



Predicting the Impact of Placing Pre-event Pharmaceuticals for Anthrax

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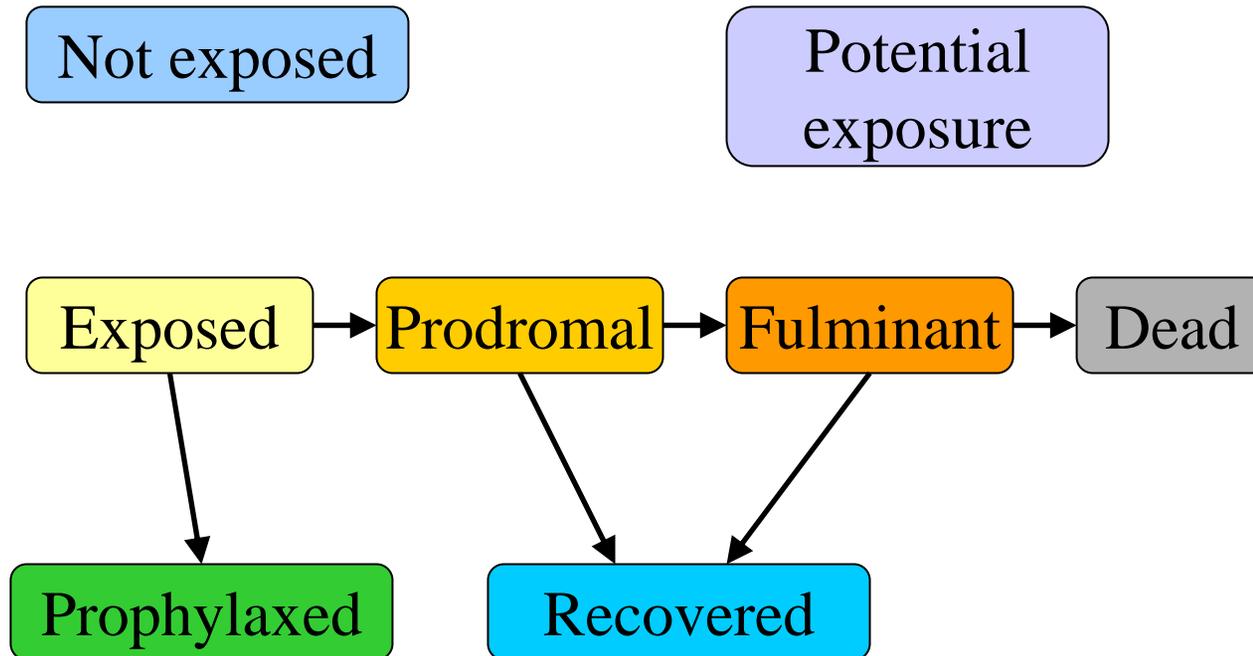
Public Health Problem

- The deliberate release of aerosolized anthrax spores in a large city could expose many thousands of residents to this deadly disease.
 - Promptly distributing antibiotics to those exposed is a key step in preventing illness and deaths.
 - Avoiding delays in this distribution is critical.
 - This work focuses on the pre-event placement of pharmaceuticals in individual households for use only as directed by public health authorities. The pre-deployed medications are commonly known as “MedKits.”
 - The use of MedKits has been advocated because it will reduce the time needed to distribute medication. Concerns about safety and the inappropriate use of MedKits have slowed the development of this option.
 - Predicting how pre-deploying MedKits would reduce the mortality resulting from an anthrax attack should be valuable to public health officials who are considering this option.
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Methodology

- *Research goal:* The purpose of the work was to develop a model that could estimate the impact of deploying MedKits in a community and to use that model to consider some possible scenarios to get some insight into the effectiveness of the MedKit strategy.
 - *Modeling approach:* We developed a compartmental model that includes both the progression of the disease and the logistics of treatment. A compartmental model represents the flows of individuals between compartments. The primary distinctions between the compartments are the exposure of the individuals, the progression of the disease (including the definitive conditions of death or recovery), the treatment status, and the possession of MedKits. Data for the model were taken from the medical literature.
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Model Overview



Potential exposure = someone will seek prophylaxis but cannot become ill.

