

Tuberculosis Tutorials



INSTITUTE FOR DISEASE MODELING
INTELLECTUAL VENTURES®

These tuberculosis (TB) tutorials were created for the EMOD QuickStart v1.8. Later versions of the QuickStart may not be completely compatible with these tutorials as installation and some of the demographics, configuration and intervention parameters have been changed. IDM continues to improve our EMOD documentation for training and research, and new and updated TB tutorial information will be added to our new documentation [site](#). As the EMOD documentation is hosted on our new site, most of the links in the PDF will not work. If you have any questions or need additional information, please contact support@idmod.org.

Tuberculosis (TB) Tutorials

In a series of tutorials, each TB-specific feature is explored, allowing the modeler to become acquainted with the range of questions that can be approached using the EMOD TB model.

There are two ways to use the tutorials. You can read the tutorials information and graphs to learn about the model; installing the Quick Start is not required. Or, for a more hands-on approach, you can also run the simulations that are associated with the tutorials and make the suggested changes to the configuration files to see the impact on the output graphs. The EMOD executable and all of the files needed to run the simulations are included in the Quick Start installation.

The initial tutorials explore the fundamental disease dynamics and age dependence of disease progression.

- [TB 1: Basic Tuberculosis \(TB\) Model](#)
- [TB 2: Age Dependent Immunity](#)

Subsequent tutorials delve into specialized topics of interest to health policy researchers including complex health systems, the cascade of care and co-transmission of drug-sensitive TB and MDR-TB.

- [TB 3: Health Care Systems](#)
- [TB 4: Cascade of Care](#)
- [TB 5: Multidrug-resistant \(MDR\) TB](#)

The final tutorial provides a simple example of using model burn-in to more realistically model a large population where TB is endemic.

- [TB 6: Population Burn-in](#)

The TB tutorial directories contain the configuration and campaign files described in the tutorials, as well as python, batch, and command files to easily run the simulations and generate output charts. If you have not installed the Quick Start, see [Installing the Quick Start](#).

NOTE: These tutorials are for learning purposes only and are not considered scientifically valid.

TB 1: Basic Tuberculosis (TB) Model

The Basic Tuberculosis (TB) Model tutorial describes how the EMOD software represents the basic progression of TB natural history in a small cohort of adults in the absence of treatment. The disease dynamics are represented by a series of state changes as individuals progress from susceptible to latent, then to active infection, followed by spontaneous cure or disease death. The latent state represents asymptomatic individuals who are TST+ (tuberculin skin test), and who are not infectious. The active state represents infectious individuals who have signs and/or symptoms of TB. Figure 1 shows all of the available states.

This tutorial also describes, in detail, the available parameters which determine the rate of progression from one state to the next. Parameters are also available to configure the varying disease presentation states for smear status, and the associated heterogeneity in infectiousness.

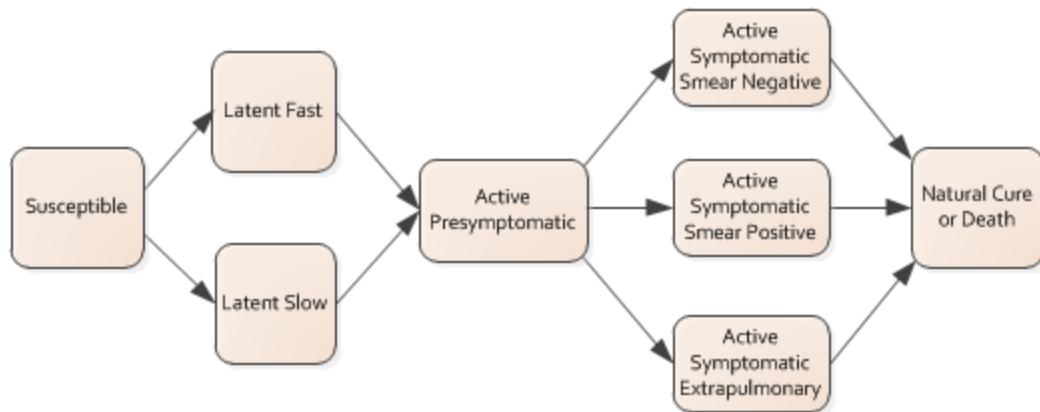


Figure 1: TB States

This tutorial consists of four scenarios:

- [SEIR Dynamics](#): The TB state-based disease progression easily replicates SEIR-like disease dynamics. Individuals progress from susceptible to latent infection, followed by active infection and recovery.
- [Active Disease Presentation](#): Individuals with active TB can have extrapulmonary or pulmonary TB. Pulmonary TB can be sputum smear positive or negative. The disease presentation can differ in adults and children, and EMOD has separate configuration parameters for adults (≥ 15 years old) and children (< 15 years old).

- **Presymptomatic Active State**: Individuals progress from latent disease to an active presymptomatic state before progressing to the active symptomatic state, reflecting the spectrum of disease from latent to active disease. The presymptomatic state represents a period of reduced infectivity where patients may have objective signs of TB (for example, an increased cough) but lack subjective symptoms (they do not notice their increased cough).
- **Heterogeneous Progression**: Heterogeneity is added in the disease progression time from latency (exposed) to active disease by subdividing the exposed population into fast and slow progressors.

Demographics Inputs

This tutorial uses a simple demographics file which describes a cohort of 10,000 people who are all 20 years old at the beginning of the simulation and live in a single homogeneously mixed population. This population is represented in the demographics file as a single node.

This demographics file is used for all of the scenarios. To view the complete demographics file, see TB_01_BasicModel_demographics in the Scenarios\InputFiles directory.

```
{
    . . .
    "Nodes": [
        {
            . . .
            "NodeAttributes": {
                . . .
                "InitialPopulation": 10000,
                "BirthRate": 0,
                . . .
            },
            . . .
            "IndividualAttributes": {
                "AgeDistributionFlag": 0,
                "AgeDistribution1": 7300,
                "AgeDistribution2": 0,
                . . .
            }
        }
    ]
}
```

SEIR Dynamics

The available states for the TB natural history (Figure 1) can be easily collapsed to an SEIR-like system (see [Generic Simulation Scenarios](#) 1 through 6). In the large population limit, this can be easily solved with ordinary differential equations (see [Generic 3: SEIR - Incubation Periods](#)).

The latent states, which represent asymptomatic individuals, correspond to the Exposed compartment in a classical SEIR model. The active states, which represent infectious individuals, correspond to the Infectious compartment. The recovered compartment includes individuals who have had a natural cure without treatment.

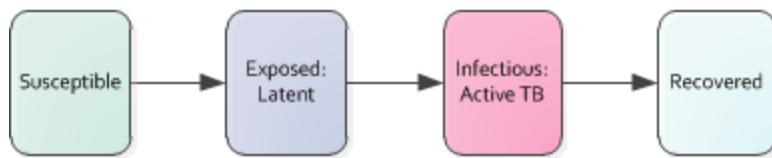


Figure 2: Schematic of TB Natural History Collapsed to an SEIR-like System

SEIR Dynamics: Key Simulation Parameters

Model Setup

By default, the TB model is configured with heterogeneity in disease progression and presentation. When running the TB model as a simple SEIR model, TB-specific heterogeneity must be disabled by configuring only one latent progression, one symptomatic state, and one disease presentation. In the SEIR Dynamics simulation, individuals go through the following disease progression and presentation path:

1. Susceptible
2. Exposed: Latent-Fast
3. Infectious: Active-symptomatic with smear positive presentation. The presymptomatic state is effectively disabled by moving individuals from the presymptomatic to the symptomatic stage in one day.
4. Recovered

Generic SEIR Model Parameters

Parameter	Value	Description
Enable_Immunity	1	Enables the ability for individuals to have protective immunity after an infection clears.

TB SEIR Model Parameters

SEIR Dynamics is configured to move all individuals to one compartment, latent-fast, when exposed to TB.

Parameter	Value	Description
Simulation_Type	"TB_SIM"	Sets the simulation type. This is a required parameter. It determines which parameter categories are valid for the simulation.
TB_Fast_Progressor_Fraction_Adult	1	Fraction of adults progressing from latent to active TB via fast progression route. In this simulation all adults are latent-fast. Fast and slow progression is included to encode heterogeneity in disease progression into the population.
TB_Fast_Progressor_Fraction_Child	1	Fraction of children progressing from latent to active TB via fast progression route. In this simulation all children are latent-fast.
TB_Fast_Progressor_Rate	0.02	Rate at which fast progressors shift from latent (exposed) to active TB. TB_Fast_Progressor_Rate is applied to both children and adults who are latent-fast. Since TB_Fast_Progressor_Fraction is set to 1 for both adults and children in this specific example, all individuals progress at TB_Fast_Progressor_Rate.

Parameter	Value	Description
TB_Presymptomatic_Rate	1	Daily probability of progressing from active presymptomatic state to active symptomatic state.

Disease Parameters

In the infectious (or active) compartment, the TB-specific disease heterogeneity is disabled. Individuals are only symptomatic, smear-positive.

Parameter	Value	Description
TB_Smear_Positive_Fraction_Adult	1	Fraction of adults with active TB that is smear positive.
TB_Smear_Positive_Fraction_Child	1	Fraction of children with active TB that is smear positive.
TB_Extrapulmonary_Fraction_Adult	0	Fraction of adults with active TB that is extrapulmonary.
TB_Extrapulmonary_Fraction_Child	0	Fraction of children with active TB that is extrapulmonary.
Base_Infectivity	0.25	Base infectivity in active, symptomatic state.
TB_Inactivation_Rate	0	Rate the individuals return to the latent state from the active state. For simplicity in this tutorial, individuals do not go back to the latent state.

Parameter	Value	Description
TB_Active_Mortality_Rate	1e-09	For individuals who have not had treatment, this rate is combined with TB_Inactivation_Rate and TB_Active_Cure_Rate to determine the duration of active disease until resolution of active phase. The fraction of TB_Active_Mortality_Rate divided by the total rate is used to determine the probability of cure.

Simulation Duration Parameters

Parameter	Value	Description
Simulation_Timestep	1	Value indicating simulation time step in days. For this simulation, the time step is one day.
Simulation_Duration	400	Duration of simulation in days.

For the complete list of simulation parameters, see the config.json file in the Scenarios\TB\01_BasicModel\A_SEIR directory.

SEIR Dynamics: Interventions

There is only one intervention which is an outbreak on day 1. All of the scenarios use this intervention.

```
{
  "Events": [
    {
      "Event_Coordinator_Config": {
        "Demographic_Coverage": 0.005,
        "Intervention_Config": {
          "Outbreak_Source": "PrevalenceIncrease",
          "class": "OutbreakIndividual"
        },
        "class": "StandardInterventionDistributionEventCoordinator"
      }
    }
  ]
}
```

```
"Event_Name": "Outbreak",
"Nodeset_Config": [
    "class": "NodeSetAll"
],
"Start_Day": 1,
"class": "CampaignEvent"
}
],
"Use_Defaults": 1
}
```

This intervention is in the campaign.json file in the Scenarios\TB\01_BasicModel\A_SEIR directory.

SEIR Dynamics: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\01_BasicModel\A_SEIR directory to run the simulation.

SEIR Dynamics: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample files, plotResults and compareScenarios, in the Scenarios\TB\01_BasicModel\A_SEIR directory to generate graphs from the simulation's Inset Chart output file.

To run plotResults, you will need to install Python and Matplotlib.pyplot on your computer. See [Pre-requisite Software for Plotting Tutorial Graphs](#) for information on installing Python and Matplotlib.pyplot.

Simulation Output Graphs

The complete course of the epidemic is observed. The initial outbreak seeds the epidemic, quickly depleting the susceptible population with latent individuals who then transition to active disease. Ultimately, the entire population gets infected and subsequently recovers.

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

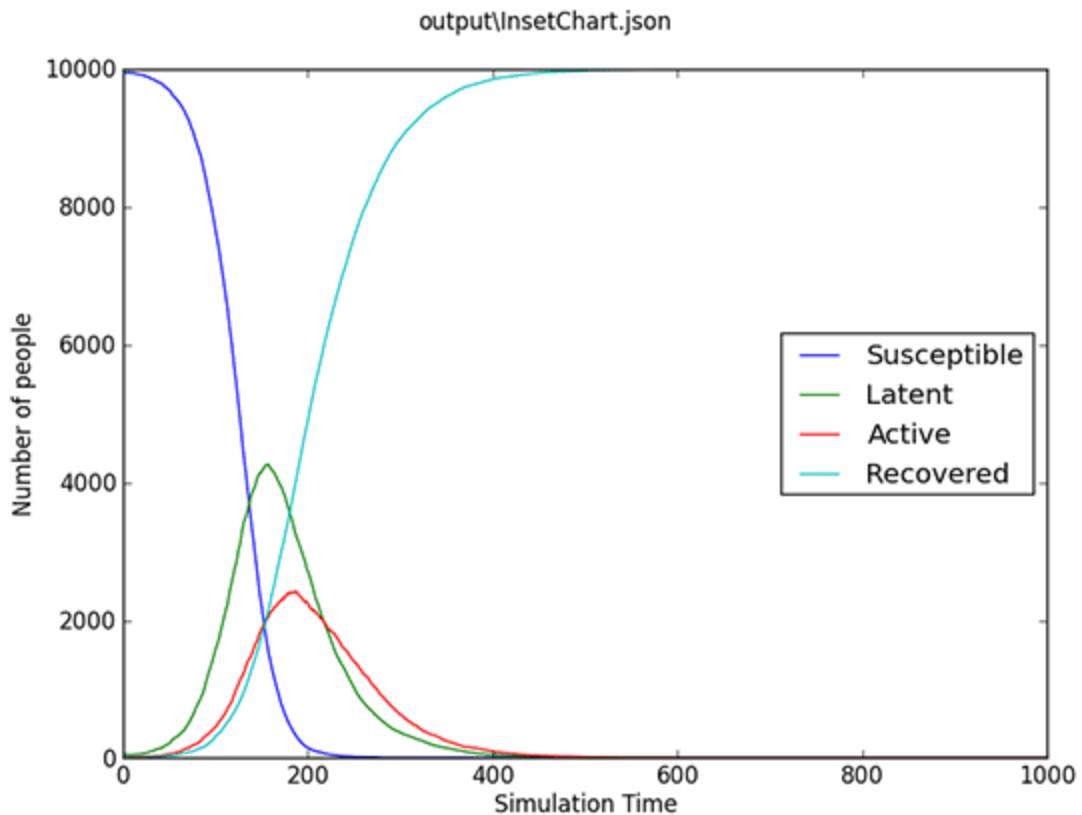


Figure 3: Individual's Progression through TB States Collapsed to an SEIR-like System

In Figure 3, all individuals start in the susceptible state. After the initial outbreak in 50 people, TB spreads amongst the population cohort. The prevalence of latent infection rises first, with a subsequent rise in active disease. Eventually, all individuals progress to the recovered state.

Figure 4 shows the prevalence of latent and active disease.

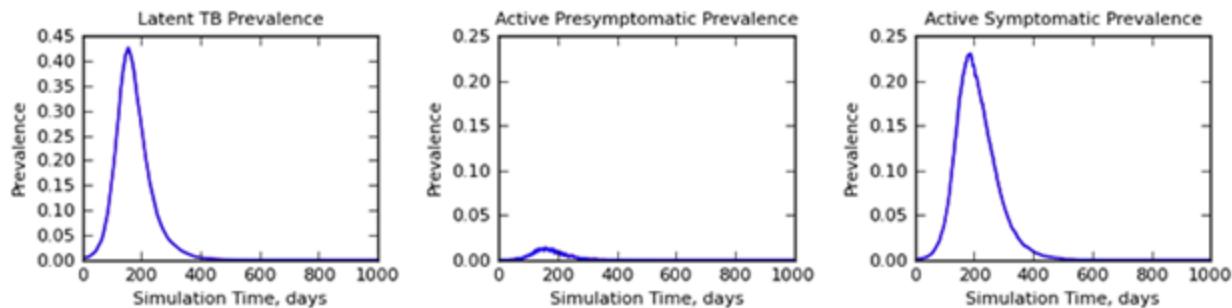


Figure 4: Prevalence of Latent and Active Disease

All individuals progress quickly from latent to active disease as the initial outbreak spreads to the population.

SEIR Dynamics: Exploring the Model

1: Exposed Compartment: Latent-Slow

Change the Latent-Fast compartment to Latent-Slow by setting the following values:

- "TB_Fast_Progressor_Fraction_Adult": 0
- "TB_Fast_Progressor_Fraction_Child": 0

If you compare the model output you will see that the Latent TB Prevalence is now entirely composed of latent-slow. The Latent Fast TB Prevalence is now zero.

2: Infectious Compartment: Active

Smear-Negative

In SEIR Model, active smear-positive represents the active compartment. You can also use smear-negative or extrapulmonary. Try setting all individuals to use smear-negative, with the following parameter values.

```
"TB_Smear_Positive_Fraction_Adult": 0,  
"TB_Smear_Positive_Fraction_Child": 0,  
"TB_Extrapulmonary_Fraction_Adult": 0,  
"TB_Extrapulmonary_Fraction_Child": 0,  
"TB_Smear_Negative_Infectivity_Multiplier": 1,
```

You can get the same output as in SEIR Dynamics except active smear-negative prevalence will have non-zero prevalence and the active smear-positive prevalence will be zero.

Smear-Negative Multiplier

Continue using smear-negative as the active compartment and set the "TB_Smear_Negative_Infectivity_Multiplier" to 0.5.

You will see that the R_0 has decreased with slower spread of the disease. This is the same result you would get if you used the SEIR Dynamics scenario but reduced base_infectivity by 50%.

Non-infectious Extrapulmonary

Set all individuals disease presentation to extrapulmonary. By definition the extrapulmonary fraction is non-infectious (not configurable) so you will see that there is no spread of infection. The only

infected people in the simulation are the original outbreak, who progress from latent-fast to active extrapulmonary.

```
"TB_Smear_Positive_Fraction_Adult": 0,  
"TB_Smear_Positive_Fraction_Child": 0,  
"TB_Extrapulmonary_Fraction_Adult": 1,  
"TB_Extrapulmonary_Fraction_Child": 1
```

Active Disease Presentation

Individuals with active TB are classified as smear positive, smear negative or extrapulmonary. The active, symptomatic compartment can be subdivided into smear-positive, smear-negative, and extrapulmonary disease presentations. Each of these disease presentations has a configurable infectiousness and rate of progression.

NOTE: Extrapulmonary has no configurable infectiousness as it is always zero.

In SEIR Dynamics, active smear-positive represented the active compartment. The other presentations, smear-negative and extrapulmonary were disabled. In Disease Presentation all three of the disease presentation are enabled.

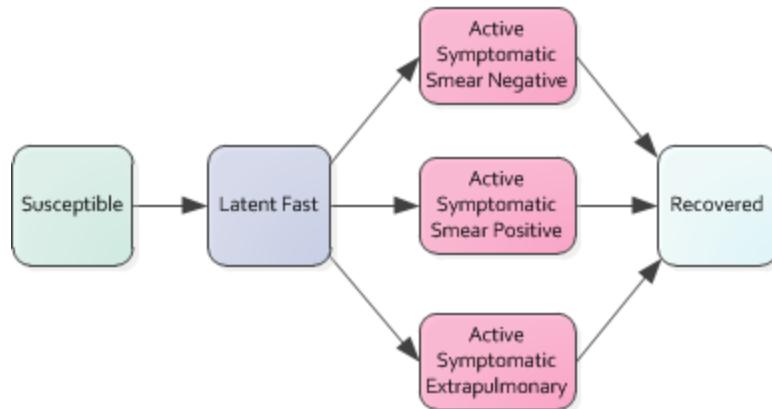


Figure 5: TB Model - Disease Presentation Heterogeneity

Active Disease Presentation: Key Simulation Parameters

Each of the three disease presentation has a configurable infectiousness and rate of progression.

- The sum of `TB_Smear_Positive_Fraction_Adult` and `TB_Extrapulmonary_Fraction_Adult` must be less than 1 because smear-positive, smear-negative, and extrapulmonary fractions compose the entire active compartment.
- The value of `Base_Infectivity` is directly applied to the smear-positive individuals.
- Smear negative individuals have a configurable infectiousness multiplier, `TB_Smear_Negative_Infectivity_Multiplier`, which is a multiplier of `Base_Infectivity`. The value of `TB_Smear_Negative_Infectivity_Multiplier` is between 0 and 1 which reflects the current belief that smear-negative individuals are less infectious than smear-positive individuals.

Parameter	Value	Description
<code>TB_Smear_Positive_Fraction_Adult</code>	0.34	Fraction of adults with active TB that is smear positive.
<code>TB_Smear_Positive_Fraction_Child</code>	0.34	Fraction of children with active TB that is smear positive.
<code>TB_Extrapulmonary_Fraction_Adult</code>	0.33	Fraction of adults with active TB that is extrapulmonary.
<code>TB_Extrapulmonary_Fraction_Child</code>	0.33	Fraction of children with active TB that is extrapulmonary.
<code>TB_Smear_Negative_Infectivity_Multiplier</code>	0.7	Used in combination with <code>Base_Infectivity</code> to define the infectiousness of smear negative individuals.
<code>TB_Extrapulmonary_Mortality_Multiplier</code>	0.4	Sets the mortality rate of extrapulmonary TB relative to smear positive.
<code>TB_Smear_Negative_Mortality_Multiplier</code>	1	Sets the mortality rate of smear negative TB relative to smear positive.

For the complete list of simulation parameters for this scenario, see the config.json file in the Scenarios\TB\01_BasicModel\B_Presentation directory.

Active Disease Presentation: Interventions

The intervention is the same as the intervention in SEIR Dynamics. You can find a copy of the campaign file in the Scenarios\TB\01_BasicModel\B_Presentation directory.

Active Disease Presentation: Running the Simulation

At your discretion, you can run the sample batch file, runEMOD, in the Scenarios\TB\01_BasicModel\B_Presentation directory.

Active Disease Presentation: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample files, plotResults and compareScenarios, in the Scenarios\TB\01_BasicModel\B_Presentation directory to generate graphs from the simulation's Inset Chart output file.

Simulation Output Graphs

The simulation output (blue), shown in Figure 6, is overlaid with the results from the previous scenario, SEIR Dynamics (red). Symptomatic disease, which previously was 100% smear positive, is now distributed among smear positive, smear negative and extrapulmonary. The overall outbreak spreads more slowly because smear negative and extrapulmonary individuals have reduced infectivity.

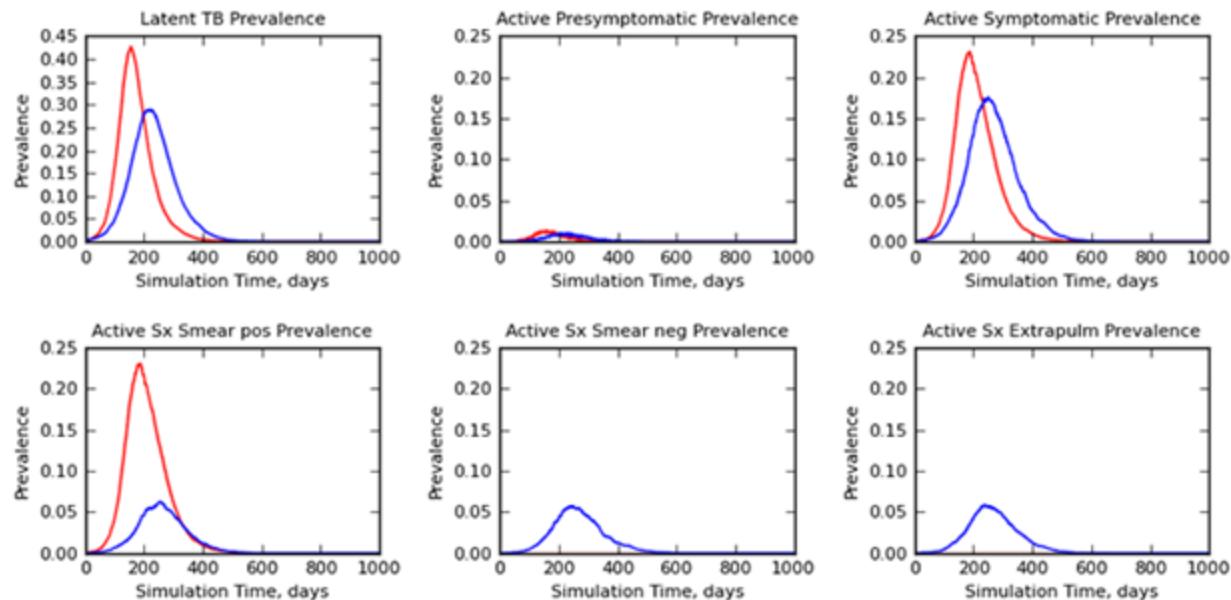


Figure 6: Longer Presymptomatic Phase Slows the Speed of Outbreak

In the previous figure, the introduction of a longer presymptomatic phase (blue) slows the spread of the outbreak compared to SEIR Dynamics (red).

