The Study of Epidemic and Endemic Diseases using Mathematical Models

Candidate: Jummy Funke David!

Supervisors: • Fred Brauer • Viviane Dias Lima

Committee members: Supervisors and Priscilla (Cindy) E. Greenwood

Dissertation Defense

January 16, 2020

Presentation Outline

1. Background Knowledge
2. Definition of some technical terms
3. PART A: **Epidemic**
   - *SIRP models with heterogeneous mixing and indirect transmission*
   - *Coupled PDE-ODE model with indirect transmission*
4. PART B: **Endemic**
   - *HIV/Syphilis co-interaction model among gbMSM*
   - *Modified HIV/Syphilis co-interaction model among gbMSM in BC*

General Background Knowledge

Epidemic:

- sudden occurrence of disease in a region above the level of normal expectancy
- modeled with no demographic effects
- by demographics, we mean birth, death and migration

Endemic:

- constant presence of disease within a particular region
- modeled with demographic effects

Pandemic: world epidemic

Definition of technical terms

Basic reproduction number ($\mathcal{R}_0$):

The average number of secondary infections caused by an average infective.

Effective reproduction number ($\mathcal{R}_e$):

Often used whenever we incorporate factors aimed at controlling the spread of disease into a model.

The final size relation:

Gives an estimate of the total number of infections and the epidemic size for the period of the epidemic from the parameters in the model.

Direct transmission of diseases:

when diseases are transmitted from *Host-Host*
e.g. **HIV, Syphilis**.

Definition of technical terms (CONTINUE...)

Indirect transmission of diseases:

when diseases are transmitted from *Host-Source-Host*
e.g. **Chickenpox, Influenza, Measles, Smallpox, Tuberculosis.**

Heterogeneous mixing:

mixing that exists between populations with different characteristics.

gbMSM:

Gay, bisexual and other men who have sex with men

Interventions:

1. **TasP:** Treatment as Prevention (HIV)
2. **PrEP:** Pre-exposure prophylaxis
3. **ART:** Antiretroviral therapy (the use of HIV medicines to treat HIV infection)

SIRP models with heterogeneous mixing and indirect transmission

- **PREVIOUS RESEARCH:**

JOURNAL OF BIOLOGICAL DYNAMICS, 2017
VOL. 11, NO. S2, 285–293
https://doi.org/10.1080/17513758.2016.1207813

OPEN ACCESS Check for updates

A new epidemic model with indirect transmission

Fred Brauer

Department of Mathematics, University of British Columbia, Vancouver, Canada

Project 1: Background

- **PREVIOUS RESEARCH:**

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- **MY WORK:**

JOURNAL OF BIOLOGICAL DYNAMICS
2018, VOL. 12, NO. 1, 375–399
https://doi.org/10.1080/17513758.2018.1467506

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Epidemic models with heterogeneous mixing and indirect transmission

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Project 1: Research Questions

- *What is the impact of varying the pathogen shedding rate and taking the age of infection into consideration?*
- *What is the nature of the epidemic in an heterogeneous mixing environment?*
- *How worst is disease spread when we consider indirect transmission pathway?*
- *What is the role of residence time on disease dynamics?*

Project 1: Heterogeneous mixing and indirect transmission for simple SIRP epidemic model

SIRP model:

$$\begin{cases} S_1' = -\beta_1 S_1 P, \\ I_1' = \beta_1 S_1 P - \alpha I_1, \\ R_1' = \alpha I_1 \end{cases} \qquad \begin{cases} S_2' = -\beta_2 S_2 P, \\ I_2' = \beta_2 S_2 P - \alpha I_2, \\ R_2' = \alpha I_2 \end{cases}$$

$P' = r_1 I_1 + r_2 I_2 - \delta P \quad (P = \text{Pathogen}, r_1, r_2 = \text{shedding rates})$

Basic reproduction number: $\mathcal{R}_0 = \beta_1 \mathcal{R}_1 + \beta_2 \mathcal{R}_2$

$$\mathcal{R}_1 = \frac{r_1 N_1}{\alpha \delta} \qquad \mathcal{R}_2 = \frac{r_2 N_2}{\alpha \delta}$$

$\mathcal{R}_0 \Longrightarrow$ *secondary infections caused indirectly through the pathogen shed by an infectious individual in* I_1 & I_2 *respectively.*

The final size relation:

$$\log \frac{S_{i0}}{S_{i\infty}} = \beta_i \left(\mathcal{R}_1 \left\{ 1 - \frac{S_1(\infty)}{N_1} \right\} + \mathcal{R}_2 \left\{ 1 - \frac{S_2(\infty)}{N_2} \right\} + \frac{2P_0}{\delta} \right), \; i = 1, 2.$$

Project 1: A two-group age of infection model with heterogeneous mixing

$A_1(\tau)$ & $A_2(\tau) \Longrightarrow$ *mean infectivity at age of infection* τ.
$\mathbf{\Gamma}(\tau) \Longrightarrow$ *fraction of pathogen remaining* τ *time units after having been shed by an infectious individuals.*

Basic reproduction number: $\mathcal{R}_0 = \beta_1\mathcal{R}_1 + \beta_2\mathcal{R}_2$

$$\mathcal{R}_1 = r_1 N_1 \int_0^\infty A_1(\tau)d\tau \int_0^\infty \mathbf{\Gamma}(\tau)d\tau,$$

$$\mathcal{R}_2 = r_2 N_2 \int_0^\infty A_2(\tau)d\tau \int_0^\infty \mathbf{\Gamma}(\tau)d\tau.$$

$\mathcal{R}_1$ & $\mathcal{R}_2 \Longrightarrow$ *secondary infections caused indirectly through the pathogen shed by an infectious individual in* I_1 & I_2 *respectively.*

Project 1: A two-group age of infection model with heterogeneous mixing

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$\mathcal{R}_1$ & $\mathcal{R}_2 \Longrightarrow$ *secondary infections caused indirectly through the pathogen shed by an infectious individual in* I_1 & I_2 *respectively.*

The final size relation:

$$\log\frac{S_{i0}}{S_{i\infty}} = \beta_i\left(\mathcal{R}_1\left[1-\frac{S_{1\infty}}{N_1}\right] + \mathcal{R}_2\left[1-\frac{S_{2\infty}}{N_2}\right]\right)$$

$N_1 - S_{1\infty}$ & $N_2 - S_{2\infty} \Longrightarrow$ often described in terms of the attack rates/ratios $\left(1-\frac{S_{1\infty}}{N_1}\right)$ and $\left(1-\frac{S_{2\infty}}{N_2}\right)$.

Project 1: Variable pathogen shedding rates

Basic reproduction number: $\mathcal{R}_0 = \beta_1 \mathcal{R}_1 + \beta_2 \mathcal{R}_2$

$$\mathcal{R}_1 = N_1 \int_0^\infty Q_1(v)dv \int_0^\infty \mathbf{\Gamma}(\mathbf{c})dc,$$
$$\mathcal{R}_2 = N_2 \int_0^\infty Q_2(v)dv \int_0^\infty \mathbf{\Gamma}(\mathbf{c})dc$$

$Q_1(v)$ & $Q_2(v) \Longrightarrow$ *shedding rates.*

$\mathbf{\Gamma}(\mathbf{c}) \Longrightarrow$ *proportion of viruses remaining for virus already shed c time units earlier.*

The final size relation:

$$\log \frac{S_{i0}}{S_{i\infty}} = \beta_i \left(\mathcal{R}_1 \left[1 - \frac{S_{1\infty}}{N_1} \right] + \mathcal{R}_2 \left[1 - \frac{S_{2\infty}}{N_2} \right] \right).$$

Project 1: Heterogeneous mixing and indirect transmission with residence time

2-Patch SIRP model with residence time:

$$\begin{cases} S_1' = -\beta_1 p_{11} S_1(p_{11}P_1 + p_{21}P_2) - \beta_2 p_{12} S_1(p_{12}P_1 + p_{22}P_2), \\ I_1' = \beta_1 p_{11} S_1(p_{11}P_1 + p_{21}P_2) + \beta_2 p_{12} S_1(p_{12}P_1 + p_{22}P_2) - \alpha I_1, \\ R_1' = \alpha I_1, \\ P_1' = r_1 I_1 - \delta P_1, \end{cases}$$

$$\begin{cases} S_2' = -\beta_1 p_{21} S_2(p_{11}P_1 + p_{21}P_2) - \beta_2 p_{22} S_2(p_{12}P_1 + p_{22}P_2), \\ I_2' = \beta_1 p_{21} S_2(p_{11}P_1 + p_{21}P_2) + \beta_2 p_{22} S_2(p_{12}P_1 + p_{22}P_2) - \alpha I_2, \\ R_2' = \alpha I_2, \\ P_2' = r_2 I_2 - \delta P_2, \end{cases}$$

Assumptions:

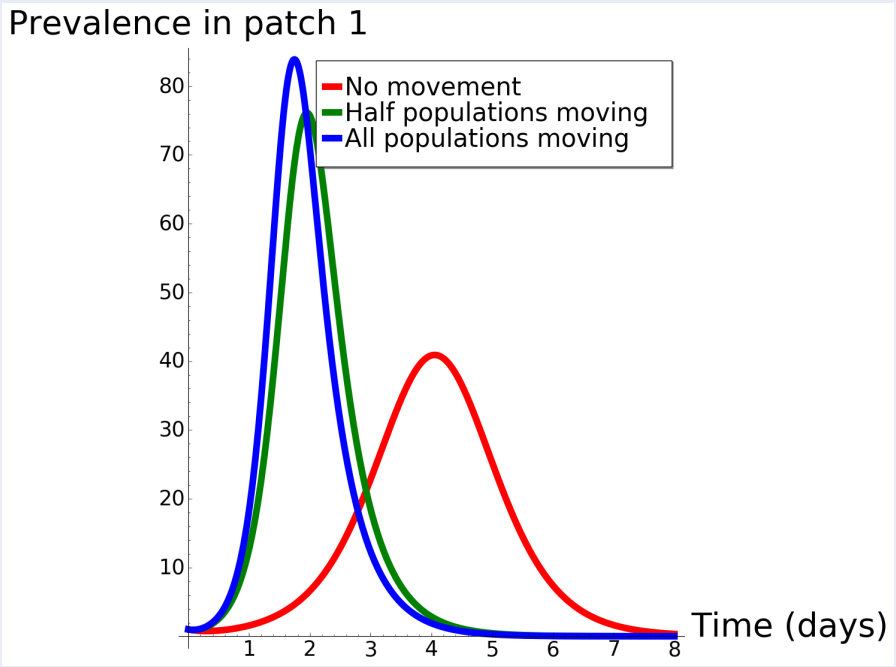
- $\beta_2 > \beta_1$, with short term travel between the two patches.
- $p_{ij}(i, j = 1, 2) \Longrightarrow$ fraction of contact made by patch i residents in patch j.
- Each patch has $p_{11} + p_{12} = 1$, $p_{21} + p_{22} = 1$.

