THEORY AND METHODS

A simple approximate mathematical model to predict the number of severe acute respiratory syndrome cases and deaths

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Background: Severe acute respiratory syndrome (SARS) is currently spreading in many countries. This paper proposes a simple approximate mathematical model for public health practitioners to predict the number of SARS cases and deaths.
Methods: The model is based on four parameters: R_o (basic reproductive number), F (case-fatality rate), i (incubation period), and d (duration of disease). The calculations can be done by hand or by using a computer spreadsheet.
Results: The best parameters to fit Canadian data as of 6 April 2003 (before infection controls took effect) are R_o = 1.5, F = 30%, i = 5 days, d = 14 days. On 6 April (day 40) there were 74 cases and 7 deaths. If this trend continues, SARS numbers in Canada are predicted to be as follows: 387 cases and 34 deaths by 26 April (day 60), 4432 cases and 394 deaths by 26 May (day 90), and 50 500 cases and 4489 deaths by 25 June (day 120). By comparison, the best parameters to fit Hong Kong data as of 10 April 2003 are R_o = 2.0, F = 20%, i = 5 days, d = 14 days.
Conclusions: Using the proposed mathematical model, it was estimated that about 1.5 to 2 new infectious cases were produced per infectious case every five days. Also, about 20% to 30% of the cases die within 14 days. The case-fatality may therefore be considerably higher than initially thought. The model indicates that SARS can spread very fast when there are no interventions.

Severe acute respiratory syndrome (SARS), a contagious and rapidly progressive infectious disease, is only months old but is already spreading in many countries.[1] The epidemic of SARS has caused a lot of concern in the media and the general public.[2–4] The World Health Organisation issued a global health alert on 12 March 2003[1 5] and set up a daily registry of reported cases on 17 March.[6] Within a matter of weeks since the first cases were reported, research results have started appearing in scientific journals on the epidemic,[1 5] epidemiological and clinical features of patient clusters in Hong Kong[7–9] and in Canada,[10] and a coronavirus as possible cause.[1 2 9–12] Scientists and health practitioners are acting fast, but still may not be fast enough.[1] Currently, public health practitioners lack a mathematical tool to assist them in predicting the number of cases and deaths in the short-term, in order to plan resources and to evaluate the effectiveness of intervention strategies.

This paper proposes a simple approximate mathematical model for public health practitioners to predict the number of SARS cases and deaths arising in the first months of an epidemic under the assumption that no intervention takes place to cut its spread. It is intended to be a user friendly epidemiological paper dealing with a highly time sensitive problem. The proposed epidemiological framework for predicting SARS morbidity and mortality is meant to be clear, simple, and applicable even in developing countries with limited resources. The calculations can be done by hand or by using a computer spreadsheet. The model is illustrated by publicly available data on the World Health Organisation web site.[6]

THE MODEL

The model, based on the standard SIR (susceptible-infected-removed) epidemic model,[13 14] assumes that transmission of SARS is contagious from person to person[1 10 11] and not point source.[15] It is further assumed that, at an initial stage of the SARS epidemic, the proportion of the population with immunity to SARS is negligible.[14]

At the initial stage of a contagious epidemic, a small number of infected people start passing the disease to a large population. Individuals can go through three states. They start out susceptible (S), then become infected and infectious (I), after which they are removed (R), either by recovery with immunity or by death. Schematically,

$$S \rightarrow I \rightarrow R.$$

The proposed model is based on four parameters: R_o (basic reproductive number—that is, the expected number of new infectious cases per infectious case), F (case fatality rate—that is, the proportion of cases who die within the symptomatic period), i (incubation period—that is, the time from infection to symptom), and d (duration of disease, or symptomatic period—that is, the time from symptom to recovery or death).[14 15]

Assumptions made in formulating the model are:

- The population at risk is large enough and time period of concern is short enough that over the time period of interest, very close to 100% of the population is susceptible.
- The epidemic is at an early stage and has not reached the point where the susceptible population decreases so much due to death or post-infection immunity that the average number of secondary cases falls.
- Unprotected contact results in infection.
- The epidemic in the population of interest begins with a single host. (Note that the equations and Excel formulas

used in computing cases and deaths are easily modified if this is not the case.)

- There is no intervention to prevent disease from spreading.
- There is homogenous mixing among the infectives and susceptibles, such that every infected person will pass the disease to exactly R_o susceptible individuals simultaneously within an incubation period of i days.
- Infectivity occurs during the incubation period only.
- The models are deterministic—that is, the four parameters take on constant values.

Predicting the number of SARS cases

This model requires only the following input parameters: R_o (basic reproductive number) and i (incubation period).

