Mitigating effects of influenza vaccination given constraints in supply and administration capacity

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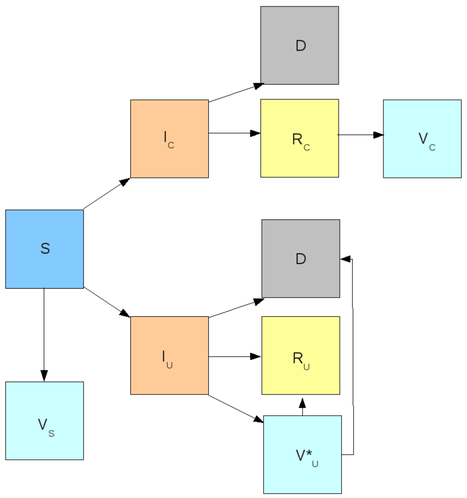
1. Overview

Influenza viruses are a major cause of morbidity and mortality worldwide. Vaccination is a powerful tool for preventing or mitigating influenza outbreaks. Yet, vaccine supplies and daily administration capacities are limited, even in developed countries. Understanding how such constraints can alter the mitigating effects of vaccination is a crucial part of influenza preparedness plans. We present a mathematical model that explicitly takes into account vaccine supply and the number of vaccines administered per day and places data-informed limits on these parameters. We use the model to test several vaccination scenarios. **The model can be used by government and medical officials to create customized pandemic preparedness plans based on the supply and administration constraints of specific communities.**

2. Epidemiological Model

We developed a SIR-like epidemiological model to study the spread of influenza (Coburn et al., 2009; Kermack and McKendrick, 1927).



S = Susceptible
V_S = Vaccinated susceptibles
I_C = Infected confirmed
I_U = Infected unconfirmed
R_C = Recovered confirmed
R_U = Recovered unconfirmed
V_C = Vaccinated confirmed
V^*_U = Vaccinated unconfirmed
D = Deceased due to infection

*still infected/infectious

The dynamics of the model are defined by:

$$\begin{aligned}
\dot{S} &= -\lambda(S,I,t) - v_S(t) \\
\dot{I}_C &= p\lambda(S,I,t) - (c+\delta)I_C \\
\dot{I}_U &= (1-p)\lambda(S,I,t) - (c+\delta)I_U - v_U(t) \\
\dot{V}_U &= v_U(t) - (c+\delta)V_U
\end{aligned}$$

$$\begin{aligned}
\dot{R}_C &= cI_C - v_R(t) \\
\dot{R}_U &= c(I_U + V_U) \\
\dot{V}_{SC} &= v_S(t) + v_R(t) \\
\dot{D} &= \delta(I_C + I_U + V_U)
\end{aligned}$$

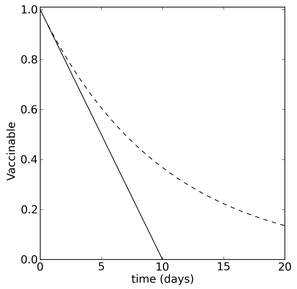
New infections per unit time are:

$$\lambda(S,I,t) = b\frac{S}{N}\left[I_C + \alpha(I_U + V_U)\right] + \phi(t),$$

where p is probability of being infected and confirmed, c is rate of recovery, δ is death rate due to infection, b is probability of infection per contact, α is infectiousness of unconfirmed cases, and $\phi(t)$ is a small pulse used to initiate an outbreak.

3. Modeling Vaccination

Modling vaccination according to *proportion* of population may over- or underestimate number of people that can realistically be vaccinated per day. We propose a *non-proportional* scheme with a daily vaccine limit.



Comparison of decay in vaccinable population over time for proportional (dashed line) and non-proportional (solid line) models of vaccination. Proportional decay is given by $x(t) = x_0 e^{-kt}$, time constant of decay is k=0.1. Non-proportional decay is given by $x(t) = x_0 - \bar{v}_D t$, where $\bar{v}_D$=kx_0 and represents max total number of vaccines per day.

