Responding to Bioterrorism: From Risk Assessment to Risk Management

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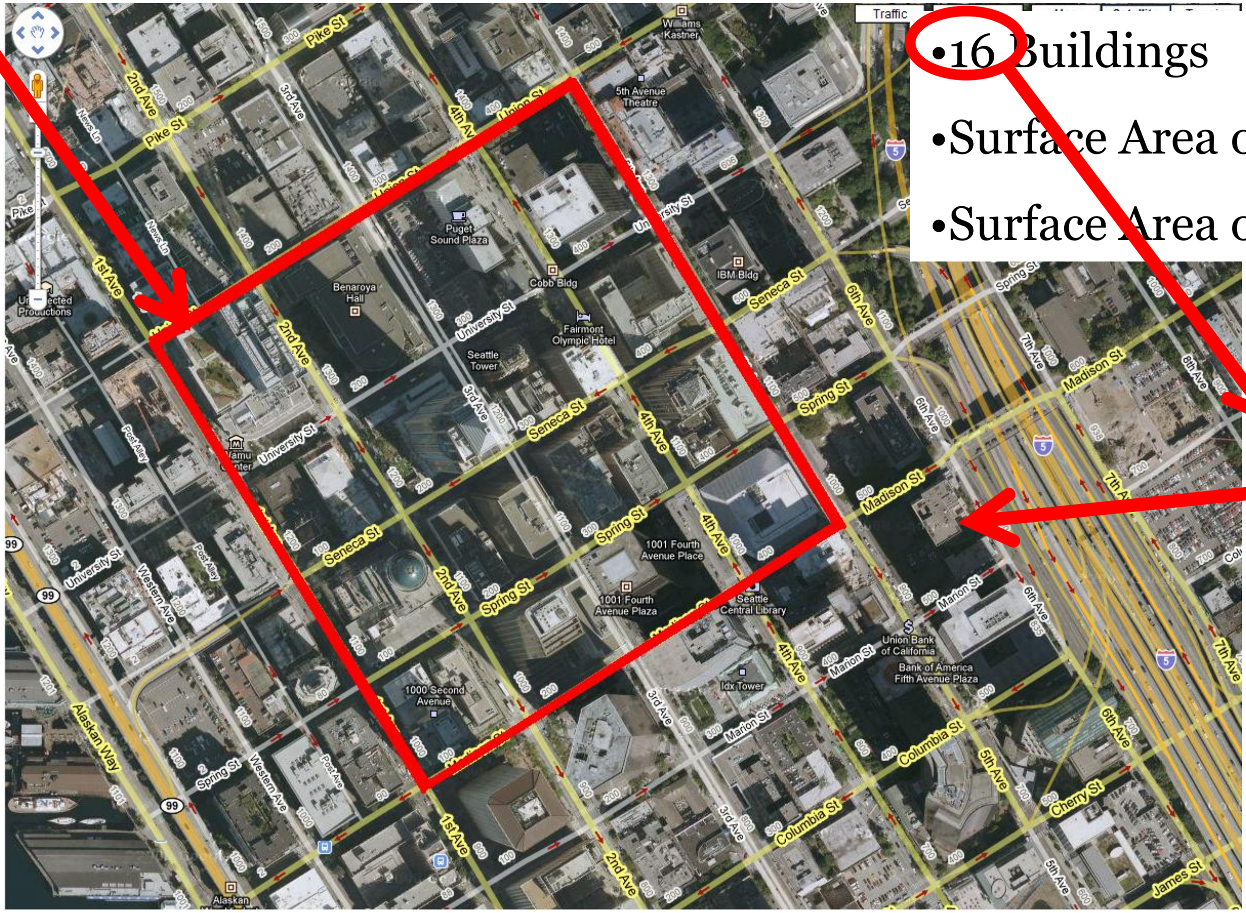
B. Anthracis release

Who drew this nice red square?



- 16 Buildings
- Surface Area of buildings
- Surface Area of sidewalks

What if I live in building #17?

- “Tolerable risk = 1 in 1,000,000”

Risk-informed Decision Making

- It’s all very well for us to talk about how “bright lines” don’t exist between acceptable and unacceptable risk
  - Voluntary vs. involuntary
  - Signal value
  - Dread
- But sometimes you either respond or don’t respond to a risk
  - Sounds kind of like a bright line.....

