SARS Outbreaks in Ontario, Hong Kong and Singapore

People wear surgical masks on Hong Kong's subway to protect against SARS. (AP Photo/Anat Givon)

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Gerardo Chowell

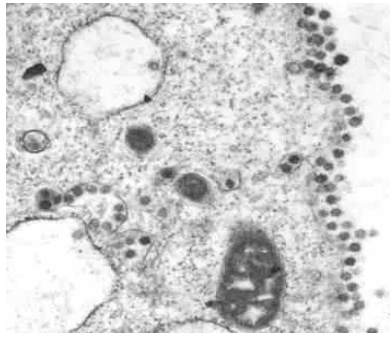
Mathematical Modeling and Analysis & Center for Nonlinear Studies
Los Alamos National Laboratory
Los Alamos, New Mexico

Outline

- SARS and its epidemiology
- A mathematical model for SARS
- The dynamics of SARS in Toronto, Hong Kong and Singapore
- Estimates of the basic reproduction number for SARS
- Comparison of the reproduction number with that of seasonal and pandemic influenza
- Conclusions

SARS

- **Severe acute Respiratory Syndrome** (SARS) is a new respiratory disease which was first identified in Guangdong's province of China.
- The outbreak of SARS was first identified in Vietnam by Dr. Carlo Urbani, a WHO expert in communicable diseases who succumbed to the disease.
- The causative agent of SARS is a new coronavirus (Drosten et al. And Ksiazek et al. 2003)
- WHO for the first time in history issued a global warning about the disease in March 2003.



Coronavirus from SARS isolated in FRhK-4 cells. Department of Microbiology, The University of Hong Kong and the Government Virus Unit.

The public image of SARS in Hong Kong

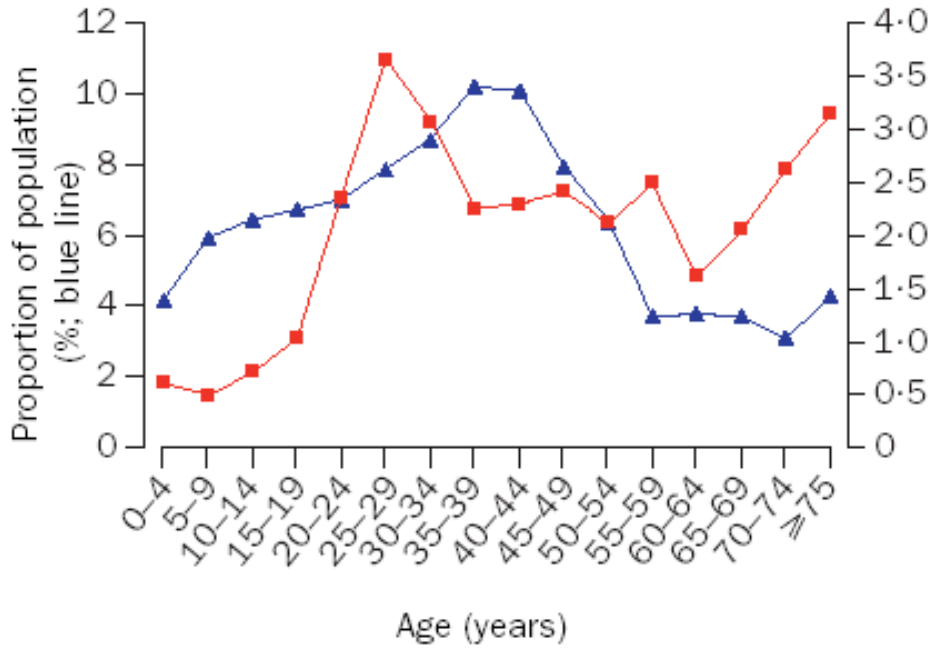
Epidemiology of SARS

- SARS is believed to be transmitted by close contact with an infectious individuals (droplets).
- An individual exposed to SARS may become infectious after an incubation period of 2-7 days.
- Infectious individuals experience similar symptoms to pneumonia including high fever, shortness of breath, dry cough, headache, stiff or achy muscles, fatigue and diarrhea.
- Most infected individuals recover typically after 7-10 days.
- The case fatality rate for patients younger than 60 years is 13.2% while for patients ages 60 or older is 43.3%.

