab, there are two other buttons for importing inputs – "Import Input File" and "Import Workbook."



Running either of these macros will open the following file selection dialog window. The "Import Input File" macro will prompt the user to select a "CEPAC Input File (*.in)", while the "Import Workbook" will prompt them for an "Excel CEPAC input workbook (*.xls)."

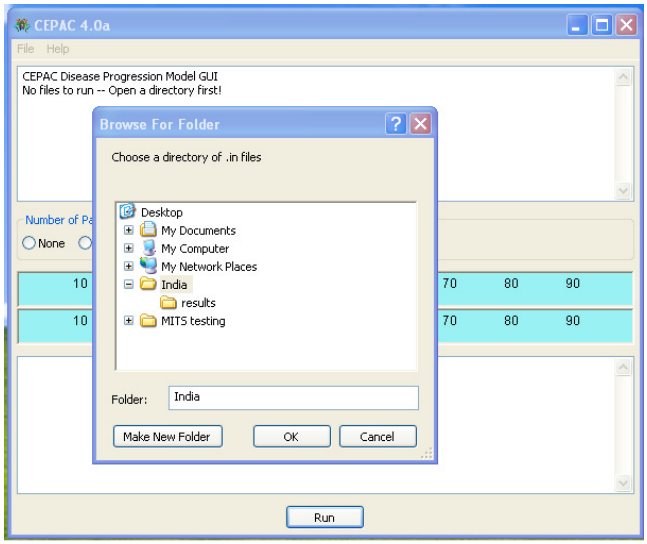


Once the file is selected, the macros will first verify that selected input file or workbook is of the same model version and display an error message if it is not. The current workbook will then have all of its input cells populated with the values specified in the selected file. The "Import Input File" macro should be used before starting any new analysis to import the appropriate default inputs. The "Import Workbook" should only be used to import into a new Excel workbook if the current one becomes corrupted or there is an issue with the macros. These macros and the "Save Run File" one can also be invoked by right clicking anywhere in the Excel workbook and selecting them from the dropdown menu.

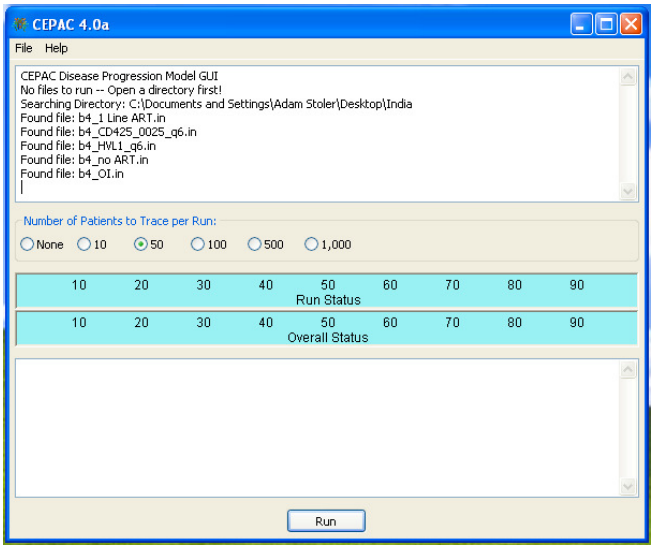
Input files from older version can be upgraded to the current version using the `upgrade_inputs4xx.exe` executable. When run, this program will scan the current directory for any older input files, perform the upgrade to the appropriate version, and place the upgraded input files in a subdirectory called "upgraded_inputs." This program can currently upgrade input files dating back to version cepac40a. The newly created input files can then be run directly with the appropriate CEPAC executable, or imported into a CEPAC inputs workbook for further modification using the "Import Input File" macro.

Note: Due to changes in the model input structure and functionality; the upgrade process cannot perfectly replicate the outcomes of the prior versions. In the absence of a perfect 1:1 correspondence between the inputs, the program attempts to convert the inputs in a logical manner to maintain the desired behavior. After upgrading, the new inputs should be verified and the outcomes validated.

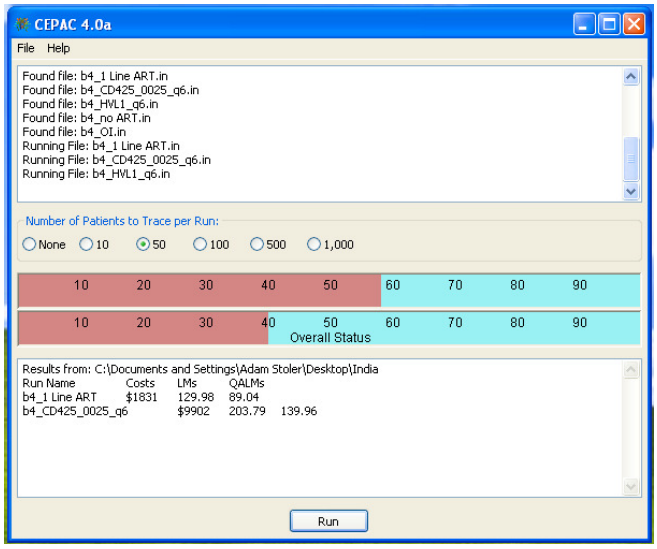
When all the run inputs are specified, the last step is to launch the `cepac4xx.exe` program. The program allows the user to select a directory where the input files for the desired batch of runs are located by selecting File->Open. The program will search for all the files in the specified directory ending with the extension "`.in`" for run inputs. After selecting a directory, the program will display all of the input files that it located. In the above picture, the file is named "`cepac_run.in`" but it's recommended that more descriptive names be used, e.g. "`1M-no_ART-PCP proph.in`". One input file must be saved for each analysis. Below is an example view of the directory selection and the resulting GUI display:



Once the input files have been located, simulation can be started by click on the Run button. If individual patient tracing is desired, the radio buttons can be used to select the number of patients to trace per run. These trace files are very useful for understanding how the model works and verifying that inputs are set up properly to produce the desired simulation. If a large number of patients is selected, these files may become quite large. It is recommended to always trace at least some patients in order to verify the program behavior.



As the program is running, there will be several status updates of its progress. The top dialog box will display the name of the input file that is currently running. The two status bars will show the progress of the current run and overall progress of all runs in the batch. The bottom dialog box will display summary statistics for the completed runs. Below is a screenshot of a running CEPAC program.



At the end of each simulation run, the program creates an "`.out`" file corresponding to the input filename in the "`results`" subdirectory of the input directory. This file contains statistics gathered during simulation of the entire cohort population. If tracing was specified, the tracing "`.txt`" files will also be created for each. The results of each analysis in the batch will be summarized in the `popstats.out` file.

In the `popstats.out` file, all summary results of the individual runs are sorted according to cost, from which incremental cost-effectiveness ratios are calculated. Often it is more useful to the user to calculate incremental cost-effectiveness ratios within smaller groups of analyses, called sets. For example, say you have 6 runs but wish to calculate incremental cost-effectiveness ratios in two separate groups of 3 runs each. The 6 runs are a batch and each group of 3 runs is a set. (Note that the number of analyses in a batch can be quite large, and the number of sets within each batch can be as numerous as you would like but not greater than the number of runs in your batch. Currently, the program is limited to a maximum of 1000 runs in a batch; but this can be easily extended if necessary.)

The name of each run set is specified by the "Set Specifier for Run" entry that is next to the "Save Run File" button in the "RunSpecs" worksheet. Note there is a current limitation for the set name: it cannot contain space characters. Typically, it is easier for the user if this name is more, rather than less, descriptive of your analysis. If you leave the field value to the default for all analyses, the cost-effectiveness ratios for the entire batch of runs will be calculated incremental to each other.

While the `cepac4xx.exe` program is actually running, do not access or modify the program's input "`.in`" files, output "`.out`" files, or the summary `popstats.out file`. However, once the program is done with an analysis, that run's "`.out`" file is available for inspection. Continuing our example, as soon as "`cepac_run.out`" appears, it is safe to open it. (Some Windows systems are set to hide file extensions. In those cases, it may be difficult to differentiate files by their extension types. The safest thing to do is to wait until the `cepac4xx.exe` completely finishes before inspecting any of the output files.)

B2. Note on Versions

Each version of the program is specified by major and minor version numbers and a build date. The current major version number is 4. The minor version numbers serve to differentiate incremental functionality of the program versions. The build date serves to denote modifications in processing that involve very little or no change in functionality. For example, a new build may be released to address logic or formatting errors that do not impact simulation results.

For example, the version "`40a (build 2009-11-03)`" contains the minor version number 0a, and was built on November 3rd, 2009. Such a version number should correspond to a program executable with the name `cepac40a.exe`.

The spreadsheets corresponding to this program version should have the names `cepac_data40a.xls` and `cepac_inputs40a.xls`. To ensure that input files are in sync with the program version, a data input version number is embedded in the spreadsheet. The same spreadsheet has the number "`201020430`" embedded within the inputs. Each executable program is hard-coded to look for such a matching version number. Because the nature of the inputs and the program logic itself change so frequently, the program will abort simulation of all runs with unmatched version inputs.

B3. Note on Discrete Events and Monthly Cycles

The basic unit of time in the model is a month. All acute events in the model occur for durations of time much smaller than a month. The result is that there are cases where the accounting of discrete events may not make much sense at initial inspection. (The halving of costs in a month of death is one simple manifestation of this issue.) The relative ordering of evaluating whether or not discrete events occur also has an impact on the results of the simulation. These events are generally arranged such that biological and disease progression events occur before any diagnostic or clinical ones. The result of this ordering is that disease progression will cause treatment changes within a given month, while the effects of the treatment changes will not manifest until the subsequent month.

B4. Note on Probabilities and Rates

The model relies heavily on the use of probabilities to determine the occurrence of discrete events and health state transitions. For the given probability of a certain event, a random number between 0 and 1 will be generated, and the event will be determined to occur if the number is below the specified probability. Many of these probabilities are fixed inputs, while others are calculated by combining multiple probabilities and/or

modifying a probability by a risk factor. In order to perform these computations, the probabilities are converted to rates, and the additive and multiplicative properties of rates are used. The following formulas are used for the conversions:

Probability to Rate:

- $P = 1 - e^{(-R)}$

Rate to Probability:

- $R = - \ln(1 - P)$

When two probabilities need to be combined to determine likelihood that either or both will occur, the additive property of rates is used. The two probabilities are converted to rates, summed together, and converted back to a probability.

When a probability needs to get modified by a risk factor to increase or decrease the likelihood of the event occurring, the multiplicative property of rates is used. The base probability is converted to a rate, this rate is multiplied by the risk factor, and the resulting rate is converted back to a probability. All of the model inputs that modify probabilities are specified as rate multipliers.

C. Detailed Model Structure

C1. Cohort Initialization

Upon model entry, individual patients are assigned chronic HIV disease characteristics drawn from initial probability distributions. Initial age (in months) and CD4 percent or count are drawn from normal distributions. Initial HVL level is broken down by percentage distribution among the possible HVL strata. A single percentage of male patients in the cohort is used to draw the gender of each individual patient.

In addition to those initial characteristics, the patient also draws for several parameters at model entry pertaining to possible treatment strategies. These include drawing from distributions of whether or not they will be eligible for ART treatments, ART response type, eligibility for OI prophylaxis, prophylaxis compliance, and criteria for clinic visits. These parameters will remain constant for the patient until death. In the CEPAC-Pediatric model, initial distributions also include maternal HIV status (CD4 $\leq$ or $>350/\mu L$ and receipt of ART) and infant feeding status (breastfeeding or replacement feeding; if breastfeeding, duration)

C1a. Prior OI History at Entry and Logging Mechanism

For patients entering the model at any age other than immediately after birth, the program can independently assess whether the patient has had a history of each OI type at the time of the start of the simulation, based on the patient's initial actual CD4 and HVL strata. Patients without a history of a particular OI are assessed a monthly probability for contracting a primary incidence of that OI. Patients with a history of an OI are assessed a different monthly probability for contracting a secondary incidence of that OI. The program treats histories of an OI acquired whether from an acute OI event in the monthly course of a patient simulation or from being assessed at patient initialization time on model entry as equivalent.

In order to generate these prior OI history probabilities, the model includes a detailed "OI history logging" mechanism. The purpose of this logging mechanism is to allow for the model simulation to generate the prior OI history probabilities, in the absence of empirical distributions. (Or, to put it another way, the simulation of a healthier cohort can be used to generate the incidences of OIs as input to another run of sicker patients, who have advanced further along in time in their disease progression.) In this sense, the user is expected to perform

an "initialization run" to produce the probabilities of prior OI histories in the resulting `.out` file. These output tables can then be used as input values into the prior OI histories at entry table for the "actual run."

The specific parameters for the OI history logging mechanism are in the `User` worksheet of the input spreadsheet:

Log Prior OI Hist Probability***			0
		0 = disabled, **1** = enabled	
Log OI Hists With # ART Failures			-1
		-**1** = N/A (prog start), **0..II** = only spec # failures**	
Log OI Hists With CD4 Counts		Upper Bnd	10000
		Lower Bnd	-1
			-1 ≤ x ≤ 10000
Log OI Hists With HVL Strata		Upper Bnd	10
		Lower Bnd	-1
			-1 ≤ x ≤ 10
Log OI Hists in Pat Mths Without Specific OIs:			
PCP	0	FUNG	0
MAC	0	BACT	0
TOXO	0	OTHER OI	0
CMV	0		
		0 = N/A (from prog start), **1** = only without this OI	

The `Log Prior OI Hist Probability` field, when set to `1`, turns the OI history logging mechanism on. When logging is enabled, the program outputs the simulated occurrences of OIs both as a proportion of all patients and in proportion to all patient months. In the former case, the program simply takes at a fixed time (i.e. the first simulated month) the numbers of OIs each patient has had and the total number of patients alive, and simply divides those two numbers. The result is the proportion of patients at that specific point in time with histories of each OI type.

The computation of OI histories by patient months needs more explanation. In certain contexts, the proportion of patient months better approximates the probability of some patient presenting at some random time to the model with some history of an OI (or multiple OIs). Users of the program can use either of these types of outputs.

The OI history logging mechanism computes the probability of a patient having a prior history of a specific OI by the formula:

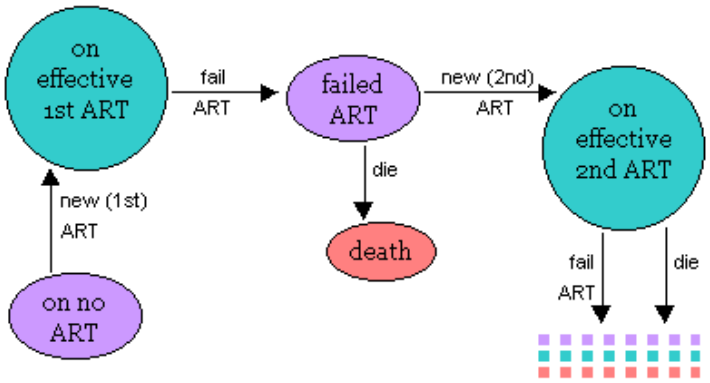
$$\frac{\textit{Number of patient months with a history of that specific OI}}{\textit{Total number of patient months}}$$

More precisely, the model simulation accumulates patient months by the patients' current true CD4 and HVL strata; the "total number of patient months" is then really the total number of patient months in a CD4 and HVL bucket. This is the reason the OI history probabilities tables are arranged jointly by CD4 and HVL. Also, the numerator can be more accurately described as those patient months when an acute incident of that OI occurs **or** for which the patient has had that OI in a previous month.

Note that the patient months included in the numerator are always a subset of the patient months in the denominator. That is to say, for every patient month contributing to the denominator, the program does a simple Boolean test to see if the patient has a history of the OI for that month, and if s/he does, contributes a patient month to the numerator. Therefore, most of the discussion below is restricted to the denominator.

The other specific parameters for the OI history logging mechanism are used to further restrict the patient months the model simulation accumulates in the denominator. For example, to consider only patients with CD4 counts less than 25, with no history of CMV, and only up to the month (but not including that month) when they either get a case of CMV or exit the simulation because of death; we set the `Upper Bnd` field for `Log OI Hists With CD4 Counts` to 25, and the `CMV` field in `Log OI Hists in Pat Mths Without Specific OIs` to 1.

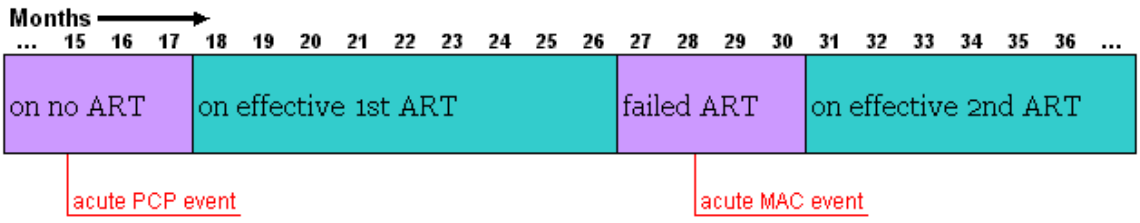
The `Log OI Hists With # ART Failures` field deserves special attention, as the rule it effects is somewhat vague. By default, its value is set to `-1`, which indicates to the model simulation to disregard the number of ARTs in determining which patient months to accumulate. For any nonnegative values in this field, the following patient state diagram is illustrative:



With nonnegative values, the only accumulated patient months are in the purple *on no ART* or *failed ART* states (in the latter case, the patient has been taken off the failed ART, and therefore is also "on no ART"). For example, with the value 2, the simulation model will only accrue those patient months after the patient has failed 2 ART regimens and until the patient begins a new ART (or exits the simulation with a death event). Currently the model allows the user to specify this "window" of patient months between ART regimens in two limited ways:

1. By a fixed number of months – this is accomplished by utilizing the existing, single `Mths Wait from ART Fail to Next` input value, also in the `User` worksheet. Say we want patients to wait 12 months from the time they're taken off a failed ART, up to the time they're begun on a new ART regimen (if any remaining): we simply set this `Mths Wait from ART Fail to Next` field to 12.
2. Indefinitely – by specifying no additional ART regimens after the failure point we're interested in.

Say we have one hypothetical patient following the timeline below:



And we set `Log OI Hists with # ART Failures` to 1. The simulation model will then accumulate 4 months (i.e. months #27, #28, #29, and #30) in the denominator. For the OI PCP, all 4 months also contribute to the numerator, as the patient has had a history of PCP since month #15. For the MAC case, only 3 patient months

would contribute to the numerator. For all the other OI's, none of the 4 relevant patient months are added to the numerator.

C2. Natural History

The natural history component of the model specifies the fundamental biological assumptions of disease progression. It includes the monthly risk of getting an acute OI event, of dying because of that OI event, and of dying from chronic AIDS-related causes (not related to an OI, or more than 30 days after the diagnosis of an OI). In addition, there is the possibility of death from non-AIDS-related causes, stratified by sex and age, including all competing mortality risks not directly attributable to AIDS. Natural history also includes the monthly decline of CD4 cells in the absence of effective ART.

CD4 percent or count is the primary driver of disease progression in the model. The patient's actual CD4 stratum determines susceptibility to OIs in the current monthly cycle, as well as the risk of dying that month due to the OI. Actual CD4 also determines the patient's specific risk to chronic AIDS death for the current month. HVL is modeled as a secondary marker of disease progression for patients after five years of age: a patient's actual HVL influences the rate of CD4 decline, which in turn drives the patient's transitions among the chronic, acute, and death states.

During program execution, the program assesses whether the patient contracts any of the specific OIs. If the patient contracts a specific OI, the program performs a second draw in that month to determine whether the patient dies from the acute OI event. If death from OI does not occur, a random draw is performed to determine whether the patient dies from chronic AIDS or non-AIDS causes. None or at most one of these events would occur in any given month. Chronic AIDS death, non-AIDS death, death from an OI, and death from medication toxicity are the only means by which patients exit the model.

