Bayesian Compartmental Modeling of Tuberculosis

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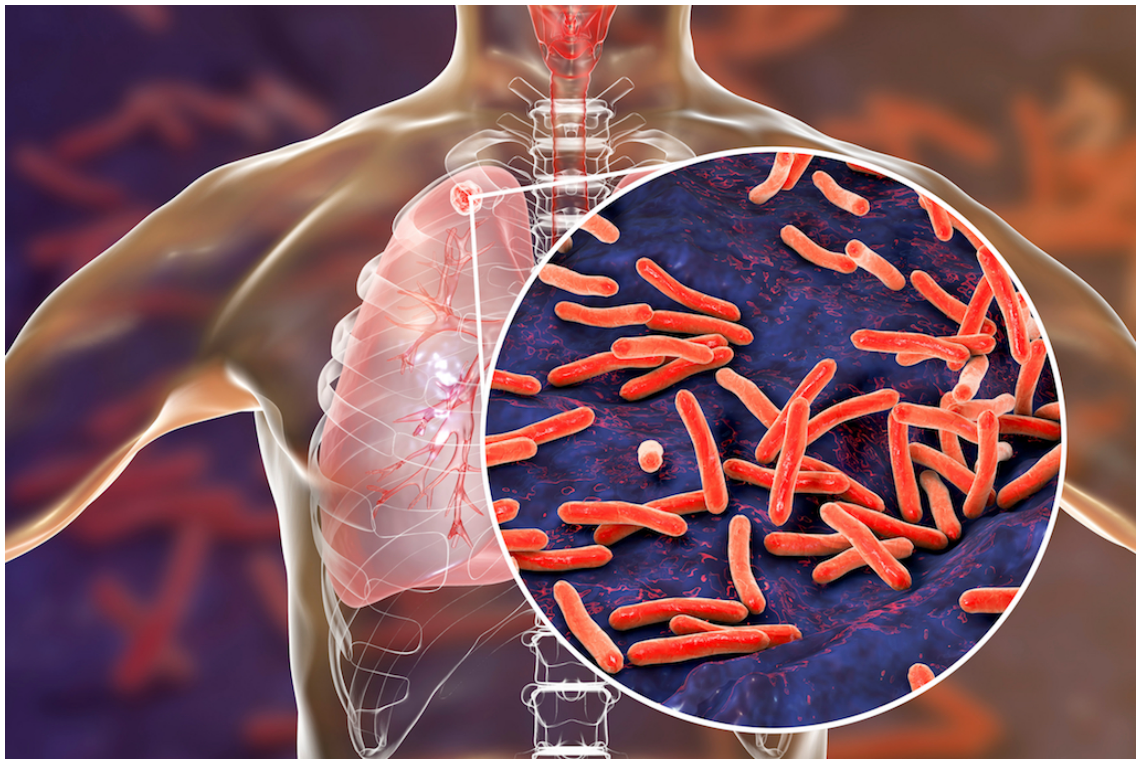
Outline

1. Background on Tuberculosis
2. Introduce Compartmental SEIRS Model Framework
3. Discuss Approximate Bayesian Computation for Bayesian Analysis
4. Apply to US data

Tuberculosis Characteristics



- The bacterium, *Mycobacterium tuberculosis* usually affects the lungs, but can also infect other parts of the body
- Tends to spread through the air not surfaces
- Globally, $\approx$ 1.5 million people die from TB each year
- second leading infectious disease after COVID-19 (above HIV/AIDS)

Tuberculosis Characteristics

- Symptoms include prolonged cough, blood is sputum, chest pain or difficulty breathing, Unintentional weight loss, Fatigue, Fever, etc
- Treatment takes 6 months of antibiotics
- You are able to spread it as long as you have bacteria in your body
- typically not infectious 1-2 weeks after starting treatment
- a study in other countries found it to be a seasonal disease [10]

Goals of Analysis

- Confirm Model of exposure probabilities
- Predict new cases of Tuberculosis
- Predict the peak of Tuberculosis
- Loosely Estimate transition probabilities

