

## **Modeling the Public Health System Response to a Terrorist Event**

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### INTRODUCTION

When seeking to model the response of the public health system to a terrorist attack on the food supply, it is logical to use the tools of risk analysis. The field of risk analysis is commonly divided into three separate but overlapping areas: risk assessment, which seeks to address the magnitude of the risk under consideration and the factors that raise or lower the risk; risk communication, which addresses the tools and techniques needed to talk about the risk in question with affected individuals (e.g. the general public, the food industry, regulatory agents, etc.); and finally risk management, which determines what can be done about the particular risk in question and which course of action is generally best,

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considering the needs of all affected individuals.<sup>1</sup>

The objective of the Public Health Response Modeling research group is to develop a mathematical model that describes the behavior of the public health system in response to a contamination event.<sup>2</sup> Ideally, the model we develop should also be able to predict the effect of interventions (e.g., food recalls or advisory messages). Although our model is being developed to specifically address deliberate contamination of the food supply, it may also be useful for accidental contamination, such as in the recent *Escherichia coli* O157:H7 contamination of bagged spinach.<sup>3</sup> This mathematical model will be a useful tool for policymakers seeking to understand the importance of various factors governing the response of the public health system to the microbial contamination of the food supply.

### CURRENT MODEL DETAILS

The current version of the mathematical model was created using the risk modeling program Analytica® (Lumina Decision Systems, Los Gatos, CA).<sup>4</sup> The model predicts a scenario that unfolds over fifty days, consisting of sixty “dose-events” (i.e. contaminated servings of food). When a contaminated serving is consumed, the simulated victim has a single probability of becoming ill, and that illness may be one of three severity levels determined randomly by the model. Figure 1 shows a series of screenshots from the model. Panel A represents the overall structure of the model showing the five modules that compose the complete model. Each of these module nodes is depicted as a rounded rectangle with a thick border. This thick border indicates that each of these nodes contain additional levels of detail. The arrows connecting the nodes indicate that information from one node is being used to calculate values in another node.

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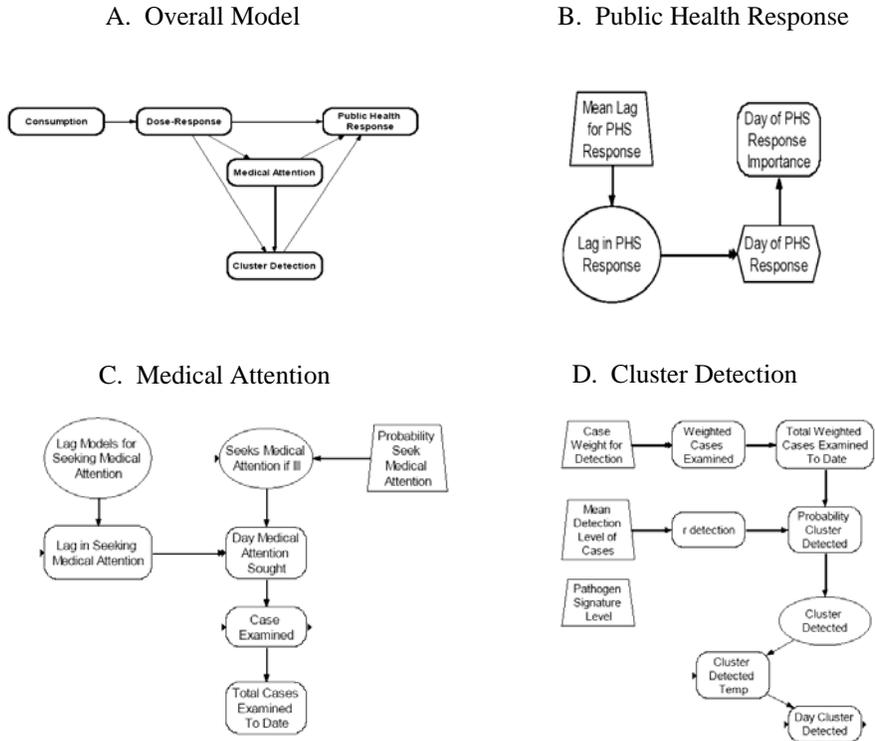
1. See generally Thomas E. McKone, *Overview of the Risk Analysis Approach and Terminology: The Merging of Science, Judgment and Values*, 7 FOOD CONTROL 69 (1996).

