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CRITICAL ROLE OF NOSOCOMIAL TRANSMISSION IN THE TORONTO SARS OUTBREAK

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Abstract. We develop a compartmental mathematical model to address the role of hospitals in severe acute respiratory syndrome (SARS) transmission dynamics, which partially explains the heterogeneity of the epidemic. Comparison of the effects of two major policies, strict hospital infection control procedures and community-wide quarantine measures, implemented in Toronto two weeks into the initial outbreak, shows that their combination is the key to short-term containment and that quarantine is the key to long-term containment.

1. **Introduction.** One of the salient features of the outbreak of severe acute respiratory syndrome (SARS) in the Greater Toronto Area (GTA) is the role of the hospital in transmission. Of 144 early patients, 111 (77%) were exposed to SARS in the hospital setting; of these, 73 patients (51%) were health-care workers, including nurses, respiratory therapists, physicians, radiology and electrocardiogram technicians, housekeepers, clerical staff, security personnel, paramedics, and research assistants [1]. The high risk of transmission within the health-care setting has a significant impact on the conduct of public-health interventions in the continuing SARS epidemic [1, 2] and potentially for other emerging respiratory diseases.

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To examine the SARS outbreak in GTA, we develop a compartmental model dividing the entire population into classes of susceptibles, exposed, infectives, hospitalized, and removed and subclasses representing the general public and individuals in the hospital setting including health-care workers and patients (HCWP). The model reflects the extremely intense exposure of HCWP to infected individuals prior to awareness of SARS by the medical community; their heightened risk continued until adequate precautions were fully operant in hospitals. In two recent analyses of SARS epidemiology [3, 4], all members of the public were considered as one class, despite evident heterogeneity in transmission, and the rapid initial spread of SARS in Vietnam, Hong Kong, and Canada in hospital wards [5]. In our analysis, the secondary infection induced by a hospitalized patient for the HCWP ($R_0 \approx 4.5$) is much larger than the secondary infection induced by an average infective for the general public ($R_0 \approx 1.6$) during the first two weeks of the SARS outbreak in GTA. These secondary infection rates decreased when hospital infection control procedures and community-wide quarantine measures were introduced.

2. **Mathematical models and analysis of dynamics.** Models were developed to correspond to the two stages of the SARS outbreak in GTA: pre-(Model I) and intra-(Model II) quarantine. Model I consists of the following compartments: *Susceptibles S* (individuals not yet infected); *Exposed E* (susceptibles who have become infected and are not yet infectious); *Infectives I* (exposed individuals who have become infected and can spread the SARS coronavirus); *Removed R* (individuals who have been exposed or infective and who are no longer considered to be susceptible); and *Hospitalized U* (infectives who are in the immediate environment of HCWP; these individuals are not considered to pose any risk to the general public, but may infect HCWP). For each class, subindices g and h represent general public and HCWP, respectively.

Model I consists of 8 coupled nonlinear differential equations describing the transfer of individuals from one compartment to another (Fig. 1):

$$\begin{cases} \frac{d}{dt}S_g(t) = -a_g S_g(t)\Big(I_g(t) + I_h(t)\Big) \\ \frac{d}{dt}S_h(t) = -a_h S_h(t)\Big(I_g(t) + I_h(t)\Big) - a_u S_h(t)\Big(U_h(t) + U_g(t)\Big) \\ \frac{d}{dt}E_g(t) = a_g S_g(t)\Big(I_g(t) + I_h(t)\Big) - b_g E_g(t) \\ \frac{d}{dt}E_h(t) = a_h S_h(t)\Big(I_g(t) + I_h(t)\Big) + a_u S_h(t)\Big(U_h(t) + U_g(t)\Big) - b_h E_h(t) \\ \frac{d}{dt}I_g(t) = b_g E_g(t) - c_g I_g(t) - r_g I_g(t) \\ \frac{d}{dt}I_h(t) = b_h E_h(t) - c_h I_h(t) - r_h I_h(t) \\ \frac{d}{dt}U_g(t) = r_g I_g(t) - \epsilon_g U_g(t) \\ \frac{d}{dt}U_h(t) = r_h I_h(t) - \epsilon_h U_h(t) \end{cases} \tag{1}$$

where a_g, a_h, and a_u are the transmission coefficients for the general public and HCWP infectives, and for hospitalized infectives for HCWP, respectively; b_g and b_h are the transmission coefficients for exposed individuals to the infective class; c_g and

