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SARS outbreaks in Ontario, Hong Kong and Singapore: the role of diagnosis and isolation as a control mechanism

G. Chowell[a,b,*], P.W. Fenimore[a], M.A. Castillo-Garsow[c], C. Castillo-Chavez[a,b]

[a] *Center for Nonlinear Studies, MS B258, Los Alamos National Laboratory, Los Alamos, NM 87545, USA*
[b] *Department of Biological Statistics and Computational Biology, Cornell University, Warren Hall, Ithaca, NY 14853, USA*
[c] *Universidad de Colima, Facultad de Ciencias & Facultad de Letras, Col. Villas de San Sebastián, 28045 Colima, Colima, Mexico*

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Abstract

In this article we use global and regional data from the SARS epidemic in conjunction with a model of susceptible, exposed, infective, diagnosed, and recovered classes of people (“SEIJR”) to extract average properties and rate constants for those populations. The model is fitted to data from the Ontario (Toronto) in Canada, Hong Kong in China and Singapore outbreaks and predictions are made based on various assumptions and observations, including the current effect of isolating individuals diagnosed with SARS. The epidemic dynamics for Hong Kong and Singapore appear to be different from the dynamics in Toronto, Ontario. Toronto shows a very rapid increase in the number of cases between March 31st and April 6th, followed by a *significant* slowing in the number of new cases. We explain this as the result of an increase in the diagnostic rate and in the effectiveness of patient isolation after March 26th. Our best estimates are consistent with SARS eventually being contained in Toronto, although the time of containment is sensitive to the parameters in our model. It is shown that despite the empirically modeled heterogeneity in transmission, SARS' average reproductive number is 1.2, a value quite similar to that computed for some strains of influenza (J. Math. Biol. 27 (1989) 233). Although it would not be surprising to see levels of SARS infection higher than 10% in some regions of the world (if unchecked), lack of data and the observed heterogeneity and sensitivity of parameters prevent us from predicting the long-term impact of SARS. The possibility that 10 or more percent of the world population *at risk* could eventually be infected with the virus in conjunction with a mortality rate of 3–7% or more, and indications of *significant* improvement in Toronto support the stringent measures that have been taken to isolate diagnosed cases.

Keywords: SARS; SEIJR; Outbreak

1. Introduction

Severe acute respiratory syndrome (SARS) is a new respiratory disease which was first identified in China's southern province of Guangdong. SARS is not merely a local endemic disease: it poses a serious risk to the medical community, is a threat to international travelers, is having a substantial negative economic impact in parts of East Asia and is spreading world-wide. The serious danger SARS poses to the medical community is illustrated by the numerous cases of transmission to health-care workers. Startlingly, the man who awakened the world to the dangers of SARS, Dr. Carlo Urbani, succumbed to the disease. Cases of transmission between aircraft passengers are suspected, and relatively short visits to epidemic regions have resulted in infection. The most striking feature of SARS, however, has proven to be its ability to rapidly spread on a global scale. One man with SARS made seven flights: from Hong Kong to Münich to Barcelona to Frankfurt to London, back to Münich and Frankfurt before finally returning to Hong Kong (Bradsher, 2003a). Another individual, a 26-year-old airport worker, appears to have transmitted the disease to 112 people (McNeil and Altmann, 2003). Clearly, there is an unfortunate interaction between the incubation period of the virus, the widely distributed severity and infectiousness of SARS in different people and the speed and volume of passenger air travel. The adverse economic impact in parts of East Asia far exceeds the disruption of previous

*Corresponding author. Center for Nonlinear Studies, MS B258, Los Alamos National Laboratory, Los Alamos, NM 87545, USA.
E-mail address: gc82@cornell.edu (G. Chowell).

