

Using Time-Dependent Sensitivity Analysis to Combat Tuberculosis

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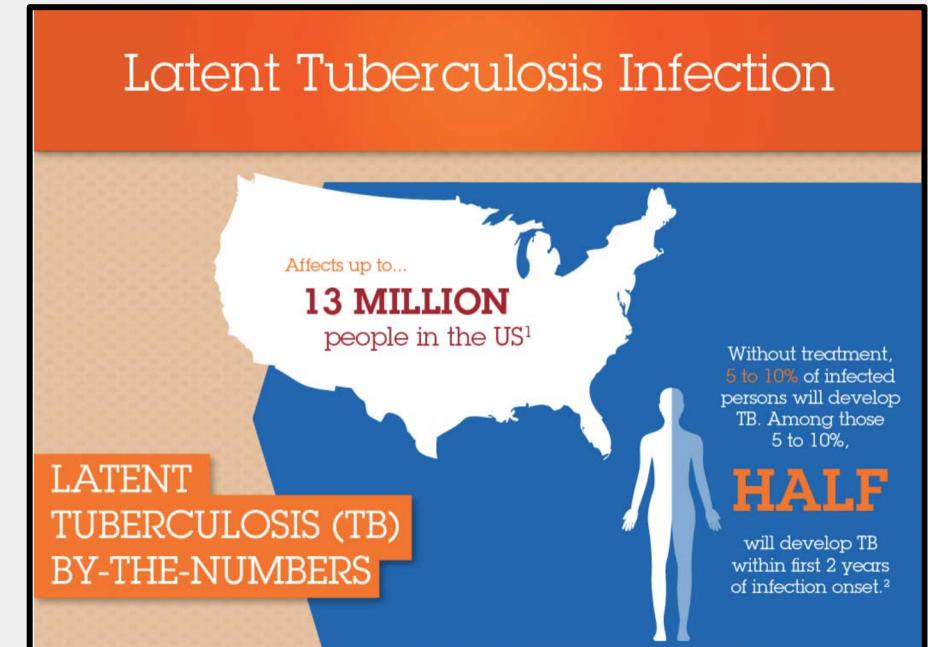
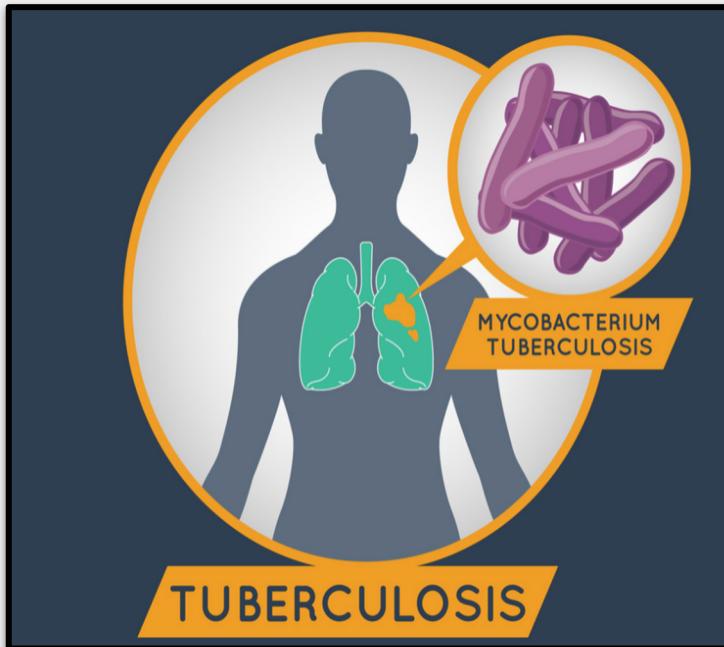


Mentored by Dr. Allison Lewis, Lafayette College





Why are we conducting this research?



