UNIVERSITY OF GEORGIA

Evolution, epidemiology, and ~~RNA virus disease~~ Highly Pathogen Avian Influenza

Justin Bahl

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A brief history

- Prior to 2007 unified nomenclature and sub-clade classification was rare
- Most studies used descriptive names
  - Gs-GD-lineage
  - Qing Hai-lineage
  - Classic Swine-lineage
  - Etc etc
- Often used geographic location/host as a descriptor
  - Potential stigmatization

What changed?

RESEARCH ARTICLE | BIOLOGICAL SCIENCES |

Emergence and predominance of an H5N1 influenza variant in China

G. J. D. Smith, X. H. Fan, J. Wang, +10, and Y. Guan Authors Info & Affiliations

November 7, 2006 | 103 (45) 16936-16941 | https://doi.org/10.1073/pnas.0608157103

Margaret Chan elected to lead the WHO on November 9, 2006

News | Published: 15 November 2006

WHO boss faces test of independence

Declan Butler

Nature **444**, 250 (2006) | Cite this article

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

EMERGING INFECTIOUS DISEASES®

Volume 14, Number 7—July 2008

Peer Reviewed Report Available Online Only

Toward a Unified Nomenclature System for Highly Pathogenic Avian Influenza Virus (H5N1)

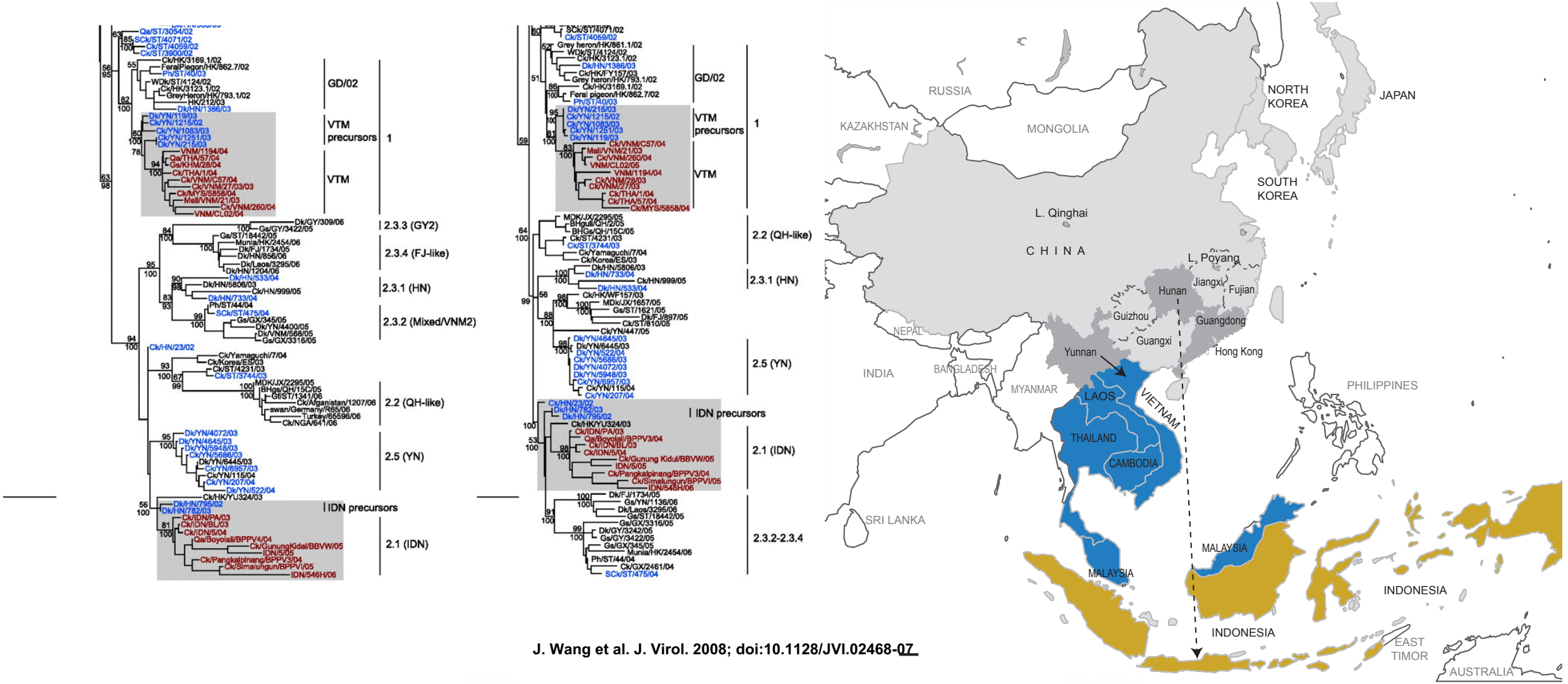
World Health Organization/World Organisation for Animal Health/Food and Agriculture Organization H5N1 Evolution Working Group.

Ruben O. Donis, **Centers for Disease Control and Prevention (CDC)**, (co-chair); Gavin J.D. Smith, **University of Hong Kong**; WHO, GIP, EPR; Veterinary Laboratories Agency, Addlestone, UK**;** Chinese Academy of Agriculture Sciences CAAS, Harbin, People's Republic of China; Erasmus University, Rotterdam, the Netherlands**;** University of Wisconsin-Madison, Madison, Wisconsin, USA; China Centers for Disease Control, Bejing, People's Republic of China; Instituto Zooprofilattico Sperimentale delle Venezie, Padova, Italy; University of Hong Kong; WHO, GIP, EPR; University of Cambridge, Cambridge, UK.

Criteria used for clade designation

No.	Criteria
1	Maintain previously designated clade numbers where possible (i.e., clade 2.2 remains 2.2 and clade 1 remains 1)
2	New clade designations based on phylogenetic tree topology derived from all available sequences (the large tree)
	H5N1 progenitors (closest to Gs/Guangdong/1/96) re-designated as clade 0
	Subsequent clades numbered starting from clade 3 (i.e., clades 3–9)
	Clades designated by presence of a distinct common node shared by at least 4 isolates (in a monophyletic group)
	Additional branches designated as a single clade evolves into more than one distinct lineage (i.e., clade 2.2 or clade 2.3.1; based on sharing of a common node and monophyletic grouping)
3	Average percentage pairwise distances between and within clades (using Kimura 2-parameter)
	Distinct clades should have >1.5% average distances between other clades
	Distinct clades should have <1.5% average distances within the clade (may be slightly higher in clades with highly evolved outliers; i.e., Ck/Shanxi/2/2006 in clade 7)
4	Bootstrap (based on 1,000 neighbor-joining bootstrap replicates) ≥60% bootstrap value at clade-defining node

Phylogenetic relationships of the HA (A) and NA (B) genes of representative influenza A viruses.



