Re-introduction of Smallpox into Dynamic, Socially-Structured and Spatially-Distributed Populations

Evaluation of Possible Responses via Meta-Population Modeling

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Outline

- Biological features of smallpox that affect its transmission in human populations and in our models, which are …
- Capable of reproducing outbreaks following disparate historical re-introductions (Bangladesh, Stockholm, and Yugoslavia) …
- … and answering policy questions (e.g., those the ACIP recently addressed)
- Meta-population modeling to reproduce the spatio-temporal pattern following the last European importation, and to …
- Explore responses to hypothetical spatially-distributed attacks to ascertain if surveillance and containment will suffice
- Or pre-emptive vaccination of hospital-based HCWs, closing schools, and mass vaccination, also are necessary
- Practical questions about control via surveillance and containment, which is more complex than other strategies

Previous work …

• Duncan, SR, S Scott and CJ Duncan 1992. Time series analysis of oscillations in a model population: the effects of plague, pestilence and famine. *Journal of Theoretical Biology* 158(2):293-311

• Duncan, SR, S Scott and CJ Duncan 1993a. An hypothesis for the periodicity of smallpox epidemics as revealed by time series analysis. *Journal of Theoretical Biology* 160(2):231-48

• Duncan, SR, S Scott and CJ Duncan 1993b. The dynamics of smallpox epidemics in Britain, 1550-1800. *Demography* 1993(3):405-23

• Scott, S, and CJ Duncan 1993. Smallpox epidemics at Penrith in the 17th and 18th century. *Transactions of the Cumberland and Westmorland Antiquarian & Archaeological Society* 93:155-60

• Duncan, SR, S Scott and CJ Duncan 1994a. Smallpox epidemics in cities in Britain. *The Journal of Interdisciplinary History* 25(2):255-71

• Duncan, SR, S Scott and CJ Duncan 1994b. Modeling different smallpox epidemics in England. *Philosophical Transactions of the Royal Society of London B* 346:407-19
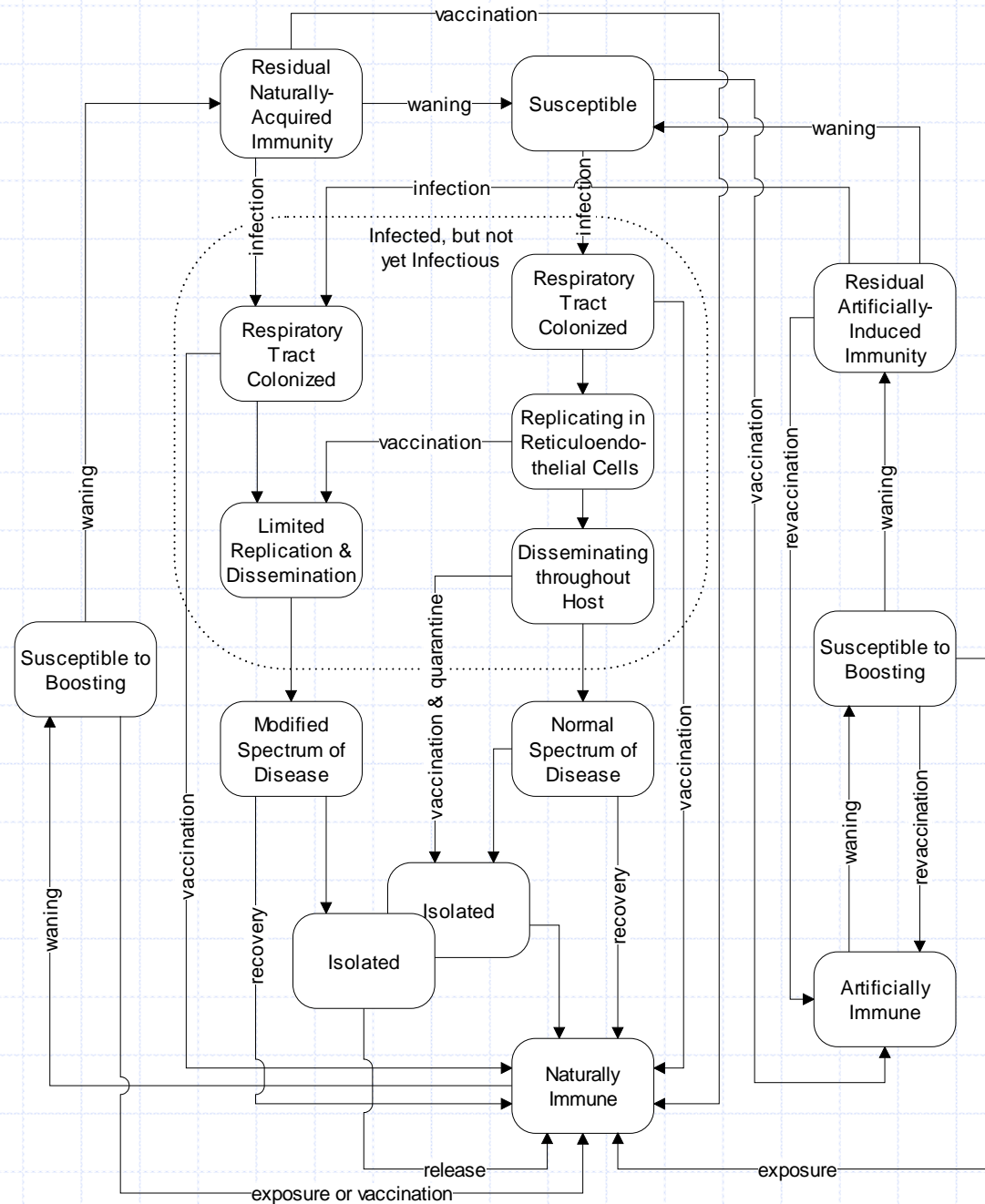
CDC Models (relative to antecedent forced SIR model)

1. Vaccination pre- and post-exposure, isolation of cases and quarantine of their contacts
2. Modification of disease spectrum via residual immunity or vaccination post-exposure
3. Distinction of artificially-induced and naturally-acquired immunity
4. Spatial mosaic of coupled sub-populations
5. Single population with gamma-distributed infection rates (for comparison with 3)
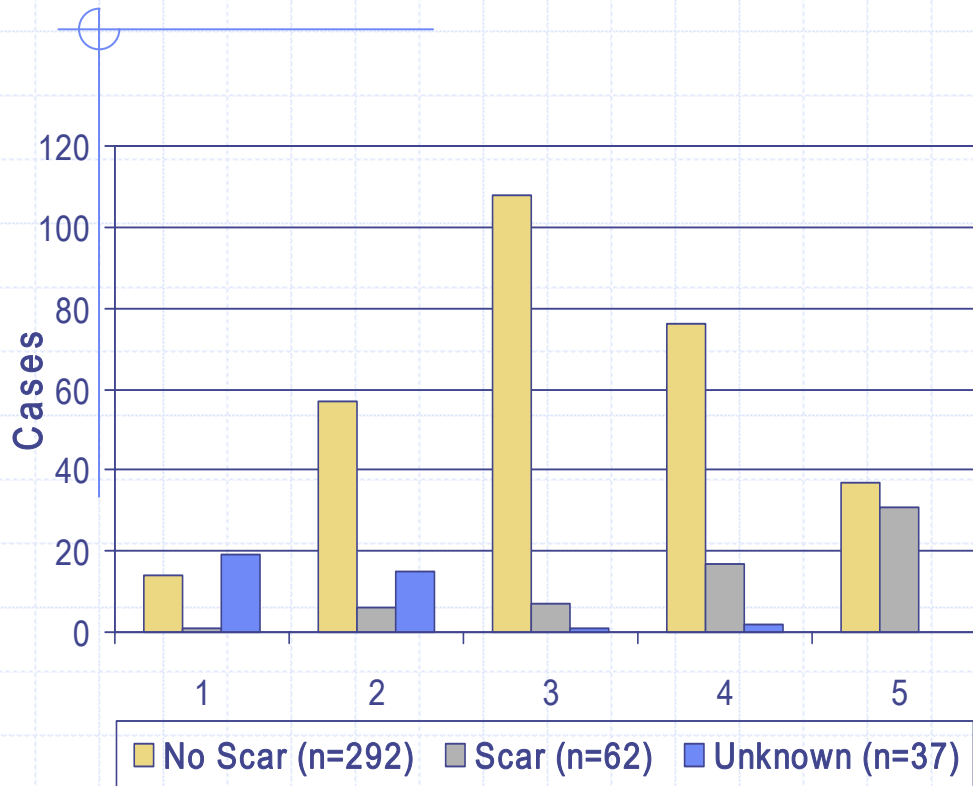6. Dynamic, age-structured meta-population with explicit contact surveillance

Why model the biological details?

- Smallpox was eradicated via a method – surveillance & containment – that took advantage of its unique biology, and which wouldn't work against polio or other vaccine-preventable diseases
- Besides HCW, the only people vaccinated via this method have already been exposed or have elevated risk of exposure by virtue of proximity to cases
- Smallpox was eliminated from the US via age-appropriate vaccinations that were re-emphasized following outbreaks, but some reactions to smallpox vaccine are life-threatening, …
- Can authorities rely on surveillance & containment, which proved so effective in Africa and Asia 30-plus years ago, to meet the challenges of bio-terrorism today?

Model 3

Residual Naturally-Acquired Immunity

vaccination

waning

Susceptible

waning

infection

infection

infection

Infected, but not yet Infectious

Respiratory Tract Colonized

Respiratory Tract Colonized

Residual Artificially-Induced Immunity

Replicating in Reticuloendo-thelial Cells

vaccination

waning

Limited Replication & Dissemination

Disseminating throughout Host

waning

Susceptible to Boosting

Susceptible to Boosting

Modified Spectrum of Disease

Normal Spectrum of Disease

vaccination

revaccination

vaccination & quarantine

vaccination

waning

revaccination

Isolated

Isolated

Artificially Immune

waning

recovery

recovery

Naturally Immune

recovery

release

exposure

exposure or vaccination

TM Mack, DB Thomas and MM Khan 1970. *Variola major* in West Pakistan. *JID* 122(6):479-88.

Lesion Density Classes:

- Hemorrhagic
1. Confluent (on face and arms)
2. Semi-confluent (on face or arms)
3. Moderate (100+ lesions on forearm)
4. Discrete (<100 lesions and 10+ lesions/100 cm^2 on forearm)
5. Sparse (<100 lesions and 1-9 lesions/100 cm^2 on forearm)
- Variola "sine eruptione"

Cases (y-axis: 0 to 120)

Legend: No Scar (n=292), Scar (n=62), Unknown (n=37)

Biological Features

- Broadly-overlapping normal and modified disease spectra for, respectively,
  - immunologically-naïve people, and …
  - ones with residual immunity or who have been vaccinated, but not soon enough post-exposure to avert disease
- Artificially-induced and naturally-acquired immunity that wane at different rates and can be boosted via exposure or vaccination
- Seasonally-varying infection rates
- Variably autonomous, spatially-distributed, age-structured, dynamic sub-populations

Reproductive Number

$$R = \sum_{\tau=0}^{D} \Pr(T \mid c, \tau) * C(\tau),$$

where t is time since onset and D duration of infectiousness, Pr(T|c,t) the probability of transmission given contact at time t, and C(t) the contact rate. What do we know about Pr(T|c,t) and C(t) vis-à-vis smallpox?