In the absence of effective ART, the patient's actual CD4 percent/count is reduced each month by an amount drawn randomly from a normal distribution with some mean and standard deviation. The program allows for stratification of this baseline CD4 decline by both current actual CD4 and HVL. In addition, each person has their own baseline CD4 decline standard deviation which is drawn once for each person at birth. This number is added to the monthly CD4 decline.

In the absence of effective ART, a patient's HVL remains stable at a HVL "setpoint." A patient's current actual HVL is decreased by effective ART; failure of ART leads to actual HVL returning up to, and no higher than, the HVL setpoint. If another effective ART regimen is not initiated, HVL remains at the setpoint value until the patient's death.

C2a. Monthly Incidence of OI

Monthly incidence of each OI is specified as an independent probability. The program allows for at most one acute OI in any given month. To draw which one OI occurs in the month, the program follows the procedure:

1. take the probability $P_0(i)$ for each OI i
2. convert OI probability to a rate, modify the OI rate by factors from OI prophylaxis (discussed later), and convert the OI rate back to a monthly probability
3. calculate the probability of no OI during the month as: $P(\text{no OI}) = \prod (1 - P(i))$
4. calculate the probability of having an OI during the month: $P(\text{OI}) = 1 - P(\text{no OI})$
5. if an OI is determined to occur in the month, determine which OI:
    a. calculate monthly rate of having each individual OI and none of the other ones:
    $$P(\text{indiv OI}) = P(i) * \prod (1 - P(j))$$
    b. normalize the individual OI probabilities by dividing by their sum

c. determine which OI occurs by randomly drawing from this distribution

C3. Mortality

There are four possible causes of death for the patient that must be evaluated for each simulated month. These include death from acute OIs, chronic AIDS, non-AIDS, and drug toxicity. In order to properly determine if death occurs in a given month and to fairly attribute the cause, these independent probabilities must be evaluated together. During model execution, the probability of each type of mortality occurring for that month is determined, and if it is greater than zero, is added to a list of mortality risks. Once all mortality risks for that month have been determined, the cause of the mortality is evaluated with the following algorithm (similar to the one used for acute OIs):

1. take the probability P(*i*) for each Mortality Risk *i*
2. calculate the probability of No Death during the month as: $P(\text{No Death}) = \prod (1 - P(i))$
3. calculate the probability of mortality during the month: $P(\text{Death}) = 1 - P(\text{No Death})$
4. roll for death occurring, and if so, determine the cause of death -
    a. calculate monthly rate of each individual cause occurring:
    $$R(i) = -\ln(1 - P(i))$$
    b. normalize the individual Mortality rates by dividing each by their sum
    $R\_normalized(i) = R(i)/(\Sigma R(i))$
    c. determine the attributable cause of death by randomly drawing from the normalized distribution of rates

C4. Clinic Visits and CD4 and HVL Tests

HIV disease progression and treatment efficacy are monitored through regular assessments of patients' OI histories and observed CD4 and HVL. The OI histories are determined at every clinic visit, based on an inputted probability of observance. The CD4 and HVL tests, when available, are normally modeled as being conducted during the clinic visit as well. They also may be conducted at special times due to the patient's ART monitoring strategy, or if a patient presents with an OI between regular clinic visits and the user wishes to have CD4/HVL tested on such occasions. The patient's observed health state is then uses to create or modify their treatment program according to the specified criteria.

Each clinic visit incurs a cost in the month in which it occurs. Additionally, the occurrence of either a CD4 or HVL test incurs an additional cost.

C4a. Scheduling of Clinic Visits

If detected as HIV positive upon entry to the model, all patients are generally assumed to undergo a clinic visit to observe their initial OI histories. The user may specify that CD4 and HVL tests should be given at this time as well, or if they should be given later on or not at all (described in the next section). At this initial visit, the program may initiate patients on prophylaxis and antiretroviral therapies as specified by the criteria for treatment. Subsequent clinic visits will then be scheduled at regular monthly intervals.

Other than the initial clinic visit on model entry, patients present to clinic visits based on their assigned clinic visit types. There are three clinic visit types that a patient can be assigned to:

1. those who make the regularly scheduled visits only if they are currently on AIDS treatments (i.e. prophylaxis or ART)
2. those who make their regularly scheduled visits if they are currently on AIDS treatments, or the special clinic visit in the event of an acute OI

3. those who make the regularly scheduled visits regardless of treatment or OI

In addition to the regularly scheduled clinic visits, certain events may trigger an emergency clinic visit to occur in that month. An emergency clinic visit works exactly like a regular one, and at most one clinic visit can occur in a given month. A user specified parameter determines whether an emergency visit should cause the next regular visit to be rescheduled based on the interval or if the existing schedule should be maintained.

The occurrence of an acute OI is one of the events that may trigger an emergency OI. The user can alternatively specify that patients will not have emergency clinic visits for OIs; the associated OI treatment costs, OI-related death costs, and OI-related mortality can be varied based on whether this special clinic visit occurs. The specific acute OI that leads to the clinic visit is always added to the patient's observed OI history. If an OI does not trigger a clinic visit, a probability can be specified for whether or not it will be observed at the subsequent clinic visit.

Regularly scheduled CD4 and HVL tests can also trigger a clinic visit if they are scheduled to occur before the next clinic visit. The only diagnostics that can occur outside of the clinic visit are the special CD4/HVL tests described below.

C4b. CD4 and HVL Tests

Regular CD4 and HVL tests are scheduled at user-specified intervals, but because they are administered only in the context of a clinic visit, they will trigger emergency clinic visits if they are scheduled to occur before the next regular visit. Testing frequency can be specified uniquely (or even set to not be administered at all) for each possible state that the patient may be in:

1. before starting any ART regimen, and with an observed CD4 above the specified threshold
2. before starting any ART regimen, and with an observed CD4 below the specified threshold
3. taken an ART regimen that is not the last one, and less than the specified number of months since init
4. taken an ART regimen that is not the last one, and greater than the specified number of months since init
5. taken the last ART regimen, and less than the specified number of months since init
6. taken the last ART regimen, and greater than the specified number of months since init
7. after the patient has been observed to fail the last available line of ART

Scheduling of either the next CD4 or HVL test is done by computing from the current month of testing when the subsequent test should occur. The basic intuition behind this structure is that it reflects a doctor's discretion of decreasing or increasing the number of intervening months to the next scheduled month of patient testing. For example, a low observed CD4 level for a sicker patient may warrant more frequent testing; a high observed CD4 for a healthier patient may allow the next CD4 test to be scheduled further out in time. The tests will be given at the next clinic visit after the desired interval between tests has been reached.

The regular schedule of CD4 and HVL testing may be interrupted in a few particular cases. When a patient first starts an ART regimen, the user may specify that CD4 and HVL tests are to be given that month and for a specified number of months after that. The user may also specify that after a test indicating ART failure occurs, additional tests will be given in the subsequent months to confirm the failure. Observation of ART regimen failure can be made by drops in observed CD4 or increases in observed HVL (or, thirdly, by observed OIs). Complete observed failure of the ART regimen is typically defined as two successive failure diagnoses, at which point an emergency clinic visit is triggered. It is also possible to specify that CD4 tests should be given to confirm clinical failure, or that HVL tests should be given to confirm immunologic or clinical failure. These special tests are given outside of the clinic visit, and always occur at the desired month.

The program allows for variability in CD4 and HVL test results. For HVL tests, the operator may specify the probability of each HVL test returning an observed HVL result one stratum higher or lower than the patient's current actual HVL. For CD4 tests, the specified percentage of the actual CD4 value is used as a standard deviation to add observed CD4 count fluctuations from a normal distribution.

C5. Costs and Life Expectancy

C5a. Discounting

Projected costs and life expectancy are discounted on a monthly basis. The program expects the discount factor to be of the form `1 + r`, where `r` is the desired discount rate. For example, a monthly discount rate of 1% would be entered as 1.01 (i.e. `1 + 0.01`) to the program. The program uses this discount factor as the divisor for all projected costs and life months accrued by each patient. The first monthly cycle for each simulated patient is always undiscounted; subsequent months are discounted by the discount factor, compounded on a monthly basis.

The default monthly discount rate used results in an annualized discount rate of 3%; the discount factor used for the program is 1.00247, calculated by $(1 + 0.03)^{1/12}$, accounting for the conversion from an annualized to a monthly basis. For debugging purposes, the discount rate is often changed to 0% – in this case, the discount factor used in the program is 1.

C5b. Routine Costs

In each month, patients accrue a monthly routine cost based on their CD4 and OI history state. If a patient has no history of OIs, the cost is based on just the patient's CD4. If a patient has a history of an OI, the cost can be based on that OI type and the patient's CD4. In the case of multiple OIs in the patient's history, the highest cost among the applicable OI types is selected for the patient's CD4 stratum.

In addition to these base routine monthly costs, patients accrue costs for each type of acute event (e.g. acute OI, toxicity, visits, tests, death) as well as monthly drug (i.e. ART, OI prophylaxes) costs.

C5c. Month of Death

All patient death events are treated in the program as if they occurred in the middle of the monthly cycle. The primary result of this generalization in terms of accounting is that patient costs and life months (both nominal and quality-adjusted) are halved in the month of death. The quality-adjusted life month is accrued according to the type of event: chronic AIDs, non-AIDS-related, OI-related, or major ART toxicity-related death.

The specific costs halved in the month of death are:

- monthly prophylaxis cost
- monthly routine care cost (e.g. by CD4, OI history, etc.)
- monthly ART treatment cost

Clinical diagnostic and treatment costs are ignored in the month of death since these are considered to be included in the cost of death. All other costs are incurred in full.

C6. OI Prophylaxis

Initiation of prophylaxis for each type of OI is usually specified by the patient's current observed CD4 stratum. Other policy criteria can include the patient's minimum observed CD4 as well as whether the patient has or has not had a history of each OI. For the OI criteria to be met, that patient must have a history of at least one of the "has history" OIs and none of the "has no history" OIs. These criteria choices can be combined through either OR or AND evaluation. If OR is selected, meeting any one of the specified criteria will trigger prophylaxis initiation. If AND is select, all of the specified criteria must be met. Additionally, a minimum month number can be set to indicate that patients cannot start prophylaxis until that month of simulation.

The stopping criteria for each type of prophylaxis, likewise, can be specified by the patient's current observed CD4 stratum, minimum observed CD4 stratum, and history of OIs. Instead of specifying a minimum month number to stop, the user can set a maximum month number or months since prophylaxis initiating to force a stop of treatment. If either of these parameters is set, they will override the other stopping criteria and cause an emergency clinic visit to occur at the specified month. The program currently reevaluates changes to a patient's prophylaxis regimen during every clinic visit.

The program allows for up to three different lines of prophylaxis drugs for each OI type. A patient will start with the first specified line and will always use that one for subsequent restarts. They will only be switched to the next line in the event of toxicity or if the prophylaxis is specified to cause an automatic switch after a given number of months. If a switch needs to occur, an emergency clinic visit will be triggered that month to enable the treatment change. If no more lines are available, the patient will stop taking prophylaxis for that particular OI.

Patients on an OI prophylaxis gain a protective benefit from that particular OI (and potentially other OIs). The prophylaxis' efficacy is specified as a rate multiplier by which the patient's monthly risk for that OI (and possibly other OIs) is reduced.

Each line of prophylaxis drug has its own independent risk of minor and major toxicity. The types of toxicity are specified by some probability of occurrence and a fixed time after prophylaxis initiation when it should occur. The toxicities are additively combined to first determine if no toxicity occurs. If toxicity is found to occur, then a distribution of the individual probabilities is used to determine whether the toxicity was major or minor. Minor and major toxicity events incur increased costs and decreased QOL in the month of the event. Major toxicity also has a specified probability of mortality that will be evaluated after the toxicity is determined to occur. Both major and minor toxicities may trigger a switch to the next line of prophylaxis; the user can individually specify whether or not each type should cause the switch.

Prophylaxis resistance, likewise, is assessed by a resistance probability at the time of initiation. If resistance does occur, the effect begins at the specified number of months after initiation. Prophylaxis resistance causes the monthly risk of that particular OI to be increased by some specified percentage. Resistance also entails a multiplicative factor by which the cost of OI treatment is increased, as well as a multiplicative factor by which the rate of death from an acute event of that OI type is increased.

C7. Pediatrics

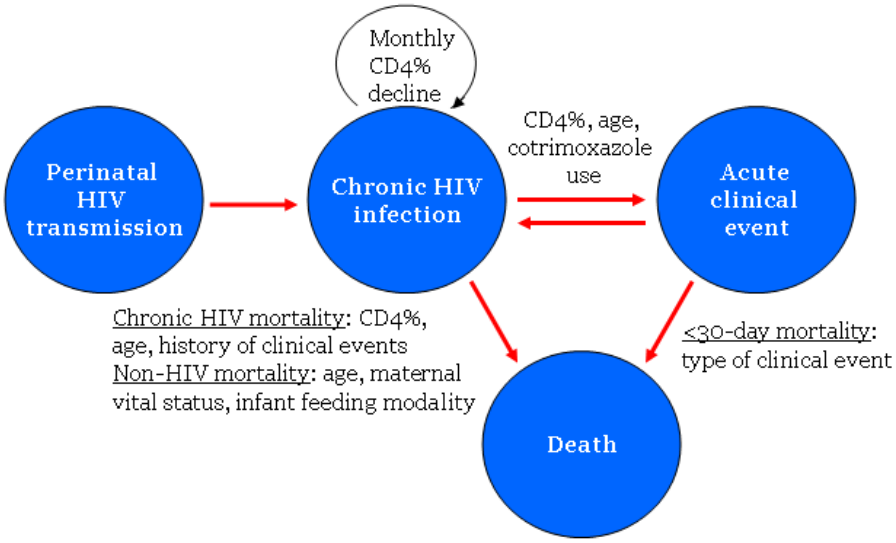
Beginning in version 43a of the model, we added an initial CEPAC-Pediatrics model to simulate HIV-infected children from ages 0-5 years. The primary focus of the initial model is on HIV disease progression in the absence of ART, although a limited ART module is included. Several key components of the initial Pediatrics model function in much the same way as in the adult model, with different input data to reflect different clinical

risks, available medications, and costs for children. In Section C7, we detail elements of the initial Pediatric model that differ importantly from the CEPAC-Adult model, and highlight ways in which the full CEPAC-Pediatric model will be substantially expanded for ongoing and proposed analyses.

C8a. Overview of CEPAC-Pediatric Model

Infants enter the model at birth, after HIV infection *in utero* or during delivery. A random number generator is used to draw from user-specified distributions of CD4% and HIV RNA level at birth. In the absence of ART, each simulated child's CD4% declines monthly at a specified rate.

Health states. Disease progression in the CEPAC-Pediatric model is characterized by monthly transitions between health states, including chronic HIV infection, acute illness, and death:



In each month of the simulation, random numbers determine transitions between these health states, based on probabilities specified as model inputs. Transition probabilities depend on current age and current CD4%. Simulated patients face monthly risks of acute "clinical events," including up to 10 discrete types of opportunistic infections (OIs) and other HIV-related illnesses. Detailed, accurate data on these risks in untreated children, and their associated costs, are critical to the model; the team has devoted great effort to identifying the best available data sources. Model analyses to date are based on International Databases for the Evaluation of AIDS (IeDEA) East African regional data (Ciaranello *et al, PIDJ* 2013, in press), and simulate 3 mutually exclusive categories of clinical events: WHO Stage 3 (excluding pulmonary and lymph node TB), WHO Stage 4 (excluding extrapulmonary TB), and TB (at any anatomic site).

Mortality risks. The CEPAC-Pediatric model simulates three causes of mortality. First, children with no history of acute clinical event face a monthly risk of HIV-related death ("chronic HIV mortality"), stratified by current age and CD4%. Second, children who experience a clinical event face "acute mortality" risks in the 30 days after an event; after this 30-day period, children with a prior event face increased monthly risks of "chronic HIV mortality." Third, the model includes a monthly risk of "non-HIV-related mortality," derived from UNAIDS age- and sex-adjusted, country-specific mortality rates that exclude the impact of HIV.

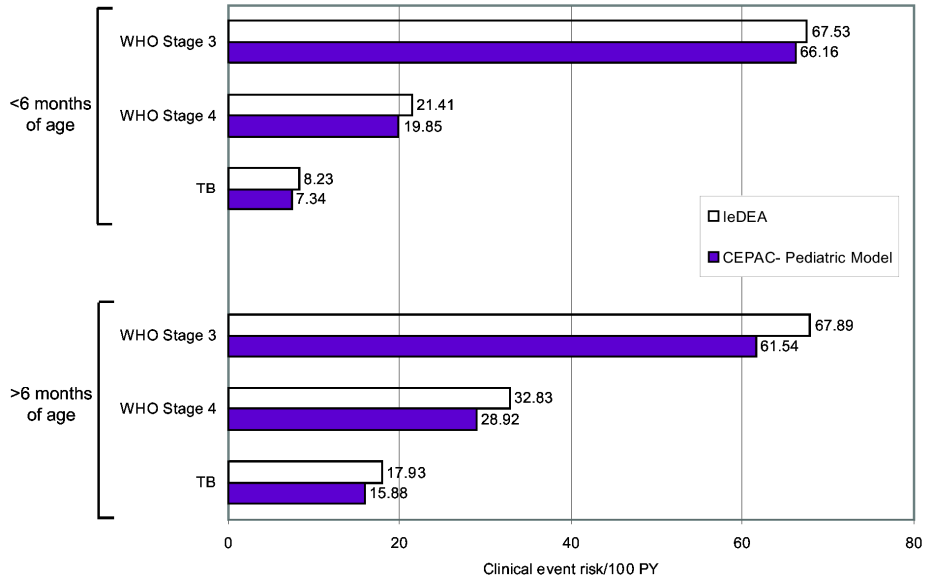
Impact of ART. Modeled patients start ART once they meet user-specified age, immunologic, virologic, and/or clinical criteria. The model can incorporate up to 10 discrete ART regimens. Each ART regimen is modeled to confer unique efficacies (probability of suppressing HIV RNA to <400c/ml; monthly CD4% gains for children

with suppressed RNA), as well as risks for development of toxicity. Children who initially suppress their HIV RNA at 24 weeks face a monthly risk of virologic failure after this time ("late failure"). The model includes an independent benefit of ART on mortality and OI risks, in addition to the effects of suppressive ART on CD4 and RNA. After failed ART, CD4% remains stable for a user-specified amount of time (usually 12 months), and then declines at the rate assigned for untreated children. The user assigns a monitoring strategy (nature and frequency of laboratory and clinical assessment) and the criteria by which ART failure is detected: virologic (e.g. no RNA decrease to <400c/ml at 24 weeks), immunologic (e.g. decline to CD4% <10%), clinical (Stage 3/4 OI), or any combination of these. After observed failure, patients can switch to the next available line of therapy. Loss to follow-up in the initial model may occur at a user-specified constant monthly rate, leading decline in CD4% and OI risk to revert to off-ART rates.

Healthcare costs. Simulated children accrue costs for each modeled health state. Costs are derived in two steps. First, we analyze resource use (number of outpatient visits, hospital days, and, if relevant to the country of focus, outpatient day-care visits) for each OI, as well as for routine HIV-related care and care in the last month of life. Next, we multiply each unit of resource use by published costs for outpatient and inpatient care.

Model outcomes. For each patient, the model tracks clinical events, changes in CD4 and RNA, time in each health state, and healthcare costs. After an individual simulated patient has died, the next patient enters the model. Cohorts of 10 million patients are simulated to generate stable model outcomes. Summary statistics are tallied for the entire cohort for each evaluated strategy of care, including key clinical outcomes (survival and life expectancy), economic outcomes (costs over 1, 5, 10-year and lifetime horizons), and incremental cost-effectiveness ratios (ICERs).

