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Inferring outbreak characteristics from a short observation period of symptomatic patients

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Problem and motivation

- **Consider a bioattack**
  - Atmospheric release of an aerosolized pathogen
    - Not caught on sensors
    - Not terribly big – $O(10^3)$ infected people
  - First intimation : successful diagnosis of an infected individual
- **Primary concern - response**
  - When did it happen, how many people got infected, what average dosage (τ, N, <D>)
- **The technical challenge**
  - *Infer (τ, N, <D>)*
  - *Inputs: $\{t_i, n_i\}$, $i = 1 \ldots M$*, time series of new symptomatics every day / every 6 hrs.
- **Restrictions**
  - Can only use 3-4 days of data, past 1st diagnosis i.e. M is small
  - Quantify uncertainty due to incomplete observation / limited data
  - Expect noise
  - Expect model errors – i.e. model (used for inference) is approximate

Methodology

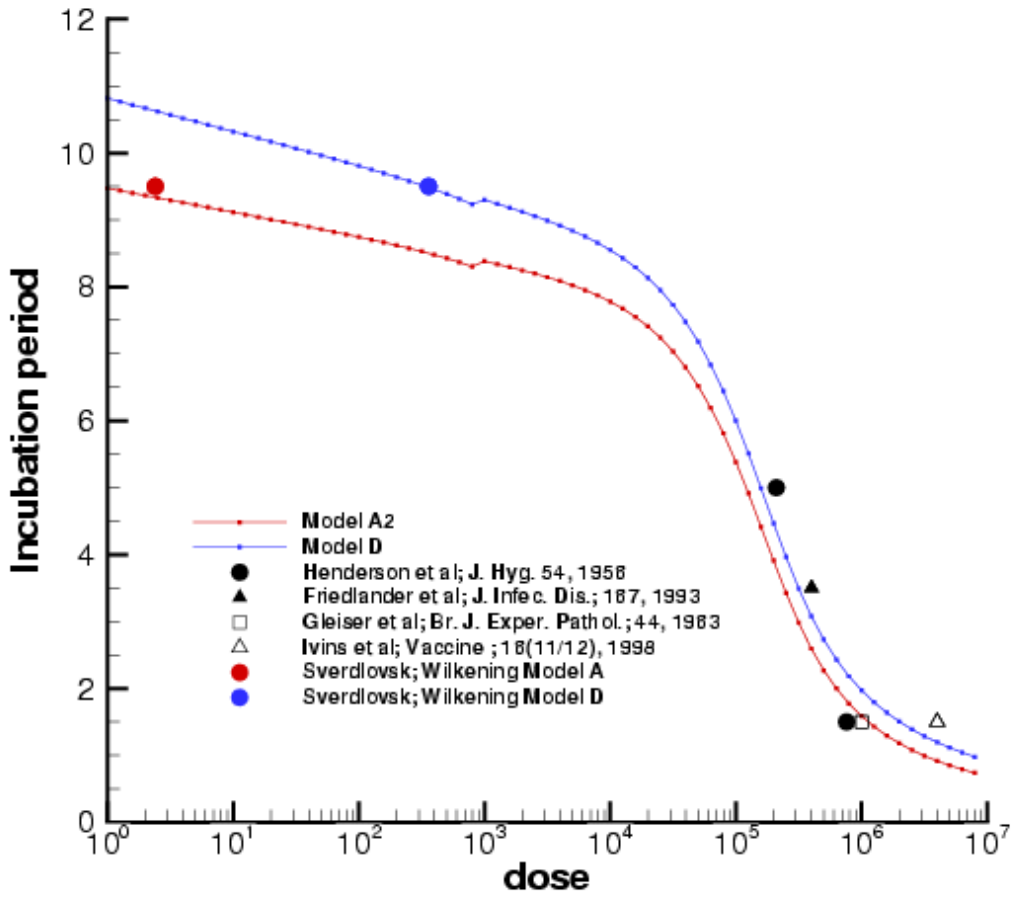
- **Bayesian Inference**
  - Likelihood of observing a $\{t_i, n_i\}$, sequence given a (τ, N, <D>) attack can be analytically derived [1]
  - Exploits the dose-dependent incubation period distribution of a disease
  - i.e. $\Lambda(\{t_i, n_i\} \mid \tau, N, \langle D \rangle)$ exists

$$P(N, \tau, \langle D \rangle \mid \{t_i, n_i\}) \propto \Lambda(\{t_i, n_i\} \mid N, \tau, \langle D \rangle) \pi_N(N) \pi_\tau(\tau) \pi_D(\langle D \rangle)$$

- **Bayes' rule**
  - π_k are priors
  - Should ideally be supplied by syndromic surveillance
  - Outputs : PDFs for N, τ, D
- **Simulated aerosol attacks to generate data**
  - Assume a city with a generic population distribution
  - Lay down a plume, infect people with different dosages
  - Dose dependent anthrax incubation period models [2]
  - Sources of errors
    - Noise
    - Difference in attack and inference models
    - Incomplete observation
- **Also invert the Sverdlovsk anthrax incident of 1979**