2. A contamination event would be an event where pathogenic microbes were allowed to contaminate a food product, either through an accident, or through deliberate introduction by a terrorist.

3. See U.S. Food and Drug Administration, *Spinach and E. coli Outbreak*, <http://www.fda.gov/oc/opacom/hottopics/spinach.html> (last visited Jan. 20, 2007).

4. Lumina Decision Systems, *What is Analytica?*, <http://www.lumina.com/ana/whatisanalytica.htm> (last visited Jan. 20, 2007).

FIGURE 1: SCREEN SNAP SHOTS SHOWING FOUR DIFFERENT AREAS OF THE ANALYTICAL® MODEL



For example, information from the Dose-Response node and the Medical Attention nodes are used in calculations in the Cluster Detection node. Panel B shows the details of the Public Health Response part of the model, while Panels C and D show details of the Medical Attention and Cluster Detection parts of the model respectively. As noted for Panel A, the arrows represent mathematical links between the different values, so in Panel C, “Lag in Seeking Medical Attention” and “Seeks Medical Attention if Ill” are both used to calculate the value of “Day Medical Attention Sought”. In some cases arrowheads without connecting lines are shown. These represent inputs or outputs to or from other nodes outside the current module used for calculations. For example, in Panel C, “Day Medical Attention Sought” plus another node, outside the “Medical Attention” module to calculate the value of “Case Examined”.

Furthermore, the value of “Case Examined” is used to calculate “Total Cases Examined to Date” as well as another node outside the “Medical Attention” module. In Panels B-D the trapezoid shapes indicate that these variables are constants that are set by the user prior to running the simulation. The oval shapes are “chance” nodes that take on a different random value for each iteration of the simulation, while the rounded rectangles with thin borders represent “general” variables. These are intermediate variables, whose values are not set by the user and may or may not be probabilistic. The other features (nodes, modules, arrows, shapes, etc.) allow the user of the software to navigate through the model and see explicitly how different calculations are made.

The simulation uses a “detection constant” to determine whether the public health system has or has not detected that an outbreak occurred. The equation that determines the probability of outbreak detection is:

$$p=1-e^{-d*twc}$$

Where “p” is the probability of detection, “e” is the base of the natural logarithm (2.71828...), “d” is the chosen value of the detection constant, and “twc” is the total number of (weighted) cases experienced to date in the simulation. The cases are weighted by severity of the illness; mild cases are weighted less than moderate cases, which are weighted less than the most severe cases. A detailed example showing the effect of different cases severities is provided in the results section below, but when the detection constant is low (e.g. 0.1) and the total weight cases is also low (e.g. 0.2, a small number ill, with mild symptoms), then the probability of detection would be one minus “e” raised to the power of -0.1 time 0.2 or about 0.02, or a one-in-fifty chance of detecting the outbreak. On the other hand, with a high detection constant (e.g. 1) and the total weighted cases is high (i.e. 1, meaning one very sick person), the probability of detecting the outbreak rises to more than 50%.

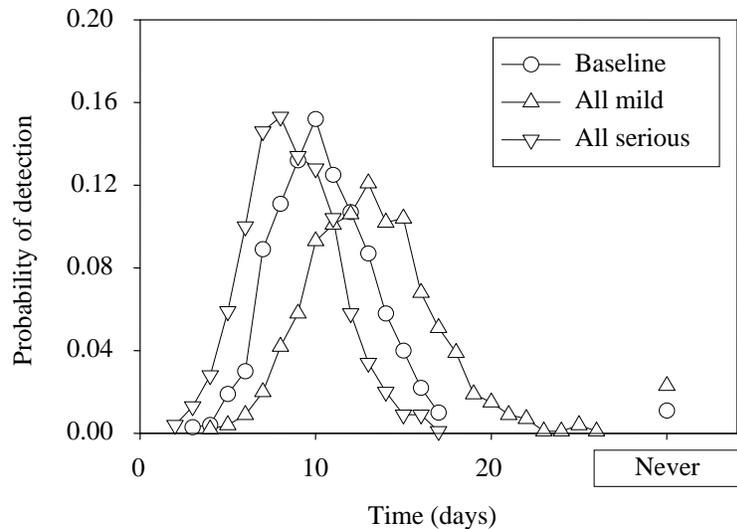
Although it is not yet implanted in the current version of the simulation, ideally the detection constant would be related to the specificity of symptoms experienced by the victims. In other words, some pathogens have a unique set of symptoms (e.g., *Clostridium botulinum* with symptoms of weakness and vertigo, followed by double vision and difficulty in speaking and

