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# MODELING AND PUBLIC HEALTH EMERGENCY RESPONSES: LESSONS FROM SARS

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**ABSTRACT**

Modelers published thoughtful articles after the 2003 SARS crisis but had limited if any real-time impact on the worldwide response and should even have inadvertently contributed to a lingering misunderstanding of how the epidemic was controlled. The impact of any intervention depends on its efficiency likewise as efficacy, and efficient isolation of infected individuals before they become symptomatic is difficult to imagine. Nonetheless, in exploring the possible impact of quarantine, the merchandise of efficiency and efficacy was varied over the whole unit interval. Another mistake was repeatedly fitting otherwise appropriate gamma distributions to times to event irrespective of whether or not they were stationary or not, particularly onset-isolation intervals whose progressive reduction evidently contributed to SARS control. Under their unknown biology, newly emerging diseases are more difficult than familiar human scourges. Influenza, as an example, recurs annually and has been modeled more thoroughly than the other communicable disease. Moreover, models were integrated into preparedness exercises, during which working relationships were established that bore fruit during the 2009 A/H1N1 pandemic. to supply the foremost accurate and timely advice possible, especially about the possible impact of measures designed to regulate diseases caused by novel human pathogens, we must appreciate the worth and difficulty of policy-oriented modeling. Effective communication of insights gleaned from modeling SARS will help to make sure that policymakers involve modelers in future outbreaks of newly-emerging infectious diseases. Accordingly, we illustrate the increasingly timely care-seeking by which, along with increasingly accurate diagnoses and effective isolation, SARS was controlled via heuristic arguments and descriptive analyses of familiar observations

**KEYWORDS:** Decision support modeling; theoretical modeling; emerging; infectious; disease emergency ;preparedness

In the summer of 2008, at a field station high within the Canadian Rockies, a couple of public health physicians met with a bigger number of communicable disease modelers to debate the intersection of modeling and public health policymaking. This workshop arose from the observation that, while the communicable disease modeling community is relatively small, it's contributing increasingly to the event of policy to handle foreseeable public health problems. Until recently, however, our role in shaping actual responses to communicable disease outbreaks had been more limited.

Modelers published thoughtful articles after the 2003 severe acute respiratory syndrome (SARS) crisis (e.g., Anderson et al. 2004), but had limited if any, real-time impact on the worldwide response. The explanation arguably is that we didn't provide what health policymakers needed, reliable projections of the impact of different actions. By overestimating the potential of managing contacts versus cases, moreover, we may even have inadvertently contributed to a lingering misunderstanding of means by which this epidemic was controlled which will affect their future responses to newly-emerging infectious diseases.

Among its many uses, modeling can improve our understanding of actual pasts, moreover as make predictions about hypothetical futures. During this spirit, we share reflections on our collective contribution to policymaking during the 2003 SARS epidemic that grew out of discussions at this retreat. While all participants shared a typical goal – increasing the utility of modeling to public health decision-makers – this essay isn't their consensus about the most effective means of accomplishing that goal. Neither is it a radical review of the SARS modeling literature. Most people also supported policymaking during the newer influenza pandemic, but SARS was tougher than our earlier experience more fully exemplifies the worth and difficulty of policy-oriented modeling.

When SARS emerged, US health policy decision-makers had hardly begun involving modelers in their deliberations, convening working groups on smallpox and anthrax modeling in 2002 and 2003, respectively. And SARS was a replacement human disease. While the causal agency was identified quickly, experience with diseases caused by other corona viruses was much less informative than the previous H1N1 and intervening pandemics and annual influenza were during 2009. Under their experience with influenza, moreover, modelers were invited to contribute to preparedness exercises during which relationships were forged that bore fruit during the particular pandemic.

The confidence in modeling that our assistance in preparing for and responding to the present foreseeable crisis engendered may reach routine public health policymaking. During unforeseen crises, however, the utility of modeling depends not only on more accurate and timely insights than we provided during the worldwide response to SARS but simpler communication. As observations are most familiar to policymakers, here we endeavor to support heuristic arguments about the contribution of varied public health measures to SARS outbreak control by descriptive analyses of salient observations.

