CEPAC TB Module Specifications

Overview

This tuberculosis (TB) module is designed to capture the natural history, diagnosis, treatment, and associated costs of TB for both HIV-infected and HIV-uninfected individuals in resource-limited settings using the framework of the CEPAC model.

This document describes the components of the module chronologically in the order that patients flow through the model. Flowchart sections are noted in parentheses (e.g., 10a) where appropriate for reference. Accompanying variable definitions and equations are provided where applicable.

Begin Month Updater (10a)

In the first month of the simulation, the module will evaluate a toggle (yes/no) to use the TB module, ignoring all of the module's functions if the toggle is set to 0. The module will also evaluate whether the TB clinic is integrated with the HIV Clinic; if toggle is set to 1 ("yes"), the diagnosis and treatment of TB will occur within the setting of an HIV clinic.

Enable TB Module	0	**0** = no, **1** = yes
TB and HIV Clinic Integrated?	0	**0** = no, **1** = yes

In the first month, patients will be distributed to one of the six natural history health states:

- Uninfected
- Latent TB
- Active Pulmonary TB
- Active Extrapulmonary TB
- Previously Treated TB
- TB Treatment Default

This initial distribution will depend on HIV status (HIV-infected or HIV-uninfected) and, for HIV-infected patients, CD4 count.

Distribution of TB states at model entry

Probability	Uninfected	Latent TB	Active Pulr	Active Extr	Prev Treat	TB Treat Default	
HIV -	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VHI	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 HI	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MHI	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MLO	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 LO	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VLO	1.0000	0.0000	0.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0

For all patients who are not in the Uninfected state, the strain of TB will be drawn as one of three variables: drug-susceptible TB (*dsTB*), multidrug-resistant TB (*MDR-TB*), or extensively drug-resistant TB (*XDR-TB*). This distribution will not depend on HIV status, CD4 count, or distribution of TB states.

Distribution of TB Strain			
dsTB	MDR-TB	XDR-TB	
0.9000	0.0000	0.1000	**Note**: row must sum to 1.0

Each patient will then be evaluated for 3 separate binary tracker variables based on their TB state:

1. TB sputum bacillary load (*sputumbacloadhi/sputumbacloadlo)*
2. Immune reactivity (*immreactyes/immreactno)*
3. Symptoms consistent with TB (*symptomyes/symptomno)*

This distribution is dependent upon HIV status, CD4 count, and TB state.

TB Sputum Bacillary Load: Sputum bacillary load is a clinical characteristic that is a surrogate for smear status and is representative of infectivity.

- Sputum bacillary load will be "low" for all Uninfected, Latent TB, Active Extrapulmonary TB, Previously Treated TB, and TB Treatment Default states.
- Sputum bacillary load can be "high" or "low" for patients in the Active Pulmonary TB state.

Immune Reactivity: Immune reactivity is a clinical characteristic that is a surrogate for tuberculin skin test (TST) and Quantiferon blood test results. It represents whether a person has mounted an immune response to tuberculosis bacterium (indicating TB exposure).

- Note that "Immune reactivity" can be falsely positive for some patients who have received the BCG vaccine or have been exposed to non-tuberculous mycobacteria, and falsely negative for patients with compromised immune systems (e.g., low CD4) and, thus, can be positive or negative in any of the health states.

Symptoms consistent with TB (which can be defined by the user and parameterized according to available data) can be present for patients in any of the health states. Patients with Active Pulmonary TB will keep their symptom flag until successfully treated for TB; patients in any other health state will keep their symptom flag for one month only.

Sputum Bacillary Load Hi at entry

Prob positive	Uninfected	Latent TB	Active Pulr	Active Extr	Prev Treat	TB Treat Default	
HIV -	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 HI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 LO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0

Immune Reactive at entry

Prob positive	Uninfected	Latent TB	Active Pulr	Active Extr	Prev Treat	TB Treat Default	
HIV -	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 VHI	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 HI	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 MHI	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 MLO	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 LO	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0
CD4 VLO	0.0000	1.0000	1.0000	1.0000	1.0000	0.0000	**Note**: row must sum to 1.0

TB symptoms at entry

Prob sympton	Uninfected	Latent TB	Active Pulr	Active Extr	Prev Treat	TB Treat Default	
HIV -	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 HI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 MLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 LO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0
CD4 VLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000	**Note**: row must sum to 1.0

TB Disease Updater (50a-50e)

This section of the module describes the natural history transitions between the 6 TB natural history states (described below). This section will appear after the HIV Infection Updater and CHRMS Updater and before the Drug Toxicity Updater. Each natural history state will have a subroutine, and the order of the subroutines will be as follows: Uninfected, Latent TB, Active Pulmonary TB, Active Extrapulmonary TB, Previously Treated TB, and TB Treatment Default.

TB Natural History States (See diagram below, next page)
All states in the model are based on the true state of the patient, rather than on diagnostic test result or clinical management/observation.

Uninfected: The patient is not infected with *Mycobacterium tuberculosis* and thus cannot develop active TB without first becoming infected.

Latent TB: The patient is infected with *Mycobacterium tuberculosis* but does not have active TB disease. This is also referred to as "latent TB infection" or "LTBI." There are no symptoms or morbidity associated with LTBI itself, and no transmission risk to others.

Active Pulmonary TB: The patient has active TB disease in the lungs. Morbidity and mortality can result from untreated or ineffectively treated active TB disease. This can be a first episode of active TB or a subsequent (recurrent) episode, which would be marked by a flag and would confer a different probability of drug resistance, treatment success, and death, and possibly trigger a different treatment regimen. This state also will include patients who have both active pulmonary and active extrapulmonary TB, as most diagnostic strategies assess for pulmonary TB.

Active Extrapulmonary TB: Similar to "Active Pulmonary TB," but the patient does not have active TB disease in the lungs and instead has active disease elsewhere. The patient may have symptoms but does not pose a transmission risk to others, and standard pulmonary tests (e.g., sputum culture) will be negative.

Previously Treated TB: The patient does not have active TB currently (and consequently no TB-associated morbidity, TB-associated mortality, or transmission risk to others) but has had active TB in the past and successfully completed TB treatment. This state also includes those who had active TB but survived via "self-cure" (i.e., "self-treatment") without actually successfully completing a TB treatment regimen.

TB Treatment Default: The patient has been treated for TB but did not complete the entire course of treatment. Those who have rolled for success will go to the TB Treatment Default state after at least 2 consecutive months of being LTFU. Those who rolled for failure will return to an Active TB state. Those in this state can experience either Relapse or Reinfection.

Dead: The patient is dead due to TB or non-TB causes. Patients can transition to this state from any other state (not shown in the diagram below for simplicity). This is an absorbing state.

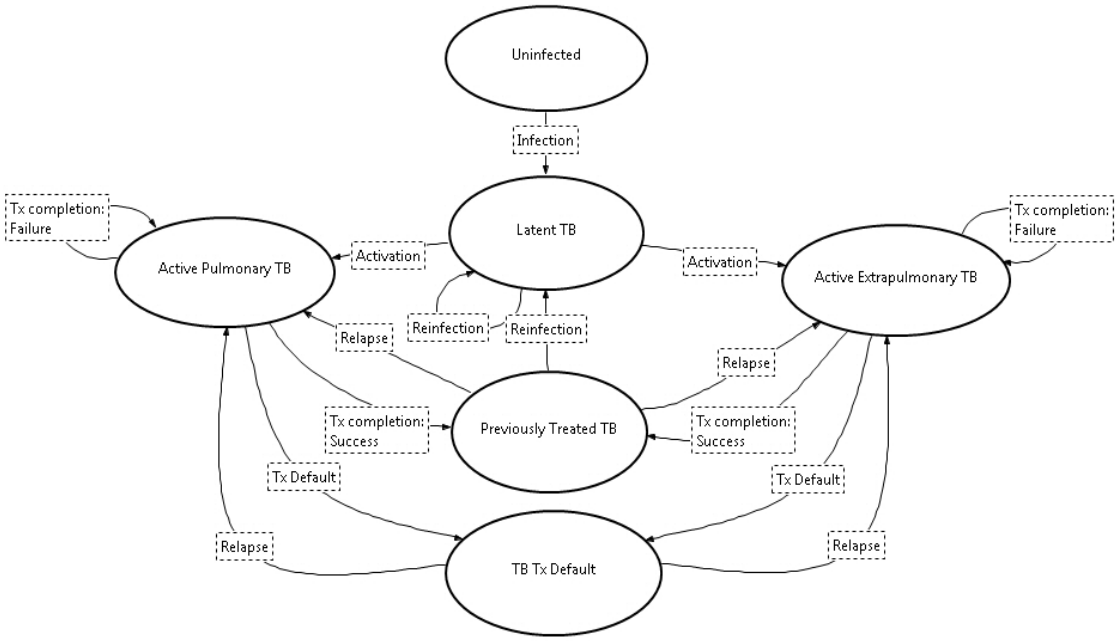

Figure 1. A simplified schematic of the natural history states and monthly transitions in the proposed CEPAC TB module. Arrows indicating remaining in the current state are omitted for clarity. Patients can transition from any of the shown states to the Dead state (not shown for simplicity).

Relapse = Active disease from the same strain that caused the previous active disease. Patient will draw for becoming *sputumbacloadhi.*
Reinfection = Exposure to, and infection by, another strain of *Mycobacterium tuberculosis* in a patient who has been infected previously. Patient will draw for a strain, which will replace the prior strain.