Project 1: Numerical simulations

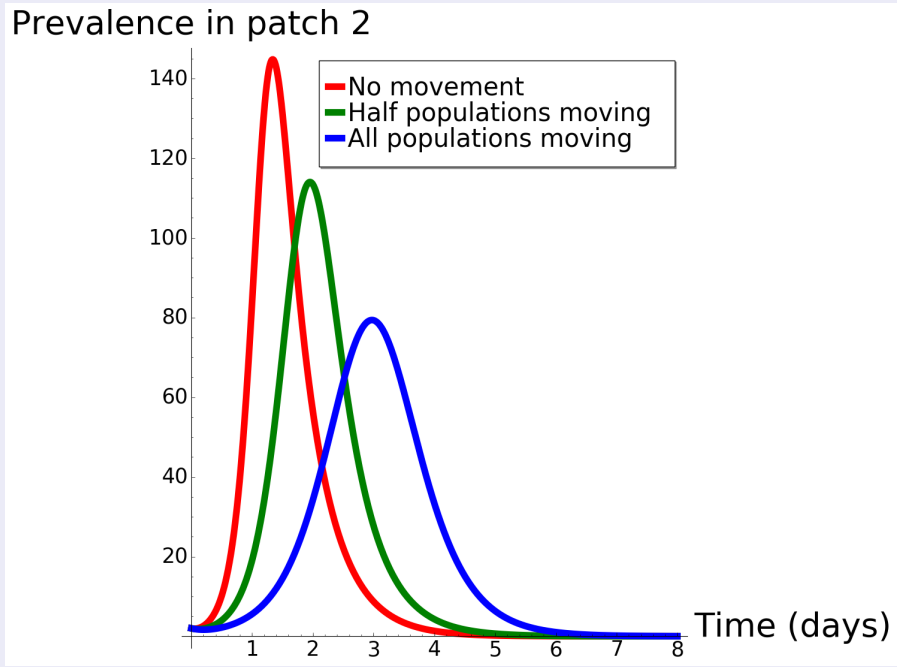
Assumptions:

- Each patch has $p_{11} + p_{12} = 1$, $p_{21} + p_{22} = 1$.

2-Patch SIRP model simulations:



(a) Infected individuals (I_1) in patch 1.



(b) Infected individuals (I_2) in patch 2.

Figure: *Dynamics of I_1 and I_2 when we vary $p_{11}, p_{12}, p_{21}, p_{22}$.*

Coupled PDE-ODE model with indirect transmission

Project 2: Background & Research Questions

Airborne disease:

any disease caused by pathogens and transmitted through the air. E.g. **Chickenpox, Influenza, Measles, Smallpox, Tuberculosis**.

Questions:

- *Can we estimate the impact of diffusion using an ODE model?*
- *How worst is the epidemic with increase or decrease in the diffusion rate?*
- *What is the effect of the patch location on the spread of infection?*

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Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/MBE

Mathematical Biosciences and Engineering, 5(x): xxx–xxx
DOI:
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Published: ...

Research article

A novel approach to modelling the spatial spread of airborne diseases: an epidemic model with indirect transmission

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[2] Interdisciplinary Studies, University of British Columbia, Vancouver, B.C., Canada.

Project 2: Model Formulation

The spatio-temporal density of pathogens $\mathcal{P}(\boldsymbol{X}, T)$ satisfies the partial differential equation (PDE) given by

$$\frac{\partial \mathcal{P}}{\partial T} = D_B \, \Delta \, \mathcal{P} - \delta \, \mathcal{P}, \quad T > 0, \quad \boldsymbol{X} \in \Omega \setminus \cup_{j=1}^{m} \Omega_j;$$

$$\partial_{n_{\boldsymbol{X}}} \mathcal{P} = 0, \quad \boldsymbol{X} \in \partial\Omega; \quad D_B \, \partial_{n_{\boldsymbol{X}}} \mathcal{P} = -r_j \, \mathcal{I}_j, \quad \boldsymbol{X} \in \partial\Omega_j, \quad j = 1, \ldots, m,$$

Dimensional Parameters:

1. $D_B > 0$ *denotes the diffusion rate of pathogens in the bulk region,*
2. δ *the dimensional decay rate of pathogens,*
3. $r_j > 0$ *the dimensional shedding rate of pathogen by an infected individual in the* j^{th} *patch,*
4. $\partial_{n_{\boldsymbol{X}}}$ *the outward normal derivative on the boundary of the domain* Ω.

Project 2: Model Formulation

The dynamics of the diffusing pathogens is coupled to the population dynamics of the j^{th} patch using:

Integro-differential system of equations:

$$\frac{d\mathcal{S}_j}{dT} = -\mu_j \mathcal{S}_j \int_{\partial\Omega_j} (\mathcal{P}/p_c)\ \mathrm{d}S_{\boldsymbol{X}};$$

$$\frac{d\mathcal{I}_j}{dT} = \mu_j \mathcal{S}_j \int_{\partial\Omega_j} (\mathcal{P}/p_c)\ \mathrm{d}S_{\boldsymbol{X}} - \alpha_j \mathcal{I}_j;$$

$$\frac{d\mathcal{R}_j}{dT} = \alpha_j \mathcal{I}_j, \qquad j = 1, \ldots, m,$$

Project 2: Dimensionless coupled model

The dimensionless density of the pathogens $P(\boldsymbol{x}, t)$ satisfies

$$\frac{\partial P}{\partial t} = D\,\Delta\, P - \ P, \quad t > 0, \quad \boldsymbol{x} \in \Omega \setminus \cup_{j=1}^{m} \Omega_{\varepsilon j};$$

$$\partial_{n_{\boldsymbol{x}}} P = \ 0, \quad \boldsymbol{x} \in \partial\Omega; \quad 2\pi\varepsilon D\, \partial_{n_{\boldsymbol{x}}} P = -\sigma_j\, I_j, \quad \boldsymbol{x} \in \partial\Omega_{\varepsilon j}, \quad j = 1, \ldots, m,$$

which is coupled to the dimensionless SIR dynamics of the j^{th} patch

$$\frac{dS_j}{dt} = -\frac{\beta_j S_j}{2\pi\varepsilon} \int_{\partial\Omega_{\varepsilon j}} P \ \mathrm{d}s_{\boldsymbol{x}};$$

$$\frac{dI_j}{dt} = \frac{\beta_j S_j}{2\pi\varepsilon} \int_{\partial\Omega_{\varepsilon j}} P \ \mathrm{d}s_{\boldsymbol{x}} - \phi_j I_j;$$

$$\frac{dR_j}{dt} = \phi_j I_j, \qquad j = 1, \ldots, m,$$

where β_j, σ_j and ϕ_j are the dimensionless transmission, shedding and recovery rates for the j^{th} patch, respectively.

Project 2: Reduced ODE model

In the limit $D = D_0/\nu,\ \nu = -1/\log(\varepsilon),\ \varepsilon \ll 1$, where $D_0 = \mathcal{O}(1)$, the coupled PDE-ODE model is reduced to an ODE system.

Leading-order ODE model:

$$\frac{dp}{dt} = -p + \frac{1}{|\Omega|}\sum_{j=1}^{m} \sigma_j\, I_j,$$

$$\frac{dS_j}{dt} = -\beta_j S_j \left(p(t) + \frac{\sigma_j\, I_j}{2\pi D_0}\right), \qquad j = 1\ldots, m\,,$$

$$\frac{dI_j}{dt} = \beta_j S_j \left(p(t) + \frac{\sigma_j\, I_j}{2\pi D_0}\right) - \phi_j I_j, \qquad j = 1, \ldots, m\,,$$

$$\frac{dR_j}{dt} = \phi_j I_j, \qquad j = 1, \ldots, m.$$

Basic reproduction number: $\mathcal{R}_0 = \mathcal{R}_\star + \mathcal{R}_D$

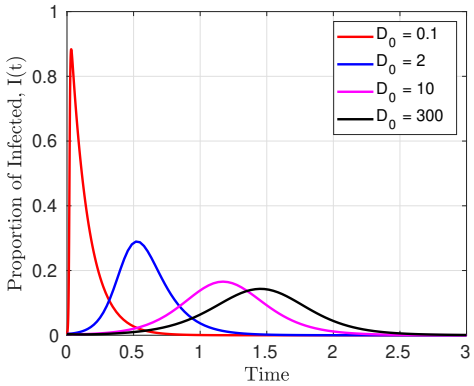
$$\mathcal{R}_\star = \frac{\beta N(0)\sigma}{\phi|\Omega|}, \text{ and } \mathcal{R}_D = \frac{\beta N(0)\sigma}{2\phi\pi D_0}$$

$\mathcal{R}_\star$ & $\mathcal{R}_D \Longrightarrow$ *secondary infections contributed by indirect transmission and diffusion respectively.*

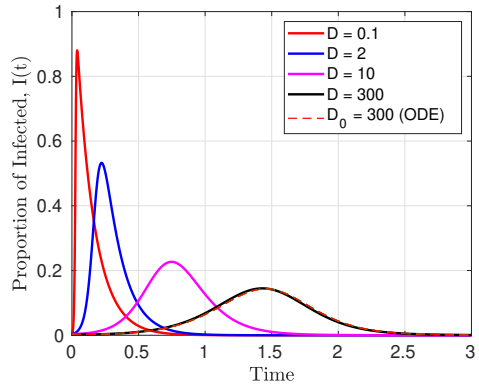
The final size relation:

$$\log \frac{S_0}{S_\infty} = \mathcal{R}_\star \left\{1 - \frac{S_\infty}{N}\right\} + \mathcal{R}_D \left\{1 - \frac{S_\infty}{N}\right\} = \mathcal{R}_0 \left\{1 - \frac{S_\infty}{N}\right\}.$$

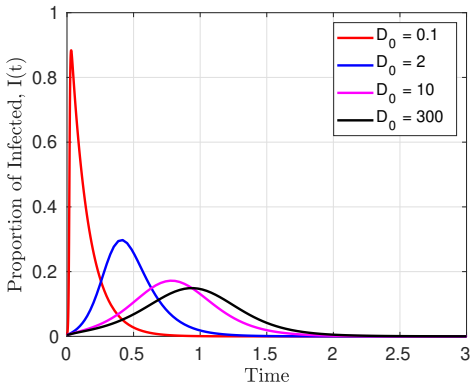
Project 2: Numerical Simulations (one-patch)