Modeling the transmission dynamics of SARS

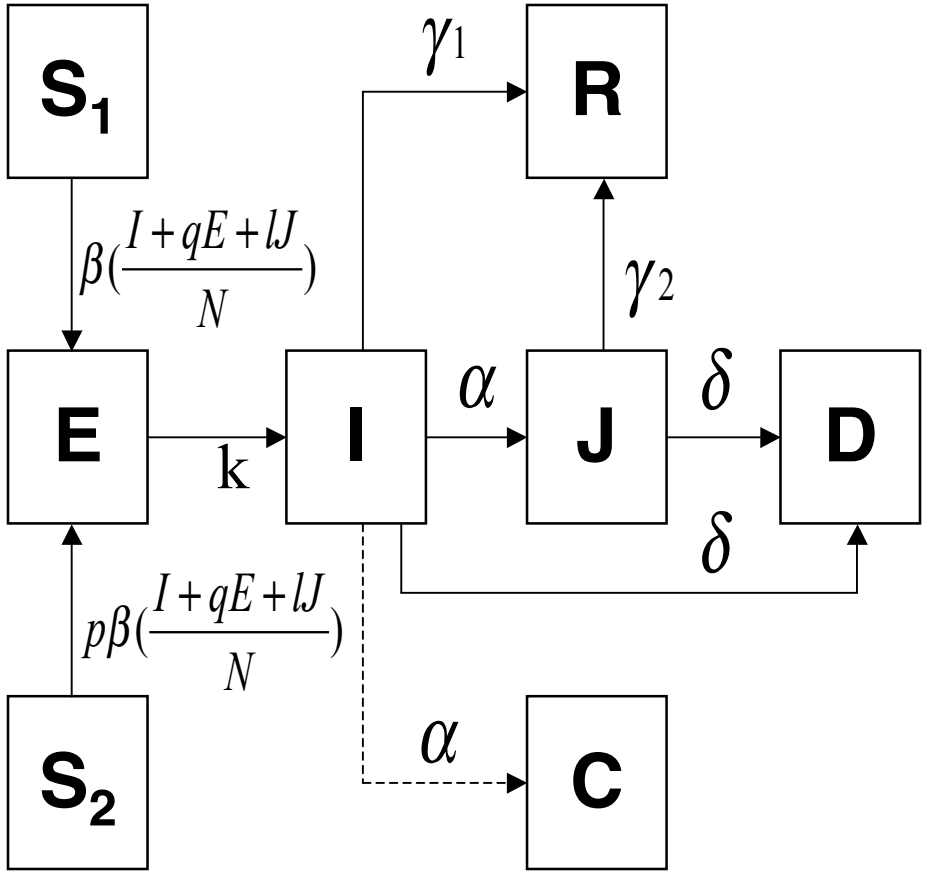
- To account for differences in susceptibility in the population, we introduce two susceptibles classes: S_1 and S_2. S_1 is the most susceptible class and S_2 is less so. For the case of Hong Kong, this can be illustrated with the following graph:

Age distribution of residents in Hong Kong (blue) and age-specific SARS incidence (red). Donnelly et al. (2003)



Compartmental model

- **E** (exposed). Asymptomatic, possibly infectious individuals.
- **I** (infectious). Infected, symptomatic not yet diagnosed individuals.
- **J** (diagnosed). Diagnosed (hospitalized) individuals.
- **R** (recovered). Individuals who recovered from the disease.
- **D** (dead). Individuals who died from the disease.



Chowell et al. (2003), Lipsitch et al. (2003), Riley et al. (2003), **Gumel et al. (2004), Lloyd-Smith (2004), Hsie et al. (2004).**

Parameter definitions and estimates

Parameter definitions and values that fit the cumulative number of "diagnosed" cases for Hong Kong.

Parameter	Definition	Value
β	Transmission rate per day	.75
q	relative measure of infectiousness for the asymptomatic class E	0.1
l	relative measure of reduced risk among diagnosed SARS cases	0.38
p	reduction in risk of SARS infection for class S_2	0.1
k	rate of progression to the infectious state per day	$\frac{1}{3}$
α	rate of progression from infective to diagnosed per day	$\frac{1}{3}$
γ_1	rate at which individuals in the infectious class recover per day	$\frac{1}{8}$
γ_2	rate at which diagnosed individuals recover per day	$\frac{1}{5}$
δ	SARS-induced mortality per day	0.006
ρ	Initial proportion of the popualtion at higher risk of SARS infection	0.4

