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The outbreak pattern of SARS cases in China as revealed by a mathematical model

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ABSTRACT

Since it first appeared in China's Guangdong Province, Severe Acute Respiratory Syndrome (SARS) has caused serious damages to many parts of the world, especially Asia. Little is known about its epidemiology. We developed a modified discrete SIR model including susceptible individuals, non-hospitalized SARS persons; hospitalized patients, cured hospital patients, and those who have died due to SARS infection. Here, we demonstrate the effective reproduction number is determined by infection rates and infectious period of hospitalized and non-hospitalized SARS patients. Both infection rate and the effective reproductive number of the SARS virus are significantly negatively correlated with the total number of cumulative cases, indicating that the control measures implemented in China are effective, and the outbreak pattern of accumulative SARS cases in China is a logistic growth curve. We estimate the basic reproduction number R_0 of SARS virus is 2.87 in mainland of China, very close to the estimations in Singapore and Hong Kong.

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1. Introduction

The first SARS case was reported in China's Guangdong Province in November of 2002. The total number of cases recorded in China climbed to over 5200 with about 5–10% mortality by the end of 2003. It has been confirmed that SARS is caused by a new coronavirus, but its epidemiology is little known (Dye and Gay, 2003; Lipsitch et al., 2003; Riley et al., 2003). Consequently, modelers are struggling to estimate the severity of the SARS epidemic, the effectiveness of control measures and to provide earlier warning of possible SARS outbreaks (Vogel, 2003). Mathematical models have been widely used to calculate and describe the dynamic evolution of epidemic threshold values and severity (Bailei, 1975; Anderson and May, 1992). The most widely used is the Kermarck-McKendrik model, also called the SIR model (Capasso and Serio, 1978), which is based on a system of three popula-

tions: susceptible, infectious and removals. Various epidemic models have been developed from the classic SIR model for different purposes, or with different assumptions, e.g. the SIRS model (Mollison, 1995), SEIR model (Keepling et al., 1997), two-level or two-stage SIR model (Ball and Neal, 2002), SIR models considering immunity (Greenhalgh et al., 2000), intermediate class (Méndez and Fort, 2000), non-linearity of infection (Moghadas, 2002; Wendi and Zhien, 2002; Ruan and Wang, 2003), etc. In classic SIR models, the effective reproductive number, R, is the threshold parameter of epidemic diseases: if $R < 1$, the disease will eventually disappear, but $R > 1$ implies that the disease will persist (Hethcote and van den Driesssche, 1995; Wallinga et al., 1999; Diekmann et al., 1990). Therefore, knowledge of R is extremely valuable for developing epidemic management strategies as it gives some indication of the effort required to reach specific goals (Wendi and Zhien, 2002; Ruan and Wang, 2003). Recently, two studies reported the

transmission epidemic of SARS in Singapore and Hong Kong (Dye and Gay, 2003; Lipsitch et al., 2003; Riley et al., 2003). Both estimated the basic reproduction number R_0 is order of 2–4. Both teams make use of mathematical models based on a system of four subpopulations: susceptible, exposed, infectious, and recovered (immune) individual, also called a SEIR model.

2. The discrete models

We developed a discrete SARS model based on the following groups: susceptible individuals, $N_1(t)$; non-hospitalized SARS persons, $N_2(t)$; hospitalized patients, $N_3(t)$; cured hospital patients, $N_4(t)$; and those who have died due to SARS infection, $N_5(t)$; (Fig. 1a). The infectious period of non-hospitalized patients, $T_1(t)$, is defined as the time non-hospitalized SARS persons from being infectious to being removed to hospitals. We assume that non-hospitalized SARS persons are infectious at the rate $P_1(t)$. Infected people with symptoms, once detected, are removed immediately to hospital for isolation and treatment. These infected patients further infect doctors, nurses and other front-line hospital staff at the rate $P_2(t)$ during the treatment period $T_2(t)$ in hospitals. Non-hospitalized SARS individuals are composed of two sub-groups: front-line hospital staff (doctors, nurses, etc.), $N_{2d}(t)$, and the general public, $N_{2n}(t)$. Non-hospitalized SARS people, $N_2(t)$, infect the general public, $N_{2n}(t)$, at the rate $P_1(t)$, while hospitalized SARS patients, $N_3(t)$, infect front-line hospital staff, $N_{2d}(t)$, at the rate $P_2(t)$. The transfer rates from $N_2(t)$ to $N_3(t)$ is determined by $T_1(t)$, and the transfer rate from $N_3(t)$ to $N_4(t)$ or $N_5(t)$ are determined by the proportion of cured patients, $P_3(t)$, and $T_2(t)$. The proportion of mortality due to SARS infection is $1 - P_3(t)$. This model is especially designed for estimating the basic and effective reproductive number of the SARS virus from the data

that has been released daily by the Chinese Ministry of Health (CMH) since April 21, 2003.