SEIR Compartmental Models

- Categorize people into 4 disease states at given time point:
- S - people **susceptible** to disease (no immunity)
- E - people who have been **exposed** to the disease, but not infectious
- I - people who are **infectious** for a disease
- R - people who are **removed** due to developing immunity or dying
- Other compartmental models exist, but are highly dependent on disease characteristics (Vaccination compartment, disease vectors)

Temporal Process Model

SEIR Compartmental Structure

Notation

S	Number of Susceptible Individuals
E	Number of Exposed Individuals
I	Number of Infectious Individuals
R	Number of Removed Individuals
N	total population, fixed
t	index for time
*	Newly exposed, infected, or removed individuals for a given time point

Equations

$$S_{(t+1)} = S_t - E_t^* + S_t^*$$
$$E_{(t+1)} = E_t + E_t^* - I_t^*$$
$$I_{(t+1)} = I_t + I_t^* - R_t^*$$
$$R_{(t+1)} = R_t + R_t^* - S_t^*$$
$$N = S_t + E_t + I_t + R_t$$

Temporal Process Model

$$E_t^* | (S_t, I_t, \pi_t^{(SE)}) \sim \text{Binomial}(S_t, \pi_t^{(SE)})$$
$$I_t^* | (E_t, \pi_t^{(EI)}) \sim \text{Binomial}(E_t, \pi_t^{(EI)})$$
$$R_t^* | (I_t, \pi_t^{(IR)}) \sim \text{Binomial}(I_t, \pi_t^{(IR)})$$

- Examples of risk factors that affect exposure ($\pi_t^{(SE)}$) could be:
  - The total population size of a county
  - The timing of an intervention (vaccine, quarantine)
  - The climate of a region
- In principle, one could also include risk factors that affect the transition from exposed to infectious ($\pi_t^{(EI)}$) or infectious to removed compartments ($\pi_t^{(IR)}$)
- However, the length of time spent in these compartments are strongly characteristic of the disease in question, so additional data provides diminishing returns in estimation.