Intervention measures

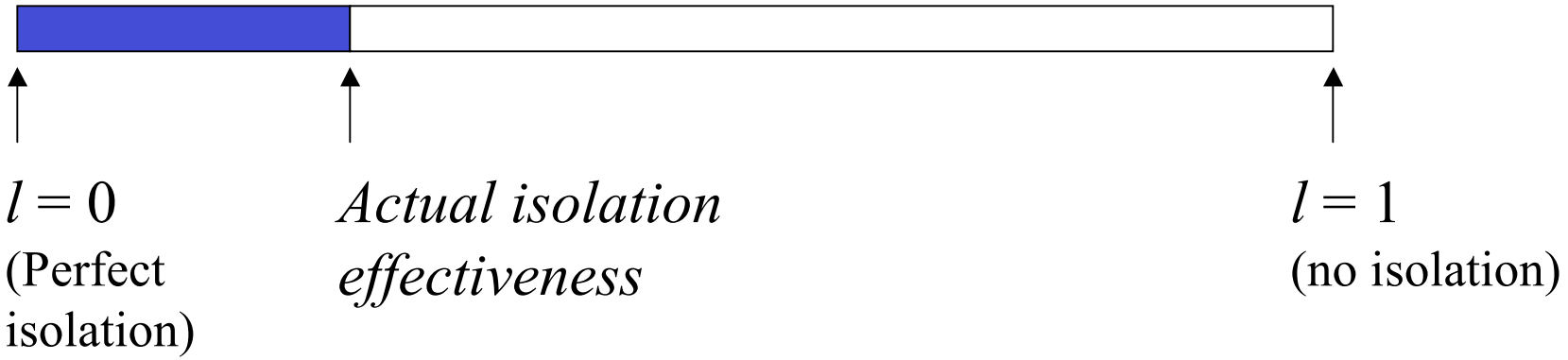
The image of SARS in hospitals

- Rapid diagnosis of patients
- Strict isolation procedures

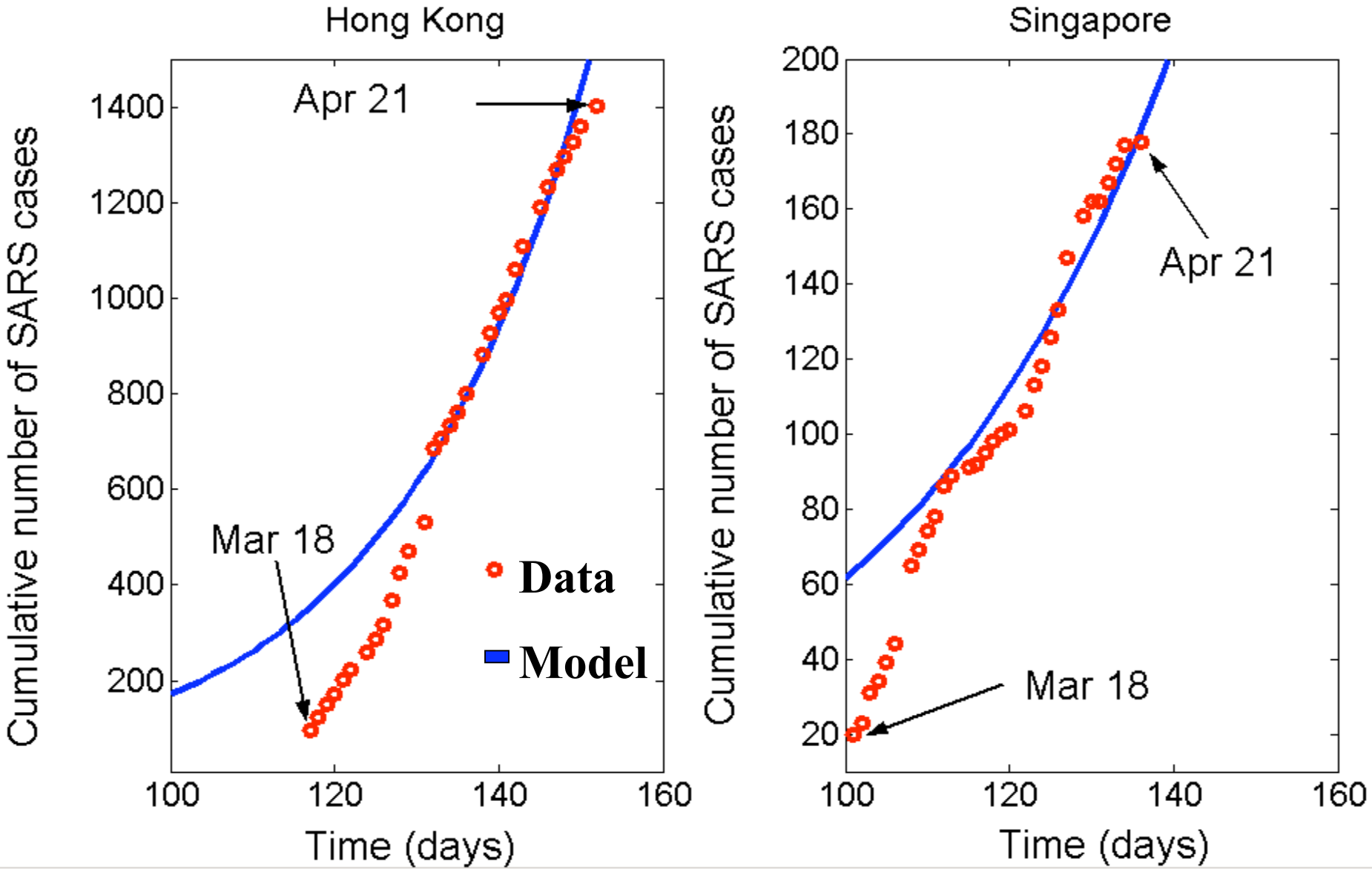
Before	***After***
Diagnostic period ~ 6 days	Diagnostic period ~ 3 days
Infectious individuals were not being properly isolated in hospitals	Isolation effectiveness was roughly 10 times better!

Isolation effectiveness (l)

