



EXPLORING HEALTH POLICIES TO PREVENT ANOTHER SARS OUTBREAK IN HONG KONG

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Abstract

The paper we read introduces a unique way of interpreting and modeling the data from the SARS outbreak in Hong Kong, and ultimately around the globe in early 2003. It introduces a "double-epidemic hypothesis" that suggests that a certain coronavirus is highly contagious but much less harmful provided a natural protection of immunity for the SARS virus. This paper tries to add on to the existing model and explore the potential effects of vaccination, i.e. an artificial protection of immunity for the SARS virus, on the outbreak, peak level, equilibrium level for SARS. Our ultimate goal is to provide a guideline for health authorities in HK on how to most effectively limit the progression and influence of the disease should there be another SARS outbreak in HK. We started by considering two separate plans: post-outbreak vaccination and pre-outbreak vaccination. For post-outbreak vaccination, we explore the possibility of controlling the disease if vaccination is given to the population at the maximal rate after the outbreak of the disease. We also tested different "threshold levels", i.e. minimum number of new daily cases, above which we trigger this post-outbreak vaccination mechanism. On the other hand, for pre-outbreak vaccination, by pre-vaccinating the population, we explore what the minimum percentage of the population must be vaccinated before an outbreak in order for the disease to be effectively controlled.