Compartments

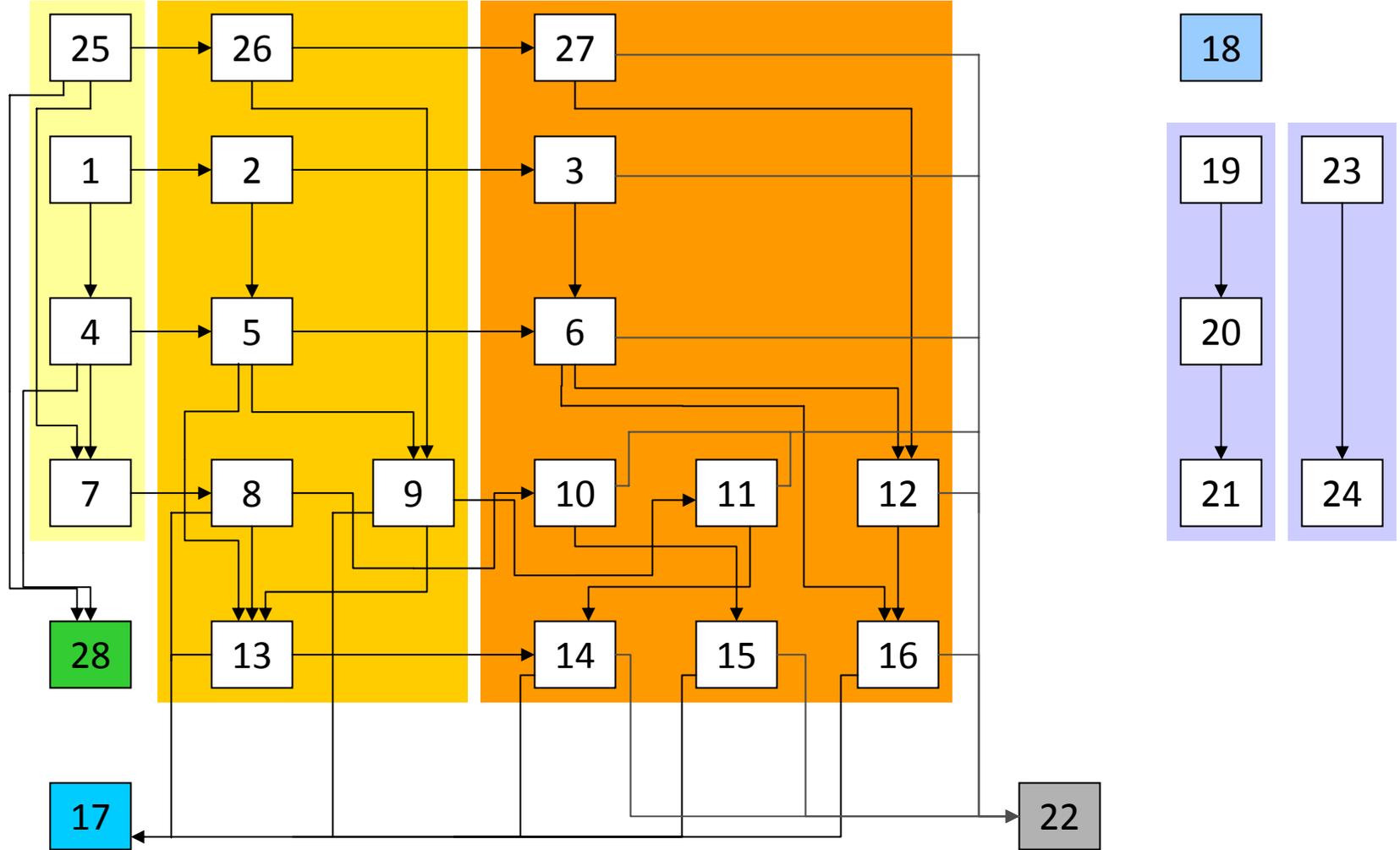


Table 1. The compartments in the MedKit model.