Tuberculosis."VectorStock.com.2018,<https://www.vectorstock.com/royalty-free-vector/tuberculosis-lgo-icon-vector-17791903>

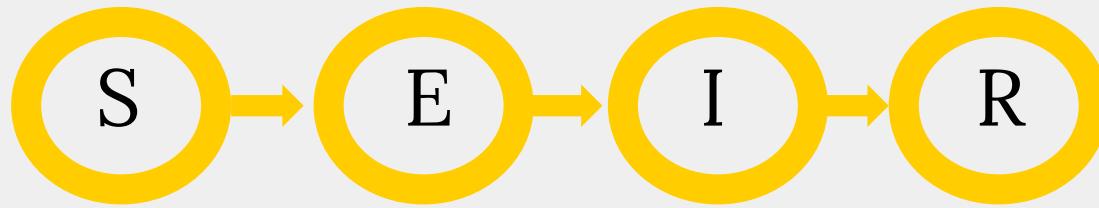
<http://www.multivu.com/players/English/7701451-sanofi-priftin-rifapentine/>

Our Research Goal

To use compartmental modeling and sensitivity analysis to determine the best method(s) of eradicating tuberculosis



Setup and Assumptions for our Model



S- Susceptible

E- Exposed

I- Infectious

R- Recovered

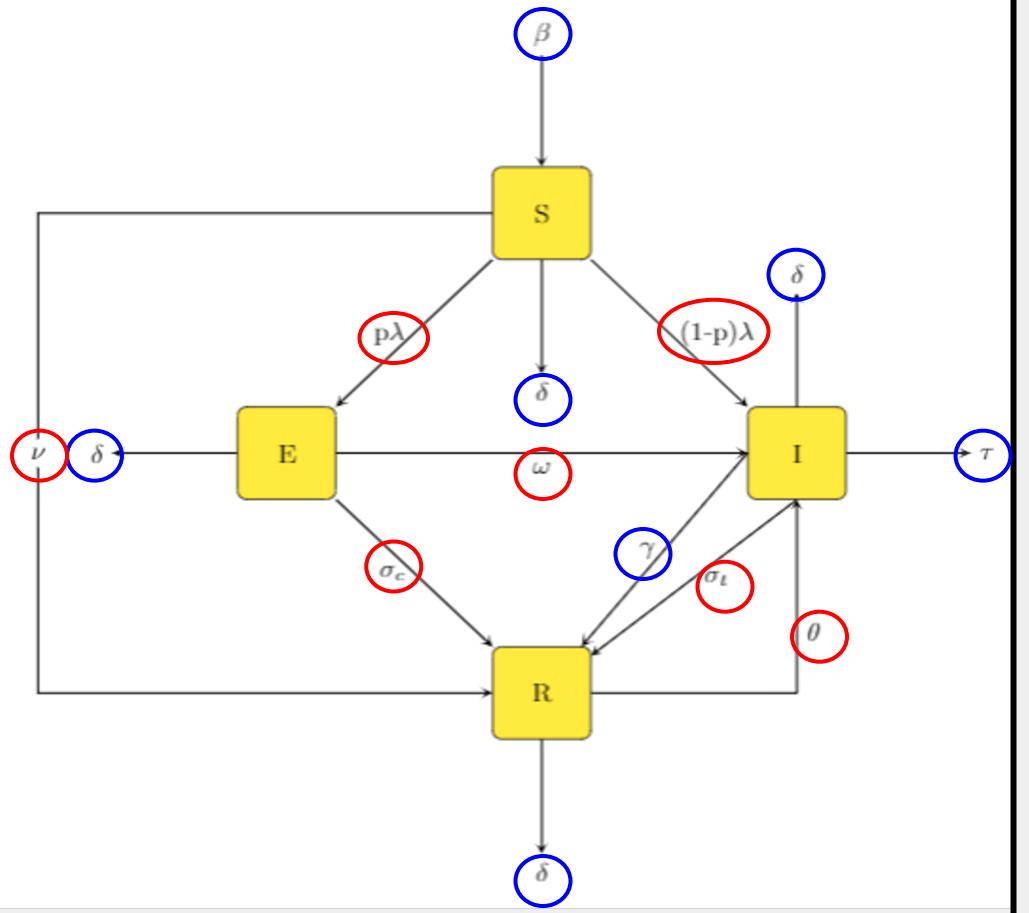


Short and Totally Not Scary Example

*the rate of change of
the human (H) population over time* $=$ *births — deaths*

$$\frac{dH}{dt} = \beta - \delta$$





$$\frac{dS}{dt} = \beta - \lambda SI - \delta S - \nu S$$

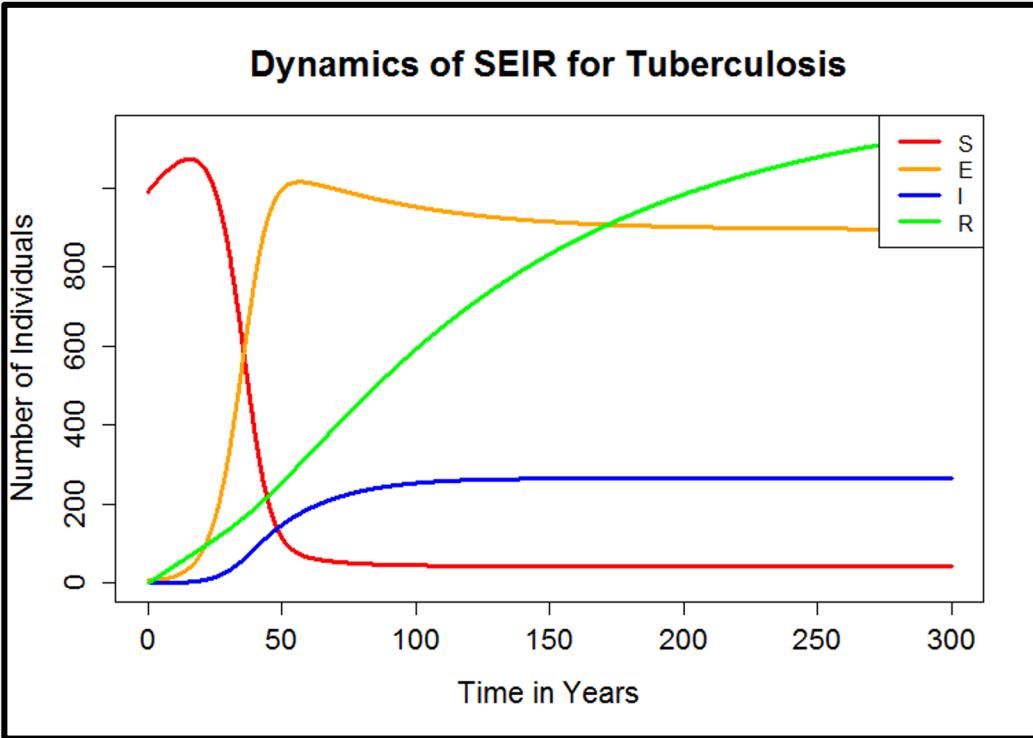
$$\frac{dE}{dt} = p\lambda SI - (\omega + \sigma_c + \delta)E$$