## LESSONS FROM SARS

Public health officials may have multiple mitigation options to contemplate within the face of emerging threats. During the 2009 influenza pandemic, as an example, there have been various pharmaceutical (vaccine, antiviral medications) and non pharmaceutical (closing schools, staying home, or wearing masks) options. Because the efficacy of existing pharmaceuticals against newly-emerging infectious diseases generally is unknown, authorities cannot depend upon them. They can, however, promulgate guidelines for managing patients or their contacts, and modelers should be able to inform their decisions.

## CONTACT MANAGEMENT

Early SARS models demonstrated the theoretical impact of isolation before symptom onset on disease transmission (e.g., Lip sitch et al. 2003; Fig. 6), and thus the potential good thing about interventions like contact tracing and quarantine. Because the impact of any intervention depends not only on its efficacy but on the proportion of targets reached, knowledgeable public health practitioners might need cautioned against overestimating the benefit of identifying asymptomatic people in whom pathogens were replicating. Where published observations permit assessment, only about 5% of infected contacts of SARS patients (i.e., susceptible people associating with infectious ones intimately enough for infection) were after all isolated before symptom onset. In Singapore, as an example, only 11 of the 238 people ultimately diagnosed as probable cases (Tan 2005) and in Taiwan, only 24 of 480 (Hsieh et al. 2005) had been quarantined. Other contacts were identified in Singapore, but evidently, their perceived risk failed to warrant movement restriction.

Could infected contacts are identified more efficiently? In Beijing, 30,178 close contacts of two, 521 probable cases were quarantined over the course of the epidemic (Pang et al. 2003). Analysis of a subset of these individuals with good records (covering 2,195 contacts of 582 patients from 5 districts) revealed a variety within the probability of diagnosed illness among quarantined individuals from 0% to

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fifteen.4%, reckoning on their relationship to the patient. The transmission was relatively high among spouses, other relatives, friends, and other household members, and low among co-workers, schoolmates, and healthcare workers. Separately, Ou et al. (2003) studied geographically representative precincts throughout the Haidian District, where 1,210 contacts of 171 patients were quarantined. The probability of infection among a subset of 383 quarantined people ranged from 0% to 31.1%, also looking on the character of their contact with patients. in keeping with the findings of Pang et al. (2003), caring for ill household members imposed the best risk, followed by visiting and residing within the same household. In sharp contrast to the case in metropolis, where a faulty sewer system at the Amoy Gardens apartment complex may have facilitated fecal-oral transmission (Hong Kong DOH, 2003), no risk was related to sharing an apartment house or workplace. In Singapore, 73.5% of cases were infected in healthcare institutions (overall, 49.3% were healthcare workers, 37.4% friends or visitors, and 13% other patients), 17.2% at home, and 3.4% within the community or workplace (Goh et al. 2006).

When infectious people infect but one susceptible person on the average, epidemics wane. Interventions to scale back the common number of secondary infections (typically denoted $\Re$) most expeditiously are preferable, provided all else (including, e.g., compliance and cost) is equal. The impact of such interventions depends crucially on pathogen life cycles and host contact patterns. Thus, in some environments, with some infectious agents, certain interventions may reduce disease transmission, whereas in other environments, or with other agents, the identical interventions might not, despite being applied with equal diligence. As are going to be apparent, the explanation of SARS readily explains why encouraging people with compatible prodromal symptoms to hunt care (and ensuring that clinicians and hospital infection control personnel had the time to diagnose and isolate them effectively) was only marginally less effective than quarantine. Because infected people are more easily identified when symptomatic, the greater efficiency of this intervention over compensated for any deficit in its efficacy.

