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The SARS epidemic

In this second contribution, we will focus on the epidemic of Severe Acute Respiratory Syndrome (SARS) caused by the Coronavirus *SARS-CoV*. This epidemic started on November 2002. We will review antecedents of this disease, look at two epidemiological models and discuss some of the measures taken during that period of time.

1 Summary

- In the first case, a model of SARS containing five different classes of individuals was considered. The model was fitted to the existing data at that moment in order to study the influence of patient isolation and diagnostic rate. The effect of quarantine was not explored. The differences observed in the dynamics of different regions are attributed to a good diagnostic rate and an efficient isolation of patients. This model is most sensitive to two parameters: the effectiveness in the isolation and the diagnostic rate. The lack of a large amount of data and the high sensitivity of these parameters make difficult for this model to predict the long-term impact of SARS.
- The second model of SARS was developed some years after the epidemic. It studies the impact of quarantine and isolation strategies. The numerical simulations performed here show that isolation strategies are very critical at an early stage of the epidemic. Suboptimal strategies provide similar results as the optimal (more restrictive and somehow less practical) strategies.
- Models are simplifications and partial descriptions of reality. They contain assumptions that imply certain idealization and approximation of phenomena. The language of mathematics allow us to formulate the behavior of an epidemic in a precise and concise way. The robustness of a model is a measure of how well the assumptions of the model correspond to reality. We evaluate the robustness of the predictions by studying different models.

2 Some antecedents on SARS

According to estimates of the World Health Organization (WHO) around 8,096 individuals were infected with SARS and 774 deaths were registered due to SARS in 55 countries [5]. The symptoms of SARS are very similar to those caused by many common respiratory pathogens (influenza viruses, *Mycoplasma pneumoniae*, *Coxiella burnetii*, etc.). In order to achieve an accurate diagnosis, the following symptoms were considered as clinical evidence of SARS [5]: documented fever $\geq 38\ ^{\circ}\mathrm{C}$, one or more symptoms of lower respiratory tract illness (cough, difficulty breathing, shortness of breath), radiographic evidence of lung infiltrates consistent with pneumonia, and the fact that no other alternative diagnosis can fully explain the disease. The diagnosis of SARS in the laboratory was mainly achieved by reverse transcription polymerase chain reaction (RT-PCR) from at least two different samples. This same method is used at the present time for testing the virus SARS-CoV-2. Serological tests were also developed and performed for SARS.

It is believed that the SARS-CoV virus is an animal virus that crossed to humans, when more contact between animals and persons took place, allowing the exposure to the virus to increase, and the virus to adapt [1]. The natural reservoir of SARS-CoV has not been identified yet but a number of wildlife species have been shown to be infected with a related coronavirus.

The first case of SARS occurred in November 2002 in the Chinese province of Guangdong. It was at the end of February 2004 that the SARS spread worldwide when a doctor of Guangdong infected several individuals at a

hotel in Kowloon, Hong Kong. Later, the disease spread by air travel. It is also known that short visits to epidemic regions resulted in infections. The outbreak of SARS was taken under control at the end of 2003, the last reported human chain of infection was broken in July 2003. However, separate outbreaks of SARS appeared later in Singapore, Taiwan and China. Three of these outbreaks were attributed to breaches in laboratory biosafety [5]. SARS posed a serious threat to the medical community because of the high number of infected health-care workers. This disease had also a severe adverse economic effect in some regions of East Asia; it was actually worse than the previous disruptions caused by the avian influenza [4].

3 A SEIJR compartmental model for SARS

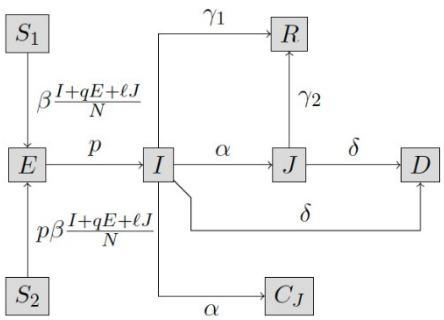
Many papers studying SARS appeared in 2003, many of them in Chinese journals, which were poorly available to international researchers. Most of the research of the virus took place in China, where the SARS epidemic hit the hardest.