J. Wang et al. J. Virol. 2008; doi:10.1128/JVI.02468-07

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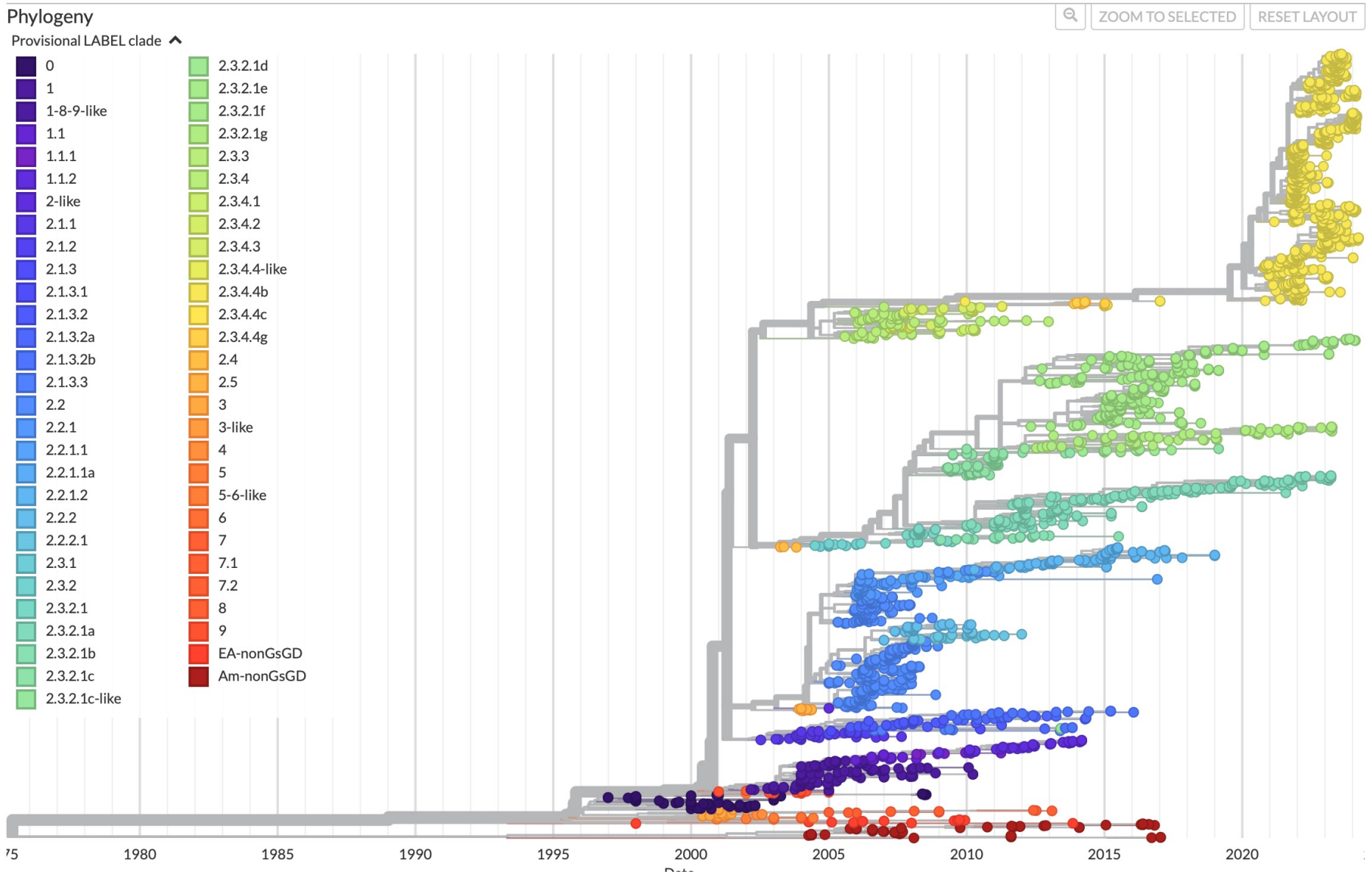
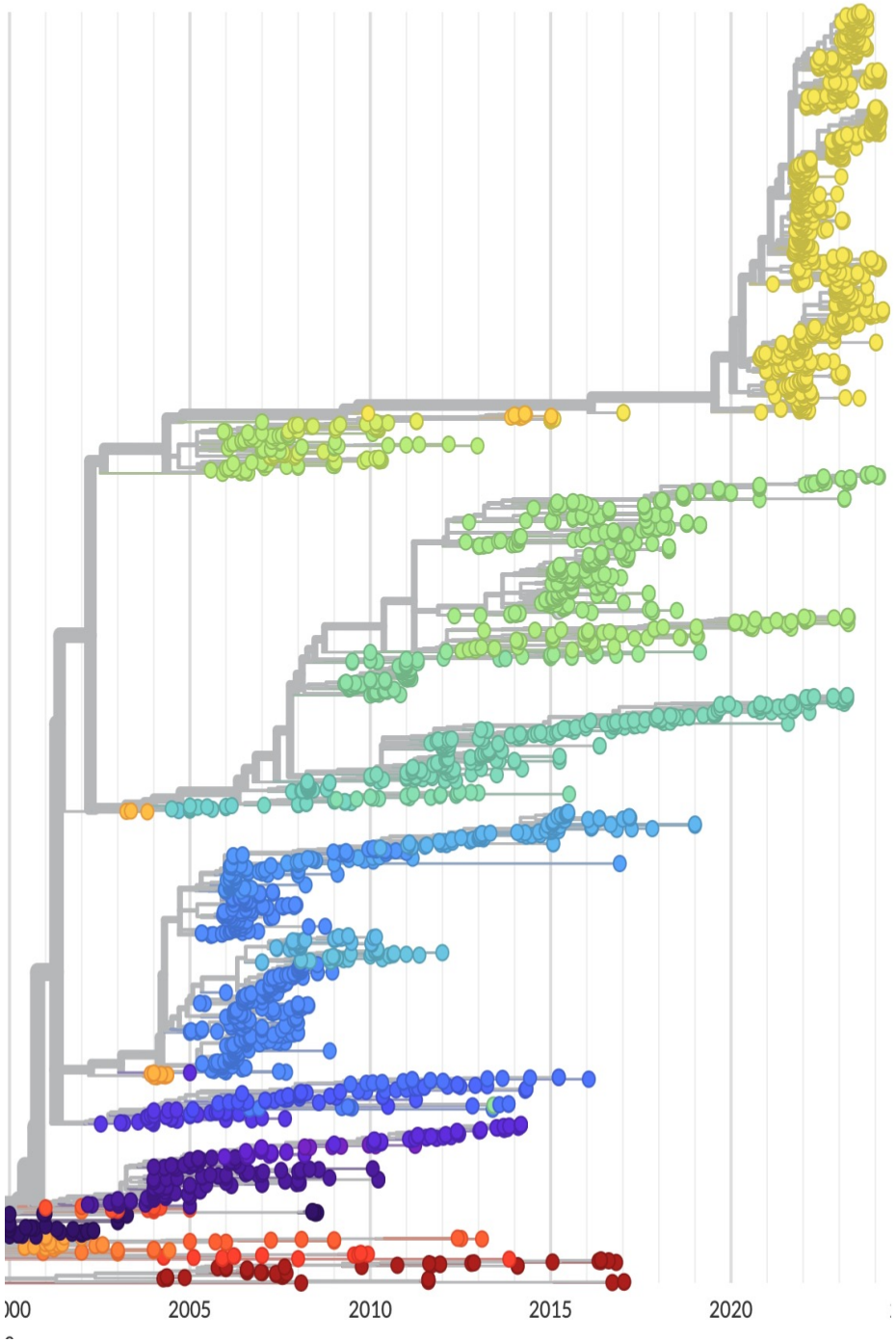
Journal of Virology

Real-time tracking of influenza A/H5N1 virus evolution

Built with nextstrain/avian-flu. Maintained by Louise Moncla. Data updated 2024-04-02. Enabled by data from GISAID.

Showing 3095 of 3095 genomes sampled between Dec 1996 and Mar 2024.





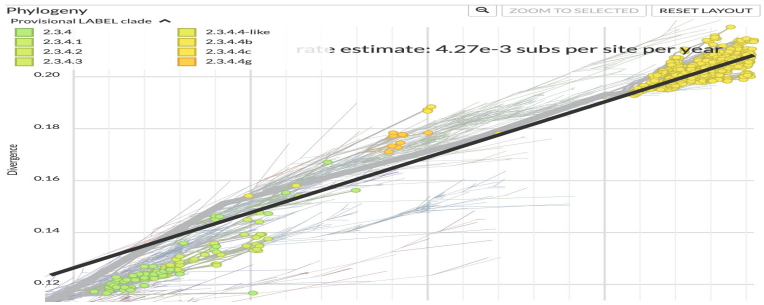
2.3.4 Global - Wild Birds, poultry, mammals, humans

