Emergency Response to an Anthrax Attack

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Why Study Anthrax

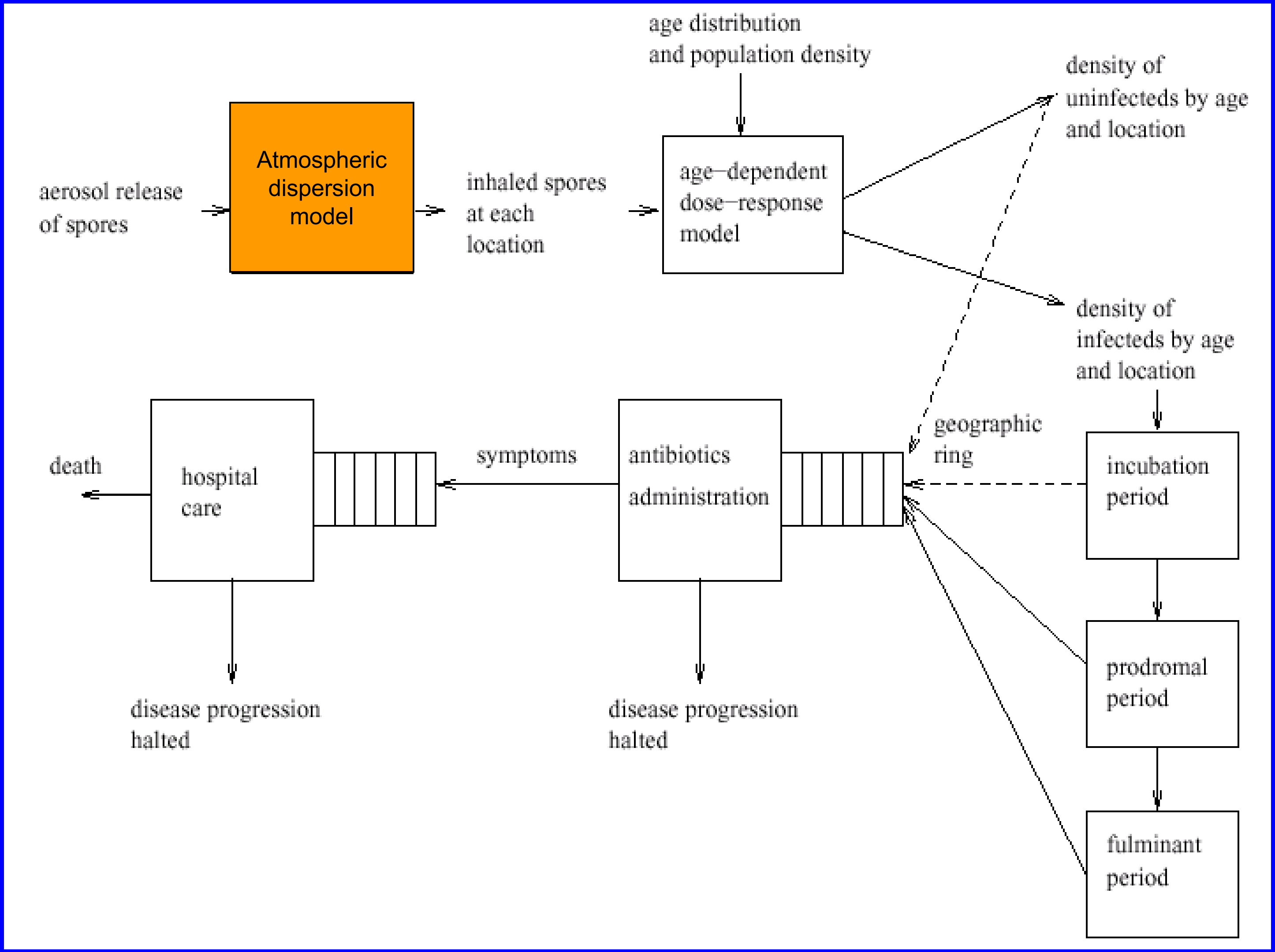
- Fatality rate > 90% if no intervention
- Highly durable (Gruinard Island = 35 years!)
- USSR (4,500 metric tons/yr), Iraq and others have weaponized it
- Proof of principle (2001 mail attacks)
- An aerosol release of 100 kg could kill up to 3 million people. Office of Technology Assessment, US Congress, 1993
- "A single SS-18 could wipe out the population of a city as large as New York"

Ken Alibek, *Biohazard*, pg 8

"Guidelines for which populations would require postexposure prophylaxis to prevent inhalation anthrax … will need to be developed. … These decisions would require estimates on the timing, location, and conditions of exposure."

Inglesby *et al.*, Working Group on Civilian Defense, (*JAMA*, May 1, 2002 page 2247)

The Model



aerosol release of spores
Atmospheric dispersion model
inhaled spores at each location
age distribution and population density
age–dependent dose–response model
density of uninfecteds by age and location
density of infecteds by age and location
geographic ring
incubation period
prodromal period
fulminant period
antibiotics administration
symptoms
hospital care
death
disease progression halted
disease progression halted

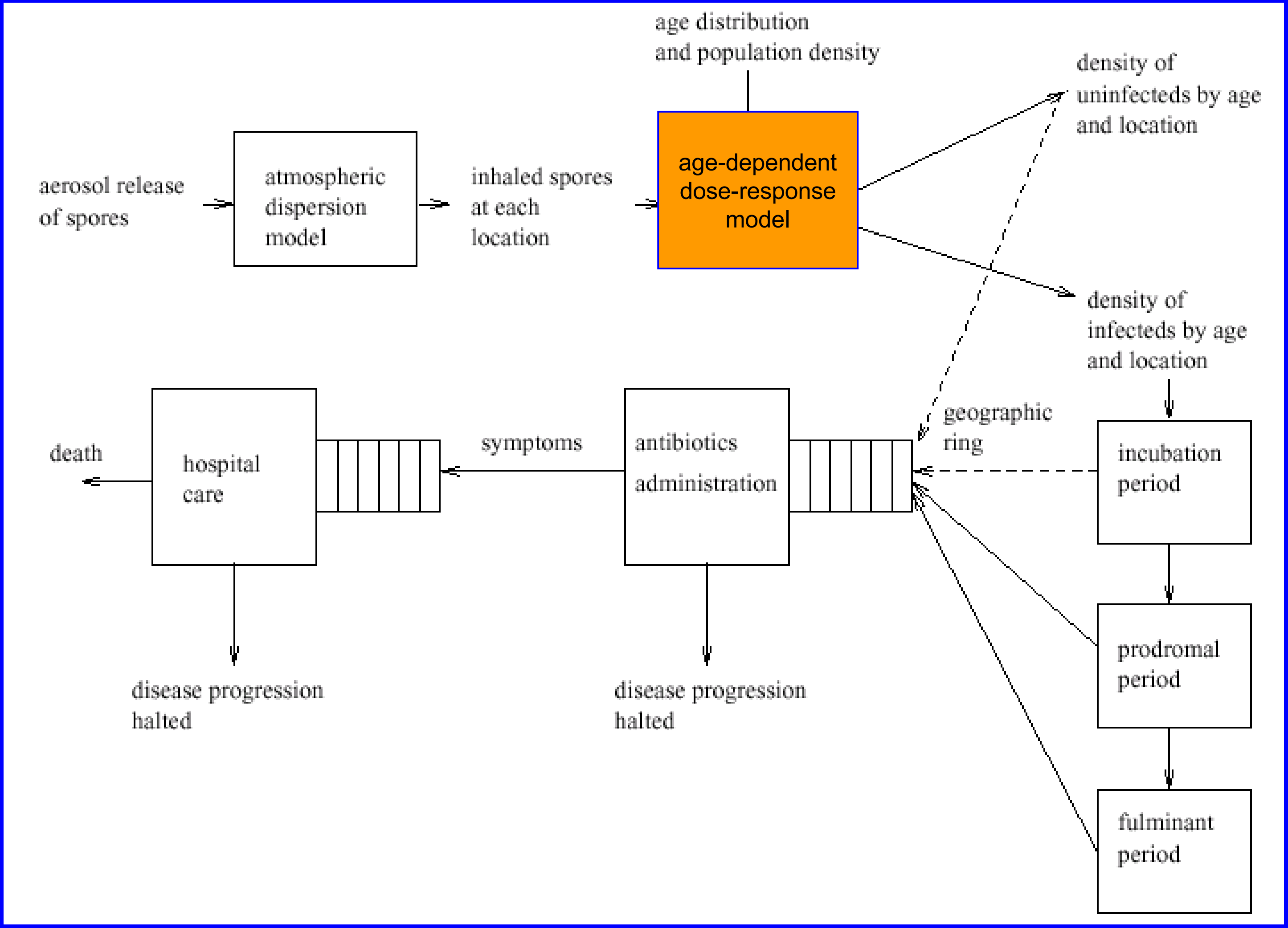
Gaussian Plume Model

- Number of spores at location (x,y) =

$$s(x,y) = \frac{bQ}{\pi u \sigma_y \sigma_z} e^{-\frac{y^2}{2\sigma_y^2} - \frac{h^2}{2\sigma_z^2}},$$

