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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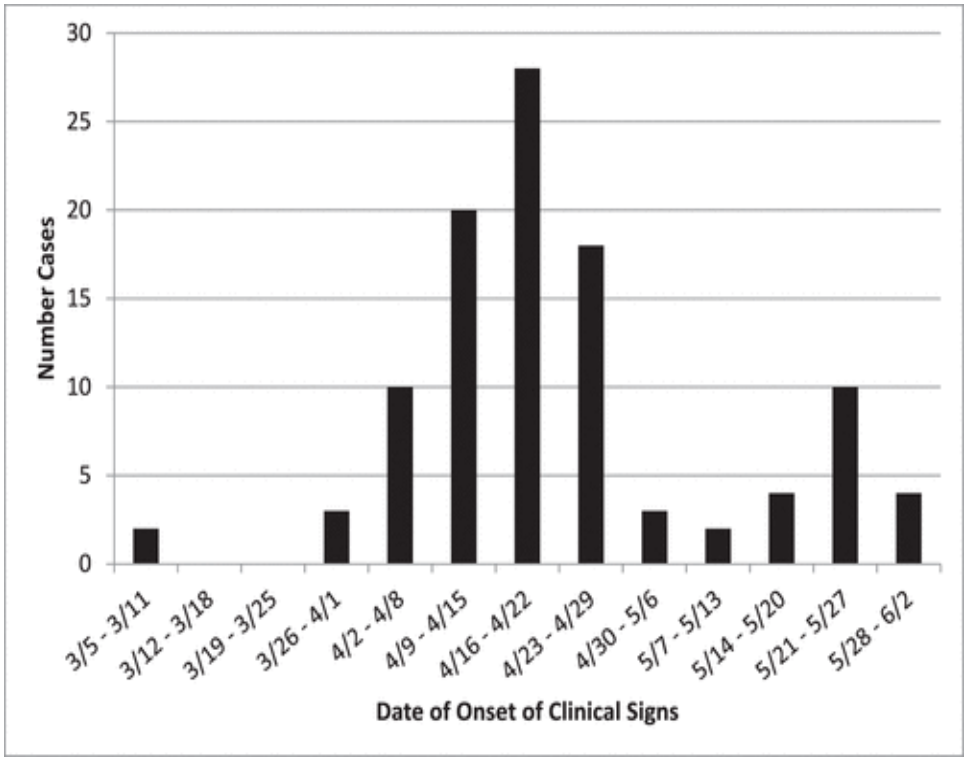
United States Department of Agriculture

MN Turkey Epidemic Curve and Details

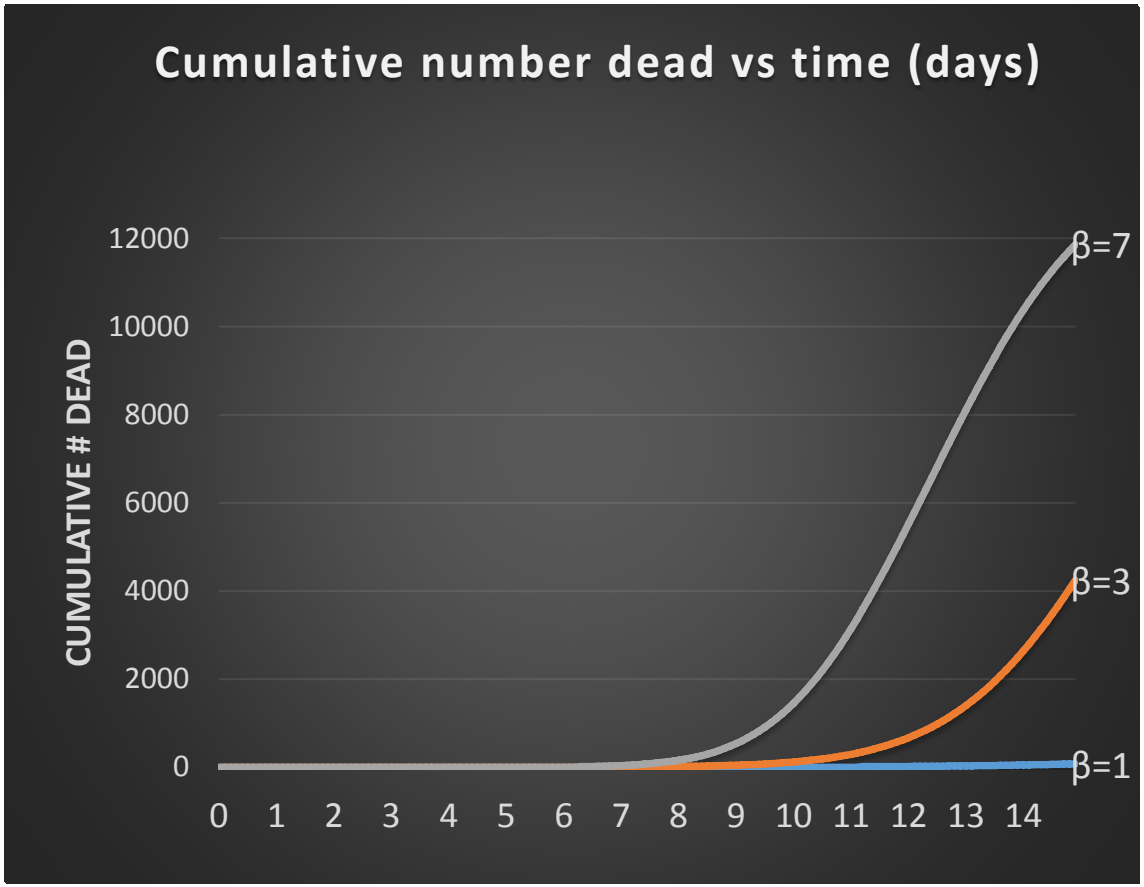
- Outbreak affected 104 commercial turkey operations in Minnesota
- Estimated total impact on U.S. economy was ~USD 3.3 billion (Greene J.L. (2015), Congressional Research Service)