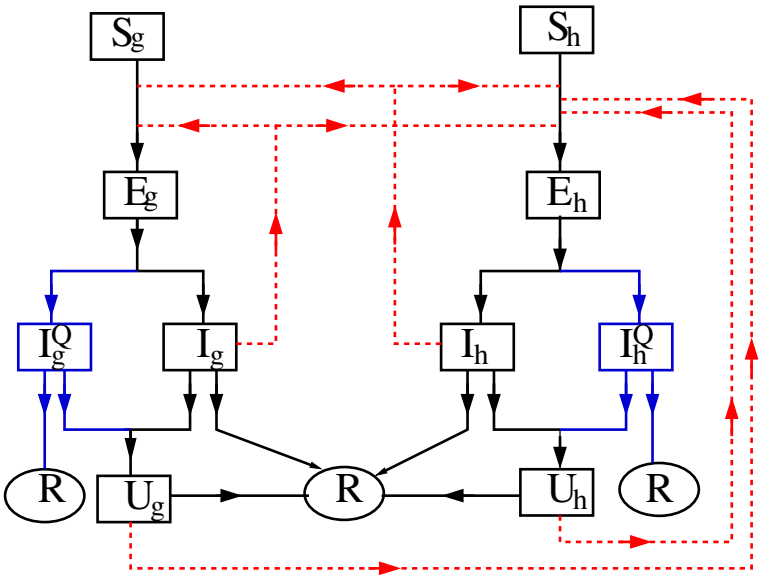


FIGURE 1. Schematic of SARS transmission when the total population is divided into the categories of the general public (g) and HCWP (h) who have direct contact with hospitalized infected patients. Each category is divided into classes of susceptibles (S), exposed (E), infectives (I), and hospitalized (U). In Model I, no quarantine (or special hospital infection control procedures) is implemented and the subclasses of infectives (I_g^Q, I_h^Q) under quarantine do not exist. Circles R indicate all individuals removed from the infective and hospitalized classes.

c_h are the transmission coefficients for infective individuals to the removed class, and r_g and r_h are the transition coefficients for infectives to hospitalization. The transition coefficients for the removed class are ϵ_g and ϵ_h, reflecting the effectiveness of treatments. The second equation in (1) describes the additional risk of HCWP resulting from their direct contact with SARS patients in the health-care setting.

The time scale considered in Model I (1) is short enough that all demographic details can be ignored. As a result, each of the total populations in the subclasses $I_g(t)$, $I_h(t)$, $E_g(t)$, $E_h(t)$, $U_g(t)$, and $U_h(t)$ eventually approaches zero, and explicit formulae can be obtained to calculate the total numbers of infected and hospitalized infectives during the entire course of the infection (see Appendix for more details).

Although simulations based on Model I correlate with the actual data in GTA [6] for the first two weeks of the outbreak (Fig. 2), the model predicted a much larger number of infectives subsequently. On March 31 (two weeks after the first cases), Ontario declared a provincial emergency to contain the spread of SARS and introduced public-health measures, including extensive contact tracing, isolation of suspect and probable cases, and voluntary home quarantine for asymptomatic contacts. Hospital infection control procedures also were enforced. Clinicians, initially unaware of the communicability of the SARS coronavirus, had used positive-pressure ventilation methods to alleviate respiratory symptoms, inadvertently augmenting dispersion of contagious droplets. Such treatments were stopped, negative-pressure

rooms were used, and face shields were introduced after masking alone proved insufficient. These more stringent hospital measures may have been important in controlling the spread of SARS in GTA [7] as well as elsewhere [3, 8], and are reflected in Model II by significant reduction of the coefficients a_h and a_u.

In Model II (2), S, E, I, R, and U represent the same groups as in Model I (Fig. 1). We introduce a second category of infectives I^Q representing infected individuals quarantined before they are admitted into (or never admitted to) the hospital. They pose no risk to HCWP and a low risk to the general public. Model II reads

$$\begin{cases} \frac{d}{dt}S_g(t) = -a_g S_g(t)\Big(I_g(t) + I_h(t)\Big) \\ \frac{d}{dt}S_h(t) = -a_h S_h(t)\Big(I_g(t) + I_h(t)\Big) - a_u S_h(t)\Big(U_h(t) + U_g(t)\Big) \\ \frac{d}{dt}E_g(t) = a_g S_g(t)\Big(I_g(t) + I_h(t)\Big) - q_g b_g E_g(t) - (1-q_g) b_g E_g(t) \\ \frac{d}{dt}E_h(t) = a_h S_h(t)\Big(I_g(t) + I_h(t)\Big) + a_u S_h(t)\Big(U_h(t) + U_g(t)\Big) \\ \qquad\qquad -q_h b_h E_h(t) - (1-q_h) b_h E_h(t) \\ \frac{d}{dt}I_g^Q(t) = q_g b_g E_g(t) - c_g I_g^Q(t) - r_g I_g^Q(t) \\ \frac{d}{dt}I_h^Q(t) = q_h b_h E_h(t) - c_h I_h^Q(t) - r_h I_h^Q(t) \\ \frac{d}{dt}I_g(t) = (1-q_g) b_g E_g(t) - c_g I_g(t) - r_g I_g(t) \\ \frac{d}{dt}I_h(t) = (1-q_h) b_h E_h(t) - c_h I_h(t) - r_h I_h(t) \\ \frac{d}{dt}U_g(t) = r_g(I_g(t) + I_g^Q(t)) - \epsilon_g U_g(t) \\ \frac{d}{dt}U_h(t) = r_h(I_h(t) + I_h^Q(t)) - \epsilon_h U_h(t) \end{cases} \tag{2}$$