- Same as Meselson *et al*. (*Science* 1994), except
  - size of release = 1 kg
  - height of release = 100 m
- Study region = within 200 km downwind and 20 km crosswind
  - Urban area < 30 km downwind (10.8 million people)
  - Rural area > 30 km downwind (0.7 million people)

The Model



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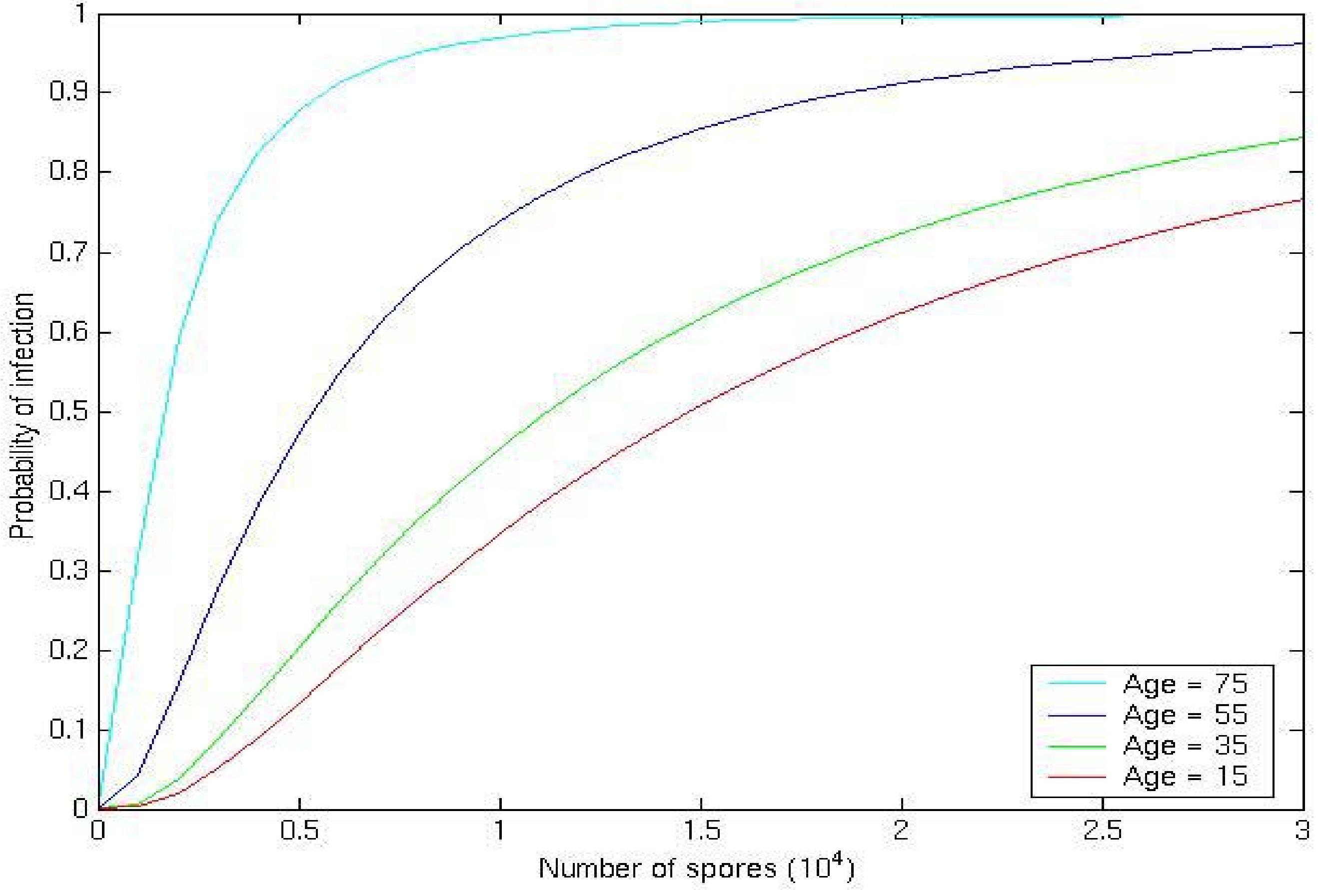
Age-dependent Dose-response Model

$$P(s,a) = \Phi(\alpha + \beta \log s + \gamma a + \delta a^2)$$



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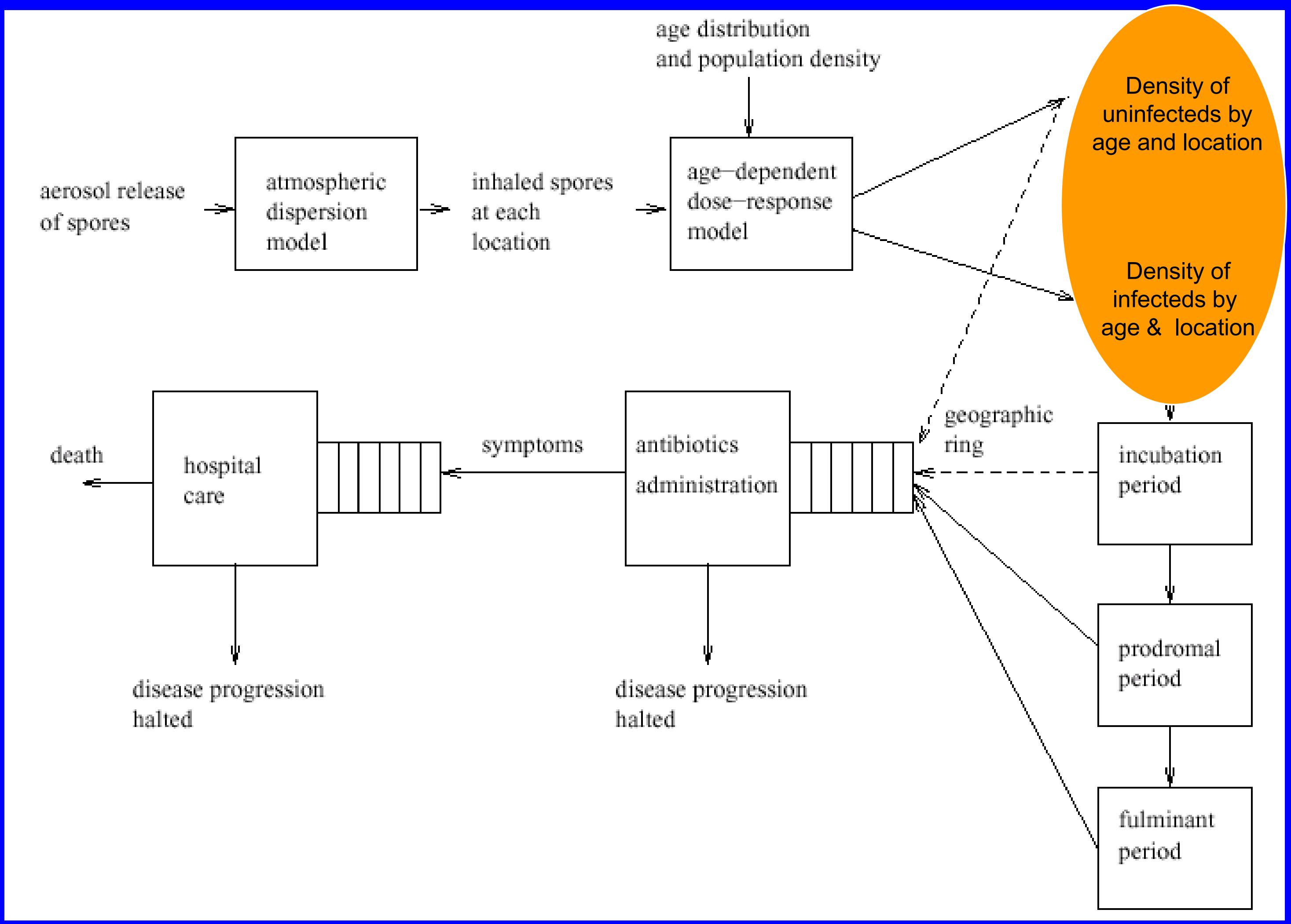