1. Ray et al, Sandia Technical. Report., SAND2006-1492
2. Wilkening, PNAS, 103(20):7589-7594, May 2006.

Attack and inference models



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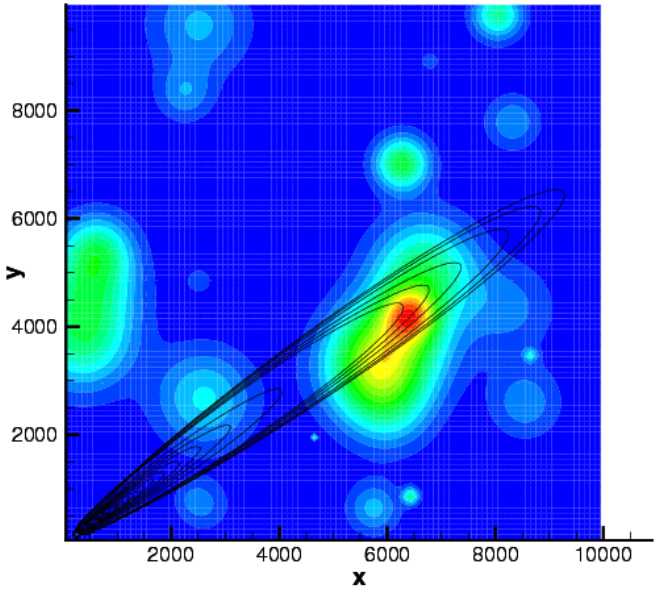
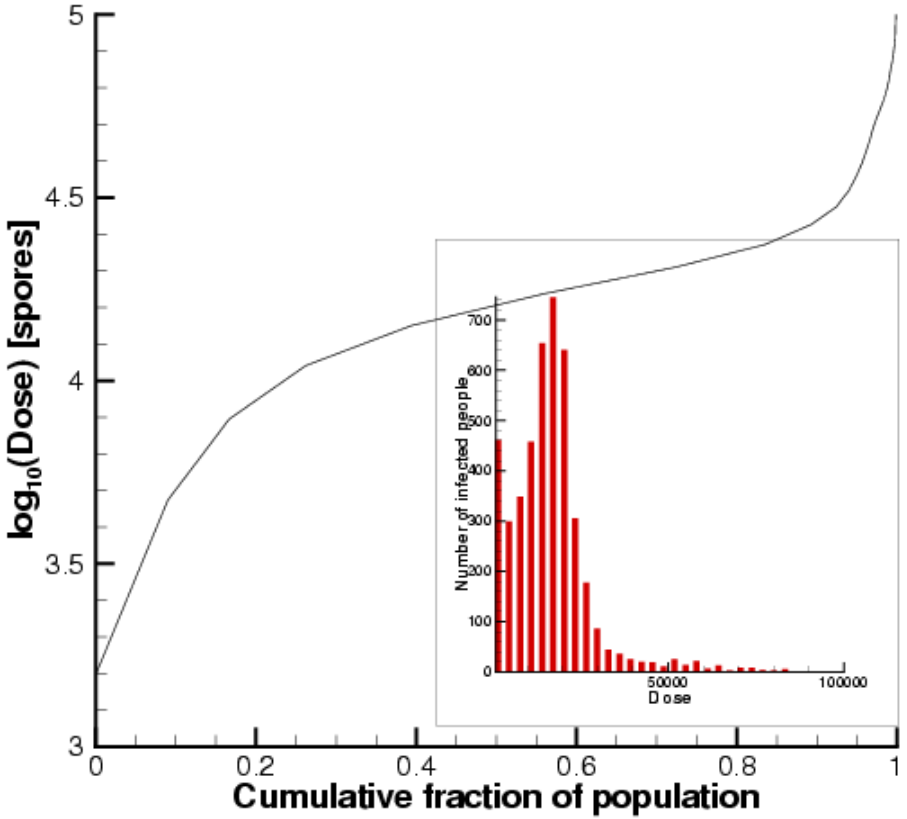
Simulated attack example

- **2 simulated attacks**
  - **Case Small :**
    - **N = 453, t = -0.75, $\log_{10}(\langle D \rangle) = 4.23$**
  - **Case Big :**
    - **N = 4453, t = -0.5, $\log_{10}(\langle D \rangle) = 4.22$**





