MODELING INTERVENTION STRATEGIES FOR UNITED STATES TB CONTROL

1. Introduction

Epidemiological models allow public health professionals to predict and analyze disease dynamics and intervention effectiveness. The most common examples of such models are compartmental differential equation models, in which the population is split between several possible health states, with flow between each state given according to deterministic differential equations. In 2012, Hill, Becerra, and Castro implemented a compartmental differential equaiton model of tuberculosis (TB) in the United States (US). Their model utilized five health states and two subpopulations, US-born (USB) and foreign-born (FB) for a total of 10 compartments. They used this model to evaluate several possible intervention strategies, and ultimately conclude that though increasing LTBI treatment was a good intervention strategy, the US was unlikely to meet their stated goal of elimination of TB in the US by 2100. In this work, the Hill model was extended in several key ways. First, additional tracking capabilities were added to the Hill model, such that it can now report further granularity in the disease dynamics. Further, economic components were added to the model in order to project the US health care system (HCS) costs due to TB given our current policy as well as for various interventions. Finally, a population level, agent based implementation of the Hill Model was created, in order to validate the Hill Model against the natural stochasticity present in real world disease spread.

2. Background

2.1. **The Hill Model.** A flowchart representation of the Hill Model is shown in Figure 1. Each compartment represents a different possible health state with respect to TB for every US-born or foreign-born individual, and arrows between different compartments represent possible transitions between states. Individuals also leave the model from all compartments due to natural death, which is left out of the figure for clarity.

The majority of USB and FB individuals fall into the Susceptible (S) category, which includes everyone who is uninfected and has not been exposed to TB. After exposure to an individual with TB, a person in the Susceptible compartment can develop Latent TB Infection (LTBI) and changes health states to either the Acute LTBI (F) or Chronic LTBI (L) compartment. Latently infected individuals are not infectious, but have some risk of developing active TB infection over time. However, the rates of disease progression are not equal, and individuals in the Acute LTBI compartment have a higher risk of developing active TB than those in the Chronic LTBI compartment. Individuals in the Chronic LTBI compartment may also be exogenously re-infected and transition to the Acute LTBI compartment.
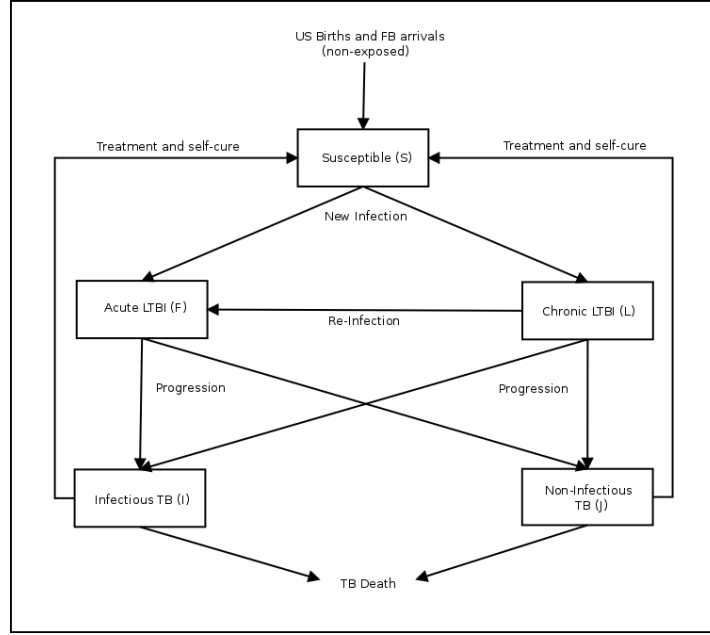
Latently infected individuals may progress to one of two active TB states: Infectious TB (I) or Non-Infectious TB (J). Individuals in both compartments have an increased risk of death from active TB infection, but only individuals in the Infectious TB compartment are contagious. In addition, individuals in all of the infected compartments (F, L, I, J) may be treated or self-cure themselves of their respective TB health condition. However, in the model, treatment or self-cure from TB does not grant immunity, and all healthy individuals are grouped in the Susceptible compartment and may be re-infected at a later time.