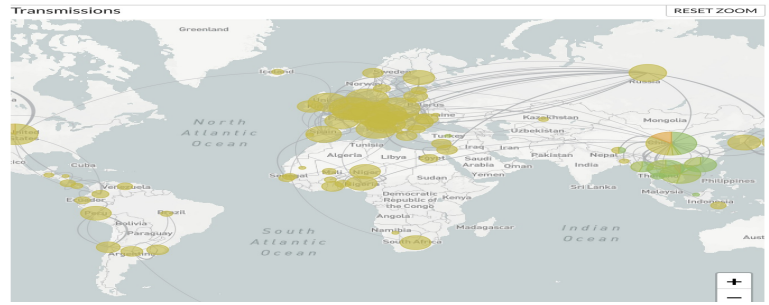
2.3.1.e Southeast Asia - Poultry

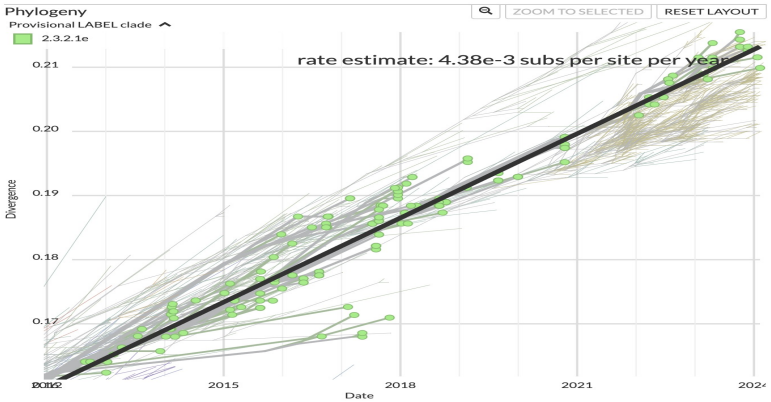
2.3.1.g Indonesia - Poultry

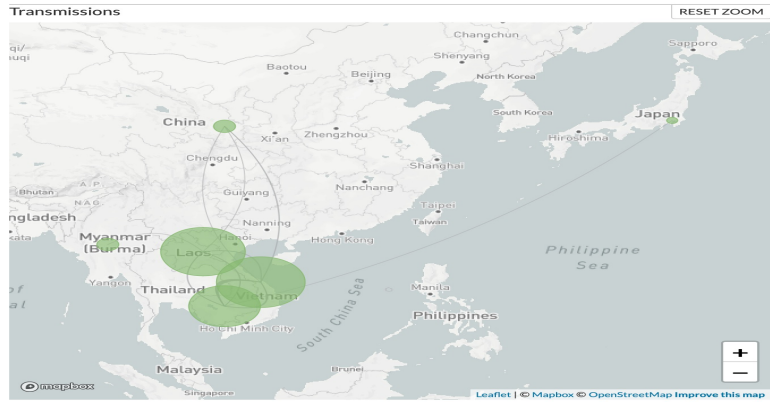
2.3.1.a Bangladesh, Nepal, India - Poultry

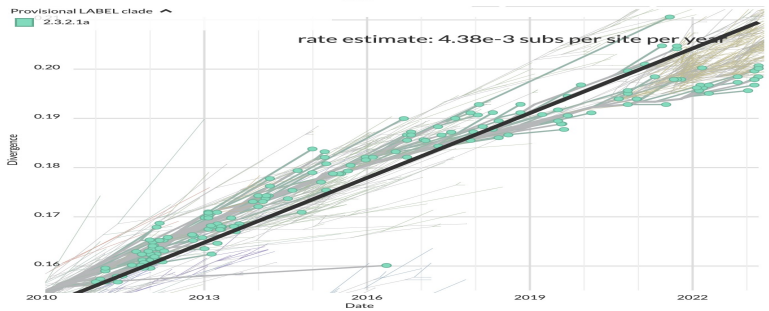
2.2 Eurasia and Middle East - Wild Bird, poultry

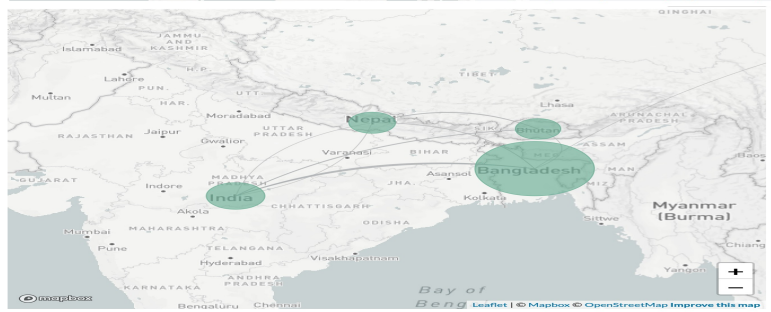

Phylogeny
ZOOM TO SELECTED
RESET LAYOUT
Provisional LABEL clade
2.3.4
2.3.4.1
2.3.4.2
2.3.4.3
2.3.4.4-like
2.3.4.4b
2.3.4.4c
2.3.4.4g
rate estimate: 4.27e-3 subs per site per year
Divergence
0.20
0.18
0.16
0.14
0.12

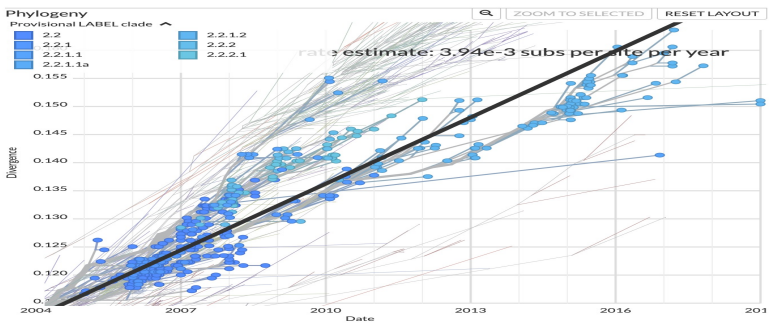

Transmissions
RESET ZOOM
North Atlantic Ocean
South Atlantic Ocean
Indian Ocean

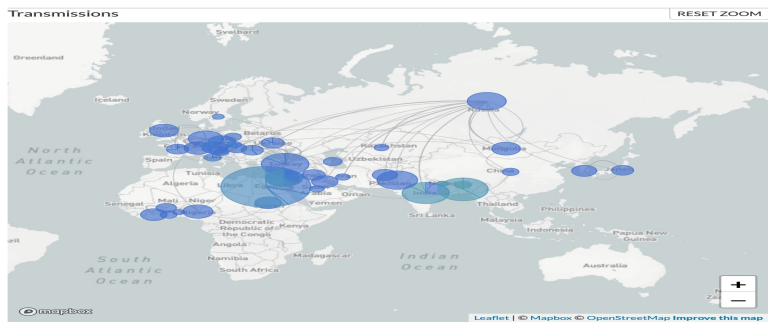

Phylogeny
ZOOM TO SELECTED
RESET LAYOUT
Provisional LABEL clade
2.3.2.1e
rate estimate: 4.38e-3 subs per site per year
Divergence
0.21
0.20
0.19
0.18
0.17
2015
2018
2021
Date

