Dynamics and Control of Infectious Diseases

Alexander Glaser

WWS556d
Princeton University

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Revision 3

Definitions

Infectious Disease

Disease caused by invasion of the body by an agent

About a quarter of all deaths worldwide are due to infectious diseases
(about 60% are due to non-communicable conditions)

An infectious disease is *contagious* if it is *easily* transmitted (from person to person)

Agent

Pathogen, i.e. a microparasite that causes disease, e.g. a virus or bacterium

Vector

Agent may be transmitted by a vector (droplet, mosquito, etc.)

Stages of an Infectious Disease

(generic)

- Incubation (latent) period
- Prodromal (initial, pre-eruptive) period
- Overtly symptomatic (infectious) period
- Recovery period (no longer infectious)

Depending on the disease, a person may or may not be able to transmit the disease during incubation and prodromal periods

Relative infectiousness in the prodromal and the symptomatic periods determine the optimal control strategy

Definitions

Epidemic

Outbreak of an infectious disease affecting
a disproportionately large number of individuals in a population,
community, or region within a short period of time

Pandemic

Spread of an epidemic to a large region (or worldwide)

Endemic

An infectious disease is endemic when it is maintained in a
population without the need for external inputs

Transmission Factor R_0

(of the microparasite, also: basic reproduction number)

Infected primary individual is placed in a large susceptible population
R_0: average number of secondary individuals infected by one primary case
(applicable in the early stages of an epidemic)

$R_0 > 1$ Epidemic $\quad$ $R_0 = 1$ Endemic $\quad$ $R_0 < 1$ Eradication

Effective transmission factor (if a fraction p is immune): $R_{\text{eff}} = R_0(1-p)$

Critical fraction of the population that has to be immune to prevent epidemic

$$R_{\text{eff}} < 1 \longrightarrow p > 1 - \frac{1}{R_0}$$

Typical Transmission Factors

Infectious Disease	R_0	$p_{(min)}$
Smallpox	3-5	70-80%
Measles	10-20	90-95%
Malaria	(100)*	99%

*Malaria needs specific “external” vector (mosquito) for transmission

Current level of U.S. population immune against smallpox: about 18%
(growth rate of epidemic today would be much higher than those of historical smallpox epidemics)

Why Mathematical Modeling?

STRENGTHS AND BENEFITS

Mathematical modeling is typically the only way to
examine the possible impact of different release and control scenarios

Questions that can be addressed:
What fraction of the population should be quarantined and/or vaccinated?
How fast have control measures to be implemented?, etc.

PROBLEMS

Simple models cannot capture the complexity of epidemics and their dynamics
Complex models are intransparent and difficult to validate

Several important aspects of epidemics are difficult to quantify
(e.g. response of population to certain events)

Dynamics of Infectious Diseases

Basic Model

based on

R. M. Anderson and R. M. May
Infectious Diseases of Humans: Dynamics and Control
Oxford University Press, 1991

Assumptions and Simplifications

(incomplete list)

Three groups: susceptible X(t), infectious Y(t), and recovering (immune) Z(t)

No age-dependency of variables and parameters

All susceptibles are equally at risk of infection ("weak homogeneous mixing")
All births into the susceptible class

Total population constant (no deaths caused by disease): $N = X(t) + Y(t) + Z(t)$
Constant mortality rate ("Type II survival")

No incubation period (only one "infectious" group)

Dynamics of Infectious Diseases

Basic model

susceptible group	$\frac{\Delta X(t)}{\Delta t} = \mu N - \lambda(t)X(t) \qquad -\mu X(t)$
infectious group	$\frac{\Delta Y(t)}{\Delta t} = \lambda(t)X(t) - \nu Y(t) - \mu Y(t)$
immune group	$\frac{\Delta Z(t)}{\Delta t} = \nu Y(t) - \mu Z(t)$

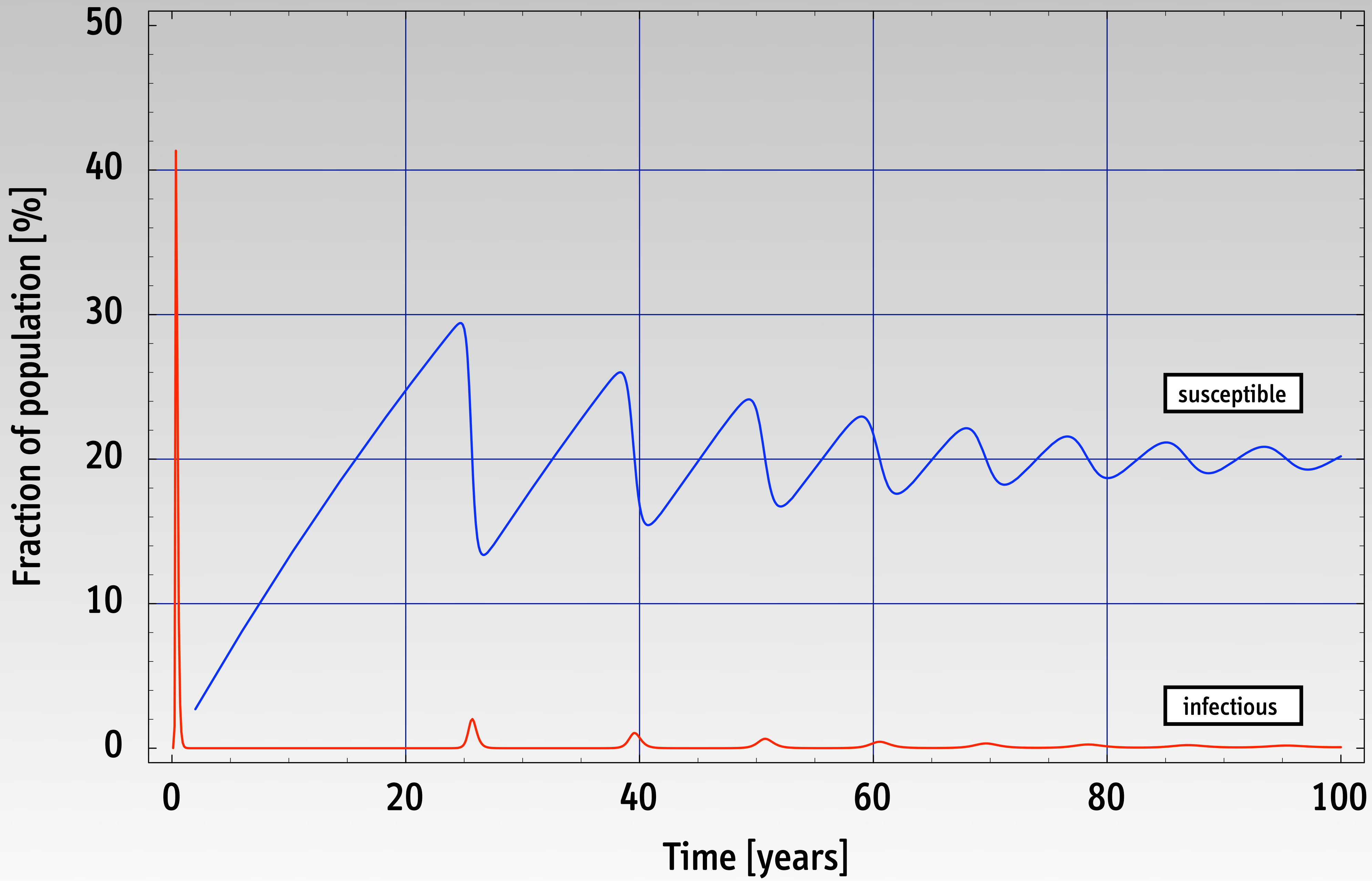
μ : Birth rate / death rate $\quad$ $\lambda(t)$: Infection rate $\quad$ ν : Recovery rate

