Epidemiology and Infection
Pandemic Risk Assessment Model (PRAM): A Mathematical Modeling Approach to Pandemic Influenza Planning
D. C. Dover, E. M. Kirwin, N. Hernandez Ceron, K. A. Nelson
Supplementary Material

The basic reproduction number $\mathcal{R}_0$ is computed for a simplified version of the PRAM, without antiviral and immunization interventions. By removing these classes, the following compartments of the PRAM remainin: Susceptible (1) $S^{(1)}$, Susceptible (2) $S^{(2)}$, Exposed (5) E, Not Medically Attended (7) NA, Medically Attended (6) MA, Not treated with AV (9) NT, Hospitalized (10) H, Recovered (12) R, and Death (11) D. Each compartment is divided into 7 age groups and 2 risks levels. The 14 sub-compartments are indexed by (a, r) where a is the age group and r is risk level.

The population size of the group (a, r) is denoted by $N_{(a,r)}$. A compartment sub indexed by $(a, \cdot)$ represents the sum of both risk groups of the compartment, for example $MA_{(k,\cdot)} = MA_{(k,1)} + MA_{(k,2)}$. The (i, j)-entry of the contact matrix is denoted by $c_{(i,j)}$.

With this notation, the ODE system is given by

$$\begin{aligned}
S^{(1)\prime}_{(a,r)} &= -\beta S^{(1)}_{(a,r)} \sum_{k=1}^{7} \frac{c_{(a,k)}}{N_{(k,\cdot)}} \left[MA_{(k,\cdot)} + NA_{(k,\cdot)} + NT_{(k,\cdot)} + H_{(k,\cdot)}\right] \\
S^{(2)\prime}_{(a,r)} &= -\beta S^{(2)}_{(a,r)} \sum_{k=1}^{7} \frac{c_{(a,k)}}{N_{(k,\cdot)}} \left[MA_{(k,\cdot)} + NA_{(k,\cdot)} + NT_{(k,\cdot)} + H_{(k,\cdot)}\right] \\
E'_{(a,r)} &= \beta \left(S^{(1)}_{(a,r)} + S^{(2)}_{(a,r)}\right) \sum_{k=1}^{7} \frac{c_{(a,k)}}{N_{(k,\cdot)}} \left[MA_{(k,\cdot)} + NA_{(k,\cdot)} + NT_{(k,\cdot)} + H_{(k,\cdot)}\right] \; - \; \pi E_{(a,r)} \\
NA'_{(a,r)} &= \left(1 - s_{(r)}\right) \pi E_{(a,r)} - \theta NA_{(a,r)} \\
MA'_{(a,r)} &= s_{(r)} \pi E_{(a,r)} - \delta MA_{(a,r)} \\
NT'_{(a,r)} &= \delta MA_{(a,r)} - \tau NT_{(a,r)} \\
H'_{(a,r)} &= h_{(r)} \tau NT_{(a,r)} - \mu H_{(a,r)} \\
R'_{(a,r)} &= \theta NA_{(a,r)} + (1 - h_{(r)}) \tau NT_{(a,r)} + (1 - m_{(r)}) \mu H_{(a,r)} \\
D'_{(a,r)} &= m_{(r)} \mu H_{(a,r)},
\end{aligned} \tag{1}$$

To find the basic reproduction number $\mathcal{R}_0$ we use the next generation matrix approach, described below.

1. Identify the disease compartments. In our case: E, NA, MA, NT, H
2. Decompose the dynamics into $\mathscr{F}$ (secondary infections) and $\mathscr{V}$ (all other transitions). Thus, we must express each sub-compartment as
$$x_{(a,r)} = \mathscr{F}^x_{(a,r)} - \mathscr{V}^x_{(a,r)}, \qquad \text{where} \quad x = E, NA, MA, NT, H.$$
This step is easy because all secondary infections enter the class E.
3. Linearized the ODE model about the disease free equilibrium (DFE) by computing the matrices F and V with entries
$$F_{(i,j)} = \frac{\partial \mathscr{F}_i}{\partial x_j}\Big|_{DFE} \qquad \text{and} \qquad V_{(i,j)} = \frac{\partial \mathscr{V}_i}{\partial x_j}\Big|_{DFE}$$
where x_i are equal to $E_{a,1}, E_{a,2}, NA_{a,1}, NA_{a,2}, \ldots, H_{a,1}, H_{a,2}$, $a = 1, \ldots, 7$, in that order. This is
$$\underbrace{E_{1,1}, \ldots, E_{7,1}, E_{1,2}, \ldots, E_{7,2}}_{x_i \ for \ i=1,\ldots,14}, \underbrace{NA_{1,1}, \ldots, NA_{7,2}}_{x_i \ for \ i=15,\ldots,28}, \ \ldots \ , \underbrace{H_{1,1}, \ldots, H_{7,2}}_{x_i \ for \ i=57,\ldots,70} \qquad \text{and} \qquad x_i = \mathscr{F}_i - \mathscr{V}_i.$$
4. Compute FV^{-1}.
5. $\mathcal{R}_0$ is equal to the largest eigenvalue of the matrix FV^{-1}, also known as the spectral radius and denoted by $\rho(FV^{-1})$.