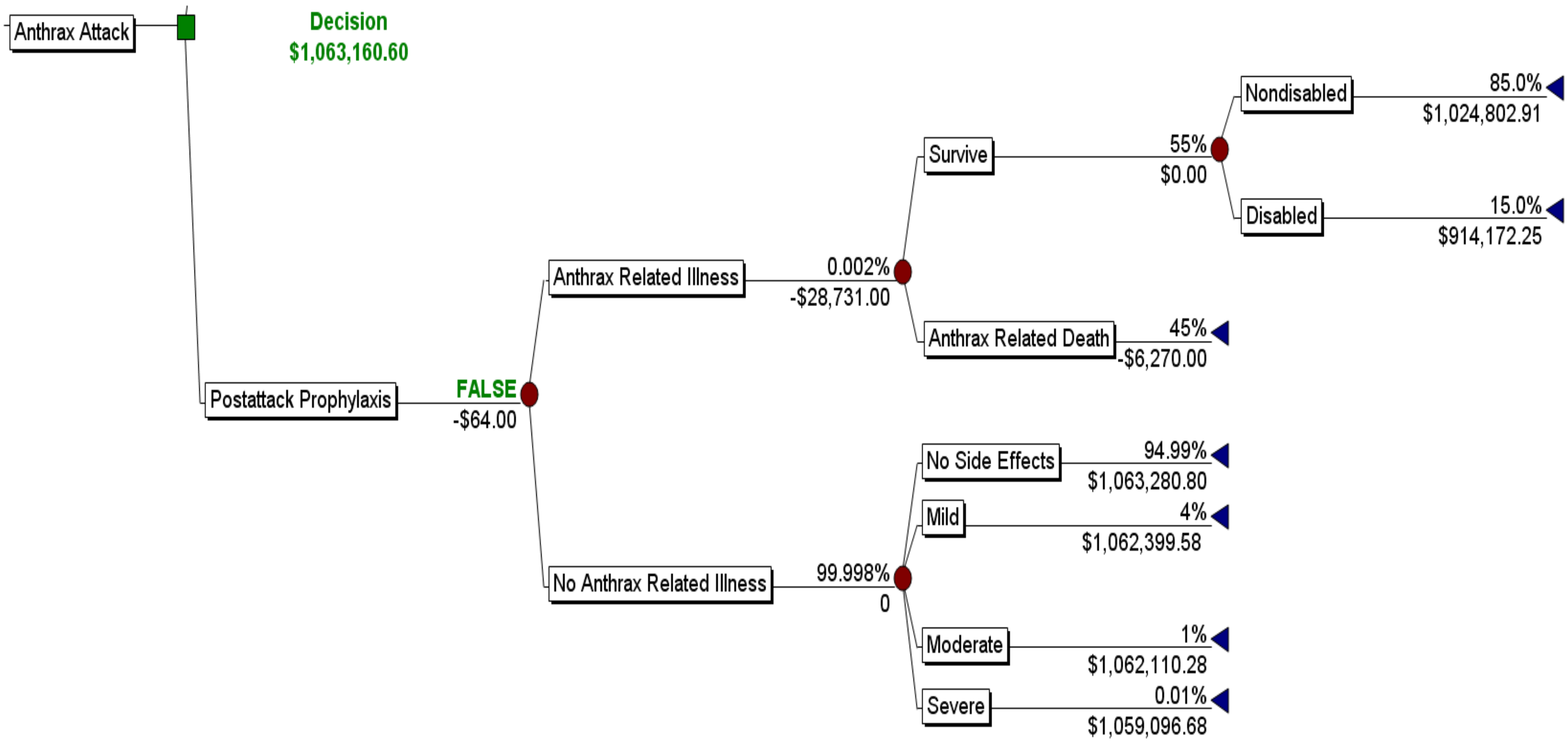
Benefit-Cost Assessment

- If we take action

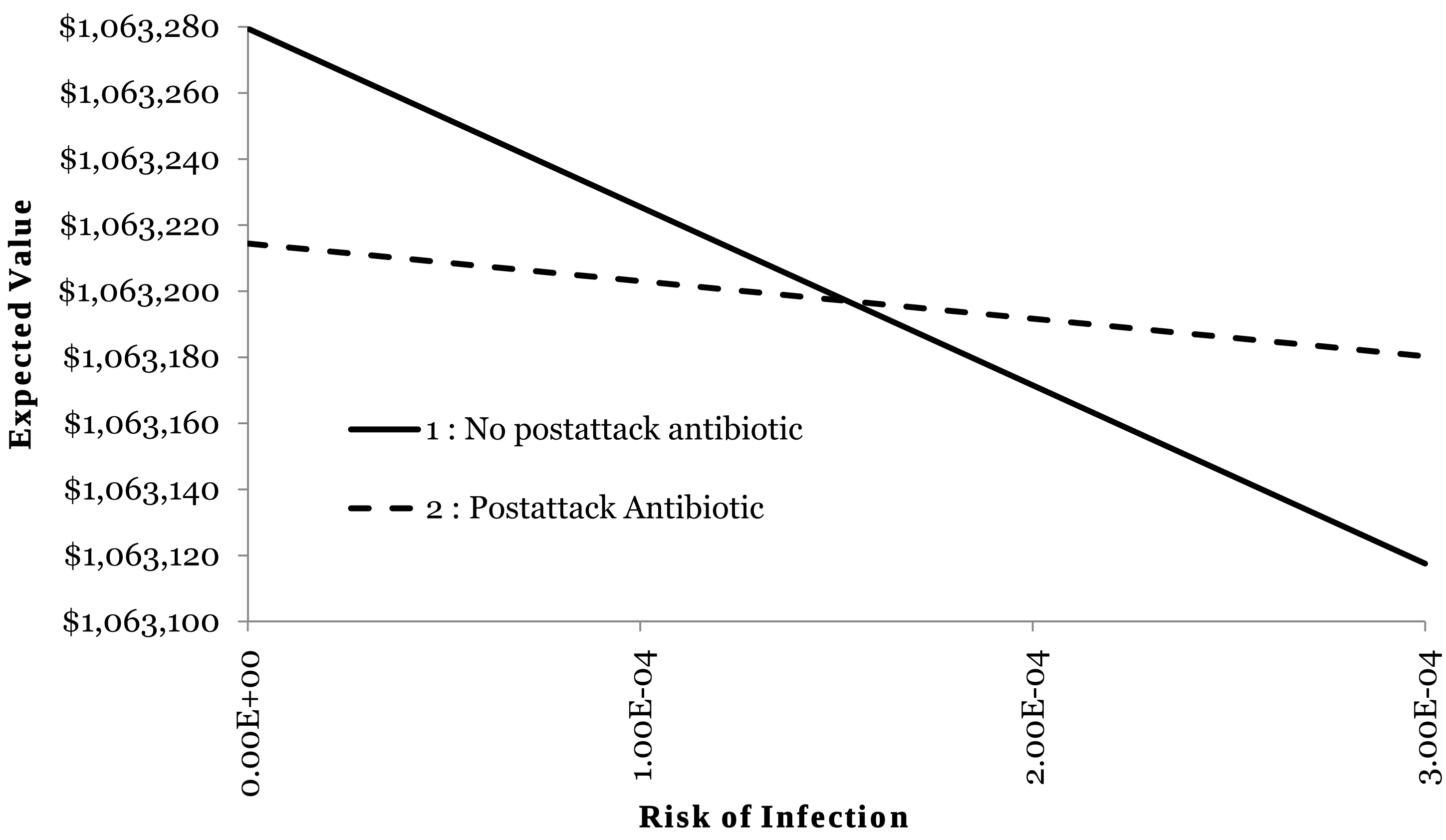
  losses = cost of action
- If we do not take action

  losses = prob * consequence
- When prob=x=cost of action/consequences outcomes have equal expected value
- When prob > x action is justified
- When prob < x action does not produce net expected benefits