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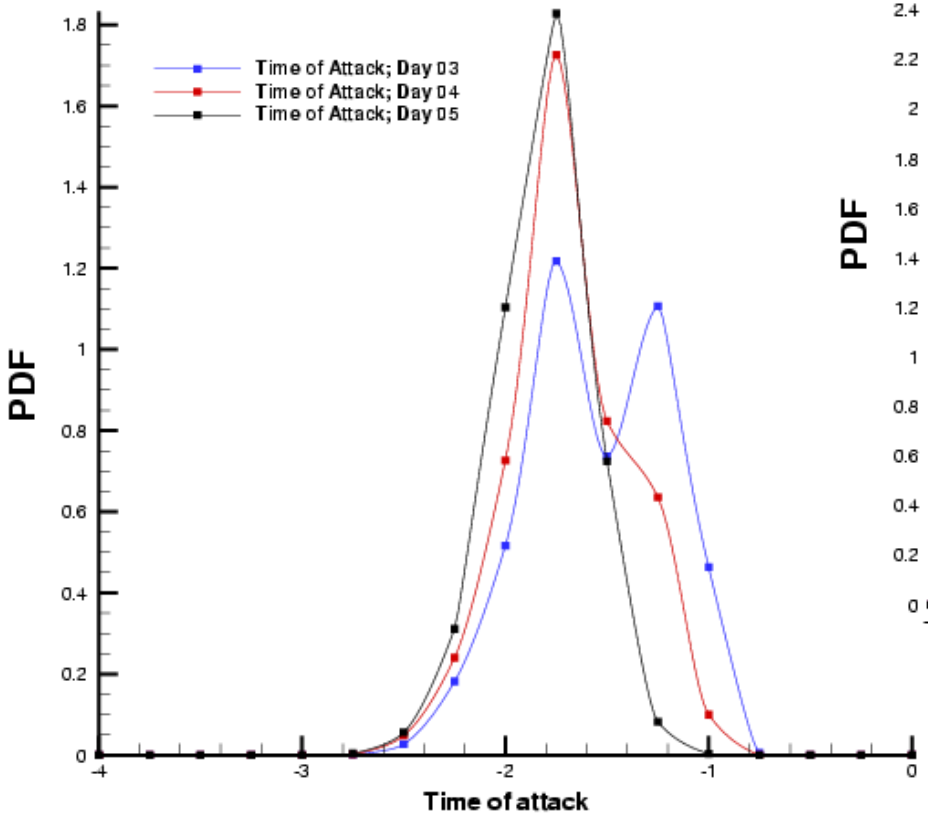
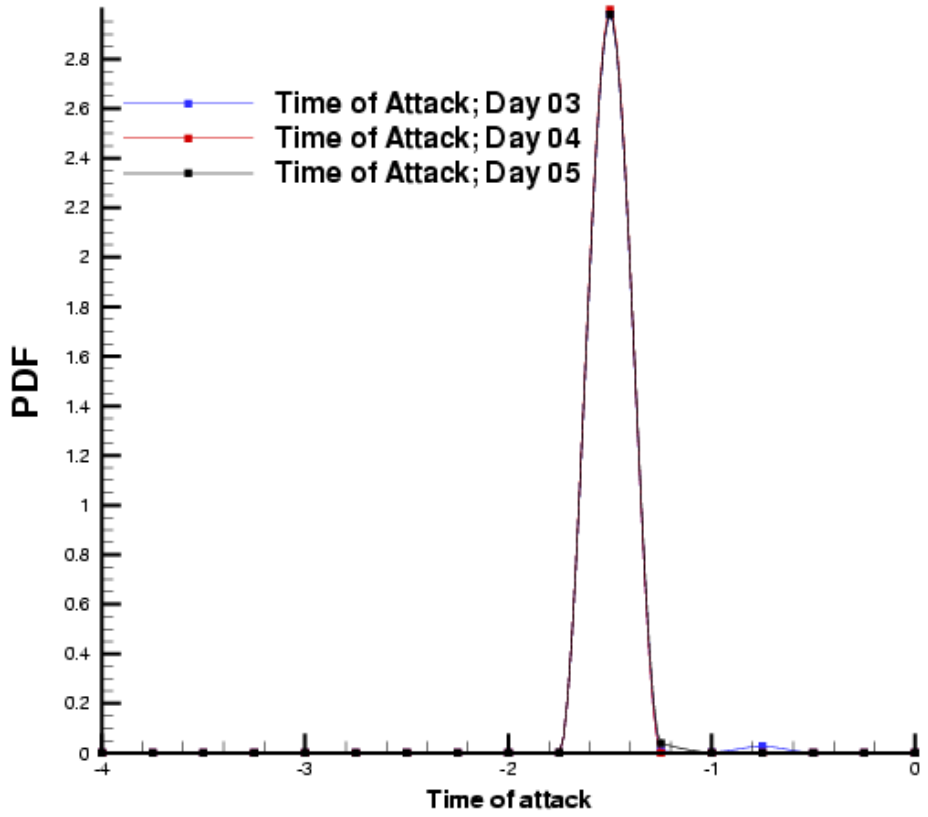
Comparison of inferred time