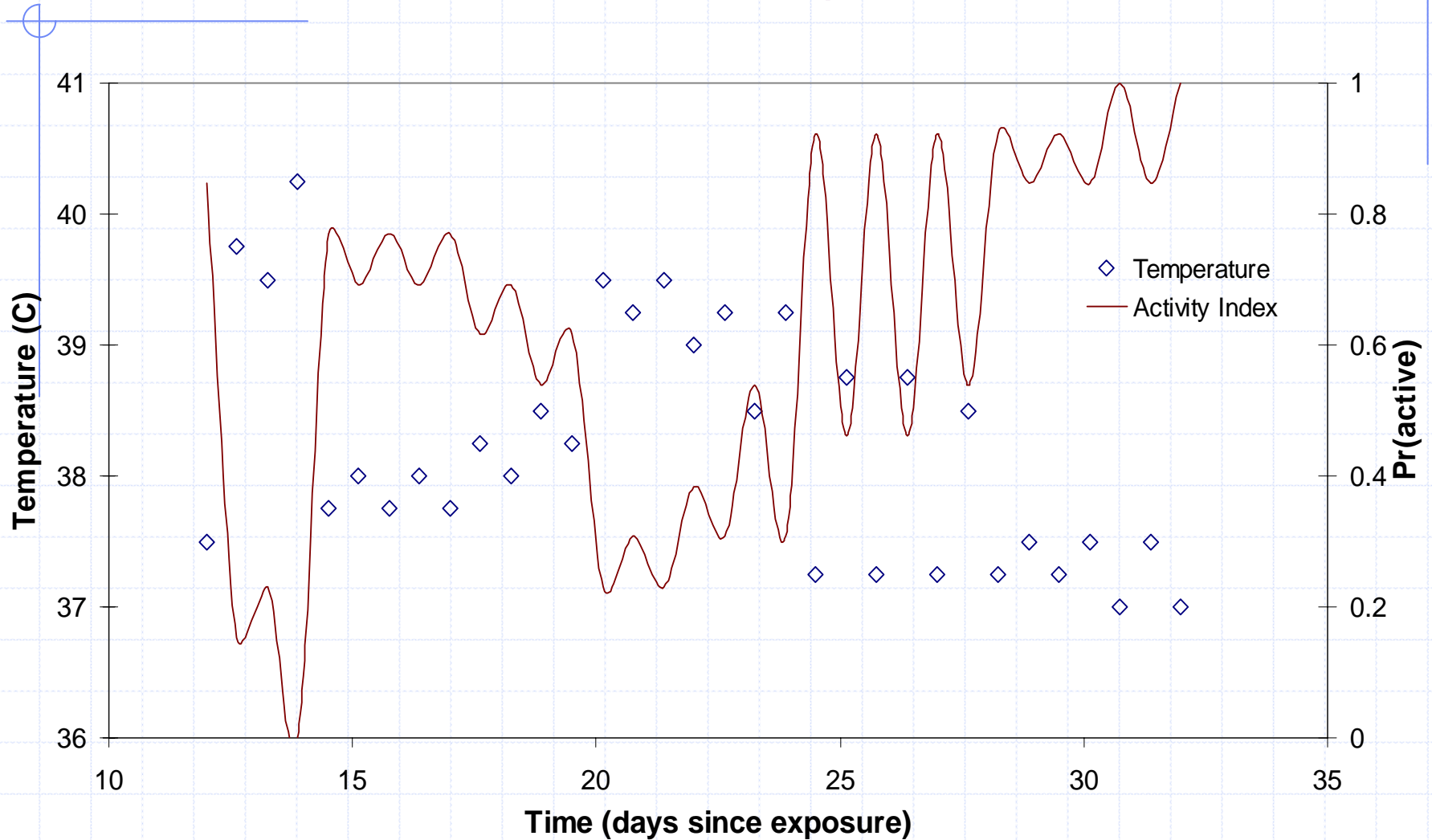# Oropharyngeal Secretions (Downie et al. 1961. Bull WHO 25:49-53)
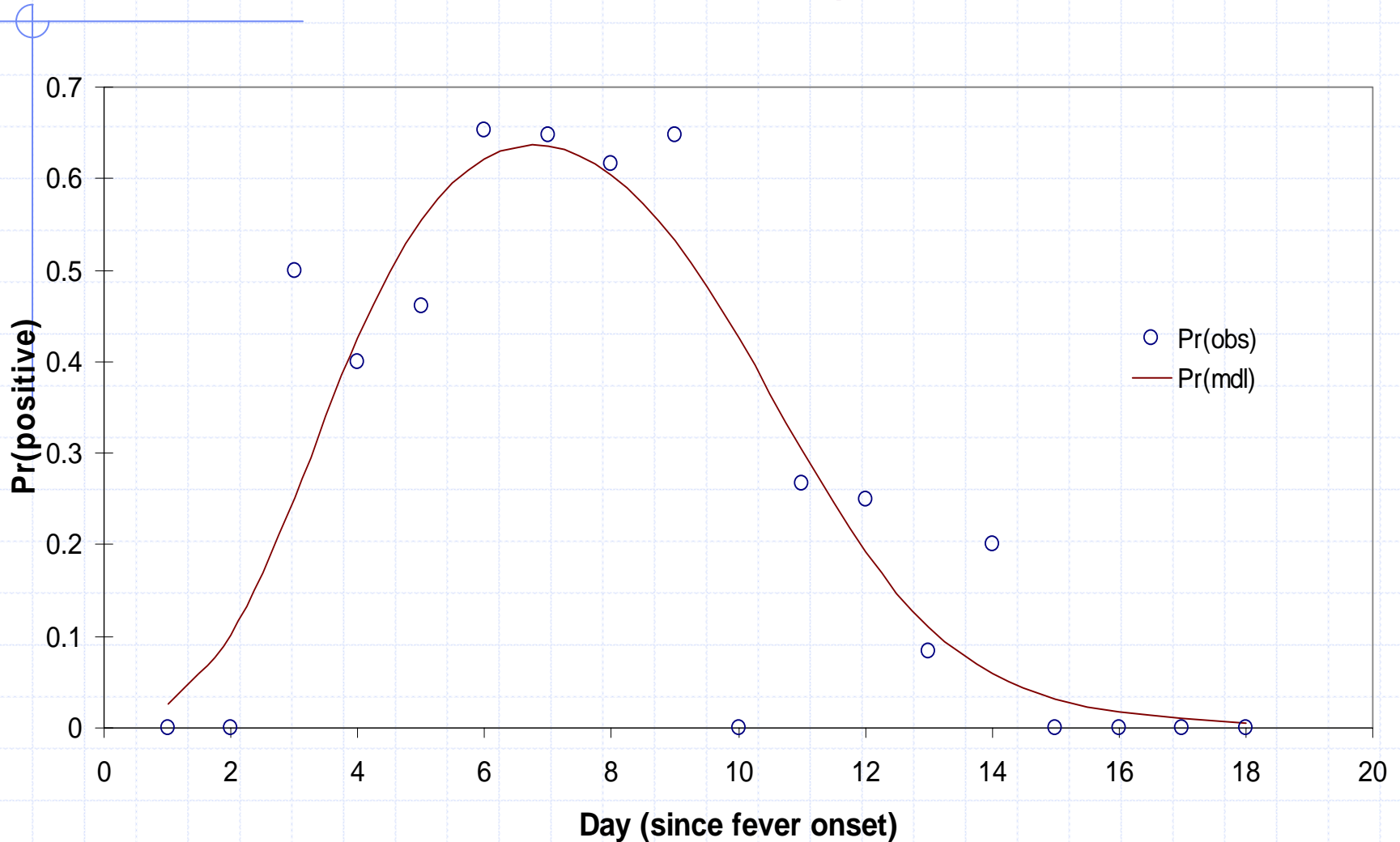
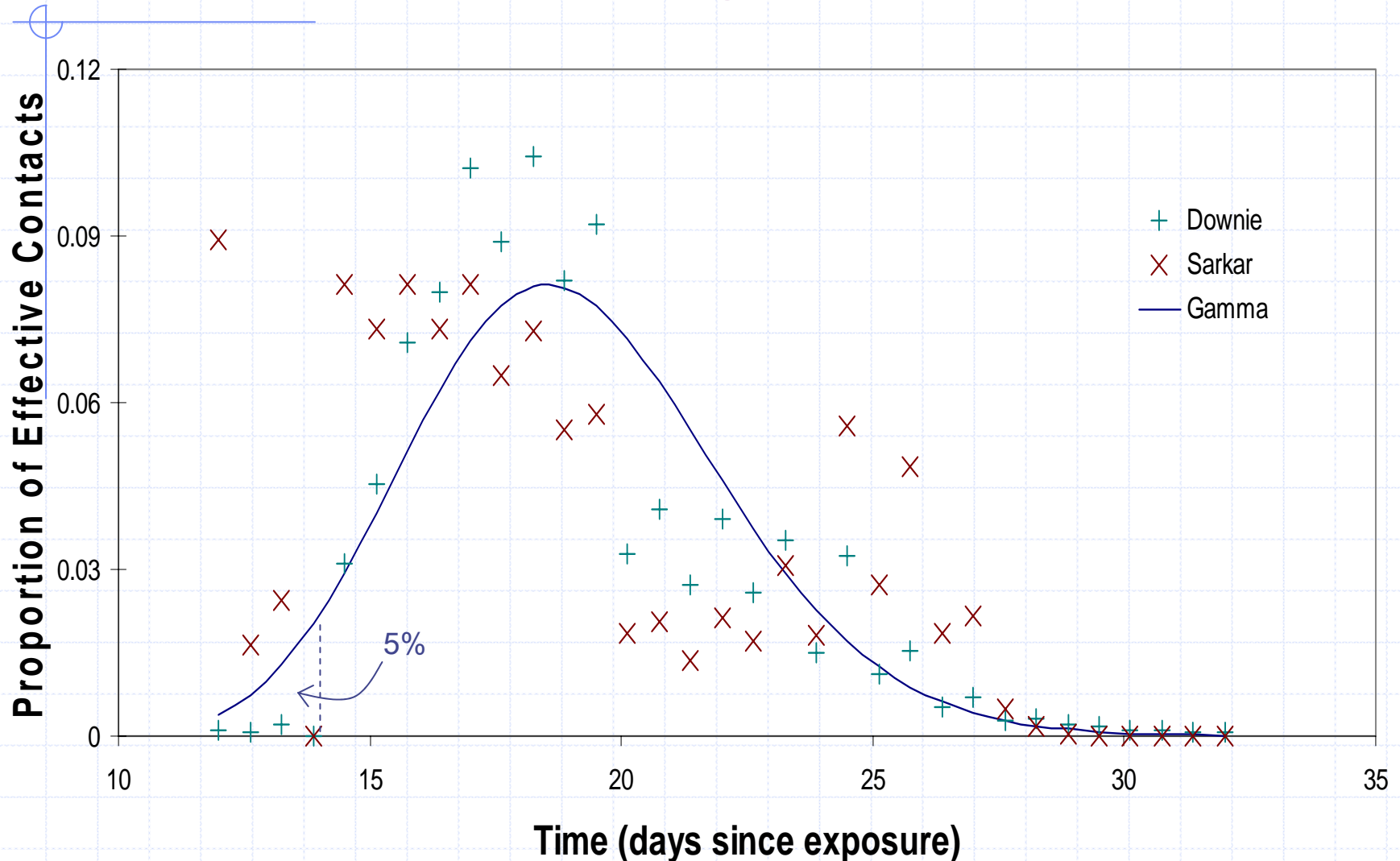# Oropharyngeal Secretions (Sarkar et al. 1973. Bull WHO 48:517-22)
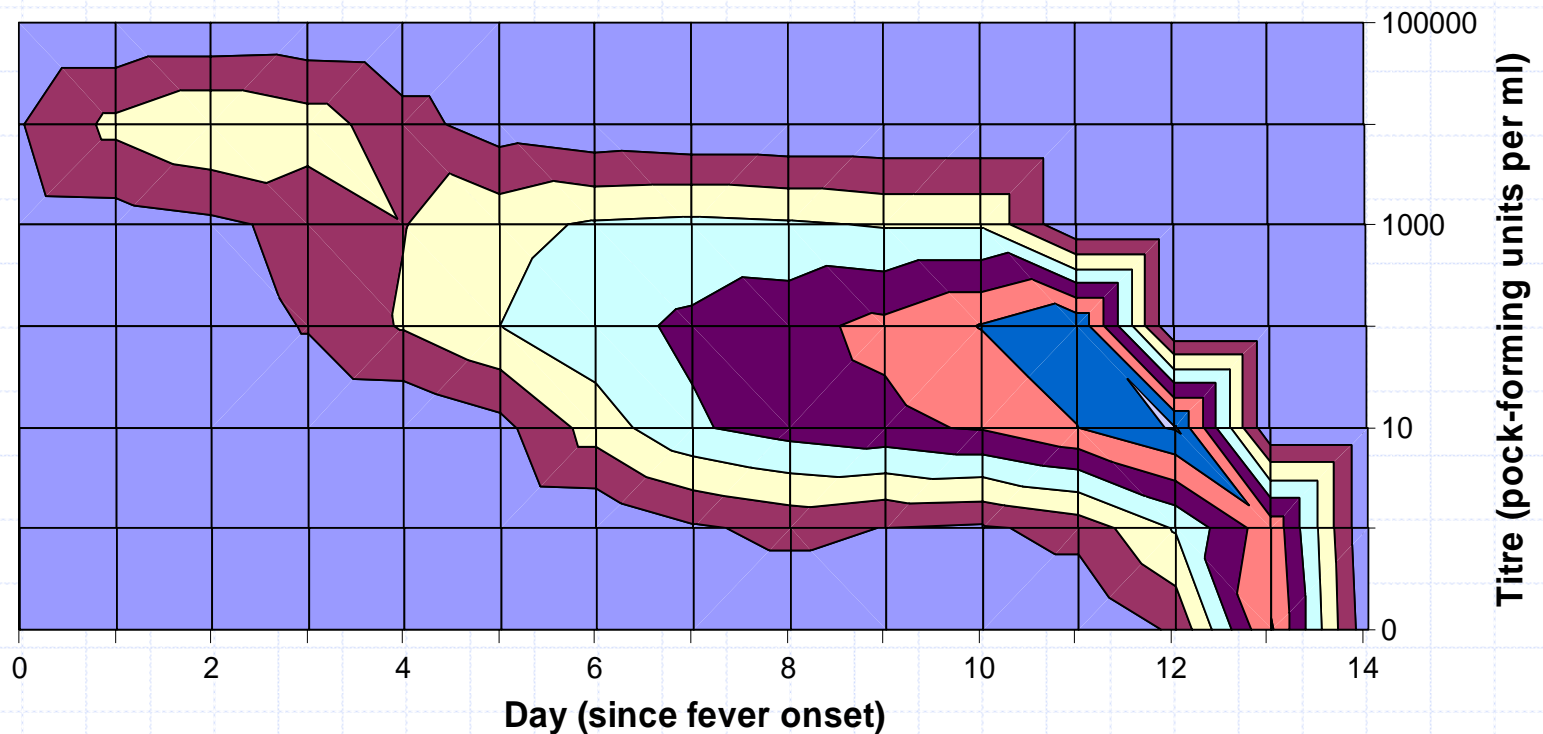
Surrogate for Contact Rate (Henderson et al. 1999. JAMA 281:2129)

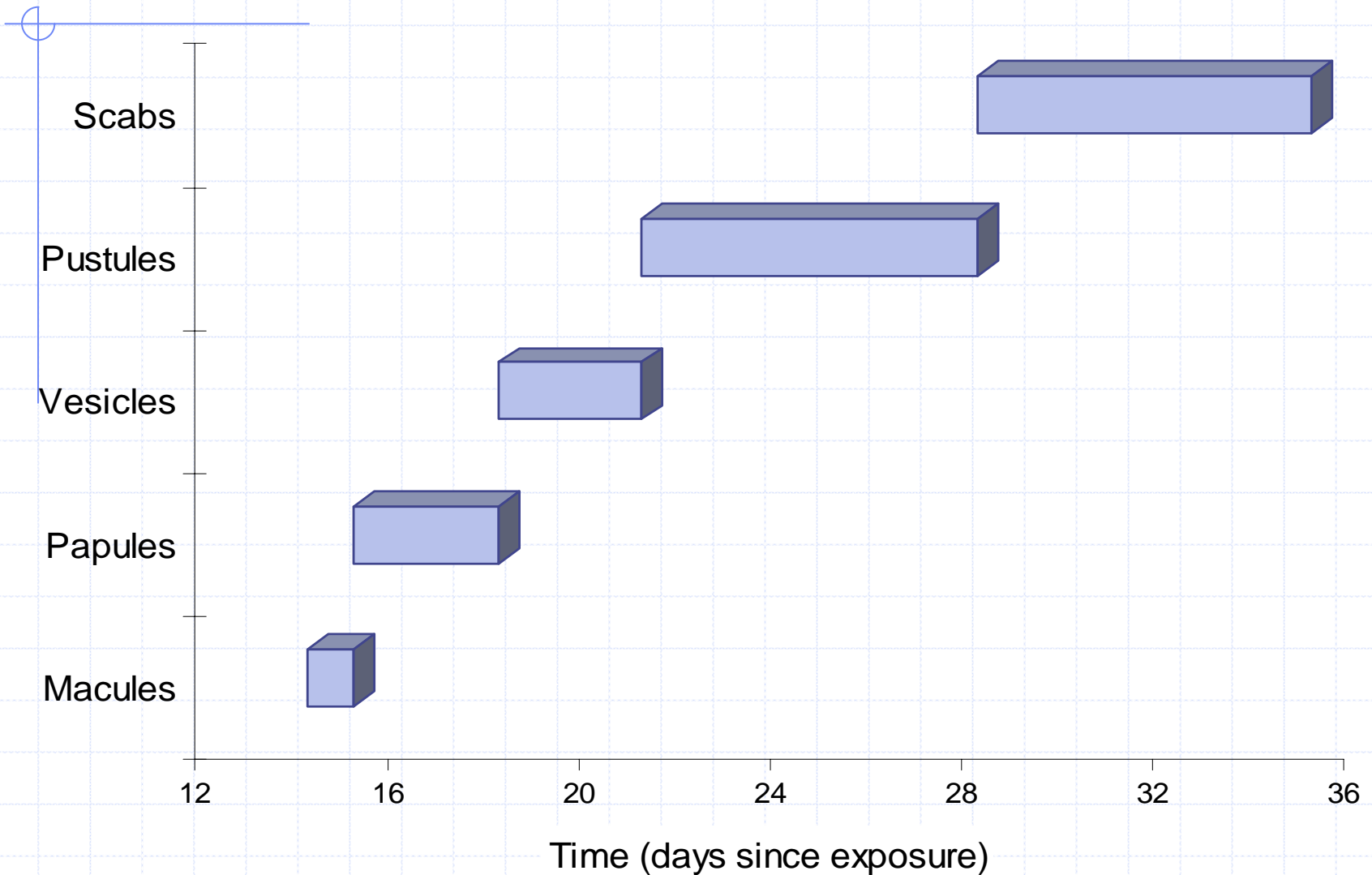# Infections during Illness

Another approach …

- Klaus Dietz (International Smallpox Modeling Meeting, 11/02) reported R_0=6.5, of which 0.32 was pre-rash, from the Faith Tabernacle outbreak in Abakaliki, Nigeria (Thompson, Foege)
- 0.32/6.5 = 4.9%

TM Mack, DB Thomas and MM Khan 1972. Epidemiology of smallpox in West Pakistan II. Determinants of intravillage spread other than acquired immunity. *Am J Epidemiol* 95(2):169-77.