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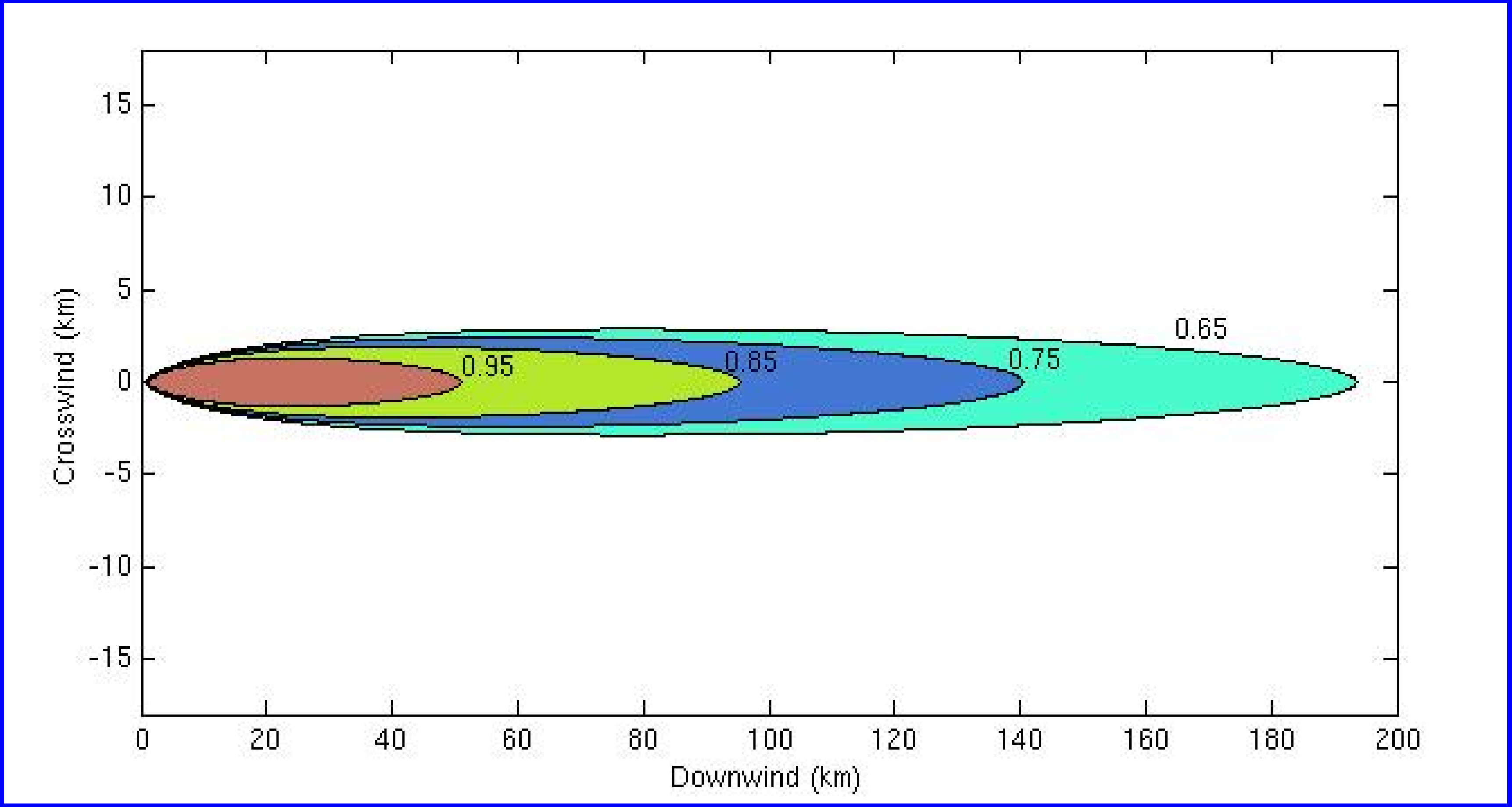
Age-aggregated Probability of Infection