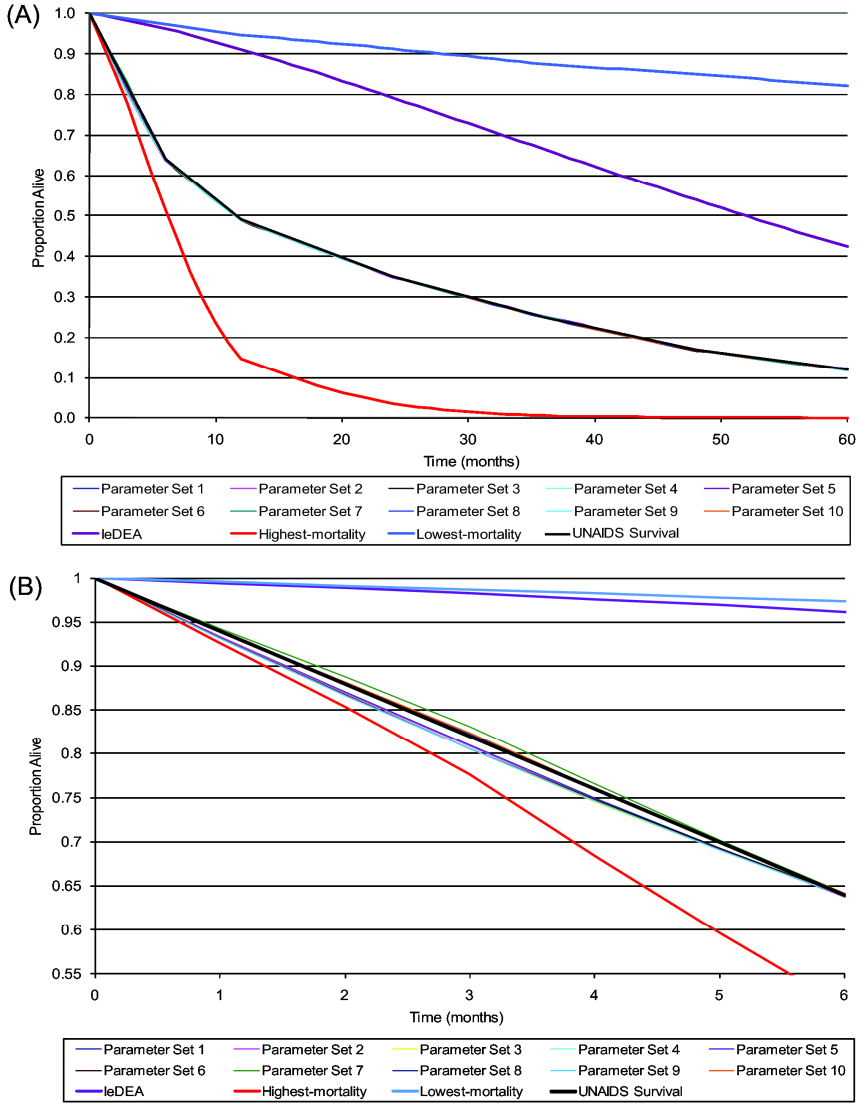
Model validation. We have internally validated the CEPAC-Pediatric model by comparing model outputs to the IeDEA data used to derive model inputs, to confirm the accuracy of the model structure (Ciaranello *et al, PLoS ONE,* 2013). Model projections that fall within 10% (relative) of the data used to derive model inputs are generally considered to be good-fitting:



Risks of clinical events from 5-16 months of age, as observed among infants in the IeDEA East Africa region and projected by the CEPAC-Pediatric model. Simulated infants enter the model with the CD4% at birth identified in the best-fitting parameter set for the internal validation survival analyses (45.0%), and CD4% values decline as per the best-fitting parameter set (6.0%/month ages 0-3 months, 0.3%/month ages ≥3 months). Simulated infants face competing risks of all three types of clinical events, as well as "acute" and "chronic" mortality. Due to differing methods of reporting, IeDEA event risks (reported for three distinct CD4 strata) could not directly be compared to model-projected event risks (reported as a cohort average, where the cohort consists of a population with a unique

distribution of CD4% each month). To generate a comparable IeDEA risk for each clinical event, we calculated an average of the three reported risks from IeDEA (CD4 <15%, CD4 15-25%, CD4 >25%) weighted by the proportion of the cohort in each CD4% strata during each month of the simulation. Model-generated rates are expected to be slightly lower than IeDEA-observed rates, due to 1) model accounting of OIs (which permits only one OI to be recorded each month), and 2) competing risks of other OIs and chronic HIV mortality in the model.
TB: tuberculosis, **PY**: person-years.
From Ciaranello et al, PLoS ONE, 2013.

Model calibration. To improve generalizability, we have calibrated the CEPAC-Pediatric model (Ciaranello *et al, PLoS ONE,* 2013). This involved examining more than 4 million parameter sets, in order to find the CD4%- and age-stratified mortality risks that best fit published survival data from >1,300 untreated, perinatally HIV-infected children ages 0-5 in six sub-Saharan African countries (UNAIDS data, Becquet *et al, PLoS Medicine*, 2012):



Model-projected survival curves from age 0-60 months for: 1) Base-case IeDEA mortality data used in the internal validation analyses (purple line); 2) the empiric UNAIDS mortality data (black line); 3) 10 of the best-fitting parameter sets (with the lowest root-mean squared error) identified in the calibration analyses (group of colored lines surrounding and almost completely overlapping with the black UNAIDS line); 4) the lowest-mortality risk parameter set from Table 3 (blue line) and 5) the highest-mortality risk parameter set (red line). The 10 sample best-fitting parameter sets from calibration analyses are almost entirely obscured by the UNAIDS survival data (black line) due to their extremely close fit to the calibration target. The IeDEA survival curve from internal validation analyses, and both the highest- and lowest-mortality risk parameter sets are all projected to 60 months of age for

comparison only, as they did not meet a threshold of UNAIDS risk ±1% at 6 months and therefore were not formally evaluated at subsequent time points in the calibration analyses.
B: A zoom plot, enlarging the results for months 0-6, shows the nearly-overlapping curves in larger detail.
From Ciaranello et al, PLoS ONE, 2013.

C7b. Patient Initialization and Stages of the Pediatric Model

Activating the Pediatrics module will cause every patient in the cohort to begin the simulation at age <5 years, with starting age specified by drawing from a user-specified distribution. At initialization, patients draw for having been infected intrauterine (IU) or intrapartum (IP). Instead of starting with an initial absolute CD4 count, pediatric patients will draw for an initial CD4 percentage. Patients will also draw for an initial HVL strata value that will be their setpoint during childhood.

Patient simulation is divided into three chronological stages – early childhood (0-59 months old), late childhood (5-12 years old), and adolescence/adulthood (13 years old and beyond). During early childhood, the patient's CD4 percentage and age are the primary drivers for disease progression and treatment policy. Their HVL level has no impact on CD4 or OI risk during this time period, but is tracked by the model to reflect probability of RNA suppression on ART and response to ART. During late childhood, the patient's absolute CD4 count and HVL strata will be the primary drivers for simulated events. This is similar to how the model functions for adults, but different input values can be specified for use during the late childhood period. Once the patient reaches age 13, they will subsequently use all of the adult input values and the model will function exactly as it would without the Pediatrics module enabled. This will allow the adult model to function as an adolescent model when parameterized with data to reflect youth and young adults ages 13-24.

The transition from early childhood to late childhood at age 5 requires some special behavior in the model. The patient's CD4 percentage is converted into an absolute CD4 count. This is currently done by drawing from a normal distribution, with the mean and standard deviation depending on the patient's CD4 percentage (effectively "mapping" the CD4% at age 5 to an absolute CD4 cell count value). We plan to examine alternate approaches to this "mapping." If a patient is on suppressive ART, a CD4 slope for the current time period will also need to be drawn. Additionally, the patient will draw for a new adult HVL setpoint using a transition matrix that specifies the likelihood of each new HVL value occurring given the setpoint established in infancy. The prior monitoring state and CD4 envelopes will also be reset to improve continuity across the age transitions.

C8c. Disease Progression

During early childhood, patients have natural history CD4 percentage declines each month that are stratified by their type of infection (intrauterine or intrapartum), age, and current CD4 percentage. The monthly probability of chronic AIDS death is calculated based on the patient's OI history, age, and CD4 percentage. The probability of non-AIDS death is stratified by age and gender like the adult inputs, but at a finer granularity of time segments. Monthly probabilities of acute OIs are stratified by OI type, prior history of that OI, age, and CD4 percentage. Mortality from OIs is stratified by OI type, OI history, whether or not OIs are treated, and patient's current age.

During late childhood, the patient will use the same CD4/HVL based natural history CD4 count decline inputs that adults use. The inputs for chronic AIDS mortality, non-AIDS mortality, acute OI incidence, and acute OI mortality will have the same structure as their adult counterparts, but may be redefined with different input values.

C8d. ART Treatment

The policy decisions to start a regimen, observe failure, or stop ART all function uniquely in the Pediatrics module. Most notably, during early childhood the patient's observed CD4 percentage count is used for immunologic criteria instead of the absolute CD4 count. These criteria are used in addition to virologic and clinical criteria, which are specified uniquely for children. The user can also specify different testing intervals for when CD4 percentage and HVL strata will be monitored during early and late childhood.

An ART regimen can be specified to start if the patient's CD4 percentage falls within a given range, if the CD4 percentage and HVL are within given ranges, or if the patient has reached a given age. Failure can be observed if there is a decrease of a given number of CD4 percentage points from the maximum, if the CD4 percentage drops below the pre-ART nadir, or if the CD4 percentage falls within a given range. In addition, the user can specify age-related criteria for both ART initiation and ART stopping.

The impact of ART treatment on disease progression is also different in the Pediatrics module. During early childhood, the "ART effect" (the CD4-independent impact of ART on the probability of chronic AIDS death and acute OI incidence) are stratified by both CD4 percentage and time on the ART regimen. In late childhood, the "ART effect" input structure is the same as what is used for adults, but the parameter values can be specified differently.

For each ART regimen, the probably of initial suppression, late failure, and costs can be specified separately for early and late childhood. During early childhood, the CD4 percentage increase while RNA is suppressed can be stratified by time on ART, age at which ART was started, and CD4 response type. During late childhood, the CD4 count increase uses the same structure as the adult inputs but may have different parameter values. The decline multiplier for failing ART, the decline multiplier off ART, and the HVL change rate use the same input structures as adults but with different values for early and late childhood.

D. Monthly Cycle of the Model

Because all events in the program occur discretely, it helpful to keep in mind the order of evaluation in each month of a simulated patient. These events are also shown in the CEPAC-Pediatric model flowcharts (available on the CEPAC website), where they are indicated as "updaters." Taking all of the mechanisms described above together, each regular monthly cycle in the program involves the following steps, in this order:

1. If the patient is on an ART regimen, see if an associated toxic event occurs
2. If an ART major toxicity event occurs, add the associated risk of mortality for all prophylaxis the patient is currently on, see if an associated toxic event occurs
3. If a prophylaxis major toxicity occurs, add the associated risk of mortality
4. Determine if an acute OI event will occur this month
    - If an OI event occurs, add the associated risk of mortality
5. Determine if death occurs this month
    - Account for risk of non-AIDS and chronic AIDS death
    - if death occurs, determine the cause and stop the patient simulation
6. Update the patient's CD4 and HVL for the month
7. For any ART or prophylaxis the patient is on:
    - Determine if any efficacy changes (suppression, resistance, failure) occurs in the drugs
8. Determine whether a regularly scheduled or emergency clinic visit should be performed this month
9. Determine if a CD4 test should occur this month and perform if so
    - Exceeded month interval since prior visit and clinic visit is occurring this month
    - Triggered by ART initiation or needed for ART failure confirmation

10. Determine if an HVL test should occur this month and perform if so
    - Exceeded month interval since prior visit and clinic visit is occurring this month
    - Triggered by ART initiation or needed for ART failure confirmation
11. If clinic visit will occur this month, perform the standard clinic visit tasks
    - Observe acute OIs and determine if prior OIs are observed
    - Determine if the current ART regimen is observed to have failed, should be stopped, or if the next line should be started
    - Determine if OI prophylaxis should be stopped or started
12. Update the patient's accumulated costs, life months, and quality adjusted life months
13. Increase the patient's age, in months

E. Program Inputs for the Model

Below is a description of all input fields in the `cepac_inputs.xls` spreadsheet that pertain to the CEPAC-Pediatric model. (Because fields in the `cepac_data.xls` workbook map directly to those in the `cepac_inputs.xls` workbook, no separate description of those inputs are given.)

	Section	Table/Field	Description	Program Variables
	Shortcuts & Miscellaneous	Set Specifier for Run	Specifies which set of runs this particular run belongs to in the simulation program's batch of runs, used for calculated ICERs within groups in a batch of runs.	runSetName
	Shortcuts & Miscellaneous	Population/Cohort Size	Specifies the number of patients in a single simulation run.	numCohorts
	Shortcuts & Miscellaneous	Annual Discount Factor	Specifies the exponential rate at which monthly costs and QOL values for the patient are discounted. This factor is converted into a monthly basis, which is then used in the program. To get undiscounted results, use the value `1`.	discountFactor
	Shortcuts & Miscellaneous	Data Set Shortcut	Specifies which set of default input values from the `cepac_data.xls` spreadsheet should be used for many of the tables in the inputs workbook.	
	Shortcuts & Miscellaneous	Maximum Patient Actual CD4	Specifies the maximum actual CD4 patients can attain in the simulation. Use the value –1 for no cap on maximum CD4.	maxPatientCD4
	Shortcuts & Miscellaneous	Longitudinal Log of Cohort	Can be either the values `0`, `1`, `2`, or `3`. A non-zero value specifies that summary information about the patient cohort longitudinally over time should be included in the run's `.out` output file. A value of `1` produces detailed summary information on a monthly basis. A value of `2` produces abridged summary information on a monthly basis. A value of `3` produces detailed summary information on a yearly basis.	longitLoggingLevel
	Shortcuts & Miscellaneous	Log as "First" OI in Simulation	Specifies a set of OIs out of which each patient may be reported as having the "first" OI in the outputs. Note that this distinction between those who have and have not encountered their "first" OI is used primarily in the longitudinal log outputs. This "first" OI setting currently does not affect a patient's disease progression.	firstOIsLongitLogging firstOIsChronicLongitLogging
	Shortcuts & Miscellaneous	Time Point 1/2/3 (Month) to Record ART Efficacy	Specifies at what number of months after ART initiation to record selected ART regimen efficacy information.	monthRecordARTEfficacy
	Shortcuts & Miscellaneous	Random Initial Seed by Curr Time	Can be either the value `0` or `1`. A value of zero specifies the use of the same starting seed for the random number generator in the program, and that it should be reseeded for each new number based on the program location, the patient number, and the month number. A value of one specifies the use of the current system time as the starting seed.	randonSeedByTime
	Shortcuts & Miscellaneous	Classification of Severe OIs	Indicates which of the specified OIs are considered severe with a value of 1. OIs considered mild, or not severe, are indicated with 0. The number of mild and severe OIs in each patient's history primarily affects the chronic AIDS death probability.	severeOIs
	Shortcuts & Miscellaneous	CD4 Strata Bounds	Allows the user to override the default boundary values for the various CD4 strata used throughout the model inputs.	CD4StrataUpperBounds
	Cohort Logging	Log Prior OI History Probability	Used to turn on/off the program recording of the proportion of patients with a given history of OIs up to some prespecified duration of time. This proportion of patients with OI histories in the output files can be used as priori OI history inputs in subsequent runs of the program.	enableOIHistoryLogging
	Cohort Logging	Log OI Histories with # ART Failures	Specifies the number of ART failures before OI history logging will begin. Use value -1 to disregard, for positive values it will record OIs after that ART line has failed and before the next line is begun.	numARTFailuresForOIHistoryLogging
	Cohort Logging	Log OI Histories with CD4 Counts	CD4 bounds for when OI history logging will begin, patients true CD4 value must be within these bounds, inclusively	CD4BoundsForOIHistoryLogging
	Cohort Logging	Log OI Histories with HVL Strata	HVL bounds for when OI history logging will begin, patients true HVL strata must be within these bounds, inclusively	HVLBoundsForOIHistoryLogging
	Cohort Logging	Log OI Histories in Patient Months without Specific OIs	Only log OIs for patients that do not have a history of any of the OIs specified with a value of 1	OIsToExcludeOIHistoryLogging