After one incubation period (i), one infectious case produces R_o new infectious cases. The cumulative total number of cases at this time is $1+R_o$. After two incubation periods (2i), there are R_o^2 cases produced by the previous R_o cases. The total number of cases is $1+R_o+R_o^2$.

Mathematically, the predicted number of incident cases on day t·i, that is, $C_{t\cdot i}$, where t is time expressed in the number of incubation periods, is

$$C_{t\cdot i}$$

The predicted total number of cases (C) is

$$C = \Sigma\ C_{t\cdot i}$$

Table 1 illustrates the application of the model to calculate the predicted number of SARS cases, using $R_o = 3$ and $i = 5$ days. It is predicted that on day 15 there are 27 new cases and that the total number of cases by day 15 is 40. The value for i can be determined from epidemiological studies of patients. The optimal values for R_o in a particular situation, for example, a country or a local area, can be determined by trying out several values to see which combination of R_o and i produces the predicted total number of SARS cases that most closely matches the observed total number of SARS cases.

Predicting the number of SARS deaths

This model requires the following input parameters: R_o (basic reproductive number), F (case fatality rate), i (incubation period) and, d (duration of disease).

After one disease duration (d), the cases are removed (by death or recovery). F percentage of them die, while 1−F percentage recover.

Mathematically, the predicted number of deaths on day t·i+d—that is, ($D_{t\cdot i+d}$), where t is time expressed in the number of incubation periods, is

$$D_{t\cdot i\cdot d} = C_{t\cdot i} \times F.$$

Table 1 Predicted number of SARS cases using $R_o = 3$ and $i = 5$ days

Number of incubation period (t)	Day (t·i)	Predicted incident cases ($C_{t\cdot i}$)	Predicted total cases (C)
0	0	1*	1
1	5	3 (=R_o)*	4 (=1+3)
2	10	9 (=R_o^2)	13 (=1+3+9)
3	15	27 (=R_o^3)	40 (=1+3+9+27)

*Mathematically, $1 = R_o^0$, $3 = R_o^1$.

Table 2 Predicted number of SARS deaths using $R_o = 3$, $i = 5$ days, $F = 10\%$ and $d = 14$ days

Number of incubation period (t)	Day	Predicted incident cases ($C_{t\cdot i}$)	Predicted new deaths ($D_{t\cdot i+d}$)	Predicted total deaths (D)
0	0 (=t×i)	1	0	0.0
1	5	3	0	0.0
2	10	9	0	0.0
	14 (=t×i+d)	0	0.1 (=1×F)*	0.1
3	15	27	0	0.1
	19	0	0.3 (=3×F)*	0.4

*Cases from day 0 are removed on day 14, after one disease duration (14 days). The one case from day 0 is expected to produce 0.1 death (1×10%) and 0.9 recovered people. Similarly, the three cases from day 5 are expected to produce on day 19 (after 14 days) 0.3 death and 2.7 recovered people.

The predicted total number of deaths (D) is

$$D = \Sigma\ D_{t\cdot i+d}.$$

Table 2 illustrates the application of the model to calculate the predicted number of SARS deaths, using $R_o = 3$, $i = 5$ days, $F = 10\%$, and $d = 14$ days. It is predicted that on day 19 there are 0.3 new deaths and that the total number of deaths by day 19 is 0.4. The value for d can be determined from epidemiological studies of patients. The optimal value for F in a particular situation, given optimal values for R_o, i and d, can be determined by trying out several values to see which combination of F, R_o, i and d produces the predicted total number of SARS deaths that most closely matches the observed total number of SARS deaths.

METHODS

The mathematical model was used to fit the observed numbers of cases and deaths posted on the World Health Organisation web site[6] available from 17 March 2003 onwards. For Canada, additional data on observed numbers of cases and deaths from 25 February (first Canadian case) to 16 March were available from Poutanen *et al*.[10]

Early epidemiological studies suggest that the incubation period ranges from 1 to 11 days, with a median of about 5 days[5 7]; therefore $i = 5$ days was used in the model. From the two deaths in Hong Kong reported in Tsang *et al*[7] and the three deaths in Canada reported in Poutanen *et al*,[10] the time from symptoms to death ranges from 8 days to 23 days, with a median of 14 days; therefore $d = 14$ days was used in the model.