Active Disease Presentation: Exploring the Model

Adjust TB_Smear_Negative_Infectivity_Multiplier to lower values, and observe the decrease in cumulative infections.

Presymptomatic Active State

Individuals progress from latent disease to an active presymptomatic state before progressing to the active symptomatic state, reflecting the spectrum of disease from latent to active disease. The presymptomatic state represents a period of reduced infectivity where patients may have objective signs of TB (for example, an increased cough) but lack subjective symptoms (they do not notice their increased cough).

The addition of the active presymptomatic state increases the overall time from initial infection to the active symptomatic state, ultimately slowing the overall spread of disease amongst the cohort.

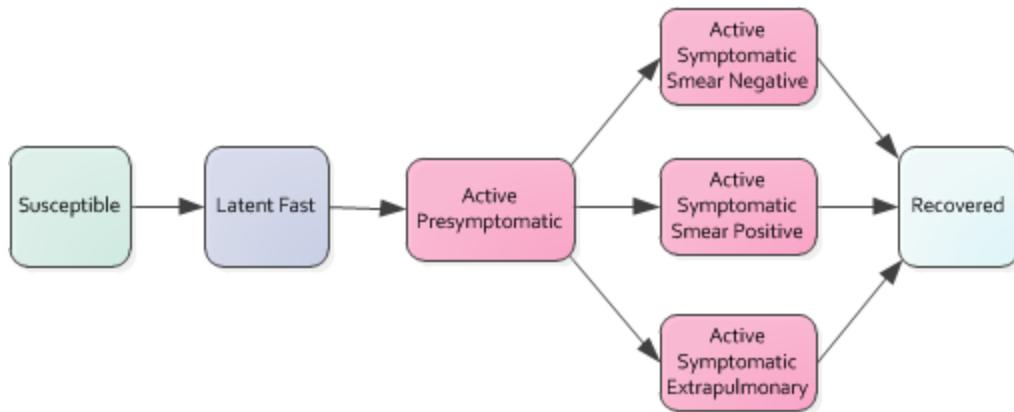


Figure 7: TB Model Configured with the Presymptomatic Stage

Presymptomatic Active State: Key Simulation Parameters

You can add the presymptomatic phase to the overall progression of disease by setting the following parameters.

Parameter	Value	Description
TB_Presymptomatic_Cure_Rate	0	This rate is added to the TB_Presymptomatic_Rate to define the total rate with which individuals progress from the presymptomatic stage to the active state.
TB_Presymptomatic_Rate	0.0333	This rate is added to the TB_Presymptomatic_Cure_Rate to define the total rate with which individuals progress from the presymptomatic stage of the active state.

For the complete list of simulation parameters for this scenario, see the config.json file in the Scenarios\TB\01_BasicModel\C_Presymptomatic directory.

Presymptomatic Active State: Interventions

The intervention is the same as the intervention in SEIR Dynamics. You can find a copy of the campaign.json file in the Scenarios\TB\01_BasicModel\C_Presymptomatic directory.

Presymptomatic Active State: Running the Simulation

At your discretion, you can run the sample batch file, runEMOD, in the Scenarios\TB\01_BasicModel\C_Presymptomatic directory.

Presymptomatic Active State: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the compare Scenarios batch file in the Scenarios\TB\01_BasicModel\C_Presymptomatic directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

The simulation output (blue), shown in Figure 8, is compared to SEIR Dynamics (red). The outbreak takes longer to spread because of the delay from infection to infectiousness which is introduced by the presymptomatic period.

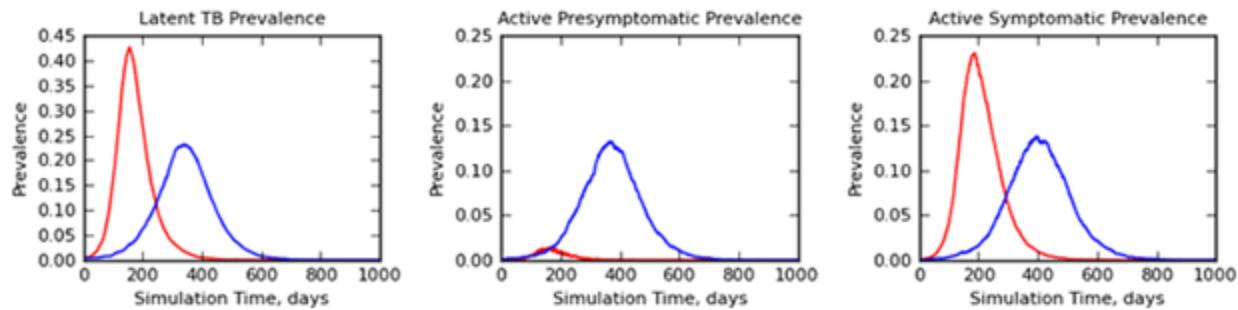


Figure 8: Introduction of a Longer Presymptomatic State Slows the Speed of the Outbreak

Presymptomatic Active State: Exploring the Model

By default, disease progression rates are exponential. For the duration of active disease only, you can alternately set `TB_Active_Period_Distribution` to `GAUSSIAN_DURATION` where the mean is set by `TB_Active_Cure_Rate` and `TB_Active_Mortality_Rate`, and the standard deviation is set by `TB_Active_Period_Std_Dev`.

For example, you can make the following change.

```
"TB_Active_Period_Distribution": "GAUSSIAN_DURATION"
```

And add the following parameter:

```
"TB_Active_Period_Std_Dev": 200,
```

For more information, see [Tuberculosis \(TB\) Parameters](#).

Heterogeneous Progression

In the TB model, the latent (or exposed) compartment can be subdivided into fast and slow compartments (see Figure 8). This can be useful to represent the bimodal distribution with which individuals may progress from latent to active disease. In the previous scenario, individuals exposed to TB progressed to only one latent compartment which was latent-fast (see Figure 8). Alternatively, all individuals could have progressed to latent-slow. For this simulation, individual progress to both latent-fast and latent-slow. The parameters `TB_Fast_Progressor_Rate` and `TB_Slow_Progressor_Rate` set the rate at which individual progress to the active compartment. The `TB_Fast_Progressor_Rate` sets the fraction of individuals which go into the latent fast state. Reflecting the differential fraction of fast progressor in adults and children, the `TB_Fast_Progressor_Rate` has been subdivided for adults and children.

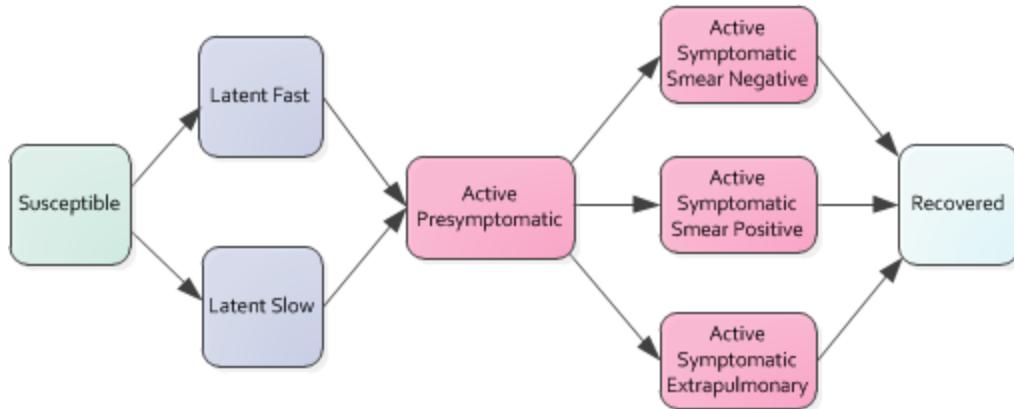


Figure 9: Latent Fast and Slow Compartments

Heterogeneous Progression: Key Simulation Parameters

Model Setup

Parameter	Value	Description
TB_Fast_Progressor_Fraction_Adult	0.5	Fraction of adults progressing from latent to active TB via fast progression route.
TB_Fast_Progressor_Fraction_Child	0.5	Fraction of children progressing from latent to active TB via fast progression route.
TB_Fast_Progressor_Rate	0.02	Rate at which fast progression shift from latency (exposed) to active TB. TB_Fast_Progressor_Rate is applied to both to children and adults who are latent-fast.
TB_Slow_Progressor_Rate	0.002	Rate at which slow progression from latency to active TB occurs in the model. TB_Fast_Progressor_Rate is applied to both to children and adults who are latent-slow.

For the complete list of simulation parameters for this scenario, see the config.json file in the Scenarios\TB\01_BasicModel\D_Progression directory.

Heterogeneous Progression: Interventions

For the complete list of campaign parameters for this scenario, see the campaign.json file in the Scenarios\TB\01_BasicModel\D_Progression directory.

Progression Heterogeneity: Running the Simulation

At your discretion, you can run the sample batch file, runEMOD, in the Scenarios\TB\01_BasicModel\D_Progression directory.

Progression Heterogeneity: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the compareScenarios batch file in the Scenarios\TB\01_BasicModel\D_Progression directory to generate graphs from the simulation's InsetChart output file.

Simulation Output Graphs

The simulation output (blue) is compared to SEIR Dynamics (red). The outbreak spreads more slowly as individuals progress through the latent slow state.

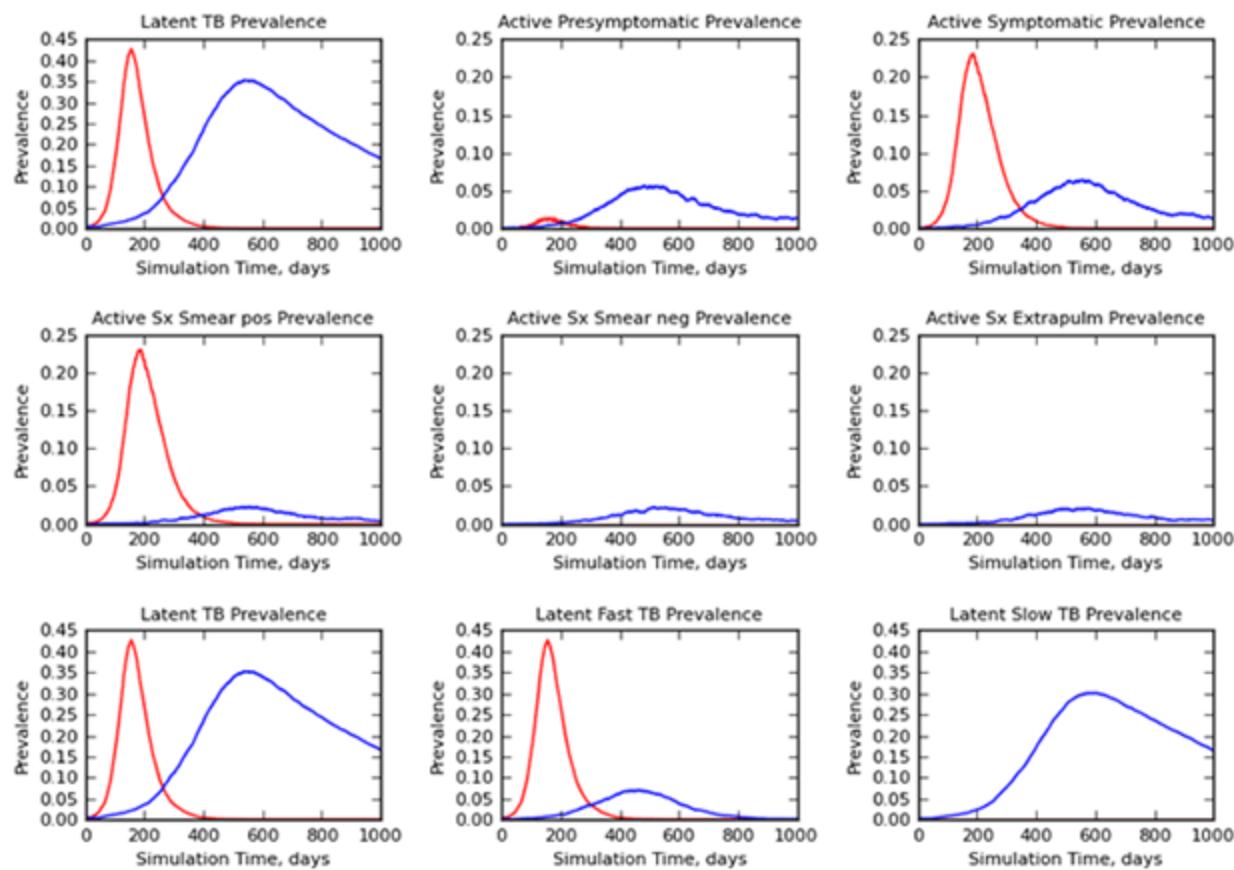


Figure 10: Latent Disease is Subdivided into Latent Fast and Slow

Compared with the baseline SEIR Dynamics (red) in this scenario (blue), latent disease is subdivided into latent fast and slow. Fast progressors progress quickly from latent to active presymptomatic and subsequently to active disease.

Heterogeneous Progression: Exploring the Model

Latent Fast and Latent Slow Progression

Change the value of `TB_Fast_Progressor_Rate` to see how the rate of disease progression in a single individual can affect the spread of TB in the cohort.

Please continue with the next scenario, [TB 2: Age Dependent Immunity](#), which illustrates how age structure can affect disease progression and the overall transmission dynamics.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Tuberculosis \(TB\) Parameters](#)

TB 2: Age Dependent Immunity

This tutorial assumes that you have read [TB 1: Basic Tuberculosis \(TB\) Model](#).

The Age Dependent Immunity tutorial illustrates how to model realistic age demographics and modulate population immunity using vaccination and post-TB infection immunity. Two age groups are defined:

- Adults: ≥ 15 years old
- Children: < 15 years old

Adults and children can have different fast progressor fractions when in the latent phase. In the active phase, adults and children can have different relative proportions of smear-positive, smear-negative and extrapulmonary disease presentations. The parameters for the susceptibility to infection and the rates of disease progression from one disease state to another are the same for both adults and children.

There are three scenarios that explore how TB immunity can be modulated by past infection or a TB vaccine.

- [Life-long Immunity](#): After an initial TB outbreak, all individuals retain 100% immunity. Ongoing new births are TB naive and get infected during a second TB outbreak.
- [Waning Immunity](#): After the initial TB outbreak, all individuals have waning immunity, which wanes to zero protection in ten years. In a second TB outbreak, the entire population of adults and children get infected.
- [Childhood Vaccines](#): BCG vaccinations are provided for all new births. The vaccination provides 100% protection from TB infection for 15 years. After the initial TB infection, all individuals have waning immunity. At the time of the second outbreak, vaccinated children are protected from infection while adults, whose immunity has waned, get infected.

Demographics Inputs

The demographics file specifies the initial population age structure and the population fertility and mortality rates. This simulation uses a simple fixed birth rate with zero background mortality so the population is growing over the duration of the simulation.

Age Distribution

To specify an age distribution, use the AgeDistribution structure in the demographics file. AgeDistribution defines cumulative distribution of the population across a range of ages. The age ranges

are defined in the `ResultValues` array, and the cumulative proportion of the population up to that age is defined in the `DistributionValues` array. The `AgeDistribution` array is enabled in the configuration file by setting `Age_Initialization_Distribution_Type` to `DISTRIBUTION_COMPLEX`.

```
"AgeDistribution": {
    "NumDistributionAxes": 0,
    "ResultUnits": "years",
    "ResultScaleFactor": 365,
    "ResultValues": [0, 5, 10, 15, 20, 25, 30,
                    35, 40, 45, 50, 55, 60, 65,
                    70, 75, 80, 85, 90, 95],
    "DistributionValues": [0, 0.095, 0.19, 0.285, 0.378, 0.466, 0.549,
                          0.627, 0.7, 0.767, 0.824, 0.872, 0.911, 0.942,
                          0.966, 0.983, 0.993, 0.998, 1, 1]
},
}
```

Using the data from the `DistributionValues` array, the following graph shows the probability of a person being in an age range.

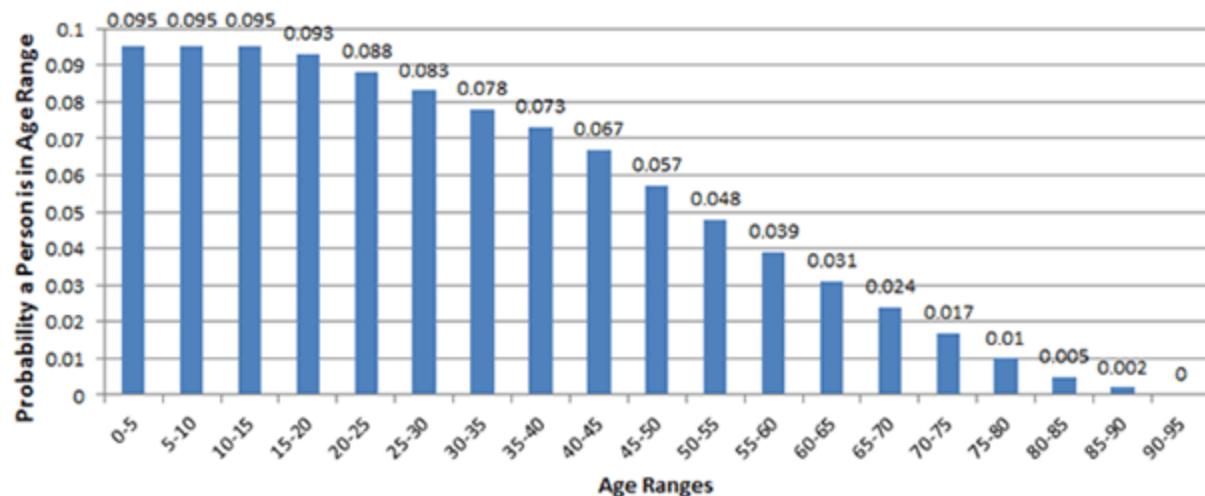


Figure 1: Age Structure of the Initialized Population.

To view the complete demographics file, see `TB_02_AgeDependentImmunity_demographics` in the `Scenarios\InputFiles` directory.

Lifelong Immunity

After an initial TB outbreak, both adults and children are infected, subsequently recover, and retain life-long immunity. Over the next 15 years, children born into the population have no immunity to TB. As a consequence, when a second TB outbreak occurs 15 years later, only children become infected.

Lifelong Immunity: Key Simulation Parameters

Demographics Parameters

The following parameters enable vital dynamics for birth and non-disease related deaths.

Parameter	Value	Description
Enable_Vital_Dynamics	1	Enables the vital process (birth and death)
Enable_Birth	1	Enables birth.
Age_Initialization_Distribution_Type	DISTRIBUTION_COMPLEX	When this parameter is set to DISTRIBUTION_COMPLEX, EMOD uses the AgeDistribution structure in the demographics file.

Immunity Parameters

The post-infection immunity is configured using the following parameters.

Parameter	Value	Description
Enable_Immunity	1	Enables the ability for individuals to have protective immunity after an infection clears.
Enable_Immune_Decay	1	Enables the ability for individuals to lose immunity. However, in this configuration, the TB_Immune_Loss_Fraction is 0, so no individuals lose immunity.

Parameter	Value	Description
TB_Immune_Loss_Fraction	0	Fraction of individuals susceptible to losing immunity.
Immunity_Acquisition_Factor	0	Reduction in TB acquisition rate for an individual who has cleared a TB infection. 1 represents full susceptibility while 0 represents full immunity to reinfection.
Acquisition_Blocking_Immunity_Decay_Rate	0	Rate at which acquisition-blocking immunity decays after the initial period indicated by the base acquisition-blocking immunity offset. In the Lifelong Immunity scenario, immune decay is enabled but the decay rates are zero.
Acquisition_Blocking_Immunity_Duration_Before_Decay	0	Number of days after a TB infection has cleared until acquisition-blocking immunity begins to decay.

Disease Parameters

The relevant configuration parameters for adults and children include the fraction who are fast progressors and the fraction that present as smear-positive, smear-negative, and extrapulmonary. For illustration purposes, all adults are set to fast progressors and children to slow progressors. Note, the actual rate of progression into active disease is the same for fast and slow progressors because output channels already aggregate latently infected individuals into latent fast and slow. This makes it easier to show the differences in adult and children disease progression.

Parameter	Value	Description
TB_Fast_Progressor_Fraction_Adult	1	Fraction of adults progressing from latent to active TB via fast progression route. In this simulation, all adults are latent-fast.

Parameter	Value	Description
TB_Fast_Progressor_Fraction_Child	0	Fraction of children progressing from latent to active TB via fast progression route. In this simulation, all children are latent-slow.
TB_Fast_Progressor_Rate	0.02	Rate of fast progression from latency to active TB. In this scenario, all adults use TB_Fast_Progressor_Rate. However, it is the same rate as TB_Slow_Progressor_Rate (so all individuals progress from latency to active at the same rate).
TB_Slow_Progressor_Rate	0.02	Rate of slow progression from latency to active TB. In this scenario, all children use TB_Slow_Progressor_Rate.

Time step and Duration Parameters

Parameter	Value	Description
Simulation_Timestep	5	Value indicating simulation time step in days. For this simulation, the time step is 5 days.
Simulation_Duration	7000	Duration of simulation in days for this simulation. The length of the simulation is 7000 days.

The complete list of parameters are in the config.json file in the Scenarios\TB\02_AgeDependentImmunity\A_Lifelong directory.

Lifelong Immunity: Interventions

All of the scenarios in this tutorial use this intervention which describes two TB outbreaks one occurring in year 1, the second occurring in year 15. The first outbreak is on day 1. The second outbreak is

1095 time steps later (`Timesteps_Between_Repetitions = 1095`). Since the time step is configured as 5 days, the second outbreak is at day 5475 or at the end of the 15th year.

`OutbreakIndividual` allows the user to specify what ages will experience the outbreak. In this intervention, the outbreak is targeted at 1 to 15 year old children.

```
{
    "Campaign_Name": "Campaign - Outbreak",
    "Events": [
        {
            "Event_Coordinator_Config": {
                "Demographic_Coverage": 0.01,
                "Intervention_Config": {
                    "Antigen": 0,
                    "Genome": 0,
                    "Outbreak_Source": "PrevalenceIncrease",
                    "class": "OutbreakIndividual"
                },
                "Number_Distributions": 50,
                "Number_Repetitions": 2,
                "Property_Restrictions": [],
                "Target_Age_Max": 15,
                "Target_Age_Min": 1,
                "Target_Demographic": "ExplicitAgeRanges",
                "Timesteps_Between_Repetitions": 1095,
                "class": "StandardInterventionDistributionEventCoordinator"
            },
            "Event_Name": "Outbreak",
            "Nodeset_Config": {
                "class": "NodeSetAll"
            },
            "Start_Day": 1,
            "class": "CampaignEvent"
        }
    ],
    "Use_Defaults": 1
}
```

You can view the `campaign.json` file is in the `Scenarios\TB\02_AgeDependentImmunity\A_Lifelong` directory.

Lifelong Immunity: Running the Simulation

At your discretion, you can use the sample batch file, `runEMOD`, in the `Scenarios\TB\02_AgeDependentImmunity\A_Lifelong` directory to run the simulation.

Lifelong Immunity: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample command script, `plotResults`, in the `Scenarios\TB\02_AgeDependentImmunity\A_Lifelong` directory to generate graphs from the simulation's `InsetChart` output file.

Simulation Output Graphs

An initial outbreak in the population results in lifelong immunity. Individuals born during the simulation get infected during the second outbreak.

In the following figure, the top left graph (Population Distribution) shows the population age structure at time 0, year 5 and year 10 of the simulation. Because no deaths are allowed in the model, each age group simply ages up to the next age group after five years while new births populate the 0-4 age bin.

The initial TB outbreak resolves as all individuals self-cure and experience lifelong immunity. The immunity in the child group falls from year 0 to year 15 as immune children age into the adult group while children born during the simulation are TB naive. At the time of the second outbreak at year 15, only children who were born during the simulation get infected.