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outbreaks of avian influenza, earning comparison with the 1998 financial market crisis in that part of the world (Schoen, 2003; MSNBC News Service, 2003a,b). Although the causative agent of SARS has been determined (Drosten et al., 2003; Ksiazek et al., 2003), a detailed understanding of the causative virus' pathogenticity and routes of transmission and the dynamics of the epidemic is still at a very early stage. It is uncertain how the virus is transmitted: by droplet or airborne transmission or person-to-person contact. The recent development of laboratory tests promises to improve the epidemiological situation somewhat (Gerberding, 2003).

SARS is a public health crisis on a scale rarely seen. The obvious question in such a crisis is, "can SARS be contained?" In this study, we report transmission parameters and epidemic dynamics from a model based on classes of people who are susceptible, exposed, infectious, diagnosed, and recovered ("SEIJR") that includes the effect of patient isolation. Our model is consistent with the possibility of containment in Toronto, Ontario.

2. SARS epidemiology and related issues

SARS was first identified in November 2002 in the Guongdong Province of China (Pomfret, 2003a). By February 26, 2003 officials in Hong Kong reported their first cases of SARS and no later than March 14th of this year the virus reached Canada (MSNBC News Service, 2003c). As of April 17th, Canada is the only location outside of Asia which has seen deaths as a result of SARS (13 so far) (MSNBC News Service, 2003c). US health officials are currently investigating 199 cases in 34 states (April 17, 2003) (Stein, 2003a).

An individual exposed to SARS may become infectious after an incubation period of 2–7 days (or longer) (CDC, 2003d) with 3–5 days being most common (Fire Chief Magazine, 2003). Most infected individuals either recover, typically after 7–10 days, or suffer 4% mortality or higher (C Health, 2003; International Society for Infectious Diseases, 2003a; BBC News, 2003). SARS appears to be most serious in people over age 40, especially those who have other medical problems such as heart or liver disease. Its symptoms are similar to pneumonia or other respiratory ailments and include a high fever ($\geqslant 38^{\circ}$C), shortness of breath, dry cough, headache, stiff or achy muscles, fatigue and diarrhoea (Stein, 2003b). These symptoms, however, are not uniform. In the US, for example, the disease seems to be a milder one than in Asia (Sloan, 2003). The result has been that SARS was, and for the moment remains, a diagnosis of exclusion.

Presently, there is no treatment for SARS (Kalb, 2003) and diagnostic tests are just becoming available (Gerberding, 2003). The mortality rate is reported to be 4% or higher world-wide (International Society for Infectious Diseases, 2003a; BBC News, 2003). Experts estimate that between 80% and 90% of people with SARS recover without medical intervention, while the condition of the remaining victims requires medical care (Stein, 2003b). As of April 17, 2003, the World Health Organization (WHO) reported 3389 cases (a mixture of probable or suspected cases) in 26 countries. One hundred and sixty-five victims are reported to have died (Stein, 2003a).

Although researchers in the Erasmus Medical Center in Rotterdam recently demonstrated that a coronavirus (some of which produce common colds) is the causative agent of SARS, the mode of transmission still remains unknown (Stein, 2003a). The current hypothesis is that SARS is transmitted mainly by close person-to-person contact which may explain the relatively slow transmission scale. However, it could also be transmitted through contaminated objects, air or by other unknown ways (CDC, 2003a). It is also a mystery how the disease originated, whether in birds, pigs or other animals, nor is it known if the origin is rural or urban (Bradsher, 2003b).