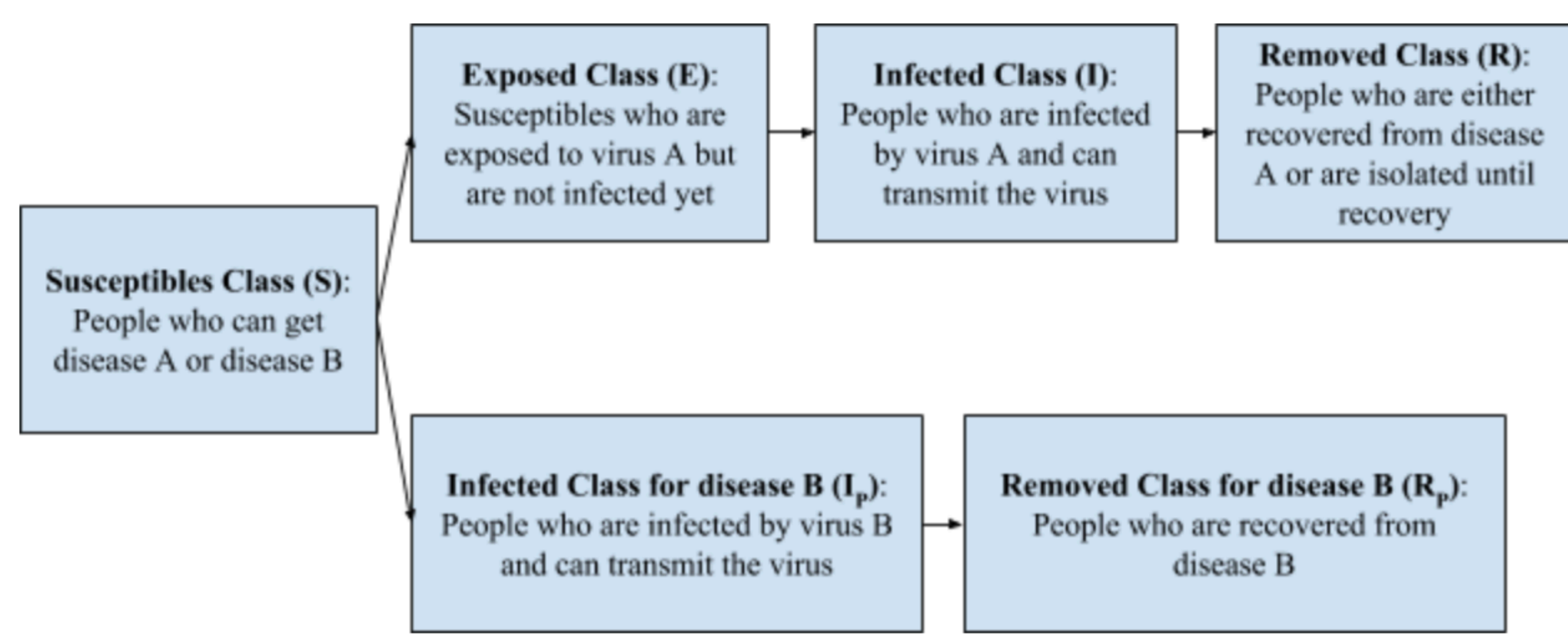
Paper on which We Based our Research

The paper we looked at was written by Professor Tuen Wai Ng at University of Hong Kong, Professor Gabriel Turinici at l'Université de Paris Dauphine and Professor Antoine Danchin at Institut Pasteur. This paper created an SEIRP model that studies the spread and outbreak of SARS in Hong Kong in early 2003. The researchers discovered that a surprisingly high percentage of the total population must have been protected against SARS virus during the outbreak by an unknown mechanism resembling the effect of vaccination. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) Thus, the researchers consider the SARS virus within the broader system that contains two co-existing coronaviruses, the SARS virus labeled virus A and another type of coronavirus that is "extremely contagious" but relatively innocuous labeled virus B. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) While virus A leads to the SARS epidemic, virus B leads to another epidemic that is much less harmful (due to the innocuousness of the virus) but no less widespread (due to its high contagiousness), with symptoms such as gastro-enteritis and diarrhea demonstrated by many people in Hong Kong and Guangdong (regions of high concentrations of SARS patients later) shortly before the SARS outbreak in 2003.

SEIRP Model - A Variation of the SIR Model

Assuming that there are no people entering or leaving the region, the traditional SIR model divides the entire population into one of the three sections in the progressive sequence S-I-R; S, the susceptible who can get the disease; I, the infected who carry the disease and can transmit the virus to others; R, the removed who are either recovered from the disease and thus immune or isolated/quarantined until recovery and are thus no longer infectious for this particular virus (note this slightly different definition of the R Class is given in the paper, and we will use this definition of R for the rest of this research). (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) Since the traditional SIR model focuses solely on a single virus and does not fit well with the data of SARS outbreak in 2003, a new model is needed to reflect the natural protective effects of virus B in the "double epidemic hypothesis" (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) We thus introduce the SEIRP model that features two major modifications to the traditional SIR model. Firstly, an interim state is added between S and I, namely, E, to represent a constant time period called the "latent period" between exposure (E) to the virus and infection by the virus, during which the person carries the virus but cannot transmit it to others. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) Secondly, a P state is introduced to represent "protection" and thus incorporate the protective effects of virus B that provides immunity for virus A to people infected by virus B.