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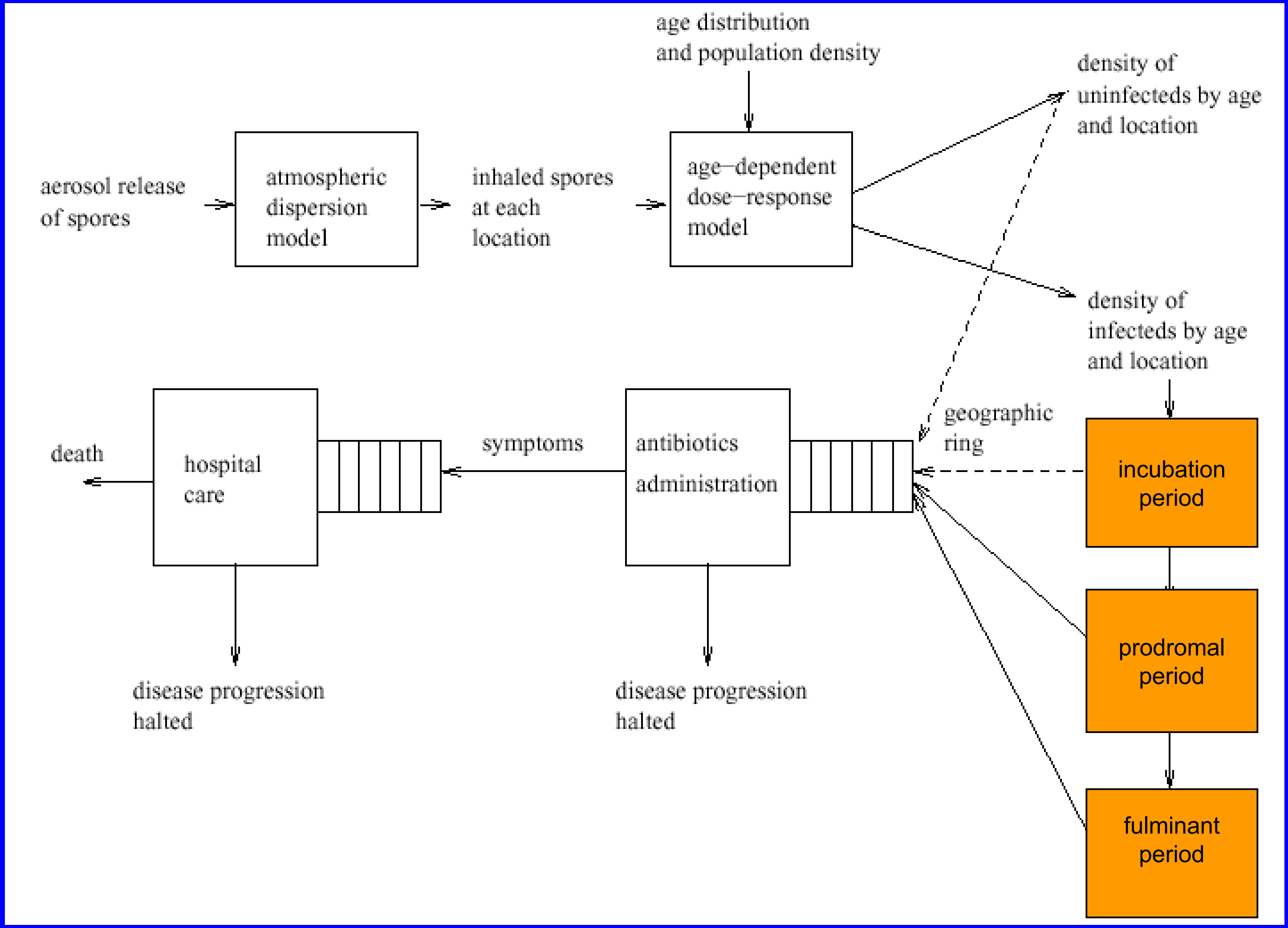
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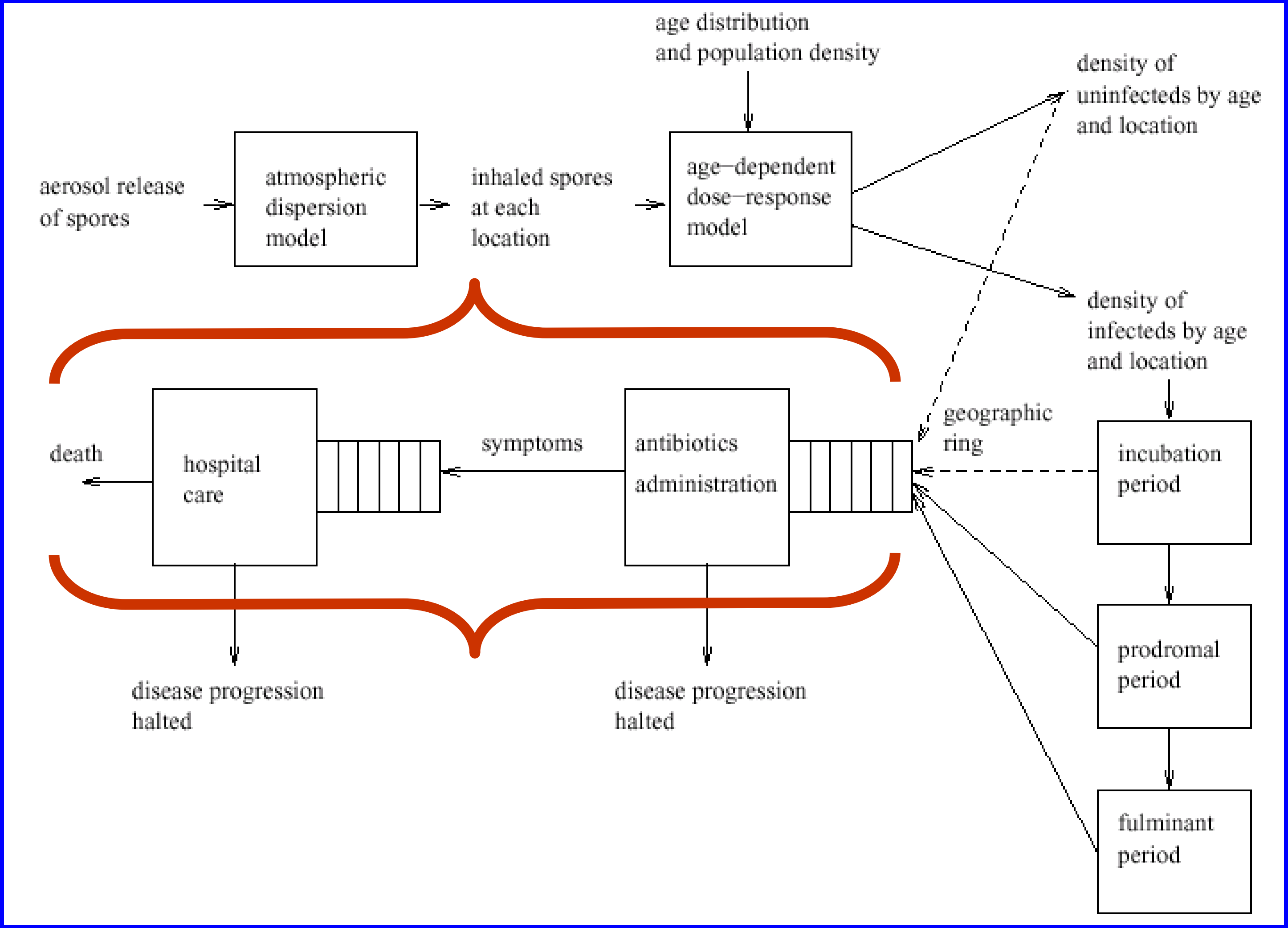
Log-normal Disease Stages

- Incubation: median = 11.0 days
  - Censored Analysis of Brookmeyer, *et al*. (*Biostatistics*, 2001)
  - We could not detect dose- or age-dependence
- Prodromal: median = 2.4 days
- Fulminant: median = 1.4 days

The Model



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Intervention

- Detection delay = 2 days (12,700 prodromals)
- Service zones
  - 9 km^2 urban zones serving 90,000
  - 81 km^2 rural zones serving 8,000
- Tandem multi-server queues
  - 7 minutes to distribute antibiotics (4 days in all)
  - 6 hours for hospital care (emergency MDs & NPs)
  - Additional mobile health care providers (federal and military personnel)

Antibiotics

- If incubating, then prevents symptoms with probability 0.9 (adherence)
- If prodromal, then:
    - prevents fulminant with probability 0.4
    - resets prodromal clock (median 2 days) with probability 0.6
- If prodromal and receive hospital care, then survive with probability 1
- If fulminant, then die with probability 1

Ring Strategy

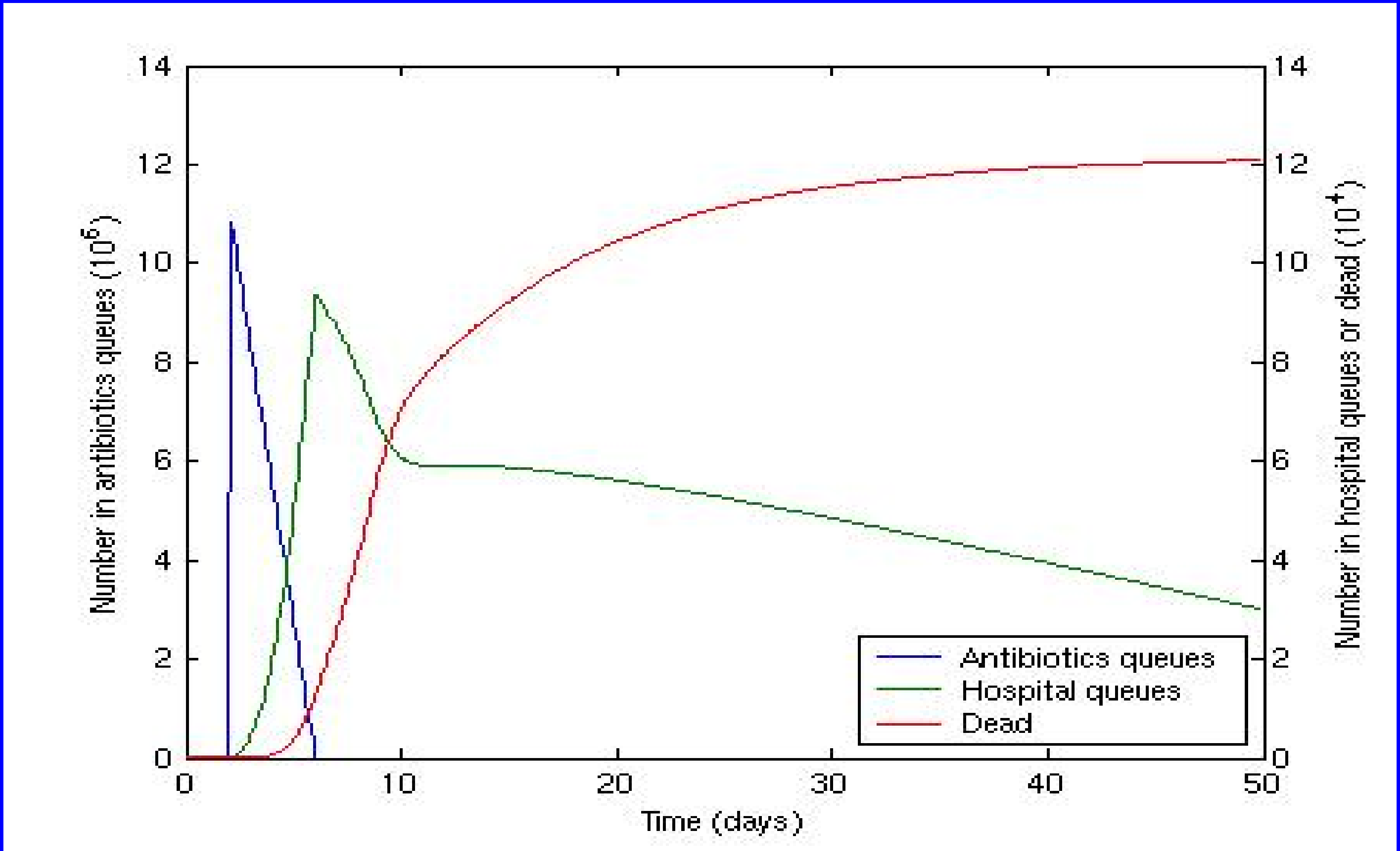
- How do asymptomatics enter antibiotics queue?
  - Anthrax burden at (x,y,t) = fraction at location (x,y) with symptoms by time t
  - Asymptomatics at location (x,y) enter antibiotics queue when anthrax burden > p
  - Base case is $p = 0$
- Symptomatics enter the antibiotics queue if not already in the ring
- Enter the hospital queue after symptoms and antibiotics

