A Bayesian Approach for Estimating Outbreak Characteristics from Patient Data

Abstract # 4469

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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
- **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
  - Noise – stochastic data
  - Expect model errors – i.e. model (used for inference) is approximate

Methodology

- **Research Challenge**
  - Little prior work – 2 published papers on the general topic
  - No contagious diseases, simplified models for non-contagious ones
  - All recent publications (oldest is 2004)
- **Bayesian Inference**
  - Likelihood Λ 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

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

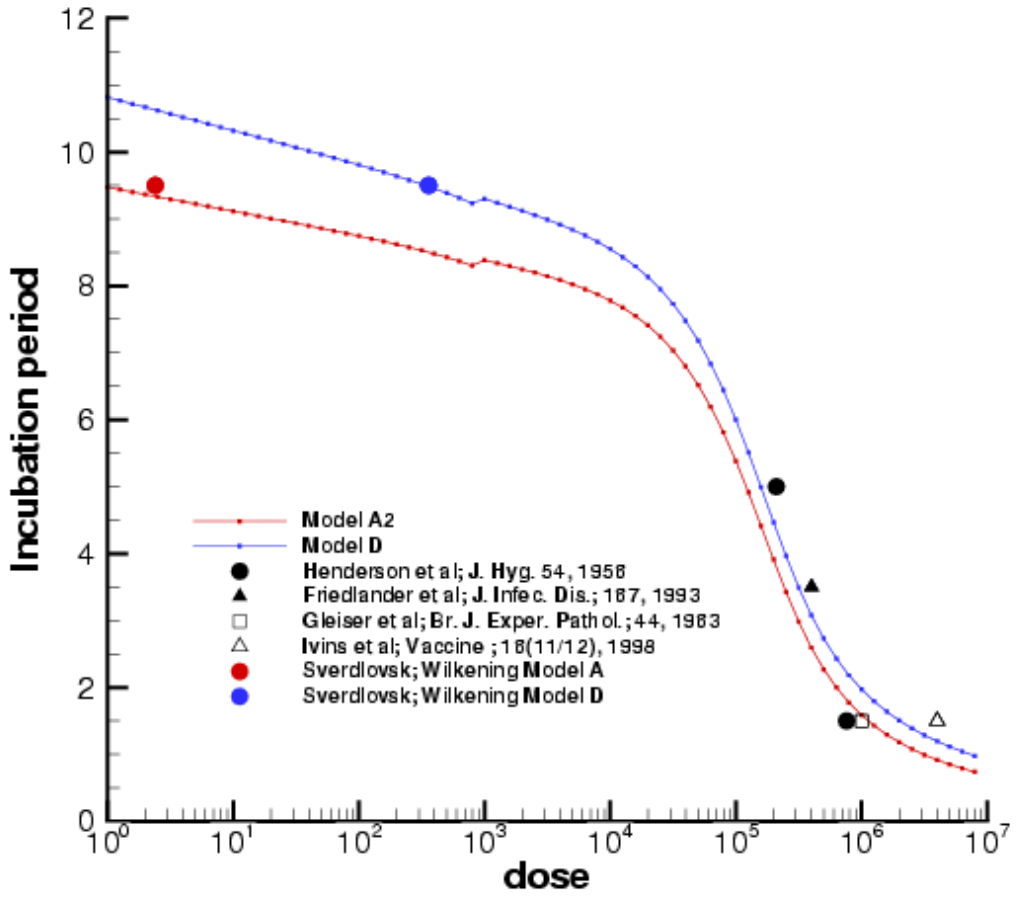
- **Simulated aerosol attacks to generate data**
  - Assume a city with a generic population distribution
  - Lay down a plume, infect people with different dosages
  - Dose dependent anthrax incubation period models [2; stochastic !]
  - Sources of errors – noise, model errors, incomplete observation
- **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.

Anthrax incubation period models

- Spores are subjected to competing processes
  - Clearance by immune system and germination into vegetative cells (rates obtained from non-human primate expts.)
  - PDF for time to germination (PDF #1)
- Vegetative cells reproduce at various rates (random variable)
- A threshold number of vegetative cells triggers symptoms
- Time from germination to symptoms, s, has a log-normal distribution (PDF #2)
- Convolution of PDF # 1 and PDF #2 gives incubation period distribution
- Parameters calculated from non-human primate experiments and Sverdlovsk, 1979.