3. Methods

3.1. **Basic Implementation.** Both the basic Hill Model and this extended Hill Model were implemented in `R` as a system of differential equations, which were solved via the `lsoda` routine. The systems of differential equations used in the Basic Hill Model and the extended Hill Model to capture basic disease dynamics are shown below in Figure 2 and Figure 3 respectively. In the extended Hill model, more differential equations were implemented to add additional tracking and economic modeling. These equations are detailed in the appendix.

The vector variables S_0, F_0, L_0, I_0, J_0 contain the number of US-born individuals in the S, F, L, I, J compartments respectively, whereas S_1, F_1, L_1, I_1, J_1 contain foreign-born individuals. N_0 and N_1 are the total populations of US-born and foreign-born individuals. The constants ρ and α are birth rates, while μ_i, and μ_d are death rates. A complete list and descriptions of all constants used in the model can be found in the appendix.

3.2. **Additional Tracking Capabilities.** In order to refine the tracking capabilities of the Hill Model, the original differential equations used to describe TB spread were separated into their component parts and each section was tracked separately.

$$
\begin{aligned}
\dot{S}_0 &= \rho(N_0 + N_1) + \sigma_0^F F_0 + \sigma^L L_0 + \varphi_0(I_0 + J_0) - \lambda_0 S_0 - \mu_0 S_0 \\
\dot{F}_0 &= p\lambda_0 S_0 + xp\lambda_0 L_0 - (\mu_0 + \nu^F + \sigma_0^F)F_0 \\
\dot{L}_0 &= (1-p)\lambda_0 S_0 - xp\lambda_0 L_0 - (\mu_0 + \nu_0^L + \sigma^L)L_0 \\
\dot{I}_0 &= q(\nu^F F_0 + \nu_0^L L_0) - (\mu_0 + \mu^d + \varphi_0)I_0 \\
\dot{J}_0 &= (1-q)(\nu^F F_0 + \nu_0^L L_0) - (\mu_0 + \mu^d + \varphi_0)J_0 \\
\dot{S}_1 &= (1-f)\alpha(N_0 + N_1) + \sigma_1^F F_1 + \sigma^L L_1 + \varphi_1(I_1 + J_1) - \lambda_1 S_1 - \mu_1 S_1 \\
\dot{F}_1 &= gpf\alpha(N_0 + N_1) + p\lambda_1 S_1 + xp\lambda_1 L_1 - (\mu_1 + \nu^F + \sigma_1^F)F_1 \\
\dot{L}_1 &= (1-gp)f\alpha(N_0 + N_1) + (1-p)\lambda_1 S_1 - xp\lambda_1 L_1 - (\mu_1 + \nu_1^L + \sigma^L)L_1 \\
\dot{I}_1 &= q(\nu^F F_1 + \nu_1^L L_1) - (\mu_1 + \mu^d + \varphi_1)I_1 \\
\dot{J}_1 &= (1-q)(\nu^F F_1 + \nu_1^L L_1) - (\mu_1 + \mu^d + \varphi_1)J_1
\end{aligned}
$$

These components were made into compartments, tracked by differential equations detailed in the appendix. These equations allowed the model to track the total number of TB cases, TB deaths, and natural deaths. Further, the model tracks, the sourced cost on the US HCS. Progressions into active TB due to activations of LTBI or exogenous infection were tracked, allowing for sourced incidence data to be generated. The entering cases of LTBI (acute or chronic) were also tracked. In the case of intervention testing, the number of cured cases of entering LTBI and the number of untreated entering LTBI were both tracked. Cured cases of LTBI entering, TB deaths, total TB cases, and total cost were also tracked discounted at 3% annually. This discounting was converted to a continuous differential equation for use within the model. In general, incidence data is calculated in the same way in the extended hill as it was in the basic Hill.

In addition, estimations of the basic reproductive number of FB or USB active, infectious TB cases were made from a theoretical and an experimental perspective. Experimental data were calculated by reducing the initial population of FB or USB active, infectious TB cases by one and allowing the model to progress otherwise as normal. The decreased number of total TB cases seen details how many infections can be thought to be due to one infected individual in the given population.

