

Estimating Epidemiological Parameters using Diagnostic Testing Data from the 2018 LPAI H5N2 Outbreak in Minnesota

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Introduction

- 8 turkey premises infected with LPAI H5N2 in Fall 2018 in Minnesota
 - 33 barns rRT-PCR (+) in total
- All infected barns were control marketed
 - Active surveillance by rRT-PCR and AGID/ELISA
- Diagnostic testing data used to estimate time of virus introduction and rate of within-house spread (adequate contact rate)



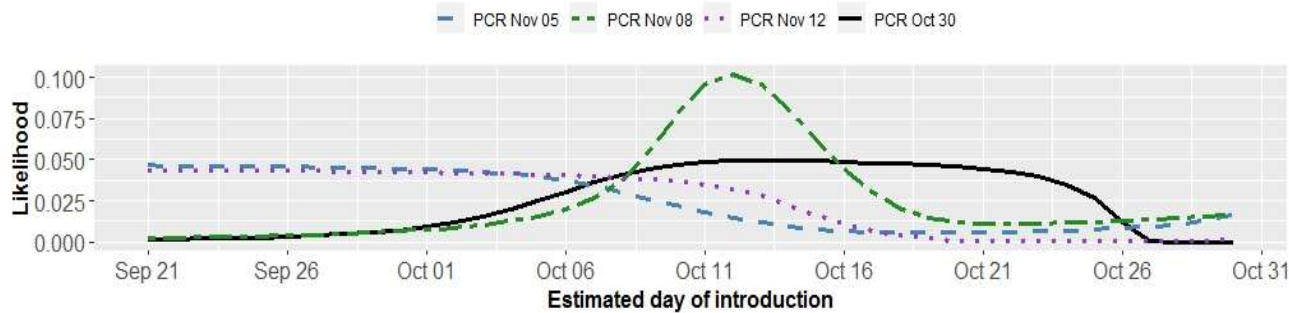
Methods

- Spread of LPAIV within a turkey house simulated for different virus introduction times and rates of spread
 - Simulation model parameters estimated from experimental and outbreak data
- Likelihood of observing diagnostic test data estimated using simulated output