	Cohort Characteristics	Distribution of Initial CD4	Mean and standard deviation distribution of patients' actual CD4 counts on entry to the simulation program. Drawing a CD4 value below zero is set to zero, a value above max CD4 is set to max CD4.	initialCD4Mean initialCD4StdDev
	Cohort Characteristics	Distribution of Initial HVL	Probability distribution of patients into the possible HVL strata on entry to the simulation program. The starting HVL stratum chosen for each patient is also the HVL setpoint for the patient. The HVL distribution is chosen dependent on the actual CD4 stratum the individual is assigned to. The probabilities across all HVL strata should sum to 1.	initialHVLDistribution
	Cohort Characteristics	Distribution of Initial Age (in Months)	Mean and standard deviation distribution of patients' age, in months, on entry to the simulation program. Ages below zero will be set zero, age over 100 years will be set to 100 years.	initialAgeMean initialAgeStdDev
	Cohort Characteristics	Gender Distribution	Percentage distribution of cohort that is male, the remainder will be female.	maleGenderDistribution
	Cohort Characteristics	Distribution of Clinic Visitor Types	Distribution of cohort into the three clinic visit types: those who make visits at the very beginning of the simulation and when on ART/prophylaxis; visits at the very beginning, on ART/prophylaxis, or at the event of an OI; and visis at the very beginning, on ART/prophylaxis, at the event of an OI, and on a regular schedule.	clinicVisitTypeDistribution
	Cohort Characteristics	Probability of Prior OI History at Entry	Probability assessed for each patient on simulation entry of having a prior history of each OI.	probOIHistoryAtEntry
	ART Regimen Starting Policy	CD4 Count	Specifies the observed CD4 range (inclusive) when eligible patients should start each line of ART regimen.	startART.CD4BoundsOnly
	ART Regimen Starting Policy	HVL Strata	Specifies the observed HVL range (inclusive) when eligible patients should start each line of ART regimen.	startART.HVLBoundsOnly
	ART Regimen Starting Policy	CD4 Count and HVL Strata	Specifies the joint observed CD4 and HVL ranges (inclusive) when eligible patients should start each line of ART regimen.	startART.CD4BoundsWithHVL startART.HVLBoundsWithCD4
	ART Regimen Starting Policy	Observed Acute OI	Specifies the OIs observed in the patient's history since the previous ART regimen was observed to have failed or was stopped to start the subsequent ART regimen. The number of observed OIs needed to start ART is subject to the `# OIs to Start ART` input.	startART.OIHistory
	ART Regimen Starting Policy	# OIs to Start ART	Specifies the number of observed OIs in `Observed Acute OI` necessary to start the subsequent line of ART.	startART.numOIs
	ART Regimen Starting Policy	CD4 Count and Observed Acute OI	Specifies the joint observed CD4 range (inclusive) and observed OIs in patient's lifetime history to start the subsequent ART regimen.	startART.OIHistoryWithCD4
	ART Regimen Starting Policy	Minimum Month # for starting ART	Specifies the minimum month number in the simulation before which each line of ART would not be started. This month condition is purely a precondition before the other CD4/HVL/OI starting conditions are considered for starting a patient on the subsequent line of ART.	startART.minMonthsNum
	ART Regimen Starting Policty	Time elapsed since prev regimen stop	Specifies the number of months since the previous ART regimen was stopped before the patient may begin the next line, used purely as a precondition before the other starting criteria are evaluated.	startART.monthsSincePrevRegimen
	Order of Administering ART Regimens	ART #	Specifies the number of ART regimen within the spreadsheet to be used for each line of ART treatment. This is a setting internal to the spreadsheet to select the order of available ART regimens; ART regimen information is ultimately input into the simulation program in the order specified here.	
	Order of Administering ART Regimens	Additional Regimen Costs At Regimen Startup	Costs added to the selected regimen's startup costs. This cost is not separately input into the program; it is combined with the corresponding ART regimen's initialization cost.	
	Order of Administering ART Regimens	Additional Regimen Costs, Monthly on Regimen	Costs added to the selected regimen's monthly costs. This cost is not separately input into the program; it is combined with the corresponding ART regimen's monthly cost.	
	ART Regimen Observed Failure Policy	Number HVL Strata Increase	Specifies the number of observed HVL strata above their minimum HVL while on the current ART regimen to indicate an observed failure diagnosis.	failART.HVLNumIncrease
	ART Regimen Observed Failure Policy	HVL Count	Range of observed HVL (exclusive) strata outside of which is considered to be a failure diagnosis of current ART regimen.	failART.HVLBounds
	ART Regimen Observed Failure Policy	HVL at Setpoint (not suppressed)	Indicates whether patients observed at HVL setpoint would be considered as a diagnosis of failing the current ART regimen.	failART.HVLFailAtSetpoint
	ART Regimen Observed Failure Policy	# Mths post-ART Init	Specifies the number of months since ART initiation after which virologic criteria will be able to count towards diagnosed failure.	failART.HVLMonthsFromInit
	ART Regimen Observed Failure Policy	CD4 Count Percent Drop	Specifies the percentage drop from maximum observed CD4 on the current ART regimen to be considered regimen failure diagnosis.	failART.CD4PercentageDrop
	ART Regimen Observed Failure Policy	CD4 Count Below pre-ART Nadir	Specifies whether or not the CD4 count reaching the pre-ART nadir level should qualify as a diagnoses of observed failure	failART.CD4BelowPreARTNadir
	ART Regimen Observed Failure Policy	(or) CD4 Count	Range of observed CD4 (exclusive) outside of which is considered to be a failure diagnosis of current ART regimen. Will be evaluated independently of the other failure criteria and at least one must be met to diagnose failure.	failART.CD4BoundsOR
	ART Regimen Observed Failure Policy	(and) CD4 Count	Range of observed CD4 (exclusive) outside of which is considered to be a failure diagnosis of current ART regimen. Will be evaluated along with other failure criteria and must also be met to count as a diagnosis.	failART.CD4BoundsAND
	ART Regimen Observed Failure Policy	# Mths post-ART Init	Specifies the number of months since ART initiation after which immunologic criteria will be able to count towards diagnosed failure.	failART.CD4MonthsFromInit
	ART Regimen Observed Failure Policy	OI Event	Specifies the observed OIs that would lead to failing the current line of ART. The user must have the number of OIs specified by the next input to be considered as an observed failure.	failART.OIsEvent
	ART Regimen Observed Failure Policy	# OIs to Fail ART	Number of the appropriate OIs needed to be observed to fail the current ART.	failART.OIsMinNum
	ART Regimen Observed Failure Policy	# Mths Post-ART Init	Number of months after ART initialization to begin counting observed OIs for failing the current ART regimen.	failART.OIsMonthsFromInit
	ART Regimen Observed Failure Policy	# Successive CD4/HVL Tests for Fail Diagnosis	Specifies the number of successive CD4 or HVL tests with observed levels to indicate observed ART regimen failure, the count resets back to zero if a test does not meet failure criteria.	failART.diagnoseNumTestsFail
	ART Regimen Observed Failure Policy	Confirm immunologic or clinical failure with HVL tests	Specifies if HVL tests should also be given to confirm failure after the criteria for immunologic or clinical failure have been reached.	failART.diagnoseUseHVLTestsConfirm

	ART Regimen Observed Failure Policy	Confirm clinical failure with CD4 tests	Specifies if CD4 tests should also be given to confirm failure after the criteria for clinical failure have been reached.	failART.diagnoseUseCD4TestsConfirm
	ART Regimen Observed Failure Policy	# Successive CD4/HVL Tests for Confirmation of Fail Diagnosis	Specifies the number of successive failed CD4/HVL tests that will be used to confirm failure if the above parameter is set, the count resets back to zero if a test does not meet failure criteria.	failART.diagnoseNumTestsConfirm
	ART Regimen Stopping Policy	Max Months on ART	Specifies the maximum number of months patients are allowed to be on the current ART regimen before the regimen is forced to be stopped, even if failure was never observed.	stopART.maxMonthsOnART
	ART Regimen Stopping Policy	On Major Toxicity	Specifies whether or not the regimen should be stopped after a major toxicity occurs, even if failure was never observed.	stopART.withMajorToxicity
	ART Regimen Stopping Policy	Stop Immediately	Specifies that the current ART regimen should be stopped immediately upon observed failure, evaluated only after observed failure	stopART.afterFailImmediate
	ART Regimen Stopping Policy	CurrCD4 <=	Specifies a CD4 lower bound (inclusive) below which the ART regimen should be stopped, evaluated only after observed failure	stopART.afterFailCD4LowerBound
	ART Regimen Stopping Policy	Observed Severe OI	Specifies if the ART regimen should be stopped after the occurrence of a severe OI, evaluated only after observed failure	stopART.afterFailWithSevereOI
	ART Regimen Stopping Policy	# Mths after observed failure	Specifies the number months after observed failure after which the regimen will be stopped, evaluated only after observed failure	stopART.afterFailMonthsFromObserved
	ART Regimen Stopping Policy	Minimum Month #	Specifies the month number after which the criteria for stopping ART will be begin to be evaluated.	stopART.afterFailMinMonthNum
	ART Regimen Stopping Policy	# Mths post-ART init	Specifies the number of months since regimen initiation after which the criteria for stopping ART will be begin to be evaluated.	stopART.afterFailMonthsFromInit
	Primary OI Prophylaxis Starting Policy	AND/OR Condition	Specifies how the various starting critieria are combined: whether one criterion is sufficient to start, or all criteria need to be met.	startProph.useOrEvaluation
	Primary OI Prophylaxis Starting Policy	Current CD4 Range	Specifies the observed current CD4 ranges (inclusive) to have a patient begin primary prophylaxis for a given OI.	startProph.currCD4Bounds
	Primary OI Prophylaxis Starting Policy	Minimum CD4 Range	Specifies the observed minimum CD4 ranges (inclusive) to have a patient begin primary prophylaxis for a given OI.	startProph.minCD4Bounds
	Primary OI Prophylaxis Starting Policy	OI History	Specifies the observed OI history criteria to have a patient begin primary prophylaxis for a given OI. Patient must have a history of at least one of the OIs specified with a 1, and none of the OIs specified with a 0. Criteria will be skipped if all OIs are set to -1.	startProph.OIHistory
	Primary OI Prophylaxis Starting Policy	Current Mth # is at least	Specifies the minimum month number in the simulation before primary prophylaxis may be started, will be evaluated as a precondition before other criteria may be evaluated.	startProph.minMonthNum
	Primary OI Prophylaxis Stopping Policy	AND/OR Condition	Specifies how the various stopping critieria are combined: whether one criterion is sufficient to stop, or all criteria need to be met.	stopProph.useOrEvaluation
	Primary OI Prophylaxis Stopping Policy	Current CD4 Range	Specifies the observed current CD4 ranges (exclusive) outside which the patient will stop primary prophylaxis for a given OI.	stopProph.currCD4Bounds
	Primary OI Prophylaxis Stopping Policy	Minimum CD4 Range	Specifies the observed minimum CD4 ranges (exclusive) outside which the patient will stop primary prophylaxis for a given OI.	stopProph.minCD4Bounds
	Primary OI Prophylaxis Stopping Policy	OI History	Specifies the observed OI history criteria to have a patient stop primary prophylaxis for a given OI. Patient must have a history of at least one of the OIs specified with a 1, and none of the OIs specified with a 0. Criteria will be skipped if all OIs are set to -1.	stopProph.OIHistory
	Primary OI Prophylaxis Stopping Policy	Current Mth # is at least	Specifies the month number in the simulation after which primary prophylaxis will automatically be stopped, will override other criteria for stopping.	stopProph.minMonthNum
	Primary OI Prophylaxis Stopping Policy	# Mths since proph init	Specifies the number of months since prophylaxis initiation after which primary prophylaxis will automatically be stopped, will override other criteria for stopping.	stopProph.monthsOnProph
	Secondary OI Prophylaxis Starting Policy	AND/OR Condition	Specifies how the various starting critieria are combined: whether one criterion is sufficient to start, or all criteria need to be met.	startProph.useOrEvaluation
	Secondary OI Prophylaxis Starting Policy	Current CD4 Range	Specifies the observed current CD4 ranges (inclusive) to have a patient begin secondary prophylaxis for a given OI.	startProph.currCD4Bounds
	Secondary OI Prophylaxis Starting Policy	Minimum CD4 Range	Specifies the observed minimum CD4 ranges (inclusive) to have a patient begin secondary prophylaxis for a given OI.	startProph.minCD4Bounds
	Secondary OI Prophylaxis Starting Policy	OI History	Specifies the observed OI history criteria to have a patient begin secondary prophylaxis for a given OI. Patient must have a history of at least one of the OIs specified with a 1, and none of the OIs specified with a 0. Criteria will be skipped if all OIs are set to -1.	startProph.OIHistory
	Secondary OI Prophylaxis Starting Policy	Current Mth # is at least	Specifies the minimum month number in the simulation before secondary prophylaxis may be started, will be evaluated as a precondition before other criteria may be evaluated.	startProph.minMonthNum
	Secondary OI Prophylaxis Stopping Policy	AND/OR Condition	Specifies how the various stopping critieria are combined: whether one criterion is sufficient to stop, or all criteria need to be met.	stopProph.useOrEvaluation
	Secondary OI Prophylaxis Stopping Policy	Current CD4 Range	Specifies the observed current CD4 ranges (exclusive) outside which the patient will stop secondary prophylaxis for a given OI.	stopProph.currCD4Bounds
	Secondary OI Prophylaxis Stopping Policy	Minimum CD4 Range	Specifies the observed minimum CD4 ranges (exclusive) outside which the patient will stop secondary prophylaxis for a given OI.	stopProph.minCD4Bounds
	Secondary OI Prophylaxis Stopping Policy	OI History	Specifies the observed OI history criteria to have a patient stop secondary prophylaxis for a given OI. Patient must have a history of at least one of the OIs specified with a 1, and none of the OIs specified with a 0. Criteria will be skipped if all OIs are set to -1.	stopProph.OIHistory
	Secondary OI Prophylaxis Stopping Policy	Current Mth # is at least	Specifies the month number in the simulation after which secondary prophylaxis will automatically be stopped, will override other criteria for stopping.	stopProph.minMonthNum
	Secondary OI Prophylaxis Stopping Policy	# Mths since proph init	Specifies the number of months since prophylaxis initiation after which secondary prophylaxis will automatically be stopped, will override other criteria for stopping.	stopProph.monthsOnProph
	OI Prophylaxis Policies	Order of Administering Primary OI Prophylaxes	This is a setting internal to the spreadsheet to select the order of primary prophylaxes for each specific OI type. Prophylaxis information is ultimately input into the simulation program in the order specified here, without this table per se.	

	OI Prophylaxis Policies	Order of Administering Secondary OI Prophylaxes	This is a setting internal to the spreadsheet to select the order of secondary prophylaxes for each specific OI type. Prophylaxis information is ultimately input into the simulation program in the order specified here, without this table per se.	
	Frequency of CD4, HVL Testing	CD4 Threshold	Specifies a threshold of observed CD4 separating the two different periods of CD4/HVL test scheduling. These two periods allow different CD4/HVL test intervals before patients have started first line ART.	testingIntervalCD4Threshold
	Frequency of CD4, HVL Testing	N1, N2	Specifies the months since ART initiation thresholds that separate the different time periods for CD4/HVL testing frequency, can be set differently for all lines before the last line and the last line.	
	Frequency of CD4, HVL Testing	Mths Between CD4 Test	Specifies the number of elapsed patient months from a month with a CD4 test before another regularly scheduled CD4 test is to be given. The CD4 test will be give with the next clinic visit after this time period has elapsed. Note that the regular schedule of CD4 tests may be interrupted by ART initiation tests or ART observed failure confirmatory tests.	CD4TestingIntervalPreARTHighCD4 CD4TestingIntervalPreARTLowCD4 CD4TestingIntervalOnART CD4TestingIntervalOnLastART CD4TestingIntervalPostART
	Frequency of CD4, HVL Testing	Mths Between HVL Test	Specifies the number of elapsed patient months from a month with a HVL test before another regularly scheduled HVL test is to be given. The HVL test will be given with the next clinic visit after this time period has elapsed. Note that the regular schedule of CD4 tests may be interrupted by ART initiation tests or ART observed failure confirmatory tests.	HVLTestingIntervalPreARTHighCD4 HVLTestingIntervalPreARTLowCD4 HVLTestingIntervalOnART HVLTestingIntervalOnLastART HVLTestingIntervalPostART
	Probability of CD4, HVL Test Errors	HVL Test Higher Error Prob	The risk of an inaccurate HVL test resulting in an observed HVL stratum one higher than the patient's current actual HVL stratum, assessed at the point of the HVL test.	probHVLTestErrorHigher
	Probability of CD4, HVL Test Errors	HVL Test Lower Error Prob	The probability of an inaccurate HVL test resulting in an observed HVL stratum one lower than the patient's current actual HVL stratum, assessed at the point of the HVL test.	probHVLTestErrortLower
	Probability of CD4, HVL Test Errors	CD4 Test Std Dev (% of curr)	Determines the error in the observed CD4 count, specified as a percentage of the actual CD4 count that will be used as a standard deviation about the mean value of the actual CD4 count.	CD4TestStdDevPercentage
	Months between Scheduled Clinic Visits		Specifies the number of elapsed patient months from a month with a clinic visit before another regularly scheduled clinic visit is to occur. Note that in the month of an acute OI event, an unscheduled clinic visit for treatment may be triggered.	clinicVisitInterval
	Probability of Detecting OIs in Patient History	Old OI at Prog Entry	Probability that prior OIs in the patient's history are detected in the patient's first clinic visit.	probDetectOIAtEntry
	Probability of Detecting OIs in Patient History	OI Since Last Visit	Probability that OIs in the patient's history since the previous clinic visit are detected in the subsequent clinic visit.	probDetectOISinceLastVisit
	Probability of Switching to Secondary Prophylaxis at Acute OI Event	Prob stop prim. Proph	Specifies the probability that a patient would stop primary prophylaxis for a particular OI and/or be eligible for secondary prophylaxis in the event of detection of that OI.	probSwitchSecondaryProph
	Wait for Regularly Scheduled Clinic Visit to Confirm ART Failure		Specifies whether the special additional HVL or CD4 tests used to confirm observed ART failure could be done outside the context of a regularly scheduled clinic visit.	ARTFailureOnlyAtRegularVisit
	Number HVL Tests Outside Clinic Visit At ART Initiation		If specified value is > 0, a HVL test will be given in the month of ART initiation and the subsequent N-1 number of months.	numARTInitialHVLTests
	Number CD4 Tests Outside Clinic Visit At ART Initiation		If specified value is > 0, a CD4 test will be given in the month of ART initiation and the subsequent N-1 number of months.	numARTInitialCD4Tests
	Emergency Clinic Visits do not count as Scheduled Visits		Specifies whether an emergency clinic visit should affect the regular schedule of clinic visits. If set to true, the OI clinic visit does not reset the number of months until the next clinic visit.	emergencyVisitIsNotRegularVisit
	Lag to CD4 Testing Availability		Determines the lag period (in months) before CD4 testing is available	CD4TestingLag
	Lag to HVL Testing Availability		Determines the lag period (in months) before HVL testing is available	HVLTestingLag
	Monthly Probability of Loss to Follow Up (LTFU)	Use LTFU?	Specifies YES or NO to indicate whether to enable or disable patients becoming LTFU after being linked to care	useLTFU
	Propensity to Respond LTFU Outcome Function (Monthly prob of becoming LTFU)	L1,L2,L1 Value, L2 Value	Response Table for monthly prob of becoming LTFU.	responseThresholdLTFU responseValueLTFU
	OI Prophylaxis Efficacy on Primary OIs		Specifies the multiplicative reduction in the probabilities of OIs, assessed in each patient month when the patient is on the given primary prophylaxis. Also used to determine if the proph is a valid one or is unspecified.	primaryOIEfficacy
	OI Prophylaxis Efficacy on Secondary OIs		Specifies the multiplicative reduction in the probabilities of OIs, assessed in each patient month when the patient is on the given secondary prophylaxis. Also used to determine if the proph is a valid one or is unspecified.	secondaryOIEfficacy
	OI Prophylaxis Toxicity	Minor Prob	Probability of developing minor toxicity while on a particular prophylaxis, assessed at a number of months since prophylaxis initiation. Both minor and major toxicity events cannot occur in the same month.	probMinorToxicity
	OI Prophylaxis Toxicity	Major Prob	Probability of developing major toxicity while on a particular prophylaxis, assessed at a number of months since prophylaxis initiation. Both minor and major toxicity events cannot occur in the same month.	probMajorToxicity
	OI Prophylaxis Toxicity	Mths to Tox	Number of months since OI prophylaxis initiation when the probabilities of minor and major toxicity are assessed.	monthsToToxicity
	OI Prophylaxis Toxicity	Prob Death Major Tox	The probability of mortality from major toxicity, determined in the same month as the toxicity occurs	probDeathMajorToxicity
	OI Prophylaxis Costs & QOL	Mth Cost*	OI prophylaxis cost incurred in each month when the patient is on the prophylaxis.	costMonthly
	OI Prophylaxis Costs & QOL	MinTox Cost	Cost incurred in the event of minor toxicity from a particular OI prophylaxis.	costMinorToxicity
	OI Prophylaxis Costs & QOL	MinTox QOL	Amount of patient QOL multiplier in the month of a minor toxicity event due to a particular prophylaxis.	QOLMinorToxicity