$$\frac{dI}{dt} = (1 - p)\lambda SI + \omega E - (\delta + \tau + \gamma + \sigma_t)I + \theta R$$

$$\frac{dR}{dt} = \nu S + \sigma_c E + (\sigma_t + \gamma)I - (\delta + \theta)R$$



SEIR Population Dynamics



- S—Susceptible (red)
 - E—Exposed (orange)
 - I—Infectious (blue)
 - R—Recovered (green)
-
- Initial Population: 1000 people (990 susceptible, 10 exposed)



Sensitivity Analysis

- Proportion of the total population that is affected by tuberculosis

$$f(t) = \frac{E(t) + I(t)}{N(t)}$$

E : Exposed population

I : Infectious population

N : Total population



Active Subspace Example (Year 68)

Singular Value Decomposition
formula:

$$G = U\Sigma V^T$$

Where is the first significant split
in diagonal values?

$$\Sigma = \begin{bmatrix} 1.00 & 0 & 0 & 0 & 0 \\ 0 & 0.64 & 0 & 0 & 0 \\ 0 & 0 & 0.06 & 0 & 0 \\ 0 & 0 & 0 & 0.01 & 0 \\ 0 & 0 & 0 & 0 & 0.01 \\ 0 & 0 & 0 & 0 & 0.004 \end{bmatrix}$$