The fitting of Canadian data was based on reported number of probable cases and deaths attributable to SARS from 25 February up to 6 April 2003 only. On 26 March 2003 Canada (Ontario) declared a public health emergency and implemented infection controls such as: strict rules on masks and protective clothing in hospitals, quarantine of suspected cases at home for 10 days, restriction of visitor access to hospitals, closing down of admissions, emergency, and non-urgent services, screening of travellers at airports, and closing of schools with suspected cases.[2 3] If these infection controls were effective, according to our model, effects on R might be seen after i+d days—that is, by 14 April (after 5+14 days), or at the earliest, by 4 April (after 1+8 days). Inspection of the observed data in Canada suggests that infection controls might have taken effect around 6 April 2003.

RESULTS

The best parameters to fit Canadian SARS data as of 6 April 2003 are $R_o = 1.5$, $F = 30\%$, $i = 5$ days, $d = 14$ days. If this

Table 3 Predicted number of probable cases and deaths attributable to SARS in Canada since 25 February 2003 based on the observed trend from 25 February to 6 April 2003, and observed numbers from 25 February to 26 May

Date	Day	Predicted incident cases	Predicted total cases	Predicted new deaths	Predicted total deaths	Observed total cases	Observed total deaths
Feb 25*	0	1	1	0	0.00	1	0
Mar 2	5	1.5	2.5	0	0.00	3	0
Mar 7	10	2.25	4.75	0	0.00	5	1
Mar 11	14	0	4.75	0.30	0.30	8	1
Mar 12	15	3.38	8.13	0	0.30	8	1
Mar 16	19	0	8.13	0.45	0.75	8	2
Mar 17	20	5.06	13.19	0	0.75	8	2
Mar 21	24	0	13.19	0.68	1.43	9	2
Mar 22	25	7.59	20.78	0	1.43	9	2
Mar 26	29	0	20.78	1.01	2.44	19	3
Mar 27	30	11.39	32.17	0	2.44	28	3
Mar 31	34	0	32.17	1.52	3.96	44	4
Apr 1	35	17.09	49.26	0	3.96	53	4
Apr 5	39	0	49.26	2.28	6.23	74	7
Apr 6	40	25.63	74.89	0	6.23	74	7
Apr 10	44	0	74.89	3.42	9.65	97	10
Apr 11	45	38.44	113.33	0	9.65	98	10
Apr 15	49	0	113.33	5.13	14.78	100	13
Apr 16	50	57.67	171.00	0	14.78	103	13
Apr 20	54	0	171.00	7.69	22.47	132	12
Apr 21	55	86.50	257.49	0	22.47	132	12
Apr 25	59	0	257.49	11.53	34.00	140	15
Apr 26	60	129.75	387.24	0	34.00	142	18
Apr 30	64	0	387.24	17.30	51.30	148	20
May 1	65	194.62	581.86	0	51.30	147	20
May 5	69	0	581.86	25.95	77.25	148	22
May 6	70	291.93	873.79	0	77.25	148	22
May 10	74	0	873.79	38.92	116.17	145	22
May 11	75	437.89	1311.68	0	116.17	145	22
May 15	79	0	1311.68	58.39	174.56	142	23
May 16	80	656.84	1968.52	0	174.56	140	23
May 20	84	0	1968.52	87.58	262.14	140	23
May 21	85	985.26	2953.78	0	262.14	140	23
May 25	89	0	2953.78	131.37	393.50	140	23
May 26	90	1477.89	4431.68	0	393.50	148	26
May 30	94	0	4431.68	197.05	590.56		
May 31	95	2216.84	6648.51	0	590.56		
Jun 4	99	0	6648.51	295.58	886.14		
Jun 5	100	3325.26	9973.77	0	886.14		
Jun 9	104	0	9973.77	443.37	1329.50		
Jun 10	105	4987.89	14961.66	0	1329.50		
Jun 14	109	0	14961.66	665.05	1994.55		
Jun 15	110	7481.83	22443.48	0	1994.55		
Jun 19	114	0	22443.48	997.58	2992.13		
Jun 20	115	11222.74	33666.22	0	2992.13		
Jun 24	119	0	33666.22	1496.37	4488.50		
Jun 25	120	16834.11	50500.34	0	4488.50		

*The first SARS case in Canada, a 78 year old woman who had returned to Toronto from Hong Kong, first noted symptoms on 25 February 2003.[10] Paremeters: R_o (basic reproductive number, the number of new infectious cases per infectious case) = 1.5, F (case fatality rate) = 30%, i (incubation period, time from infection to symptom) = 5 days, and d (duration of SARS, from symptom to recovery or death) = 14 days. Predicted numbers are based on the mathematical model. Observed numbers from 25 February to 16 March are given by Poutanen *et al*[10]; observed numbers since 17 March are from the WHO web site (http://www.who.int/csr/sarscountry/en/).

early trend continues, SARS numbers in Canada are predicted to be as follows: 387 cases and 34 deaths by 26 April (day 60), 4432 cases and 394 deaths by 26 May (day 90), and 50 500 cases and 4489 deaths by June 25 (day 120) (table 3).