Once the infectious stages have been identified, step 2 is fairly easy because all secondary infections enter the class E. Therefore

$$\mathscr{V}^E_{(a,r)} = \pi E'_{(a,r)}, \qquad \mathscr{F}^E_{(a,r)} = \beta \left(S^{(1)}_{(a,r)} + S^{(2)}_{(a,r)}\right) \sum_{k=1}^{7} \tfrac{c_{(a,k)}}{N_{(k,\cdot)}} \left[MA_{(k,\cdot)} + NA_{(k,\cdot)} + NT_{(k,\cdot)} + H_{(k,\cdot)}\right],$$
$$\mathscr{V}^x_{(a,r)} = -x'_{(a,r)}, \qquad \mathscr{F}^x_{(a,r)} = 0, \qquad \text{for} \quad x = NA, MA, NT \ \text{ and } \ H.$$

To complete step 3, notice that the DFE is $S^{(1)}_{(a,r)} = S^{(1)}_{(a,r)}(0)$, $S^{(2)}_{(a,r)} = S^{(2)}_{(a,r)}(0)$ and all other compartments equal to zero. In particular $S^{(1)}_{(a,r)} + S^{(2)}_{(a,r)} = N_{(a,r)}$. Then compute the Jacobian and evaluate at DFE

$$\frac{\partial \mathscr{F}^E_{(a',r')}}{\partial E_{(a,r)}} = 0, \qquad \frac{\partial \mathscr{F}^E_{(a',r')}}{\partial E_{(a,r)}}\Bigg|_{DFE} = 0$$
$$\frac{\partial \mathscr{F}^E_{(a',r')}}{\partial NA_{(a,r)}} = \beta \left(S^{(1)}_{(a',r')} + S^{(2)}_{(a',r')}\right) \frac{c_{(a',a)}}{N_{(a,\cdot)}}, \qquad \frac{\partial \mathscr{F}^E_{(a',r')}}{\partial NA_{(a,r)}}\Bigg|_{DFE} = \beta c_{(a',a)} \frac{N_{(a',r')}}{N_{(a,\cdot)}}$$
$$\frac{\partial \mathscr{F}^E_{(a',r')}}{\partial MA_{(a,r)}} = \beta \left(S^{(1)}_{(a',r')} + S^{(2)}_{(a',r')}\right) \frac{c_{(a',a)}}{N_{(a,\cdot)}}, \qquad \frac{\partial \mathscr{F}^E_{(a',r')}}{\partial MA_{(a,r)}}\Bigg|_{DFE} = \beta c_{(a',a)} \frac{N_{(a',r')}}{N_{(a,\cdot)}}$$
$$\frac{\partial \mathscr{F}^E_{(a',r')}}{\partial NT_{(a,r)}} = \beta \left(S^{(1)}_{(a',r')} + S^{(2)}_{(a',r')}\right) \frac{c_{(a',a)}}{N_{(a,\cdot)}}, \qquad \frac{\partial \mathscr{F}^E_{(a',r')}}{\partial NT_{(a,r)}}\Bigg|_{DFE} = \beta c_{(a',a)} \frac{N_{(a',r')}}{N_{(a,\cdot)}}$$
$$\frac{\partial \mathscr{F}^E_{(a',r')}}{\partial H_{(a,r)}} = \beta \left(S^{(1)}_{(a',r')} + S^{(2)}_{(a',r')}\right) \frac{c_{(a',a)}}{N_{(a,\cdot)}}, \qquad \frac{\partial \mathscr{F}^E_{(a',r')}}{\partial H_{(a,r)}}\Bigg|_{DFE} = \beta c_{(a',a)} \frac{N_{(a',r')}}{N_{(a,\cdot)}}$$

