LECTURE 2. Avian & Zoonotic Influenza: Ecology and Threats

Focus: How influenza viruses spill over, circulate in nature, and threaten humans.

Introduction to Avian Influenza Ecology

- Wild birds as reservoirs.
- LPAI vs HPAI.
- Flyways, mixing, and the ecology of transmission in wild & domestic bir

Emergence of H5Nx & HPAI in Poultry & Wild Birds

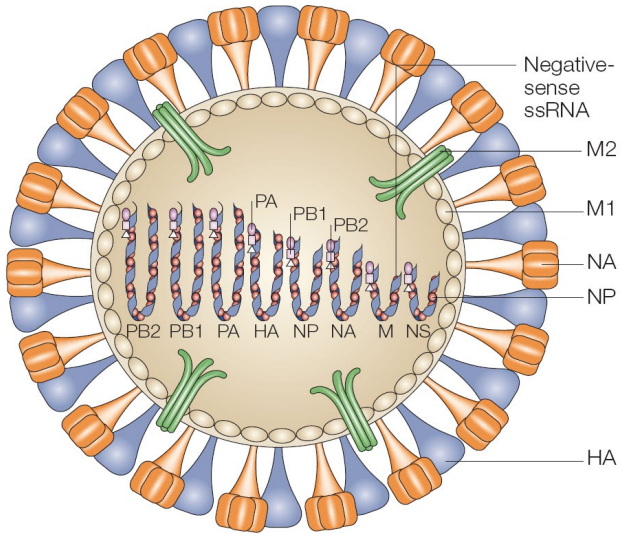
- History of H5N1 & emergence of 2.3.4.4 clade.
- Dynamics in poultry vs wild birds.
- Recent global spread, factors driving persistence.

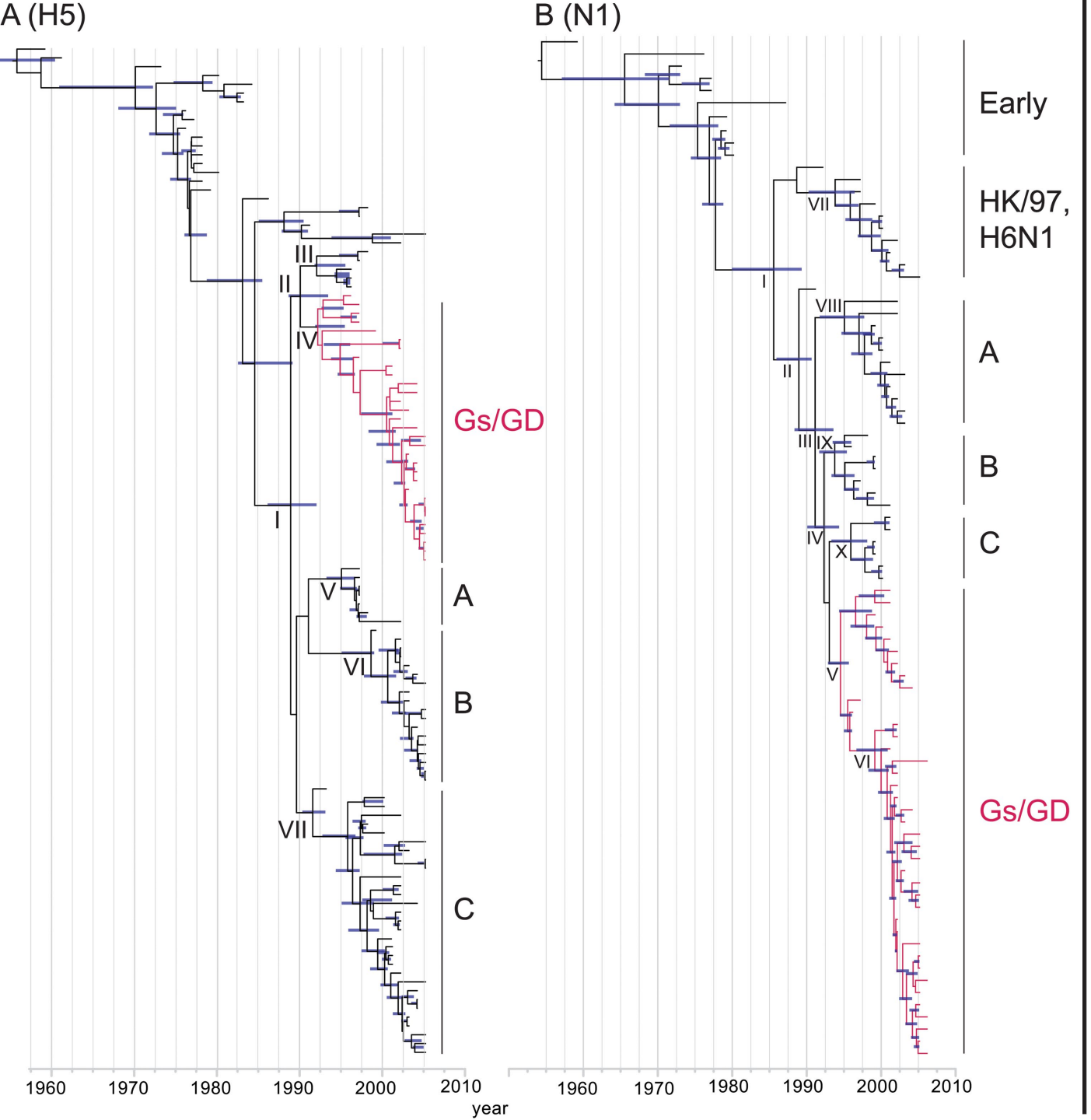
Zoonotic Infections & Recent Mammalian Cases (30 min)

- Human infections with H5, H7, H9.
- Recent reports of mammalian infections & their implications.
- Molecular markers of adaptation.

Synthesis & Future Threats (20 min)

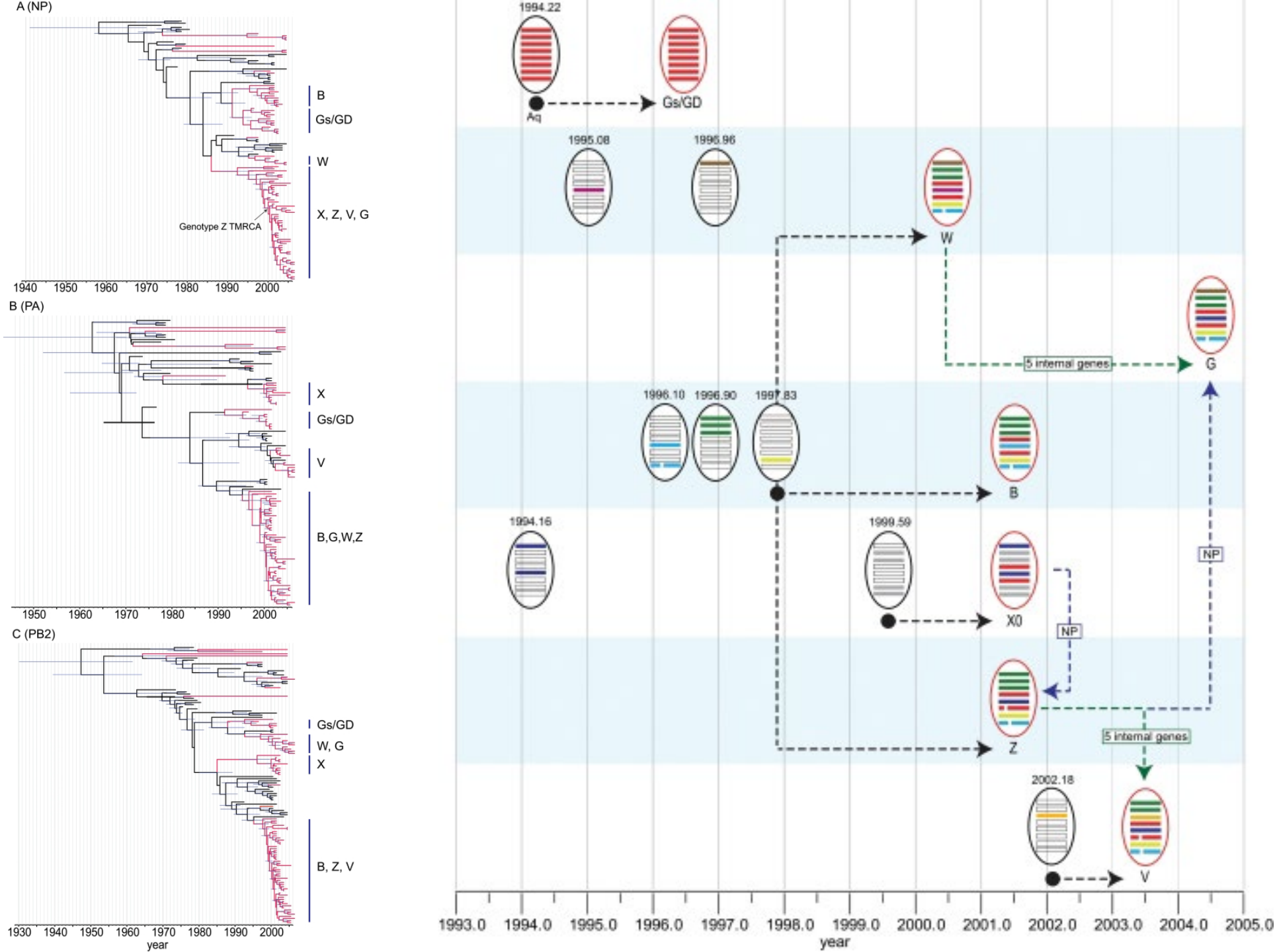
- Why surveillance in birds & mammals matters.
- Role of ecological change (agriculture, climate, migration).
- Prospects for pandemic potential.