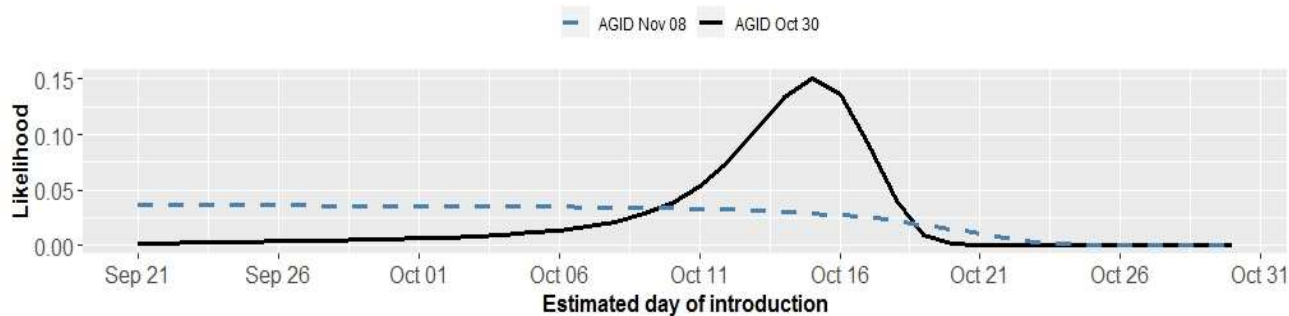


Estimated Likelihood of LPAI Introduction for Stearns 1, House 2

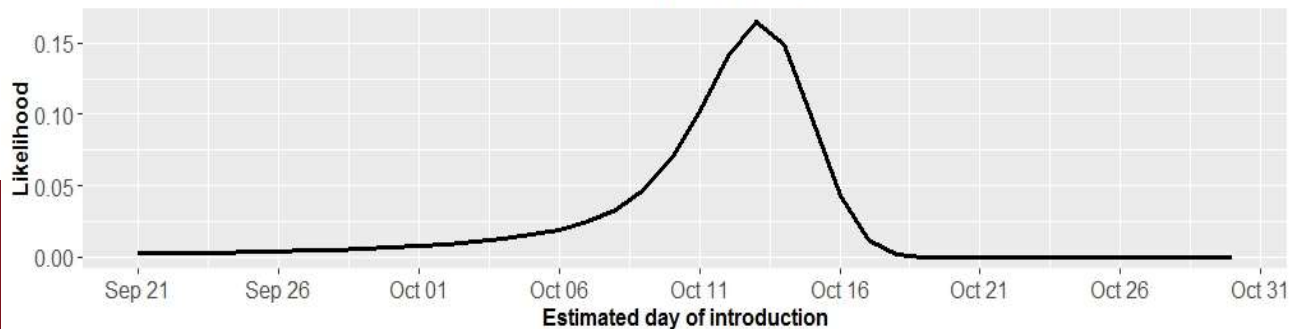
PCR Likelihoods