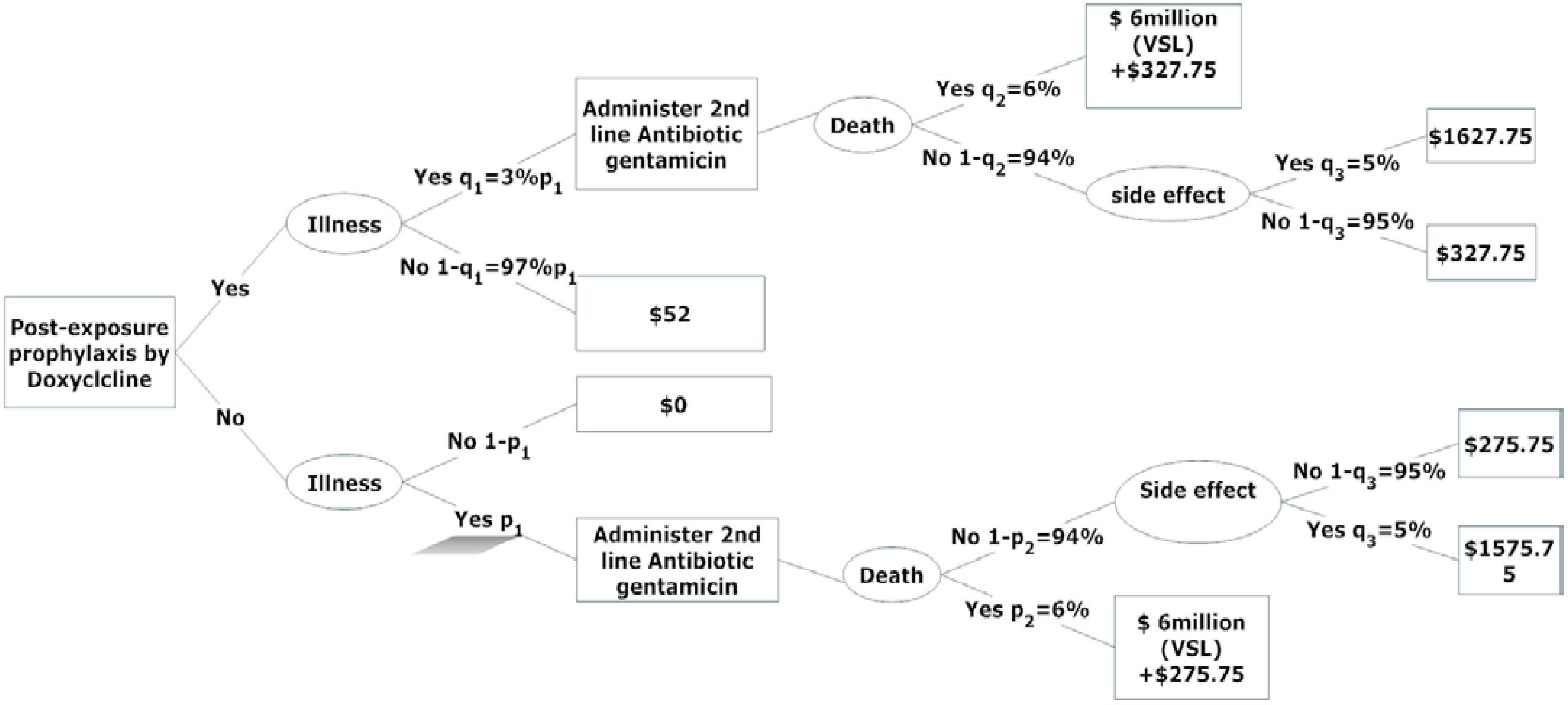
Antibiotic prophylaxis for anthrax



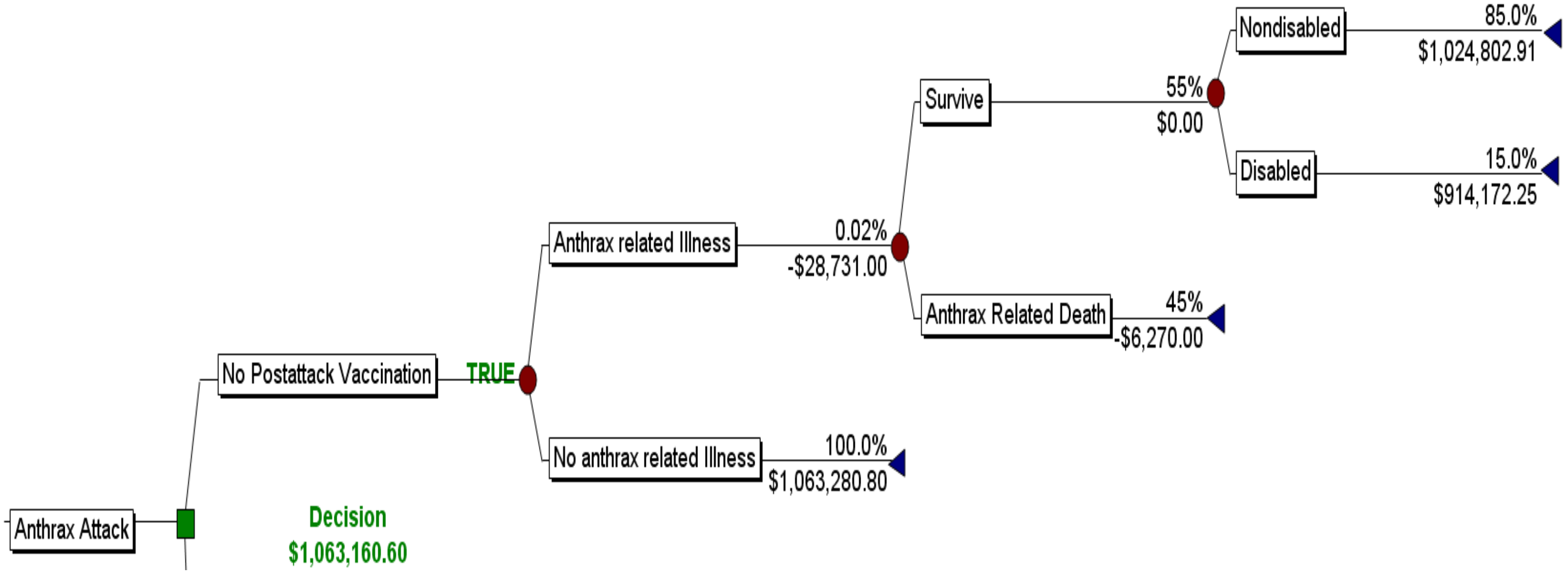
Antibiotic prophylaxis for Anthrax: Switchover point in low 10^{-4} range