Notable Flags

Infecting TB Strain (*dsTB*, *MDR-TB*, *XDR-TB*)

Observed TB Strain (*ObserveddsTB, ObservedMDRTB, ObservedXDRTB*)

PriorActiveTBn (where n is the number of previous active TB episodes since model entry)

PriorTreatmentDefault

OnTBProphylaxisX (where X is the number of the prophylaxis regimen)

OnTBTreatmentX (where X is the number of the treatment regimen)

TBTreatmentFail

TBTreatmentSuccess

Transitions between TB States (monthly)

A: Uninfected → Uninfected (50b)
This "transition" involves remaining in the current Uninfected state. The probability will effectively be the product of one minus each of the other transition probabilities (i.e., the default is to remain in the current state).

B: Uninfected → Latent TB (50f)

This event is infection. The probability will be defined according to published data from South Africa or another setting of interest and will be independent of HIV status and CD4. Upon this state transition, a flag will be assigned describing the strain of TB with which the patient has been infected, drawn from a distribution of drug-susceptible TB (dsTB), multidrug-resistant TB (MDR-TB), and extensively drug-resistant TB (XDR-TB). Uninfected patients who are on prophylaxis or treatment for TB (either due to a false positive diagnostic result or because they receive empiric therapy) will have a marked reduction in infection probability. Patients in any TB state *other* than Uninfected/Active TB are at risk of obtaining a new infection, but the rate of infection is decreased as those who have been exposed to TB previously are somewhat "protected" against new infection and disease.

Patients who undergo this transition will roll for becoming either *immreactyes* or *immreactno*, which depends on HIV status and CD4. If the patient is on TB prophylaxis (*onTBprophylaxisX*) when infected, the patient can roll for a more resistant strain.

INFECTION

Monthly Incidence of TB Infection (Primary and Reinfection)

	<18	18-25	26-30	31-35	36-40	41-45	46+
HIV -	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 VHI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 HI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 MHI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 MLO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 LO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 VLO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

	Uninfected	Latent TB	Active Pulm TB	Active Extrapulm TB	Prev Treat TB	TB Treat Default
Infection Multiplier	0.2000	1.0000	0.0000	0.0000	1.0000	1.0000

Probability of Immune Reactive Once Infected

Probability	
HIV -	0.0000
CD4 VHI	0.0000
CD4 HI	0.0000
CD4 MHI	0.0000
CD4 MLO	0.0000
CD4 LO	0.0000
CD4 VLO	0.0000

C: Uninfected → Dead (60a)

Death occurs from a non-TB cause as defined in the remainder of the CEPAC model for HIV-infected patients (chronic AIDS death, OI acute mortality, ART toxicity, non-AIDS death, etc.), or as defined in the monthly non-AIDS death probability in the Natural History tab for HIV-negative patients. Also, death can occur from toxicity of prophylaxis or treatment of TB, though the number of cases is expected to be quite small.

D: Latent TB → Latent TB (50c)

There are two pathways for this "transition":

1) Similar to **A**, this pathway is the default for patients with latent TB infection. Factors that will effectively increase the likelihood of no transition include the *OnTBProphylaxisX* or *OnTBTreatmentX* (due to false positive diagnostic result or empiric treatment) flag, HIV-negative status, and high CD4 count for HIV-infected patients.

2) Reinfection: In this pathway, a patient with latent TB infection has a monthly probability of becoming infected with a different strain of *Mycobacterium tuberculosis*. The new infecting strain will always replace the previous infecting strain, as it is believed that relapse is most likely to occur with the newest strain. [**Note:** It was decided that the newest infecting strain should trump the previous infected strain instead of the more resistant strain trumping the less resistant strain;

3/17/15] Patients will first draw for reinfection from the same probabilities for infection as described in **B**. If reinfected, the patient will draw from the distribution of TB strains. If patients are reinfected and were previously *immreactno*, they will draw again for either *immreactyes* or *immreactno*.

Note: *although reinfection can technically occur in any infected or active TB state, we simplify and assume that only those in the Latent TB, Previously Treated TB, or TB Treatment Default states can become reinfected.*

E: Latent TB → Active Pulmonary TB (50c)

There are two pathways for this transition:

1) Activation of latent TB: There is a monthly probability of activation (termed "reactivation TB" in most literature) dependent on the following factors: time since infection, HIV status, and CD4 count.
    a. Patients experience a risk of activating to active TB disease in a step-wise fashion; typically, the activation rate is highest in the first two years since infection, and this risk is greatly reduced after 2 years. Model users are able to define two activation rates stratified by time since TB infection.

2) Primary progressive TB: This transition to active disease occurs in the same month of either infection or reinfection; thus the patient enters the Latent TB state in that month but essentially bypasses it and moves directly on to Active Pulmonary TB or Active Extrapulmonary TB within the same month. [**Note:** The ordering of the Uninfected, Latent TB, and Active Pulmonary TB and Active Extrapulmonary TB subroutines allows a person to go from Uninfected to Active Pulmonary TB or Active Extrapulmonary TB in the same month; this is primary progressive TB.] The probability of primary progressive TB will equal the probability of activation in the first month and will be higher than activation probabilities in subsequent months (see equations above).

After this transition, patients will draw for becoming *sputumbacloadhi*, which will depend on CD4 status. [**Note**: In the future, this distribution may depend on age for pediatric-related analyses]

ACTIVATION

Incidence of TB Activation

	Time Since Infection	
N1 =	24	
Probability	x <= 24 mths	x > 24 mths
HIV -	1.0000	1.0000
CD4 VHI	1.0000	1.0000
CD4 HI	1.0000	1.0000
CD4 MHI	1.0000	1.0000
CD4 MLO	1.0000	1.0000
CD4 LO	1.0000	1.0000
CD4 VLO	1.0000	1.0000

Distribution of Pulmonary and Extra Pulmonary

	Pulm	ExtraPulm
HIV -	1.0000	0.0000
CD4 VHI	1.0000	0.0000
CD4 HI	1.0000	0.0000
CD4 MHI	1.0000	0.0000
CD4 MLO	1.0000	0.0000
CD4 LO	1.0000	0.0000
CD4 VLO	1.0000	0.0000

Sputum Bacillary Load Hi Once Activated (Pulm only)

Probability	
HIV -	0.0000
CD4 VHI	0.0000
CD4 HI	0.0000
CD4 MHI	0.0000
CD4 MLO	0.0000
CD4 LO	0.0000
CD4 VLO	0.0000

F: Latent TB → Active Extrapulmonary TB (50c)

There are two pathways for this transition, essentially the same as those described in **E**. The ratio of active extrapulmonary to pulmonary TB cases rises as CD4 falls. Patients will not draw for *sputumbacloadhi* after this

transition as patients with extrapulmonary TB do not have high bacillary load in their sputum (and in fact are sputum smear-negative).

G: Latent TB → Dead (60a)
Death occurs from a non-TB cause, toxicity from TB prophylaxis, or toxicity from TB treatment.

H: Active Pulmonary TB → Active Pulmonary TB (50f)
This is the default for this state. A patient will remain in this state while on treatment, and current treatment will be marked with a time-counted flag (*onTBtreatmentX)*. A patient who draws treatment failure (defined clinically as positive culture at end of treatment course) or who is lost to follow-up (having initially rolled for failure) will remain in this state. Those who fail from treatment will be flagged as such and will have a higher probability of acquiring drug resistance (i.e., developing MDR-TB or XDR-TB). Patients who fail and are flagged as *sputumbacloadhi* will keep this flag.

I:Active Pulmonary TB → TB Treatment Default
Patients who are on TB treatment and who roll for TB treatment default will transition to the TB Treatment Default state, unless they roll for failure in which case they will remain in the Active TB state.

J: Active Pulmonary TB → Previously Treated TB (50d)
Patients who achieve treatment success (completion of appropriate treatment for strain and negative culture at end of treatment course) undergo this transition. They will be flagged as having successfully completed treatment and having had a prior episode of active TB.

Patients who do not successfully complete treatment, or who were never on treatment despite having active TB, have a probability of self-cure after a user-defined period of time (though they are subject to the monthly mortality risk from untreated TB until then). After this user-defined period of time, the patient transitions to the Previously Treated TB state and is flagged as having had a prior episode of active TB.

Patients who default on treatment will have a probability of success weighted by the proportion of their treatment that they complete. Those who default and roll for success will transition to the Previously Treated TB state and will be considered treatment successes, though they will have flagged as having defaulted. They will be flagged as having had a prior episode of active TB.

Patients who undergo this transition will lose their *sputumbacloadhi* tracker variable if it is present. *(Refer to "TB clinic treatment subroutine" section below for details on treatment success/failure.)*

K: Active Pulmonary TB → Dead (60a)
Death occurs from active pulmonary TB, including untreated or undertreated TB (e.g. treatment for ds TB when the patient in fact has MDR-TB), toxicity from TB treatment, or a non-TB cause.

L: Active Extrapulmonary TB → Active Extrapulmonary TB (50f)
Similar to the description provided in **H**.

M: Active Extrapulmonary TB → Previously Treated TB (50d)
Similar to the description provided in **J**.

N: Active Extrapulmonary TB → Dead (60a)
Similar to the description provided in **K**.

O: Previously Treated TB → Previously Treated TB (50d)

This is the default for this state. A patient will remain in this state as long as he/she does not die, develop reinfection, or relapse.

