Training in Infectious Diseases Modeling

A reflection on factors that may render an infectious disease outbreak controllable

Prepared for the 2nd Episouth Workshop by Nathalie Elomeiri; Camelia Savulescu & Fernando Simón

Participant's Guide

Isolation *properly refers only to the confinement of symptomatic patients in the hospital (or at home) so that they will not infect others.* ***Quarantine*** *has traditionally been defined as the separation from circulation in the community of asymptomatic people who may have been exposed to infection and might—or might not—become ill.* ***Home quarantine*** *refers to voluntary confinement of known contacts of infectious disease cases in their own homes.* ***Large-scale quarantine*** *typically refers to confinement of large groups of possibly infected people—for example, all passengers on an airplane, or the residents of an apartment building or an entire city—for periods of days to weeks. In recent years the term social distancing has come into use.* ***Social distancing*** *has been used to refer to a range of measures that might serve to reduce contact between people. These may include closing schools or prohibiting large gatherings, such as church services and sporting events. Others have used the term to refer to actions taken to increase the distance of individuals from each other at the work site or in other locations—for example, substituting phone calls for face-to-face meetings or avoiding hand-shaking. The term has come to describe fundamentally different approaches to disease mitigation.*

Introduction

Two basic public health policy options exist for controlling the spread of an infectious disease in the absence of effective vaccines or treatment: (1) effective isolation of symptomatic individuals and (2) tracing of the contacts of symptomatic cases and quarantining. Different combinations and variations of these control measures have been proposed.

Although isolation is probably always an acceptable public health measure, quarantine is more controversial. Mass quarantine can inflict significant social, psychological, and economic costs without resulting in the detection of many infected individuals.

By the end of this session, you will be able to:

1. Define variables necessary for studying the dynamics of a disease.
2. Examine the effect of different control measures on the reduction of the reproductive rate of a disease.
3. Use defined disease parameters in preparedness for an emerging disease outbreak

Part I

Q1. What basic information would help for deciding on effective infectious disease control measures (consider isolation, contact tracing and quarantine and their variations)? What would you like to know about the disease or the intervention capacity?

Q2. How would you translate this information into useful variables for understanding disease dynamics and control opportunities?

Part II

Reminder-definitions:

*- The basic reproduction number **R0**, defined as the number of secondary infections generated by a primary infection in a susceptible population and which thus measures the intrinsic transmissibility of an infectious agent; it can be calculated as the area under the infectiousness curve. For an epidemic to expand in the early stages of spread, more than one secondary case has to be generated by the primary case, and hence we need an R0 > 1.*

*- The disease generation time **Tg**, which is the mean time interval between infection of one person and infection of the people that individual infects(minimun and maximun Tg can also be estimated); together with R0, Tg sets the time scale of epidemic growth and thereby the speed with which intervention measures need to be put in place to avoid a large outbreak. Specifically, the doubling time for the number of cases in a growing outbreak is of order ln (2) Tg/(R0 /1).*

*- **The proportion of transmission** occurring prior to symptoms (or **asymptomatically**), θ, which determines the potential for symptom-based public health control measures to reduce the number of infections.*
(Factors that make an infectious disease outbreak controllable-Christophe Fraser, Steven Riley, Roy M. Anderson, and Neil M. Ferguson).

"The proportion of transmission that occurs before the onset of symptoms or via asymptomatic transmission, which we call θ, is a useful new statistic for summarizing the likely feasibility of isolation- or contact-tracing-based intervention measures in controlling an epidemic outbreak. For control through isolation alone, we need $\theta<1/R0$. For diseases in which $\theta>1/R0$, contact tracing needs to be added to the set of control measures used.".
(Factors that make an infectious disease outbreak controllable-Christophe Fraser, Steven Riley, Roy M. Anderson, and Neil M. Ferguson).

