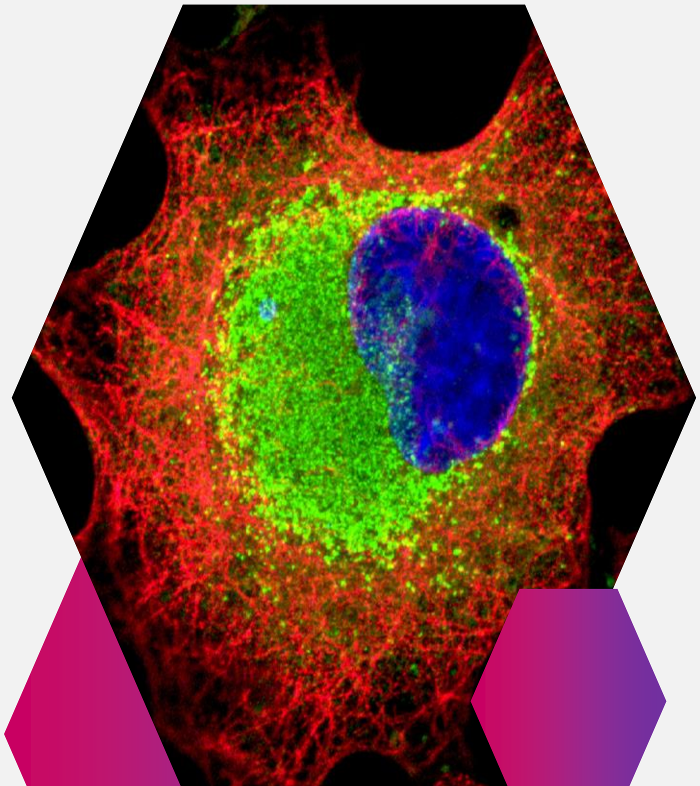

The current global panzootic of H5N1 and its risk to humans

Prof Ian Brown

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Preparing for containment and mitigation of pandemic H5N1 influenza