P: Previously Treated TB → Latent TB (50f)

This transition involves reinfection with any strain of *Mycobacterium tuberculosis*. The probability of reinfection will be defined as that described for infection in **B**. The patient can then go on to develop active TB disease via the two pathways described in **E**. The reinfecting strain will replace the prior strain (e.g., if a patient completed treatment for MDR-TB in the past and now becomes infected with dsTB, then they will be flagged as having only dsTB, and potential subsequent activation will reflect dsTB). If patients are reinfected and were previously *immreactno*, they will draw again for either *immreactyes* or *immreactno.*

Q: Previously Treated TB → Active Pulmonary TB (50g)

This direct transition involves relapse of active disease from the same strain of *Mycobacterium tuberculosis* that caused the previous active disease. The incidence of relapse depends on months since completion of successful TB treatment or since self-cure (i.e., time since transitioning from Active TB to Previously Treated TB state; relapse incidence declines over time and is CD4-dependent). After this transition, patients will draw for becoming *sputumbacloadhi*, which will depend on CD4 status. This will follow the approach outlined in section E (Latent TB to Active Pulmonary TB) with the following change:

As data suggests that the transition rate stabilizes at approximately 5 years (60 months), for HIV-negative patients, we will have:

$$p(transition\ at\ time\ t) = PTtoARateMultiplier * e^{-x_{PTtoA}(\min[t,60])}$$

where $-x_{PTtoA}$ is determined from the literature of HIV-negative patients from the rate at which relapse decrease over time, while the PTtoARateMultiplier is included so that the integrated value from t=0 to t=life expectancy of

($PTtoARateMultiplier * e^{-x_{PTtoA}(\min[t,60])}$) equals the estimated proportion of individuals with previously treated TB who will relapse to active pulmonary TB over their lifetime.

This change will also be used in the monthly relapse rate for HIV-infected individuals. Patients who relapse will face a probability of increasing strain resistance.

RELAPSE

Incidence of TB Relapse

probRelapse=F(CD4)*Multiplier*e^(-x*(min[t,threshold]))/(propTxComp)

Multiplier	x	threshold (months)
0.0000	0.0000	60

	F(CD4)
CD4 VHI	1.0000
CD4 HI	1.0000
CD4 MHI	1.0000
CD4 MLO	1.0000
CD4 LO	1.0000
CD4 VLO	1.0000

Distribution of Pulmonary and Extra Pulmonary

	Pulm	ExtraPulm
HIV -	1.0000	0.0000
CD4 VHI	1.0000	0.0000
CD4 HI	1.0000	0.0000
CD4 MHI	1.0000	0.0000
CD4 MLO	1.0000	0.0000
CD4 LO	1.0000	0.0000
CD4 VLO	1.0000	0.0000

Sputum Bacillary Load Hi Once Relapsed (Pulm only)

Probability	
HIV -	0.0000
CD4 VHI	0.0000
CD4 HI	0.0000
CD4 MHI	0.0000
CD4 MLO	0.0000
CD4 LO	0.0000
CD4 VLO	0.0000

R: Previously Treated TB → Active Extrapulmonary TB (50g)
Similar to the description provided in **Q**, adjusted for probability of developing extrapulmonary rather than pulmonary TB.

S: **Previously Treated TB → Dead (60a)**
Death occurs from a non-TB cause or toxicity from TB treatment.

T: TB Treatment Default → Active Pulmonary (27e) or Active Extrapulmonary TB (50g)
This transition represents relapse to the either the Active Pulmonary TB state or the Active Extrapulmonary TB state, dependent upon CD4 and time.

Upon defaulting, those who had initially rolled for treatment success now roll again for success vs. failure: this time, the probability of success is proportional to the number of months of treatment completed before defaulting (e.g., if the patient completed 2 months of the planned 6 months of treatment, then the probability of success is 0.33). Those who roll for failure this time go to one of the "Active TB" states (whichever one they were in previously). They have a probability of increased resistance (i.e., a more drug-resistant strain of TB) after defaulting, as defined in the TB treatment tab. Those who again roll for success go to the "Default" state; they do not have active TB, but they are at higher risk for relapse.

If a patient who defaults subsequently becomes reinfected, then they are flagged with the new strain.

U: TB Treatment Default → Latent TB (50f)
Patients who have defaulted can get reinfected with Latent TB and will be flagged with *PriorTreatmentDefault* and will have an increased risk of developing Active TB.

After evaluating each natural history subroutine, all patients will be evaluated for the symptom flag (*symptomyes*/*symptomno*), which indicated the presence of symptoms consistent with TB and can be defined by the user.

TB SYMPTOMS

Monthly Incidence of TB symptom occurence

Prob symptoms	Uninfected	Latent TB	Active Pul	Active Extr	Prev Treat	TB Treat Default
HIV -	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 VHI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 HI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 MHI	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 MLO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 LO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
CD4 VLO	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

- If a patient is not symptomatic (*symptomno*), he/ she will roll for acquiring symptoms this month, which will depend on TB state and CD4.
- If a patient is currently symptomatic (*symptomyes*), he/ she will clear that flag and roll again if not in the Active Pulmonary TB or Active Extrapulmonary TB state. If the patient is in one of those two states, he/she will keep the *symptomyes* flag (assumption).

Drug Toxicity Updater (30a)

TB prophylaxis and treatment toxicities will be evaluated in CEPAC in the same section as ART toxicities and other OI prophylaxis toxicities. Patients who are currently on prophylaxis or treatment (described later in the specifications) will be flagged with the variables *onTBprophylaxisX* or *onTBtreatmentX*, respectively, where *X* refers to the prophylaxis or

treatment regimen that the patient is receiving. Currently, this module does not consider interactions between TB drugs and *specific* HIV drugs, but it does allow for a higher likelihood of toxicity if a patient is on both TB and HIV regimens.

TB Prophylaxis Toxicity (30d)

Each month that a patient carries the *onTBprophylaxisX* flag, he/she will roll for toxicity, stratified by on/off ART to simulate increased toxicity for patients on ART (e.g., hepatotoxicity). If the toxicity is rolled for, the patient will accrue a cost (*TBprophtoxcost*) and quality of life (QOL) modification (*TBprophtoxQOL*).

The patient will also accrue a mortality risk (*TBprophtoxmortality*) to be added and evaluated in the Mortality Updater (60a).

TB Prophylaxis Toxicity

		Minor Tox Monthly Prob		Major Tox Monthly Prob		
Number	Prophylaxis Name	Off ART	On ART	Off ART	On ART	Prob Dth (Maj)
0	Isoniazid	0.000000	1.0000	0.000000	1.0000	0.000000
1	Rifampin	0.000000	1.0000	0.000000	1.0000	0.000000
2	User Proph 1	0.000000	1.0000	0.000000	1.0000	0.000000
3	User Proph 2	0.000000	1.0000	0.000000	1.0000	0.000000
4	User Proph 3	0.000000	1.0000	0.000000	1.0000	0.000000

Patients who are HIV-uninfected will be scheduled for an Emergency TB Clinic Visit in the same month that they experience a toxicity event. Patients who are HIV-infected will be scheduled for an Emergency TB Clinic Visit this month in both HIV/TB integrated clinic settings and non-integrated settings.

TB Treatment Toxicity (30d)

Similar to TB prophylaxis toxicity, each month that a patient carries the *onTBtreatmentX* flag, he/she will roll for toxicity. If the toxicity is rolled for, the patient will accrue a cost (*TBtreatmenttoxcost*) and quality of life (QOL) decrement (*TBtreatmenttoxQOL*).

Toxicity

	Minor Tox Monthly Prob		Major Tox Monthly Prob		
	Off ART	On ART	Off ART	On ART	Prob Dth (Maj)
HIV -	0.000000	0.000000	1.000000	1.000000	0.500000
HIV +	0.000000	0.000000	1.000000	1.000000	0.500000

	Minor Tox Cost	Minor Tox QOL Mult	Major Tox Cost	Major Tox QOL Mult
HIV -	0.00	1.0000	0.00	1.0000
HIV +	0.00	1.0000	0.00	1.0000

The patient will also accrue a mortality risk (*TBtreatmenttoxmortality*) to be added and evaluated in the Mortality Updater (60a).

Patients who are HIV-uninfected will be scheduled for an Emergency TB Clinic Visit in the same month that they experience a toxicity event. Patients who are HIV-infected will be scheduled for an Emergency TB Clinic Visit this month in both HIV/TB integrated clinic settings and non-integrated settings.

General Mortality Updater (60a)

The General Mortality Updater is already a framework within the CEPAC module which accrues all of the mortality probabilities in the Disease section of CEPAC and evaluates whether a patient dies in that month. This TB module will not change this structure at all, but will need: untreated TB mortality (*untreatedTBmortalityCD4xxx*, where xxx denotes CD4 stratum [e.g., vhi, hi, mhi, etc.]), TB prophylaxis toxicity mortality (*TBprophtoxmortality*), and TB treatment toxicity mortality (*TBtreatmenttoxmortality*). Those who rolled for treatment success (*TBTreatmentSuccess*) will have a mortality risk while on treatment that is equal to the product of probability of mortality from active, untreated TB and the multiplier for mortality while on successful treatment (the probability of treatment success depends on the

appropriateness of the regimen for that strain). Those who rolled for treatment failure (*TBTreatmentFail*) will have a mortality risk equivalent to the product of the probability of mortality from active, untreated TB and the multiplier for mortality while on failed treatment.

TB mortality may be adjusted by a multiplier dependent on calendar month. This feature was added to the module to prevent excess TB deaths in the first month, as patients in the active TB state were subject to probability of TB mortality in month 0 before they even have a chance to roll for entering the diagnostic algorithm and initiating TB treatment (patients essentially go through this mortality updater prior to clinic updater). The user may specify a time point to demarcate different multipliers to TB mortality in the cell for "N=". For example, if N=1, and month <=N is set to 0.0, then patients with untreated, active TB will face 0% chance of dying from TB in months 0 and 1.