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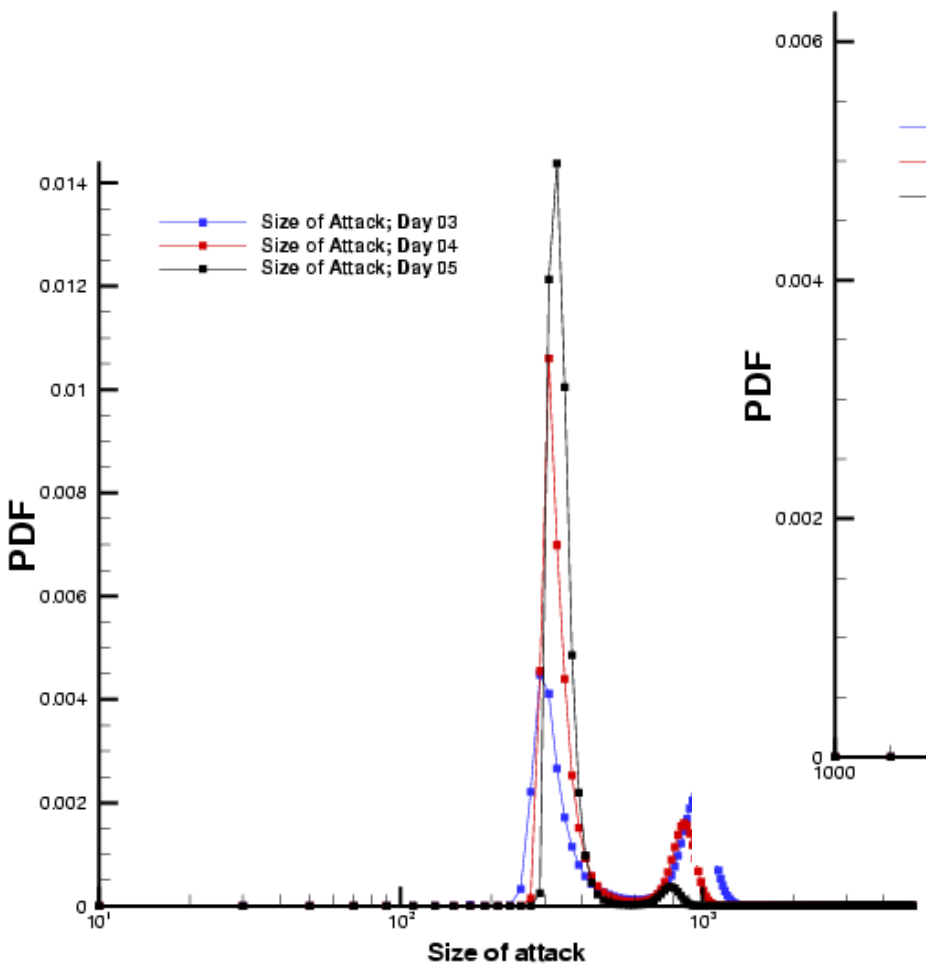
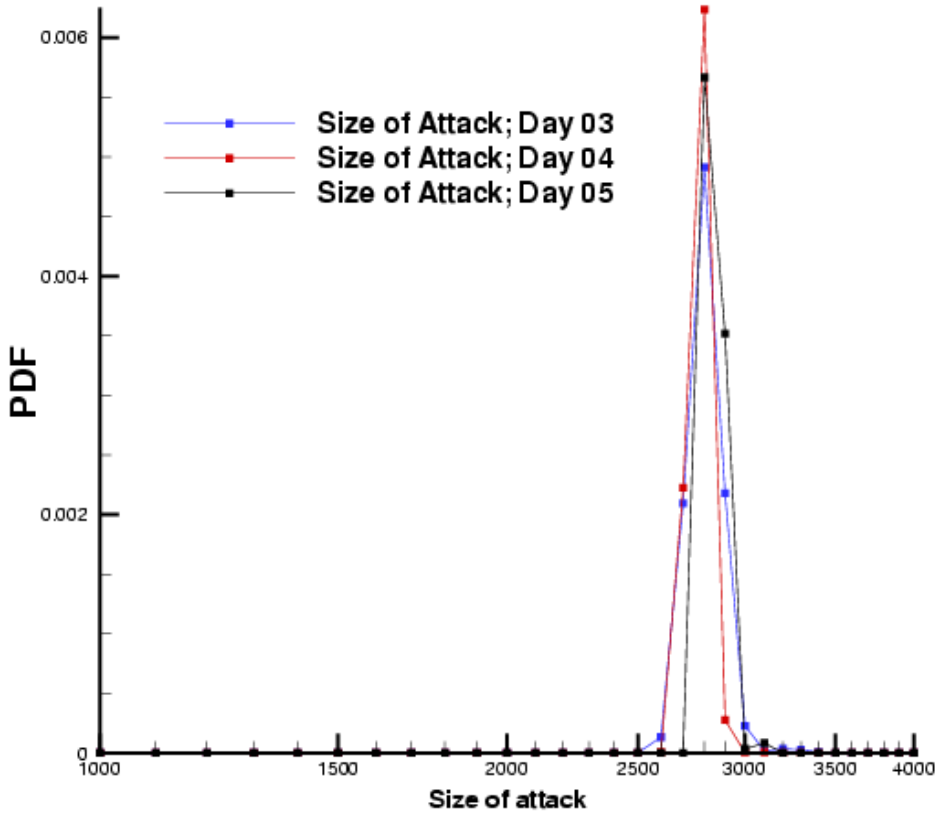
Comparison of inferred size





