

Overview of HPAI spillover events – quo vadis?

Ian Brown

Pirbright Institute

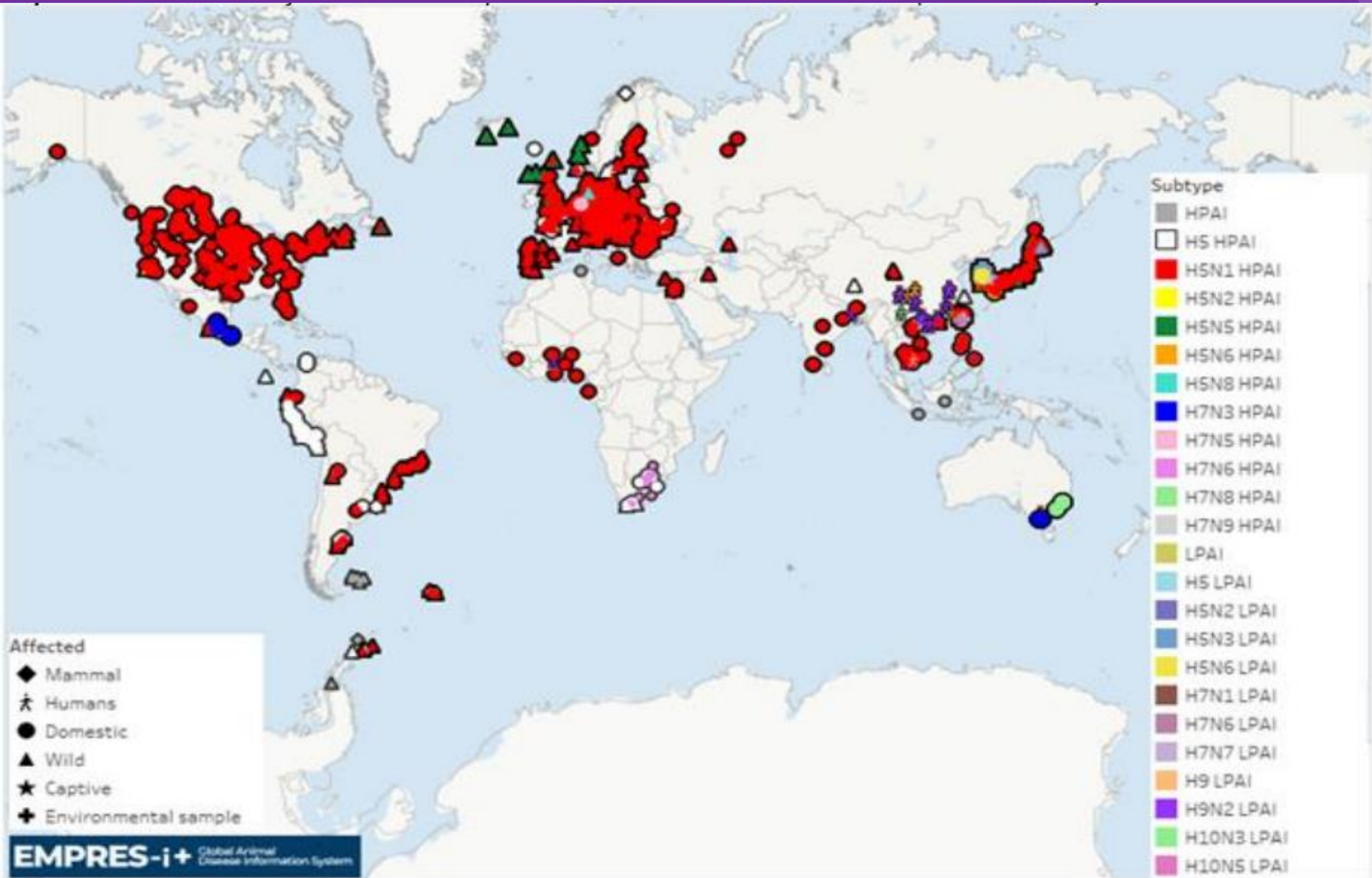
FVE webinar 27/2/25

Key new developments in HPAI epidemiology

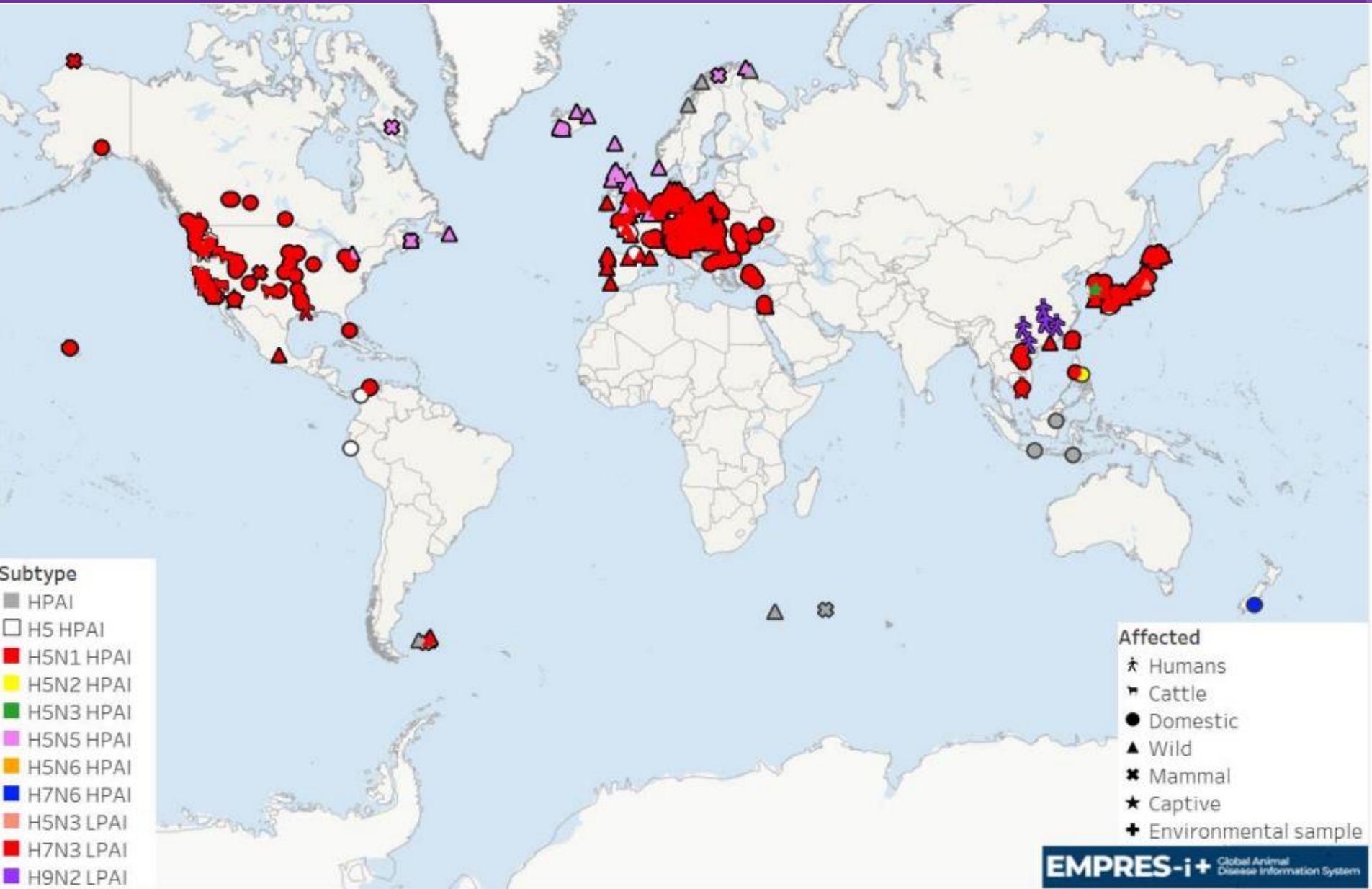
- Exceptional global spread; panzootic most continents affected
- High infection pressure
 - Increased spread to domestic birds
 - High environmental contamination
 - Exposure to greater range of species of wild bird
- Mammalian infections: spillover to scavengers, some M2M transmission
- Dairy cattle infection in USA: sustained transmission non respiratory, back spill to domestic birds
- H5 HPAI virus evolving with high fitness traits
- Antigenically HA clade 2.3.4.4b moderately stable

Global distribution of Avian Influenza

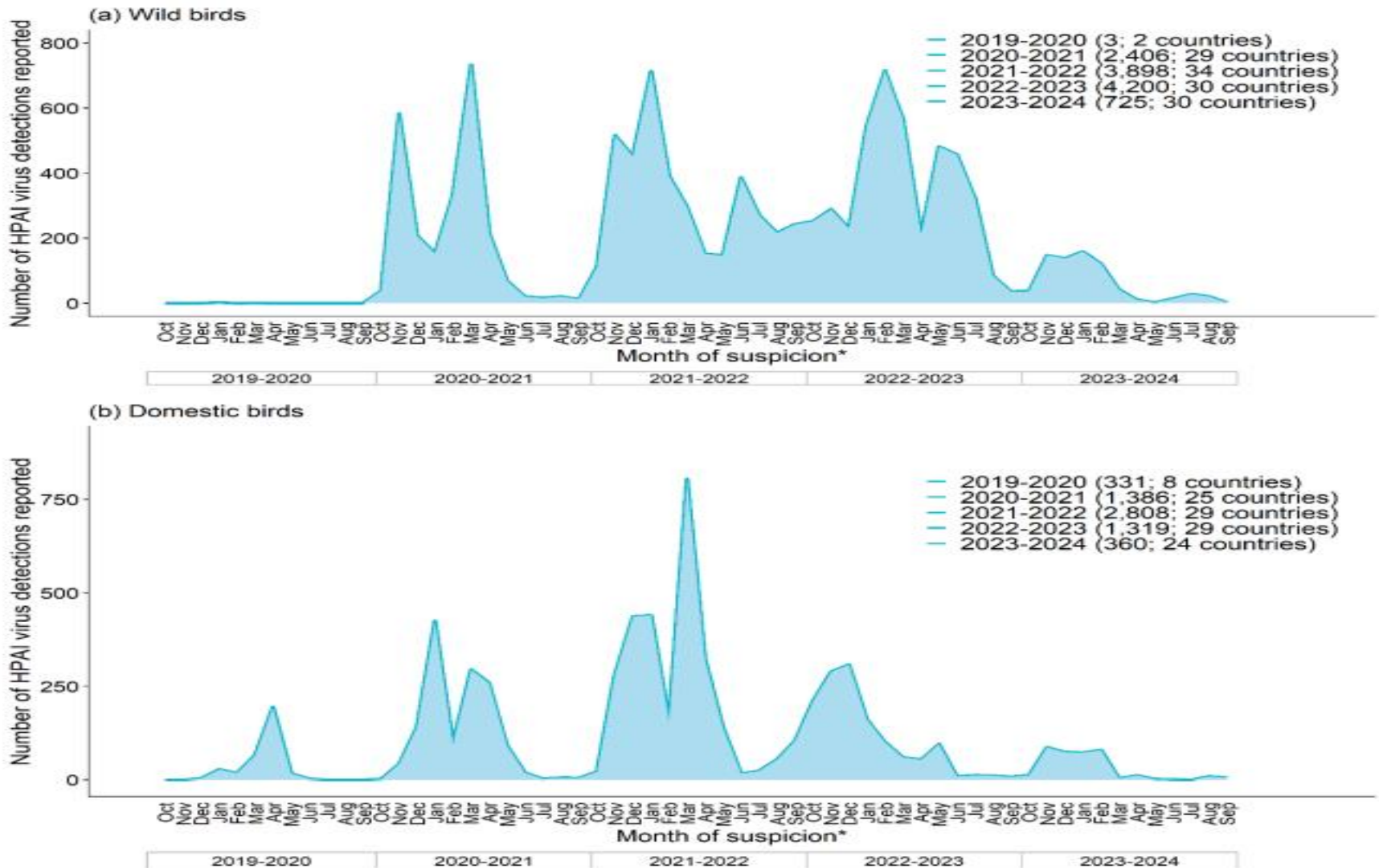
1st October 2023- 26th September 2024



Global distribution of AIV since 1 October 2024 (i.e. current wave) ; H5 HPAI predominant