Compartment	Exposure, treatment status	Progression of disease	Treatment began	MedKit
1	Exposed, unaware of exposure	Incubation stage	n.a.	No
2	Exposed, unaware of exposure	Prodromal stage	n.a.	No
3	Exposed, unaware of exposure	Fulminant stage	n.a.	No
4	Aware of exposure	Incubation stage	n.a.	No
5	Aware of exposure	Prodromal stage	n.a.	No
6	Aware of exposure	Fulminant stage	n.a.	No
7	Not adhering to prophylaxis	Incubation stage	Prophylaxis begun in incubation stage	Both
8	In prophylaxis	Prodromal stage	Prophylaxis begun in incubation stage	Both
9	In prophylaxis	Prodromal stage	Prophylaxis begun in prodromal stage	Both
10	In prophylaxis	Fulminant stage	Prophylaxis begun in incubation stage	Both
11	In prophylaxis	Fulminant stage	Prophylaxis begun in prodromal stage	Both
12	In prophylaxis	Fulminant stage	Prophylaxis begun in fulminant stage	Both
13	In treatment	Prodromal stage	Treatment begun in prodromal stage	Both
14	In treatment	Fulminant stage	Prophylaxis or treatment begun in prodromal stage	Both
15	In treatment	Fulminant stage	Prophylaxis begun in incubation stage, treatment begun in fulminant stage	Both
16	In treatment	Fulminant stage	No prophylaxis or prophylaxis begun in fulminant stage	Both
17	Exposed	Recovered	n.a.	Both
18	Not exposed	n.a.	n.a.	Both
19	Potential exposure, not seeking prophylaxis	n.a.	n.a.	No
20	Potential exposure, seeking prophylaxis	n.a.	n.a.	No
21	Potential exposure, in prophylaxis	n.a.	n.a.	No
22	Exposed	Dead	n.a.	Both

Table 1 (continued)

Compartment	Exposure, treatment status	Progression of disease	Treatment began	MedKit
23	Potential exposure, not seeking prophylaxis	n.a.	n.a.	Yes
24	Potential exposure, in prophylaxis	n.a.	n.a.	Yes
25	Exposed, unaware of exposure	Incubation stage	n.a.	Yes
26	Exposed, unaware of exposure	Prodromal stage	n.a.	Yes
27	Exposed, unaware of exposure	Fulminant stage	n.a.	Yes
28	Adhering to prophylaxis	Prophylaxed	Prophylaxis begun in incubation stage	Both



Scenarios Considered

- We employed the MedKit model to estimate the number of deaths in scenarios with the following parameters:
 - Population size = 5,000,000.
 - Time to detect attack = 48 hours.
 - Delay until local supplies are available = 5 hours.
 - Delay until push pack is available = 12 and 24 hours.
 - Number exposed = 50,000, 500,000, and 1,250,000.
 - Percentage of non-exposed persons who will seek prophylaxis (potential exposures) = 1%, 10%, and 50%.
 - Adherence rate = 65% and 90%.
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Response Resources