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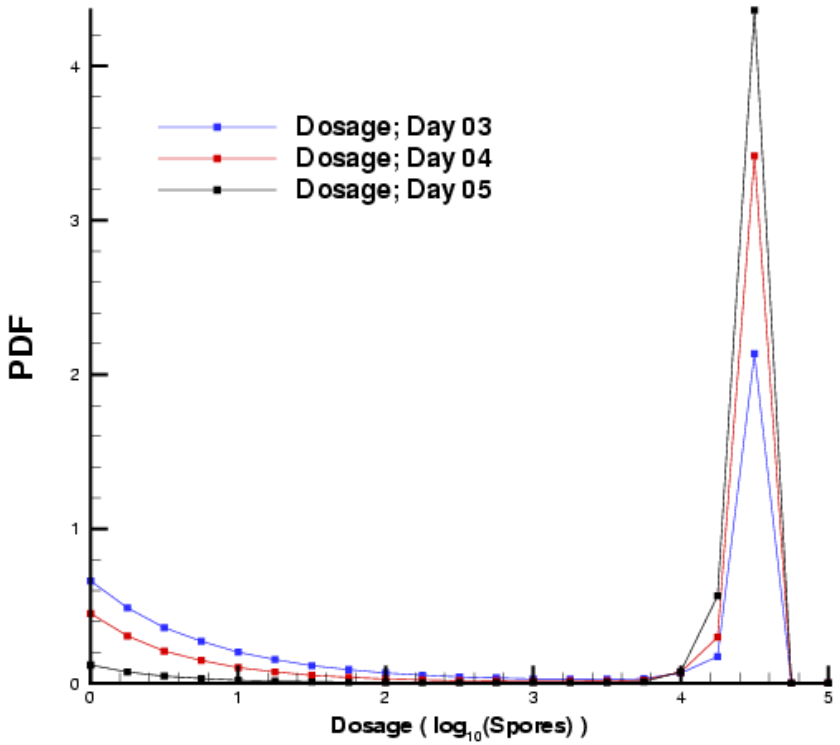
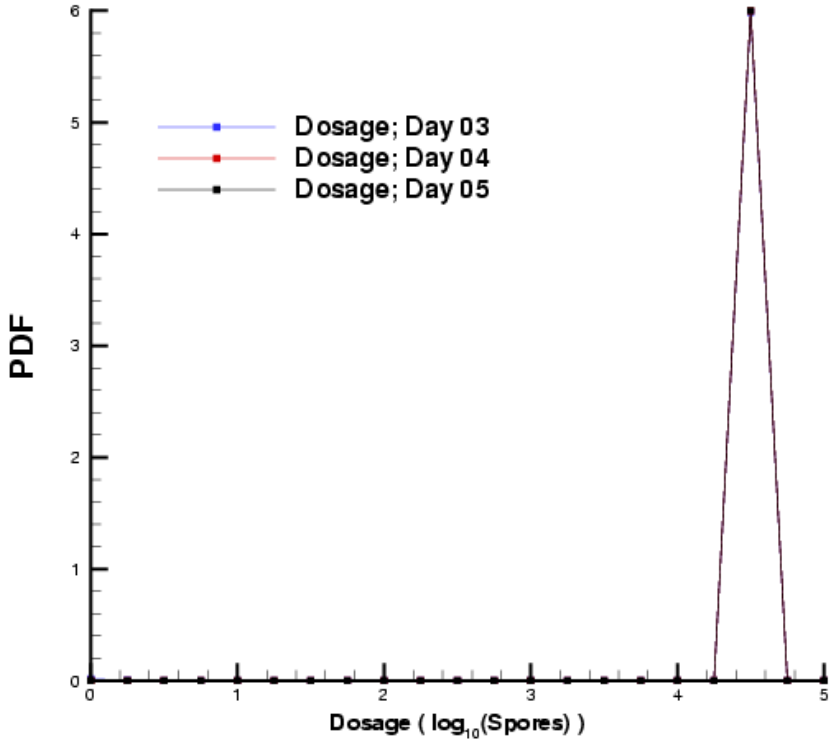
Comparison of inferred dosage





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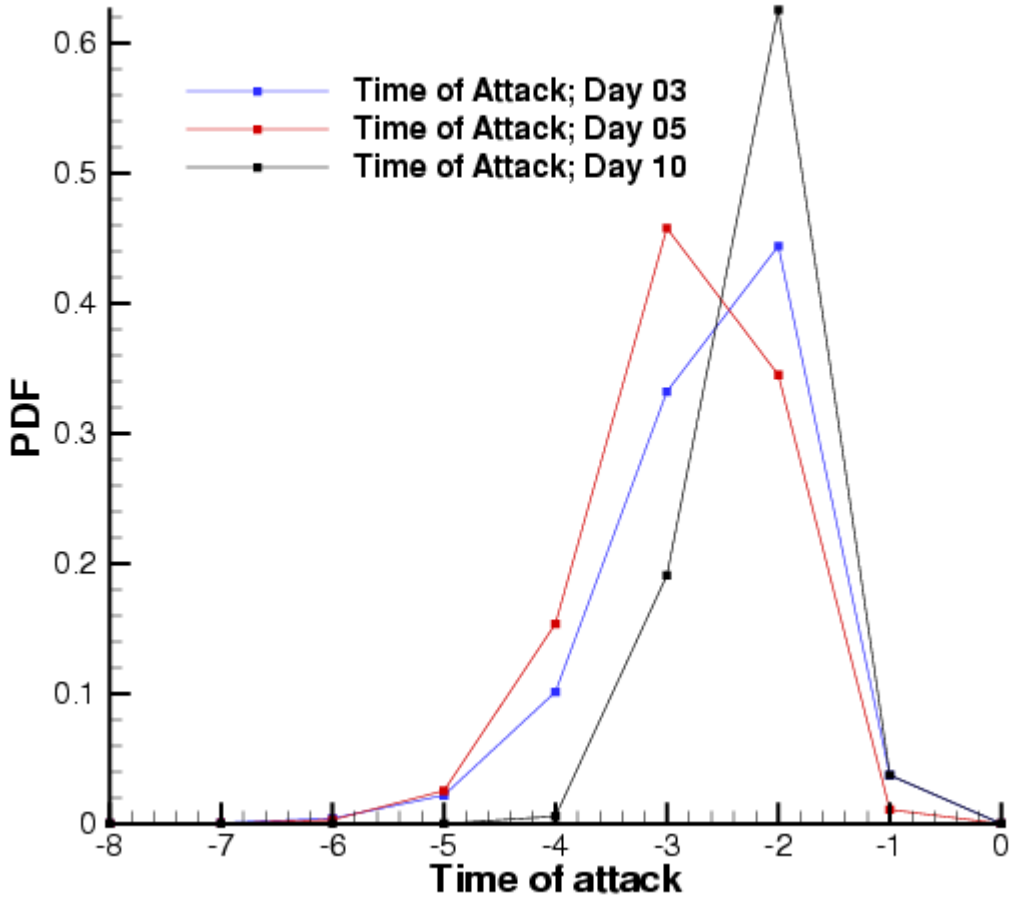
Sverdlovsk,1979