- "The mean inter-generation interval of same compound cases closely approximates the incubation period calculated from … transient exposure[s]. This indicates that *prodromal contagion is infrequent*, and that … designation of rash appearance as … time … of first infectiousness is reasonable.
- "Transmission appeared to take place *in the home of the transmitter*, and *high relative risk* among older children was attributed to their *propensity for visiting* other compounds.
- "Although sociologic determinants of spread between compounds were demonstrated, the *most important identifiable determinant* … was the *severity of the transmitter* case.
- "Seasonal variation in incidence was mostly due to transmission within the village, and was attributed at least in part to *seasonal variation in the ambient survival time* of emitted virus."

NB: the italics are mine

Evolution of Rash

Scabs

Pustules

Vesicles

Papules

Macules

12   16   20   24   28   32   36

Time (days since exposure)

Why is smallpox's R_0 half that of measles in similar settings?

- People are infectious only after their lesions ulcerate, with those in the throat preceding skin by about 12 hours, …

- … by which time they are no longer mixing as usual (i.e., working, attending school, playing with children in the neighborhood, …)

- Disease is more likely to be transmitted person-to-person in households and hospitals than shopping malls, …

Strategy I

- Fit model 3 to historical re-introductions, adjusting only infection rates, to demonstrate that we could reproduce diverse phenomena (i.e., model structure and consensus biological parameters seem reasonable)

- Simulate re-introductions into hypothetical US cities via same model insofar as possible (i.e., initial conditions, responses, … differ), adjusting infection rates to vary R_0 over range inferred from historical observations

Stockholm, 1963

- Typical of several re-introductions to Europe from southern Asia (e.g., institutional, small [only 27 cases and 4 deaths], …)

- But vaccination status and other clinical details[†] permit assignment to disease spectra

- And the response, which extended far beyond the affected community, is informative

- 8,000 neighbors, and roughly 300,000 other residents were vaccinated, of whom 1,076 reported complications, 77 serious

[†]Thanks to Peter Merkle and John Bombardt for sharing the original articles

Smallpox in Stockholm
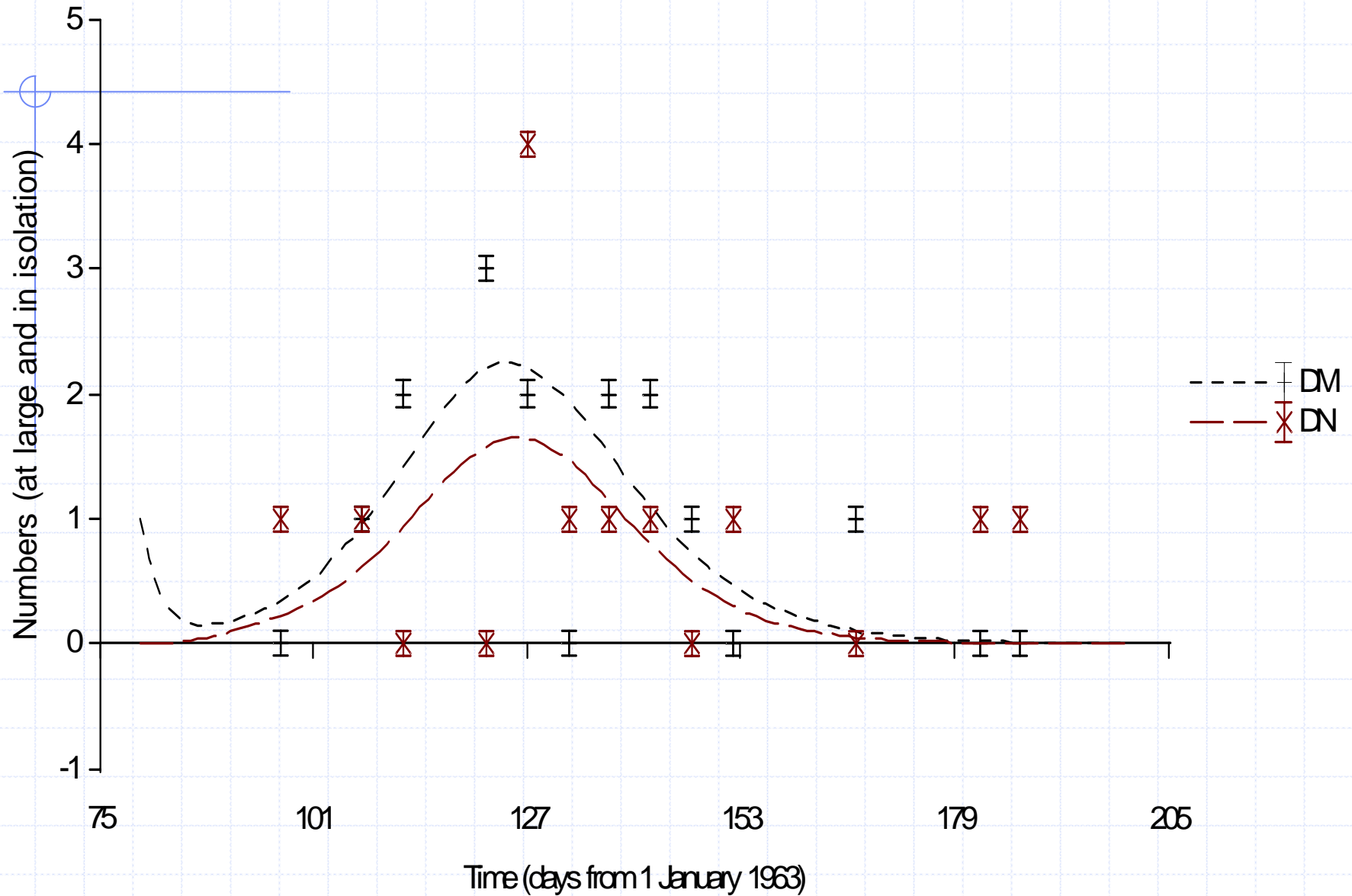
Bangladesh

- No cases of smallpox were reported during 1971, possibly indicating elimination

- But 10 millions fled to India during East Pakistan's struggle for independence

- Some were infected in 4 refugee camps and returned incubating or infectious

- Magnitude of the problem not immediately apparent by virtue of disrupted infrastructure
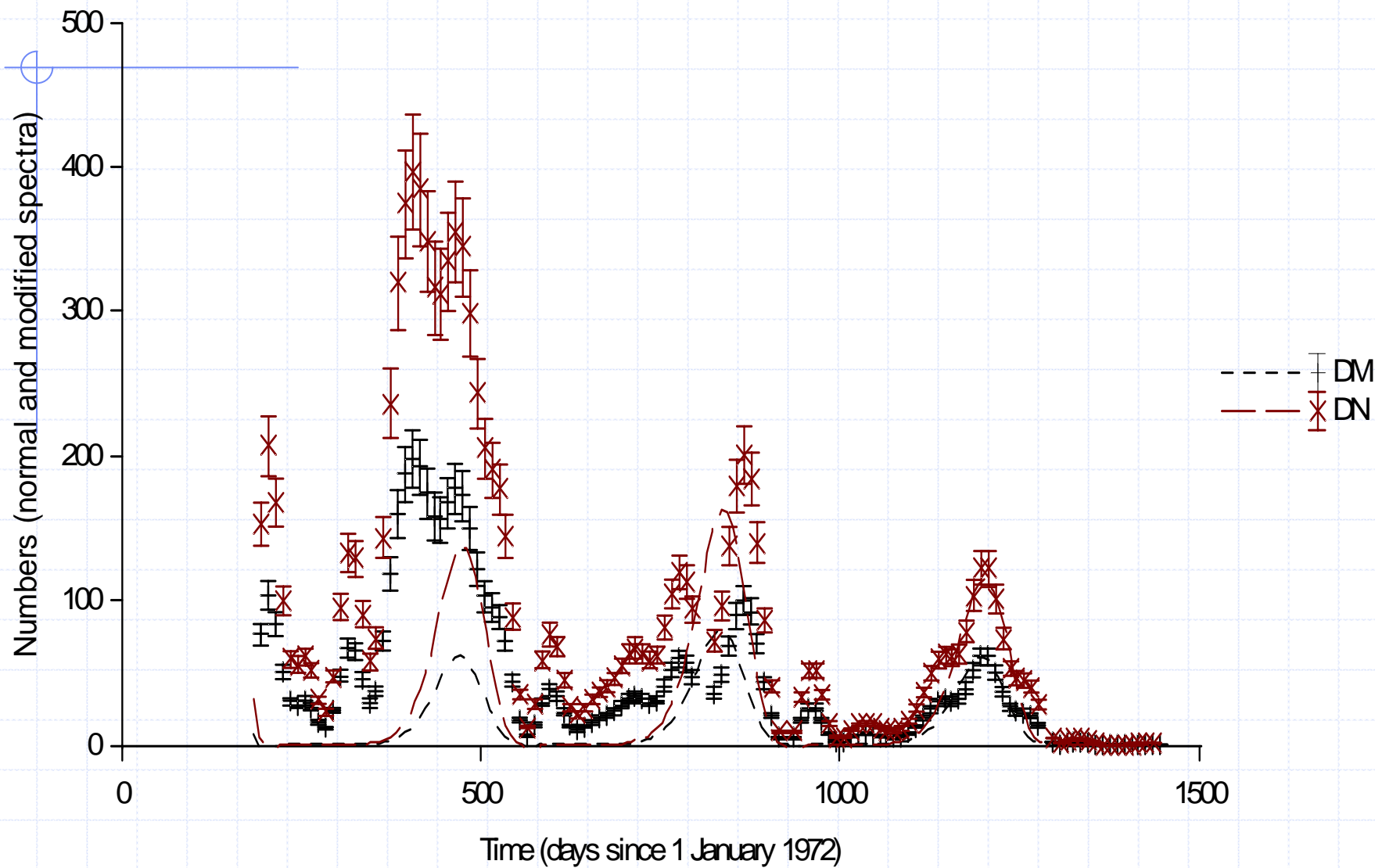
Smallpox in Bangladesh
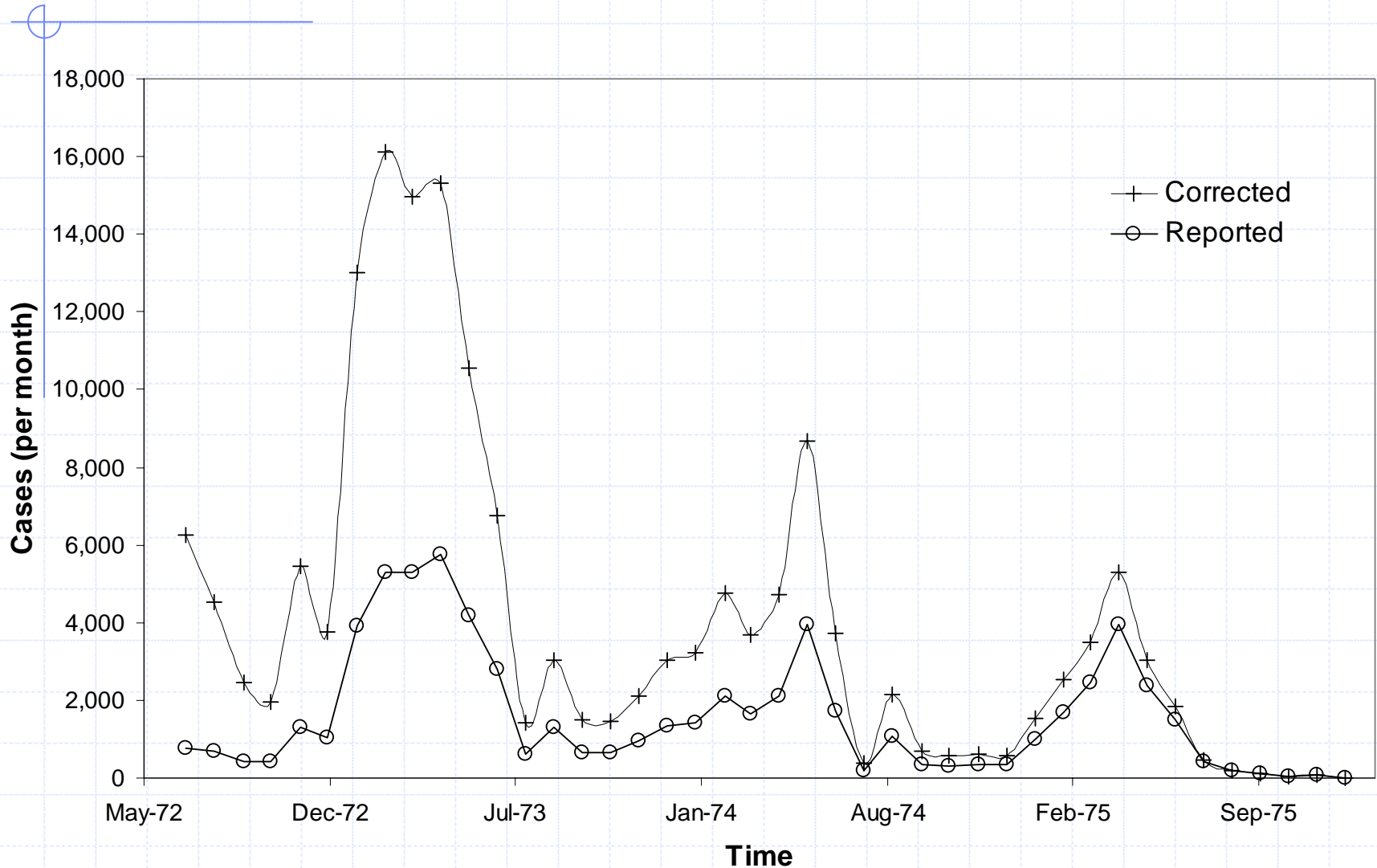
Smallpox Scar Survey, 1976