We assume that the immigration and emigration rates of infected individuals are the same. Clinical observations indicate that cured SARS patients are unlikely to be infectious again (Yang, 2003). We will ignore the effect of natural birth and mortality rates because we are only interested in the dynamics of the SARS epidemic over a period of short time (e.g. a few weeks or months). The dynamic model is described as below:

$$N_1(t + 1) = N_1(t) - P_1(t) \cdot N_2(t) - P_2(t) \cdot N_3(t) \tag{1}$$

$$N_2(t + 1) = N_2(t) + P_1(t) \cdot N_2(t) + P_2(t) \cdot N_3(t) - \frac{N_2(t)}{T_1(t)} \tag{2}$$

$$N_3(t + 1) = N_3(t) + \frac{N_2(t)}{T_1(t)} - P_3(t) \cdot \frac{N_3(t)}{T_2(t)} - (1 - P_3(t)) \cdot \frac{N_3(t)}{T_2(t)} \tag{3}$$

$$N_4(t + 1) = N_4(t) + P_3(t) \cdot \frac{N_3(t)}{T_2(t)} \tag{4}$$

$$N_5(t + 1) = N_5(t) + (1 - P_3(t)) \cdot \frac{N_3(t)}{T_2(t)} \tag{5}$$

Notice that, $P_1(t) \cdot N_2(t)$ is the number of new SARS cases among the general public caused by $N_2(t)$; and $P_2(t) \cdot N_3(t)$ is the number of new SARS cases among front-line hospital staff caused by $N_3(t)$. We assume the $T_1(t)$ of $N_{2n}(t)$ and $N_{2d}(t)$ is same, then:

$$N_{2n}(t + 1) = N_{2n}(t) + P_1(t) \cdot N_2(t) - \frac{N_{2n}(t)}{T_1(t)} \tag{6}$$

$$N_{2d}(t + 1) = N_{2d}(t) + P_2(t) \cdot N_3(t) - \frac{N_{2d}(t)}{T_1(t)} \tag{7}$$

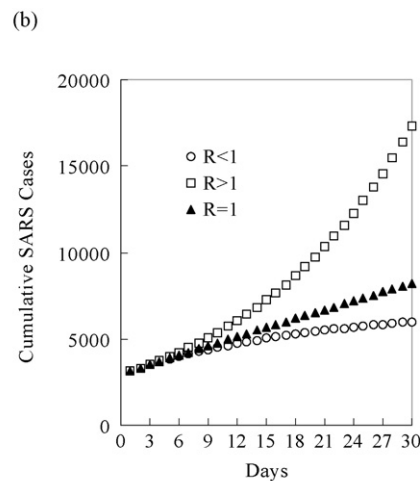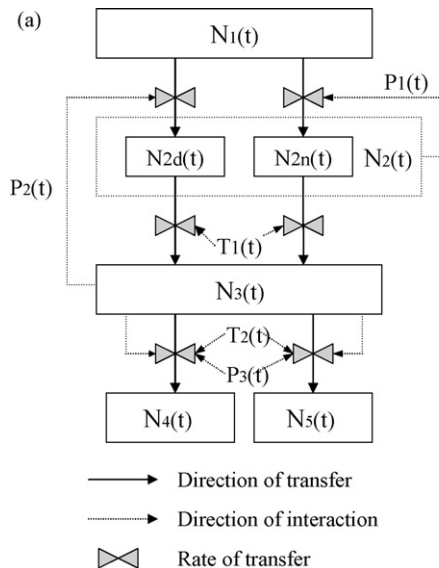The time step in our models is set as one day.