- **Suspected atmospheric release of weapon-grade anthrax formulation from a military compound**
  - **Estimated date : April 2nd, 1979.**
  - **First symptomatic: April 4th, 1979**
  - **Estimated number of infected people: 75 ; 70 died**
- **Challenges**
  - **Small size**
  - **Reconstructed data**
  - **Low dose; estimated dose per person:**
    - **9 spores (Meselson, *Science*, 1994, using Glassman's numbers)**
    - **1-10 spores (Wilkening, PNAS, 103(20), 2006)**
  - **Effect of prophylaxis (initiated April 12th, 1979)**
  - **Vaccination (started : April 15th, 1979 (approx))**

Sverdlovsk, 1979 - Time of infection



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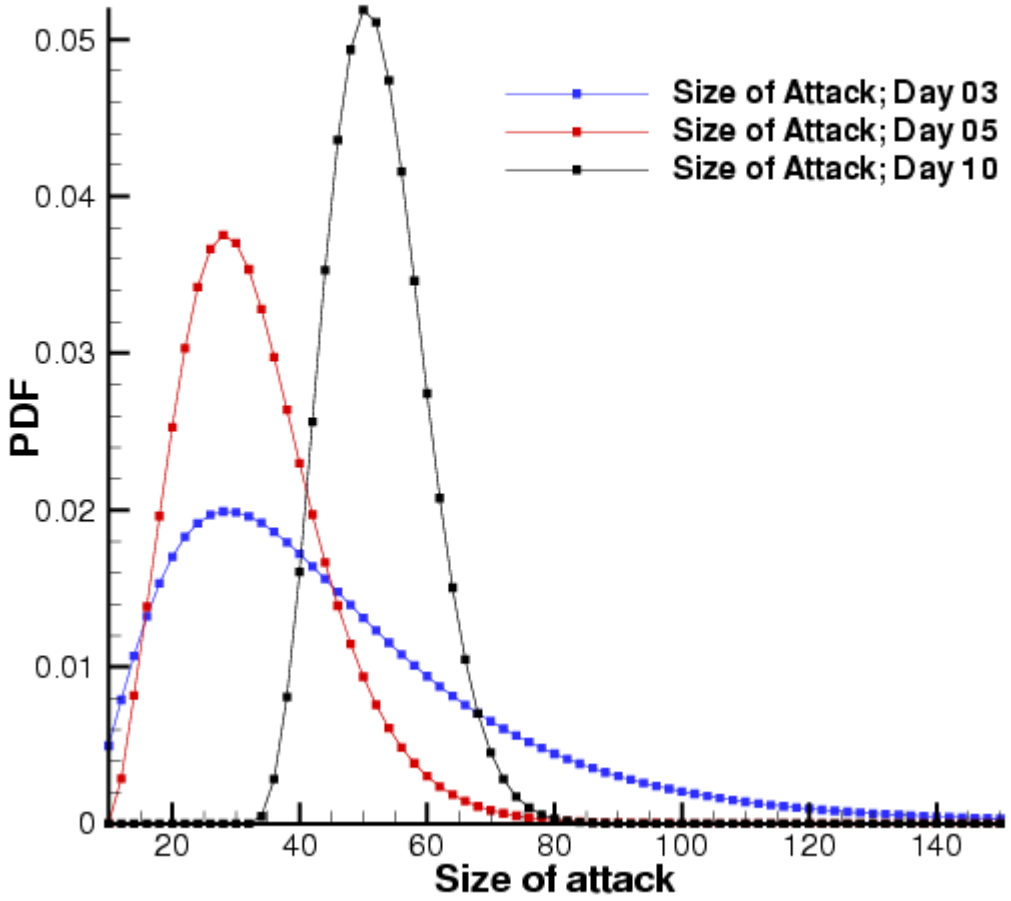
Sverdlovsk, 1979 – Size of infected population