Infection rate: $\lambda(t) = \beta Y(t)$ $\quad$ β : transmission parameter (equivalent to R_0)

$$\mu = \frac{1}{70\,\text{yrs}} \quad \nu = \frac{1}{0.1\,\text{yrs}} \quad \beta = \frac{1}{0.02\,\text{yrs}} \quad x(0) = 1 \quad \lambda(0) = 0.0001\frac{1}{\text{yrs}}$$

Epidemic and Endemic Phases

(of an infectious disease)



Epidemic and Endemic Phases

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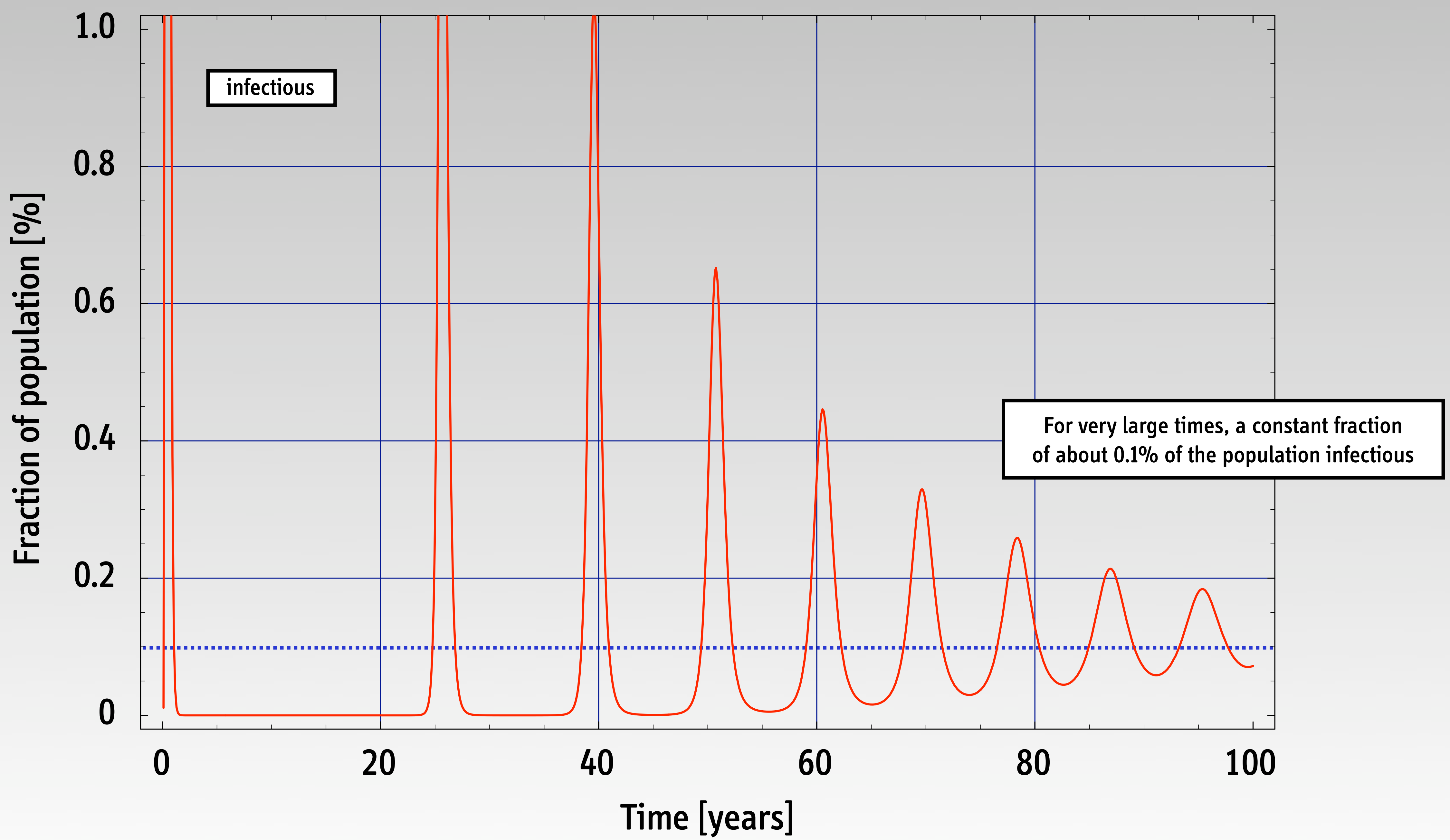
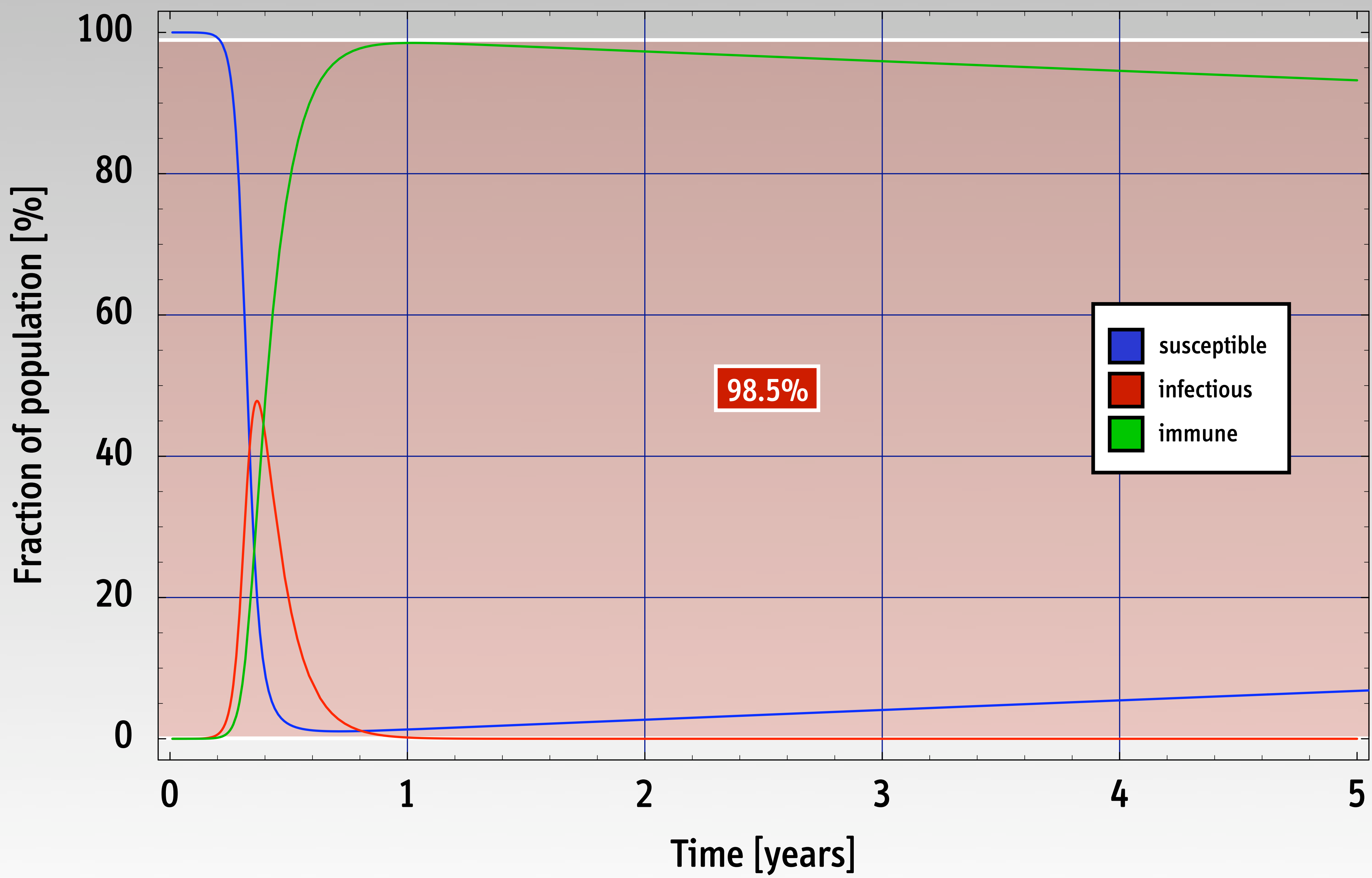