Base Case Results

Priority Policy	Deaths	% Reduction in Deaths
Mass Service	123,400	-
Symptomatic	118,100	4.3%
Symptomatic-age	114,700	7.1%
Symptomatic/prodromal	117,400	4.9%
Symptomatic-age/prodromal	113,900	7.7%

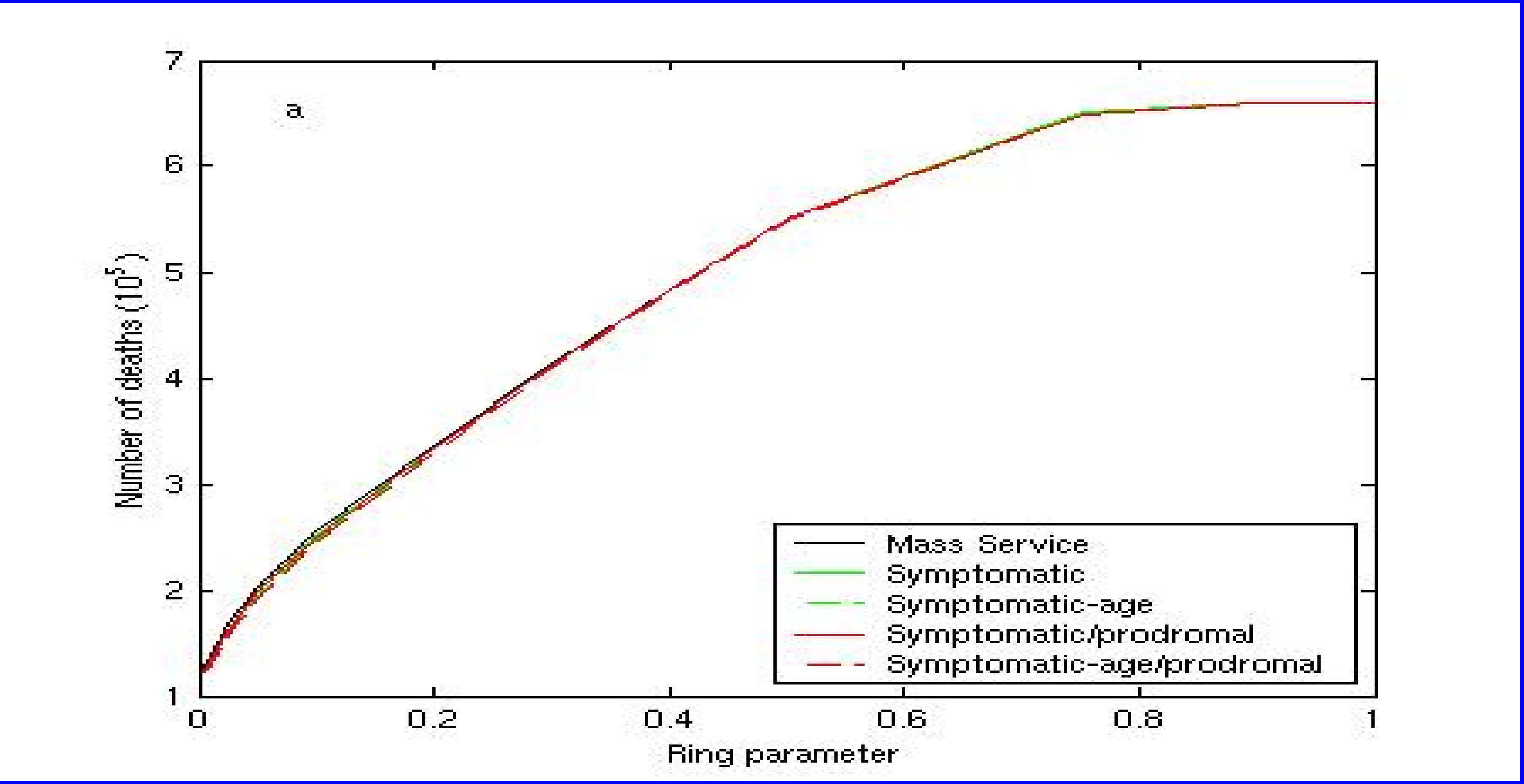
Symptomatic (4.3%) > Age (2.8%) > Prodromal (0.6%)