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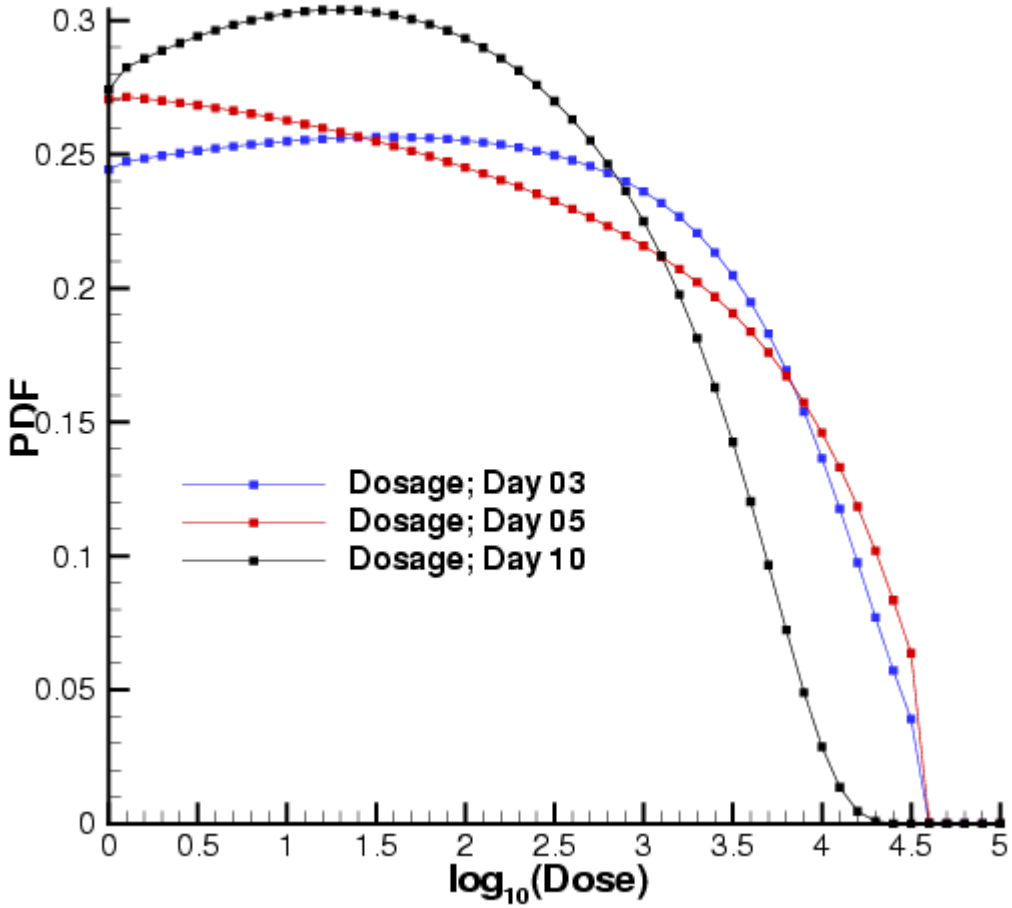
Sverdlovsk, 1979 – Dosage



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Conclusions

- **Rigorous Bayesian formulation to characterize bioterrorist attacks**
  - **Based on when people exhibit symptoms**
  - **Syndromic surveillance acts as a means for forming efficient priors**
  - **Based on evidence i.e. diagnosed patients**
    - **Syndromic surveillance does *not* have to disprove the null hypothesis**
    - **Brings in a spatial component to the anlysis.**
- **Syndromic surveillance + Incident characterization can :**
  - **Quantitatively characterize attacks**
  - **Formulate requirements for medical resources**
  - **Help in logistics.**

Background

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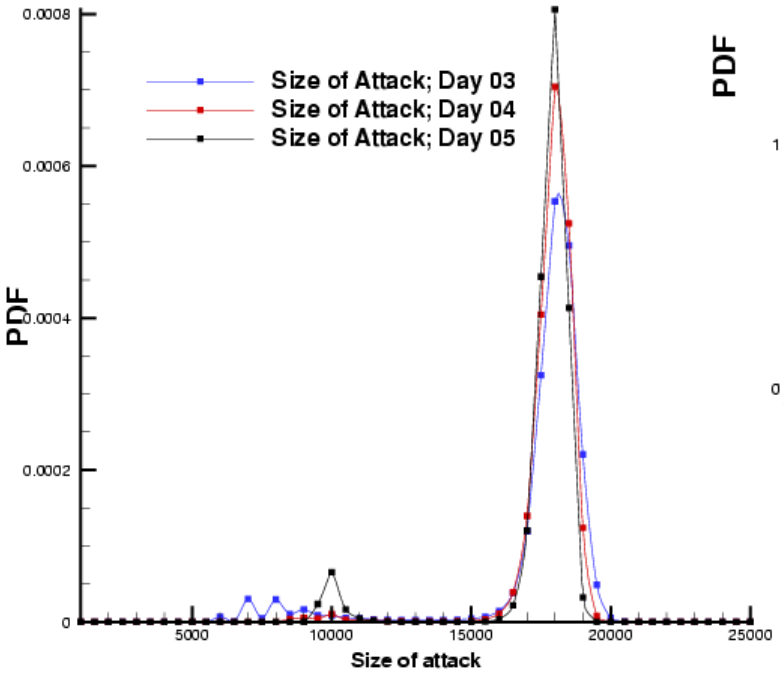
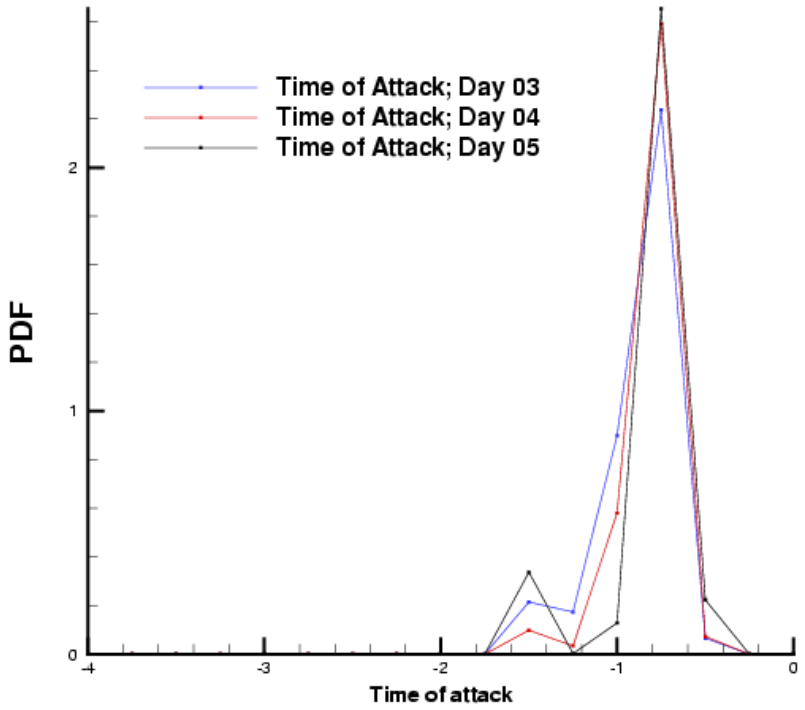
A spectacular failure

