A Viewing COVID-19 as two diseases

A recent study shows that patients with severe COVID-19 tend to have a high viral load and a long virus-shedding period [2]. We imagine that the transmission might depend on the state of the carrier (e.g., because higher viral load means transmission more likely to lead to symptomatic). We revise the baseline model in [3] by viewing COVID-19 as two diseases. The infected individuals can be either asymptomatic, I_a, or symptomatic I_s. Symptomatic cases may have higher viral load and therefore are more infectious. The susceptible individuals S preferentially become symptomatic exposed individuals E_s after getting infected by symptomatic infected individuals I_s. The baseline model is as follows (without age structure)

$$
\begin{aligned}
\dot{S} &= -\beta_a S I_a - \beta_s S I_s \\
\dot{E}_a &= (1 - \epsilon_a)\beta_a S I_a + \epsilon_s \beta_s S I_s - \gamma_{Ea} E_a \\
\dot{E}_s &= \epsilon_a \beta_a S I_a + (1 - \epsilon_s)\beta_s S I_s - \gamma_{Es} E_s \\
\dot{I}_a &= p\gamma_{Ea} E_a + (1 - q)\gamma_{Es} E_s - \gamma_a I_a \\
\dot{I}_s &= (1 - p)\gamma_{Ea} E_a + q\gamma_{Es} E_s - \gamma_s I_s \\
\dot{R} &= \gamma_a I_a + (1 - f)\gamma_s I_s \\
\dot{D} &= f\gamma_s I_s \ .
\end{aligned}
\tag{A.1}
$$

B $\mathcal{R}_0$ calculation

To compute the basic reproduction number, we use next-generation matrix [1]. The infected subsystem of Eq. A.1 can be written as

$$
\begin{bmatrix} \dot{E}_a \\ \dot{E}_s \\ \dot{I}_a \\ \dot{I}_s \end{bmatrix} = \left(\begin{bmatrix} 0 & 0 & (1 - \epsilon_a)\beta_a & \epsilon_s \beta_s \\ 0 & 0 & \epsilon_a \beta_a & (1 - \epsilon_s)\beta_s \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} + \begin{bmatrix} -\gamma_{Ea} & 0 & 0 & 0 \\ 0 & -\gamma_{Es} & 0 & 0 \\ p\gamma_{Ea} & (1 - q)\gamma_{Es} & -\gamma_a & 0 \\ (1 - p)\gamma_{Ea} & q\gamma_{Es} & 0 & -\gamma_s \end{bmatrix} \right) \begin{bmatrix} E_a \\ E_s \\ I_a \\ I_s \end{bmatrix},
\tag{B.2}
$$

where the first matrix in the bracket is called transmission matrix T and the second matrix is refered as transition matrix Σ. Then, we define a matrix Q whose columns consist of unit vectors relating to non-zero rows of T only, i.e., $Q = [e_1, e_2]$ where e_i is the ith unit vector in $\mathbb{R}^4$. The next-generation matrix, $\Phi = -Q^T T \Sigma^{-1} Q$, is

$$
\Phi = \begin{bmatrix} \frac{\beta_s \epsilon_s (1-p)}{\gamma_s} + \frac{\beta_a (1-\epsilon_a)p}{\gamma_a} & \frac{\beta_s \epsilon_s q}{\gamma_s} + \frac{\beta_a (1-\epsilon_a)(1-q)}{\gamma_a} \\ \frac{\beta_s (1-\epsilon_s)(1-p)}{\gamma_s} + \frac{\beta_a \epsilon_a p}{\gamma_a} & \frac{\beta_s (1-\epsilon_s)q}{\gamma_s} + \frac{\beta_a \epsilon_a (1-q)}{\gamma_a} \end{bmatrix}.
\tag{B.3}
$$

