

January 13, 2018  
Heroin Model

S=susceptibles

P=prescribed opioid users, A=addicted to opioids, H=heroin users/addicted, R=treatment/rehabilitation

$S(0) = S_0, P(0) = P_0, A(0) = A_0, H(0) = H_0, R(0) = R_0$

Assume  $H_0 > 0, \mu_H > \mu_A$  and  $\theta_1 > \theta_2, \theta_3$

$$\frac{dS}{dt} = -\alpha S - \beta(1 - \xi)SA - \beta\xi SP - \theta_1 SH + \epsilon P + \delta R + \mu(P + R) + (\mu + \mu_A)A + (\mu + \mu_H)H$$

$$\frac{dP}{dt} = \alpha S - \epsilon P - \gamma P - \theta_2 PH - \mu P$$

$$\frac{dA}{dt} = \gamma P + \sigma_A R + \beta(1 - \xi)SA + \beta\xi SP - \zeta A - \theta_3 AH - (\mu + \mu_A)A$$

$$\frac{dH}{dt} = \theta_1 SH + \theta_2 PH + \theta_3 AH + \sigma_H R - \nu H - (\mu + \mu_H)H$$

$$\frac{dR}{dt} = \zeta A + \nu H - \delta R - \sigma_A R - \sigma_H R - \mu R$$

The following is a brief description of each parameter in the system:

$\alpha$ : the rate at which people are prescribed opioids

$\beta$ : total probability of becoming addicted to opioids other than by prescription

$\beta(1 - \xi)$ : proportion of which the non-prescribed, susceptible population becomes addicted to opioids by black market drugs and other addicts

$\beta\xi$ : proportion of which the non-prescribed, susceptible population obtains extra prescription opioids and becomes addicted

$\theta_1$ : rate at which the non-prescribed, susceptible population becomes addicted to heroin by black market drugs and other addicts

$\epsilon$ : rate at which people come back to the susceptible class after being prescribed opioids (i.e. not addicted)

$\delta$ : rate at which people come back to the susceptible class after successfully finishing treatment

$\mu$ : natural death rate

$\mu_A$ : enhanced death rate for opioid addicts ( $\mu + \text{overdose rate}$ )

$\mu_H$ : enhanced death rate for heroin addicts ( $\mu + \text{overdose rate}$ )

$\gamma$ : rate at which prescribed opioid users become addicted

$\theta_2$ : rate at which opioid prescribed user population becomes addicted to heroin

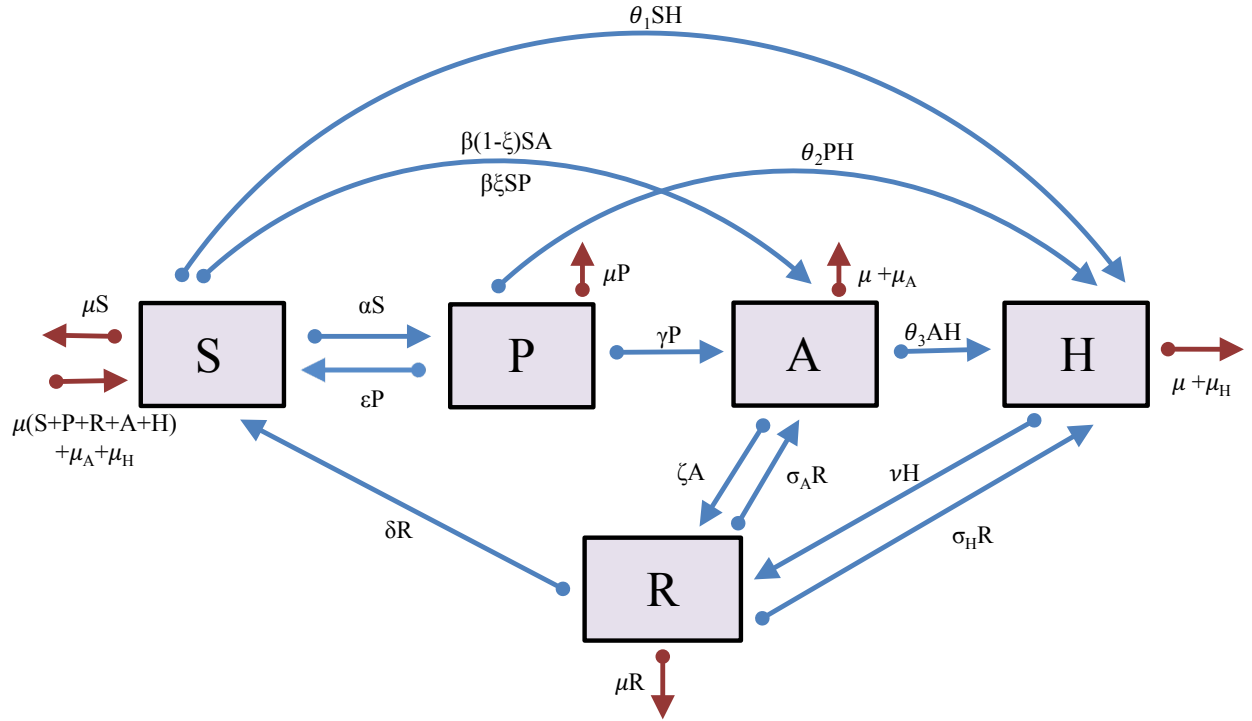
$\sigma_A$ : rate at which people relapse from treatment into the opioid addicted class

$\zeta$ : rate at which addicted opioid users enter treatment/rehabilitation

$\theta_3$ : rate at which the opioid addicted population becomes addicted to heroin

$\sigma_H$ : rate at which people relapse from treatment into the heroin addicted class