Fig. 1 – (a) Diagramatic representation of the SARS model. See text for symbol definitions; (b) the outbreak pattern and the effective reproductive number of the SARS model. When $R < 1$ (○), the outbreak curve is a power curve ($P_1 = 0.0062$, $P_2 = 0.1473$, $T_1 = 4.5$, $T_2 = 14$); when $R > 1$ (□), the outbreak curve is exponential ($P_1 = 0.0378$, $P_2 = 0.2144$, $T_1 = 4.5$, $T_2 = 14$); when $R = 1$ (▲), the outbreak curve is linear ($P_1 = 0.01404$, $P_2 = 0.1785$, $T_1 = 4.5$, $T_2 = 14$). The initial values of total cumulative cases, cumulative mortality, cumulative recovered patients and cumulative cases are 3106, 139, 1306 and 653, respectively.

3. Theoretical analysis

First, let us assume that the growth pattern of total cumulative SARS cases is linear against time t, and let $N_s(t)$ be total cumulative SARS cases at time t, then:

$$N_s(t) = b_0 + b_1 \cdot t$$
$$N_s(t+1) = b_0 + b_1 \cdot (t+1)$$

Here, b_0, b_1 are constants.

$$N_s(t+1) - N_s(t) = b_1$$

b_1 is the number of new SARS cases at time t. That is to say, if b_1 is constant, the growth pattern of SARS cases is linear against time t. From Eq. (3), the number of new cases of SARS removed to $N_3(t)$ is $N_2(t)/T_1(t)$, then $N_s(t+1) - N_s(t) = N_2(t)/T_1(t)$. If $N_2(t+1) - N_2(t) = 0$, $N_s(t+1) - N_s(t)$ is constant and the growth pattern of SARS cases will be linear; if $N_2(t+1) - N_2(t) > 0$ it will be exponential; if $N_2(t+1) - N_2(t) < 0$ it will be a power curve. From Eq. (2):

$$N_2(t+1) - N_2(t) = P_1(t) \cdot N_2(t) + P_2(t) \cdot N_3(t) - \frac{N_2(t)}{T_1(t)} = 0$$

$$P_1(t) \cdot T_1(t) + P_2(t) \cdot T_1(t) \cdot \frac{N_3(t)}{N_2(t)} = 1 \tag{8}$$

For a linear growth pattern $N_2(t)$ has to be stable. To satisfy the Eq. (8), $N_3(t)$ also has to be stable: $N_3(t+1) - N_3(t) = 0$. From Eq. (3):

$$N_3(t+1) - N_3(t) = \frac{N_2(t)}{T_1(t)} - \frac{N_3(t)}{T_2(t)}$$

If $N_3(t+1) - N_3(t) = 0$, $N_3(t)/N_2(t) = T_2(t)/T_1(t)$. From Eq. (8), then

$$P_1(t) \cdot T_1(t) + P_2(t) \cdot T_2(t) = 1 \tag{9}$$

Let $R(t) = P_1(t) \cdot T_1(t) + P_2(t) \cdot T_2(t)$, the outbreak pattern of SARS cases is determined by the following conditions: $R(t) = 1$, linear growth; $R(t) > 1$, exponential growth; $R(t) < 1$, power growth. If $P_2(t) = 0$, i.e. SARS infection among front-line hospital staff is completely controlled, then the Eq. (9) is written as: $R(t) = P_1(t) \cdot T_1(t) = 1$. Through qualitative analysis, we conclude that the outbreak pattern of SARS cases is determined by four parameters: the infection rate among the general public $P_1(t)$ and front-line hospital staff $P_2(t)$, the infectious period of non-hospitalized patients $T_1(t)$ and the treatment period of SARS patients in hospital $T_2(t)$.

4. Model parameter estimation

The data provided by the CMH include total cumulative SARS cases, cumulative SARS cases among front-line hospital staff, cumulative SARS mortality, cumulative cured SARS cases, and cumulative suspected SARS cases on the Chinese Mainland (Table 1). Let us define:

Table 1 – The cumulative SARS cases in Mainland China from April 21 to May 12, 2003, released by the Chinese Ministry of Health

Date	Days	Total	Dead	Cured	Doctors[a]
April 21	1	2158	97	1213	480
April 22	2	2305	106	1231	517
April 23	3	2422	110	1254	541
April 24	4	2601	115	1277	578
April 26	6	2753	122	1285	588
April 27	7	2914	131	1299	610
April 28	8	3106	139	1306	653
April 29	9	3303	148	1322	709
April 30	10	3460	159	1332	727
May 1	11	3638	181	1351	753
May 2	12	3799	322	1372	778
May 3	13	3971	190	1406	810
May 4	14	4125	197	1416	832
May 5	15	4280	206	1433	851
May 6	16	4409	214	1460	883
May 7	17	4560	219	1487	901
May 8	18	4698	224	1529	917
May 9	19	4805	230	1582	925
May 10	20	4884	235	1620	931
May 11	21	4948	240	1652	935
May 12	22	5013	252	1693	941

Source: Chinese Ministry of Health.