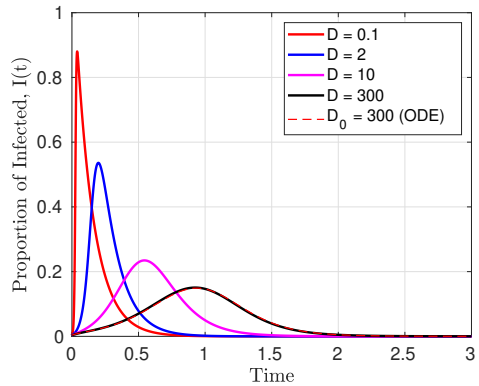
(a) Reduced ODE



(b) Coupled PDE-ODE



(c) Reduced ODE

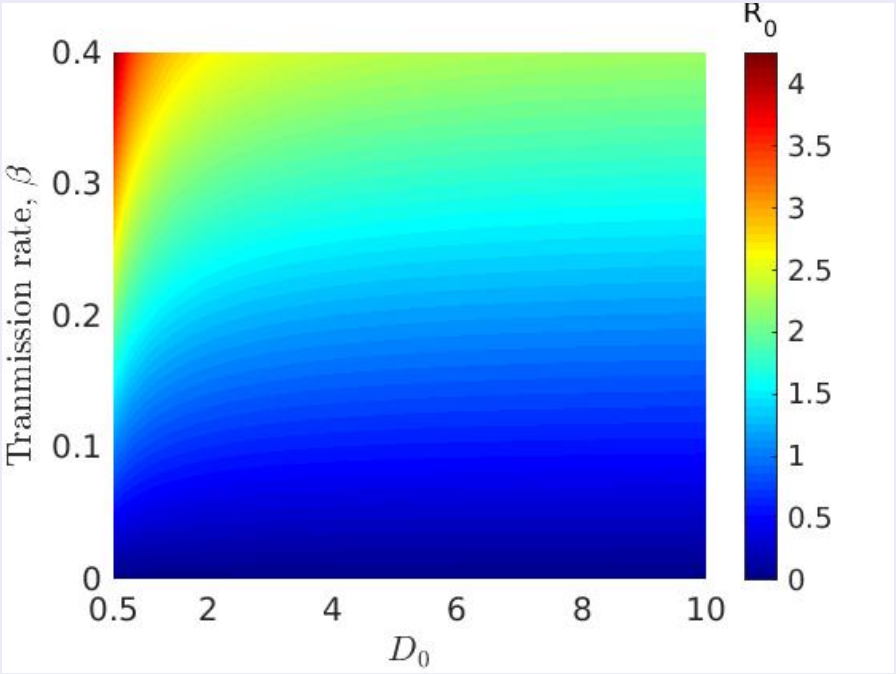


(d) Coupled PDE-ODE

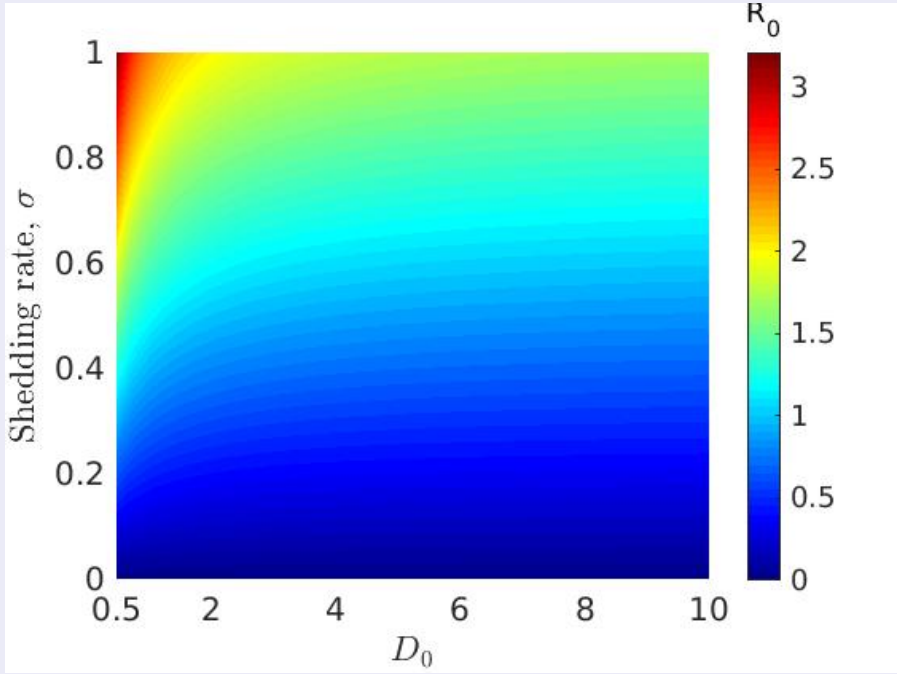
Figure: *(a) & (b) ODE & coupled PDE-ODE with* $(S(0), I(0), R(0)) = (249/250, 1/250, 0)$ *and* $p(0) = P(0) = 0$. *(c) & (d) ODE & coupled PDE-ODE with* $(S(0), I(0), R(0)) = (249/250, 1/250, 0)$ *and* $p(0) = P(0) = 1$.

Project 2: Numerical Simulations (one-patch)

Surface plots:



(a)



(b)

Figure: *Surface plots of the basic reproduction number $\mathcal{R}_0$ with respect to the diffusion rate of pathogens D_0 and transmission rate, and shedding rate. (a) D_0 and the transmission rate β, while (b) D_0 and the shedding rate σ.*

Project 2: Two-Patch model

Basic reproduction number: $\mathcal{R}_0^\infty = \beta_1\mathcal{R}_1 + \beta_2\mathcal{R}_2$

In the well-mixed limit $D_0 \gg 1$, *the* **basic reproduction number** $\mathcal{R}_0$ *for the two-patch model reduces to*

$$\mathcal{R}_0^\infty = \frac{\beta_1 N_1(0)\sigma_1}{\phi_1|\Omega|} + \frac{\beta_2 N_2(0)\sigma_2}{\phi_2|\Omega|}.$$

$\mathcal{R}_1 = \dfrac{N_1(0)\sigma_1}{\phi_1|\Omega|}$, and $\mathcal{R}_2 = \dfrac{N_2(0)\sigma_2}{\phi_2|\Omega|}$

$\mathcal{R}_1$ & $\mathcal{R}_2 \Longrightarrow$ *secondary infections contributed by patch* 1 *and* 2 *respectively.*

Project 2: Two-Patch model

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$$\mathcal{R}_1 = \frac{N_1(0)\sigma_1}{\phi_1|\Omega|}, \text{ and } \mathcal{R}_2 = \frac{N_2(0)\sigma_2}{\phi_2|\Omega|}$$

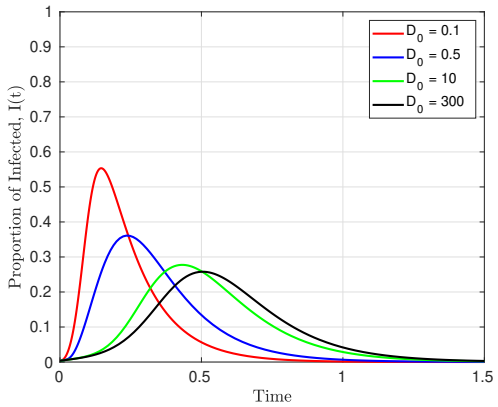
$\mathcal{R}_1$ *&* $\mathcal{R}_2 \Longrightarrow$ *secondary infections contributed by patch* 1 *and* 2 *respectively.*

The final size relation:

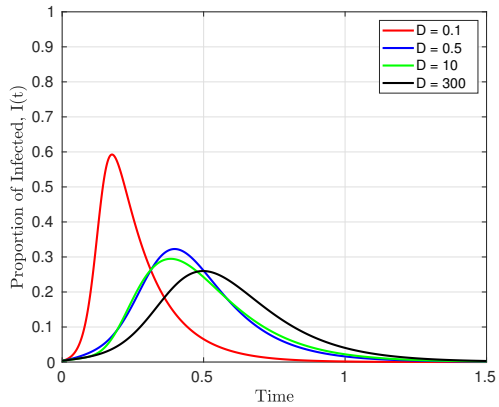
$$\log\frac{S_{10}}{S_{1\infty}} = \beta_1\Big(\mathcal{R}_1\Big\{1-\frac{S_{1\infty}}{N_1(0)}\Big\} + \mathcal{R}_2\Big\{1-\frac{S_{2\infty}}{N_2(0)}\Big\} + \frac{\sigma_1 N_1(0)}{2\pi\phi_1 D_0}\Big\{1-\frac{S_{1\infty}}{N_1(0)}\Big\}\Big),$$

$$\log\frac{S_{20}}{S_{2\infty}} = \beta_2\Big(\mathcal{R}_1\Big\{1-\frac{S_{1\infty}}{N_1(0)}\Big\} + \mathcal{R}_2\Big\{1-\frac{S_{2\infty}}{N_2(0)}\Big\} + \frac{\sigma_2 N_2(0)}{2\pi\phi_2 D_0}\Big\{1-\frac{S_{2\infty}}{N_2(0)}\Big\}\Big).$$

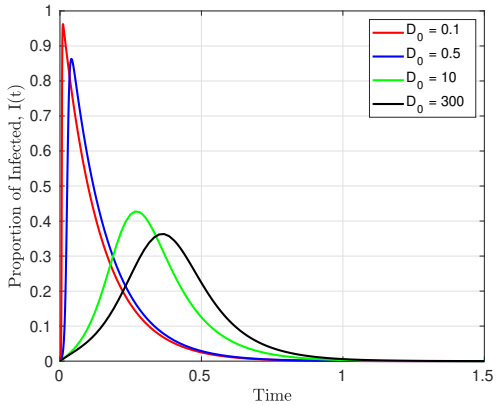
Project 2: Two-patch Numerical Simulation



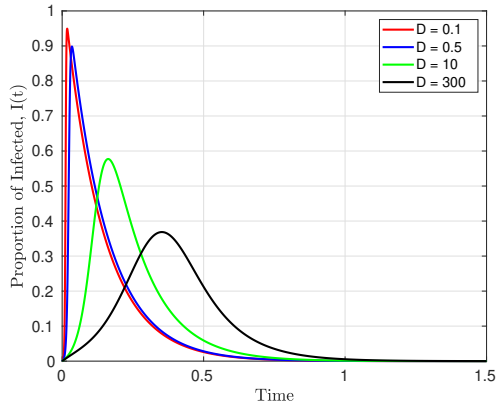
(a) Patch 1 ODE



(b) Patch 1 PDE-ODE



(c) Patch 2 ODE



(d) Patch 2 PDE-ODE

Figure: *Patch 1 ((a) & (b)) and Patch 2 ((c) & (d)) with* $(S_1(0), I_1(0), R_1(0)) = (299/300, 1/300, 0)$, $(S_2(0), I_2(0), R_2(0)) = (250/250, 0, 0)$, *and* $p(0) = 1$ *and* $P(0) = 1$ *for the diffusing pathogens.*

PART A: Summary (Projects 1 & 2)

1. *SIRP model was proposed*
2. *The model explored the impact of age of infections, varying the pathogen shedding rates and human mobility*
3. *The SIRP model in Project 1 was improved by proposing a coupled PDE-ODE models which includes diffusion of pathogens*
4. *The coupled PDE-ODE model was reduced to an ODE system, which was used to compute $\mathcal{R}_0$ and the final size relation*

PART A: Summary (continue...)

1. *PDE-ODE model numerically agreed with the reduced ODE*
2. *Both model predicted a decrease in the epidemic as the diffusion rate of pathogens increases*
3. *Diffusion is important when modelling airborne diseases, and some diseases may be difficult to control if overlooked*
4. *Individuals infected through indirect transmission medium in an heterogeneous mixing populations, which had been omitted in some other previous works is worth taking into account.*

PART A: Future work (Projects 1 & 2)

Can we obtain more credible estimates of the final epidemic sizes if we

- *incorporate human mobility between patches?*
- *incorporate multiple class of hosts and sources in order to compare disease spread among different populations and viruses.*

Explore model behaviour when vaccination and treatment are involved:

- *reduce contact rates?*
- *lower $\mathcal{R}_0$?*
- *decrease the final epidemic size?*

Can we use this novel approach to model the dynamics of mosquito-borne diseases (malaria, dengue, ...) where mosquitoes diffuse in the air?