- Sampled age group within which known proportion of cases occurred

- Counted people with pockmarks, corrected for mortality due to disease, …

- … fading of pocks and all cause mortality during the intervening period

- Inflated by reciprocals of sampling and age group fractions

Smallpox in Bangladesh

Smallpox in Bangladesh

Reproductive Numbers

Time (days since 1 January 1972)

Ro
Rt
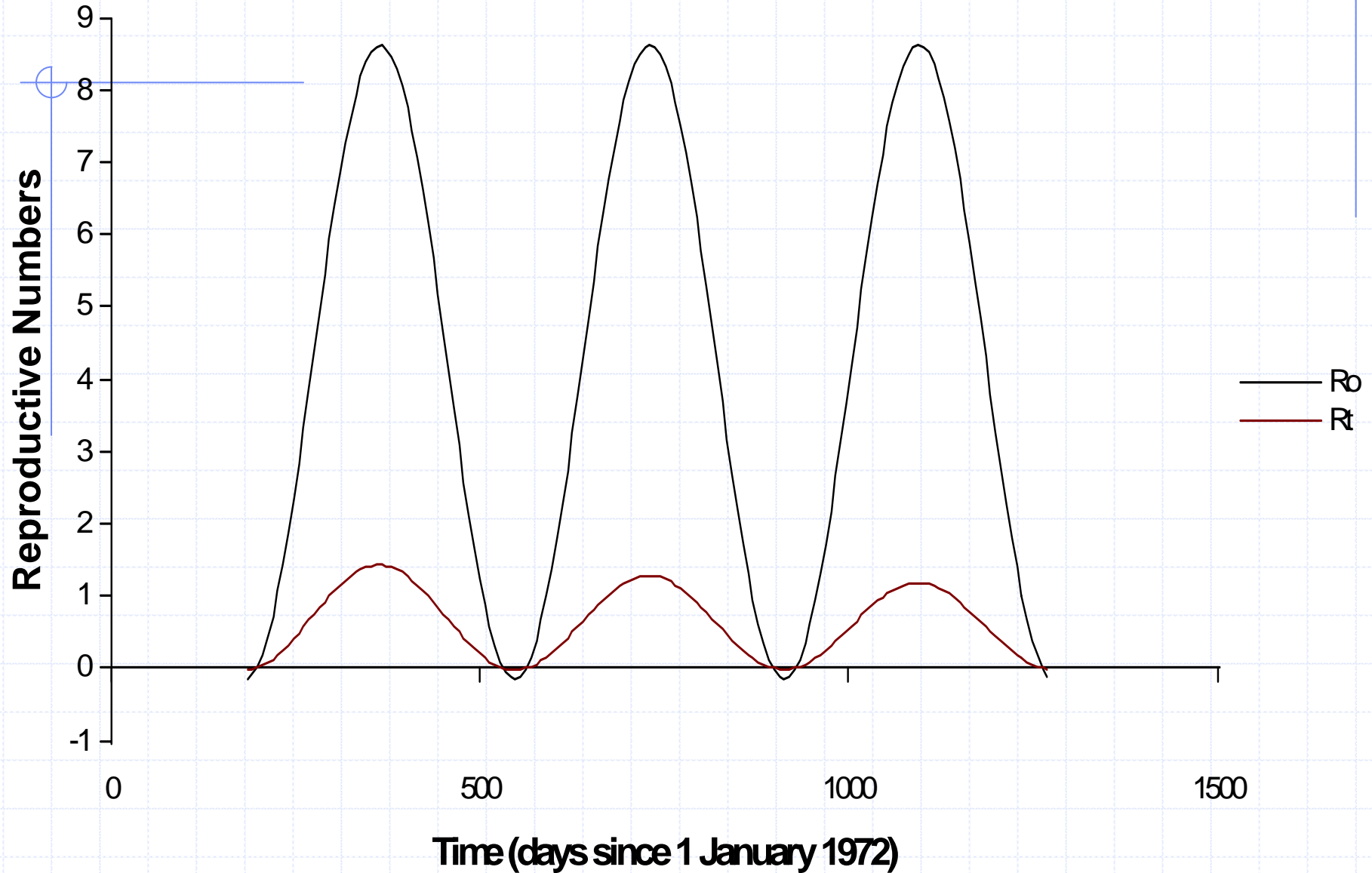
Seasonality

- Most attribute this to climatic factors (e.g., temperature and humidity) affecting survival of pathogens between hosts

- Others believe that it's due to social customs (e.g., harvest festivals), whose timing may however be due to climatic conditions

- Among Bill Foege's insights was that, because low season cases spawned multiple high season ones, efforts should focus …

Cannot observe R_0, but …

- R(t) is the ratio of the numbers of cases, N, in successive epidemic generations
- Epidemiologists estimated r from N(t) = N(0)exp(rt) during outbreaks in Bangladesh
- And observed that the doubling time, t = ln(2)/r, approximated the latent period
- Thus, on average, cases infected ~2 susceptible people during the season

Modeling Process (i.e., where we were when the ACIP met during June of 2002)

- Model is faithful to our collective understanding of smallpox transmission in human populations

- Fits historical datasets reasonably well with informed opinions about parameters that can no longer be estimated independently

- Able to contribute to policy debate, by simulating consequences of alternative decisions (i.e., experimenting)

To *prepare* for the possible re-introduction[†] of smallpox by terrorists, the ACIP was asked if …

1. … we should resume vaccination, terminated in the US almost a decade before smallpox was eradicated[‡]?
2. And if so, whom?
   - Specially-trained response teams ($\sim 10^3$)
   - Selected staff at designated[§] facilities ($\sim 10^4$)
   - First responders ($\sim 10^5$)
   - …

[†]   Smallpox was introduced to the New World from the Old (McNeill, WH 1977. *Plagues and Peoples*. Doubleday, New York, 340 pp.)

[‡]   the risk of adverse reactions was believed to outweigh the risk of importation

[§]   all versus designated regional facilities increases this to an estimated 510k

Practical Questions

- Should authorities vaccinate only face-to-face contacts or neighborhoods?
- What are the relative contributions of vaccinating and quarantining contacts?
- Is control sensitive enough to quarantine and isolation to justify enforcement?
- How inefficient can identifying/tracing become without jeopardizing control?
- How much delay in identifying cases and tracing their contacts is tolerable?

Strategy II

- Model 3 can assist policymakers in preparing for a possible terrorist attack
- And in guiding our response, insofar as it involves only face-to-face contacts. But if neighborhood (in a mathematical sense) vaccination is indicated, optimization requires a spatially heterogeneous model
- Model 4 is composed of multiple sub-populations, each with model 3's features

Model 4

m_{ij}
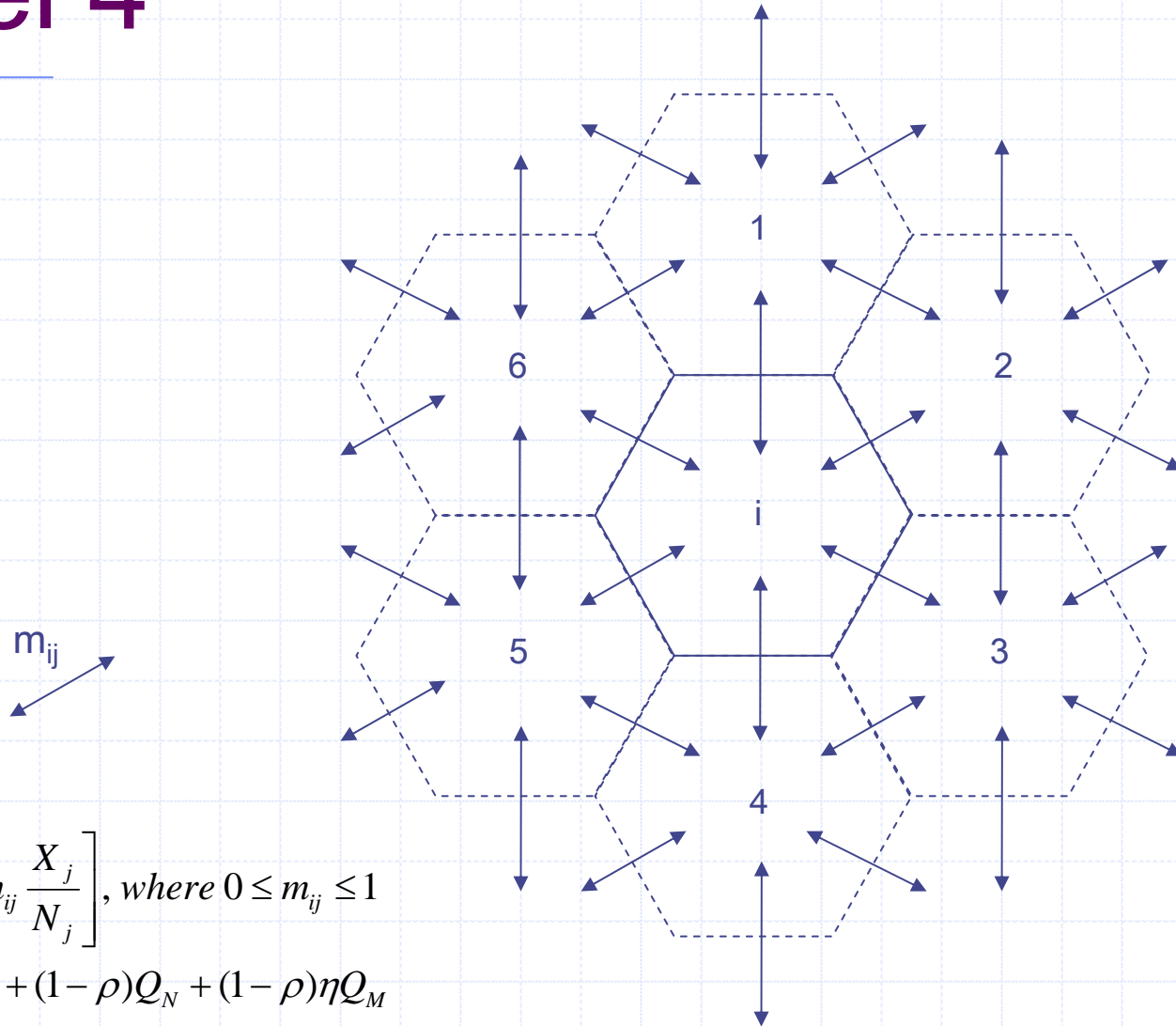
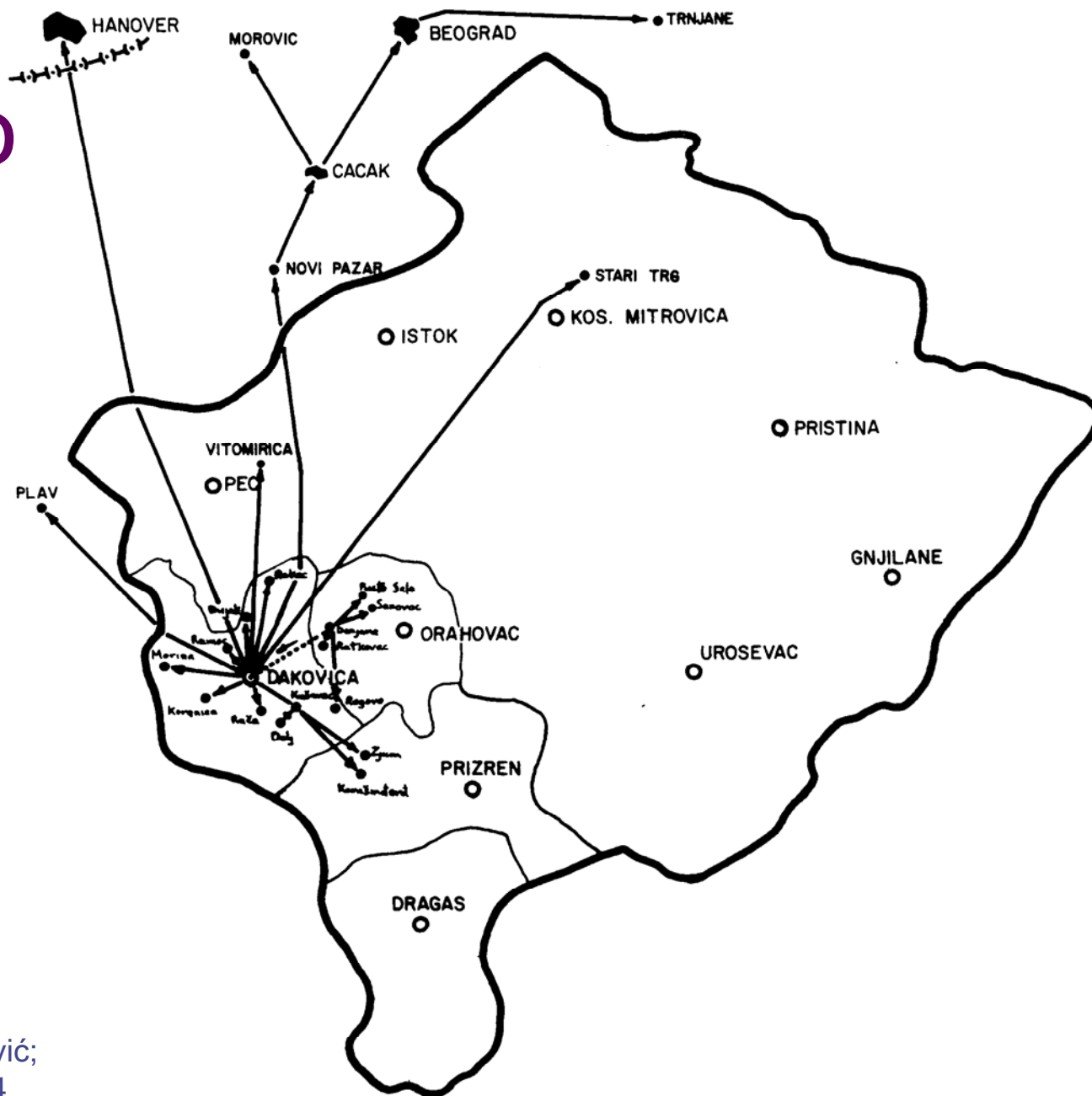$$\lambda_i = \beta\left[\frac{X_i}{N_i} + \sum_{j=1}^{6} m_{ij}\frac{X_j}{N_j}\right], where\ 0 \le m_{ij} \le 1$$