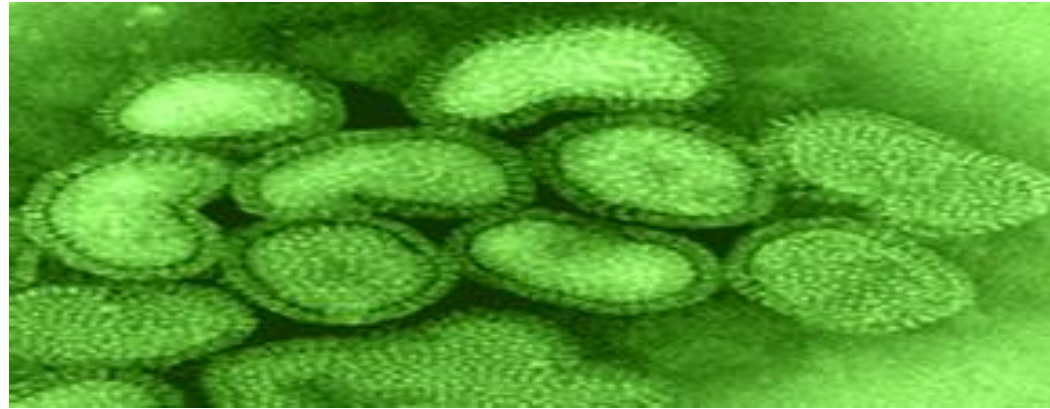


European epidemic waves with H5 HPAI



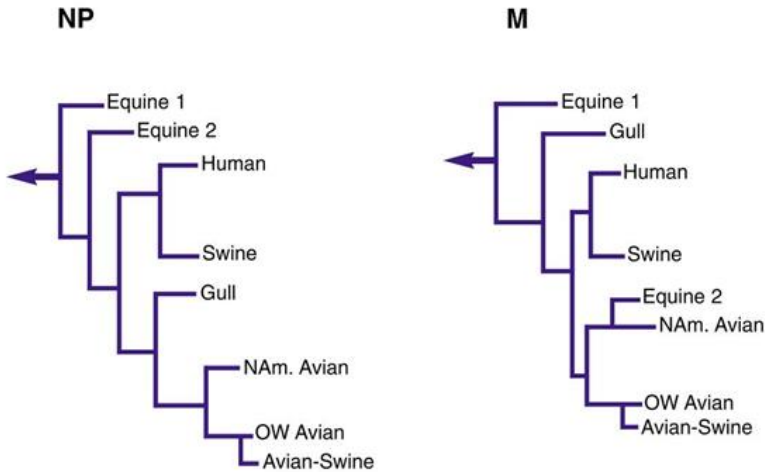
How do avian influenza viruses change in nature?

Segmented genome: shift
Point mutations in HA/NA: drift



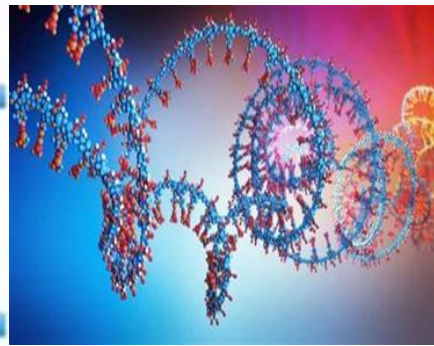
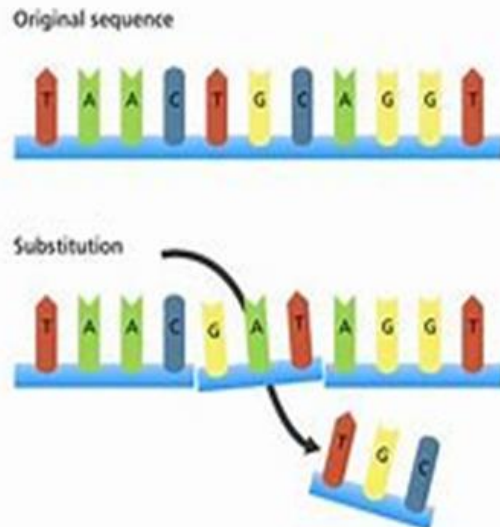
Gene signatures carry host of origin traits
Useful for tracking virus change – genetic reassortment or SHIFT

Point mutations in each gene segment; HA gene most relevant – genetic DRIFT



O. T. Gorman et al.

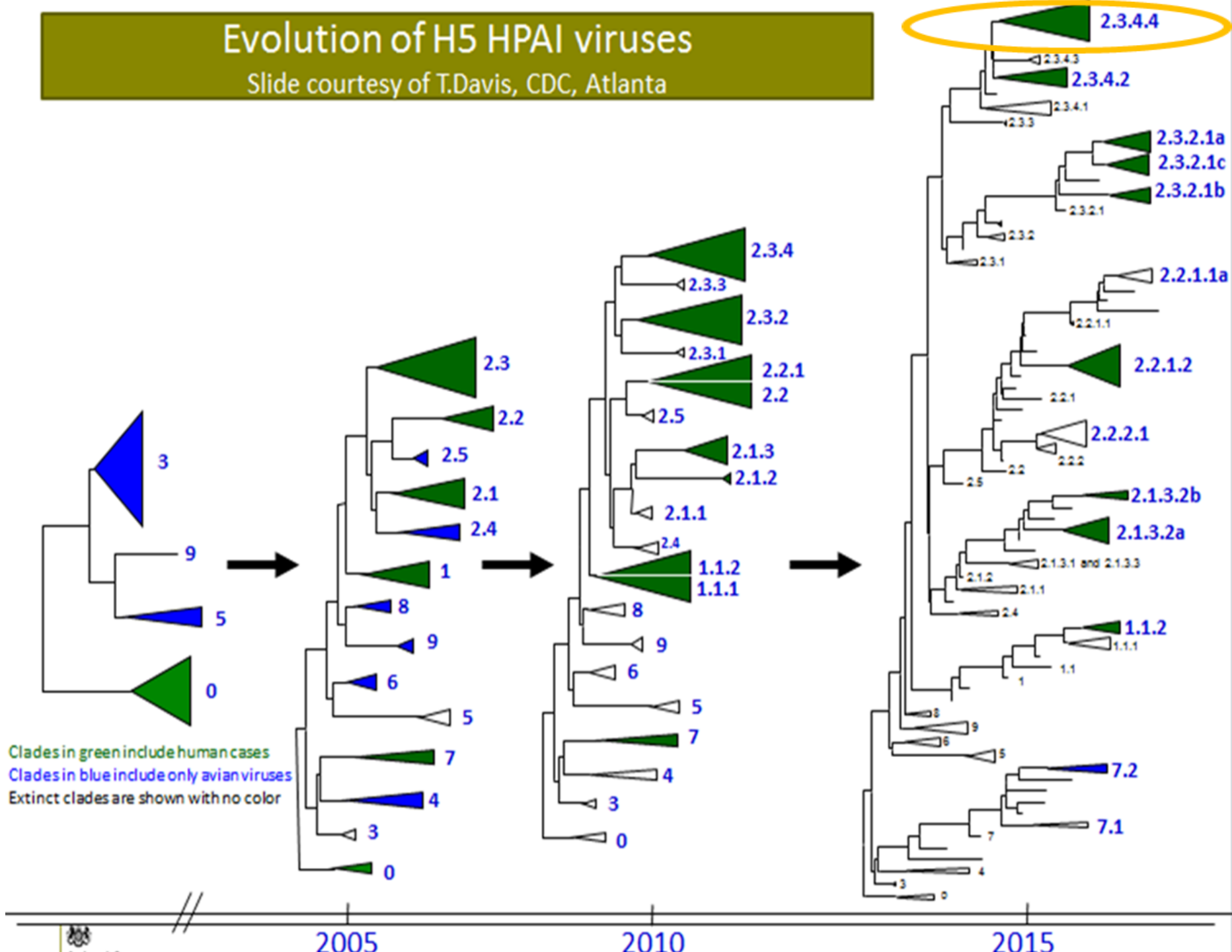
Defines genotypes on whole genome characteristics