AGID Likelihoods



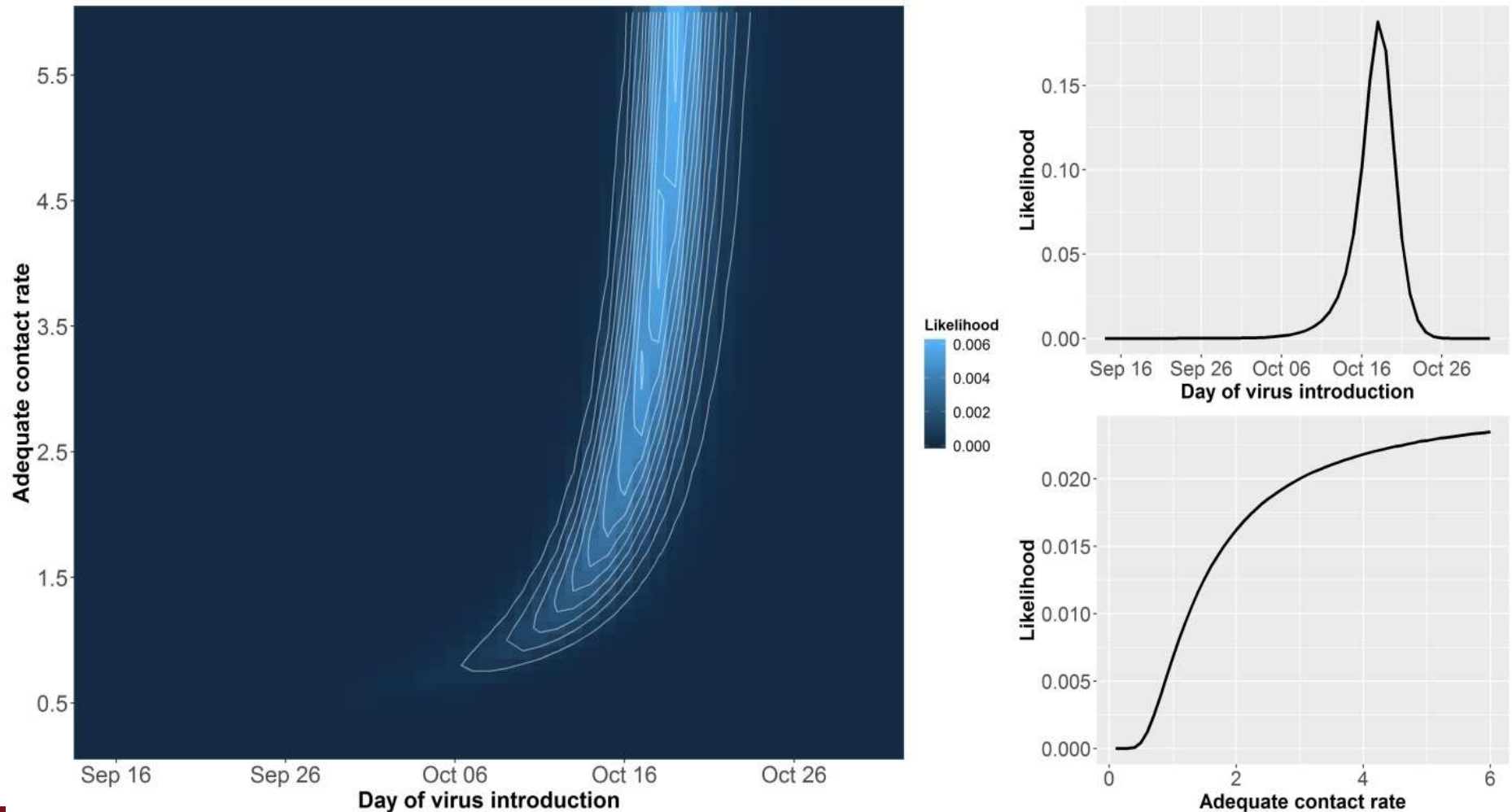
Overall Likelihood



Test Date	Result
10/30	2/2 PCR (+)
10/30	7/10 AGID (+)
11/05	0/1 PCR (+)
11/08	1/3 PCR (+)