Transition Probabilities

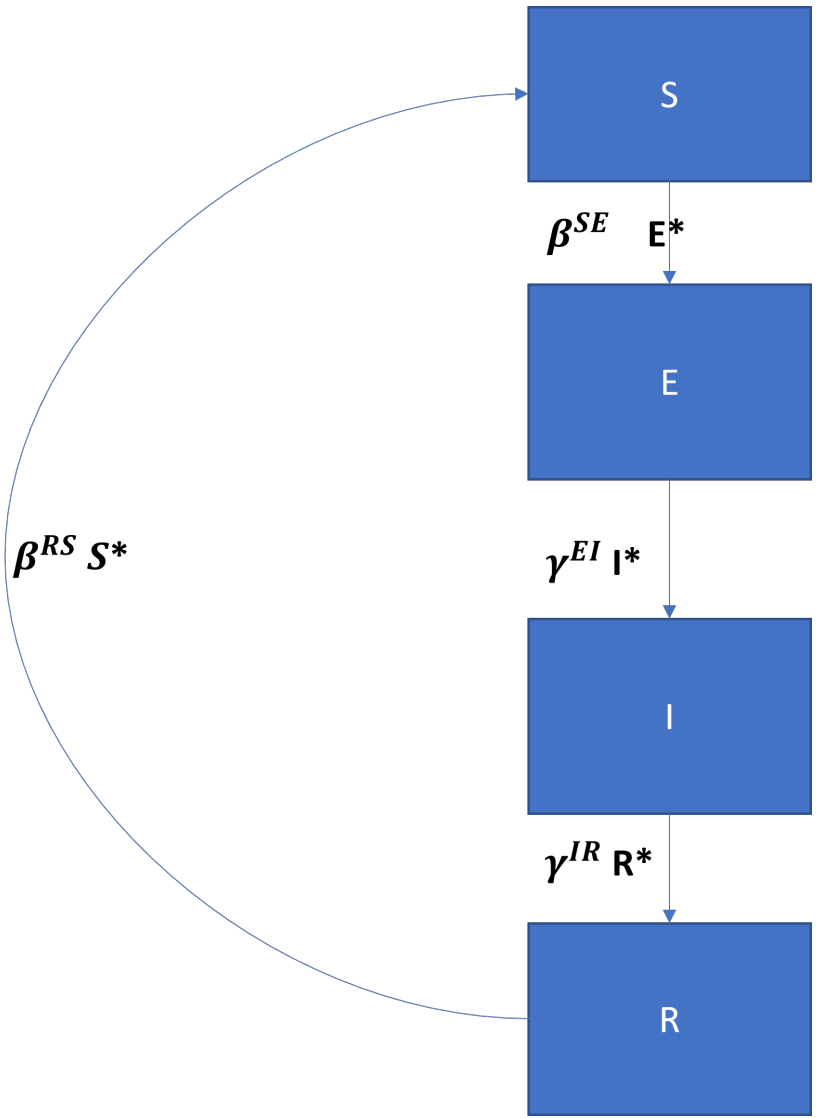
Notation

X_t	A **vector** of exposure covariates
β	A **vector** of exposure/reinfection effects
γ_{EI}	The reciprocal of the average latent period
γ_{IR}	The reciprocal of the average infectious period

Distributional Assumptions

$$\pi_t^{(SE)} = 1 - \exp\{-\frac{I_t}{N}\exp\{\beta^{(SE)\prime} X_t^{(SE)}\}\}$$
$$\pi_t^{(EI)} = 1 - \exp\{-\gamma_{EI}\}$$
$$\pi_t^{(IR)} = 1 - \exp\{-\gamma_{IR}\}$$
$$\pi_t^{(RS)} = 1 - \exp\{-exp\{\beta^{(RS)\prime} X_t^{(RS)}\}\}$$

Diagram



Approximate Bayesian Computation

- A fast approach for fitting Bayesian models is the Approximate Bayesian Computation (ABC) algorithm
- Only requires that the data is able to be simulated, 'likelihood-free'.
- Can be used to conduct Bayesian Inference on models whose likelihoods are computationally expensive or intractable to evaluate

Notation

y	The observed data
$d(\cdot, \cdot)$	A distance measure between two numbers/vectors
$S(\cdot)$	A summary statistic of the data
ε	The max tolerable discrepancy between the two statistics

Do Until N points accepted:

1. Draw $\theta_i \sim p(\theta)$
2. Simulate $x_i \sim p(x|\theta_i)$
3. Reject if θ_i if $d(S(x_i), S(y)) > \varepsilon$

Approximate Bayesian Computation

- You have an sample of $P(\theta|d(S(x_i), S(y)) \leq \varepsilon)$
- If $\varepsilon = 0$, then one is sampling exactly from the posterior distribution
- This is not feasible as the probability of generating the exact same data set is ≈ 0 in most applications.
- Thus, ABC accepts data that is 'close enough' $(\leq \varepsilon)$, where we want ε as small as practically possible
- The rejection algorithm is intuitive, but is very inefficient especially when the prior distribution is diffuse with the true parameter distribution.

Approximate Bayesian Computation

Sequential Monte Carlo Algorithm

1. Pick a decreasing sequence of $\varepsilon_1, \varepsilon_2, \cdots, \varepsilon_T$
2. If t $= 1$
   - Do until N acceptances
     - Draw $\theta_i \sim \pi(\theta)$
     - Simulate $x_i \sim p(x|\theta_i)$
     - Reject if θ_i if $d(S(x_i), S(y)) > \varepsilon_0$
   - Set $w_i^{(1)} = \frac{1}{N}$; $\tau_1^2 = 2var(\theta^{(1)})$; t $= 2$;
3. If t >1
   - Do until N acceptances
     - Draw θ_i^* from $\theta^{(t-1)}$ weighted by $w_i^{(t-1)}$
     - Draw $\theta_i^{(t)} \sim N(\theta_i^*, \tau^2)$
     - Simulate $x_i \sim p(x|\theta_i)$
     - Reject if θ_i if $d(S(x), S(y)) > \varepsilon_t$
   - Set $w_i^{(t)} \propto \frac{\pi(\theta_i^{(t)})}{\sum_{j=1}^{N} w_j^{(t-1)} \phi_j(\theta_i^{(t)})}$; $\tau_t^2 = 2var(\theta^{(t)})$; t $=$ t $+ 1$;