Antibiotic prophylaxis for plague: Switchover point in low 10^{-4} range

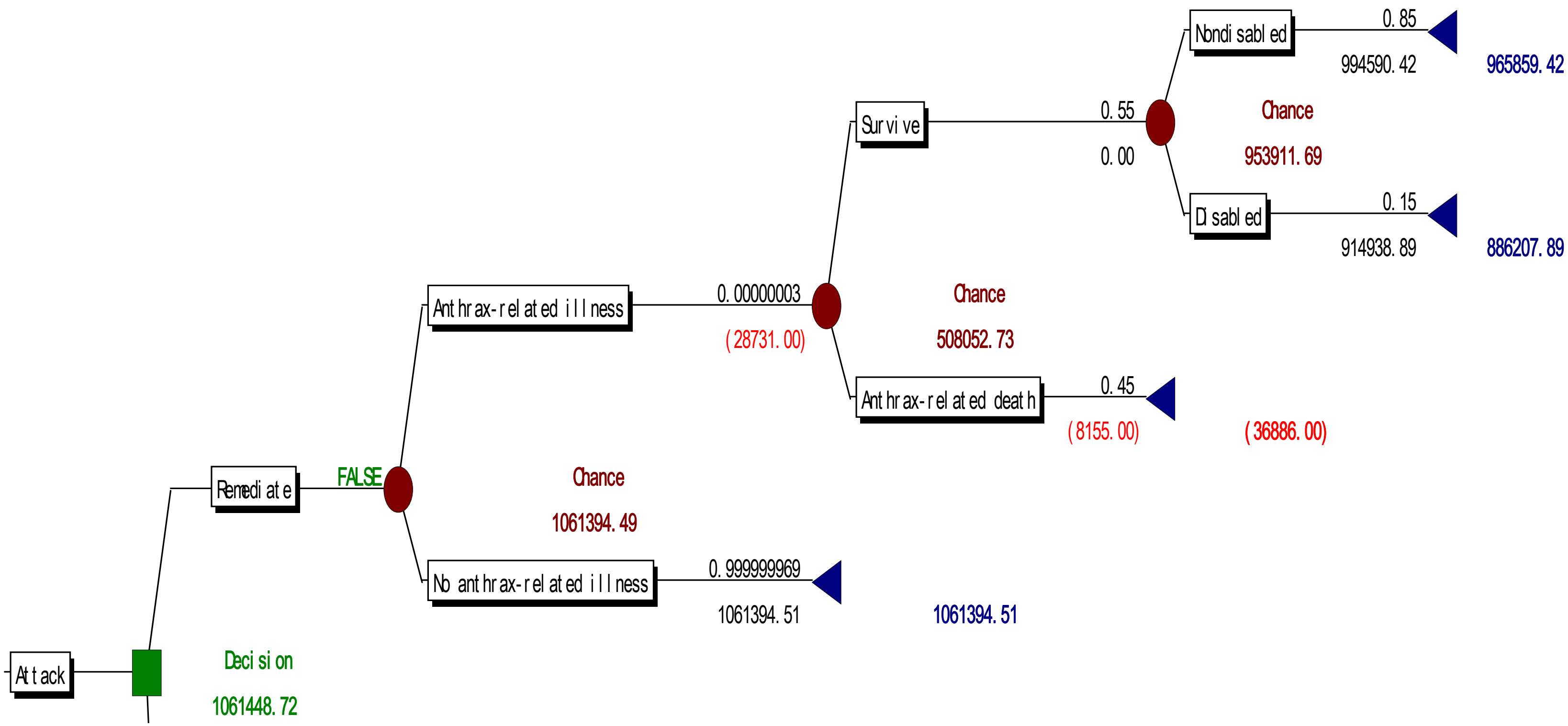


Vaccination for Anthrax: Switchover point in low 10^{-4} range



B. anthracis Environmental remediation: Substantially higher

Vaccination would be preferred

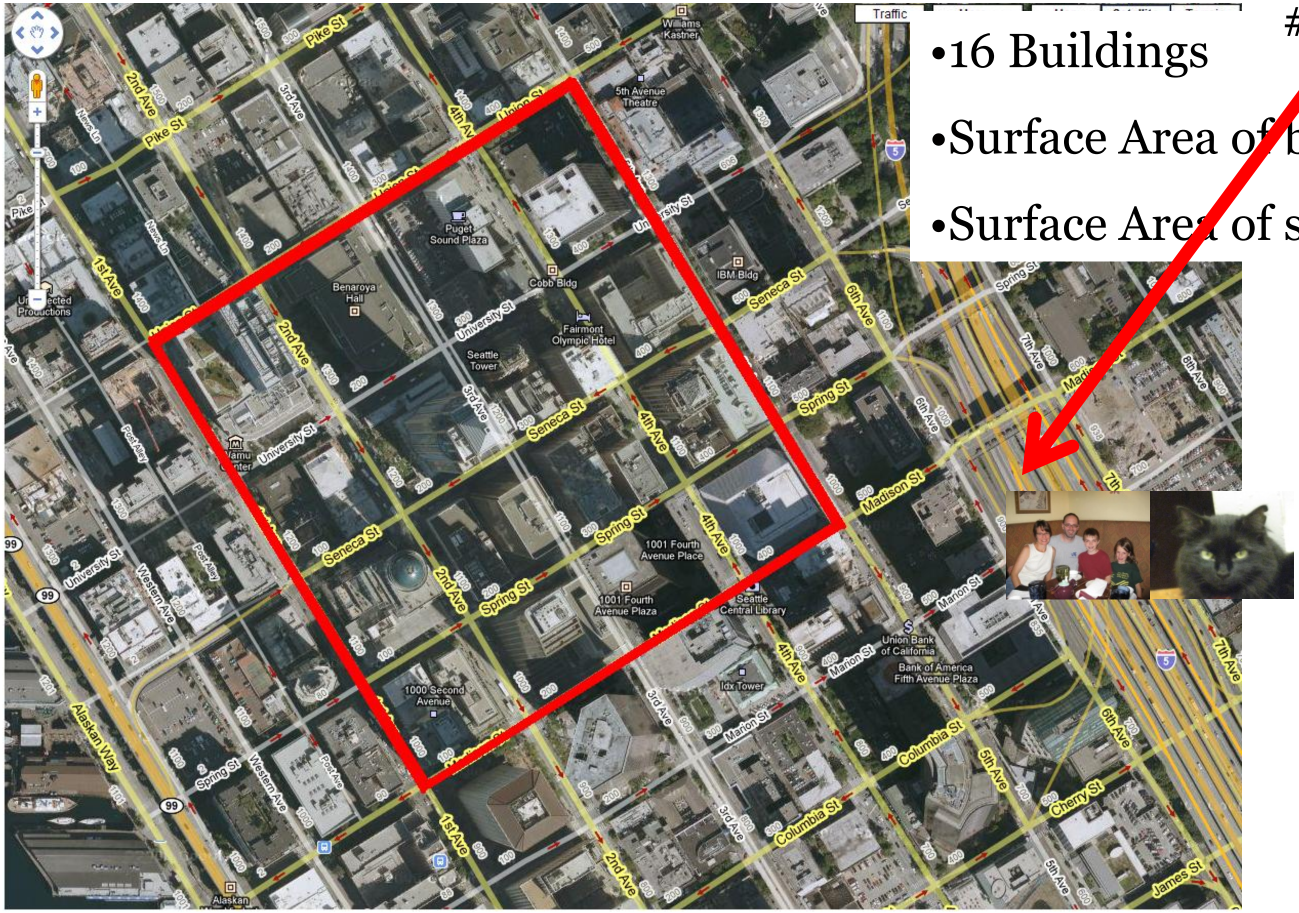


This does not dictate decision making

- Taking antibiotics and getting vaccinations are and will remain private decisions
- People may look to government and academia for guidance with difficult decisions
  - It may not hurt to think about whether on average those who follow our advice would on average be better off
  - to the extent that we can monetize benefits

B. *Anthracis* release

What if I live in building #17?



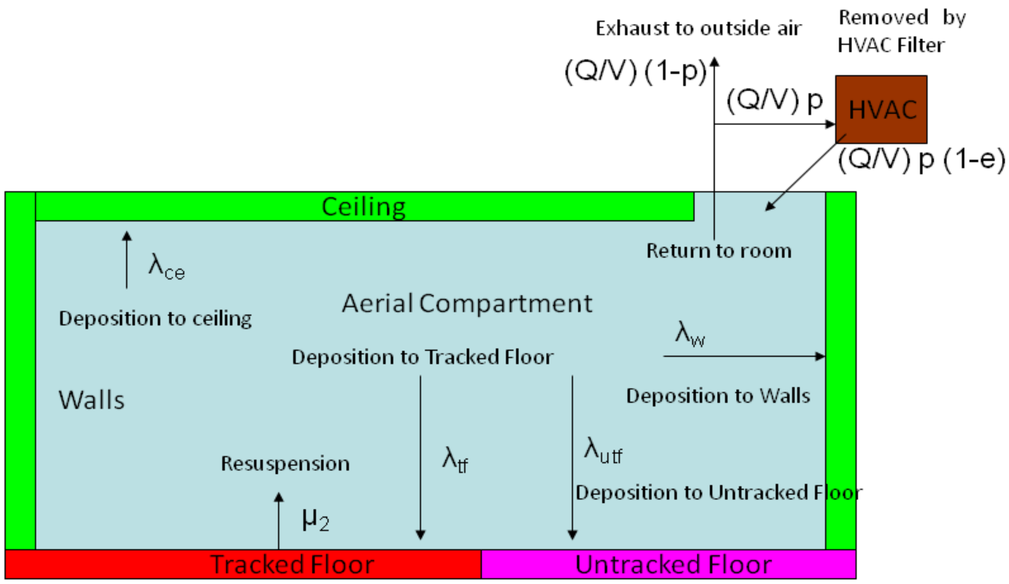
- •16 Buildings
- •Surface Area of buildings
- •Surface Area of sidewalks

How do I link risk with what I can measure?

"Total number of spores may be uncertain – triangular distribution"

Min	$2.68(10^{12})$
Likeliest	$6(10^{15})$
Max	$2.68(10^{17})$

- Need an integrated model
- From release to exposure and risk
- From release to surface concentrations
- Link surface concentrations with risk



Fate and Transport Equation

$$
\begin{pmatrix} \dot{M}_{air} \\ \dot{M}_{htf} \\ \dot{M}_{ltf} \\ \dot{M}_{utf} \\ \dot{M}_{cw} \\ \dot{M}_{f} \\ \dot{M}_{ec} \\ \dot{M}_{n} \\ \dot{M}_{h} \\ \dot{M}_{d} \end{pmatrix}
=
\begin{pmatrix}
[(1-e)p-1]\frac{Q}{V}-(\lambda_{htf}+\lambda_{ltf}+\lambda_{utf}+\lambda_{cw}+\frac{Inh\ e_n}{V}+\gamma_{air}) & \mu_2 & \mu_2 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\lambda_{htf} & -(\mu_2+\gamma_{htf}+r_{sh}f_{sh}) & 0 & 0 & 0 & 0 & 0 & 0 & r_{hs}f_{hs} & 0 \\
\lambda_{ltf} & 0 & -(\mu_2+\gamma_{ltf}) & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
\lambda_{utf} & 0 & 0 & -\gamma_{utf} & 0 & 0 & 0 & 0 & 0 & 0 \\
\lambda_{cw} & 0 & 0 & 0 & -\gamma_{cw} & 0 & 0 & 0 & 0 & 0 \\
ep\frac{Q}{V} & 0 & 0 & 0 & 0 & -\gamma_f & 0 & 0 & 0 & 0 \\
(1-p)\frac{Q}{V} & 0 & 0 & 0 & 0 & 0 & -\gamma_{ec} & 0 & 0 & 0 \\
\frac{I\ e_n}{V} & 0 & 0 & 0 & 0 & 0 & 0 & -\gamma_n & 0 & 0 \\
0 & r_{sh}f_{sh} & 0 & 0 & 0 & 0 & 0 & 0 & -(\gamma_h+r_{hs}f_{hs}) & 0 \\
\gamma_{air} & \gamma_{htf} & \gamma_{ltf} & \gamma_{utf} & \gamma_{cw} & \gamma_f & \gamma_{ec} & \gamma_n & \gamma_h & 0
\end{pmatrix}
\begin{pmatrix} M_{air} \\ M_{htf} \\ M_{ltf} \\ M_{utf} \\ M_{cw} \\ M_{f} \\ M_{ec} \\ M_{n} \\ M_{h} \\ M_{d} \end{pmatrix}
$$

- Subscript s, h, hts, lth, utf, cw, f, ec, n, and d represent for surface, hand, higher tracked floor, lower tracked floor, untracked floor, ceiling and walls, HVAC filter, external, human nasal, and decay, respectively.
- r is the frequency human contacts
- f is the mass transfer fraction for different human contact
- γ is pathogen's decay rate
- λ is the pathogen's deposition rate to various compartents surface (table surface), which equals the product of pathogen's deposition velocity (ν) and surface area (A)
- e, and e_n are HVAC filter and human nasal passage hair's abilities of filtering pathogen