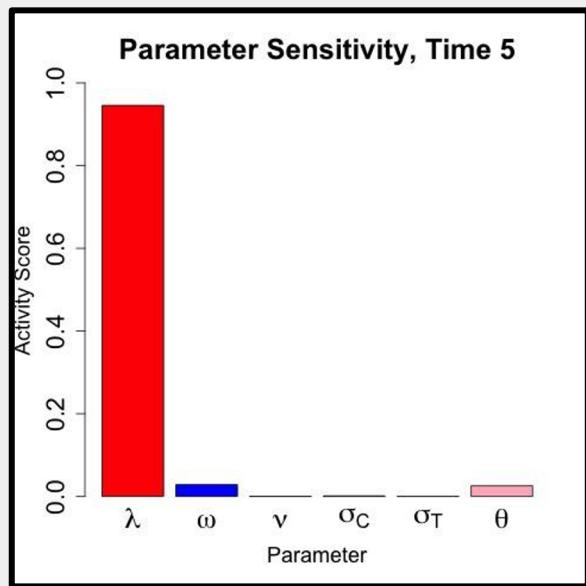
First two columns = active subspace

$$U = \begin{bmatrix} -0.26 & -0.90 & 0.33 & -0.07 & -0.02 & -0.07 \\ 0.31 & -0.25 & -0.32 & 0.40 & 0.76 & 0.01 \\ 0.04 & 0.06 & -0.04 & -0.11 & 0.06 & -0.99 \\ 0.74 & -0.31 & -0.34 & -0.25 & -0.42 & 0.02 \\ 0.12 & -0.01 & 0.18 & 0.87 & -0.43 & -0.13 \\ -0.52 & -0.14 & -0.80 & 0.12 & -0.23 & -0.03 \end{bmatrix}$$

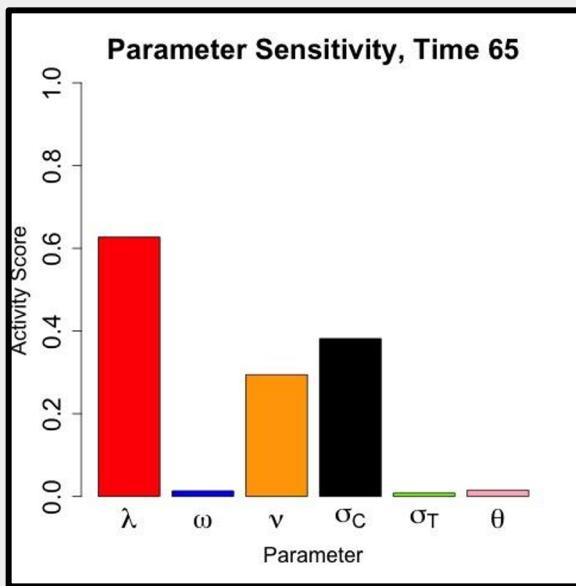
Two Dimensional



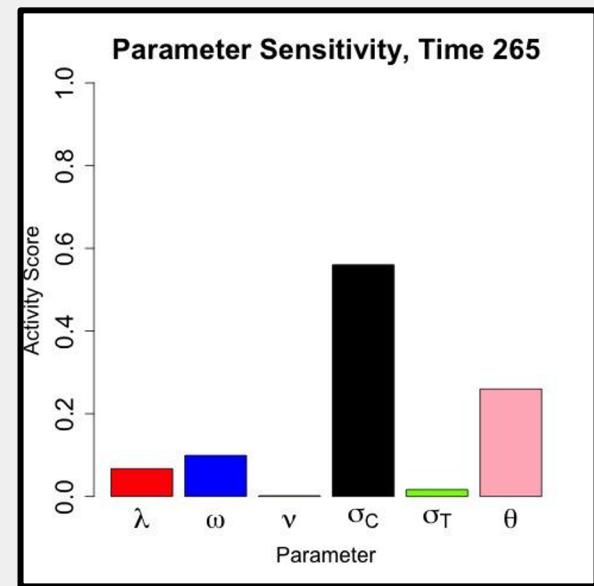
Methods of Targeting TB Based on our Results