MORTALITY				
Mortality from TB (Active, untreated TB)				
Prob death		Active Pulm TB	Active Extrapulm TB	
	HIV -	1.0000	1.0000	
	CD4 VHI	1.0000	1.0000	
	CD4 HI	1.0000	1.0000	
	CD4 MHI	1.0000	1.0000	
	CD4 MLO	1.0000	1.0000	
	CD4 LO	1.0000	1.0000	
	CD4 VLO	1.0000	1.0000	
Multiplier by Tx and fail/success draw:				
If on successful treatment				0.0000
If on failed treatment				0.0000
Multiplier by calender month				
N =	0			
month <= 0	1.0000			
month > 0	1.0000			

Behavior Updater (90a/b)

The Behavior Updater in CEPAC handles loss to follow-up (LTFU) and return to care (RTC). The default is to assume that HIV care and TB care are not integrated (i.e., they operate independently of each other), though we plan to allow for integration of HIV care and TB care, designated by a toggle (yes/no).

If HIV care and TB care are not integrated, HIV-infected patients who are LTFU in HIV care are not automatically LTFU in TB care. Patients who are LTFU will be moved into the "TB Treatment Default" state if they have not attended a TB clinic for a user-defined number of months (usually 2 months). Patients who are LTFU for less than the user-defined number of months for defaulting will remain in the TB state they were in upon LTFU. Note that HIV-uninfected patients will skip the Behavior Updater (as they currently do) since they cannot be LTFU to HIV care.

When HIV care and TB care are integrated, being LTFU in HIV care will automatically signify being LTFU in TB care. When a patient rolls for LTFU in HIV care, the module will evaluate if the patient is on TB prophylaxis (*onTBprophlyaxisX*) or on TB treatment (*onTBtreatmentX*), and will clear these flags, thus stopping both TB prophylaxis and treatment for patients who are LTFU. Patients who were destined to fail treatment will still fail and remain in the Active TB state. Patients who were destined to complete treatment successfully will draw for treatment failure based on the proportion of their treatment they completed before going LTFU upon defaulting. Patients who fail will draw for *sputumbacloadhi*.

HIV Clinic Visit Updater (130a)

The Clinic Visit Updater currently describes the HIV clinic visit and all of its subroutines. We propose to add a TB Treatment Program Subroutine and a TB Proph Program Subroutine (identical to the TB Treatment and TB Proph subroutines, respectively, in the TB Clinic Visit Updater) when the TB Module is enabled and when HIV care and TB care are integrated at the HIV Clinic.

TB Testing at HIV Clinic Updater (135b)

The TB Testing at HIV Clinic Updater is used to simulate the diagnosis and treatment of TB within the setting of an HIV clinic and to ultimately link patients to TB treatment via the TB linkage subroutine (130p). Patients receiving TB testing at an integrated HIV/TB clinic will always link to TB treatment and care.

Attendance at HIV clinic this month will be evaluated. These specifications are already in use in CEPAC and, thus, are not described here. Patients not attending clinic in this month skip the rest of the TB Testing at HIV Clinic Updater.

Patients who attend HIV clinic this month will be evaluated for Active Pulmonary TB or Extrapulmonary TB. As a simplifying assumption, patients who are on successful TB therapy will not be subject to further diagnostic testing.

For patients to enter the TB diagnostics subroutine, the TB Diagnostics Tab must be turned on (set to 0). If this is turned off, patients will automatically link to TB care upon incidence of active TB.

If patients should be automatically linked to TB care in month 0 (and we still want TB diagnostics to be turned ON for subsequent months), patients can roll for a probability of starting in TB care upon entry to the model based on their TB state. Because these patients have not undergone DST prior to initiating care, their observed strain will be equal to their true strain for all states except for TB uninfected, which will default to observed dsTB.

Prob of starting in TB Care					
Uninfected	Latent TB	Active Pulm TB	Active Extrapulm TB	Prev Treat	TB Treat Default
0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

By default, patients are only allowed to accept and take one TB test a month and are unable to move onto the next test until the results of the previous test are picked up. If a patient fails to accept their initial test, the patient will have to start the entire testing sequence over again should s/he need to be tested again. The testing sequence is not re-offered unless the patient meets initiation criteria again.[1]

However, if 'Allow Multiple Tests in Same Month' is turned on, patients will continue TB testing (tests and order of testing as defined below) until they fail to accept a test, fail to pick-up the results of a previous test, or finish all tests specified in the same month.

Enable TB Diagnostics	1	**0** = no, **1** = yes
Allow Multiple Tests in Same Month?	0	**0** = no, **1** = yes

Patients who are not on TB therapy will be tested for TB if: a) they are due for scheduled TB screening this month, or b) they meet the criteria to be tested. Other criteria for the timing of screening will include:

1. Upon HIV diagnosis

[1]This is so that a patient can be offered a test (in month 0, for instance), not accept a test (proxy for inability to produce sputum), but still begin empiric treatment. If they meet initiation criteria again after undergoing empiric treatment (for example, develop TB symptoms later on), they can restart the testing sequence.

2. Presentation with TB symptoms, defined as a probability (0 to 1)
3. At HIV clinic visit with CD4<200 (or other CD4 criterion)
4. With any OI
5. At month X in model simulation (one-time)
6. Every Y months (recurring)

Initiation Policy for TB Testing

Use Policy?						
					0	**Note:** use 0="AND", 1="OR"
1	YES	Upon HIV Diagnosis			AND	
1	YES	With TB Symptoms			AND	
0	NO	With any OI			AND	
0	NO	0	**< CurrCD4 <**	350	AND	
0	NO	Calendar month		0	AND	
0	NO	Months between testing		1	AND	

If these criteria are met (either any criteria if using 'OR' and all specified criteria when using 'AND'), the patient will be subject to diagnostic testing. If not, the patient will skip the rest of the TB Testing at HIV Clinic Updater.

Patients will be eligible for up to 4 diagnostic tests (which can include combinations of chest X-ray, sputum smear, sputum culture, sputum GeneXpert, and urine LAM, though the four tests can be parameterized to represent any type, number, or order of tests). All test results, except for sputum culture, will be evaluated in the month of screening, and the results will be drawn in that month.

Each test will be associated with a "Time to results" parameter, signifying the delay to result associated with each test (i.e., sputum smear results are available immediately whereas sputum culture results require up to 2 months, and longer for conventional drug-susceptibility testing). This parameter will be a probability distribution with mean month and standard deviation. If the test results are positive and available in that month, the patient will be flagged as diagnosed with TB, which will inform TB treatment decisions later that month in the module. If a test result is not available in that month, the patient will receive the test result in a subsequent month, and that test result can inform clinical decisions only after it has been received.

The tests will be ordered and performed according to the test matrix below. A value of "1" indicates that the test should be performed, and a value of "0" indicates that the test should not be performed. For example, if Test 1 is sputum smear, and the result is positive, one may forgo additional diagnostic tests. Users may also specify whether a particular test should be linked to or associated with a drug susceptibility test, which tests for the drug resistance pattern of the TB strain causing TB disease.

Test Ordering

	Test Number	Test Name	Include DST?	
1st	0	*Test 0*	0	**0** = no, **1** = yes
2nd	1	*Test 1*	0	**0** = no, **1** = yes
3rd	2	*Test 2*	0	**0** = no, **1** = yes
4th	3	*Test 3*	0	**0** = no, **1** = yes
	-1 = none			

There is an additional test ordering sequence section for patients being treated a second time (e.g., for surveillance for relapse after an initial treatment regimen has been completed).

Test Sequence Matrix										
	If 2 tests									
	Perform test 1 when	Test 0 +	1	**0** = no, **1** = yes						
		Test 0 -	0	**0** = no, **1** = yes						
	If 3 tests		Test 1 +	Test 1 -						
	Perform test 2 when	Test 0 +	0	1	**0** = no, **1** = yes					
		Test 0 -	1	1	**0** = no, **1** = yes					
	If 4 tests	**Test 2 +**				**Test 2 -**				
	Perform test 3 when		Test 1 +	Test 1 -			Test 1 +	Test 1 -		
		Test 0 +	0	1	**0** = no, **1** = yes	Test 0 +	1	1	**0** = no, **1** = yes	
		Test 0 -	1	1	**0** = no, **1** = yes	Test 0 -	1	1	**0** = no, **1** = yes	

Each test will have a defined sensitivity (the probability of a positive test result for those in the Active Pulmonary TB and Active Extrapulmonary TB states) and specificity (the probability of a negative test result for those who truly do not have active TB).

TB Test 0

Test Name:	Test 0					
Test characteristics						
TB Positive Test Rate	Uninfected	Latent TB	Active Pulm TB	Active Extrapulm TB	Prev Treat TB	TB Treat Default
HIV -	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 VHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 HI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 MHI	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 MLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 LO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000
CD4 VLO	0.0000	0.0000	1.0000	0.0000	0.0000	0.0000

Each test will also have a probability of test acceptance, probability of result pick-up, and time to result pick-up. Patients will roll for a one-time probability of picking up the results of each diagnostic test. For patients who roll to pick up their results, they roll for a "time to result pick up". If these patients pick up the results before the time defined in the "repeat all tests if not picked up by n months" cell, then they move onto the next test (if available) or receive a diagnosis. If these patients pick up the results after the time defined in the "repeat all tests if not picked up by n months," then they will repeat all diagnostic tests when they "show up" to pick up their results.

For patients who roll to **not** pick up their results: if they present for testing again before the time defined by the "repeat all tests if not picked up by n months" cell (because they still fall under the criteria described in the TB testing initiation policy), then they will simply have to repeat the current test. If they show up after that time frame, they will have to repeat all diagnostic tests.

Probability of test acceptance	1.0000	
Probability of result pick-up	1.0000	
Repeat all tests if not picked up by n months:	6	
	Mean	SD
Time to result pickup (mth)	6.0000	0.0000

Drug Resistance Testing Subroutine (135c')

Tests that include drug resistance testing will enter the "Drug Resistance Testing Subroutine" via a yes/no toggle under the Test Ordering section.