Source: Dargatz et. al, Avian Diseases 60(2):467-472. 2016

Impact of Transmission Parameters on Disease Dynamics

- Within-flock transmission dynamics inform disease control measures
- β: 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 = β x infectious period



Modeling Approaches

- Back-calculation using mortality data from outbreak
- Forward simulation and curve-fitting using mortality data from outbreak

Why Estimate β and R_0?

- Within-flock β and R_0 inform
  - Secure poultry supply risk assessments
  - Evaluation of active and passive surveillance protocols
  - Between-premises disease spread models
- Thus far β estimates from U.S outbreak data were unavailable, and estimates from other countries were used
- Although β has been previously estimated from experimental data, extrapolation to commercial flocks is not straight forward

Back-calculation: Data Preparation

- Ideally, estimation of β 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, β 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 β was used

Back-calculation: Results

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

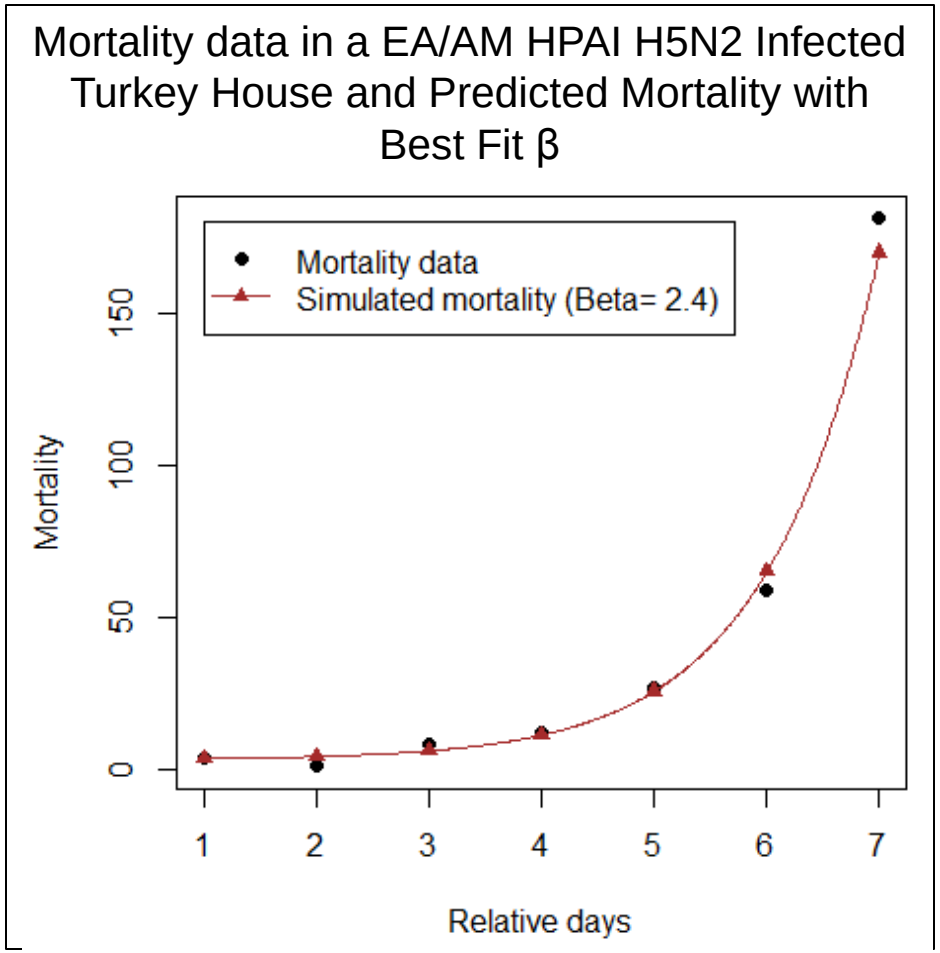
	β (95% CI)	R_0 (95% CI)
Outbreak data: Default scenario	2.87 (2.19 – 3.76)	11.49 (8.77 – 15.04)
Outbreak data: Sensitivity analysis	9.38 (5.13 – 17.14)	37.52 (20.52 – 68.56)
Validation on synthetic data	2.43 (1.52 – 4.31)	9.72 (6.08 – 17.24)