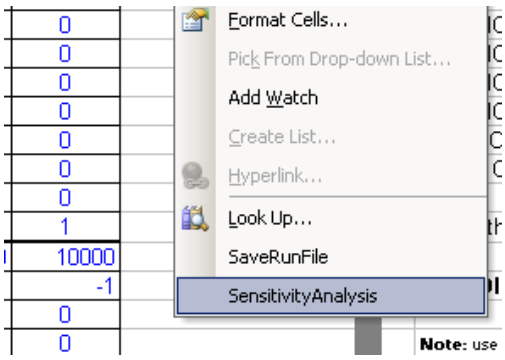
	OI Prophylaxis Costs & QOL	MajTox Cost	Cost incurred in the event of major toxicity from a particular OI prophylaxis.	costMajorToxicity
	OI Prophylaxis Costs & QOL	MajTox QOL	Amount of patient QOL multiplier in the month of a major toxicity event due to a particular prophylaxis.	QOLMajorToxicity
	OI Prophylaxis Switching	Mths from Init	The number of months since prophylaxis initiation after which the current line will be stopped and the patient will be switched to the next line, if one is available	monthsToSwitch
	OI Prophylaxis Switching	On MinTox	Indicates whether or not this prophylaxis should require a switch to the next line after a minor toxicity	switchOnMinorToxicity
	OI Prophylaxis Switching	On MajTox	Indicates whether or not this prophylaxis should require a switch to the next line after a major toxicity	switchOnMajorToxicity
	ART Description		A brief textual description of the ART regimen.	regimenName
	Regimen Cost, Startup		Cost incurred as soon as the patient is initiated on an ART regimen. This is a one-time cost incurred only at ART regimen startup. Also used to determine if the ART regimen is a valid one or is unspecified.	costInitial
	Regimen Cost, Monthly*		Ongoing cost incurred at the end of patient month if the patient is on the ART regimen. Also used to determine if the ART regimen is a valid one or is unspecified.	costMonthly
	Eff Time Horizon		Specifies the number of months after ART regimen initiation constituting the primary, initial efficacy time horizon. Patient will be subject to a monthly probability of late failure or late partial suppression after this time.	efficacyTimeHorizon
	Force Fail at Mth		Specifies number of months after ART initiation when all patients still in suppressed or partially suppressed state to transition into failure state, can be set to -1 to disable.	forceFailAtMonth
	Mth CD4 change on Suppressed ART	N1, N2	Specifies the month bounds after ART initiation for the CD4 effect of suppressed ART regimens.	stageBoundsCD4ChangeOnART
	Mth CD4 change on Suppressed ART	Mean, StdDev	Specifies the slopes of CD4 change for each of the three time stages for patients on suppressed ART. The slope will be drawn once at the beginning of each time period and will remain constant for the remainder of the time period. The specified max patient CD4 level cannot be exceeded. If the nadir CD4 level is reached, the rate of decline cannot exceed the base natural history decline rate.	CD4ChangeOnARTMean CD4ChangeOnARTStdDev
	Mth CD4 change on Partially Suppressed ART	N1, N2	Specifies the month bounds after ART initiation for the CD4 effect of partially suppressed ART regimens.	stageBoundsCD4ChangeOnART
	Mth CD4 change on Partially Suppressed ART	Mean, StdDev	Specifies the slopes of CD4 change for each of the three time stages for patients on partially suppressed ART. The slope will be drawn once at the beginning of each time period and will remain constant for the remainder of the time period. The specified max patient CD4 level cannot be exceeded. If the nadir CD4 level is reached, the rate of decline cannot exceed the base natural history decline rate.	CD4ChangeOnARTMean CD4ChangeOnARTStdDev
	Mth Nat Hist CD4 Multiplier on Failed ART	N1, N2	Specifies the month bounds after ART failure for the CD4 effect of failed ART regimens.	stageBoundsCD4ChangeOnART
	Mth Nat Hist CD4 Multiplier on Failed ART	Multiplier	Specifies the multiplicative factors on natural history CD4 decline for patients who have failed but are not taken off the current ART regimen for each of the three stages. If the nadir CD4 level is reached, the rate of decline cannot exceed the base natural history decline rate.	CD4MultiplierOnFailedART
	Monthly CD4 Std Dev On ART		Specifies a secondary standard deviation that will be used monthly in addition to the CD4 effect while on ART. Used to create some variability around the constant CD4 slopes. Is applied monthly on for all ART efficacy states.	secondaryCD4ChangeOnARTStdDev
	CD4 change multiplier off ART		Specifies the multiplicative factors on natural history CD4 decline for patients who have been taken off the ART regimen. Different multipliers can be specified based on the ART suppression state when they were taken off of ART, and whether or not they have reached their HVL setpoint. If the nadir CD4 level is reached, the rate of decline cannot exceed the base natural history decline rate.	monthlyCD4MultiplierOffArtPreSetpoint monthlyCD4MultiplierOffArtPostSetpoint
	HVL Change Rate	Mth Prob	Monthly probability of the patient's HVL moving the specified number strata towards the target HVL for the fully suppressed, partially suppressed, or failed state.	monthlyProbHVLChange
	HVL Change Rate	Strata /Mth	Number of strata that patient's HVL is changed in the month when patient's HVL is determined to change.	monthlyNumStrataHVLChange
	Toxicity Minor	Prob	Specifies the probability of a minor toxicity occurring after the given number of months from the start of the ART subregimen	toxicity.probToxicity
	Toxicity Minor	Time to tox: Mean (mth) Time to tox: Std Dev (mth)	Specifies the distribution of months until toxicity that will be drawn from when the patient initiates the ART subregimen	toxicity.timeToToxicityMean toxicity.timeToToxicityStdDev
	Toxicity Minor	Tox cost	Specifies the toxicity cost to be applied while the toxicity effect is active	Toxicity.costAmount
	Toxicity Minor	Tox cost duration	Specifies the duration that the toxicity cost will be incurred each month – 0 is one month, 1 is while on this subregimen, 2 is while on this regimen, and 3 is until death	Toxicity.costDuration
	Toxicity Minor	On Tox, Swith to sub-regimen	Specifies the subregimen to switch to upon this toxicity occurring, -1 means the patient will not switch subregimens after a toxicity	Toxicity.switchSubRegimenOnToxicity
	Toxicity Major	Prob	Specifies the probability of a minor toxicity occurring after the given number of months from the start of the ART subregimen	toxicity.probToxicity
	Toxicity Major	Time to tox: Mean (mth) Time to tox: Std Dev (mth)	Specifies the distribution of months until toxicity that will be drawn from when the patient initiates the ART subregimen	toxicity.timeToToxicityMean toxicity.timeToToxicityStdDev
	Toxicity Major	QOL mult	Specifies the QOL multiplier to be applied while the toxicity effect is active	toxicity.QOLMultiplier
	Toxicity Major	QOL duration	Specifies the duration that the QOL multiplier effect will be incurred each month – 0 is one month, 1 is while on this subregimen, 2 is while on this regimen, and 3 is until death	toxicity.QOLDuration
	Toxicity Major	Tox cost	Specifies the toxicity cost to be applied while the toxicity effect is active	toxicity.costAmount
	Toxicity Major	Tox cost duration	Specifies the duration that the toxicity cost will be incurred each month – 0 is one month, 1 is while on this subregimen, 2 is while on this regimen, and 3 is until death	toxicity.costDuration
	Toxicity Major	Acute death prob	Specifies the probability of acute toxicity death occurring the month that the toxicity begins	toxicity.probAcuteDeathMajorToxicity

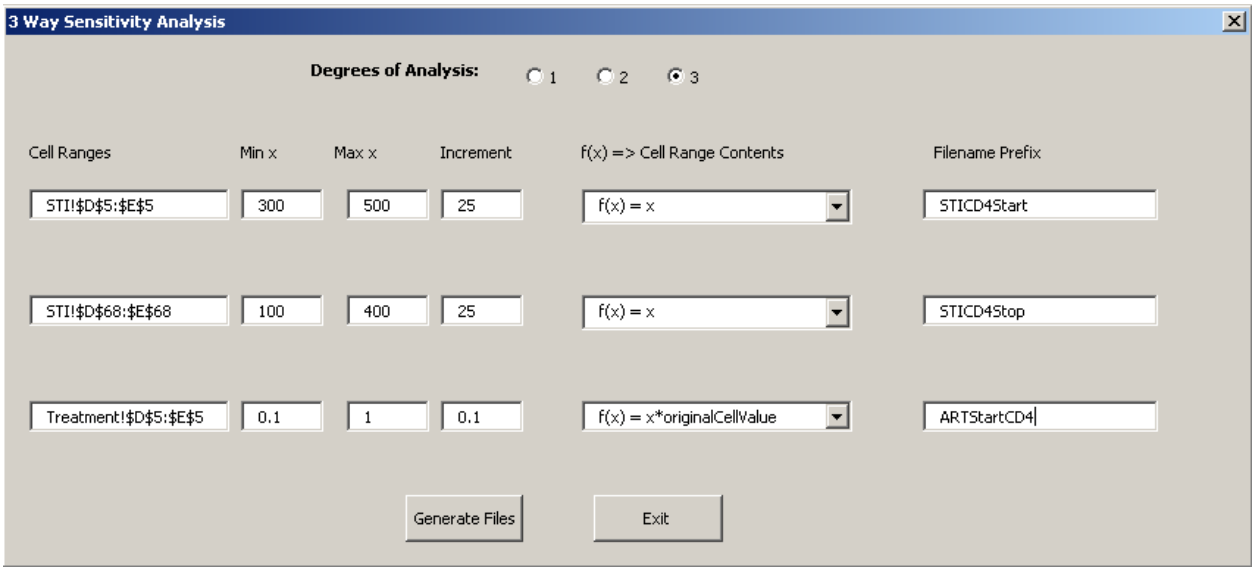
	Toxicity Major	Acute dth cost	Specifies the cost incurred due to acute toxicity death	toxicity.costAcuteDeathMajorToxicity
	Time to swith (mth)		Specifies the number of months since starting the subregimen after which the patient will be switched to the next subregimen, can be set to -1 to disable.	monthsToSwitchSubRegimen
	Chronic AIDS Death Probability	Off ART	Probability of chronic AIDS death assessed in each month that patient is not on a current ART regimen. The probabilities are divided into 3 states: no OI history, history of any OIs except those considered severe, and history of OIs including at least one considered severe.	chronicAIDSDeathProbOffART
	Chronic AIDS Death Probability	On ART	Probability of chronic AIDS death assessed in each month that patient is on a current ART regimen. The probabilities are divided into 3 states: no OI history, history of any OIs except those considered severe, and history of OIs including at least one considered severe.	chronicAIDSDeathProbOnART
	OI Probability, Off ART	No OI History	Probability of acute OI event assessed in each month that patient is not on a current ART regimen. The probability of each OI is pulled from the No OI History table if the patient does not have a history of that specific OI. Only one acute OI event may occur in a given patient month.	monthlyOIProbOffART
	OI Probability, Off ART	OI History	Probability of acute OI event assessed in each month that patient is not on a current ART regimen. The probability of each OI is pulled from the OI History table if the patient has a history of that specific OI. Only one acute OI event may occur in a given patient month.	monthlyOIProbOffART
	OI Probability, On ART Multiplier		A rate multiplier used to adjust the acute OI probabilities for those months when the patient is on a current ART regimen. Note that this table is internal to the spreadsheet; the on ART inputs are fed into the program by multiplying the off ART values.	
	OI Probability, On ART	No OI History	Probability of acute OI event assessed in each month that patient is on a current ART regimen. The probability of each OI is pulled from the No OI History table if the patient does not have a history of that specific OI. Only one acute OI event may occur in a given patient month.	monthlyOIProbOnART
	OI Probability, On ART	OI History	Probability of acute OI event assessed in each month that patient is on a current ART regimen. The probability of each OI is pulled from the OI History table if the patient has a history of that specific OI. Only one acute OI event may occur in a given patient month.	monthlyOIProbOnART
	Death from OI Probability	Treated, No OI Hist	Probability of death from acute OI event. This probability is assessed if the patient is treated for the OI (patient is of type that goes to clinic for OIs) and has not had the OI previously.	probDeathFromOITreated
	Death from OI Probability	Treated, OI History	Probability of death from acute OI event. This probability is assessed if the patient is treated for the OI (patient is of type that goes to clinic for OIs) and has had the OI previously.	probDeathFromOITreated
	Death from OI Probability	Untreated, No OI Hist	Probability of death from acute OI event. This probability is assessed if the patient is not treated for the OI (patient is of type that does not go to clinic for OIs) and has not had the OI previously.	probDeathFromOIUntreated
	Death from OI Probability	Untreated, OI History	Probability of death from acute OI event. This probability is assessed if the patient is not treated for the OI (patient is of type that does not go to clinic for OIs) and has had the OI previously.	probDeathFromOIUntreated
	Baseline CD4 Decline, Monthly	Mean, Std Dev	Distribution of monthly CD4 decline for patient not on effective ART regimen and not in lag period to baseline CD4 decline after ART failure. Amount of CD4 decline determined each month independently by mean and standard deviation.	monthlyCD4DeclineMean monthlyCD4DeclineStdDev
	Baseline CD4 Decline, Monthly	Between Subject	Std Deviation of CD4 decline for each specific patient. Drawn once for each person at start.	monthlyCD4DeclineBtwSubject
	Non AIDS Death Probability		Probability of non AIDS death based on age and gender, used monthly to determine mortality from non AIDS causes.	monthlyNonAIDSDeathProb
	Acute OI Event Costs	Off-ART, Treated	Cost incurred at an acute OI event, when the patient is treated for the OI (patient is of type that goes to clinic for OIs) and is not on a current ART regimen.	acuteOICostTreated
	Acute OI Event Costs	Off-ART, Untreated	Cost incurred at an acute OI event, when the patient is not treated for the OI (patient is of type that does not go to clinic for OIs) and is not on a current ART regimen.	acuteOICostUntreated
	Acute OI Event Costs	On-ART, Treated	Cost incurred at an acute OI event, when the patient is treated for the OI (patient is of type that goes to clinic for OIs) and is on a current ART regimen.	acuteOICostTreated
	Acute OI Event Costs	On-ART, Untreated	Cost incurred at an acute OI event, when the patient is not treated for the OI (patient is of type that does not go to clinic for OIs) and is on a current ART regimen.	acuteOICostUntreated
	CD4 Test Costs		Cost incurred at the time of an administered CD4 test.	CD4TestCost
	HVL Test Costs		Cost incurred at the time of an administered HVL test.	HVLTestCost
	Death Costs	Off-ART, Treated	Cost incurred in the event of an OI death, chronic AIDS death, or non AIDS death. The cost is assessed when the patient is not on a current ART regimen and, for an OI death, when the OI event is treated (patient is of type that goes to clinic for OIs).	deathCostTreated
	Death Costs	Off-ART, Untreated	Cost incurred in the event of an OI death, chronic AIDS death, or non AIDS death. The cost is assessed when the patient is not on a current ART regimen and, for an OI death, when the OI event is not treated (patient is of type that does not go to clinic for OIs).	deathCostUntreated
	Death Costs	On-ART, Treated	Cost incurred in the event of an OI death, chronic AIDS death, or non AIDS death. The cost is assessed when the patient is on a current ART regimen and, for an OI death, when the OI event is treated (patient is of type that goes to clinic for OIs).	deathCostTreated
	Death Costs	On-ART, Untreated	Cost incurred in the event of an OI death, chronic AIDS death, or non AIDS death. The cost is assessed when the patient is on a current ART regimen and, for an OI death, when the OI event is not treated (patient is of type that does not go to clinic for OIs).	deathCostUntreated
	Contact/Visit Costs		Cost incurred at the time of each clinical contact/visit with each patient.	clinicVisitCost
	Routine Care Costs	HIV-neg	Routine state cost incurred for HIV-negative patients, stratified by gender and age.	routineCareCostHIVNegative
	Routine Care Costs	HIV-pos, Off-ART	Routine state cost incurred for HIV-negative patients that are not on ART, stratified by CD4, gender, and age.	routineCareCostHIVPositive

	Routine Care Costs	HIV-pos, On-ART	Routine state cost incurred for HIV-negative patients that are on ART, stratified by CD4, gender, and age.	routineCareCostHIVPositive

E1. Sensitivity Analysis Tool

Starting with version cepac30i, an automated linear sensitivity analysis tool has been made available. This tool allows the user to quickly create input files for one-way, two-way, and three-way sensitivity analyses. The macro can be invoked by right clicking anywhere on the input spreadsheet and selecting the 'SensitivityAnalysis' option. The '3 Way Sensitivity Analysis' form will then pop-up –





To use this form:

- Select desired degree of analysis. If user selects 1 degree, then the boxes for the 2 – 3 way analyses will be grayed out.
- For each desired degree of analysis
  - Double-click on form Cell Ranges. A pop-up window will allow you to select cells from any sheet within the workbook. If you have already selected those cells for another degree, a user prompt will ask you to pick different cells.
  - Select the f(x) you wish to use to fill in the selected input sheet values
  - Select the min and max value of x that will be used to fill in the selected input sheet values. The increment will determine which values are used between the min and max.

- Enter a 'Filename Prefix' for the degree of analysis. This prefix will appear in the filenames of the generated input sheet so that you can identify the sensitivity analysis data point.

- Click Generate Files
- A file dialog will ask you to name a directory and base filename for all generated input sheets. Enter a filename and click 'Save'
- The sensitivity analysis tool will now generate the input files that correspond to each data point of the sensitivity analysis. It does this by replacing the selected cells with the value of f(x) for each x that was indicated. It will create input sheets for all combinations of f(x) of each degree of analysis.

For the example inputs on the above file, if we were to choose a base filename of exampleSA, the tool will create files (with the indicated values in the selected input cells) that are named:

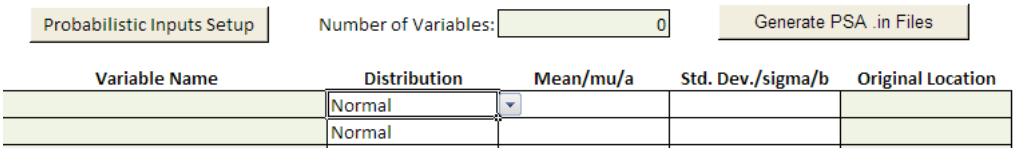
exampleSA,STICD4Start=300,STICD4Stop=100,ARTSTARTCD4=0.1.in
exampleSA,STICD4Start=300,STICD4Stop=100,ARTSTARTCD4=0.2.in
exampleSA,STICD4Start=300,STICD4Stop=100,ARTSTARTCD4=0.3.in
…
exampleSA,STICD4Start=300,STICD4Stop=125,ARTSTARTCD4=0.1.in
exampleSA,STICD4Start=300,STICD4Stop=125,ARTSTARTCD4=0.2.in
exampleSA,STICD4Start=300,STICD4Stop=125,ARTSTARTCD4=0.3.in
…
exampleSA,STICD4Start=300,STICD4Stop=150,ARTSTARTCD4=0.1.in
exampleSA,STICD4Start=300,STICD4Stop=150,ARTSTARTCD4=0.2.in
exampleSA,STICD4Start=300,STICD4Stop=150,ARTSTARTCD4=0.3.in
…
…

This will happen until all combinations of the values of STICD4Start, STICD4Stop, and ARTSTARTCD4 have been generated.

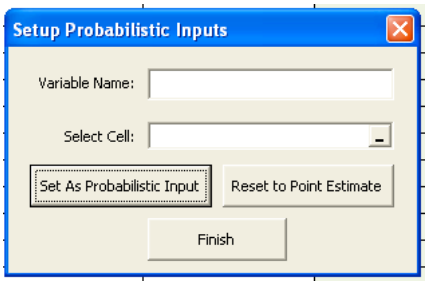
E2. Probabilistic Sensitivity Analysis Tool

In addition to the regular sensitivity analysis tool, a Probabilistic Sensitivity Analysis (PSA) tool was added starting in version cepac41. This has been debugged and implemented for the adolescent/adult model (age >13 years), and will be added to the Pediatric model as part of proposed work. PSA works by having the user specify distributions for a number of input parameters and the tool generates input sets by performing random draws from these distributions. Such an analysis is useful for accounting for the uncertainty in input parameters and the affects of this uncertainty on the outcomes. This is different from the "3-way Sensitivity Analysis" tool discussed previously which instead focuses on how hypothetical changes to input parameters will affect outcomes.

A Probabilistic Sensitivity Analysis can be setup under the "Probabilistic Params" tab of the inputs workbook with the "Probabilistic Inputs Setup" and the "Generate PSA .in Files" buttons, and the parameters table –



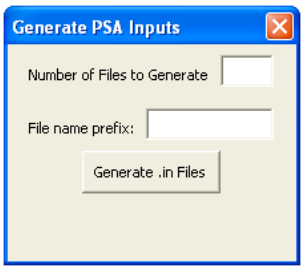
The "Probabilistic Inputs Setup" allows the user to specify parameters for PSA and brings up the following dialog when run –



For each parameter of the PSA run, the user must specify a unique name for this input. The user can then select a range of worksheet cells for the input values to be modified. This can either be specified by manually writing the range identifier, or clicking in the "Select Cell" value and selecting the range from the spreadsheet. Once the input is specified, click on the "Set As Probabilistic Input" to add it as a PSA input. To remove a PSA input from the selected list, click on the "Reset to Point Estimate" button. This script can also be invoked by right clicking anywhere in the Excel workbook and selecting it from the menu.

The user can specify the distributions for the selected PSA input parameters in the table under the "Probabilistic Parameters" tab. The available distributions for selection are normal, log normal, and beta. The mean/mu/a and stdDev/sigma/b parameters for these distributions can then be specified in the appropriate column. There is also a "Parameter Help" section that generates the mean and standard deviations for different settings of the log normal and beta distribution parameters.