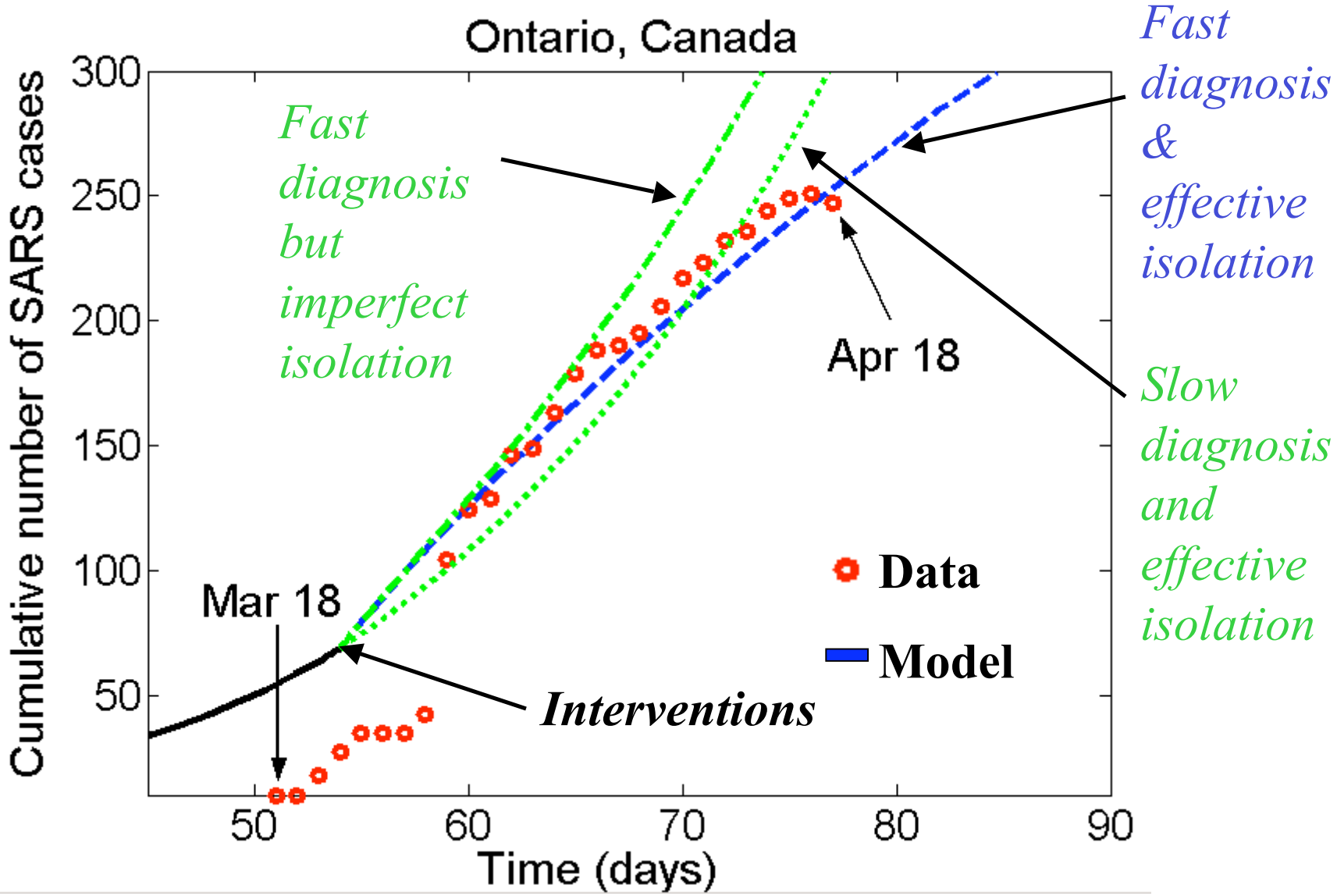
- $0 < l < 1$ is a measure of the effectiveness of the isolation procedures implemented in hospital wards (i.e appropriate nursing-barrier techniques, etc.)
- 94% of SARS cases in Taiwan occurrred in hospital wards.



The cases of Hong Kong and Singapore



The case of Toronto



The Basic reproduction number R_0

The number of secondary cases generated by a primary infectious case during its period of infectiousness in an entirely susceptible population is known as the **basic reproduction number R_0**.

A more practical quantity is the **reproduction number (R)** which measures the transmissibility in a partially immune population, where a fraction of individuals is effectively protected against infection before the start of the epidemic, because of residual immunity from previous exposure to influenza, or vaccination. For example, if a proportion p of a completely susceptible population is successfully immunized prior to an epidemic, the relation between the basic and the effective reproductive number is $R = (1\text{-}p)\ R_0$.