WHO workshop 14 November 2024

Statistical and Mathematical Modeling for H5N1 Pandemic

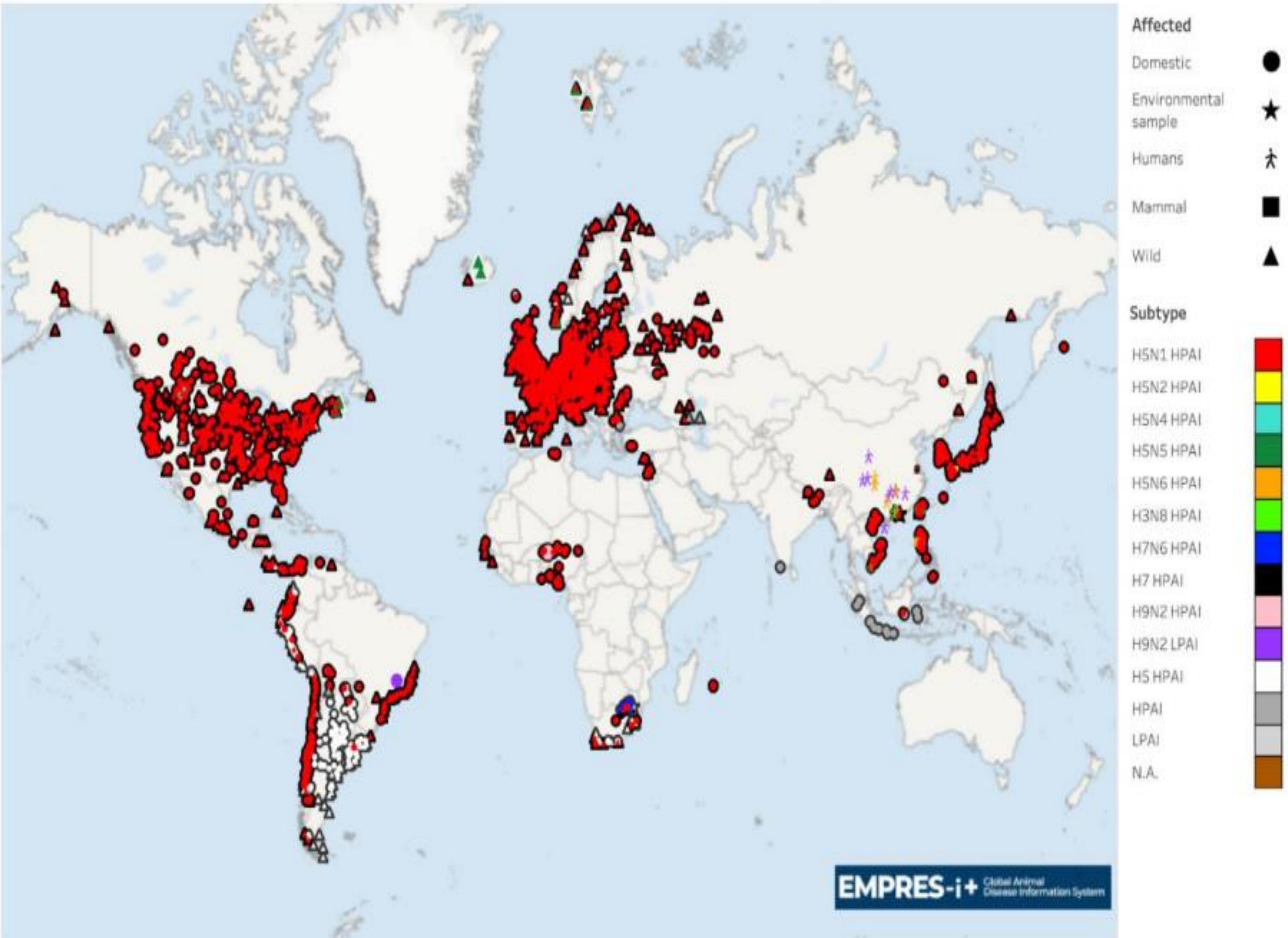
Biotechnology and Biological Sciences Research Council