We define $\mathcal{R}_a = \beta_a/\gamma_a$ and $\mathcal{R}_s = \beta_s/\gamma_s$, the Eq. B.3 read as

$$
\Phi = \begin{bmatrix} \overbrace{\mathcal{R}_s \epsilon_s (1-p)}^{E_a \to I_s \to E_a} + \overbrace{\mathcal{R}_a (1-\epsilon_a)p}^{E_a \to I_a \to E_a} & \overbrace{\mathcal{R}_s \epsilon_s q}^{E_s \to I_s \to E_a} + \overbrace{\mathcal{R}_a (1-\epsilon_a)(1-q)}^{E_s \to I_a \to E_a} \\ \underbrace{\mathcal{R}_s (1-\epsilon_s)(1-p)}_{E_a \to I_s \to E_s} + \underbrace{\mathcal{R}_a \epsilon_a p}_{E_a \to I_a \to E_s} & \underbrace{\mathcal{R}_s (1-\epsilon_s)q}_{E_s \to I_s \to E_s} + \underbrace{\mathcal{R}_a \epsilon_a (1-q)}_{E_s \to I_a \to E_s} \end{bmatrix}.
\tag{B.4}
$$

First, we calculate $\mathcal{R}_0$ for a special case, $\epsilon_a = \epsilon_s = 0$, then the NGM is

$$
\Phi_0 = \begin{bmatrix} \overbrace{\mathcal{R}_a p}^{E_a \to I_a \to E_a} & \overbrace{\mathcal{R}_a (1-q)}^{E_s \to I_a \to E_a} \\ \underbrace{\mathcal{R}_s (1-p)}_{E_a \to I_s \to E_s} & \underbrace{\mathcal{R}_s q}_{E_s \to I_s \to E_s} \end{bmatrix}.
\tag{B.5}
$$

1

Remember that for a 2×2 matrix the dominant eigenvalue, and hence $\mathcal{R}_0$, can be obtained from the trace and the determinant of the matrix as

$$
\begin{aligned}
\mathcal{R}_0 &= \frac{1}{2}\left(\mathrm{trace}(\Phi_0) + \sqrt{\mathrm{trace}(\Phi_0)^2 - 4\mathrm{Det}(\Phi_0)}\right) \\
&= \frac{1}{2}\left(\mathcal{R}_a p + \mathcal{R}_s q + \sqrt{(\mathcal{R}_a p + \mathcal{R}_s q)^2 - 4\mathcal{R}_a \mathcal{R}_s (p + q - 1)}\right)
\end{aligned}
\tag{B.6}
$$

Second, we calculate $\mathcal{R}_0$ for another special case, $p = q = 1$, the NGM is

$$
\Phi_1 = \begin{bmatrix} \overbrace{\mathcal{R}_a(1-\epsilon_a)}^{E_a \to I_a \to E_a} & \overbrace{\mathcal{R}_s \epsilon_s}^{E_s \to I_s \to E_a} \\ \underbrace{\mathcal{R}_a \epsilon_a}_{E_a \to I_a \to E_s} & \underbrace{\mathcal{R}_s(1-\epsilon_s)}_{E_s \to I_s \to E_s} \end{bmatrix}.
\tag{B.7}
$$

In this case, we find

$$
\begin{aligned}
\mathcal{R}_0 &= \frac{1}{2}\left(\mathrm{trace}(\Phi_1) + \sqrt{\mathrm{trace}(\Phi_1)^2 - 4\mathrm{Det}(\Phi_1)}\right) \\
&= \frac{1}{2}\left(\mathcal{R}_a(1-\epsilon_a) + \mathcal{R}_s(1-\epsilon_s) + \sqrt{(\mathcal{R}_a(1-\epsilon_a) + \mathcal{R}_s(1-\epsilon_s))^2 - 4\mathcal{R}_a \mathcal{R}_s(1 - \epsilon_a - \epsilon_s)}\right)
\end{aligned}
\tag{B.8}
$$