Figure 1: The SEIRP Model



This double-virus SEIRP model is illustrated by the box-model shown in Figure 1 above, which describes a two-virus system involving viruses A (the one causing SARS) and B, and we consider the developments of the diseases with respect to time (t). (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) As shown by the six distinct boxes, the box-model divides the population into six different classes whose relationships with each other are clearly demonstrated by the arrows between boxes: Susceptible Class (S) that stands for the class of people who can get either disease A or disease B, Exposed Class (E) that represents the susceptible people in Class S who are exposed to virus A (SARS virus) first but are not infected yet, Infected Class (I) that stands for the people in Class E who end up being infected by virus A (SARS virus) and can thus transmit the virus to others, Removed Class (R) that represents the people in Class I who are no longer infectious, i.e., those who either recovered from disease A (SARS) or are isolated/quarantined until recovery, Infected Class for disease B (I_p) that stands for the susceptible in Class S who are infected by virus B and can transmit the virus to others, and finally the Removed Class for disease B (R_p) that represents the people in Class I_p who recovered from disease B (no longer infectious) and thus gained natural protection against virus A (SARS virus). (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation)

Explaining the Parameters

The parameter r is a constant that can be interpreted as the infection rate of disease A that has the unit $(\frac{1}{\text{unit time} \cdot \text{person}})$. It is calculated as part of $rS(t)I(t)$, which is a number proportional to the number of infected people with disease A (I) multiplied by the number of susceptible people (S). This number calculates the number of people who become exposed to disease A over a unit time (t). A higher r means that in a unit time, a greater number of the susceptible population becomes exposed to disease A.

The parameter r_p is similar to r , but is the infection rate for disease B that has unit $(\frac{1}{\text{unit time} \cdot \text{person}})$ and is calculated as part of $r_p S(t)I_p(t)$, which is a number proportional to the number of people infected with disease B (I_p) multiplied by the number of susceptible people (S). This number calculates the number of people who are infected by disease B over a unit time (t). A higher r_p means that in a unit time, a greater number of the susceptible population becomes infected with disease B.