HIV/Syphilis co-interaction model gbMSM

HIV/Syphilis co-interaction model gbMSM

Background:

1. *The population of gay, bisexual and other men who have sex with men (gbMSM) remain the most affected by HIV infection in BC*
2. *Majority of infectious syphilis cases (over 80% of all cases) in BC were among gbMSM*
3. *Currently, TasP, Condom use, and PrEP have been highly effective for HIV prevention and control in gbMSM*
4. *Similarly, Condom use, Test & Treat diagnosed cases of syphilis have also been effective*

Project 3: Background

- **PREVIOUS RESEARCH:**

Bull Math Biol (2018) 80:437–492
https://doi.org/10.1007/s11538-017-0384-0

Society for Mathematical Biology

CrossMark

ORIGINAL RESEARCH

Mathematical Analysis of the Transmission Dynamics of HIV Syphilis Co-infection in the Presence of Treatment for Syphilis

A. Nwankwo[1] · D. Okuonghae[1]

Project 3: Background

- **PREVIOUS RESEARCH:**

Bull Math Biol (2018) 80:437–492
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Society for Mathematical Biology

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ORIGINAL RESEARCH

Mathematical Analysis of the Transmission Dynamics of HIV Syphilis Co-infection in the Presence of Treatment for Syphilis

A. Nwankwo[1] · D. Okuonghae[1]

- **MY WORK:**

A co-interaction model of HIV and syphilis infection among gay, bisexual and other men who have sex with men

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Project 3: Research Questions & Population

Research question:

- *How does syphilis epidemic affect HIV prevalence and vice versa?*
- *What is the impact of a change in transmission rate on disease dynamics?*
- *Can we test and treat mono-infected individuals more to reduce disease prevalences?*

Project 3: Research Questions & Population

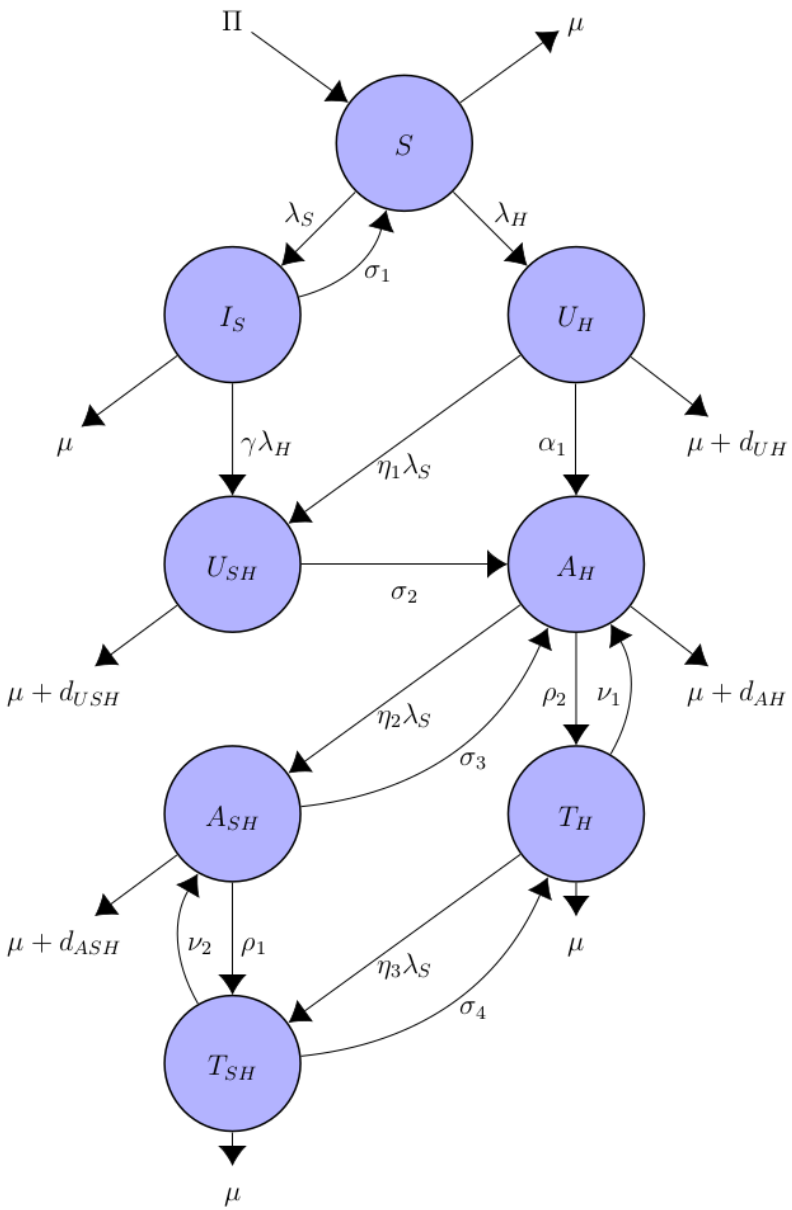
Research question:

- *How does syphilis epidemic affect HIV prevalence and vice versa?*
- *What is the impact of a change in transmission rate on disease dynamics?*
- *Can we test and treat mono-infected individuals more to reduce disease prevalences?*

Study population:

- *Gay, bisexual and other men who have sex with men (gbMSM)*
- *Co-interaction of HIV and Syphilis*
- *Testing and treament*

Project 3: HIV/Syphilis Flow Diagram



Force of infection associated with HIV infection:

$$\lambda_H = \beta_H \frac{(U_H + \kappa_1 A_H + \kappa_2 U_{SH} + \kappa_3 A_{SH})}{N}$$

Force of infection associated with syphilis infection:

$$\lambda_S = \beta_S \frac{(I_S + \phi_1 U_{SH} + \phi_2 A_{SH} + \phi_3 T_{SH})}{N}$$

Project 3: HIV & Syphilis sub-models

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Pi - (\mu + \lambda_H)S, \\ \dfrac{\mathrm{d}U_H}{\mathrm{d}t} = \lambda_H S - (\mu + d_{UH} + \alpha_1)U_H, \\ \dfrac{\mathrm{d}A_H}{\mathrm{d}t} = \alpha_1 U_H + \nu_1 T_H - (\mu + d_{AH} + \rho_2)A_H, \\ \dfrac{\mathrm{d}T_H}{\mathrm{d}t} = \rho_2 A_H - (\mu + \nu_1)T_H, \end{cases}$$

$$\text{where} \quad \lambda_H = \beta_H \frac{(U_H + \kappa_1 A_H)}{N_H},$$

with total population given as $N_H(t) = S(t) + U_H(t) + A_H(t) + T_H(t)$.

$$\begin{cases} \dfrac{\mathrm{d}S}{\mathrm{d}t} = \Pi + \sigma_1 I_S - (\mu + \lambda_S)S, \\ \dfrac{\mathrm{d}I_S}{\mathrm{d}t} = \lambda_S S - (\mu + \sigma_1)I_S, \end{cases}$$

$$\lambda_S = \beta_S \frac{I_S}{N_S}, \quad \text{with total population given as} \quad N_S(t) = S(t) + I_S(t)$$

Project 3: Effective reproduction Number

HIV sub-model

$$\mathcal{R}_{eH} = B_U + B_A,$$

$$B_U = \frac{\beta_H}{(\mu + d_{UH} + \alpha_1)},$$

$$B_A = \frac{\beta_H \alpha_1 \kappa_1 (\mu + \nu_1)}{(\mu + d_{UH} + \alpha_1)\left((\mu + \nu_1)(\mu + d_{AH}) + \mu\rho_2\right)}.$$

Project 3: Effective reproduction Number

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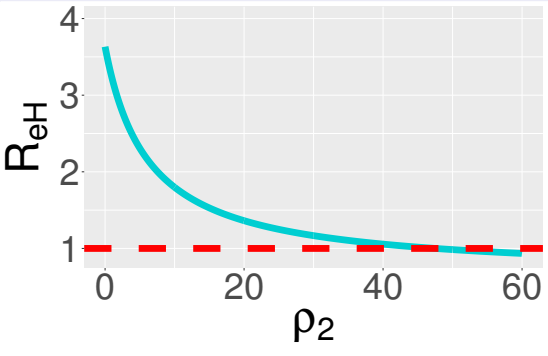
Syphilis sub-model

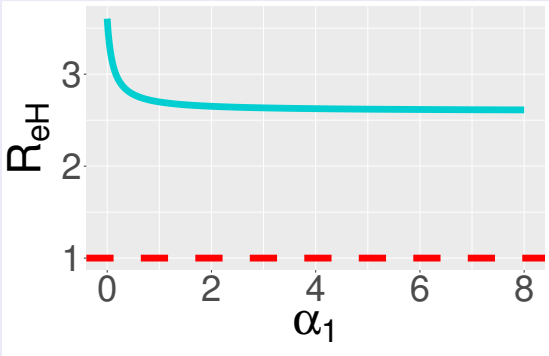
$$\mathcal{R}_{eS} = \frac{\beta_S}{(\mu + \sigma_1)}.$$

- *Mathematically*, the product of the transmission of syphilis infection and the rate that an infective progresses out of syphilis class.
- *Biologically*, the number of syphilis infection produced by one syphilis infective during the period of infectiousness when introduced in a totally syphilis susceptible population.

Project 3: Sensitivity analyses

Sensitivity analysis of $\mathcal{R}_{eH}$:





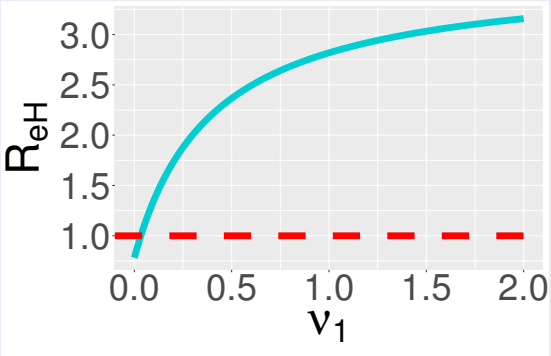


Figure: *Impact of increasing testing rate α_1, treatment rate ρ_2 and rate of increase in treatment failure ν_1 on HIV reproduction number $\mathcal{R}_{eH}$.*

Sensitivity analysis of $\mathcal{R}_{eS}$:

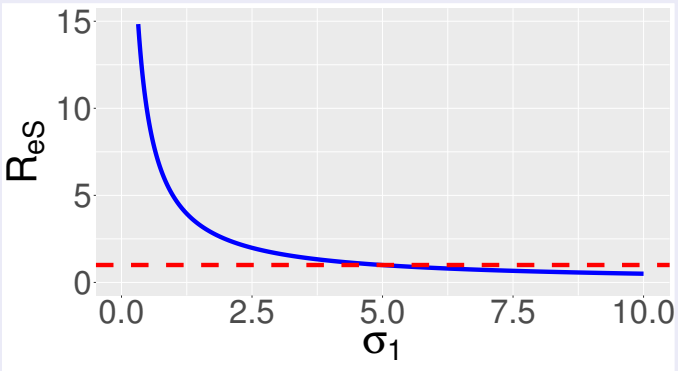


Figure: *Impact of increasing testing and treatment rate σ_1 on syphilis reproduction number $\mathcal{R}_{eS}$.*