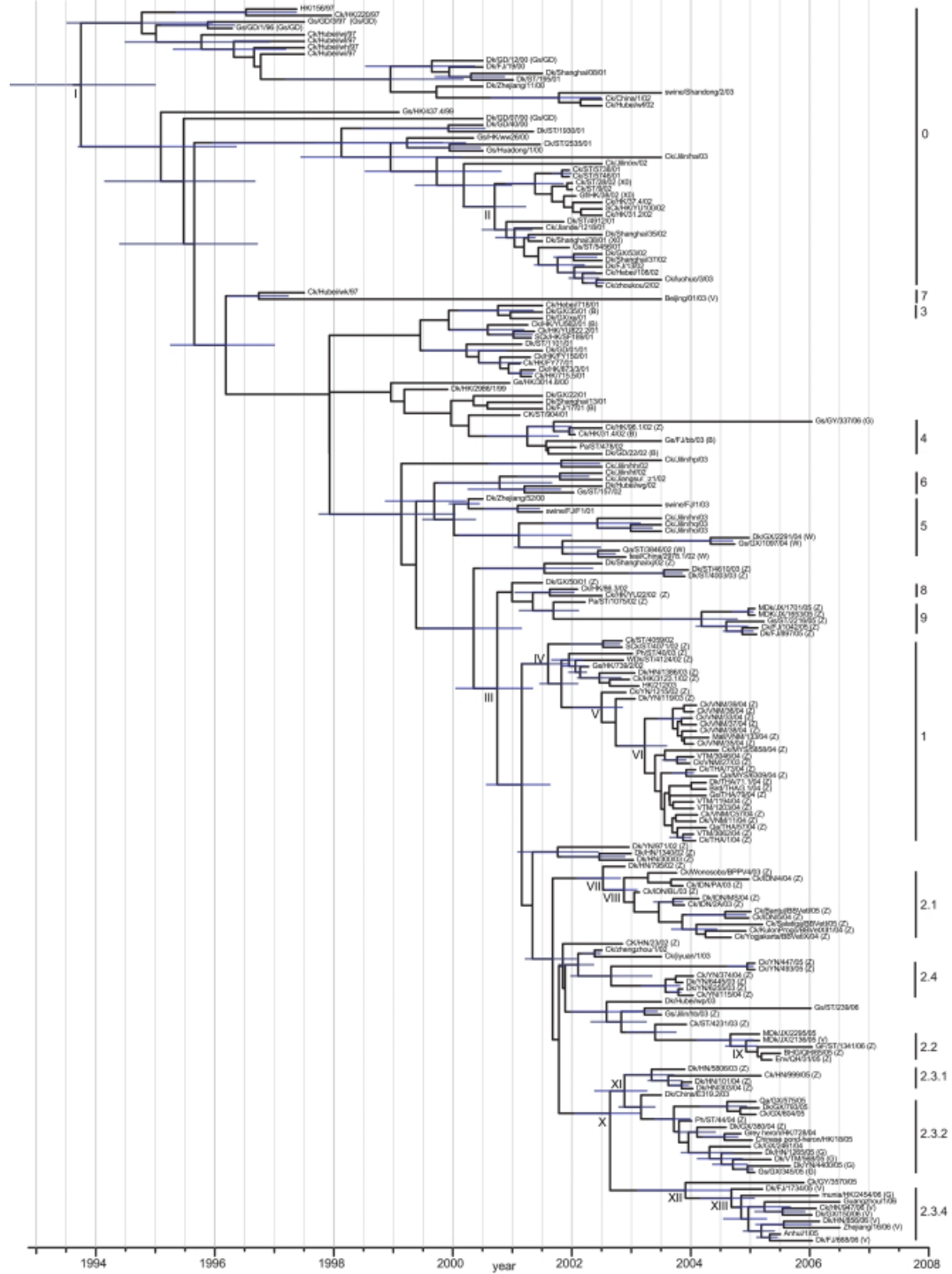


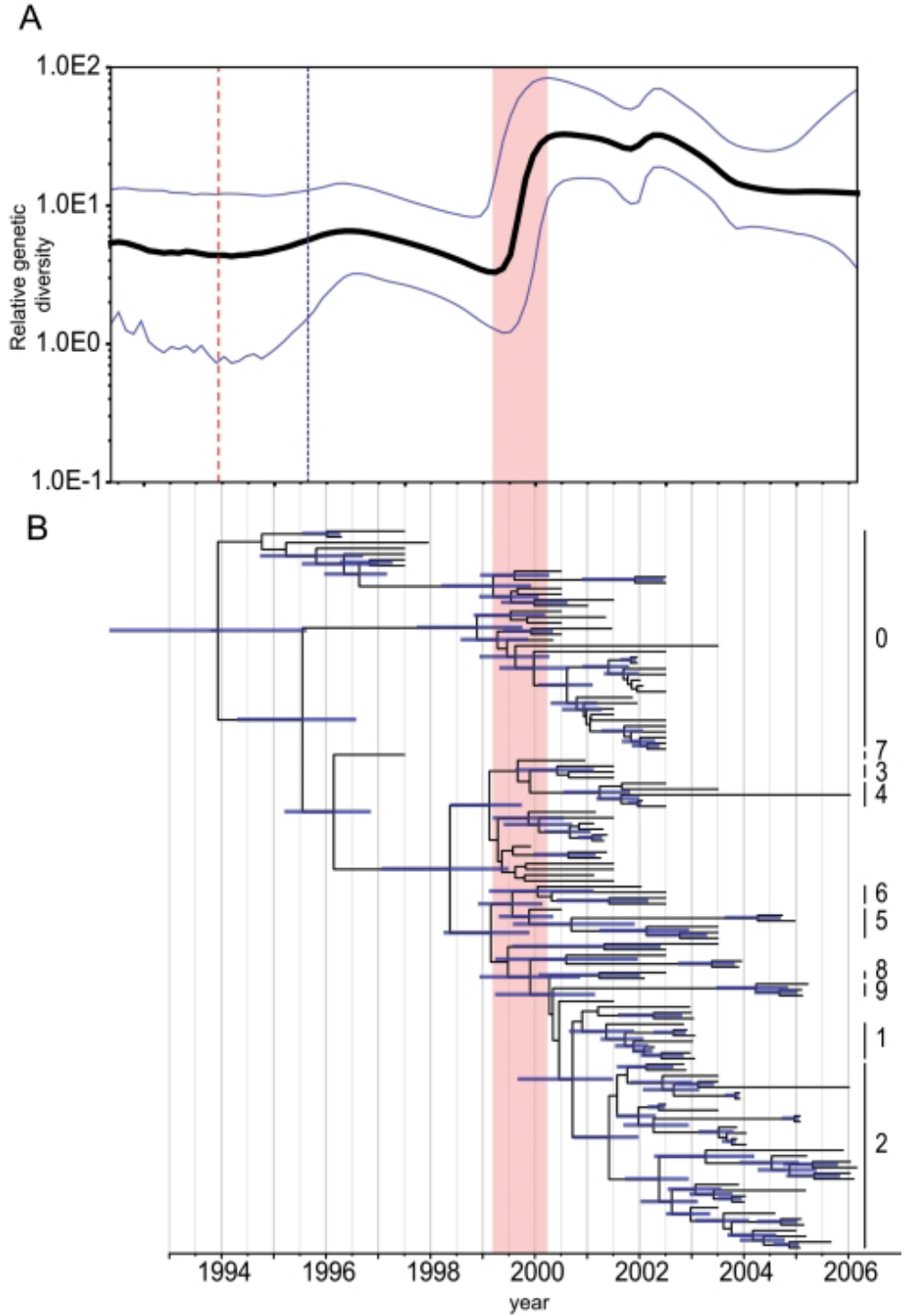


Dataset	Node[1]	Description	Mean TMRCA (95% HPD)[2]
H5 HA dataset	I	Current Eurasia	1989.51 (1986.52–1992.42)
	II	Gs/GD+out-group	1991.69 (1989.06–1993.83)
	III	Hokkaido/Singapore	1994.21 (1992.19–1995.91)
	IV	Gs/GD H5N1	1994.04 (1992.27–1995.84)
	V	Europe A	1995.64 (1993.64–1997.06)
	VI	Europe B	1997.88 (1995.47–1999.39)
	VII	Eurasia C	1992.48 (1992.71–1993.49)
N1 NA dataset	I	Current Eurasia	1985.83 (1980.32–1989.67)
	II	Eurasia	1989.21 (1986.30–1991.01)
	III	Eurasia	1991.40 (1988.73–1993.94)
	IV	Eurasia	1992.59 (1990.45–1994.71)
	V	GsGD	1994.81 (1993.23–1996.02)
	VI	GsGD with 20 AA deletion	1999.42 (1997.05–2001.23)
	VII	HK97	1994.08 (1990.61–1996.79)
	VIII	Eurasia A	1995.33 (1992.10–1998.08)
	IX	Eurasia B	1994.03 (1992.04–1995.75)
	X	Eurasia C	1996.19 (1993.68–1998.49)

[1]Nodes indicate TMRCAs of major H5 and N1 lineages, as shown in Figures 1A, B.
[2]The dates are presented as year followed by proportion of days.
doi:10.1371/journal.ppat.1000161.t002


A (NP)
B
Gs/GD
W
X, Z, V, G
Genotype Z TMRCA
1940 1950 1960 1970 1980 1990 2000
B (PA)
X
Gs/GD
V
B,G,W,Z
1950 1960 1970 1980 1990 2000
C (PB2)
Gs/GD
W, G
X
B, Z, V
1930 1940 1950 1960 1970 1980 1990 2000
year
1994.22
Aq
Gs/GD
1995.08
1995.96
W
5 internal genes
G
1996.10
1996.90
1997.83
B
1994.16
1999.59
X0
NP
NP
Z
5 internal genes
2002.18
V
1993.0 1994.0 1995.0 1996.0 1997.0 1998.0 1999.0 2000.0 2001.0 2002.0 2003.0 2004.0 2005.0
year


I
II
III
IV
V
VI
VII
VIII
IX
X
XI
XII
XIII
0
7
3
4
6
5
8
9
1
2.1
2.4
2.2
2.3.1
2.3.2
2.3.4
1994
1996
1998
2000
2002
2004
2006
2008
year


A
1.0E2
1.0E1
1.0E0
1.0E-1
Relative genetic diversity
B
0
7
3
4
6
5
8
9
1
2
1994
1996
1998
2000
2002
2004
2006
year

Edwards et al. 2023. *EID*

EMERGING INFECTIOUS DISEASES®

EID Journal > Volume 29 > Number 1—January 2023 > Main Article

Volume 29, Number 1—January 2023

Dispatch

Detection of Clade 2.3.4.4b Avian Influenza A(H5N8) Virus in Cambodia, 2021

Kimberly M. Edwards, Jurre Y. Siegers, Xiaoman Wei, Ammar Aziz, Yi-Mo Deng, Sokhoun Yann, Chan Bun, Seng Bunnary, Leonard Izzard, Makara Hak, Peter Thielen, Sothyra Tum, Frank Wong, Nicola S. Lewis, Joe James, Filip Claes, Ian G. Barr, Vijaykrishna Dhanasekaran[1], and Erik A Karlsson[1]

Xie et al. 2023. *Nature*

nature

Explore content | About the journal | Publish with us | Subscribe

nature > articles > article

Article | Published: 18 October 2023

The episodic resurgence of highly pathogenic avian influenza H5 virus

Ruopeng Xie, Kimberly M. Edwards, Michelle Wille, Xiaoman Wei, Sook-San Wong, Mark Zanin, Rabeh El-Shesheny, Mariette Ducatez, Leo L. M. Poon, Ghazi Kayali, Richard J. Webby & Vijaykrishna Dhanasekaran

Nature **622**, 810–817 (2023) | Cite this article

18k Accesses | **727** Altmetric | Metrics

Yang et al. 2024. *J Virol*

Genetic diversity of highly pathogenic avian influenza H5N6 and H5N8 viruses in poultry markets in Guangdong, China, 2020-2022

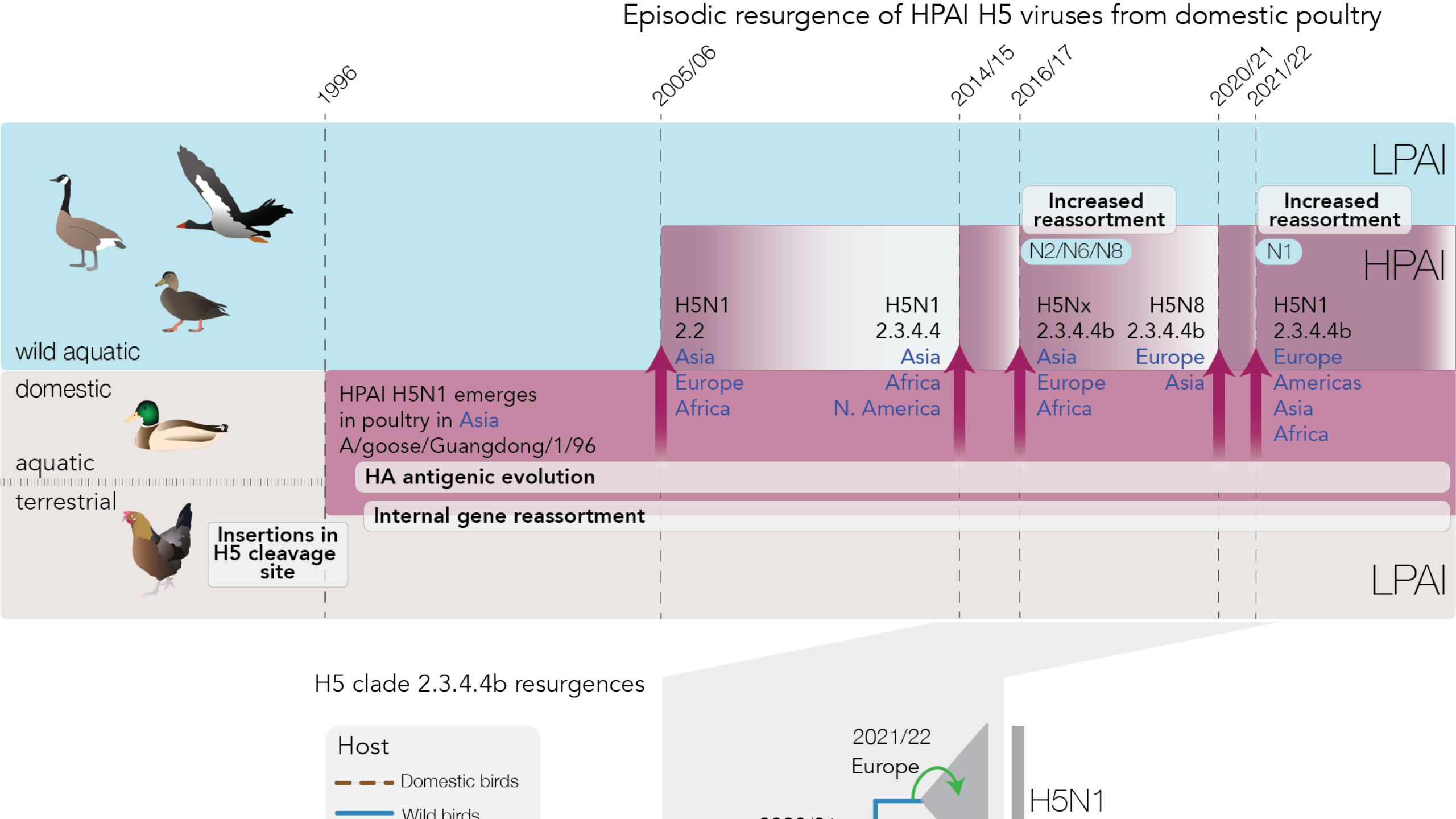
Kang Yang[1,2], Sarea Nizami[3], Shu Hu[3,4], Lirong Zou[1], Huishi Deng[1], Jiamin Xie[1], Qianfang Guo[1], Kimberly M. Edwards[3,4], Vijaykrishna Dhanasekaran[3,4], Hui-Ling Yen[3], Jie Wu[1]

[1]Guangdong Provincial Center for Disease Control and Prevention, Guangzhou, Guangdong, China
[2]School of Public Health, Sun Yat-Sen University, Guangzhou, Guangdong, China
[3]School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong
[4]HKU-Pasteur Research Pole, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, Hong Kong

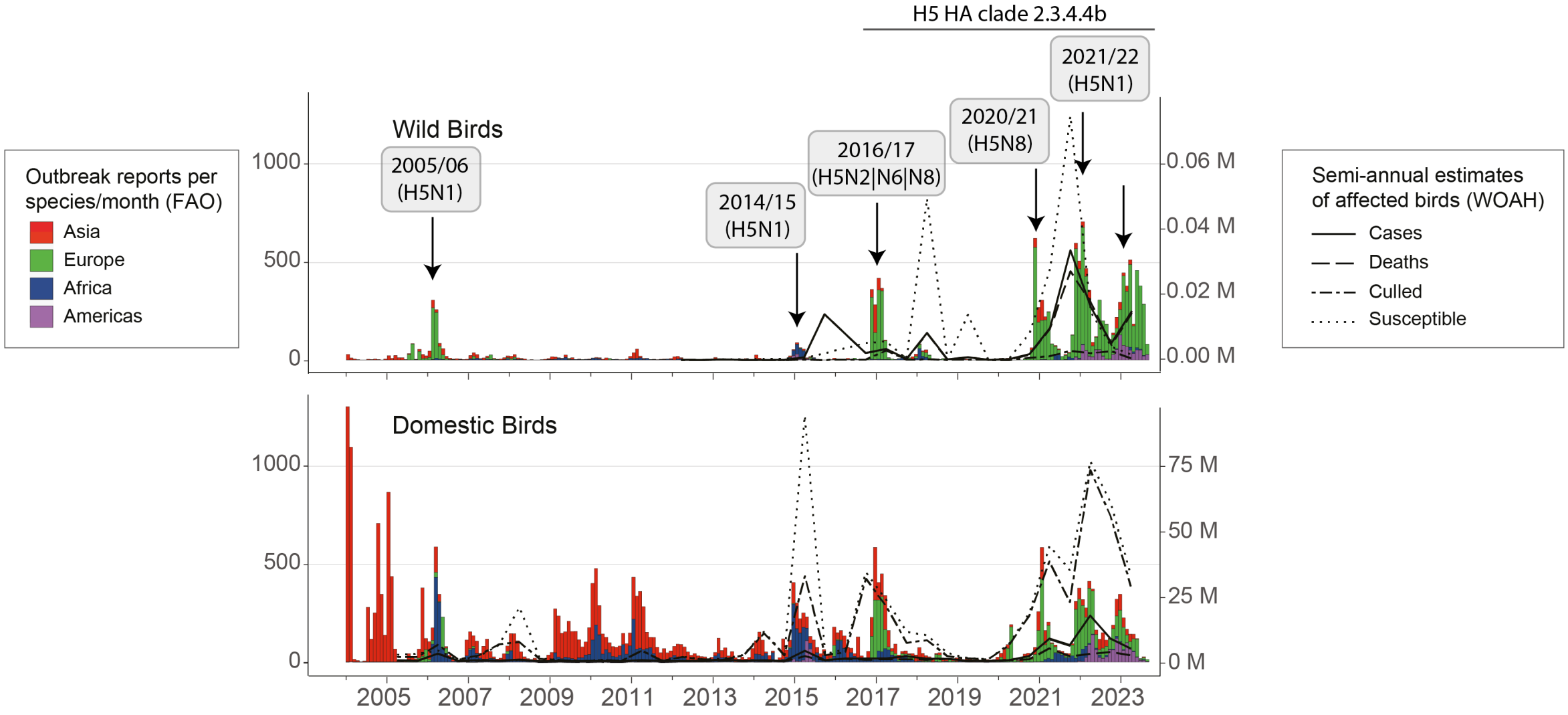
Karlsson et al. (In Press)