11/08	10/10 AGID (+)
11/12	0/3 PCR (+)



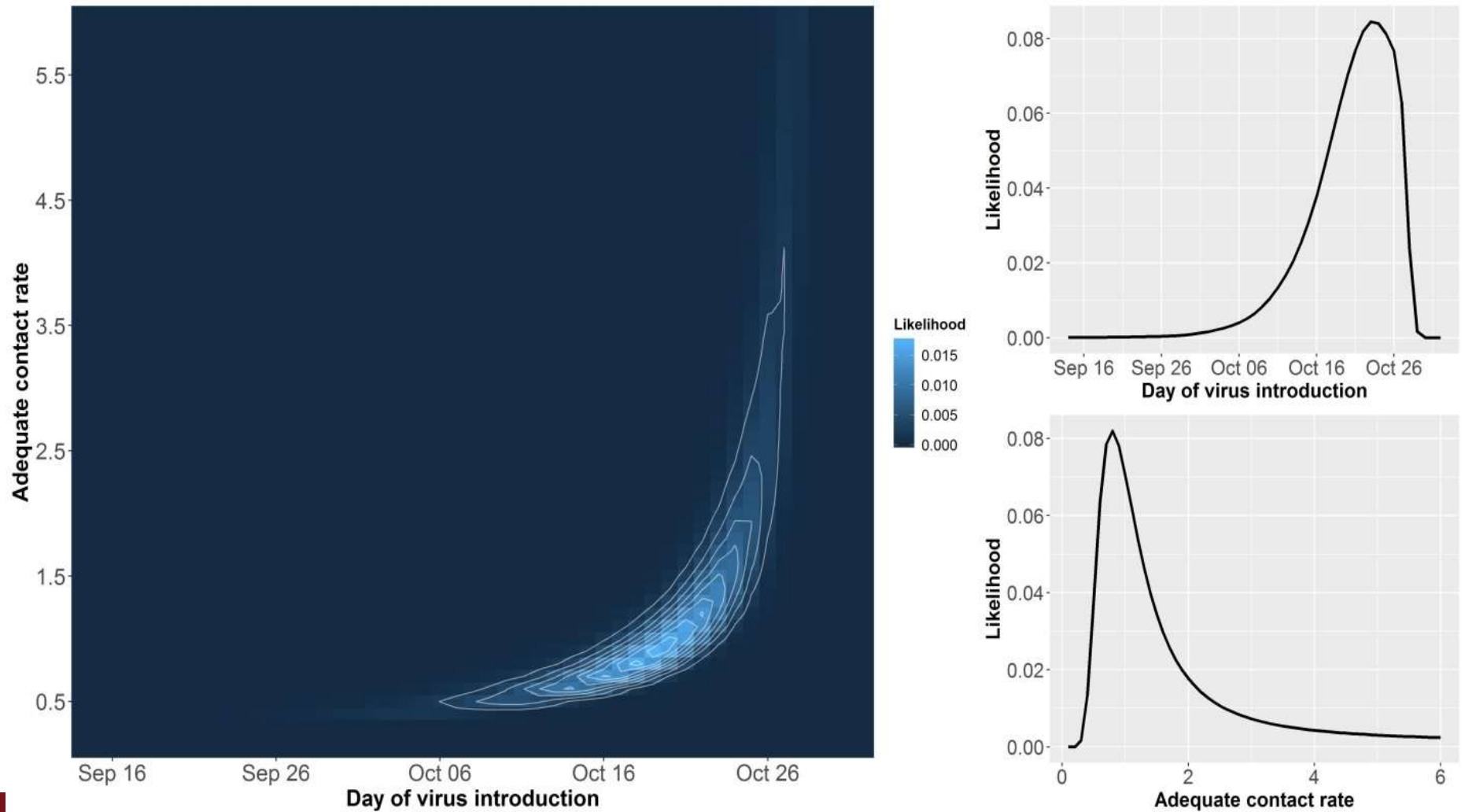
Estimated Likelihood of LPAI Introduction and Rate of Virus Spread for Kandiyohi 1, House 1