In this article, a simple model for SARS outbreaks is formulated (see Anderson and May, 1991 or Brauer and Castillo-Chavez, 2000). The model is used in conjunction with *global and local* SARS data to estimate the initial growth rate of the SARS epidemic. These rates are used to estimate SARS' *basic reproductive number*, R_0, the classical epidemiological measure associated with the reproductive power of a disease. R_0 estimates the *average* number of secondary cases of infection generated by a *typical* infectious individual in a population of susceptibles (Diekmann and Heesterbeek, 2000) and hence, it is used to estimate the initial growth of a SARS outbreak. We estimate (using data from Ontario, Hong Kong and Singapore) that R_0 is about 1.2. This value is not too different from past estimates of R_0 for influenza (see Castillo-Chavez et al., 1989) despite the fact that *superspreaders* of SARS have been identified. In fact, the parameter values resulting on this R_0, on our population-scaled model, can lead to extremely high levels of infection. We show, via simple extrapolation, that the estimated rate of growth is consistent with the reported date for the first cases of SARS in Hong Kong, however the first cases in Toronto may be several weeks earlier than the February 23 date of the first case reported by the Canadian Health Ministries (Canadian Ministry of Health, 2003). Our best "rough" estimate for Toronto is that the first case occurred sometime around January 29th, and not later than February 28th. The data for Hong Kong are fitted by fixing the parameters k, δ and γ_1 based on estimates of the observed rates for the corresponding processes. The growth rate β is estimated from observed "model-free" exponential growth in Singapore and Hong Kong.

The *average* diagnostic rate α and the measure of heterogeneity between the two susceptible classes p and the effectiveness of patient isolation measures (related to l) are then varied to fit the initial data for Hong Kong and Singapore. To model the data in Toronto, we must postulate that the parameters describing the rate of diagnosis (α) and isolation (l) in the Canadian outbreak changed radically on March 27. Two hospitals in Toronto were closed about that time: Scarborough Grace Hospital on March 25th and York Central Hospital on March 28th (Private Communication, April 21st, 2003). The remainder of this article is organized as follows: Section 4 introduces the basic model and gives an R_0 expression for the basic reproductive rate; Section 5 describes the results of simulations and connections to data; and, Section 6 collects our final thoughts.

3. SARS' transmission model

US data are limited and sparsely distributed (International Society for Infectious Diseases, 2003b; Coomer, 2003), while the quality of China's data is hard to evaluate (Pomfret, 2003b). On the other hand, there appears to be enough data for Toronto (Canadian Ministry of Health, 2003), Singapore and Hong Kong (World Health Organization, 2003) to make limited preliminary predictions using a model that includes the effects of *suspected* mechanisms for the spread of SARS. Limited data and inconclusive epidemiological information place severe restrictions on efforts to model the global spread of the SARS etiological agent.

Thus, we model *single* outbreaks, ignoring demographic processes other than the impact of SARS on survival. The model is applied to data from Toronto, Hong Kong and Singapore. Because the outbreak dynamics in Singapore and Hong Kong are different from those in Toronto, some of the results may only be indicative of what is happening in those regions of the world (in particular our parameters α and l may change). The situation must be re-evaluated frequently as SARS continues its travels around the world.

Here we describe a model that incorporates, in a *rather crude* way, some of the important characteristics suggested in the literature (unequal susceptibility, symptomatic and asymptomatic individuals, mode of transmission, superspreaders, etc.) (CDC, 2003a, b, c; International Society for Infectious Diseases, 2003b). The goal is to use the results for single outbreaks as a first step in our efforts to gauge the *global* impact of SARS. Hence, we focus on three "closed" populations (Southern Ontario (Toronto), Singapore and Hong Kong) and postulate differences in the degree of susceptibility to SARS (McNeil and Altmann, 2003; Stein, 2003b). These differences may be due to variations in contact rates, age-dependent susceptibility or "unknown" genetic factors. This last assumption is handled (in a rather crude and arbitrary way) via the introduction of two distinct susceptible classes: S_1, the most susceptible, and S_2, less so. Initially, $S_1 = \rho N$ and $S_2 = (1-\rho)N$ where ρ is the proportion of the population size N that is initially at higher risk of SARS infection. The parameter p is a measure of reduced susceptibility to SARS in class S_2 (Stein, 2003b; McNeil and Altmann, 2003). E ("exposed") denotes the class composed of asymptomatic, possibly infectious (at least some of the time) individuals. Typically, it takes some time before asymptomatic infected individuals become infectious. The possibility of limited transmission from class E is included, in a rather crude way, via the parameter q (see Table 1). The class I denotes infected, symptomatic, infectious, and undiagnosed individuals. I-individuals move into the diagnosed class J at the rate α. Individuals recover at the rates γ_1 (I class) and γ_2 (J class). The rate δ denotes SARS' disease-induced mortality. The classes R is included to keep track of the cumulative number of diagnosed and recovered, respectively. Furthermore, it is assumed that diagnosed individuals are handled with *care*. Hence, they might not be (*effectively*) as infectious as those who have not been diagnosed (if l is small). The parameter l takes into account their reduced impact on the transmission process (small l represents effective measures taken to isolate diagnosed cases and vice versa). Table 1 includes parameters' definitions and the initial values used. Our SARS epidemiological model is given by the following nonlinear system of