Pathogens' Virulence Coefficients and Decay Rates

- By bootstrapping the available data, virulence coefficients' distribution are acquired:

Pathogen	Virulence coefficient	Decay rate in the air (Min. Max) (hr^{-1})	Decay rate on fomites (Min. Max) (hr^{-1})
B.anthracis	Weibull (3.18×10^{-6}, 1.29×10^{1})	Very Persistent	Very Persistent
Y.Pestis	Weibull (1.10×10^{-3}, 3.47×10^{1})	(2.10, 3.49)	(0.04, 1.24)
F. tularesis	Normal (5.60×10^{-2}, 9.50×10^{-4})	(0.55, 9.20)	(0.01, 0.46)
Variola major	Gamma (5.65, 4.20×10^{-7})	(1.00×10^{-5}, 0.13)	(5.45×10^{-3}, 9.95×10^{-3})
Lassa	Lognormal(-4.20, 1.93)	(0.78, 4.14)	(0.68, 0.92)

Other Inputs

Symbol	Meaning	Units	Diameter	Value scale: Lower bound	Source	Upper bound	Source	Input value
V_{uf}, V_{tf}	Deposition velocity on untracked and tracked floor	m/s	1μM	3.5×10^{-5}	(Lai and Nazaroff 2000)	8.0×10^{-4}	(NRC 2005)	6.9×10^{-5}
			3μM	2.0×10^{-4}	(NRC 2005)	6.0×10^{-3}	(Riley, McKone et al. 2002)	4.2×10^{-4}
			5μM	3.0×10^{-4}		1.4×10^{-2}		1.4×10^{-3}
			10μM	7.0×10^{-4}		2.7×10^{-2}		5.6×10^{-3}
V_w	Deposition velocity on walls	m/s	1μM	3.5×10^{-8}	(Lai and Nazaroff 2000)	9.0×10^{-5}	(Schneider, Kildeso et al. 1999)	3.9×10^{-5}
			3μM	1.5×10^{-8}		2.1×10^{-4}		1.6×10^{-4}
			5μM	1.0×10^{-8}		4.0×10^{-4}		3.1×10^{-4}
			10μM	7.0×10^{-9}		6.0×10^{-4}		3.5×10^{-4}
V_{ce}	Deposition velocity on ceiling	m/s	1μM				(NRC 2005)	6.2×10^{-7}
e_n	Nasal passages particle remove efficiency		1μM	0.02	(Landahl 1950)	0.25	(Roger O. McClellan and Henderson 1989)	0.14
			3μM	0.22		0.68		0.45
			5μM	0.42		0.81		0.62
			10μM	0.62		0.91		0.77
I	Breathing rate		m^3/hr	0.8	(Kowalski 2003)	2.0	(Kowalski 2003)	1.02
p	Recirculation fraction			0	(ASHRAE 2005)	1	(ASHRAE 2005)	0.8

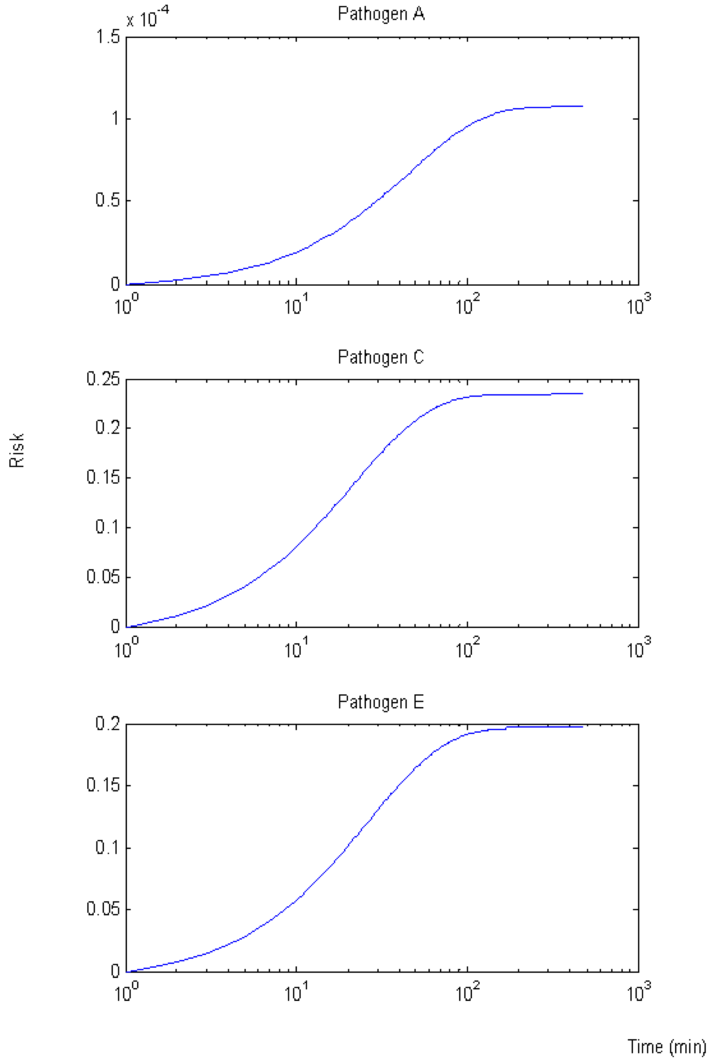
Other Inputs

Symbol	Meaning	units	Value		Source
V	Room dimensions	m^3	5.6×5.6×2.5		Assumed a typical office (EPA 1997; Sextro, Lorenzetti et al. 2002)
A_{tf}	Area-tracked floor	m^2	5.6×5.6×0.75		
A_{utf}	Area-untracked floor	m^2	5.6×5.6×0.25		
A_{ce}	Area- ceiling	m^2	5.6×5.6		
A_w	Area- wall	m^2	5.6×2.5×4		
A_f	Filter area	m^2	3.82×10^{-2} (2.81×10^{-2}-5.62×10^{-2})		Q/A = 137m/min (91-183 m/min)
A_n	Area of nasal passages	m^2	0.8		(Landahl 1950)
ACH	Air changes per hour		4		(ASHRAE 2005)
Q	Discharge	m^3/s	0.087		Q = V×ACH/3600 (in seconds)
f	Proportion tracked		0.75		(ASHRAE 2005)
μ_2	Resuspension rate	s^{-1}	D=1μM	3.3×10^{-8}	(Thatcher and Layton 1995; Sextro, Lorenzetti et al. 2002)
			D=3μM	5.3×10^{-7}	
			D=5μM	2.2×10^{-7}	
			D=10μM	1.1×10^{-6}	
e	Filter efficiency		D=1μM	0.098	(Sextro, Lorenzetti et al. 2002)
			D=3μM	0.49	
			D=5μM	0.74	
			[illegible]	[illegible]	