From an experimental perspective, the spread of TB was thought to be a geometric series. If one infectious individual infects x people annually, over the course of N years the total number of infections caused by this individual can be approximated by the geometric series of N terms with rate x and initial term 1. In this case, $N = 100$, and the ratios for FB infectious individuals and USB infectious individuals were obtained from RATIO CITATION COLIN.

3.3. **Economic Modeling.** When tracking the economic implications of current US TB load and various intervention strategies, active TB costs were given by $14,000. This cost is the weighted mean of the costs of cases requiring hospitalization (happening 49% of the time) and cases not requiring hospitalization (51%). These data were found in DYLAN COST STUDY CITATION. LTBI treatment costs were given by $468.00. These data were based on the cost of a successfull treatment, given by DYLAN COST STUDY CITATION, as well as adherence and efficacy data found in ADHERENCE CITATION.

From these estimated cost per treatment, total costs were obtained by assuming that every patient with active TB in the US is treated at full price, though the treatment may fail. As individuals with active TB are charged upon entry to the active TB compartment, the model can also accurately estimate sourced US HCS cost data. Cost data were separately tracked due to incoming active TB costs stemming from activation of LTBI vs exogenous reinfection. These data were modelled as additional compartments and also solved by `lsoda`. For LTBI treatment cost, treatment was charged upon leaving the LTBI compartment due to the cumulative self-cure and treatment rate given in the Hill Model. The fraction of these indviduals who leave this compartment due to self cure was assumed to be zero. Given the uncertainty in measurments of LTBI treatment cost, extensive sensitivity analysis was performed on this parameter relative to final cost outcomes. In addition to US HCS cost, the system was implemented so as to also track projected intervention implementation cost, given user-inputted parameters relating to various possible intervention cost strategies. The extended Hill Model was used to track the effect of many interventions tested by the Hill Model. In particular, the intervention strategy of curing entering cases of LTBI proved very promising and elimination year, final cost, and cost per case averted were tracked for various levels of entering LTBI cure rate. The interventions were implemented so as to take effect during the year 2013 and run to 2100. The numerical DE solver `lsoda` used was run with a time step of 0.8. Sensitivity analysis was performed on this parameter and reducing the time step was shown to have minimal effect on final size or cost values.

3.4. **Agent Based.** The population level agent based model was implemented in several ways. Early implementations were built in `Netlogo` and `Java`, but final implementations were constructed in `C++`. An implementation was made that tracked the hill model exactly, up to still including the Acute Latent compartment in the model. Probabilites of agent progression between various health states were computed given rates in the hill model and a variety of approximations. The model maintained scaled individual records for every individual with LTBI, with susceptible individuals not modelled as agents. Instead, a binomial distribution was used to probabilistically pick the number of new infections each time step. Similarlly, immigration was also handeled outside of the agent-based modelling. The final size standard deviation and distribution data was collected via 2160 (MINUS SOME) runs with each agent in the model truly representing one infected individual and a time step of 0.01. These data were analyzed in R. This model was also made to track deaths, total TB cases, and infection sources. This data were consistent with the deterministic model, and not reproduced in this write-up.

Further implementations of the `C++` model were made that deviated from the basic Hill Model. Specifically, the acute latent compartment in the basic Hill Model is a vestigal necessity of compartmental modeling and not reflective of the biology of tuberculosis, and an agent based model was implemented that more closely respects the biology of tuberculosis. Results from this model or the strict Hill model did not differ significantly.

4. Results

4.1. **Basic Population Breakdown.** The additional tracking capabilities offered several key insights into US TB dynamics. Figure 1 shows the yearly incidence of US TB, broken down into infection source. It can be seen that the majority