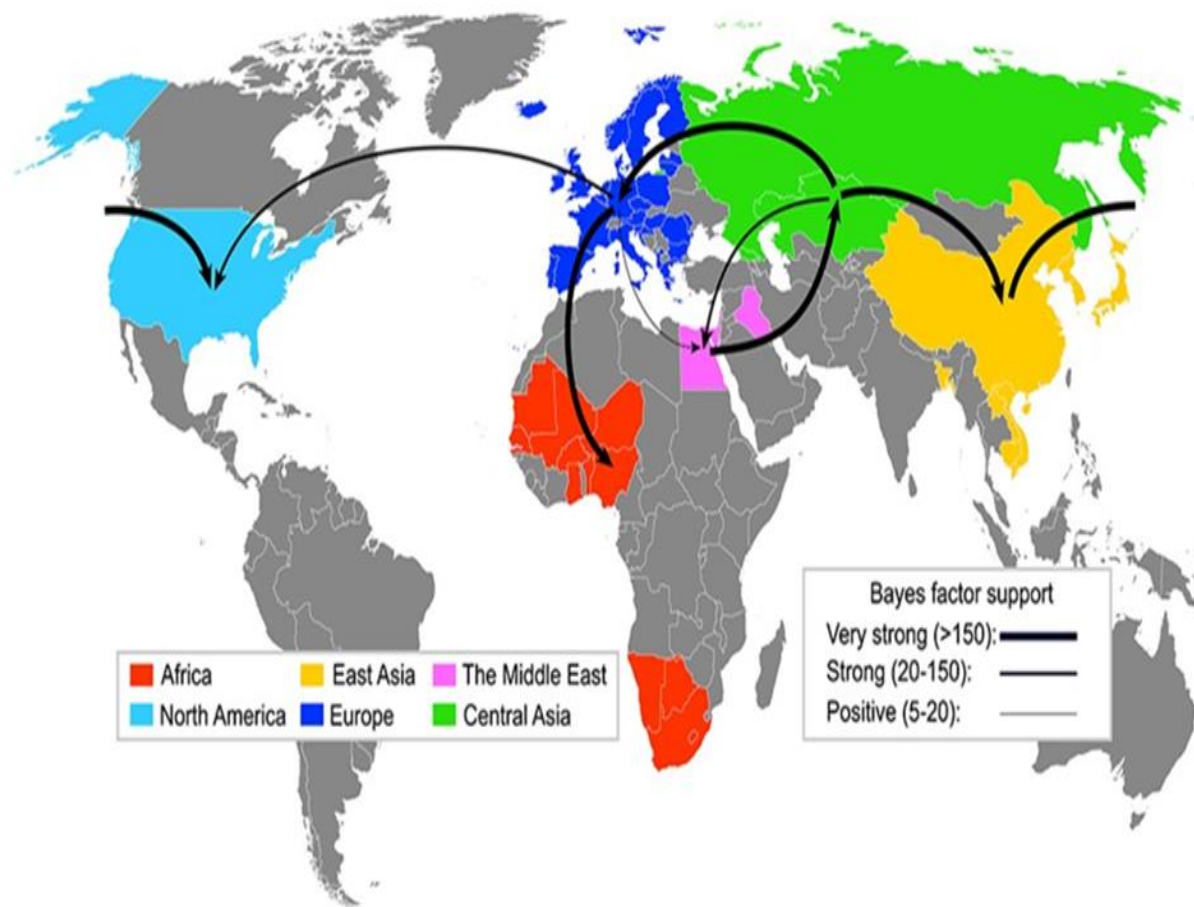
Defines HA or NA clades

Evolution of H5 HPAI viruses

Slide courtesy of T.Davis, CDC, Atlanta



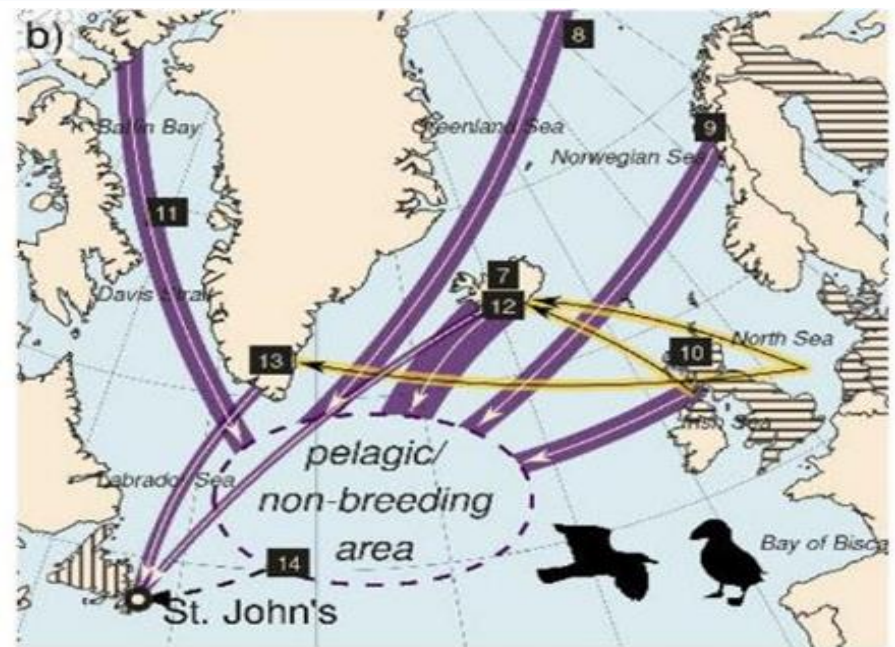
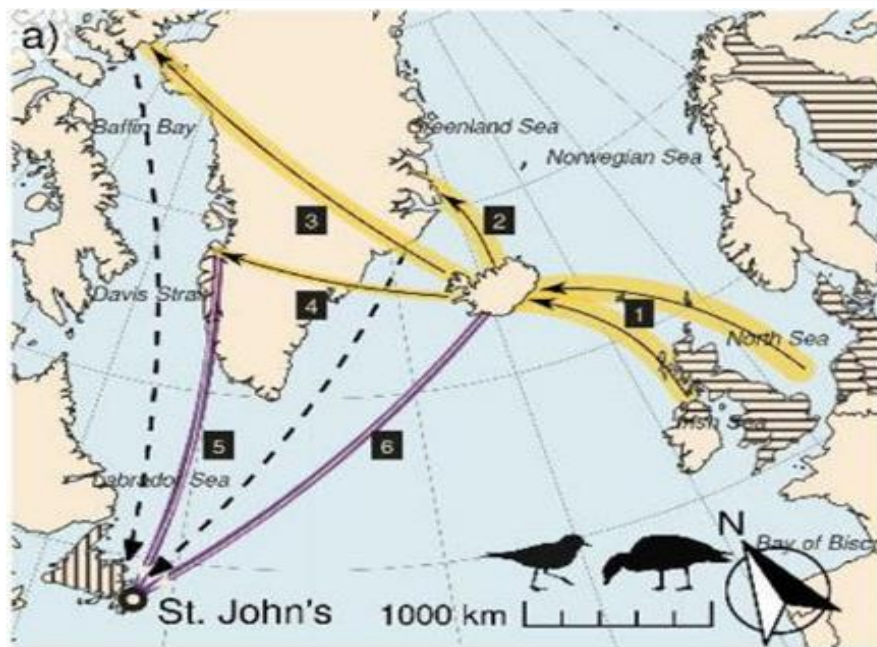
Global migration rates among the geographic regions of clade 2.3.4.4b (2020-2022)



Fusaro et al High pathogenic avian influenza A(H5) viruses of clade 2.3.4.4b in Europe—Why trends of virus evolution are more difficult to predict, *Virus Evolution*, Volume 10, Issue 1, 2024, veae027, <https://doi.org/10.1093/ve/veae027>

Transatlantic transmission

Putative transmission pathways between Europe and Newfoundland via migratory waterfowls/shorebirds



■ spring ■ autumn H5N1 detected spring/summer 2021 November 2021



scientific reports

www.nature.com/scientificreports



Communication
Recurring Trans-Atlantic Incursion of Clade 2.3.4.4b H5N1 Viruses by Long Distance Migratory Birds from Northern Europe to Canada in 2022/2023

Tamiru N. Alkie^{1,†}, Alexander M. P. Byrne^{2,4}, Megan E. B. Jones^{3,4}, Benjamin C. Mollett², Laura Bourque³, Oliver Lung¹, Joe James^{2,8}, Carmencita Yason⁴, Ashley C. Banyard^{2,8}, Daniel Sullivan¹, Anthony V. Signore^{1,2}, Andrew S. Lang⁶, Meghan Baker⁷, Beverly Dawe⁷, Ian H. Brown^{2,5,4} and Yohannes Berhane^{1,8,9,*}

OPEN

Transatlantic spread of highly pathogenic avian influenza H5N1 by wild birds from Europe to North America in 2021

V. Callendo^{1,6}, N. S. Lewis^{2,5,10}, A. Pohlmann^{2,10}, S. R. Baillie^{11,12}, A. C. Banyard⁸, M. Beer¹, I. H. Brown⁵, R. A. M. Fouchier¹, R. D. E. Hansen¹, T. K. Lameris¹³, A. S. Lang⁶, S. Laurentou⁷, O. Lung⁷, G. Robertson⁸, H. van der Jeugd¹⁴, T. N. Alkie¹, K. Thorup^{15,16}, M. L. van Toor⁹, J. Waldenström⁸, C. Yason¹⁰, T. Kulken¹⁷ & Y. Berhane^{1,2}

Expansion in wild bird host range: susceptibility?

Primary hosts: Often highly susceptible



- Many long distance migratory species may be tolerant to infection with HPAIV in the absence of disease

Mortality

Secondary hosts: Differential susceptibility



Expansion in wild bird host range: susceptibility

Tertiary: Medium-Low Susceptibility



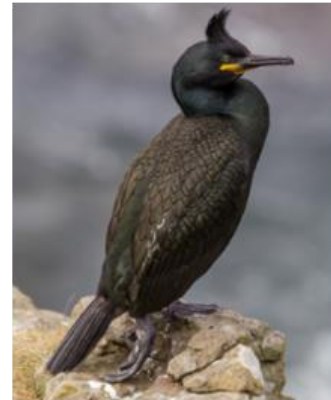
Occasionally seen to succumb to infection.

Quaternary: Resistant?

*Dalmatian
pelican*



*European
shag*

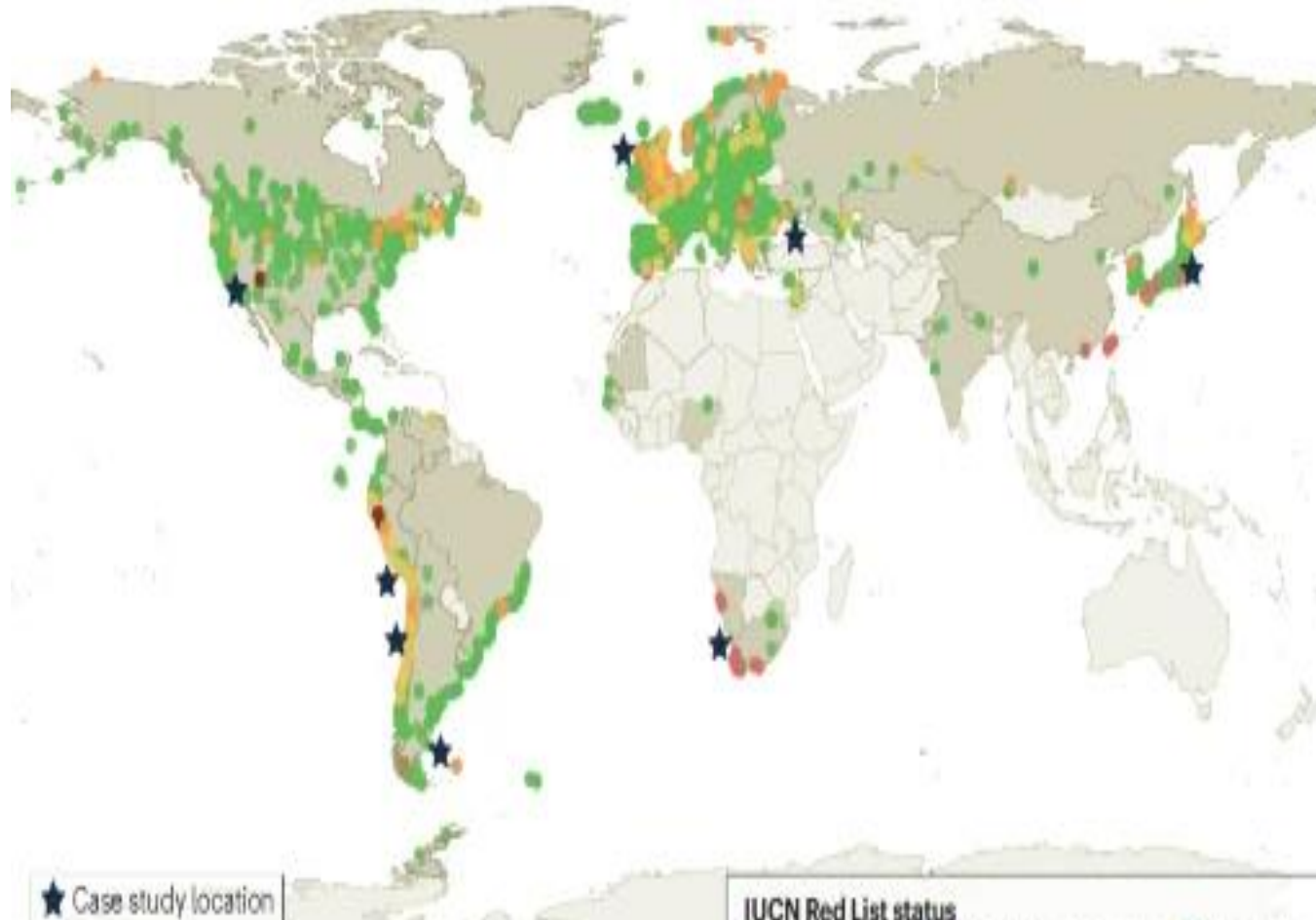


Impacts on biodiversity

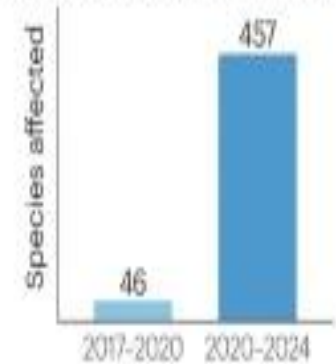


Impacts of H5 HPAI on biodiversity

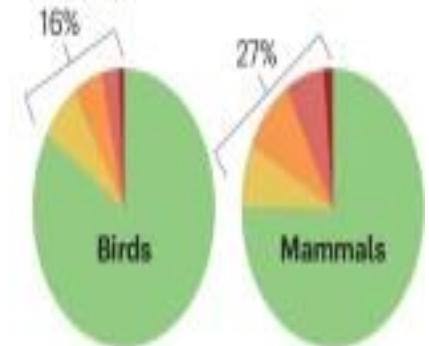
a Locations of H5N1 cases during 2020–2024 outbreak



b Number of infected species



c IUCN Red List status of infected species



Comment | Published: 15 January 2025

The threat of avian influenza H5N1 looms over global biodiversity

Sergio A. Lambertucci , Andrea Santangeli & Pablo I. Plaza

[Nature Reviews Biodiversity](#) 1, 7–9 (2025) | [Cite this article](#)

Increased infectivity in effective bridging species?