Rate of infection (λ)



Latent treatment (σ_C)
Vaccination rate (ν)



Relapse Rate (θ)



Acknowledgements

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References

- Blower, S. M., Mclean, A. R., Porco, T. C., Small, P. M., Hopewell, P. C., Sanchez, M. A., & Moss, A. R. (1995). The intrinsic transmission dynamics of tuberculosis epidemics. *Nature Medicine*, 1(8), 815-821. doi:10.1038/nm0895-815
- Constantine, P. G., & Diaz, P. (2017). Global sensitivity metrics from active subspaces. *Reliability Engineering & System Safety*, 162, 1-13. doi:10.1016/j.ress.2017.01.013
- Chaisson, R. E., & Churchyard, G. J. (2010, March 01). Recurrent Tuberculosis: Relapse, Reinfection, and HIV | The Journal of Infectious Diseases | Oxford Academic. Retrieved June/July, 2018, from <https://academic.oup.com/jid/article/201/5/653/861944>
- Global tuberculosis report 2017. (2017, December 06). Retrieved from http://www.who.int/tb/publications/global_report/en/



References

Kozicharow, Allison, and Bernice Born. "WiRED International Launches Airborne Diseases Module." *WiRED Launches Prevention Education Program on Ebola in East Africa/WiREDInternational.org*, WiRED International Health Education and Information, www.wiredinternational.org/Airborne%20Diseases_Module_Launched.html.

Newswire, MultiVu - PR. "Sanofi Launches New Priftin® (Rifapentine) Packaging." *Multivu*, Sanofi, www.multivu.com/players/English/7701451-sanofi-priftin-rifapentine/.

South Africa Birth rate. (n.d.). Retrieved July 23, 2018, from
https://www.indexmundi.com/south_africa/birth_rate.html

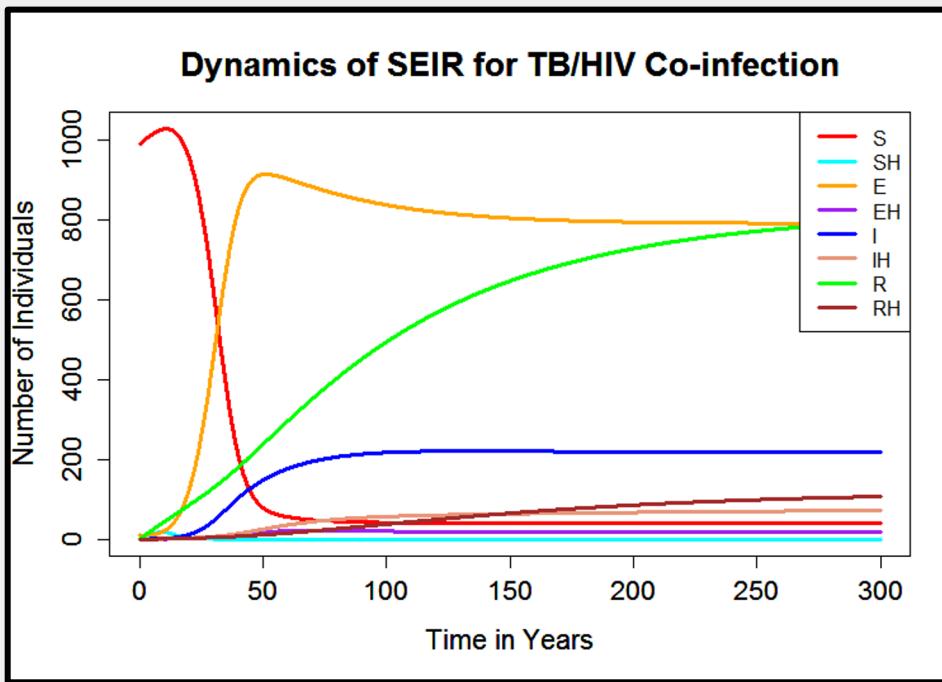
TB Facts | TB, tests, drugs, statistics. (n.d.). Retrieved July 23, 2018, from <https://www.tbfacts.org/>



