A Comparison of Modeling Approaches for Estimating Within-flock Disease Transmission Parameters for the 2015 H5N2 HPAI Virus Outbreak in the U.S.

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• Outbreak affected 104 commercial turkey operations in Minnesota

• Estimated total impact on U.S. economy was ~USD 3.3 billion (Greene J.L. (2015), Congressional Research Service)

Impact of Transmission Parameters on Disease Dynamics

• Within-flock transmission dynamics inform disease control measures

• $\beta$: adequate contact rate or transmission parameter = mean number of birds infected by each infectious bird per unit time: determines disease spread rate

• $R_0$: basic reproduction number = $\beta \times$ infectious period
Modeling Approaches

• Back-calculation using mortality data from outbreak

• Forward simulation and curve-fitting using mortality data from outbreak
Why Estimate $\beta$ and $R_0$?

• Within-flock $\beta$ and $R_0$ inform
  • Secure poultry supply risk assessments
  • Evaluation of active and passive surveillance protocols
  • Between-premises disease spread models

• Thus far $\beta$ estimates from U.S outbreak data were unavailable, and estimates from other countries were used

• Although $\beta$ has been previously estimated from experimental data, extrapolation to commercial flocks is not straight forward
Back-calculation: Data Preparation

• Ideally, estimation of $\beta$ requires data on number of newly infected birds ($C$), Susceptible ($S$), Infectious ($I$), and total number of birds ($N$) at different time points—yet only mortality is observed in the field.

• Through back-calculation, we estimate these 4 variables from mortality data assuming fixed latent and infectious periods.

• Once $C$, $S$, $I$ & $N$ are obtained, $\beta$ is estimated using accepted GLM-based approaches.
Back-calculation: Parameters Used

• Default scenario: 1 day latent and 4 days infectious period based on inoculation studies using EA/AM HPAI H5N2 virus turkey field isolate was used

• For purposes of sensitivity analysis, the latent period was adjusted to 2 days in the back-calculation procedure

• For validating the estimation procedure, synthetic simulated mortality data with a known $\beta$ was used
## Back-calculation: Results

Estimated $\beta$ using infectious period of 4 days with latent period of 1 day for default scenario and 2 days for sensitivity analysis as well as $\beta$ from validation with synthetic data (input 2.87)

<table>
<thead>
<tr>
<th></th>
<th>$\beta$ (95% CI)</th>
<th>$R_0$ (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outbreak data: Default scenario</td>
<td>2.87 (2.19 – 3.76)</td>
<td>11.49 (8.77 – 15.04)</td>
</tr>
<tr>
<td>Outbreak data: Sensitivity analysis</td>
<td>9.38 (5.13 – 17.14)</td>
<td>37.52 (20.52 – 68.56)</td>
</tr>
<tr>
<td>Validation on synthetic data</td>
<td>2.43 (1.52 – 4.31)</td>
<td>9.72 (6.08 – 17.24)</td>
</tr>
</tbody>
</table>
Possible Limitations for Back-calculation

• Back-calculation with GLM-based estimation studies are limited by
  • the assumption of deterministic latent and infectious periods
  • ignoring between-bird variation
  • using whole-integers for these durations e.g., not considering the exact moment of infection

• Alternative approaches are being explored e.g., forward simulation and curve-fitting
Simulation and Curve-fitting: Methods

- A new approach is proposed based on least squares curve-fitting.
- Disease mortality is predicted using deterministic differential equation models.
- A goodness of fit measure (approximate likelihood) is then maximized to estimate $\beta$.

Mortality data in a EA/AM HPAI H5N2 Infected Turkey House and Predicted Mortality with Best Fit $\beta$. 

![Graph showing mortality data and simulated mortality with $\beta = 2.4$.]
Simulation and Curve-fitting: Results

• Performed well for estimating $\beta$ on synthetic datasets

• Uses smaller time steps and non-integer latent and infectious periods

• The $\beta$ estimate was sensitive to the mean latent period

Approximate likelihoods for $\beta$ from 5 HPAI infected turkey flocks
Comparison in Five Selected Flocks

- For comparison purposes, 5 flocks were selected, individual-flock β’s and combined-flocks β were estimated.
- The combined β estimate and those for flocks # 1, 2, and 3 are in close agreement.
- Forward simulation approach also considers uncertainty in the time of flock infection and hence has greater uncertainty in β estimate.

<table>
<thead>
<tr>
<th>Flock</th>
<th>β (90%CI): FIVE flocks in outbreak data</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Back – calculation</td>
</tr>
<tr>
<td>Flock1</td>
<td>4.16</td>
</tr>
<tr>
<td>Flock2</td>
<td>2.25</td>
</tr>
<tr>
<td>Flock3</td>
<td>1.42</td>
</tr>
<tr>
<td>Flock4</td>
<td>2.13</td>
</tr>
<tr>
<td>Flock5</td>
<td>10</td>
</tr>
<tr>
<td>5 flocks combined</td>
<td>2.8 (2.1 – 3.7)</td>
</tr>
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</table>
Concluding Remarks

• Back-calculation is a computationally fast method that uses accepted GLM-based procedures to obtain reasonable estimates for $\beta$

• $\beta$ is a key parameter in a number of modeling analyses for decision support and active surveillance

• Developing multiple methods to estimate $\beta$ will improve the accuracy of within-flock HPAI spread models results