[a] Includes all front-line hospital staff.

$N_s(t)$ is total cumulative SARS cases at time t;
$N_d(t)$, cumulative SARS cases among front-line hospital staff at time t;
$N_n(t)$, cumulative SARS cases among general public at time t;
$N_5(t)$ is cumulative SARS mortality at time t;
$N_4(t)$ is cumulative cured SARS cases at time t.

Then:

$$N_3(t) = N_s(t) - N_4(t) - N_5(t) \tag{10}$$

$$N_2(t) = T_1(t) \cdot [N_s(t+1) - N_s(t)] \tag{11}$$

$$N_n(t) = N_s(t) - N_d(t) \tag{12}$$

$$N_{2n}(t) = T_1(t) \cdot [N_n(t+1) - N_n(t)] \tag{13}$$

$$N_{2d}(t) = T_1(t) \cdot [N_d(t+1) - N_d(t)] \tag{14}$$

From Eqs. (6) and (13):

$$P_1(t) = \frac{\{T1(t) \cdot [N_n(t+2) - N_n(t+1)] - T_1(t) \cdot [N_n(t+1) - N_n(t)] + [N_n(t+1) - N_n(t)]\}}{N_2(t)} \tag{15}$$

From Eqs. (7) and (14):

$$P_2(t) = \frac{\{T_1(t) \cdot [N_d(t+2) - N_d(t+1)] - T_1(t) \cdot [N_d(t+1) - N_d(t)] + [N_d(t+1) - N_d(t)]\}}{N_3(t)} \tag{16}$$

Table 2 – Estimated values of $P_{1\_w}(t)$, $P_{2\_w}(t)$, $R(t)$ and their standard errors S_1, S_2 and S											
Date	Day	N_s	r	$\sum N_3(t)$	$P_{2\_w}(t)$	S_2	$\sum N_2(t)$	$P_{1\_w}(t)$	S_1	$R(t)$	S
April 21	1	2158	0.0659								
April 22	2	2305	0.0495								
April 23	3	2422	0.0713								
April 24	4	2601	0.0568								
April 26	6	2753	0.0568								
April 27	7	2914	0.0638	6841	0.0378	0.0023	4266	0.2144	0.0063	1.4937	0.0159
April 28	8	3106	0.0615	8502	0.0169	0.0014	5152.5	0.2031	0.006	1.1503	0.0130
April 29	9	3303	0.0464	9505	0.0230	0.0015	5197.5	0.2329	0.0059	1.3706	0.0137
April 30	10	3460	0.0502	10506	0.0150	0.0012	5472	0.1786	0.0052	1.014	0.0118
May 1	11	3638	0.0433	11565	0.0259	0.0015	5391	0.1835	0.0053	1.1875	0.0125
May 2	12	3799	0.0443	12461	0.0178	0.0012	5481	0.1760	0.0051	1.0413	0.0118
May 3	13	3971	0.0381	13490	0.0085	0.0008	5449.5	0.1708	0.0051	0.8867	0.0112
May 4	14	4125	0.0369	14572	0.0062	0.0007	5283	0.1473	0.0049	0.7492	0.0106
May 5	15	4280	0.0297	15552	0.0112	0.0008	4977	0.1818	0.0055	0.9749	0.0120
May 6	16	4409	0.0337	16454	0.0078	0.0007	4950	0.1598	0.0052	0.8289	0.0113
May 7	17	4560	0.0298	17339	0.0051	0.0005	4770	0.1529	0.0052	0.7589	0.0112
May 8	18	4698	0.0225	18167	0.0017	0.0003	4527	0.1232	0.0049	0.5773	0.0104
May 9	19	4805	0.0163	19055	0.0021	0.0003	4108.5	0.1139	0.0050	0.542	0.0106
May 10	20	4884	0.0130	19709	0.0023	0.0003	3703.5	0.1009	0.0050	0.4854	0.0106
May 11	21	4948	0.0131	20253	−0.002	–	3298.5	0.1608	0.0064	0.6895	–
May 12	22	5013	0.0145	20680	0.0000	3.4E−05	3046.5	0.0552	0.0041	0.2485	0.0088

N_s is the total cumulative SARS cases. r is the instantaneous increase rate. "–" S_2 and S are not calculated due to the negative value of $P_2(t)$.