Attack and inference models



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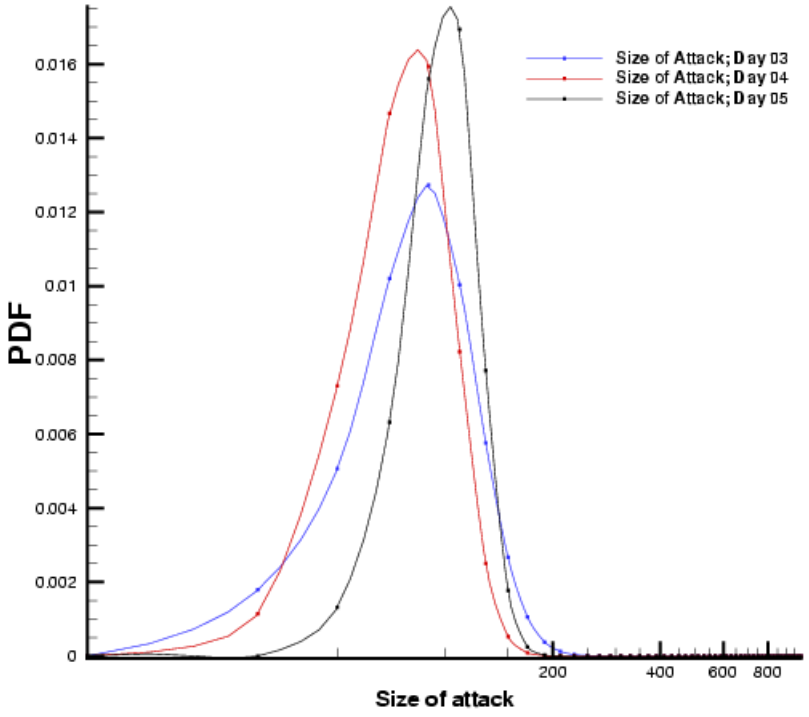
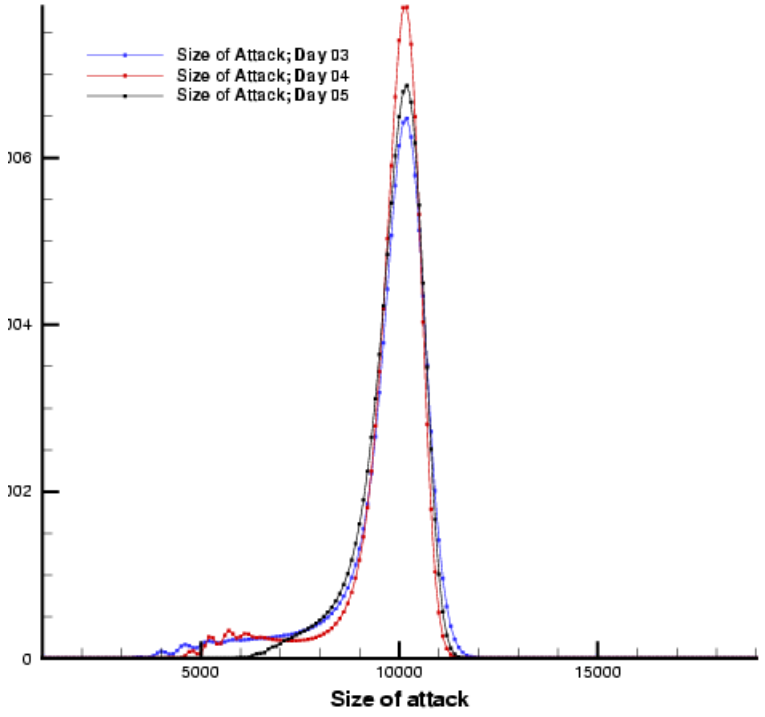
Check No. 1 – Ideal case

- Does the method work in the ideal case?
- Approach :
  - Simulate 2 "ideal" attacks
    - Case B : 100 infected people
    - Case E : 10,000 infected people
  - Every infected person receives a dose of 100 spores
  - The disease progresses as per the blue model
  - Collect observations (# of symptomatic people) over 6-hr intervals
  - Inference as per blue mode too
    - No model errors !
  - Infer characteristics of attack based on 3-5 days of data
- Discrepancy between characterization and simulation due to:
  - Noise in the observations
  - Incomplete observation

Inference of size of attack





Case B : N = 100, τ = -2.25, $\log_{10}(D) = 2$

Case E : N = 10,000, τ = -1.0, $\log_{10}(D) = 2$

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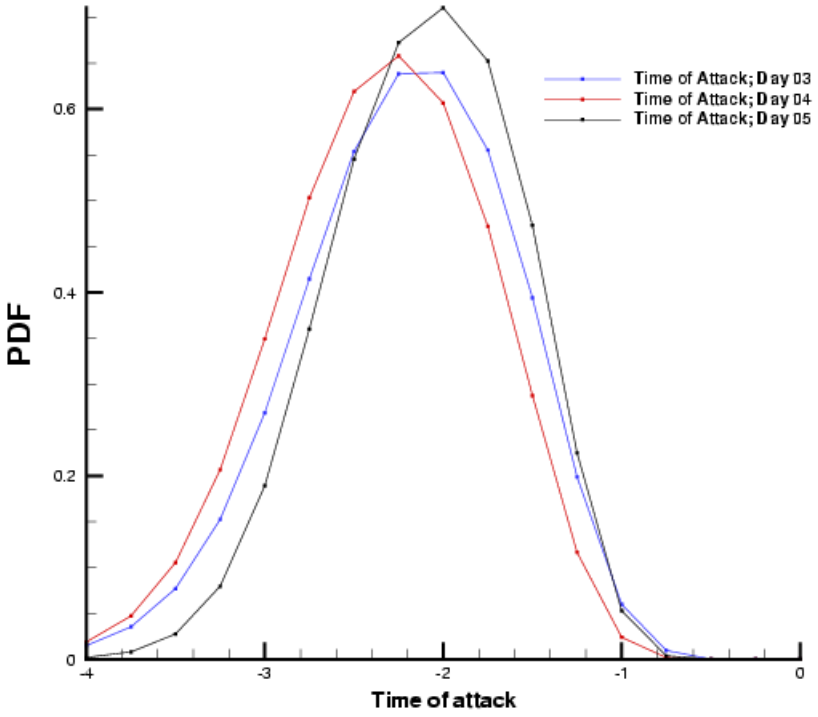
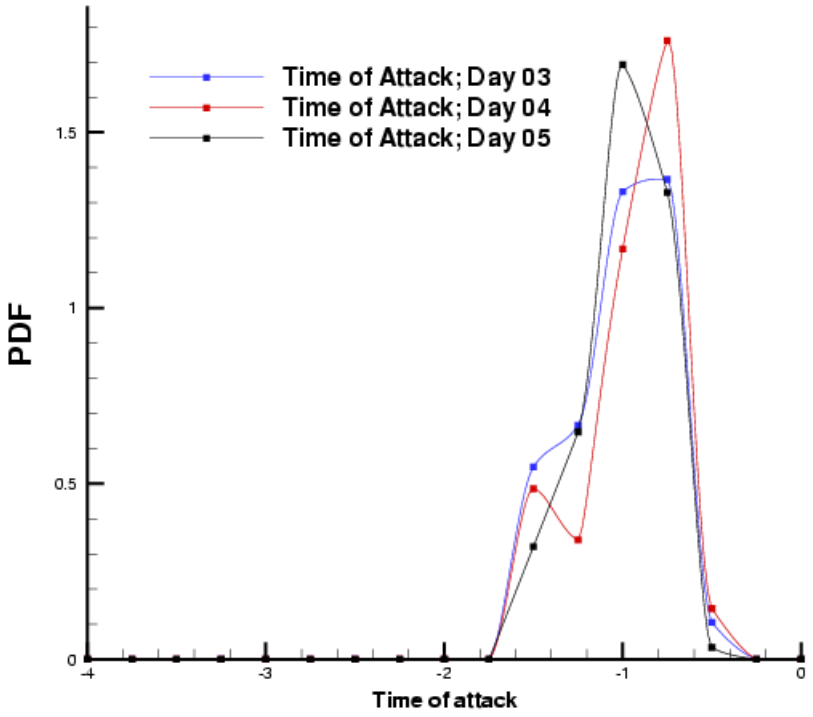
Inference of time of attack