where parameters q_g and q_h are the fractions of exposed general public and HCWP that have been quarantined, respectively.

Note that in the case where $q_g = q_h = 0$, $I_g^Q = I_h^Q = 0$ if their initial values are zero; thus Model II reduces to Model I. The rates of transfer from the E class to I class are described by new equations on $I_g^Q(t)$ and $I_h^Q(t)$ to reflect the effect of quarantine measures (see Appendix).

This model allows analysis of the dependence of the total number of infected and hospitalized individuals $X(t)$ at time t on the parameters a_g, a_h, a_u, q_g, and q_h. This model also provides an explicit formula for the lowest possible ultimate number of infected and hospitalized ($X(\infty)$) when hospital infection control measures and quarantine measures are strictly enforced, and for the most conservative estimation of the quarantine fraction for $X(\infty)$ to fall below a specified level (see Appendix for details).

3. **Results.** The parameters and initial conditions for the simulations are based on the 1996 census adjusted by 1999 intercensus estimates for the year 2003. The total population in GTA (by PHU) is the following: PEEL: 1,107,504; CITY OF

TORONTO: 2,620,228; DURHAM: 544,069; HALTON: 398,592; and YORK REGION: 778,295. Also, according to the statistics from Health Canada [6], we have the initial population data in Table 1, where the initial $t = 0$ corresponds to March 18.

$S_g(0)$	$S_h(0)$	$E_g(0)$	$E_h(0)$	$I_g(0)$	$I_h(0)$	$U_g(0)$	$U_h(0)$
5, 443, 104	3, 000	3	12	1	2	6	1

TABLE 1. Initial population data for Model I, $t = 0$ corresponds to March 18.

Although it is difficult to estimate a_h, a_g and a_u, we know that $a_g \leq a_h << a_u$. In a crude approximation in which the total population is divided into three classes (susceptible, infective, and removed) and where the transition coefficients from S class to I class and from I class to R class are a and c, respectively, the reproductive number (R_0) is given by aN/c. The reproductive number is defined as the average number of secondary infections that occur when one infective is introduced into a completely susceptible host population ([11, 10, 13, 12]). If we take $R_0 = 1.2$ (a value very similar to that calculated for some strains of influenza virus [9] despite the heterogeneity in transmission of the SARS coronavirus, and if we use $N = 5,446,104$ and an estimated 3 days as the median time for symptomatic individuals to be admitted to hospitals [1], then $c = 1/3$ and $a = 1.2c/N = 0.000000075$. We use this value for a_g in the simulations for both models. In the study carried out in [3, 14], R_0 is estimated as 3, 2.7, and 1.2. These estimated values of R_0 do not address different transmission rates in the general community and in the health care setting. However, the ratio a_u/a_g reflects the effectiveness of hospital infection control measures, and is used as a parameter in the simulation of the second model. Since stringent hospital control measures were absent pre-March 30 in the first model, hence we take $a_h = 100a_g$, and $a_u = 1000a_g$. Hence the average infective induced secondary infection is $R_0 \approx 1.6$ for the general community, and the average hospitalized patient induced secondary infection is $R_0 \approx 4.5$ for the health care setting.

Because the average exposed period prior to becoming infectious is $1/b$, and the median time from self-reported earliest known exposure to symptoms onset is 6 days [1], we use $b_g = b_h = 1/6$. The average period before an infective individual dies without being admitted to a hospital is $1/c$. This number is small, reflecting a relatively low death rate. The 21-day survival in a Toronto cohort of 144 hospitalized cases was 93.5%, with negative outcomes most often associated with diabetes or other co-morbid conditions [1]. Estimates for case fatality rates are also associated with age, with a fatality rate of 13.2% for those under 60, rising to 43.3% for those ($\geq$) 60 reported in Hong Kong [8]. We use $c_g = c_h = 0.001$. Because $1/r$ is the average period for an infective individual before admission to a hospital, $r_g = r_h = 1/3$ [1]. Assuming that this rate improved over the course of the epidemic, we use $r_g = r_h = 1/4$ for the first 12 days. For the remaining course (simulation for Model II), $r_g = r_h = 1/3$. Finally, $\epsilon_g = \epsilon_h = 0.1$. (The median hospital stay is 10 days [1], but assuming that the hospital stay for the infectives in the early stage is longer, $r^{-1} = 20$ days. Therefore, for Model I, $\epsilon_g = \epsilon_h = 0.05$.) All the parameters involved in Model I and II are summarized in Table 2.