Aggregated Queue Dynamics: Mass Service Policy



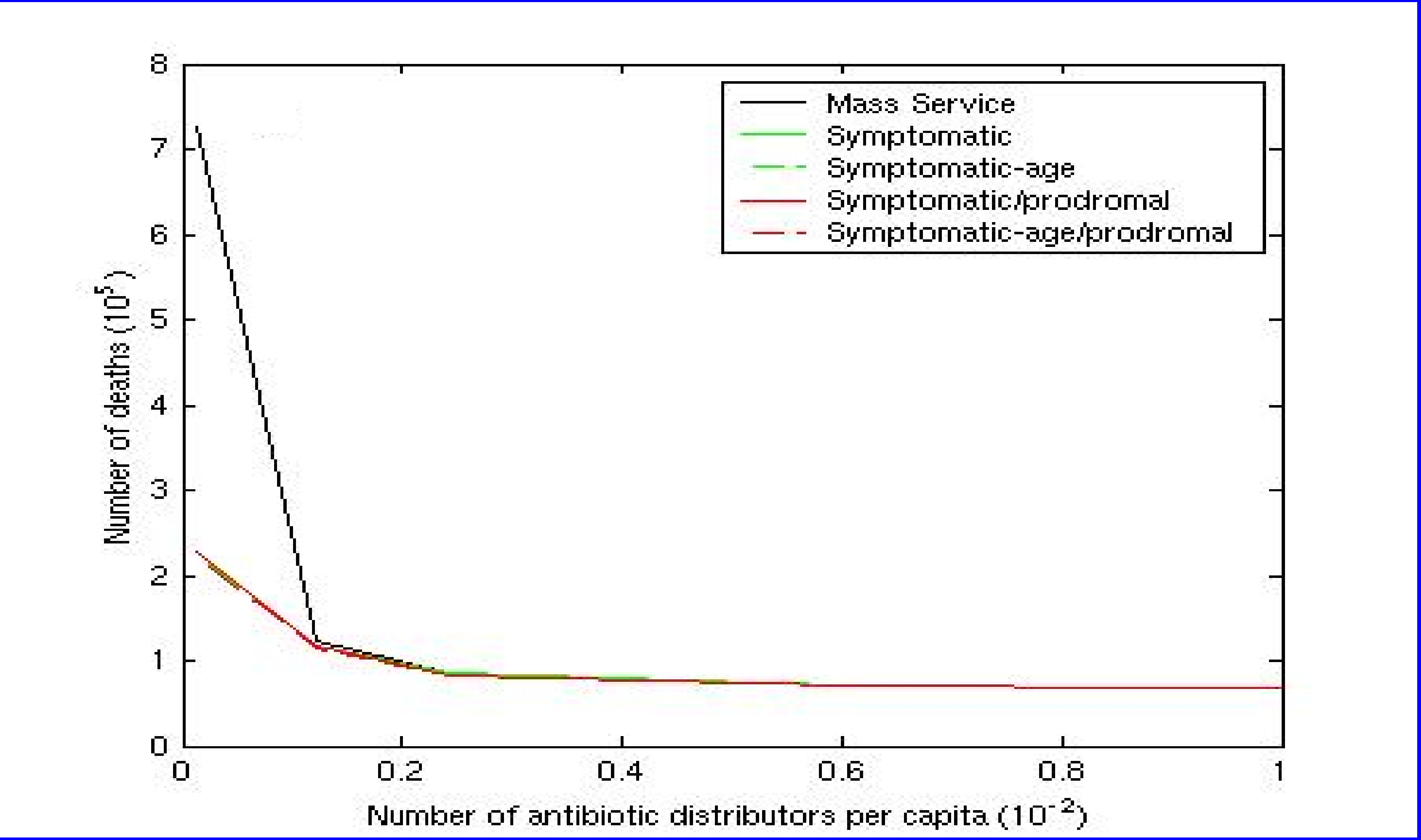
Sensitivity to Ring Parameter

- Aggressive prophylactic strategy is required
- Deaths double if *p* increased from 0 to 0.07
- 660,000 (44% of infected) die if $p = 1$ (no prophylaxis)



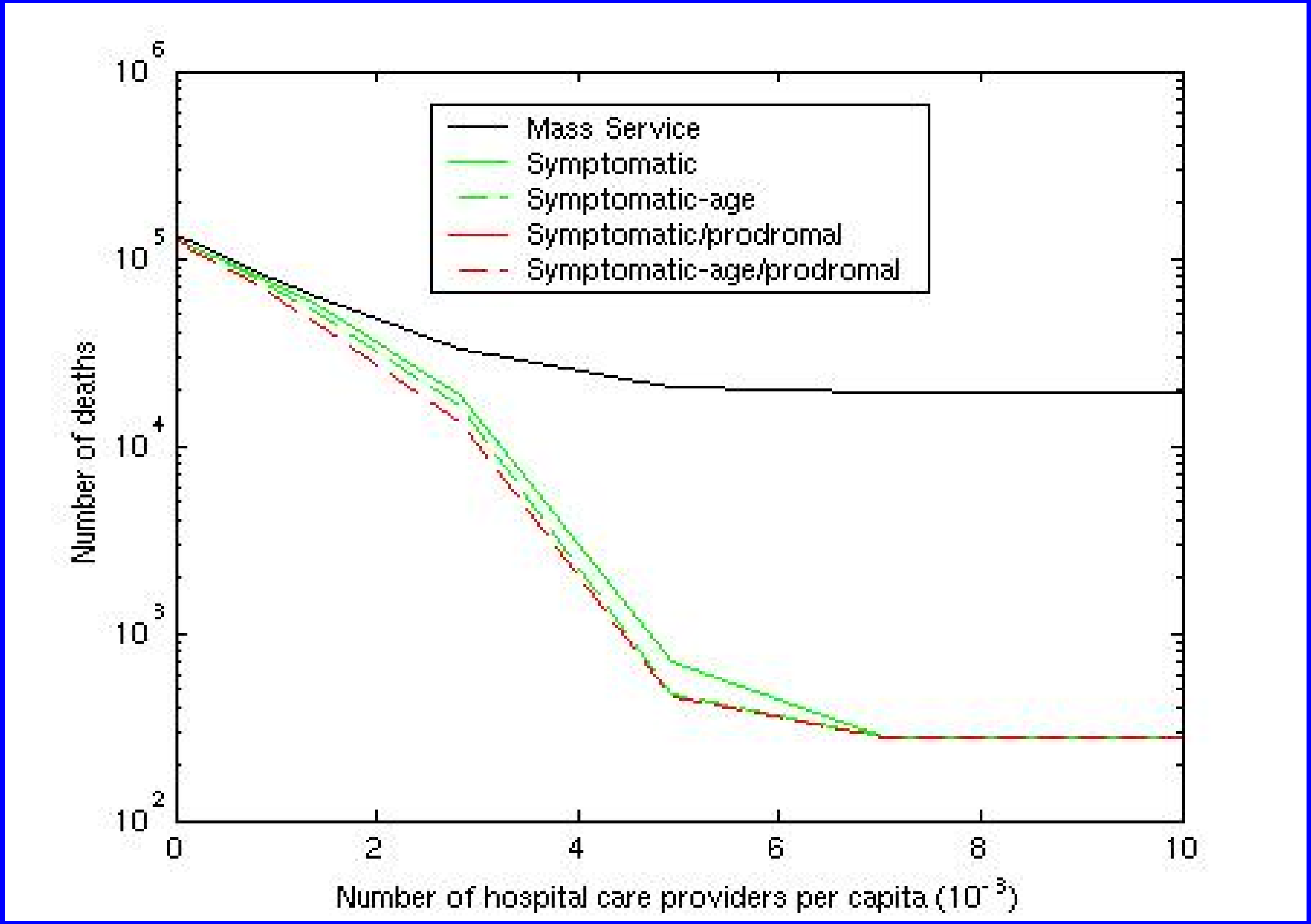
Sensitivity to Number of Antibiotic Distributors

- This eases the bottleneck at hospital
- Deaths nearly halved with 7.5-fold increase in capacity or pre-attack distribution