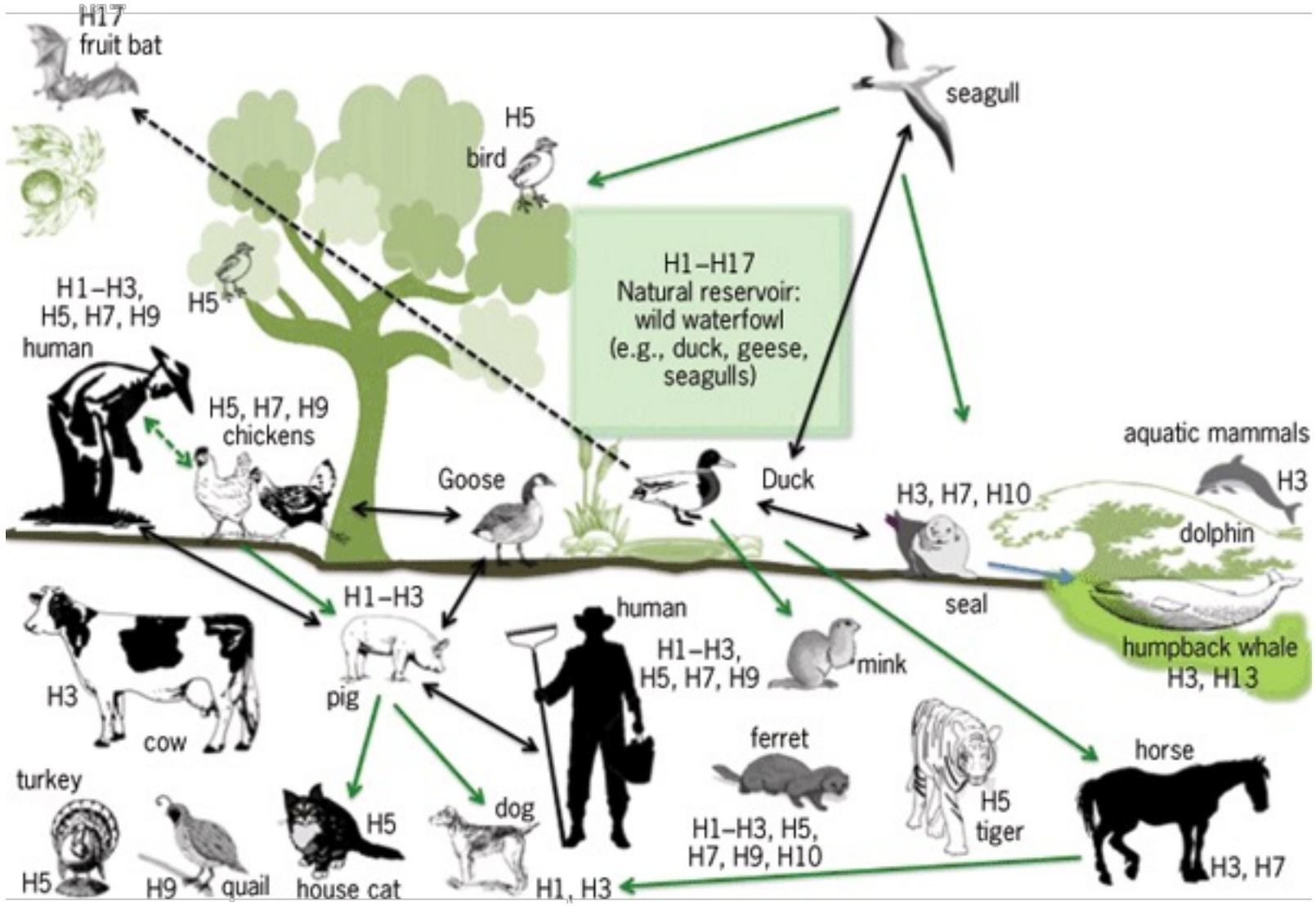

Transmissions
RESET ZOOM
China
Japan
Myanmar (Burma)
Laos
Thailand
Vietnam
Philippines
Philippine Sea
South China Sea
Malaysia
Leaflet | © Mapbox © OpenStreetMap Improve this map


Provisional LABEL clade
2.3.2.1a
rate estimate: 4.38e-3 subs per site per year
Divergence
0.20
0.19
0.18
0.17
0.16
2010
2013
2016
2019
2022
Date


Nepal
Bangladesh
India
Myanmar (Burma)
Leaflet | © Mapbox © OpenStreetMap Improve this map


Phylogeny
ZOOM TO SELECTED
RESET LAYOUT
Provisional LABEL clade
2.2
2.2.1
2.2.1.1
2.2.1.1a
2.2.1.2
2.2.2
2.2.2.1
rate estimate: 3.94e-3 subs per site per year
Divergence
0.155
0.150
0.145
0.140
0.135
0.130
0.125
0.120
2004
2007
2010
2013
2016
Date


Transmissions
RESET ZOOM
North Atlantic Ocean
South Atlantic Ocean
Indian Ocean
Leaflet | © Mapbox © OpenStreetMap Improve this map


H17
fruit bat
seagull
H5
bird
H1–H17
Natural reservoir:
wild waterfowl
(e.g., duck, geese,
seagulls)
H1–H3,
H5, H7, H9
human
H5
H5, H7, H9
chickens
Goose
Duck
aquatic mammals
H3
dolphin
H3, H7, H10
seal
humpback whale
H3, H13
H1–H3
pig
human
H1–H3,
H5, H7, H9
mink
H3
cow
ferret
H1–H3, H5,
H7, H9, H10
H5
tiger
horse
H3, H7
turkey
H5
H9
quail
H5
house cat
dog
H1, H3

2006 1 24

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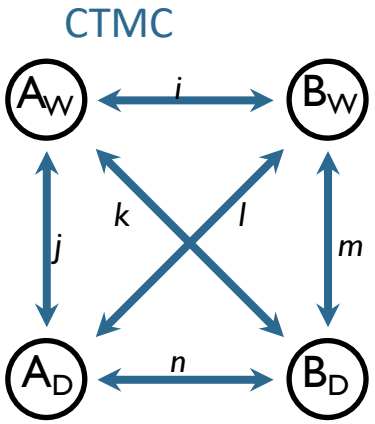
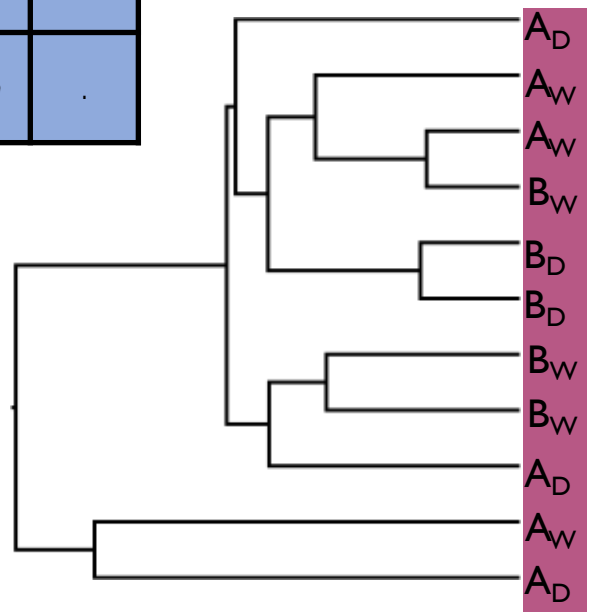
Ecosystem interaction model

- Discrete Model:

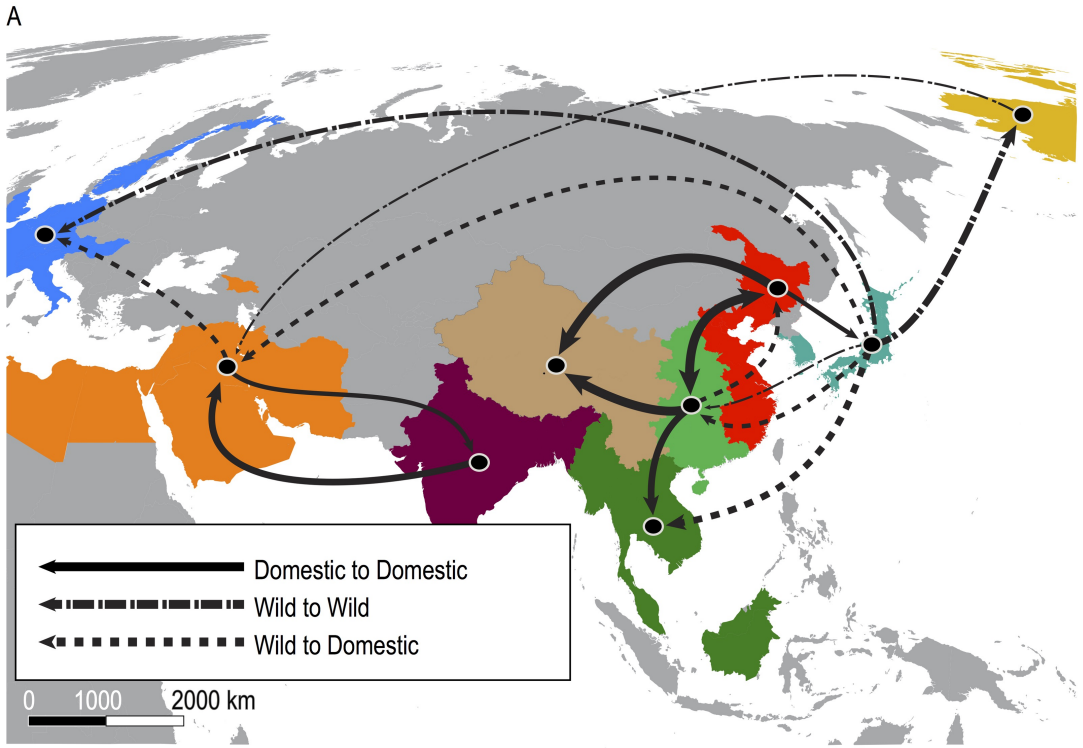


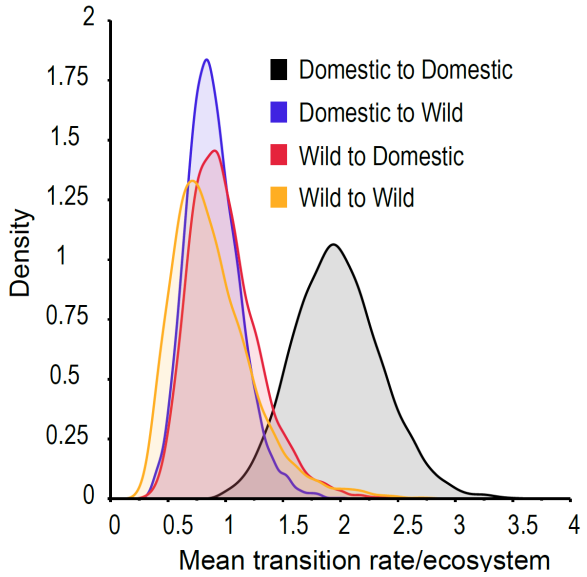
	A_D	B_D	A_W	B_W
A_D	.	π_{Bi}	π_{Cj}	π_{Dk}
B_D	π_{Ai}	.	π_{Cl}	π_{Dm}
A_W	π_{Aj}	π_{Bl}	.	π_{Dn}
B_W	π_{Ak}	π_{Bm}	π_{Cn}	.

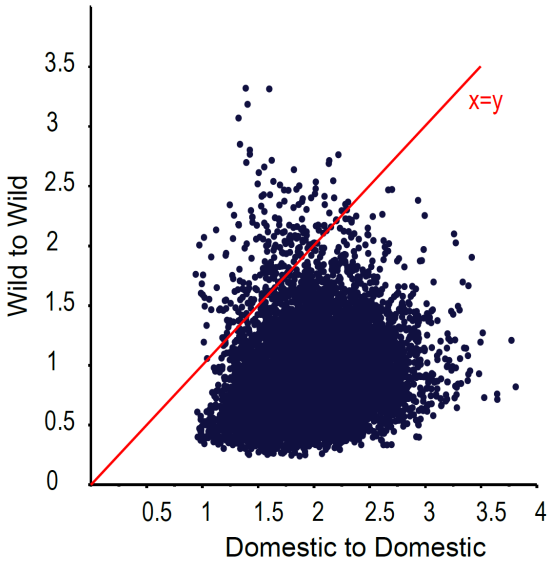


Supported migration rates between ecosystems

- Bahl J et al. *PLoS Pathogens* doi.org/10.1371/journal.ppat.1005620



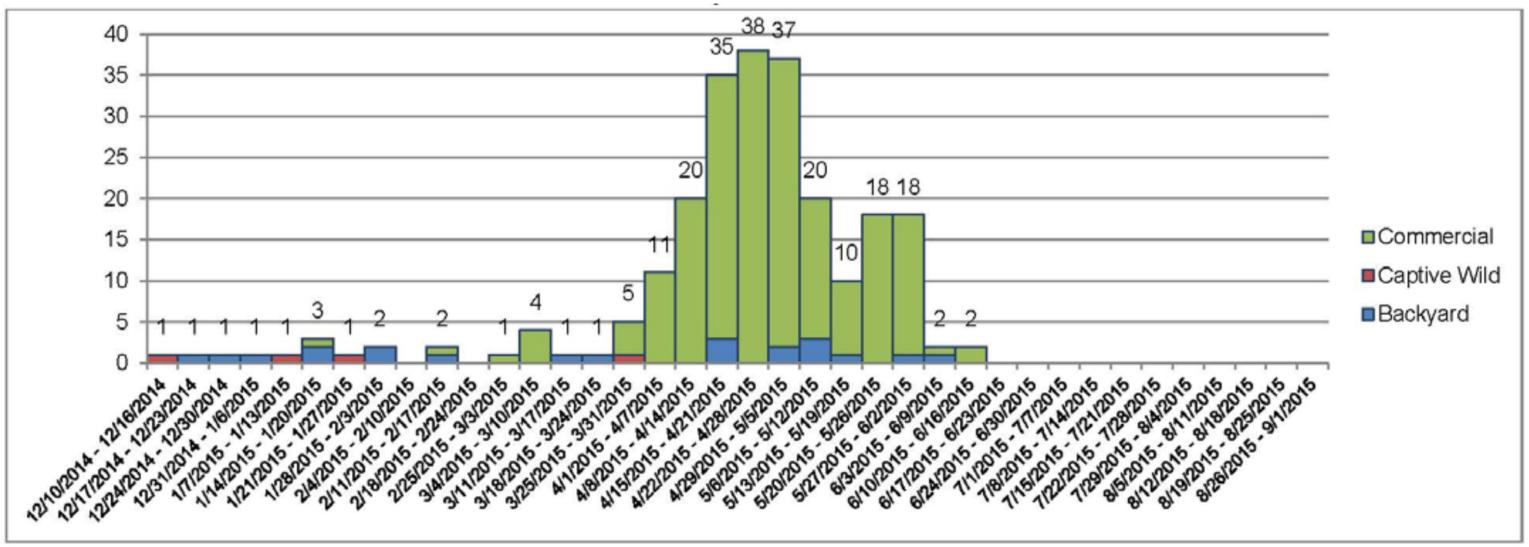




2014–2015 HPAI H5Nx Outbreak

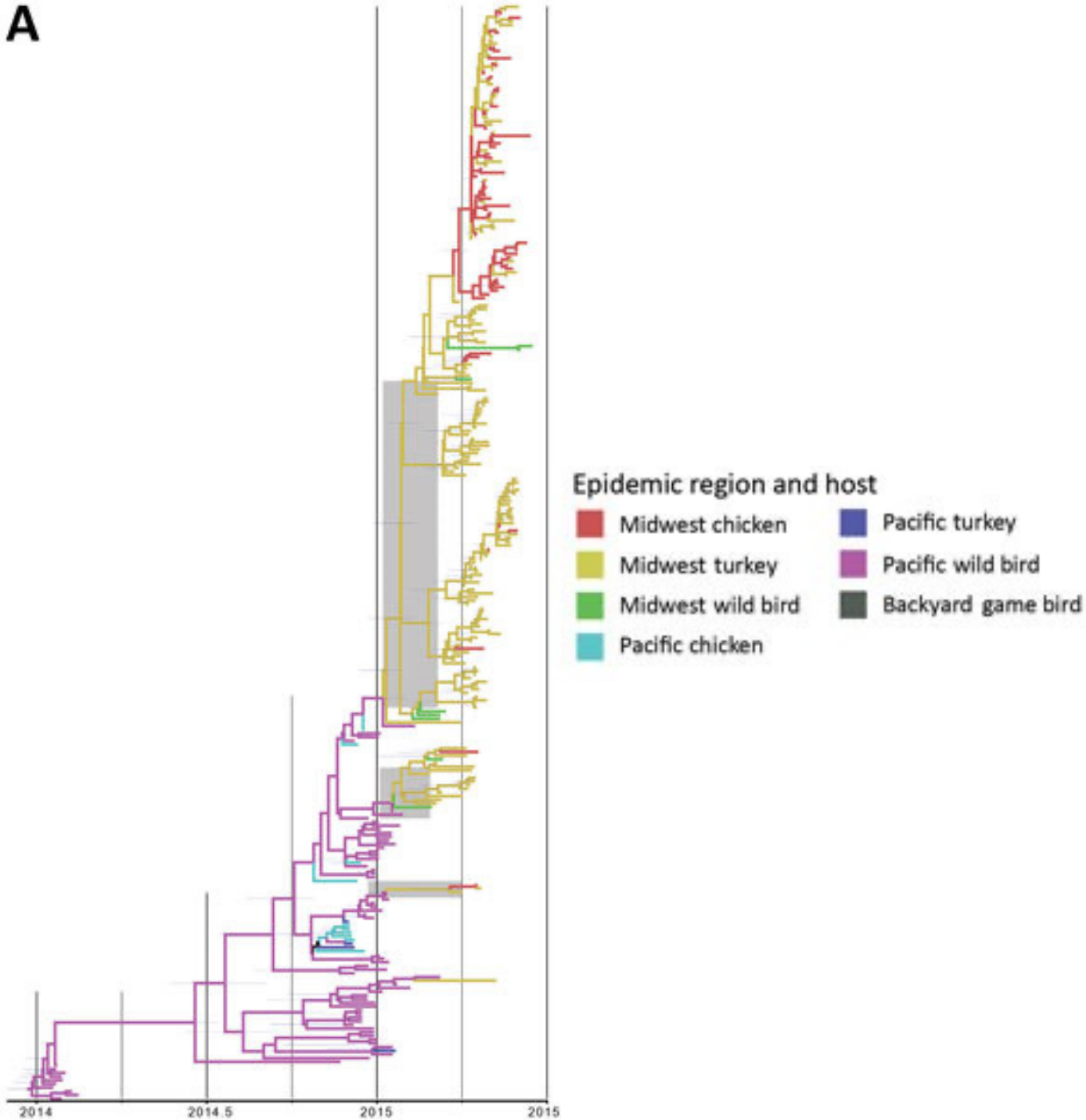
- December 2014: H5N2 detection in British Columbian commercial poultry
- December 2014: H5N8 and H5N2 detection in Pacific northwest wild birds and backyard poultry
- January 2015: First US commercial poultry detection (California)