Plots of the predicted and observed numbers of SARS cases and deaths on linear and log scales are shown in figures 1–4.

The proposed model is easy to use. Table 3 and figures 1–4 were generated, using Excel (Microsoft Corporation), in less than an hour. The model can also be done by hand, with a calculator and graph paper; it took about four hours to generate the table and the four figures.

DISCUSSION

The method described in this paper is easy to understand and to use. It can be useful in at least two situations. Firstly, a public health officer can estimate the size of an outbreak before control measures are effectively put into practice. Secondly, it may be useful for public education to illustrate what could happen in a population where no action is taken to stop the epidemic.

Under the contagious epidemic assumption, SARS is passed from person to person and the initial rise in the number of cases and deaths is slow. However, the model indicates a possible devastating effect in just a few months' time, if proper measures to control the epidemic are not available or enforced to reduce the number of new infectious cases per infectious case (R_o) to below 1.0. Exponential growth of the SARS epidemic in the absence of interventions has also been suggested by other authors.[16–18]

The model can be used to evaluate the success of interventions by monitoring the reduction of R_o (success in controlling the spread) and the reduction of F (effectiveness of the treatment) needed to produce the best fitting model for new observed data. Furthermore, if the actual numbers of

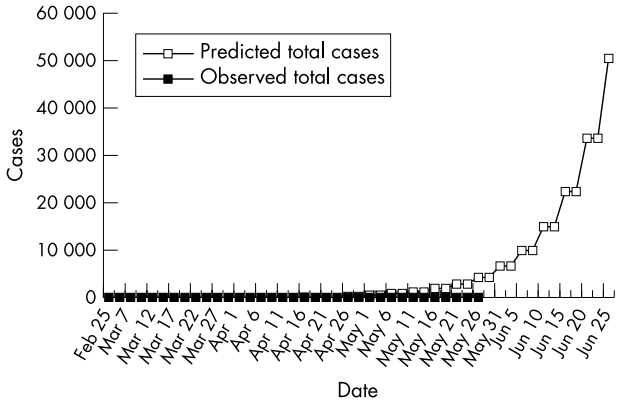

Figure 1 Predicted and observed probable cases of SARS in Canada, February to June 2003.

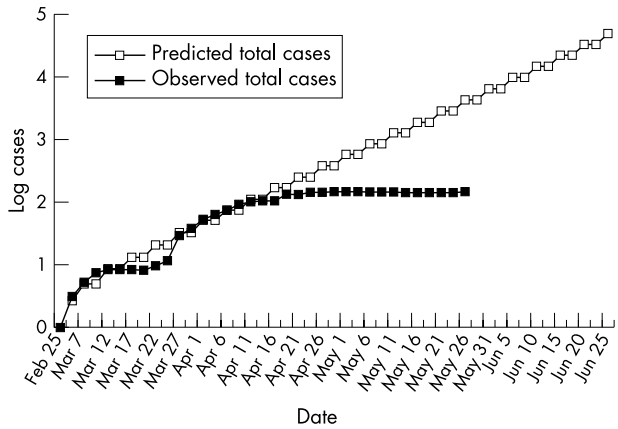

Figure 2 Predicted and observed probable cases (log scale) of SARS in Canada, February to June 2003.

cases and deaths are increasingly lower than the predicted numbers, as current Canadian data appear to show, health practitioners may be reassured that the interventions are doing well. The gradual fall off of the observed number of cases and deaths after 6 April 2003 from the expected curves based on the initial trend indicates that control measures in Canada implemented since 26 March 2003 probably have taken effect. In evaluating success, however, confounding by natural intervention must also be considered, for example, it is possible that R_o may change and diminish regardless of control measures, simply as the weather becomes warmer.[18]

The model can also be used to provide a more accurate estimate for the case fatality rate than the traditional method. Under the traditional method, which is based on a cross sectional approach, case fatality is simply the number of deaths divided by the number of cases in a specified time period. For example, the traditional method estimates that, as of 3 April 2003, the case fatality is 10% (6 of 62) for Canada and 2% (17 of 734) for Hong Kong.[19] However, at the initial stage of an epidemic, there is an accelerating increase of daily new cases. These new cases are not likely to die within the same day. Their inclusion results in an underestimation of case fatality. Using our model, which is based on a cohort approach, it is estimated that the case fatality is 30% in Canada and 20% in Hong Kong, assuming a disease duration of 14 days. The case fatality estimate varies depending on the disease duration, for example, it becomes 20% for Canada and 5% for Hong Kong if a disease duration of seven days is used. Our predictions are confirmed by a recent report based on 1425 cases in Hong Kong that SARS death rate is higher than WHO estimate; and that about 20% of the SARS cases in Hong Kong are dying (13% for cases younger than 60 years; 43% for cases 60 years and older).[18 20] After the study, the WHO has revised its SARS death rate from 6% to 15%.[21]