The weekly average values of $P_1(t)$, $P_2(t)$ last week at time t are calculated as:

$$P_{1\_w}(t) = \frac{\sum\{T_1(t) \cdot [N_n(t+2) - N_n(t+1)] - T_1(t) \\ \cdot [N_n(t+1) - N_n(t)] + [N_n(t+1) - N_n(t)]\}}{\sum N_2(t)} \quad (17)$$

$$P_{2\_w}(t) = \frac{\sum\{T_1(t) \cdot [N_d(t+2) - N_d(t+1)] - T_1(t) \\ \cdot [N_d(t+1) - N_d(t)] + [N_d(t+1) - N_d(t)]\}}{\sum N_3(t)} \quad (18)$$

The standard errors were estimated by following Krebs (1999). Let $p_1 = P_{1\_w}(t)$; $q_1 = 1 - p_1$; $n_1 = \sum N_2(t)$; $p_2 = P_{2\_w}(t)$; $q_2 = 1 - p_2$; $n_2 = \sum N_2(t)$; S_1, S_2 and S are standard errors of $P_{1\_w}(t)$, $P_{2\_w}(t)$ and $R(t)$, then:

$$S_1 = \sqrt{\frac{p_1 \cdot q_1}{n_1}}$$
$$S_2 = \sqrt{\frac{p_2 \cdot q_2}{n_2}}$$
$$S = \sqrt{T_1 \cdot S_1^2 + T_2 \cdot S_2^2}$$

It is obvious that using the rolling weekly averages of infection rates reduces estimation errors since the higher the $\sum N_2(t)$ or $\sum N_3(t)$, the lower the standard errors.

Clinical observations indicate that in mainland of China, the infectious period of the non-hospitalized persons is usually between 4 and 5 days with an average of 4.5 days (Yang, 2003). The average treatment period (admission to discharge) of hospitalized SARS patients is 14 days. About 95% of patients are completely cured. Thus, we assume that the parameters of $T_1(t)$, $T_2(t)$ and $P_3(t)$ are constant, and let $T_1 = 4.5$, $T_2 = 14$, $P_3 = 0.95$. The model parameters $P_{1\_w}(t)$, $P_{2\_w}(t)$, $R(t)$, and their standard errors are shown in Table 2.

The instantaneous rate of increase in cumulative SARS cases $N_s(t)$ is defined as: $r = \ln[N_s(t+1)/N_s(t)]$. If the instantaneous rate of increase is negative and linear correlated with

cumulative SARS cases, the growth pattern of cumulative SARS cases is a logistic (Zhang et al., 2003).

5. Results

Fig. 1b illustrates how effective reproductive number R determines the outbreak pattern of SARS cases. The initial values of $N_1(0)$, $N_2(0)$, $N_3(0)$, $N_4(0)$, $N_5(0)$ are from the data of April 21, 2003, released by CMH. Changing the values P_1, P_2, P_3, T_1 and T_2 produce different curves for the total number of cumulative cases. The simulation results further support the conclusion that R is the threshold for the outbreak pattern of SARS.

Sensitivity analysis indicates that T_1 and P_1 are the most sensitive parameters, T_2 and P_2 are less sensitive and P_3 is the least sensitive (Fig. 2). Therefore, R is mainly determined by P_1, P_2, T_1 and T_2.

Fig. 3a shows that the effective reproductive number (R) and infection rates (P_1, P_2) among front-line hospital staff and the general public are significantly negatively correlated with total cumulative SARS cases (N_s). The instantaneous rate of increase in total cumulative cases is also significantly negatively correlated with the number of total cumulative cases, indicating that the outbreak pattern of cumulative SARS cases in China is a logistic growth curve. Table 3 shows the results of linear regression between dependents variables (R, P_2, P_1, r) and independent variable (N_s). From Table 3, the maximum R (equal basic reproductive number R_0), P_2, P_1, r (equal b_0 in Table 3) are 2.8716, 0.0684, 0.4245 and 0.1129 when the cumulative SARS case (N_s) is approaching zero. Therefore, in the early stage of SARS outbreak, each SARS infect 1.9 ($P_1 \cdot T_1 = 0.4245 \times 4.5$) members of the general public, 0.9576 ($P_2 \cdot T_2 = 0.0684 \times 14$) front-line hospital staff. During the study period, we estimate that each infected individual infects 0.48–1.49 individuals, average 0.93 (0.18 front-line hos-