Case B : N = 100, τ = -2.25,
$\log_{10}(D)$ = 2



Case E : N = 10,000, τ = -1.0,
$\log_{10}(D)$ = 2

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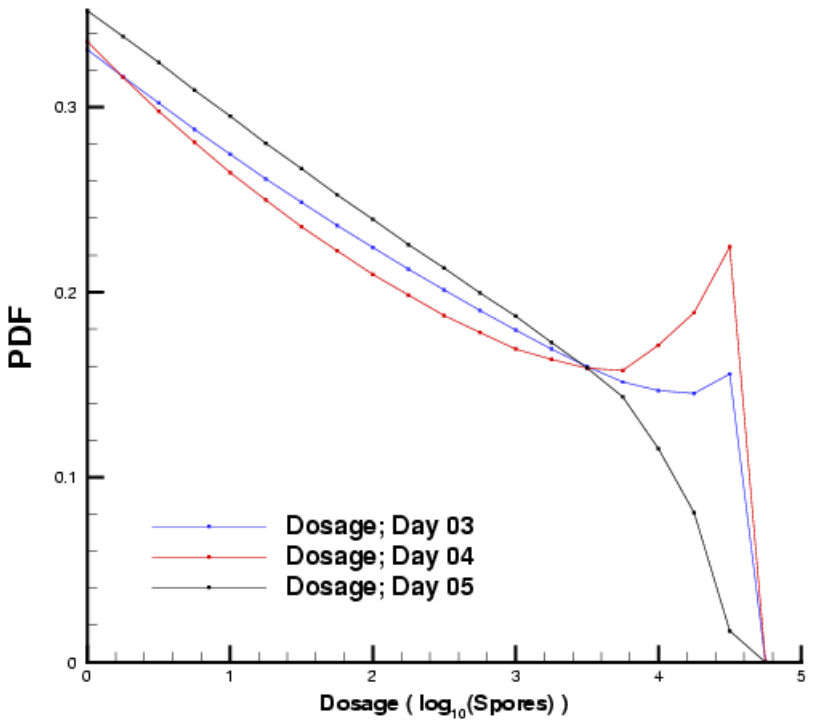
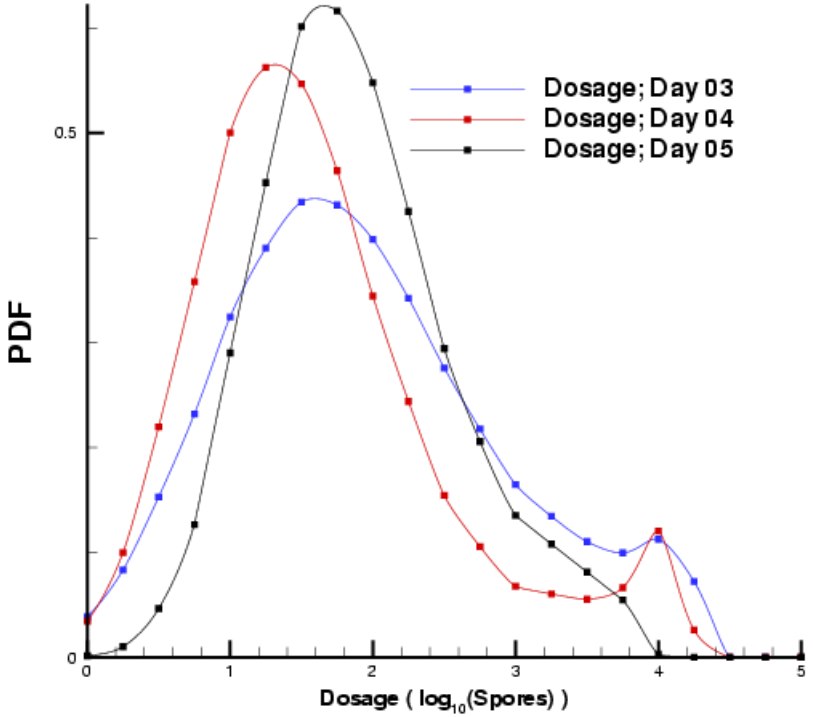
Inference of dosage received during attack