R_0 for SARS

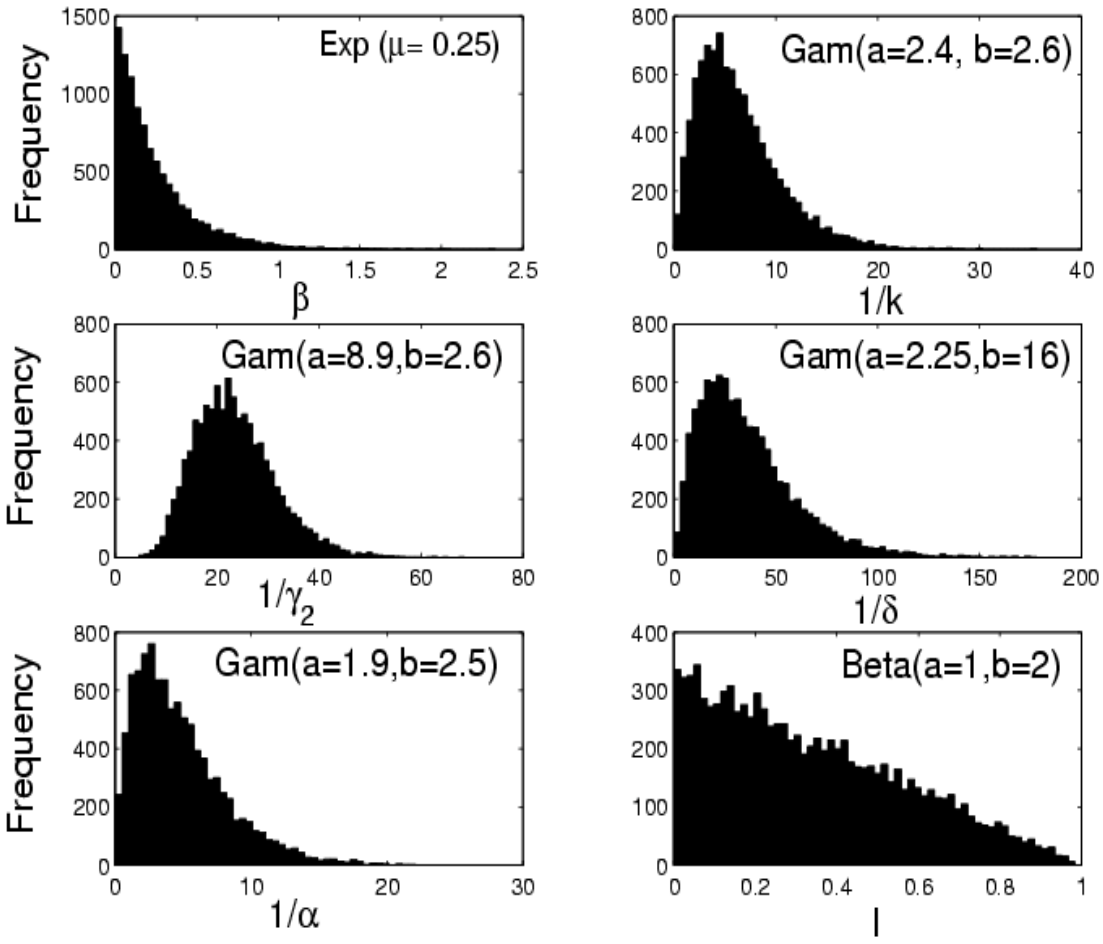
- Following the second generation approach (Diekmann and Heesterbeek, 2000), we can obtain the following expression for the basic reproductive number:

$$\mathcal{R}_0 = \{\beta\,[\rho + p(1-\rho)]\}\left\{\frac{q}{k} + \frac{1}{\alpha+\gamma_1+\delta} + \frac{\alpha l}{(\alpha+\gamma_1+\delta)(\gamma_2+\delta)}\right\}$$

- For Hong Kong $R_0 = 1.2$ and $R_0 = 1.1$ for Singapore.

Uncertainty analysis for R_0

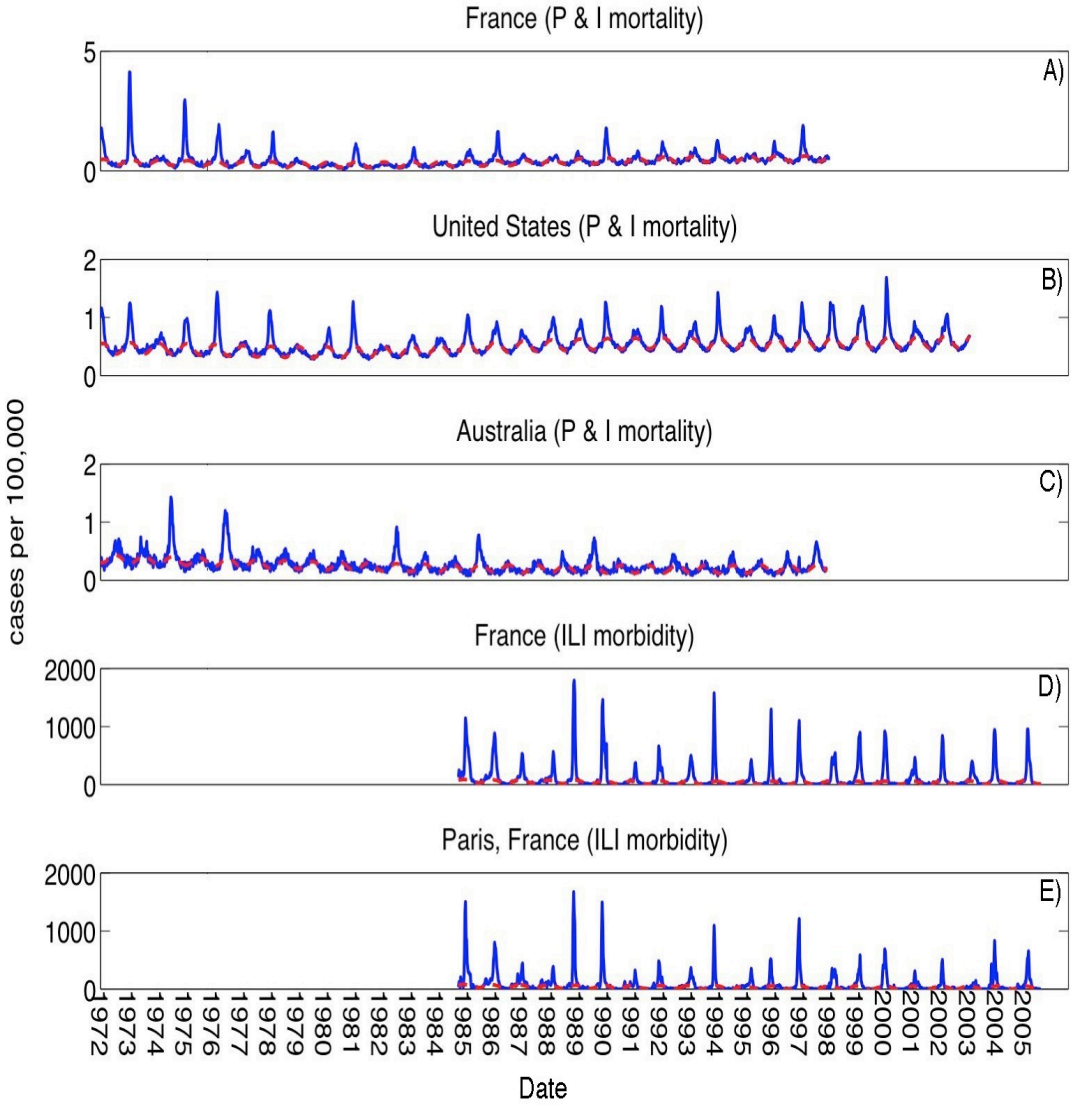
Parameter distributions (Donnelly et al. 2003)