An interesting observation from using the model is that, for fitting the spread of SARS in Hong Kong as of 10 April 2003, the best parameters are $R_o = 2.0$, $F = 20\%$, $i = 5$ days, $d = 14$ days (data not shown). It is understandable that, because of the higher population density, R_o in Hong Kong is higher than in Canada. The lower case fatality in Hong Kong (20%), as compared with that in Canada (30%), may be attributable to a difference in attribution of deaths to SARS, as different rules may govern the coding of a death when a SARS patient dies of a non-SARS related cause.

Our model has been developed for the rapid calculation of predicted cases and deaths for the short term at this initial stage of the SARS epidemic. It is intended to help front line public health practitioners in their planning. The model is not intended to replace more sophisticated mathematical methods at a later stage when more data on the epidemic pattern of SARS are available. To keep the model simple and user friendly for the average public health officer, a number of assumptions are made that may reduce the validity, compared with more sophisticated models. As the model is simple to use, it may result in situations where assumptions are not fulfilled. As an illustration, according to current knowledge, mortality risk seems to be strongly dependent on age[18 21] but this dependency is not taken account into the

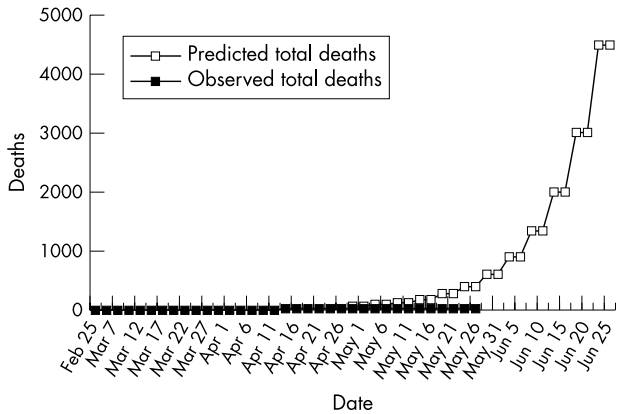

Figure 3 Predicted and observed SARS deaths in Canada, February to June 2003.

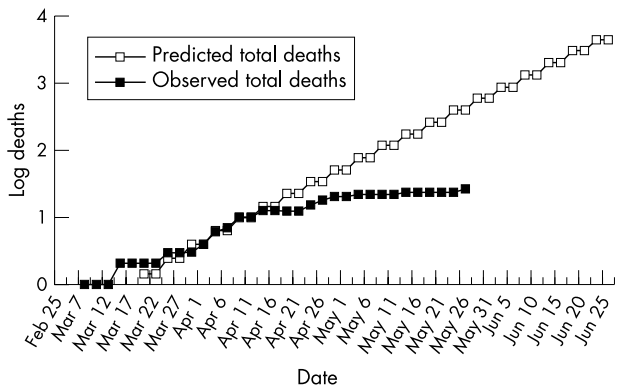

Figure 4 Predicted and observed SARS deaths (log scale) in Canada, February to June 2003.

model. Also, the basic reproductive number may not be homogenous, for example, it may be higher in certain subgroups (in particular hospitals) and lower in others.[17]

For simplicity, the model fitting is carried out by ''trying out several values'' (eyeballing) instead of some formal fitting algorithm that then requires extensive computer programming. The models are deterministic to avoid the complex stochastic models where, for example, i and d take values from a specific distribution with mean and variance. Also, 95% confidence intervals for the curves or sensitivity analyses are not suggested. The model does not address issues such as evaluating the efficacy of interventions by shortening the period between onset of symptoms and hospital admission.

When this paper was first developed based on available data up to mid-April 2003, it was our hope that our estimates for Canada will be off in a month or two. This will then show that the recent infection control measures have been effective. The predicted numbers based on the early trend only illustrate the hypothetical situation if the early trend continues, for example, when control measures are either not available or not enforced. By late May, when this paper was finalised, the estimates are already off. The departure of observed numbers from the predicted can be considered a measure of the success of infection controls, in terms of the number of potential cases and deaths prevented.

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