One can assess the potential impact of any intervention on a transmissible disease by calculating its effect on the reproduction number. The naming of this quantity reflects its demographic origin (Heesterbeek 2002), but communicable disease modelers focus instead on the typical number of effective contacts while infectious, where effective means sufficiently intimate for infection of susceptible individuals; the consensus for SARS is roughly 3 (World Health Organization, 2003). Because $\Re = \Re0(1 - p)$, where $\Re0$ is that the basic reproduction number and p is that the product of any intervention’s efficiency and efficacy, we solve for the $\Re0$ at which $\Re = 1$, below which threshold outbreaks subside. With the aforementioned 5% efficiency observed in Singapore and Taiwan, and assuming 100% efficacy (i.e., quarantined people infected no one), evidently, quarantine couldn’t control any disease whose $\Re0 > 1.05$. Thus, while implementing this measure may have communicated authorities’ concern about matters – possibly increasing compliance with recommended hand washing, mask-wearing, and social distancing practices – evidently quarantine intrinsically contributed little to SARS control.

Because contact management is socially disruptive, potential costs and benefits must be weighed realistically. Identifying only 11 probable cases among 7,863 contacts restricted to their homes in Singapore and 47 among 4,331 telephoned daily (Tan 2005) imposed significant (if un quantified) costs, apparently for minimal gains. we’ve got dates of symptom onset and isolation for clinically diagnosed cases in Singapore but don’t know which had been quarantined or telephoned daily, so cannot determine if identified contacts were isolated to any extent further quickly than others, as Tan’s (2006) juxtaposition of weekly proportions of probable cases who had been identified as contacts and mean onset-isolation intervals suggests. Similarly, in Taiwan, only 24 probable cases were identified by quarantining 55,632 contacts and none by quarantining 95,828 travelers from SARS-affected areas (Hsieh et al. 2005). We don’t know the way many probable cases were quarantined in Beijing, but the ratio of contacts to patients reported by Pang et al. (2003) was 12; in Taiwan, this factor was 116 (316 including travelers), and in Singapore, it had been 33 (51 including those telephoned).

Tailoring activities to specific risk groups – those defined by Ou, Pang, and their co-workers, for instance – could mitigate the social cost. In Beijing, quarantine was most appropriate for those who cared for ill household members. Being instructed to quickly seek medical aid should any symptom which may herald SARS develop, however, was appropriate even for contacts with lower risk exposures. In Singapore, paradoxically, those telephoned actually were at much greater risk (47/4,331) than those quarantined (11/7,863). Case management can also be problematic. In Taiwan, as an example, the incidence of laboratory-confirmed influenza was elevated among young adults hospitalized during 2003, with the surplus presumably suspected of getting SARS. The proportion of suspect cases not reclassified as probable – an overestimate absent consistent laboratory analyses – was nonetheless modest, relative to misclassification of uninfected people as contacts (in Singapore, e.g., 1–58/12,194 > 99.5% were misclassified), and most patients enjoy medical aid.

## CASE MANAGEMENT

If not by contact management, how was SARS controlled? Available evidence suggests that the reduction in time from symptom onset to clinical presentation and diagnosis during the course of this outbreak, along with increasingly effective isolation and other infection-control procedures, contributed most to containment.

This hypothesis can also be explored mathematically. Because $\Re0$ is that the sum (while infectious) of products of contact rates and probabilities of transmission on contact, either or both of which can vary with time since infection or symptom onset, in essence estimating the impact of isolating infected people at any time is easy. If we make the simplifying assumptions that probabilities of transmission on contact reflect infectiousness, which is proportional to viral load (successive logarithms of which may, in turn, be represented via a nonstop statistical distribution), which contact rates don’t change substantially during illnesses, we are able to determine from the suitable cumulative distribution function when isolation would have prevented ℜ0 − 1 infection.

Such an estimate may be derived from analyses of samples collected during the SARS epidemic. Within the most exhaustive of several quantitative RT-PCR studies thus far, He et al. (2007) analyzed 614 serological samples, 96 throat washes, and 224 fecal samples from SARS patients to see viral loads at successive times after symptom onset. because the cause was transmitted primarily via respiratory secretions (except possibly among residents of the Amoy Gardens apartment complex), it seems prudent to base our estimate on results from the throat washes. Given the assumptions outlined above, along with a gamma distribution, these results suggest that for a disease with ℜ0 = 3, the isolation that was 100% effective in blocking transmission could prevent ℜ0 − 1 infection (and thus cause epidemic control) if implemented up to five.2 days after symptom onset, on the average (Fig. 1). The operational requirements may be calculated for any efficacy. as an example, an isolation that was only 80% effective should suffice to effect disease containment if implemented up to 4.4 days after symptom onset under the given assumptions, and so on. Analyses of the sooner studies of Peiris et al., 2003, Cheng et al., 2004 yield similar results. That said, we must emphasize that these simple calculations are intended to be heuristic. If contact rates declined sharply after symptom onset, as an example, the time available for isolation would be overestimated. Day et al., 2006, Fraser et al., 2004, Lloyd-Smith et al., 2003 have developed frameworks for evaluating such questions more rigorously in future outbreaks of newly-emerging infectious diseases.