of the US TB load is driven by activations of FB LTBI, followed by USB LTBI activations. This data further agrees with the conclusions drawn by Hill, Becerra, and Castro about the necessity of LTBI treatment in any valuable intervention strategy. Further, figure 2 shows a similarly sourced plot, but analyzing the final
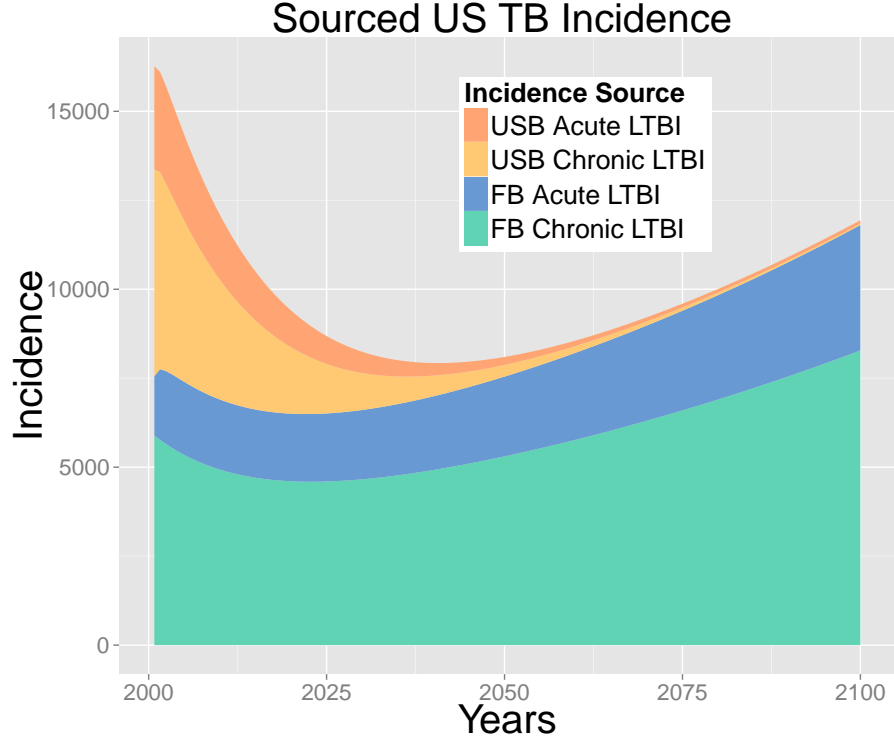

FIGURE 1. Sourced yearly incidence data generated by the extended Hill Model.

US HCS costs due to TB. One can see that in this plot, roughly half of the US TB HCS costs are due to activations of LTBI. In this data, it is appropriate to think of the costs due to acute LTBI are due to exogenous re-inection, whereas active TB costs due to chronic LTBI are activations of LTBI into active TB. Note that both of these plots underestimate the impact LTBI activations play in the spread of TB, as every LTBI activation to infectious TB contributes not only to incidence and costs directly, but also indirectly by causing additional future cases, which is not captured in these graphs. Further, there is also US HCS costs due to treating LTBI, which is not illustrated in these graphs.