We calculate weights of each subpopulation (epidemiological class):

$$w_S(t) = \frac{S(t)}{M(t)}, \quad w_U(t) = \frac{I_U(t)}{M(t)}, \quad w_R(t) = \frac{R_C(t)}{M(t)},$$

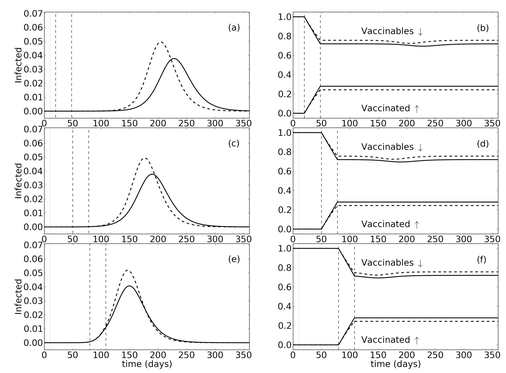
where $M(t) = S(t) + I_U(t) + R_C(t)$ is total eligible for vaccination at time t.

Max number of vaccines per day each subpopulation can receive is then:

$$\bar{v}_S(t) = \bar{v}_D w_S(t), \quad \bar{v}_U(t) = \bar{v}_D w_U(t), \quad \bar{v}_R(t) = \bar{v}_D w_R(t).$$

For more details on the model, see Cruz-Aponte et al. (2011)

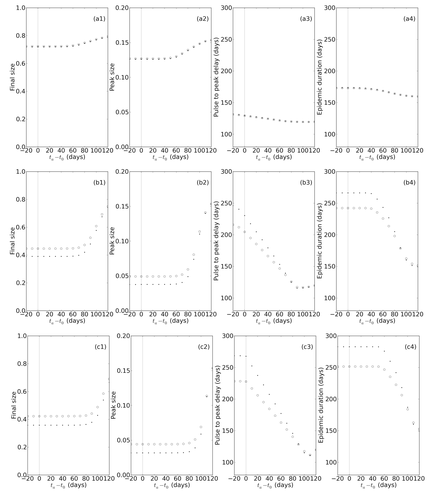
4. Results



Comparison of proportional (dashed) and non-proportional (solid) models for different vaccination campaign starts. Initial outbreak occurs on day 10 (t_0=10; solid vertical line). Vaccination campaign initiated on days 20 **(a, b)**, 50 **(c, d)**, or 80 **(e, f)**, and lasts for 28 days, at rate of 1% of population per day (proportional; k=0.01), or maximum of 10^6 vaccines per day (non-proportional, $\bar{v}_D = 10^6$).

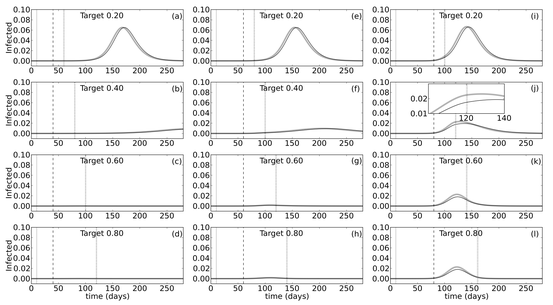
■ Proportional model predicts epidemics that peak sooner with larger peak, but are often shorter, than non-proportional model epidemics.

5. Results



Quantification of final size, peak size, peak time, and epidemic duration for proportional (open circles) and non-proportional (filled circles) models. Measures plotted as function of difference between vaccination start time (t_a) and initial outbreak (t_0; solid gray line). Vaccination scenarios were: (1) 60 day campaign with k=0.001 (proportional) or $\bar{\nu}_D = 10^5$ (non-proportional) **(a1-a4)**, (2) 30 day campaign with k=0.01 or $\bar{\nu}_D = 10^6$ **(b1-b4)**, and (3) 5 day campaign with k=0.1 or $\bar{\nu}_D = 10^7$ **(c1-c4)**.

■ In moderate/aggressive regime, final and peak sizes are smaller, while peak times and epidemic durations are larger, in non-prop. vs. proportional model.



Effects of vaccine coverage, start times, and unconfirmed cases in non-prop. model ($\bar{v}_D$=10^6). Outbreak at t_0=10. Vaccination starts t_a=20 **(a)-(d)**, 50 **(e)-(h)**, or 80 **(i)-(l)**. Confirmed case probablity, p, 0.20 (thick gray) or 0.65 (thin black).

■ 20% coverage does not mitigate outbreak. 40-60% coverage effective in mitigating outbreak, the earlier the better. Beyond 60% coverage, no additional benefits, vaccines are wasted. Confirmed case probablity has little effect.

References

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