The parameter a might be the most difficult to understand, and it describes the removal process from the Infected Class (I) to the Removed Class (R). (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) Since we defined our Removed Class (R) as the class of infected population who are no longer infectious, i.e. those who are either recovered or are isolated from the general population, the parameter a should be interpreted as the identification rate of potential cases that has unit $(\frac{1}{\text{unit time}})$ (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) It is calculated as part of $aI(t)$, which is a number proportional to the total number of people infected by virus A. This number calculates the number of people infected with virus A (SARS virus) who are identified as infected and thus removed from the disease A infected class to the disease A removed class per unit time. A higher a means that in a unit time, a larger number of the infected population for virus A is identified, becomes removed, and joins the removed population.

The parameter a_p is similar to a , but it describes the removal process from the Infected Class for disease B (I_p) to the Removed Class for disease B (R_p). (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) Similarly, the parameter a_p should be interpreted as the identification rate of potential cases that has unit $(\frac{1}{\text{unit time}})$. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) It is calculated as part of $a_p I_p(t)$, which is a number proportional to the total number of people infected by virus B. This number calculates the total number of people infected with virus B who have been identified as infected, given medical treatments, and thus moved to the removed population over a unit time. A higher a_p means that in a unit time, a larger number of the infected population for virus B is identified, given treatment or taken care of, recovers, and joins the removed population.

The parameter b is a constant that can be interpreted as the rate of evolution from Exposed Class (E) to the Infected Class (I) that has the unit $(\frac{1}{\text{unit time}})$. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) It is calculated as part of bE , which is a number proportional to the total number of exposed people. This number calculates the number of exposed people who have evolved to become infected per unit time. A higher b means that in a unit time, a larger number of the exposed population for disease A leaves the exposed class to join the infected class for disease A. It is important to notice that $1/b$ is related to disease A's latent period. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation)

Explaining the Equations

Rate of change for the susceptible population: $\frac{dS}{dt} = -rS(t)I(t) - r_p S(t)I_p(t)$
 $-rS(t)I(t) - r_p S(t)I_p(t)$ is a negative rate of change that measures over a unit time the number of susceptible people decreased who either become exposed to disease A ($=rS(t)I(t)$) or infected by disease B ($=r_p S(t)I_p(t)$)

Rate of change for the population exposed to disease A: $\frac{dE}{dt} = rS(t)I(t) - bE(t)$
 $rS(t)I(t) - bE(t)$ is a relative rate of change that measures over a unit time the change in the number of people exposed to disease A. The rate of change becomes more positive when there is a greater number of susceptible people who becomes exposed to virus A ($=rS(t)I(t)$) and becomes more negative when a greater number of exposed people become infected with disease A ($=bE(t)$). If $rS(t)I(t)$ is greater than $bE(t)$, the rate of change for the number of population exposed to disease A is positive and if $rS(t)I(t)$ is less than $bE(t)$, the rate of change for the number of population exposed to disease A is negative.

Rate of change for the population infected with disease A: $\frac{dI}{dt} = bE(t) - aI(t)$
 $bE(t) - aI(t)$ is a relative rate of change that measures over a unit time the change in the number of people infected with disease A. The rate of change becomes more positive when a greater number of exposed people become infected with disease A ($=bE(t)$) and becomes more negative when a greater number of people infected with disease A become identified with having disease A and are placed in the removed population for disease A ($=aI(t)$). $bE(t)$ is greater than $aI(t)$, the rate of change for the number of population infected with disease A is positive and if $bE(t)$ is less than $aI(t)$, the rate of change for the number of population infected with disease A is negative.