Table 3 – Linear regressions between dependents (R, P_2, P_1, r) and independent N_s by using linear models: $r = b_0 + b_1 N_s$, $R = b_0 + b_1 N_s$, $P_2 = b_0 + b_1 N_s$, $P_1 = b_0 + b_1 N_s$

Dependent	Mth	R^2	d.f.	F	Sigf	b_0	b_1
R	LIN	0.875	16	111.80	0.000	2.8716	−0.0005
P_2	LIN	0.833	16	79.57	0.000	0.0684	−0.00001
P_1	LIN	0.745	16	46.83	0.000	0.4245	−0.00007
r	LIN	0.909	22	218.51	0.000	0.1129	0.00002
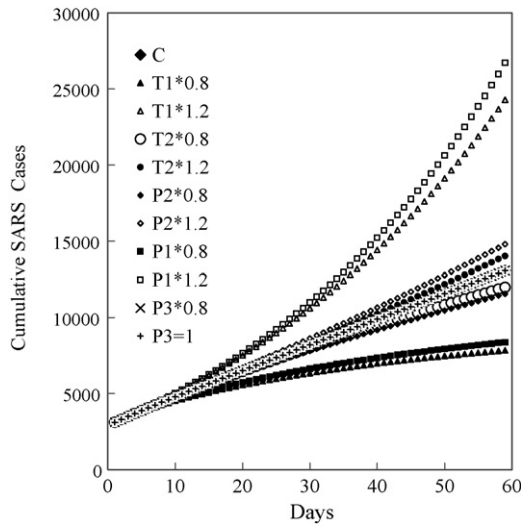
Fig. 2 – Sensitivity analysis of model parameters P_1, P_2, P_3, T_1, T_2. Each parameter was increased or reduced by 20% while the other parameters remained unchanged. The linear curve is the contrasting curve (C) ($R = 1$, $P_1 = 0.01404$, $P_2 = 0.1785$, $T_1 = 4.5$, $T_2 = 14$). The initial values of total cumulative cases, cumulative mortality, cumulative recovered patients and cumulative cases are 3106, 139, 1306 and 653, respectively. The curves of $P_3^* 1.2$ and $P_3^* 0.8$ are totally overlapped with the contrasting curve (C).

pital staff and 0.75 members of the general public) during the study period of 3 weeks. In general, the infection of SARS person to front-line hospital staff is better managed due to the improved protection measures taken in hospitals.

Fig. 3b shows the simulated and observed values of total cumulative cases, cumulative cases among front-line hospital staff and the general public. The negative relationship between infection rates and cumulative cases has been incorporated into the model. In general, the simulation curves are a good fit to the observed growth patterns, but the discrepancy between observed and expected became a little larger over the last week. Higher accuracy of simulation is achieved if it is conducted within a 1-week time frame (Fig. 4). These results indicate that the model is generally a good predictor of the dynamics of SARS epidemic.

6.   Discussions

Although there have been no reported cases of transmission of SARS during pre-symptomatic period (Lipsitch et al., 2003), our study suggests that such transmission by SARS person before hospitalized is quite high; about 2–4 times higher than transmission from hospitalized patients. At present, the transmission process by non-hospitalized persons is not completely understood. Infection paths of nearly 20–30% SARS patients are not clear in mainland of China. Though it is gener-
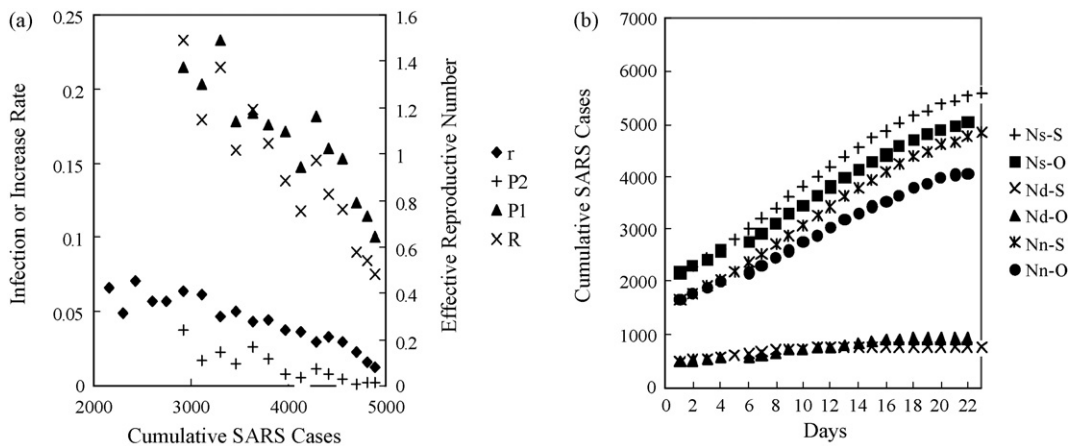