$$and\ X = D_N + \eta D_M + (1-\rho)Q_N + (1-\rho)\eta Q_M$$
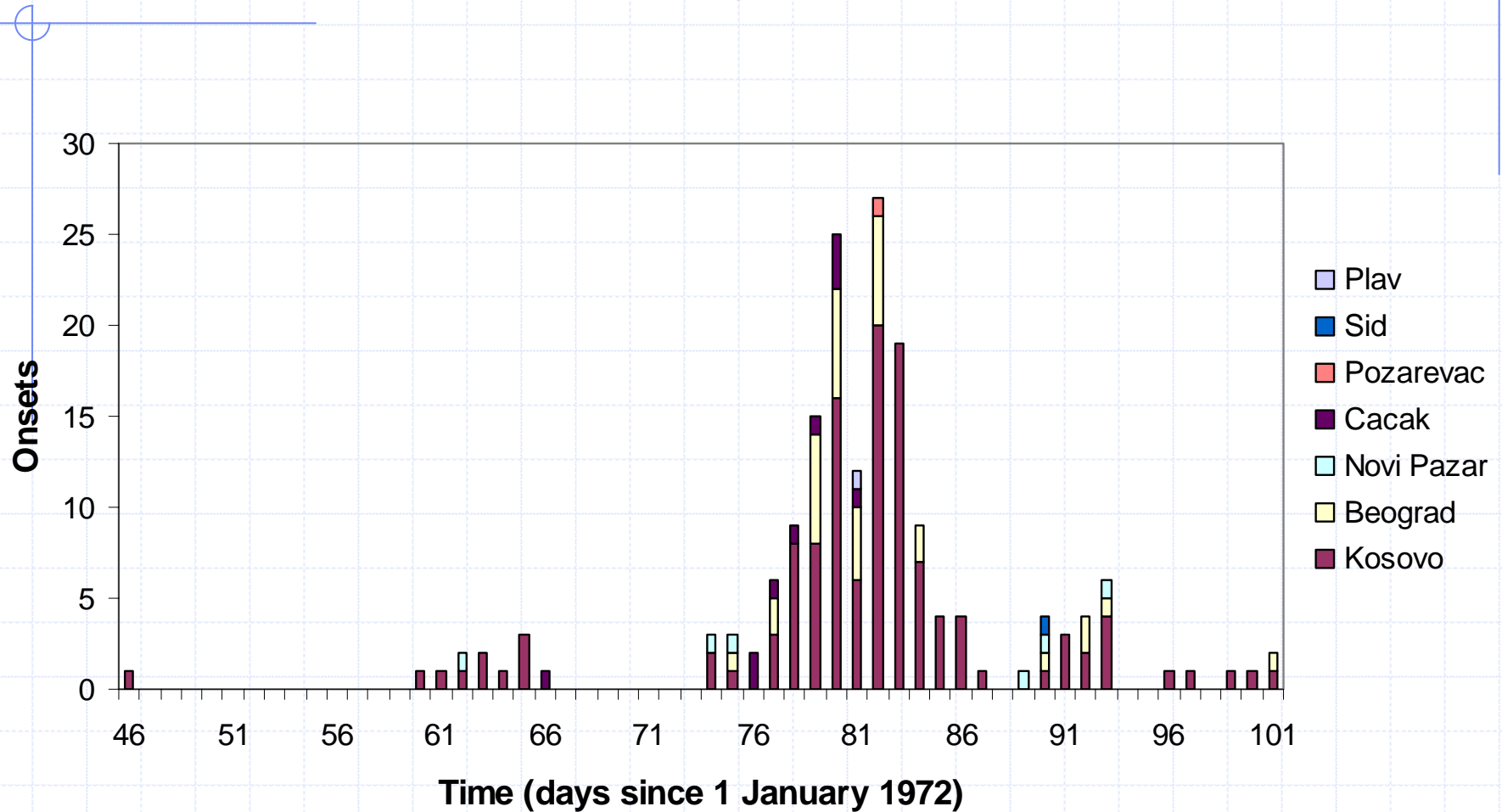
Neighborhoods …

- Houses,
- Multi-family dwellings
- Residential sub-divisions
- (Pre-)schools, workplaces
- Airports, bus and train stations
- Hospitals, shopping centers, malls
- Villages, towns, cities, …

i

Kosovo

Smallpox in Yugoslavia

Can our meta-population model reproduce this spatio-temporal pattern following the 1972 re-introduction to Kosovo?

- Modeling all cases as though normal spectrum in the two semi-autonomous provinces, Belgrade, three other Serbian municipalities and in Montenegro

- Trying to distinguish clinical course, outcome, and municipality (5 in Kosovo, 12 in greater Serbia [9 of which comprise Belgrade] and 1 each in Montenegro and Voivodina), whose interventions also differed

- Amra Uzicanin, a Bosnian physician who was re-vaccinated as a child during this crisis, is working with us; Mike Lane led the US response

Normal Spectrum Disease
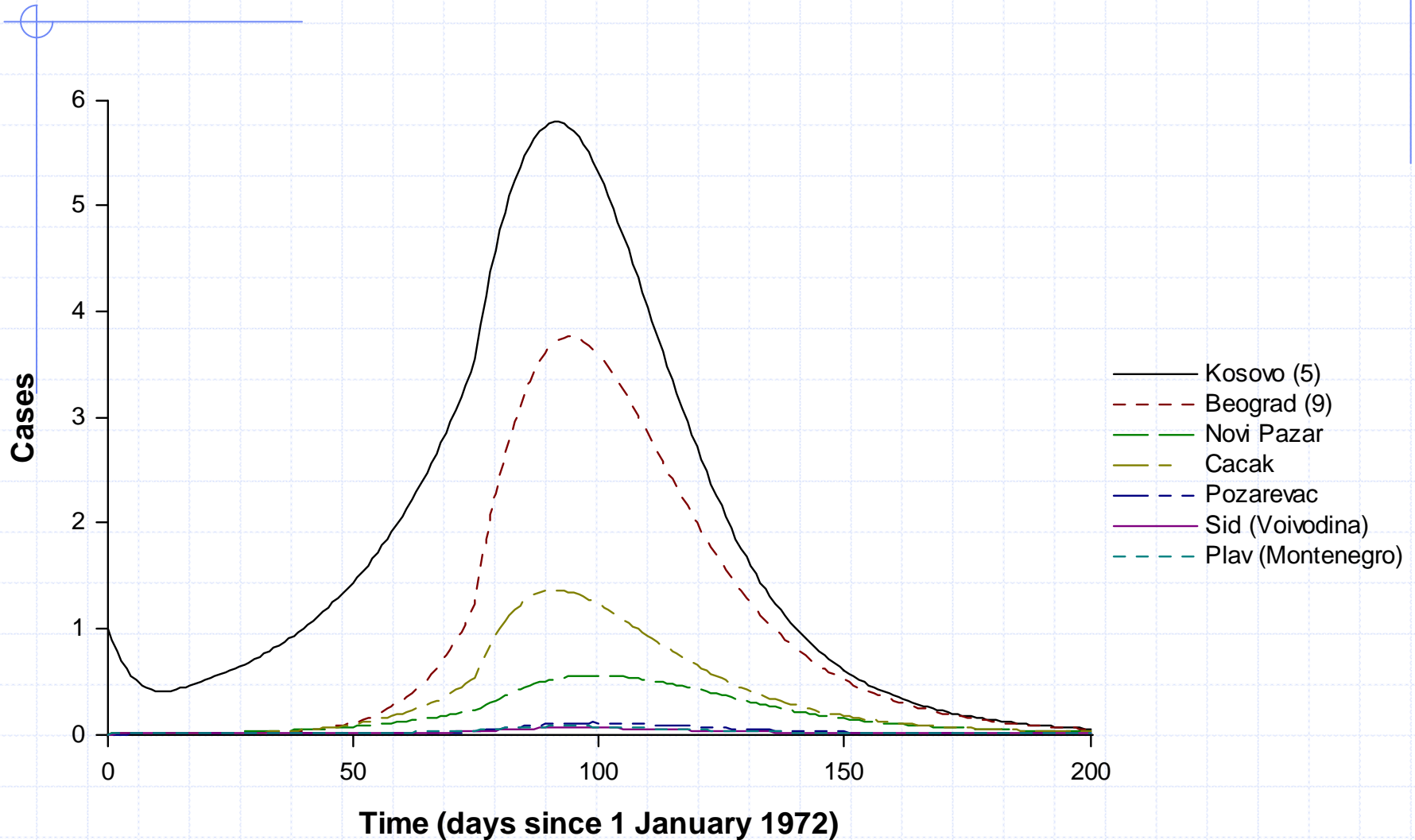
Yugoslavia, 1972
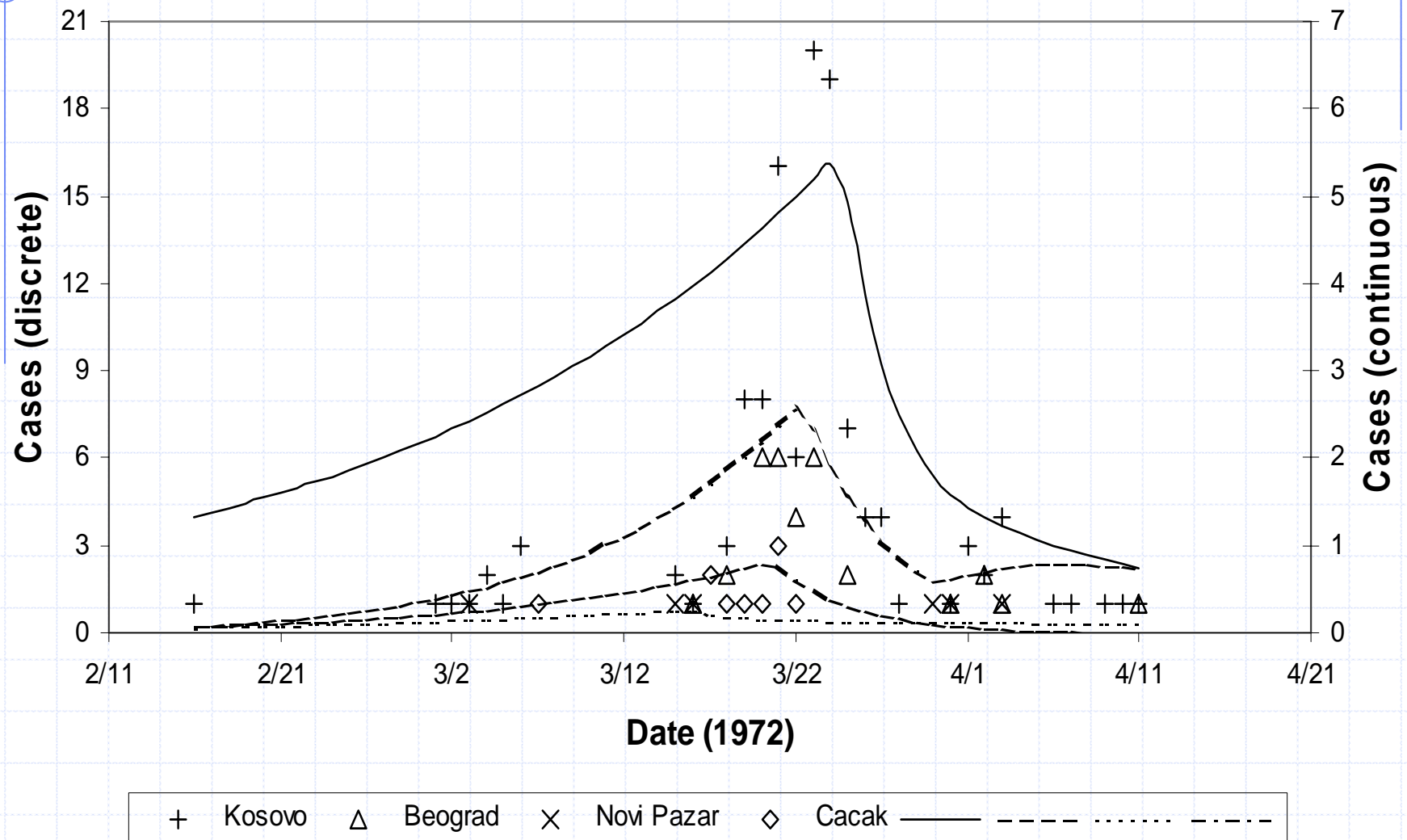
b_{ii}	m_{ij}	Kosovo	Beograd	Novi Pazar	Cacak	Pozarevac	Sid (Voivodina)	Plav (Montenegro)
0.85	Kosovo	1	0	0	0	0	0	0
0.83	Beograd	0	1	0	0.25	0	0	0
0.68	Novi Pazar	0.13	0	1	0	0	0	0
0.86	Cacak	0	0	0.68	1	0	0	0
0.13	Pozarevac	0	0.14	0	0	1	0	0
0.23	Sid (Voivodina)	0	0	0	0.71	0	1	0
0.47	Plav (Montenegro)	0.05	0	0	0	0	0	1

DHHS Working Group's Re-introduction Scenarios

- 10 to 10K infected via aerosol in settings frequented by people differing in age, and hence residual immunity

- Populations from 6K to 1.6M w/age-distributions from 2000 census, but differently allocated among …

- … commercial districts, hospitals (mostly adults), schools (mostly children), and residential neighborhoods (mixed)
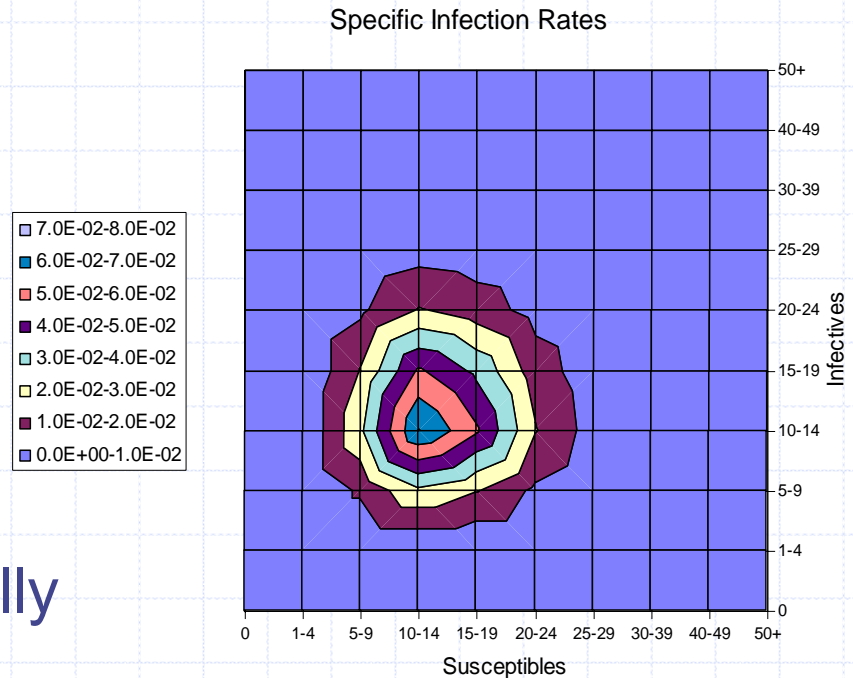
Biological Parameters