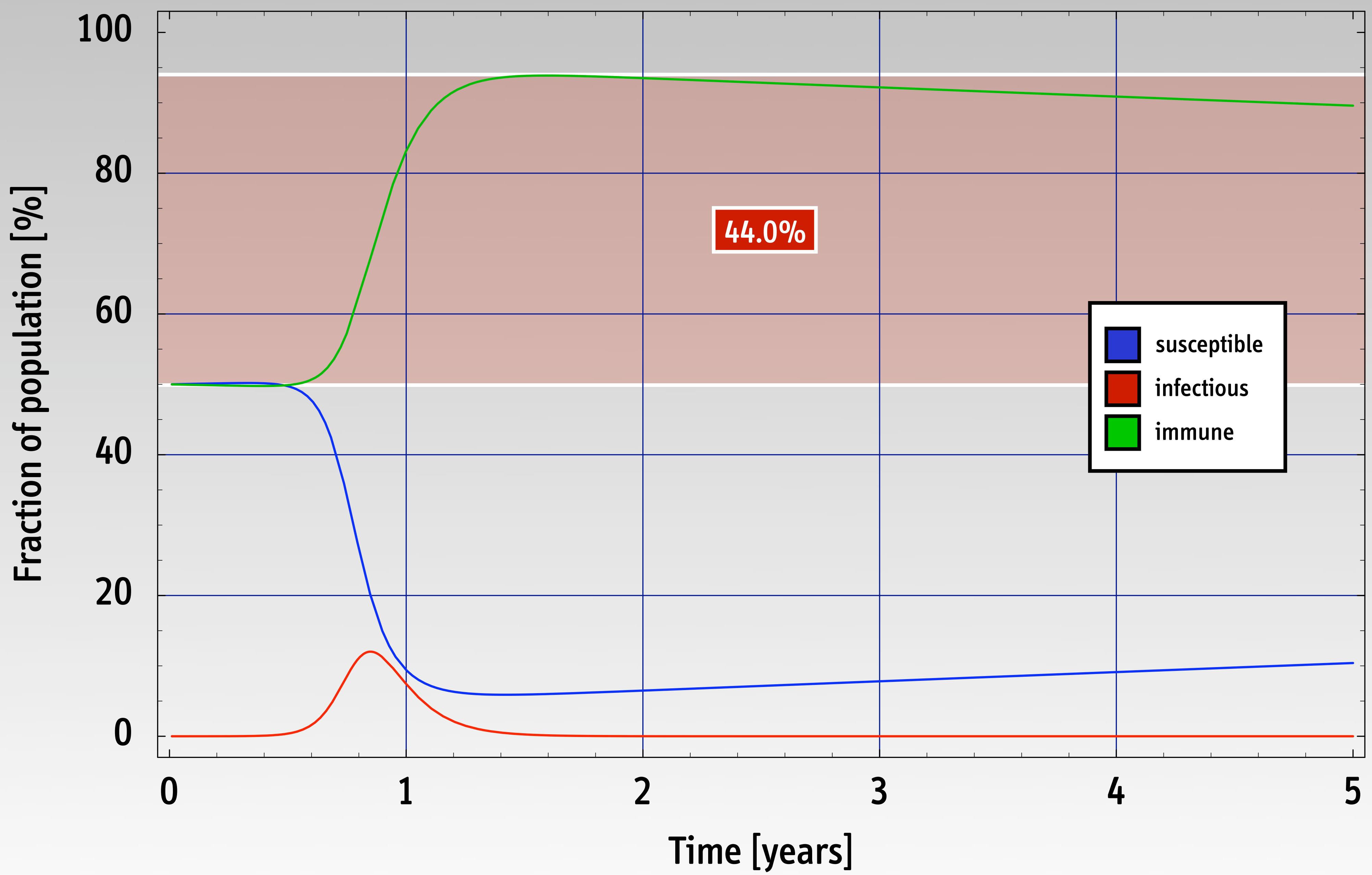
Severity of an Epidemic

(initial immunity level: 0%)