There is resistance testing for the 3 strains (ds-TB, MDR-TB, XDR-TB) of TB.

Drug Resistance Positive Test Rate		ds-TB	MDR-TB	XDR-TB	Months to Result
	ds-TB	1.0000	0.0000	0.0000	2
	MDR-TB	0.0000	1.0000	0.0000	2
	XDR-TB	0.0000	0.0000	1.0000	2
			Note: columns must sum to 1.0 for all strains		

The sensitivities and specificities of the drug resistance tests will be used to populate the cells. Those testing positive for MDR-TB will receive the tracker variable *ObservedMDRTB*. Those testing positive for XDR-TB will receive the tracker variable *ObservedXDRTB*. Like the result of a test without DST, the result of DST will be evaluated in that month but will be made available only after a user-specified amount of time. Patients who receive the diagnosis of MDR-TB or XDR-TB in a given month will begin treatment or switch to the correct treatment that month.

If the drug resistance test is not linked to the diagnostic test result, patients will roll for a probability of results pick-up for each drug susceptibility test.

Is DST linked to diagnostic test?	1	**0** = no, **1** = yes
If not linked, probability of DST result pick-up:	0.5000	

Each test also has associated costs and QOL multipliers.

Initial TB test cost	0.00
Initial TB test QOL multiplier	0.00
Addit. Cost for drug sensitivity testing	555.00

Because we are including the possibility of multiple diagnostic assays, we will also need to include a diagnostic "Result Interpretation Matrix" to determine the clinical diagnosis based on the combination of results from the test sequence matrix. For example, if two tests are performed, we are likely to consider the patient diagnosed with TB if both tests are positive, or if one of the tests is positive, but not if neither test is positive. Patients can be diagnosed with TB and begin treatment after having undergone multiple diagnostic tests even if they do not accept the final test(s) or pick up the results of the final test(s).[2] In each combination of tests and results, the user must specify the clinical diagnosis.

[2] This can be used as a proxy for the ability or inability to produce sputum for diagnostics that use sputum as a medium (i.e., sputum smear, sputum culture, sputum GeneXpert). In this case, the sputum test(s) would have to be indicated at the end of the diagnostic algorithm. For example, clinical assessment and chest x-ray could be listed as the first and second tests, and sputum smear and sputum Xpert could be listed as the third and fourth tests. A patient unable to provide a sputum specimen would undergo the first two tests but not the third or fourth tests.

Result Interpretation Matrix

If 1 test	Test 0 +	1	0 = no, 1 = yes						
Diagnosed TB when	Test 0 -	0	0 = no, 1 = yes						
If 2 tests		Test 1 +	Test 1 -						
Diagnosed TB when	Test 0 +	1	1	0 = no, 1 = yes					
	Test 0 -	1	0	0 = no, 1 = yes					
If 3 tests	**Test 2 +**				**Test 2 -**				
Diagnosed TB when		Test 1 +	Test 1 -			Test 1 +	Test 1 -		
	Test 0 +	1	1	0 = no, 1 = yes	Test 0 +	1	1	0 = no, 1 = yes	
	Test 0 -	1	1	0 = no, 1 = yes	Test 0 -	1	0	0 = no, 1 = yes	
If 4 tests	**Test 3 +**								
Diagnosed TB when	Test 2 +				Test 2 -				
		Test 1 +	Test 1 -			Test 1 +	Test 1 -		
	Test 0 +	0	0	0 = no, 1 = yes	Test 0 +	1	1	0 = no, 1 = yes	
	Test 0 -	0	1	0 = no, 1 = yes	Test 0 -	1	1	0 = no, 1 = yes	
	Test 3 -								
	Test 2 +				Test 2 -				
		Test 1 +	Test 1 -			Test 1 +	Test 1 -		
	Test 0 +	1	1	0 = no, 1 = yes	Test 0 +	1	1	0 = no, 1 = yes	
	Test 0 -	1	1	0 = no, 1 = yes	Test 0 -	1	1	0 = no, 1 = yes	

Recall that there is an additional test ordering section for patients repeating the testing sequence (e.g., for surveillance for relapse after an initial treatment regimen has been completed). Results from the tests of both patient populations (those undergoing initial testing and those undergoing subsequent testing) go through the same result interpretation matrix, though the number and types of tests may differ between the two test ordering sequences (for example, a patient might be tested via sputum smear microscopy, sputum culture, and chest x-ray the first time, but only by sputum culture the second time).

A patient can be given empiric treatment for active TB, even in the absence of a definitive diagnosis of active TB. Scenarios in which this can occur include: 1) no additional diagnostic testing is done; 2) the clinician is waiting for the result of a diagnostic test (especially sputum culture); or 3) the clinician believes that the patient has active TB despite negative or inconclusive diagnostic test results.

Regimen

The majority of patients who are given empiric treatment for active TB are presumed to have dsTB, and accordingly will be given a first-line multidrug treatment regimen for dsTB. The only patients who may be given an empiric treatment regimen targeting MDR-TB or XDR-TB will be those who have a known history (flag) of active TB disease with either of these strains since entering the model; these patients will have a probability of being given an empiric treatment regimen for MDR-TB or XDR-TB. The empiric treatment regimens to be given for presumed dsTB, MDR-TB, or XDR-TB are defined by the user.

Empiric Therapy

Probablility of Empiric MDR-TB treatment for those with known history of MDR-TB	1.0000
Probablility of Empiric XDR-TB treatment for those with known history of XDR-TB	1.0000

Empiric Therapy Treatment Num

DS-TB	MDR-TB	XDR-TB
0	1	2
Treatment 0	*Treatment 1*	*Treatment 2*

Initiation of empiric treatment

Empiric treatment can be *initiated* in the following scenarios, dependent on HIV status and CD4 count:

1) Patient is symptomatic; awaiting result of TB Text X
2) Patient is asymptomatic; awaiting result of TB Test X
3) Patient is symptomatic; TB Test X comes back positive (a non-definitive test such as chest x-ray) and clinician is still awaiting the result of TB Test Y
4) Patient is asymptomatic; TB Test X comes back positive (a non-definitive test such as chest x-ray) and clinician is still awaiting the result of TB Test Y
5) Patient is symptomatic; has been offered test (whether or not they have accepted it)
6) Patient is asymptomatic; has been offered test (whether or not they have accepted it)

Probability of initiating empiric treatment				
	While Awaiting Results		Upon Positive Result	
	Symptomatic	Asymptomatic	Symptomatic	Asymptomatic
HIV -	0.0000	0.0000	0.0000	0.0000
CD4 VHI	0.0000	0.0000	0.0000	0.0000
CD4 HI	0.0000	0.0000	0.0000	0.0000
CD4 MHI	0.0000	0.0000	0.0000	0.0000
CD4 MLO	0.0000	0.0000	0.0000	0.0000
CD4 LO	0.0000	0.0000	0.0000	0.0000
CD4 VLO	0.0000	0.0000	0.0000	0.0000

If modeling a scenario where all symptomatic patients are given empiric treatment and no additional diagnostic tests are performed, the user can specify that a clinician's "detection" of symptoms is a positive test result (TB Test 0), and the probability of symptomatic patients starting empiric treatment given this positive test result is 1.

Cessation or continuation of empiric treatment

Empiric treatment can be *stopped* in the following scenarios:

1) Patient is symptomatic; pending TB Test X comes back negative
2) Patient is asymptomatic; pending TB Test X comes back negative

The probability of each of these is defined by the user in the input sheet ("probability of stopping empiric therapy upon negative result").

Probability of stopping empiric therapy upon negative result		
	Symptomatic	Asymptomatic
	0.0000	0.0000

Empiric treatment can be *continued* in the following scenarios:

1) Patient is symptomatic; pending TB Test X comes back negative
2) Patient is asymptomatic; pending TB Test X comes back negative

The probability of each of these is defined in the input sheet as 1 minus the "probability of stopping empiric therapy upon negative result."

Duration of treatment

If a patient is on empiric treatment and a subsequent test result (e.g., sputum culture) returns positive, then the same treatment will be continued assuming that it's for the same strain; e.g., if normal treatment duration for dsTB is 6 months and the patient received empiric dsTB treatment for 2 months before getting a positive sputum

culture, then dsTB treatment will be continued for an additional 4 months. However, if the patient's observed strain turns out to be different from the strain targeted by empiric treatment (e.g., patient received 2 months of empiric dsTB therapy but then is observed to have MDR-TB by a test result indicating such), then the patient will start an MDR-TB treatment regimen from scratch; the 2 months of dsTB treatment do not count.

Costs and toxicities

While on an empiric treatment regimen, the patient accrues costs and toxicity probabilities defined for that regimen, identical to those defined for those on non-empiric treatment. If a patient experiences minor toxicity from empiric treatment, the treatment will be continued. If a patient experiences major toxicity while on empiric treatment, the treatment will be stopped; the patient will not be switched to a different regimen. However, if a pending test results subsequently returns positive, the patient can start "non-empiric" treatment with the next regimen.

Empiric treatment as prophylaxis

Empiric treatment, when the full duration is completed, should also be considered as effective prophylaxis; in other words, it will reduce the risk of infection, reinfection, and activation in a manner similar to prophylaxis.

Once all test results for a month have been evaluated, if the patient is diagnosed with TB (*ObservedxxxTB*) he/she will be flagged to begin treatment in that month if not already on treatment. Patients flagged to begin treatment will roll for linking to TB clinic if HIV/TB care is not integrated (schedule Emergency TB Clinic Visit).