swallowing<sup>5</sup>) very different from typical food borne disease symptoms of vomiting and diarrhea. These unique symptoms make it easier to detect outbreaks of certain types of food borne disease over others. Incorporating a measure of the specificity of symptoms in the detection constant should improve the accuracy of the model, so that for example, an outbreak which consists of ten cases of botulism is much more easily detected than an outbreak with ten cases of mild diarrhea caused by *Salmonella*.

## RESULTS

Graph 1 shows the relationship between the probability of detection over time and a mixture of illness profiles for three different situations: all mild illnesses, all serious illnesses and the baseline scenario with a mixture of illnesses (60% mild illness, 30% moderate illness and 10% severe illness).

GRAPH 1. THE PROBABILITY OF DETECTION FOR A MIXTURE OF ILLNESS PROFILES



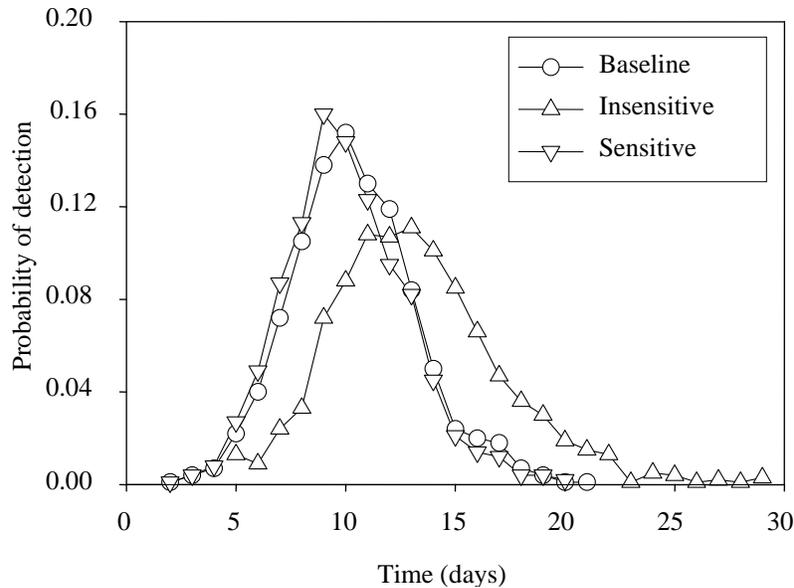
In the baseline scenario the maximum probability of detecting the outbreak occurred at day ten, with a probability of about 16%. It should be noted that because the detection probability

5. U.S. Food and Drug Administration, *Food borne Pathogenic Microorganisms and Natural Toxins Handbook*, <http://www.cfsan.fda.gov/~mow/chap2.html> (Jan. 1992 with periodic updates).

is evaluated each day, the probability that the illness will not be detected becomes smaller and smaller over time. As expected, in those situations in which the mix of illness severity becomes more serious, the probability of detection rises more rapidly. When all of the illnesses are serious, the probability that the outbreak will be detected peaks after eight days, instead of ten. When the illnesses are all mild, the detection probability peaks after thirteen days. It is interesting, however, that even in the most severe situation, it still takes eight days for the probability of detection to reach its peak and probabilities of detection are always quite low at the beginning of an outbreak. This length of time is attributable to the number of delays inherent in the system, such as: the incubation period in each person, delays in seeking medical attention once the illness manifests, and delays in transmission of the medical information to public health officials.