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Estimated Likelihood of LPAI Introduction and Rate of Virus Spread for Kandiyohi 1, House 1

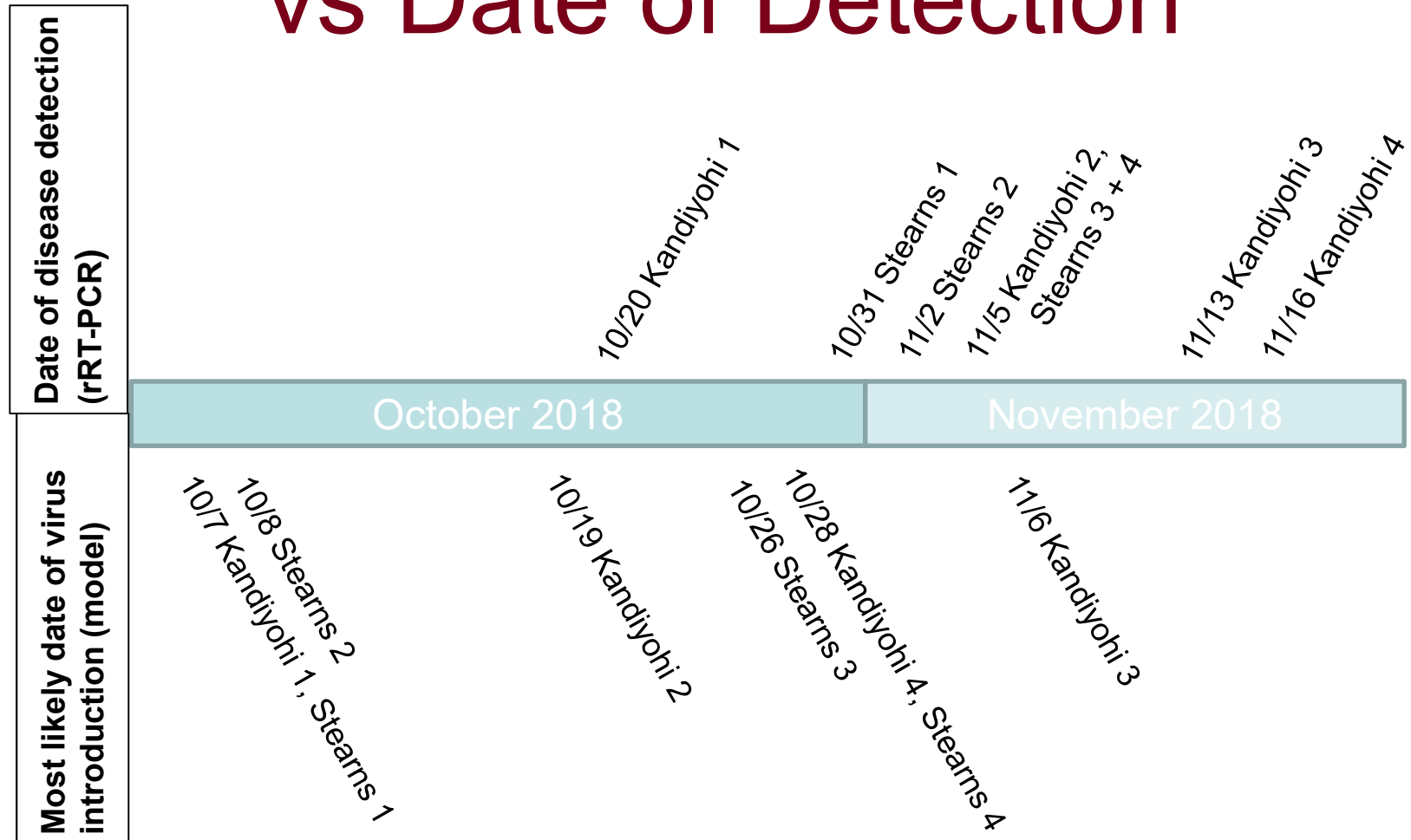


Estimated Date of LPAI Introduction

Premises	Most likely date of virus introduction (95% CI)
Kandiyohi 1	October 7 (Sep 13 – Oct 09)
Stearns 1	October 7 (Sep 22 – Oct 11)
Stearns 2	October 8 (Sep 22 – Oct 13)
Kandiyohi 2	October 19 (Oct 12 – Oct 22)
Stearns 3	October 26 (Oct 19 – Oct 28)
Stearns 4	October 28 (Oct 14 – Oct 29)
Kandiyohi 4	October 28 (Oct 19 – Nov 8)
Kandiyohi 3	November 6 (Oct 31 – Nov 8)



Estimated Date of Introduction vs Date of Detection



Estimated Date of LPAI Introduction: Results Summary

- Variable amounts of time between the first and last house infected on a premises
- Average of 9 days (5th-95th percentile: 4-21 days) between time of exposure and first positive rRT-PCR
- Average of 26 days (5th-95th percentile: 17-42 days) between time of exposure and first negative rRT-PCR result with all subsequent tests negative
 - 20 days (5th-95th percentile: 11-30 days) between exposure and first virus isolation negative



Method Validation

- Estimation method applied to diagnostic test data simulated with known parameters
- Several scenarios evaluated:
 - Fast and slow rates of spread
 - Different times of exposure relative to first test
 - Two testing schedules: one based on Kandiyohi 2, one with rRT-PCR and serology testing every 3 days
 - Combining results from multiple barns



Selected Validation Results

Scenario	Most likely date of virus introduction (95% CI)
<ul style="list-style-type: none"> • Slow spread • Infected 10/14 (6 days prior to first test) • Kandiyohi 2 test schedule 	<p>Single barn results: Oct 21 (Oct 10 – Oct 25)</p> <p>Combined results from 5 barns: Oct 16 (Oct 9 – Oct 22)</p>
<ul style="list-style-type: none"> • Fast spread • Infected 10/14 (6 days prior to first test) • Kandiyohi 2 test schedule 	<p>Single barn results: Oct 13 (Sep 24 – Oct 15)</p> <p>Combined results from 5 barns: Oct 13 (Oct 8 – Oct 15)</p>
<ul style="list-style-type: none"> • Slow spread • Infected 10/14 (6 days prior to first test) • Increased testing 	<p>Single barn results: Oct 15 (Oct 7 – Oct 20)</p> <p>Combined results from 5 barns: Oct 14 (Oct 10 – Oct 17)</p>



Validation Discussion

- The given time of virus introduction was in the estimated 95% CI for every scenario
- The method performs better
 - For fast within-house rates of spread
 - When the first test is performed at least several days prior to 100% seroconversion in the flock
 - The greater the amount and frequency of testing performed
 - When results from multiple barns can be combined