Fig. 3 – (a) The negative relationship between the SARS infection rate among the general public (P_1, ▲) ($R^2 = 0.743$, $p = 0.000$), the infection rate among front-line hospital staff (P_2, +) ($R^2 = 0.740$, $p = 0.000$), the effective reproductive number (R, ×) ($R^2 = 0.813$, $p = 0.000$), the relative rate of increase of total cumulative cases (r, ●) ($R^2 = 0.934$, $p = 0.000$) against total cumulative cases of SARS in China. (b) The simulated total cumulative SARS cases ($N_s - S$, +), observed values of the total cumulative SARS cases ($N_s - O$, ■), the simulated cumulative SARS cases among front-line hospital staff ($N_d - S$, ×), the observed cumulative SARS cases among front-line hospital staff ($N_d - O$, ▲), the simulated cumulative SARS cases among the general public ($N_n - S$, *) and the observed cumulative SARS cases among the general public ($N_d - O$, ●) in China from April 21 to May 12, 2003.
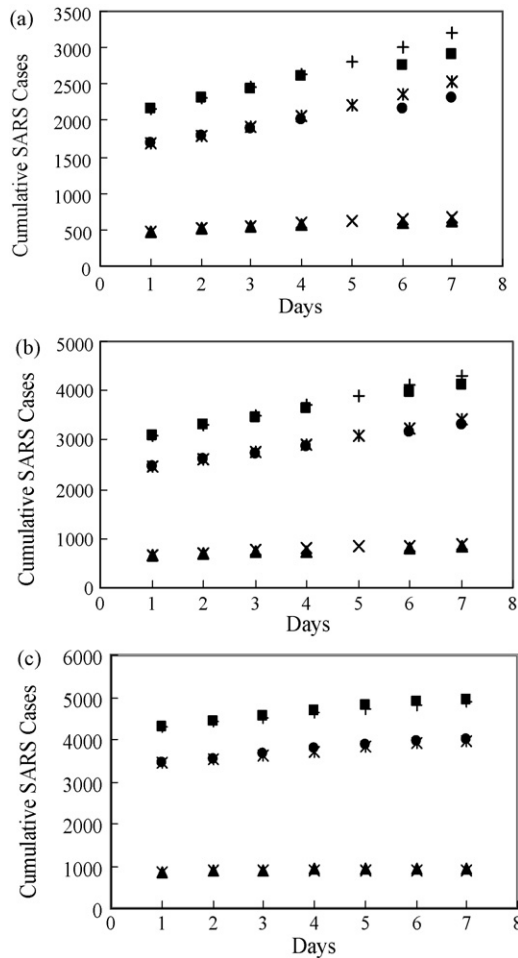
Fig. 4 – Simulations conducted within a 1-week time frame with the simulated total cumulative SARS cases (+), the simulated cumulative SARS cases among front-line hospital staff (×), the simulated cumulative SARS cases among the general public (*); the observed values of the total cumulative SARS cases (■), the observed cumulative SARS cases among front-line hospital staff (▲), and the observed cumulative SARS cases among the general public (●) in China from April 21 to May 12, 2003. (a) First week, (b) Second week and (c) Third week.

ally believed SARS persons are only infectious during the few days with symptoms, alternative infection paths may exist. According to a survey in China, the SARS virus can survive several days outside the body of SARS persons. It is possible these viruses explain the high proportion of SARS cases without unknown origins.

We estimate that the basic reproductive number R_0 for a single infected individual in the early stage is 2.8716, which is very close to the estimation of R_0 in Singapore and Hong Kong by Lipsitch et al. (2003) and Riley et al. (2003). The rate of SARS transmission is not very high compared to some airborne diseases, which suggests that transmission of the SARS virus requires a relatively long-term period of close contact. This is supported by the fact that SARS cases most often occur among family members, residents or workers in the same

apartment complex or office building and front-line hospital staff.