Graph 2 shows the relationship between probability of detection over time and the value of the outbreak detection constant “d” noted in the equation above. The figure compares three different values for the detection constant: a baseline value (-0.5) representing on average ten cases needed to detect an outbreak a sensitive value (-5) representing on average only a single case needed to detect an outbreak, and an insensitive value (-0.05) representing on average one hundred cases needed to detect an outbreak.

GRAPH 2. PROBABILITY OF DETECTION FOR VARIOUS VALUES OF THE OUTBREAK DETECTION CONSTANT



While making the model more sensitive to the detection of an outbreak, an average of one out of ten cases needed to trigger detection might be expected to significantly raise the probability of outbreak detection; the simulation results indicate that this may not be the case. As noted in the discussion of Graph 1 above, the delays inherent in the system prevent immediate detection, regardless of sensitivity to cases. Likewise, raising the number of cases needed to trigger detection has only a very slight effect on the day at which the probability of detection is at a maximum. This is likely because the number of simulated doses (in this case sixty) still result in a significant “signal” reaching the public health system. As noted above, even if the probability of detection on any given day is low, the chance of repeatedly failing to detect an outbreak falls dramatically the longer the outbreak goes on.

These results show that even with a simple model, the simulation has the important ability to assist in reasoning through the implications and consequences of our assumptions about how the public health system might be expected to behave. We do, however, acknowledge that this model is still a preliminary one and needs a significant number of refinements

before it matches what most public health officials would consider the real world. The remainder of this paper will focus on enhancements to the model that are planned for the near future.

### IMPROVEMENTS AND FUTURE DIRECTIONS

The model described above includes many assumptions about the public health system that can be refined through the addition of more realistic public health data. Two different approaches are being used at this time: (1) expert elicitation, which uses expert opinion (from carefully designed questionnaires) to fill in needed gaps in the assumptions used in the simulation, and (2) the addition of real public health data. In the latter case, few data are available, but one notable exception is the Enteric Disease Investigation Timeline Study (EDITS).<sup>6</sup> A brief summary of the EDITS data is shown in Table 1.

TABLE 1. EDITS DATA SUMMARY<sup>7</sup>

	Salmonella	Shigella	Campy	E. coli	Listeria
Onset of Illness	328	162	145	163	31
Specimen Collection Date	479	194	174	175	36
Initial Report Date	258	99	117	55	19
State Report Date	196	94	96	32	13
Isolate Submission Date	441	165	91	160	24
PFGE Set Up Date	117	35	0	79	0
PFGE Sub-typing Date	351	114	0	147	19
Interview Date	225	98	105	154	21
Total observations	537	253	251	188	45
Complete records, all dates	3	0	0	8	0

The database contains information on five pathogens: *Salmonella*, *Shigella*, *Campylobacter*, *Escherichia coli* O157:H7

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6. See generally CRAIG HEDBERG, COUNCIL OF STATE AND TERRITORIAL EPIDEMIOLOGISTS, THE ENTERIC DISEASE TIMELINE STUDY (2005), available at <http://www.cste.org/pdf/files/2005/EDITS-final-report.pdf>.

7. *Id.*

and *Listeria monocytogenes*. For each of these five pathogens, the database contains information from real-world cases in six states. That real-world data contains:

- The date of illness onset;
- The date a fecal specimen was collected;
- The date an initial report was filed;
- The date a report with the state health department was filed;
- The date a fecal sample isolate was submitted to the Centers for Disease Control and Prevention (CDC) for entry into PulseNet;<sup>8</sup>
- The date that genetic fingerprinting, called Pulsed Field Gel Electrophoresis (PFGE), was set up by the CDC, the date the genetic fingerprinting was complete; and
- The date the affected individual was interviewed by state or local epidemiologists.