Once all of the parameters and their distributions have been set, the "Genera PSA .in Files" macro can be invoked to create the input files –



The user can specify the number of input files to generate and a prefix for the name of the input files. After clicking on the "Generate .in Files" button, the files will be created in the same directory as the input sheet and be named "<prefix><file #>.in". After PSA is finished, all input parameters should be reset back to their initial values using the "Probabilistic Inputs Setup" macro and the "Reset to Point Estimate".

F. Program Outputs of the Model

F1. Cohort Summary File

At the end of program execution, the program writes primary outcomes of the batch of runs to the `popstats.out` file. If the file does not exist, the program creates one with that name; if it already exists, the program appends to that file. It is important not to access the file, especially during program execution. If the file cannot be modified, the program will write the output to a new file, `popstats.out-tmp`.

The `popstats.out` file is tab-delimited and uses one line for each completed run. Information for each run includes average projected costs, average expected life months, average expected quality-adjusted life months, and the numbers of primary OI events per thousand patients. The runs are ordered by set, and by cost in ascending order. Incremental cost effectiveness ratios are calculated for runs within the same set. This ratio is

defined as the additional cost divided by its additional clinical benefit (i.e. life months or quality-adjusted life months), compared to the next least costly strategy.

The initial columns of the summary file are as follows:

		RUN DATE	RUN TIME		TOTAL COHORT					HIV+ PATIENTS		
RUN SET	RUN NAME			Cohort	COST	LMs	QALMs	COST/LY	Cost/QALY	COST	LMs	QALMs
DefaultSet	noTst-3%dsc	12/17/2001	22:11:55	18347	46870	238.125	231.052			85992	215.574	202.598
DefaultSet	HIVtst-3%dsc	12/17/2001	22:11:46	18538	61475	242.484	235.076	dominated	dominated	111745	223.467	209.735
DefaultSet	noTst-0%dsc	12/17/2001	22:11:51	18347	92477	399.282	386.144	3396	3529	169668	338.864	314.760
DefaultSet	HIVtst-0%dsc	12/17/2001	22:11:40	18538	120022	407.916	394.061	38281	41753	218753	354.772	329.087

The remaining columns are:

PRIMARY OI CASES PER THOUSAND HIV+ PATIENTS							DTHS /1000		
pcp	mac	toxo	cmv	fungal	bactl	other	chrAIDS	nonAIDS	toxART
290.2	85.4	35	183.5	134	0	367.4	660.3	203.3	0
235.6	79.6	35.7	188.2	141.4	0	362.2	621.7	244.6	0
290.2	85.4	35	183.5	134	0	367.4	660.3	203.3	0
235.6	79.6	35.7	188.2	141.4	0	362.2	621.7	244.6	0

F2. Run Summary File

At the completion of each run, an output summary file is created with the file extension "`.out`" describing the results of the run. The output summary file of each run is a tab delimited text file, and can loaded by programs such as Microsoft Excel for viewing. The file contains the results of the cohort simulation, which will be described below.

If the file cannot be modified, the output will instead be written to a file with the extension "`.out-tmp`"

F2a. Broad Measures

The very first section of the file characterizes broad measures:

POPULATION SUMMARY MEASURES (run completed 11/05/09,14:41:27)
[Program version 40a, build 2009-11-03]

Outcome/Measure	Average	Std Dev	LB	UB
Costs	98257	62072	97040	99473
Life Months	113.9894	66.4215	112.6876	115.2913
Quality-Adj Life Mths	99.0623	58.739	97.911	100.2135
	Avg Costs	Avg LMs	Avg QALMs	
Up to 0 ART(s) obsv fail	55271	53.1263	46.62	
Up to 1 ART(s) obsv fail	64815	59.2301	51.8512	
Up to 2 ART(s) obsv fail	69218	62.2393	54.4455	
Up to 3 ART(s) obsv fail	71629	64.2679	56.2187	
Up to 4 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 5 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 6 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 7 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 8 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 9 ART(s) obsv fail	98257	113.9894	99.0623	
Up to 10 ART(s) obsv fail	98257	113.9894	99.0623	
Total Clinic Visits	395471			
Only HIV+ patients	98850	113.9019	98.9393	

The first and second lines indicate the date and time the run was completed, and the version and build of the executable program. These items are intended to aid in bookkeeping, in particular noting when and how the file was produced.

The first table specifies the mean, standard deviation, and 95% confidence interval (specified by lower and upper bounds) of aggregate cohort costs in discounted dollars and life expectancies in discounted life months and discounted quality-adjusted life months. The second table describes a cross section of costs and life expectancies as the cohort progresses through each line of ART. "`Up to 0 ART(s) obsv fail`" describes all costs and life months accrued by patients before they are observed to have failed any ART regimen; "`Up to 1 ART(s) obsv fail`" describes all costs and life months accrued by patients observed to have failed at least one ART regimen; and so on.

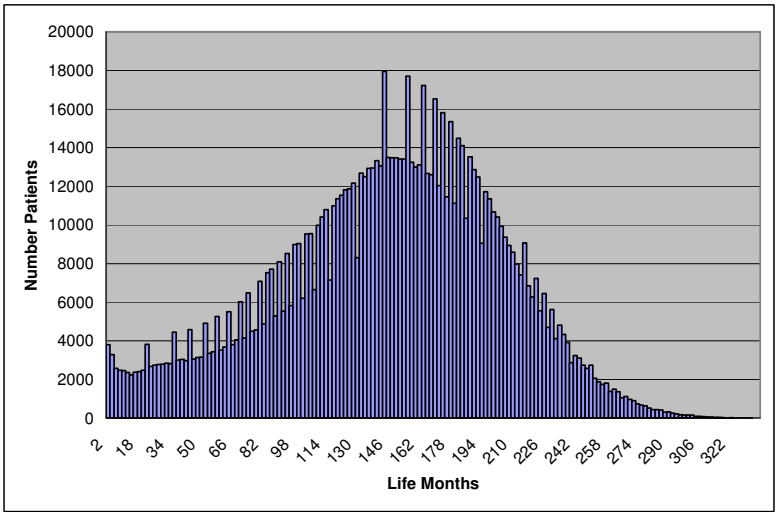
The last line indicates the total number of clinic visits made in the cohort simulation.

F2b. Detailed Life Expectancy

Next is a breakdown of patients' discounted life expectancy:

LIFE MONTH SURVIVAL OF ENTIRE COHORT							
LM bucket (UB, excl):	2	4	6	8	10	12	14
# Patients:	146	144	126	102	78	102	97
LM Min:	0.5		LM Max:	341.5195			
LM Median:	116.7788		LM AvgDev:	54.6104			
LM Mean:	113.9894		LM StdDev:	66.4215		LM AvgDev:	54.6678
LM Variance:	4411.8111		LM Skew:	0.1303		LM Kurtosis:	-0.595
Cost Mean:	98256.66		Cost StDv:	62072.32			
QALM Mean:	99.0623		QALM StDv:	58.739			
LIFE MONTH SURVIVAL EXCLUDING LONGEST 5% (500 patients)							
LMs							
LM bucket (UB, excl):	1	2	3	4	5	6	7
# Patients:	84	62	74	70	66	60	55
LM Min:	0.5		LM Max:	223.7071			
LM Median:	113.1888		LM AvgDev:	50.3534			
LM Mean:	106.804		LM StdDev:	59.8727		LM AvgDev:	50.5885
LM Variance:	3584.7421		LM Skew:	-0.1292		LM Kurtosis:	-1.0044
Cost Mean:	97696.06		Cost StDv:	61224.6			
QALM Mean:	92.4806		QALM StDv:	52.3245			
LIFE MONTH SURVIVAL EXCLUDING SHORTEST 5% (500 patients)							
LMs							
LM bucket (UB, excl):	9	11	13	15	17	19	21
# Patients:	59	90	100	89	84	88	105
LM Min:	7.44		LM Max:	341.5195			
LM Median:	121.731		LM AvgDev:	51.3866			
LM Mean:	119.8038		LM StdDev:	62.9892		LM AvgDev:	51.4047
LM Variance:	3967.6381		LM Skew:	0.1674		LM Kurtosis:	-0.482
Cost Mean:	102450.74		Cost StDv:	60746.4			
QALM Mean:	104.1193		QALM StDv:	55.8587			
LIFE MONTH SURVIVAL EXCLUDING LONGEST & SHORTEST 5% (1000 patients)							
LMs							
LM bucket (UB, excl):	8	9	10	11	12	13	14
# Patients:	18	41	37	53	49	51	46
LM Min:	7.44		LM Max:	223.7071			
LM Median:	116.7788		LM AvgDev:	46.9563			
LM Mean:	112.5422		LM StdDev:	56.1964		LM AvgDev:	47.0962
LM Variance:	3158.0327		LM Skew:	-0.1269		LM Kurtosis:	-0.9322
Cost Mean:	102092		Cost StDv:	59790.8			
QALM Mean:	97.453		QALM StDv:	49.1934			

These statistics were intended only for debugging of patient survival. The model keeps track of only the first 1,000,000 HIV-positive patients to avoid excessive memory usage. The number of patients in each LM bucket can be used to produce a histogram of patient survival by life months, as in the following graph of a run with 1 million patients:



F2c. Initial Characteristics

Next is a section describing the initial characteristics of the cohort:

INITIAL DISTRIBUTIONS							
CD4 Count Level	# Patients		HVL Setpt Lvl	# Patients		Curr HVL Lvl	# Patients
VHI (>500)	6325		VHI (>100k)	0		VHI	0
HI (300-500)	1762		HI (30k-100k)	2544		HI	2544
MHI (200-300)	1095		MHI (10k-30k)	2516		MHI	2516
MLO (100-200)	389		MED (3k-10k)	2451		MED	2451
LO (50-100)	123		MLO (500-3k)	1574		MLO	1574
VLO (0-50)	246		LO (20-500)	855		LO	855
			VLO (0-20)	0		VLO	0
Avg Init Age(Mths):	417						
			Female				
Male Patients:	9940		Patients:	0			
	PCP	MAC	TOXO	CMV	FUNG	BACT	NONE1
Prior OI Histories Distrib:	410	435	435	414	377	0	0

The first set of tables here describes the distribution of patients on entry to the model by CD4 strata (for children <5 years of age, this is shown as CD4%), HVL setpoints, and actual HVL. The other statistics are the average age (in months), gender breakdown, and numbers of patients with histories of each OI type at the time of initialization.

F2d. Opportunistic Infections and Death Events

The following tables describe the numbers of OI events (shown here is an example for adults in US-based runs):

OI SUMMARIES					
Type/OI	PCP	MAC	TOXO	CMV	FUNG
# Primary OIs	2300	796	237	1163	680
# Secondary OIs	286	410	231	8473	51
Primary OIs	PCP	MAC	TOXO	CMV	FUNG
CD4vhi	197	50	27	44	50
CD4_hi	137	67	25	54	53
CD4mhi	273	55	32	115	54
CD4mlo	627	126	27	126	142
CD4_lo	403	107	44	125	113
CD4vlo	663	391	82	699	268
Secondary OIs	PCP	MAC	TOXO	CMV	FUNG
CD4vhi	64	145	131	2462	21
CD4_hi	28	49	47	664	8
CD4mhi	33	45	24	807	4
CD4mlo	53	37	9	727	7
CD4_lo	29	27	4	421	5

CD4vlo	79	107	16	3392	6
Detected OIs	PCP	MAC	TOXO	CMV	FUNG
CD4vhi	500	447	385	2447	304
CD4_hi	226	185	125	720	112
CD4mhi	338	135	100	856	98
CD4mlo	621	169	48	784	150
CD4_lo	414	129	41	502	115
CD4vlo	744	480	89	3717	276
Total	2843	1545	788	9026	1055

The first table details the total number of OI events of the cohort. Primary OIs are defined as the first occurrence of each OI type for each patient. Any subsequent OI event of the same type as one in each patient's history is accrued as a secondary OI. Incidence of primary OIs, secondary OIs, and detected OIs is further broken down by patients' actual CD4 strata in the month of those events.

The following tables provide results of the optional OI history logging mechanism, if not enabled these values will all be N/A. Actual outputs provide results for each program defined OI type – only PCP and MAC are given here for reasons of brevity.

PRIOR OI HIST PROB AS PROPORTION OF PATIENTS (LOGGED)

OI: pcp	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total
HVLvhi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HVL_hi	N/A	0	0.166666667	0	0	0.6	0.16
HVLmhi	N/A	0	0.166666667	0.333333	0	0	0.085714
HVLmed	N/A	0	0.25	0.333333	0.5	1	0.222222
HVLmlo	N/A	0.333333	0	0	0.666667	N/A	0.333333
HVL_lo	N/A	0	0	N/A	0	N/A	0
HVLvlo	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total	N/A	0.0625	0.15	0.2	0.333333	0.5	
OI: mac	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total
HVLvhi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HVL_hi	N/A	0	0	0	0	0.4	0.08
HVLmhi	N/A	0	0	0	0	0.5	0.028571
HVLmed	N/A	0	0	0.333333	0	0	0.055556
HVLmlo	N/A	0	0	0	0	N/A	0
HVL_lo	N/A	0	0.333333333	N/A	0	N/A	0.142857
HVLvlo	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total	N/A	0	0.05	0.066667	0	0.375	

…

PRIOR OI HIST PROB BY PATIENT MTHS (LOGGED)

OI: pcp	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total
HVLvhi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HVL_hi	0.293006	0.114973	0.139784946	0.150289	0.233766	0.142857	0.193294
HVLmhi	0.099432	0.05896	0.056372549	0.09611	0.090426	0.009404	0.070524
HVLmed	0.098985	0.141689	0.191836735	0.145833	0.22807	0.235294	0.134284
HVLmlo	0.123649	0.041588	0.15819209	0.068966	0.130435	0.027027	0.095211
HVL_lo	0.097054	0.101907	0.139186296	0.101933	0.151832	0.184211	0.107087
HVLvlo	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total	0.120502	0.088906	0.12744437	0.108944	0.148479	0.092616	
OI: mac	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total
HVLvhi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
HVL_hi	0.166352	0.168449	0	0	0.090909	0.087912	0.114398
HVLmhi	0.008523	0.001156	0	0	0	0.144201	0.018144
HVLmed	0.007614	0.002725	0.204081633	0.140625	0.017544	0.323529	0.057041
HVLmlo	0.010804	0.00189	0.016949153	0.017241	0.021739	0	0.009014
HVL_lo	0.027946	0.015495	0.047109208	0.010545	0.010471	0.105263	0.026119
HVLvlo	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total	0.033261	0.024128	0.050573163	0.023537	0.019678	0.116395	

…

The first section details the proportion of patients with a history of each OI type by patients' current actual CD4 and HVL. Note that this proportion represents an arbitrary month for each patient, specifically the first month for each patient in which the OI history logging criteria apply. There are two primary reasons for this. Because the OI history logging mechanism is intended to bootstrap the OI history characteristics of some randomized cohort at some particular point in time, it makes sense to use at most one arbitrary month for each patient and imagine all such selected patient months as concurrent for the desired cohort. Second, picking other specific,

non-random points in time may skew cohort characteristics – for example, using the patients' last months of life skews results away from a truly randomized starting cohort.

The second section details the proportion of patient months with a history of each OI type by patients' current actual CD4 and HVL. The actual calculation of this proportion of patient months with a given OI history over the total number of patient months is described in more detail in the *Prior OI History at Entry and Logging Mechanism* description.

The following tables detail statistics about death events:

CAUSES OF DEATH					
CD4 Count Level	PCP	MAC	TOXO	CMV	FUNG
CD4vhi	9	5	28	129	4
CD4_hi	4	4	9	41	3
CD4mhi	12	5	8	35	1
CD4mlo	37	10	11	44	5
CD4_lo	13	9	12	23	3
CD4vlo	16	19	18	185	8
# Deaths	91	52	86	457	24
HIVnegs	N/A	N/A	N/A	N/A	N/A
Death Distrib	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo
HVLvhi	0	0	0	0	0
HVL_hi	339	188	173	248	154
HVLmhi	422	214	219	250	157
HVLmed	483	223	234	322	175
HVLmlo	408	186	187	232	124
HVL_lo	230	102	106	96	53
HVLvlo	155	30	19	9	2

The total number of deaths is given by each possible cause of death, as well as stratified by CD4 level at the time of death. The possible causes of death include acute OI, chronic AIDS, non AIDS, and ART toxicity. The second table shows the distribution of CD4 and HVL levels at the time of death.

F2e. Aggregate Survival and Costs

The following sections describe the total life months and costs accrued by the simulated cohort:

Total discounted life months accrued by all patients in the cohort are broken down by several dimensions. The first table (below) breaks down overall life months by current actual CD4 strata of each patient month, and by whether the patient has a history of any OI.

OVERALL SURVIVAL							
CD4 Strata:	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total
Life Months [woOIHist]	395317	161711	122366	61104	21232	35496	797226
Life Months [w.OIHist]	57224	21321	18733	16720	10443	31416	155858
Life Months [Total]	452541	183032	141099	77824	31674	66912	953084
HVL Strata:	HVLvhi	HVL_hi	HVLmhi	HVLmed	HVLmlo	HVL_lo	HVLvlo
Life Mths, HVL Setpt	0	222985	238981	242141	151236	97741	0
Life Mths, Curr HVL	0	167512	202850	228038	178645	117761	58277
OI:	PCP	MAC	TOXO	CMV	FUNG	BACT	NONE1
Life Mths, no OI hist	906147	927408	936371	933161	930041	953084	953084
Life Mths, with OI hist	46937	25676	16713	19923	23043	0	0
	HIVneg	unidentHIV+	identHIV+	(HIVpos)			
LMs by HIV State:	186810	61553	891531	953084			
	LMs	QALMs					
LMs in HIV Scr Module:	186810	172633		LMs in "Reg CEPAC":	953084		

The second table (below) breaks down total life months by patients' HVL setpoints and by patients' current actual HVL strata. This table breaks down for each OI the total number of patient months spent with and

without a history of that OI. The total life months and quality-adjusted life months accrued in the HIV screening module as well as the total life months spent in the cohort simulation outside of the HIV screening module are given at the end.

OVERALL COSTS								
CD4 Strata:	CD4vhi	CD4_hi	CD4mhi	CD4mlo	CD4_lo	CD4vlo	Total	
Costs [woOIHist]	276614259	137953754	119893892	62323143	18461623	53050844	668297515	
Costs [w.OIHist]	95401386	39138830	37013492	31151257	15877097	95686974	314269036	
Costs [Total]	372015646	177092584	156907384	93474399	34338720	148737818	982566551	
HVL Strata:	HVLvhi	HVL_hi	HVLmhi	HVLmed	HVLmlo	HVL_lo	HVLvlo	
Costs, HVL Setpt	0	239856994	242245013	231266408	135547129	133651006	0	
Costs, Curr HVL	0	151179269	184263268	208843649	179905709	165501466	92873190	
Direct Proph Costs	PCP	MAC	TOXO	CMV	FUNG	BACT	NONE1	NONE2
Proph 1	0	0	0	0	0	0	0	0
Proph 2	0	0	0	0	0	0	0	0
Proph 3	0	0	0	0	0	0	0	0
Total Proph Costs	0	0	0	0	0	0	0	0
	ART 1	ART 2	ART 3	ART 4	ART 5	ART 6	ART 7	ART 8
Direct ART Costs:	110315226	86480953	72058628	61572022	0	0	0	0
	CD4 Tests	HVL Tests	ClinicVisits					
Testing Costs:	26843141	39920632	0					
	Tests	Misc						
HIV Screening Costs:	0	0						
	Direct Medical	DirectNon Medical	TimeCosts	Indirect	Unclassified		DrugCosts	Toxicity
Total Undiscounted Costs:	884435835	0	0	0	0		413736214	0

Like total cohort life months, overall discounted costs accrued by all the patients are broken down by current actual CD4 (with and without any history of an OI), and HVL setpoint and current actual HVL strata. The discounted direct costs of drugs and testing incurred by the entire cohort are given for all the possible prophylaxis drugs, ART regimens, and CD4 and HVL testing strategies. Total undiscounted costs are also given in the final table for the various classifications of total costs, and drug and toxicity costs.