In the last contribution we considered a model with susceptible, infected and recovered individuals. We will now explore a more complicated model with susceptible, exposed, infected, diagnosed, and recovered classes of individuals, which in the literature is known as "SEIJR". This particular model was developed by Chowell et al [2] based on data from Toronto, Hong Kong and Singapore. It was observed that the epidemic dynamics for Hong Kong and Singapore appeared to be different from the dynamics in Toronto, Ontario. The difference could be attributed to variations in contact rates, age-dependent susceptibility or unknown "genetic" (or other) factors. To handle this situation the authors introduce two different susceptible classes: S_1 the most susceptible and S_2 the less susceptible, which reflects more the reality since human populations are heterogeneous. People are more susceptible because of preexisting health conditions or because they live in an epidemic zone. The compartmental model they proposed is given by a system of ordinary differential equations:

$$
\begin{aligned}
\frac{d}{dt}S_1(t) &= -\beta S_1(t)\frac{I(t)+qE(t)+\ell J(t)}{N}\\
\frac{d}{dt}S_2(t) &= -\beta p S_2(t)\frac{I(t)+qE(t)+\ell J(t)}{N}\\
\frac{d}{dt}E(t) &= -\beta(S_1(t)+pS_2(t))\frac{I(t)+qE(t)+\ell J(t)}{N} - kE(t)\\
\frac{d}{dt}I(t) &= kE(t) - (\alpha+\gamma_1+\delta)I(t)\\
\frac{d}{dt}J(t) &= \alpha I(t) - (\gamma_2+\delta)J(t)\\
\frac{d}{dt}R(t) &= \gamma_1 I(t) + \gamma_2 J(t)
\end{aligned}
$$

The total of the population is $N = S_1 + S_2 + I + J + R$. At the beginning, $S_1 = \rho N$ and $S_2 = (1-\rho)N$, where ρ is the proportion of the population that is at higher risk of getting infected. Parameter p is a measure of reduced susceptibility to the infection in class S_2. β is the transmission rate per day. Class E denotes the "exposed" individuals, asymptomatic but possibly infected. The possibility of transmission from class E is included with a parameter q. Class I represents the symptomatic, infected and undiagnosed individuals. The I-individuals evolve into class J of diagnosed persons at the rate α. The individuals recover at the rate γ_1 for class I and γ_2 for class J. The class of recovered individuals R keeps track of the number of diagnosed and recovered individuals. Parameter δ indicates the SARS-induced mortality. The model also assumes that the individuals are carefully treated and diagnosed, therefore they are not as infectious as those who are not diagnosed. Finally parameter ℓ is a measure of the reduced impact of those individuals who are diagnosed, a small value of ℓ indicates that effective measures were taken in order to isolate diagnosed cases.

The following flow diagram summarizes the evolution of classes in this model. Note that not all exposed individuals have to evolve to class I of infected persons. Only a proportion of them will be infected.



Quantity C_J is included only for comparison with epidemiological statistics. It tracks the total number of diagnosed cases. The values of p and q are fixed arbitrarily, since they are not known in advance, while parameters α and ℓ are varied to fit the existing data from Hong Kong, Toronto and Singapore. The other parameters were roughly estimated from literature. In this model, the effect of isolating diagnosed individuals is explored through these parameters.

The authors found estimates of the basic reproduction number R_0 ranging between 1.1 and 1.2. They also conclude that the changes introduced after the identification of the first case result in a dramatic reduction in the number of cases and mortality in Toronto. According to their model, local outbreaks should follow similar pat- terns (even in the presence of superspreaders). Their model is quite sensitive to the parameters ℓ (effectiveness of isolation) and α (diagnostic rate).

4 A SEQIJR model of SARS

The previous model we looked at was developed at the moment that the epidemic was taking place with the data available at that moment, and the model was fitted to those data. A few years later several papers on SARS appeared, and among them paper [6] that considered a SEQIJR model. The population is split into six classes: susceptible, asymptomatic, quarantined, symptomatic, isolated, and recovered individuals. This model was originally proposed in [3]. A system of differential equations describes this epidemic model:

$$\begin{aligned}
\frac{d}{dt}S(t) &= \Lambda - S(t)\frac{\beta I(t) + \varepsilon_E \beta E(t) + \varepsilon_Q \beta Q(t) + \varepsilon_J \beta J(t)}{N} - \mu S(t) \\
\frac{d}{dt}E(t) &= p + S(t)\frac{\beta I(t) + \varepsilon_E \beta E(t) + \varepsilon_Q \beta Q(t) + \varepsilon_J \beta J(t)}{N} - (u_1(t) + k_1 + \mu)E(t) \\
\frac{d}{dt}Q(t) &= u_1(t)E(t) - (k_2 + \mu)Q(t) \\
\frac{d}{dt}I(t) &= k_1 E(t) - (u_2(t) + d_1 + \sigma_1 + \mu)I(t) \\
\frac{d}{dt}J(t) &= u_2(t)I(t) + k_2 Q(t) - (d_2 + \sigma_2 + \mu)J(t) \\
\frac{d}{dt}R(t) &= \sigma_1 I(t) + \sigma_2 J(t) - \mu R(t)
\end{aligned} \tag{1}$$

In this model, the total of the population $N = S + E + I + Q + J + R$. It assumes a natural death rate $\mu > 0$ in each group of the subpopulations and a constant recruitment rate Λ. This includes the inflow of asymptomatic persons into the region at rate p per time unit: new births, immigration and emigration. The transmission coefficients for the four classes of infected individuals are β, $\varepsilon_E \beta$, $\varepsilon_Q \beta$, $\varepsilon_J \beta$, respectively. An asymptotic person flows into the symptomatic class at a rate k_1, and a quarantine individual into the isolated class at a rate k_2. The parameters d_1 and d_2 are per-capita disease induced death rates for the symptomatic and isolated persons, respectively. Likewise, the parameters σ_1 and σ_2 are per-capita recovery rates for the symptomatic and isolated individuals, respectively. The control variable $u_1(t)$ is the rate of quarantining of individuals who have been in contact with an infected person, while $u_2(t)$ represents the rate of isolating of symptomatic individuals by an isolation program.

The mathematical problem for this model consists in minimizing a certain cost function

$$J(u_1, u_2) = \int_0^{t_f} \left[B_1 E(t) + B_2 Q(t) + B_3 I(t) + B_4 J(t) + \frac{C_1}{2} u_1^2(t) + \frac{C_2}{2} u_2^2(t) \right] dt \tag{2}$$

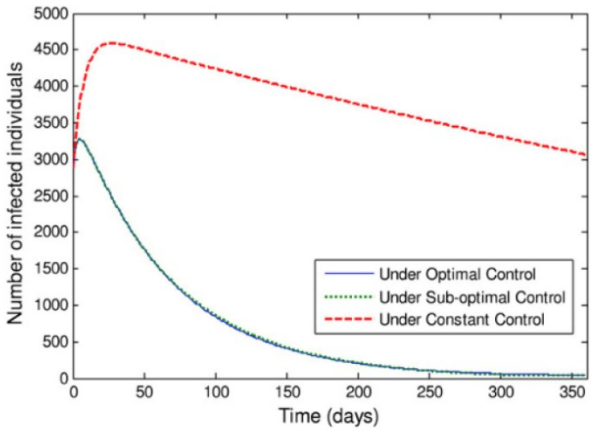
subject to the system (1) and certain boundary conditions. The coefficients, B_1, B_2, B_3, B_4, C_1 and C_2, are balancing cost factors and t_f is the final time. The main idea is to find an optimal control pair of functions u^*_1, u^*_2 such that

$$J(u_1^*, u_2^*) = \min_{\Omega} J(u_1, u_2), \tag{3}$$

where Ω is a certain space of functions. The so-called Pontryagin's maximum principle provides necessary conditions for finding solutions to optimal control problems. With this result, the problem is transformed into minimizing a Hamiltonian system H, with respect to u_1 and u_2. Through numerical simulation based on a

genetic algorithm, the authors obtain a suboptimal solution, that means a solution where the functions u^*_1, u^*_2 are not the global minimum, for the optimal quarantine and isolation control to the problem (3). They compute likewise an optimal solution. The comparison between the suboptimal and the optimal solution is very interesting since both provide very similar performance for reducing the number of infected individuals. In general, for practical implementations it is easier to use suboptimal solutions, since they are less restrictive and the results are similar.

The next figure was taken from [6] (Figure 4). Here, we can see that the curves corresponding to the optimal and the suboptimal solutions are practically indistinguishable. Both strategies result in the same reduction of the number of infected individuals.



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