Figure 5. Total Incidence of HPAI in the United States by Week



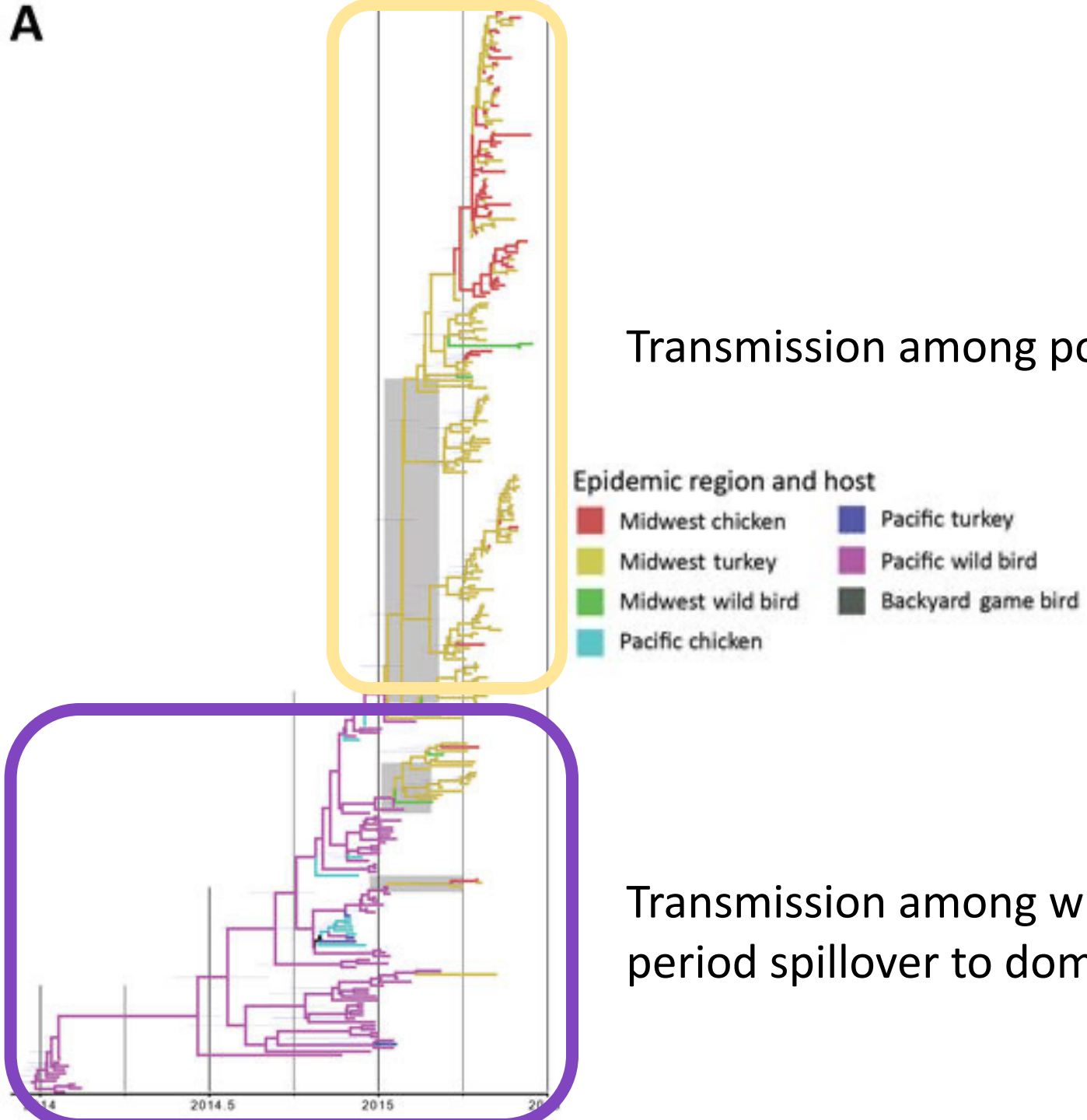
Note: Date pictured is earliest available date indicating clinical signs. This is a clinical sign date if known, a suspect status, or a presumptive positive status. Some premises may only have a confirmed positive status date.

USDA APHIS. 2016. Final Report for the 2014–2015 Outbreak of Highly Pathogenic Avian Influenza (HPAI) in the United States



Lee et al *EID* (2018) doi: 10.3201/eid2410.171891

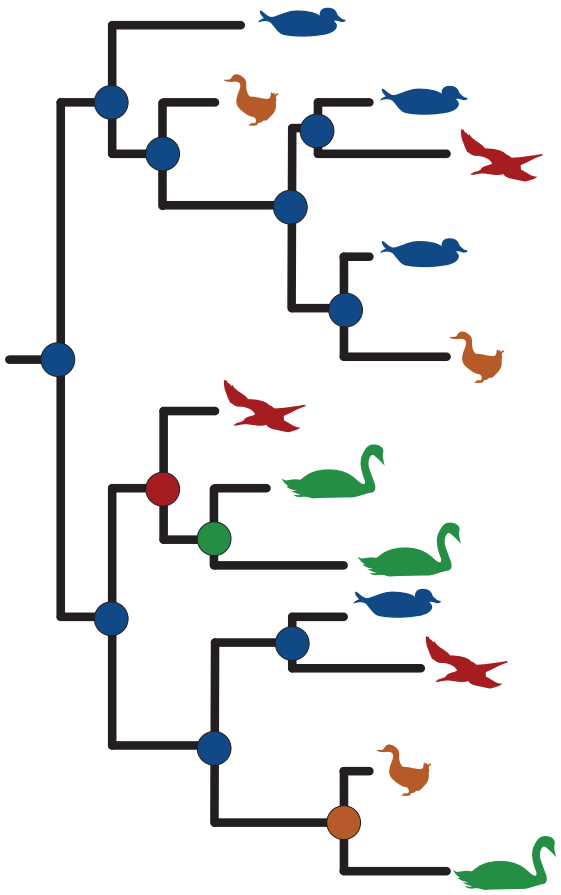
Lee et al *EID* (2018) doi: 10.3201/eid2410.171891