C Age-dependent model structure

The dynamics of infected compartments in an age-structured Covid-SIR model can be written as

$$
\begin{aligned}
\dot{I}_{a,i} &= \overbrace{\beta_a \sigma_{a,i} S_i\left(\sum_{j=1}^{N} C_{i,j} I_{a,j}\right)}^{a \to a \text{ transmission}} + \overbrace{\beta_s \sigma_{a,i} S_i\left(\sum_{j=1}^{N} C_{i,j} I_{s,j}\right)}^{s \to a \text{ transmission}} - \delta_a I_{s,i} \\
\dot{I}_{s,i} &= \underbrace{\beta_a \sigma_{s,i} S_i\left(\sum_{j=1}^{N} C_{i,j} I_{a,j}\right)}_{a \to s \text{ transmission}} + \underbrace{\beta_s \sigma_{s,i} S_i\left(\sum_{j=1}^{N} C_{i,j} I_{s,j}\right)}_{s \to s \text{ transmission}} - \delta_s I_{s,j},
\end{aligned}
\tag{C.9}
$$

where $C_{i,j}$ is the contact matrix (N by N). Note that $\sigma_{s,i} = \alpha_i p_i$, where α_i is the susceptibility of people in age i to infection and p_i is the probability of symptomatic infection for age i. Similarly, we have $\sigma_{a,i} = \alpha_i(1 - p_i)$. Though we cannot distinguish (or identify) the parameters p_i and α_i from model, we do expect that $\sigma_{s,i}/\sigma_{a,i} = p_i/(1 - p_i)$.

To derive the next-generation matrix, we define the vector of infected compartments,

$$
I = [-I_{a,i} - | - I_{s,i}-]^T,
$$

where $i = 1, ..., N$ and so that $I \in \mathbb{R}^{2N}$. We decouple the linearized infected subsystem as $\dot{I} = (T + \Sigma)I$, where T is the transmission matrix and Σ is the transition matrix. Note that the transmission matrix T can be viewed as a matrix with four blocks, each block suggests one way of transmission: $x \to y$, where $x, y \in \{a, s\}$. Specifically, we define four N by N matrices:

$$
\begin{aligned}
[T_{a \to a}]_{i,j} &= \beta_a \sigma_{a,i} S_i^0 C_{i,j}, \\
[T_{s \to a}]_{i,j} &= \beta_s \sigma_{a,i} S_i^0 C_{i,j}, \\
[T_{a \to s}]_{i,j} &= \beta_a \sigma_{s,i} S_i^0 C_{i,j}, \\
[T_{s \to s}]_{i,j} &= \beta_s \sigma_{s,i} S_i^0 C_{i,j},
\end{aligned}
\tag{C.10}
$$

where S_i^0 is the initial fraction of age i group. Therefore, the transmission matrix T can be written as

$$
T = \begin{bmatrix} T_{a \to a} & T_{s \to a} \\ T_{a \to s} & T_{s \to s} \end{bmatrix}.
\tag{C.11}
$$

The transition matrix Σ is a diagonal matrix: $\Sigma = -\text{diag}[-\delta_a - | - \delta_s -]$, *i.e.*, the diagonal elements on the first N rows are $-\delta_a$ and the diagonal elements of rest rows are $-\delta_s$. The NGM Φ can be computed as $-T\Sigma^{-1}$ and we obtain

$$\Phi = \begin{bmatrix} \frac{T_{a \to a}}{\delta_a} & \frac{T_{s \to a}}{\delta_s} \\ \frac{T_{a \to s}}{\delta_a} & \frac{T_{s \to s}}{\delta_s} \end{bmatrix}, \tag{C.12}$$

where $(.)/\delta_a$ and $(.)/\delta_s$ are performed elementwise on matrix.

References

[1] Odo Diekmann, JAP Heesterbeek, and Michael G Roberts. The construction of next-generation matrices for compartmental epidemic models. *Journal of the Royal Society Interface*, 7(47):873–885, 2010.

[2] Yang Liu, Li-Meng Yan, Lagen Wan, Tian-Xin Xiang, Aiping Le, Jia-Ming Liu, Malik Peiris, Leo LM Poon, and Wei Zhang. Viral dynamics in mild and severe cases of covid-19. *The Lancet Infectious Diseases*, 2020.

[3] Sang Woo Park, Daniel M Cornforth, Jonathan Dushoff, and Joshua S Weitz. The time scale of asymptomatic transmission affects estimates of epidemic potential in the covid-19 outbreak. *medRxiv*, 2020.