Project 3: HIV-syphilis co-interaction model

1. **Disease free equilibrium point (DFE):**

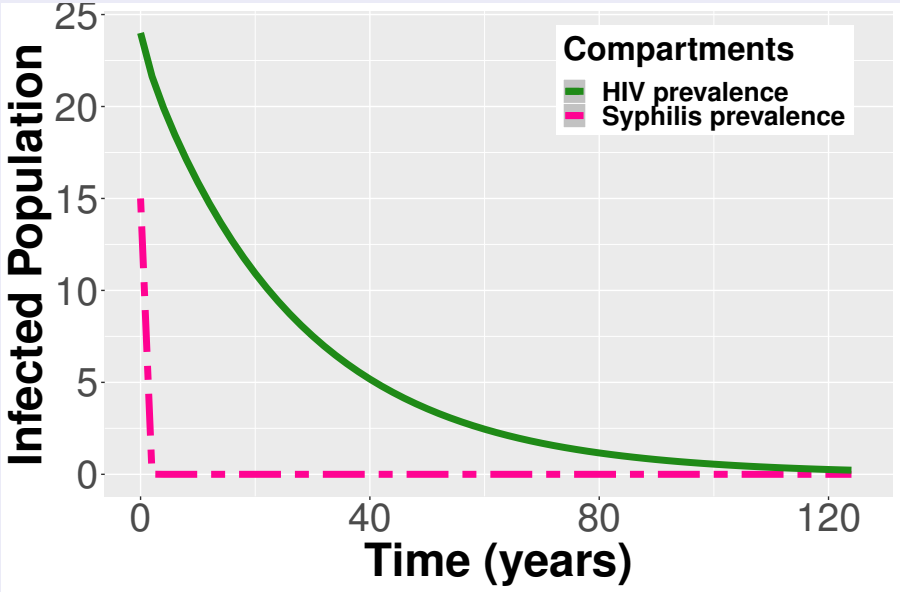
   $E_0 = (S_0, I_{0S}, U_{0H}, A_{0H}, T_{0H}, U_{0SH}, A_{0SH}, T_{0SH}) = \left(\frac{\Pi}{\mu}, 0, 0, 0, 0, 0, 0, 0\right)$.

2. **Effective reproduction Number:** $\mathcal{R}_e = \max\{\mathcal{R}_{eS}, \mathcal{R}_{eH}\}$

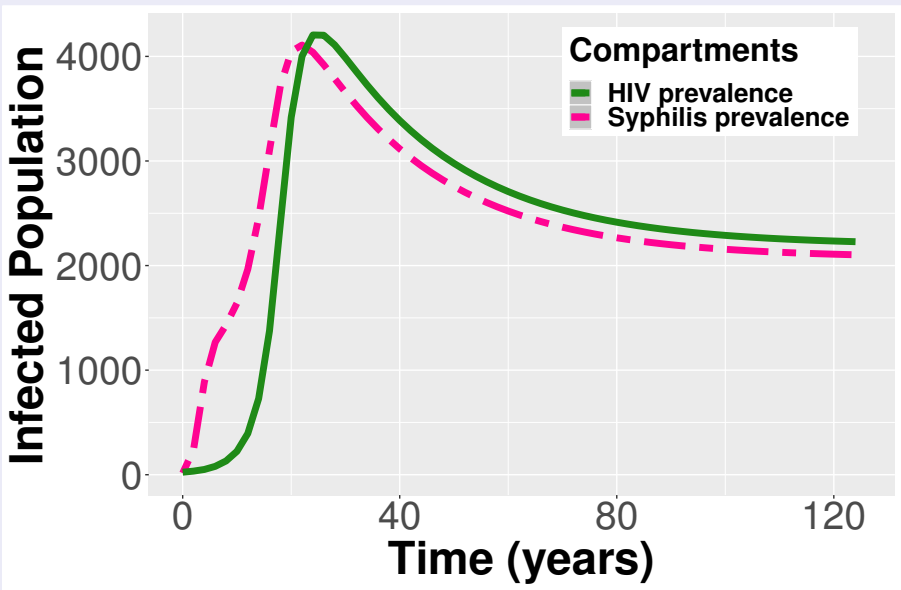
3. **Endemic equilibrium point:**

   - $E_1 = (S1, I_{S1}, 0, 0, 0, 0, 0, 0)$, similar to *HIV free equilibrium* (E_S^*),
   - $E_2 = (S2, 0, U_{H2}, A_{H2}, T_{H2}, 0, 0, 0)$, *syphilis free equilibrium* (E_H^*),
   - $E_3 = (S3, I_{S3}, U_{H3}, A_{H3}, T_{H3}, U_{SH3}, A_{SH3}, T_{SH3})$, *HIV-syphilis co-interaction equilibrium*.

Project 3: Numerical simulations



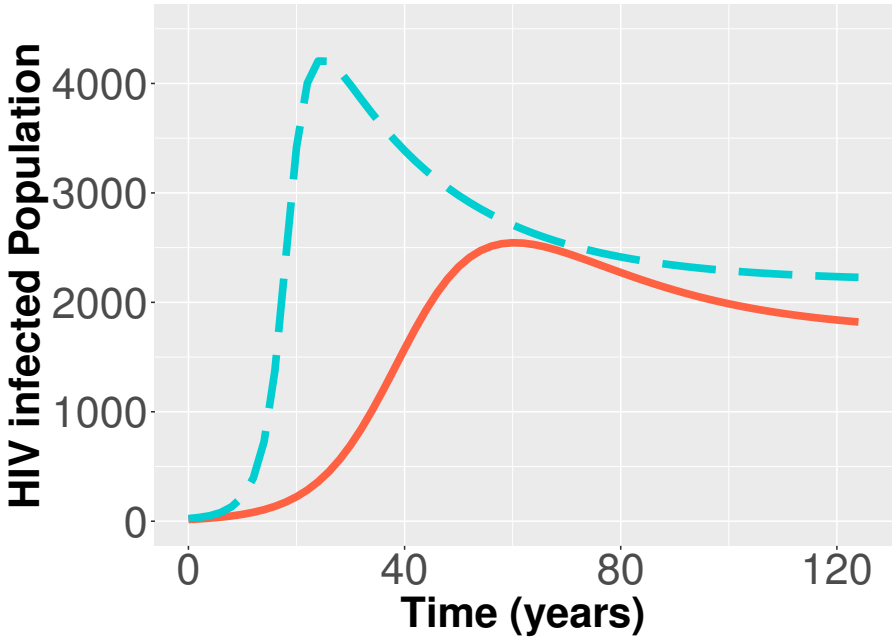
(a) Disease free equilibrium.



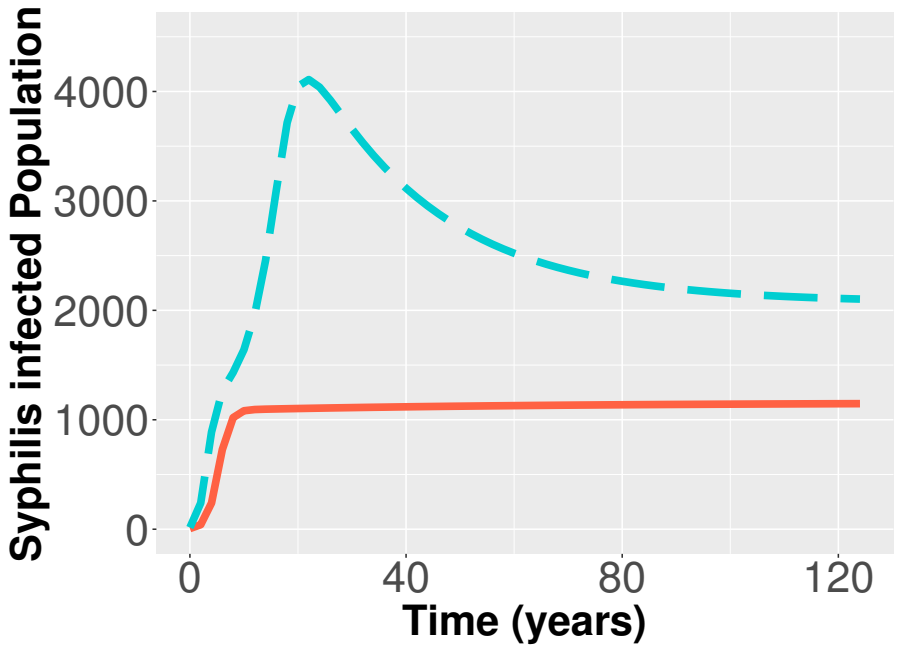
(b) Endemic equilibrium.

Figure: *Number of HIV infected individuals (green) and syphilis infected individuals (red), with different transmission rates and reproduction number:* $\beta_H = 0.02, \beta_S = 0.1, \mathcal{R}_e = 0.139$ *(left);* $\beta_H = 0.4, \beta_S = 5.0, \mathcal{R}_e = 2.780$ *(right)*

Project 3: Prevalence of HIV & syphilis infections



(a) HIV positive individuals



(b) Syphilis positive individuals

Figure: *Prevalence of HIV and syphilis with* $\beta_H = 0.4$ *and* $\beta_S = 5.0$ *(*$\mathcal{R}_{eH} = 2.780 > 1, \mathcal{R}_{eS} = 1.245 > 1, \mathcal{R}_e = 2.780 > 1$*). (a) The prevalence of HIV with syphilis at the initial stage of the epidemic (blue dashed line) and without syphilis (red solid line). (b) The prevalence of syphilis infection with HIV at the initial stage of the epidemic (blue dashed line) and without HIV (red solid line)*

Assessing the combined impact of interventions on HIV and syphilis epidemics among gbMSM in BC: a co-interaction model

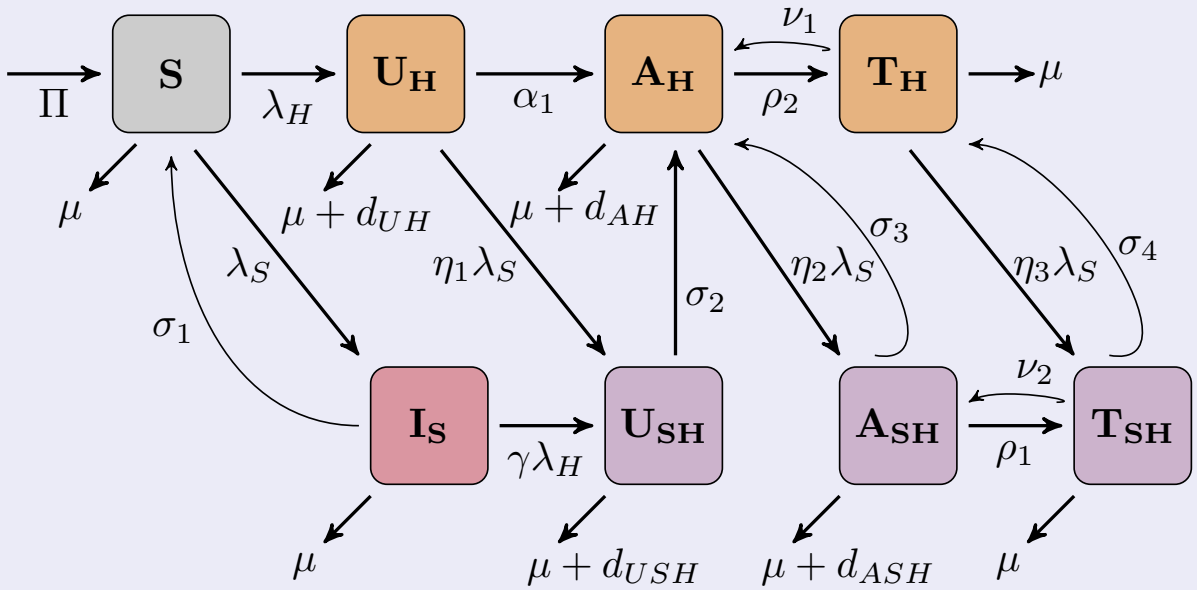
Assessing the combined impact of interventions on HIV and syphilis epidemics among gbMSM in BC: a co-interaction model