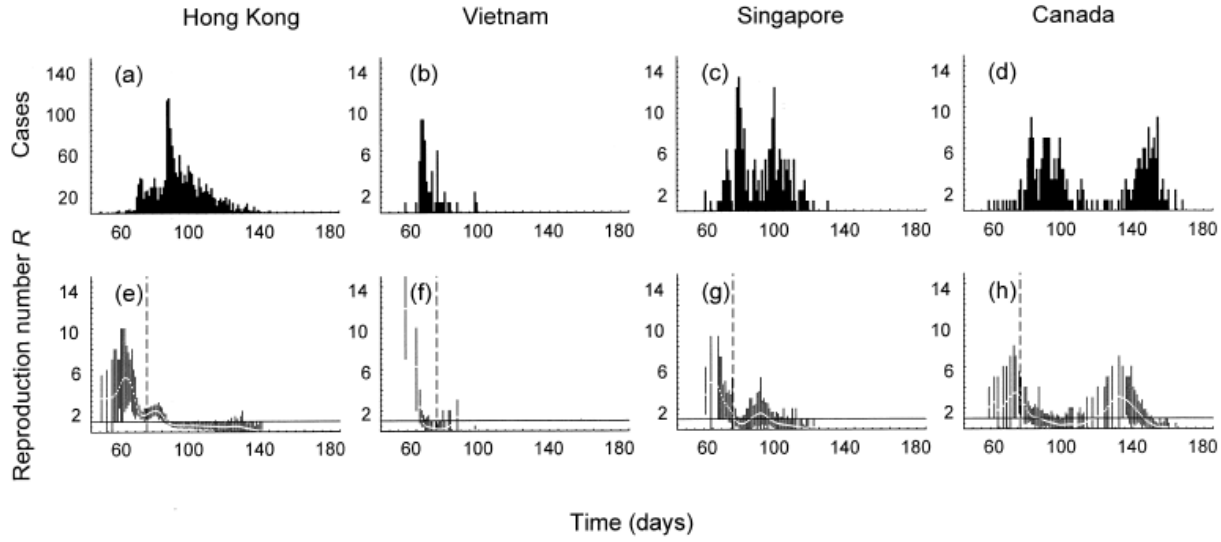


FIGURE 1. Epidemic curves (numbers of cases by date of symptom onset) for severe acute respiratory syndrome (SARS) outbreaks in *a*) Hong Kong, *b*) Vietnam, *c*) Singapore, and *d*) Canada and the corresponding effective reproduction numbers (*R*) (numbers of secondary infections generated per case, by date of symptom onset) for *e*) Hong Kong, *f*) Vietnam, *g*) Singapore, and *h*) Canada, 2003. Markers (white spaces) show mean values; accompanying vertical lines show 95% confidence intervals. The vertical dashed line indicates the issuance of the first global alert against SARS on March 12, 2003; the horizontal solid line indicates the threshold value $R = 1$, above which an epidemic will spread and below which the epidemic is controlled. Days are counted from January 1, 2003, onwards.

(Different Epidemic Curves for Severe Acute Respiratory Syndrome reveal similar impacts of control measures, Jacco Wallinga, Peter Teunis).

Q3. Interpret the above figures. Generate hypothesis for explaining why SARS could be rapidly controlled?

Q4. Use the information provided below and previous answers to discuss usefulness of control measures for SARS and H5N1. Would you need any other information?

