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Mathematical Models of Isolation and Quarantine

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THE RECENT EMERGENCE OF SEVERE ACUTE RESPIRATORY syndrome (SARS) has drawn attention to the strategies of isolation and quarantine (I&Q) as a method of disease control. The fundamental dilemma associated with the implementation of I&Q is how to predict the population-level efficacy of individual quarantine: Which and how many individuals need to be quarantined to achieve effective control at the population level? Although some forms of I&Q have proven effective in SARS,[1,2] they are not appropriate for all infectious diseases. Diseases like varicella, for which costs of quarantine may be high (many work and school days are lost when noninfected contacts are kept at home) and the return minimal (a relatively mild disease is avoided), require a different approach. Furthermore, in some cases, I&Q may be not only costly but harmful. An I&Q policy for varicella, in the long run, may actually increase the average age (and therefore the severity) of first infection. Using I&Q to control rubella in China could actually lead to higher levels of disease because under the current system (of no control), about 97% of the population has rubella antibodies obtained from direct exposure to infectious individuals.[2] Such a level of natural immunity would be impossible to accomplish under the current effective US and Canadian vaccination policies.

Mathematical modeling can help determine when I&Q are the best strategies for disease control as well as how they might affect short- and long-term disease dynamics. Mathematical modeling offers ways of integrating population-level knowledge based on previous epidemics with available individual and population data to predict the outcomes of several alternative scenarios. This kind of mathematical epidemiology is particularly well suited to problems for which formal experimentation is impossible for logistical or ethical reasons. In these situations, mathematical models can play a role in planning and experimental design in epidemiology, ecology, and immunology.

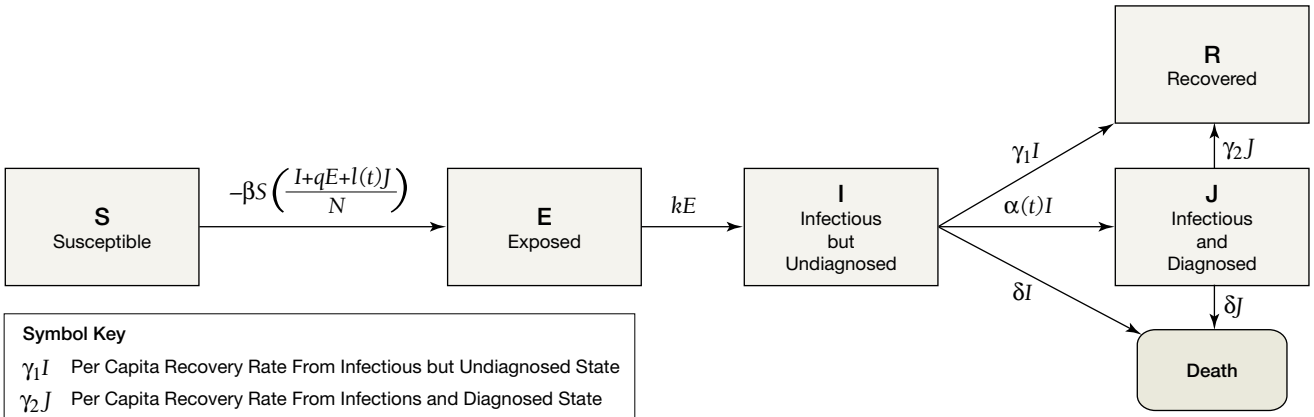
Mathematical disease modeling is an attempt to fit empirical data to abstract processes. Decisions must always be made about which variables to exclude from the model. Although inclusion of more variables (for example, the baseline health status of every individual) would make the model more accurate, such models would be impossibly complex. The balance between predictive power and its level of detail depends on the questions the model is intended to answer. Variables that can influence the outcome of I&Q policies include the number of contacts an infected person has per unit of time, the probability of infection per contact, and the proportion of the population that is vaccinated, quarantined, isolated, or educated to avoid infection. In general, it is difficult to judge the effects and interactions of these variables at the population level. A simple model is usually mathematically "tractable" (ie, easy to manipulate and to calculate outcomes for), thus allowing the entire range of possible outcomes to be studied. Addition of detail and complexity can make models more accurate, but this also complicates their mathematics. Current computer technology, however, allows studies of extremely detailed models.

