AN EVALUATION OF THE RISK DECISION LEVEL FOR PROPHYLAXIS AND TREATMENT AFTER AN ANTHRAX RELEASE

Jade Mitchell-Blackwood, Patrick L. Gurian, Ph.D., and Cara O’Donnell
Acknowledgements

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OBJECTIVES

To link the technical research on bio-threats conducted in other CAMRA projects with the societal goal of managing the risk of bioterrorism

Current Research Questions

1. What is the decision level for anthrax risk?
2. What dose corresponds to this risk level? How do we use animal dose-response studies to inform this estimate?
3. How do we relate what we measure in the environment to dose and risk?
Flow of Information

Bacillus anthracis Aerosol
Transport Model - environmental concentrations producing dose which produces risk at which action is warranted

Bacillus anthracis Dose-Response Model - dose producing risk at which action is warranted

Decision model - risk at which action is warranted

Minimum Sampling Area/Volume
Such that a negative sample establishes that environmental concentrations would not produce a dose which produces a risk at which action is warranted

Response Decision
Decision level for anthrax risk

- Evaluate the cost-effectiveness of strategies for prophylaxis and treatment after an aerosolized release of *B. anthracis* (Fowler et al. 2005)

- Risk of infection is variable based on the size of the release and/or the amount of exposure to which a person is subjected

- In many situations there will be a few highly exposed individuals and a much larger number of individuals who receive much lower exposures

- At what point is medical treatment not justified?

Exposure Scenarios

- Prospective Scenario
  - Post-event re-occupancy of a building
  - Spores have settled and deposited on tracked surfaces

- Retrospective Scenario
  - *Bacillus anthracis* spores have been released in an indoor venue
  - People in the immediate vicinity will receive treatment
  - People on the outskirts may or may not require treatment (in other rooms or outside of the building)
Methods

- Decision analytic model (Fowler et al. 2005)
  - Societal perspective for costs and benefits
  - Discounted at 3% annually
  - Monetize remaining expected lifespan of an individual
  - All costs are in 2004 dollars
- Precision Tree 1.0 for Excel
  - Expected Value of Costs and Utilities
### Model Inputs

### Probabilities

- Clinical inhalational anthrax after attack and exposure:
  - No vaccination, no antibiotics: 0.95
  - No vaccination, receive antibiotics: 0.2
  - Vaccination, no antibiotics: 0.07
  - Vaccination, receive antibiotics: 0.02
  - Baseline mortality given clinical disease: 0.45
  - Nondisabled state if survive clinical illness: 0.85

### Costs, 2004 $

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine costs (6 doses)</td>
<td>18</td>
</tr>
<tr>
<td>Vaccine administration</td>
<td>46</td>
</tr>
<tr>
<td>Antibiotic and administration costs (adult dosing):</td>
<td></td>
</tr>
<tr>
<td>Doxycycline, 100 mg, orally twice daily</td>
<td>12</td>
</tr>
<tr>
<td>Severe inhalational anthrax estimated cost of care</td>
<td>28,731</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>6,270</td>
</tr>
</tbody>
</table>
Model Inputs

Utilities

<table>
<thead>
<tr>
<th>Utilities</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population baseline</td>
<td>0.92</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>0.90</td>
</tr>
<tr>
<td>Severe inhalational anthrax</td>
<td>0.64</td>
</tr>
<tr>
<td>Post anthrax healthy state</td>
<td>0.9</td>
</tr>
<tr>
<td>Post anthrax disabled state</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Vaccine & Antibiotic Side Effects:

<table>
<thead>
<tr>
<th>Effects</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>0.9</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.8</td>
</tr>
<tr>
<td>Severe</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Baseline Case Assumptions for Hypothetical Cohort

- Reside or work in metropolitan U.S. area like New York City
- Mean age = 36 years
- Life expectancy = 76 years
- Value of a QALY = $50,000
- Utilized least expensive medication
- Anthrax related illness is severe

Summary of Base Case Utilities
Valuing Side Effects

- FOR ANTIBIOTICS — Reduced utilities were considered for a period of 60 days for mild and moderate and 7 days for severe side effects.

- FOR VACCINATION — Reduced utilities were considered for a period of 7 days for mild and moderate and 21 days for severe side effects.
Valuing Side Effects

AN EXAMPLE CALCULATION for a person who receives vaccination, does not get anthrax related illness, but suffers severe side effects

Expected Value =
- Present value of the Cost of Treatment
+ Present Value of the (Monetized QALY at the Population Baseline Utility for 39 years)
+ (Monetized QALY at Reduced Utility for 21 days + Monetized QALY at the Population Baseline Utility for the Remaining Days of the Year)

\[ EV = -2473 +(((0.92 \times 22.7893 \times $50,000) + ((0.6) \times $50,000 \times (21/365)) + (0.92 \times $50,000 \times (344/365))) \times 0.9709) \]
Decision level for prospective anthrax risk