$$\phi_j \equiv \text{pdf of } N(\theta_j^{(t-1)}, \tau_{t-1}^2)$$

Notation

M_j	Proposed model j
$A_i^{(M_j)}$	0-1 indicator

Do until N total Draws from each model

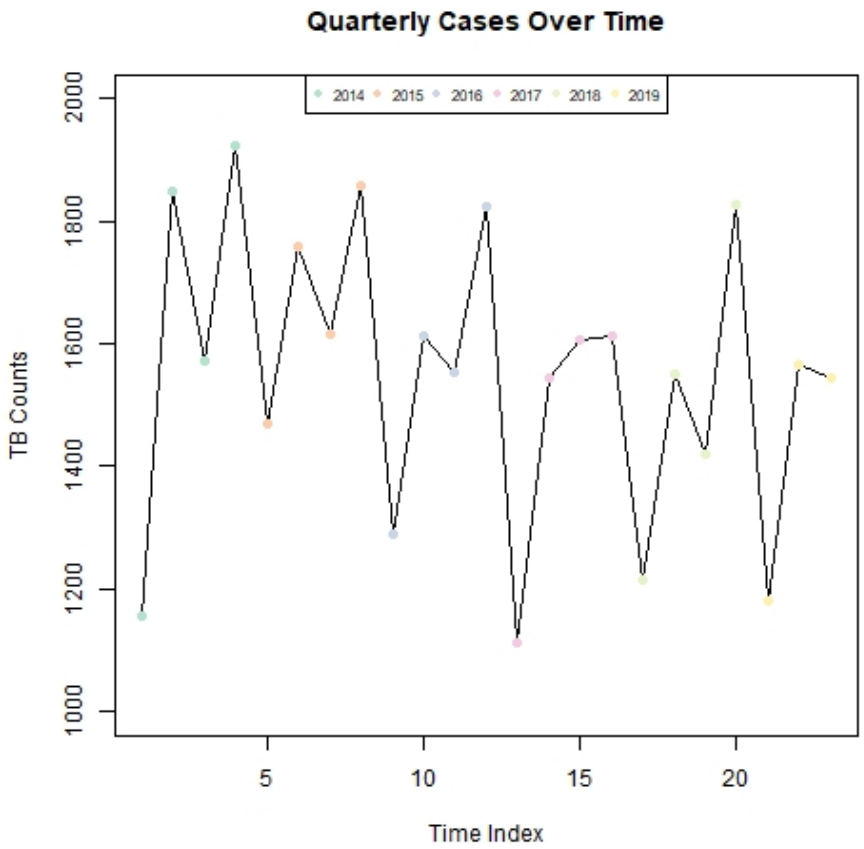
1. Draw a model $m_j \sim P(M_j)$
2. Draw $\theta_i \sim p(\theta|M_j = m_j)$
3. Simulate $x_i \sim p(x|\theta_i, M_j = m_j)$
4. $A_i^{(M_j)} = \mathbb{I}_{d(x_i,y)<\varepsilon}$

$$\frac{1}{N}\sum_i A_i^{(M_j)} \to \mathbb{E}(A_i^{(M_j)}) = P(d(x_i, y)) < \varepsilon | M_j = m_j)$$

- Recall the $BF_{1,2} = \frac{P(y|M_1)}{P(y|M_2)}$
- Sometimes people skip the model draw part and just reweight the sum at the end

Data

Quarterly United States TB Data



- Data is from DATA.CDC.GOV
- Reported quarterly from 2014-2019
- Last year used for prediction