4.1.1. *Basic Reproduction Number.* The basic reproduction number of FB or USB cases of infectious TB was also estimated by this system. From a theoretical perspective, we can think of the total number of secondary infections over 100 years due to a FB or USB infectious TB case as describing a geometric series in a large population. Presuming there are no overlaps in infectious contacts, if a single case
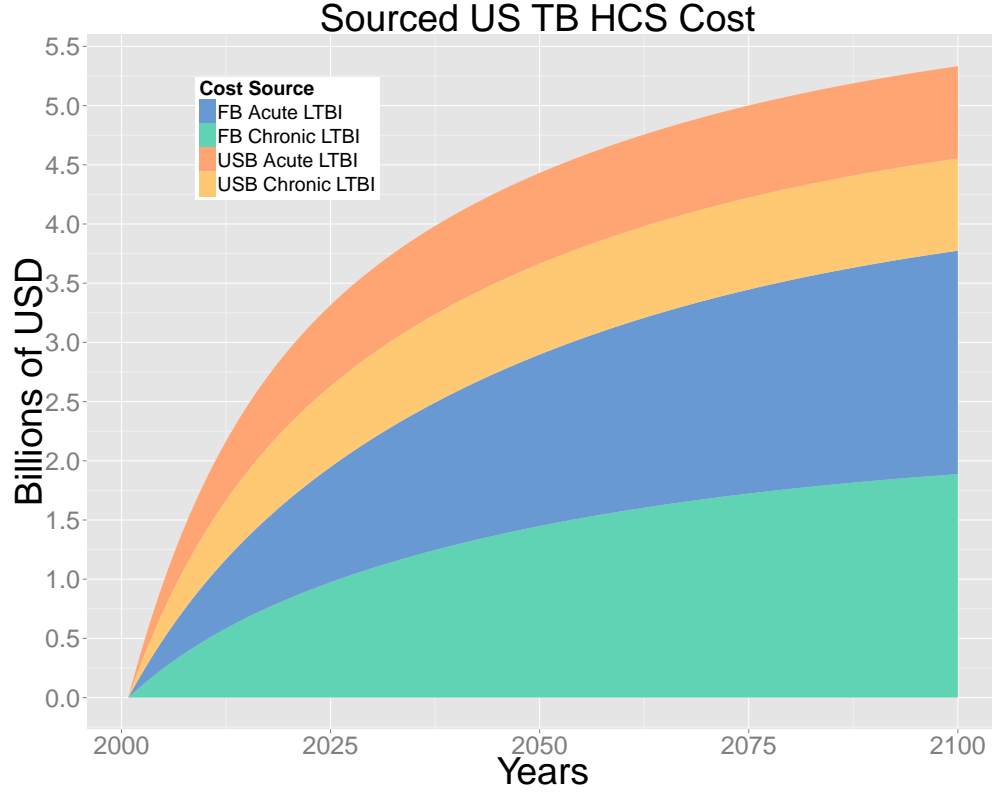
FIGURE 2. Sourced US HCS economic TB load. Note that this data only illustrates the load due to treating active TB, but illustrates where the infections driving this cost come from.

of infectious TB in either population infects p_f, p_u new cases in one year, respectively, then we can say that over the course of 100 years, the total number of cases infected will follow a geometric series. This analysis predicts that over 100 years, one USB infection will lead to 1.03 subsequent infections, whereas one FB infection will lead to .64 subsequent infections. The full calculations are included in the appendix. Experimentally, these data were also analyzed, with results of 1.04 and .8, respectively. WHAT CAUSES THIS DIFFERENCE? WE NEED TO ANSWER THAT.

4.2. **Intervention Analysis.** The primary interventions analyzed by the extended Hill were those that analyzed curing various percentages of entering LTBI cases. Four indicative percentages chosen were 20%, 35%, 50%, and 65%. Note that the Hill model does not distinguish documented immigration from undocumented immigration, and as such estimates of entering LTBI cure rates higher than 65% become much more difficult to achieve. It was seen that in this model as well as in the basic Hill, no analyzed intervention predicted elimination by 2100. In order to obtain elimination by 2100, at least 95% of entering LTBI cases had to be cured, which is practically impossible. However, it was seen that curing entering cases

	red20	red35	red50	red65
2000	ND	ND	ND	ND
2025	67722.96	67527.15	67332.53	67138.90
2050	28759.00	28581.09	28404.13	28227.50
2075	20876.80	20709.13	20541.77	20374.49
2100	17967.39	17804.94	17642.64	17480.33

TABLE 1. Cost Per Case Averted by Reducing Incoming LTBI by 20%, 35%, 50%, and 65% (in dollar per case)

of LTBI resulted in a net US HCS cost per case averted of $67,722.96 at 2025, $28,759.00 at 2050, and $17,967.39 at 2100 (assuming 20% reduction with one cure costing $XXXX; see Table 1 for other percentages). Given the variable nature of LTBI treatment cost, the model code is extendible such that a user can adjust these costs themselves to explore more specific methods of curing entering LTBI. Further, it was also found that the relationship between total incidence at 2100 and percentage of incoming LTBI cases cured was linear, and from this estimates were made of the yearly average US HCS savings garnered by curing one case of entering LTBI over the time scale 2000 to 2025, 2000 to 2050, and 2000 to 2100. This value peaked at $1.026 million at 2100 (20% reduction). This illustrates that it would be cost saving to cure cases of LTBI at the cost of $1.026 million "2000" dollars over the time period 2000-2100. These intervention strategies also resulted in 23,870; 41,952; and 60,189 fewer cases of TB seen in the US, and 2,056; 3,614; and 5,185 fewer TB deaths, for 20%, 35%, and 50% reduction, respectively.