Case B : N = 100, τ = -2.25, $\log_{10}(D) = 2$



Case E : N = 10,000, τ = -1.0, $\log_{10}(D) = 2$

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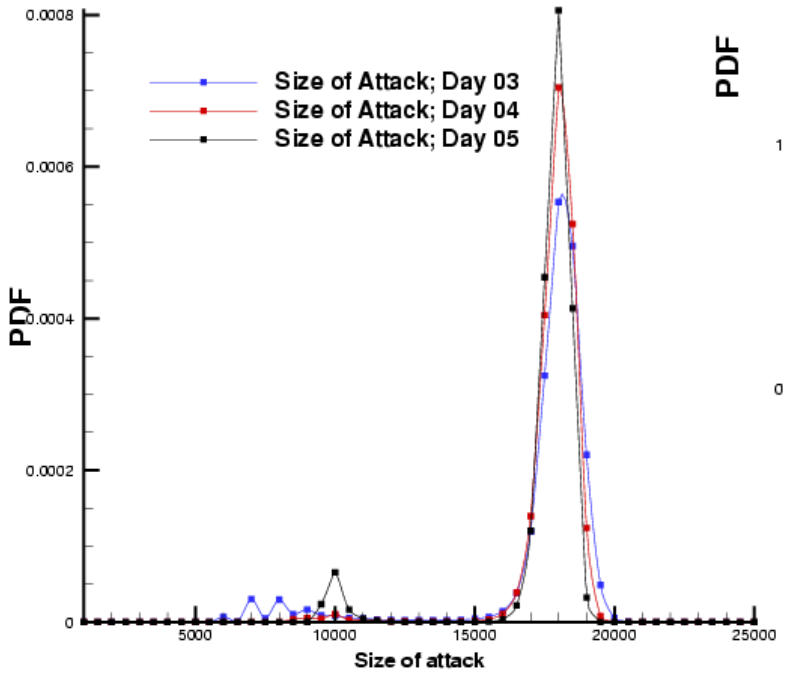
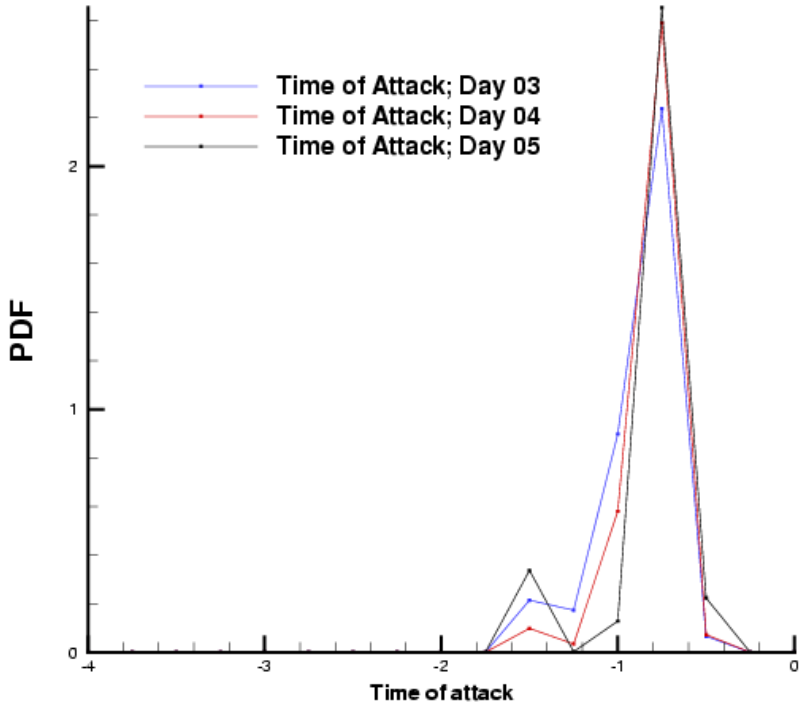
A spectacular failure

- Inferring with partial observations can lead to spectacular failures
- Time series : {2, 369, 938, 1102, 958}
- Attack : N = 10^4, τ = - 1.5, D = 10^4





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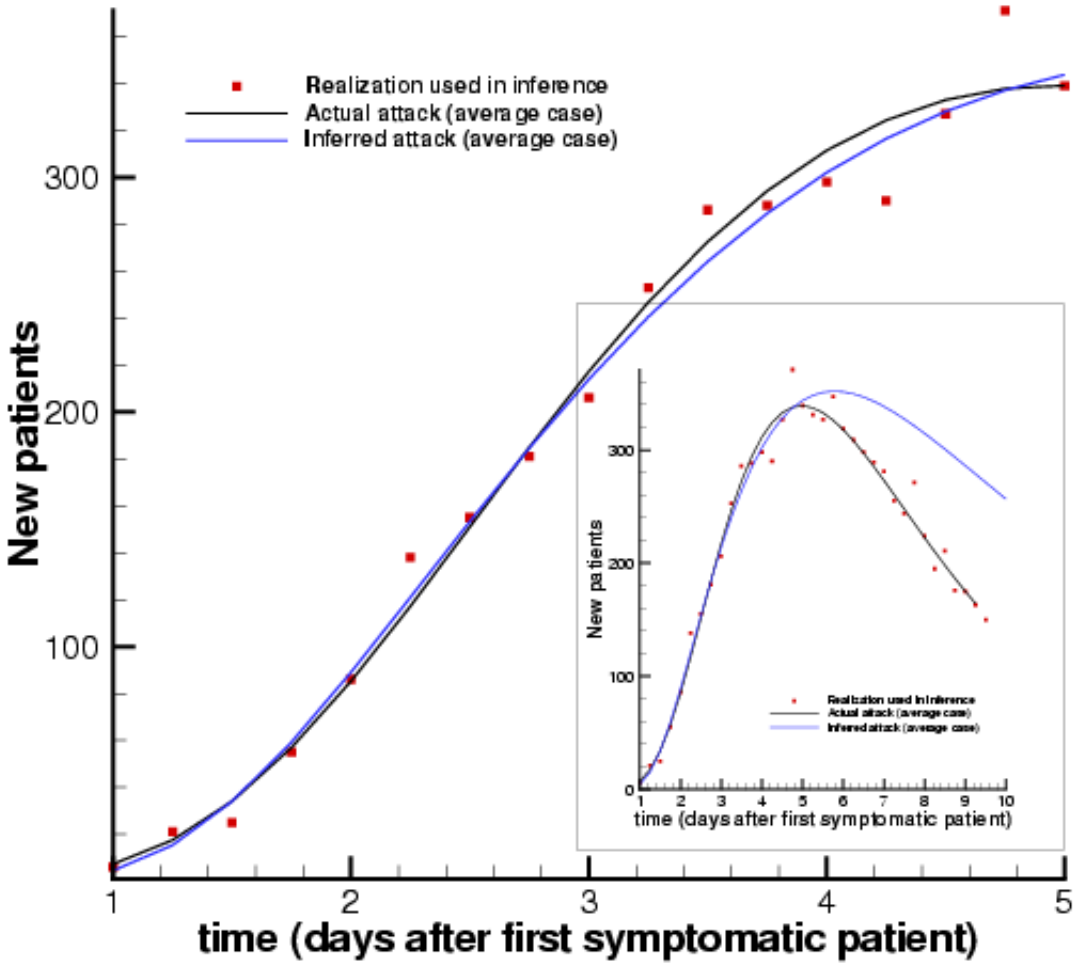
Why?