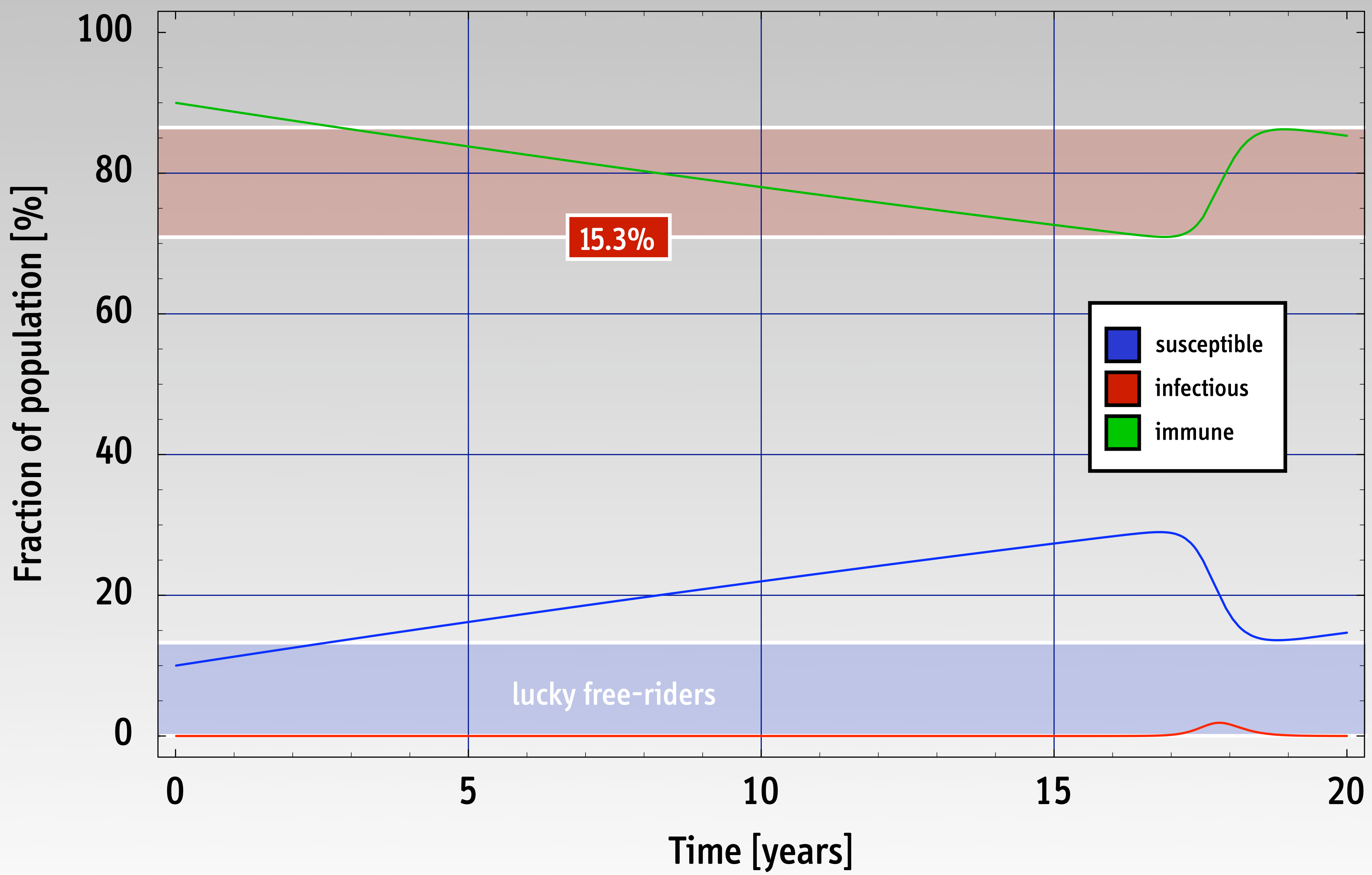
Severity of an Epidemic

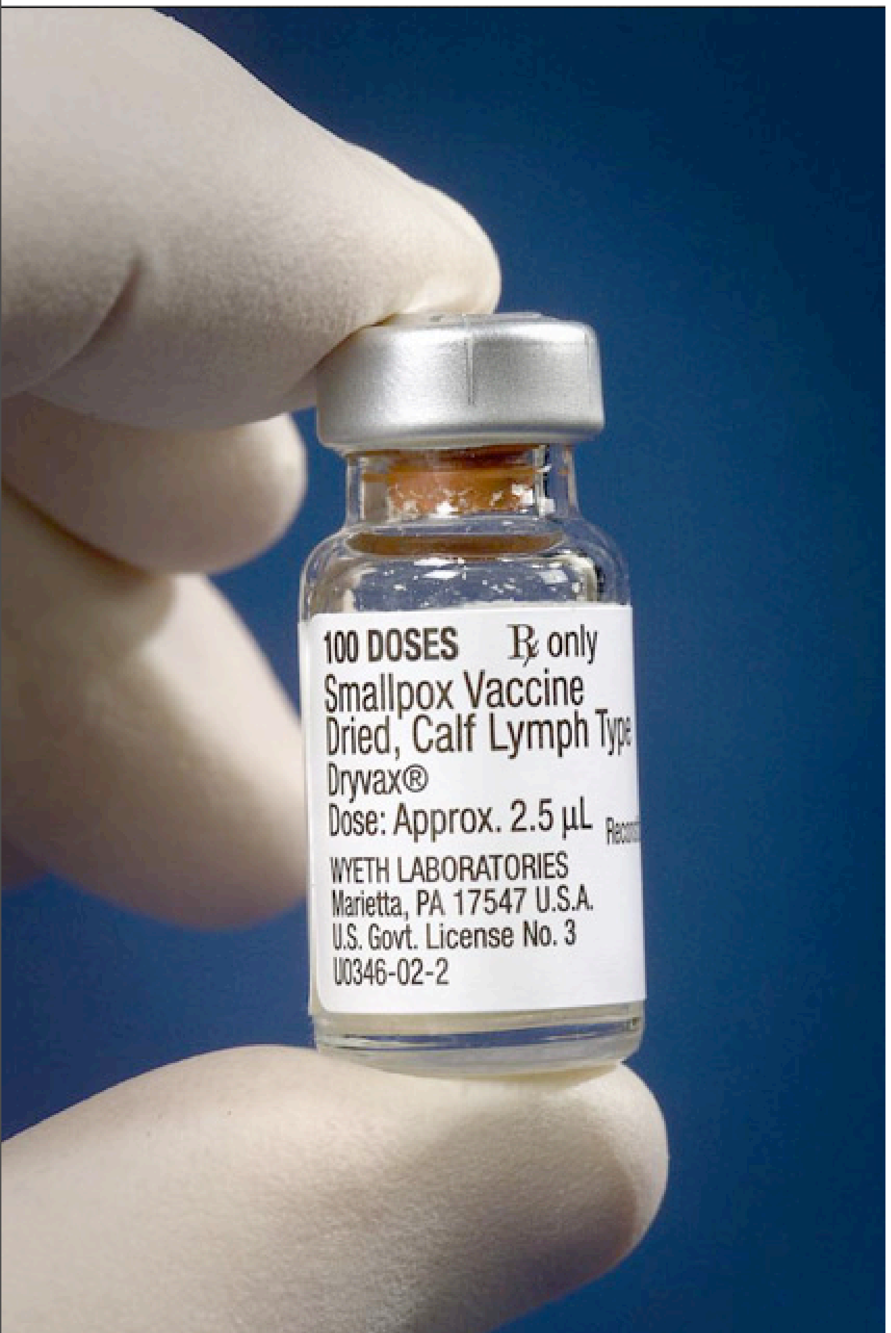
(initial immunity level: 50%)



Severity of an Epidemic

(initial immunity level: 90%)





Smallpox

Response Options to an Outbreak

and the Potential Role of Mathematical Modeling to Identify Optimal Control Strategies

About Smallpox

Agent: variola virus
Mode of transmission: infective droplets via face-to-face contact

Lethality: about 30% (depending on many factors, some types > 98%)

Long incubation period: about 2-3 weeks (possibility of localized control measures)

Once endemic in humans; eradicated in 1979, primarily by mass vaccination
Humans are (or have been) only known host of virus

About Smallpox

1947 smallpox incident in New York City
one infectious person traveling to the city by bus from Mexico
mass vaccination of several million people