Pirbright receives strategic funding from BBSRC UKRI

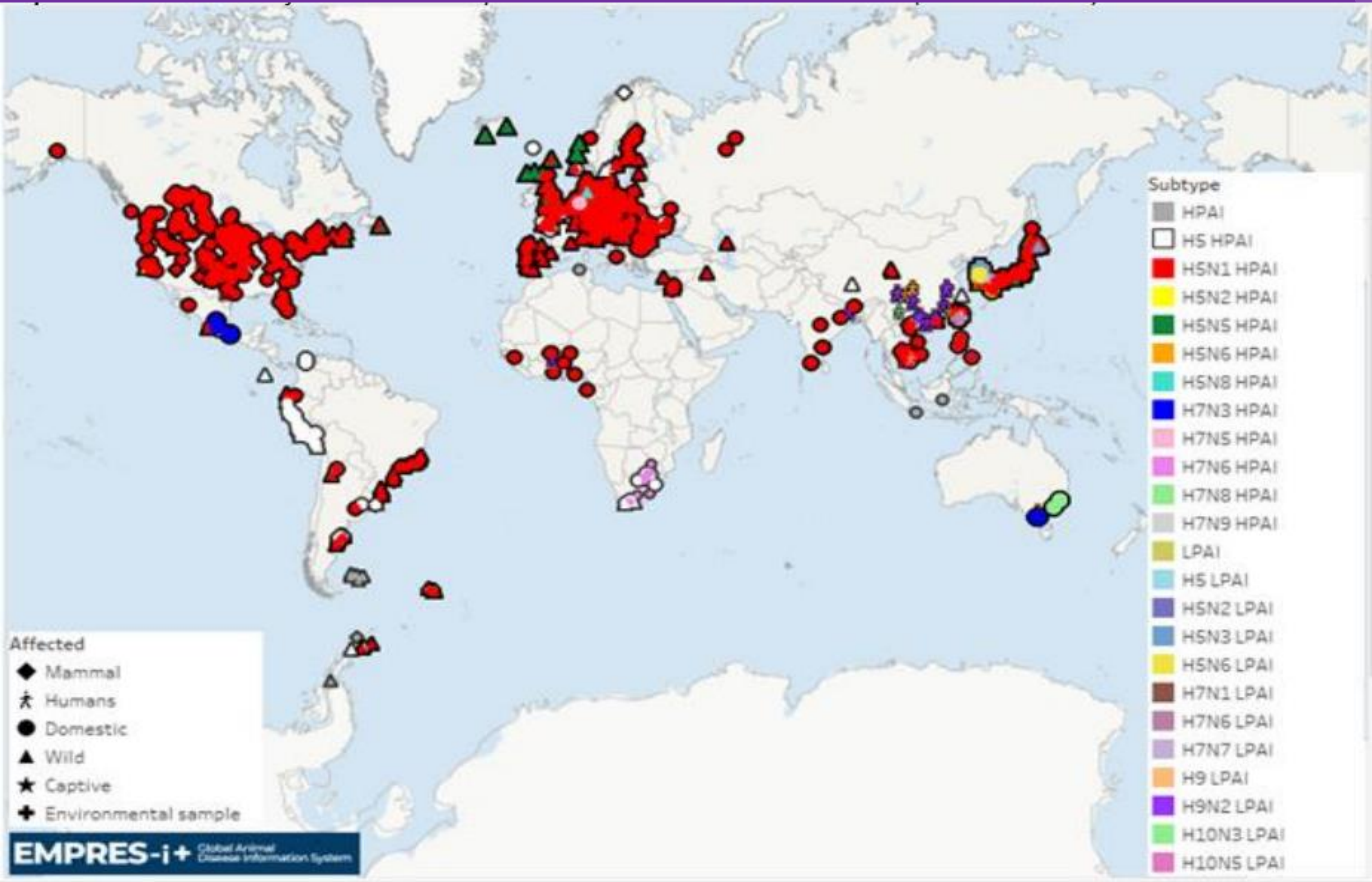
Key recent developments in HPAI epidemiology

- 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
- ‘Regular’ spill over to humans; occupational exposure
- H5 HPAI virus evolving with high fitness traits
- Antigenically clade 2.3.4.4b moderately stable