Table 1
Parameter definitions and values that fit the cumulative number of cases in class J ("diagnosed") for Hong Kong

Parameter	Definition	Value
β	Transmission rate per day	0.75
q	Relative measure of infectiousness for the asymptomatic class E	0.1
l	Relative measure of reduced risk among diagnosed SARS cases	0.38
p	Reduction in risk of SARS infection for class S_2	0.1
k	Rate of progression to the infectious state per day	$\frac{1}{3}$
α	Rate of progression from infective to diagnosed per day	$\frac{1}{3}$
γ_1	Rate at which individuals in the infectious class recover per day	$\frac{1}{8}$
γ_2	Rate at which diagnosed individuals recover per day	$\frac{1}{5}$
δ	SARS-induced mortality per day	0.006
ρ	Initial proportion of the population at higher risk of SARS infection	0.4

These parameters are used to compute the basic reproductive number R_0.

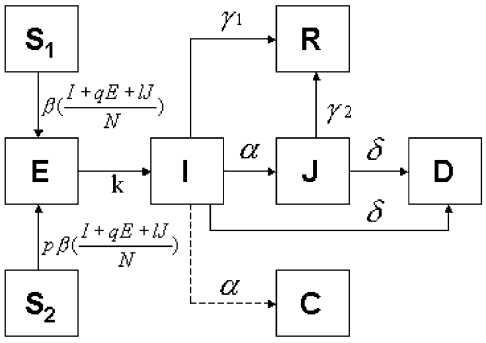

Fig. 1. A schematic representation of the flow of individuals between the different classes. The model considers two distinct susceptible classes: S_1, the most susceptible, and S_2. $\beta(I+qE+lJ)/N$ is the transmission rate to S_1 from E, I and J. p is a measure of reduced susceptibility to SARS in class S_2. E is the class composed of asymptomatic, possibly infectious individuals. The class I denotes infected, symptomatic, infectious, and undiagnosed individuals. I-individuals move into the diagnosed class J at the rate α. Individuals recover from class I at the rate γ_1 and γ_2 from the J class. The rate δ is SARS' disease-induced mortality. The classes R and D are included to keep track of the cumulative number of diagnosed, recovered and dead individuals, respectively. The quantity C is for comparison with epidemiological statistics; it tracks the total number of diagnosed individuals.

differential equations:

$$\begin{aligned}
\dot{S}_1 &= -\beta S_1 \frac{(I+qE+lJ)}{N},\\
\dot{S}_2 &= -\beta p S_2 \frac{(I+qE+lJ)}{N},\\
\dot{E} &= \beta(S_1+pS_2)\frac{(I+qE+lJ)}{N} - kE,\\
\dot{I} &= kE - (\alpha+\gamma_1+\delta)I,\\
\dot{J} &= \alpha I - (\gamma_2+\delta)J,\\
\dot{R} &= \gamma_1 I + \gamma_2 J,
\end{aligned} \tag{1}$$

which is referred to as "SEIJR," after the variables used to name the classes (see Fig. 1).