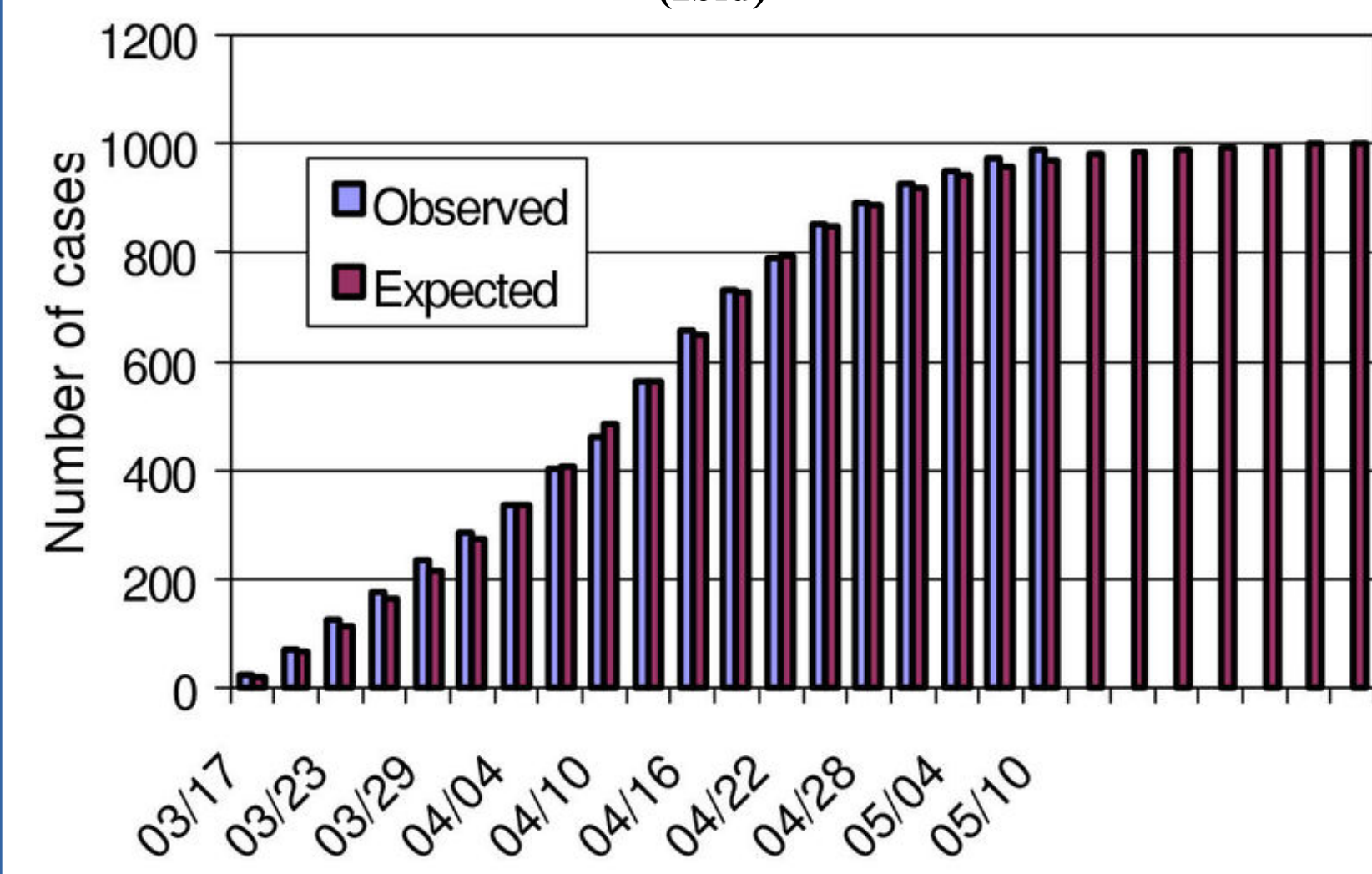
Rate of change for the removed population for disease A: $\frac{dR}{dt} = aI(t)$
 $aI(t)$ is a relative rate of change that measures over a unit time the change in the number of removed people for disease A. The rate of change increases when a greater number of people infected with disease A become identified with having disease A and are placed in the removed population for disease A ($=aI(t)$)

Rate of change for the population infected with disease B: $\frac{dI_p}{dt} = r_p S(t)I_p(t) - a_p I_p(t)$
 $r_p S(t)I_p(t) - a_p I_p(t)$ is a relative rate of change that measures over a unit time the change in the number of people infected with disease B. The rate of change becomes more positive when a greater number of susceptible people become infected with disease B ($=r_p S(t)I_p(t)$) and become more negative when a greater number of people infected with disease B become identified with having disease B and are placed in the removed population for disease B ($=a_p I_p(t)$). If $r_p S(t)I_p(t)$ is greater than $a_p I_p(t)$, the rate of change for the number of people infected with disease B is positive and if $r_p S(t)I_p(t)$ is less than $a_p I_p(t)$, the rate of change for the population infected with disease B is negative.