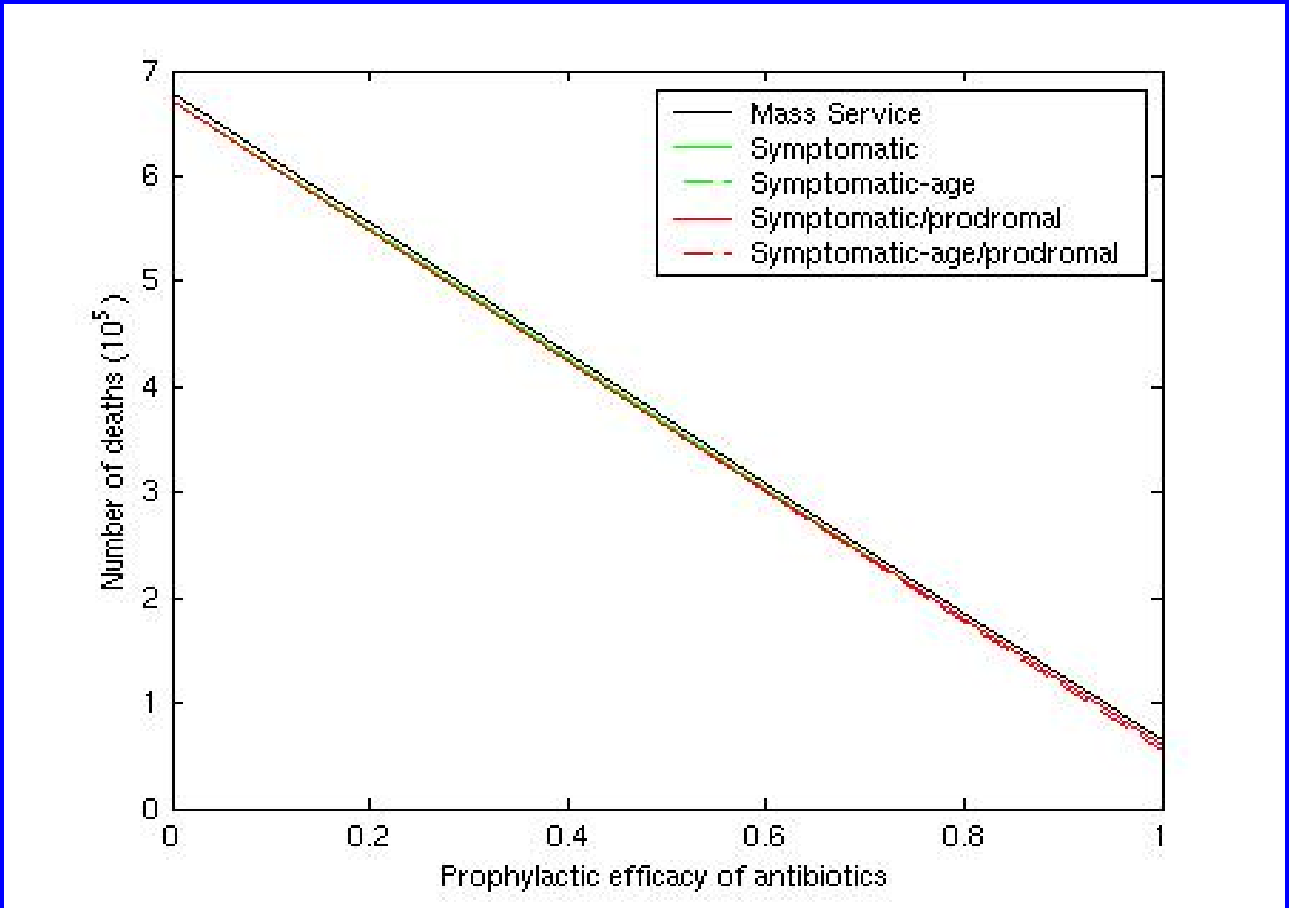
Sensitivity to Number of Hospital Care Providers

- Congestion disappears at 75 times the base case



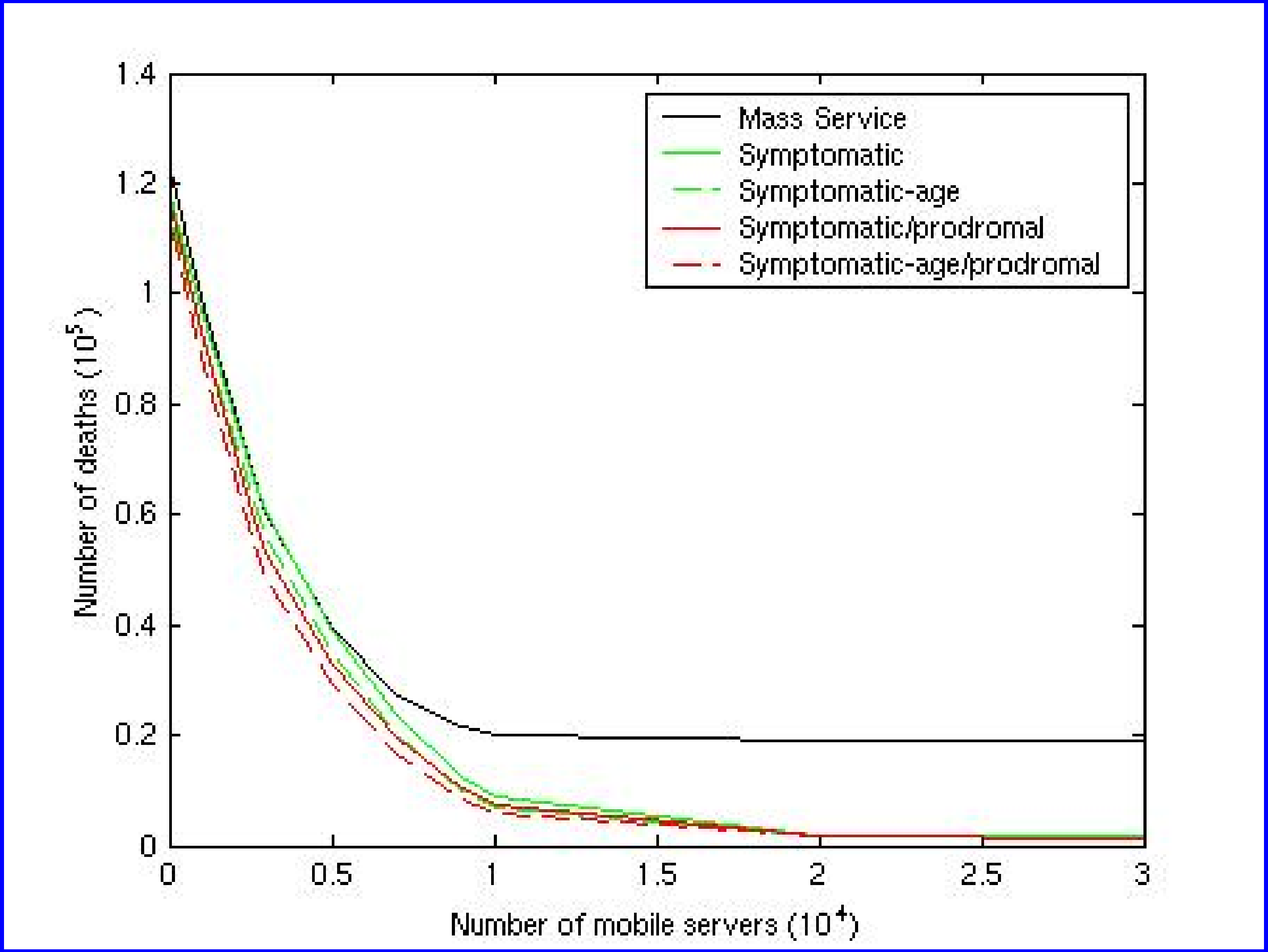
Sensitivity to Prophylactic Efficacy (Adherence)