The values of p and q are not known and are fixed arbitrarily while l and α are varied and optimized to fit the existing data (least-squares criterion) for Hong Kong, Singapore and Toronto. We did not explore the sensitivity of the model to variations in p and q because they are not known and cannot be controlled. All other parameters were roughly estimated from data (Canadian Ministry of Health, 2003; World Health Organization, 2003) and current literature (CDC, 2003a, d; Fire Chief Magazine, 2003; C Health, 2003). In particular, the transmission rate β is calculated from the dominant root of the third-order equation obtained from the linearization around the disease-free equilibrium (Diekmann and Heesterbeek, 2000). The parameters l and α were allowed to vary when fitting the data for each location (Singapore, Hong Kong and Toronto). Some restrictions apply, for example, the value of $\alpha > \gamma_1$. We also require that $1/\gamma_2 = 1/\gamma_1 - 1/\alpha$, a statement that members of the diagnosed class J recover at the same rate as members of the undiagnosed class I. $1/\gamma_1$ has been reported to be between 7 and 10 days (International Society for Infectious Diseases, 2003a; C Health, 2003). From the second generator approach (Diekmann and Heesterbeek, 2000), we obtain the following expression for the basic reproductive number:

$$\mathcal{R}_0 = \{\beta[\rho + p(1-\rho)]\} \times \left\{\frac{q}{k} + \frac{1}{\alpha+\gamma_1+\delta} + \frac{\alpha l}{(\alpha+\gamma_1+\delta)(\gamma_2+\delta)}\right\} \tag{2}$$

which can be easily given an epidemiological interpretation. The use of parameters estimated from Hong Kong (Table 1) gives a value of $R_0 = 1.2$ (Hong Kong) and $R_0 = 1.2$ (Toronto, assuming exponential growth) and $R_0 = 1.1$ (Singapore).

4. Simulation results

Initial rates of growth for SARS outbreaks in different parts of the world (see Fig. 2) are computed using the data provided by WHO (World Health Organization, 2003) and the Canadian Ministry of Health (Canadian Ministry of Health, 2003). These rates are computed exclusively from the number of cases reported between March 31 and April 14. The values obtained are 0.0405 (world data), 0.0496 (Hong Kong), 0.054 (Canada), 0.054 (Toronto) and 0.037 (Singapore).

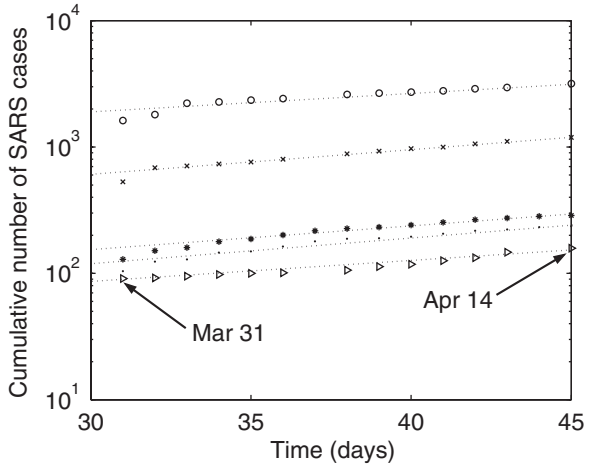

Fig. 2. The cumulative number of SARS cases from March 31 to April 14 (lin-log scale) for the World (top data), Hong Kong (second row), Ontario, Canada (fourth row), all of Canada (third row) and Singapore (bottom row). The data were obtained from WHO (World Health Organization, 2003) except for the Canadian data which are from the Canadian Ministry of Health (2003). The Ontario data includes suspected and probable cases since March 31. This inclusion explains the jump in the data for Ontario on March 31st. The rates of growth of the SARS outbreak (computed using data from March 31 to April 14) are: 0.041 (world), 0.050 (Hong Kong), 0.037 (Singapore), 0.054 (Canada) and 0.054 (Ontario).