Based on these parameters given in Table 2, the numerical simulations were carried out using Maple and Mathematica. The simulated result from Model I and

	a_g	a_h	a_u	b_g	b_h	r_g	r_h	ϵ_g	ϵ_g	q_g	q_h
Model I	7.5E-8	$100a_g$	$1000a_g$	$\frac{1}{6}$	$\frac{1}{6}$	$\frac{1}{3}$	$\frac{1}{3}$	0.05	0.05	0.0	0.0
Model II	7.5E-8	$10a_g$	$10a_g$	$\frac{1}{6}$	$\frac{1}{6}$	$\frac{1}{3}$	$\frac{1}{3}$	0.1	0.1	0.8	0.9

TABLE 2. The parameters value for both of the Models I and II used in the numerical simulations

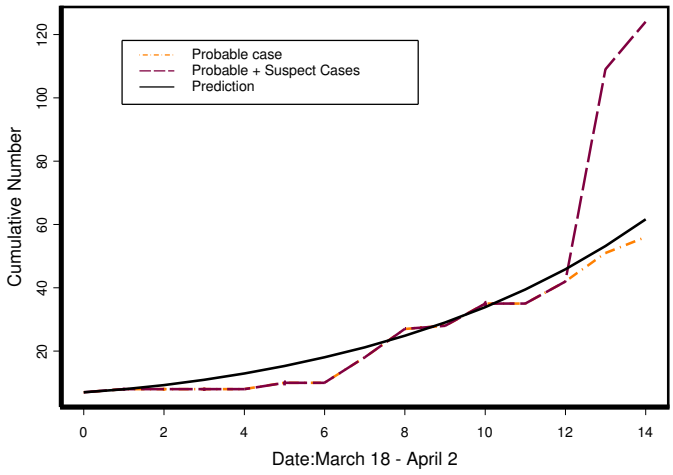


FIGURE 2. SARS in GTA: Comparison of the reported data based on Health Canada statistics [6] and Model I predictions of hospitalized patients and removed individuals from March 18 ($t = 0$) until April 1 ($t = 14$). On March 30, the number of probable cases from the Health Canada statistics is 42; the model prediction number, $X(12) = 46$.

the actual data (Fig. 2) compare well for the first two weeks of the outbreak. After March 30 ($t = 12$), however, the simulation yields a much higher number of infectives than actually occurred. This inconsistency clearly indicates the effectiveness of the combination of hospital control procedures and quarantine measures, providing the basis for Model II. The ratio of infectives between HCWP and the general public is close to constant ($\approx 50\%$) which indicates the proportional risk of HCWP during the initial outbreak, but it changes after an effective quarantine policy is established for the public and infection controls are used in health-care facilities. After March 30, both hospital control measures and quarantine were implemented in GTA; thus, for Model II we use the same parameters as in Model I, except $a_h = 10a_g$, $a_u = 10a_g$, $q_g = 0.8$, and $q_h = 0.9$, to reflect the effectiveness of quarantine measures. Initial conditions for Model II correspond to the values from Model I reached on March 30 ($t = 12$) and are in agreement with the actual data. From the predictions using Model I, we get the initial data for Model II (Table 3), where $t = 0$ corresponds to March 30. However, the actual data available do not enumerate the infectives/hospitalized/removed and HCWP/public distinctions.