Resurgence of zoonotic highly pathogenic avian influenza A(H5N1) infections in Cambodia

Erik A. Karlsson, Ph.D.[1#], Jurre Y. Siegers, Ph.D.[1*], Ruopeng Xie, Ph.D.[2*], Kimberly M. Edwards, MSc.[2*], Alexander M.P. Byrne, Ph.D.[3*], Shu Hu[2], Ruixuan Wang[2], Sokhoun Yann[1], Sarath Sin[1], Songha Tok[1], Kimlay Chea[1], Sreyviseth Horm[1], Chenthearath Rith[1], Seangmai Keo[1], Leakhena Pum[1], Veasna Duong[1], Heidi Auerswald[1], Yisuong Phou[1], Sonita Kol[1], Andre Spiegel[1], Ruth Harvey[3], Sothyra Tum[4], San Sorn[4], Bunnary Seng[4], Yi Sengdoeurn[5], Chau Darapheak[6], Chin Savuth[6], Makara Hak[7], Vanra Ieng[8], Sarika Patel[8], Peter Thielen[9], Filip F. Claes[10], Nicola S. Lewis[3], Ly Sovann[5], Vijaykrishna Dhanasekaran, Ph.D.[2#]

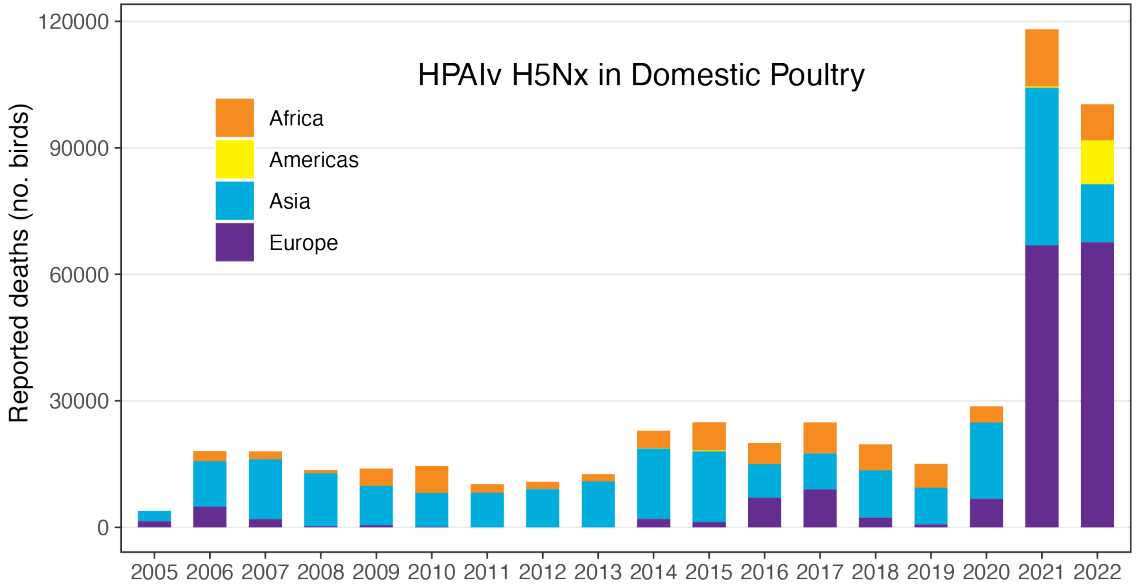

Episodic resurgence of HPAI H5 viruses from domestic poultry
1996
2005/06
2014/15
2016/17
2020/21
2021/22
LPAI
Increased reassortment
Increased reassortment
N2/N6/N8
N1
HPAI
wild aquatic
domestic
aquatic
terrestrial
H5N1
2.2
Asia
Europe
Africa
H5N1
2.3.4.4
Asia
Africa
N. America
H5Nx
2.3.4.4b
Asia
Europe
Africa
H5N8
2.3.4.4b
Europe
Asia
H5N1
2.3.4.4b
Europe
Americas
Asia
Africa
HPAI H5N1 emerges in poultry in Asia
A/goose/Guangdong/1/96
HA antigenic evolution
Internal gene reassortment
Insertions in H5 cleavage site
LPAI
H5 clade 2.3.4.4b resurgences
Host
Domestic birds
Wild birds
2021/22
Europe
H5N1

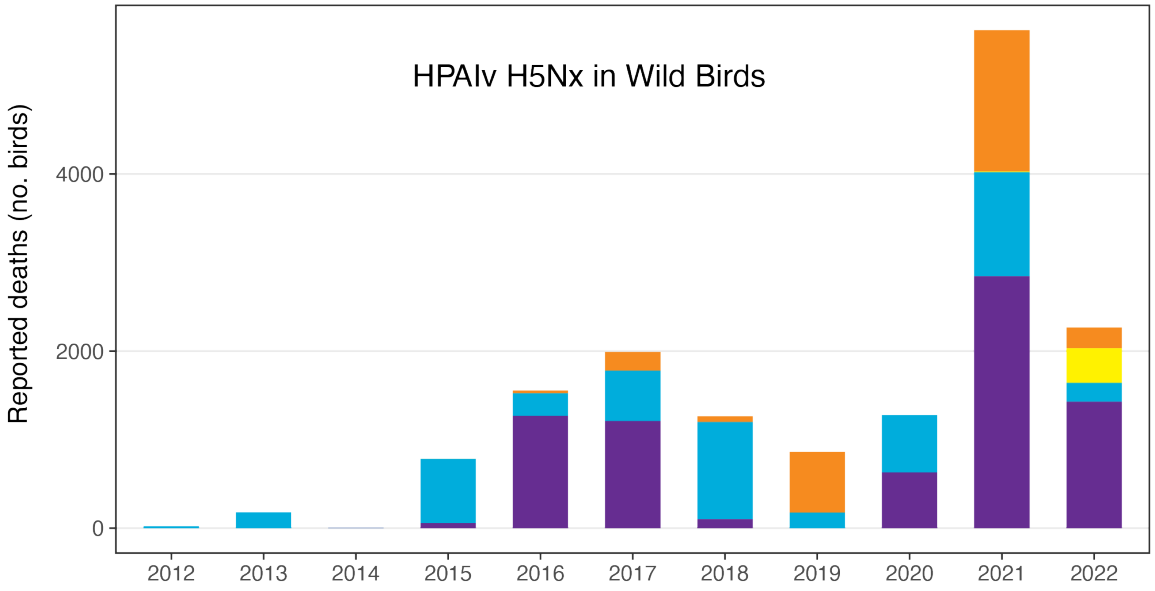
Epidemiology of resurgent HPAI H5 outbreaks

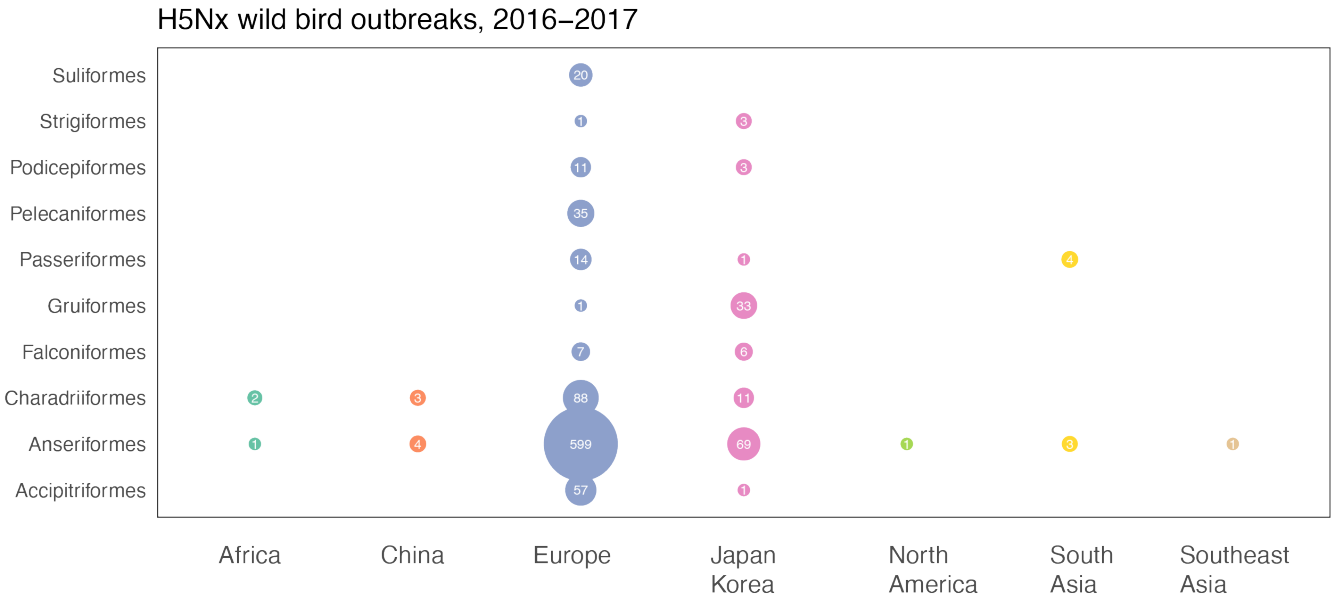


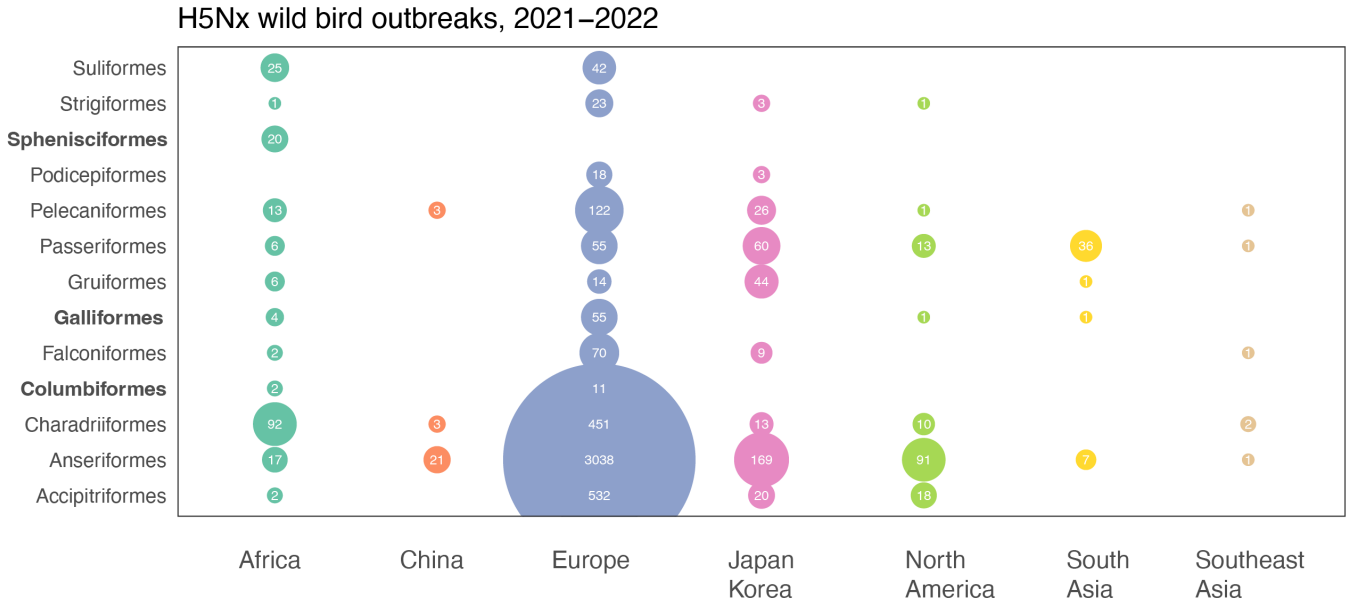
World Animal Health Information System (WAHIS), WOAH (https://wahis.woah.org/)
EMPRESS-ii+ Global Animal Disease Information System, FAO (https://empress-ii.fao.org/)
Xie et al. 2023 *Nature*