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

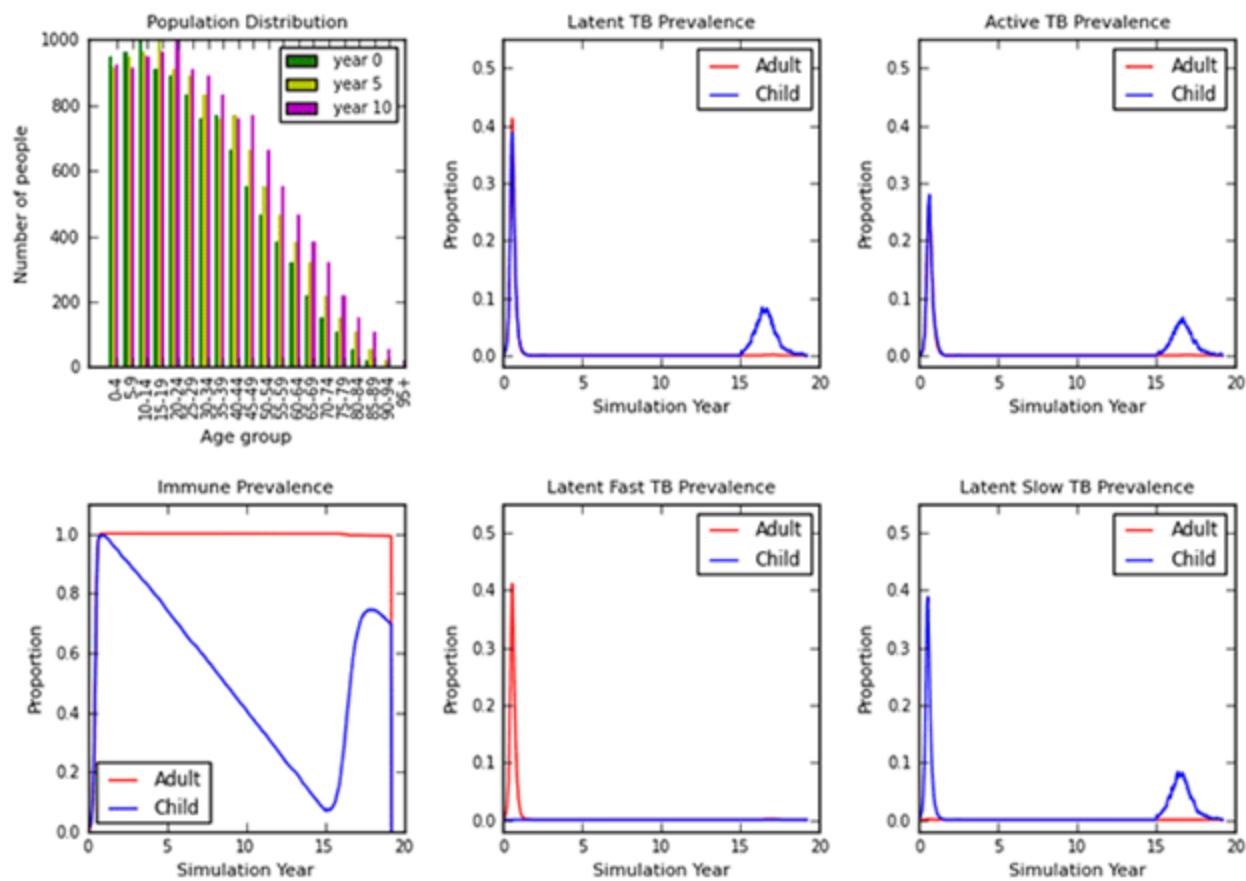


Figure 2: Only Children Born after the 1st Outbreak are Susceptible during the 2nd Outbreak

Over the course of the simulation, the population grows as individuals are born. After the initial outbreak, both adults (red) and children (blue) gain post-infection immunity. At the time of the second outbreak, only TB-naive children are susceptible to TB.

Waning Immunity

For this scenario, adults have waning immunity. Immunity provides 100% protection for 10 years (set by `Acquisition_Blocking_Immunity_Duration_Before_Decay`) and then declines exponentially (mean 15 days) for both children and adults. Fifteen years later, both adults and children are susceptible to disease and participate in the epidemic when the second outbreak occurs.

Waning Immunity: Key Simulation Parameters

Immunity Parameters

Parameter	Value	Description
Acquisition_Blocking_Immunity_Decay_Rate	0.05	Rate at which acquisition-blocking immunity decays after the initial period indicated by the base acquisition-blocking immunity offset.
Acquisition_Blocking_Immunity_Duration_Before_Decay	3650	Number of days after a TB infection has cleared until acquisition-blocking immunity begins to decay.

The complete config.json file is in the Scenarios\TB\02_AgeDependentImmunity\B_Waning directory.

Waning Immunity: Interventions

This scenario has the same interventions as Life-Long Immunity. You can view the campaign.json file in the Scenarios\TB\02_AgeDependentImmunity\B_Waning directory.

Waning Immunity: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\02_AgeDependentImmunity\B_Waning directory to run the simulation.

Waning Immunity: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample command script, plotResults, in the Scenarios\TB\02_AgeDependentImmunity\Waining directory to generate graphs from the simulation's InsetChart output file.

Simulation Output Graphs

The initial outbreak in the population results in immunity which provides protection for 10 years before waning quickly to zero. All individuals are susceptible to the second outbreak that occurs 15 years later.

In the following figure, the Population Distribution graph shows the population age structure at time 0, year 5 and year 10 of the simulation. The population structure is exactly the same as in Lifelong Immunity.

The initial TB outbreak resolves as all individuals self-cure. However, the protective immunity remains at 100% for 10 years before declining quickly to zero. From year 0 to 10, child immunity falls as new births are added to the child group. Twelve years after the initial outbreak, the entire population is susceptible. At the time of the second outbreak at year 15, all individuals get infected.

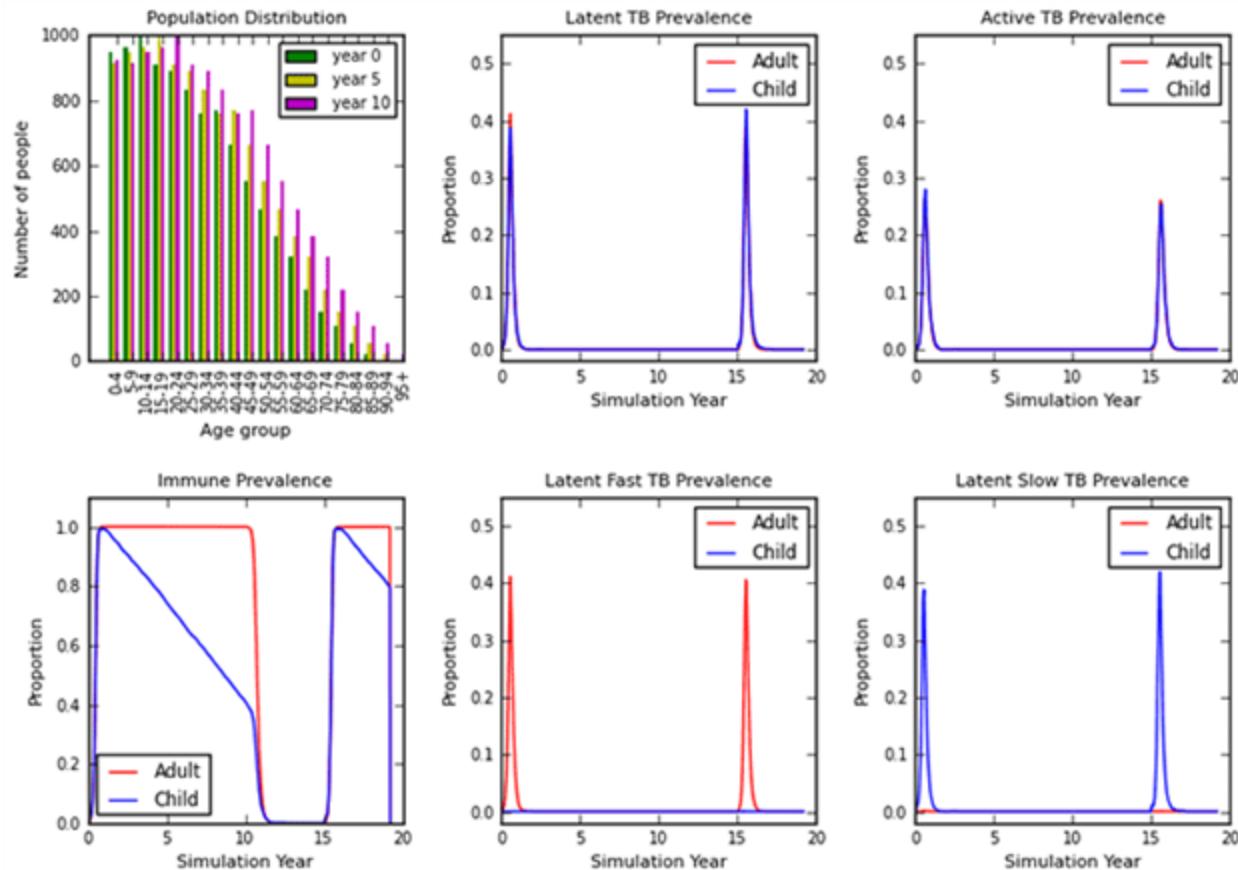


Figure 3: Immunity from the 1st Outbreak Lasts for 10 years, then Quickly Wanes to Zero.

After the first outbreak, the post-infection immunity provides 100% protection for 10 years, then quickly wanes to zero.

Childhood Vaccines

In Childhood Vaccines, BCG vaccinations given at birth provide 15 years of protection from acquiring TB. The duration of protective immunity is decreased from the 10 years in Waning Immunity to 2

years. At the time of the second outbreak at year 15, only adults, who all experienced waning immunity after the first outbreak, participate in the second outbreak.

Childhood Vaccines: Key Simulation Parameters

This scenario has the same configuration file as Waning Immunity. The complete list of parameters are in the config.json file in the Scenarios\TB\02_AgeDependentImmunity\C_Vaccines directory.

Childhood Vaccines: Interventions

This scenario uses the interventions as in the previous scenarios. However, an additional vaccine intervention is added. It models a simple vaccine with 100% protection for 15 years.

For additional information about how to parameterize vaccines, see [Generic 2: SIR - Targeted Vaccination Campaigns](#).

```
    . . .
    "Intervention_Config": {
        "Actual_IndividualIntervention_Config": {
            "Cost_To_Consumer": 1,
            "Durability_Time_Profile": "BOXDURABILITY",
            "Primary_Decay_Time_Constant": 5475,
            "Reduced_Acquire": 1,
            "Vaccine_Take": 1,
            "Vaccine_Take_Age_Decay_Rate": 0,
            "Vaccine_Type": "AcquisitionBlocking",
            "class": "BCGVaccine"
        },
        "Trigger_Condition": "Births",
        "class": "NodeLevelHealthTriggeredIV"
    },
    . . .
```

You can view the campaign.json file in the Scenarios\TB\02_AgeDependentImmunity\C_Vaccines directory.

Childhood Vaccines: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\02_AgeDependentImmunity\C_Vaccines directory to run the simulation.

Childhood Vaccines: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample Windows Command script to create graphs. From the EMODQuick Start command window, navigate to this scenario's directory and enter plotResults.

Simulation Output Graphs

An initial outbreak in the population results in immunity which provides protection for two years before waning quickly to zero. All individuals are susceptible to the second outbreak that occurs 15 years later.

The population age structure remains the same as in the first two scenarios. The protective immunity remains at 100% for only two years before declining quickly to zero. The population immunity falls slightly in children as new TB-naive births are added to the child group, Fifteen years after the initial outbreak, the entire adult population is susceptible and all children are protected by vaccine derived immunity. At the time of the second outbreak at year 15, all adults get infected.

Note: The plotted immunity represents only disease-acquired immunity and does not include the vaccine derived immunity.

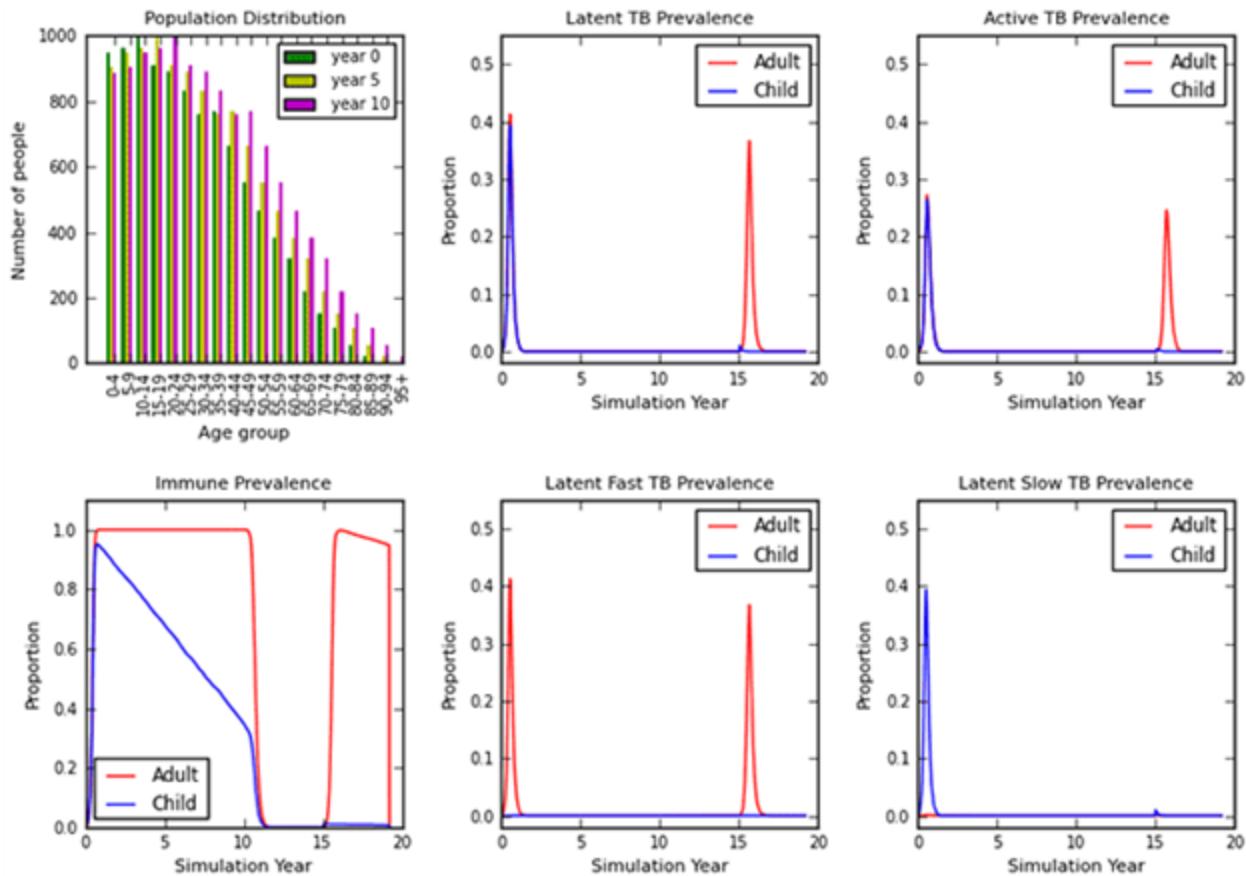


Figure 4: Population and TB dynamics - Childhood Vaccines

Exploring the Model

Example 1:

Vary the `TB_Immune_Loss_Fraction` to adjust what proportion of individuals lose their immunity.

Example 2:

Adjust the rate of immune decay by adjusting `Acquisition_Blocking_Immunity_Decay_Rate`.

Please continue with the next tutorial, [TB 3: Health Care Systems](#) which illustrates how to model multiple health care systems.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Tuberculosis \(TB\) Tutorials](#)

[Parameter Reference](#)

TB 3: Health Care Systems

This tutorial assumes that you have read [TB 2: Age Distribution and Childhood Immunity](#).

The Health Care Systems tutorial illustrates how to model multiple health care systems. It categorizes patients into those who receive no care, those who receive care in the private health care system, and those who receive care in the public health care system. The scenario also illustrates how to dynamically change the quality of care within a health care system during the simulation.

There are four scenarios in this tutorial. The first scenario, Multiple Systems, demonstrates how to configure multiple health care systems. Each of the three subsequent scenarios build upon Multiple Systems by adding interventions that improve either individual's access to care, or the quality of care within a health system.

In general, public health systems have been found to offer more effective treatment with higher cure rates than private health systems, as seen in China and India. For purposes of illustration, these differences are exaggerated in the scenarios: all in public care get cured, while all in private care return to latent disease but relapse to active disease.

- [Multiple Systems](#): Individuals are equally divided into three health care systems. All individuals are infected at the beginning of the simulation. One hundred days after TB activation, individuals who have private and public health care receive treatment with the quality of care dependent on the health care system.
- [No Care to Public Health Care](#): Infected individuals who do not have access to health care are shifted to the public health system on day 750. On day 850 they receive curative treatment.
- [Private to Public Health Care](#): Individuals in the private health system receive a treatment and subsequently relapse to active disease. When they relapse, they immediately shift from the private to the public health system. One hundred days after the shift, they receive curative treatment in the public health system.
- [Private Health Care Improvement](#): At day 75, the quality of care in the private health care system is improved such that all treatments in the private health system provided after day 75 are curative treatments.

Demographics Inputs

IndividualProperties

Use IndividualProperties to divide individuals into three health care groups (None, Private and Public) which are treated differently in the simulation using targeted interventions.

```

"Defaults": {
    "IndividualProperties": [
        {
            "Property": "QualityOfCare",
            "Values": [
                "None",
                "Private",
                "Public"
            ],
            "Initial_Distribution": [0.33, 0.33, 0.34],
            "Transitions": []
        }
    ],
}

```

Property and Values

The IndividualProperties structure creates groups using the Property and Values.

The EMOD-defined Property parameter specifies the property type. For this scenario, the property type QualityOfCare was chosen because the name represents the characteristic that is different between the three groups in this scenario.

The Values array defines the groups. Each user-defined element in the array is a group. In this scenario, groups are None, Private and Public. These represent the groups of patients who have no access to care, who access care in the private health system, and who access care in the public health system respectively.

Note: Property and Values creates the groups. However, the different behavior of the three groups must be configured with targeted interventions in the campaign file.

Initial Distribution

The elements in the Initial_Distribution array correspond to the elements (groups) in the Values array. At the beginning of the simulation or at birth, individuals are assigned to a group using the probabilities in the Initial_Distribution array. In this scenario, individuals have a 33% chance of having no health care, 33% chance of private health care, and a 34% chance of public health care. For more information, see [Creating Heterogeneous Groups](#).

This demographics file is used for all of the scenarios. To view the complete demographics file, see TB_03_HealthSystems_demographics in the Scenarios\InputFiles directory.

Multiple Systems

This scenario follows a cohort of adults who are all infected at time step 1. They are all fast progressors and move quickly from initial infection to active disease. After TB activation, there is a fixed delay of 100 days until individuals receive a 50 day treatment. Treatment in the public sector is 100% curative while treatment in the private sector causes 100% of the patients to go into a latent state, after which they will relapse back into active disease.

Note: Described in IndividualProperties, individuals have been randomly assigned to not access care (1/3), to access care in the private health system (1/3) or to access care in the public health system (1/3).

The treatment cure rate parameters for both the private and public health care are configured to be very high. In the public health system, individuals are assumed to experience total cure, and return to uninfected state. While in the private health system, individuals are assumed to subsequently relapse to active, symptomatic disease.

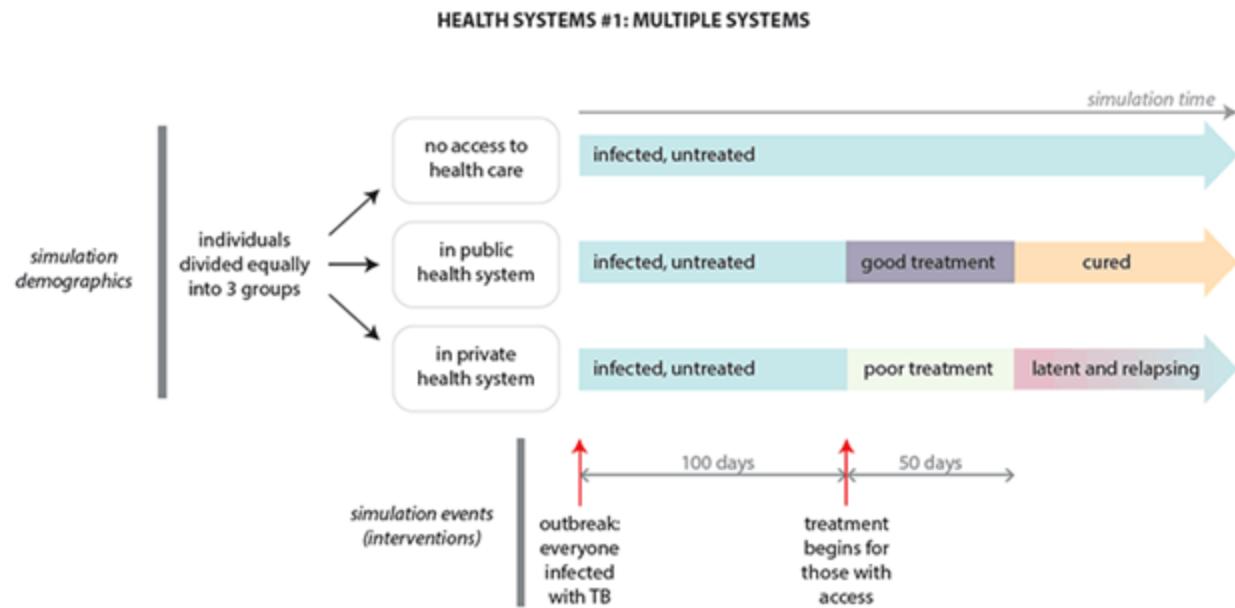


Figure 1: Multiple Systems

Multiple Systems: Key Simulation Parameters

In this scenario, all individuals progress through the latent fast compartment, immediately moving from latent infection through active presymptomatic to active disease. A very small number is used

for the TB_Active_Mortality_Rate and the TB_Active_Cure_Rate so that no individuals have a natural resolution of their active disease.

Parameter	Value	Description
TB_Active_Mortality_Rate	1e-9	For individuals who have not had treatment, this rate is combined with TB_Inactivation_Rate and TB_Active_Cure_Rate to determine the duration of active disease until resolution of active phase. The fraction of TB_Active_Mortality_Rate divided by the total rate is used to determine the probability of cure.
TB_Active_Cure_Rate	1e-9	For individuals who have not had treatment, this rate is combined with TB_Inactivation_Rate and TB_Active_Mortality_Rate to determine the duration of active disease until resolution of the active phase. The fraction of TB_Active_Cure_Rate divided by the total rate. The fraction is used to determine the cure probability.
TB_Presymptomatic_Rate	1	For individuals in the presymptomatic stage, this rate is combined with the TB_Presymptomatic_Cure_Rate to define the duration of presymptomatic period.

Parameter	Value	Description
TB_Fast_Progressor_Fraction_Adult	1	Fraction of adults progressing from latent to active TB via fast progression route. In this simulation all children are latent-fast.
TB_Fast_Progressor_Fraction_Child	1	Fraction of children progressing from latent to active TB via fast progression route. In this simulation all children are latent-fast.
TB_Relapsed_to_Active_Rate	0.01	Rate of progressing from relapsed to active state.

Simulation Setup Parameters

Parameter	Value	Description
Simulation_Timestep	5	Value indicating simulation time step in days. For this simulation, the time step is five days.
Simulation_Duration	1000	Duration of simulation, in days.

Multiple Systems: Interventions

Initial Outbreak

An OutbreakIndividual intervention initially seeds the infection in the entire population with 100% prevalence.

```

        {
      "Event_Coordinator_Config": {
        "Demographic_Coverage": 1,
        "Intervention_Config": {
          "Antigen": 0,
          "Genome": 0,
          "Outbreak_Source": "PrevalenceIncrease",
          "class": "OutbreakIndividual"
        },
        "Number_Distributions": -1,
        "Number_Repetitions": 1,
        "Property_Restrictions": [],
        "Target_Demographic": "Everyone",
        "class": "StandardInterventionDistributionEventCoordinator"
      },
      "Event_Name": "Outbreak",
      "Nodeset_Config": {
        "class": "NodeSetAll"
      },
      "Start_Day": 1,
      "class": "CampaignEvent"
    },
  
```

Active TB Interventions

There are two `NodeLevelHealthTriggeredIV` interventions that are triggered when an individual progresses to active TB.