Model Parameters

- Exposure Covariates Used
  - Model 1: Basis Spline expansion of the time index, 3 df
  - Model 2: Trigonometric Temporal Basis
  - $\beta_0 + \beta_1 sin(\frac{2\pi t}{4}) + \beta_2 cos(\frac{2\pi t}{4}) + \beta_3 sin(\frac{2\pi t}{4}) cos(\frac{2\pi t}{4})$
- Initializing Compartments
  - Loosely Fixed on Rough estimates
  - (S0=300e6,E0=1000,I0=9000/4,R0=3*9000/4)

Prior Distribution on Parameters

- $\beta_k^{(SE)} \sim N(0, \text{precision} = 0.5)\ \forall k$
- $\beta^{(RS)} \sim N(\approx 0.0118, \text{precision} \approx 313000)$
  - estimated from a study[12]
- $\gamma_{EI} \sim Gamma(100, -log(1 - 0.536)/100) =$
  - chosen such that 90% chance of becoming infectious by 9 months on average
- $\gamma_{IR} \sim Gamma(10, -log(1 - 0.437)/10)$
  - chosen such that 90% chance of becoming removed by 1 year on average

Results: Posterior Predictive Distribution

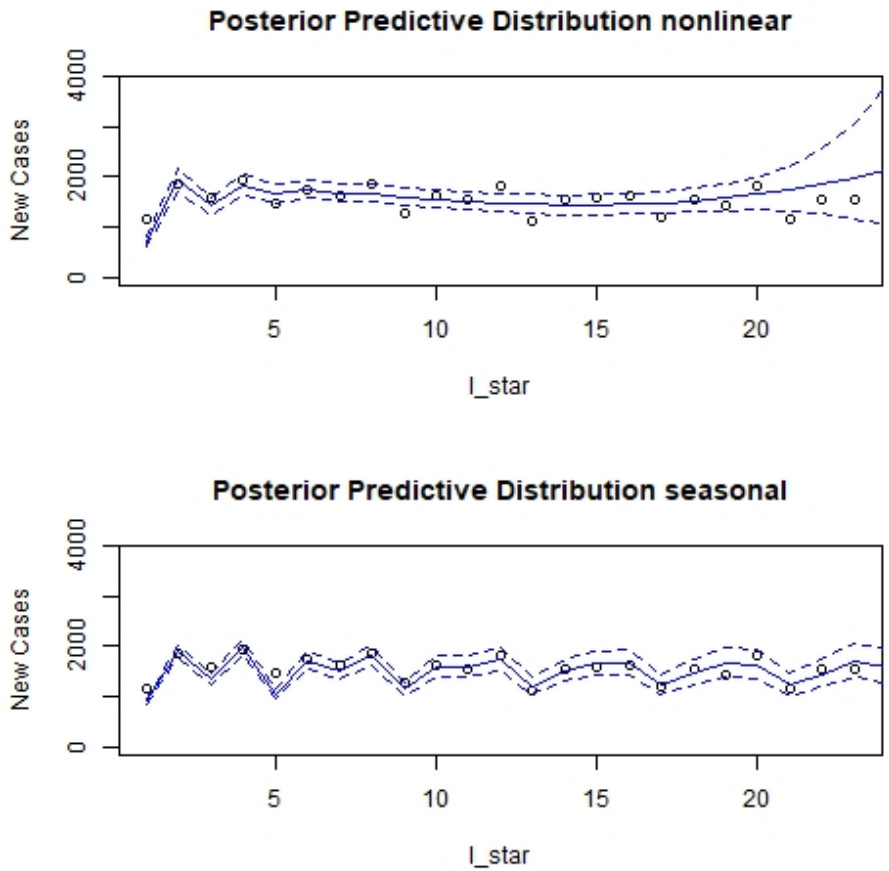


Figure: Posterior Predictive Distribution and 95% CI

$P(max\{I_{21}^*, I_{22}^*, I_{23}^*\} = I_2^*2) = 0.01524$; Num Post Pred sample $= 50000$

Results: Bayes Factor

Table: Terminating Epsilon of models

	Terminating.Epsilon
Nonlinear	950.413
Seasonal	597.479

- Extremely different terminating epsilon
- In general, we use the mean of these two epsilons to assess Bayes factor
- $BF_{seasonal,nonlinear} = Inf$. Does it make sense why?

