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journal homepage: [www.elsevier.com/locate/jtbi](http://www.elsevier.com/locate/jtbi)Timely identification of optimal control strategies for emerging infectious diseases<sup>☆</sup>Zhilan Feng<sup>a</sup>, Yiding Yang<sup>a</sup>, Dashun Xu<sup>a,1</sup>, Pei Zhang<sup>a,2</sup>, Mary Mason McCauley<sup>b</sup>, John W. Glasser<sup>b,\*</sup><sup>a</sup> Department of Mathematics, Purdue University, 150 North University Street, West Lafayette, IN 47907, USA<sup>b</sup> National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, NE Atlanta, GA 30333, USA

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## ABSTRACT

**Background:** Health authorities must rely on quarantine, isolation, and other non-pharmaceutical interventions to contain outbreaks of newly emerging human diseases.

**Methods:** We modeled a generic disease caused by a pathogen apparently transmitted by close interpersonal contact, but about which little else is known. In our model, people may be infectious while incubating or during their prodrome or acute illness. We derived an expression for  $\mathfrak{R}$ , the reproduction number, took its partial derivatives with respect to control parameters, and encoded these analytical results in a user-friendly Mathematica™ notebook. With biological parameters for SARS estimated from the initial case series in Hong Kong and infection rates from hospitalizations in Singapore, we determined  $\mathfrak{R}$ 's sensitivity to control parameters.

**Results:** Stage-specific infection rate estimates from cases hospitalized before quarantine began exceed those from the entire outbreak, but are qualitatively similar: infectiousness was negligible until symptom onset, and increased 10-fold from prodrome to acute illness. Given such information, authorities might instead have emphasized a strategy whose efficiency more than compensates for any possible reduction in efficacy.

**Conclusions:** In future outbreaks of new human diseases transmitted via close interpersonal contact, it should be possible to identify the optimal intervention early enough to facilitate effective decision-making.

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## 1. Introduction

Early in 2003, a physician infected while treating patients with atypical pneumonia in Guangdong Province, China, infected other travelers in their Hong Kong hotel. On returning home to Singapore, Taiwan, Toronto, and Vietnam, they transmitted the pathogen causing the disease, later named severe acute respiratory syndrome (SARS), to local residents. Global spread of this hitherto unknown pathogen led WHO to issue travel advisories and some national health authorities to quarantine travelers from affected areas. As subsequent infections were largely nosocomial, hospital infection-control procedures were increasingly enforced. Absent knowledge of the onset of infectiousness, local authorities also quarantined community contacts.

Faced with an infectious disease of unknown etiology, policy-makers acted quickly (Gerberding, 2003). Case-series were among the earliest sources of information (e.g., presenting symptoms, duration of distinguishable clinical stages, and outcomes). Upon isolation of the etiologic agent, experience with illnesses caused by related pathogens became germane. While these actions were thoughtful, in retrospect some were unnecessary. We have since developed a model with which policymakers could use similar information—which should be available in future outbreaks, especially of new diseases causing serious morbidity—to assess the likely impact of available interventions.

Because identifying infected people before they become ill is difficult, quarantine is inefficient; e.g., only 11 of 238 probable cases were identified before symptom onset in Singapore (Tan, 2005) and 24 of 480 in Taiwan (Hsieh et al., 2005). Isolating people with symptoms that may herald disease, especially if they might have been exposed to someone since diagnosed, would be more efficient. Impact is proportional to the product of efficiency and efficacy, which must exceed  $1 - 1/\mathfrak{R}_0$  for control, where  $\mathfrak{R}_0$  is the average number of sufficiently intimate contacts for transmission while infectious. Consequently, infected people must be highly infectious or infectious long before becoming ill for quarantine to be a better strategy than simply encouraging those

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