Rate of change for the removed population with disease B: $\frac{dR_p}{dt} = a_p I_p(t)$
 $a_p I_p(t)$ is a relative rate of change that measures over a unit time the change in the number of removed people with disease B. The rate of change increases when a greater number of people infected with disease B become identified with having disease B and are placed in the removed population for disease B ($=a_p I_p(t)$)

Hong Kong SARS Data

Figure 2: The cumulative SARS cases in the Hong Kong community from 3/17/2003 to 5/10/2013 (Ibid)



As shown in Figure 2, the expected number of cumulative SARS cases in Hong Kong community from March 17th to May 10th, 2003 produced by the model (curve for R) fits extremely well with the actual cases observed in that time period. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation) The model also allows us to simulate and predict the equilibrium level of cumulative cases, which results in a limiting value of 1011 for the R curve. (Ng, Turinici, Danchin, A double epidemic model for the SARS propagation)

Figure 3: Number of new SARS cases in HK community every three days from 3/17/2003 to 5/10/2013 (Ibid)

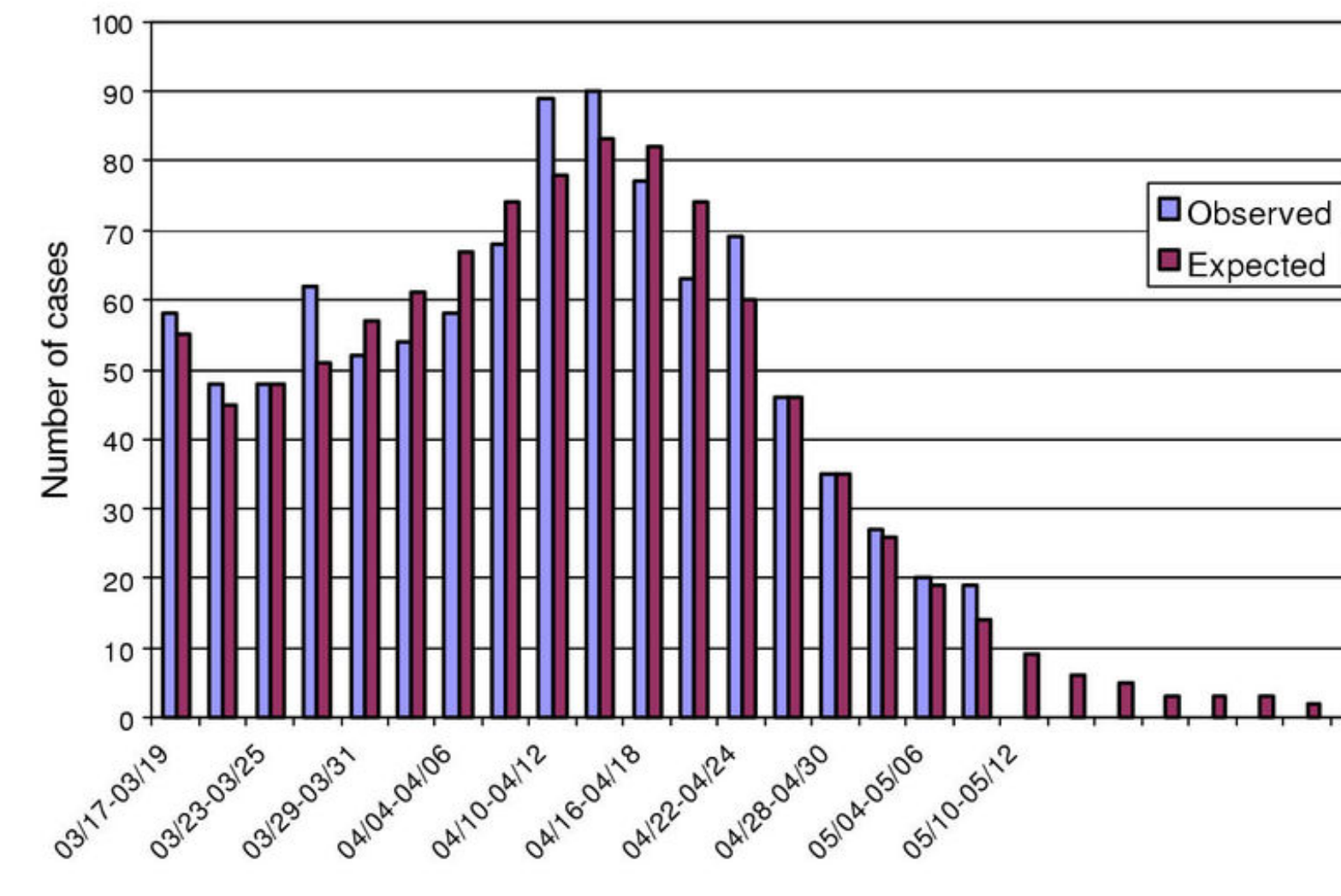


Figure 3 demonstrates the number of new cases every three days and thus illustrates the progression of the outbreak in a more detailed fashion. From Figure 3, we can see that the predicted peak of the outbreak is about 83 cases per three days in mid-April, while the actual peak of the outbreak is 90 cases per three days in the same three-day period. (Ibid) The model also allows us to simulate and predict the equilibrium level of new cases per three days, which results in a limiting value of around 4 cases per three days forming the "constant background infection level on which superimposes sudden local outbreaks". (Ibid)

Our Model

The figure above shows projections of SARS cases under the assumption that people start getting vaccinated after the outbreak of the disease. Here we have four scenarios:

- Blue bars: people getting vaccinated on the first day of the outbreak, when there are only 14 cases of the disease
- Green bars: people getting vaccinated on the second day, when there are 18 cases that day
- Purple bars: people getting vaccinated on the 9th day, with 22 daily cases
- Yellow bars: people getting vaccinated on the 26th day, with 26 daily cases

Also, described by the orange bars, we have the actual data from 2003.

As can be seen from the cumulative graphs and the trend, the blue bars represent the lowest number of people who became infected with SARS, followed by green, purple, and yellow bars. It could thus be inferred that if people only start to get vaccinated after the outbreak of the disease, the sooner they get vaccinated, fewer people would get infected. The most ideal situation would be that vaccinations become readily available and are given to people on the first day of the outbreak. Going back to our model, our original parameter e describes the daily number of people who are immune to SARS after vaccination. A note to be made on e is that not everyone getting vaccinated is immune, because 0.001% of people vaccinated can still get infected with SARS. This is why we multiplied 152640 (daily number of people getting vaccinated) with 0.99997768115 to get a realistic e . In our model, we subtracted e from the susceptible population, as these people are now immune. The earlier we start subtracting e , the fewer people in the susceptible population, and the curve will be flatter towards the end. As shown by the graphs, when no vaccination was available, which was the actual situation, 975 people in total were infected in the end. If vaccines were available after we start to have 26 new daily cases, there would be a total of 934 cases. If vaccines were available after we start to have 22 new daily cases, there would be a total of 734 cases. If vaccines were available after we start to have 18 new daily cases, there would be a total of 623 cases. If vaccines were available after we start to have 14 new daily cases, there would be a total of 577 cases.