Other Inputs

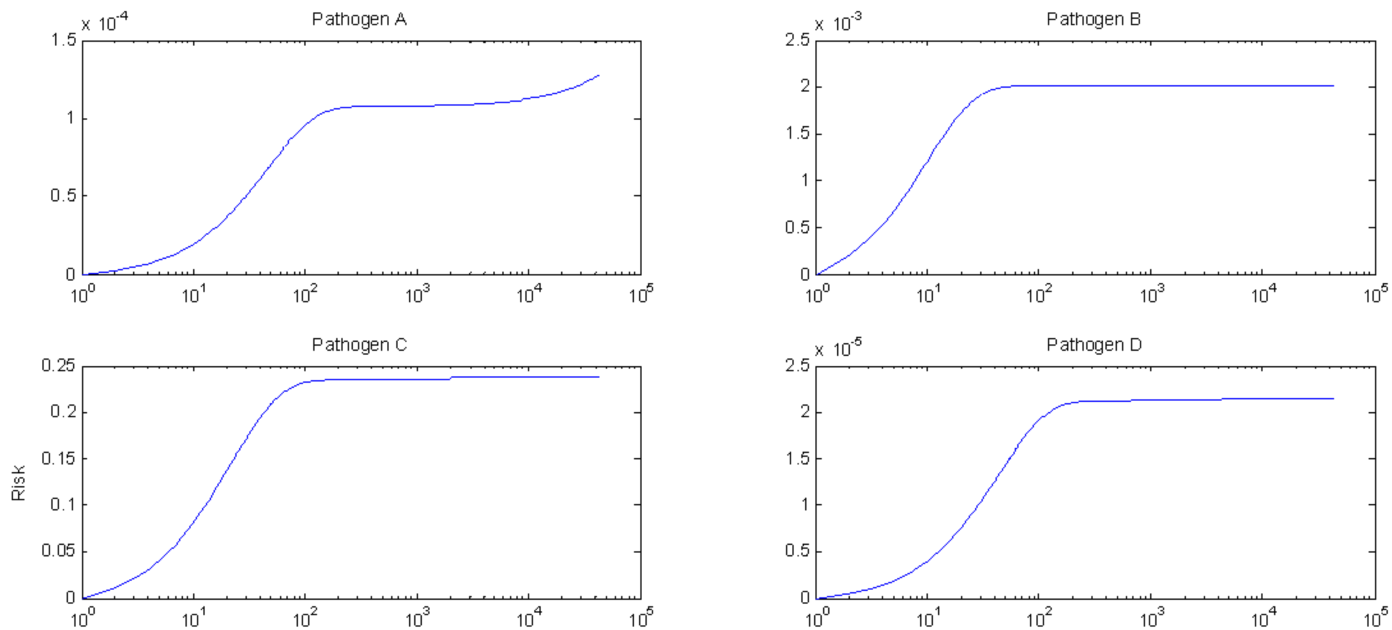
Symbol	Meaning (Unit)	Upper bound	Source	Lower bound	Source	Best estimate	Source
$f_{h\text{-}s}$	Mass transfer fraction from hand to surface during each contact	0.338	(Ansari, Sattar et al. 1988)	0.010	(Ansari, Springthorpe et al. 1991)	0.174	Middle point
$f_{s\text{-}h}$	Mass transfer fraction from surface to hand during each contact	0.658	(P. Rusin 2002)	0.008	(Ansari, Springthorpe et al. 1991)	0.333	Middle point
$f_{h\text{-}m}$	Mass transfer fraction from hand to mouth during each contact	0.410	(P. Rusin 2002)	0.330	(P. Rusin 2002)	0.350	(Nicas and Best 2008)
$r_{h\text{-}m}$	Hand-mouth contacting rate (hr^{-1})	8	Decide by author	5	Decide by author	8	(Nicas and Best 2008)
$r_{h\text{-}s}$	Hand-surface contacting rate (hr^{-1})	6	Decide by author	3	Decide by author	6	Decide by author

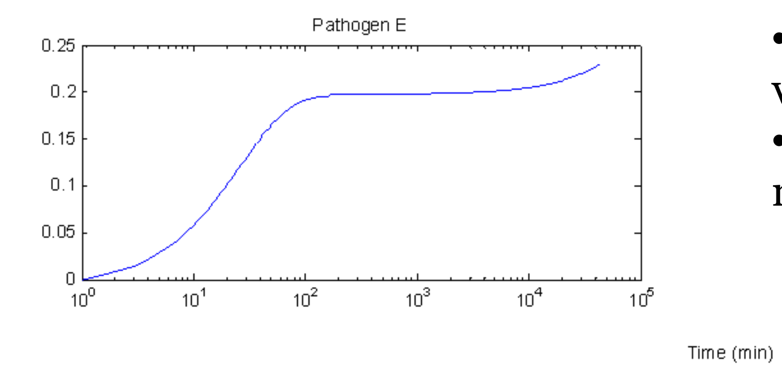
Result
(D=1 micron, released in the air)



- Y axis is positively correlated with pathogen’s virulence
- The time to reach asymptote is positively related to pathogen’s overall environmental persistence

Result
(D=1 micron, released on the surface)





- Y axis is positively correlated with pathogen's virulence
- Pathogen A and E have the relative slow decay rates

Linking risk with Surface Concentrations

- The majority of released pathogens are in the air
- Inhalation is the major exposure pathway
- Samples collected from surfaces can be used directly to characterize:
  1. The quantity of released pathogens

$$M_{air\ 0} = \frac{M_{utf}\left(\sum k_{dep} + k_{air} - k_{utf}\right)}{k_{dep\_utf}\, e^{-k_{utf} t}\left[1 - e^{-\left(\sum k_{dep} + k_{air} - k_{utf}\right)t}\right]}$$

  2. The possible inhalation dose

$$Dose = \frac{I\left(\sum k_{dep} + k_{air} - k_{floor}\right)}{V\left(\sum k_{dep} + k_{air}\right)\left(k_{dep\_utf}\, e^{-k_{floor} t}\right)}\Delta\left[\frac{M_{utf}}{1 - e^{-\left(\sum k_{dep} + k_{air} - k_{floor}\right)t}}\right]$$

$$\Delta = \left(e^{-\left(\sum k_{dep} + k_1\right)t_1} - e^{-\left(\sum k_{dep} + k_1\right)t_2}\right)$$

  - Where k is pathogen's loss due to decay, and kdep is pathogen's loss due to deposition

Interpreting Surface Concentrations

- The majority of released pathogens are on the surface
- The risk is mainly due to ingestion of spores via fomite-hand-mouth transmission route
- Solutions are relative complex, General solution of the equation 2 can be expressed in terms of eigenvalues (D), and eigenvectors (ν)

$$\begin{pmatrix} \dot{M}_{air} \\ \dot{M}_{htf} \\ \dot{M}_{ltf} \\ \dot{M}_{h} \end{pmatrix} = \begin{pmatrix} [(1-e)p-1]\frac{Q}{V}-(\lambda_{htf}+\lambda_{ltf}+\lambda_{utf}+\lambda_{ce}+\frac{Inh\,n}{V}+\gamma_{air}) & \mu_2 & \mu_2 & 0 \\ \lambda_{htf} & -(\mu_2+\gamma_{htf}+r_{sh}\times f_{sh}) & 0 & r_{hs}\times f_{hs} \\ \lambda_{ltf} & 0 & -\mu_2 & 0 \\ 0 & r_{sh}\times f_{sh} & 0 & -\gamma_h - r_{hs}\times f_{hs} \end{pmatrix} \begin{pmatrix} M_{air} \\ M_{htf} \\ M_{ltf} \\ M_{h} \end{pmatrix}$$

$$M_h = C_1 \nu_{4,1} e^{-D_{1,1}t} + C_2 \nu_{4,2} e^{-D_{2,2}t} + C_3 \nu_{4,3} e^{-D_{3,3}t} + C_4 \nu_{4,4} e^{-D_{4,4}t}$$