Vaccination may have severe side effects

Mass vaccination campaign likely to cause more deaths

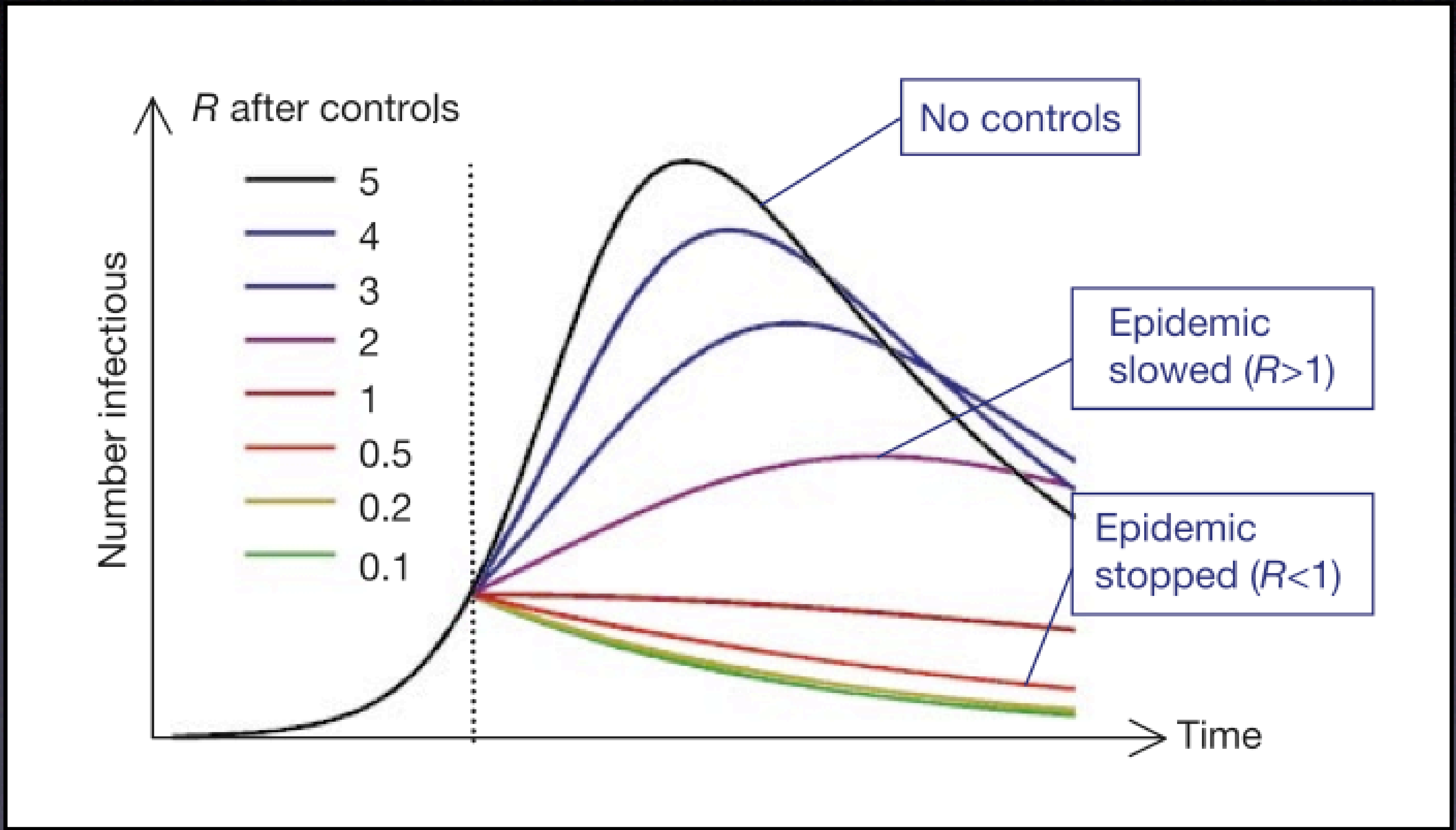
than locally isolated smallpox epidemic

Temporary retention of samples (officially) in only two locations today

Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America (about 400 strains)
Russian State Centre for Research on Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation (about 120 strains)

Destruction of samples originally scheduled for June 30, 1999

Objective of Control Strategies



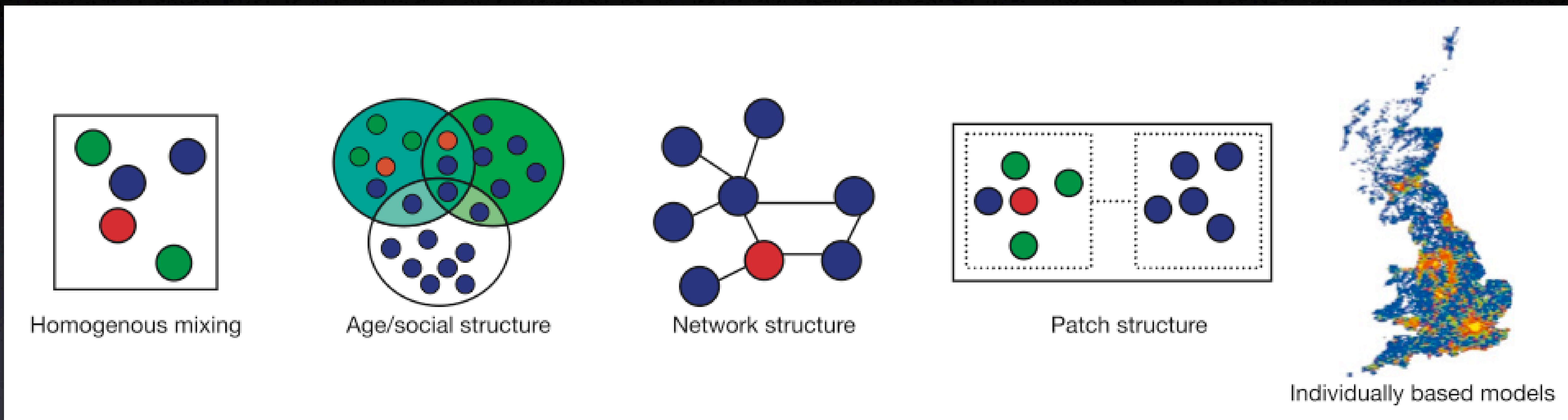
Source: Ferguson et al., Nature (425), 2003

Outbreak Control Options

		BENEFITS	DRAWBACKS
CONTAINMENT	Isolation and quarantine	Highly effective at reducing transmission from known cases	Needs adequate facilities; compulsory policy coercive; requires rapid detection of cases
	Movement restrictions	Potentially useful in containing a small outbreak	Difficult to police, compromised by any "illegal" movements, coercive
VACCINATION	Ring vaccination	Minimizes use of vaccine	Contacts need to be found at an early stage of incubation
	Targeted ("local mass") vaccination	Highly effective during eradication campaign (with background levels of herd immunity high)	Less effective in "mobile" society
	Mass vaccination	Effective at stopping widespread dissemination; not dependent on contact tracing	Large numbers have to be vaccinated quickly; unnecessary morbidity and mortality
	Prophylactic vaccination	Useful for protecting first-responders; if used for entire population, no need for rapid implementation	If used for entire population, high long-term costs and (unnecessary) morbidity and mortality