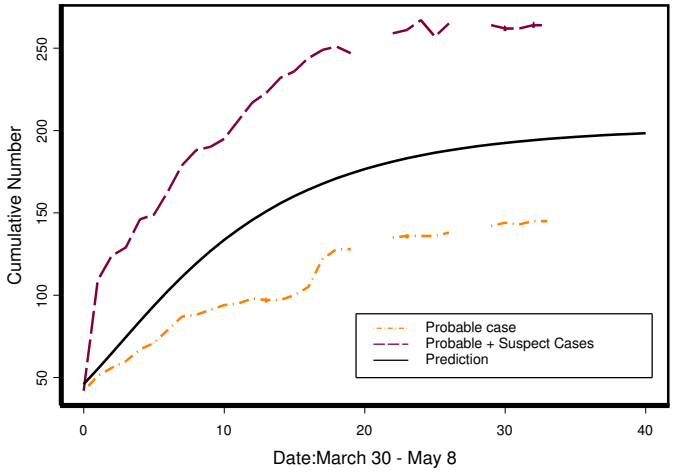


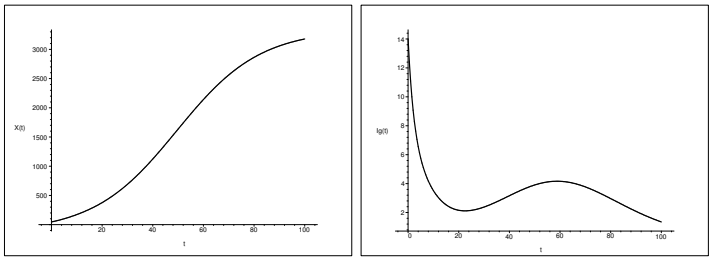
FIGURE 3. SARS in GTA: Comparison of actual data and simulations from March 30 ($t = 0$), $t = 39$ corresponds to May 8, when Health Canada statistics [6] indicated the cumulative number of probable and suspect cases in GTA were 140 and 122, respectively. The model prediction indicates on May 08, $X(39) = 198$. On May 23 when our work was nearly complete, 33 new cases were reported.

$S_g(0)$	$S_h(0)$	$E_g(0)$	$E_h(0)$	$I_g^Q(0)$	$I_h^Q(0)$	$I_g(0)$	$I_h(0)$	$U_g(0)$	$U_h(0)$
5, 443, 041	2, 951	36	28	0	0	14	13	18	18

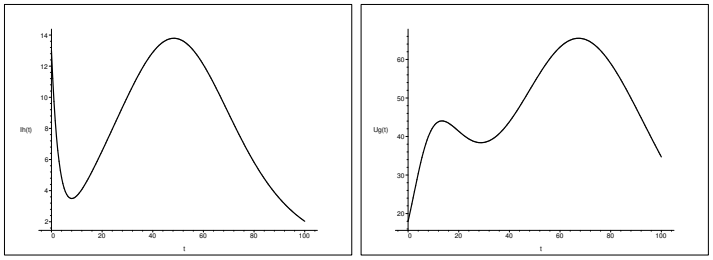
TABLE 3. Initial population data for Model II, $t = 0$ corresponds to March 30.

The actual data and simulation results for Model II until $t = 40$, ($t = 39$ corresponds to May 8, when the World Health Organization [WHO] officially lifted its travel warning after two incubation periods had elapsed since the last new reported probable case) are closely aligned (Fig. 3) and illustrate the effects of reducing transmission rates for HCWP from $a_h = 100a_g$ and $a_u = 1000a_g$ to $a_h = a_u = 10a_g$ (due to strict hospital infection control measures) and raising quarantine parameters from $q_g = q_h = 0.0$ to $q_g = 0.8$ and $q_h = 0.9$ (corresponding to the implementation of aggressive quarantine measures).

A key issue in the GTA SARS epidemic, and for future outbreaks, is identifying which of these two policies was most effective in containing the outbreak. Further simulations of Model II show that hospital control measures must be strict to contain the virus. The results of the simulations in Fig. 3 (pre-March 30 values $a_h = 100a_g$ and $a_u = 1000a_g$ changed to $a_u = a_h = 10a_g$) and Fig. 4(a) (no change post-March 30) are sharply different. In the latter case, even when the quarantine fraction is high ($q_g = 0.8$ and $q_h = 0.9$) but nosocomial transmission rates remain as for Model I, the total hospitalized and removed individuals on May 8th would be 1324, the outbreak would last > 100 days, and about 3, 000 individuals would