Part III

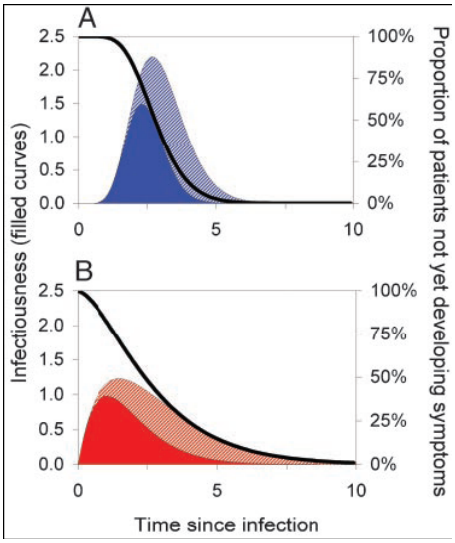


Fig 2. Filled curves represent infectiousness through time since infection (left axis) (measured in arbitrary units). The black curve represents the probability of a person not having developed symptoms by a certain time (right axis). The basic reproduction number *R*0 is the area under the infectiousness curve (solid color plus cross-hatched section). The solid-colored area represents transmission arising prior to symptoms such that θ, the proportion of presymptomatic transmission, is the proportion of the total area under the infectiousness curve that is solid-colored. (*A* and *B*) Low- and high-variance incubation and infectiousness distributions, respectively. Both cases have *R*0 = 5, *T*g = 3 (in arbitrary time units),and θ=0.5;*A*showsalowvariance of 0.1 mean^2,whereas*B*showsahigh variance of 0.5 mean^2.

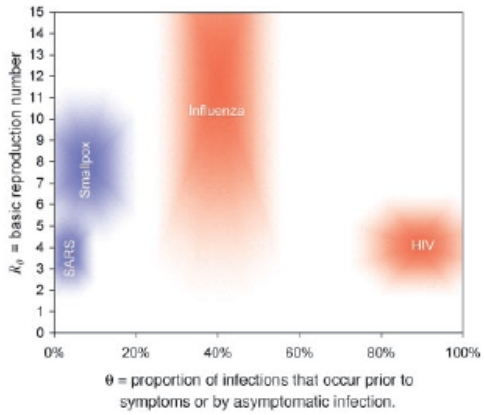


Fig 3. Parameter estimates. Plausible ranges for the key parameters R0 and θ for four viral infections of public concern are shown as shaded regions. The size of the shaded area reflects the uncertainties in the parameter estimates.

Table 1. Comparison of disease characteristics for SARS and H5N1.

	SARS	**H5N1**
Viral shedding in relation to onset of symptoms	After	2-3 days before
Peak viral shedding	2nd week of illness	1st-2nd days of illness
Time between successive cases	8-10 days	2-4 days
R0	2-4	~2

Q5. Which diseases in the figure above could be controlled isolating symptomatic cases only? Why? Would quarantine help for controlling the other diseases? Why?

Use the information provided in the annex (Estimated values of the basic reproductive rate, R0 for various infections, Anderson) and below as needed.

SARS. *The basic reproduction number R0 for SARS has been estimated in a number of ways: for the Hong Kong outbreak, using a fitting a detailed transmission model to the incidence time series, which gave estimates of 2–4 . Lipsitch et al estimated R0 from exponential doubling times of several epidemics, which resulted in a wider range of 1–7.*
Estimated θ of 11%, no minimum value available (because there is no evidence of pre-symptomatic transmission having occurred).

Smallpox. *R0 and θ have been determined from a detailed analysis of an outbreak in Nigeria by Eichner and Dietz. They concluded $4 < R0 < 10$ and $0 < \theta < 20\%$ (defining symptoms as the appearance of rash).*

HIV. *In populations for which spread into the general population has been seen (e.g., sub-Saharan Africa), R0 is by definition>1. We are not aware of published estimates of Ro for these generalized heterosexual epidemics; however, based on the formulas shown by Anderson and May, an upper bound of <5 can be obtained. If most transmission occurs during primary infection, then $\theta \approx 100\%$. If transmission is more uniform, then the distribution of time to AIDS leads to a lower bound: $\theta > 80\%$.*

Pandemic Influenza. *Maximum bound for Ro obtained by analysing the case data from an outbreak of the 1978 H1N1 flu in a boys boarding school yielding an upper bound of $R0 < 21$. No lower bound can be defined for a novel recombinant influenza strain. $30\% < \theta < 50\%$.*

Q6. How would the effectiveness in the implementation affect the success of the control measure applied for controlling the disease?