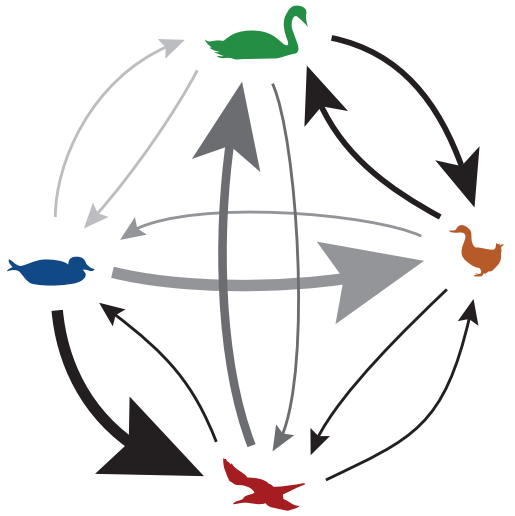


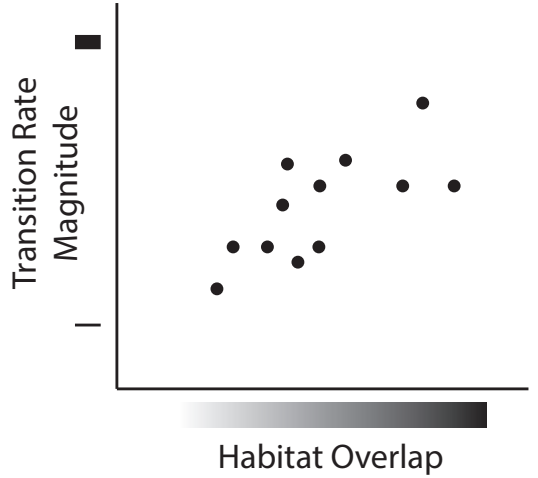
Transmission among poultry farms

Transmission among wild bird with period spillover to domestic birds

Dr. Joe Hicks
Imperial College

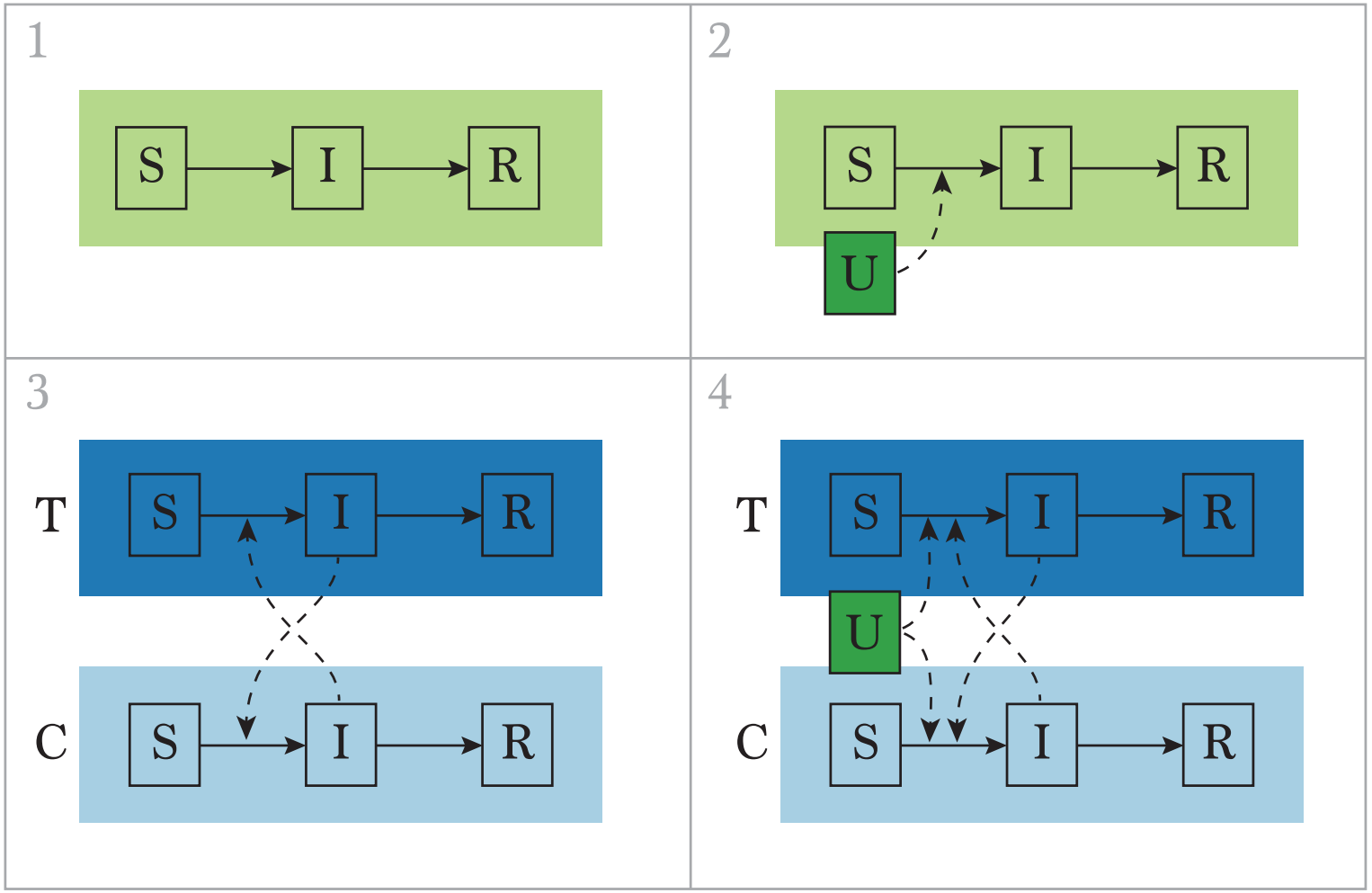






Hicks JT et al. *PLoS Pathogens* (2020) doi.org/10.1371/journal.ppat.1007857

Hypothesized Models

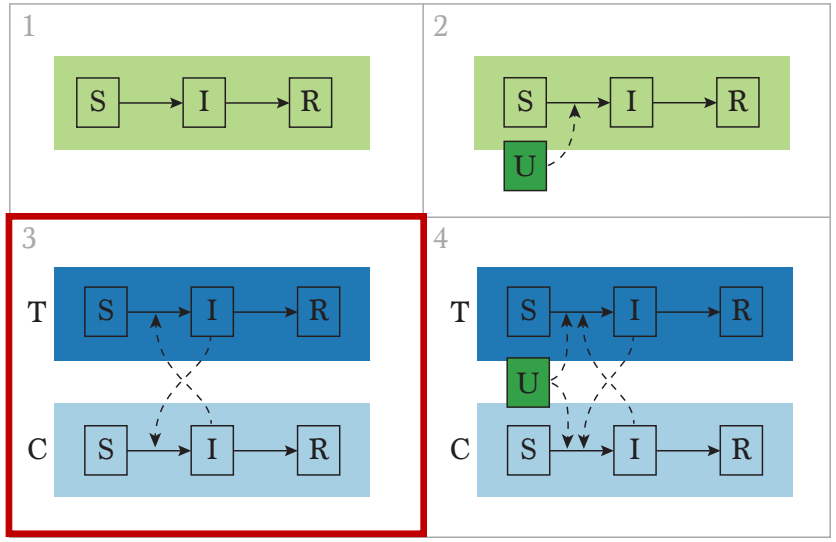


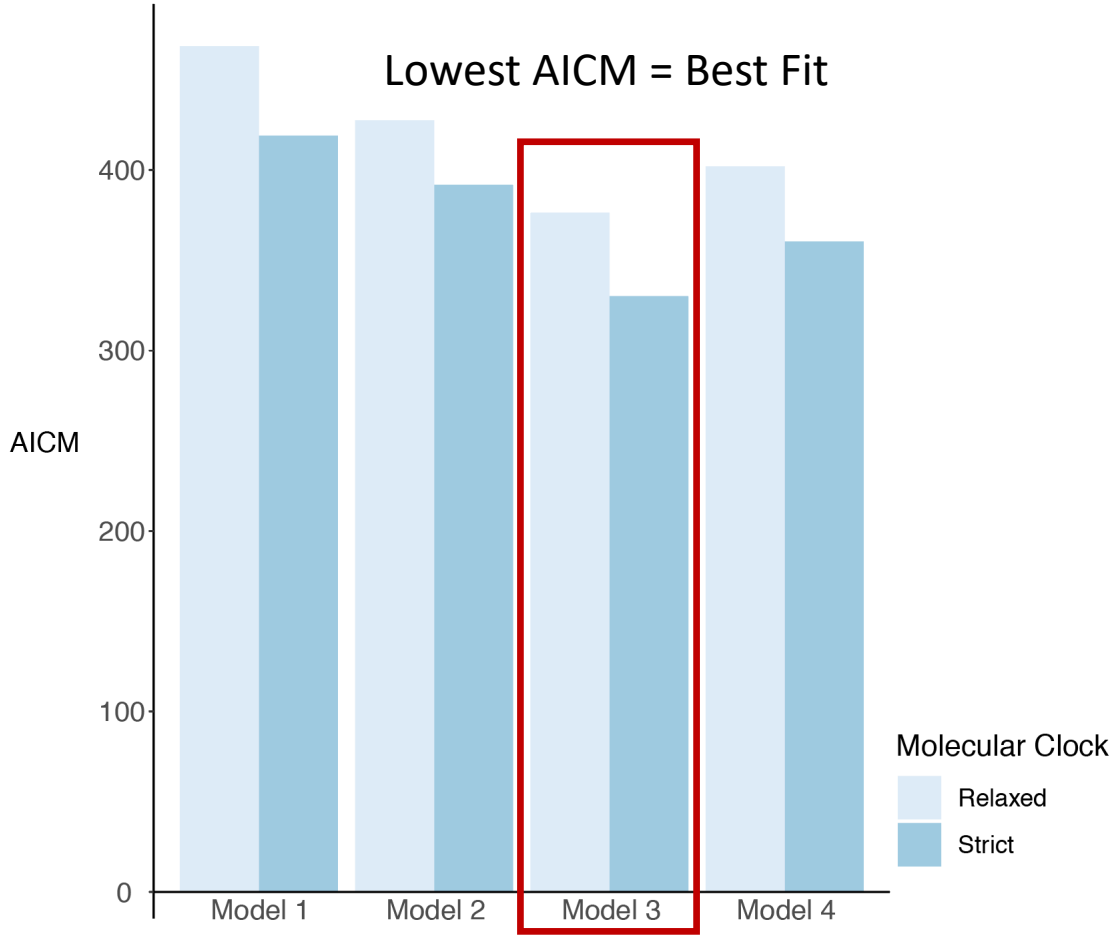
S = Susceptible Farm
I = Infected Farm
R = Culled Farm

U = Unknown external viral source

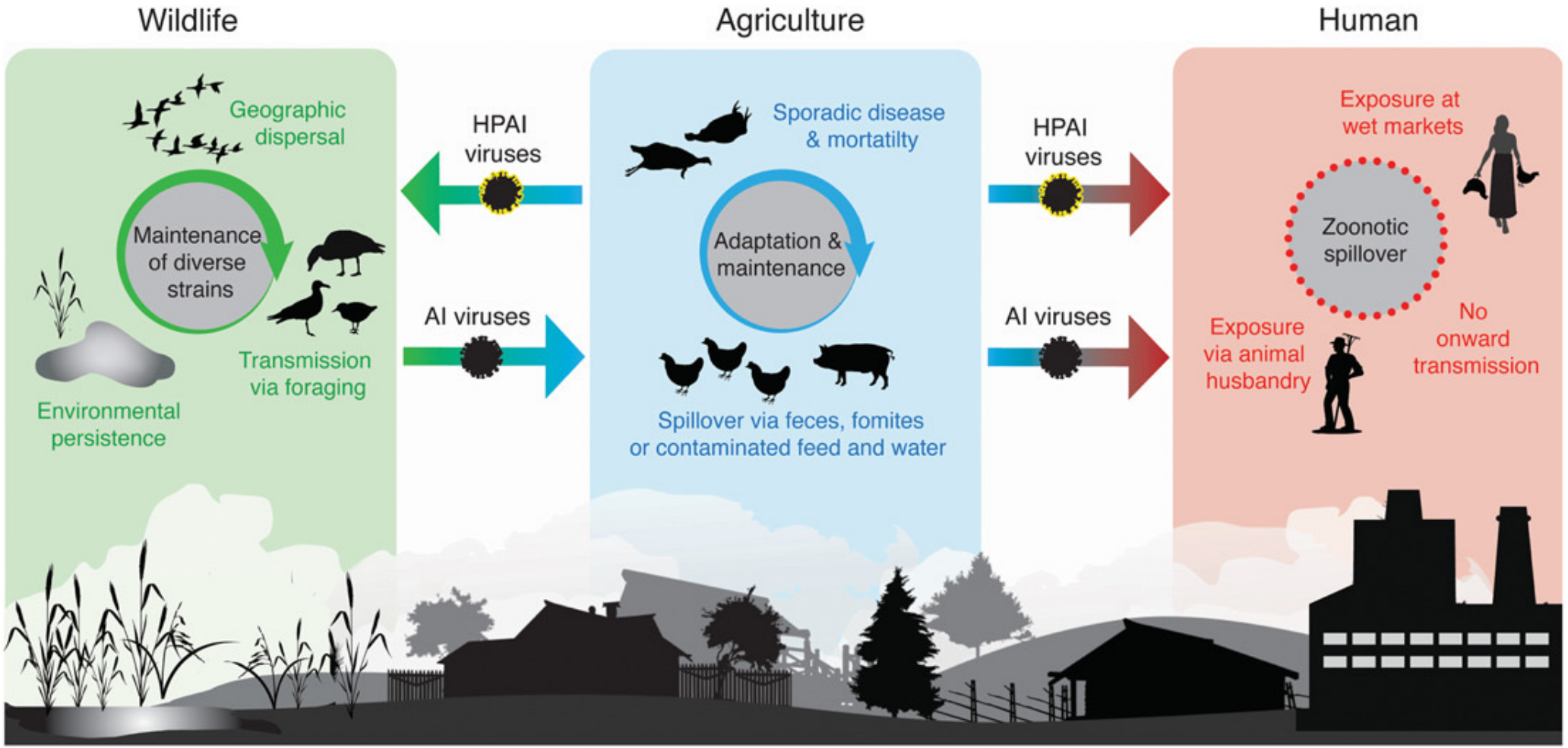
T = Turkey production system
C = Layer chicken production system

Model Fit Comparison





Highly pathogenic avian influenza is a disease threat that crosses ecological systems and scales



Ramey et al J Wildl Manag, 2022, DOI: (10.1002/jwmg.22171)

H5N1 emergence

- Resulted from complex ecology of farms & live-poultry markets in southern China
- Different bird species harbor different influenza A subtypes
- Markets allow interaction between different bird species
  - Aquatic poultry (goose, duck)
  - Terrestrial poultry (chicken)
  - Minor poultry (especially quail)
- Regional lineages – likely determined by trade
- Spillover to wild avian populations have resulted in widescale spread

A sub-clade classification system should be useful

- For HPAI – viral ecology, epidemiology determine how evolutionary mechanisms
- **Pathogen Diversity:** is driven by natural selection, mutation, drift, migration