- Prophylaxis (for exposed and potential exposures without MedKits)
 - Points of dispensing (PODs): 10 PODs that can each dispense medication to 1,000 persons per hour, 14 hours per day.
 - Antibiotics: the local stockpile has 50,000 doses (3,571 abbreviated regimens), the push pack provides 2,718,000 doses (194,143 abbreviated regimens), and the vendor-managed inventory provides sufficient doses for everyone to receive a complete regimen.
 - Treatment (for the ill in prodromal and fulminant states)
 - Intravenous (IV) antibiotics: the local stockpile has 500 days of IV antibiotics, the push pack provides 21,492 days of IV antibiotics, and the vendor-managed inventory provides sufficient IV antibiotics for everyone who is being treated.
 - Ventilators: 100 are available when the attack occurs, and the push pack provides 100 more.
 - Respiratory technicians: each can monitor 10 patients, and 200 are available when the attack occurs.
 - ICU beds: 2,000 are available when the attack occurs.
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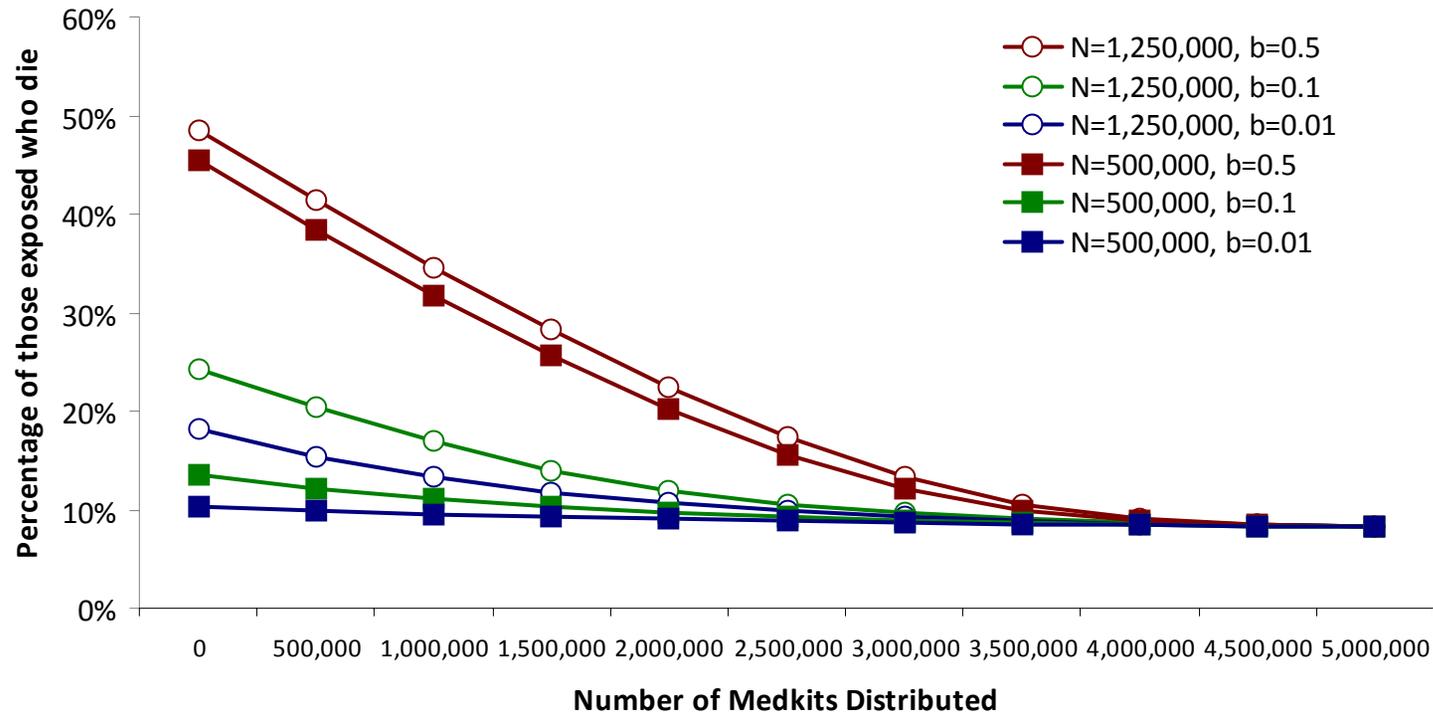


MedKits Model

- The MedKits model can estimate the number of deaths that result from an anthrax attack when a community pre-deploys MedKits and uses PODs to dispense prophylaxis to those without MedKits.
 - **The model can be used to consider a wide range of scenarios and local factors.**
 - The findings show that, as more MedKits are pre-deployed, fewer deaths occur, but the decrease in the number of deaths slows.
 - The impact of using MedKits depends on the percentage of non-exposed persons who will seek prophylaxis (potential exposures).
 - **When the population has more potential exposures, deploying MedKits is more effective.** The MedKits reduce the number of potential exposures who seek prophylaxis, which allows those truly exposed (but without MedKits) to receive medication sooner, which saves lives.
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Deaths decrease as more Medkits are distributed.