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

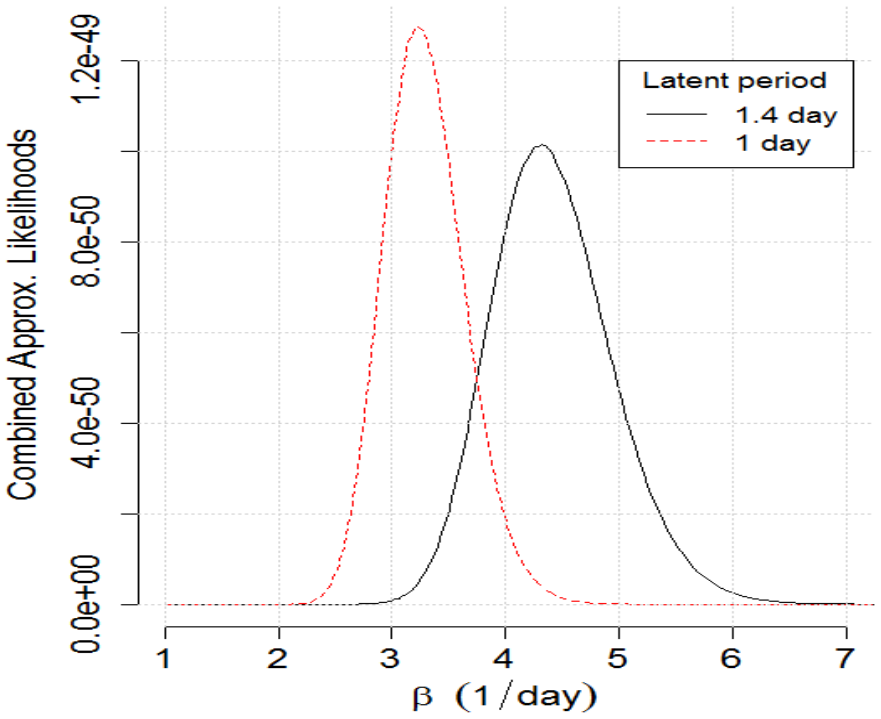
- A new approach is proposed based on least squares curve-fitting
- Disease mortality is predicted using deterministic differential equation models
- A goodness of fit measure (approximate likelihood) is then maximized to estimate β



Simulation and Curve-fitting: Results

- Performed well for estimating β on synthetic datasets
- Uses smaller time steps and non-integer latent and infectious periods
- The β estimate was sensitive to the mean latent period

Approximate likelihoods for β 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

	β (90%CI): FIVE flocks in outbreak data	
	Back – calculation	Forward simulation
Flock1	4.16	4.9 (3.9 – 6.6)
Flock2	2.25	2.5 (2.1 – 3.1)
Flock3	1.42	1.0 (1.0 – 1.1)
Flock4	2.13	7.4 (4.9 – 17)
Flock5	10	15.5 (10.0 – 19.4)
5 flocks combined	2.8 (2.1 – 3.7)	3.2 (2.8 – 3.9)

Concluding Remarks

- Back-calculation is a computationally fast method that uses accepted GLM-based procedures to obtain reasonable estimates for β
- β is a key parameter in a number of modeling analyses for decision support and active surveillance
- Developing multiple methods to estimate β will improve the accuracy of within-flock HPAI spread models results

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