Table 2
Estimated starting times of the SARS outbreak

Country	Estimated start of the outbreak
Canada	February 1st
Hong Kong	November 20th
Singapore	December 6th
World data	November 5th

For our numerical simulations, we start with an infectious individual (not yet diagnosed, $I(0) = 1$) and *crude* estimates for the start of SARS outbreaks (t_0) are obtained from the formula $t_0 = t - (\frac{1}{r}\log(x(t)))$, which assumes initial exponential growth (r, the estimated "model-free" rate of growth from the time series $x(t)$ of the cumulative number of SARS cases). Results for Toronto, Hong Kong, Singapore and aggregated world data are shown in Table 2. The estimated "world" start of the outbreak is November 5, a date consistent with the fact that the first SARS case was detected in Guangdong, China in November (Pomfret, 2003a). These dates are used as the starting time of the respective outbreaks.

For the case of the Province of Ontario, Canada the total population N is approximately 12 million. We assume that the population at *major* risk of SARS infection lives in Ontario's southern part (particularly Toronto), and is approximately 40% of the total population ($\rho = 0.4$ in our model). It is worth pointing out that this value of ρ is not critical (that is, the most sensitive) in the model. The "model-free" approximately exponential growth rates for the various regions of the world are roughly similar *except for Canada* from March 31st (day 61) to April 6th (beginning the day of the jump in the number of reported Canadian cases), the number of diagnosed cases grew $\sim\exp(0.081t)$, where t is measured in days. This rate is substantially higher than elsewhere in the world. In the subsequent week (beginning April 7th, day 68) the number of probable or suspected Canadian cases rapidly rolls over to a smaller growth rate not too far from the rest of the world. We conclude, based on the coincidence of the Canadian hospital closures, the jump in the reported number of Canadian SARS cases on March 31st and the rapid rise in recognized cases in the following week, that Canadian doctors were rapidly diagnosing pre-existing cases of SARS (in either class E or I on March 26th). If we make the assumption that the fundamental disease spreading parameters other than α and l are roughly constant throughout the world prior to March 26th, we can reach two important conclusions. Beginning on March 26th, in Toronto:

- α changed from a number $1/\alpha \approx 1/\gamma_1 - 2 \approx 6$ days to $1/\alpha_1 \leqslant 3$ days, and
- l changed from an uncertain and relatively large value $l > 1/2$ to $l \leqslant 0.1$.

If we assume that the fundamental growth rate β is essentially constant from one region of the world to another, it is difficult for our model to produce growth rates r well above the world average, except as a transient response to differences in diagnostic rate α (due to delays in response or change in policy). Similarly, the SEIJR model requires fairly small values of l to achieve a rapid roll-over in the growth rate of recognized cases. The parametric details of how a "second" initial condition for Toronto on March 26th is generated do not affect the qualitative aspect of this argument: the Canadian data prior to March 31st (the day of the large jump) are probably not as meaningful as data after that date, and hence only bound the model from below prior to March 26th. The essential aspect of this before-and-after hospital closure argument is that there were substantially more undiagnosed people in classes E and I than in class J on March 26th. This is a reasonable assumption given that the number of cases reported by Canadian officials more than double