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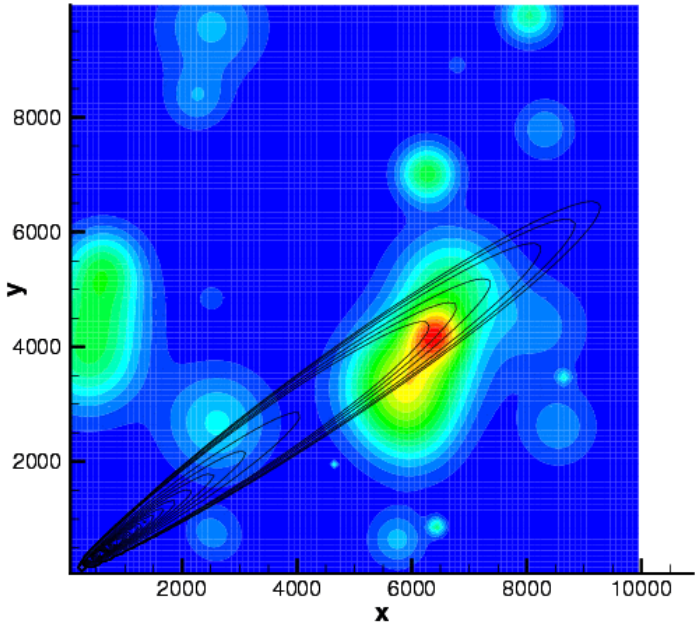
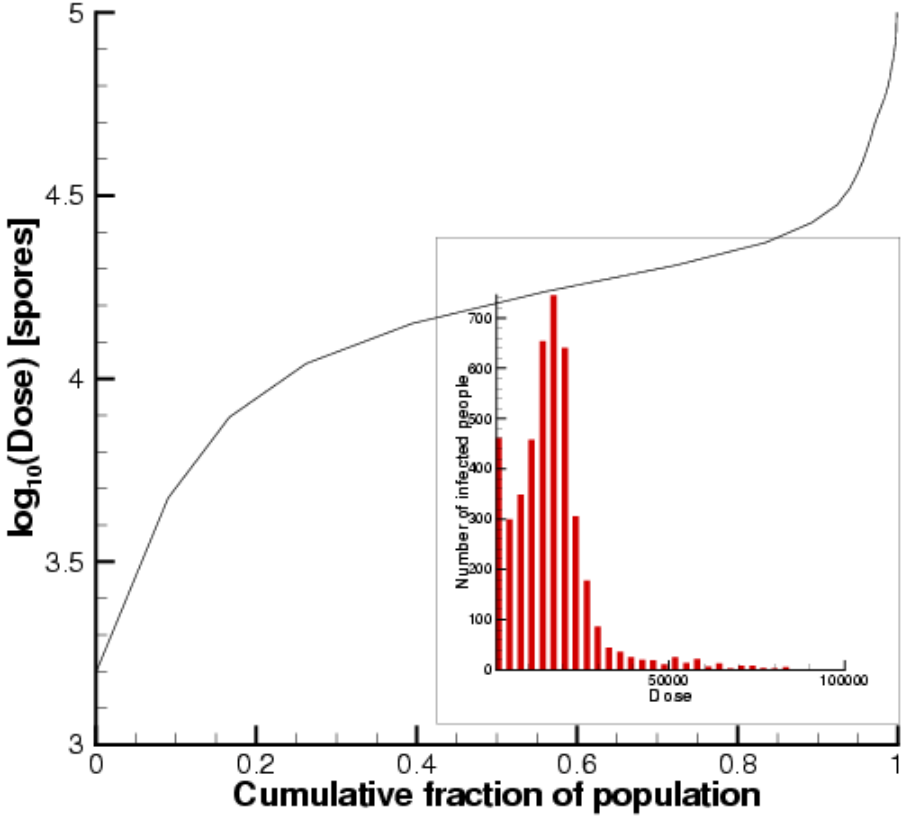
Synopsis of the first check

- Given ideal case (accurate model and uniform dose), the inverse problem
  - Reliably infers size and time
  - Dosage is hard for small attacks
  - Large attacks are easier to infer
  - Characterizations can go wrong when based on incomplete observations, *but....*
  - Always recovers to correct one when more data becomes available.
- The method is mathematically consistent, *but….*
- *Is it useful / applicable in non-ideal cases?*

Simulated attack example

- **Simulated attack**
  - **Case: N = 453, t = -0.75, $\log_{10}(<D>) = 4.23$**
  - **Time series: {1,36,57,55,56}**