AntiTBDDrug

The `AntiTBDDrug` intervention enables specific parameters for the relative probabilities of several different treatment outcomes. The `TB_Drug_Clearance_Rate`, `TB_Drug_Relapse_Rate`, and `TB_Drug_Mortality_Rate` represent the rates that cure, relapse or death will occur as a result of the treatment.

- The `Primary_Decay_Time_Constant` determines the duration of treatment when the `Durability_Profile` is `FIXED_DURATION_CONSTANT_EFFECT`. In this scenario, the duration of treatment is 50 days.
- The `TB_Drug_Clearance_Rate` is the cure rate of the drug.
- The `TB_Drug_Relapse_Rate` is the probability that an individual will be cured but subsequently relapse.

In the model, clearance represents a true cure, that is, a return to the uninfected state, while relapse represents an infection which is initially appears cured but subsequently relapses to active symptomatic disease. Rates for clearance, relapse, and mortality are used to determine the weighted probability each of these events might occur during each time step. Only a single event can occur for the duration of a single treatment, and the probabilities are held fixed during the entire treatment. Thus, it is the combination of these rates and the total duration of treatment which determines the overall cure/relapse/mortality rate of a treatment episode. If no event occurs during the treatment, then the individual is categorized as having failed treatment.

The TB_Drug_Resistance_Rate is an independent probability that a drug sensitive person will acquire drug resistance. This primarily pertains to failed patients.

Public Health Care Intervention

Property_Restrictions_Within_Node restricts this intervention to individuals in public health care.

When an individual progresses to active TB, there is a treatment delay which is set by DelayedIntervention. The treatment delay (Delay_Period) is 100 days. The treatment lasts for 50 days (Primary_Decay_Time_Constant). The TB_Drug_Clearance_Rate is 0.1 and the TB_Drug_Relapse_Rate is 1e-09 which means that public sector treatment is effectively 100% curative.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Actual_IndividualIntervention_Config": {
        "Actual_IndividualIntervention_Configs": [
          {
            "Cost_To_Consumer": 1,
            "Drug_Type": "FirstLineCombo",
            "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
            "Dose_Interval": 1,
            "Fraction_Defaulters": 0,
            "Primary_Decay_Time_Constant": 50,
            "Remaining_Doses": 1,
            "Reduced_Transmit": 1,
            "TB_Drug_Clearance_Rate": 0.1,
            "TB_Drug_Inactivation_Rate": 1e-09,
            "TB_Drug_Mortality_Rate": 1e-09,
            "TB_Drug_Relapse_Rate": 1e-09,
            "TB_Drug_Resistance_Rate": 1e-09,
            "class": "AntiTBD"
          }
        ]
      }
    }
}
```

```

    "Coverage": 1,
    "Delay_Period": 100,
    "Delay_Distribution": "FIXED_DURATION",
    "class": "DelayedIntervention
},
"Demographic_Coverage": 1,
"Property_Restrictions_Within_Node":
[
    "QualityOfCare:Public"
],
"Trigger_Condition": "TBActivation",
"class": "NodeLevelHealthTriggeredIV"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [],
"Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "Public Health Care: Drugs after TB activation",
"Nodeset_Config": {
    "class": "NodeSetAll"
},
"Start_Day": 1,
"class": "CampaignEvent"
},

```

Private Health Care Intervention

Property_Restrictions_Within_Node restricts this intervention to individuals in private health care.

The delay and timing of the intervention is the same as the public health care intervention. However, AntiTBDDrug has different values. The TB_Drug_Clearance_Rate is set to 1e-9 and the TB_Drug_Relapse_Rate is set to 0.1. This means that effectively 100% of the patients go into a latent state and will later relapse back into active disease.

```

{
    "Event_Coordinator_Config": {
        "Demographic_Coverage": 1,
        "Intervention_Config": {
            "Actual_IndividualIntervention_Config": {
                "Actual_IndividualIntervention_Configs": [
                    {
                        "Cost_To_Consumer": 1,
                        "Dose_Interval": 1,

```

```
        "Drug_Type": "FirstLineCombo",
        "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
        "Fraction_Defaulters": 0,
        "Primary_Decay_Time_Constant": 50,
        "Reduced_Transmit": 1,
        "Remaining_Doses": 1,
        "TB_Drug_Clearance_Rate": 1e-09,
        "TB_Drug_Inactivation_Rate": 1e-09,
        "TB_Drug_Mortality_Rate": 1e-09,
        "TB_Drug_Relapse_Rate": 0.1,
        "TB_Drug_Resistance_Rate": 1e-09,
        "class": "AntiTBDDrug"
    },
],
"Coverage": 1,
"Delay_Distribution": "FIXED_DURATION",
"Delay_Period": 100,
"class": "DelayedIntervention
},
"Duration": -1,
"Property_Restrictions_Within_Node": [
    "QualityOfCare:Private"
],
"Trigger_Condition": "TBActivation",
"class": "NodeLevelHealthTriggeredIV"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [],
"Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "Private Health Care: Drugs after TB activation",
Nodeset_Config": {
    "class": "NodeSetAll"
},
"Start_Day": 1,
"class": "CampaignEvent"
},
```

You can view the complete campaign.json file is in the Scenarios\TB\03_HealthSystems\A_MultipleSystems directory.

Multiple Systems: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\03_HealthSystems\A_MultipleSystems directory to run the simulation.

Multiple Systems: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample script file, plotResults, in the Scenarios\TB\03_HealthSystems\A_MultipleSystems directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

After the initial infection of the cohort, all individuals progress quickly through latent to active disease. Individuals who have no access to care remain in the active state. For individuals in the private and public sector, there is a 100-day delay until all individuals receive a 50-day treatment.

Public Health Care

Individuals in the public sector receive curative treatment and are no longer active. See the decline in the green curve in the Active TB Population.

Private Health Care

Individuals eventually progress back to active disease.

- Individuals who receive private care receive non-curative treatment and progress to a latent state. See the blue line in Latent TB Population and Latent Pending Relapse Population.
- After relapse, individuals progress to Active TB Population PostRelapse.

No Health Care

Individuals with no health care remain in the active state. See the red in Active TB Population.

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

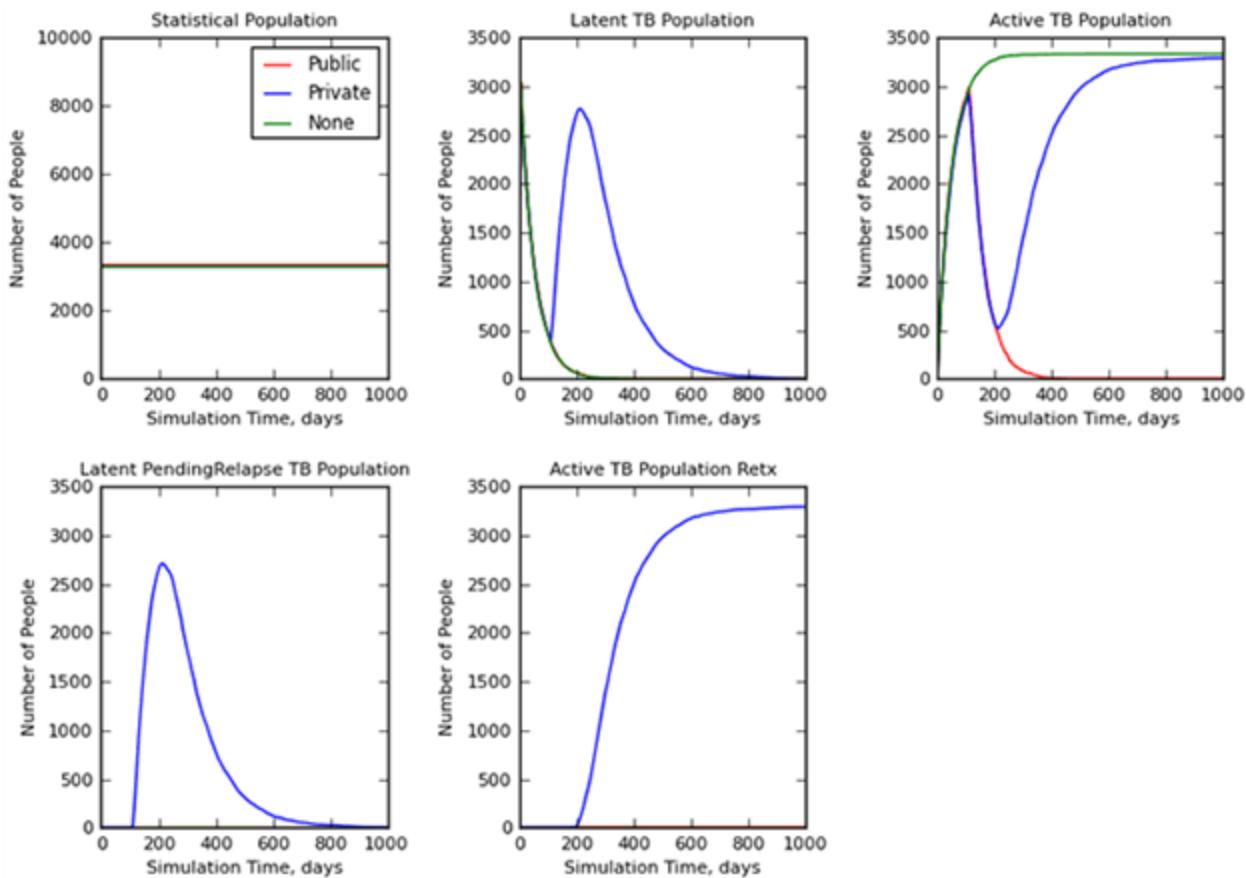


Figure 2: Multiple Systems.

One third of individuals have no access to care (green). One third receive care in the private health care system (blue). One third are in the public health care system (red). In this simulation, individuals are cured in the public health care system. Individuals cured in the private health care system subsequently relapse.

No Care to Public Health Care

Infected individuals who do not have access to health care are shifted to the public health system on day 750. On day 850 they receive curative treatment. The treatment is from a public health care system and lasts for 100 days.

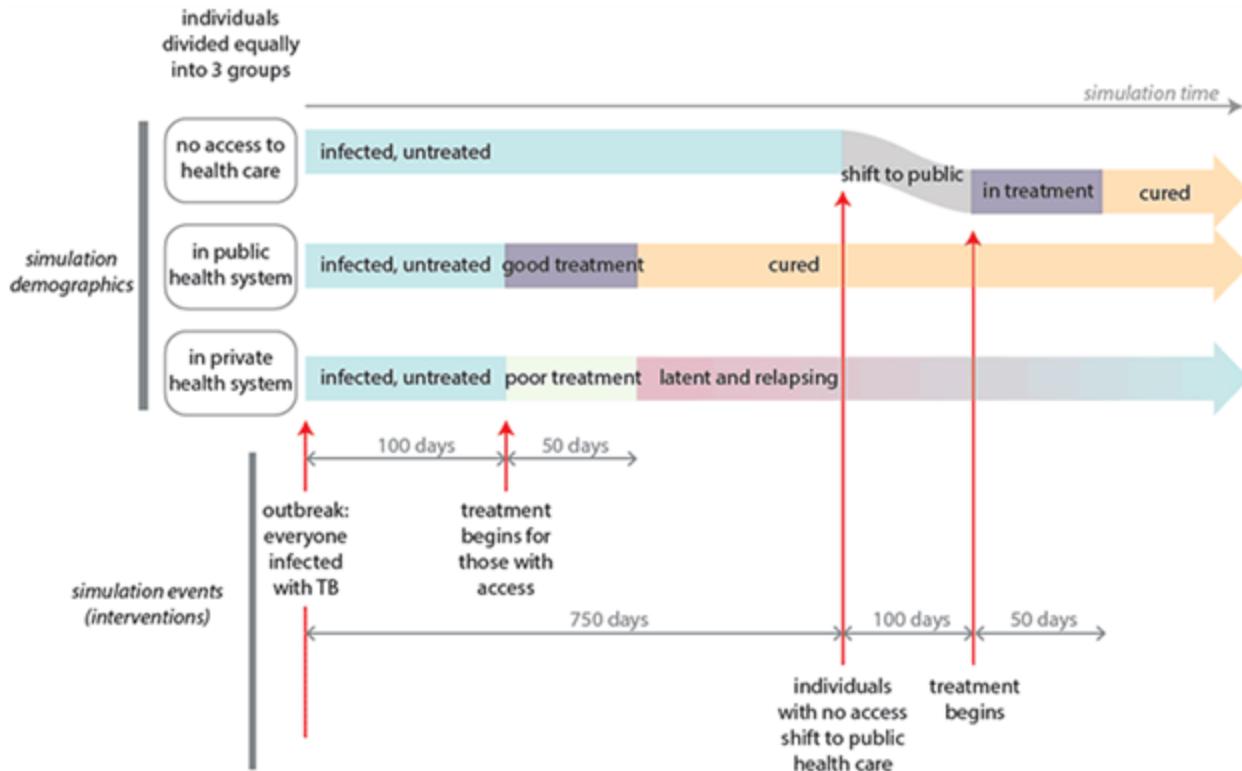


Figure 3: No Care to Public Health Care:

No Care to Public Health Care: IKey Simulation Parameters

The configuration parameters are the same as in Multiple Systems. The config.json for No Care to Public Health Care is in the Scenarios\TB\03_HealthSystems\B_NoneToPublic directory.

No Care to Public Health Care: Interventions

In addition to the interventions used in Multiple Systems, interventions are added to shift patients from no care to public health care on day 750. This is done using the PropertyValueChanger intervention. This intervention is only distributed to individuals who have None as their QualityofCare.

One hundred days after shifting to public health care, these individuals are given the same AntiTBDrug curative treatment given to individuals who were in the public health care system at the beginning of the simulation.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
```

```

    "Intervention_List": [
        {
            "Daily_Probability": 1,
            "Maximum_Duration": 1000000000.0,
            "Revert": 0,
            "Target_Property_Key": "QualityOfCare",
            "Target_Property_Value": "Public",
            "class": "PropertyValueChanger"
        },
        {
            "Actual_IndividualIntervention_Configs": [
                {
                    "Cost_To_Consumer": 1,
                    "Dose_Interval": 1,
                    "Drug_Type": "FirstLineCombo",
                    "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
                    "Fraction_Defaulters": 0,
                    "Primary_Decay_Time_Constant": 50,
                    "Reduced_Transmit": 1,
                    "Remaining_Doses": 1,
                    "TB_Drug_Clearance_Rate": 0.1,
                    "TB_Drug_Inactivation_Rate": 1e-09,
                    "TB_Drug_Mortality_Rate": 1e-09,
                    "TB_Drug_Relapse_Rate": 1e-09,
                    "TB_Drug_Resistance_Rate": 1e-09,
                    "class": "AntiTBDDrug"
                }
            ],
            "Coverage": 1,
            "Delay_Distribution": "FIXED_DURATION",
            "Delay_Period": 100,
            "class": "DelayedIntervention"
        }
    ],
    "class": "MultiInterventionDistributor"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [
    "QualityOfCare:None"
],
Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
,
"Event_Name": "PropertyValueChanger from None to Public",
"Nodeset_Config": {

```

```
        "class": "NodeSetAll"
    },
    "Start_Day": 750,
    "class": "CampaignEvent"
}
```

No Care to Public Health Care: Running the Simulation

At your discretion, you can use the sample file, runEMOD, in the Scenarios\TB\03_HealthSystems\B_NoneToPublic directory to run the simulation.

No Care to Public Health Care: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample file, plotResults, in the Scenarios\TB\03_HealthSystems\B_NoneToPublic directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

Infected individuals who do not have access to health care are shifted to the public health system on day 750. On day 850 they receive curative treatment. This is clearly observed in the graphs at day 750 where there is a drop in the statistical population in None (red line). The active TB population in None goes to 0 and the active TB population in public (green line) increases. This population is resident in Public for only 100 days, after which they receive treatment.

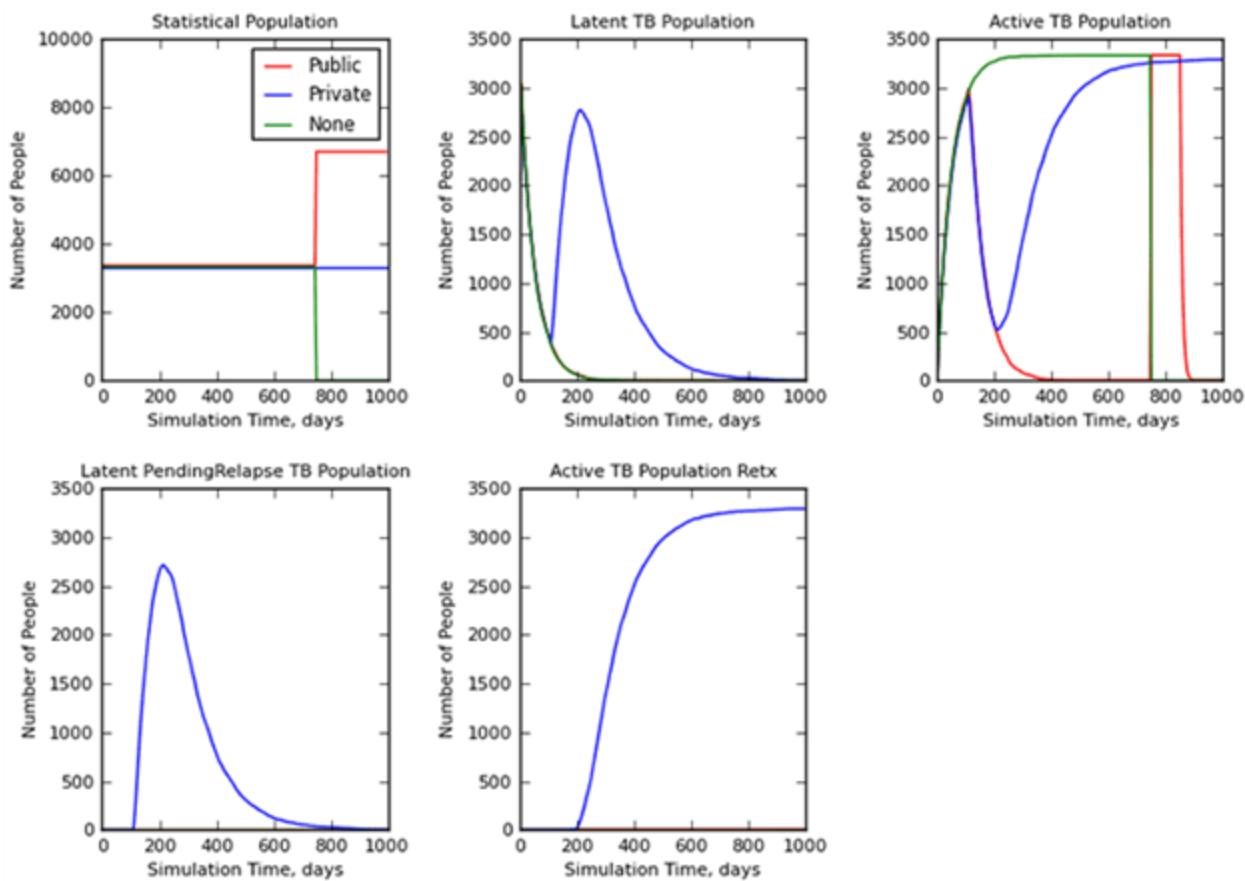


Figure 4; Individuals shift from no care to public health care at time step 750. They subsequently receive care and are cured.

Private to Public Health Care

Individuals in the private health system receive a treatment go into a temporary latent state and subsequently relapse to active disease. In this scenario, at the time of relapse, individuals immediately shift from the private to the public health system. One hundred days after the shift, they receive curative treatment in the public health system.

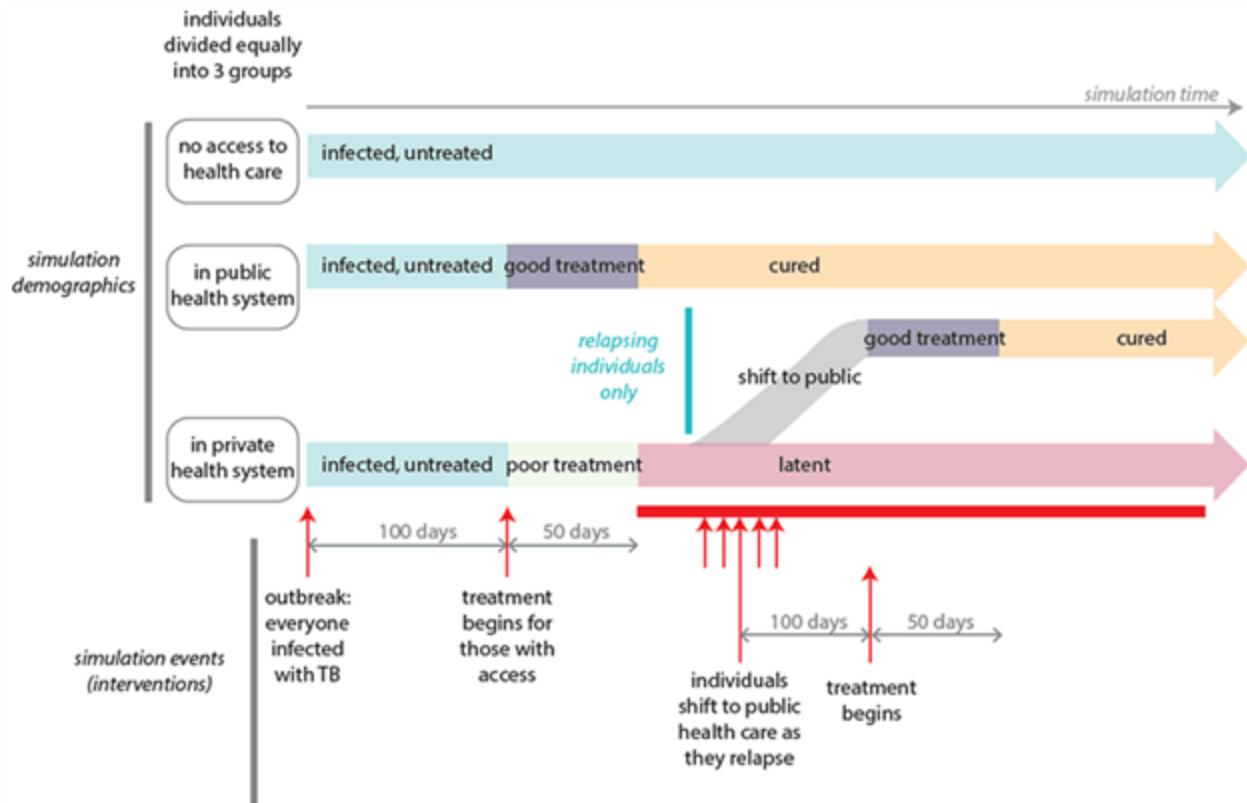


Figure 5: Private to Public Health Care

Private to Public Health Care: Key Simulation Parameters

The configuration parameters are the same as in Multiple Systems. However, a copy of the config.json file is in the Scenarios\TB\03_HealthSystems\C_PrivateToPublic directory.