Probability of Linking to TB Treatment Upon TB-positive diagnosis:	
Integrated HIV/TB Clinic	1.0000
Non-integrated HIV/TB Clinic	1.0000

Patients who are HIV-infected but undetected (and not linked to HIV care) and receive a TB-positive diagnosis will also roll for becoming detected as having an HIV infection upon linking to TB care.

Probability of HIV Detection Upon Linkage to TB Care	
Integrated HIV/TB Clinic	1.0000
Non-integrated HIV/TB Clinic	1.0000

TB Clinic Visit Updater (135a)

The TB Clinic Visit Updater is used to simulate the diagnosis and treatment of TB within the setting of a TB clinic that is not integrated with the HIV clinic in the CEPAC model. Thus, patients can be in or out of care at either clinic independently. Additionally, HIV-negative patients who do not cycle through the HIV clinic in CEPAC are able to cycle through the TB Clinic Visit Updater to manage their TB care. HIV-infected individuals who are diagnosed with TB during their HIV clinic visit (see previous section "TB Testing at HIV Clinic Updater") can link to the TB Clinic Visit updater.

Will Attend TB Clinic This Month (135b)

As with the HIV Clinic in CEPAC, patients will be evaluated for attendance at a TB clinic visit this month.

- Patients who are TB LTFU and who do not return to care will not attend clinic.
- Patients who are HIV-uninfected will attend TB clinic only if they are symptomatic and roll to present to TB clinic. HIV-uninfected patients can also have a probability of showing up to TB clinic via a screening intervention (this will allow us to model TB-screening interventions in HIV-negative patients and how

wide of a "net" the intervention must cast.) Patients who are HIV-uninfected will enter directly into the TB Clinic Diagnostics Subroutine.

- HIV-infected patients will not attend TB clinic if HIV/TB care is integrated. If HIV/TB care is not integrated, patients who link to TB clinic from the "TB Testing at HIV Clinic Updater" will skip the diagnostic portion of the TB Clinic Visit updater, so as not to cycle twice through the diagnostic algorithm. HIV-infected patients who have not been linked to TB clinic from the HIV clinic will cycle through the TB Clinic Diagnostics Subroutine.
- All patients awaiting a TB diagnosis, on TB treatment, scheduled to start or stop prophylaxis, or experiencing a treatment or prophylaxis toxicity this month will attend TB clinic, unless they are LTFU.

TB Clinic Diagnostics Subroutine (135c)

The TB Clinic Diagnostics Subroutine and drug resistance testing subroutine will function almost identically to the "TB Testing at HIV Clinic" subroutine with the following exceptions:

1. No evaluation of "Will attend HIV Clinic this month?"
2. No linking to TB care after positive diagnosis (patient is already in TB care).

TB Clinic Treatment Subroutine (135g)

The TB Clinic Treatment Subroutine links patients who have been diagnosed with TB to TB treatment. It deals with the clinical management of TB and the efficacy of treatment. All patients can receive TB treatment, regardless of true TB natural history state. This will allow treatment of those who do not truly have TB (false positives).

Based on the presence of the diagnosed drug strain tracker variables (*ObserveddsTB*¸ *ObservedMDRTB*, *ObservedXDRTB*), patients will have a probability of receiving each line of therapy as initial treatment. The probabilities for each strain must sum to one. Patients not identified as having drug-resistant TB will be assumed to have drug-susceptible TB.

Probability of Receiving Each line as initial treatment

			Prob Initial		
	TB Treatment #	Name of Treatment	Observed ds-TB	Observed MDR-TB	Observed XDR-TB
	0	*Treatment 0*	1.0000	0.0000	0.0000
	1	*Treatment 1*	0.0000	1.0000	0.0000
	2	*Treatment 2*	0.0000	0.0000	1.0000
	3	*Treatment 3*	0.0000	0.0000	0.0000
	4	*Treatment 4*	0.0000	0.0000	0.0000
	5	*Treatment 5*	0.0000	0.0000	0.0000
	6	*Treatment 6*	0.0000	0.0000	0.0000
	7	*Treatment 7*	0.0000	0.0000	0.0000
	8	*Treatment 8*	0.0000	0.0000	0.0000
	9	*Treatment 9*	0.0000	0.0000	0.0000
			Must sum to 1	**Must sum to 1**	**Must sum to 1**

Users can specify a time lag to the start of treatment initiation. Each line of treatment will have a user-specified intended duration.

Months Lag to Treatment Initiation	Mean	Std Dev
	0.00	0.00

The user can define the name of each treatment line and specify the intended treatment duration and initial/monthly costs.

Treatment Name:	Treatment 0	
Treatment Duration Mths	0	
	Initial	Monthly
Cost of Treatment	0.00	0.00

When starting a line of treatment, a patient will roll for a destined treatment outcome. The two options will be *TBTreatmentSuccess* and *TBTreatmentFailure*. The distribution will be dependent upon HIV status, CD4 count, and the true TB strain.

Overall Probability of Treatment Success(Those not in active TB states automatically roll success)			
	ds-TB	MDR-TB	XDR-TB
HIV -	1.0000	1.0000	1.0000
CD4 VHI	0.0000	0.0000	0.0000
CD4 HI	0.0000	0.0000	0.0000
CD4 MHI	0.0000	0.0000	0.0000
CD4 MLO	0.0000	0.0000	0.0000
CD4 LO	0.0000	0.0000	0.0000
CD4 VLO	0.0000	0.0000	0.0000

Patients with Active Pulmonary TB or Active Extrapulmonary TB who roll for treatment success will not face monthly probabilities of TB mortality; these patients will lose their *sputumbacloadhi* flag if present. Patients in the Active Pulmonary TB or Active Extrapulmonary TB states who successfully complete treatment will move to the Previously Treated TB health state.

Those who roll for treatment failure (*TBTreatmentFail*) will continue to face monthly TB mortality equal to that of those with untreated TB.

Treatment as Prophylaxis

Patients in the Uninfected, Latent TB, Previously Treated TB, or TB Treatment Default states who are treated due to false positive diagnostic results or empiric therapy will remain in their respective health states upon treatment completion and automatically roll for treatment success. However, their risks of infection and reinfection will be reduced while on TB treatment. Also, for those in the Latent TB state, completion of a full course of TB treatment without default will count as “prophylaxis,” thereby reducing their risk of subsequent activation in a manner similar to that if they had completed a course of prophylaxis. These risks are stratified similarly to TB prophylaxis and are dependent upon HIV status and CD4 count.

Patients with Uninfected Status			
Efficacy of treatment against TB infection			
HIV-	1.0000		
CD4 VHI	1.0000		
CD4 HI	1.0000		
CD4 MHI	1.0000		
CD4 MLO	1.0000		
CD4 LO	1.0000		
CD4 VLO	1.0000		
Months of Efficacy after stopping	0		

Patients in Latent state			
Efficacy of treatment against TB activation			
	ds-TB	MDR-TB	XDR-TB
HIV-	1.0000	1.0000	1.0000
CD4 VHI	1.0000	1.0000	1.0000
CD4 HI	1.0000	1.0000	1.0000
CD4 MHI	1.0000	1.0000	1.0000
CD4 MLO	1.0000	1.0000	1.0000
CD4 LO	1.0000	1.0000	1.0000
CD4 VLO	1.0000	1.0000	1.0000
Months of Efficacy after stopping	0	0	0

Patients in Latent, Prev Treated, or Default states			
Efficacy of treatment against reinfection			
	ds-TB	MDR-TB	XDR-TB
HIV-	1.0000	1.0000	1.0000
CD4 VHI	1.0000	1.0000	1.0000
CD4 HI	1.0000	1.0000	1.0000
CD4 MHI	1.0000	1.0000	1.0000
CD4 MLO	1.0000	1.0000	1.0000
CD4 LO	1.0000	1.0000	1.0000
CD4 VLO	1.0000	1.0000	1.0000
Months of Efficacy after stopping	0	0	0

Patients who roll for treatment failure will have a probability of experiencing observed early failure before the end of a treatment regimen. Patients who are observed to experience early failure will have a probability of switching to the next user-defined treatment regimen.

Monthly Probability of Observed Early Failure		0.0000
Probability of Switching Treatment Lines Upon Observed Early Failure		0.0000
Next Treatment Upon Observed Early Failure		
TB Treatment #	Name of Treatment	
-1	*N/A*	

Patients who completed a treatment line but failed can move to the next regimen.

Next Treatment Upon Failure (Non early)	
TB Treatment #	Name of Treatment
-1	*N/A*
-1=N/A	

Patients who fail treatment can also have a probability of repeating the same regimen that they had just failed. Patients can have a probability of increased drug resistance upon treatment failure or default (i.e., *dsTB* changing to *MDR-TB* or *MDR-TB* changing to *XDR-TB;* for simplification, patients cannot directly change from dsTB to XDR-TB).

Repeating line as retreatment after failure					
				Probability of Increased Resistance	
TB Treatment #	Name of Treatment	Prob Repeat	Max # of Repeats	After Failure	After Treatment Default
0	*Treatment 0*	0.0000	0	0.0000	1.0000
1	*Treatment 1*	0.0000	0	0.0000	0.0000
2	*Treatment 2*	0.0000	0	0.0000	0.0000
3	*Treatment 3*	0.0000	0	0.0000	0.0000
4	*Treatment 4*	0.0000	0	0.0000	0.0000
5	*Treatment 5*	0.0000	0	0.0000	0.0000
6	*Treatment 6*	0.0000	0	0.0000	0.0000
7	*Treatment 7*	0.0000	0	0.0000	0.0000
8	*Treatment 8*	0.0000	0	0.0000	0.0000
9	*Treatment 9*	0.0000	0	0.0000	0.0000
			0=No repeat		

In addition, patients who were previously treated for TB (and either completed or defaulted from treatment) carry a flag indicating such. If these patients are treated for TB again, their regimen is specified according to a different treatment sequence: "Probability of receiving line as treatment among those with recurrent TB". This allows the user to specify different regimens, or the same regimens but with different probabilities of treatment success/failure.