Charadriiformes: diverse order live near water

Sub group Laridae (gulls, terns, noddies, skimmers, kittiwakes); ubiquitous
100 species from 22 genera many of which have become infected with H5N1

Genetic changes in virus

High susceptibility and virus shedding

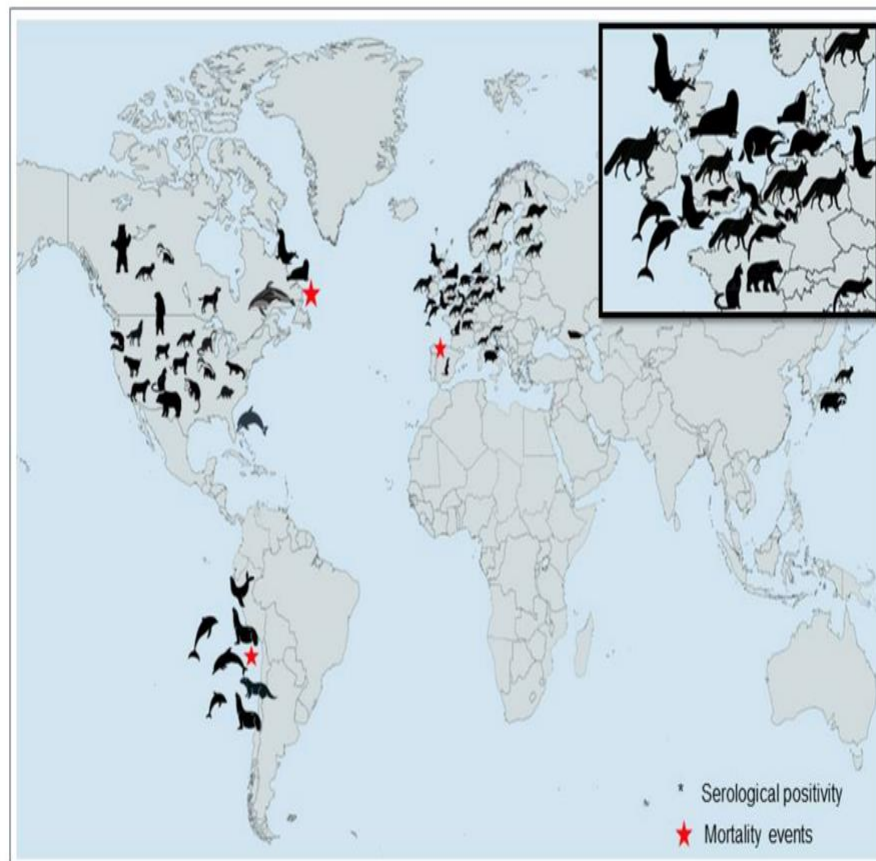
Behavioural; move between habitats (land, sea, remote land masses)

Increasing environmental contamination/exposure (naïve populations)



Spread to mammals

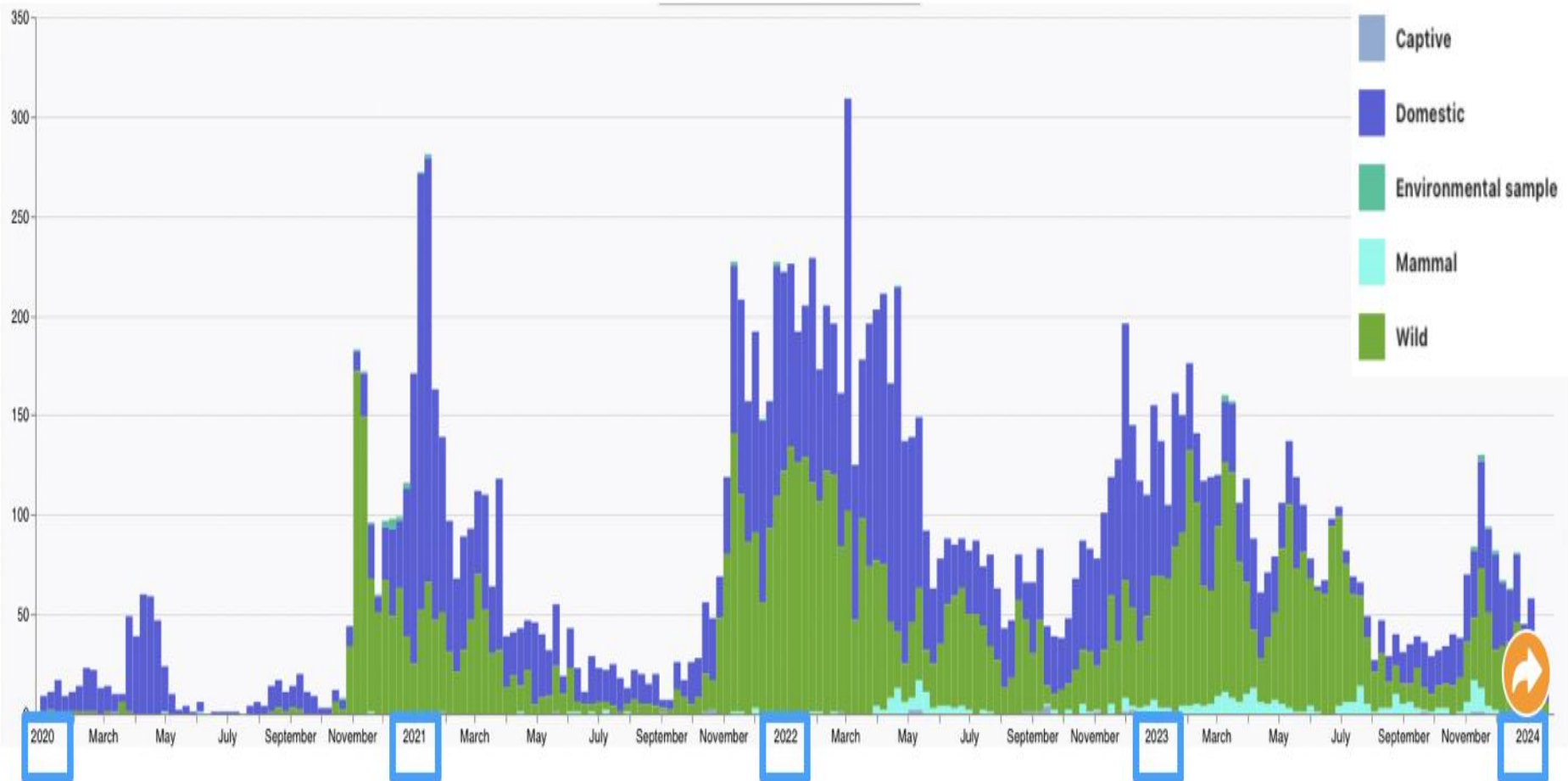
- Captive bred animals: mink, foxes
- Wild Scavengers; ie foxes, seals, stoat, otter
- Domestic ; cats



American black bear (<i>Ursus americanus</i>)	Burmeister's porpoise (<i>Phocoena spinipinnis</i>)	European polecat (<i>Mustela putorius</i>)	Porpoise (<i>Phocoena phocoena</i>)
American mink (<i>Neogale vison</i>)	Caspien seal (<i>Pusa caspica</i>)	Ferret (<i>Mustela furo</i>)	Raccoon (<i>Procyon lotor</i>)
American pine marten (<i>Martes americana</i>)	Cat (<i>Felis catus</i>)	Fisher cat (<i>Pekania pennanti</i>)	Red fox (<i>Vulpes vulpes</i>)
Amur leopard (<i>Panthera pardus orientalis</i>)	Chilean dolphin (<i>Cephalorhynchus eutropia</i>)	Grey seal (<i>Halichoerus grypus</i>)	Skunk (<i>Mephitis mephitis</i>)
Amur tiger (<i>Panthera tigris</i>)	Common dolphin (<i>Delphinus delphi</i>)	Harbour seal (<i>Phoca vitulina</i>)	South America fur seal (<i>Arctophoca australis</i>)
Asiatic black bear (<i>Ursus thibetanus</i>)	Coyote (<i>Canis latrans</i>)	Japanese raccoon dog (<i>Nyctereutes viverrinus</i>)	South American bush dogs (<i>Speothos venaticus</i>)
Bobcat (<i>Lynx rufus</i>)	Dog (<i>Canis familiaris</i>)	Kodiak grizzly bear (<i>Ursus arctos horribilis</i>)	South American sea lion (<i>Otaria flavescens</i>)
Beech marten (<i>Martes foina</i>)	Eurasian badger (<i>Meles meles</i>)	Marine otter (<i>Lontra felina</i>)	Virginia opossum (<i>Didelphis virginiana</i>)
Bottlenose dolphin (<i>Tursiops truncatus</i>)	Eurasian lynx (<i>Lynx lynx</i>)	Mountain lion (<i>Puma concolor</i>)	White-sided dolphin (<i>Lagenorhynchus acutus</i>)
Brown bear (<i>Ursus arctos</i>)	Eurasian otter (<i>Lutra lutra</i>)	North American river otter (<i>Lontra canadensis</i>)	Pig (<i>Sus scrofa</i>)

H5 detections: Expanded host range

Timeline of number of outbreaks of HPAI from 2020 to present



Semi-aquatic mammals in South America

Mammal to mammal transmission



nature communications

Article <https://doi.org/10.1038/s41467-024-53766-5>

Epidemiological data of an influenza A/H5N1 outbreak in elephant seals in Argentina indicates mammal-to-mammal transmission

Received: 19 April 2024

Marcela M. Uhart^{1,2}, Ralph E. T. Vanstreels¹, Martha I. Nelson¹,
Valeria Olivera¹, Julieta Campagna¹, Victoria Zavattieri¹, Philippe Lemey¹,
Claudio Campagna¹, Valeria Falabella¹ & Agustina Rimondi^{1,2}