Private to Public Health Care: Interventions

In addition to the interventions used in Multiple Systems, an intervention is added when individuals relapse, they shift to the public health care system, and then receive treatment 100 days later.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Actual_IndividualIntervention_Config": {
        "Intervention_List": [
          {
            "Daily_Probability": 1,
            "Maximum_Duration": 1000000000.0,
            "Revert": 0,
            "Type": "Shift"
          }
        ]
      }
    }
  }
}
```

```

        "Target_Property_Key": "QualityOfCare",
        "Target_Property_Value": "Public",
        "class": "PropertyValueChanger"
    },
    {
        "Actual_IndividualIntervention_Configs": [
            {
                "Cost_To_Consumer": 1,
                "Dose_Interval": 1,
                "Drug_Type": "FirstLineCombo",
                "Durability_Profile": "FIXED_DURATION_CONSTANT_"
            },
            {
                "Fraction_Defaulters": 0,
                "Primary_Decay_Time_Constant": 50,
                "Reduced_Transmit": 1,
                "Remaining_Doses": 1,
                "TB_Drug_Clearance_Rate": 0.1,
                "TB_Drug_Inactivation_Rate": 1e-09,
                "TB_Drug_Mortality_Rate": 1e-09,
                "TB_Drug_Relapse_Rate": 1e-09,
                "TB_Drug_Resistance_Rate": 1e-09,
                "class": "AntiTBDDrug"
            }
        ],
        "Coverage": 1,
        "Delay_Distribution": "FIXED_DURATION",
        "Delay_Period": 100,
        "class": "DelayedIntervention"
    }
],
"class": "MultiInterventionDistributor"
},
"Property_Restrictions_Within_Node": [
    "QualityOfCare:Private"
],
"Trigger_Condition": "TBActivationPostRelapse",
"class": "NodeLevelHealthTriggeredIV"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [],
"Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "PostRelapseActivation shift from private to public",
"Nodeset_Config": {

```

```
        "class": "NodeSetAll"
    },
    "Start_Day": 1,
    "class": "CampaignEvent"
}
```

Private to Public Health Care: Running the Simulation

At your discretion, you can use the sample file, runEMOD, in the Scenarios\TB\03_HealthSystems\C_PrivateToPublic directory to run the simulation.

Private to Public Health Care: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\03_HealthSystems\C_PrivateToPublic directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

In this scenario, individuals in the private sector who relapse to active disease shift to the public sector. After treatment, they stay in the latent pending relapse phase (within the private health care system), but once they activate (active post relapse) they move into the public health system. They immediately receive curative treatment so the second bump in the active TB population reaches a smaller peak than the initial peak.

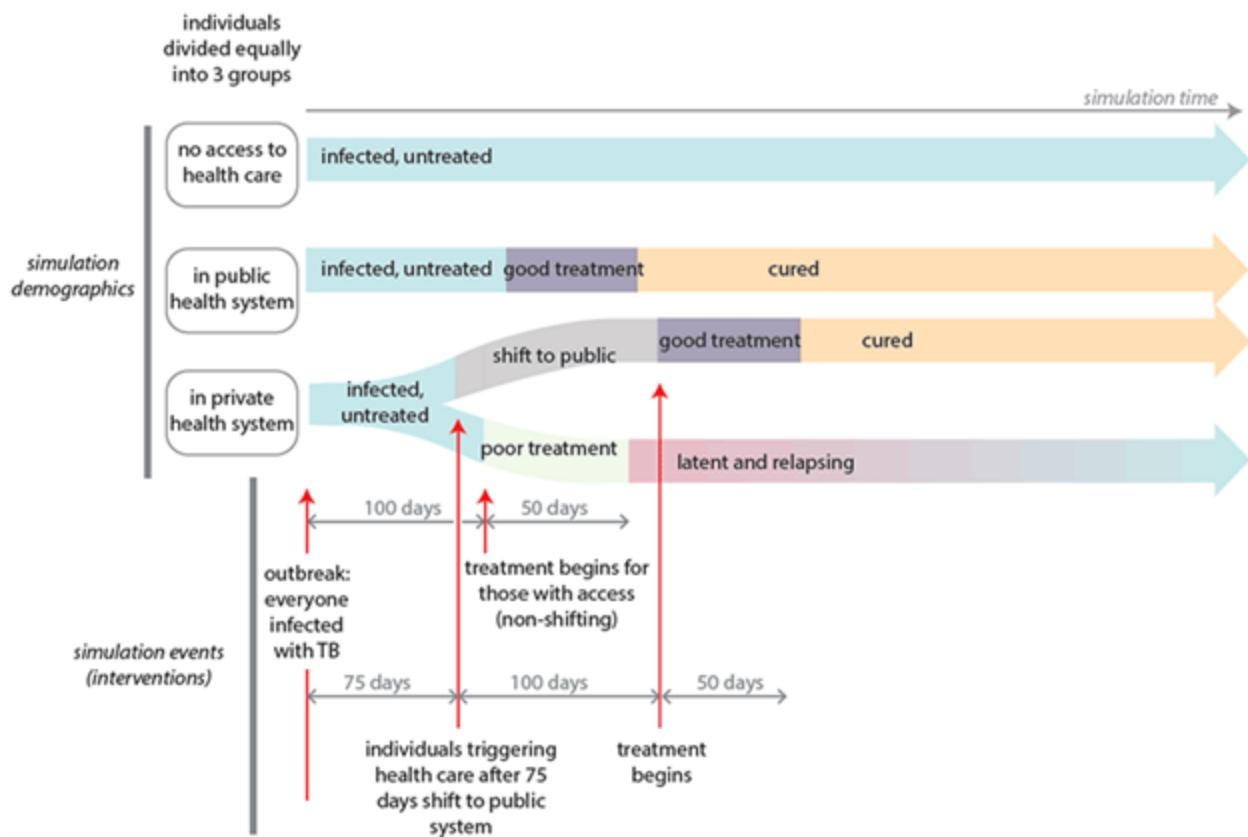


Figure 6: Individuals who are initially treated in the private health system, and subsequently relapse, are shifted to the public health care system. There, they receive curative treatment.

Private System Improvement

The quality of care in the private care health system is improved so that all individuals who start treatment after day 75 receive curative treatment. This lowers the number of individuals in the private sector who relapse.

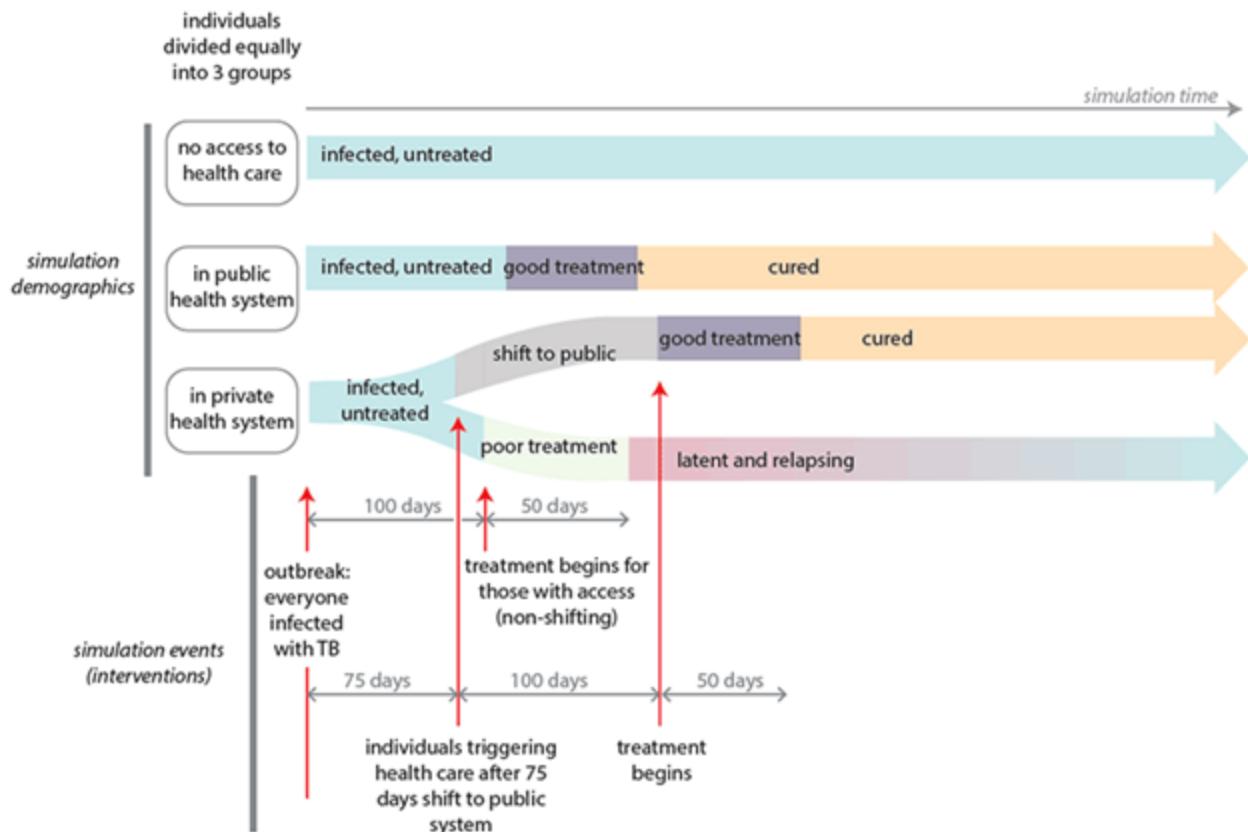


Figure 7: Private System Improvement

Private System Improvement: Key Simulation Parameters

The configuration parameters are the same as in Multiple Systems. However, a copy of the config.json file is in the Scenarios\TB\03_HealthSystems\Private\SystemImprovement directory.

Private System Improvement: Interventions

In addition to the interventions used in Multiple Systems, interventions are added for improving the private health care system.

At day 75, the private health care intervention that is triggered by the TBActivation event is replaced with a drug intervention that is the same as the public health care intervention. Individuals who go into active TB after day 75 receive the improved TB treatment.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Actual_IndividualIntervention_Config": {
```

```

    "Actual_IndividualIntervention_Configs": [
        {
            "Cost_To_Consumer": 1,
            "Dose_Interval": 1,
            "Drug_Type": "FirstLineCombo",
            "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
            "Fraction_Defaulters": 0,
            "Primary_Decay_Time_Constant": 50,
            "Reduced_Transmit": 1,
            "Remaining_Doses": 1,
            "TB_Drug_Clearance_Rate": 0.1,
            "TB_Drug_Inactivation_Rate": 1e-09,
            "TB_Drug_Mortality_Rate": 1e-09,
            "TB_Drug_Relapse_Rate": 1e-09,
            "TB_Drug_Resistance_Rate": 1e-09,
            "class": "AntiTBDDrug"
        }
    ],
    "Coverage": 1,
    "Delay_Distribution": "FIXED_DURATION",
    "Delay_Period": 100,
    "class": "DelayedIntervention"
},
"Property_Restrictions_Within_Node": [
    "QualityOfCare:Private"
],
"Trigger_Condition": "TBActivation",
"class": "NodeLevelHealthTriggeredIV"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [],
"Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "Improve quality of care in the private sector, should expire the top one",
"Nodeset_Config": {
    "class": "NodeSetAll"
},
"Start_Day": 75,
"class": "CampaignEvent"
}
}

```

Private System Improvement: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\03_HealthSystems\D_SystemImprovement directory to run the simulation.

Private System Improvement: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\03_HealthSystems\D_SystemImprovement directory to generate graphs.

Simulation Output Graphs

At time 75, the quality of treatment in the private sector is improved such that all individuals who start treatment after time 75 receive curative treatment. This lowers the number of individuals in the private sector who relapse.

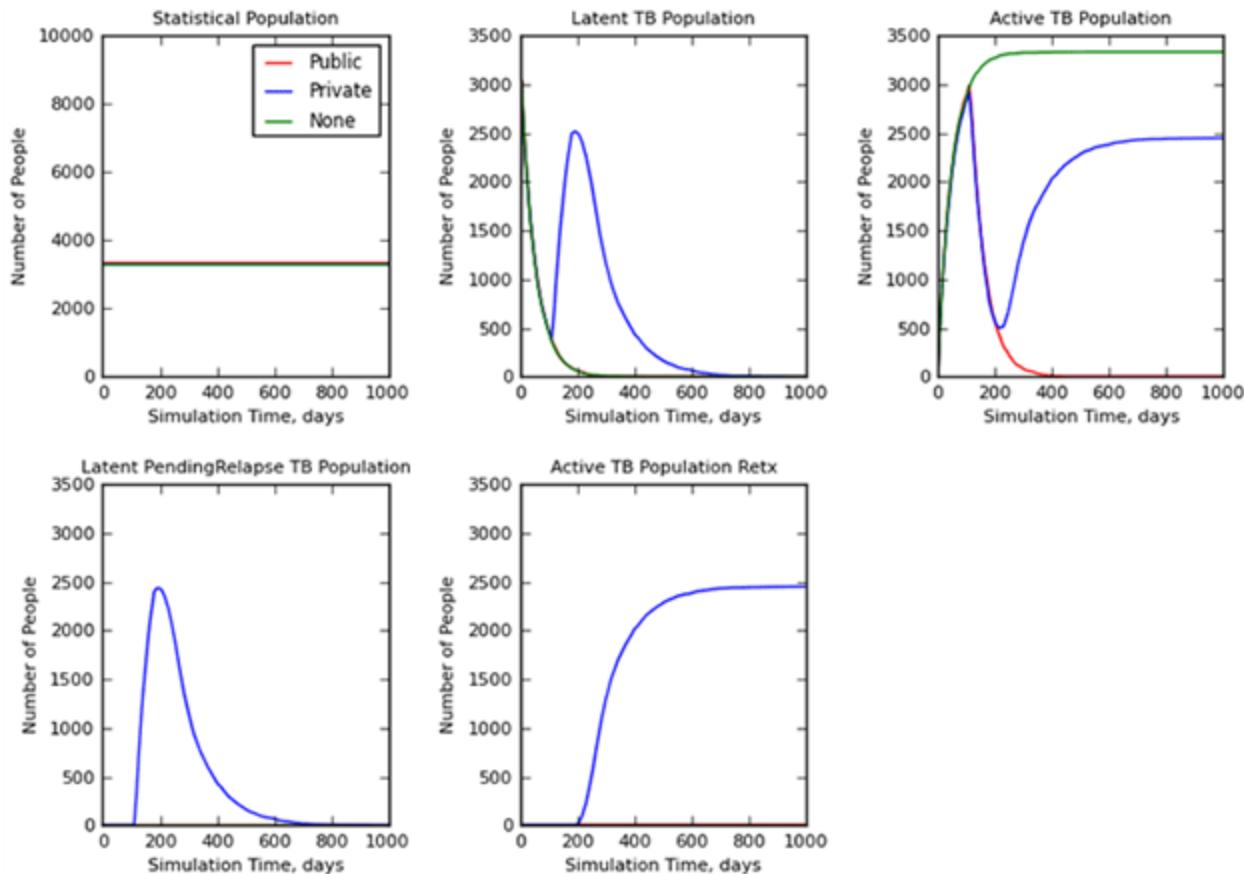


Figure 8: Individual in the private health system who are treated after day 75, are provided with curative treatment lowering the total number of individuals who relapse.

Exploring the Model

Simultaneously increase the quality of care in the private sector and shift individuals from no care to the private health system.

Please continue with the next scenario, [TB 4: Cascade of Care](#) which demonstrates the effect of the cascade of care on the disease outcome of individuals who received treatment for TB.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Tuberculosis \(TB\) Tutorials](#)

[Parameter Reference](#)

TB 4: Cascade of Care

The Cascade of Care tutorial assumes that you have read [TB 3: Health Care Systems](#).

This tutorial demonstrates how the cascade of care can be represented in EMOD, using a series of dependent interventions. It illustrates the use of model “events”, which occur at the time of a state transition, and are used to link dependent interventions together into a care cascade. Examples of events include when an individual progresses from one disease state to another (NewInfectionEvent when an individual goes from susceptible to latent) or specific steps in the care cascade (ProviderOrdersTBTest when an individual visits a health care provider). The use of events also enables a simple computational interface for dynamically changing the cascade of care during the course of the simulation. Detailed reporting within the cascade of care can add insight into why patients ultimately do or do not receive curative treatment.

There are two scenarios in this tutorial:

- [Passive Case Finding](#): Symptomatic individuals must present themselves to health care providers, who subsequently order a TB test. Individuals must return to get their test results before they can receive treatment.
- [Active Case Finding \(ACF\)](#): After the cohort progresses through passive case finding, individuals who are treatment experienced and initial defaulters are brought back to the clinic for a second provider visit

Demographics Inputs

At the beginning of the simulation, all individuals are 20 years old (7300 days). There are no births and deaths

```
"Nodes": [
  {
    "IndividualAttributes": {
      "AgeDistribution1": 7300,
      "AgeDistribution2": 0,
      "AgeDistributionFlag": 0,
      ...
    }
    "MortalityDistribution": {
      ...
      "ResultUnits": "annual deaths per 1000 individuals",
      "ResultValues": [
        [ 0 ],
        [ 0 ]
      ]
    }
  }
]
```

```

    },
    . . .
},
"NodeAttributes": {
    . . .
    "BirthRate": 0,
    "InitialPopulation": 10000,
    . . .
},
. . .
}
]

```

IndividualProperties

IndividualProperties divides individuals into three health care groups (None, Private and Public) which are treated differently in the simulation using targeted interventions. The values in the Initial_Distribution array indicate the probabilities of an individual being assigned into one of the three health care groups. In this case, the probability is that all individuals will be assigned to public health care (Public).

```

"Defaults": {
    "IndividualProperties": [
        {
            "Property": "QualityOfCare",
            "Values": [
                "None",
                "Private",
                "Public"
            ],
            "Initial_Distribution": [0, 0, 1],
            "Transitions": []
        }
    ],
}

```

To view the complete demographics file, see TB_04_CascadeOfCare_demographics.json in the Scenarios\Inputs directory. This demographics file is used for both scenarios.

Passive Case Finding

This scenario illustrate a simple cascade of care that represents symptomatic individuals who present themselves to providers (Figure 1). As most individuals do not immediately present to health care providers, this scenario models “healthseekingbehavior” where individuals present to health

care providers at an exponential rate after TBActivation. Once they visit the provider, they receive a diagnostic test for TB. Some individuals may not return to get their test result (defaulters), which can occur for various reasons, including lack of trust in the provider or lack of time and funds to make a second trip to this provider. Individuals who do return to get their test result may receive either a positive or negative test result. If the TB test is positive, providers may order higher quality treatment, which in this illustration, is highly effective against TB. If the TB test is negative, providers may order empiric treatment, which in this illustration, is not effective against TB. At the close of their treatment, patients would continue to be symptomatic and again re-seek treatment. Further description and parameterization of each of these steps in the care cascade is described in the Interventions section.

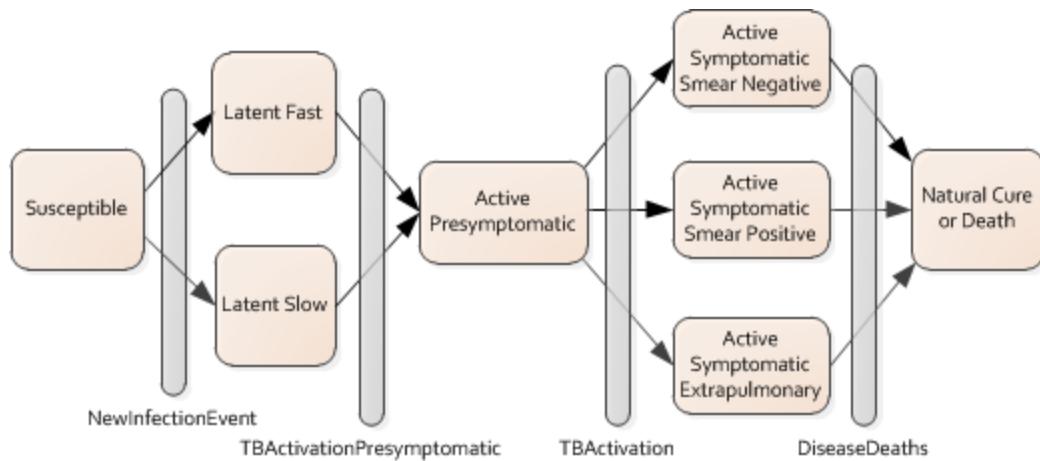


Figure 1: Disease Progression Events (gray bars)

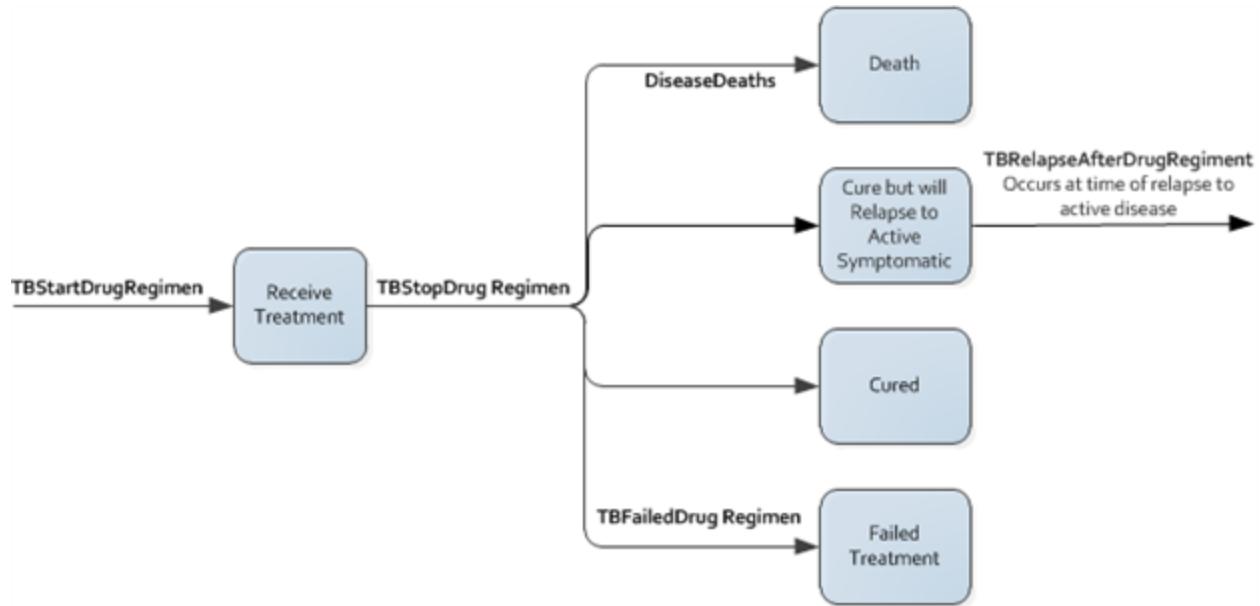


Figure 2: Non-disease Events

Passive Case Finding: Key Simulation Parameters

Disease Parameters

The active symptomatic individuals have a 50% probability of being smear positive, a 50% probability of being smear negative, and a 0% probability of being extrapulmonary.

Parameter	Value	Description
TB_Extrapulmonary_Fraction_Adult	0	Fraction of adults with active TB that is extrapulmonary.
TB_Extrapulmonary_Fraction_Child	0	Fraction of children with active TB that is extrapulmonary.
TB_Smear_Positive_Fraction_Adult	0.5	Fraction of adults with active TB that is smear positive.
TB_Smear_Positive_Fraction_Child	0.5	Fraction of children with active TB that is smear positive.

Drug Parameters

This tutorial parameterizes two drugs: high quality treatment (DOTS), and empiric treatment. The empiric treatment is parametrized directly in the campaign file.

The high quality treatment is parameterized using CDCDrug in the config.json. The CDCDrug drug regimen lasts 50 days, and because the daily probability of cure is set to 0.1, all individuals who are given the CDCDrug regimen will effectively be cured. The drug is distributed during the simulation using the AntiTBPropDepDrug intervention.

```
, , ,
    "TB_Drug_Parms": {
        "CDCDrug": {
            "TB_Drug_Clearance_Rate": 0.1,
            "TB_Drug_Inactivation_Rate": 1e-09,
            "TB_Drug_Mortality_Rate": 1e-09,
            "TB_Drug_Primary_Decay_Time_Constant": 180.0,
            "TB_Drug_Relapse_Rate": 1e-09,
            "TB_Drug_Resistance_Rate": 1e-09
        },
        . . .
    }
```

```

},
"TB_Drug_Types_For_This_Sim": [
    "CDCDrug",
    . . .
],
. . .

```

The complete config.json file is in the Scenarios\TB\04_CascadeOfCare\A_PassiveCaseFinding directory.

The EmpiricTreatment lasts 50 days and because the clearance, mortality and relapse rates are very small, all individuals fail the treatment, that is, the treatment does not affect their disease state. The drug is distributed during the simulation using the AntiTBDDrug intervention.

```

. . .
"Cost_To_Consumer": 1,
"Dose_Interval": 1,
"Drug_Type": "EmpiricTreatment",
"Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
"Fraction_Defaulters": 0,
"Primary_Decay_Time_Constant": 50,
"Reduced_Transmit": 1,
"Remaining_Doses": 1,
"TB_Drug_Clearance_Rate": 1e-09,
"TB_Drug_Inactivation_Rate": 1e-09,
"TB_Drug_Mortality_Rate": 1e-09,
"TB_Drug_Relapse_Rate": 1e-09,
"TB_Drug_Resistance_Rate": 1e-09,
"class": "AntiTBDDrug"
. . .