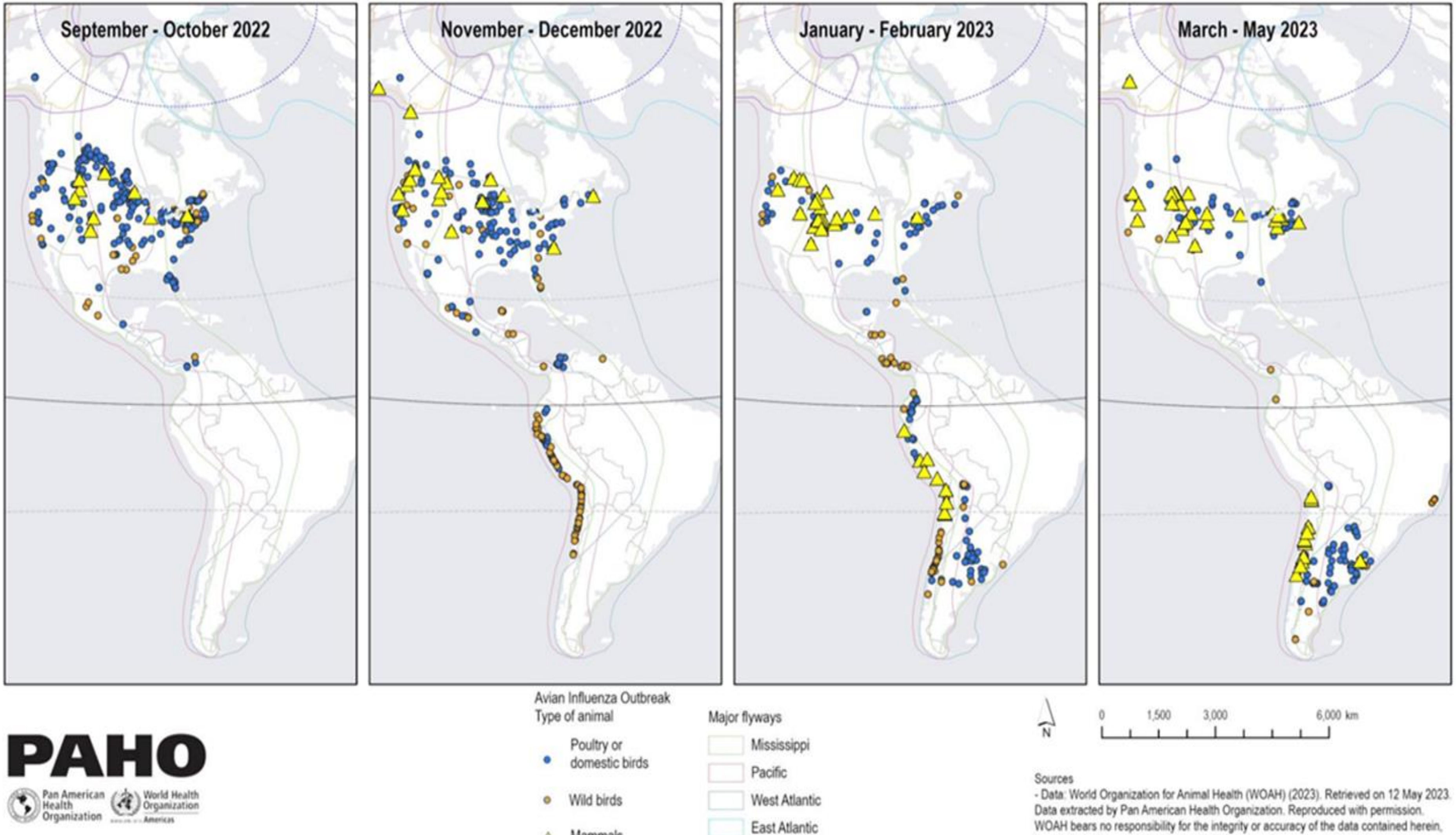
Confirmed Avian influenza events worldwide from 1 October 2022 to 30 September 2023