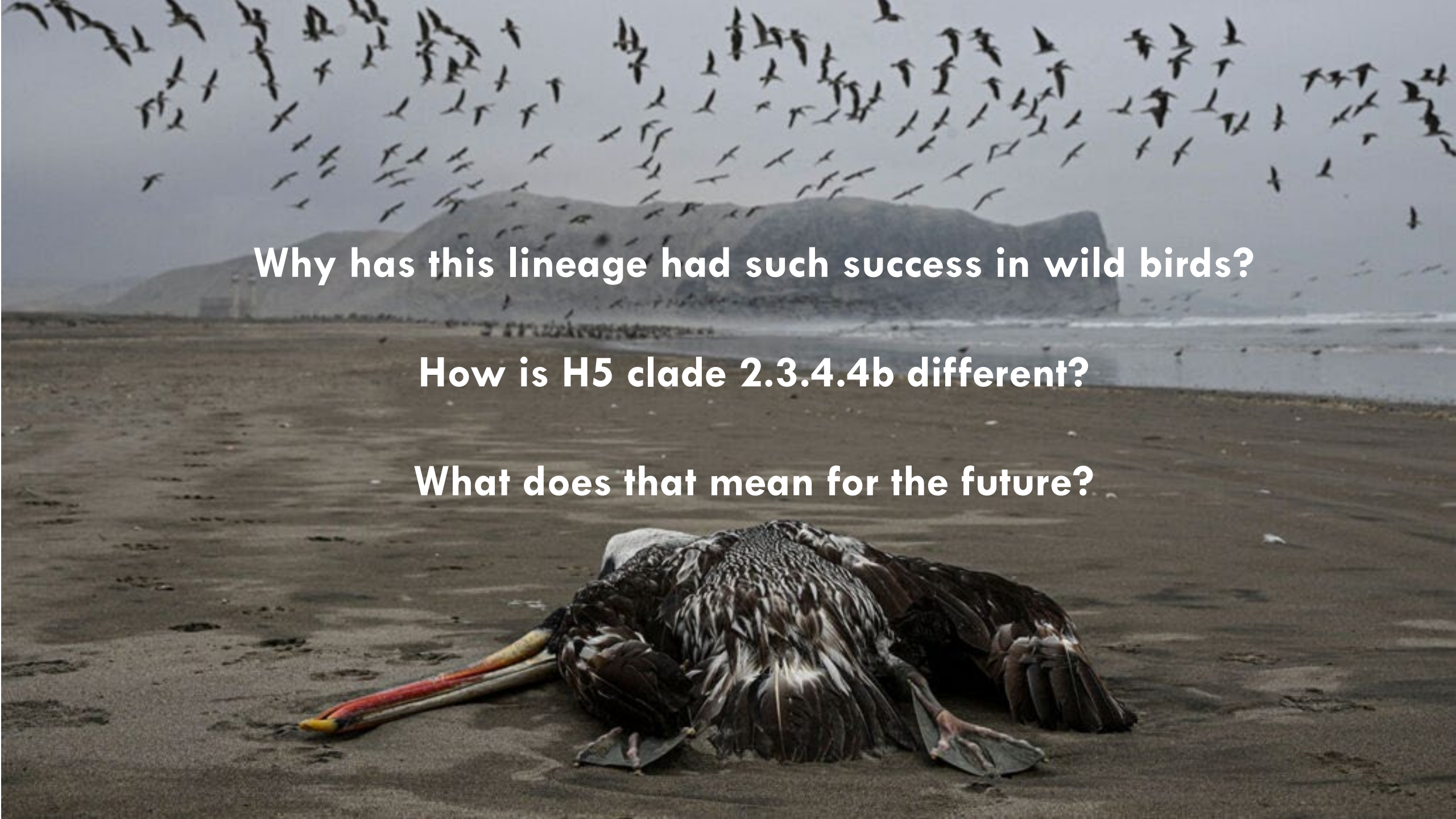
Epidemiology of resurgent HPAI H5 outbreaks



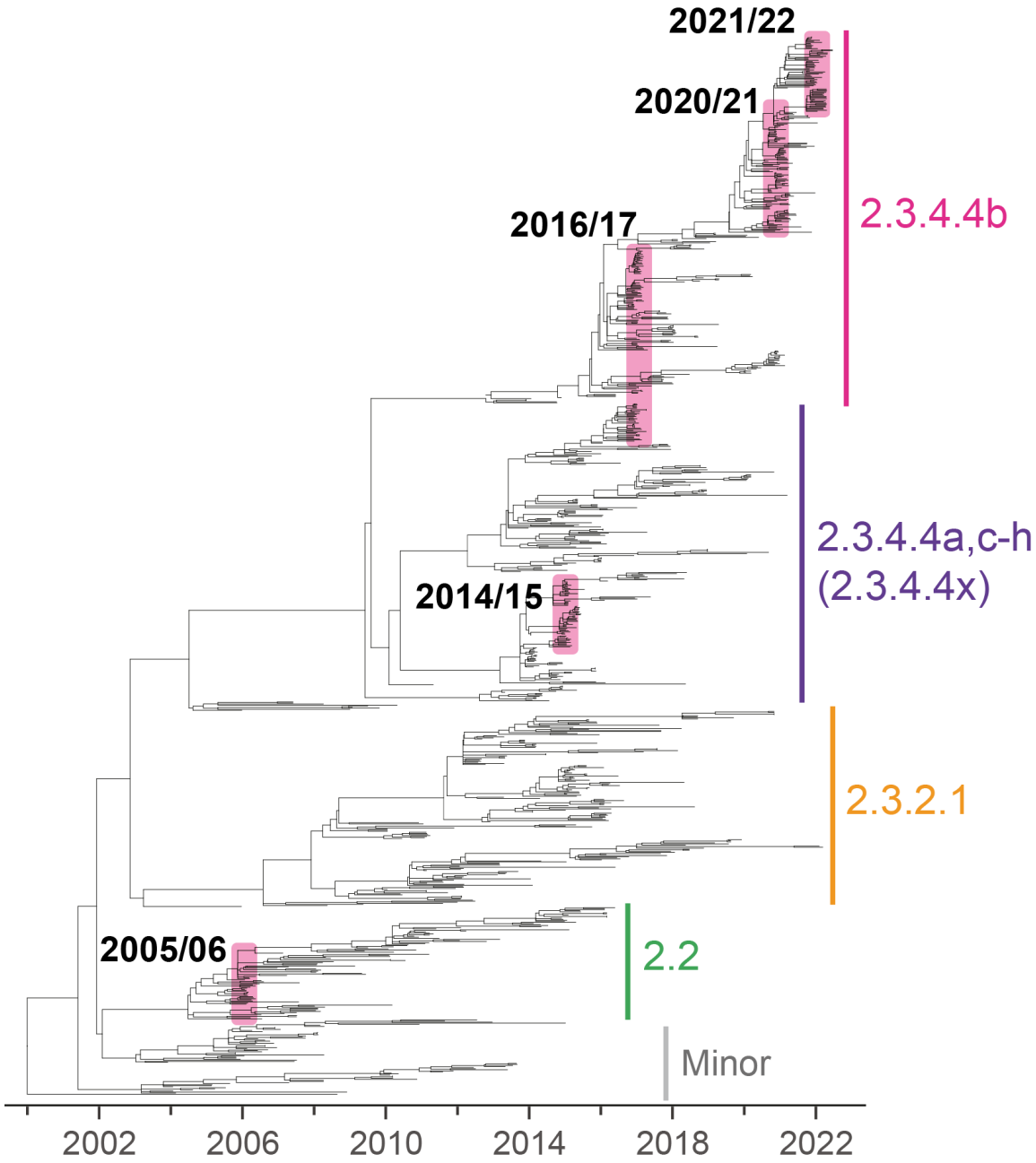




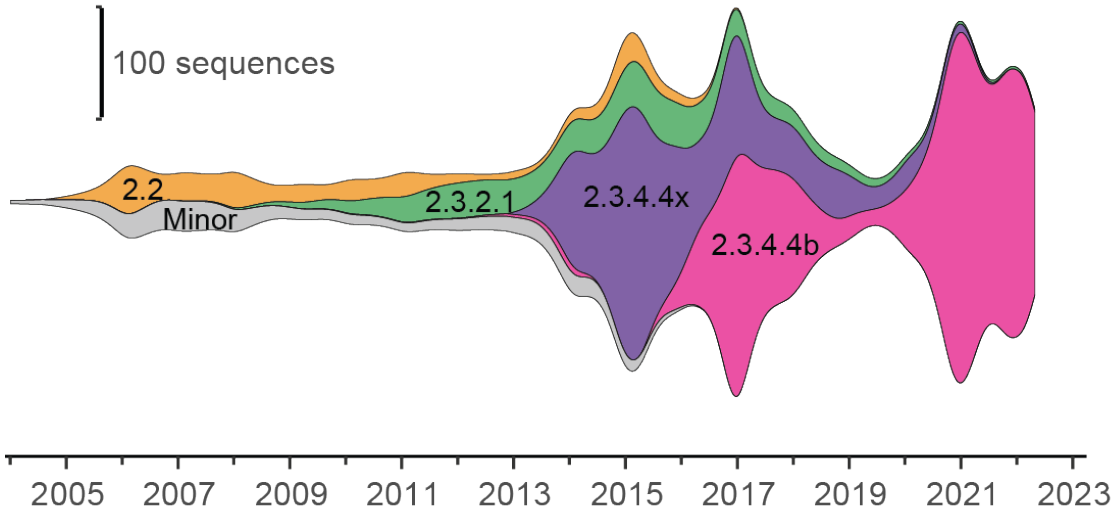



Why has this lineage had such success in wild birds?
How is H5 clade 2.3.4.4b different?
What does that mean for the future?

Genomic epidemiology of resurgent HPAI H5 outbreaks



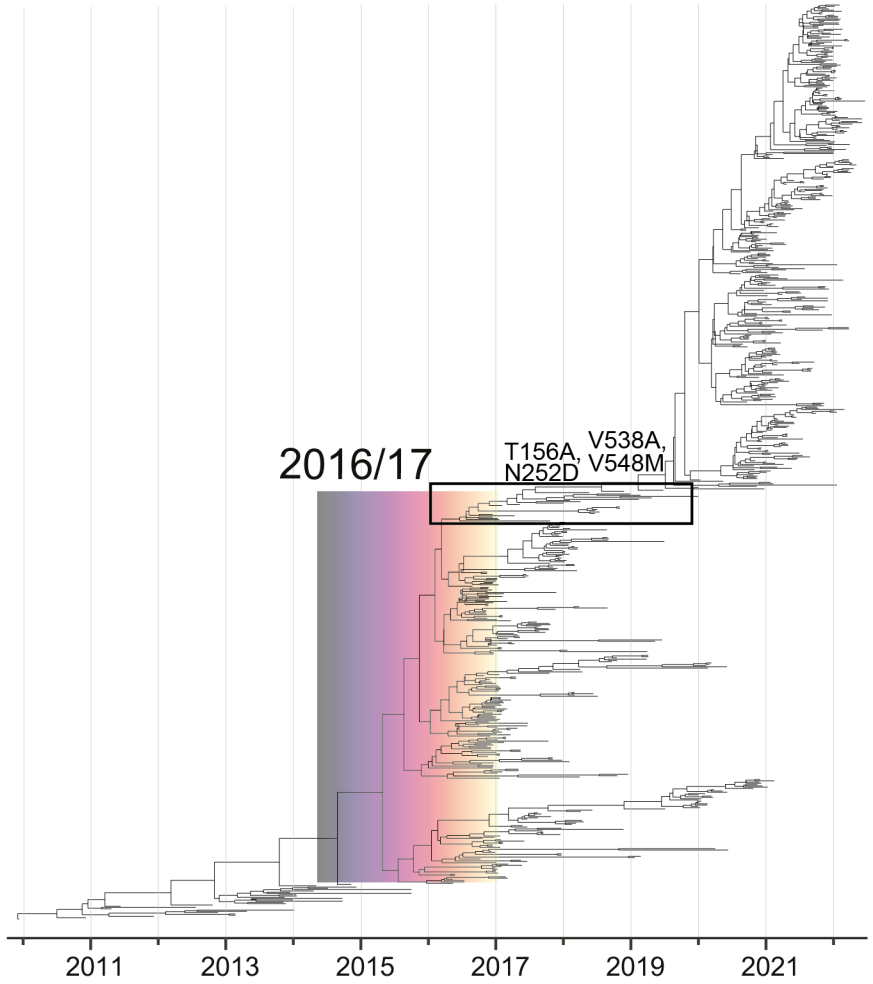
Temporal changes in HPAI H5 HA clade prevalence

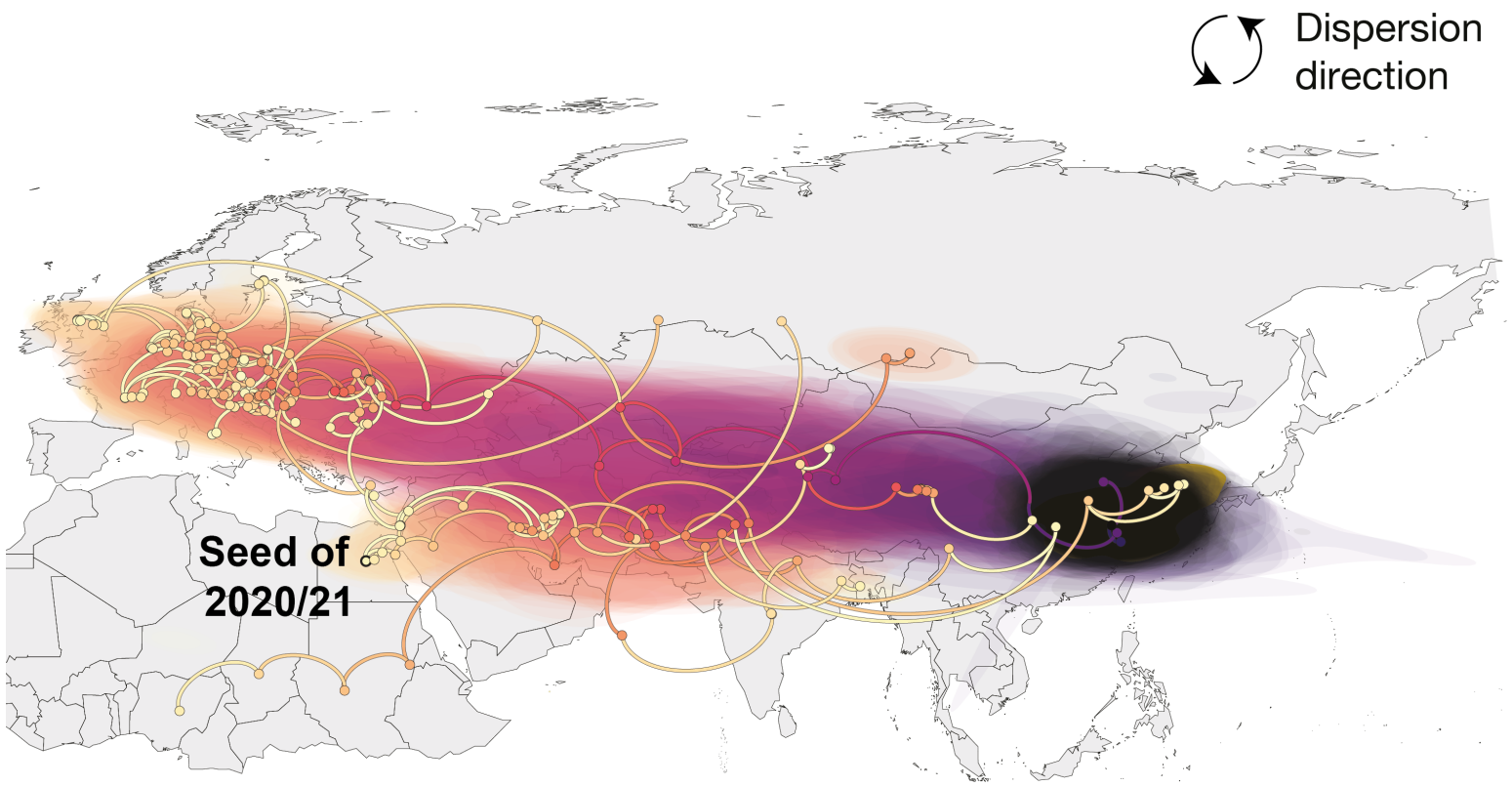


GISAID (https://gisaid.org/)
NCBI Influenza Virus Resource (https://www.ncbi.nlm.nih.gov/genomes/FLU/)

