April 10, 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 $\theta_3 > \theta_1, \theta_2$

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

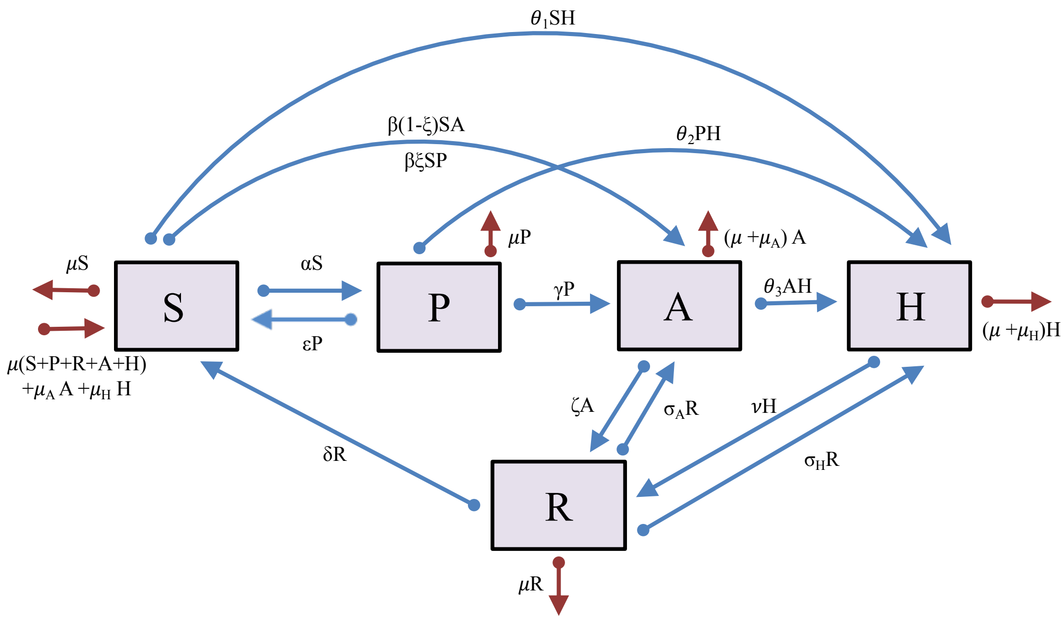
$$\frac{\mathrm{d}P}{\mathrm{d}t} = \alpha S - \epsilon P - \gamma P - \theta_2 PH - \mu P$$

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

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

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \zeta A + \nu H - \delta R - \sigma_A R - \sigma_H R - \mu R$$

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 (overdose rate which results in death)
$\mu_H$: enhanced death rate for heroin addicts (overdose rate which results in death)
$\gamma$: 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:

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

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 $\mathscr{F}$ and $\mathscr{V}$ shown below. Note that $\mathscr{F}_i$ represents the rate that secondary infections enter infected compartment $i$ and $\mathscr{V}_i$ 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:

$$
\mathscr{F} = \begin{pmatrix} 0 \\ 0 \\ \beta S A \\ \theta_1 S H + \theta_2 P H \\ 0 \end{pmatrix}
$$

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

$$
F = \begin{pmatrix} \beta S^* & 0 & 0 \\ 0 & \theta_1 S^* + \theta_2 P^* & 0 \\ 0 & 0 & 0 \end{pmatrix}
$$

$$
V = \begin{pmatrix} \zeta + \mu + \mu_A & 0 & -\sigma_A \\ 0 & \nu + \mu + \mu_H & -\sigma_H \\ -\zeta & -\nu & \delta + \sigma_A + \sigma_H + \mu \end{pmatrix}
$$

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

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

$\mathscr{R}_0$ may then be determined as the spectral radius of $FV^{-1}$:

$$\mathscr{R}_0 = \frac{(r+s)+\sqrt{(r-s)^2+4\beta S^* z\sigma_A\zeta\sigma_H\nu}}{2det(V)}$$

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 $det(V) = a(bc - \sigma_H\nu) - \sigma_A\zeta b$.

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 $-\sigma_A\zeta(\nu + \mu + \mu_H) - \sigma_H\nu$.