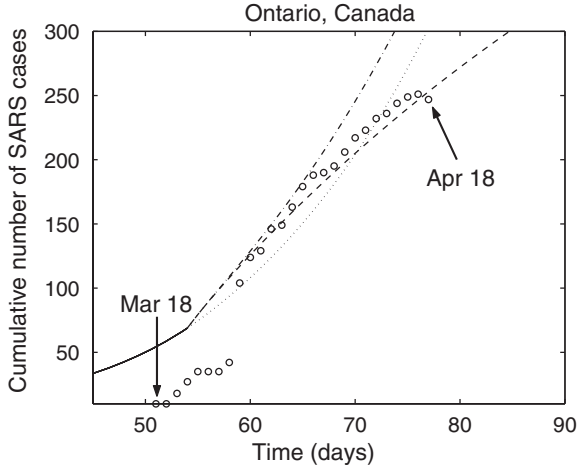

Fig. 3. The circles are the cumulative number of suspected or probable SARS cases in Ontario beginning on day 61 (March 31st, the day of the jump) and the number of probable cases up until day 60. The data prior to day 61 only bound the model from below. The lines are the cumulative number of "diagnosed" cases C from the SEIJR model (C is the running sum of all diagnosed cases J). The fit to the data is given by a change in the values of α and l on March 26th. Prior to March 26th, $\alpha = 1/6$, $l = 0.76$. Because the model is poorly constrained prior to day 61, the real purpose of this part of the model is to generate sufficiently large classes of E and I relative to J on March 26th to give the fast increase in C from day 61 to day 67. After March 26th, three scenarios are shown. The fit to the data is given by $\alpha = 1/3$, $l = 0.05$ (rapid diagnosis and effective isolation of diagnosed cases, dashed line). The second curve is given by $\alpha = 1/6$, $l = 0.05$ (slow diagnosis and effective isolation, dotted line) and the third curve by $\alpha = 1/3$, $l = 0.3$ (rapid diagnosis with improved but imperfect isolation, dash–dot line). An index case is assumed on February 1st. The transmission rate β is computed using the estimated rate of growth ($r = 0.0543$) for the Ontario data as described in the text.

Table 3
Long-time model results for Ontario, Canada, assuming various changes in behavior on March 26th, 2003

l	α	Infected with SARS (%)	Diagnosed with SARS (%)
0.05	1/3	0.0077	0.0055
0.3	1/3	18	13
0.05	1/6	21	13

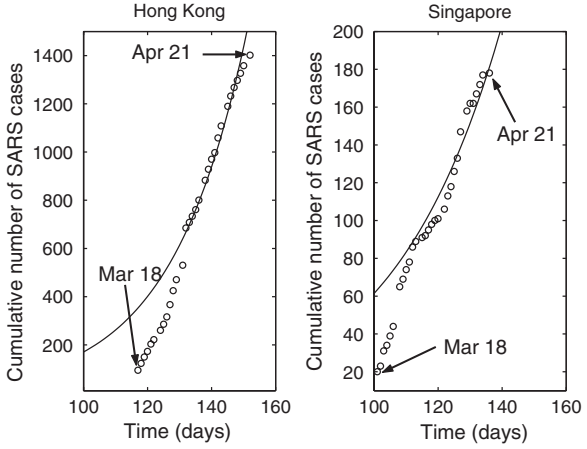

Fig. 4. Cumulative number of SARS cases in Hong Kong and Singapore as a function of time (SEIJR model) with $l = 0.38$ (Hong Kong) and $l = 0.40$ (Singapore). Singapore has $\beta = 0.68$, all other parameter are from Table 1. The data are fitted starting March 31 (see Fig. 2) because of the jump in reporting on March 30th.

from March 30th to March 31st. The introduction of behavioral changes starting on March 26 ($t = 57$ days), alters the fate of the disease in a dramatic fashion (see Fig. 3, Table 3).

Fitting the model to the Hong Kong and Singapore data is carried out in a similar fashion with $\rho = 0.4$ (Hong Kong has about 7.5 million inhabitants, Singapore 4.6 million). The estimated transmission rate from Hong Kong data is $\beta \approx 0.75$ and for Singapore $\beta \approx 0.68$. Both Hong Kong and Singapore's data are fit with the value $q = 0.1$. Hong Kong and Singapore's measure of contact between diagnosed SARS cases and susceptibles are $l = 0.38$ and 0.40, respectively (see Fig. 4). Even though there is some heterogeneity in the parameters for Hong Kong and Singapore, they provide an important calibration of our model. Their values for l and α are roughly consistent with each other, indicating that the difference with Toronto is significant within our model, and pointing to the joint importance of rapid diagnosis $\alpha \approx 1$ and good isolation of diagnosed patients $l \approx 0$ in controlling an outbreak. While there is some indication in the data from Hong Kong of a possible slowing of the outbreak, we did not attempt to analyse the slowing or assess its significance.