F2f. Prophylaxis

This section simply summarizes the total number of minor and major toxicity events due to OI prophylaxes:

OI PROPH TOXICITY EVENTS							
Minor Tox Events	pcp	mac	toxo	cmv	fungal	bactl	other
Proph 1	8	0	0	0	0	0	0
Proph 2	0	0	0	0	0	0	0
Proph 3	0	0	0	0	0	0	0
Proph 4	0	0	0	0	0	0	0
Proph 5	0	0	0	0	0	0	0
Total	8	0	0	0	0	0	0
Major Tox Events	pcp	mac	toxo	cmv	fungal	bactl	other
Proph 1	3	0	0	0	0	0	0
Proph 2	0	0	0	0	0	0	0
Proph 3	0	0	0	0	0	0	0
Proph 4	0	0	0	0	0	0	0
Proph 5	0	0	0	0	0	0	0
Total	3	0	0	0	0	0	0

The following section details the number of primary/secondary OI prophylaxis that were initiated, and the true CD4 and observed CD4 at the time of initiation -

PRIMARY OI PROPH MEAN CD4 AT INIT									
	Proph1 True	Obsv CD4	Times Init'd	Proph2 True	Obsv CD4	Times Init'd	Proph3 True	Obsv CD4	Times Init'd
BCIM	0	0	0	0	0	0	0	0	0
BCIS	0	0	0	0	0	0	0	0	0
FNGM	0	0	0	0	0	0	0	0	0
FNGS	0	0	0	0	0	0	0	0	0
MLR	0	0	0	0	0	0	0	0	0
ISO	0	0	0	0	0	0	0	0	0
TOXO	0	0	0	0	0	0	0	0	0

MAC	0	0	0	0	0	0	0	0	0
PCP	0	0	0	0	0	0	0	0	0
NONE1	0	0	0	0	0	0	0	0	0
NONE2	0	0	0	0	0	0	0	0	0
NONE3	0	0	0	0	0	0	0	0	0
NONE4	0	0	0	0	0	0	0	0	0
OTHM	0	0	0	0	0	0	0	0	0
OTHS	0	0	0	0	0	0	0	0	0

SECONDARY OI PROPH MEAN CD4 AT INIT

	Proph1 True	Obsv CD4	Times Init'd	Proph2 True	Obsv CD4	Times Init'd	Proph3 True	Obsv CD4	Times Init'd
BCIM	0	0	0	0	0	0	0	0	0
BCIS	0	0	0	0	0	0	0	0	0
FNGM	0	0	0	0	0	0	0	0	0
FNGS	0	0	0	0	0	0	0	0	0
MLR	0	0	0	0	0	0	0	0	0
ISO	0	0	0	0	0	0	0	0	0
TOXO	0	0	0	0	0	0	0	0	0
MAC	0	0	0	0	0	0	0	0	0
PCP	0	0	0	0	0	0	0	0	0
NONE1	0	0	0	0	0	0	0	0	0
NONE2	0	0	0	0	0	0	0	0	0
NONE3	0	0	0	0	0	0	0	0	0
NONE4	0	0	0	0	0	0	0	0	0
OTHM	0	0	0	0	0	0	0	0	0
OTHS	0	0	0	0	0	0	0	0	0

F2g. ART Statistics

This first section details the number of months in each suppression state for each ART line, stratified by the patient's true HVL that month -

MONTHS IN SUPPRESSED/PARTIALLY SUPPRESSED/FAILED STATES ON ART

	ART1	ART2	ART3	ART4	ART5	ART6	ART7	ART8	ART9	ART10	Total
Months suppressed	32998	23809	17704	13412	0	0	0	0	0	0	87923
Months partially suppressed											
HVLvhi	0	0	0	0	0	0	0	0	0	0	0
HVL_hi	5471	4180	2617	2111	0	0	0	0	0	0	14379
HVLmhi	5920	4428	3205	2294	0	0	0	0	0	0	15847
HVLmed	6868	5051	3591	2692	0	0	0	0	0	0	18202
HVLmlo	3512	2782	1842	1353	0	0	0	0	0	0	9489
HVL_lo	2113	1520	1152	834	0	0	0	0	0	0	5619
HVLvlo	0	0	0	0	0	0	0	0	0	0	0
Total	23884	17961	12407	9284	0	0	0	0	0	0	
Months failed											
HVLvhi	13221	11575	8232	6237	0	0	0	0	0	0	39265
HVL_hi	7161	6401	4703	3616	0	0	0	0	0	0	21881
HVLmhi	5613	4525	3340	2528	0	0	0	0	0	0	16006
HVLmed	3846	2957	2125	1665	0	0	0	0	0	0	10593
HVLmlo	2893	2073	1507	1214	0	0	0	0	0	0	7687
HVL_lo	2059	1498	1068	880	0	0	0	0	0	0	5505
HVLvlo	0	0	0	0	0	0	0	0	0	0	0
Total	34793	29029	20975	16140	0	0	0	0	0	0	

Each line of ART regimen is summarized as follows:

ART 1 STATS

	# Total	# Supp	Avg TrueCD4	Avg ObsvCD4	#Drawn Supp	#Drawn Part Supp	#Drawn Fail
At Init:	9989	791	584	584	8458	0	1531

	# Total	AvgTrueCD4	AvgObsvCD4	MthsToFail(Mean)	MthsToFail(StdDev)
At ART true fail:	9646	1026.45	1013.65	44.46	43.55

At ART obsv fail:	# Total	# with true fail	AvgTrueCD4	AvgObsvCD4	MthsToObsvFail(Mean)	MthsToObsvFail(StdDev)
Any fail diagnosis	9591	9591	1004.86	1009.82	49.58	43.73
Virologic	9591	9591	1004.86	1009.82	49.58	43.73
Immunologic	0	0	0	0	0	0
Clinical	0	0	0	0	0	0
No fail diagnoses	398					

At ART stop:	# Total	# with true fail	AvgTrueCD4	AvgObsvCD4	MthsToStop(Mean)	MthsToStop(StdDev)
All	8411	8411	474.22	474.79	148.06	109.27
Max Months on ART	0	0	0	0	0	0
On Observed Failure	0	0	0	0	0	0
Fail and CD4	8411	8411	474.22	474.79	148.06	109.27
Fail and Severe OI	0	0	0	0	0	0
Fail and Max Months	0	0	0	0	0	0
LTFU	0	0	0	0	0	0
Never stopped	1578					

	# at Mth 1	# Supp, Mth 1	# at Mth 2	# Supp, Mth 2	# at Mth 6	# Supp, Mth 6
Number Patients:	9982	2201	9974	4308	9339	8497

	Mean, Mth 1	SD, Mth 1	Mean, Mth 2	SD, Mth 2	Mean, Mth 6	SD, Mth 6
HVL Drops:	0.8467	0.3603	1.6266	0.735	3.0964	1.5661

Pat Distrib at Init:	HVLvhi	HVL_hi	HVLmhi	HVLmed	HVLmlo	HVL_lo	HVLvlo
CD4vhi	0	1577	1542	1511	1051	502	0
CD4_hi	0	457	469	491	307	150	0
CD4mhi	0	304	291	295	182	95	0
CD4mlo	0	112	105	106	65	22	0
CD4_lo	0	33	32	38	21	8	0
CD4vlo	0	52	60	60	37	14	0
Minor Tox Cases:	0	0	0	0	0	0	0
Chronic Tox Cases:	0	0	0	0	0	0	0
Major Tox Cases:	0	0	0	0	0	0	0
Death Tox Cases:	0	0	0	0	0	0	0

	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5+		Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5+		Cycle 1	…
Interruptions:	0	0	0	0	0	Restarts:	0	0	0	0	0	STI Endpoint:	0	…

All numbers in this table represent hard counts of the appropriate items, i.e. are not discounted. The total number of months patients spend on each ART regimen is given, with the counts of patients who get initiated as well as stay on the ART regimen after the specified number of months. The given number of months after initiation can be adjusted via modifying user inputs. At the specified time points, the number of patients actually suppressed is also given. The next table provides the mean and standard deviation of the number of HVL strata that patients on the ART regimen has decreased by from their HVL setpoints. (Therefore the description *HVL Drops* is not entirely accurate in that the difference is calculated from the patients' HVL setpoint, and not current actual HVL strata at the time of ART initiation). Finally the numbers of patients at each different actual CD4 strata, encountering an ART-related minor toxicity event, encountering an ART-related major toxicity event, and encountering death from the major toxicity are given broken down by patients current actual HVL strata.

F2h. Longitudinal Log of Cohort

The program allows for longitudinal snapshots of overall cohort characteristics over time. Such longitudinal logs can be done on a monthly or yearly basis. When done on a monthly basis, outputs can be in detailed or in shortened form. The type of logging enabled is specified in the user inputs.

Below is an example of one year's cohort summary (referred to as "yearly detail"):

COHORT SUMMARY FOR YEAR 1 END

	HIVneg	unidentHIV+	identHIV+	Total
# Alive:	179	5	3	187

Mean True CD4 (/infd): 335 (145 SD) Mean True CD4 (/cohort): 14 (74 SD) Mean Obsv CD4 (/infd): 356 (142 SD)
Mean True HVL (/infd): 9219 (9295 SD) Mean True HVL (/cohort): 394 (2598 SD) Mean Obsv HVL (/infd): 9219 (9295 SD)

CD4 Strata Distrib	CD4vlo	CD4_lo	CD4mlo	CD4mhi	CD4_hi	CD4vhi
True CD4:	0	1	0	2	5	0
Obsv CD4:	0	1	0	2	5	0

HVL Strata Distrib	HVLvlo	HVL_lo	HVLmlo	HVLmed	HVLmhi	HVL_hi	HVLvhi
True HVL:	0	3	0	2	3	0	0
Obsv HVL:	0	3	0	2	3	0	0

OIs Distrib	pcp	mac	toxo	cmv	fungal	bactl	other	
Prim OI evts:	0	0	0	0	0	0	0	
Sec OI evts:	0	0	0	0	0	0	0	
# w/ OIhist:	0	0	0	0	0	0	0	# None OI hist: 187

	CD4&HVL	HIVtests	HIVmisc
Testing costs:	2863	0	0

Total Cohort Mth costs: 139408.4

Proph Costs	pcp	mac	toxo	cmv	fungal	bactl	other
Proph 1	65	0	336	0	0	0	0
Proph 2	0	0	0	0	0	0	0
Proph 3	0	0	0	0	0	0	0
Proph 4	0	0	0	0	0	0	0
Proph 5	0	0	0	0	0	0	0

	ART 1	ART 2	ART 3	ART 4
ART Costs:	34014	0	0	0

Below is an example of one month's cohort summary (referred to as "monthly detail"):

COHORT SUMMARY FOR MONTH 1

	HIVneg	unidentHIV+	identHIV+	Total	Total QOL applied
# Alive:	0	0	1000	1000	1000

Mean True CD4 (/infd): 335 (145 SD) Mean True CD4 (/cohort): 14 (74 SD) Mean Obsv CD4 (/infd): 356 (142 SD)
Mean True HVL (/infd): 9219 (9295 SD) Mean True HVL (/cohort): 394 (2598 SD) Mean Obsv HVL (/infd): 9219 (9295 SD)

CD4 Strata Distrib	CD4vlo	CD4_lo	CD4mlo	CD4mhi	CD4_hi	CD4vhi
True CD4:	0	0	0	999	1	0
Obsv CD4:	0	0	0	1000	0	0

HVL Strata Distrib	HVLvlo	HVL_lo	HVLmlo	HVLmed	HVLmhi	HVL_hi	HVLvhi
True HVL:	0	694	167	82	39	18	0
Obsv HVL:	0	66	164	274	245	251	0

OIs Distrib	pcp	mac	toxo	cmv	fungal	bactl	other		
Prim OI evts:	5	0	3	2	1	0	5		
Sec OI evts:	0	0	0	0	0	0	0		
# w/ OIhist:	5	0	3	2	1	0	5	# None OI hist:	984

	CD4&HVL	HIVtests	HIVmisc
Testing costs:	0	0	0

Total Cohort Mth costs: 1761424.82

Proph Costs	pcp	mac	toxo	cmv	fungal	bactl	other
Proph 1	0	0	0	0	0	0	0
Proph 2	0	0	0	0	0	0	0
Proph 3	0	0	0	0	0	0	0
Proph 4	0	0	0	0	0	0	0
Proph 5	0	0	0	0	0	0	0

	ART 1	ART 2	ART 3	ART 4
ART Costs:	956742	0	0	0

COHORT SUMMARY FOR MONTH 1

	HIVneg	unidentHIV+	identHIV+	Total		
# Alive:	0	0	1000	1000	MeanTrueCD4 (/infd): 266	MeanTrueHVL (/infd): 2949

OIs Distrib	pcp	mac	toxo	cmv	fungal	bactl	other		
Tot OI evts:	5	0	3	2	1	0	5		
# w/ OIhist:	5	0	3	2	1	0	5	# None OI hist:	984

F3. Trace Output File

The following are examples of traces produced by the program. Note that life months (LMs), quality adjusted (QA) life months, and patient costs are cumulative, discounted values.

Each line in the patient trace is preceded by a month number – this is the number of months since the hypothetical patient has enterred the model.

Here is an example of such a trace file –

```
BEGIN PATIENT 2
  gender: male, init age: 396 mths (33.00 yrs)
  init VisitType sched, Implement proph YES art YES;
  HIV state: HIVneg
**0 HIV SCREENING STARTUP, $ 0
**0 HIV TEST ACCEPT, RETURN, TRUE NEGATIVE, $ 0
  0 mth: LM 1.00 QA 0.00, $ 0;
  1 mth: LM 2.00 QA 1.00, $ 0;
  2 mth: LM 2.99 QA 1.99, $ 0;
  3 mth: LM 3.99 QA 2.99, $ 0;
  4 mth: LM 4.98 QA 3.98, $ 0;
  5 mth: LM 5.96 QA 4.96, $ 0;
  6 mth: LM 6.95 QA 5.95, $ 0;
  7 mth: LM 7.93 QA 6.93, $ 0;
  8 mth: LM 8.91 QA 7.91, $ 0;
  9 mth: LM 9.89 QA 8.89, $ 0;
  10 mth: LM 10.87 QA 9.87, $ 0;
  11 mth: LM 11.84 QA 10.84, $ 0;
**12 HIV TEST ACCEPT, RETURN, TRUE NEGATIVE, $ 0
  12 mth: LM 12.81 QA 10.84, $ 0;
  13 mth: LM 13.78 QA 11.81, $ 0;
  14 mth: LM 14.74 QA 12.77, $ 0;
  15 mth: LM 15.71 QA 13.74, $ 0;
  16 mth: LM 16.67 QA 14.70, $ 0;
  17 mth: LM 17.63 QA 15.66, $ 0;
  18 mth: LM 18.59 QA 16.61, $ 0;
  19 mth: LM 19.54 QA 17.57, $ 0;
  20 mth: LM 20.49 QA 18.52, $ 0;
  21 mth: LM 21.44 QA 19.47, $ 0;
  22 mth: LM 22.39 QA 20.42, $ 0;
  23 mth: LM 23.33 QA 21.36, $ 0;
**24 HIV TEST ACCEPT, RETURN, TRUE NEGATIVE, $ 0
  24 mth: LM 24.28 QA 21.36, $ 0;
  25 mth: LM 25.22 QA 22.30, $ 0;
  26 mth: LM 26.15 QA 23.24, $ 0;
**27 HIV INFECTION;
  27 init CD4: 266;
  27 init HVL: HVLmlo, setpt: HVLmlo;
  27 upd: true CD4 262, true HVL HVLmlo;
  27 mth: LM 27.09 QA 24.18, $ 0;
  28 upd: true CD4 258, true HVL HVLmlo;
  28 mth: LM 28.02 QA 25.11, $ 0;
**29 HIV ACUTE TO CHR: CD4 258, HVLsetpt HVLmlo;
  29 upd: true CD4 254, true HVL HVLmlo;
  29 mth: LM 28.95 QA 26.04, $ 0;
  30 upd: true CD4 251, true HVL HVLmlo;
  30 mth: LM 29.88 QA 26.97, $ 0;
  31 upd: true CD4 247, true HVL HVLmlo;
  31 mth: LM 30.81 QA 27.90, $ 0;
  32 upd: true CD4 243, true HVL HVLmlo;
  32 mth: LM 31.73 QA 28.82, $ 0;
  33 upd: true CD4 240, true HVL HVLmlo;
  33 mth: LM 32.66 QA 29.74, $ 0;
  34 upd: true CD4 236, true HVL HVLmlo;
  34 mth: LM 33.58 QA 30.66, $ 0;
  35 upd: true CD4 232, true HVL HVLmlo;
  35 mth: LM 34.49 QA 31.58, $ 0;
**36 HIV TEST ACCEPT, RETURN, FALSE NEGATIVE, $ 0
  36 upd: true CD4 228, true HVL HVLmlo;
  36 mth: LM 35.41 QA 31.58, $ 0;
  37 upd: true CD4 224, true HVL HVLmlo;
  37 mth: LM 36.32 QA 32.49, $ 0;
  38 upd: true CD4 221, true HVL HVLmlo;
  38 mth: LM 37.23 QA 33.40, $ 0;
  39 upd: true CD4 217, true HVL HVLmlo;
  39 mth: LM 38.14 QA 34.31, $ 0;
  40 upd: true CD4 213, true HVL HVLmlo;
  40 mth: LM 39.05 QA 35.22, $ 0;
  41 upd: true CD4 210, true HVL HVLmlo;
  41 mth: LM 39.95 QA 36.12, $ 0;
```