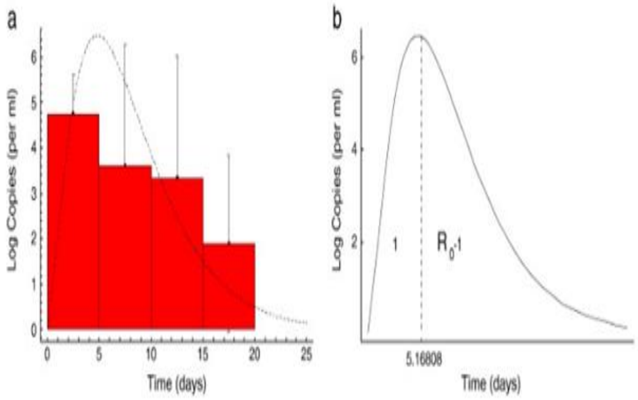

Fig. 1. a) Estimated viral load (log copies per ml) from quantitative RT-PCR on throat washings from SARS patients (means and 95% CI within 5-day intervals post-symptom onset), fitted gamma distribution (α = 2.49, β = 3.23), and b) time post-symptom onset by which isolation that was 100% effective would prevent ℜ0 − 1 infection.

Fig. 2, Fig. 3 illustrate daily mean intervals between symptom onset and diagnosis and proportions diagnosed within 4 days of symptom onset (i.e., during the largely noninfectious prodrome), respectively, by onset date in Singapore and Taiwan. The remarkable similarity of those observations in societies valuing different aspects of attribute suggests a standard behavioral mechanism for the control progressively attained globally (Wallinga and Teunis 2004): As patients weren’t very infectious until acutely ill, evidently SARS was controlled by their earlier and doubtless progressively more practical isolation after symptom onset (Feng et al. 2009, Table 2), phenomena that authorities facilitated mainly (recall that only 58 of 238 probable cases in Singapore and 24/480 in Taiwan were traced) via effective health communications (Menon 2006) with healthcare providers additionally because the general population (Chen et al. 2006). Others have noted that these times to event weren’t stationary (e.g., Anderson et al. 2004), which precludes fitting the otherwise appropriate gamma distribution (Donnelly et al., 2003, Riley et al., 2003), even by epoch (Leung et al. 2005).

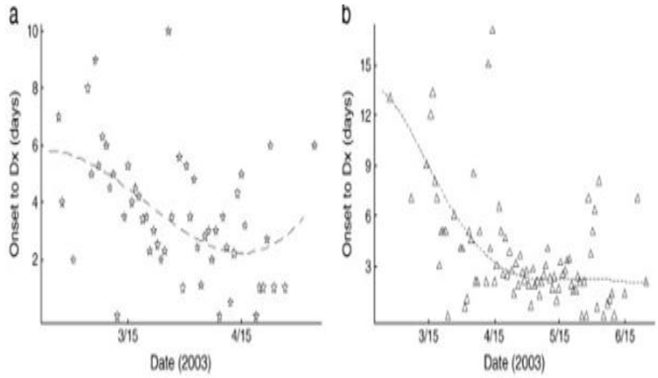

Fig. 2. a) Intervals from symptom onset to diagnosis and polynomial regressions, which account for temporal variation in daily numbers of persons in danger, by onset date in Singapore (stars) and b) Taiwan (triangles). While fifteen stars and twenty-six triangles represent single individuals, the mean quickly became but that at which ℜ = 1.