Adapted from N. M. Ferguson et al., Planning for Smallpox Outbreaks, *Nature*, Vol. 425, October 2003

Modeling Complexity



Source: Ferguson et al., *Nature* (425), 2003

Deterministic models
Solve equations (fast), "hopefully" capture the average epidemic behavior

Stochastic models
Simulation (slow), recognize random nature of transmission events (important in early/late stages of epidemic)

Advanced Methods: Example 1

(Deterministic Model)

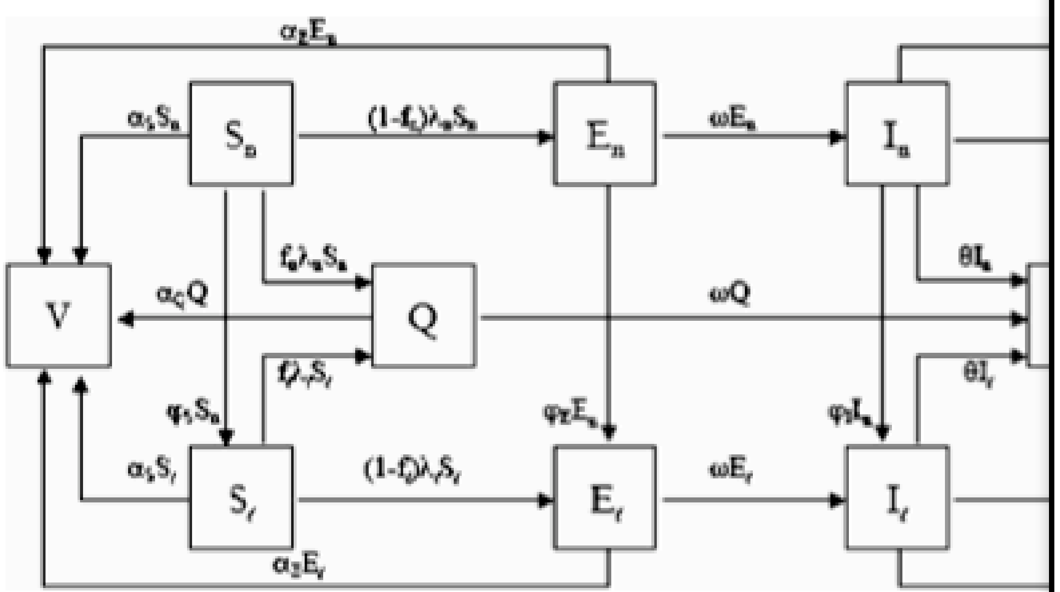


Fig. 1. Schematic relationship between normally active and less active individuals (j
arrows that connect the boxed groups represent movement of individuals from
Susceptible individuals (S_j) can become exposed (E_j), be quarantined (Q) or vaccin
can either become infectious (I_j) after an incubation period or be vaccinated (V). Qua
be vaccinated (V) or isolated (W). Infectious individuals (I_j) can be isolated (W) or
Similarly, isolated individuals (W) can either recover (R) or die (D).

$$\dot{V} = \alpha_S(S_n + S_\ell) + \alpha_E(E_n + E_\ell) + \alpha_Q Q,$$

$$\dot{S}_n = -\lambda_n S_n - (\varphi_S + \alpha_S)S_n,$$

$$\dot{S}_\ell = -\lambda_\ell S_\ell + \varphi_S S_n - \alpha_S S_\ell,$$

$$\dot{Q} = f_n\lambda_n S_n + f_\ell\lambda_\ell S_\ell - (\omega + \alpha_Q)Q$$

$$\dot{E}_n = (1 - f_n)\lambda_n S_n - (\varphi_E + \omega + \alpha_E)E_n,$$

$$\dot{E}_\ell = (1 - f_\ell)\lambda_\ell S_\ell + \varphi_E E_n - (\omega + \alpha_E)E_\ell,$$

$$\dot{I}_n = \omega E_n - (\varphi_I + \mu + \delta + \theta)I_n,$$

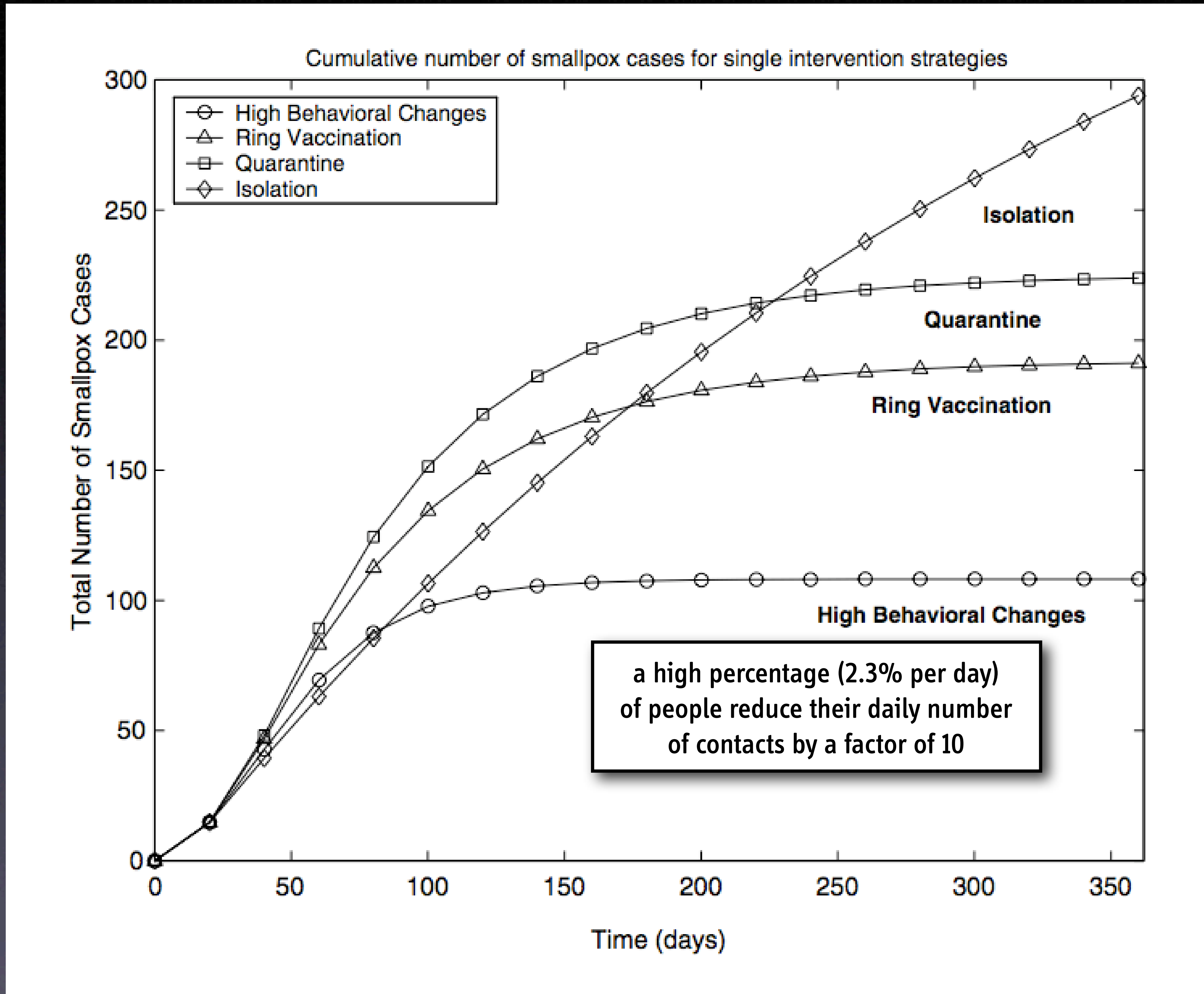
$$\dot{I}_\ell = \omega E_\ell + \varphi_I I_n - (\mu + \delta + \theta)I_\ell,$$