Objectives:

1. *To assess how the combination of TasP, Condom use, PrEP, and Test & Treat syphilis can be used to prevent/eliminate HIV and syphilis epidemics among gbMSM in BC.*
2. *To assess the impact of PrEP on the HIV epidemic in BC.*

Project 4: Methods

HIV/syphilis flow diagram:



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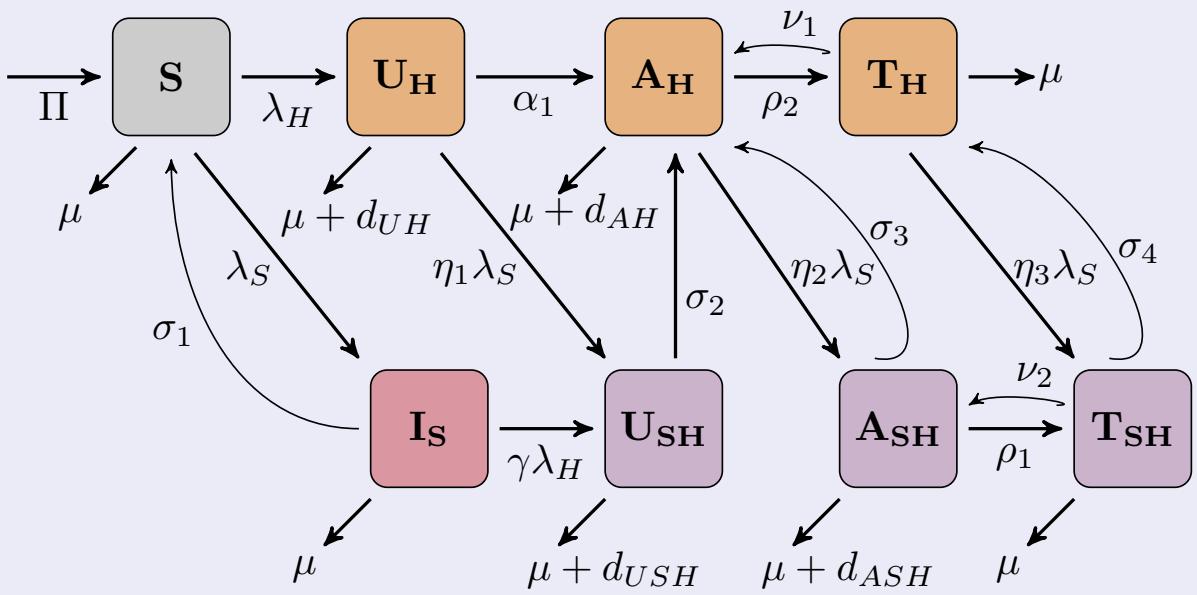


Modeling the force of HIV/syphilis infection:

1. $\lambda_H =$
$$\beta_H(1-\epsilon\xi)((1-\psi)+(1-\theta)\psi R_P)\frac{(U_H+\kappa_1 A_H+\kappa_2 U_{SH}+\kappa_3 A_{SH})}{N}$$
2. $$\lambda_S = \beta_S(1-\epsilon\xi)((1-\psi)+\psi R_P)\frac{(I_S+\phi_1 U_{SH}+\phi_2 A_{SH}+\phi_3 T_{SH})}{N}$$

Project 4: Methods

Transmission parameters fitted and calibrated on:

- *Public Health Agency of Canada (PHAC) estimates of HIV incidence and Prevalence for gbMSM in BC*,
- *Annual HIV diagnoses from HIV Cascade of Care in British Columbia Centre for Excellence in HIV/AIDS (BC-CfE), and*
- *Annual syphilis diagnoses from British Columbia Centre for Disease Control*

Assessed the impact of optimizing:

1. TasP
2. Test & Treat syphilis,
3. Condom use
4. PrEP

Project 4: Methods & Intervention scenarios:

TasP:

- Status Quo: *based on model calibration*
- Intervention according to Low, Medium and High:
  1. *decreasing the time to HIV diagnosis*
  2. *decreasing time to antiretroviral (ART) treatment*
  3. *increasing the time retained on ART*

Test & Treat syphilis:

- Status Quo: *based on model calibration*
- Intervention according to Low, Medium and High:
  1. *decreasing the time from syphilis infection to treatment*

PrEP:

- Status Quo: *4000*
- Intervention: *linearly increases to maximum PrEP uptake in 2028 according to Low: 5000; Medium: 7000; High: 10,000*

Project 4: Methods & Intervention scenarios:

Condom use(%):

- Status Quo: *65*
- Intervention: *linearly increases to maximum condom use in 2028 according to Low: 70; Medium: 75; High: 80*

Project 4: Methods & Intervention scenarios:

Condom use(%):

- Status Quo: *65*
- Intervention: *linearly increases to maximum condom use in 2028 according to Low: 70; Medium: 75; High: 80*

Impact of interventions at the end of 10 years measured on:

1. *HIV point prevalence, HIV and syphilis incident cases*
2. *All-cause mortality cases among PLWH*
3. *WHO threshold for disease elimination as a public health concern*
4. *univariate sensitivity coefficients for HIV and syphilis incidence changes under three PrEP uptake, TasP and Test & Treat scenarios at the end of 2028*
5. *percent change in the number of cumulative HIV and syphilis incident cases with respect to the Status Quo scenario from 2019 to 2028.*

Project 4: Model outcomes

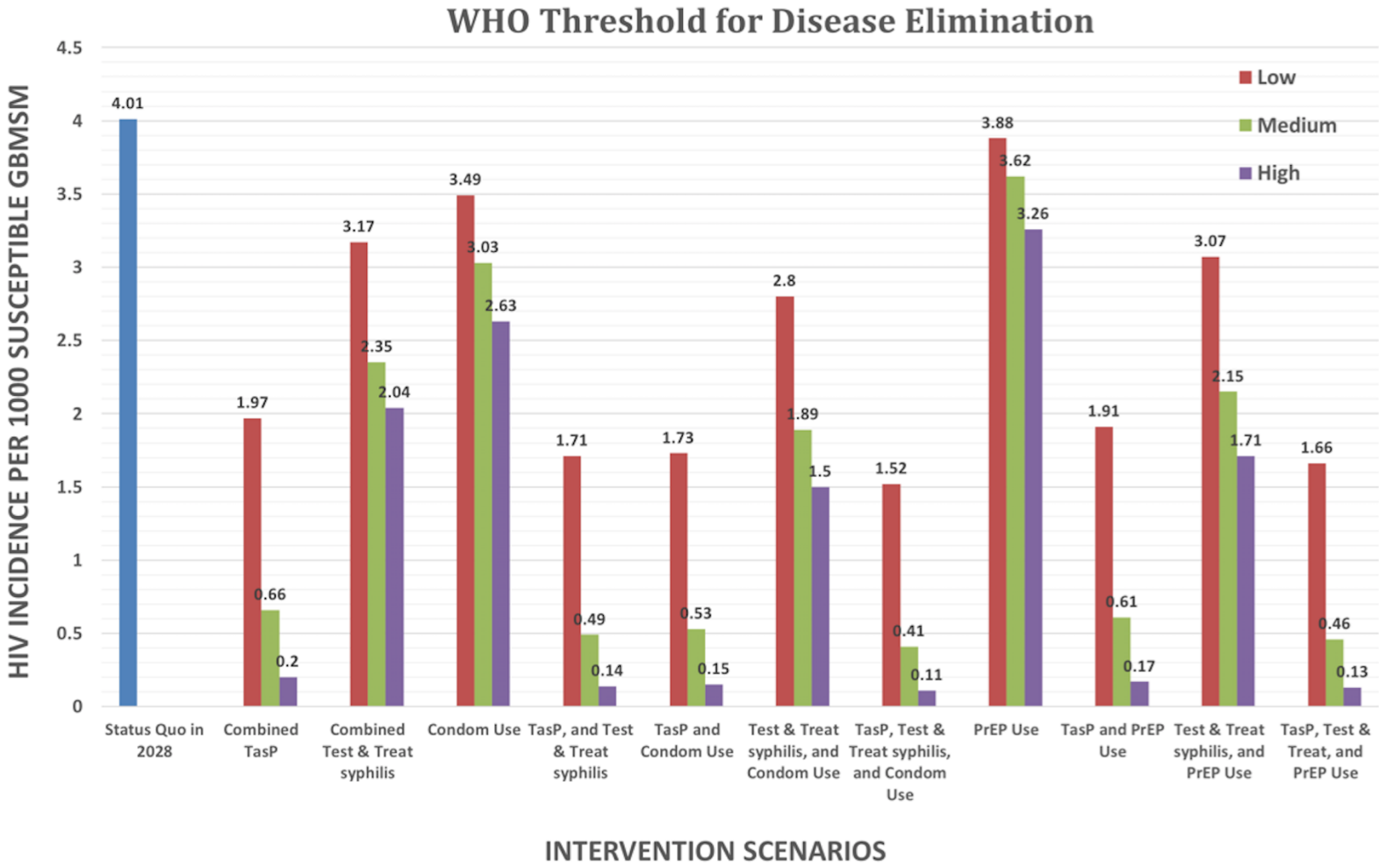


Figure: *HIV incidence rate under different intervention scenarios in comparison to the WHO threshold for disease elimination as a public health concern at the end of* 2028