- Residence times
  - en route to normal- and modified-spectra disease: colonization, replication, dissemination, and infectious (7)
  - artificially-induced and naturally-acquired immunity: full, boost-able and residual (6)
- Vaccine efficacies – boosting of immunity, prevention and modification of disease
- Infection rate – mean (sub-populations can differ) and harmonic coefficients, diminution, if any, due to modification of disease
- Demographic – age-specific proportions female, birth and death rates, disease-induced as well as due to other causes
- Mixing – among age groups within sub-populations and among sub-populations, extent to which ill people, family members and others stay home

Models whose details are fabricated are meretricious (… in and gospel out)

- Age groups mix similarly in all sub-populations, which is tantamount to asserting that differences observed between schools and workplaces, e.g., are due to their age-distributions (some evidence for this)

- Age-specific mixing loosely based on experience with other VPDs, which may be inappropriate – insofar as they are largely transmitted during the prodrome and people may mix as usual during outbreaks, whereas only about 5% of smallpox infections occur then and mixing likely changed during outbreaks – as it almost certainly would following terrorist attacks

- Mixing among sub-populations is guesstimated, but could in principle be measured, were we modeling real entities. I know too little about spatial units to make up unique age-specific mixing parameters

Age-specific mixing

- Generalized mixing matrix has a gamma-distributed diagonal

- Mixing is assortative, but disposition to mix with others the same age …

- … decays exponentially with age

Specific Infection Rates

Legend:
- 7.0E-02-8.0E-02
- 6.0E-02-7.0E-02
- 5.0E-02-6.0E-02
- 4.0E-02-5.0E-02
- 3.0E-02-4.0E-02
- 2.0E-02-3.0E-02
- 1.0E-02-2.0E-02
- 0.0E+00-1.0E-02

Infectives (y-axis): 0, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-39, 40-49, 50+

Susceptibles (x-axis): 0, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-39, 40-49, 50+

Residual Immunity, US

- Ever vaccinated from 1971 United States Immunization Survey
- If artificially-induced immunity decays exponentially …
- … with a mean of 30 ± 5 years, about 30% remains

Age	Proportion
<1	0.14
1-4	0.62
5-19	0.94
20-64	0.91
65+	0.74

Possible Responses

Surveillance & containment:

- 90% of cases is identified
- 75% of their contacts, and everyone in hospitals receiving patients are vaccinated

Evaluate:

1. Pre-emptively …
   a. vaccinating 10 or 30% of HCW
   b. (re-vaccinating 25 and 50% of people w/residual artificially-induced immunity)
2. After 1st case is detected (day 20), …
   a. (vaccinating all HCW in entire town or city)
   b. vaccinating in schools and workplaces
   c. closing schools for 14 days in affected neighborhoods
   d. MV of 0, 25, 50 and 80% of population w/in 10 days
3. Beginning a week later (day 27), MV …

Programming the Scenarios

- Initial conditions:
  - o residual artificially-induced immunity
  - o pre-emptive vaccination of 10 or 30% of HCW
  - o infection of 10 adults in a restaurant, 500 people of all ages in a movie theater, and 10,000 in a sports arena
- Programming:
  - o vaccinate 95% of hospital-based HCW within 2 days of first diagnosis
  - o find 90% of cases and 75% of their contacts; isolate cases at home or in hospital, normal- more effectively than modified-spectrum; vaccinate and observe contacts
  - o vaccinate 40 or 80% of those susceptible or partially immune, save infants, within 10 days of detection
- Dynamic links:
  - o simulate school closing by setting m_{ij} involving schools to zero temporarily
  - o simulate staying home by multiplying m_{ij} involving neighborhoods by 1-proportion infected

Initial Public Health Response

- Mean incubation period (exposure to onset of symptoms) is 11.5 days
- By fever plus 7 days (vesicular rash), all normal- and 75% of modified-spectrum cases are recognized in 1st wave
- Remaining 25% of modified-spectrum cases recognized by day fever plus 10
- Recognition of subsequent cases depends …

Incubation Period (Fenner et al.)
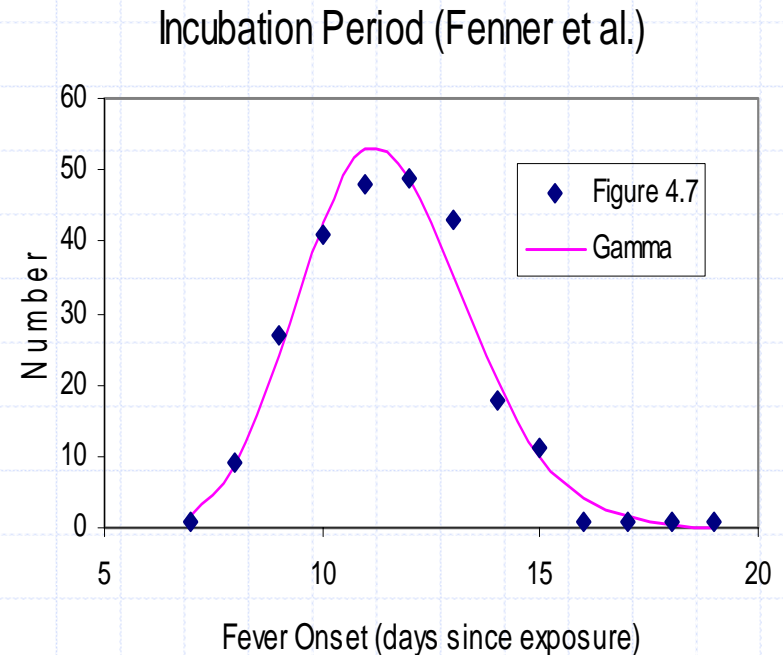
Subsequent PH Response

- Subsequently-identified cases are diagnosed
  - ○ when fever occurs (mean 11.5 days post-exposure) or after the papular rash appears (fever + 6 days), …
  - ○ … depending on whether they are known contacts (i.e., under surveillance) or not
- CDC models don't track individuals, but if 0.75*0.9 of contacts were found, this would be day 0.675*11.5 + 0.325*17.5 ° 13.45 on average

Individual Responses

- 95% of normal- and 50% of modified-spectrum cases are isolated (in home or hospital) by day 13, and remainder are isolated by day 15
- Simulate staying home by multiplying the mixing of age k in residential neighborhood i with other sub-populations
- … by 1-weighted proportion (those with modified- count 1/3 those with normal-spectrum disease) age k who are ill

Hospitalized
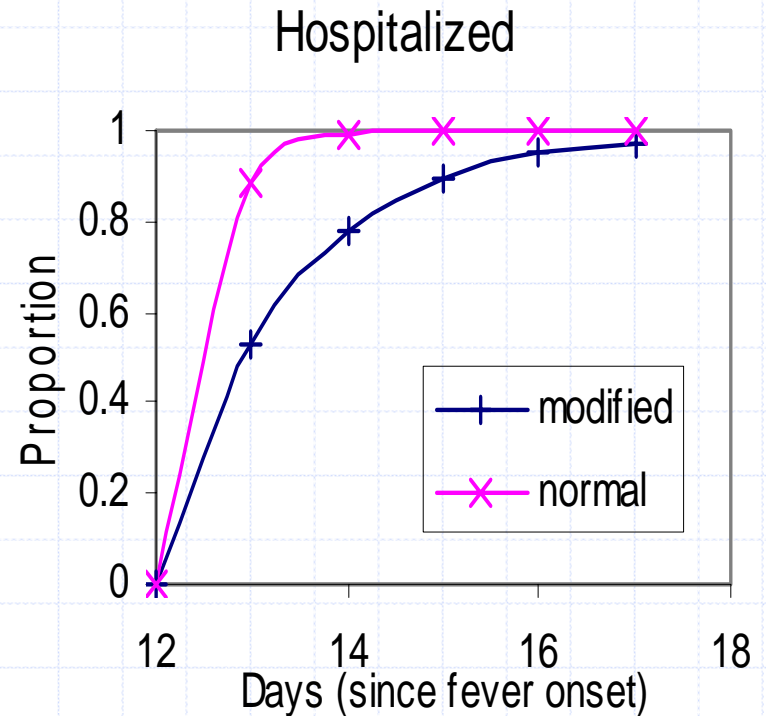
Community Structures

Age	Pr(2000)
<1	0.014
1-14	0.199
15-19	0.072
20-29	0.132
30-54	0.369
55+	0.214

Sub-Pop	N	P-T
Residential	2-18	0.67
Low/Mid Schools	2-6	0.07
High Sch	1-3	0.03
Business	1-4	0.2
Hospital	1-6	0.03

Winter R_0

Weighted average ≈ 4

- Residential neighborhoods ≈ 4
- Schools ≈ 6
- Hospital ≈ 8 (estimate ~ 7 in Kosovo, Beograd and Cacak, where hospitals were major sites of transmission)
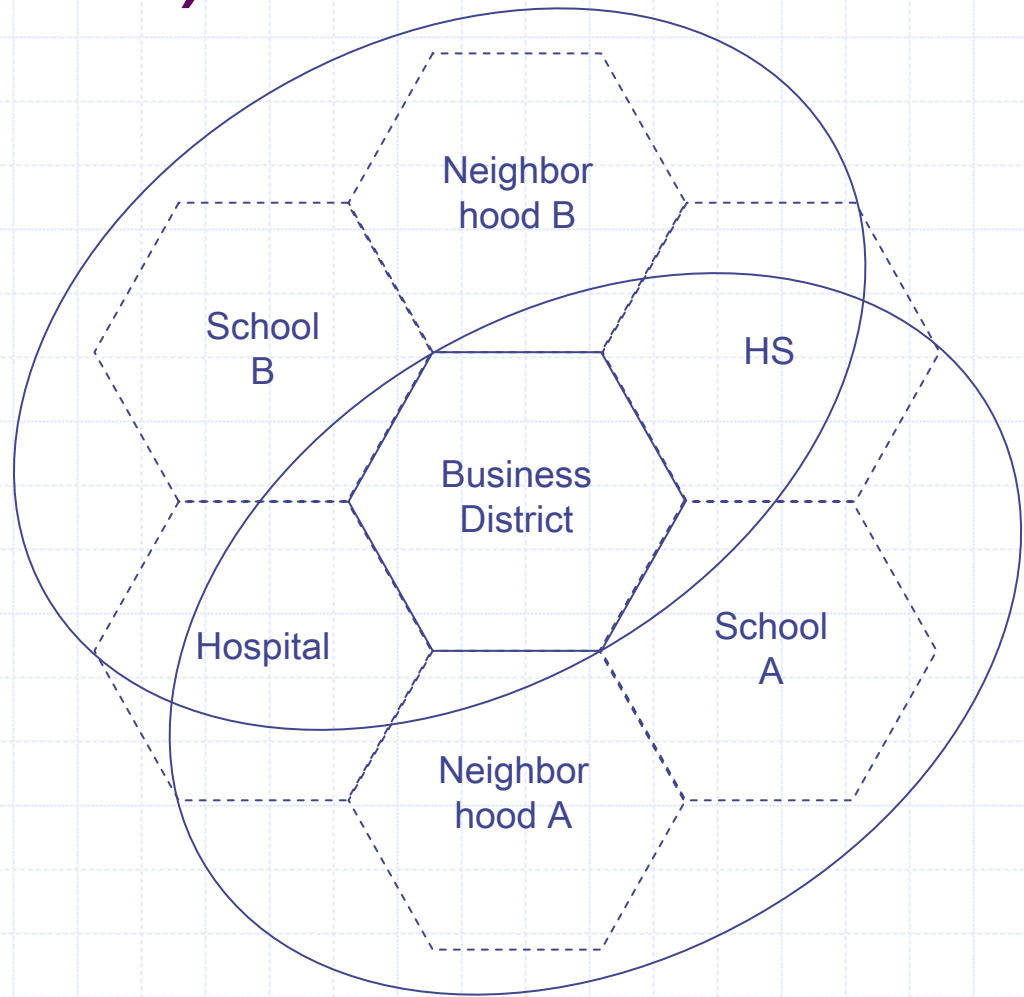- Business district(s) ≈ 2

Please note that …

- Given the other biological parameters, fitting this model to historical outbreaks by adjusting the infection rate, **b**, and calculating R_0 …

- … is equivalent mathematically to setting the harmonic coefficients, $\mathbf{b}_1$ and $\mathbf{b}_2$, to zero, and adjusting the mean, $\mathbf{b}_0$, to attain some R_0