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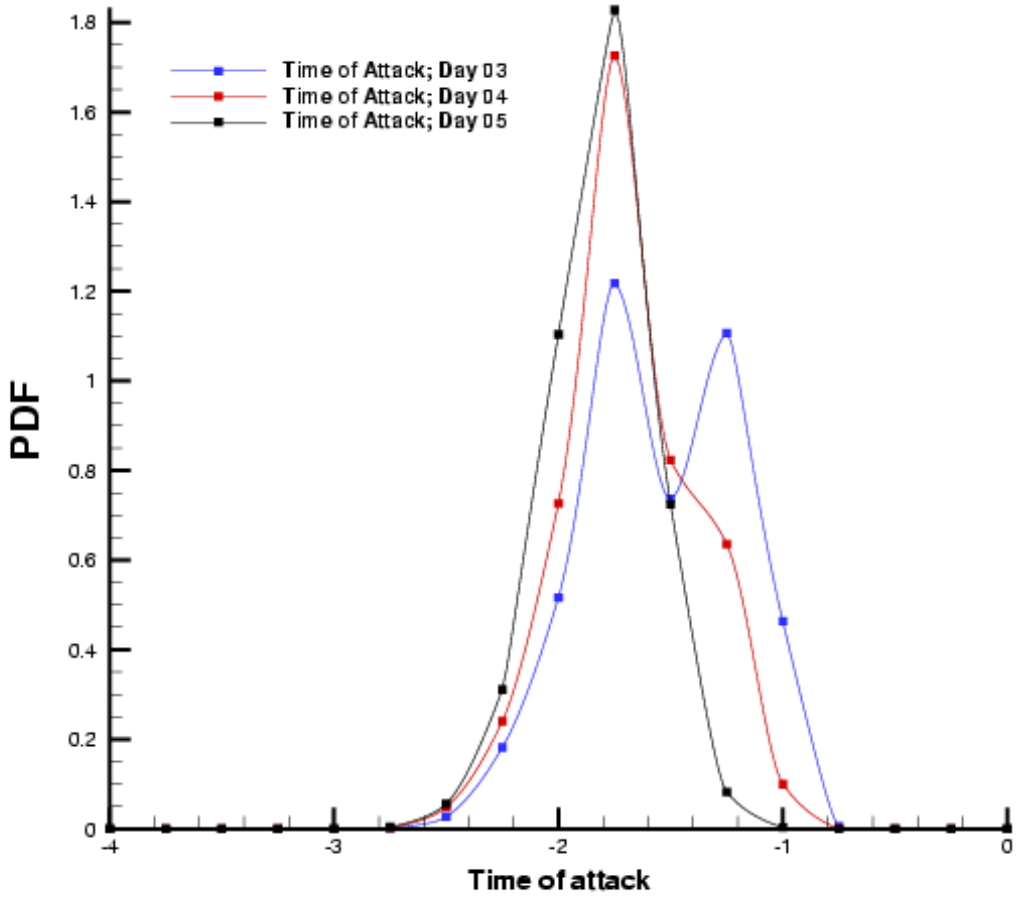
Comparison of inferred time



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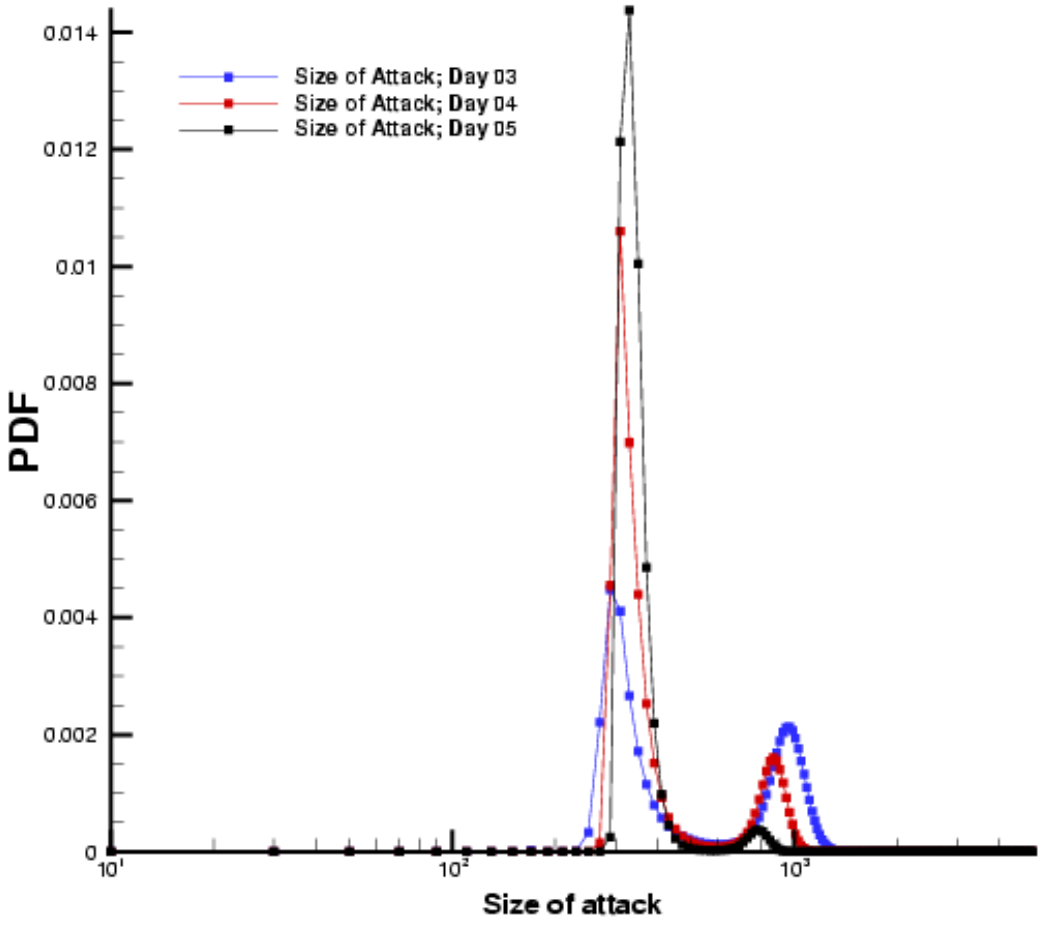
Comparison of inferred size