Project 4: Model outcomes

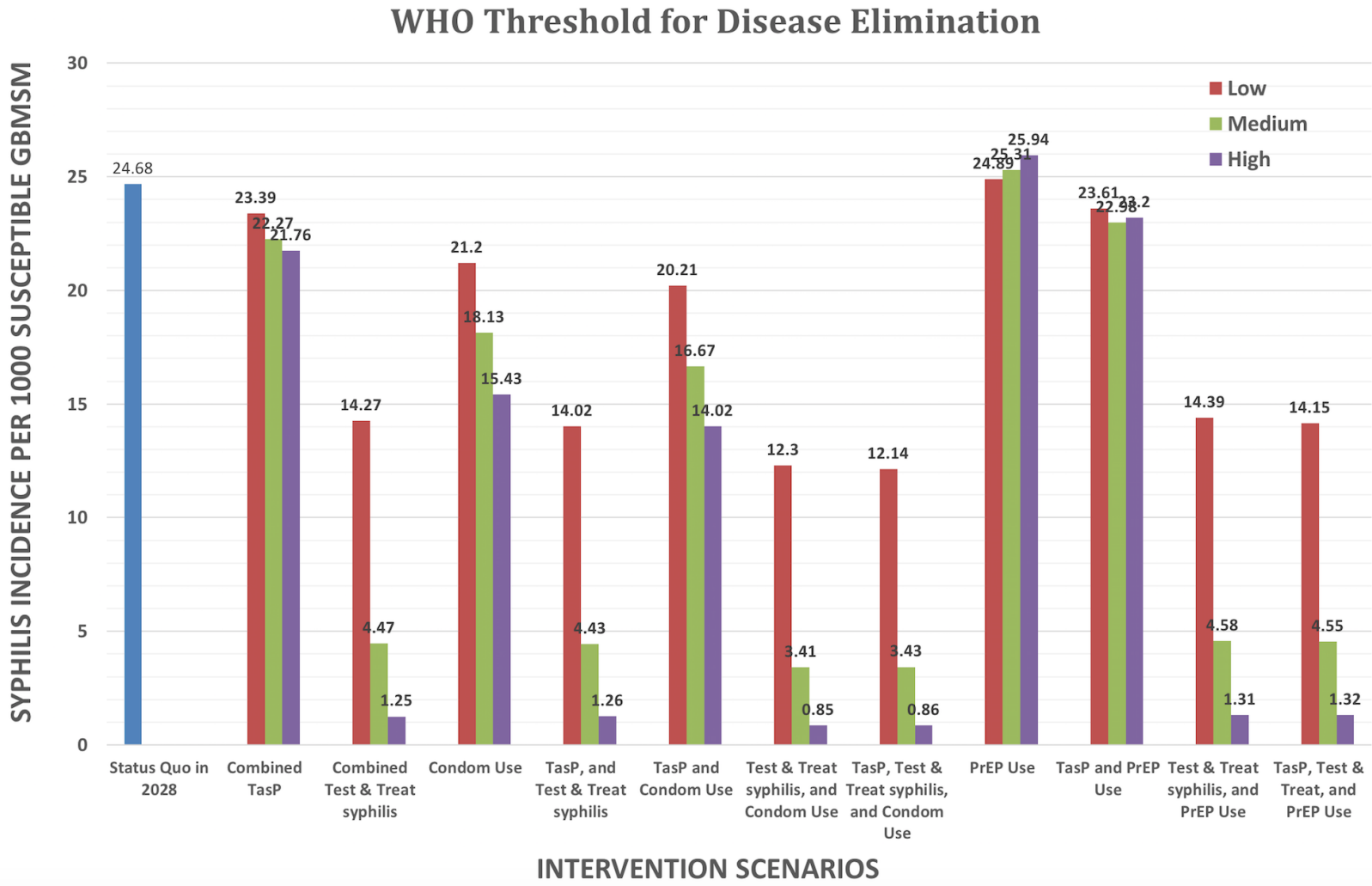
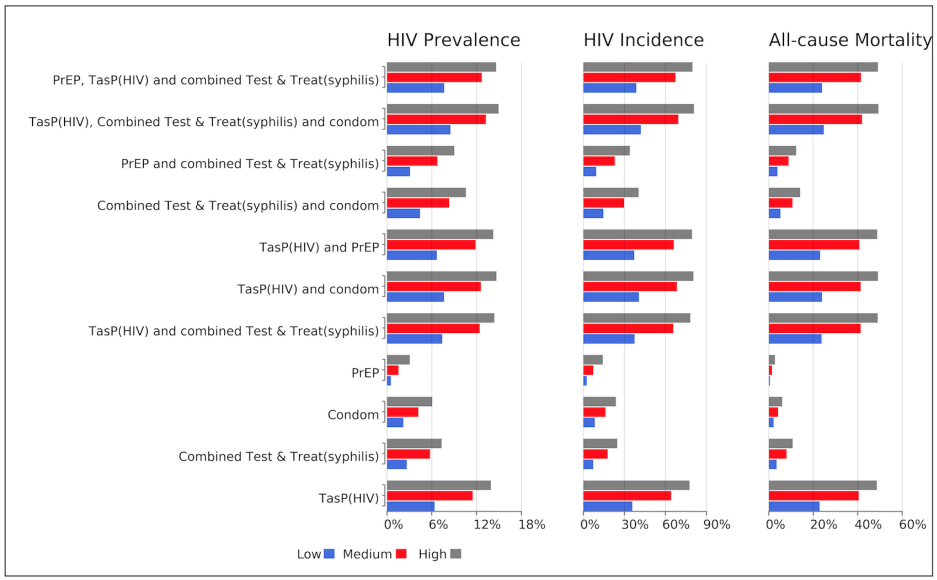
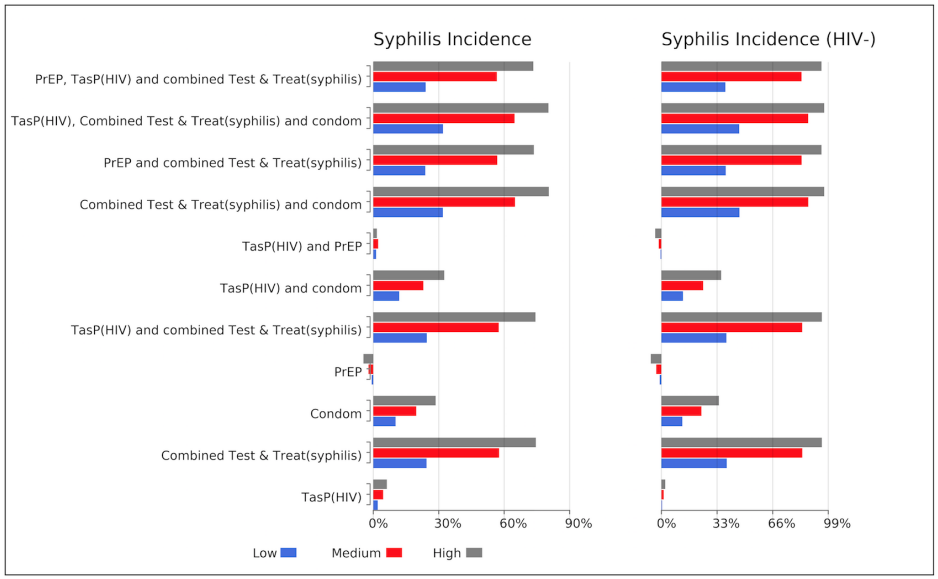


Figure: *Syphilis incidence rate under different intervention scenarios in comparison to the WHO threshold for disease elimination as a public health concern at the end of 2028*

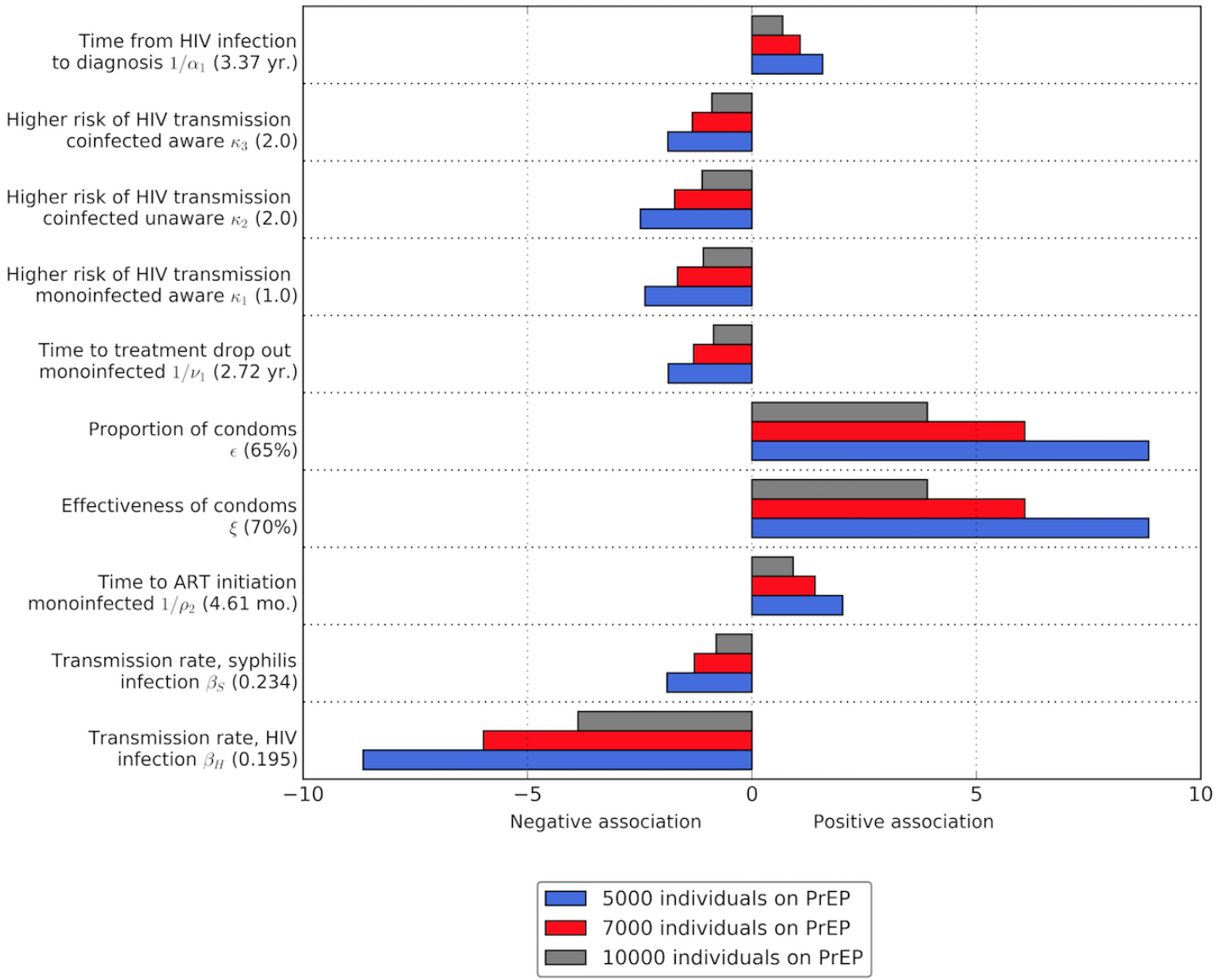
Paper 4: Model outcomes

Reduction in HIV point prevalence, the cumulative number of HIV incident cases, and all-cause mortality cases among PLWH (left), and the cumulative number of syphilis incident cases (right), among gbMSM after 10 years of TasP, PrEP, condom use, and Test & Treat (syphilis) interventions