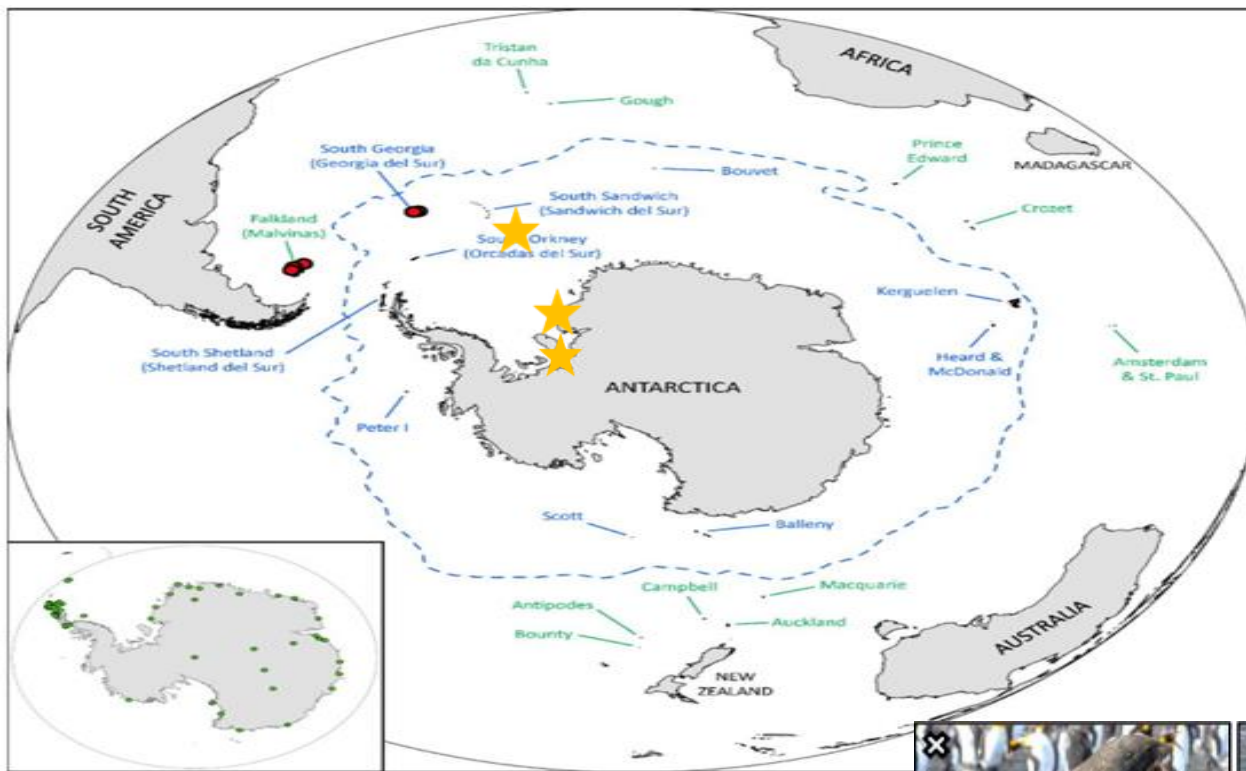
Accepted: 18 October 2024

Published online: 11 November 2024

www.pirbright.ac.uk

Spread to Antarctica

OFFLU ad-hoc group on HPAI H5 in wildlife of South America and Antarctica (2023) Continued expansion of high pathogenicity avian influenza H5 in wildlife in South America and incursion into the Antarctic region.



Separate introductions into South Georgia, South Sandwich Islands and Falkland islands; spread to shelf



Highly Pathogenic Avian Influenza A (H5N1) Suspected in penguins and shags on the Antarctic Peninsula and West Antarctic Coast

Fabiola León, Céline Le Bohec, Eduardo J. Pizarro, Loïcka Baille, Robin Cristofari, Aymeric Houston, Daniel P. Zitterbart, Gonzalo Barriga, Elie Poulin, Juliana A. Vianna
 doi: <https://doi.org/10.1101/2024.03.16.585360>

This article is a preprint and has not been certified by peer review [what does this mean?]



Abstract Full Text Info/History Metrics

Preview PDF

nature communications

Article

<https://doi.org/10.1038/s41467-024-51490-8>

Detection and spread of high pathogenicity avian influenza virus H5N1 in the Antarctic Region

Received: 23 November 2023

Accepted: 8 August 2024

Published online: 03 September 2024

Ashley C. Banyard^{1,2}, Ashley Bennison³, Alexander M. P. Byrne^{1,4}, Scott M. Reid¹, Joshua C. Lynton-Jenkins^{1,2}, Benjamin Mollert¹, Dilhani De Silva¹, Jacob Peers-Dent¹, Kim Finlayson⁵, Rosamund Hall³, Freya Blockley², Marcia Blyth³, Marco Fatchieri¹, Zoe Fowler⁶, Elaine M. Fitzcharles², Ian H. Brown^{1,2} & Joe James^{1,2}

Outbreaks in captive bred mammals

Spain ; Oct 22 outbreak in mink farm (52k)

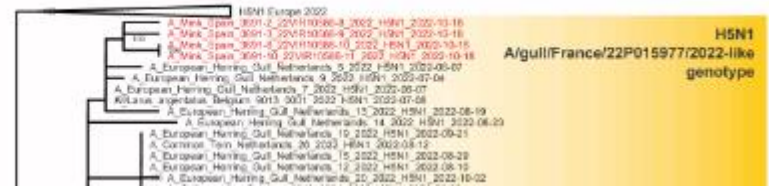


A. Gene composition of H5N1 A/gull/France/22P015977/2022-like genotype



■ H5N1 A/duck/Saratov/29-02/2021-like
■ Gull-adapted H13 subtype

HA gene



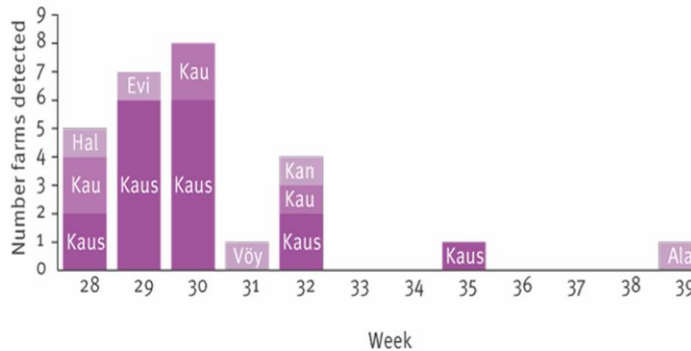
Limited adaptive changes in the virus (T271A) in the PB2 gene

Montserrat et al (<https://doi.org/10.2807/1560-7917.ES.2023.28.3.2300001>)

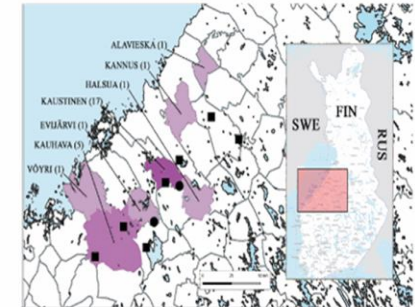
H5N1 HPAI in fur farms in Finland July-Oct 2023



A. Detection of fur farms with HPAI A(H5N1), by week and municipality



B. Location of fur farms with HPAI A(H5N1)



- Initial point introductions from wild birds
- Secondary spread between fur farms
- Up to 7 genetic changes associated with mammalian adaptation but not all viruses
- Depopulation and other control measures
- Prophylactic vaccination of fur farms workers now offered

Eurosurveillance Europe's journal on infectious disease surveillance, epidemiology and global health

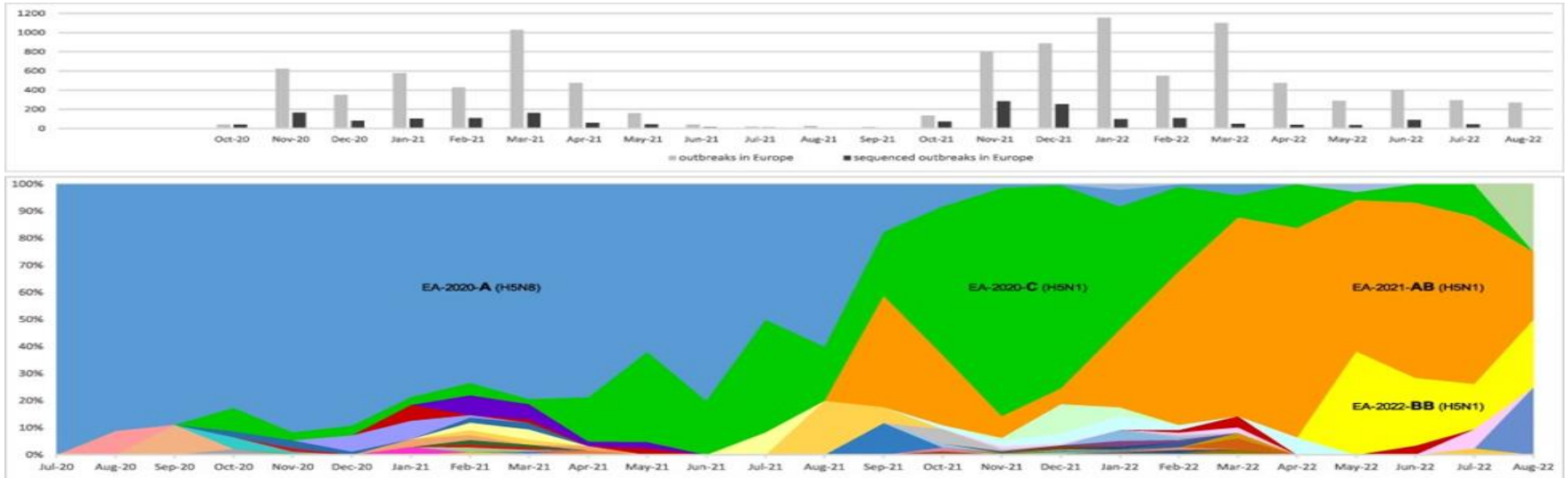
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Outbreaks Open Access

Highly pathogenic avian influenza A(H5N1) virus infections on fur farms connected to mass mortalities of black-headed gulls, Finland, July to October 2023 Like 0 Download

Lauri Kareinen¹, Niina Tammiranta¹, Ari Kauppinen², Bianca Zecchin³, Ambra Pastori², Isabella Monne², Calogero Terregino², Edoardo Giussani², Riikka Kaarto⁴, Veera Karkamo⁴, Tanja Lähtinen¹, Hanna Lounela¹, Tuuja Kantala¹, Ilona Laamanen¹, Tiina Nokireki¹, Laura London¹, Otto Helve⁴, Sohvi Kärriläinen⁴, Niina Ikonen⁴, Jari Jalava⁴, Laura Kalin-Mänttärin⁴, Anna Katz⁴, Carita Savolainen-Kopra⁴, Erika Lindh⁴, Tarja Siironen⁴, Essi M Korhonen⁵, Kirsi Aaltonen⁵, Monica Galliano⁶, Alice Fusaro⁶, Tuija Paakkilä¹