Table of Parameter Values

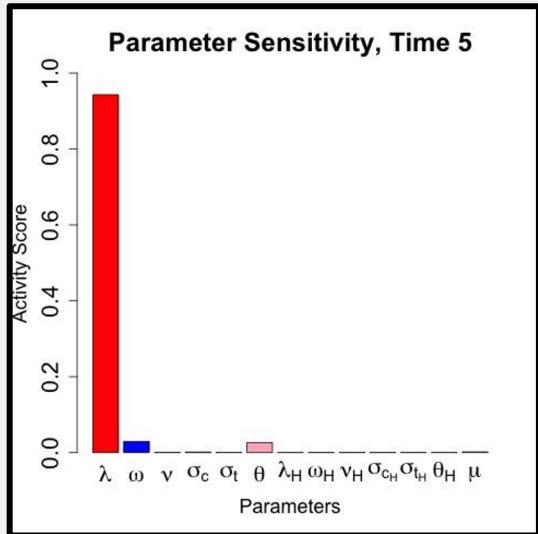
Parameter	Units	Nominal	Source
(ν) rate of vaccination	$\frac{1}{\text{time}}$	0.00445	WHO
(λ) rate of infection	$\frac{1}{\text{people} * \text{time}}$	0.0018	Estimated
(ω) rate of deterioration	$\frac{1}{\text{time}}$	0.0084	TB Facts
(σ_c) latent TB treatment	$\frac{1}{\text{time}}$	0.005	Estimated
(σ_t) active TB treatment	$\frac{1}{\text{time}}$	0.005	Estimated
(θ) rate of reinfection	$\frac{1}{\text{time}}$	0.0005	Blower

SEIR Dynamics (Co-infection Model)

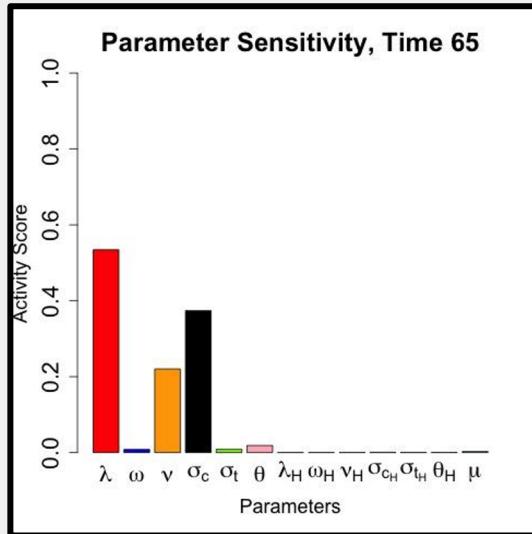




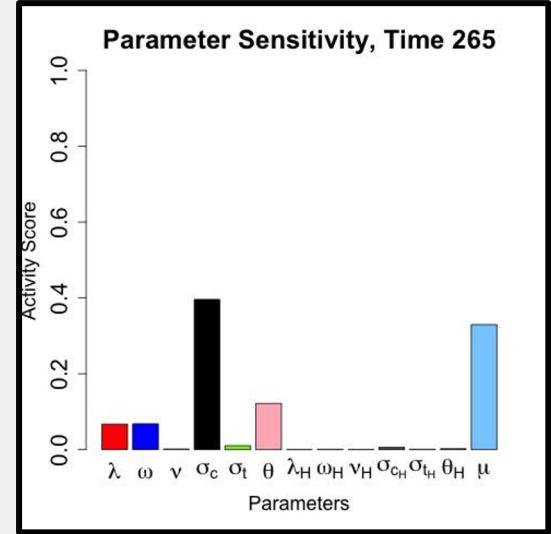
Results For Our Co-infection Model



Rate of infection (λ)



Latent treatment (σ_c)
Vaccination rate (ν)



HIV incidence rate (μ)