- Anthrax Attack
  - $1,063,160.60
  - Decision
- No Postattack Vaccination
  - Anthrax related Illness
    - Anthrax Related Death
      - Disabled
        - 15.0%
        - $914,172.25
      - Nondisabled
        - 85.0%
        - $1,024,802.91
  - No anthrax related Illness
    - Survive
      - 55%
      - $0.00
    - Anthrax Related Death
      - 45%
      - $6,270.00

- Decision
  - $1,063,280.80
Decision level for prospective anthrax risk
Decision level for prospective anthrax risk

- Anthrax Attack
  - No Postattack Vaccination: TRUE
    - Decision: $1,063,160.60
    - Anthrax related Illness: 0.022%
      - $28,731.00
      - Anthrax Related Death: 45%
        - $6,270.00
  - Anthrax Attack
    - Postattack Vaccination: FALSE
      - $64.00
      - Anthrax Related Illness: 0.002%
        - $28,731.00
        - Anthrax Related Death: 45%
          - $6,270.00
          - No Side Effects: 94.99%
            - $1,063,280.80
            - Mild: 4%
              - $1,062,399.58
              - No Anthrax Related Illness: 99.998%
                - $0.00
                - Moderate: 1%
                  - $1,062,110.28
                  - Severe: 0.01%
                    - $1,059,096.68

Nondisabled: 85.0%
- $1,024,802.91
- Disabled: 15.0%
- $914,172.25
Decision level for prospective anthrax risk

No action alternative is preferred for probability of infection $<$ 0.022%, or 1 people in 4,495

This risk can be related to aerosol exposure using a dose-response function
Decision level for retrospective anthrax risk

- Anthrax Attack
  - No postattack antibiotics
    - Anthrax related illness
      - 0.054%
        - Survive
          - 55%
            - Nondisabled
              - 85%
                - $1,024,802.91
            - Disabled
              - 15%
                - $914,172.25
          - Anthrax related death
            - 45%
              - $6,270.00
    - No anthrax related illness
      - 99.946%
        - $1,063,280.80

Decision
$1,062,991.24
Decision level for retrospective anthrax risk

Anthrax Attack

- Postattack Antibiotics
  - FALSE
    - Anthrax Related Illness
      - 0.011%
        - Anthrax related death
          - 45%
            - Anthrax related death
              - $-6,270.00
            - No Side Effects
              - 79.99%
                - $1,063,280.80
            - Mild
              - 19.0%
                - $1,062,293.84
            - Moderate
              - 1.0%
                - $1,061,402.84
            - Severe
              - 0.01%
                - $1,059,692.52

  - TRUE
    - Anthrax Related Illness
      - 0.011%
        - Anthrax related death
          - 45%
            - Anthrax related death
              - $-6,270.00
            - No Side Effects
              - 79.99%
                - $1,063,280.80
            - Mild
              - 19.0%
                - $1,062,293.84
            - Moderate
              - 1.0%
                - $1,061,402.84
            - Severe
              - 0.01%
                - $1,059,692.52

Decision
$1,062,991.24

Nondisabled
85%
$1,024,802.91

Disabled
15%
$914,172.25
Decision level for retrospective anthrax risk

No postattack antibiotics
- TRUE

Anthrax Attack
- Decision $1,062,991.24

No anthrax related illness
- 99.946%
- $1,063,280.80

Anthrax related illness
- 0.054%
- -$28,731.00

No postattack antibiotics
- FALSE

Postattack Antibiotics
- $-22.00

Anthrax Related Illness
- 0.011%
- -$28,731.00

Anthrax related death
- 45%
- -$6,270.00

No Side Effects
- 79.99%
- $1,063,280.80

Mild
- 19.0%
- $1,062,293.84

Moderate
- 1.0%
- $1,061,402.84

Severe
- 0.01%
- $1,059,692.52
Decision level for retrospective anthrax risk

No action alternative is preferred for probability of infection < 0.054%, or 1 person in 1,866

This risk can be related to aerosol exposure using a dose-response function
## Sensitivity Analysis

<table>
<thead>
<tr>
<th>QALY=$50K</th>
<th>Prospective/Vaccination</th>
<th>Retrospective/Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 in 4,495</td>
<td>1 in 1,866</td>
</tr>
<tr>
<td></td>
<td>0.022%</td>
<td>0.054%</td>
</tr>
<tr>
<td>QALY=$100K</td>
<td>1 in 6,151</td>
<td>1 in 1,917</td>
</tr>
<tr>
<td></td>
<td>0.016%</td>
<td>0.052%</td>
</tr>
<tr>
<td>QALY=$200K</td>
<td>1 in 7,620</td>
<td>1 in 1,945</td>
</tr>
<tr>
<td></td>
<td>0.013%</td>
<td>0.051%</td>
</tr>
</tbody>
</table>
Conclusion

- Benefit-cost analysis can suggest a level at which the decision to treat is justified
  - Many assumptions required about both empirical uncertainties and values
  - An expected-value analysis such as this may not be appropriate for all decision makers
- The conclusion will be sensitive to many factors including the value of a QALY
Future Work

- Sensitivity analysis for all uncertain model inputs
- Evaluation of the model for new treatments
- Consideration of the decision to remediate