Results: Exposure Parameters

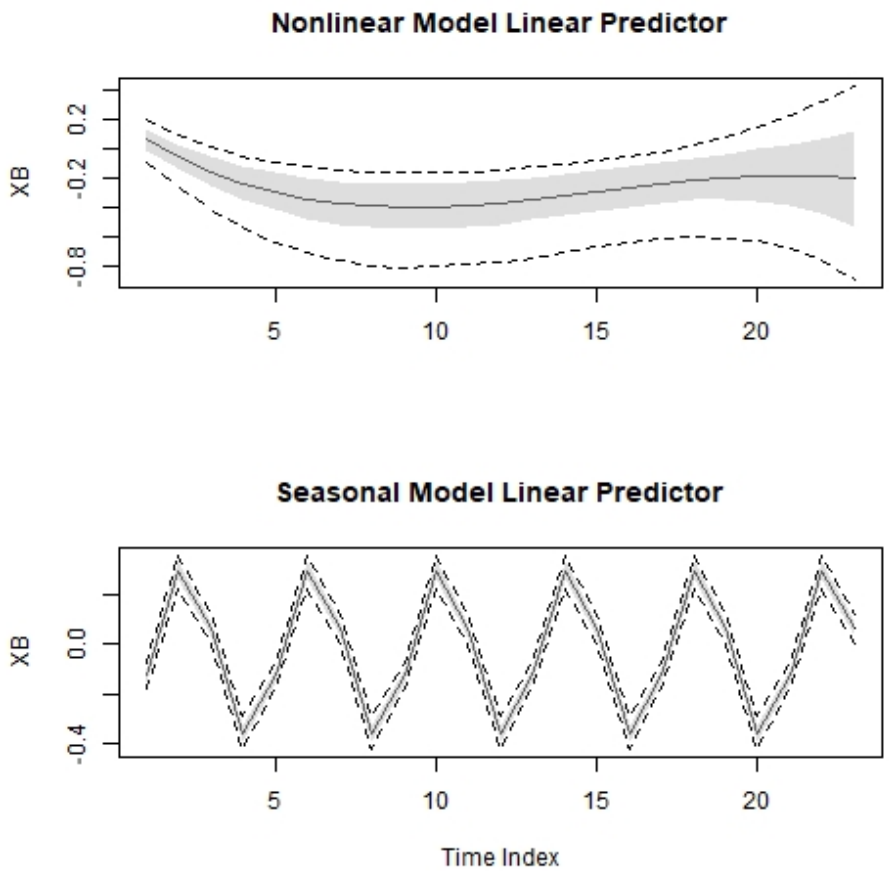


Figure: Plot of exposure over time Index

Results: Transition Parameters

Table: Transition Parameter Estimates

	Mean	SD	95% LB	95% UB
Beta_RS_1	1.200e-02	0.000*	1.2000	1.2000
γ_{EI}	2.457	0.208	2.0780	2.9140
γ_{IR}	3.862	0.402	3.1530	4.7160
$\pi^{(EI)}$	0.912	1.780e-02	0.8747875	0.9457200
$\pi^{(IR)}$	0.977	8.837e-03	0.9572694	0.9910503
$\pi^{(RS)}$	0.636	1.787e-05	0.636	0.636

Table: Mean transition parameters and 95% credible intervals for the seasonal model. SD not truly zero. N = 1000

Discussion

- The posterior update is quite different the the prior beliefs for E-I, I-R compartments
- R-S is pretty much the same
- decent at prediction, not great at finding peaks
- Ignores spatial heterogeneity (Alaska, Hawaii)
- Ignores underreporting

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