(a) $(t, X(t))$ (b) $(t, I_g(t))$

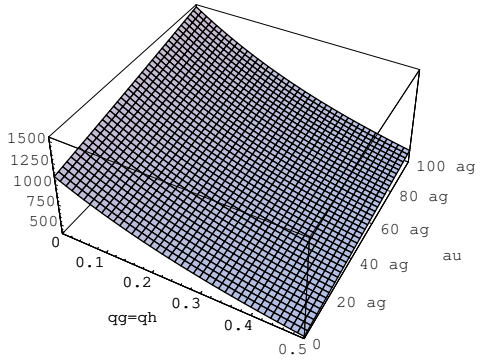


(c) $(t, I_h(t))$ (d) $(t, U_g(t))$

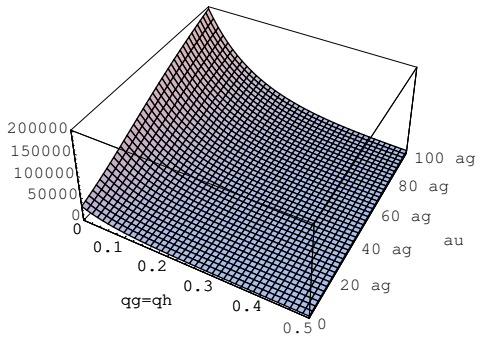
FIGURE 4. Model II simulations starting March 30 ($t = 0$) with $a_h = 100a_g$ and $a_u = 1000a_g$. (a) shows that if strict hospital control measures are not taken, there would be 3000 infected, and the epidemic would last > 100 days; (b)-(d) depict I_g, I_h, and U_g as functions of the time, and illustrate multiple peaks of infection.

be either hospitalized or removed (Fig. 4(a)). The multiple local maxima indicating possible multiple peaks should hospital control procedures not be taken (Fig. 4(b)-(d)), mirror the actual patterns in other regions: an initial peak reflective of early exposures mostly to HCWP followed by a second peak that includes both those exposed through hospital and general population contacts [3]. Following this second peak, with improved control measures, the number of new cases declines as the outbreak comes under control ($R_0 < 1$).

The simulations of Model II indicate that both hospital infection control and quarantine measures are important in containing the epidemic. In Fig. 5, we set $q_g = q_h = q$, and all other parameters and initial values are as in Model I, except that $a_h = a_g$. The total number $X(t)$ of infected and hospitalized cases are functions of a_u and q. By 40 days, hospital control and quarantine measures, if sufficiently strong, substantially reduce $X(t)$ (Fig. 5(a)), but quarantine measures are essential for long-term (150 days) containment of the epidemic (Fig. 5(b)). If enhanced measures for hospital infection control and quarantine are relaxed prematurely, the number of hospitalized individuals continue to diminish for several days, and then rise again (Fig. 6). The reported SARS cases in GTA on May 23 illustrate the consequences of premature relaxation of infection control measures.



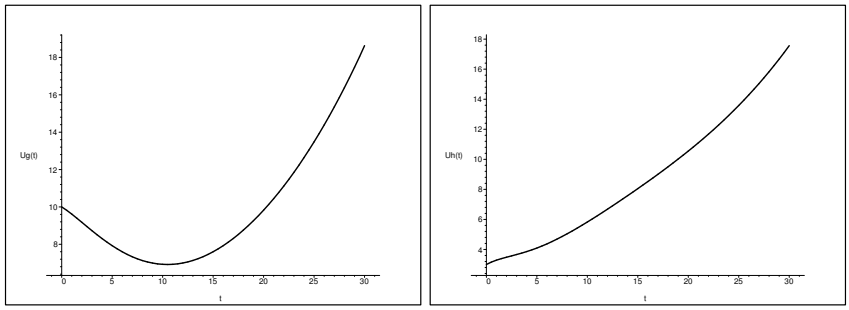
(a) 40 days



(b) 150 days

FIGURE 5. The number $X(t)$ of infected and hospitalized at (a): 40 days, (b): 150 days, after the first two weeks (t = 0 = March 30) as a function of the hospital transmission parameter a_u vs. the fraction quarantined $q = q_g = q_h$. Substantially reducing *either* a_u *or* increasing q significantly is sufficient to reduce the number of cases to low levels at 40 days. At 140 days reducing hospital transmission to 0 without quarantine results in $\approx 25,000$ cases, whereas increasing the hospital transmission parameter to $a_u = 100a_g$ and the quarantine fraction to .5 results in only $\approx 3,000$ cases. To contain the epidemic over time, quarantine of exposed individuals is necessary, because $R_0 > 1$ for the general public.

4. **Discussion.** In total, our simulations show that the combination of moderate quarantine but strict hospital infection control procedures was the key to the containment of SARS in GTA; increasing the effectiveness of quarantine $> 85\%$ did



(a) $(t, U_g(t))$ (b) $(t, U_h(t))$

FIGURE 6. This simulation shows the consequences of relaxation of hospital infection control measures and quarantine measures. The simulation starts on May 9 ($t = 0$, using the initial data obtained from Model II) and under the assumption that parameters a_h and a_u are increased to $a_h = 100a_g$ and $a_u = 500a_g$ and q_g and q_h are decreased to $q_g = 20\%$ and $q_h = 40\%$, respectively. The total number of the removed and hospitalized individuals will increase by 32 after 20 days on May 29.

not significantly reduce the total number of hospitalized and removed individuals [15]. Conversely, without strict hospital control procedures, the outbreak duration will be significantly longer (> 100 days), with multiple peaks of infection during the entire course and affecting greater numbers of individuals (Fig. 4).