Extensive genetic heterogeneity: large genotype diversity in Europe



Subtype	Genotype	Genotype name-Representative European viruses	W1 - 2020-2021										N. viruses NW1	Color legend	Reference sequences	
			P82	P81	PA	HA	NP	HA	MP	NS						
H5N1	EA-2020-A	H5N1_A/duck/Chelyabinsk/1/2021-like	20	20	20	20	20	20	20	20	20	20	706	80.7	1	A/Eurasian_Wigeon/Netherlands/1/2020_H5N1
	EA-2020-B	H5N1_A/chicken/Russia_Novosibirsk_region/1/2020-like	15	16	1	1	1	1	1	1	1	1	20	0.3	2	A/wigeon/legend_gull/Netherlands/15-03/2019/3035/2021_H5N1
	EA-2020-M	H5N1_A/goose/Poland/011/2020-like	20	20	14	20	20	20	20	20	20	20	3	0.3	3	A/duck/Ringledive/1/2021_H5N1
	EA-2021-Q	H5N1_A/gemina/Belgium/2021/01/2021-like	20	20	14	20	20	20	20	20	20	20	20	2.3	4	A/duck_Wild/NL_Groningen/2021/03/2021_H5N1
	EA-2021-Q	H5N1_A/canada_goose/Belgium/2021/01/2021-like	20	20	20	20	26	20	20	20	20	20	8	0.9	5	A/chicken/Netherlands/2020/05/2021_H5N1
	EA-2020-C	H5N1_A/Eurasian_Wigeon/Netherlands/1/2020-like	1	1	1	1	1	1	1	1	1	1	61	7.0	6	A/duck/Mongolia/1/2021_H5N1
	EA-2021-V	H5N1_A/duck/Czech_Republic/2/2021-like	1	1	1	1	1	1	1	1	1	1	2	0.2	7	A/duck/Netherlands/2020/03/2020_H4N6
	EA-2020-X	H5N1_A/Eurasian_outflow/Netherlands/20016890/001/2020-like	20	9	14	20	11	20	20	20	20	20	1	0.1	8	A/duck/Netherlands/2020/03/2020_H4N6
	EA-2020-D	H5N1_A/gemina/NL/1_federation_Cornwall/06/02/2020-like	20	20	20	20	20	20	20	20	20	20	3	0.3	9	A/chicken/Netherlands/1/2021/03/2021_H5N1
	EA-2020-E	H5N1_A/bussard/Germany/MA/0216/2020-like	20	20	29	20	20	20	20	20	20	20	17	1.9	10	A/turkey/England/05/18/2021_H5N1
EA-2020-F	H5N1_A/yeminge_falcon/Germany/1/37/6/2/2020-like	20	20	29	20	20	20	20	20	20	20	1	0.1	11	A/gemina/fowl/Germany/WW/00318/02/2020_H5N1	
EA-2021-H	H5N1_A/chicken/Denmark/DA/21/2020/04/06/2021-like	20	20	29	20	20	20	20	20	20	20	3	0.3	12	A/duck/Poland/1/2021/01/2021_H5N1	
EA-2021-I	H5N1_A/hoopoe_wann/Romania/20123_21V1849/1/2021-like	18	14	10	20	26	13	20	20	20	20	9	1.0	13	A/duck/Mongolia/1/2021_H5N1	
EA-2021-L	H5N1_A/duck_wann/Poland/06/05/2021-like	1	1	1	1	1	1	1	1	1	1	1	0.1	14	A/duck/Poland/1/2021_H5N1	
EA-2021-N	H5N1_A/huffid_duck/Poland/06/05/2021-like	18	14	10	20	26	13	20	20	20	20	1	0.1	15	A/duck/Poland/1/2021_H5N1	
EA-2021-H	H5N1_A/huffid_duck/Poland/06/05/2021-like	20	20	29	20	20	20	20	20	20	20	11	1.3	16	A/duck/Poland/1/2021_H5N1	
EA-2020-G	H5N1_A/red_bird/Germany/SK/003419/2020-like	11	31	11	20	12	11	20	20	20	20	12	1.4	17	A/duck/Netherlands/1/2021_H5N1	
EA-2021-J	H5N1_A/Laridae/Germany/SK/003419/2021-like	11	23	5	20	26	20	20	20	20	20	3	0.3	18	A/duck/Netherlands/1/2021_H5N1	
EA-2021-P	H5N1_A/yellow-legged_gull/Netherlands/05-0039_21V18305/2021-like	11	23	5	20	26	20	20	20	20	20	4	0.5	19	A/duck/Netherlands/1/2021_H5N1	

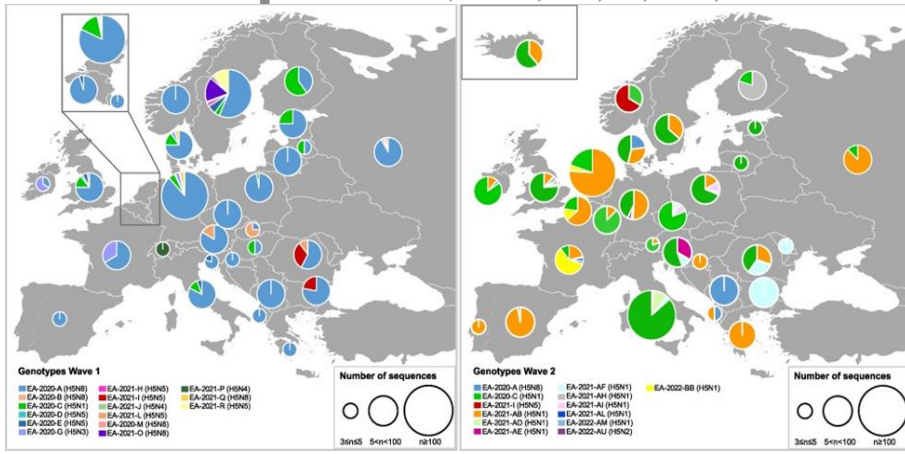
JOURNAL ARTICLE

High pathogenic avian influenza A(H5) viruses of clade 2.3.4.4b in Europe—Why trends of virus evolution are more difficult to predict

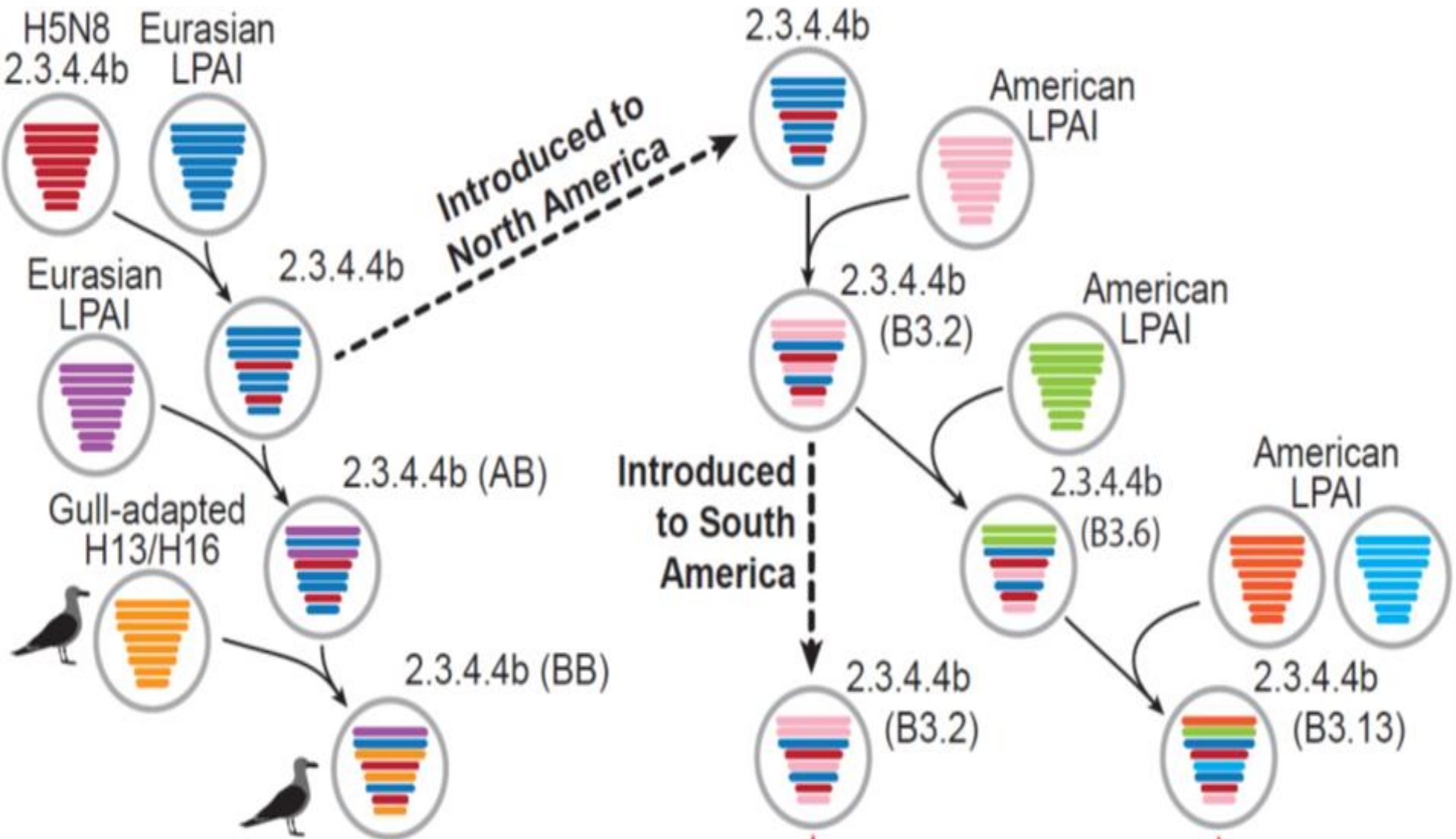
Alice Fusaro, Bianca Zecchin, Edoardo Giussani, Elisa Palumbo, Montserrat Agüero-García, Claudia Bachofen, Adam Bálint, Fereshteh Banihashem, Ashley C Banyard, Nancy Beerens ... Show more

Author Notes

Virus Evolution, Volume 10, Issue 1, 2024, veae027,

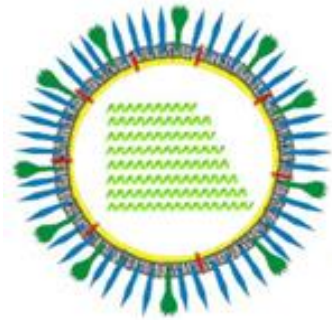


Iterative reassortment drove the emergence and propagation of the H5N1 panzootic



Peacock et al, 2024 (Figure credit Martha Nelson and David VanInsberghe)

The virus driving the impact!



The 2021-24 H5N1 HPAI is the most infectious and dangerous of strains to date

Multiple evolved traits

Spread of H5N1 HPAI to dairy cattle

H5N1 HPAI dairy cattle outbreak 10th March 2024 to present

Choose time period

Choose species

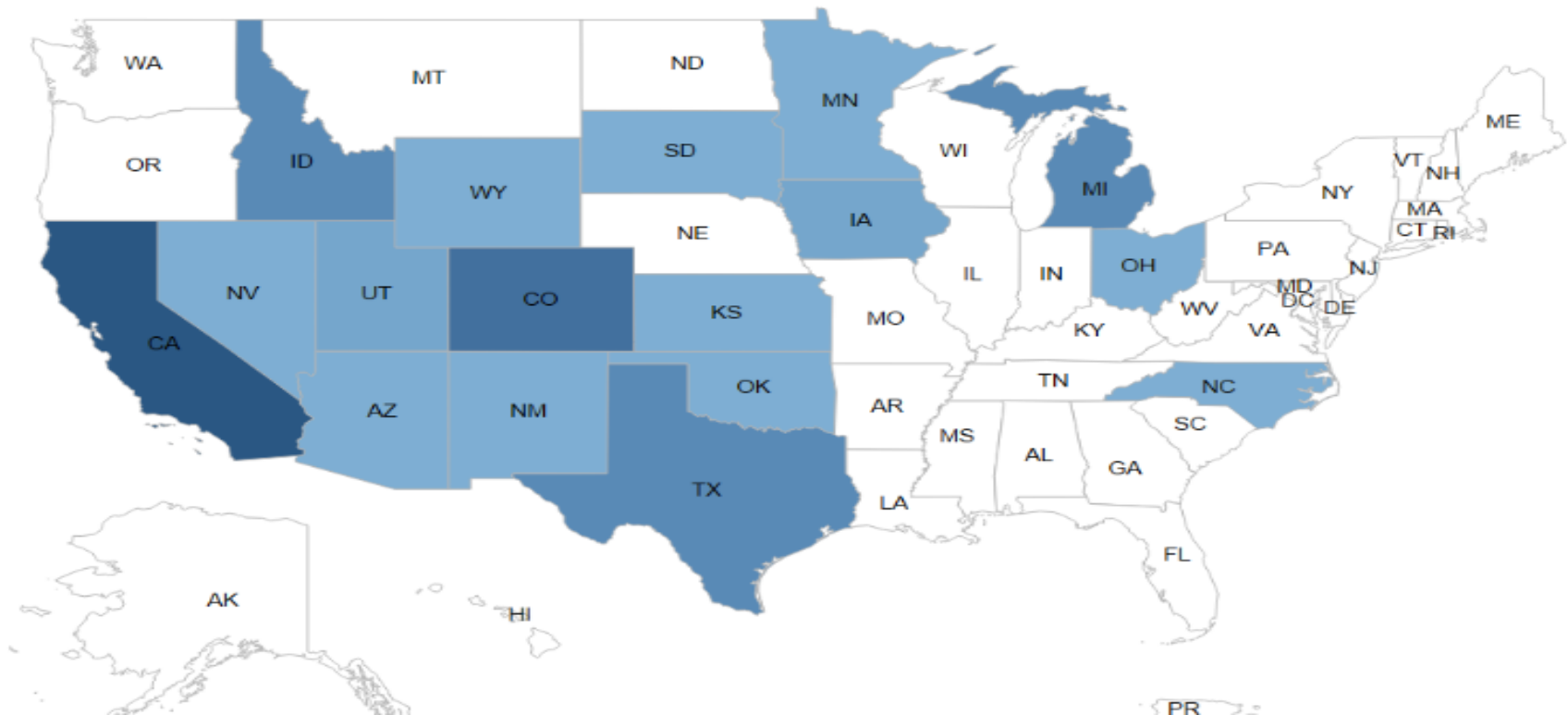
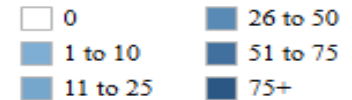
Situational Update