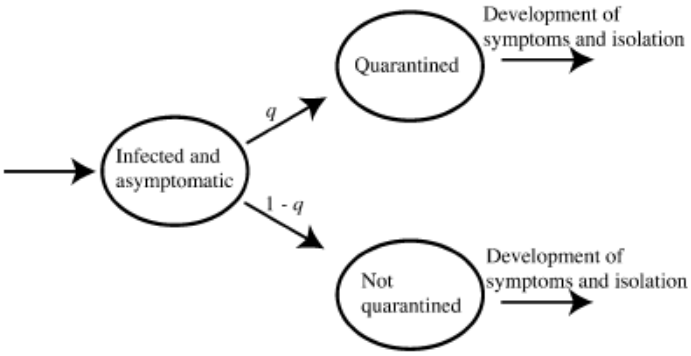


FIGURE 1. A schematic diagram of the two pathways down which an infected individual can move when quarantine protocols are in place.

SARS H5N1

Q7. Interpret the graphs below, how are the different parameters reflected in the different scenarios?

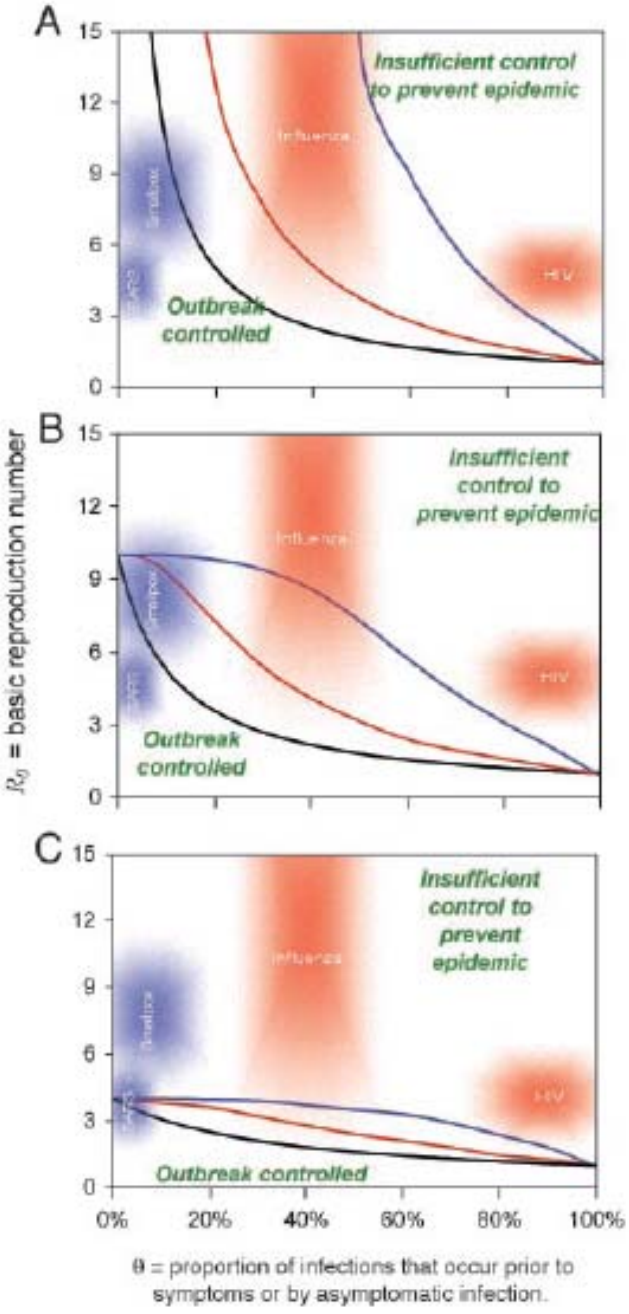


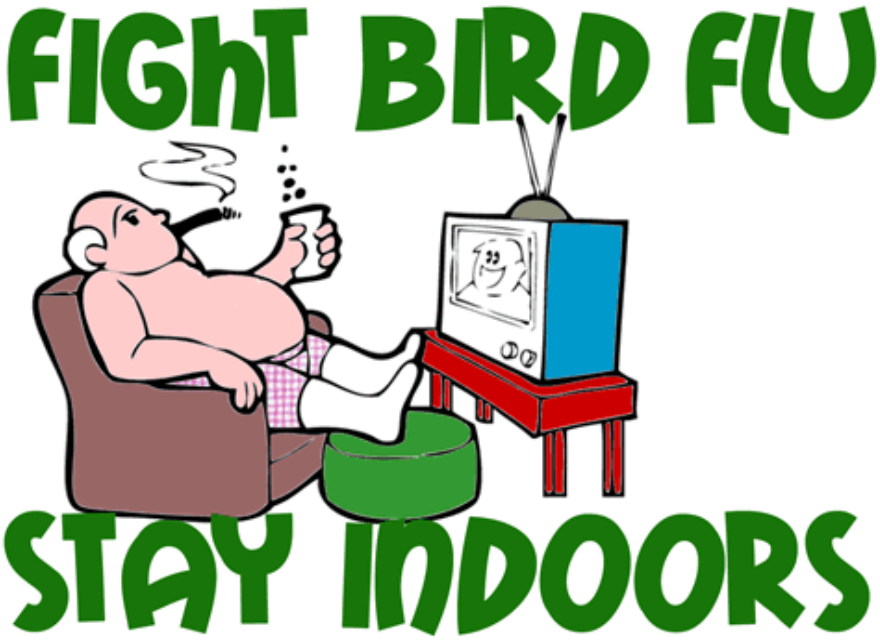
Fig. 3. Criteria for outbreak control. Each curve represents a different scenario, consisting of a combination of interventions and a choice of parameters. For each scenario, if a given infectious agent is below the R_0–θ curve, the outbreak is always controlled eventually. Above the curve, additional control measures (e.g., movement restrictions) would be required to control spread. Black lines correspond to isolating symptomatic individuals only. Colored lines correspond to the addition of immediate tracing and quarantining of all contacts of isolated symptomatic individuals. The black (isolation only) line is independent of distributional assumptions made (low or high variance), whereas the colored (isolation + contact tracing) lines match the variance assumptions made in Fig. 1 (red = high variance; blue = low variance). The efficacy of isolation of symptomatic individuals is 100% in *A*, 90% in *B*, and 75% in *C*. Contact tracing and isolation is always assumed 100% effective in the scenarios in which it is implemented (colored lines). Curves are calculated by using a mathematical model of outbreak spread incorporating quarantining and contact tracing (see main text).

Q8. The threat of an influenza pandemic has alarmed countries around the globe and given rise to an intense interest in disease mitigation measures. How would you apply what has been learned from previous influenza pandemics as well as the SARS and H5N1 examples to pandemic flu preparedness?