Some epidemiologists have suggested that the apparently linear growth in SARS cases is due to the slow rate of transmission of the virus, and estimate that each infected individual infects no more than two other people (Vogel, 2003). Our study generally supports this speculation, but indicates that the outbreak pattern of the accumulative SARS cases in China is logistic in general, rather than linear. The infection rates, effective reproductive number and the instantaneous rate of increase in total cumulative cases are significantly negatively correlated with the total number of cumulative cases. This is a good indication that the SARS epidemic can be well managed by using traditional prevention measures like isolation, reduction of contacts, etc.

The basic and effective reproductive numbers are good indicators of the severity of epidemic diseases and effectiveness of control (Hethcote and van den Driesssche, 1995). In general, estimation of these parameters from disease outbreak data is not easy since the actual process of infection is not observed, data are often incomplete and the rate of infection is often non-linear. Kramer (1994) accurately simulated the growth of an HIV infected population. Some other methods are also proposed to estimate model parameters, like the Martingale method (Fine and Clarkson, 1982; Yip, 1989; Becker, 1989, 1993; Haydon et al., 1997; Becker and Britton, 1999), Markov Chain Monte Carlo method (O'Neill, 2002). The SARS model described here is a variant of the SIR model with the addition of two-stage infections and two sub-compartments that reflect unique features of the SARS virus. The model has the advantage that its parameters are easy to estimate from the data released by the CHM. The advantage of our estimation is that R_0, R, P_1, P_2 can be estimated by using simple data of cumulative SARS cases as shown in Table 1.

Our model also includes three basic components: susceptible (N_1), infectious (N_2, N_3) and removals (N_4, N_5). Thus, it is basically a SIR model used widely in epidemiological studies (e.g. Capasso and Serio, 1978; Mollison, 1995; Keepling et al., 1997; Ball and Neal, 2002; Greenhalgh et al., 2000; Dye and Gay, 2003; Lipsitch et al., 2003; Riley et al., 2003). The difference of our model from the classic SIR model is that we further divide the infectious component into two parts: hospitalized and non-hospitalized populations, and we divide the removal component into two parts: cured and dead populations. These modifications were specially done for SARS transmissions. The other difference is that we define the infectious rate differently. Let $S(t)$ is the number of susceptible population at time t, $I(t)$ is the number of infectious population at time t, α is the maximum infection rate, τ is the incubation time. In the classic SIR model (e.g. Monteriro et al., 2006a,b), the contribution of $I(t)$ to the increase of newly infection population is calculated as: $\Delta = \alpha \cdot S(t) \cdot I(t - \tau)$. In our model, we define $P(t)$ as the infection rate of infectious individual of $I(t)$ at time t. Thus, we have the following equation: $\Delta = P(t) \cdot I(t)$. The parameter $P(t)$ varies in time. It contains the combined effect of incubation time, immunity and control efforts. In the classic SIR model, α is assumed to be constant, only $S(t)$ and $I(t - \tau)$ determine the increase of newly infected population. In fact, isolation measures by human obviously affect the infection rate α. Such an effect is not well presented in the classic SIR model.

It is obvious that our model has advantages over the conventional SIR model because it has fewer parameters. This will make parameter estimation easier without knowing detailed mechanism of disease transmission (e.g. incubation time, immunity and control efforts) and the susceptible population size. Although the parameters of $P_1(t)$, $P_2(t)$, $T_1(t)$, $T_2(t)$ vary in time, it is reasonable to assume they are stable when they are estimated at the rolling interval of 1 week.

Using our model, the infection rate of one infectious individual can easily be estimated at any time if the accumulative numbers of infection and dead cases are given. Though this epidemiological model and the parameter estimation method are specially designed for SARS transmission, they are also applicable to other infectious diseases, and to population growth of other organisms.

The decline of the effective reproductive number indicates that the measures adopted to control SARS in China are effective. One of the key preventative measures in China is the complete isolation of those confirmed or suspected of having been infected, including anyone likely to have had close contact with confirmed or suspected SARS carriers. This measure is strongly recommended because the model shows that both the infectious period (T_1) and the infection rate (P_1) are very sensitive parameters. In addition to isolating confirmed cases reducing the infectious period (T_1) is an effective means of reducing SARS infection. This requires the early identification of infected individuals using modern diagnostic techniques.

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