```

The complete campaign.json file is in the Scenarios\TB\04_CascadeOfCare\A_PassiveCaseFinding directory.

Passive Case Finding: Interventions

Outbreak

For both scenarios, the simulation starts with an initial outbreak.

```

{
"Event_Coordinator_Config": {
    "Demographic_Coverage": 1,

```

```
"Intervention_Config": {  
    "Antigen": 0,  
    "Genome": 0,  
    "Outbreak_Source": "PrevalenceIncrease",  
    "class": "OutbreakIndividual"  
},  
"Number_Distributions": -1,  
"Number_Repetitions": 1,  
"Property_Restrictions": [],  
"Target_Demographic": "Everyone",  
    "class": "StandardInterventionDistributionEventCoordinator"  
},  
"Event_Name": "Outbreak",  
"Nodeset_Config": {  
    "class": "NodeSetAll"  
},  
"Start_Day": 1,  
    "class": "CampaignEvent"  
},
```

Care Cascades

The cascade of care shown in Figure 3 is translated into a series of dependent interventions which are linked by events (see Figure 4).

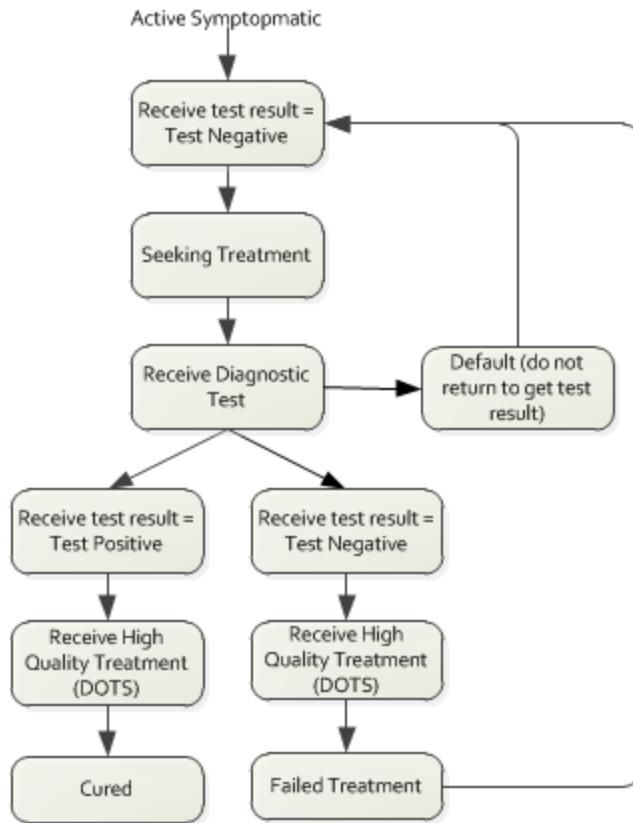


Figure 3: Cascade of Care

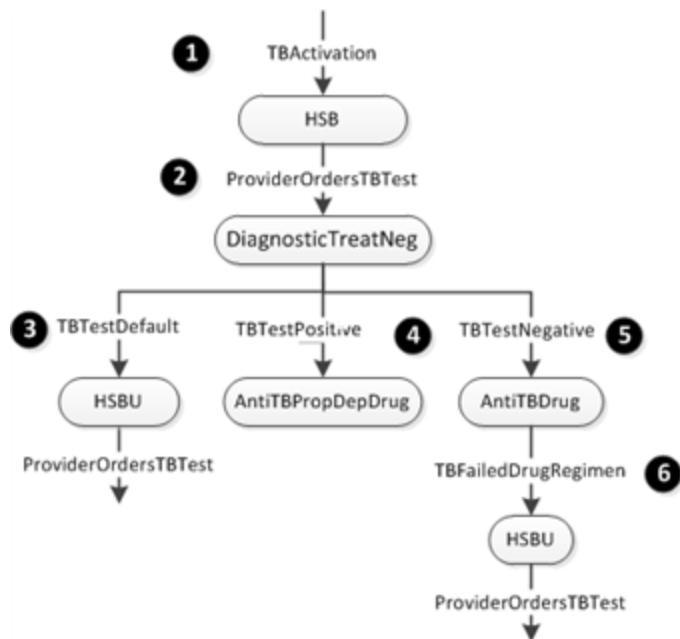
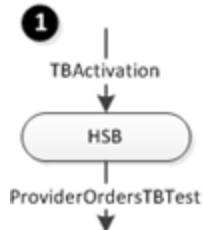


Figure 4: Cascade of Care as represented in the EMOD campaign.json file

Numbers represent the campaign event number. Events, such as TBActivation and ProviderOrdersTest, are represented as text overlaid on arrows. Text in ovals describe the intervention class used as the actual intervention in the campaign event.

Treatment Seeking (1)

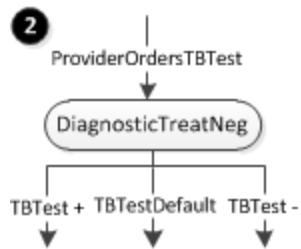


TBActivation occurs when the individual progresses to the active symptomatic stage. To represent the behavior that not all individuals immediately seek care when they become symptomatic, The TBActivation event triggers a health seeking behavior (HSB). The parameter Tendency describes the daily probability that an individual seeking care will go to a provider who orders a TB test (marked by the event ProviderOrdersTBTest).

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Event_Or_Config": "Event",
        "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",
        "Single_Use": 1,
        "Tendency": 0.05,
        "class": "SimpleHealthSeekingBehavior"
    },
    "Demographic_Coverage": 1,
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "TBActivation",
    "class": "NodeLevelHealthTriggeredIV"
},
  
```

Diagnostic Test (2)



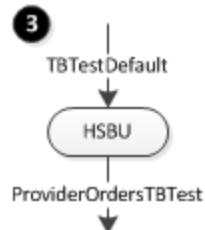
Once the provider orders a TB test, not all individuals will actually receive the test. In this campaign file, this is controlled by the Demographic_Coverage of the second campaign event. In this case,

`Demographic_Coverage` is set to 1, so 100% of individuals who get the TB test order actually receive the diagnostic test.

The diagnostic test is based on the individual's smear status. In this simple scenario, the `base_sensitivity` and the `base_specificity` are set to 1, representing a perfect smear test. The treatment fraction describes the fraction of individuals who receive the test and return to get the test result, which is set to 0.5 in this example. Individuals who do not return to get their test result are considered defaulters. Of those who return to get their test result, individuals who are smear positive receive a positive test result, while individuals who test negative receive a negative test result.

```
"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Base_Sensitivity": 1,
        "Base_Specificity": 1,
        "Cost_To_Consumer": 10,
        "Days_To_Diagnosis": 50,
        "Event_Or_Config": "Event",
        "Defaulters_Event": "TBTestDefault",
        "Negative_Diagnosis_Event": "TBTestNegative",
        "Positive_Diagnosis_Event": "TBTestPositive",
        "Treatment_Fraction": 0.5,
        "class": "DiagnosticTreatNeg"
    },
    "Demographic_Coverage": 1,
    "Duration": -1,
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "ProviderOrdersTBTest",
    "class": "NodeLevelHealthTriggeredIV"
},
```

Default from TB Diagnostic Test (3)



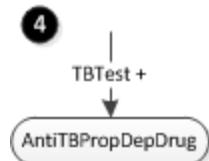
Individuals who received the TB diagnostic test but do not return to get their test result are considered defaulters. In this cascade of care, defaulters return to seek care. However, this has been parameterized to a very low rate in the passive case finding simulation, such that effectively none of the defaulters visit a second health care provider. In the ACF scenario, all defaulters are found and brought to a clinic, which is done by updating the rate these individuals re-seek care.

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Event_Or_Config": "Event",
        "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",
        "Single_Use": 1,
        "Tendency": 5e-06,
        "class": "HealthSeekingBehaviorUpdateable"
    },
    "Demographic_Coverage": 1,
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "TBTestDefault",
    "class": "NodeLevelHealthTriggeredIV"
}

```

Positive Test Result (4)



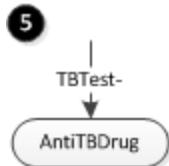
Individuals who test positive receive the AntiTBPropDepDrug CDCDrug, which is parameterized in the config.json. The CDCDrug drug regimen lasts 50 days, and because the daily probability of cure is set to 0.1, all individuals who are given the CDCDrug regimen will effectively be cured.

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Cost_To_Consumer": 1,
        "Drug_Type_by_Property": {
            "QualityOfCare:Public": "CDCDrug"
        },
        "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
        "Enable_State_Specific_Treatment": 1,
        "Primary_Decay_Time_Constant": 50,
        "Remaining_Doses": 1,
        "class": "AntiTBPropDepDrug"
    },
    "Demographic_Coverage": 1,
    "Duration": -1,
    "Trigger_Condition": "TBTestPositive",
    "class": "NodeLevelHealthTriggeredIV"
}

```

Negative Test Result (5)



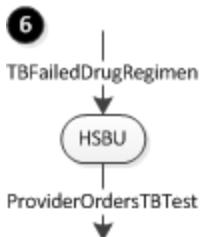
Individuals who test negative receive the empiric treatment. The empiric treatment lasts 50 days, and because the daily probability of cure, relapse and mortality are set to 1e-9, all individuals who are given the empiric treatment fail the treatment (the treatment does not affect their disease state).

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Cost_To_Consumer": 1,
        "Dose_Interval": 1,
        "Drug_Type": "EmpiricTreatment",
        "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
        "Fraction_Defaulters": 0,
        "Primary_Decay_Time_Constant": 50,
        "Reduced_Transmit": 1,
        "Remaining_Doses": 1,
        "TB_Drug_Clearance_Rate": 1e-09,
        "TB_Drug_Inactivation_Rate": 1e-09,
        "TB_Drug_Mortality_Rate": 1e-09,
        "TB_Drug_Relapse_Rate": 1e-09,
        "TB_Drug_Resistance_Rate": 1e-09,
        "class": "AntiTBDrug"
    },
    "Demographic_Coverage": 1,
    "Duration": -1,
    "Trigger_Condition": "TBTestNegative",
    "class": "NodeLevelHealthTriggeredIV"
},

```

Treatment Failure(6)



Individuals who fail treatment are still symptomatic and return to seek care. As with the defaulters, the rate of care-seeking is set to a very small number, such that effectively none of these treatment experienced individuals visit a second health care provider. In the ACF scenario, these treatment

experienced individuals are found and brought to the clinic, which is done by updating the rate these individuals re-seek care.

```
"Intervention_Config": {  
    "Actual_IndividualIntervention_Config": {  
        "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",  
        "Event_Or_Config": "Event",  
        "Single_Use": 1,  
        "Tendency": 5e-06,  
        "class": "HealthSeekingBehaviorUpdateable"  
    },  
    "Demographic_Coverage": 1,  
    "Property_Restrictions_Within_Node": [],  
    "Trigger_Condition": "TBFailedDrugRegimen",  
    "class": "NodeLevelHealthTriggeredIV"  
},
```

You can view the campaign.json file is in the Scenarios\TB\04_CascadeOfCare\A_PassiveCaseFinding directory.

Passive Case Finding: Running the Simulation

At your discretion, you can use the sample batch file runEMOD, in the Scenarios\TB\04_CascadeOfCare\A_PassiveCaseFinding directory to run the simulation.

Passive Case Finding: Expected Simulation Output

Generating Simulation Graphs

You can use the sample file, plotResults, in the Scenarios\TB\04_CascadeOfCare\A_PassiveCaseFinding directory to generate graphs.

Simulation Output Graphs

In this simple example, 50% of the active symptomatic cohort are smear positive and 50% are smear negative. After the first provider visit, 100% of the population is tested, but 50% of the cohort does not return to get their test result. The half of the smear positive individuals who did not default (25% of the total cohort) get cured while the smear negative individuals who did not default get empiric treatment, which leads to treatment failure.

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

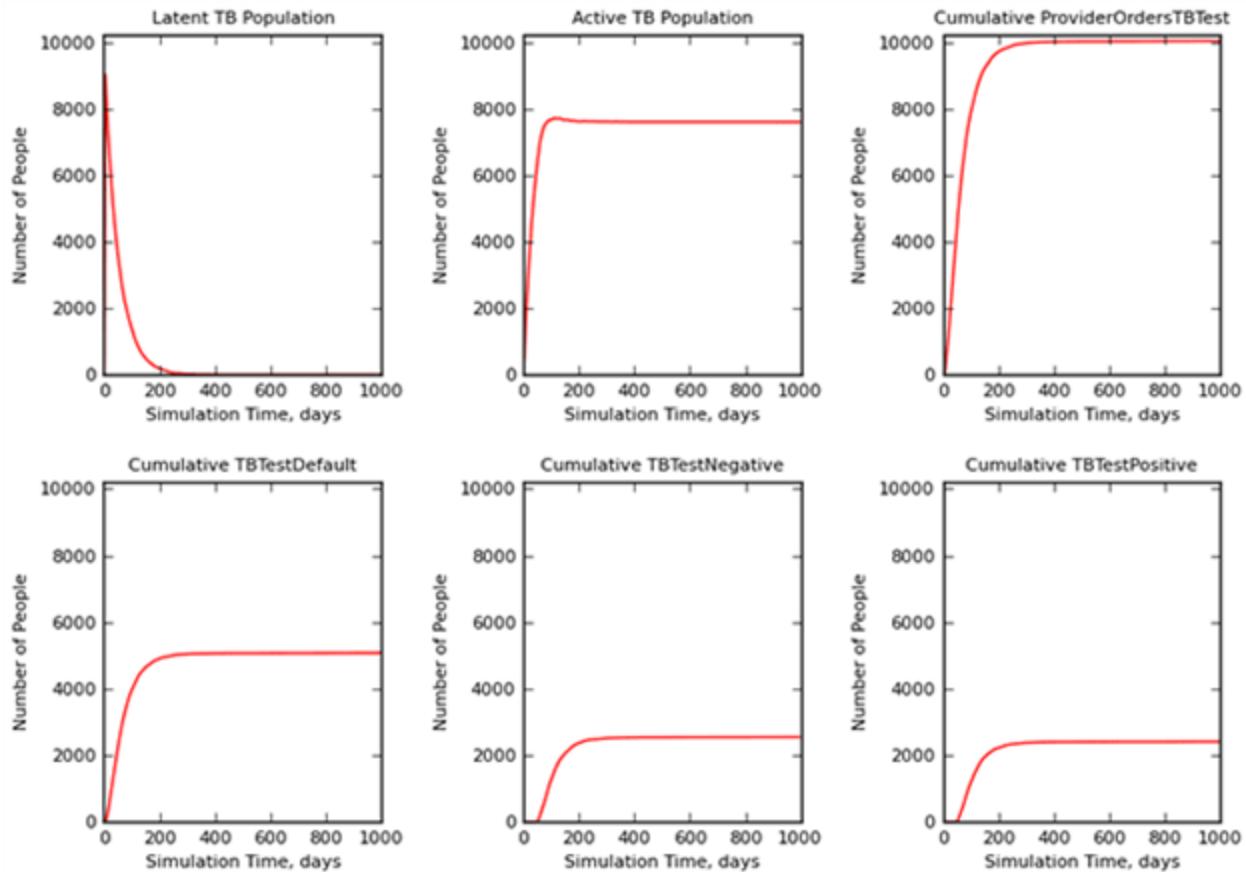


Figure 5: Passive Case Finding

Active Case Finding (ACF)

At the end of the Passive Case Finding scenario, 25% of the cohort is cured, 25% of the population is treatment experienced (the smear negatives who got empiric treatment) and the remaining 50% of the population is treatment naïve because they initially defaulted. The defaulters are composed of half smear positive and smear negative individuals. Thus, of all individuals in the active symptomatic state, 2/3 are smear negative and 1/3 are smear positive. All of the non-cured individuals are seeking care at such a low rate that by the end of the simulation, none of them have returned for a second provider visit.

This scenario models active case finding where all diseased individuals are brought into a clinic, given a TB test, and given treatment based on the test result, therefore, default is zero.

ACF: Key Simulation Parameters

The simulation parameters are the same as Passive Case Finding. The config.json file is in the Scenarios\TB\04_CascadeOfCare\B_ACF directory.

ACF: Interventions

The simulation starts with a TB outbreak at TB Activation.

Add ACF

All individuals are brought into the clinic immediately at time 500. In this example, Tendency is updated to 1 in the HSB of the treatment experienced and defaulters.

```
{  
    "Event_Coordinator_Config": {  
        "Demographic_Coverage": 1,  
        "Intervention_Config": {  
            "New_Tendency": 1,  
            "class": "HealthSeekingBehaviorUpdate"  
        },  
        "Property_Restrictions": [],  
        "class": "StandardInterventionDistributionEventCoordinator"  
    },  
    "Event_Name": "ACF",  
    "Nodeset_Config": {  
        "class": "NodeSetAll"  
    },  
    "Start_Day": 500,  
    "class": "CampaignEvent"  
},
```

To dynamically change the care cascade during the simulation, set a fixed duration to the original intervention in the care cascade and introduce the new intervention at the desired time.

```
{  
    "Event_Coordinator_Config": {  
        "Intervention_Config": {  
            "Actual_IndividualIntervention_Config": {  
                "Base_Sensitivity": 1,  
                "Base_Specificity": 1,  
                "Cost_To_Consumer": 10,  
                "Days_To_Diagnosis": 50,  
                "Event_Or_Config": "Event",  
                "Defaulters_Event": "TBTestDefault",  
                "Negative_Diagnosis_Event": "TBTestNegative",  
                "Positive_Diagnosis_Event": "TBTestPositive",  
                "Treatment_Fraction": 0.5,  
                "class": "DiagnosticTreatNeg"  
            },  
        },  
    },  
}
```

```

    "Duration": 500,
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "ProviderOrdersTBTest",
    "class": "NodeLevelHealthTriggeredIV"
},
"Property_Restrictions": [],
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "when a provider orders a test, the patient can default or get the
intervention appropriate to test result",
"Nodeset_Config": {
    "class": "NodeSetAll"
},
"Start_Day": 1,
"class": "CampaignEvent"
},

```

To reduce default at time 500, set the duration to 500 for the high default test and introduce the zero default test at time 500.

```

{
"Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
        "Actual_IndividualIntervention_Config": {
            "Base_Sensitivity": 1,
            "Base_Specificity": 1,
            "Cost_To_Consumer": 10,
            "Days_To_Diagnosis": 50,
            "Event_Or_Config": "Event",
            "Defaulters_Event": "TBTestDefault",
            "Negative_Diagnosis_Event": "TBTestNegative",
            "Positive_Diagnosis_Event": "TBTestPositive",
            "Treatment_Fraction": 1,
            "class": "DiagnosticTreatNeg"
        },
        "Demographic_Coverage": 1,
        "Duration": -1,
        "Property_Restrictions_Within_Node": [],
        "Trigger_Condition": "ProviderOrdersTBTest",
        "class": "NodeLevelHealthTriggeredIV"
},
"Property_Restrictions": [],
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "new: when a provider orders a test, the patient gets mdr testing

```

```
and smear",
    "Nodeset_Config": {
        "class": "NodeSetAll"
    },
    "Start_Day": 500,
    "class": "CampaignEvent"
}
```

You can see all of the interventions in the campaign.json file is in the Scenarios\TB\04_CascadeofCare\B_ACF directory.

ACF: Running the Simulation

At your discretion, you can use the sample batch file, runEmod, in the Scenarios\TB\04_CascadeofCare\B_ACF directory to run the simulation.

ACF: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\04_CascadeofCare\B_ACF directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

After the initial round of passive case finding, ACF is introduced to the cohort at time 500. The individuals who remain in the active symptomatic state are 2/3 smear negative and 1/3 smear positive. All diseased individuals are brought into the clinic, given a TB test, and receive their results (default is zero). Smear negative individuals (2/3) receive a negative test, followed by empiric treatment, while smear positive individuals (1/3) receive a positive test and curative treatment.

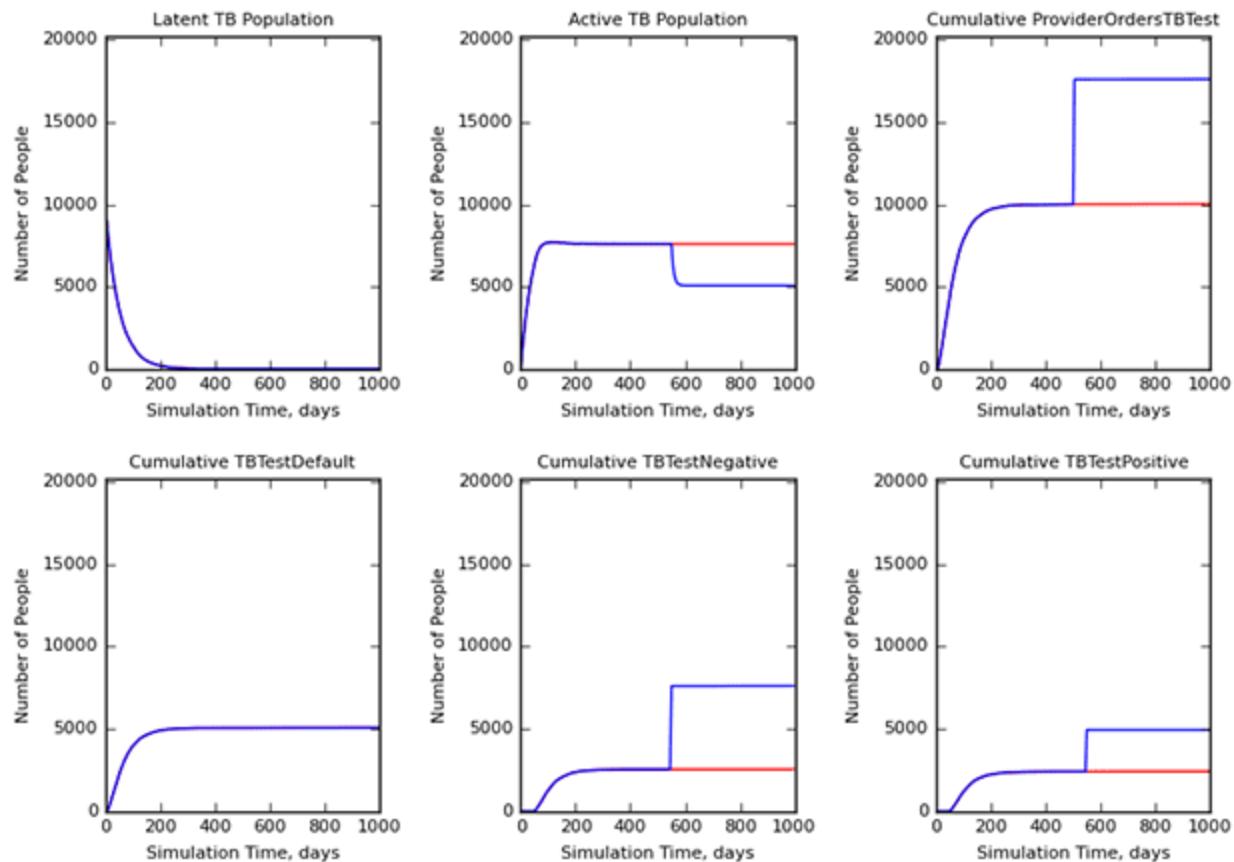


Figure 6: Impact of ACF

Please continue with the next tutorial, [TB 5: Multidrug-resistant \(MDR\) TB](#).

Exploring the Model

Example 1

Vary the proportion of individuals who have an TB test ordered by their health providers but who do not follow up and actually receive the diagnostic test. This introduces additional leaks into the care cascade.

Example 2

Increase the rate that treatment experienced or defaulters return for a second provider visit. This can be used to represent repeated provider visits.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Parameter Reference](#)

TB 5: Multidrug-Resistant (MDR) TB

The Multidrug-resistant TsB tutorial assumes that you have read [TB 4: Cascade of Care](#).

Multidrug-resistant TB (MDR-TB) is disease involving a strain of *M. tuberculosis* that is resistant to at least two of the four drugs in the standard first-line regimen, isoniazid (INH) and rifampicin (RIF). While such strains are believed to occur naturally during infection at low frequencies, the use of four drugs in the standard first-line regimen, each with a different mode of action, typically ensures that such strains do not replicate to high frequencies in an infected individual.