- Because …

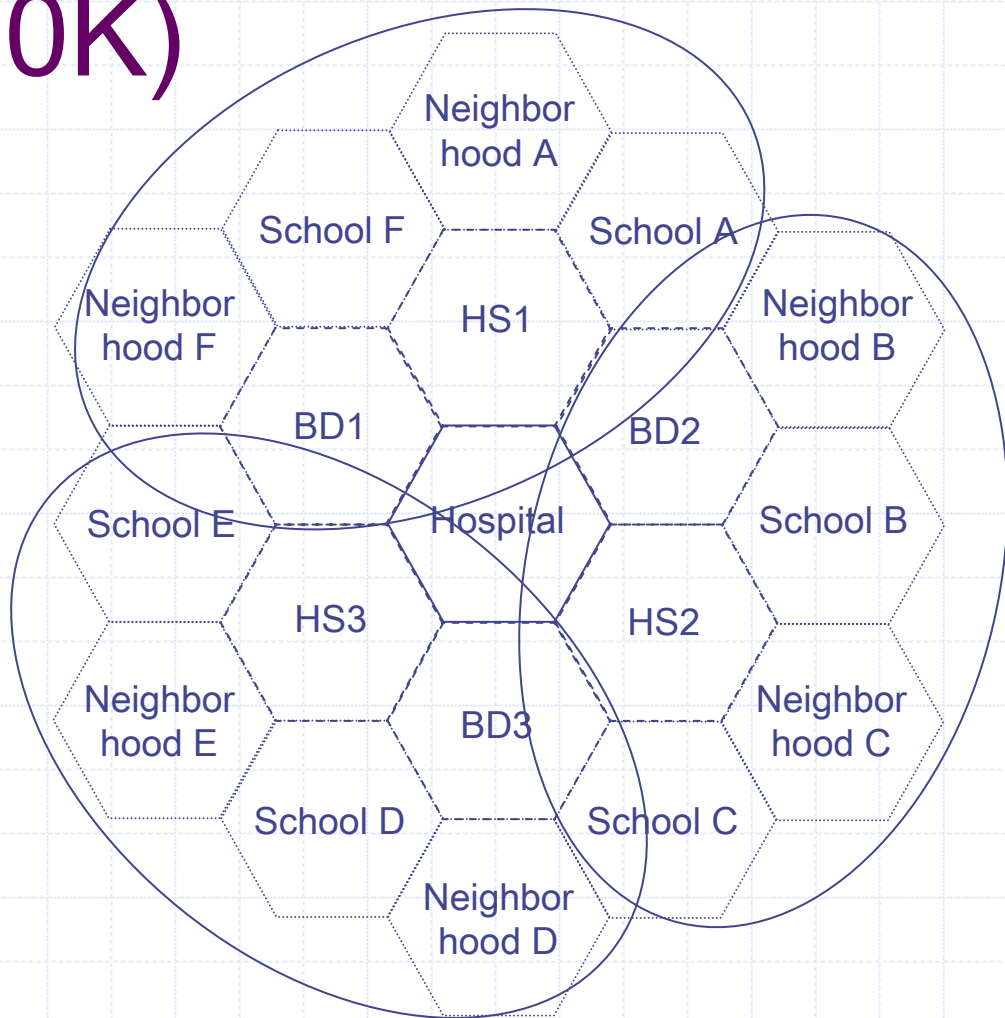$$R_0 = \frac{\alpha_N \beta \gamma \delta}{(\alpha_N + \mu)(\gamma + \mu)(\delta + \mu)(\sigma_N + \kappa\mu)},$$
$$where \ \beta = \beta_0 + \beta_1 \sin(2\pi t) + \beta_2 \cos(2\pi t)$$

Village (N=6K)

Town (N=50K)

Neighbor hood A

School F

School A

Neighbor hood F

HS1

Neighbor hood B

BD1

BD2

School E

Hospital

School B

HS3

HS2

Neighbor hood E

BD3

Neighbor hood C

School D

School C

Neighbor hood D

City (N=1.6M)

Hospital (6)

Business District (4)

Neighborhood (18)

High School (3)

Lower/middle School (6)
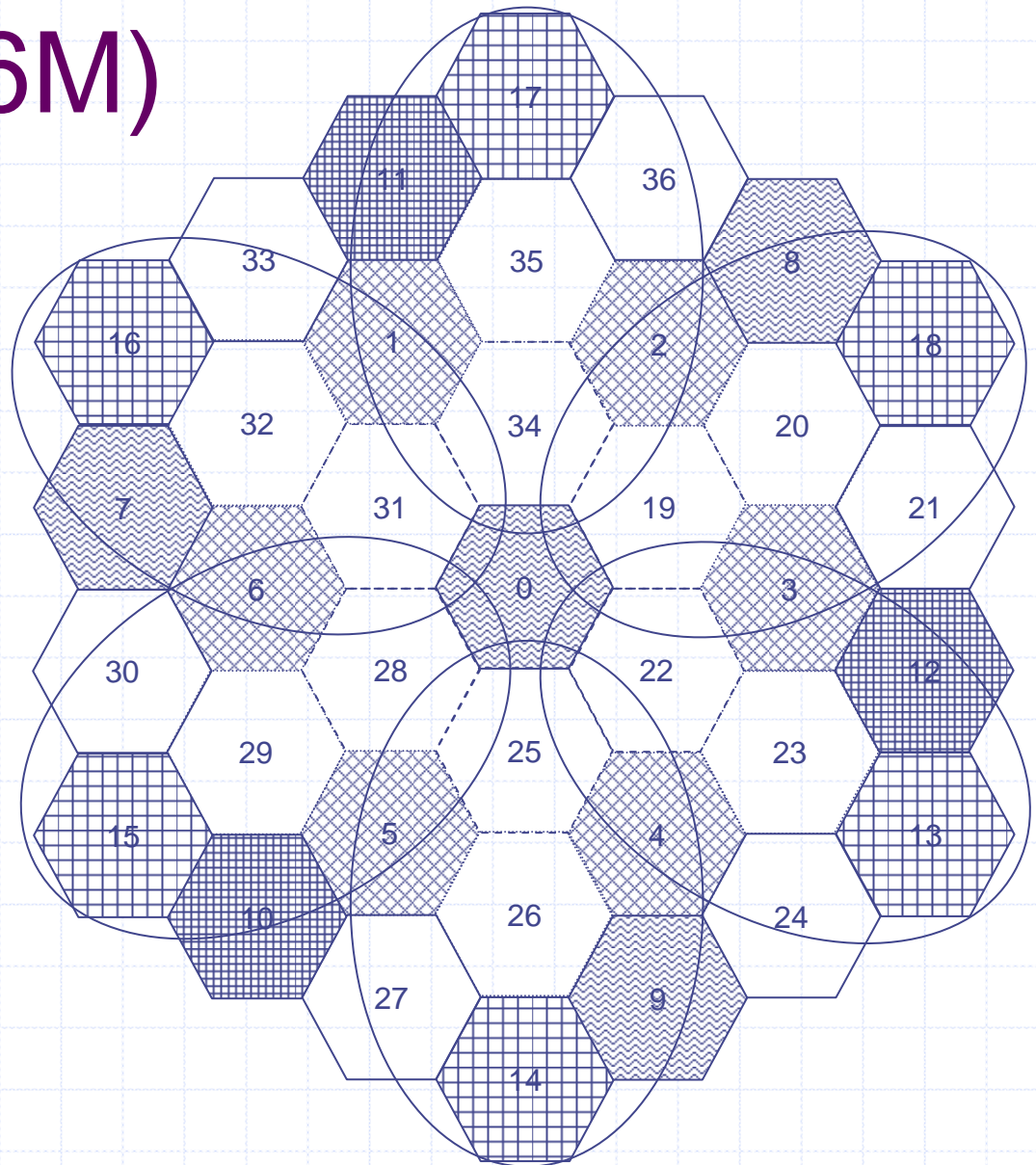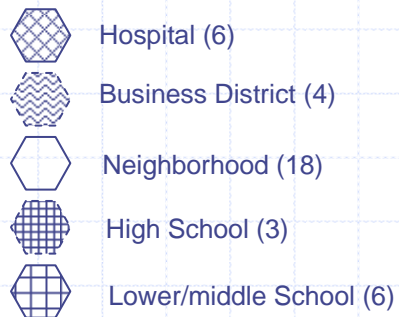
Social Mixing

b_{ii}		m_{ij}	Business District(s)	Neighbor-hoods	High School(s)	Schools	Hospital
0.25		Business District(s)	0.1	0.2	0	0	0.005
0.5		Neighborhoods	0.2	0.1	0.01	0.05	0.015
0.75		High School(s)	0	0.01	0.0025	0	0
0.75		Schools	0	0.05	0	0	0
1.0		Hospital	0.005	0.015	0	0	0.001

NB: 1) this diagonal is *among* business districts, …. 2) each neighborhood has a lower/middle school, but shares a high school and local business district with another. Connections with other business districts are half those with local districts in our town, but vary inversely with distance squared in our city

Spatial Mixing

- Estimated m_{ij} between Yugoslavian municipalities range from 0.05 to 0.71, but insofar as spread outside Kosovo (via a desperately ill person seeking care, and being misdiagnosed at successive hospitals) is hardly mixing as usual, …

- … this historical experience doesn't help to parameterize meta-population models. On the other hand, if it disabuses us of the mistaken notion that "usual" mixing would prevail during smallpox outbreaks, it may prove invaluable

- Need rules that make sense to social scientists, if not measurements in real towns and cities