Several other intervention strategies analyzed by the Hill Model were refined with the Extended Hill, and economic properties about each of them were tracked. The results for these interventions, which are less effective than curing entering LTBI cases across the board, are given in the appendix.

4.3. **Agent Based Evaluation.** The Agent Based Model allowed the statistical properties of the system to be analyzed and verified. In particular, they illustrated that the deterministic Hill model provides a robust and consistent statistical measure of TB epidemic behavior in the US conditions. We found that the distribution of incidence and final population sizes were normal, with mean accurate to the deterministic model and standard deviations given in table X, in the appendix.

4.4. **Sensitivity Analysis.**

5. Discussion

These results confirm the hypothesis that curing incoming LTBI rates is a necessary step towards elimination and indicate that it is a cost effective option.

5.1. **Future Work.** This work could be extended by examining different classes of interventions or more accurately estimating intervention cost with the deterministic extended Hill. Further work could also be done with the agent-based Hill Model, by using it to examine the effect contact structure plays on US TB incidence levels or to examine the effects drug-resistant TB will have on US TB dynamics.

6. Appendix

6.1. **Hill Constants.** Below, we detail some of the relevant constants in the Basic Hill Model. A full listing of constants used in the original Hill Model can be found in CITATION! ¡++¿

```
sigmaLBase  <- 0.057
fBase       <- 0.187
transBase   <- 1
incLTBIBase <- 1


#Treatment Effectiveness Data:
probHosp      <- .49 #Probability of hospitalization for active TB treatment
efficacyLTBI <- .9  #LTBI treatement efficacy
adherenceLTBI <- .64 #LTBI treatment adherence
probLTBItreatsuccess <- efficacyLTBI*adherenceLTBI

#Cost Parameter Values:
costtb   <- 2985   #TB treatment cost w/o hopsitalization <- Dylan supp. p.11-12
costhosp <- 25495  #TB treatment cost w/ hospitalization  <- Dylan supp. p.10
costLTBI <- 403.45 #LTBI treatment cost
Ct       <- costtb*(1-probHosp) + costhosp*probHosp #Cost of active TB treatment
Cl       <- costLTBI/probLTBItreatsuccess          #Cost of LTBI treatment

parms <- c(
mu0  = 1/78,     #Natural mortality rate USB per year
mu1  = 1/53,     #Natural mortality rate FB per year
ro   = 0.018,    #USB birth rate per year
alpha = 0.005,   #FB arrival rate per year
p    = 0.103,    #Fraction of new infections which are acute (fast
progressors)
vF   = 1.5,      #Progression rate of acute infection per year
l0   = 0.015,    #Prevalence of LTBI in the USB population in 2000
l1   = 0.211,    #Prevalence of LTBI in the FB population in 2000:
r0   = 0.667,    #Fraction of cases due to reactivation in the USB population
r1   = 0.780,    #Fraction of cases due to reactivation in the FB population
vL0  = 0.0014,   #Progression rate for reactivation (chronic LTBI) in the USB
population per year
vL1  = 0.0010,   #Progression rate for reactivation (chronic LTBI) in the FB
population per year
q    = 0.708,    #Fraction of infections progressing to infectious disease
mud  = 0.115,    #Mortality rate due to TB per year
x    = 0.111,    #Fraction of re-infected chronic LTBI moving to acute
infection
ARI0 = 0.030/100, #Annual risk of infection for USB in 2000
beta = 10.39,    #Effective contact rate per year
e0   = 0.965,    #Fraction of preferred contacts with own population for USB
e1   = 0.985,    #Fraction of preferred contacts with own population for FB
g    = 0.0047,   #Fraction of FB arrivals with LTBI who are fast progressors
phi0 = 1.114,    #Cumulative fraction self-cure and treatment of active
disease for both populations pre year RATES (USB)
phi1 = 1.167,    #Cumulative fraction self-cure and treatment of active
disease for both populations pre year RATES (FB)
sigmaF0 = 1.296, #Cumulative fraction of treatment for acute infection for
both populations per year RATES (USB)
sigmaF1 = 1.301, #Cumulative fraction of treatment for acute infection for
both populations per year RATES (FB)
sigmaLBase = sigmaLBase, #Treatment rate for chronic LTBI per year
fBase = fBase,   #Fraction of FB arrivals with LTBI

#2010 New Cases in Population i (millions)
#source: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5105a3.htm
newCases0 = .008714,  #US-born
newCases1 = .007554,  #Foreign-born

CtBase = Ct,
ClBase = Cl
)
```

