SEIR MODEL: SARS OUTSIDE THE HOSPITAL

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Some Questions of SARS Epidemic

- **Epidemics in hospital vs. outside hospital**

Different dynamics?

Medical staff had higher risk, at least in the first weeks of SARS outbreak.

Rapid initial spread of SARS occured in hospital in Vietnam, Hong Kong, Singapore, Canada.

• **Superspreading vs. normal spreading**

Different modes of transmission?

Hong Kong: Prince of Wales hospital, 125 infected by one.

Guangzhou: 130 infected by one.

Singapore: 103 infected by 5.

Before having complete understood of these questions, we began with examining the epidemic dynamics outside hospital.

Population Outside Hospital Divided Into 4 Groups

$\mathcal{S}$: Susceptible, can contract the virus.

$\mathcal{E}$: Exposed, exposed to the virus but not yet infective.

$\mathcal{I}$: Infective, contract SARS and can infect others.

$\mathcal{R}$: Removed, former infective who are no longer infectious (quarantined in hospital, recovered, died).

$$\mathcal{S} \Longrightarrow \mathcal{E} \Longrightarrow \mathcal{I} \Longrightarrow \mathcal{R}$$

Assumptions

1. The total population N is constant.

The populations in the class $\mathcal{S}$, $\mathcal{E}$, $\mathcal{I}$ and $\mathcal{R}$ are $S(t)$, $E(t)$, $I(t)$ and $R(t)$ respectively.

$$S(t) + E(t) + I(t) + R(t) = N.$$

2. The rate of change in $\mathcal{S}$ is proportional to the number of contacts between members of $\mathcal{S}$ and $\mathcal{I}$.

The number of contact is proportional to $I(t)S(t)$ if $I(t)$ is small, and proportional to $S(t)$ if $I(t)$ is large.

The strength of the virus decays in time.

$$S' = -F(I, S, t)S,$$

$$F > 0, \qquad \frac{\partial F}{\partial t} < 0,$$

$$F \sim \lambda I \quad \text{for small } I \text{ and } t,$$

$$F \text{ is bounded for large } I.$$

In practice, we may take

$$F = F(I, t).$$

3. During the incubation period the individual does not infect others.

Let the incubation period be τ days. It is the time length an individual stays in the group $\mathcal{E}$.

$$E(t) = S(t - \tau) - S(t).$$

An infective individual is capable of transmitting the virus to others.

4. The individual will be quarantined in hospital immediately after having been infective for T days.

Thus T is the time length the infective individual stays in the class $\mathcal{I}$.

$$R'(t) = I(t - T).$$

SEIR Model

$$\begin{cases} S'(t) = -F(I,t)S, \\ E(t) = S(t-\tau) - S(t), \\ I'(t) = F\big(I(t-\tau), t-\tau\big)S(t-\tau) - I(t-T), \\ R'(t) = I(t-\tau). \end{cases} \tag{1}$$

Initial conditions are given on the interval $[-\tau, 0]$, assuming $T < \tau$.

Consider that the infective are not quarantined exactly T days after being infective, the model is modified to

$$\begin{cases} S'(t) = -F(I,t)S, \\ E(t) = S(t-\tau) - S(t), \\ I'(t) = F\big(I(t-\tau), t-\tau\big)S(t-\tau) - \sum\limits_{0\le j<T} k_j I(t-T+j), \\ R'(t) = \sum\limits_{0\le j<T} k_j I(t-T+j). \end{cases} \tag{2}$$

SARS Epdemic Outside Hospital in Singapore

We computed the model against the data from March 13 to April 26, 2003. $t = 0$ on the day March 19. To fit the data, we choose

$$F(I,t) = e^{-h(t)} g(I),$$

where, for I not very large,

$$g(I) = \frac{bI}{1 + c_1 I + c_2 I^2 + c_3 I^3}, \qquad h(t) = \frac{\beta t + \delta t^2}{1 + \gamma t}.$$

Value of Parameters

$$\tau = 5, \qquad T = 3, \qquad b = \frac{2.8}{N}.$$

$$N = 3500000,$$

$$K_0 = K_1 = K_2 = 0.3,$$

$$c_1 = 0.08, \qquad c_2 = 0.03, \qquad c_3 = 0.1,$$

$$\beta = 0.62, \qquad \delta = 0.003, \qquad \gamma = 0.99.$$

Observation From Computation

The model fits the data best when

$$\tau = 5, \qquad T = 3, \qquad b = \frac{2.8}{N}.$$

• **Incubation period**: After we had finished the computation we learned that in Singapore, $\tau = 5.2$. Morbidity and Mortality Weekly Report **52**, 405 (2003).

In Hong Kong, $\tau = 6.4$ days, Donnell et al, Lancet, 361 (2003).