Evolution of clade 2.3.4.4b and early migration patterns of resurgent HPAI

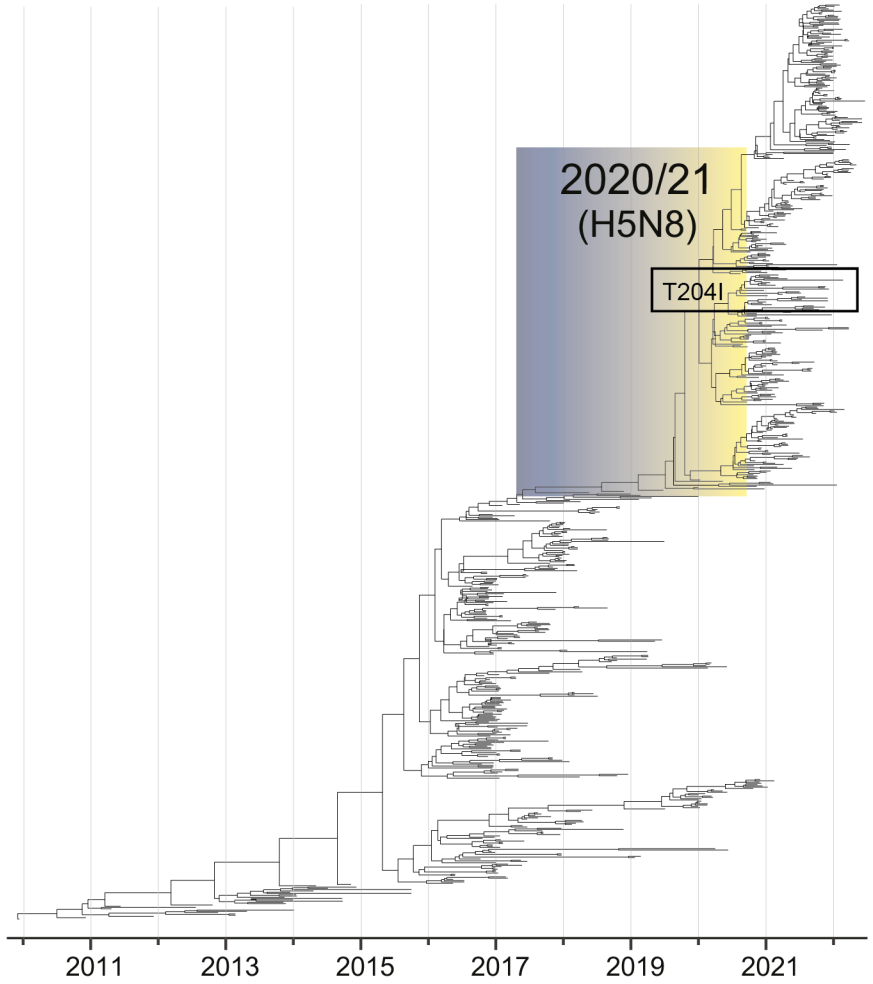
LKS Faculty of Medicine

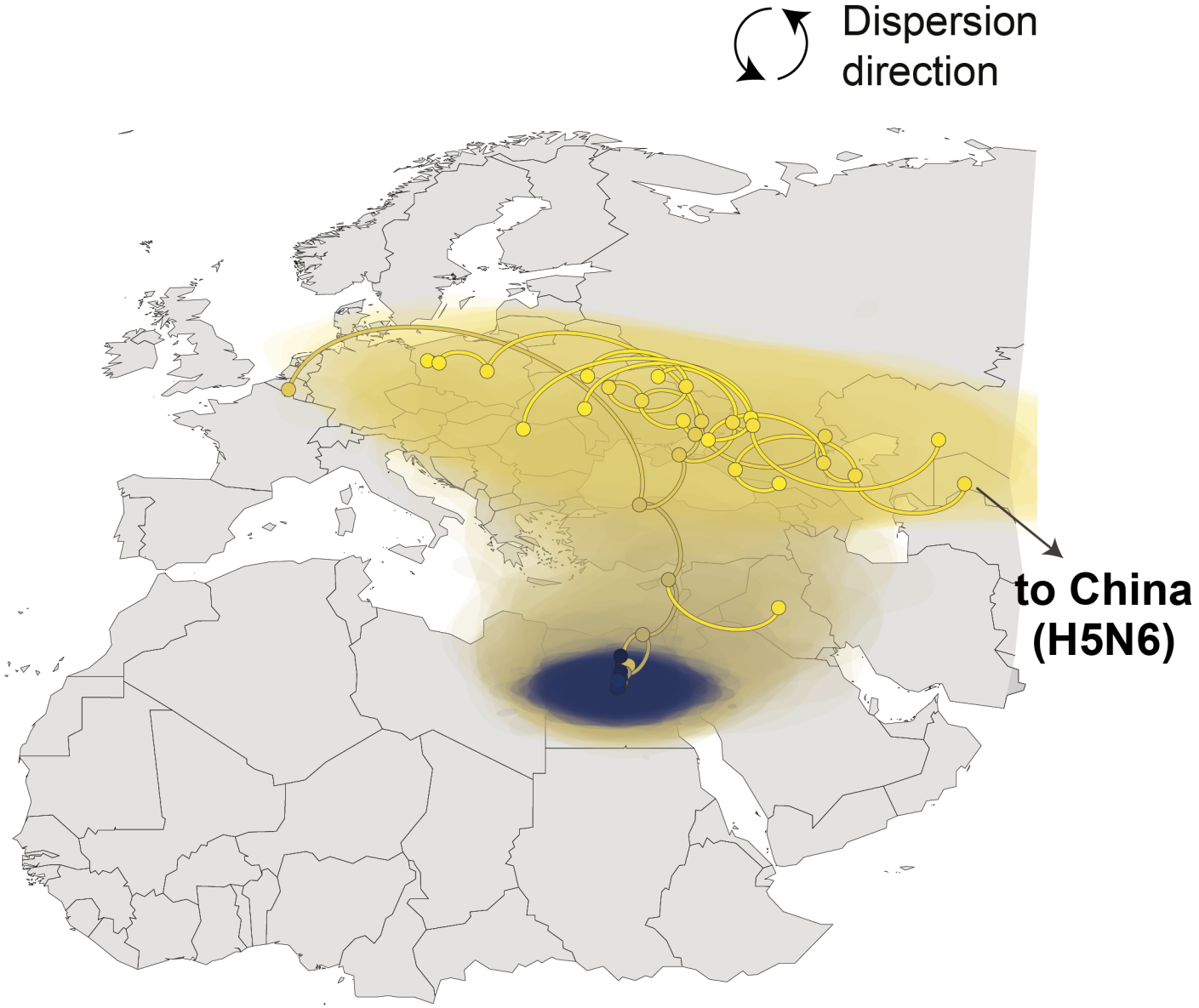




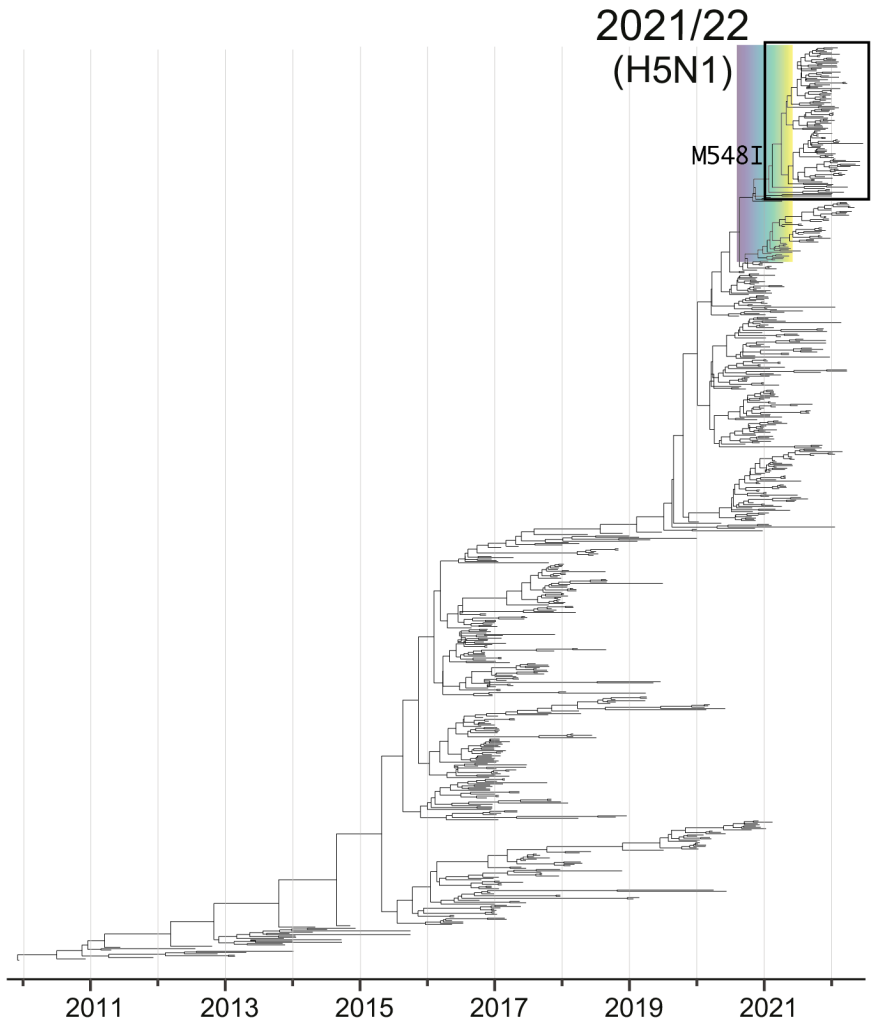
Evolution of clade 2.3.4.4b and early migration patterns of resurgent HPAI