Figure 3. A list of relevant constants in the Basic & Extended Hill Model

6.2. **The Extended Hill Equations.** Below, we detail the full equations used in the extended hill model. These equations extend those used in the standard Hill

Model. In many cases, the equations of the Hill model were split into their component parts, which could then be tracked separately. Here, a continuous discounting

```
discV    <- 1/(1.03^t)  #amount costs, health states discount constant

#parameter values initialized for each time step
c01           <- (1-e0)*((1-e1)*N1)/((1-e0)*N0 + (1-e1)*N1)    #proportion of contacts made with FB individuals  (USB)
c00           <- 1 - c01                                        #proportion of contacts made with USB individuals (USB)
c10           <- (1-e1)*((1-e0)*N0)/((1-e0)*N0 + (1-e1)*N1)    #proportion of contacts made with USB individuals (FB)
c11           <- 1 - c10                                        #proportion of contacts made with FB individuals  (FB)
dLTBIEn       <- f*alpha*(N0+N1)                                #FB arrivals with LTBI entering
dnatdeath0    <- mu0 * N0                                       #Natural deaths (USB)
dnatdeath1    <- mu1 * N1                                       #Natural deaths (FB)
dtbdeath0     <- mud * (I0 + J0)                                #TB deaths (USB)
dtbdeath1     <- mud * (I1 + J1)                                #TB deaths (FB)
dtbdeathD0    <- discV * dtbdeath0                              #TB deaths with discounting (USB)
dtbdeathD1    <- discV * dtbdeath1                              #TB deaths with discounting (FB)
dprogAcute0   <- vF*F0                                          #Acute LTBI progressions to Active TB disease (USB)
dprogAcute1   <- vF*F1                                          #Acute LTBI progressions to Active TB disease (FB)
dprogChron0   <- vL0*L0                                         #Chronic LTBI progressions to Active TB disease (USB)
dprogChron1   <- vL1*L1                                         #Chronic LTBI progressions to Active TB disease (FB)
dprogTotal0   <- dprogAcute0 + dprogChron0                      #Progression to Active TB (USB)
dprogTotal1   <- dprogAcute1 + dprogChron1                      #Progression to Active TB (FB)
dprogTotalD0  <- discV * dprogTotal0                            #Progression to Active TB with discounting (USB)
dprogTotalD1  <- discV * dprogTotal1                            #Progression to Active TB with discounting (FB)
lambda0       <- transmission*(beta*(c00*(I0/N0) + c01*(I1/N1)))  #Forces of Infection (USB)
lambda1       <- transmission*(beta*(c10*(I0/N0) + c11*(I1/N1)))  #Forces of Infection (FB)
dexogenous0   <- x*p*lambda0*L0                                 #Exogenous re-infections of Chronic LTBI to Acute LTBI (USB)
dexogenous1   <- x*p*lambda1*L1                                 #Exogenous re-infections of Chronic LTBI to Acute LTBI (FB)
dInterventionCost <- discV * (iCnewCases*1e6*(dprogTotal0+dprogTotal1) + iCtotPop*1e6*(N0+N1) + iCLTBIEn*1e6*dLTBIEn*(1-incLTBI))

#Difference Equations (USB)