Discussion

- Diagnostic testing data can provide information on spread dynamics
 - Supports epidemiological investigations
 - Improves models used in risk analysis
 - Data collection during an outbreak is critical for understanding disease transmission
- Uncertainty in parameters and variability in disease spread
 - Lack of LPAI H5N2 experimental data leading to use of proxy strains in model
 - Number and frequency of diagnostic tests



Acknowledgements

- Thank you to Michelle Kromm, Jill Nezworski, Megan Lighty, Dale Lauer, Shauna Voss, Mary Donahue, Stacy Pollock, and Mia Torchetti for assistance in obtaining diagnostic testing data to support model development.
- Thank you to Erica Spackman for providing experimental inoculation data for parameter estimation and the Minnesota Supercomputing Institute for providing supercomputing resources used to perform the analysis.



Acknowledgements

- Authors Peter Bonney, Sasidhar Malladi, Emily Walz, and Carol Cardona acknowledge funding of their work by sponsored project contract number CON000000075615 (Secure Food Systems Team Contract with the State of Minnesota Board of Animal Health) and partial funding from a cooperative agreement between the Center for Epidemiology and Animal Health (CEAH) of the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS) Veterinary Services (VS) and the University of Minnesota (UMN) as USDA Award # AP18VSCEAH00C016 (Risk Analysis and Modeling to Manage HPAI and Other Animal Disease Emergencies). Carol Cardona is also funded by the B.S. Pomeroy Chair in Avian Health at the University of Minnesota College of Veterinary Medicine.



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Funding

- *This material was made possible, in part, through the University of Minnesota's Secure Food Systems Team Contract with the State of Minnesota Board of Animal Health (BAH) as sponsored project contract number CON000000075615 and from a cooperative agreement between the Center for Epidemiology and Animal Health (CEAH) of the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS) Veterinary Services (VS) and the University of Minnesota (UMN) as USDA Award # AP18VSCEAH00C016.*



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Questions?



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Transmission Model Parameters

Parameter name	Parameter description	Distribution/Value
Contact rate	Mean number of contacts a bird has that are sufficient to transmit infection per unit time	Grid of 0.5 to 10.0 contacts per day discretized at 0.1 intervals
Latent period distribution	Length of the latent period	~ Gamma (shape = 2.58, scale = 0.24); mean = 0.63 days, standard deviation = 0.39 days
Infectious period distribution	Length of the infectious period	~ Gamma (shape = 4.04, scale = 2.92); mean = 11.78 days, standard deviation = 5.86 days
Time to seroconversion	Time to seroconversion post-infection	~ Gamma (shape = 3.56, scale = 1.63); mean = 5.80 days, standard deviation = 3.07 days
Proportion seroconverting	Proportion of LPAI infected turkeys that seroconvert	0.99



rRT-PCR vs Virus Isolation

- In 8/29 barns at least one positive rRT-PCR result observed after 100% seropositive result
 - rRT-PCR positive observed up to 2 weeks after 100% seropositivity
- All rRT-PCR samples tested by Virus Isolation after 100% seropositivity were negative
 - rRT-PCR samples taken same day as 100% seropositive result were positive by Virus Isolation in 4 barns
- Virus recovered from 1/31 rRT-PCR positive results with Ct > 35
- Risk analysis needed for interpretation of diagnostic test results as related to product movement decisions



rRT-PCR vs Virus Isolation by Barn

Premises	Barn	Days from 1 st 100% seropositive to 1 st rRT-PCR (-) (with no subsequent rRT-PCR (+))	Days from 1 st 100% seropositive test result until first VI (-)
Kandiyohi1	Barn 1	11 days	0 days
	Barn 2	15 days	8 days
	Barn 3	14 days	0 days
	Barn 4	14 days	0 days
Stearns 3	Barn 1	8 days	7 days
	Barn 2	7 days	7 days
	Barn 3	0 days	0 days
	Barn 4	0 days	0 days