- Deaths 50% higher if adherence is 80% rather than 90%



Sensitivity to Number of Mobile Servers

- Mobile servers more effective than additional local servers

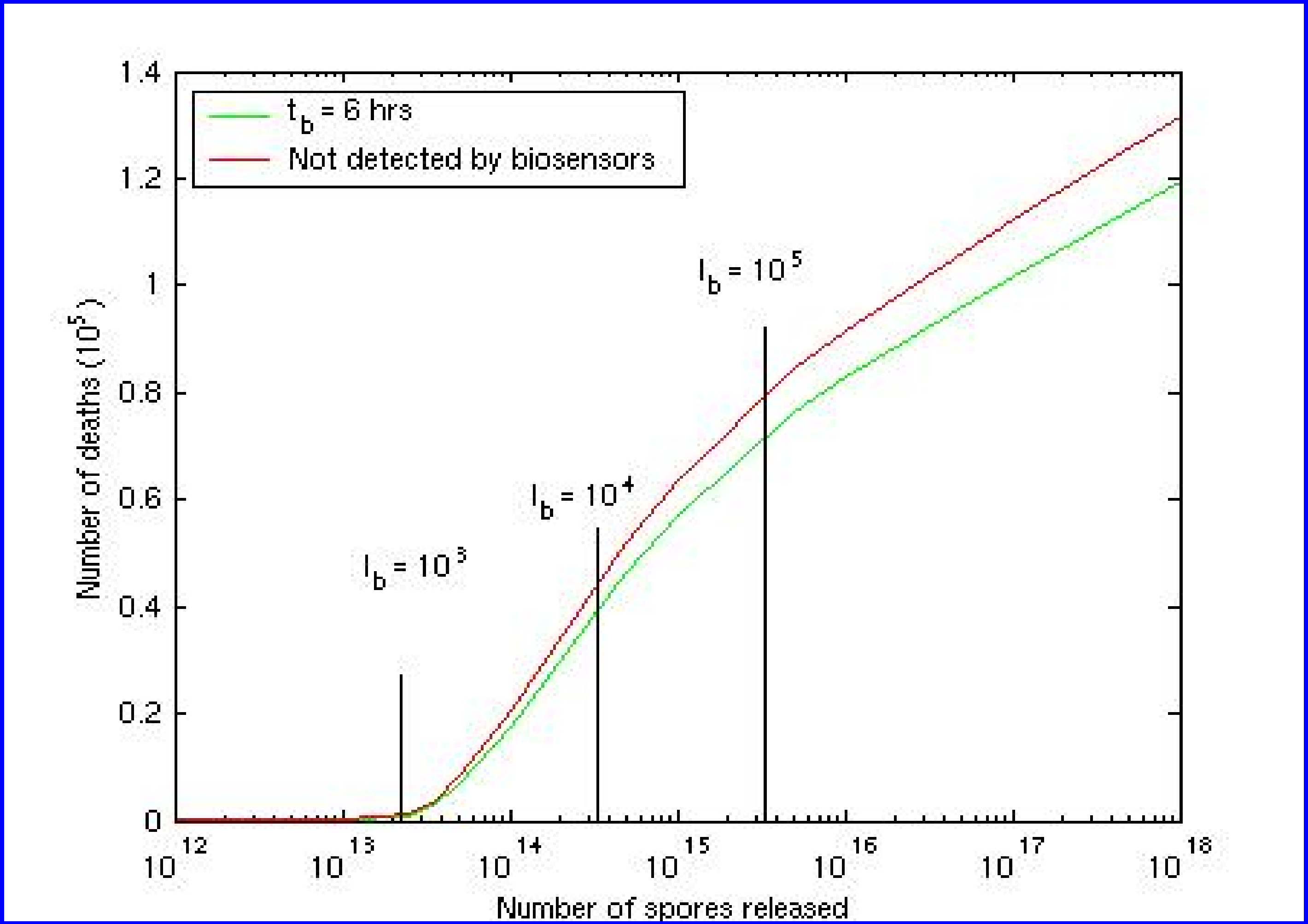


Assessing Biosensors

- Time delay to get results (t_b)
- Detection limit (l_b)
- Geographic density (d_b)
- Detection Delay = $\begin{cases} t_b \text{ if max spore count by biosensor} > l_b \\ \text{2 days otherwise} \end{cases}$
- Assume pre-attack antibiotic distribution and priority to prodromals

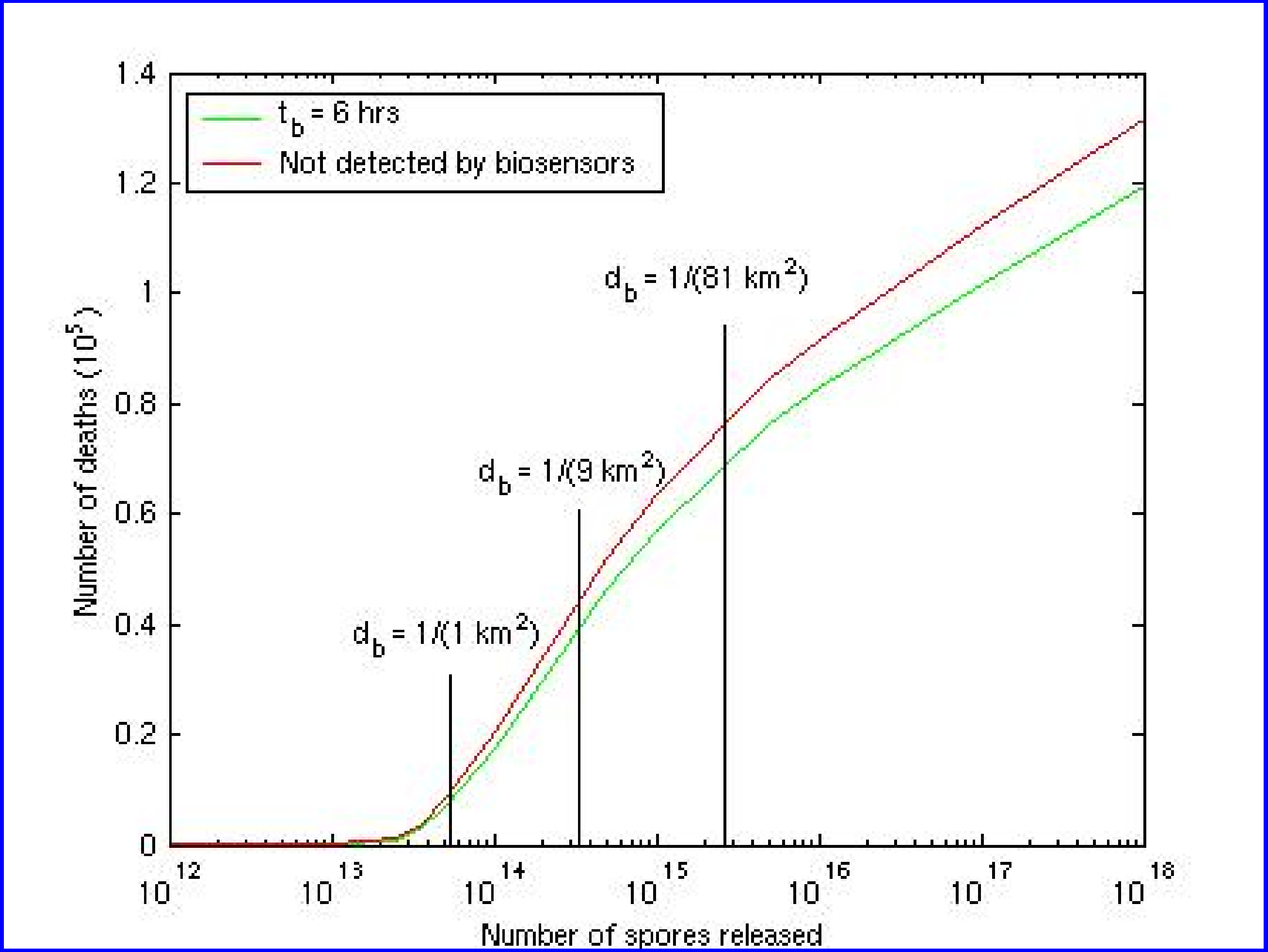
Assessing Biosensor Detection Limit

- Deaths discontinuous in release size: a jump down at vertical line



Assessing Biosensor Geographic Density

- High detection limit can be compensated for by high geographic density



Pre-Attack Antibiotic Distribution vs. Biosensors

Time Intervention Begins	Time to Deliver all Antibiotics	Deaths
48 hours	4 days	123,000
6 hours (biosensors)	4 days	70,000
48 hours	0 days (pre-attack distn)	60,000
6 hours (biosensors)	0 days (pre-attack distn)	50,000

Pre-attack antibiotic distribution and biosensors are:

- substitutes
- not additive => adherence becomes bottleneck
  surge hospital care capacity required

Policy Implications

- Aggressive prophylactic strategy
  - spatial (*p = 0* in ring)
  - temporal (pre-attack distribution, use nonprofessionals)
  - educate to increase adherence
  - prioritize by disease, then age
- Surge hospital care capacity
  - Expanded training (e.g., non-emergency MDs, NPs & EMTs)
  - National Guard, Red Cross, DMATs, NDMS, DoD, VA
  - Pre-attack vaccination of first responders
  - Avoid secondary bottlenecks (e.g., antibiotics, transportation, ventilators)
  - Prioritize to maximize lives saved (military MD training?)

Policy Implications

- Biosensor deployment
  - Necessary but not sufficient – also need rapid service
  - Limited value to improving technology beyond

    time delay = 1 day

    detection limit = 10^4 spores

    geographical density = 1 sensor per 9 km^2
  - Detection limit can be compensated for by geographical density
  - Gaussian plume, so regard with caution

Pre-attack Mass Vaccination?

- Non-negligible probability of attack
- Irreducible uncertainties
  - attack size
  - antibiotic treatment efficacy without hospital care
  - dose-dependent incubation period?
- Cost and difficulty of mounting a response

But this option is several years away …