Chowell, Castillo-Chavez, Fenimore, Kribs-Zaleta, Arriola, Hyman, Emerging Infectious Diseases (2004).

- For Hong Kong, R_0 = 1.8 (0.5, 2.5) and R_0 = 1.7 (0.4, 2.3) for Singapore.
- Under perfect isolation, 25% of the R_0 distribution lies at $R_0 > 1$. This highlights the importance of simultaneously applying more than one method of control.
- Lipstich et al. (2003), Riley et al. (2003) R0 ~ 2-3, assuming an exponential epidemic growth phase (may overestimate initial growth rate, Razum et al. 2003).

Seasonal influenza

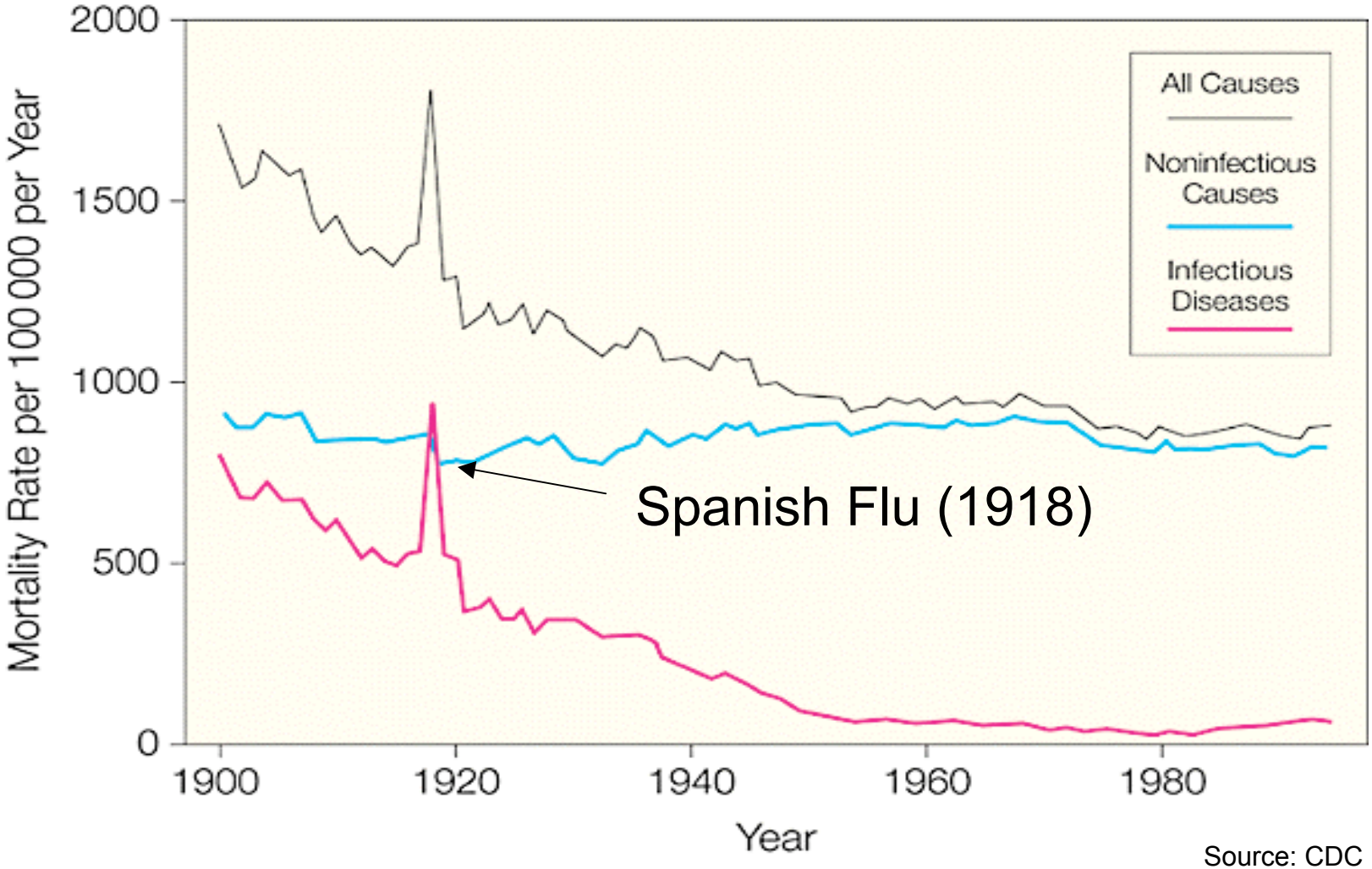