Patients who experience a major toxicity event have a user-defined probability of stopping their current line of treatment. They then roll for a probability of starting a different line of treatment; the user can define the next line of treatment.This structure also appears separately for empiric therapy. The user can thus define the patient's probability of switching treatments (and to which treatment s/he switches) while on any empiric therapy, and also define these parameters for each individual line of (non-empiric) treatment.

TB Clinic Proph Subroutine (135f and 135f')

The user can specify the order of prophylaxis administration and define the duration of each prophylaxis line.

Order of Administering Prophylaxes			
	Proph #	Proph Name	Proph Duration (Mths)
Line 0	0	*Isoniazid*	6
Line 1	-1	*N/A*	6
Line 2	-1	*N/A*	6
Line 3	-1	*N/A*	6
Line 4	-1	*N/A*	6
	Note: use "-1" to indicate unused proph.		

TB Prophylaxis initiation criteria will be evaluated and will include: CD4 count, known history of active TB, presence of *immreactyes* tracker variable, or at ART initiation. If either or all of these criteria (and/or evaluated by a toggle) are met, the patient will start the next line of prophylaxis and will gain the *onTBprophylaxisX* time-counted flag.

Prophylaxis Starting Policy for HIV+			
		0	Note: use 0="AND", 1="OR"
	All on proph	1	0 = no, 1 = yes
AND	CurrCD4 <=	350	
	CurrCD4 >=	0	
AND	ART Initiation	0	0 = no, 1 = yes
AND	History of Active TB	0	0 = no, 1 = yes
AND	Immune Reactive	0	0 = no, 1 = yes

Prophylaxis Starting Policy for HIV -			
		0	Note: use 0="AND", 1="OR"
	All on proph	1	0 = no, 1 = yes
AND	History of Active TB	0	0 = no, 1 = yes
AND	Immune Reactive	0	0 = no, 1 = yes

Patients who qualify for prophylaxis will experience a probability of actually receiving treatment based on HIV status and whether they are on or off ART. There can be a user-defined time delay in starting prophylaxis treatment, characterized by months (mean and standard deviation) of lag.

Proportion of Patients who Qualify for Proph to Receive Proph:		
HIV-	Off ART	On ART
1.0000	1.0000	1.0000
	Mean	Std Dev
Lag to Start	0	0

Patients already on prophylaxis who experience toxicity this month will be evaluated for availability of a second line of prophylaxis, as defined by the order of prophylaxis administration.

Move onto next line of prophylaxis upon toxicity:	
0	0=no, 1=yes

If so, the patient will switch to that line (*onTBprophylaxisX*), and the prophylaxis efficacy will be updated. If another line of prophylaxis is not available, the patient will lose the *onTBprophylaxisX* flag and will no longer be conferred the benefit, toxicity risks, or costs of being on prophylaxis. Patients will also experience continued protection against TB infection or activation for a user-defined period of time after stopping prophylaxis treatment.

Patients with Uninfected Status					
Efficacy of prophylaxis against TB infection					
Number	0	1	2	3	4
Prophylaxis Name	Isoniazid	Rifampin	User Proph 1	User Proph 2	User Proph 3
HIV-	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VHI	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 HI	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MHI	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MLO	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 LO	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VLO	1.0000	1.0000	1.0000	1.0000	1.0000
Months of Efficacy after stopping	0	0	0	0	0

Patients in Latent state									
Efficacy of prophylaxis against activation									
Prophylaxis Name	Isoniazid			Rifampin			User Proph 1		
	ds-TB	MDR-TB	XDR-TB	ds-TB	MDR-TB	XDR-TB	ds-TB	MDR-TB	XDR-TB
HIV-	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VHI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 HI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MHI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MLO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 LO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VLO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
Months of Efficacy after stopping	0	0	0	0	0	0	0	0	0

Patients in Latent, Prev Treated, or Default states

Efficacy of prophylaxis against reinfection

Prophylaxis Name	Isoniazid			Rifampin			User Proph 1		
	ds-TB	MDR-TB	XDR-TB	ds-TB	MDR-TB	XDR-TB	ds-TB	MDR-TB	XDR-TB
HIV-	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VHI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 HI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MHI	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 MLO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 LO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
CD4 VLO	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
Months of Efficacy after stopping	0	0	0	0	0	0	0	0	0

TB Prophylaxis Cost and QOL

Number	Prophylaxis Name	Mth Cost	MinTox Cost	Min Tox QOL	Maj Tox Cost	Maj Tox QOL
0	Isoniazid	0.00	0.00	0.00	0.00	0.00
1	Rifampin	0.00	0.00	0.00	0.00	0.00
2	User Proph 1	0.00	0.00	0.00	0.00	0.00
3	User Proph 2	0.00	0.00	0.00	0.00	0.00
4	User Proph 3	0.00	0.00	0.00	0.00	0.00

TB Prophylaxis Toxicity

		Minor Tox Monthly Prob		Major Tox Monthly Prob		
Number	Prophylaxis Name	Off ART	On ART	Off ART	On ART	Prob Dth (Maj)
0	Isoniazid	0.000000	1.0000	0.000000	1.0000	0.000000
1	Rifampin	0.000000	1.0000	0.000000	1.0000	0.000000
2	User Proph 1	0.000000	1.0000	0.000000	1.0000	0.000000
3	User Proph 2	0.000000	1.0000	0.000000	1.0000	0.000000
4	User Proph 3	0.000000	1.0000	0.000000	1.0000	0.000000

Patients who have received TB prophylaxis may also develop a more resistant-strain of TB due prophylaxis upon activation of a latent TB infection.

TB Prophylaxis Increase Resistance After Activation

Number	Prophylaxis Name	Prob Resist
0	Isoniazid	0.000000
1	Rifampin	0.000000
2	User Proph 1	0.000000
3	User Proph 2	0.000000
4	User Proph 3	0.000000

Each month on prophylaxis, the patient will roll to default, or 'drop off', from TB prophylaxis.

Of Patients who are Taking Proph

Monthly Probability of Drop Off	1.0000

If the patient does not default from prophylaxis, he/she will be evaluated for whether TB prophylaxis should be stopped (criteria based on HIV status, CD4 count, number of months since prophylaxis initiation, ART initiation, and a major toxicity event). If none of the criteria are met, the patient will continue the same line of prophylaxis until the duration of prophylaxis is complete. If the stopping criterion is met, the patient will stop TB prophylaxis and will lose the *onTBprophylaxisX* flag.

Prophylaxis Stopping Policy for HIV+

		0	**Note:** use 0="AND", 1="OR"
	CurrCD4 <=	350	
	CurrCD4 >=	0	
AND	# Months on Proph	10000	
AND	Major Toxicity	0	**0** = no, **1** = yes

Prophylaxis Stopping Policy for HIV-

		0	**Note:** use 0="AND", 1="OR"
	# Months on Proph	100000	
AND	Major Toxicity	0	**0** = no, **1** = yes

Patients who have completed prophylactic therapy can have a probability of increased drug resistance (i.e., *dsTB* changing to *MDR-TB* or *MDR-TB* changing to *XDR-TB)* upon activating, though the probability of activating may be reduced by the prophylactic therapy.

TB Prophylaxis Increase Resistance After Activation

Number	Prophylaxis Name	Prob Resist
0	Isoniazid	0.000000
1	Rifampin	0.000000
2	User Proph 1	0.000000
3	User Proph 2	0.000000
4	User Proph 3	0.000000

TB Clinic LTFU Subroutine (135d)

The TB Clinic LTFU Subroutine will be used to simulate TB treatment default when HIV and TB clinics are not integrated, for TB-infected, HIV-negative patients, and for TB-infected, HIV-positive but undetected (not linked to HIV care) patients.

Those who are LTFU do not incur treatment or toxicity costs when they are LTFU. For patients who are on treatment and not already LTFU, there will be a monthly probability of being LTFU based on TB state; those who roll to be LTFU can then again roll for treatment success vs. failure:

- Patients who initially rolled for destined treatment failure (*TBTreatmentFail*) will automatically fail upon becoming lost to follow-up.
- Patients who initially rolled for destined treatment success (*TBTreatmentSuccess*) will roll again (after being loss to follow-up for the minimum number of months required to be defined as default (2 months) using a treatment success probability weighted by the proportion of time spent on treatment. If Y is the intended duration of treatment and X is the number of months on treatment prior to becoming LTFU, then the probability of success will be (X/Y)**ProbTBTreatmentSuccess*. Patients who roll for success the second time will lose their *sputumbacloadhi* flag and will go to the Default state; patients who roll for failure the second time will redraw for the *sputumbacloadhi* flag and will remain in the Active TB state.
- Patients in the Uninfected, Latent TB, or Previously Treated TB states who are unnecessarily receiving treatment will automatically stay in their respective states upon being LTFU.

Use TB LTFU?	0	**0**=no, **1**=yes

Monthly Probability of Going LTFU

Uninfected	1.0000
Latent TB	1.0000
Active Pulm TB	0.5000
Active Extrapulm TB	1.0000
Prev Treat TB	1.0000
TB Treat Default	1.0000

Patients who are currently LTFU from TB treatment will face a monthly probability of returning to care based on TB state, HIV status, and CD4 count. We will assume that patients in the Uninfected, Latent TB, and Previously Treated TB states who are LTFU from TB treatment will not return to TB treatment. However, patients in the Uninfected, Latent TB, and Previously Treated TB states who default from TB prophylaxis will have a monthly probability of returning to TB care to recommence prophylaxis.