Historically, it has been all but impossible to prevent influenza from being imported into a country or political jurisdiction, and there has been little evidence that any particular disease mitigation measure has significantly slowed the spread of flu. The clinical and epidemiologic characteristics of influenza explain why:
• The influenza virus is known to spread rapidly from one person to the next, with a second generation of patients occurring within 2–4 days following exposure.
• People infected with influenza may shed virus for 1–2 days before becoming symptomatic.
• Some flu-infected individuals may be asymptomatic and so would not be recognized as being infected. In seasonal flu outbreaks, this group may represent a significant proportion of infected people. Asymptomatic individuals infected with flu have been shown to shed virus, although the extent to which these individuals transmit infection to others is not known.
• Many patients who are symptomatic are not readily diagnosed because their symptoms differ little from individuals with other respiratory illnesses or allergies.

Q9. (Optional) In your opinion, what would be the benefits and consequences of the following measures in the situation of an influenza pandemic. Discuss each one in terms of feasibility, acceptability and ethics.

- Large-scale community vaccination
- Isolation of sick people in hospitals
- Home isolation of sick people
- Use of antiviral medications
- Home quarantine
- Travel restrictions
- Large-scale quarantine measures
- School closures
- Prohibition of social gatherings
- Hand-washing and respiratory etiquettes
- Use of masks and personal equipment


FIGHT BIRD FLU
STAY INDOORS