• **Value of T:** We were not able to find reported value of T in Singapore.

In Hong Kong: T is between 3 and 5 days, longer earlier in the epidemic. Donnell et al, Lancet, 361 (2003).

• The model is sensitive in b.

But is robust in other parameters.

• Not as the standard SIR model where the curve exhibits one peak, the solution of SEIR model exhibits oscillation.

A Consequence

$F(I,t) = g(I)e^{-h(t)} \sim$ probability of a person outside hospital contracting the virus per day,

$\frac{g(I)e^{-h(t)}}{I}S \sim \frac{g(I)e^{-h(t)}}{I}N \sim$ number of persons infected by an infective outside hospital per day.

Consider an infective who stays outside hospital in the time

interval $[t_0, t_0 + T]$. We may use

$$\int_{t_0}^{t_0+T} g_0(I(t))e^{-h(t)}dt$$

to give a rough estimate of the expected number of secondary infections generated by him outside hospital, where

$$g_0(I) = \frac{2.8}{1 + 0.08I + 0.03I^2 + 0.1I^3},$$

$$h(t) = \frac{0.62t + 0.003t^2}{1 + 0.99t}.$$

For large t,

$$h(t) \sim \frac{0.62}{0.99} \sim 0.63.$$

If we choose $I = 2$ (which is close to the average), we can estimate the integral by

$$3g_0(2)e^{-0.63} = 3 \times 1.35 \times 0.53 \sim 2.1.$$

Lipsitch et al. estimated that in Singapore, including the transmission in hospitals, a single infective produced $2.2 \sim 3.6$ secondary cases.

Note that

$$F(I,t) = g_0(I)e^{-h(t)}\frac{I}{N}.$$

For large t, as above, choosing the average infective $I = 2$, we may estimate the probability of a person outside hospital contracting the virus per day by

$$F(I,t) \sim 1.35 \times 0.53 \times \frac{2}{N} \sim \frac{1.4}{N}.$$

Next Step

To understand SARS epidemic we have to examine the transmission in hospital, and understand the superspreading events. The phenomenon is very complicated. We do not expect any simple model.

Let us try a ...

Two-population model: a model including superspreaders

The total population is divided into 5 groups.

- $\mathcal{S}$: Susceptible, can contract the virus.

$$\mathcal{S} = \mathcal{S}_m \cup \mathcal{S}_n,$$

$\mathcal{S}_m$: medical staff,

$\mathcal{S}_n$: others.

The population in the classes $\mathcal{S}_m$ and $\mathcal{S}_n$ are $S_m(t)$ and $S_n(t)$

respectively,

$$S(t) = S_m(t) + S_n(t).$$

- $\mathcal{E}$: Exposed, exposed to the virus but not yet infective.

The population in the class $\mathcal{E}$ is $E(t)$.

• $\mathcal{I}$: Infective, contract SARS and can infect others.

$$\mathcal{I} = \mathcal{I}_w \cup \mathcal{I}_g,$$

$\mathcal{I}_w$: weakly infective;

$\mathcal{I}_g$: strongly infective (super-spreaders).

The population in the classes $\mathcal{I}_w$ and $\mathcal{I}_g$ are $I_w(t)$ and $I_g(t)$ respectively,

$$I(t) = I_w(t) + I_g(t).$$

• $\mathcal{P}$: Patients, quarantined in hospital. The population in the class $\mathcal{P}$ is $P(t)$.

$$\mathcal{P} = \mathcal{P}_w \cup \mathcal{P}_g,$$

$\mathcal{P}_w$: patients who are weakly infective;

$\mathcal{P}_g$: patients who are strongly infective (super-spreaders).

The population in the classes $\mathcal{P}_w$ and $\mathcal{P}_g$ are $P_w(t)$ and $P_g(t)$ respectively,

$$P(t) = P_w(t) + P_g(t).$$

• $\mathcal{R}$: Removed, former infective who are no longer infectious (including recovered, died, isolated).

The population in the class $\mathcal{R}$ is $R(t)$.

$$\mathcal{S} \Longrightarrow \mathcal{E} \Longrightarrow \mathcal{I} \Longrightarrow \mathcal{P} \Longrightarrow \mathcal{R}$$

Assumptions

1. The total population N is constant.

$$S(t) + E(t) + I(t) + P(t) + R(t) = N.$$

2. Patients in hospital contact only medical staff.

The members in $\mathcal{S}_n$ can be infected by members in $\mathcal{I}$ only.

The members in $\mathcal{S}_m$ can be infected by members both in $\mathcal{I}$ and in $\mathcal{P}$.