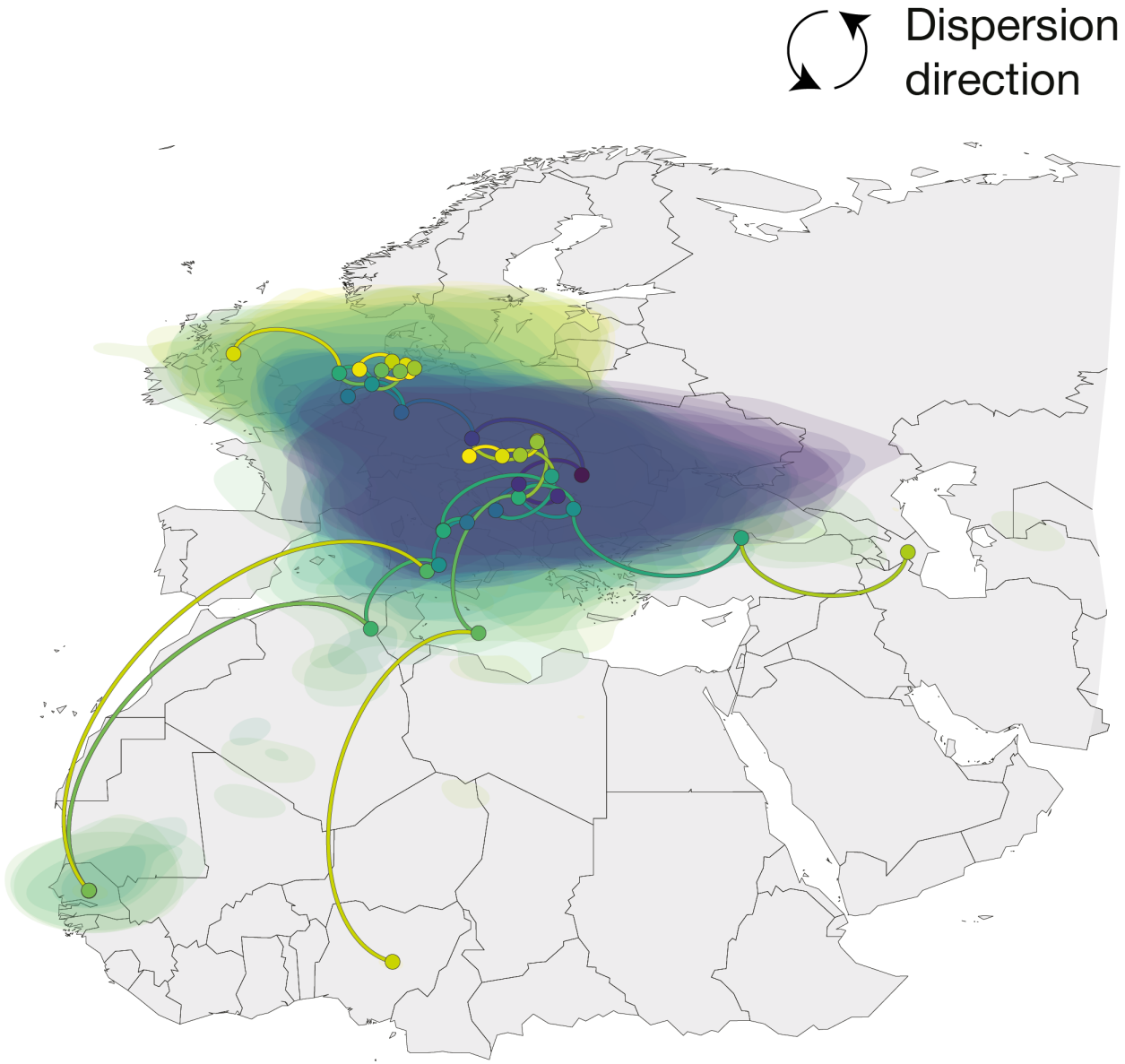
LKS Faculty of Medicine



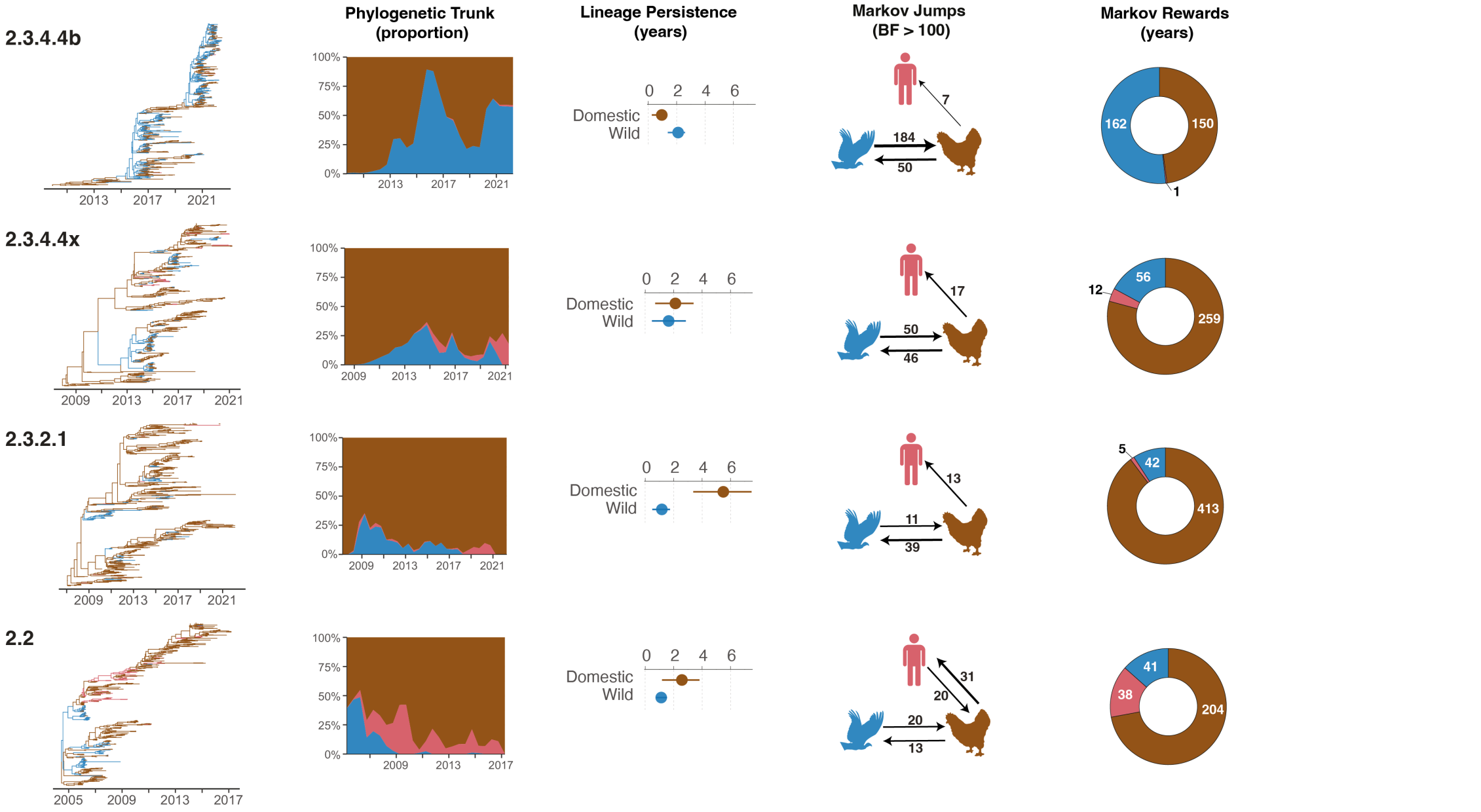


Evolution of clade 2.3.4.4b and early migration patterns of resurgent HPAI



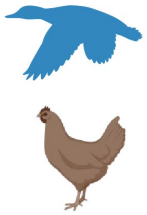


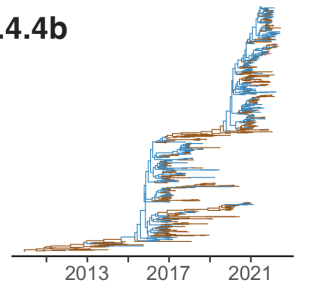
Host maintenance of HPAI H5Nx

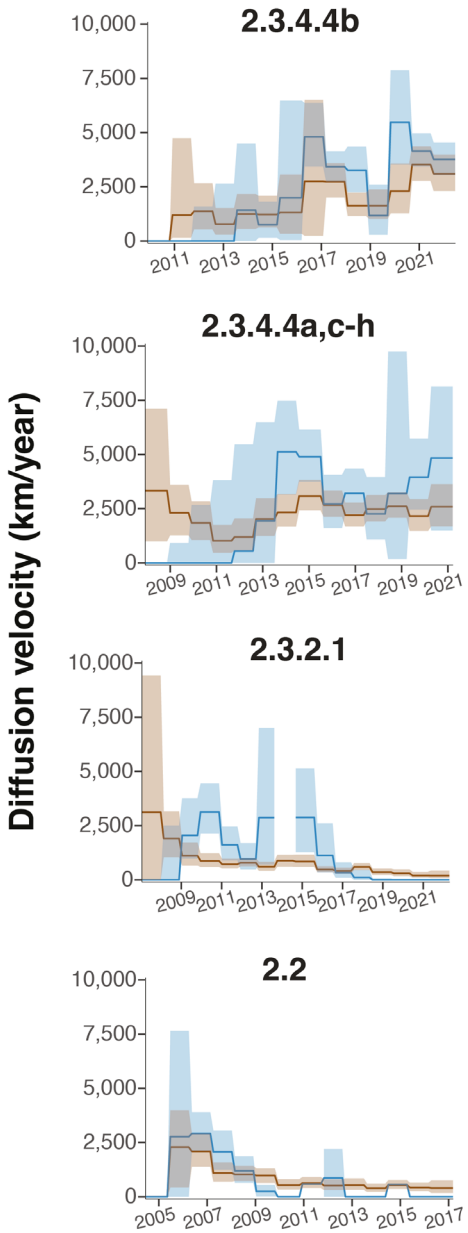


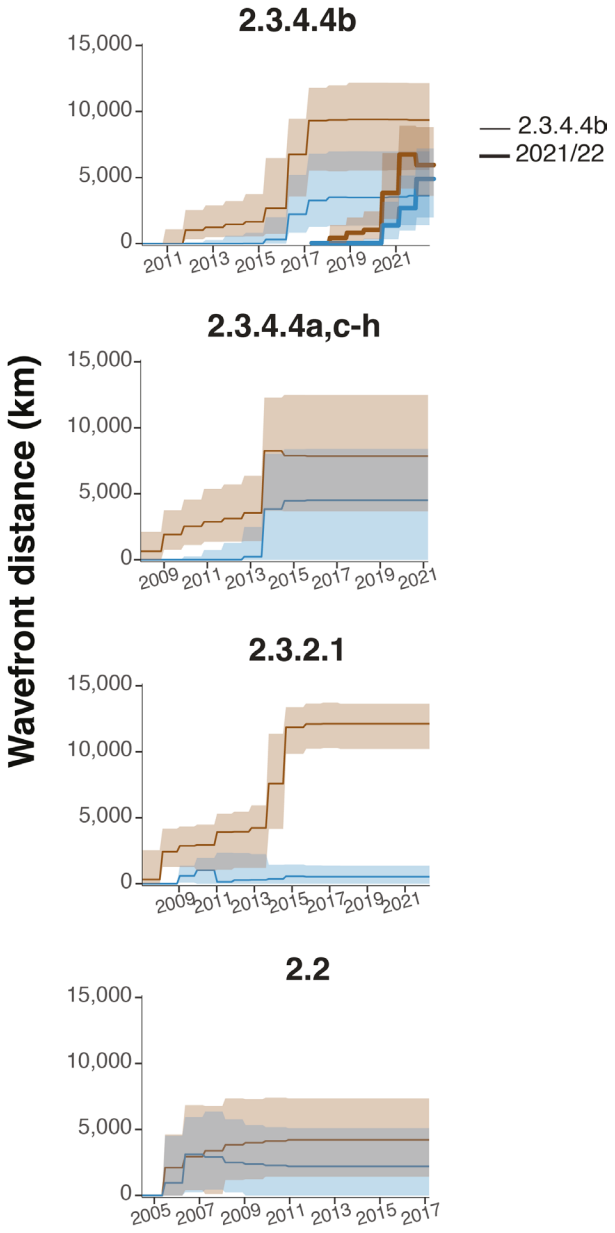
Asymmetric discrete-trait model with Bayesian Stochastic Search Variable Selection (BSSVS) and the continuous-time Markov chains model

Host contribution to HPAI H5Nx spread

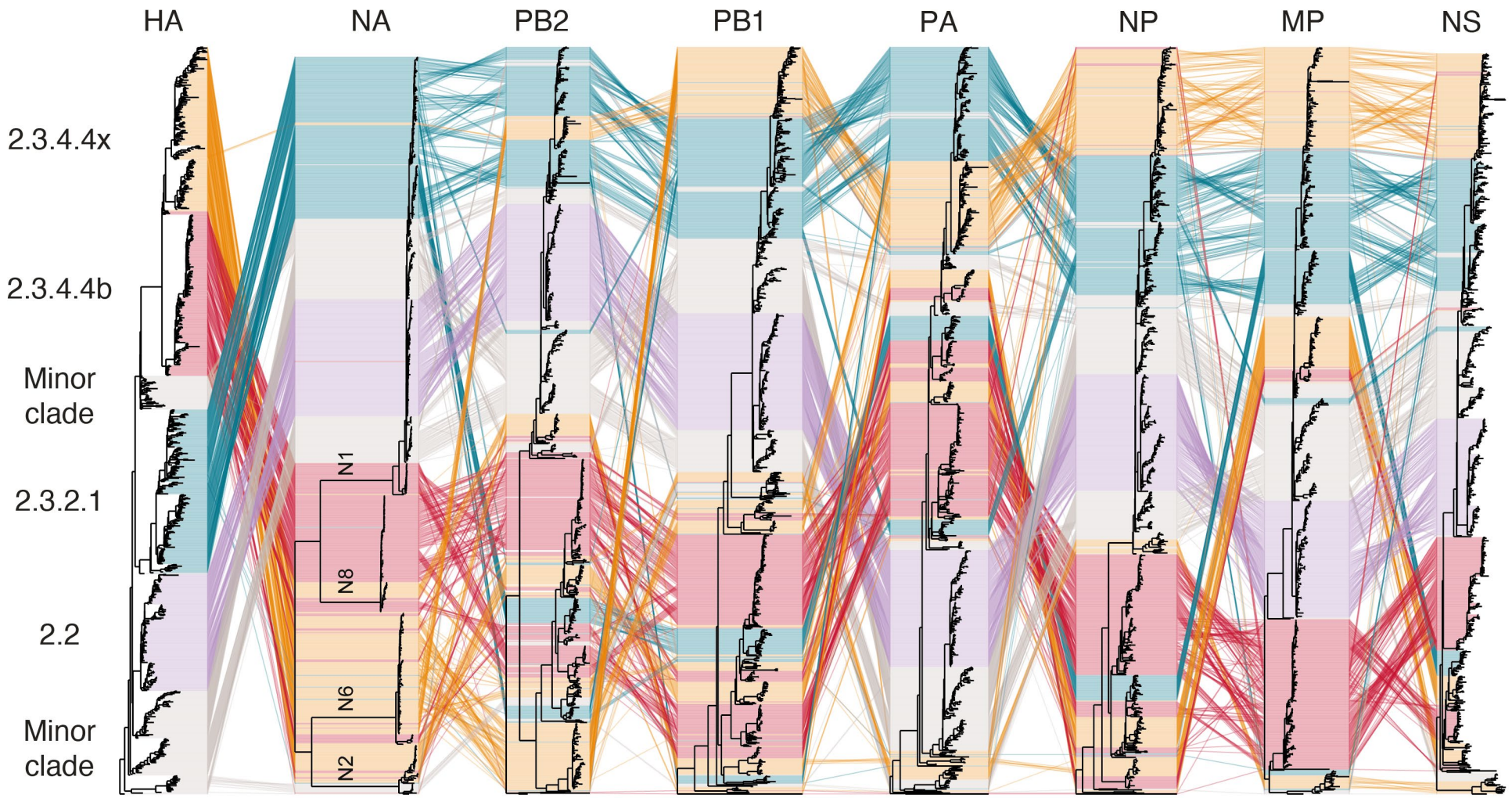




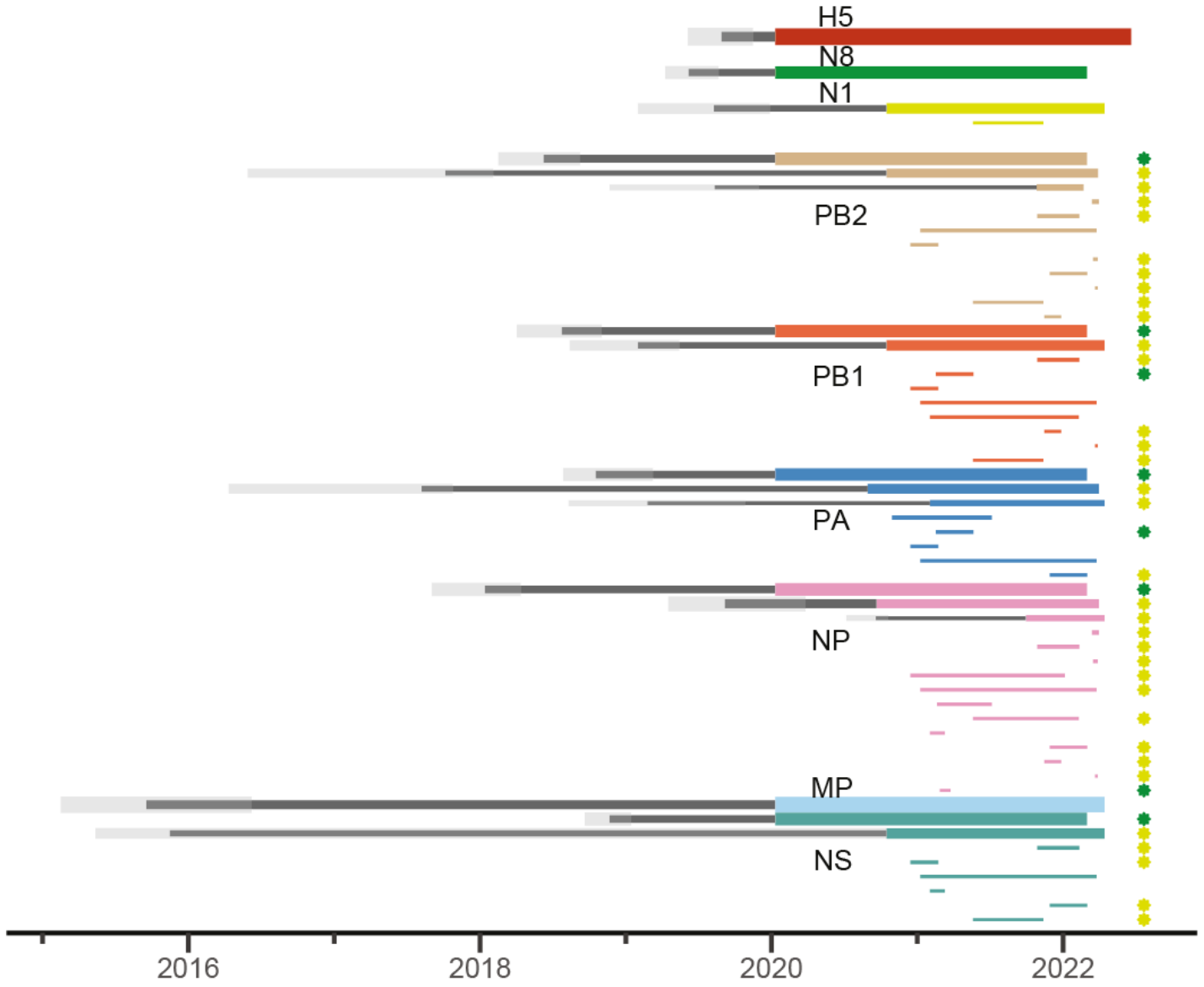


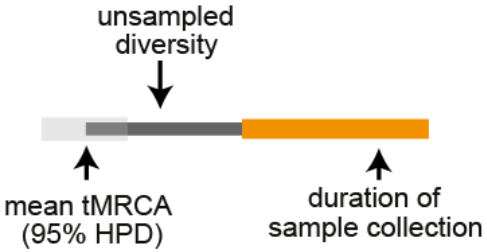


Increasing reassortment of clade 2.3.4.4 viruses



Frequent reassortment of H5N1 clade 2.3.4.4b viruses





Subtype

- H5N1 (2021/22)
- H5N8 (2020/21)