- Attack : N = 10^4, τ = - 1.5, D = 10^4
- 3-5 days of data





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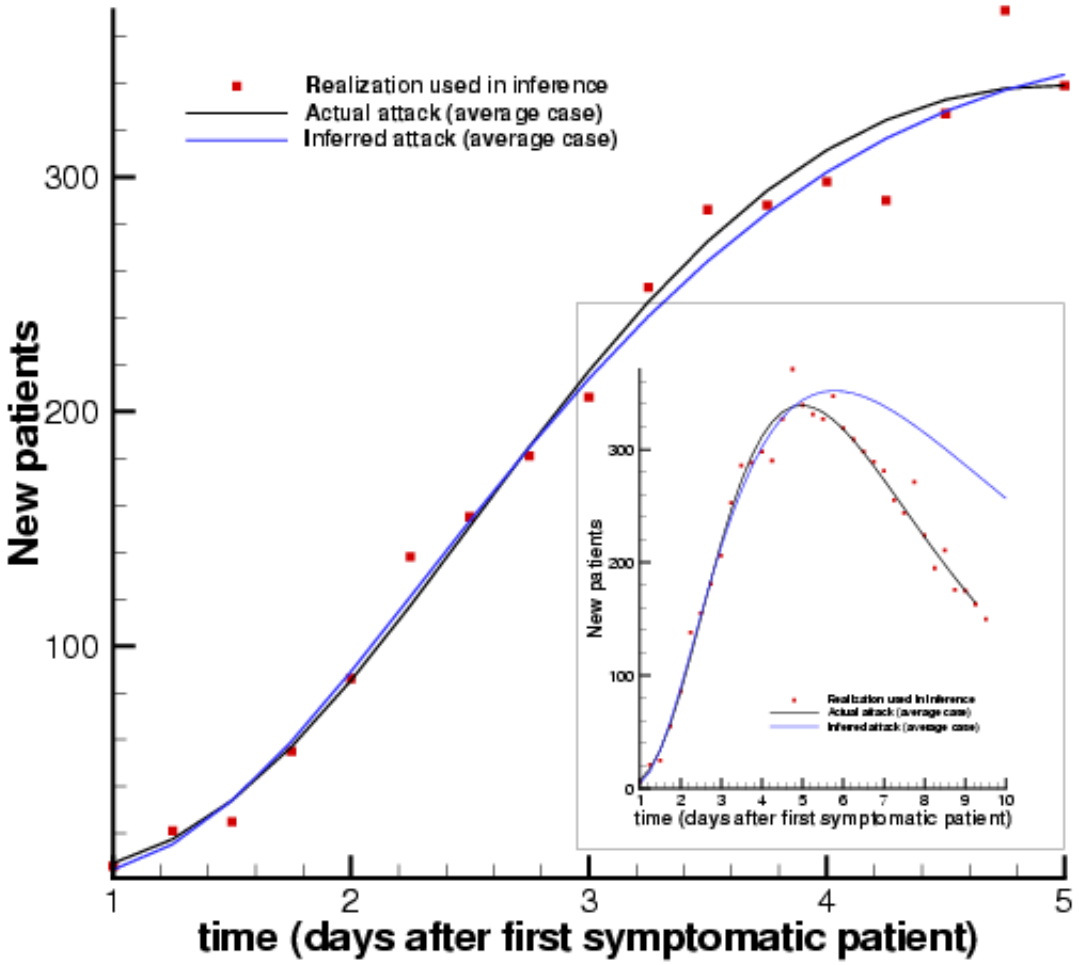
Why?



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