09052024 ImmunoSEIRS Flu Mathematical Model (Work in Progress)

Note 1: I have incorporated important notation suggestions from Lauren & Dave.

Note 2: for simplicity, I have dropped all subscripts F because that stands for flu, and here we are exclusively discussing flu.

- t: time
- a: age group
- A: set of age groups
- $\mathcal{I} := \{\mathrm{H1}, \mathrm{H3}, \mathrm{V}\}$: the set of types of immunity-inducing events: infection by H1N1, infection by H3N2, and vaccination, respectively.
- $\boldsymbol{O}$: $|A| \times |\mathcal{I}|$ matrix, where the (a, ℓ)th element is the positive constant modeling the saturation of antibody production in individuals in age group a who had immunity-inducing event ℓ.

Population-level immunity against <u>infection</u> (derived from H1N1 infections, H3N2 infections, and vaccinations respectively)

$$\frac{dM^I_{a,H1}(t)}{dt} = \frac{g^I_{H1} p_{H1}(t) R_a(t)}{N_a \left(1 + \sum_{\ell \in L} O_{a,\ell} M^I_{a,\ell}(t)\right)} - w^I_{H1} M^I_{a,H1}(t) \tag{1}$$

$$\frac{dM^I_{a,H3}(t)}{dt} = \frac{g^I_{H3} p_{H3}(t) R_a(t)}{N_a \left(1 + \sum_{\ell \in L} O_{a,\ell} M^I_{a,\ell}(t)\right)} - w^I_{H3} M^I_{a,H3}(t) \tag{2}$$

$$\frac{dM^I_{a,V}(t)}{dt} = g^I_V V(t - \tau) - w^I_V M^I_{a,V}(t) \tag{3}$$

where

- g^I_{H1}: factor by which population-level immunity against infection grows after each H1N1 case that recovers
- g^I_{H3}: factor by which population-level immunity against infection grows after each H3N2 case that recovers
- g^I_V: factor by which population-level immunity against infection grows after each vaccination
- N_a: total population of age group a
- $p_{H1}(t)$, $p_{H3}(t)$: prevalence of H1N1, H3N2 respectively
- w^I_{H1}: rate at which H1N1 infection-induced immunity against infection wanes
- w^I_{H3}: rate at which H3N2 infection-induced immunity against infection wanes
- w^I_V: rate at which vaccine-induced immunity against infection wanes

- $V(t)$: number of vaccine doses administered at time t
- τ: delay in number of days of dose administration.

Population-level immunity against hospitalization (derived from H1N1 infections, H3N2 infections, and vaccinations respectively)

$$\frac{dM^H_{a,H1}(t)}{dt} = \frac{g^H_{H1} p_{H1}(t) R_a(t)}{N_a \left(1 + \sum_{\ell \in L} O_{a,\ell} M^H_{a,\ell}(t)\right)} - w^H_{H1} M^H_{a,H1}(t) \tag{4}$$

$$\frac{dM^H_{a,H3}(t)}{dt} = \frac{g^H_{H3} p_{H3}(t) R_a(t)}{N_a \left(1 + \sum_{\ell \in L} O_{a,\ell} M^H_{a,\ell}(t)\right)} - w^H_{H3} M^H_{a,H3}(t) \tag{5}$$

$$\frac{dM^H_{a,V}(t)}{dt} = g^H_V V(t) - w^H_V M^H_{a,V}(t) \tag{6}$$

where

- $p_{H1}(t)$, $p_{H3}(t)$, $V(t)$, τ: see above
- g^H_{H1}: factor by which population-level immunity against hospitalization grows after each H1N1 case that recovers
- g^H_{H3}: factor by which population-level immunity against hospitalization grows after each H3N2 case that recovers
- g^H_V: factor by which population-level immunity against hospitalization grows after each vaccination
- w^H_{H1}: rate at which H1N1 infection-induced immunity against hospitalization wanes
- w^H_{H3}: rate at which H3N2 infection-induced immunity against hospitalization wanes
- w^H_V: rate at which vaccine-induced immunity against hospitalization wanes