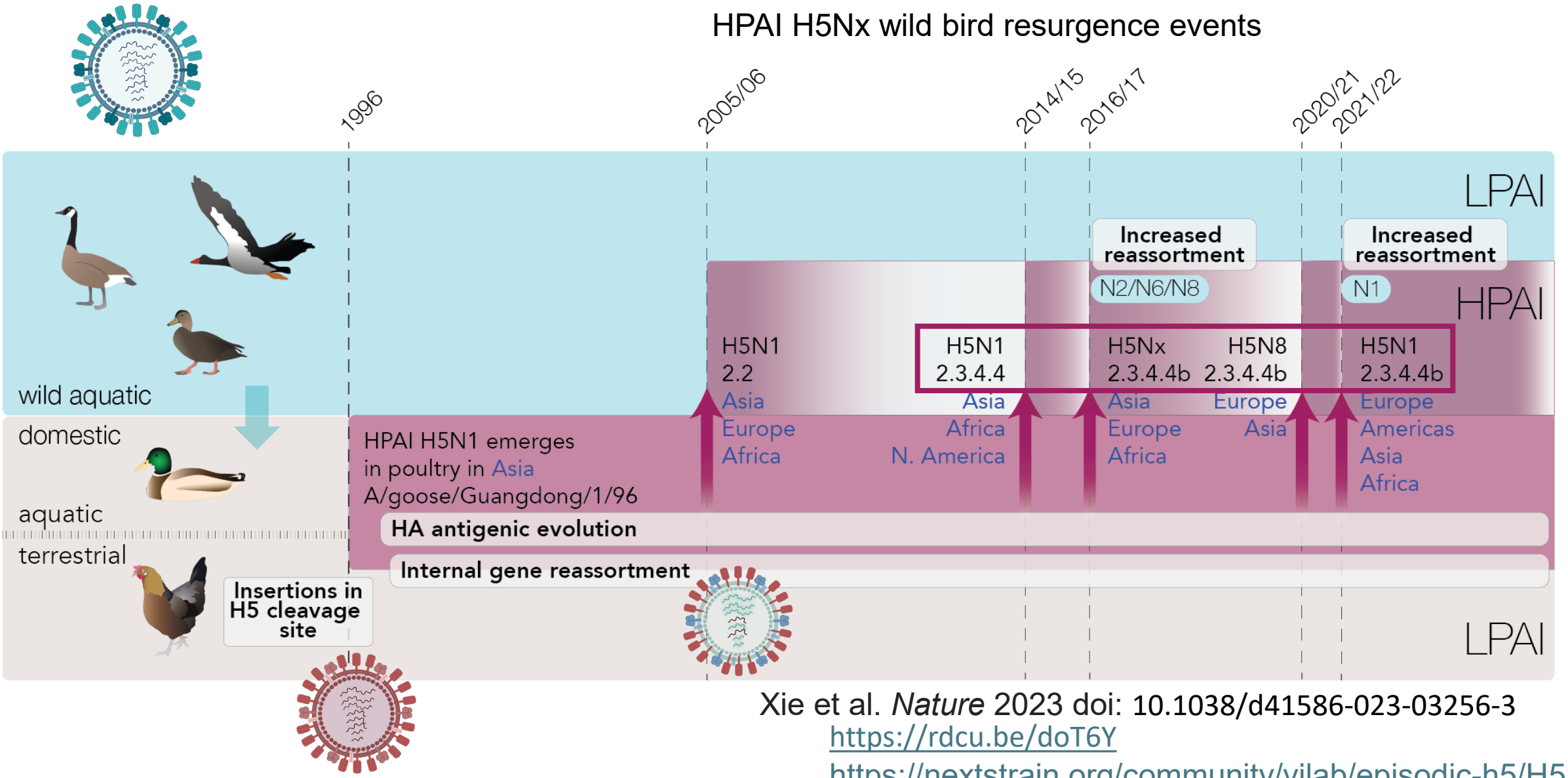
Number of sequences

- 100
- 500
- 1000
- 2000

Conclusions

- Dynamic **shift in the ecological source** of HPAI H5 outbreaks from Asia to Africa and Europe
  - Reinforce surveillance capacity
- HPAI H5 is increasingly **persistent in wild bird populations**
  - Accelerating dispersion velocity, expanding host and geographic range, and creating more opportunities for reassortment
- Major implications for public health, wildlife conservation, poultry production, food security, veterinary husbandry
  - Vaccination???
- Multi-faceted mitigation and prevention strategies
  - Biosecurity and surveillance in addition to culling and vaccination

HPAI H5Nx wild bird resurgence events

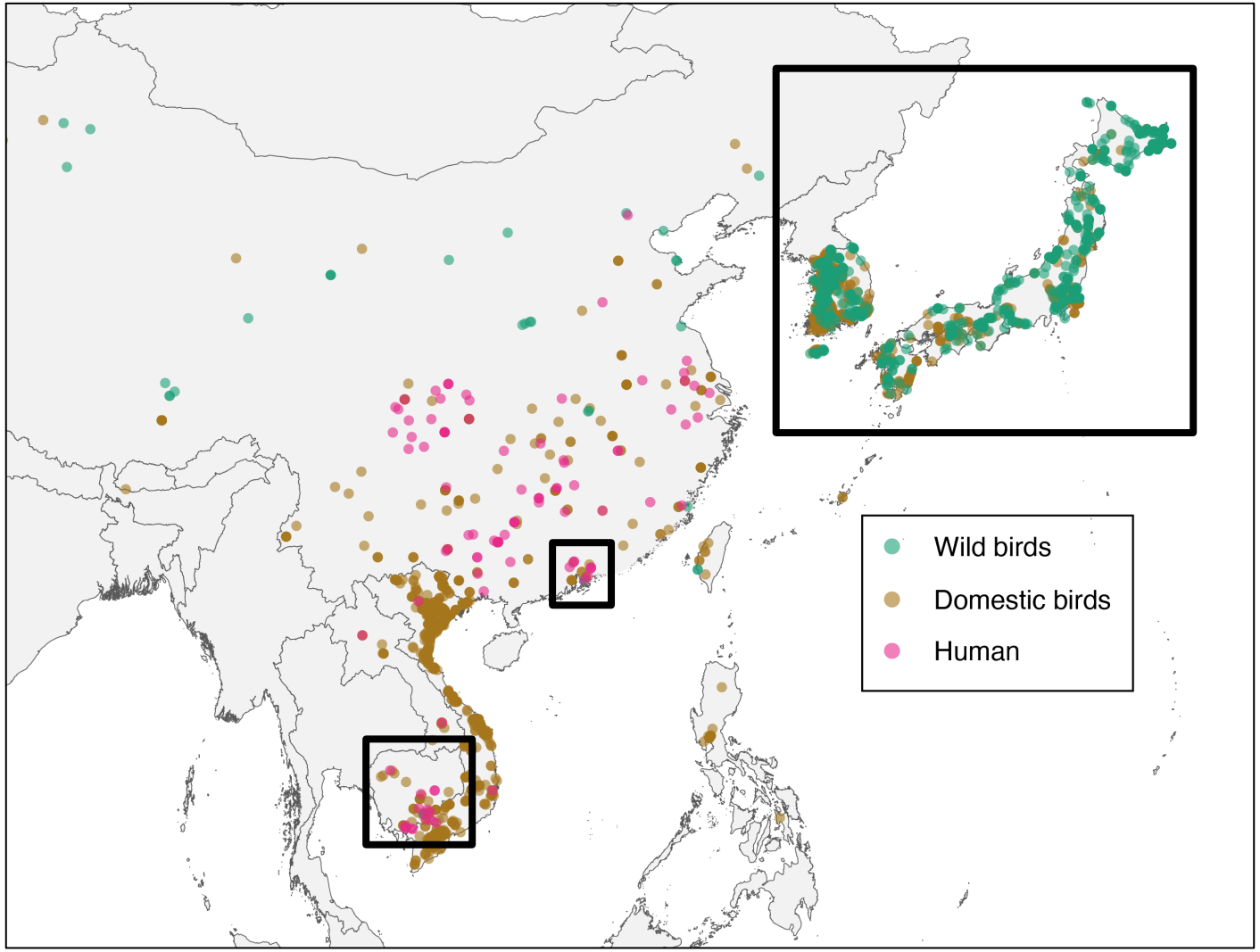


Xie et al. *Nature* 2023 doi: 10.1038/d41586-023-03256-3

https://rdcu.be/doT6Y

https://nextstrain.org/community/vjlab/episodic-h5/H5

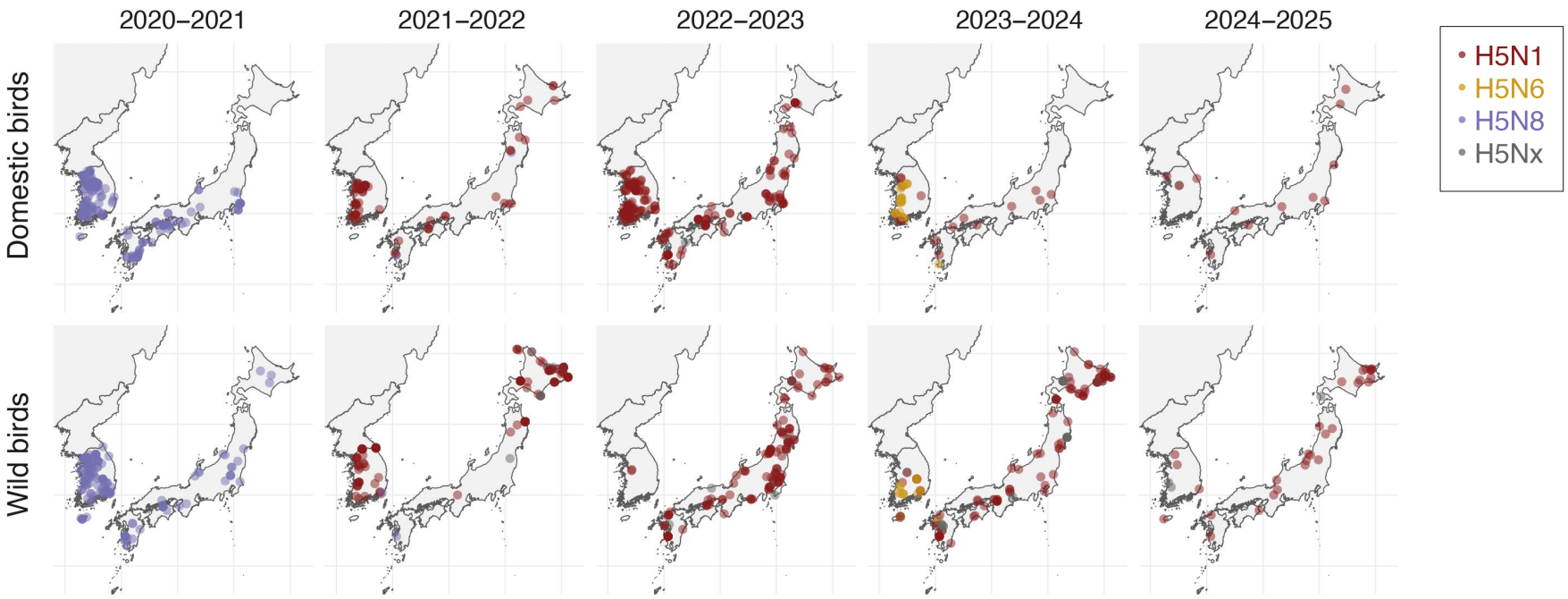
Regional impact of HPAI H5Nx clade 2.3.4.4b reintroductions in Asia