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In the Total Outbreak, in Cattle, there were:
973 Confirmed Cases in 17 States

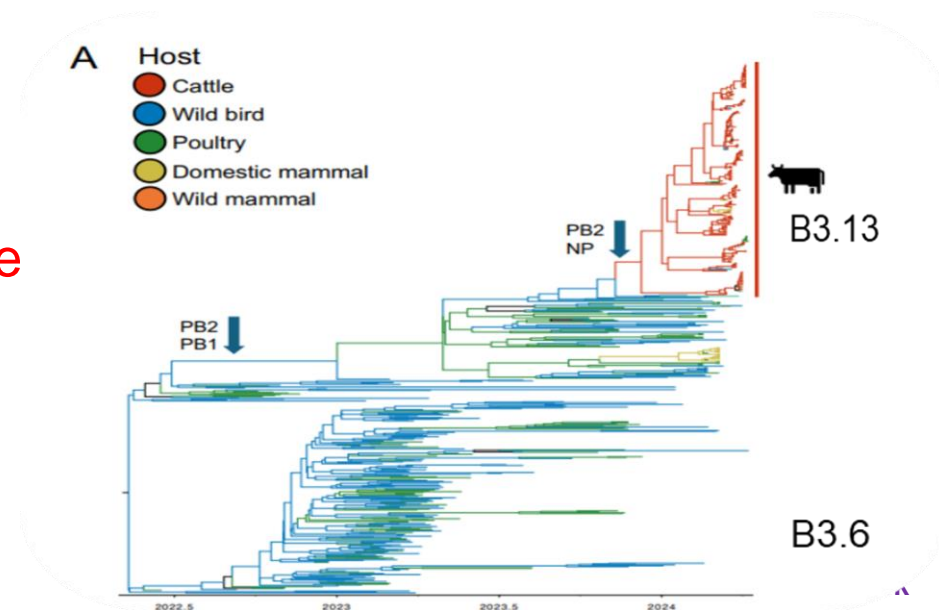
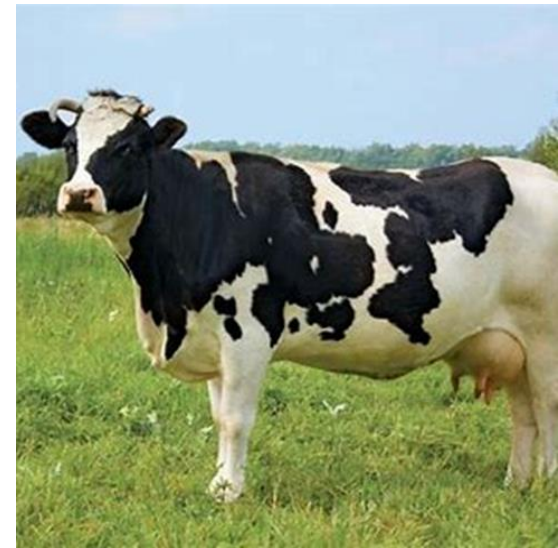
Number of Confirmed Cases in Cattle by State, Total Outbreak

Legend



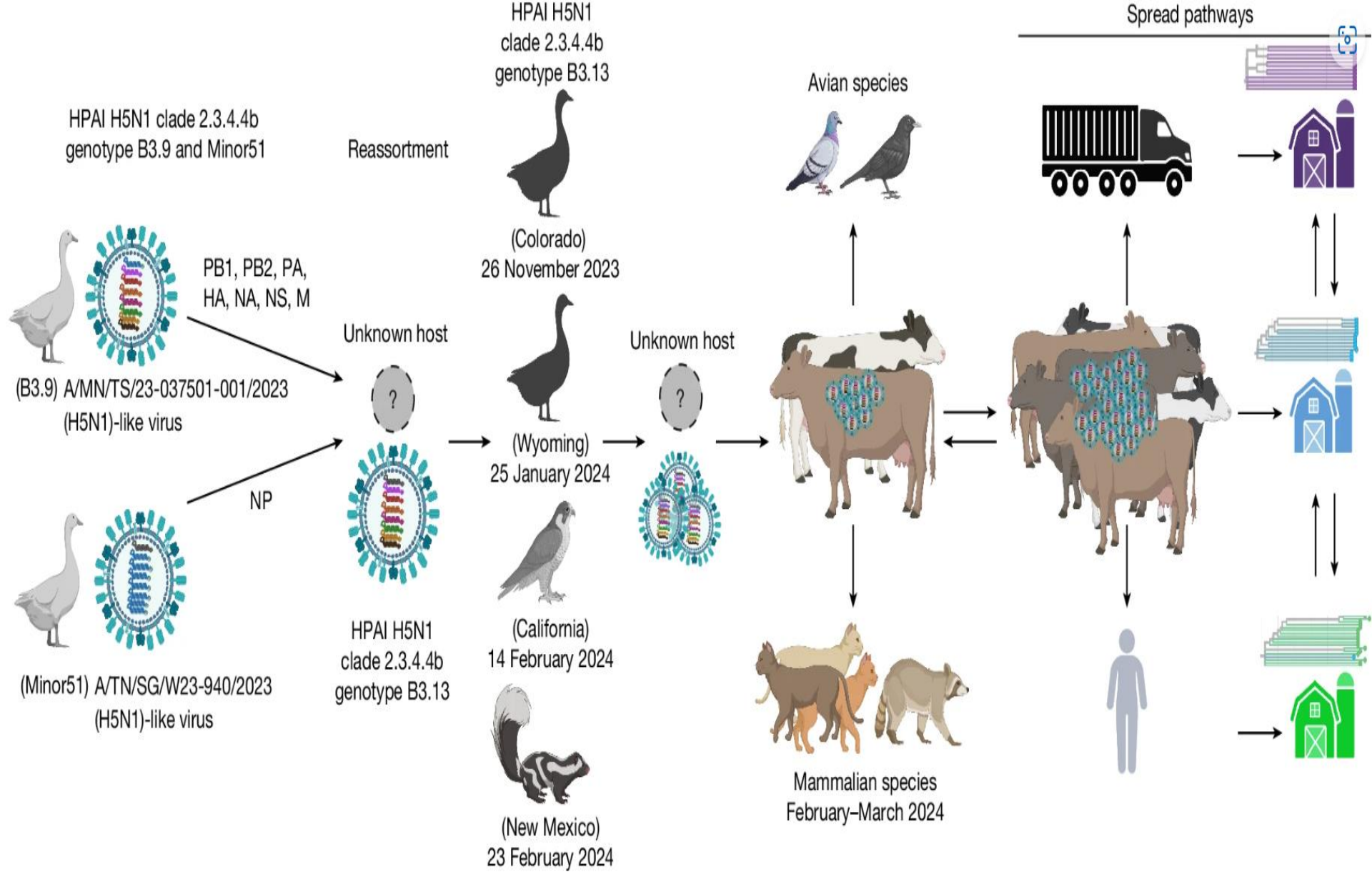
Dairy cattle; infection and epidemiology

- 3 spill overs of H5N1 HPAI (B3.13 genotype dominant)
 - Initial signs are drop in feed intake and milk output
 - Mastitis
 - Symptoms range from asymptomatic to lethal
 - Viral load in milk can be very high
 - Almost exclusively lactating cows
-
- Replication largely in mammary gland
 - Respiratory infection at best transient
-
- Spread via movement of infected cattle
 - Fomite : equipment, people etc



Nguyen et al bioRxiv

<https://doi.org/10.1101/2024.05.01.591751>



Caserta, L.C., Frye, E.A., Butt, S.L. et al. Spillover of highly pathogenic avian influenza H5N1 virus to dairy cattle. *Nature* (2024). <https://doi.org/10.1038/s41586-024-07849-4>

Human case summary associated with dairy cattle epidemic (24/2/25)

National Total Cases: 70

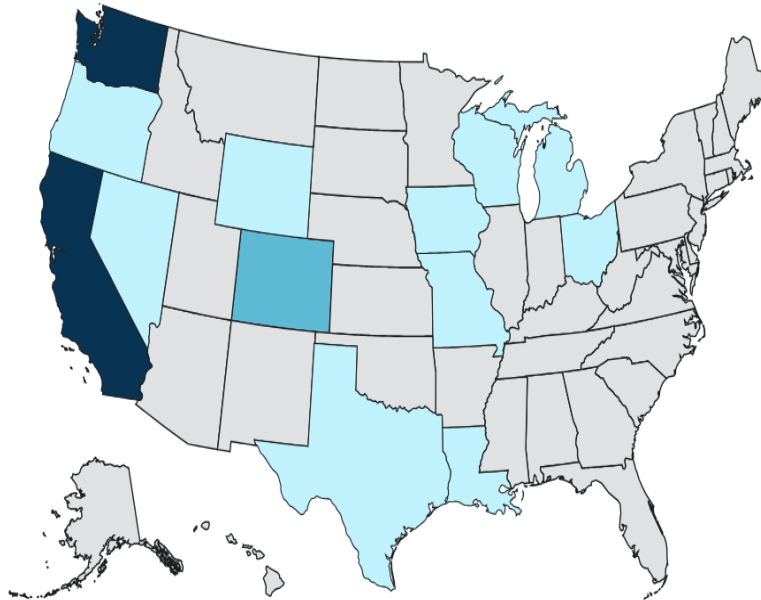
Cases	Exposure Source
41	Dairy Herds (Cattle)*
24	Poultry Farms and Culling Operations*
2	Other Animal Exposure†
3	Exposure Source Unknown‡

NOTE: One additional case was previously detected in a poultry worker in Colorado in 2022. Louisiana reported the first H5 bird flu death in the U.S.