Thus, the F matrix is given by the block matrix

$$F = \begin{bmatrix} 0 & F^* & F^* & F^* & F^* \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

where each zero represents a 14×14 zero matrix,

$$F^* = \beta \begin{bmatrix} F^{(1)} & F^{(1)} \\ F^{(2)} & F^{(2)} \end{bmatrix},$$

and $F^{(1)}, F^{(2)}$ can be decomposed as

$$F^{(r)} = \begin{bmatrix} c_{(1,1)} \frac{N_{(1,r)}}{N_{(1,\cdot)}} & \cdots & c_{(1,7)} \frac{N_{(1,r)}}{N_{(7,\cdot)}} \\ c_{(2,1)} \frac{N_{(2,r)}}{N_{(1,\cdot)}} & \cdots & c_{(2,7)} \frac{N_{(2,r)}}{N_{(7,\cdot)}} \\ \vdots & \ddots & \vdots \\ c_{(7,1)} \frac{N_{(7,r)}}{N_{(1,\cdot)}} & \cdots & c_{(7,7)} \frac{N_{(7,r)}}{N_{(7,\cdot)}} \end{bmatrix}, \qquad F^{(r)}_{i,j} = c_{(i,j)} \frac{N_{(i,r)}}{N_{(j,\cdot)}}.$$

Similarly, we can find the matrix V. Compute

$$\frac{\partial \mathscr{V}^{E}_{(a',r')}}{\partial E_{(a,r)}} = \pi, \qquad \frac{\partial \mathscr{V}^{E}_{(a',r')}}{\partial x_{(a,r)}} = 0 \quad \text{where } x = NA, MA, NT, H$$

$$\frac{\partial \mathscr{V}^{NA}_{(a',r')}}{\partial E_{(a,r)}} = -\left(1 - s_{(r)}\right)\pi, \quad \frac{\partial \mathscr{V}^{NA}_{(a',r')}}{\partial NA_{(a,r)}} = \theta, \quad \frac{\partial \mathscr{V}^{NA}_{(a',r')}}{\partial x_{(a,r)}} = 0 \quad \text{where } x = MA, NT, H$$

$$\frac{\partial \mathscr{V}^{MA}_{(a',r')}}{\partial E_{(a,r)}} = -s_{(r)}\pi, \quad \frac{\partial \mathscr{V}^{MA}_{(a',r')}}{\partial MA_{(a,r)}} = \delta, \quad \frac{\partial \mathscr{V}^{MA}_{(a',r')}}{\partial x_{(a,r)}} = 0 \quad \text{where } x = NA, NT, H$$

$$\frac{\partial \mathscr{V}^{NT}_{(a',r')}}{\partial MA_{(a,r)}} = -\delta, \quad \frac{\partial \mathscr{V}^{NT}_{(a',r')}}{\partial NT_{(a,r)}} = \tau, \quad \frac{\partial \mathscr{V}^{NT}_{(a',r')}}{\partial x_{(a,r)}} = 0 \quad \text{where } x = E, NA, H$$

$$\frac{\partial \mathscr{V}^{H}_{(a',r')}}{\partial NT_{(a,r)}} = -h_{(r)}\tau, \quad \frac{\partial \mathscr{V}^{H}_{(a',r')}}{\partial H_{(a,r)}} = \mu, \quad \frac{\partial \mathscr{V}^{H}_{(a',r')}}{\partial x_{(a,r)}} = 0 \quad \text{where } x = E, NA, MA$$

Then V can be separated in 14×14 block matrices

$$V = \begin{bmatrix} \mathrm{Diag}[\pi] & 0 & 0 & 0 & 0 \\ -\mathrm{Diag}\left[\left(1 - s_{(1)}\right)\pi, \left(1 - s_{(2)}\right)\pi\right] & \mathrm{Diag}[\theta] & 0 & 0 & 0 \\ -\mathrm{Diag}\left[s_{(1)}\pi, s_{(2)}\pi\right] & 0 & \mathrm{Diag}[\delta] & 0 & 0 \\ 0 & 0 & -\mathrm{Diag}[\delta] & \mathrm{Diag}[\tau] & 0 \\ 0 & 0 & 0 & -\mathrm{Diag}[h_{(1)}\tau,\ h_{(2)}\tau] & \mathrm{Diag}[\mu] \end{bmatrix}$$

where Diag$[z]$ is a 14×14 diagonal matrix with entries equal to z and Diag$[z_1, z_2]$ is also a diagonal matrix with its first 7 entries equal to z_1 and the remaining 7 equal to z_2. To find the inverse of V we use the formula

$$\begin{bmatrix} A & 0 \\ C & D \end{bmatrix}^{-1} = \begin{bmatrix} A^{-1} & 0 \\ -D^{-1}CA^{-1} & D^{-1} \end{bmatrix}$$