Deaths as Medkits Distribution Increases
(alpha = 90%, t = 24 hours)



N = the number exposed.

b = the fraction of non-exposed persons who will seek prophylaxis (potential exposures).

alpha = prophylaxis adherence rate

t = delay until push pack is available



Useful References

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- Brookmeyer R, Blades N, Hugh-Jones M, Henderson DA, “The statistical analysis of truncated data: application to the Sverdlovsk anthrax outbreak,” *Biostatistics*, Volume 2, Number 2, pages 233–47, 2001.
 - Brookmeyer, R., E. Johnson, and R. Bollinger, “Public health vaccination policies for containing an anthrax outbreak,” *Nature*, Volume 432, pages 901-904, 2004.
 - Centers for Disease Control and Prevention, “Emergency MedKit Evaluation Study Summary,” November 15, 2007.
 - Holty, J.E., D.M. Bravata, H. Liu, R.A. Olshen, K. McDonald, and D.K. Owens, “Systematic review: a century of inhalational anthrax cases from 1900 to 2005,” *Annals of Internal Medicine*, Volume 144, Number 4, pages 270–280, 2006.
 - Hupert, N., Wattson, D., Cuomo, J., Hollingsworth, E., and Neukermans, K., “Predicting hospital surge after a large-scale anthrax attack: a model-based analysis of CDC's cities readiness initiative prophylaxis recommendations,” *Medical Decision Making*, Volume 29, pages 424-437, 2009.
 - Jacquez, John A., *Compartmental Analysis in Biology and Medicine*, third edition, BioMedware, Ann Arbor, Michigan, 1996.
 - Shepard, Colin W., Montse Soriano-Gabarro, Elizabeth R. Zell, James Hayslett, Susan Lukacs, Susan Goldstein, Stephanie Factor, Joshua Jones, Renee Ridzon, Ian Williams, Nancy Rosenstein, and the CDC Adverse Events Working Group, 2002, “Antimicrobial postexposure prophylaxis for anthrax: adverse events and adherence,” *Emerg Infect Dis*, Volume 8, Number 10, pages 1124–1132.
 - Walter, Gilbert G., and Martha Contreras, *Compartmental Modeling with Networks*, Birkhäuser, Boston, 1999.
 - Wein, Lawrence M., David L. Craft, and Edward H. Kaplan, “Emergency response to an anthrax attack,” *Proc Natl Acad Sci*, Volume 100, Number 7, pages 4346–4351, 2003.
 - Zaric, Gregory S., Dena M. Bravata, Jon-Erik Cleophas Holty, Kathryn M. McDonald, Douglas K. Owens and Margaret L. Brandeau, “Modeling the Logistics of Response to Anthrax Bioterrorism,” *Medical Decision Making*, Volume 28, pages 332-350, 2008.
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Looking Ahead

- Operations research (OR) is the academic discipline concerned with using analytical models to improve planning and decision-making.
 - More opportunities exist to apply OR modeling, simulation, and analysis techniques to public health problems.
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A Final Thought

- Modeling should create a conversation, not answer a question.





For more information

- Contact Jeffrey W. Herrmann at jwh2@umd.edu or 301-405-5433
 - Visit the Public Health Preparedness Modeling blog at blog.umd.edu/phpm/
 - Visit our project web site at www.isr.umd.edu/Labs/CIM/projects/clinic/
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