42 upd: true CD4 206, true HVL HVLmlo;
42 mth: LM 40.85 QA 37.02, $ 0;
43 upd: true CD4 203, true HVL HVLmlo;
43 mth: LM 41.75 QA 37.92, $ 0;
44 upd: true CD4 198, true HVL HVLmlo;
44 mth: LM 42.65 QA 38.82, $ 0;
45 upd: true CD4 195, true HVL HVLmlo;
45 mth: LM 43.54 QA 39.71, $ 0;
46 upd: true CD4 191, true HVL HVLmlo;
46 mth: LM 44.44 QA 40.61, $ 0;
47 upd: true CD4 187, true HVL HVLmlo;
47 mth: LM 45.33 QA 41.50, $ 0;
**48 HIV TEST ACCEPT, RETURN, TRUE POSITIVE, $ 0
48 CD4 TEST: obsv CD4 184, $ 74;
48 HVL TEST: obsv HVL HVLmlo, $ 172;
**48 CLINIC VISIT, $ 172;
**48 INIT NEW ART 1, $ 172;
**48 ART DRAW suppressed;
48 upd: true CD4 184, true HVL HVLmlo;
48 mth: LM 46.22 QA 41.50, $ 1707;
49 CD4 TEST: obsv CD4 194, $ 1781;
49 HVL TEST: obsv HVL HVL_lo, $ 1878;
49 upd: true CD4 194, true HVL HVL_lo;
49 mth: LM 47.10 QA 42.25, $ 3409;
50 upd: true CD4 205, true HVL HVLvlo;
50 mth: LM 47.99 QA 43.01, $ 4937;
51 CD4 TEST: obsv CD4 224, $ 5010;
51 HVL TEST: obsv HVL HVLvlo, $ 5107;
**51 CLINIC VISIT, $ 5107;
51 upd: true CD4 224, true HVL HVLvlo;
51 mth: LM 48.87 QA 43.77, $ 6705;
52 upd: true CD4 244, true HVL HVLvlo;
52 mth: LM 49.75 QA 44.53, $ 8299;
53 upd: true CD4 262, true HVL HVLvlo;
53 mth: LM 50.62 QA 45.28, $ 9888;
54 CD4 TEST: obsv CD4 286, $ 9961;
54 HVL TEST: obsv HVL HVLvlo, $ 10058;
**54 CLINIC VISIT, $ 10058;
54 upd: true CD4 286, true HVL HVLvlo;
54 mth: LM 51.50 QA 46.03, $ 11643;
**55 ART LATE PARTIAL;
55 upd: true CD4 315, true HVL HVLvlo;
55 mth: LM 52.37 QA 46.79, $ 13225;
56 upd: true CD4 344, true HVL HVL_lo;
56 mth: LM 53.24 QA 47.53, $ 14803;
**57 ART LATE FAIL;
57 CD4 TEST: obsv CD4 372, $ 14876;
57 HVL TEST: obsv HVL HVLmlo, $ 14971;
**57 CLINIC VISIT, $ 14971;
57 upd: true CD4 372, true HVL HVLmlo;
57 mth: LM 54.11 QA 48.28, $ 16225;
58 HVL TEST: obsv HVL HVLmlo, $ 16320;
58 upd: true CD4 365, true HVL HVLmlo;
58 mth: LM 54.98 QA 49.03, $ 17571;
59 HVL TEST: obsv HVL HVLmlo, $ 17666;
59 upd: true CD4 356, true HVL HVLmlo;
59 mth: LM 55.85 QA 49.77, $ 18913;
60 CD4 TEST: obsv CD4 345, $ 18985;
60 HVL TEST: obsv HVL HVLmlo, $ 19080;
**60 CLINIC VISIT, $ 19080;
**60 ART 1 FAIL OBSV BY HVL;
**60 TAKEN OFF ART 1 by NEXT_REGIMEN_TO_START;
**60 INIT NEW ART 2, $ 19080;
**60 ART DRAW failure;
60 upd: true CD4 345, true HVL HVLmlo;
60 mth: LM 56.71 QA 50.51, $ 20643;
61 CD4 TEST: obsv CD4 337, $ 20714;
61 HVL TEST: obsv HVL HVLmlo, $ 20809;
61 upd: true CD4 337, true HVL HVLmlo;
61 mth: LM 57.57 QA 51.25, $ 22368;
62 HVL TEST: obsv HVL HVLmlo, $ 22462;
62 upd: true CD4 330, true HVL HVLmlo;
62 mth: LM 58.43 QA 51.99, $ 24017;
63 CD4 TEST: obsv CD4 320, $ 24088;
63 HVL TEST: obsv HVL HVLmlo, $ 24183;
**63 CLINIC VISIT, $ 24183;
**63 ART 2 FAIL OBSV BY HVL;
**63 TAKEN OFF ART 2 by NEXT_REGIMEN_TO_START;
**63 INIT NEW ART 3, $ 24183;
**63 ART DRAW partial_suppressed;
63 upd: true CD4 320, true HVL HVLmlo;
63 mth: LM 59.28 QA 52.73, $ 25734;
64 CD4 TEST: obsv CD4 349, $ 25805;
64 HVL TEST: obsv HVL HVLmlo, $ 25899;
64 upd: true CD4 349, true HVL HVLmlo;
64 mth: LM 60.14 QA 53.46, $ 27446;
65 HVL TEST: obsv HVL HVLmlo, $ 27540;
65 upd: true CD4 383, true HVL HVLmlo;
65 mth: LM 60.99 QA 54.20, $ 29083;
66 CD4 TEST: obsv CD4 413, $ 29154;
66 HVL TEST: obsv HVL HVLmlo, $ 29247;
**66 CLINIC VISIT, $ 29247;
**66 ART 3 FAIL OBSV BY HVL;
**66 TAKEN OFF ART 3 by NEXT_REGIMEN_TO_START;
**66 INIT NEW ART 4, $ 29247;
**66 ART DRAW partial_suppressed;
66 upd: true CD4 413, true HVL HVLmlo;
66 mth: LM 61.84 QA 54.93, $ 30474;
67 CD4 TEST: obsv CD4 443, $ 30544;
67 HVL TEST: obsv HVL HVLmlo, $ 30637;
67 upd: true CD4 443, true HVL HVLmlo;
67 mth: LM 62.69 QA 55.66, $ 31861;
68 HVL TEST: obsv HVL HVLmlo, $ 31954;
68 upd: true CD4 472, true HVL HVLmlo;
68 mth: LM 63.53 QA 56.38, $ 33174;
69 CD4 TEST: obsv CD4 502, $ 33244;
69 HVL TEST: obsv HVL HVLmlo, $ 33337;
**69 CLINIC VISIT, $ 33337;
**69 ART 4 FAIL OBSV BY HVL;
**69 TAKEN OFF ART 4 by STOP_ON_FAIL;
69 upd: true CD4 502, true HVL HVLmlo;
69 mth: LM 64.38 QA 57.12, $ 33543;
70 upd: true CD4 472, true HVL HVLmlo;
70 mth: LM 65.22 QA 57.84, $ 33748;
71 upd: true CD4 443, true HVL HVLmlo;
71 mth: LM 66.06 QA 58.56, $ 33953;
72 CD4 TEST: obsv CD4 412, $ 34023;
72 HVL TEST: obsv HVL HVLmlo, $ 34115;
**72 CLINIC VISIT, $ 34115;
72 upd: true CD4 412, true HVL HVLmlo;
72 mth: LM 66.90 QA 59.28, $ 34383;
73 upd: true CD4 385, true HVL HVLmlo;
73 mth: LM 67.73 QA 60.00, $ 34651;
74 upd: true CD4 354, true HVL HVLmlo;
74 mth: LM 68.56 QA 60.72, $ 34919;
75 CD4 TEST: obsv CD4 325, $ 34988;
75 HVL TEST: obsv HVL HVLmlo, $ 35079;
**75 CLINIC VISIT, $ 35079;
75 upd: true CD4 325, true HVL HVLmlo;
75 mth: LM 69.40 QA 61.43, $ 35652;
76 upd: true CD4 295, true HVL HVLmlo;
76 mth: LM 70.22 QA 62.15, $ 36224;
77 upd: true CD4 263, true HVL HVLmlo;
77 mth: LM 71.05 QA 62.86, $ 36794;
78 CD4 TEST: obsv CD4 233, $ 36863;
78 HVL TEST: obsv HVL HVLmlo, $ 36954;
**78 CLINIC VISIT, $ 36954;
78 upd: true CD4 233, true HVL HVLmlo;
78 mth: LM 71.88 QA 63.57, $ 37523;
79 upd: true CD4 202, true HVL HVLmlo;
79 mth: LM 72.70 QA 64.27, $ 38090;
80 upd: true CD4 184, true HVL HVLmlo;
80 mth: LM 73.52 QA 64.97, $ 38657;
81 CD4 TEST: obsv CD4 180, $ 38725;
81 HVL TEST: obsv HVL HVLmlo, $ 38815;
**81 CLINIC VISIT, $ 38815;
81 upd: true CD4 180, true HVL HVLmlo;
81 mth: LM 74.34 QA 65.67, $ 39311;
82 upd: true CD4 176, true HVL HVLmlo;
82 mth: LM 75.16 QA 66.36, $ 39806;

```
  83 upd: true CD4 173, true HVL HVLmlo;
  83 mth: LM 75.97 QA 67.06, $ 40300;
  84 CD4 TEST: obsv CD4 170, $ 40368;
  84 HVL TEST: obsv HVL HVLmlo, $ 40457;
**84 CLINIC VISIT, $ 40457;
  84 upd: true CD4 170, true HVL HVLmlo;
  84 mth: LM 76.79 QA 67.75, $ 40950;
  85 upd: true CD4 166, true HVL HVLmlo;
  85 mth: LM 77.60 QA 68.44, $ 41441;
  86 upd: true CD4 162, true HVL HVLmlo;
  86 mth: LM 78.41 QA 69.12, $ 41931;
  87 CD4 TEST: obsv CD4 158, $ 41998;
  87 HVL TEST: obsv HVL HVLmlo, $ 42087;
**87 CLINIC VISIT, $ 42087;
  87 upd: true CD4 158, true HVL HVLmlo;
  87 mth: LM 79.21 QA 69.81, $ 42576;
  88 upd: true CD4 155, true HVL HVLmlo;
  88 mth: LM 80.02 QA 70.50, $ 43064;
  89 upd: true CD4 151, true HVL HVLmlo;
  89 mth: LM 80.82 QA 71.18, $ 43550;
  90 CD4 TEST: obsv CD4 147, $ 43617;
  90 HVL TEST: obsv HVL HVLmlo, $ 43705;
**90 CLINIC VISIT, $ 43705;
  90 upd: true CD4 147, true HVL HVLmlo;
  90 mth: LM 81.62 QA 71.86, $ 44190;
  91 upd: true CD4 143, true HVL HVLmlo;
  91 mth: LM 82.42 QA 72.54, $ 44674;
  92 upd: true CD4 139, true HVL HVLmlo;
  92 mth: LM 83.22 QA 73.22, $ 45157;
  93 CD4 TEST: obsv CD4 136, $ 45223;
  93 HVL TEST: obsv HVL HVLmlo, $ 45311;
**93 CLINIC VISIT, $ 45311;
  93 upd: true CD4 136, true HVL HVLmlo;
  93 mth: LM 84.01 QA 73.89, $ 45793;
  94 upd: true CD4 132, true HVL HVLmlo;
  94 mth: LM 84.81 QA 74.57, $ 46273;
  95 upd: true CD4 128, true HVL HVLmlo;
  95 mth: LM 85.60 QA 75.24, $ 46753;
  96 CD4 TEST: obsv CD4 125, $ 46818;
  96 HVL TEST: obsv HVL HVLmlo, $ 46905;
**96 CLINIC VISIT, $ 46905;
  96 upd: true CD4 125, true HVL HVLmlo;
  96 mth: LM 86.39 QA 75.91, $ 47383;
  97 upd: true CD4 121, true HVL HVLmlo;
  97 mth: LM 87.18 QA 76.58, $ 47860;
  98 upd: true CD4 117, true HVL HVLmlo;
  98 mth: LM 87.96 QA 77.25, $ 48336;
  99 CD4 TEST: obsv CD4 113, $ 48401;
  99 HVL TEST: obsv HVL HVLmlo, $ 48488;
**99 CLINIC VISIT, $ 48488;
  99 upd: true CD4 113, true HVL HVLmlo;
  99 mth: LM 88.74 QA 77.91, $ 48962;
**100 PRIMARY OI OTHEROI;
**100 OBSV OI OTHEROI;
**100 CLINIC VISIT, $ 53332;
  100 upd: true CD4 110, true HVL HVLmlo;
  100 mth: LM 89.53 QA 78.45, $ 53806;
  101 upd: true CD4 106, true HVL HVLmlo;
  101 mth: LM 90.31 QA 79.11, $ 54278;
  102 upd: true CD4 102, true HVL HVLmlo;
  102 mth: LM 91.08 QA 79.78, $ 54749;
  103 CD4 TEST: obsv CD4 98, $ 54814;
  103 HVL TEST: obsv HVL HVLmlo, $ 54899;
**103 CLINIC VISIT, $ 54899;
  103 upd: true CD4 98, true HVL HVLmlo;
  103 mth: LM 91.86 QA 80.44, $ 55096;
  104 upd: true CD4 94, true HVL HVLmlo;
  104 mth: LM 92.63 QA 81.09, $ 55291;
  105 upd: true CD4 91, true HVL HVLmlo;
  105 mth: LM 93.41 QA 81.75, $ 55487;
  106 CD4 TEST: obsv CD4 88, $ 55551;
  106 HVL TEST: obsv HVL HVLmlo, $ 55635;
**106 CLINIC VISIT, $ 55635;
  106 upd: true CD4 88, true HVL HVLmlo;
  106 mth: LM 94.18 QA 82.40, $ 55830;
  107 upd: true CD4 84, true HVL HVLmlo;
  107 mth: LM 94.94 QA 83.06, $ 56024;
  108 upd: true CD4 81, true HVL HVLmlo;
  108 mth: LM 95.71 QA 83.71, $ 56218;
  109 CD4 TEST: obsv CD4 77, $ 56282;
  109 HVL TEST: obsv HVL HVLmlo, $ 56366;
**109 CLINIC VISIT, $ 56366;
  109 upd: true CD4 77, true HVL HVLmlo;
  109 mth: LM 96.48 QA 84.36, $ 56559;
  110 upd: true CD4 74, true HVL HVLmlo;
  110 mth: LM 97.24 QA 85.01, $ 56752;
  111 upd: true CD4 70, true HVL HVLmlo;
  111 mth: LM 98.00 QA 85.65, $ 56945;
  112 CD4 TEST: obsv CD4 67, $ 57008;
  112 HVL TEST: obsv HVL HVLmlo, $ 57091;
**112 CLINIC VISIT, $ 57091;
  112 upd: true CD4 67, true HVL HVLmlo;
  112 mth: LM 98.76 QA 86.30, $ 57283;
**113 DEATH chrAIDS;
  LMs 99.14 QA 86.62 $ 64524 ;
  END PATIENT
```

F4. Generalized Data Extraction

Starting in version cepac40c, the Generalized Data Extraction executable, "data_extraction_*xx*.exe", was created to help pull out useful information from multiple CEPAC output files (*.out). When run, this program will first scan the current directory for any data extraction parameter "*.gde-in" files. These files describe which data to extract and how to format the output. For each of these parameter files, the program will then extract the specified data from all of CEPAC "*.out" files in that directory and generate corresponding data extraction output "*.gde-out" files. The format for the data extraction parameter files is described below –

Examples for specifying which data to extract are shown below. These can be specified anywhere in the file, as long as they are specified on their own lines and have the correct format. There are two main types of data extraction that can be used - individual data and repeating data. The possible calculations that can be done are the ICER calculation or the user defined individual one. There is also a parameter for specifying the format of the output table.

The following TABLE_FORMAT parameter can be set to specify if the outputs should be organized by rows or columns. If "orientation" is set to "row", the filenames will appear in the first column with all outputs for that file will be in its row. If set to "column", the filenames will appear in the first row and all outputs will be in its column. If unspecified, the default is "row". The value specified for "sort" will be the label of extracted data that the output files should be ordered by, will default to alphabetical by "filename".

TABLE_FORMAT: orientation="row", sort="filename"

The SINGLE_DATA type indicates a single data entry. The "label" value is the label that will be used in the output file and for calculated entries. The "section" value is the section header in the output file under which the desired date will be found. The entire section name does not need to be listed, a shortened prefix that distinguishes it from other sections is sufficient. The "rowoffset" and "column" values are the number of rows down from the section header and the column of the desired cell.

SINGLE_DATA: label="Costs", section="POPULATION SUMMARY", rowoffset="3", column="C"
SINGLE_DATA: label="LMs", section="POPULATION SUMMARY", rowoffset="4", column="C"

If ICERs should be calculated, use the CALC_ICER type with the specified labels of extracted data for the costs, "costs_label", and time period, "time_label". This should only be specified once and will also override the "sort" value and cause the outputs to be sorted by the "costs_label".

CALC_ICER: costs_label="Costs", time_label="LMs"

Single calculated entries can be specified with type SINGLE_CALC. The "label" value is the label that will be used in the output file. The "equation" value is an equation that uses the labels of the single data values and can have any basic math functions: +,-,*,/,(,). An example is shown below after some additional single data values.

SINGLE_DATA: label="chrAIDSDth", section="CAUSES OF DEATH", rowoffset="8", column="R"
SINGLE_DATA: label="nonAIDSDth", section="CAUSES OF DEATH", rowoffset="8", column="S"
SINGLE_CALC: label="percChrAIDSDth", equation="chrAIDSDth / (chrAIDSDth + nonAIDSDth)"

Repeated data entries can be specified with type REPEAT_DATA. The "label" value is the base label that will be used in the output file, it will be followed by the iteration number. The "section", "rowoffset", and "column" values specify how far off from the repeating section header the data can be found. The "repeatnum" label specifies how many times to repeat this data extraction. The following example extracts the number alive values for each month for a year.

REPEAT_DATA: label="numAlive", section="COHORT SUMMARY", rowoffset="2", column="F", repeatnum="12"

G. Programming Notes

The code, which is developed with Microsoft Visual Studio, is mostly written in standard ANSI C++, to support compilation and execution on both MS Windows PCs, Mac OS X, and Unix workstations. Compilation with both Windows Visual C++ and Linux G++ compiler is currently supported.

Microsoft Excel has been retained as the primary user interface for data input. Its advantages over, say, custom modal dialogs include reduced code modification to support data changes, more flexibility in manipulating data

inputs as the operator sees fit, and the leveraging of common user proficiency in Excel. Its primary disadvantage is the manual nature of manipulating inputs into the format required by the program. There is the possibility of changing to a custom graphical user interface within the next few years.

G1. Random Numbers

In the simulation, random draws determine the occurrence of acute events and transitions between patient health states. In general, event risks and state transitions are assumed to be stochastic, or near-stochastic, in nature. Random number generators work by repeatedly performing mathematical operations to generate a series of numbers that appear to be random. This process can be thought of as black box, with the only input being the initial seed to start the sequence. Anytime the model needs to perform a random draw, it will use the next number in the sequence coming out of this black box.

The CEPAC treatment program utilizes the Mersenne Twister random number generator algorithm developed by Takuji Nishimura and Makoto Matsumoto. The implementation used in the model is based on MT19937, and was ported to C++ by Jasper Bedaux. For more information about this algorithm and implementation, see http://www.bedaux.net/mtrand/. The algorithms produce random numbers uniformly distributed from 0 to 1. In multiple contexts, the model utilizes normal, or Gaussian, probability distribution functions (PDFs) – normally distributed deviates with 0 mean and unit variance. These Gaussian deviates are obtained by transforming uniformly distributed deviates by the polar form of the Box-Muller transform.

The model can be specified to either use a fixed seed or current time seed for initializing the random number generator. A description of the functionality of each of these options and when they should be used is described below -

Fixed seed:
Fixed seed initializes the random number generator using a constant number. This results in a sequence of numbers that will be identical between different runs of the model. Using this option will cause the exact same outputs to be generated for any set of input files. In prior versions, if an input file was changed at all then the outputs would be completely different. Even though the model was generating the same sequence of random numbers, the model would request them in a different order. For example, if toxicity was disabled in one run and then enabled in the next, there would need to be an extra random number draw every month in the second run to determine if toxicity occurred. In month 1, patient 1 would use the next random number for its toxicity draw and the subsequent random number draw for OIs would not be consistent with the run that did not have toxicity.
Starting in cepac42a, this fixed seed behavior has been changed to fix such problems. Now, for every random number that the model needs, it will reseed the random number generator based on what part of the model is running, the patient number, and the month number. This will guarantee that at the same point in the model for patient X in month Y, the same random number will be used across different runs. For example, when determining if patient 25 gets PCP in month 47, the same result will occur across different runs. This will even hold true across different model versions, given that that specific component of the model was not modified. **Fixed seed should only be used for debugging and consistency checking**. Due to the reseeding, this new functionality greatly slows down the model. It will allow the user to make changes to the inputs of certain modules and verify that these do not have unpredictable consequence for other modules. If the same set of inputs are imported to the next model version, the effects of the model changes on the outputs can be analyzed. Both of these features should be very useful for debugging and validation.

Current time seed:
Current time seed initializes the random number generator based on the system time of the computer. This results in a sequence of numbers that will be more "random" and will vary between different runs of the model. **Current time seed should be used for ALL policy analysis**. If there is a large amount of variability between model runs, it means that the cohort size is too small and that there is a lot of noise. The results from fixed seed are no more accurate than any single run using random seed. Final results for publication should be verified as being sufficiently accurate by performing multiple random seed runs or by calculating confidence intervals.