- We find similar average reproduction numbers for inter-pandemic influenza in the three countries: 1.3 in the US (95% Confidence Interval (CI) 1.2-1.4), [Wilcoxon test for between country differences, $P>0.87$].

- Estimates of the reproduction number using morbidity data for France and the greater Paris area are in close agreement with those obtained using mortality data.

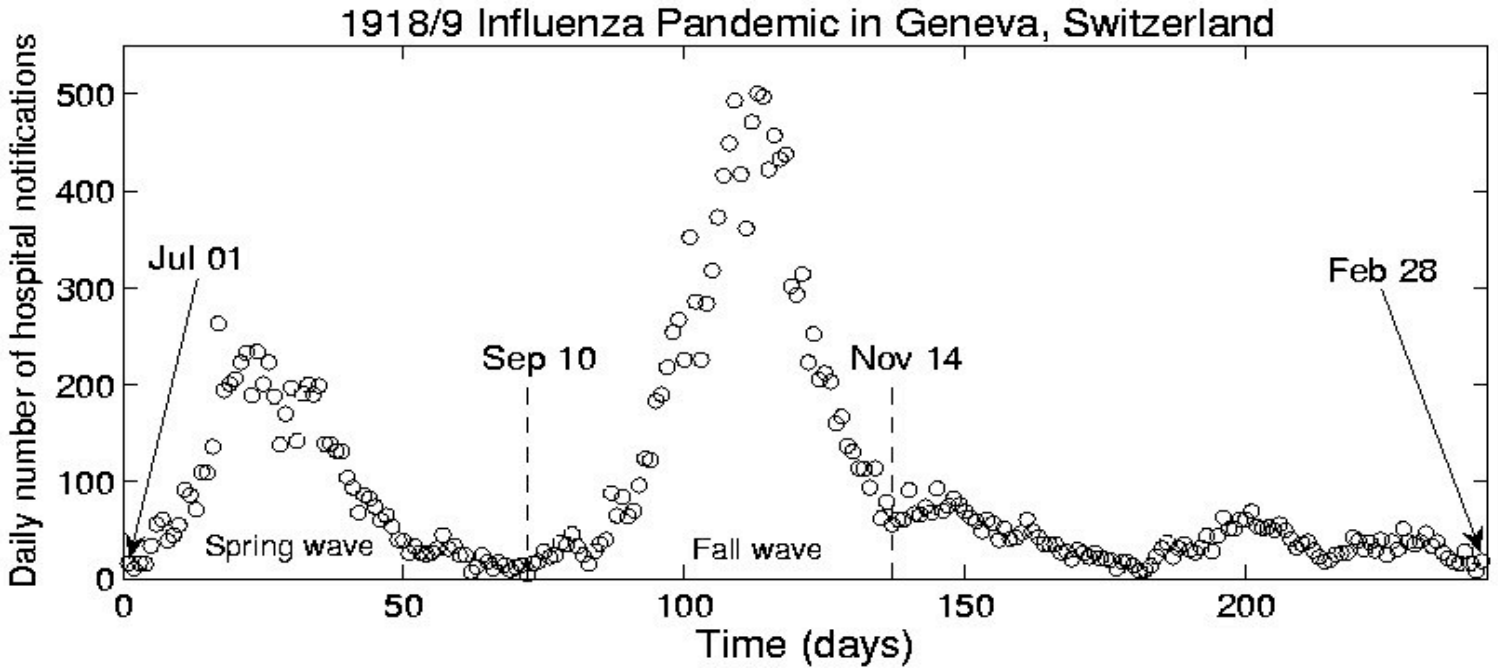
Chowell, Miller, Viboud. Transmission of Seasonal Influenza in the United States, France, and Australia, and prospects for control (in revision).