$\nu$ : rate at which heroin users enter treatment/rehabilitation



To find the addiction-free equilibrium (AFE), we set Eqs. (FILL IN) equal to zero and require that  $A = H = R = 0$ . We are left with the system

$$\begin{aligned}
 0 &= -\alpha S^* - \beta \xi S^* P^* + \epsilon P^* + \mu P^* \\
 0 &= \alpha S^* - \epsilon P^* - \gamma P^* - \mu P^* \\
 0 &= \gamma P^* + \beta \xi S^* P^*
 \end{aligned}$$

If  $P = 0$ , then the only solution is  $S^* = P^* = H^* = R^* = 0$ . Thus, will assume  $P \neq 0$ . This forces  $\gamma + \beta \xi S^* = 0$  and since all of our parameters and variables are non-negative, then it must be  $\gamma = 0$  and either  $\beta = 0$  or  $\xi = 0$ . Under the assumption that  $\gamma = 0 = \xi$  to ensure the existence of our AFE and that  $1 = S + P + A + H + R$ , we calculate the AFE to be

$$\begin{aligned}
 S^* &= \frac{\epsilon + \mu}{\alpha + \epsilon + \mu} \\
 P^* &= \frac{\alpha}{\alpha + \epsilon + \mu} \\
 A^* &= 0 \\
 H^* &= 0 \\
 R^* &= 0
 \end{aligned}$$

## Calculating the Basic Reproduction Number, $R_0$

From this point on, we will assume  $\gamma = 0$  and  $\xi = 0$  (thus,  $\beta \neq 0$ ) in order to ensure the existence of the AFE. This results in the infected compartment Eqns. (FILL IN) reducing to:

$$\begin{aligned}\frac{dA}{dt} &= \sigma_A R + \beta S A - \zeta A - \theta_3 A H - (\mu + \mu_A) A \\ \frac{dH}{dt} &= \theta_1 S H + \theta_2 P H + \theta_3 A H + \sigma_H R - \nu H - (\mu + \mu_H) H \\ \frac{dR}{dt} &= \zeta A + \nu H - \delta R - \sigma_A R - \sigma_H R - \mu R\end{aligned}$$

Thus, under the assumption of A, H and R as the infected compartments and parameter restrictions stated above, the assumptions of the Next Generation Method are satisfied for matrices  $\mathcal{F}$  and  $\mathcal{V}$  shown below. Note that  $\mathcal{F}_i$  represents the rate that secondary infections enter infected compartment  $i$  and  $\mathcal{V}_i$  represents the difference between the rate of transfer out of compartment  $i$  and the rate of transfer into compartment  $i$  by means different than a secondary infection. Using this method results in the following matrices:

$$\begin{aligned}\mathcal{F} &= \begin{pmatrix} 0 \\ 0 \\ \beta S A \\ \theta_1 S H + \theta_2 P H \\ 0 \end{pmatrix} \\ \mathcal{V} &= \begin{pmatrix} \alpha S + \beta S A + \theta_1 S H - \epsilon P - \delta R - \mu(P + R + A + H) - \mu_A A - \mu_H H \\ -\alpha S + \epsilon P + \theta_2 P H + \mu P \\ -\sigma_A R + \zeta A + \theta_3 A H + (\mu + \mu_A) A \\ -\theta_3 A H - \sigma_H R + \nu H + (\mu + \mu_H) H \\ -\zeta A - \nu H + \delta R + \sigma_A R + \sigma_H R + \mu R \end{pmatrix} \\ F &= \begin{pmatrix} \beta S^* & 0 & 0 \\ 0 & \theta_1 S^* + \theta_2 P^* & 0 \\ 0 & 0 & 0 \end{pmatrix} \\ V &= \begin{pmatrix} \zeta + \mu + \mu_A & 0 & -\sigma_A \\ 0 & \nu + \mu + \mu_H & -\sigma_H \\ -\zeta & -\nu & \delta + \sigma_A + \sigma_H + \mu \end{pmatrix}\end{aligned}$$

The eigenvalues of  $FV^{-1}$  are calculated to be:

$$\sigma(FV^{-1}) = \left\{ 0, \frac{(r+s) - \sqrt{(r-s)^2 + 4\beta S^* z \sigma_A \zeta \sigma_H \nu}}{2 \det(V)}, \frac{(r+s) + \sqrt{(r-s)^2 + 4\beta S^* z \sigma_A \zeta \sigma_H \nu}}{2 \det(V)} \right\}$$

$R_0$  may then be determined as the spectral radius of  $FV^{-1}$ :

$$R_0 = \frac{(r+s) + \sqrt{(r-s)^2 + 4\beta S^* z \sigma_A \zeta \sigma_H \nu}}{2 \det(V)}$$

where  $a = \zeta + \mu + \mu_A$ ,  $b = \nu + \mu + \mu_H$ ,  $c = \delta + \sigma_A + \sigma_H + \mu$ ,  $z = \theta_1 S^* + \theta_2 P^*$ ,  $r = \beta S^*(bc - \sigma_H \nu)$ ,  $s = z(ac - \sigma_A \zeta)$ , and  $\det(V) = abc - \sigma_A \zeta(\nu + \mu + \mu_H) - \sigma_H \nu$ .

We note that the radicand  $(r-s)^2 + 4\beta S^* z \sigma_A \zeta \sigma_H \nu$  is positive, since all parameters are positive. In addition,  $r$  is positive since  $bc$  contains the term that cancels with  $-\sigma_H \nu$ ,  $s$  is positive since  $ac$  contains the term that cancels with  $-\sigma_A \zeta$  and finally,  $\det(V)$  is positive since  $abc$  contains terms that cancel with  $-\sigma_A \zeta(\nu + \mu + \mu_H) - \sigma_H \nu$ .

\*\*wording on this?