We developed a model to predict whether I&Q could stop the spread of SARS in greater Toronto, Ontario.[1,2] We limited the time frame of the model to the duration of a single SARS outbreak. The simplicity of the question and the simplicity of our assumptions reduced the amount of data required to test the SARS model. Our "simple" SARS model has about 11 parameters. Obviously, completely accurate and specific predictions from such a model were impossible, but the model was able to illustrate the power of I&Q as control measures. The model predicted that these policies would help and showed how dramatically they could reduce the size of a SARS outbreak (by a factor of 1000). These results agreed with actual observations.[1,2] Models can provide rapid estimates of the impact of control strategies even before data from other areas are available (before epidemic spread occurs) and when experimental data may be incomplete or inaccurate.

Mathematical models are frequently represented by a box diagram showing the categories of persons the model addresses (boxes), the movement between categories as the disease progresses (arrows), and the mathematical rates at which this movement occurs (formulas on arrows). An example for the SARS model is provided below. There are 5 categories of persons: susceptible (S), capable of catching the disease; exposed (E), infected with the disease but in a latent state; infectious (I), capable of infecting others but undiagnosed; infectious and diagnosed (J); and recovered (R).

In this model, γ_i represents the (per capita) recovery rate (ie, the movement from one of the infected categories, I or J, to recovered, R); δ is the (per capita) SARS-induced death rate (ie, the movement from I or J out of the system); $\alpha(t)$ is the time-dependent (per capita) diagnosis rate (ie, the movement from I to J), and $l(t)$, β, and q are coefficients representing estimates of how much contact exists between persons and how infectious they are. These coefficients therefore determine how quickly movement from S to E occurs. $l(t)$ is the time-dependent reduction in infectiousness from isolation, β is the transmission coefficient

Figure. Box Diagram Illustrating a Mathematical Model of Outcomes of a SARS Epidemic



Symbol Key

$\gamma_1 I$	Per Capita Recovery Rate From Infectious but Undiagnosed State
$\gamma_2 J$	Per Capita Recovery Rate From Infections and Diagnosed State
δ	Per Capita SARS-Induced Death Rate
$\alpha(t)$	Time-Dependent Per Capita Diagnosis Rate
$l(t)$	Time-Dependent Reduction in Infectiousness From Isolation
β	Transmission Coefficient
q	Relative Infectiousness of Individuals With a Latent Infection
N	Total Population, Sum of S + E + I + J + R

(the expected number of contacts per unit of time per person that result in an infection), and q measures the relative infectiousness of individuals who are in a latent state.

A fundamental concept of mathematical epidemiology is that a "threshold" can be identified. The basic reproductive number, R_0, a dimensionless quantity, introduced in the early 20th century by Ross,[3] and Kermack and McKendrick,[4,5] estimates the average number of secondary infections generated by a typical infectious individual with a given infection. The theory is based on the understanding that a basic reproductive number greater than 1 generates an increasing number of infected persons and results in an epidemic outbreak, while no epidemic will emerge if R_0 is less than 1. Important factors in controlling a disease's spread can be identified by examining their effect on R_0. One of the most important contributions in mathematical epidemiology has been to show that the most important factor in any I&Q or treatment campaign is the speed of response. Irrespective of other measures, the longer a case goes undiagnosed, the more likely it will be that the infected individual will be able to spread the disease before he or she is treated; hence, the more likely that R_0 will be greater than 1. Mathematical epidemiology provides a way of studying and characterizing these influences in a systematic way. But devising strategies to decrease R_0 is not the only issue. Finding realistic diagnostic or isolation strategies quickly can be difficult and costly. Theoretical and mathematical epidemiologists have frequently assumed a perfect world (a world in which there are no complicating variables or random variability in behavior), where response times are not particularly relevant, where perfect isolation is possible, and where individuals are all well informed and compliant with government policy. These scenarios are simpler to model. However, it is impossible to maintain perfect I&Q strategies in the real world. The often irrational but predictable social aspects associated with disease transmission and control have a significant impact. Epidemiologists are beginning to incorporate more of these elements into their models, thanks to the increased availability of powerful and inexpensive computers. The impact of the SARS model in Toronto provides an example of this.[1,2] The addition of more realistic elements, however, often requires that researchers make unrealistic assumptions, particularly about the nature of human interactions (social dynamics). Hence, every theoretical and numerical result needs to be observed cautiously until the underlying model assumptions are verified.

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