US mortality in 20th century



Source: CDC

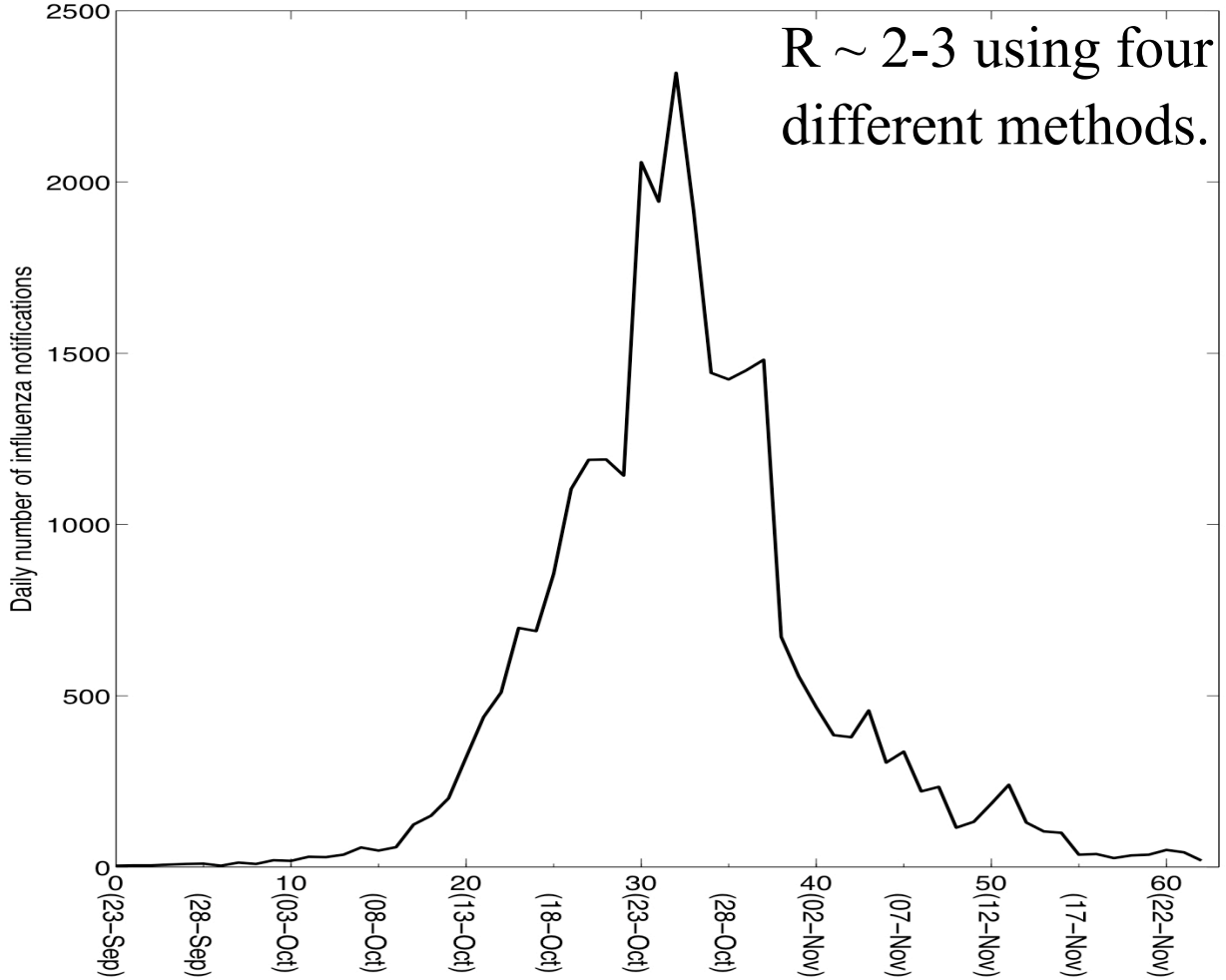
Influenza pandemic in Geneva, Switzerland



Flu wave	Case fatality (%)	R	S.D. R	Reporting (%)	S. D. Reporting (%)
1st wave	0.7	1.49	0.02	59.7	2.0
2nd wave	3.25	3.75	0.09	83.0	2.0

Chowell, Ammon, Hengartner, Hyman,
***J Theor Biol* (2006).**

Influenza pandemic in San Francisco, California



- Mills et al., Nature (2004). R ~ 2-3 around 10 major US cities.
- Gani et al. Emerg. Inf. Dis. (2005) in the UK estimated R ~12.

Chowell, Nishiura, Bettencourt,
J. Royal Society Interface (to appear)

Conclusions

• A model that considers the effect of average infectiousness in an heterogeneous population has been introduced to explore the role of patient isolation and diagnostic rate in controlling a SARS outbreak.

• By examining two cases with relatively clean exponential growth curves we are able to calibrate the SEIJR model. We then use our SEIJR model to study the non-exponential dynamics of the Toronto Outbreak where the rapid slowing in the growth of new recognized cases, robustly constrain the SEIJR model by requiring that $l \approx 0.05$ and $\alpha > 1/3$ days^{-1}.

• The fitting of data shows that initial rates of SARS growth are quite similar in most regions leading to mean estimates of R_0 1.7-1.8

Conclusions, cont'

• In our model "good control" means (a) *at least* a factor of 10 reduction in *l* (effectiveness of isolation) and (b) simultaneously a *maximum* diagnostic period of 3 days. The model is sensitive to these parameters, so they should be treated as absolutely minimal requirements: better is better.

• The reproduction number of the Spanish Flu pandemic is approximately twice larger than that of seasonal flu ($R \sim R_0$).

• The reproduction number of the first (herald) pandemic wave is in agreement with that of seasonal flu.