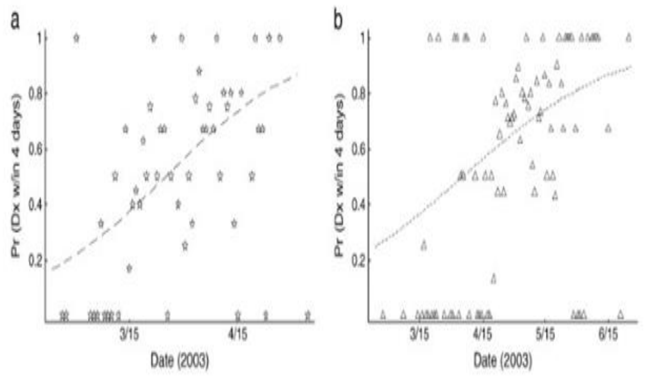

Fig. 3. a) Proportions diagnosed during the prodrome (within 4 days of symptom onset) and logistic regressions, which account for temporal variation in daily numbers of persons in danger, by onset date in Singapore and b) Taiwan. Proportions diagnosed during their prodrome increased from about 0.2 to 0.8 during both outbreaks.

It is safe to assume that shortening intervals between the onset of clinical symptoms and isolation of patients with communicable diseases will reduce their effective infectious periods and thus the extent of onward transmission. Could modelers have demonstrated that timely isolation – not quarantine – was the key to controlling SARS early enough to possess influenced the general public health response to the current crisis (especially in light of the Amoy Gardens event, which can have biased responsible officials towards more aggressive interventions)? Feng et al. (2009) demonstrate that the ratios of infection rates during the prodrome and acute phases fitted to the primary 30 days and every one hospital admissions are similar, answering this question affirmatively. But could we’ve convinced health authorities to allocate more resources to encourage people – especially people who may need been exposed to someone subsequently diagnosed – to hunt treatment upon experiencing symptoms which may herald SARS, and to assist clinicians in diagnosing, and infection control personnel in isolating patients? Also, looking ahead, as participants within the Canadian workshop endeavored to try and do, what lessons from SARS might increase the utility of modeling the subsequent time that a brand new communicable disease emerges?

## APPLYING THE TEACHINGS

Evaluating models is difficult, especially within the throes of public health emergencies, but the disparate predicted and realized impacts of quarantine during the SARS epidemic reinforce the importance of such evaluations and also the care with which they have to be performed. Even the most effective modeling is restricted by inaccurate or incomplete information. and through health crises, humanitarian needs trump record-keeping. Nonetheless, to make sure that interventions are modeled realistically, epidemiologists must scrutinize all available information lest observations that appear invaluable in hindsight be underappreciated or maybe overlooked. as an example, Lipsitch et al. (2003; Fig. 1d) observed that the mean number of secondary infections per case in Singapore climbed dramatically when time from onset to isolation exceeded four days. To our knowledge, however, the implication of this observation vis-à-vis the potential impact of a case versus contact management has not heretofore been articulated. Nonetheless, the inference that infected people weren’t particularly infectious until acutely ill was subsequently substantiated by the isolation of the SARS coronavirus and assessment of viral loads and shedding as functions of your time from symptom onset. Shortening the amount between such observations and deductions will make sure that timely public health decisions are supported credible science within the future.

## INFLUENCING PUBLIC POLICY

Once models are evaluated and any deficiencies remedied, pertinent analytical or simulation results must be translated into actionable information for policymakers. Mathematicians could also be convinced by the relative magnitude of partial derivatives of control reproduction numbers concerning alternative parameters, but to possess any impact whatsoever on higher cognitive process, such results must be expressed within the language of public health practice and concerning readily available (or quickly improvise) interventions. Until recently, few modelers had been intimately involved in emergency response or policy development, so facilitators with practical experience in these areas, who understood the potential of modeling in elucidating the relevant issues, were indispensable. Recent experiences may have narrowed the gap between the health and mathematical sciences, but field observations or results of natural experiments still carry more weight among most public health practitioners.