Tentative Rules

- Adults most likely shop, work, … in local business districts
- Probabilities of shopping, working, … elsewhere diminish with intervening distance (e.g., inverse square)
- Ignore bussing, which affects children and schools?
- Would children stay home, social events be cancelled, and parents remain closer to home during outbreaks?
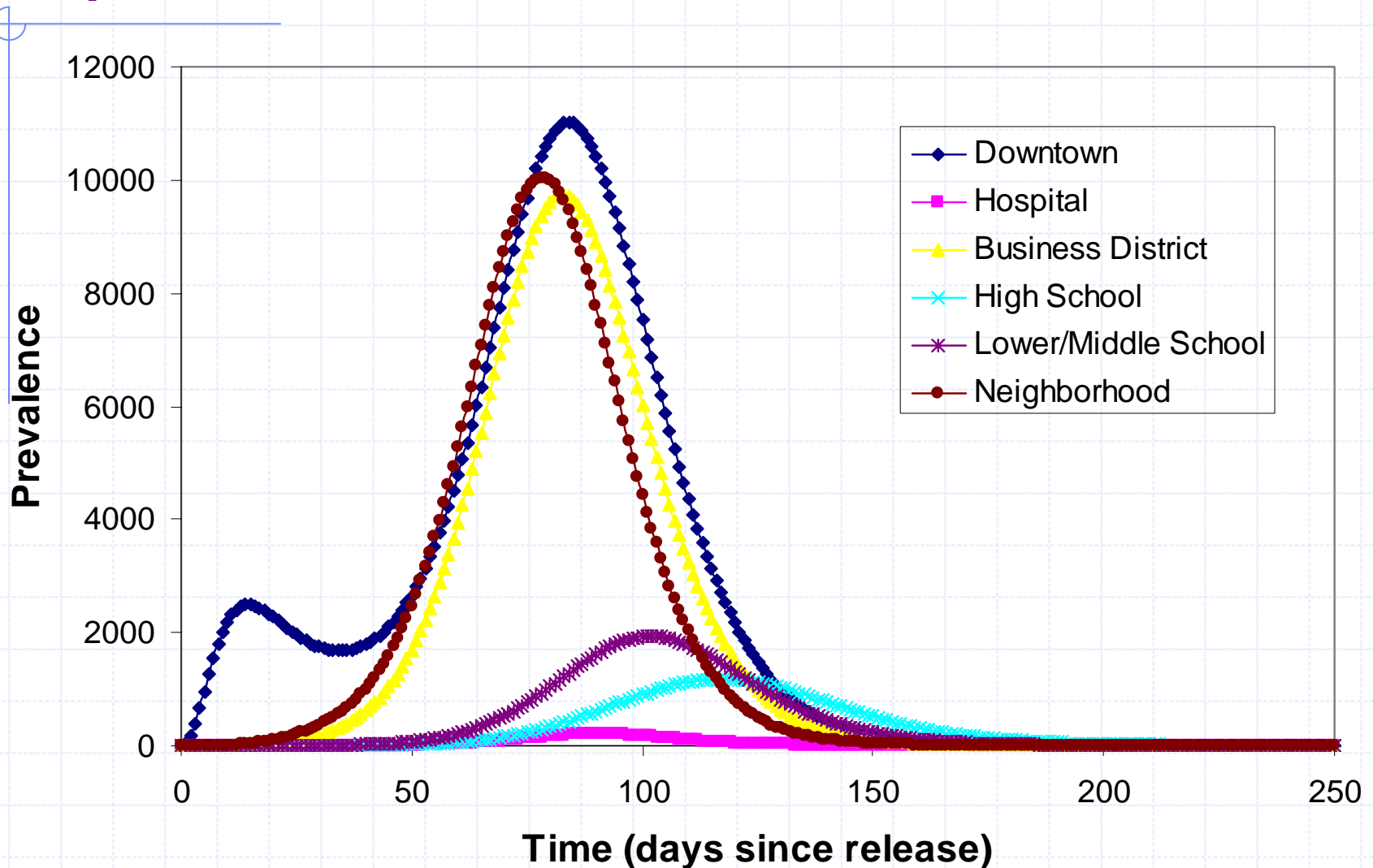
10 Adults Infected via Aerosol in a Restaurant, No Intervention
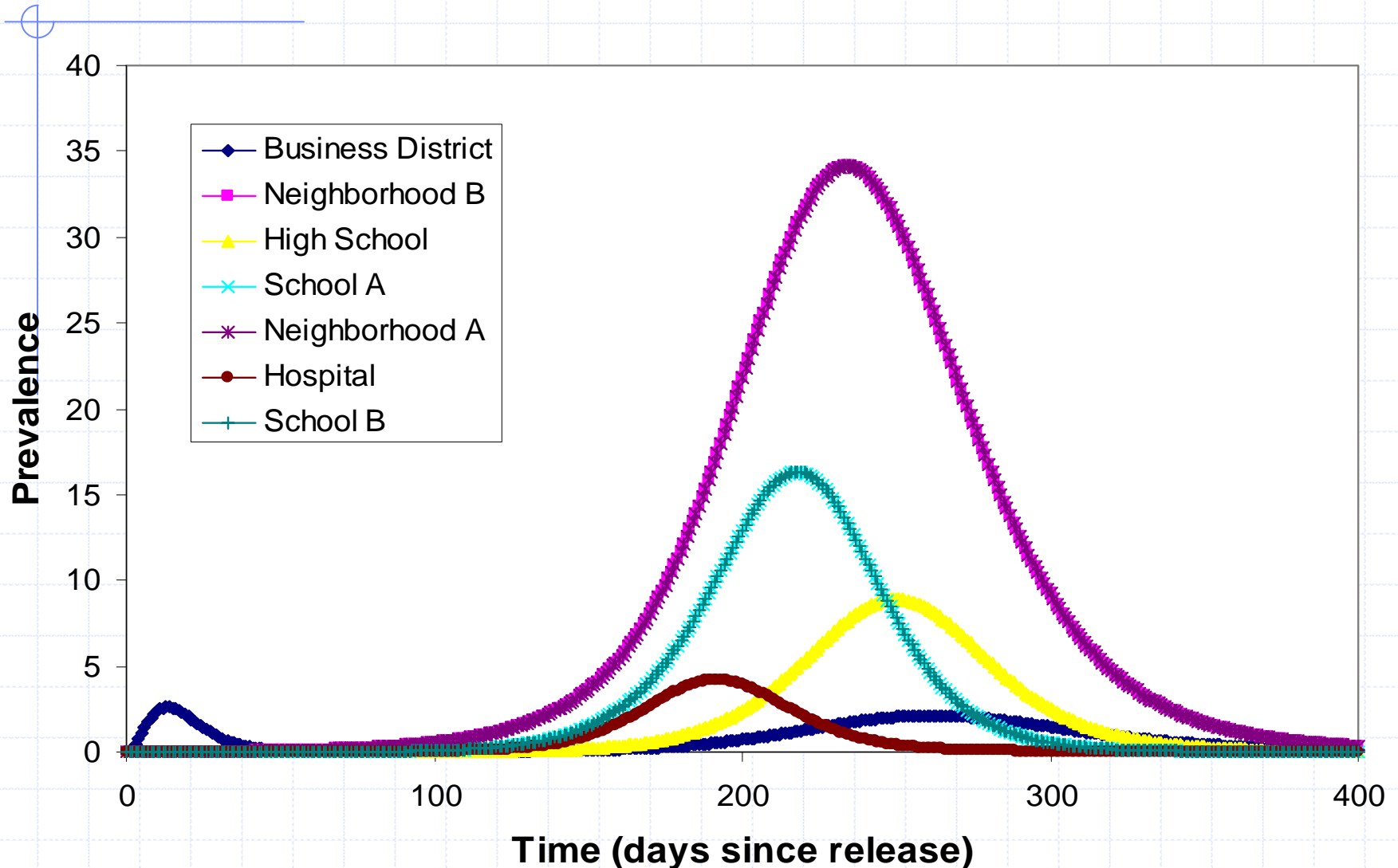
500 Infected via Aerosol in a Movie Theater, No Intervention
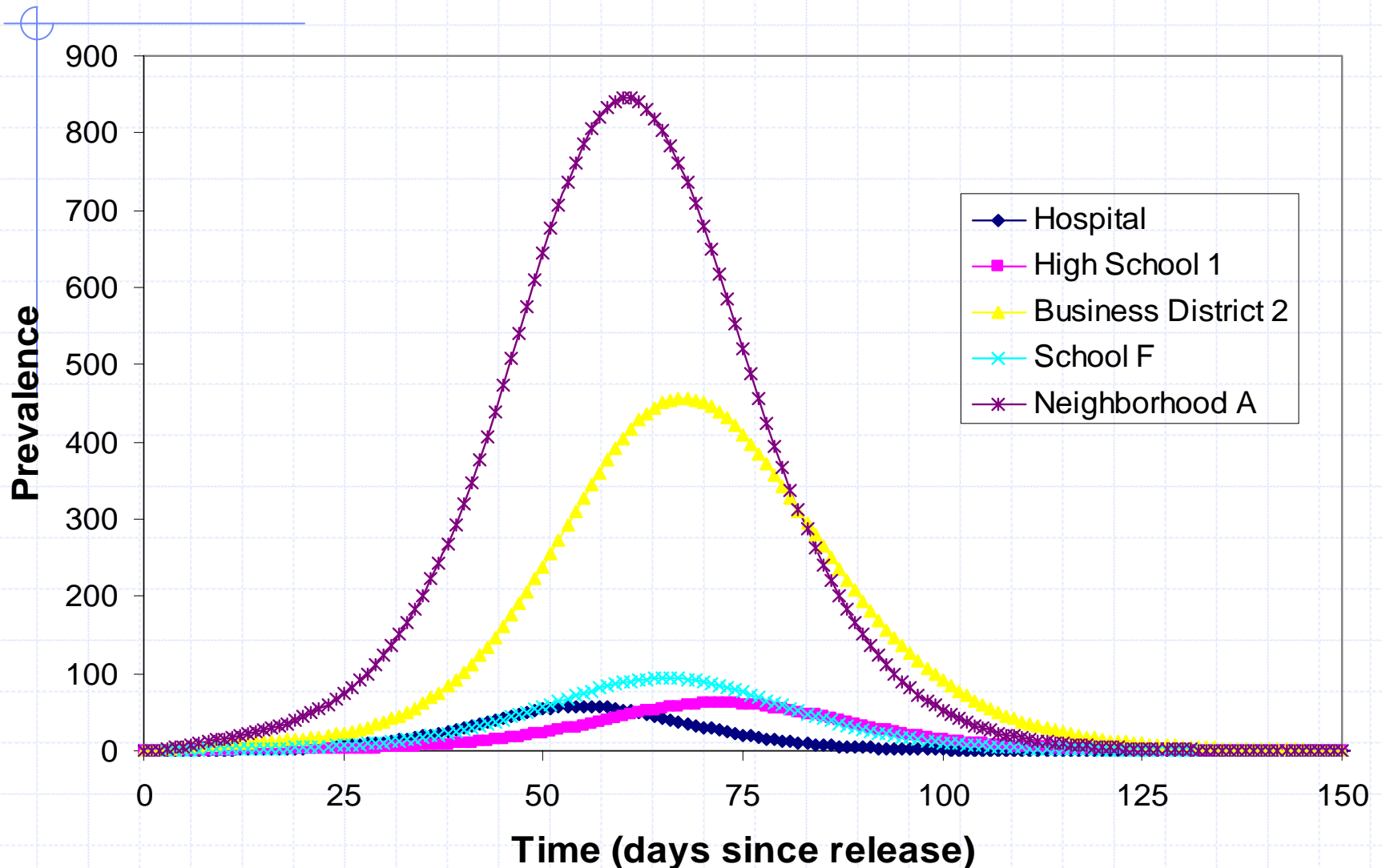
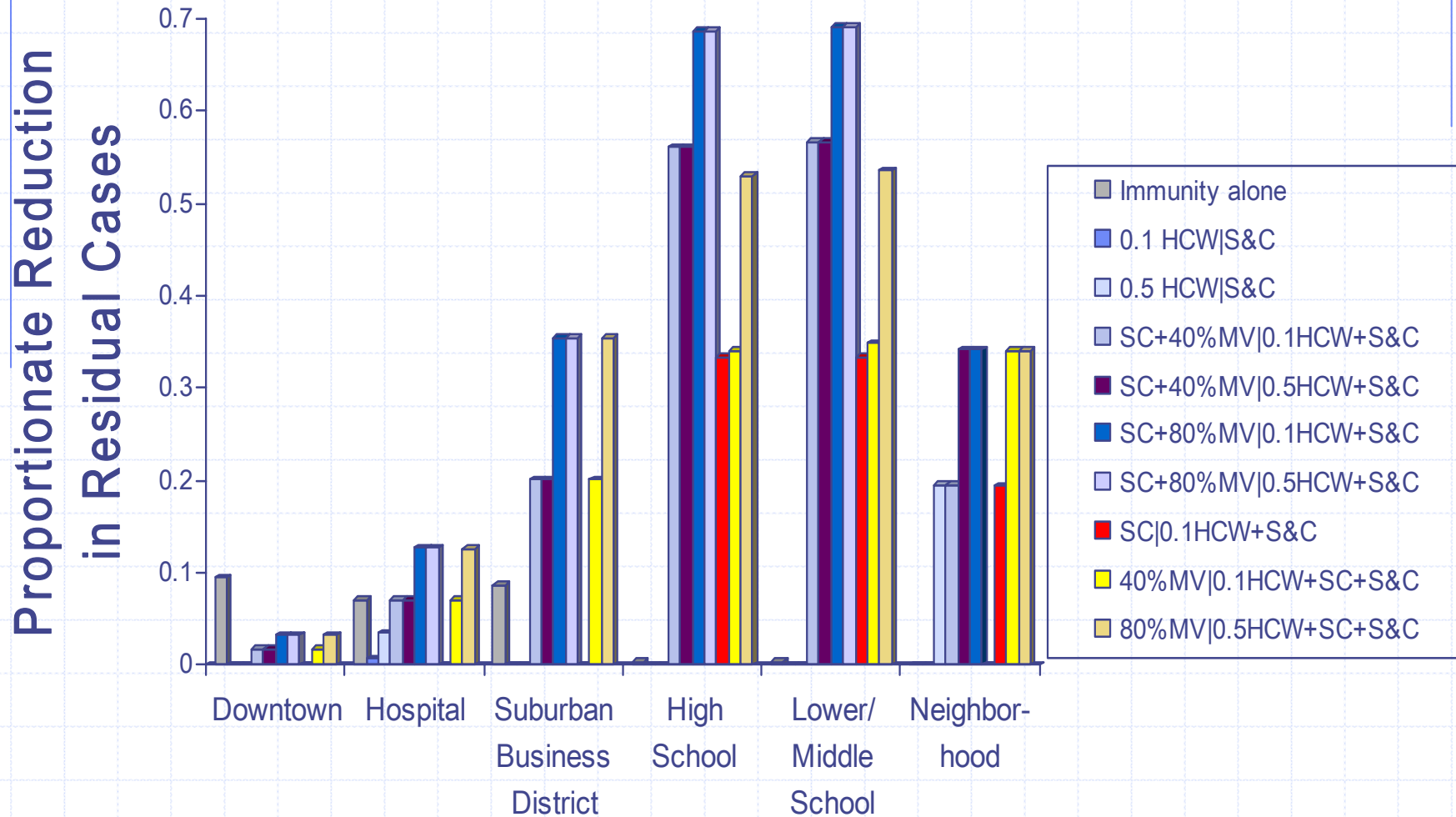# 10K Infected via Aerosol in a Sports Arena, No Intervention

Because these Scenarios are Nested, Comparisons are Experiments

Key	Scenario
1	Susceptible population
2	10% over 30 years of age wholly- and 30% partially-immune
3	#2 plus S&C plus 95% of hospital-based HCW w/in 2 days of diagnosis
4	#3 plus pre-emptive vaccination of 0.1 of hospital-based HCW
5	#3 plus pre-emptive vaccination of 0.3 of hospital-based HCW
6	#4 plus school closing for 10 days while 40% of populace is vaccinated
7	#5 plus school closing for 10 days while 40% of populace is vaccinated
8	#6 except that 80% of the populace is vaccinated
9	#7 except that 80% of the populace is vaccinated
10	#4 plus school closing

Experimental Results

- Comparison of simulations differing in some respect are experiments that evaluate the difference conditional on whatever is common, including the model

- Because sub-populations differ in size, age-distribution, and interconnections, differences per se are uninformative

- Express events relative to person-times or populations at risk (i.e., as rates and proportions)

- What is the population at risk? Events in the scenario without however they differ (immunity or an intervention that affects them)

- Because these differences reduce events, we express results as proportionate reductions, (events w/o difference-events w/ difference)/events w/o difference

- Because we have 7-37 subpopulations, we report weighted average reductions and ranges

Supplementary Interventions

Proportionate Reduction in Residual Cases (y-axis)

Categories (x-axis): Downtown, Hospital, Suburban Business District, High School, Lower/Middle School, Neighbor-hood

Legend:
- Immunity alone
- 0.1 HCW|S&C
- 0.5 HCW|S&C
- SC+40%MV|0.1HCW+S&C
- SC+40%MV|0.5HCW+S&C
- SC+80%MV|0.1HCW+S&C
- SC+80%MV|0.5HCW+S&C
- SC|0.1HCW+S&C
- 40%MV|0.1HCW+SC+S&C
- 80%MV|0.5HCW+SC+S&C

NB: S&C includes vaccinating 95% of hospital-based HCW within 2 days of the first diagnosis

In General, …

- Quantitative details depend on community structure (social & spatial), but …
- Surveillance & Containment reduce cases by 83 to 99%, depending on setting
- Small marginal benefits associated with other interventions (mostly direct effects)
  - o Vaccinating 10-30% of HCW pre-emptively
  - o Closing schools for 10 days and …
  - o … vaccinating 40-80% aged one year and older

Limitations

- Experience with social phenomena that may be important (e.g., relevant sub-populations, interconnections); involve social scientists?
- Observations that might permit evaluation; explore Angulo's outbreak?
- Differential equations don't permit fine spatial resolution (vaccinate entire households)
- Deterministic; make complementary event-time models?
- Crude logistics; vary intensity of interventions (cf. emerging ID model) during outbreaks?

Juan Angulo's observations analyzed by Bruce Sayers

"This self-contained epidemic of *Variola minor* occurred during 1955-56 in the municipality of Bragança Paulista (population about 62,000 at the time), State of São Paulo (population about 6.5 million). The epidemic was followed from the first case (introduced from another State) up to extinction some 11 months later; the data on every reported case (484 clinical cases in 210 households) were collected and carefully verified. There were thus 210 initial cases in households and 274 other intra-household cases. Two of the infected individuals had contracted *Variola* 12 or 14 years previously, 97 had received vaccinations against *Variola*: 66 of these more than 5 years before infection, and 31 more recently - nine within 14 days."

Conclusions

- Smallpox differs from other vaccine-preventable diseases
- Surveillance and containment, which exploited those differences, eradicated smallpox where mass vaccination had failed
- CDC models faithfully represent biological features affecting smallpox transmission …
- … and affirm the historical experience, namely that surveillance and containment is VERY effective
- Unless widespread attack were certain, mass vaccination would not be indicated

Surveillance & Containment (SC)

- A proportion E_1 of contacts is traced, after an arbitrary delay, vaccinated, and those in whom virus is disseminating also are quarantined

- Tracing, vaccination and quarantine occur at rate $-\ln(1-E_1)$/latent period; compliance is reasonable (e.g., 0.75)

- Vaccination rescues recently infected contacts and ameliorates illness among those in whose reticuloendothelial cells virus is replicating

- Simultaneously, proportion E_2 of cases is isolated [i.e., rate = $-\ln(1-E_2)$/infectious period]; compliance is excellent (e.g., 0.95)

As Control via Surveillance & Containment is Complex, …

$$(1-\Pr(R))*(1-\Pr(Q))*\left[\begin{array}{l}\Pr(A)*\Pr(I)*\left[\sum_{\tau=0}^{\tau_I}\Pr(T\,|\,c_M,\tau)*C_M(\tau)+\Pr(C\,|\,I)*\sum_{\tau=\tau_I}^{D_M}\Pr(T\,|\,c_M,\tau)*C_M(\tau)\right]+\\[1em]\Pr(A)*(1-\Pr(I))*\sum_{\tau=0}^{D_M}\Pr(T\,|\,c_M,\tau)*C_M(\tau)+\\[1em](1-\Pr(A))*\Pr(I)*\left[R_I+\Pr(C\,|\,I)*\sum_{\tau=\tau_I}^{D_N}\Pr(T\,|\,c_N,\tau)*C_N(\tau)\right]+\\[1em](1-\Pr(A))*(1-\Pr(I))*R_0\end{array}\right]<1,$$

$$where\ R_I=\sum_{\tau=0}^{\tau_I}\Pr(T\,|\,c_N,\tau)*C_N(\tau),\ R_0=\sum_{\tau=0}^{D_N}\Pr(T\,|\,c_N,\tau)*C_N(\tau),...$$

we have made a spreadsheet, which calculates these probabilities and numbers, and …

Dynamics of S&C (following a 1-day delay, 0.672 of contacts are vaccinated, some are quarantined, and 0.9 of cases are isolated, during their respective latent and infectious periods)