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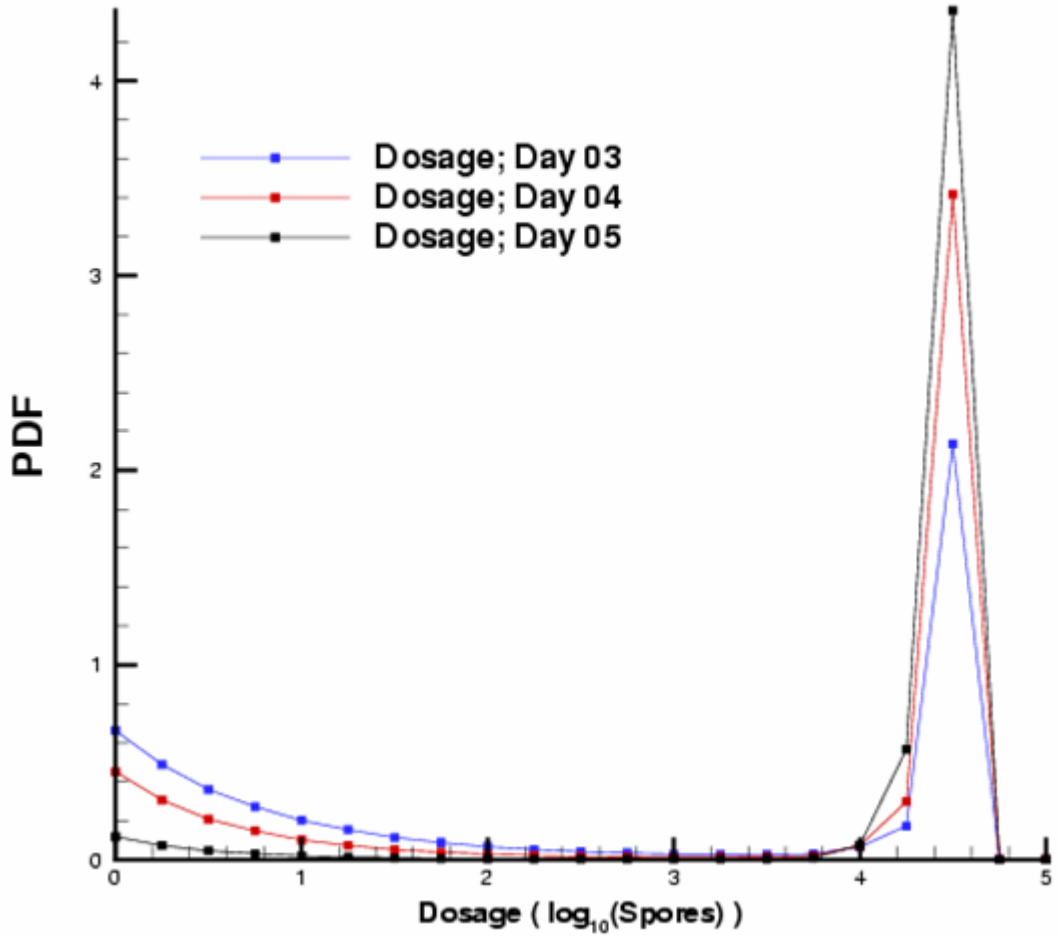
Comparison of inferred dosage



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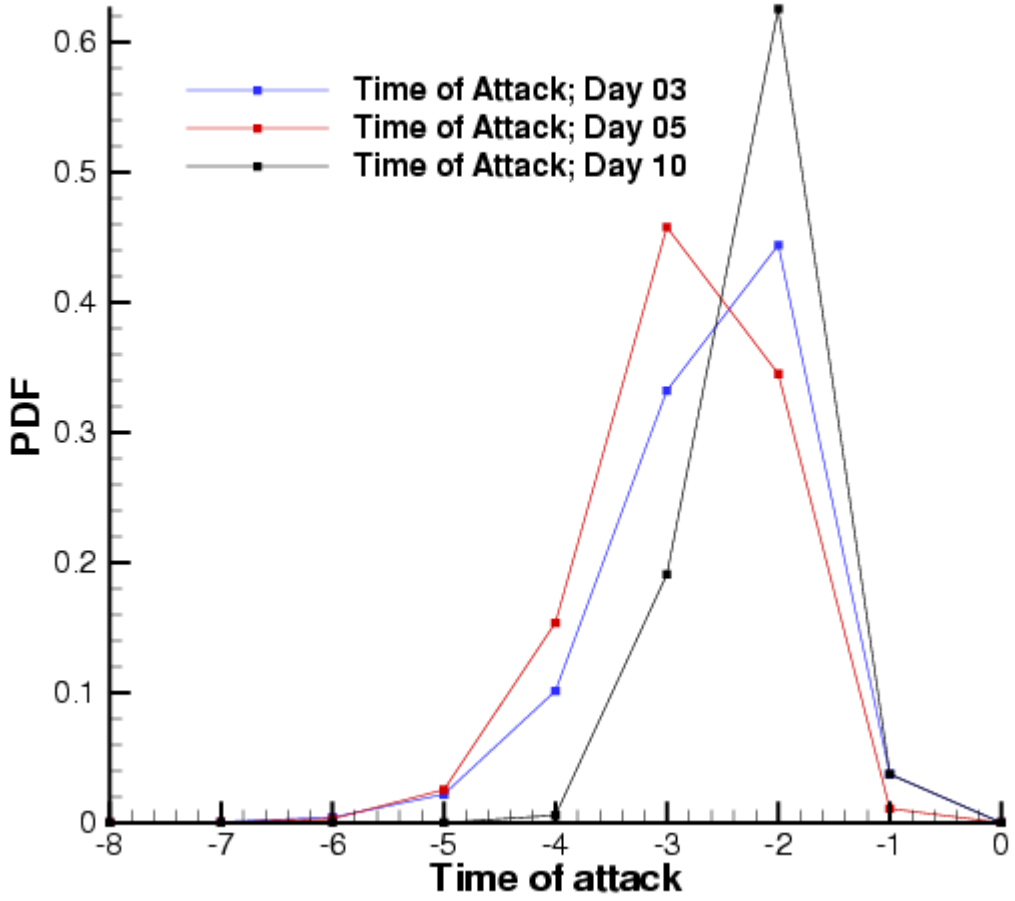
Sverdlovsk,1979