dS0 <- ro*(N0+N1) + sigmaF0*F0 + sigmaL*L0 + phi0*(I0+J0) - lambda0*S0 - mu0*S0
dF0 <- p*lambda0*S0 + dexogenous0 - (mu0 + vF + sigmaF0)*F0
dL0 <- (1-p)*lambda0*S0 - dexogenous0 - (mu0 + vL0 + sigmaL)*L0
dI0 <- q*(dprogAcute0 + dprogChron0) - (mu0 + mud + phi0)*I0
dJ0 <- (1-q)*(dprogAcute0 + dprogChron0) - (mu0 + mud + phi0)*J0

#Difference Equations (FB)
dS1 <- (1-incLTBI)*dLTBIEn+(1-f)*alpha*(N0+N1) + sigmaF1*F1 + sigmaL*L1 + phi1*(I1 + J1) - lambda1*S1 - mu1*S1
dF1 <- g*p*dLTBIEn*incLTBI + p*lambda1*S1 + dexogenous1 - (mu1 + vF + sigmaF1)*F1
dL1 <- (1-g*p)*dLTBIEn*incLTBI + (1-p)*lambda1*S1 - dexogenous1 - (mu1 + vL1 +sigmaL)*L1
dI1 <- q*(dprogAcute1 + dprogChron1) - (mu1 + mud + phi1)*I1
dJ1 <- (1-q)*(dprogAcute1 + dprogChron1) - (mu1 + mud + phi1)*J1

dN0 <- dS0 + dF0 + dL0 + dI0 + dJ0
dN1 <- dS1 + dF1 + dL1 + dI1 + dJ1

#Cost calculations
dcL0 <- discV * Cl * sigmaL  * 1e6 * L0                     #cost for Chronic LTBI cures     (USB)
dcF0 <- discV * Cl * sigmaF0 * 1e6 * F0                     #cost for Acute LTBI cures       (USB)
dcI0 <- discV * Ct * q*(dprogAcute0 + dprogChron0) * 1e6    #cost for Infectious TB cures    (USB)
dcJ0 <- discV * Ct * (1-q)*(dprogAcute0 + dprogChron0) * 1e6 #cost for Non-Infectious TB cures (USB)
dcI0dL0 <- discV * Ct * q*(dprogChron0) * 1e6      #cost for Infectious TB cures    (USB)
dcI0dF0 <- discV * Ct * q*(dprogChron0) * 1e6      #cost for Infectious TB cures    (USB)
dcJ0dL0 <- discV * Ct * (1-q)*(dprogAcute0) * 1e6 #cost for Non-Infectious TB cures (USB)
dcJ0dF0 <- discV * Ct * (1-q)*(dprogAcute0) * 1e6 #cost for Non-Infectious TB cures (USB)
dcL1 <- discV * Cl * sigmaL  * 1e6 * L1                     #cost for Chronic LTBI cures     (FB)
dcF1 <- discV * Cl * sigmaF1 * 1e6 * F1                     #cost for Acute LTBI cures       (FB)
dcI1 <- discV * Ct * q*(dprogAcute1 + dprogChron1) * 1e6    #cost for Infectious TB cures    (FB)
dcJ1 <- discV * Ct * (1-q)*(dprogAcute1 + dprogChron1) * 1e6 #cost for Non-Infectious TB cures (FB)
dcI1dL1 <- discV * Ct * q*(dprogChron1) * 1e6      #cost for Infectious TB cures    (USB)
dcI1dF1 <- discV * Ct * q*(dprogChron1) * 1e6      #cost for Infectious TB cures    (USB)
dcJ1dL1 <- discV * Ct * (1-q)*(dprogAcute1) * 1e6 #cost for Non-Infectious TB cures (USB)
dcJ1dF1 <- discV * Ct * (1-q)*(dprogAcute1) * 1e6 #cost for Non-Infectious TB cures (USB)
dcN0 <- dcF0 + dcL0 + dcI0 + dcJ0                          #Total cost for all treatments (USB)
dcN1 <- dcF1 + dcL1 + dcI1 + dcJ1                          #Total cost for all treatments (FB)
```

FIGURE 4. The equations defining the Extended Hill Model, shown in R syntax. In this model, compartments share the same names as they did in the Hill Model, *i.e.* S1 is the Foreign Born susceptible population.

approximation is used to a discount rate of 3% yearly, found via *discV*. In many of the differential equations, a small *c* is used to denote *cost of*.

6.3. Estimations for Infectious Rates of FB and USB. Colin to add.

6.4. Statistical Qualities of the Agent Based Model.

6.5. Finer Intervention Analysis.

6.6. Sensitivity Analysis.