Our considerations here also may be relevant to the spread of other respiratory infections, including pneumonic plague or other emerging respiratory infections. Hospitals have been amplifiers of diseases that involve the general public [such as influenza (respiratory), and enteropathogenic *E. coli* (enteric)]; our models should be useful to address issues related to their control. The epidemiology of SARS has been complex with rapid spread in some areas (e.g., Beijing) but not others, (e.g. Shanghai) despite introduction of the causative agent, as well as the control of the epidemic in many localities without continuous community spread [16]. These patterns are more consistent with secondary infection in the health-care setting being much greater than in the general community, with an overall $R_0 > 1$ [3]. The ability of relatively modest quarantine measures to decrease $R_0 < 1$ in the general community suggests a pathogen that is not well-adapted to human hosts, and implies strong selection for transmission. Thus, stringent control measures in hospital settings-the major amplifiers of transmission-are needed to minimize the risk for pandemic spread of SARS.

5. **Appendix: Analysis of dynamics for Models I and II.** In this section, we give the analysis of dynamics for Models I and II. In particularly, we give the optional quarantine fractions to control the total number of hospitalized and removed individuals below a specified level.

5.1. **Total numbers of infected and hospitalized infectives, without quarantine.** If $U_g(0) = U_h(0) = 0$, then

$$\lim_{t\to\infty}(I_g(t), I_h(t), E_g(t), E_h(t), U_g(t), U_h(t)) = (0,0,0,0,0,0),$$

$$\lim_{t\to\infty} S_g(t) = S_g(0)e^{-a_g(I_g^\infty + I_h^\infty)},$$

$$\lim_{t\to\infty} S_h(t) = S_h(0)e^{-a_h(I_g^\infty + I_h^\infty) - a_u(U_g^\infty + U_h^\infty)}$$

where $I_g^\infty = \int_0^\infty I_g(s)ds,\ U_g^\infty = \int_0^\infty U_g(s)ds,\ I_h^\infty = \int_0^\infty I_h(s)ds,\ U_h^\infty = \int_0^\infty U_h(s)ds$ describe the total numbers of infected and hospitalized infectives during the entire course of infection, and these values are determined as follows:

$$\begin{cases} U_g^\infty = \frac{r_g}{\epsilon_g} I_g^\infty,\ \ U_h^\infty = \frac{r_h}{\epsilon_h} I_h^\infty, \\ S_g(0) + E_g(0) + I_g(0) = S_g(0)e^{-a_g(I_g^\infty + I_h^\infty)} + (c_g + \epsilon_g)I_g^\infty, \\ S_h(0) + E_h(0) + I_h(0) = S_h(0)e^{-a_h(I_g^\infty + I_h^\infty) - a_u(U_g^\infty + U_h^\infty)} + (c_h + \epsilon_h)I_g^\infty. \end{cases}$$

5.2. **Total numbers of infected and hospitalized infectives, with quarantine.** For Model II, we have

$$\lim_{t\to\infty}(I_g(t), I_h(t), I_g^Q(t), I_h^Q(t), E_g(t), E_h(t), U_g(t), U_h(t)) = (0,0,0,0,0,0,0,0),$$

$$S_g(\infty) := \lim_{t\to\infty} S_g(t) = S_g(0)e^{-a_g(I_g^\infty + I_h^\infty)},$$

$$S_h(\infty) := \lim_{t\to\infty} S_h(t) = S_h(0)e^{-a_h(I_g^\infty + I_h^\infty) - a_u(U_g^\infty + U_h^\infty)}$$

where

$$\begin{cases} I_g^\infty = \int_0^\infty I_g(s)ds, I_g^{Q\infty} = \int_0^\infty I_g^Q(t)dt, E_g^\infty = \int_0^\infty E_g(t)dt, U_g^\infty = \int_0^\infty U_g(s)ds, \\ I_h^\infty = \int_0^\infty I_h(s)ds, I_h^{Q\infty} = \int_0^\infty I_h^Q(t)dt, E_h^\infty = \int_0^\infty E_h(t)dt, U_h^\infty = \int_0^\infty U_h(s)ds \end{cases}$$

and these parameters are determined by

$$\begin{cases} U_g^\infty = \frac{r_g}{\epsilon_g}(I_g^\infty + I_g^{Q\infty}) + \frac{1}{\epsilon_g}U_g(0), \\ E_g^\infty = \frac{1}{b_g}E_g(0) + \frac{1}{b_g}S_g(0)[1 - e^{-a_g(I_g^\infty + I_h^\infty)}], \\ (c_g + r_g)I_g^\infty - I_g(0) - (1-q_g)b_g E_g^\infty = 0, \\ (c_h + r_h)I_h^\infty - I_h(0) - (1-q_h)b_h E_h^\infty = 0, \\ (c_g + r_g)I_g^{Q\infty} - q_g g b_g g E_g^\infty - I_g^Q(0) = 0, \\ (c_h + r_h)I_h^{Q\infty} - q_h b_h E_h^\infty - I_h^Q(0) = 0. \end{cases}$$