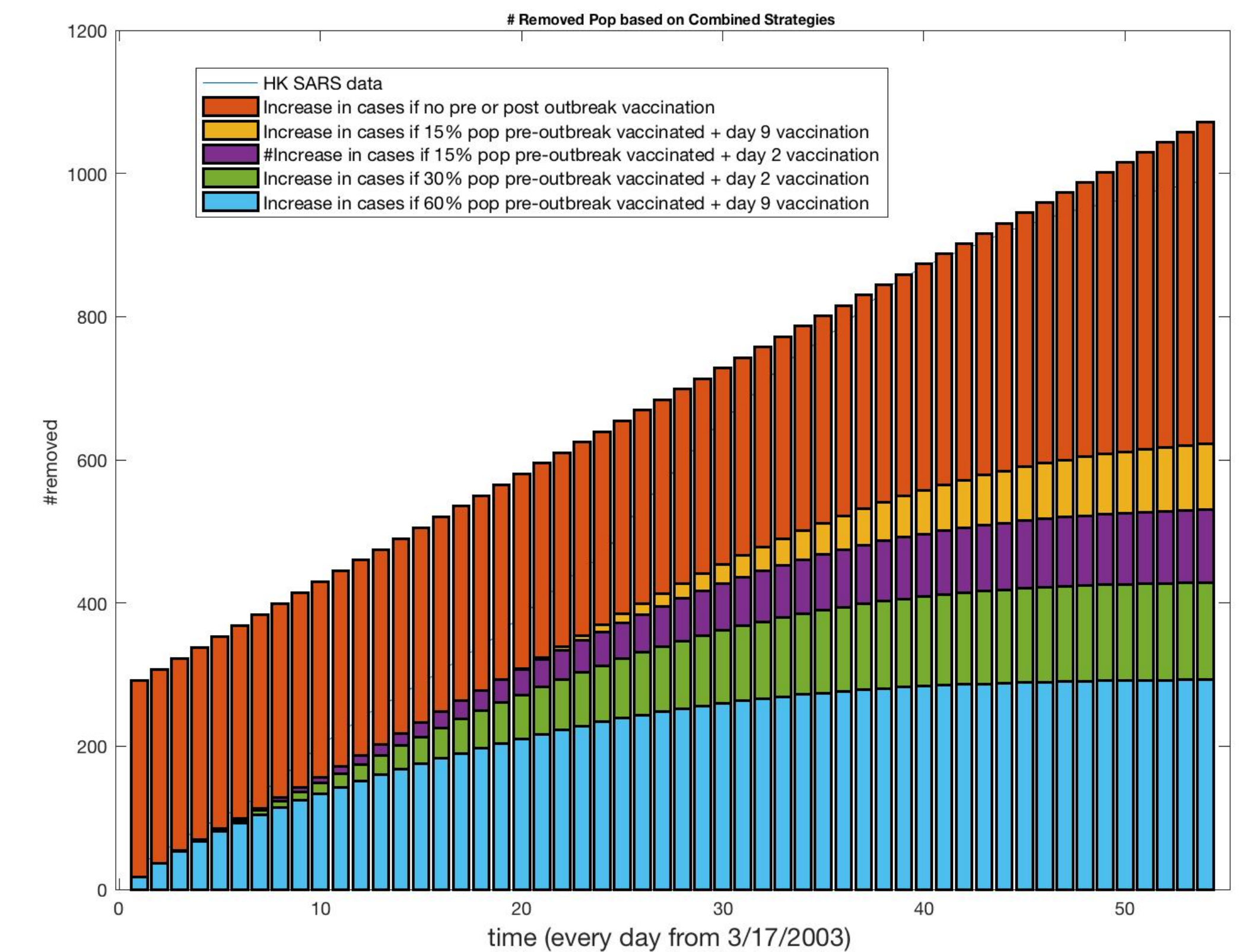
The figure above shows projections of SARS cases under the assumption that people get vaccinated before the outbreak. Here we have six scenarios:

- Dark blue bars: 90% of the population get vaccinated
- Maroon bars: 75% of the population get vaccinated
- Light blue bars: 60% of the population get vaccinated
- Green bars: 45% of the population get vaccinated
- Purple bars: 30% of the population get vaccinated
- Yellow bars: 15% of the population get vaccinated

Also, described by the orange bars, we have the actual data from 2003.

As can be seen from the cumulative graphs and the trend, the dark blue bars represent the lowest number of people who became infected with SARS, followed by maroon, light blue, green, purple, and yellow bars. Going back to our model, if more people could be vaccinated before the outbreak of the disease, e would be higher as e is a proportion of the people who get vaccinated. As a result, as we subtract greater e from the susceptible population, fewer people would be infected in the end. As shown by the graphs, when only 15% of the people get vaccinated beforehand, there would be 815 cases in the end, which would still be better than the original, 975 cases. When 30% of the people get vaccinated, that number would be reduced to 621. With 45% of the people getting the vaccine, there would be 559 cases. With 60% of the people getting the vaccine, there would be 327 cases. With 75% of the people getting the vaccine, there would be 245 cases. In the ideal situation, with 90% of the people vaccinated before the outbreak, the number of cases would be further reduced to 191.