Drug resistance arises through inappropriate treatment which undermines the efficacy of first-line treatment. When this occurs, *M. tuberculosis* strains resistant to one or more drugs may replicate to high frequencies and become the predominant strain in an infected individual. From an epidemiological point of view, this presents two difficulties: Not only are individuals who have acquired a drug-resistant *M. tuberculosis* strain more difficult to treat, but they may also transmit the drug-resistant strain to others. Resistance to INH and RIF commonly co-occurs in the same individual, accounting for the inclusion of these drugs in the definition of MDR-TB.

The scenarios in this tutorial demonstrate various aspects of MDR-TB in TB model:

- [Acquired MDR-TB](#): Individuals are originally infected with drug-sensitive straint but treatment is ineffective and individuals acquire MDR-TB. In this scenario all individuals acquire MDR-TB so there is no transmitted MDR-TB.
- [Transmitted MDR-TB](#): Individuals who acquire MDR-TB through ineffective treatment infect susceptible individuals.
- [Ineffective Treatment](#): Inappropriate use of first-line regimen to treat MDR-TB.
- [Effective Treatment](#): Use of MDR-TB diagnostics and regimen to treat MDR-TB.

Demographics Inputs

This tutorial utilizes a population of 10,000 individuals identical to the demographics used in [TB 1: Basic Tuberculosis \(TB\) Model](#) and [TB 3: Health Care Systems](#). To view the complete demographics file, see TB_05_MDR_demographics in the Scenarios\inputFiles directory.

Key MDR Parameters

The various TB drug-specific parameters in the campaign file (such as TB_Drug_Clearance_Rate and TB_Drug_Inactivation_Rate) follow a special nomenclature where the third word refers to a change of state in the individual's infection (for example, from active TB to cleared TB or latent TB,

respectively), not to a change to the drug itself (for example, from metabolically active drug to a drug cleared from the body). From active TB, several next states are possible: clearance (uninfected), inactivation (latent TB), mortality, and resistance (of the TB strain, still with active infection). Rates are specified as a probability per time step.

Simulation Parameters

Parameter	Values	Description
Number_Basestrains	1	Number of base strains in the simulation (see General Disease). For TB, the closest analogue is the different TB lineages, for example, East Asian, Euro-American. For a friendly introduction to TB lineages, see Lehrman 2013. Scientific American 309:80.
Number_Substrains	2	Number of substrains in the simulations (see General Disease). For TB, The value is set to 2 for the purposes of simulating drug-sensitive and drug-resistant strains.
TB_MDR_Fitness_Multiplier	0 to 1	Relative infectiousness of MDR strains

The complete list of simulation parameters is in the config.json file which is located in each of the tutorial directories at Scenarios\TB\05_MDR.

Intervention Parameters

These parameters are used in OutbreakIndividual.

Parameter	Value	Description
Antigen	1	Identifier for the specific TB base strain in the model being targeted, numbering from 0 to Number_Basestrains - 1. Because Number_Basestrains was set to 1, only one Antigen can be set in the campaign file. All drugs and other interventions target this strain.
Genome	2	Identifier for the variant strains of the TB base strains, numbering from 0 to Number_Substrains - 1. Because Number_Substrains was set to 2, two identifiers for Genome can be used. The convention used in this tutorial is to set 0 for drug-sensitive and 1 for drug-resistant strains.
TB_Drug_Resistance_Rate	0.1	Property of AntiTBDDrug describing the rate at which resistance is acquired while an individual is taking the drug.
Reduced_Transmit	0.9	Relative reduction in infectiousness while an individual is taking drug, with 0 being no reduction and 1 being total cessation

Acquired MDR-TB

Acquired MDR-TB demonstrates how individuals become infected with MDR-TB in the model when their own drug-sensitive infection becomes drug-resistant. This is known as acquired or secondary drug resistance.

The complete list of simulation parameters is in the config.json file in the Scenarios\TB\05_MDR\A_Acquired directory.

Acquired MDR-TB: Interventions

Initially, all individuals are infected with drug-sensitive TB.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 0.005,
    "Intervention_Config": {
      "Antigen": 0,
      "Event_Or_Config": "Event",
      "Genome": 0,
      "Outbreak_Source": "PrevalenceIncrease",
      "class": "OutbreakIndividual"
    },
    ...
  },
  "Start_Day": 1,
  ...
}
```

Through a single round of inappropriate treatment administered at day 100, all of the drug-sensitive TB-infected individuals develop MDR-TB. For illustration purposes, the duration of treatment, specified by `Primary_Decay_Time_Constant`, is set to 90 days rather than the DOTS-specified 180 days.

The rate at which individuals acquire MDR-TB is specified by the parameter `TB_Drug_Resistance_Rate`. The parameter is set to 0.1 / day, so that the average time required for an individual on treatment to acquire MDR-TB is $1 / (0.1 \text{ / day}) = 10 \text{ days}$.

The parameter `Reduced_Transmit` is set to the value of 0.9. This value is less than the maximum value of 1 which corresponds to the complete elimination of transmission while on treatment so, theoretically, transmission is still possible. However, because the entire population is infected, no susceptible individuals exist.

No further diagnostics or follow-up treatment is added..

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Base_Sensitivity": 1,
      "Base_Specificity": 1,
      "Days_To_Diagnosis": 1,
      "Event_Or_Config": "Config",
      "Positive_Diagnosis_Config": {
        "Cost_To_Consumer": 1,
        ...
      }
    }
  }
}
```

```
        "Dose_Interval": 1,  
        "Drug_Type": "FirstLineCombo",  
        "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",  
        "Fraction_Defaulters": 0,  
        "Primary_Decay_Time_Constant": 90,  
        "Reduced_Transmit": 0.9,  
        "Remaining_Doses": 1,  
        "TB_Drug_Clearance_Rate": 1e-09,  
        "TB_Drug_Inactivation_Rate": 1e-09,  
        "TB_Drug_Mortality_Rate": 1e-09,  
        "TB_Drug_Relapse_Rate": 1e-09,  
        "TB_Drug_Resistance_Rate": 0.1,  
        "class": "AntiTBDDrug"  
    },  
    "Treatment_Fraction": 1,  
    "class": "ActiveDiagnostic"  
},  
...  
},  
"Start_Day": 100,  
...  
}
```

You can view the all of the interventions in the campaign.json file in the Scenarios\TB\05_MDR\A_Acquired directory.

Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\05_MDR\A_Acquired directory to run the simulation.

MDR-TB: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\05_MDR\A_Acquired directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

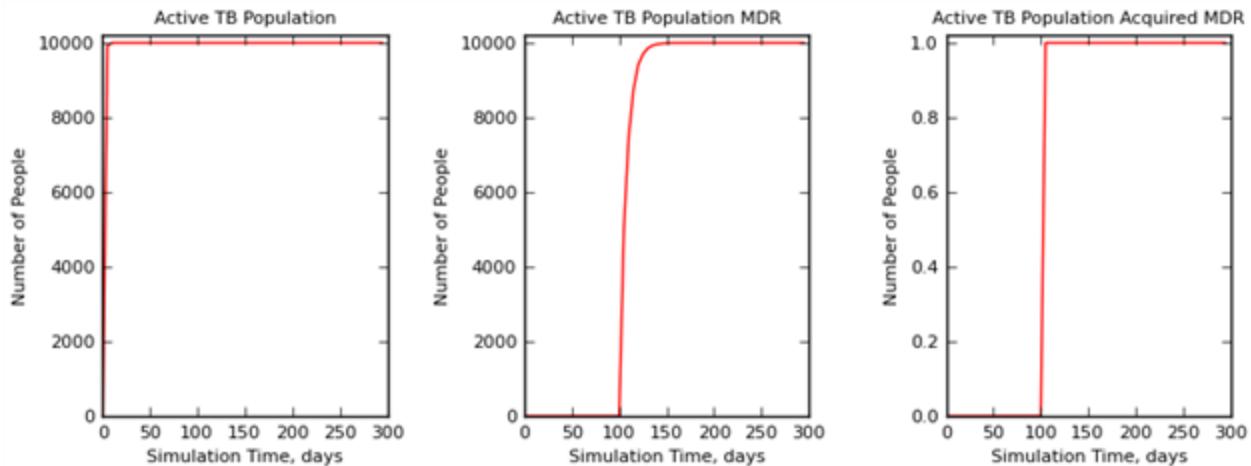


Figure 1: All individuals who are Treated at Time 100 and Acquire Drug Resistance

Transmitted MDR-TB

In this scenario, transmitted MDR-TB is added so both modes of transmission are in the scenario. As in Acquired MDR-TB, individuals are initially infected with drug-sensitive TB. However, in this scenario, only 1% of the total susceptible population is initially infected. While there is some degree of transmission of drug-sensitive TB, most of the population remains uninfected by day 100.

Transmitted MDR-TB: Interventions

At day 100, a single round of inappropriate treatment is given, resulting in all drug-sensitive TB-infected individuals acquiring MDR-TB. As in the last scenario, Reduced_Transmit is set to 0.9, so that transmission while on treatment is still possible. However, in this scenario, susceptible individuals are still present in the population at day 100. These individuals become infected with MDR-TB through transmission beginning at day 100 and then at an increased rate beginning on day 190 after treatment elapses and the effect of Reduced_Transmit ends.

You can view the campaign.json file is in the \Scenarios\TB\05_MDR\B_Transmitted directory.

Transmitted MDR-TB: Running the Simulation

At your discretion, you can use the sample batch file, runEmod, in the \Scenarios\TB\05_MDR\B_Transmitted directory to run the simulation. For information about different methods for running the DTK, see Running a DTK Simulation.

Transmitted MDR-TB: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\05_MDR\B_Transmitted directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

The impact of different treatment availabilities can be seen by comparing output from this scenario with the other scenarios where ineffective or effective treatment is provided for MDR. As a reminder, in this scenario, 1% of the population is initially infected with drug-sensitive TB then given inappropriate treatment between days 100 and 190 resulting in the acquisition of MDR-TB. From day 100 onward, MDR-TB is also transmitted to the remaining, susceptible population.

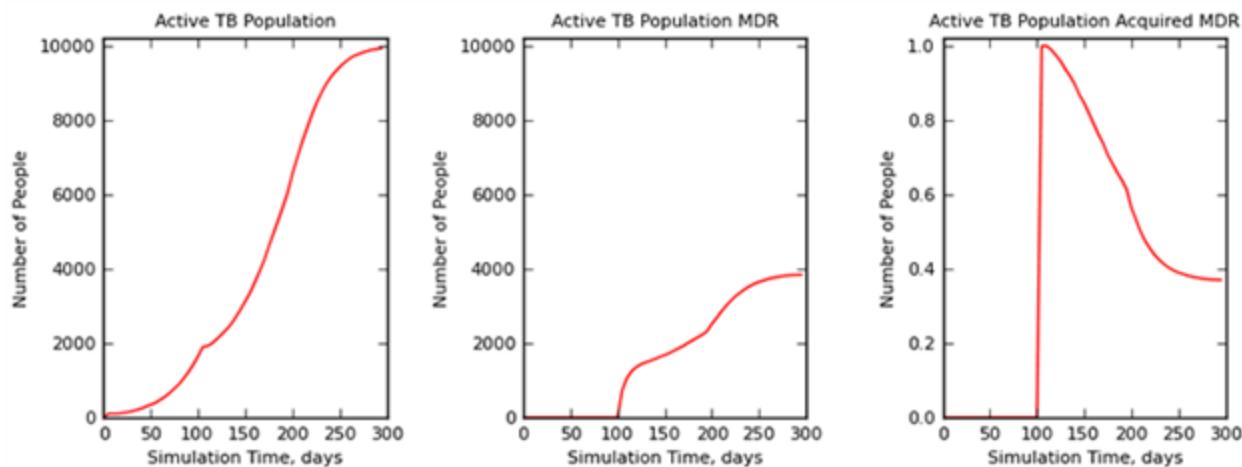


Figure 2: MDR-TB is Acquired at Time 100 and Subsequently Transmitted to the Susceptible Population

Ineffective Treatment

Ineffective Treatment builds on the previous MDR-TB scenario to show what happens in an MDR-TB-infected population when MDR-specific diagnostics and treatments are unavailable and first-line treatments are futilely applied. Following inappropriate treatment for drug-sensitive TB and acquisition of MDR-TB, infected individuals are considered to have failed treatment and subsequently seek additional treatment for a period of a few days. However, in the absence of MDR-specific second-line treatments, these individuals receive a second round of first-line treatment. This may occur in resource-limited settings that lack either the capacity to diagnose MDR-TB or the means to provide expensive second-line treatments. In general, treatment initiated in the absence of a full diagnosis is called "empiric treatment" and has previously been recommended by WHO for MDR-TB.

Ineffective Treatment: Interventions

A failure outcome from a TB drug regimen, which in real life is usually associated with MDR-TB that was either already present at the beginning of treatment or developed during the course of treatment, is used to trigger an additional round of treatment. The class NodeLevelHealthTriggeredIV is used with the Trigger_Condition specified as TBFailedDrugRegimen. However, as stated previously in this tutorial only first-line treatment is available.

First-line treatment is assumed to have a relatively benign effect on MDR-TB: the infected individual's outcome does not change but transmission is reduced while on treatment. (The default value of Reduced_Transmit is used, 0.9) Even in this best-case situation, the effect on the epidemic is minimal. Compared to the output from Transmitted MDR-TB, the number of individuals in the active MDR-TB population is reduced only slightly, while the fraction of MDR-TB cases that are acquired is increased slightly, reflecting reduced transmission. Under more conservative assumptions -- for example, if first-line treatment was assumed to be less effective in reducing the transmission of MDR-TB than of drug-sensitive TB and the value of Reduced_Transmit was set closer to 0 -- the output would resemble that of Transmitted MDR-TB scenario even more closely.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Actual_IndividualIntervention_Config": {
        "Actual_IndividualIntervention_Configs": [
          {
            "Cost_To_Consumer": 1,
            "Dose_Interval": 1,
            "Drug_Type": "EmpiricTreatment",
            "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
            "Fraction_Defaulters": 0,
            "Primary_Decay_Time_Constant": 90,
            "Reduced_Transmit": 0.9,
            "Remaining_Doses": 1,
            "TB_Drug_Clearance_Rate": 1e-09,
            "TB_Drug_Inactivation_Rate": 1e-09,
            "TB_Drug_Mortality_Rate": 1e-09,
            "TB_Drug_Relapse_Rate": 1e-09,
            "TB_Drug_Resistance_Rate": 0.1,
            "class": "AntiTBDDrug"
          }
        ],
        "Coverage": 1
      }
    }
  }
}
```

```

        "Delay_Distribution": "FIXED_DURATION",
        "Delay_Period": 10,
        "class": "DelayedIntervention"
    },
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "TBFailedDrugRegimen",
    "class": "NodeLevelHealthTriggeredIV"
},
"Number_Distributions": -1,
"Number_Repetitions": 1,
"Property_Restrictions": [],
"Target_Demographic": "Everyone",
"class": "StandardInterventionDistributionEventCoordinator"
},
"Event_Name": "Failed people get an ineffective re-treatment after time delay",
"Nodeset_Config": {
    "class": "NodeSetAll"
},
"Start_Day": 1,
"class": "CampaignEvent"
},
...
[remainder identical to MDR scenario (1c)]

```

You can view the all of the interventions in the campaign.json file in the Scenarios\TB\05_MDR\C_Ineffective Treatment.

Ineffective Treatment: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\05_MDR\C_Ineffective Treatment directory to run the simulation.

Ineffective Treatment: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\05_MDR\C_Ineffective Treatment directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

The impact of attempting to treat MDR-TB (Transmitted MDR scenario) using first-line drugs is observed. When the same set of output channels as those from Figure 2 (transmitted MDR) are plotted, the futility of this course of action is readily observed. Small effects are seen in MDR-TB prevalence and the fraction of MDR-TB that is acquired, but the dynamics of the epidemic are essentially unchanged.

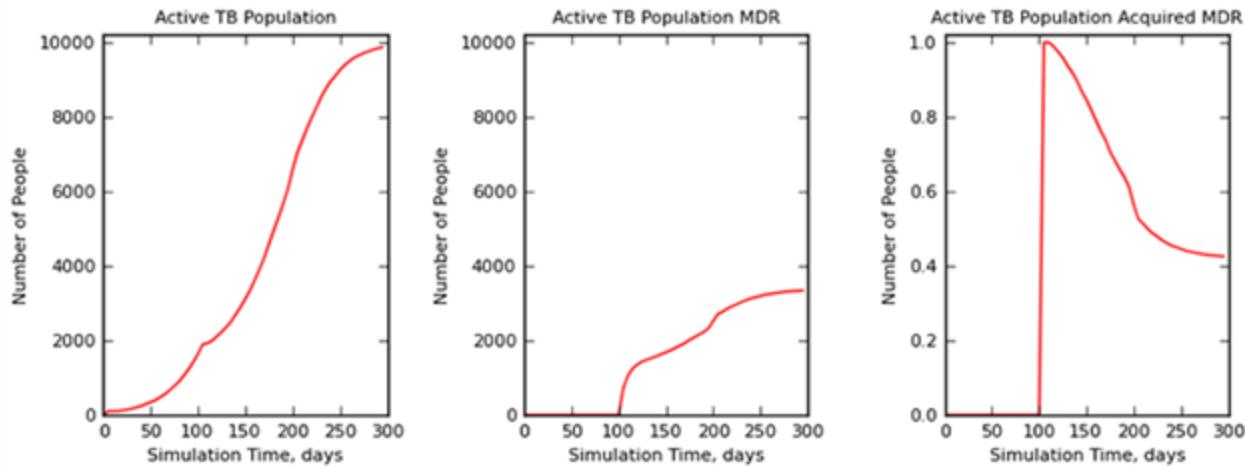


Figure 3: Ineffective Treatment Does Not Affect the Course of the Epidemic

Effective Treatment

This scenario shows the improvements that are gained by the availability of MDR-TB diagnostics and second-line treatment. The scenario begins similarly, with the initial infection of a few individuals with drug-sensitive TB, a round of inappropriate treatment, and acquisition of MDR-TB. However, in this scenario, a diagnostic is available for all individuals who have reached the end of their first-line treatment course and are considered to have failed treatment. At that time, an additional test is given that can discriminate drug-sensitive from drug-resistant infection.

Effective Treatment: Interventions

After a period of 50 days, representing the time required to obtain results from culture-based tests for MDR-TB, a course of second-line treatment is given. In this scenario, for illustration purposes, second-line treatment is assumed to quickly cure MDR-TB-infected individuals. (The relevant parameter, `TB_Drug_Clearance_Rate`, is set to 0.1 / day, resulting in a mean time to cure of $1 / (0.1 \text{ / day}) = 10 \text{ days}$.) In the output, the fraction of MDR-TB that is acquired can be seen to drop to nearly 0 after second-line treatment. However, because the MDR-TB diagnostic is only made available to infected individuals failing a treatment course, individuals who were infected with MDR-TB by transmission do not receive this diagnostic and continue to be infected.

```
{
  "Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
      "Actual_IndividualIntervention_Config": {
        "Base_Sensitivity": 1,
```

```
        "Base_Specificity": 1,
        "Cost_To_Consumer": 1,
        "Days_To_Diagnosis": 50,
        "Event_Or_Config": "Event",
        "Defaulters_Event": "TBMDRTestDefault",
        "Negative_Diagnosis_Event": "TBMDRTestNegative",
        "Positive_Diagnosis_Event": "TBMDRTestPositive",
        "Treatment_Fraction": 1.0,
        "class": "MDRDiagnostic"
    },
    "Trigger_Condition": "TBFailedDrugRegimen",
    "class": "NodeLevelHealthTriggeredIV",
    ...
},
...
},
"Start_Day": 1,
...
},
{
    "Event_Coordinator_Config": {
        "Demographic_Coverage": 1,
        "Intervention_Config": {
            "Actual_IndividualIntervention_Config": {
                "Cost_To_Consumer": 1,
                "Dose_Interval": 1,
                "Drug_Type": "SecondLineCombo",
                "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
                "Fraction_Defaulters": 0,
                "Primary_Decay_Time_Constant": 90,
                "Reduced_Transmit": 1,
                "Remaining_Doses": 1,
                "TB_Drug_Clearance_Rate": 0.1,
                "TB_Drug_Inactivation_Rate": 1e-09,
                "TB_Drug_Mortality_Rate": 1e-09,
                "TB_Drug_Relapse_Rate": 1e-09,
                "TB_Drug_Resistance_Rate": 1e-09,
                "class": "AntiTBDrug"
            },
            "Trigger_Condition": "TBMDRTestPositive",
            "class": "NodeLevelHealthTriggeredIV",
            ...
},
...
},
"Start_Day": 1,
...
```

```
},
...
[remainder identical to Transmitted MDR scenario]
```

You can view all of the interventions in the campaign.json file in the Scenarios\TB\05_MDR\D_SecondLineDrugs directory.

Effective Treatment: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\05_MDR\D_SecondLineDrugs directory to run the simulation.

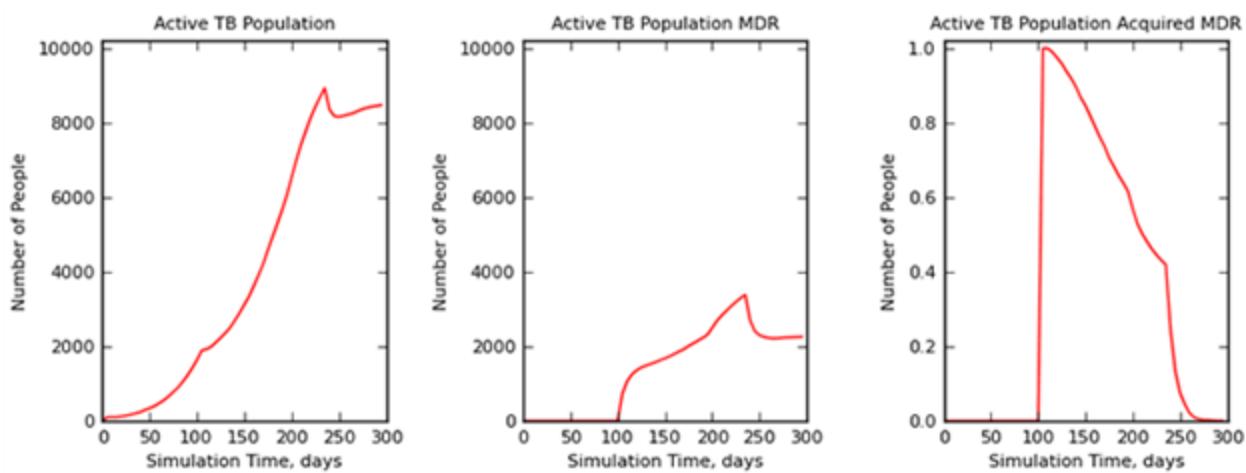
Effective Treatment: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotInsetChart, in the Scenarios\TB\05_MDR\D_SecondLineDrugs directory to generate graphs.

Simulation Output Graphs

The impact of treating MDR-TB using a MDR-TB-specific diagnostic linked to effective second-line drugs is observed. As a reminder, in this simulation, infected individuals who complete treatment but continue to have active TB are immediately given a MDR-TB diagnostic. Individuals who test positive are immediately given an effective second-line treatment. This time, when the same output channels as those from Transmitted MDR scenario are plotted, the impact is immediately apparent. In particular, the fraction of MDR-TB that is acquired plummets as acquired MDR-TB cases are detected right away and treated.



Exploring the Model

Example 1: Vary infectiousness during empiric treatment and second-line treatment.

As suggested in Ineffective Treatment, the effect of various treatments on the infectiousness of MDR-TB cases (for example, the number of viable bacilli expectorated per cough while on treatment) is largely unknown. Explore the effect of different assumptions on the change in infectiousness while on treatment in the model. To change the infectiousness while on treatment, vary the AntiTBDDrug campaign parameter, Reduced_Transmit.

Example 2: MDR Fitness

One config parameter specific to MDR-TB is the fitness of MDR-TB strains, called TB_MDR_Fitness_Multiplier. In the model, this parameter works by setting the infectiousness of MDR-TB. (The AntiTBDDrug intervention parameter, Reduced_Transmit, does something similar, but only during the drug treatment itself.) For all of the scenarios in this section, the value of this parameter has been set to 1, giving MDR-TB an equal infectiousness to drug-sensitive TB. However, in general, drug-resistant strains of any pathogen (including those for TB) are assumed to have a lower fitness and infectiousness than wild-type, drug-sensitive strains, especially in the absence of drug pressure. Explore the effect of setting MDR fitness in the model to values less than 1 to represent the reduced fitness of MDR-TB strains. Compare the total number of active TB cases over time, as well as the number of MDR-TB cases.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Tuberculosis \(TB\) Tutorials](#)

[Parameter Reference](#)

TB 6: Population Burn-in

This tutorial assumes that you have read and understand the first five tutorials as it uses concepts and configuration examples from them.

Population Burn-in implements a more realistic simulation with a larger population where TB is endemic but present at a low absolute prevalence. To accomplish this, the tutorial utilizes two key features:

- A larger population size that allows a small number of infected individuals to be represented. Nevertheless, the population is sampled, so that an individual may represent more than one person in the population. The population age distribution remains constant throughout the scenario by the application of a fixed birth rate and an age-dependent mortality rate.
- Simulation burn-in is a modeling concept borrowed from the electronics industry where the first items produced by a manufacturing process are discarded before the process is applied. For software modeling, the points of a simulation are discarded before the simulation is usefully applied.

Two scenarios within this tutorial demonstrate using burn-in with a large population and how to use a simulation after burn-in:

- [Steady State](#): At the start of the simulation, 50% of the population is initialized with TB, resulting in an initial peak of active disease. The simulation is run until steady-state dynamics are observed, showing that disease endemicity has been reached. A steady state in the disease is observed after approximately a 100-year burn-in period where latent disease is more highly prevalent in older individuals and incidence results from a combination of new transmissions and reactivation from latent disease. The simulation continues past the burn-in period with little change in the epidemic aside from stochastic noise.
- [Private to Public Health Care](#): An intervention is applied after the burn-in period which moves 50% of the population to higher quality care. The simulation is run for an additional 10 years to observe the impact of improving the quality of care.

Demographics Inputs

To view the complete demographics file, see `TB_06_PopulationBurnIn_demographic` in the `Scenarios\InputFiles` directory.

Nodes

NodeAttributes

This simulation uses a population of 100 000 individuals with a fixed birth rate, as indicated in the NodeAttributes section of the demographics file. Birthrate is set to 7.25. In the configuration file, Birth_Rate_Dependence has been set to FIXED_BIRTH_RATE which indicates that the value represents a constant, daily rate. On average, 7.25 individuals are added to the simulation per day.