5.3. **Optional quarantine fractions.** The dependence of $X(\infty)$ on the parameters (a_h, a_u, q_g, q_h) can be calculated. Since

$$\dot{X} = \dot{U}_g + \dot{U}_h + c_g(I_g^Q + I_h^Q) + (c_g I_g + c_h I_h) + \epsilon_g U_g + \epsilon_h U_h$$

then $X(\infty) = X(0) + (c_g + r_g)(I_g^\infty + I_g^{Q\infty}) + (c_h + r_h)(I_h + I_h^{Q\infty})$.

For the sake of simplicity, we let $q = q_g = q_h, b = b_g = b_h, \epsilon = \epsilon_g = \epsilon_h, r = r_g = r_h, \alpha = c_g + r_g = c_h + r_h$. Denote by $I(0) = I_g(0) + I_h(0), U(0) = U_g(0) + U_h(0), E(0) = E_g(0) + E_h(0)$, and $I^\infty = I_g^\infty + I_h^\infty, I^{Q\infty} = I_g^{Q\infty} + I_h^{Q\infty}$, $U^\infty = U_g^\infty + U_h^\infty, E^\infty = E_g^\infty + E_h^\infty$ and recall that $I_g^Q(0) = I_h^Q(0) = 0$, we get

$$\begin{aligned} \alpha I^\infty &= I(0) + (1-q)bE^\infty, \\ \alpha I^{Q\infty} &= qbE^\infty, \\ U^\infty &= \tfrac{r}{\epsilon}(I^\infty + I^{Q\infty}) + \tfrac{1}{\epsilon}U(0) = \tfrac{r}{\epsilon\alpha}(I(0) + bE^\infty) + \tfrac{1}{\epsilon}U(0). \end{aligned}$$

Therefore,

$$\begin{aligned} bE^\infty &= E(0) + S_g(0)(1 - e^{-\frac{a_g}{\alpha}I(0)})e^{-\frac{a_g}{\alpha}(1-q)bE^\infty} \\ &\quad + S_h(0)(1 - e^{-\frac{a_h}{\alpha}I(0)}e^{-\frac{a_u}{\epsilon\alpha}rI(0) - \frac{a_u}{\epsilon}U(0)}e^{-\frac{a_h}{\alpha}(1-q)bE^\infty}e^{-\frac{a_u}{\epsilon\alpha}rbE^\infty}). \end{aligned}$$

It is straightforward to show that the above equation always has a unique positive solution $Y = bE^\infty$, and hence when all others are fixed, $bE^\infty = f(a_h, a_u, q)$ is a function of a_h, a_u, and q. This is an increasing function of either a_u or a_h, when all others are fixed, and a decreasing function of q, when all others are fixed. The same is true for $X(\infty)$, since $X(\infty) = X(0) + I(0) + bE^\infty$.

The above equation also allows calculations of the minimal quarantine fraction to control the total number of hospitalized and removed individuals below a specified level. As an illustration, we note that there clearly is a limit to what can be achieved by both quarantine and hospital control procedures. In the best possible case, in which $a_u = 0$ and $q = 1$,

$$bE^\infty = E(0) + S_g(0)(1 - e^{-\frac{a_g}{\alpha}I(0)}) + S_h(0)(1 - e^{-\frac{a_g}{\alpha}I(0)}) = E(0) + S(0)(1 - e^{-\frac{a}{\alpha}I(0)})$$

and

$$X(\infty) = X(0) + E(0) + I(0) + S(0)(1 - e^{-\frac{a}{\alpha}I(0)}) := X(best).$$

Assuming the hospital control procedures are so strictly enforced that $a_u = 0$, and we want to control the outbreak so that $X \le X^*$, a given number. Note that necessarily, $X^* \ge X(best)$. Let $Y^* = X^* - X(0) - I(0)$. Then, we can find $q^* \in [0, 1]$ so that

$$Y^* = E(0) + S_g(0)(1 - e^{-\frac{a}{\alpha}I(0)}e^{-\frac{a}{\alpha}(1-q)Y^*}) + S_h(0)(1 - e^{-\frac{a}{\alpha}I(0)}e^{-\frac{a}{\alpha}(1-q)Y^*}).$$

Thus, $X(\infty) \le X^*$ if and only if $q \ge q^*$.

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