Optimal Immunization Strategy Against SARS



The graph above shows projections with respect to "combined strategy". Through "combined strategy", we are looking at a more realistic situation where some people would get vaccinated before the outbreak, and there will also be people who get vaccinated after the outbreak. To simplify the question, we have combined trends with similar results. Also, getting 90% of the population vaccinated before the outbreak is rather unrealistic - flu vaccination coverage is typically around 45%, and given the fact that SARS outbreaks would happen on a much less frequent basis than flu, the likelihood of getting 90% of the population vaccinated with no imminent threat in sight would be improbable. (Flu Vaccination Coverage, United States, 2016-17 Influenza Season)

In total we have 9 scenarios:

- 15% pre-outbreak vaccination +
Vaccination starts with 14 daily new cases. Total number of cases: 516
Vaccination starts with 18 daily new cases. Total number of cases: 530
Vaccination starts with 22 daily new cases. Total number of cases: 622
- 30% pre-outbreak vaccination +
Vaccination starts with 14 daily new cases. Total number of cases: 419
Vaccination starts with 18 daily new cases. Total number of cases: 429
Vaccination starts with 22 daily new cases. Total number of cases: 494
- 60% pre-outbreak vaccination +
Vaccination starts with 14 daily new cases. Total number of cases: 265
Vaccination starts with 18 daily new cases. Total number of cases: 269
Vaccination starts with 22 daily new cases. Total number of cases: 293

From these projections we could see that the optimal case would be to have 60% of the population vaccinated before an outbreak, and start vaccination as soon as there were signs of an outbreak (with 14 people already infected).



http://www.chinadaily.com.cn/hkedition/2009-05/05/content_7742501.htm



https://www.hongkongfp.com/2017/02/19/pictures-hong-kong-2003-sars-epidemic/

Discussion

While it makes sense to think that we want as many people vaccinated before the outbreak as possible, and that we want to start vaccinating people as soon as the outbreak starts, we can't always achieve these goals given that it would be extremely costly to do so. In order to obtain the most cost-efficient and realistic solution, we calculated the rate of change in the number of infected cases as variables (percentage of population vaccinated before an outbreak, number of days after the outbreak for vaccination to start) change. We discovered that in terms of the percentage of people vaccinated before the outbreak, 60% seems to be a rather critical value, as the number of cases would increase much more significantly around this value than around other values. In terms of the number of daily new cases occurring before vaccination takes place, 22 (Day 9 in the original data) seems to be a critical value for the same reason. Also, as we examined "combined strategies", we could see that the differences among the three groups divided by the percentage covered are much greater than the differences among the subgroups (divided by daily new cases). Hence it would seem that pre-outbreak coverage is a more important factor than post-outbreak vaccination in reducing the total number of cases. The optimal solution we would like to propose would be to cover 60% of the population before an outbreak, and to start vaccination when there are 22 daily new cases (Day 9 in the original data) after the outbreak. While starting vaccination when there are 22 daily new cases will cause the number of cases to rise slightly as compared to starting it when there are only 14 or 18, we do think that this difference could be offset by the benefits of having enough time to produce enough vaccines and distribute them to hospitals in an organized manner.

References

- "Frequently Asked Questions About SARS." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 2 July 2012, http://www.cdc.gov/sars/about/faq.html.
- Wallinga, Jacco, and Peter Teunis. "Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures." American Journal of Epidemiology | Oxford Academic. OUP Academic, Oxford University Press, 15 Sept. 2004, academic.oup.com/aje/article/160/6/509/79472.
- Ng, Tuen Wai, et al. "A Double Epidemic Model for the SARS Propagation." BMC Infectious Diseases, BioMed Central, 10 Sept. 2003, bmcfid.biomedcentral.com/articles/10.1186/1471-2334-3-19#Abs1
- "Ask the Experts." Http://www.immunize.org/, www.immunize.org/askexperts/experts_inf.asp.
- "Vaccine Management: Recommendations for Handling and Storage of Selected Biologicals." Centers for Disease Control, National Center for Prevention Services Division of Immunization, Atlanta, GA. Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 3 Mar. 1991, wonder.cdc.gov/wonder/prevguid/p0000075/p0000075.asp.
- "Vaccines." Http://us.gsk.com, Nov. 2017, us.gsk.com/en-us/about-us/what-we-do/vaccines/.
- "Influenza (Flu)." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 28 Sept. 2017, www.cdc.gov/flu/fluavxview/coverage-1617estimates.htm.
- Feng, Zhang. "First SARS Vaccine Trials a Success." China Aims to Boost Industries along Yangtze River, 15 Jan. 2005, www.chinadaily.com.cn/english/doc/2005-01/15/content_409255.htm.