```
"Nodes": [
  {
    . . .

    "NodeAttributes": {
      "BirthRate": 7.25,
      "InitialPopulation": 100000,
    }
  }
]
```

IndividualAttributes

Initial Age Distribution

Similarly to [TB 2: Age Dependent Immunity](#), the initial age distribution is explicitly specified.

```
"Nodes": [
  {
    "IndividualAttributes": {
      "AgeDistribution": {
        "DistributionValues": [
          0, 0.11861136002893, 0.243120423759721, 0.342944119572159,
          0.438070229201696, 0.5214270550481, 0.594815231666682,
          0.666855737751466, 0.731896027864999, 0.790430805636026,
          0.843312403517271, 0.886324004910257, 0.925078059704281,
          0.955212492980567, 0.977864680991485, 0.990698956452811,
          0.997190887837509, 1
        ],
        "ResultScaleFactor": 365,
        "ResultValues": [
          0, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85
        ]
      },
      . . .
    }
]
```

```

    . . .
}
]

```

Mortality Distribution

The mortality distribution is specified explicitly by age and gender. Males and females are assigned the same mortality rate.

```

"Nodes": [
{
  "IndividualAttributes": {
    . . .

    "MortalityDistribution": {
      "AxisNames": [
        "gender",
        "age"
      ],
      "AxisScaleFactors": [
        1,
        1
      ],
      "AxisUnits": [
        "male=0,female=1",
        "days"
      ],
      "NumDistributionAxes": 2,
      "NumPopulationGroups": [
        2,
        39
      ],
      "PopulationGroups": [
        [ 0, 1 ],
        [ 0, 364, 365, 1824, 1825.0, 3649, 3650.0, 5474,
          5475.0, 7299, 7300.0, 9124, 9125.0, 10949, 10950.0, 12774,
          12775.0, 14599, 14600.0, 16424, 16425.0, 18249, 18250.0, 20074,
          20075.0, 21899, 21900.0, 23724, 23725.0, 25549, 25550.0, 27374,
          27375.0, 29199, 29200, 31024, 31025, 36499, 37500 ]
      ],
      "ResultScaleFactor": 0.00273972602,
      "ResultUnits": "annual deaths per 1000 individuals",
      "ResultValues": [
        [ 0.13117, 0.13117, 0.00252, 0.00252, 0.00084, 0.0084, 0.0055,
          0.0055, 0.0295, 0.0295, 0.0295, 0.0295, 0.01, 0.01, 0.01, 0.01,
          0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.01971, 0.01971,
          0.0198, 0.0198, 0.03424, 0.03424, 0.15943, 0.15943, 0.17944,

```

```

        0.17944, 0.17944, 0.17944, 0.17944, 5000, 5000, 5000 ],
[ 0.13117, 0.13117, 0.00252, 0.00252, 0.00084, 0.0084, 0.0055,
  0.0055, 0.0295, 0.0295, 0.0295, 0.0295, 0.01, 0.01, 0.01,
  0.01, 0.03, 0.03, 0.03, 0.03, 0.03, 0.03, 0.01971, 0.01971,
  0.0198, 0.0198, 0.03424, 0.03424, 0.15943, 0.15943, 0.17944,
  0.17944, 0.17944, 0.17944, 5000, 5000, 5000 ]
],
},
. . .
}
. . .
]

```

Prevalence Distribution

Fifty percent of the population is initialized with latent TB using the prevalence distribution flag. Setting the PrevalenceDistributionFlag to 0 tells the simulation software to use a fixed value, as opposed to setting the value to 1 which would result in a draw from a distribution. The fixed number is given by PrevalenceDistribution1 which is set to 0.5.

```

"Nodes": [
{
  "IndividualAttributes": {
    . . .

    "PrevalenceDistribution1": 0.5,
    "PrevalenceDistributionFlag": 0,
  }
},
. . .
]

```

Defaults

Individual Properties

As in [TB 3: Health Care Systems](#), three health care groups are created: None, Private and Public. However, in this tutorial all individuals start out in the private sector which has low-quality care.

```

"Defaults": {
  "IndividualProperties": [
    {
      "Property": "QualityOfCare",

```

```

        "Values": [
            "None",
            "Private",
            "Public"
        ],
        "Initial_Distribution": [1e-08, 0.9999998, 1e-08 ],
    },
],
}

```

Steady State

Key Simulation Parameters

Demographics Parameters

The following parameters enable vital dynamics for birth, non-disease related deaths, and mortality.

Parameter	Value	Description
Enable_Vital_Dynamics	1	Enables the vital process (birth, death)
Enable_Birth	1	Enables birth (vital process).
Birth_Rate_Dependence	“FIXED_BIRTH_RATE”	Determines how the birth rate specified in the demographics file is used. The value Birth_Rate_Dependence indicates that the rate in the demographics file is an absolute rate at which new individuals are born.
Death_Rate_Dependence	NONDISEASE_MORTALITY_BY_AGE_AND_GENDER	Enables death (vital process).

TB Parameters

The TB parameters are set to the following values. These values are typically used in TB modeling.

TB Model Parameters

```
"TB_Active_Cure_Rate": 0.000245,  
"TB_Active_Mortality_Rate": 9.5e-05,  
"TB_Active_Period_Distribution": "EXPONENTIAL_DURATION",  
"TB_Extrapulmonary_Mortality_Multiplier": 0.15,  
"TB_Fast_Progressor_Fraction_Adult": 0.15,  
"TB_Fast_Progressor_Fraction_Child": 0.05,  
"TB_Fast_Progressor_Rate": 0.006,  
"TB_Immune_Loss_Fraction": 0,  
"TB_Inactivation_Rate": 0,  
"TB_Latent_Cure_Rate": 0,  
"TB_MDR_Fitness_Multiplier": 1,  
"TB_Presymptomatic_Cure_Rate": 0,  
"TB_Presymptomatic_Rate": 0.0012,  
"TB_Relapsed_to_Active_Rate": 0.004,  
"TB_Slow_Progressor_Rate": 8.2e-6,  
"TB_Smear_Negative_Mortality_Multiplier": 0.15,
```

TB Disease Parameters

```
"TB_Extrapulmonary_Fraction_Adult": 0.1,  
"TB_Extrapulmonary_Fraction_Child": 0.4,  
"TB_Smear_Negative_Infectivity_Multiplier": 0.15,  
"TB_Smear_Positive_Fraction_Adult": 0.65,  
"TB_Smear_Positive_Fraction_Child": 0.25,
```

TB Drug Parameters

The parameterization for the CDCDrug is for illustration purposes only.

```
"TB_Drug_Parms": {  
    "CDCDrug": {  
        "TB_Drug_Clearance_Rate": 0.1,  
        "TB_Drug_Inactivation_Rate": 1e-09,  
        "TB_Drug_Mortality_Rate": 1e-09,  
        "TB_Drug_Primary_Decay_Time_Constant": 180.0,  
        "TB_Drug_Relapse_Rate": 1e-09,  
        "TB_Drug_Resistance_Rate": 1e-09  
    },  
    . . .  
    "HospitalDrug": {  
        "TB_Drug_Clearance_Rate": 0.0111,  
        "TB_Drug_Inactivation_Rate": 1e-09,  
        "TB_Drug_Mortality_Rate": 0.00142,  
        "TB_Drug_Primary_Decay_Time_Constant": 30.0,  
        "TB_Drug_Relapse_Rate": 0.00243,  
        "TB_Drug_Resistance_Rate": 1e-09
```

```

    },
    ...
}
```

The complete config.json file is in the Scenarios\TB\06_PopulationBurnIn\A_SteadyState directory.

Steady State: Interventions

This simulation uses a cascade of care similar to the those demonstrated in [TB 4: Cascade of Care](#).

Upon TBActivation, individuals seek care with a Poisson rate of 0.005 per day, that is, with a mean waiting time of $1 / (0.005 \text{ per day}) = 200 \text{ days}$, at which time they can receive a TB test.

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",
        "Tendency": 0.005,
        "Event_Or_Config": "Event",
        "class": "SimpleHealthSeekingBehavior"
    },
    "Demographic_Coverage": 1,
    "Property_Restrictions_Within_Node": [],
    "Trigger_Condition": "TBActivation",
    "class": "NodeLevelHealthTriggeredIV"
}
```

When individuals receive a test with any result, 50% of the time they default and do not receive treatment.

```

"Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Base_Sensitivity": 1,
        "Base_Specificity": 1,
        "Cost_To_Consumer": 10,
        "Days_To_Diagnosis": 50,
        "Event_Or_Config": "Event",
        "Defaulters_Event": "TBTestDefault",
        "Negative_Diagnosis_Event": "TBTestNegative",
        "Positive_Diagnosis_Event": "TBTestPositive",
        "Treatment_Fraction": 0.5,
        "class": "DiagnosticTreatNeg"
    },
    "Demographic_Coverage": 1,
    "Duration": -1,
    "Property_Restrictions_Within_Node": []
}
```

```

    "Trigger_Condition": "ProviderOrdersTBTest",
    "class": "NodeLevelHealthTriggeredIV"
}

```

Individuals who default re-seek care with a Poisson rate of 0.005 per day, that is, with a mean waiting time of $1 / (0.005 \text{ per day}) = 200 \text{ days}$.

```

"Event_Coordinator_Config": {
    "Demographic_Coverage": 1,
    "Intervention_Config": {
        "Actual_IndividualIntervention_Config": {
            "Event_Or_Config": "Event",
            "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",
            "Single_Use": 1,
            "Tendency": 0.005,
            "class": "HealthSeekingBehaviorUpdateable"
        },
        "Demographic_Coverage": 1,
        "Property_Restrictions_Within_Node": [],
        "Trigger_Condition": "TBTestDefault",
        "class": "NodeLevelHealthTriggeredIV"
    }
}

```

Individuals who are tested to be smear-positive receive treatment based on their health care sector. The efficacy information for specific treatments is configured with the TB_Drug_Types_For_This_Sim structure in the config.json file.

```

[Intervention_Config": {
    "Actual_IndividualIntervention_Config": {
        "Cost_To_Consumer": 1,
        "Drug_Type_by_Property": [
            {"QualityOfCare:Private": "HospitalDrug"},
            {"QualityOfCare:Public": "CDCDrug"}],
        "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
        "Enable_State_Specific_Treatment": 1,
        "Primary_Decay_Time_Constant": 50,
        "Remaining_Doses": 1,
        "class": "AntiTBPropDepDrug"
    },
    "Demographic_Coverage": 1,
    "Duration": -1,
    "Trigger_Condition": "TBTestPositive",
}

```

```

    "class": "NodeLevelHealthTriggeredIV"
}

```

Individuals who are tested to be smear negative receive empirical treatment which is ineffective.

```

[Intervention_Config": {
  "Actual_IndividualIntervention_Config": {
    "Cost_To_Consumer": 1,
    "Dose_Interval": 1,
    "Drug_Type": "EmpiricTreatment",
    "Durability_Profile": "FIXED_DURATION_CONSTANT_EFFECT",
    "Fraction_Defaulters": 0,
    "Primary_Decay_Time_Constant": 50,
    "Reduced_Transmit": 1,
    "Remaining_Doses": 1,
    "TB_Drug_Clearance_Rate": 1e-09,
    "TB_Drug_Inactivation_Rate": 1e-09,
    "TB_Drug_Mortality_Rate": 1e-09,
    "TB_Drug_Relapse_Rate": 1e-09,
    "TB_Drug_Resistance_Rate": 1e-09,
    "class": "AntiTBDDrug"
  },
  "Demographic_Coverage": 1,
  "Duration": -1,
  "Trigger_Condition": "TBTestNegative",
  "class": "NodeLevelHealthTriggeredIV"
}

```

Individuals who re-activate after relapsing or who fail treatment re-seek care but at a slower rate with a mean waiting time of $1 / (0.0005 \text{ per day}) = 2000 \text{ days}$.

Seek Treatment After Failed Treatment

```

[Intervention_Config": {
  "Actual_IndividualIntervention_Config": {
    "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",
    "Event_Or_Config": "Event",
    "Tendency": 0.0005,
    "class": "HealthSeekingBehaviorUpdateable"
  },
  "Demographic_Coverage": 1,
  "Property_Restrictions_Within_Node": [],
  "Trigger_Condition": "TBFailedDrugRegimen",
  "class": "NodeLevelHealthTriggeredIV"
}

```

Seek Treatment after Relapse

```
"Intervention_Config": {  
    "Actual_IndividualIntervention_Config": {  
        "Actual_IndividualIntervention_Event": "ProviderOrdersTBTest",  
        "Event_Or_Config": "Event",  
        "Tendency": 0.0005,  
        "class": "HealthSeekingBehaviorUpdateable"  
    },  
    "Demographic_Coverage": 1,  
    "Property_Restrictions_Within_Node": [],  
    "Trigger_Condition": "TBActivationPostRelapse",  
    "class": "NodeLevelHealthTriggeredIV"  
}
```

You can view the campaign.json file is in the Scenarios\TB\06_PopulationBurnIn\A_SteadyState directory.

Steady State: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\06_PopulationBurnIn\A_SteadyState directory to run the simulation.

Steady State: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\06_PopulationBurnIn\A_SteadyState directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

After the burn-in period there is little change in the epidemic aside from stochastic noise.

NOTE: Because the EMOD model is stochastic, your graphs may appear slightly different from those given below.

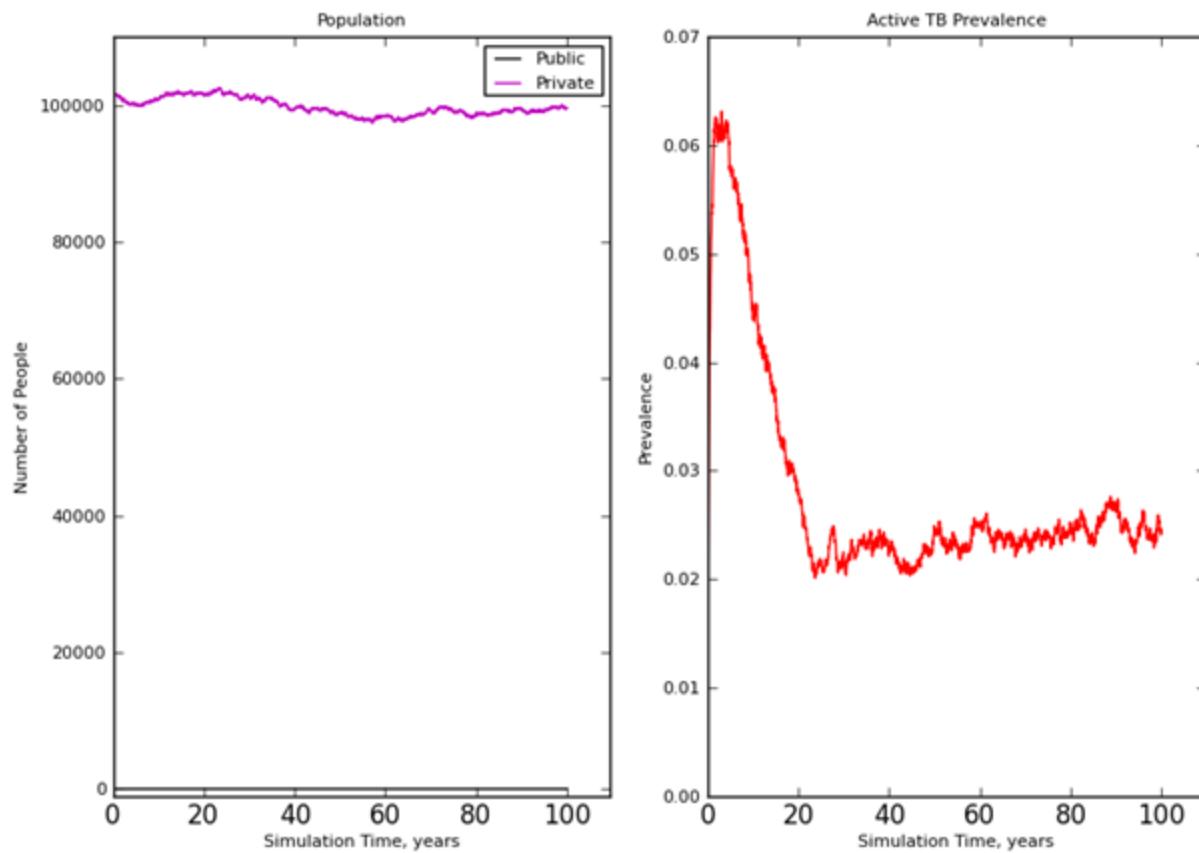


Figure 1: Proportion of individuals in each sector of care (left) and Active TB prevalence in the population (right)

Private to Public Health Care System

This simulation uses the same parameter values in the configuration and campaign files as Steady State. An intervention is added that moves individuals from the lower quality private health care to higher quality public health care.

Private to Public Health Care: Key Simulation Parameters

The simulation uses the same the simulation parameter values as Burn-in. However, you can find a copy of the configuration file in the Scenarios\TB\06_PopulationBurnIn\B_PrivateToPublic directory.

Private to Public Health Care: Interventions

Individuals who have access to inferior private care system are shifted over to the public health care after the 80-year burn-in period.

```
{  
    "Event_Coordinator_Config": {  
        "Demographic_Coverage": 1,  
        "Intervention_Config": {  
            "Distribution_Rate": 1,  
            "Target_Property_Key": "QualityOfCare",  
            "Target_Property_Value": "Public",  
            "class": "PropertyValueChanger"  
        },  
        "Number_Distributions": -1,  
        "Number_Repetitions": -1,  
        "Timesteps_Between_Repetitions": 73,  
        "Property_Restrictions": [  
            "QualityOfCare:Private"  
        ],  
        "Target_Demographic": "Everyone",  
        "class": "StandardInterventionDistributionEventCoordinator"  
    },  
    "Event_Name": " shift from private to public",  
    "Nodeset_Config": {  
        "class": "NodeSetAll"  
    },  
    "Start_Day": 29200,  
    "class": "CampaignEvent"  
}
```

You can view the campaign.json file is in the \Scenarios\TB\06_PopulationBurnIn\B_PrivateToPublic directory.

Private to Public Health Care: Running the Simulation

At your discretion, you can use the sample batch file, runEMOD, in the Scenarios\TB\06_PopulationBurnIn\B_PrivateToPublic directory to run the simulation.

Private to Public Health Care: Expected Simulation Output

Generating Simulation Graphs

At your discretion, you can use the sample batch file, plotResults, in the Scenarios\TB\06_PopulationBurnIn\B_PrivateToPublic directory to generate graphs from a simulation's InsetChart output file.

Simulation Output Graphs

The impact of shifting individuals from private to public care can be seen in many of the output channels comparing the baseline outcome to the scenario. In one of these channels, Active TB Prevalence, the expected decrease is seen following the burn-in period.

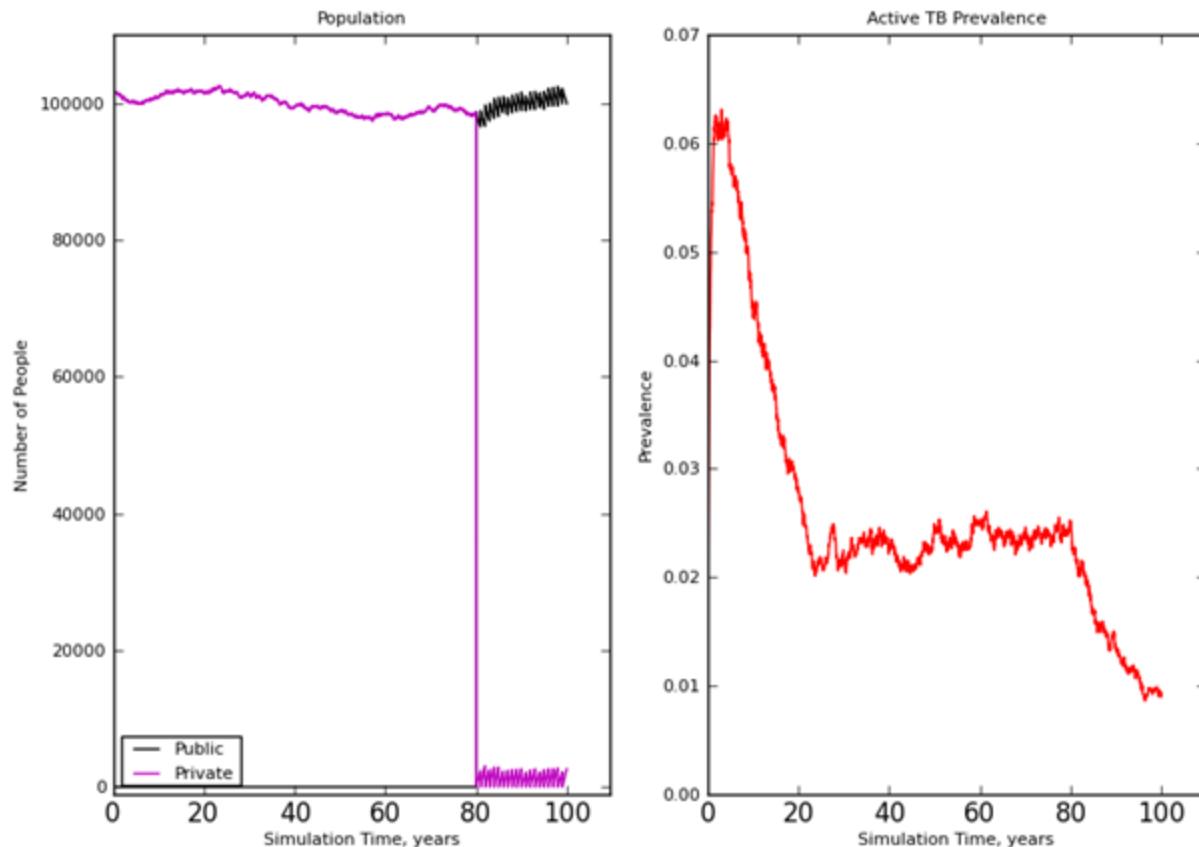


Figure 2: Proportion of individuals in each sector of care (left) and Active TB prevalence in the overall population (right)

There is a post burn-in shift of individuals from lower-quality health care to high quality health care.

Related Topics:

[Tuberculosis \(TB\) Overview](#)

[Tuberculosis \(TB\) Tutorials](#)

[Parameter Reference](#)