- Where C_i is the coefficient determined by the ratio of eigenvectors and the initial conditions (Init)

$$C_i = \frac{\nu}{Init}$$

Interpreting Surface Concentrations

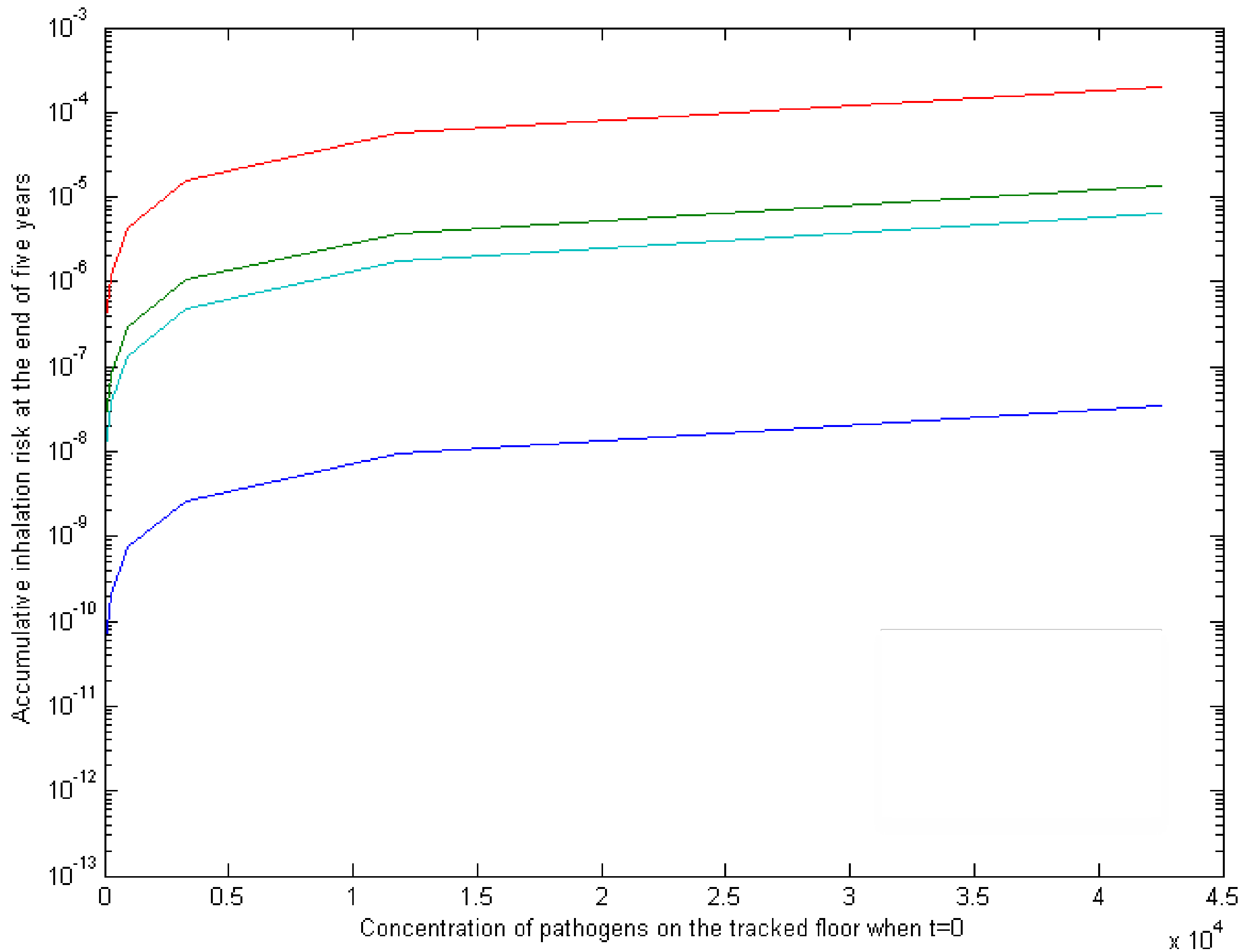
- Exposure dose

$$Dose = Dose_{Inh} + Dose_{Ing} \approx Dose_{Ing} = (r_{hm} \times f_{hm}) \int_{t_1}^{t_2} \frac{M_h}{A_h} dt$$

- The maximum dose can be achieved at $t_1=0$, $t_2=\infty$

$$Dose_{\max} = (r_{hm} \times f_{hm}) \sum_{i=1}^{4} \frac{C_i v_{2,i}}{D_{i,i}}$$

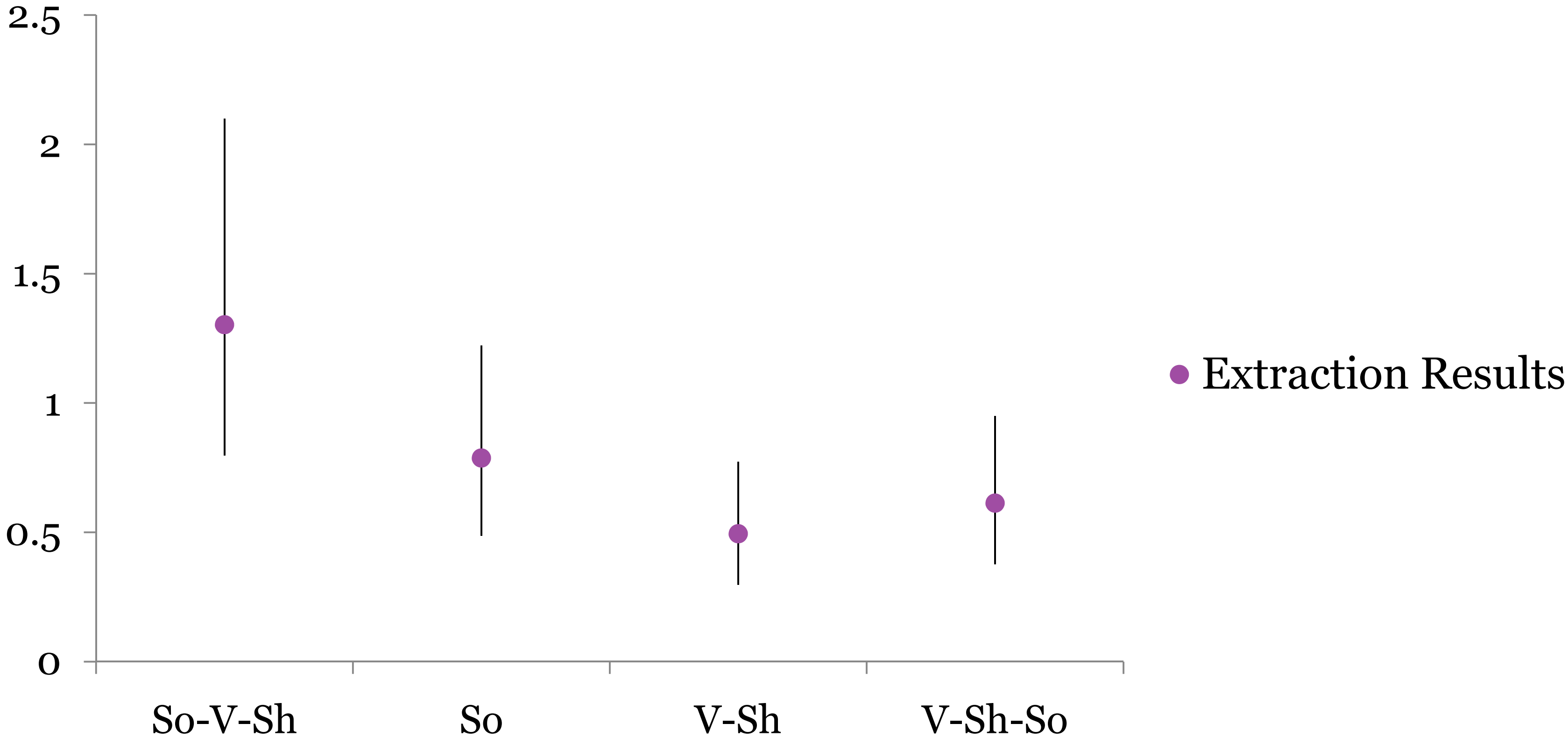
Re-aerosolization risk vs. concentration



1/1000 Retrospective Risk Levels for Environmental Sampling for B. anthracis
(1 µM spores/M^2)

Tracked (Untracked) floor	Range	Filter	Range
35	$9.0\times10^{-1} – 4.0\times10^{3}$	9.2×10^{4}	$0^{*} - 1.5\times10^{6}$