- **Ecology:** HPAI has a massive host range. Behavior, contact rates, transmission mechanism, and population size differs and can impact phylogenetic patterns
- **Epidemiology:** timing of transmission and risk associated with climate in wild birds, distribution and epizootic size associated with established trade routes for domestic animals

Acknowledgements

Applied molecular epidemiology team

Joseph Hicks, Sachin Subedi, Jiani Chen, Tosin Babasola, Guppy Stott, Gabriella Veytsel, Leke Lyu, Mohamed Bahkeet, Xueting Qiu, MHM Mubassir, Cody Dailey

Dong-Hun Lee, Gavin Smith, Andy Ramey, Nichola Hill, Yi Guan, Malik Pieris, Vijay Dhanasekaren

CEIRS
NIAID Centers of Excellence for Influenza Research and Surveillance

Funding

NIAID-NIH

SJCEIRS (NIAID HHSN266200700005C and HHSN272201400006C)

UGA CIDER (75N93021C00018)

UGA CIVIC (75N93019C00052)

Centers for Disease Control and Prevention

Georgia Pathogen Genomics Center of Excellence

Influenza (75D30119C06826, 75D30121C11990)

SARS-CoV-2 (75D30121C11159, 75D30121C10133)

NSF RAPID: 2029595

CENTERS FOR DISEASE CONTROL AND PREVENTION

National Science Foundation
WHERE DISCOVERIES BEGIN

Terrible Assumptions!

- Virus behaves the same in all wild and domestic populations
- Assume all anseriformes migrate in the same patterns
  - Host specific migration behaviors are irrelevant
- Our sampling is representative
  - A few thousand birds are sampled out of millions of breeding pairs