$$\dot{W} = \theta(I_n + I_\ell) + \omega Q - (\mu + \delta)W,$$

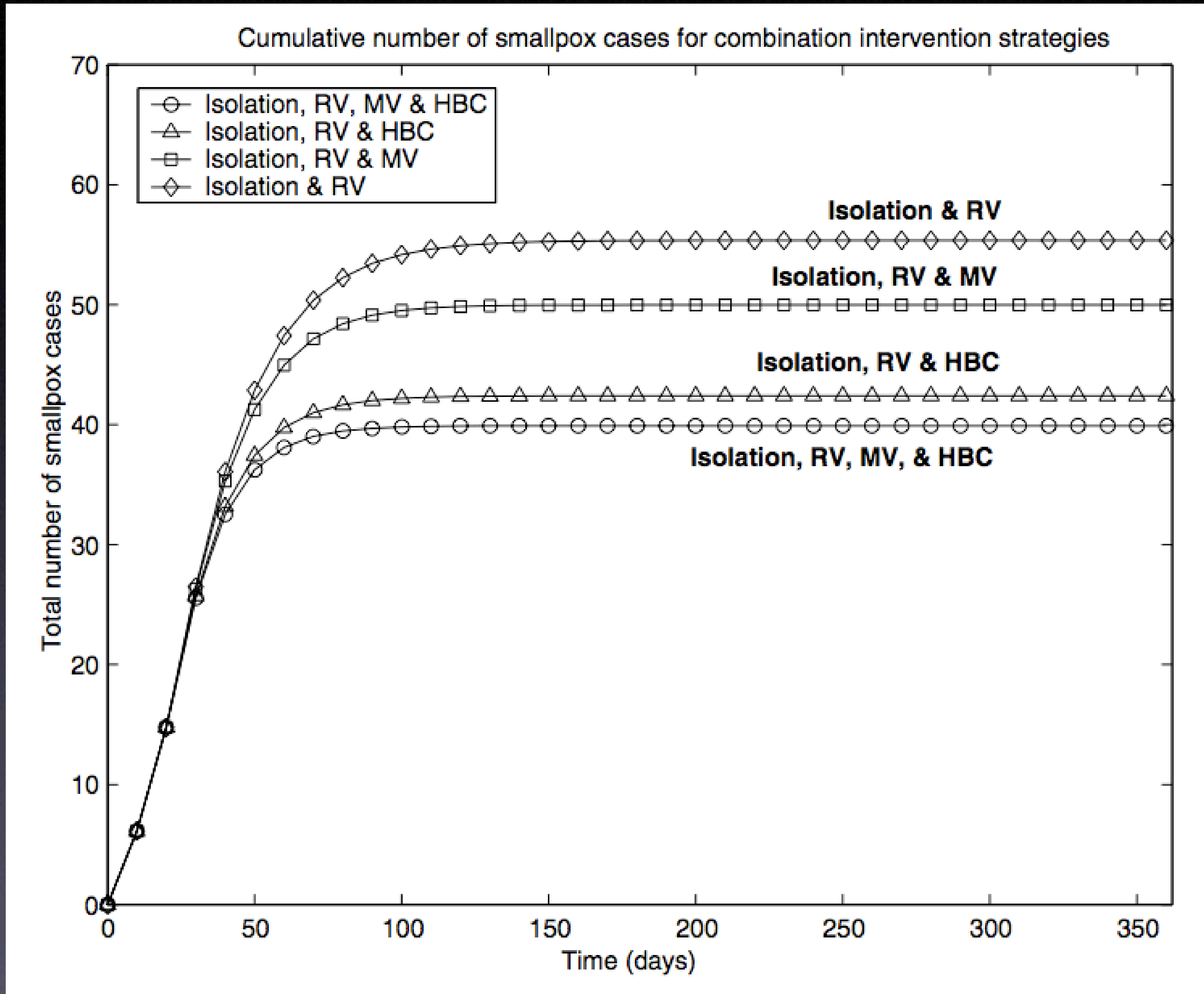
$$\dot{R} = \delta(I_n + I_\ell + W),$$

$$\dot{D} = \mu(I_n + I_\ell + W),$$

S. Del Valle et al.,
Effects of behavioral changes in a smallpox attack model,
Mathematical Biosciences 195 (2005)



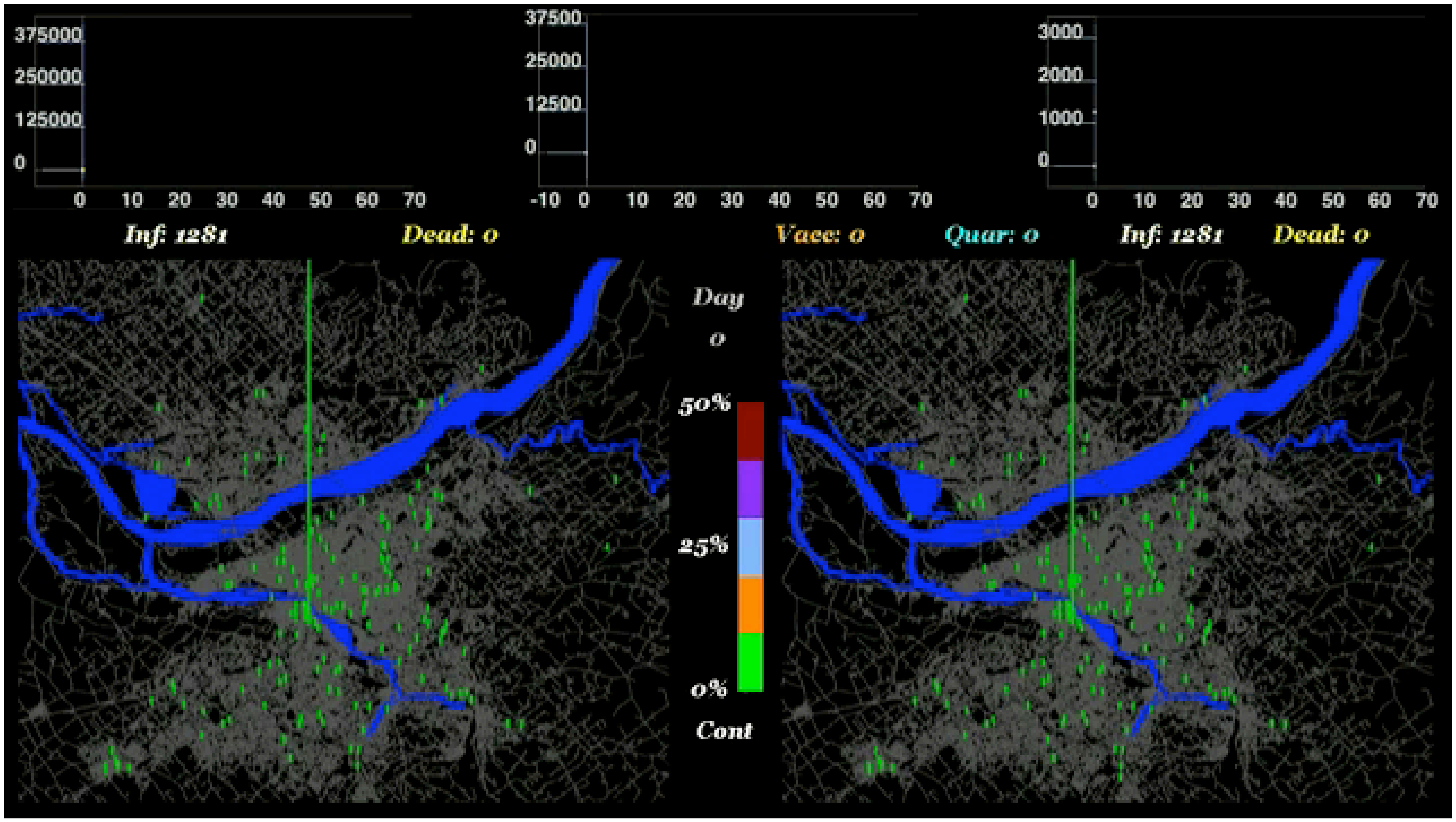
S. Del Valle et al., *Mathematical Biosciences* 195 (2005)