Modeling may guide or support observational studies. While the impact of closing schools and canceling large public gatherings during future influenza pandemics was predicted by modeling (Ferguson et al., 2006, Germann et al., 2006), it’s going to are more persuasively communicated by analyses of actions taken by state and native policymakers in cities throughout the u. s. during the 1918 pandemic (Hatchett et al. 2007). By their own account, the epidemiologists who performed the latter study wouldn’t have known what patterns to hunt in historical records without the guidance provided by modeling. But do the apparently beneficial effects of school closures reliably translate into similar contemporary effects, given secular changes in family and workforce structure? whether or not contacts among schoolchildren may well be reduced, any possible benefit may well be offset by increased contacts between children and adults, some elderly (e.g., grandparents caring for youngsters so parents could continue working). And elderly people are more likely to die of complications.

Similarly, at a time when elected officials were deeply concerned about the threatened reintroduction of smallpox by terrorists and a few modelers were asserting the resumption of universal vaccination (e.g., Kaplan et al. 2002), most public health officials were persuaded that contact tracing, vaccination, and surveillance of contacts would suffice (as they'd during the age of eradication) by observations indicating little pre-symptomatic transmission (Eichner and Dietz 2003) and substantial residual immunity among previously vaccinated members of the population (Eichner 2003). In fact, biological inaccuracies in early models (compared by Ferguson et al. 2003) caused some policymakers with firsthand knowledge of smallpox to eschew modeling. From a policy perspective, therefore, modeling can serve many functions. Besides making qualitative predictions, models can even function tools or instruments with which to explore the character of problems iteratively. Feng et al. (2009), as an example, have embedded analytical results from a generic model of a respiratory disorder transmitted by close contact, but about which little else is thought, in software that allows end users to explore a range of possible responses. With such a modeling environment, one can evaluate control efforts for SARS, deduce the more general results of Day et al., 2006, Fraser et al., 2004, and possibly even guide official responses during future emergences of recent human diseases. Models mustn't function the only real basis for policy decisions, but they're a minimum of capable of illustrating the results of alternatives, including inaction, during a manner readily appreciable by policymakers.

While it certainly is less complicated to publish modeling studies in periodicals catering to mathematicians, the people whose decisions modelers hope to tell are more likely to read medical or general science journals. A dominant theme within the modeling literature about vaccine-preventable diseases, for instance, is that everybody needn't be vaccinated to regulate transmission. Indeed, to shield those that cannot receive live vaccines or who respond poorly, if in any respect (e.g., elderly people), it's essential to vaccinate people who might otherwise infect them. Thus, while endeavoring to "stockpile enough [smallpox] vaccine for each man, woman, and child" (Thompson 2002) may have reassured an electorate whose homeland had recently been violated, it also may have generated an expectation which will haunt us within the future (when, e.g., production problems result in shortages of influenza vaccine). Clearly, during this era of evidence-based medicine, a bridge between the 2 worlds must be forged to induce all relevant information (even if model-based) to those charged with applying it through the expenditure of taxpayer dollars.

## SUMMARY

Public health officials must decide a way to deploy available resources most advantageously. Modelers can contribute to their decision planning by exploring the impact of other scenarios. Lest results are misleading, however, models must be faithful to available information, including expert opinion. Knowledgeable public health practitioners may need cautioned against overestimating the potential impact of managing contacts of SARS patients and interpreted observations suggesting that infected people weren't particularly infectious until acutely ill as a sign for managing cases instead. on reflection, we'd encourage policymakers to interpret the progressive shortening of intervals between symptom onset and isolation characterizing most if not all SARS outbreaks as tangible evidence of the potential of effective health communications, which may be invaluable in future crises. Absent such observations, conveying complex and infrequently nonintuitive results supporting policy decisions to public health and medical professionals is challenging. Lay audiences are even tougher. Underage variation in vaccine efficacy, as an example, modelers know that individuals in danger of influenza complications could also be better protected by vaccinating those that might otherwise infect them than by being vaccinated themselves (Bansal et al. 2006). But do health policymakers? Nonetheless, where infectious diseases are concerned, citizens likely will act in ways they perceive as congruent with their own survival or self-interest, which of their loved ones. Effective risk communication, including balanced presentations of modeled outcomes, ensures that the self-interested actions of people align with socially desirable outcomes.

## DISCLAIMERS

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