Patients with Active Pulmonary TB, Active Extrapulmonary TB, and TB Treatment Default states who return to care will be placed on a treatment regimen based on the time spent LTFU. They can reinitiate the original treatment regimen from the beginning, resume the original treatment regimen according to the month during which they were LTFU, roll to be re-tested for active TB, or initiate the next treatment line if available.

Monthly Probability of Return to Care (RTC)

	Uninfected	Latent TB	Active Pulm TB	Active Extrapulm TB	Prev Treat TB	TB Treat Default
HIV -	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
HIV +	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

Returning to TB care (Active State only)

	Number of months since LTFU				
	0-2 months	2-4 months	4-6 months	6-8 months	8+ months
Reinitiate original treatment regimen	0.0000	0.0000	0.0000	0.0000	0.0000
Resume original treatment regimen	0.0000	0.0000	0.0000	0.0000	0.0000
Re-testing for new regimen	0.0000	0.0000	0.0000	0.0000	0.0000
Move onto next treatment regimen	1.0000	1.0000	1.0000	1.0000	1.0000
	must sum to 1.0	must sum to 1.0	must sum to 1.0	must sum to 1.0	must sum to 1.0

TB Care Costs

Patients with untreated, active TB incur monthly direct medical, direct non-medical, time, and indrect costs.

Monthly Costs Related to Untreated TB

	Direct Medical	Direct Non-medical	Time Costs	Indirect Costs	Total
Untreated	0.00	0.00	0.00	0.00	0.0000

Patients who are currently receiving TB treatment can incur costs associated with a TB or HIV/TB clinic visit with a provider or a TB medication pick-up visit. The user may specify the frequency of these costs to simulate how often these visits occur.

Costs Related to Treated TB

	Direct Medical	Direct Non-medical	Time Costs	Indirect Costs	Frequency of Costs	Total
Clinic visit with provider	0.00	0.00	0.00	0.00	3	0.0000
Medication pick-up visit	0.00	0.00	0.00	0.00	3	0.0000

End Month Updater (140a/b/c)

In the end month updater, which handles the majority of costing in CEPAC, we propose to add the costs of TB prophylaxis, TB prophylaxis toxicity, TB treatment, TB treatment toxicity, and TB diagnostic tests. We will include the option of an HIV/TB integrated care multiplier, which will allow us to examine the effects of cost reductions and/or increases associated with integrated care. We will include an option to increase or decrease TB care cost by a specified dollar amount or percentage until a specified month, after which TB care costs can be increased or decreased by another

specified dollar amount or percentage. This functionality will allow us to examine cost reductions or increases associated with coordinated care.

We will also include TB-specific death costs and QOL in the End Month Updater if the patient dies of TB in that month.

Model Output

TB SUMMARY EVENTS											
	TB State On Entry:	dsTB	mdrTB	xdrTB							
	uninfected	0									
	Latent	0	0	0							
	Active Pulmonary	907	74	19							
	Active Extrapulmonary	0	0	0							
	Previously Treated	0	0	0							
	Treatment Default	0	0	0							
	Start on TB Treatment:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	Dropout TB Treatment:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	TB Cure at Treatment Dropout:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	Complete TB Treatment:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	TB Cure at Treatment Completion:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	TB Increase Resistance at Treatment Completion:	0	1	2	3	4	5	6	7	8	9
	dsTB	0	0	0	0	0	0	0	0	0	0
	mdrTB	0	0	0	0	0	0	0	0	0	0
	xdrTB	0	0	0	0	0	0	0	0	0	0
	Total TB Incident Infections/Reinfections	dsTB	mdrTB	xdrTB							
	Uninfected	0	0	0							
	Latent	0	0	0							
	Active Pulmonary	0	0	0							
	Active Extrapulmonary	0	0	0							
	Previously Treated	0	0	0							
	Treatment Default	0	0	0							
		dsTB	mdrTB	xdrTB							
	Total Activations (Pulm) from Latent TB	0	0	0							
	Total Activations (Extrapulm) from Latent TB	0	0	0							
	Total Activations (All) from Latent TB	0	0	0							
	Total Relapses (Pulm)	0	0	0							
	Total Relapses (Extrapulm)	0	0	0							
	Total Relapses (All)	0	0	0							
	Total TB Spontaneous Resolution	0	0	0							
	Total Deaths from TB	0	0	0							
		3	3	3	3	3	3	3	3	3	3
	Total TB Treatment Minor Toxicity	0	0	0	0	0	0	0	0	0	0
	Total TB Treatment Major Toxicity	0	0	0	0	0	0	0	0	0	0
		Proph1	Proph2	Proph3							
	Total TB Proph Minor Toxicity	0	0	0							
	Total TB Proph Major Toxicity	0	0	0							

TB MONTHLY SUMMARY						
	Uninfected	Latent	Active Pulmonary	Active Extrapulmonary	Previously Treated	Treatment Default
TB State	0	0	1000	0	0	0
TB Tracker	Sputum Bacillary Load Hi	Immune Reactive	TB Symptoms			
HIV-	0	0	0			
HIV+undetected	0	0	0			
HIV+unlinked(detected not in care	0	0	0			
HIV+in_care	1000	1000	1000			
HIV+LTFU	0	0	0			
HIV+RTC	0	0	0			
CD4vlo	0	0	0			
CD4_lo	0	0	0			
CD4mlo	0	0	0			
CD4mhi	0	0	0			
CD4_hi	0	0	0			
CD4vhi	1000	1000	1000			
	Proph 0	Proph 1	Proph 2	Proph 3	Proph 4	
Num On TB Prophylaxis	0	0	0	0	0	
	Treatment 0	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5
Num On TB Treatment	0	0	0	0	0	0
Num On Empiric TB Treatment	0	0	0	0	0	0
	dsTB	mdrTB	xdrTB			
Num With TB Strain	907	74	19			
Total TB Incident Infections/Reinfections						
Uninfected	0	0	0			
Latent	0	0	0			
Active Pulmonary	0	0	0			
Active Extrapulmonary	0	0	0			
Previously Treated	0	0	0			
Treatment Default	0	0	0			
	dsTB	mdrTB	xdrTB			
Total Activations (All) from Latent TB	0	0	0			
Total Activations (Pulm) from Latent TB						
HIV Negative	0	0	0			
CD4vlo	0	0	0			
CD4_lo	0	0	0			
CD4mlo	0	0	0			
CD4mhi	0	0	0			
CD4_hi	0	0	0			
CD4vhi	0	0	0			
Total Activations (Extrapulm) from Latent TB						
HIV Negative	0	0	0			
CD4vlo	0	0	0			
CD4_lo	0	0	0			
CD4mlo	0	0	0			
CD4mhi	0	0	0			
CD4_hi	0	0	0			
CD4vhi	0	0	0			
Total Relapses (All)	0	0	0			
Total Relapses (Pulm)	0	0	0			
Total Relapses (Extrapulm)	0	0	0			

True Strain	dsTB	mdrTB	xdrTB	TB Uninfected		
Observed dsTB	0	0	0	0		
Observed mdrTB	0	0	0	0		
Observed xdrTB	0	0	0	0		
TB Pos Test Result	Test 0	Test 1	Test 2	Test 3		
Uninfected	0	0	0	0		
Latent	0	0	0	0		
Active Pulmonary	0	0	0	0		
Active Extrapulmonary	0	0	0	0		
Previously Treated	0	0	0	0		
Treatment Default	0	0	0	0		
TB Neg Test Result	Test 0	Test 1	Test 2	Test 3		
Uninfected	0	0	0	0		
Latent	0	0	0	0		
Active Pulmonary	0	0	0	0		
Active Extrapulmonary	0	0	0	0		
Previously Treated	0	0	0	0		
Treatment Default	0	0	0	0		
	Uninfected	Latent	Active Pulmonary	Active Extrapulmonary	Previously Treated	Treatment Default
TB Diagnostic Result Pos	0	0	0	0	0	0
TB Diagnostic Result Neg	0	0	0	0	0	0
	Treatment 0	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5
Num On Successful Treatment (All)	0	0	0	0	0	0
Num On Successful Treatment (Pulm)	0	0	0	0	0	0
Num On Successful Treatment (Extrapulm)	0	0	0	0	0	0
Num On Failed Treatment (All)	0	0	0	0	0	0
Num On Failed Treatment (Pulm)	0	0	0	0	0	0
Num On Failed Treatment (Extrapulm)	0	0	0	0	0	0
Num Treatment Defaults (All)	0	0	0	0	0	0
Num Treatment Defaults (Pulm)	0	0	0	0	0	0
Num Treatment Defaults (Extrapulm)	0	0	0	0	0	0
Num Dropout TB Treatment:						
dsTB	0	0	0	0	0	0
mdrTB	0	0	0	0	0	0
xdrTB	0	0	0	0	0	0
TB Deaths (All)	0					
TB Deaths (Pulm)						
HIV Negative	0					
CD4vlo	0					
CD4_lo	0					
CD4mlo	0					
CD4mhi	0					
CD4_hi	0					
CD4vhi	0					
TB Deaths (Extrapulm)						
HIV Negative	0					
CD4vlo	0					
CD4_lo	0					
CD4mlo	0					
CD4mhi	0					
CD4_hi	0					
CD4vhi	0					
TB Deaths While TB LTFU						
HIV Negative	0					
CD4vlo	0					
CD4_lo	0					
CD4mlo	0					
CD4mhi	0					
CD4_hi	0					
CD4vhi	0					