HVAC filter extraction results with 95% CI



Metric to Evaluate Pathogens' Threatens

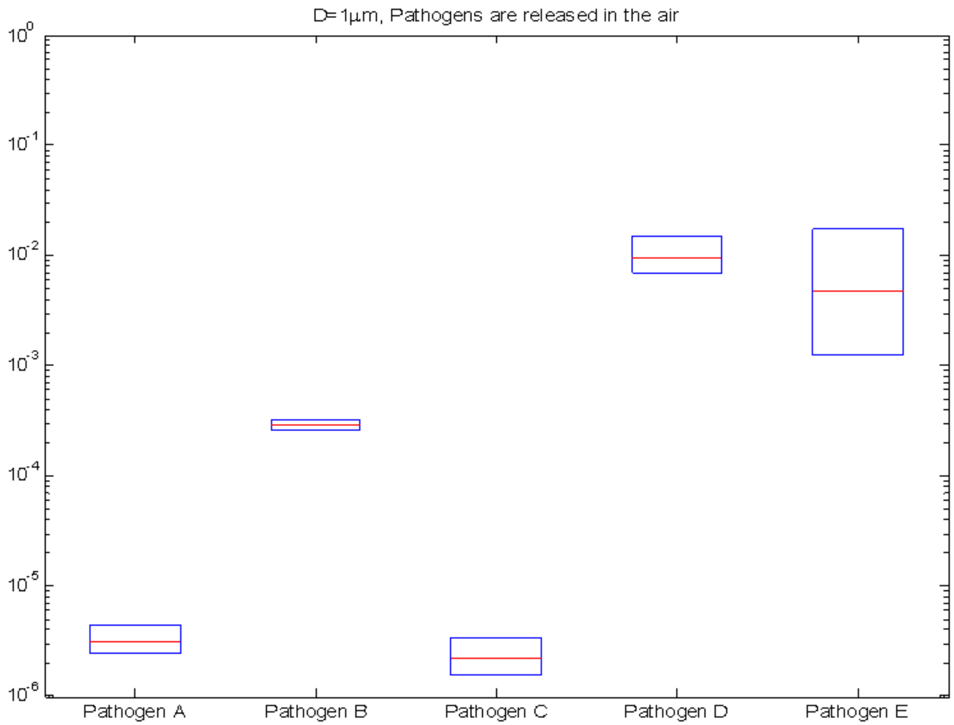
- Pathogen's threaten has a positive correlation with their virulence, fate and transport properties, and environmental persistence (deposition, resuspension, and decay, representing by k)
- For aerosolized pathogens

$$risk = r \times I \int_{t_1}^{t_2} C_{air} dt = r \times I \int_{t_1}^{t_2} C_{air0} e^{-kt} dt = r \times I \times C_{air0} \int_{t_1}^{t_2} e^{-kt} dt \propto \frac{r}{k_{dep} + k_{decay} - resus}$$

- For surface released pathogens

$$risk = r \times r_{hm} \times f_{hm} \int_{t_1}^{t_2} C_{htf} dt = r \times r_{hm} \times f_{hm} \int_{t_1}^{t_2} C_{htf0} e^{-kt} dt \propto \frac{r}{k_{decay} + resus}$$

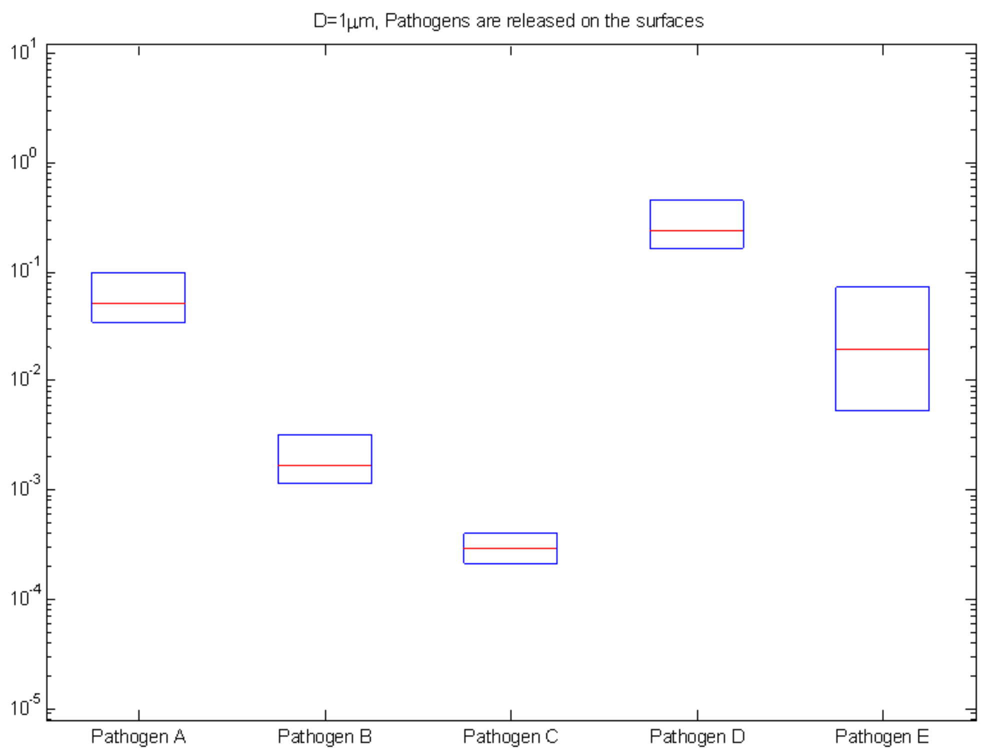
Metric to Evaluate Risk and Uncertainty



- If r and k are fed with distributions

D=1 (μm) Released in the air						
Correlation Coefficient		Pathogen A	Pathogen B	Pathogen C	Pathogen D	Pathogen E
Risk	K_{floor}	**-6.91×10^{-1}**	**-5.65×10^{-1}**	**-5.43×10^{-1}**	-1.60×10^{-1}	-2.72×10^{-2}
	K_{wall}	-1.79×10^{-1}	-1.34×10^{-1}	-1.32×10^{-1}	-3.95×10^{-2}	-7.60×10^{-3}
	K_{HVAC}	-3.84×10^{-1}	-2.75×10^{-1}	-2.82×10^{-1}	-7.86×10^{-2}	-2.59×10^{-2}
	K_{nose}	2.19×10^{-2}	2.16×10^{-2}	1.05×10^{-2}	-4.21×10^{-3}	-5.06×10^{-3}
	Decay	-5.26×10^{-15}	**-7.10×10^{-1}**	**-9.16×10^{-2}**	**-8.39×10^{-1}**	-7.46×10^{-2}
	Resuspension	1.38×10^{-2}	5.57×10^{-3}	5.86×10^{-3}	-1.08×10^{-2}	-5.64×10^{-3}
	r	1.46×10^{-1}	2.30×10^{-1}	**6.27×10^{-1}**	1.51×10^{-2}	**9.46×10^{-1}**

Metric to Evaluate Risk and Uncertainty



D=1 (μm) Released on the fomite						
Correlation Coefficient		Pathogen A	Pathogen B	Pathogen C	Pathogen D	Pathogen E
Risk	Decay	-1.18×10^{-15}	$\mathbf{-6.92\times10^{-1}}$	-3.61×10^{-1}	$\mathbf{-6.42\times10^{-1}}$	-2.07×10^{-2}
	Resuspension	$\mathbf{-4.08\times10^{-1}}$	8.91×10^{-3}	1.06×10^{-3}	-1.60×10^{-2}	-1.94×10^{-3}
	r	3.25×10^{-2}	4.07×10^{-2}	$\mathbf{9.11\times10^{-1}}$	1.22×10^{-2}	$\mathbf{9.96\times10^{-1}}$

Closing Thoughts

1. CAMRA has developed an approach for characterizing microbial risk, delineating affected areas, and making treatment and re-occupation decisions
2. Uncertainties exist both in parameters for specific organisms and in the structure of the approach
3. It would be unreasonable to assume that this approach can be implemented without practice
4. We will learn by doing if we give ourselves time to practice

    Budgets must be reasonable-IKEA approach to bioterrorism drills

5. From properly designed drills, tools, techniques, and basic knowledge can emerge

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