5. Conclusions

A simple model that can capture the effect of average infectiousness in a heterogeneous population and the effect of isolating diagnosed patients has been introduced to explore the role of patient isolation and diagnostic rate in controlling a SARS outbreak. By examining two cases with relatively clean exponential growth curves for the number of recognized cases, we are able to calibrate a SEIJR model with parameters $\alpha = 1/3$ (SARS' diagnostic rate) and $l \approx 0.4$ (isolation effectiveness). We then use our SEIJR model to examine the non-exponential dynamics of the Toronto outbreak. Two features of the Toronto data, the steep increase in the number of recognized cases after March 31st and rapid slowing in the growth of new recognized cases, robustly constrained the SEIJR model by requiring that $l \approx 0.05$ and $\alpha > 1/3$ days^{-1}.

The model is also used to look at the impact of drastic control measures (isolation). The fitting of data shows that the initial rates of SARS' growth are quite similar in most regions leading to estimates of R_0 between 1.1 and 1.2 despite the recent identification of *superspreaders*. Model simulations are fitted to SARS reported data for the province of Ontario, Hong Kong and Singapore. Good fits are obtained for reasonable values of α, the rate of identification of SARS infections; "reasonable" values of the control parameters l (a measure of isolation); possible values of p, a *crude* measure of reduced susceptibility (due to genetic factors, age or reduced contact rates); q a *crude* measure of the relative degree of infectiousness of asymptomatic individuals; possible values of ρ a measure of initial levels of population heterogeneity; and, reasonable values of N the *effective* population size. It is worth noting that for values of N larger than 100,000 the predictions (proportion of cases at the end of the outbreak, etc.) are *roughly* the same. The introduction of behavioral changes that follow the identification of the first case (reduce values of l at the time of the identification and moving aggressively to identify cases of SARS by increasing $1/\alpha$) result in a dramatic reduction in the total number of cases and on mortality in Toronto. Given the fact that SARS appears to kill between 3% and 7% of infected (diagnosed) cases (BBC News, 2003), it seems quite appropriate to isolate diagnosed people. Although we do not examine the effect of quarantine by varying q, it seems intuitive that quarantining those who came into close contact with positively diagnosed individuals will reduce the total number of cases.

Model results and simple estimates suggest that *local* outbreaks may follow similar patterns. Furthermore, the use of relative extreme isolation measures in conjunction with rapid diagnosis has strong impact on the local dynamics (Toronto's situation). However, if SARS has shown us anything it is that "undetected" and

"unchecked" local disease dynamics can rapidly become a global issue.

The research on this article used the latest data available (April 18 for Canada and April 21 for Hong Kong and Singapore). Recent disclosures (Pomfret, 2003c) reaffirm the importance of carrying out the analysis excluding data from China. We have redone the analysis including the data collected up to April 25 and, our conclusions, remain the same. Current data seem to support higher values for SARS induced mortality rates (BBC News, 2003). However, our model is *most sensitive* to the parameters l (effectiveness of isolation) and (α) diagnostic rate. It is not as sensitive to changes in δ. In fact, the consideration of a 7% mortality ($\delta \approx 0.01$) rather than 4% reduces the number of cases by about 12%. In Toronto, we have estimated 612 diagnosed cases with ($l = 0.05$ and $\alpha = 1/3$ after March 26th). Perfect isolation after March 26th ($l = 0.00$) reduces this number to 396 diagnosed cases. The assumption of homogenous mixing implies that our model is likely to overestimate the size of the outbreak. Hence, the situation in Toronto seems to support the view that this *outbreak* is being contained. Obviously, the case of the crude model (by design) cannot handle high levels of variability (a stochastic model would be desirable). This possibility is tested (as it is often done in deterministic models) by looking at the sensitivity of the model to parameters (α and l being the most critical). Such sensitivity analyses can also help "estimate" the variability in R_0.

A series of articles recently available online (www.sciencemag.org/feature/data/sars/) report higher values of R_0. A direct comparison with our formula (2) identifies some key differences and model assumptions that partially account for these quantitative differences. Table 3 highlights the large variations in final epidemic size predicted by our model due to its sensitivity to changes in the key control parameters (α and l). (A stochastic version of this model supports great variability in R_0).

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