S. Del Valle et al., *Mathematical Biosciences* 195 (2005)

Advanced Methods: Example 2

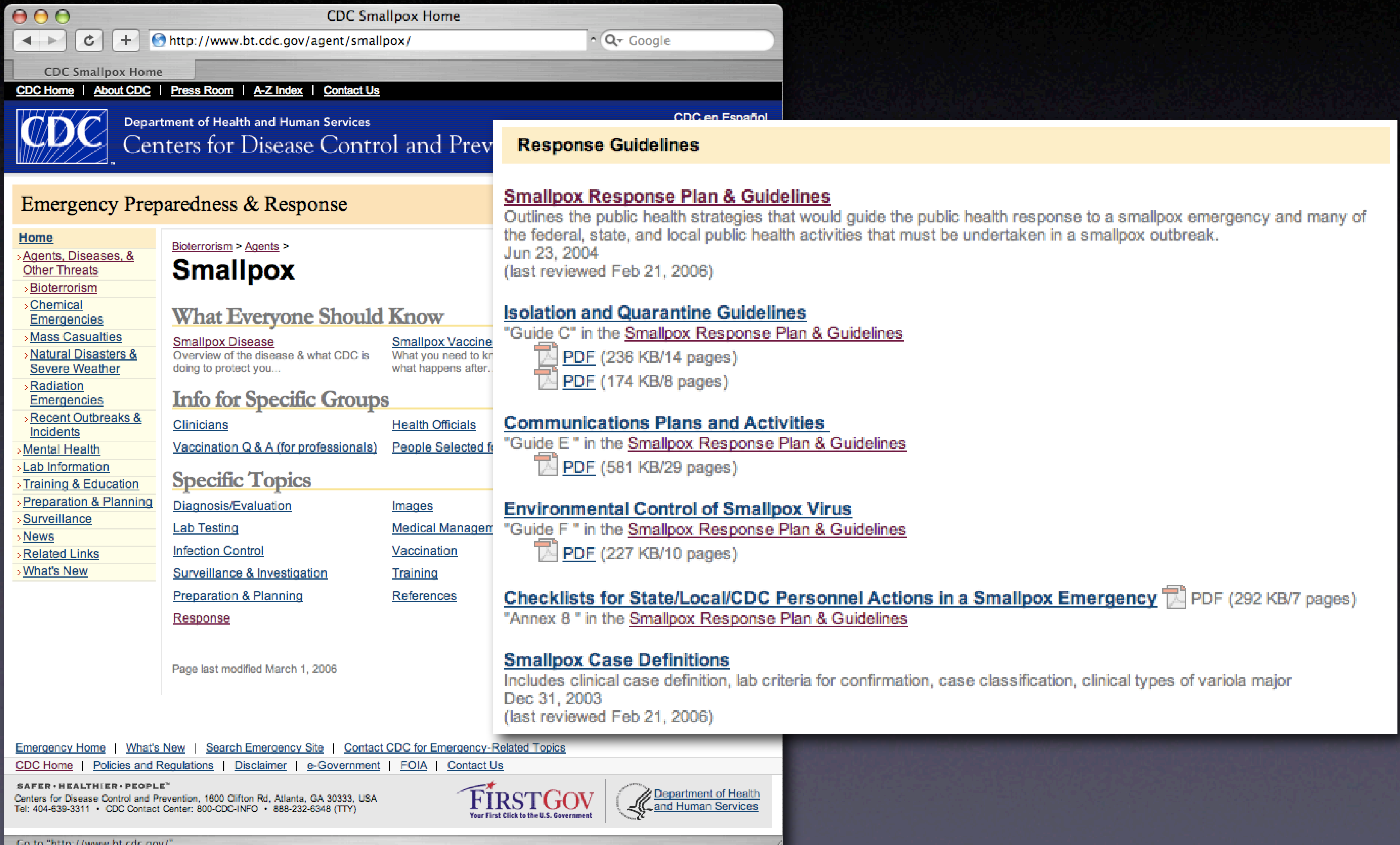
(Stochastic Model)



Covert smallpox attack on a generic city (attack site is university in city center)

EpiSimS
Los Alamos National Laboratory
Computer and Computational Sciences Division (CCS)

Centers for Disease Control



Concluding Remarks

Modeling can be a useful tool to identify a “credible” set of control options and to assess their relative effectiveness under certain conditions

Modeling can also suggest certain trigger thresholds, i.e. when to escalate responses

There are no “single most efficient” response strategies

In the event of an outbreak of an infectious disease:
Real-time data collection and modeling

How much information would be available in the early stages of an epidemic?
(potentially insufficient to “feed” the available models adequately)

References

- R. M. Anderson and R. M. May, *Infectious Diseases of Humans: Dynamics and Control,* Oxford University Press, 1991
- N. M. Ferguson et al., Planning for Smallpox Outbreaks, *Nature*, Vol. 425, October 2003, pp. 681-685
- S. Del Valle, H. Hethcote, J.M. Hyman, and C. Castillo-Chavez, Effects of Behavioral Changes in a Smallpox Attack model, *Mathematical Biosciences*, 195 (2005), pp. 228-251
- R. N. Nelson, *Mathematical Models of Smallpox Epidemic*, WWS556d Lecture Slides, 2003
- Centers for Disease Control and Prevention, http://www.bt.cdc.gov/agent/smallpox/