FAO Empress-i+

Global Animal Disease Information System

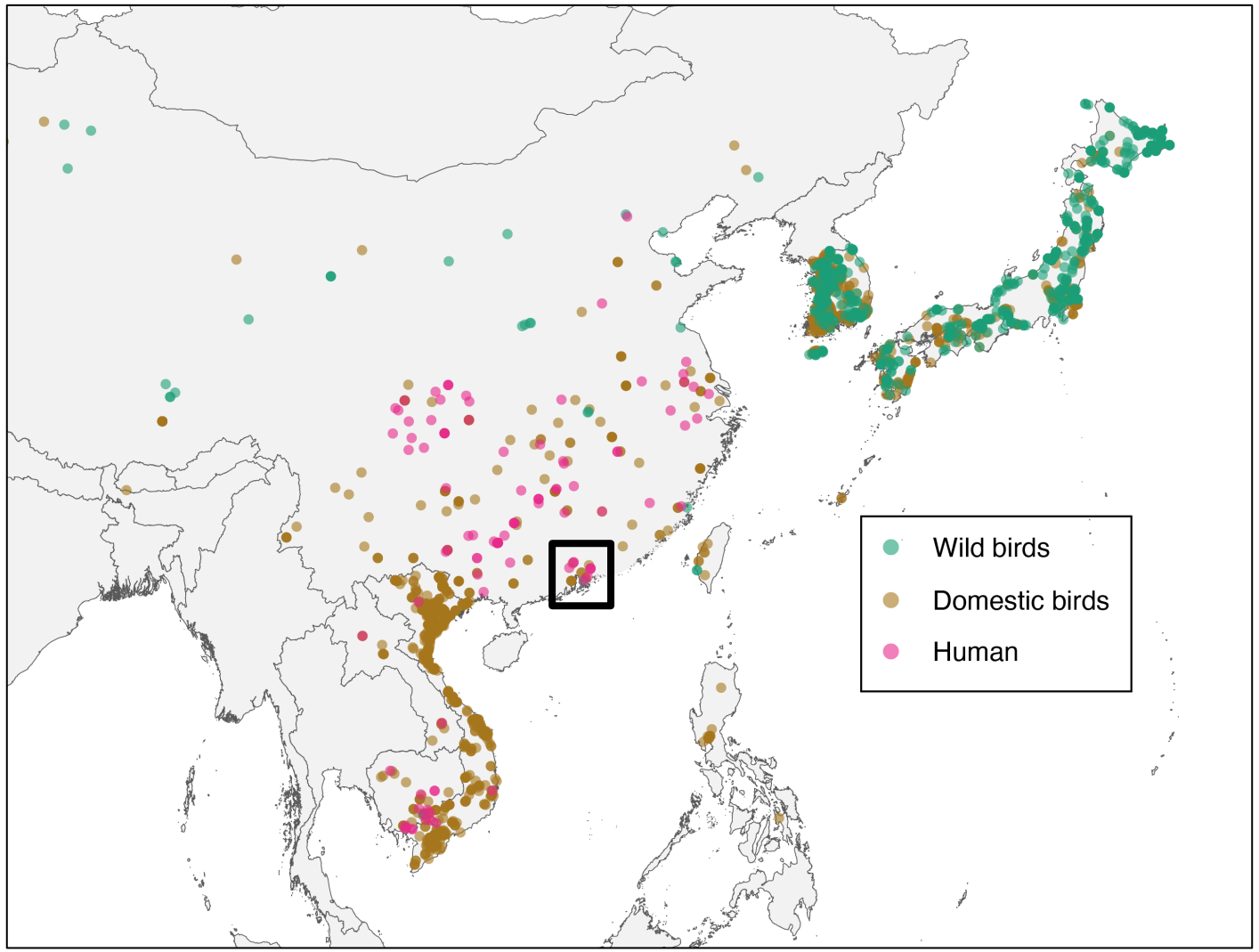
Regional impact of HPAI H5Nx clade 2.3.4.4b reintroductions: Japan & Korea



- Two 2.3.4.4b H5N8 genotypes in 2020/21
- Displaced by two H5N1 introductions in 2021
- Extensive reassortment, impact on poultry production
- 2023/24 reintroduction of H5N5, impacting wild birds

GISAID.org & FAO Empress-i+
Global Animal Disease Information System

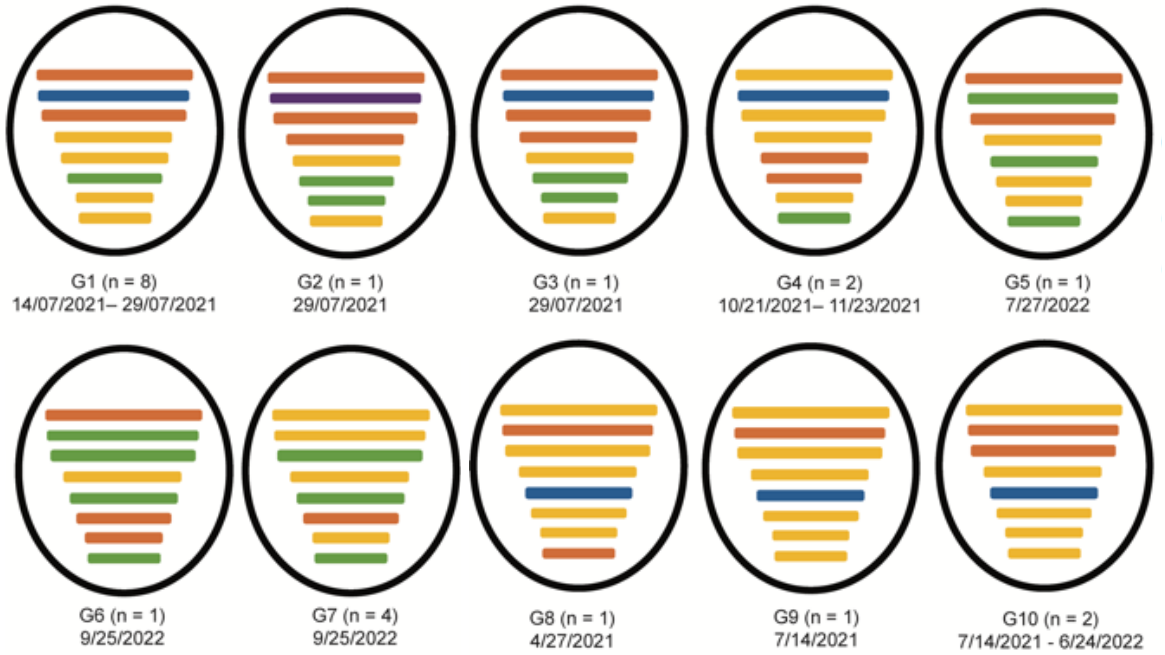
Regional impact of HPAI H5Nx clade 2.3.4.4b reintroductions in Asia



FAO Empress-i+

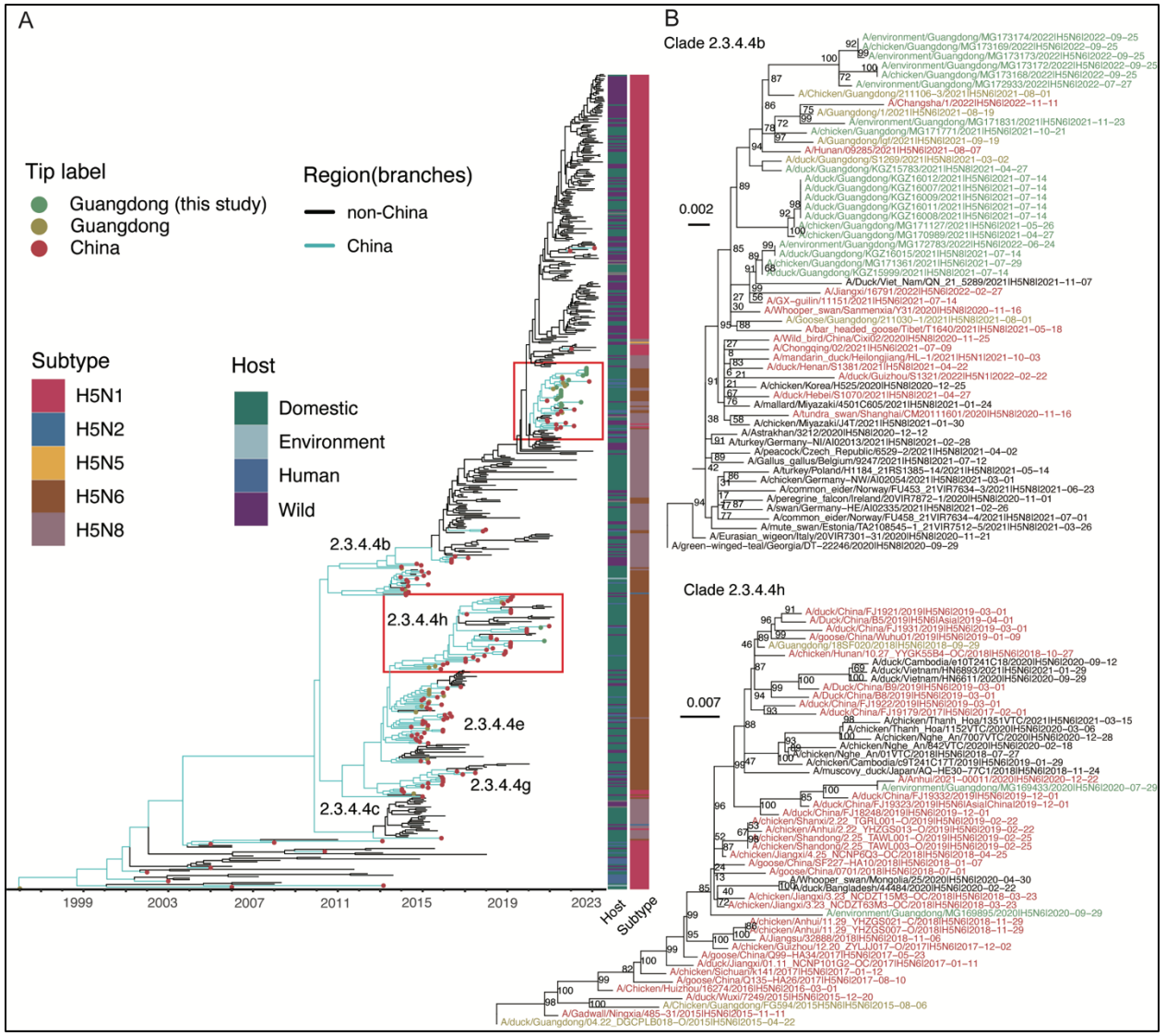
Global Animal Disease Information System

Genomic characterization of H5N6 and H5N8 from live poultry markets in Guangdong, China

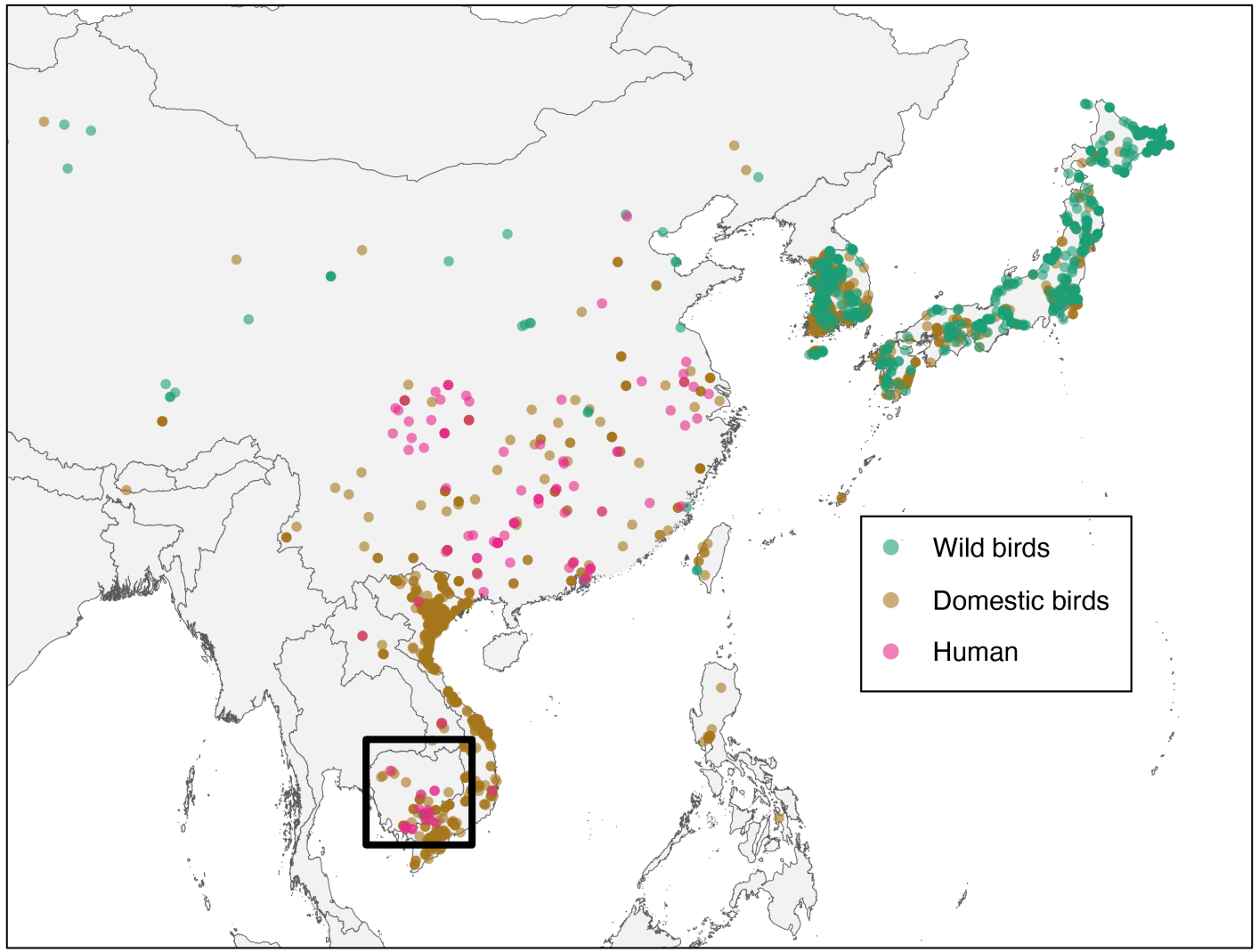


Vaccination against H5|H7|H9

N = 22 H5N6|N8 isolates; 10 genotypes
HA clades 2.3.4.4h and 2.3.4.4b



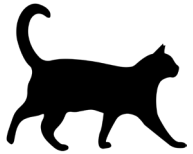
Regional impact of HPAI H5Nx clade 2.3.4.4b reintroductions in Asia



FAO Empress-i+

Global Animal Disease Information System

Impact of HPAI H5 clade 2.3.4.4b reintroductions in Asia



Feral cats, Korea
(clade 2.3.4.4b H5N1)



Raccoon dog, Red fox, Japan
(clade 2.3.4.4b H5N1)



Mink, Canine, China
(clade 2.3.4.4b H5N6)



Brown rat, China
(clade 2.3.4.4h H5N6)

GISAID.org

Impact of HPAI H5 clade 2.3.4.4b reintroductions in Asia: genotypes of human infections

China

South Asia

Southeast Asia

GISAID.org