- **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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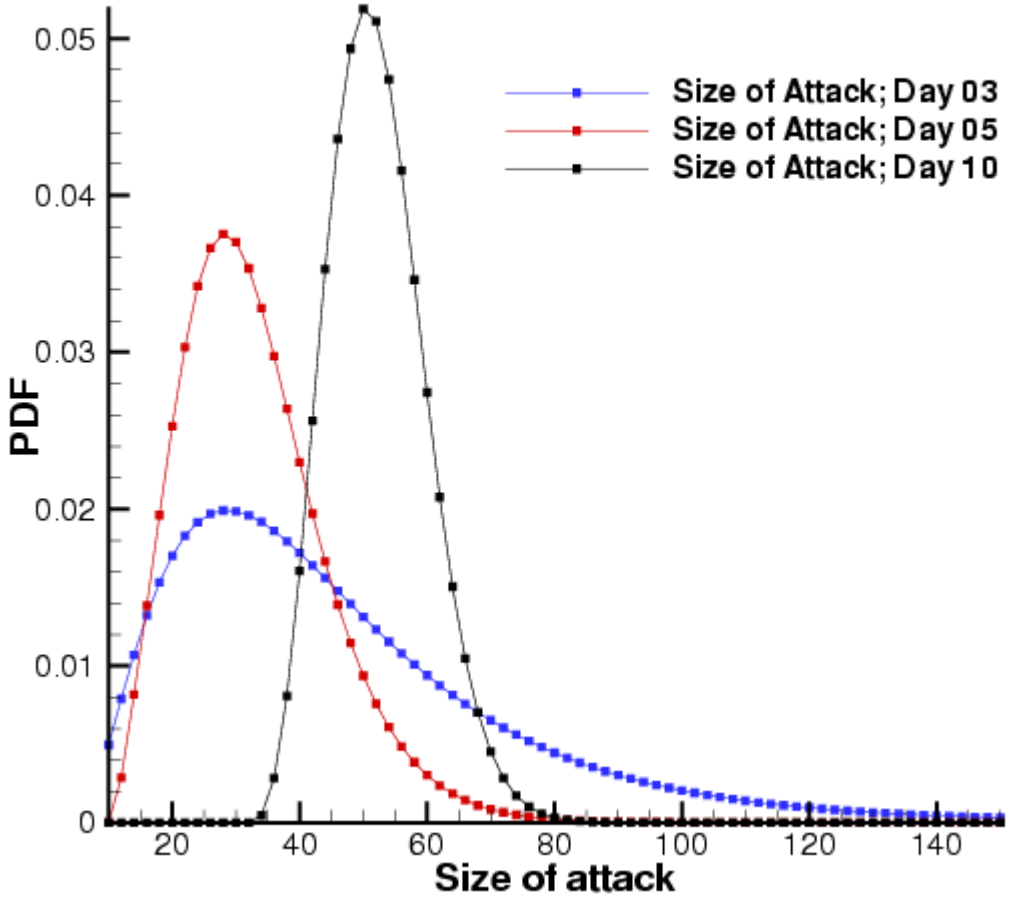
Sverdlovsk, 1979 – Size of infected population



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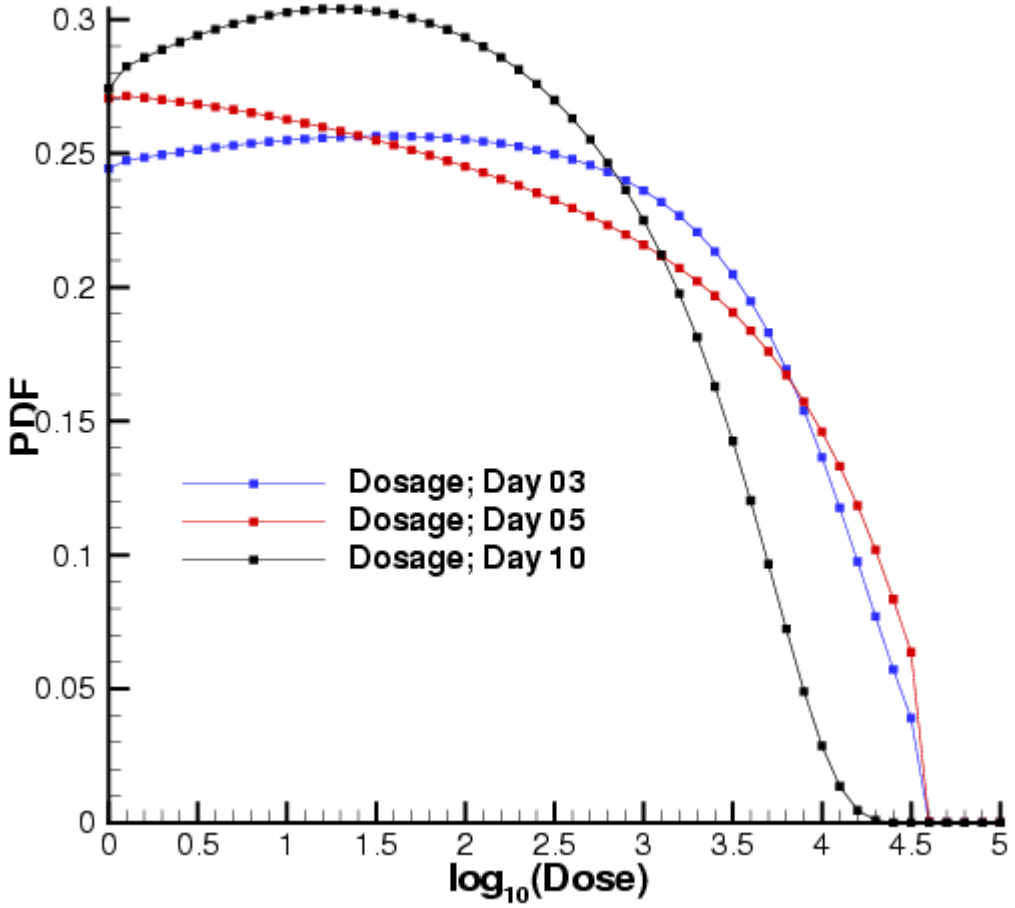
Sverdlovsk, 1979 – Dosage



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Conclusions

- **We have**
  - **A rigorous Bayesian formulation to characterize bioterrorist attacks (anthrax)**
  - **Can be extended to smallpox, plague and other disease with a *symptomatic* contagious period.**
- **We need, in short order,**
  - **To bring in a spatial component into the inverse problem,**
  - **Ditto, contagious diseases**
- **Ultimately, need to design a risk-based response plan**
  - **Characterization not very useful if the cavalry rides in every time someone sneezes.**
- **More Information :**
  - **Ray et al, "A Bayesian method for characterizing distributed micro-releases", Sandia Technical Report, SAND2006-7568, Printed December 2006. Unclassified, unlimited release.**

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