*Exposure Associated with Commercial Agriculture and Related Operations

†Exposure was related to other animals such as backyard flocks, wild birds, or other mammals

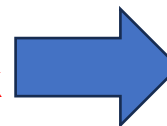
‡Exposure source was not able to be identified



Total cases



Pasteurisation kills live virus in the milk

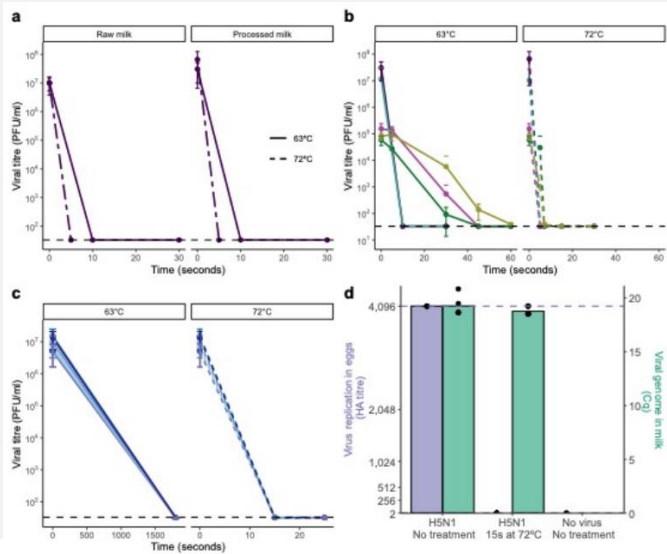


https://www.cdc.gov/bird-flu/situation-summary/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fbird-flu%2Fphp%2Favian-flu-summary%2Findex.html

Virus survival in milk?



Pasteurisation

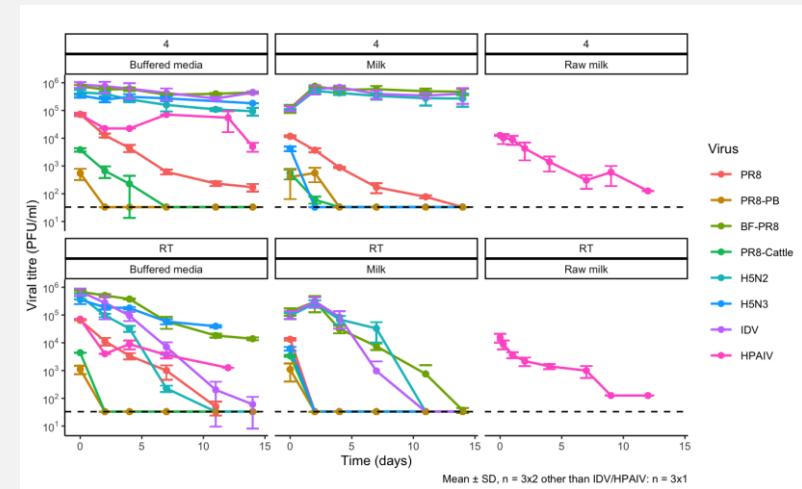


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Pasteurisation temperatures effectively inactivate influenza A viruses in milk

[Jenna Schafers](#), [Caroline J. Warren](#), [Jiayun Yang](#), [Junsen Zhang](#), [Sarah J. Cole](#), [Jayne Cooper](#), [Karolina Drewek](#), [B Reddy Kolli](#), [Natalie McGinn](#), [Mehnaz Qureshi](#), [Scott M. Reid](#), [Thomas P. Peacock](#), [Ian Brown](#), [Joe James](#), [Ashley C. Banyard](#), [Munir Iqbal](#), [Paul Digard](#), [Ed Hutchinson](#)

doi: <https://doi.org/10.1101/2024.05.30.24308212>

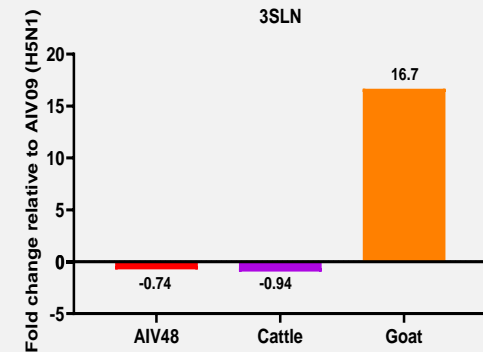
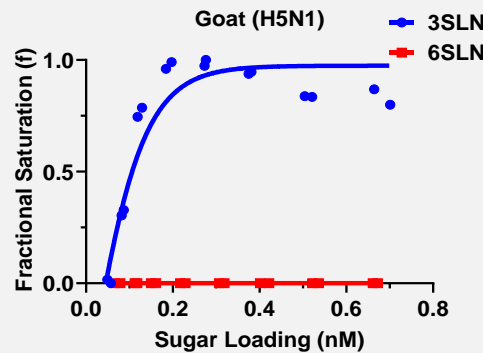
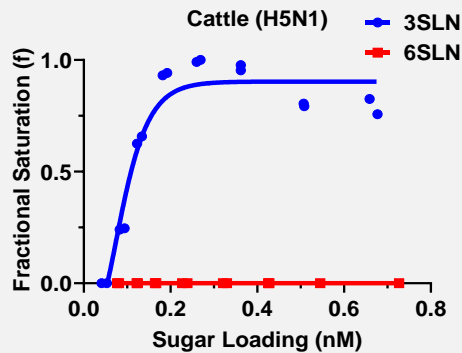
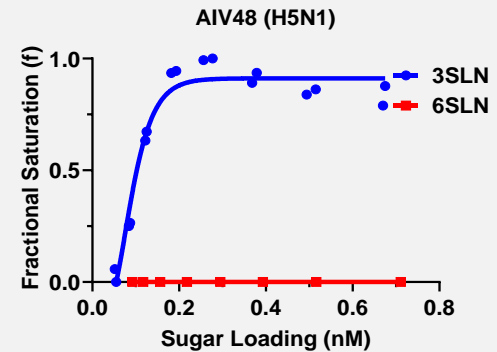
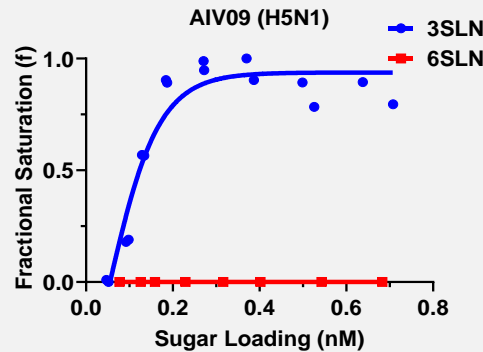
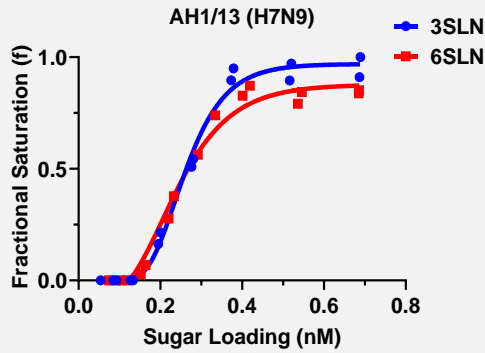


Raw milk an unsafe commodity!



Do the cattle and goat H5N1 viruses pose risk to humans?

Receptor Binding studies



Cattle and goat H5N1 viruses retain affinity for avian-like receptor analogue 3SLN.

Dairy cattle epidemic; implications for poultry?

- Dairy farms often close proximity to poultry
- Poorer biosecurity practices
- Shared personnel/household contacts between sectors
- Cattle virus whilst replicating in mammary gland phenotypically avian
- Fully infectious for domestic birds
 - Human cases; mild
- No evidence to date for spill over into wild birds of dairy cattle B3.13 virus
- Infection confined to USA
- Reduction of threat from cattle via vaccination?



- Field Studies with Nonviable, Non-replicating Veterinary Vaccines Targeting Highly Pathogenic Avian Influenza in Livestock

<https://www.aphis.usda.gov/news/program-update/cvb-notice-24-13-field-studies-nonviable-non-replicating-veterinary-vaccines>

Companion animals: H5 HPAI

- H5N1 HPAI infections in cats have been widely reported
- Variable clinical manifestations, including respiratory and neurological signs, often fatal outcomes.
- Infection via exposure to infected birds, other animals, raw or contaminated feed or in the milking parlour!
- Multiple independent cases in Poland; feed?
- Captivity die offs ie Large cats in zoos

RESEARCH

Outbreak of highly pathogenic avian influenza A(H5N1) clade 2.3.4.4b virus in cats, Poland, June to July 2023

Katarzyna Domańska-Blicharz¹, Edyta Świętoń², Agnieszka Świątańska³, Isabella Monne⁴, Alice Fusaro⁴, Karolina Tarasiuk¹, Krzysztof Wyrostek¹, Natalia Styś-Fijol¹, Aleksandra Giza², Marta Pietruk², Bianca Zecchin⁴, Ambra Pastori⁴, Łukasz Adaszek⁴, Małgorzata Pomorska-Mól⁴, Grzegorz Tomczyk¹, Calogero Terregino⁴, Stanisław Winiarczyk^{1,2}

- Dogs susceptible
- Very infrequent reports





Could vaccination solve the problem?

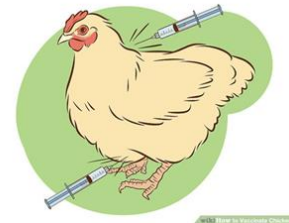


Vaccination will only work when applied in combination with other measures

Vaccination is not a substitute for weak farm biosecurity

Considering vaccination as part of available avian influenza control measures

- **Prevention and control of outbreaks in vaccinated domestic bird populations** resulting in reduced virus circulation within and between flocks and lower risk of spillover to wildlife
- **Reduced economic losses**, both direct (e.g. bird deaths) and indirect (e.g. mass culling and trade disruption). When properly implemented, avian influenza vaccination is compatible with safe trade, according to WOAHP international standards
- **Lower risk of human exposure to avian influenza viruses**, and thus of a potential pandemic, in line with the One Health
- **Minimised environmental impact** by reducing the risk of spill over to wild animals
- **Protecting food security**
- **Incentives for innovative research**



Key Conclusions

- Exceptional global spread; panzootic most continents affected
 - Continues to be a significant threat to biodiversity
- High infection pressure resulting in increased wild bird host range and continuing if not declining cases in domestic birds
- Mammalian infections: spillover to scavengers, some M2M transmission
- Dairy cattle infection in USA: continuing outbreak with spread (17 states); **vaccination in future?**
- H5 HPAI virus evolving with high fitness traits
- Antigenically dominant clade 2.3.4.4b moderately stable
- **Vaccination remains an important tool for prevention/control in some countries/regions**



Animal & Plant Health Agency

Ash Banyard
Joe James
Marek Slomka
Cecilia Di Genova
Lizzie Billington
Sofia Riccio
Kajal Ralh
Jafar Hassan

Caroline Warren
DES, Animal Sciences, Pathology

RVC Royal Veterinary College
University of London

Pablo Alarcon
Guillaume Fournie
Javier Guitan
Stephen Vickers
Sarah Hill



Imperial College London

Wendy Barclay
Jess Quantrill



James Wood
Paniz Hussein



UNIVERSITY OF LEEDS
Alastair Ward



Ed Hutchinson



Emma Cunningham
Jenna Schafers



Munir Iqbal
Jiayun Yang
Thomas Peacock
Jean Remy Sadeyen
Rebecca Daines
Mehnaz Qureshi
Kolli Reddy
Samuel Richardson
Toby Carter



Department of Agriculture, Environment and Rural Affairs



UK Health Security Agency



Paul Digard
Rute Pinto
Sam Lycett
Rowland Kao



The University of Nottingham

UNITED KINGDOM · CHINA · MALAYSIA

Kin-Chow Chang
Lamyaa Al-Dalawi
Leah Goulding



Biotechnology and Biological Sciences Research Council



Department for Environment Food & Rural Affairs



Llywodraeth Cymru
Welsh Government



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