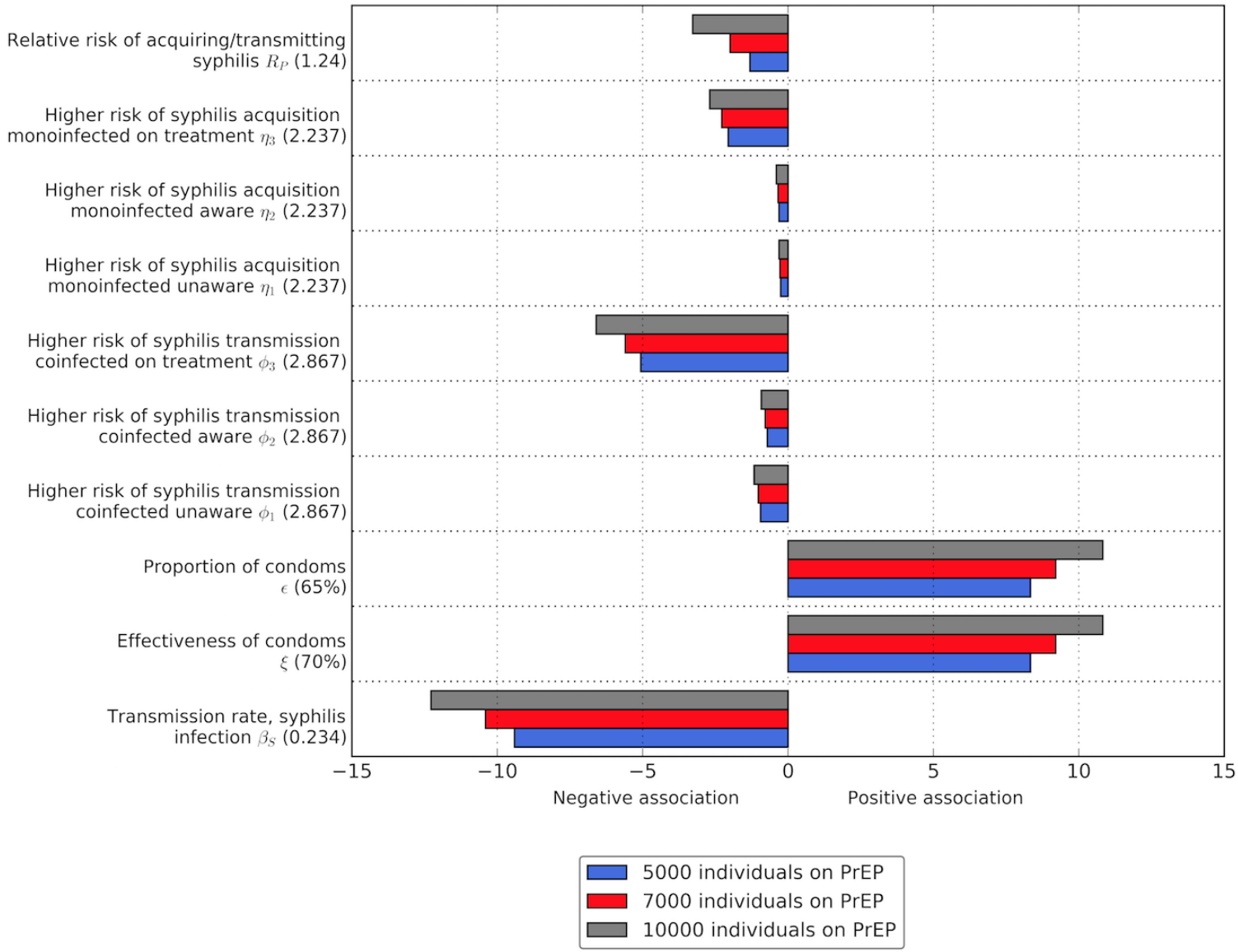




Project 4: Sensitivity Analysis (HIV Incidence)

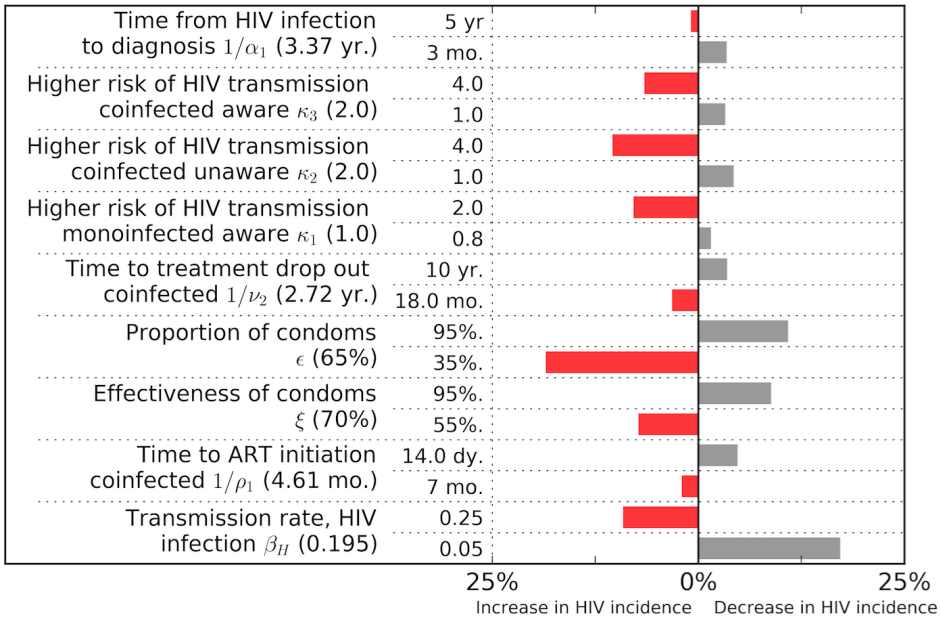


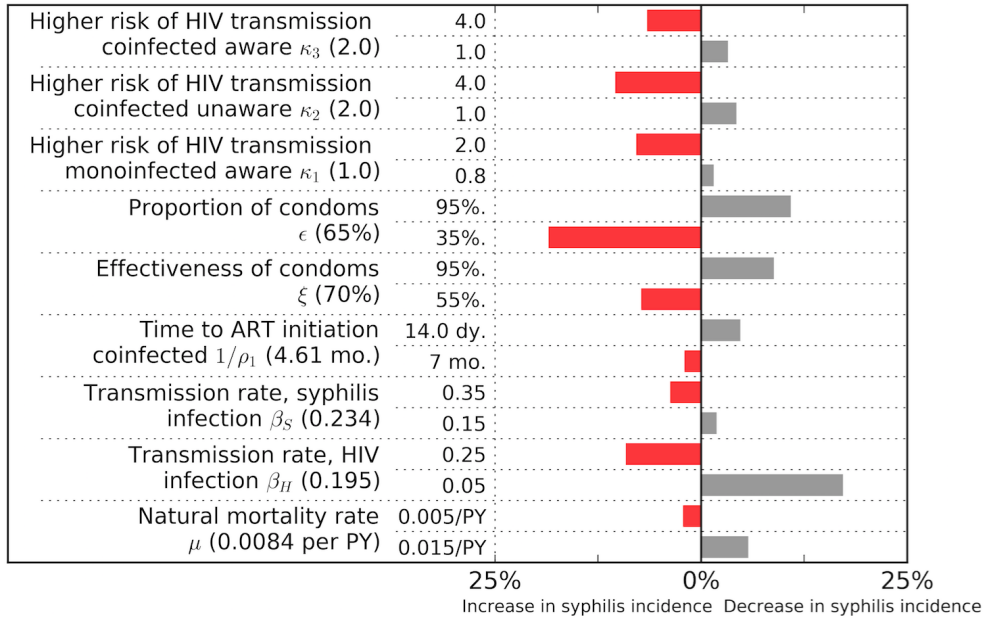
Project 4: Sensitivity Analysis (Syphilis Incidence)



Project 4: Sensitivity Analysis

Sensitivity analysis for the parameters with the most uncertainty based on the available literature. Left: *Percent change in the cumulative number of HIV incident cases* in comparison to the Status Quo at the end of 2028; Right: *Percent change in the cumulative number of syphilis incident cases* in comparison to the Status Quo at the end of 2028





PART B: Summary (Projects 3 & 4)

Analytical & numerical results:

- disease-free equilibra are locally and globally asymptotically stable whenever $\mathcal{R}_e$ (i.e $\mathcal{R}_{eS}$ & $\mathcal{R}_{eH}$)< 1 .
- endemic equilibra are locally and globally asymptotically stable whenever $\mathcal{R}_e$ (i.e $\mathcal{R}_{eS}$ & $\mathcal{R}_{eH}$)> 1 .
- Stable HIV free endemic equilibra whenever $\mathcal{R}_{eS} > 1$ & $\mathcal{R}_{eH} < 1$.
- Stable syphilis free endemic equilibra whenever $\mathcal{R}_{eS} < 1$ & $\mathcal{R}_{eH} > 1$.

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- Stable syphilis free endemic equilibra whenever $\mathcal{R}_{eS} < 1$ & $\mathcal{R}_{eH} > 1$.

- increasing σ_1 decreases $\mathcal{R}_{eS}$ below unity (possiblity of eradicating syphilis among mono-infected individuals).
- increasing ρ_2, α_1, ν_1 decreases $\mathcal{R}_{eH}$, but not below unity.
- HIV infection increases syphilis prevalence and vice versa (one of the possible ways).

PART B: Summary (Projects 3 & 4)

1. *Optimizing TasP or combining TasP with any other interventions to at least the medium scenario significantly reduced the HIV incidence, and elimination of HIV disease was possible.*
2. *Optimizing Test & Treat syphilis, and increased proportion of condom use with or without TasP to the high scenario reduced the syphilis incidence, and elimination of syphilis was possible.*
3. *Optimizing TasP, Test & Treat syphilis, combined with condom use resulted in HIV & syphilis incident rate as low as 0.11 & 0.86 respectively and elimination of both diseases was possible.*
4. *Only TasP significantly decreased mortality while PrEP increased syphilis incidence by about 5%.*

PART B: Conclusions (Projects 3 & 4)

1. *Optimizing TasP, through promotion of timely HIV diagnosis, treatment initiation and higher retention, or combined with improving time from syphilis infection to treatment and the distribution of PrEP was the most successful strategy to control the HIV epidemic.*
2. *Optimizing Test & Treat syphilis, and increased condom use was the most successful strategy to control the syphilis epidemic.*
3. *Frequent testing for syphilis and other STIs, particularly among gbMSM using PrEP should be prioritized to control the syphilis epidemic.*
4. *Consistent use of condoms should continue to be encouraged and promoted to simultaneously reduce HIV and syphilis transmission.*

PART B: Future work (Projects 3 & 4)

1. Expand the model to adjust for age and risk level:
   - how do individuals in each age and risk group contribute to disease spread?
   - what proportion of infected individuals in each age and risk group do we need to treat more?

2. If we have range of data and parameters, can we construct confidence intervals for our model outcomes?
   - Bootstrap method
   - Monte carlo filtering method

3. If we have enough information about the prior, can we use this to inform the posterior?
   - Bayesian approach

Summary of main contributions

Different infectious disease models with possible elimination strategies:

Indirect transmission models (epidemic models):

1. *epidemic models with heterogeneous mixing & indirect transmission,*
2. *the epidemic model designed using a coupled PDE-ODE system*

Direct transmission models (endemic models)

1. *the co-interaction model of HIV and syphilis infections,*
2. *HIV/Syphilis co-interaction model modified to assess the impact of different interventions in BC.*

Conclusions:

With my convincing story of innovation trends:

1. *I consider myself an* **astonishing innovator**.

2. *My* **innovative strategies** *to eliminating epidemic and endemic diseases through direct and indirect transmission pathways are*

   - *computationally cheaper* compared to other existing PDE models,
   - *richer and better* compared to other existing ODE models.

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- Paul Gustafson

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