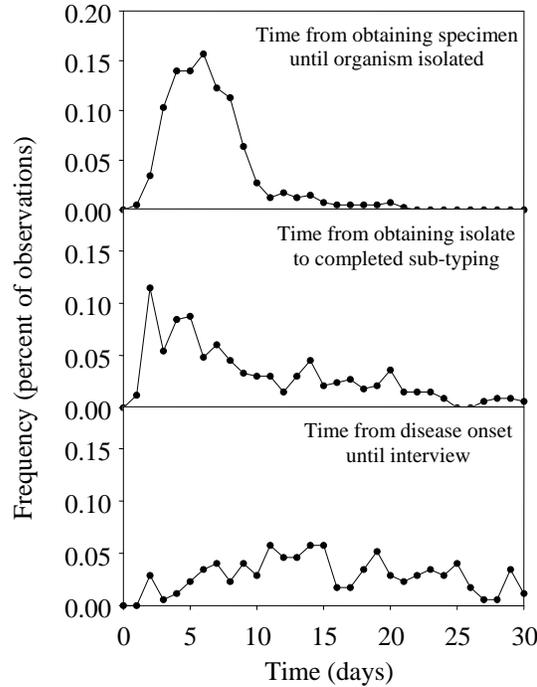
Although this database is state of the art and quite extensive, it should be noted that because it contains real-world data, it is by its very nature incomplete, and although it contains over one thousand records, only three records are fully complete and contain information on all eight types of data.

Graph 3 shows three representative examples of frequency distributions for three different steps in the timeline for a salmonellosis outbreak investigation from the enteric disease timeline study database.

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8. See Centers for Disease Control and Prevention, *PulseNet*, <http://www.cdc.gov/pulsenet/> (last visited Jan. 20, 2007).

GRAPH 3. REPRESENTATIVE EXAMPLES OF FREQUENCY DISTRIBUTIONS FOR THREE DIFFERENT STEPS IN A SAMONELLOSIS OUTBREAK TIMELINE



It is clear from the data shown in the top panel that, in the case of *Salmonella*, the time from obtaining a specimen until an organism is isolated follows an essentially normal distribution, with an average of about one week. In almost no cases does it take longer than two weeks to obtain an isolate. The time from when this isolate is obtained until it is sub-typed is more variable, as shown in the middle panel. In this case the sub-typing is most commonly completed within three days, but the average time to completion was closer to two weeks, with some samples not typed until three or more weeks after isolation. Finally, the bottom panel shows that the time from disease onset until the patient is interviewed is highly variable, with an average time to interview of about eighteen days, but with some interviews taking place after two days, and others not completed until three or four weeks after disease onset.

The analysis depicted in Graph 3 can be repeated for the

other organisms in the EDITS database and for the timelines described in Table 1. Although not presented here, EDITS found that *E coli* O157:H7 cases are reported one to three days sooner than *Salmonella* cases,<sup>9</sup> consistent with the predictions of the model, based on severity of illness. The EDITS study also predicted the timelines observed in the reporting of cases associated with the recent spinach outbreak. Thus, this real world dataset can, with careful review and analysis, become part of the data used to enhance the current simulation model.

#### OTHER IMPROVEMENTS

As noted above, the model does not currently distinguish between pathogens with a unique signature (like *C. botulinum*) and others that present as more classical food borne pathogens (like *Salmonella*). The addition of a pathogen signature variable to flag distinct pathogens easily would be an important enhancement to the model.

Another important aspect of the public health system, which is not currently considered in the model, is the ability of the hospitals and other health care providers to react to epidemics. One member of our team works for a large Minnesota hospital, and her objective in the coming year is to add data on the hospital system capacity to the model. This enhancement will allow us to consider the mitigating effects of various interventions on public health, such as ventilator capacity or anti-toxin availability in the case of a *C. botulinum* outbreak.

A third enhancement to the model that we envision over the next year will be the addition of time dependent feedback on the model predictions, so that as a simulated event unfolds on the computers, the effect of various interventions (i.e. recalls or announcements from public health officials) can be considered. We also hope to further model the effect of various messaging strategies through data provided via collaboration with risk communication researchers at the National Center for Food Protection and Defense.

#### SUMMARY

The model presented here is still a work in progress and we still require more realistic public health data, more pathogen specific data, and the ability to model the mitigating effect of intervention, but in the end we hope that our finished

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9. HEDBERG, *supra* note 6, at 3.

product will be useful in optimizing the performance of the public health system.

Through the data presented here we hope to have illustrated that mathematical modeling can be a useful tool in solving public health problems because it helps to pinpoint uncertainties or knowledge gaps, while at the same time serving as a tool for investigating the impact of potential changes to the system.