SEIHRD equations

$$\frac{dS_a(t)}{dt} = \underbrace{-S_a(t) \cdot \sum_{a' \in A} \frac{\beta(t)\phi_{a,a'}(t)I_{a'}(t)}{N_{a'}(1 + \boldsymbol{K_a^I}(\boldsymbol{p})^T \boldsymbol{M_a^I})}}_{\text{new exposed}} + \underbrace{\eta R_a(t)}_{\text{new susceptible}} \tag{7}$$

$$\frac{dE_a(t)}{dt} = \underbrace{S_a(t) \cdot \sum_{a' \in A} \frac{\beta(t)\phi_{a,a'}(t)I_{a'}(t)}{N_{a'}(1 + \boldsymbol{K_a^I}(\boldsymbol{p})^T \boldsymbol{M_a^I})}}_{\text{new exposed}} - \underbrace{\sigma E_a(t)}_{\text{new infected}} \tag{8}$$

$$\frac{dI_a(t)}{dt} = \underbrace{\sigma E_a(t)}_{\text{new infected}} - \underbrace{(1 - \tilde{\mu}_a)\gamma I_a(t)}_{\text{new recovered from home}} - \underbrace{\frac{\zeta \tilde{\mu}_a I_a(t)}{1 + \boldsymbol{K_a^H}(\boldsymbol{p})^T \boldsymbol{M_a^H}}}_{\text{new hospitalized}} \tag{9}$$

$$\frac{dH_a(t)}{dt} = \underbrace{\frac{\zeta \tilde{\mu}_a I_a(t)}{1 + \boldsymbol{K_a^H}(\boldsymbol{p})^T \boldsymbol{M_a^H}}}_{\text{new hospitalized}} - \underbrace{(1 - \tilde{\nu}_a)\gamma_H H_a(t)}_{\text{new recovered from hospital}} - \underbrace{\frac{\pi \tilde{\nu}_a H_a(t)}{1 + \boldsymbol{K_a^D}(\boldsymbol{p})^T \boldsymbol{M_a^H}}}_{\text{new dead}} \tag{10}$$

$$\frac{dR_a(t)}{dt} = \underbrace{(1 - \tilde{\mu}_a)\gamma I_a(t)}_{\text{new recovered from home}} + \underbrace{(1 - \tilde{\nu}_a)\gamma_H H_a(t)}_{\text{new recovered from hospital}} - \underbrace{\eta R_a(t)}_{\text{new susceptible}} \tag{11}$$

$$\frac{dD_a(t)}{dt} = \underbrace{\frac{\pi \tilde{\nu}_a H_a(t)}{1 + \boldsymbol{K_a^D}(\boldsymbol{p})^T \boldsymbol{M_a^H}}}_{\text{new dead}} \tag{12}$$

where

- $\beta(t) = \beta_0(1 + q(t))$: time-dependent transmission rate
- $q(t)$: seasonality parameter based on absolute humidity
- $\phi_{a,a'}(t)$: mixing rates between age groups based on contact matrices
- γ, γ_H: recovery rates for infected and hospital compartments respectively
- σ: infection rate (exposed to infected transition rate)
- $[\tilde{\mu}_a]$, where $\tilde{\mu}_a = \frac{\mu_a \gamma}{\zeta - \mu_a(\zeta - \gamma)}$: adjusted hospitalization rate vector (as in, proportion hospitalized based on age group) actually used in model – adjustment necessary to ensure actual proportion hospitalized recapitulates $[\mu_a]$
- $[\mu_a]$: hospitalization rate vector (as in, proportion hospitalized based on age group)
- ζ: hospitalization rate (infected to hospital transition rate)

- $[\tilde{\nu}_a]$, where $\tilde{\nu}_a = \frac{\nu_a \gamma_H}{\pi - \nu_a(\zeta - \gamma_H)}$: adjusted hospitalization rate vector (as in, proportion hospitalized based on age group) actually used in model – adjustment necessary to ensure actual proportion hospitalized recapitulates $[\nu_a]$

- $[\nu_a]$: in-hospital mortality rate vector (as in, proportion who die based on age group)

- π: death rate from hospital

- η: rate at which recovered individuals become susceptible

- The following are all $|A| \times |\mathcal{I}|$ matrices
  - $\boldsymbol{K^I(p)} = [K^I_{H1}(p_{H1}), K^I_{H3}(p_{H3}), K^I_V]$: reduction in infection risk from given immunity-inducing event
  - $\boldsymbol{K^H(p)} = [K^H_{H1}(p_{H1}), K^H_{H3}(p_{H3}), K^H_V]$: reduction in hospitalization risk from given immunity-inducing event
  - $\boldsymbol{K^D(p)} = [K^D_{H1}(p_{H1}), K^D_{H3}(p_{H3}), K^D_V]$: reduction in death risk from given immunity-inducing event
  - $\boldsymbol{M^I} = \boldsymbol{M^I}(t) = [M^I_{H1}(t), M^I_{H3}(t), M^I_V(t)]$: population-level immunity from infection (induced by H1 infection, H3 infection, vaccination respectively)
  - $\boldsymbol{M^H} = \boldsymbol{M^H}(t) = [M^H_{H1}(t), M^H_{H3}(t), M^H_V(t)]$: population-level immunity from hospitalization (induced by H1 infection, H3 infection, vaccination respectively)