3. During the incubation period the individual does not infect others. The incubation period is τ days.

4. The weakly and strongly infective patients are recovered at the rate c_w or c_g respectively:

$$R'(t) = c_g P_g(t) + c_w P_w(t), \qquad c_g \ll c_w.$$

5. An infective individual is capable of transmitting the virus to others. The individual will be quarantined in hospital immediately after having been infective for T days.

The model is:

$$
\begin{aligned}
S_n'(t) &= -F_n\big(I_g(t), I_w(t), t\big) S_n(t), \\
S_m'(t) &= -\Big[F_n\big(I_g(t), I_w(t), t\big) + F_m\big(P_g(t), P_w(t), t\big)\Big] S_m(t), \\
E(t) &= S_n(t-\tau) + S_m(t-\tau) - S_n(t) - S_m(t), \\
I_w'(t) &= H_{wn}(I_g(t-\tau), I_w(t-\tau), t-\tau) S_n(t-\tau) \\
&\quad + H_{wm}\big(I_g(t-\tau), I_w(t-\tau), t-\tau\big) S_m(t-\tau) \\
&\quad + Q\big(P_g(t-\tau), P_w(t-\tau), t-\tau\big) S_m(t-\tau) - I_w(t-T),
\end{aligned}
$$

$$
\begin{aligned}
I_g'(t) = &\Big[F_n\big(I_g(t-\tau), I_w(t-\tau), t-\tau\big) \\
&\quad - H_{wn}\big(I_g(t-\tau), I_w(t-\tau), t-\tau\big)\Big] S_n(t-\tau) \\
&+ \Big[F_n\big(I_g(t-\tau), I_w(t-\tau), t-\tau\big) \\
&\quad + F_m\big(P_g(t-\tau), P_w(t-\tau), t-\tau\big) \\
&\quad - H_{wm}\big(I_g(t-\tau), I_w(t-\tau), t-\tau\big) \\
&\quad - Q\big(P_g(t-\tau), P_w(t-\tau), t-\tau\big)\Big] S_m(t-\tau) - I_g(t-T), \\
P_g'(t) = &\, I_g(t-T) - c_g P_g(t), \\
P_w'(t) = &\, I_w(t-T) - c_w P_w(t), \\
R'(t) = &\, c_g P_g(t) + c_w P_w(t).
\end{aligned}
$$

where $c_g \ll c_w$.

The model can be modified to reflect the fact that the infective are not quarantined exactly T days after being infective,

In practice, we can take F, H, Q to be linear functions.

$$
\begin{aligned}
S_n'(t) &= -\Big(\alpha_{ng} I_g(t) + \alpha_{nw} I_w(t)\Big) S_n(t), \\
S_m'(t) &= -\Big(\alpha_{ng} I_g(t) + \alpha_{nw} I_w(t) + \alpha_{mg} P_g(t) + \alpha_{mw} P_w(t)\Big) S_m(t), \\
E(t) &= S_n(t-\tau) + S_m(t-\tau) - S_n(t) - S_m(t), \\
I_w'(t) &= \Big[\beta_{ng} I_g(t-\tau) + \beta_{nw} I_w(t-\tau)\Big] S_n(t-\tau) \\
&\quad + \Big[\beta_{mg} I_g(t-\tau) + \beta_{mw} I_w(t-\tau)\Big] S_m(t-\tau) \\
&\quad + \Big[\gamma_g P_g(t-\tau) + \gamma_w P_w(t-\tau)\Big] S_m(t-\tau) - I_w(t-T),
\end{aligned}
$$

$$
\begin{aligned}
I'_g(t) &= \Big[(\alpha_{ng} - \beta_{ng})I_g(t-\tau) + (\alpha_{nw} - \beta_{nw})I_w(t-\tau)\Big]S_n(t-\tau) \\
&\quad + \Big[(\alpha_{mg} - \beta_{mg})I_g(t-\tau) + (\alpha_{mw} - \beta_{mw})I_w(t-\tau)\Big]S_m(t-\tau) \\
&\quad + \Big[(\alpha_{mg} - \gamma_g)P_g(t-\tau) + (\alpha_{mw} - \gamma_w)P_w(t-\tau)\Big]S_m(t-\tau) \\
&\quad - I_g(t-T), \\
P'_g(t) &= I_g(t-T) - c_g P_g(t), \\
P'_w(t) &= I_w(t-T) - c_w P_w(t), \\
R'(t) &= c_g P_g(t) + c_w P_w(t),
\end{aligned}
$$

where

$$\alpha_{ng} \gg \alpha_{nw}, \quad \alpha_{mg} \gg \alpha_{mw}, \quad \alpha_{ng} \gg \alpha_{nw}, \quad c_w \gg c_g.$$

We are now trying to simplify the model. However, recently C. Dye and N. Gay wrote:

"On a conceptual level, the next generation of SARS models may have to become yet more complex ....."

——Science.1086925, 23 May 2003.

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