twice. This gives us

$$V^{-1} = \begin{bmatrix} \text{Diag}\left[\frac{1}{\pi}\right] & 0 & 0 & 0 & 0 \\ \text{Diag}\left[\frac{1-s_{(1)}}{\theta}, \frac{1-s_{(2)}}{\theta}\right] & \text{Diag}\left[\frac{1}{\theta}\right] & 0 & 0 & 0 \\ \text{Diag}\left[\frac{s_{(1)}}{\delta}, \frac{s_{(2)}}{\delta}\right] & 0 & \text{Diag}\left[\frac{1}{\delta}\right] & 0 & 0 \\ \text{Diag}\left[\frac{s_{(1)}}{\tau}, \frac{s_{(2)}}{\tau}\right] & 0 & \text{Diag}\left[\frac{1}{\tau}\right] & \text{Diag}\left[\frac{1}{\tau}\right] & 0 \\ \text{Diag}\left[\frac{s_{(1)}h_{(1)}}{\mu}, \frac{s_{(2)}h_{(2)}}{\mu}\right] & 0 & \text{Diag}\left[\frac{h_{(1)}}{\mu}, \frac{h_{(2)}}{\mu}\right] & \text{Diag}\left[\frac{h_{(1)}}{\mu}, \frac{h_{(2)}}{\mu}\right] & \text{Diag}\left[\frac{1}{\mu}\right] \end{bmatrix}$$

To complete step 4 we compute

$$\begin{aligned} FV^{-1} &= \begin{bmatrix} 0 & F^* & F^* & F^* & F^* \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} \text{Diag}\left[\frac{1}{\pi}\right] & 0 & 0 & 0 & 0 \\ \text{Diag}\left[\frac{1-s_{(1)}}{\theta}, \frac{1-s_{(2)}}{\theta}\right] & * & 0 & 0 & 0 \\ \text{Diag}\left[\frac{s_{(1)}}{\delta}, \frac{s_{(2)}}{\delta}\right] & 0 & * & 0 & 0 \\ \text{Diag}\left[\frac{s_{(1)}}{\tau}, \frac{s_{(2)}}{\tau}\right] & 0 & * & * & 0 \\ \text{Diag}\left[\frac{s_{(1)}h_{(1)}}{\mu}, \frac{s_{(2)}h_{(2)}}{\mu}\right] & 0 & * & * & * \end{bmatrix} \\ &= \begin{bmatrix} F^*\left(\text{Diag}\left[\frac{1-s_{(1)}}{\theta} + \frac{s_{(1)}}{\delta} + \frac{s_{(1)}}{\tau} + \frac{s_{(1)}h_{(1)}}{\mu}, \frac{1-s_{(2)}}{\theta} + \frac{s_{(2)}}{\delta} + \frac{s_{(2)}}{\tau} + \frac{s_{(2)}h_{(2)}}{\mu}\right]\right) & * & * & * & * \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix} \end{aligned}$$

The entries $*$ have not been computed because those will not be relevant when finding the eigenvalues of FV^{-1}.

Finally, we must compute the eigenvalues of FV^{-1}. To find the nonzero eigenvalues it is enough to focus on the first block matrix $M = F^*\left(\text{Diag}[(1-s)/\theta + s/\delta + s/\tau] + \text{Diag}[sh_{(1)}/\mu,\ sh_{(2)}/\mu]\right)$.

$$\begin{aligned} M &= F^*\left(\text{Diag}\left[\frac{1-s_{(1)}}{\theta} + \frac{s_{(1)}}{\delta} + \frac{s_{(1)}}{\tau} + \frac{s_{(1)}h_{(1)}}{\mu}, \frac{1-s_{(2)}}{\theta} + \frac{s_{(2)}}{\delta} + \frac{s_{(2)}}{\tau} + \frac{s_{(2)}h_{(2)}}{\mu}\right]\right) \\ &= \beta \begin{bmatrix} F^{(1)} & F^{(1)} \\ F^{(2)} & F^{(2)} \end{bmatrix} \text{Diag}\left[\frac{1-s_{(1)}}{\theta} + \frac{s_{(1)}}{\delta} + \frac{s_{(1)}}{\tau} + \frac{s_{(1)}h_{(1)}}{\mu}, \frac{1-s_{(2)}}{\theta} + \frac{s_{(2)}}{\delta} + \frac{s_{(2)}}{\tau} + \frac{s_{(2)}h_{(2)}}{\mu}\right] \\ &= \begin{bmatrix} aF^{(1)} & bF^{(1)} \\ aF^{(2)} & bF^{(2)} \end{bmatrix}, \end{aligned}$$

where

$$a = \beta\left(\frac{1-s_{(1)}}{\theta} + \frac{s_{(1)}}{\delta} + \frac{s_{(1)}}{\tau} + \frac{s_{(1)}h_{(1)}}{\mu}\right) \qquad \text{and} \qquad b = \beta\left(\frac{1-s_{(2)}}{\theta} + \frac{s_{(2)}}{\delta} + \frac{s_{(2)}}{\tau} + \frac{s_{(2)}h_{(2)}}{\mu}\right).$$

The matrix M cannot be simplified further, so there is not a simple formula for its eigenvalues and numeric methods must be used to compute $\mathcal{R}_0$.