Global distribution of Avian Influenza
1st October 2023- 26th September 2024



Introduction into Central and Latin America

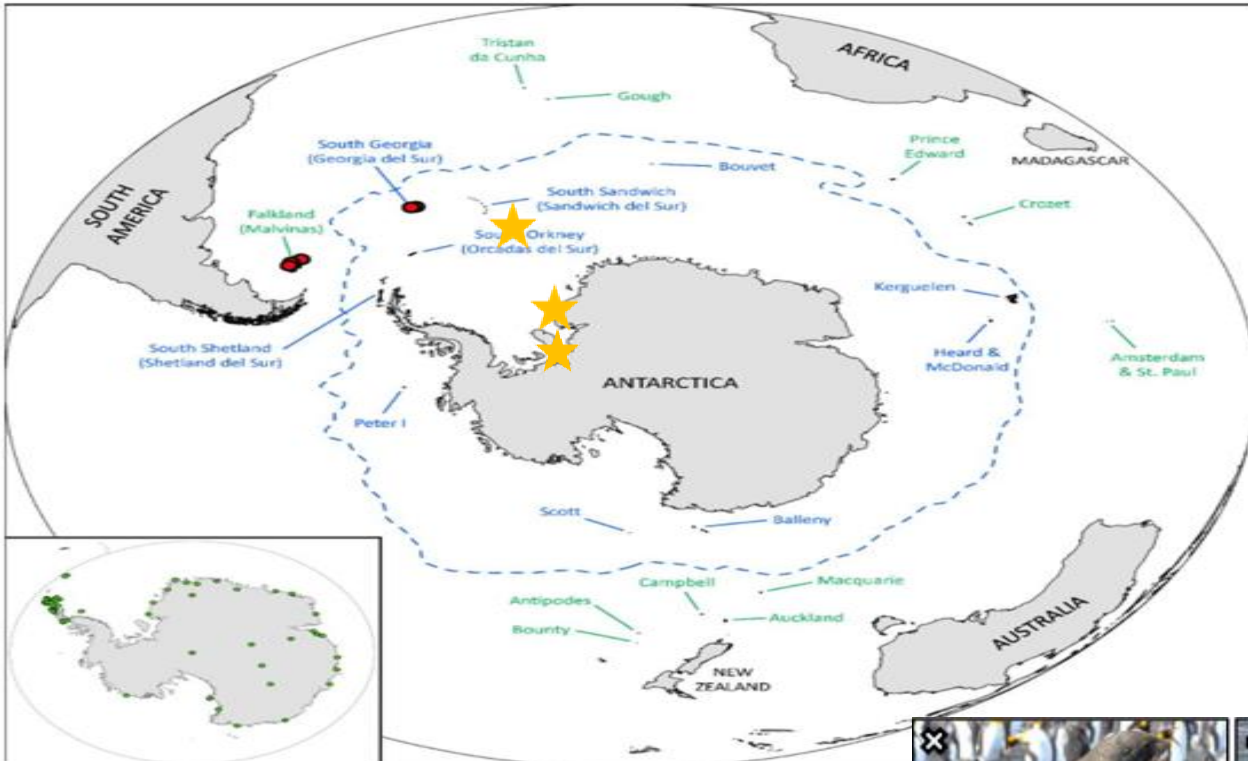


Map production: PAHO Health Emergencies Department/ Health Emergency Information and Risk Assessment Unit. GIS Team.

Sources
- Data: World Organization for Animal Health (WOAH) (2023). Retrieved on 12 May 2023. Data extracted by Pan American Health Organization. Reproduced with permission. WOAH bears no responsibility for the integrity or accuracy of the data contained herein, but not limited to, any deletion, manipulation, or reformatting of data that may have occurred beyond its control
- Cartography: WHO Detailed ADM0 Boundaries; Conservation of Artic Flora and Fauna - Data Service (SHP) Major flyways of Artic Birds Shapefile Accessed February 2023.

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

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
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Ashley C. Banyard[1,2], Ashley Bennison[3], Alexander M. P. Byrne[1,4], Scott M. Reid[1], Joshua G. Lynton-Jenkins[1,2], Benjamin Mollett[1], Dilhani De Silva[1], Jacob Peers-Dent[1], Kim Finlayson[5], Rosamund Hall[3], Freya Blockley[3], Marcia Blyth[3], Marco Falchieri[1], Zoe Fowler[6], Elaine M. Fitzcharles[3], Ian H. Brown[1,2] & Joe James[1,2]

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, Loicka Baille, Robin Cristofari, Aymeric Houstin, Daniel P. Zitterbart, Gonzalo Barriga, Elie Poulin, Juliana A. Vianna

doi: https://doi.org/10.1101/2024.03.16.585360

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Abstract Full Text Info/History Metrics Preview PDF

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Wild bird species affected: >300 species/25+orders

Wild bird orders affected by Gs/Gd H5Nx HPAI		
	Since 2021	
Accipitriformes (n=51)	Galliformes (n=19)	Psittaciformes (n=25)
Anseriformes (n=94)	Gaviiformes (n=3)	Rheiformes (n=1)
Caprimulgiformes (n=1)	Gruiformes (n=16)	Sphenisciformes (n=4)
Casuariiformes (n=1)	Passeriformes (n=49)	Strigiformes (n=18)
Cathartiformes (n=2)	Pelecaniformes (n=31)	Struthioniformes (n=1)
Charadriiformes (n=111)	Phoenicopteriformes (n=4)	Suliformes (n=25)
Ciconiiformes (n=6)	Piciformes (n=3)	Trogoniformes (n=1)
Columbiformes (n=7)	Podicipediformes (n=8)	
Falconiformes (n=13)	Procellariiformes (n=14)	

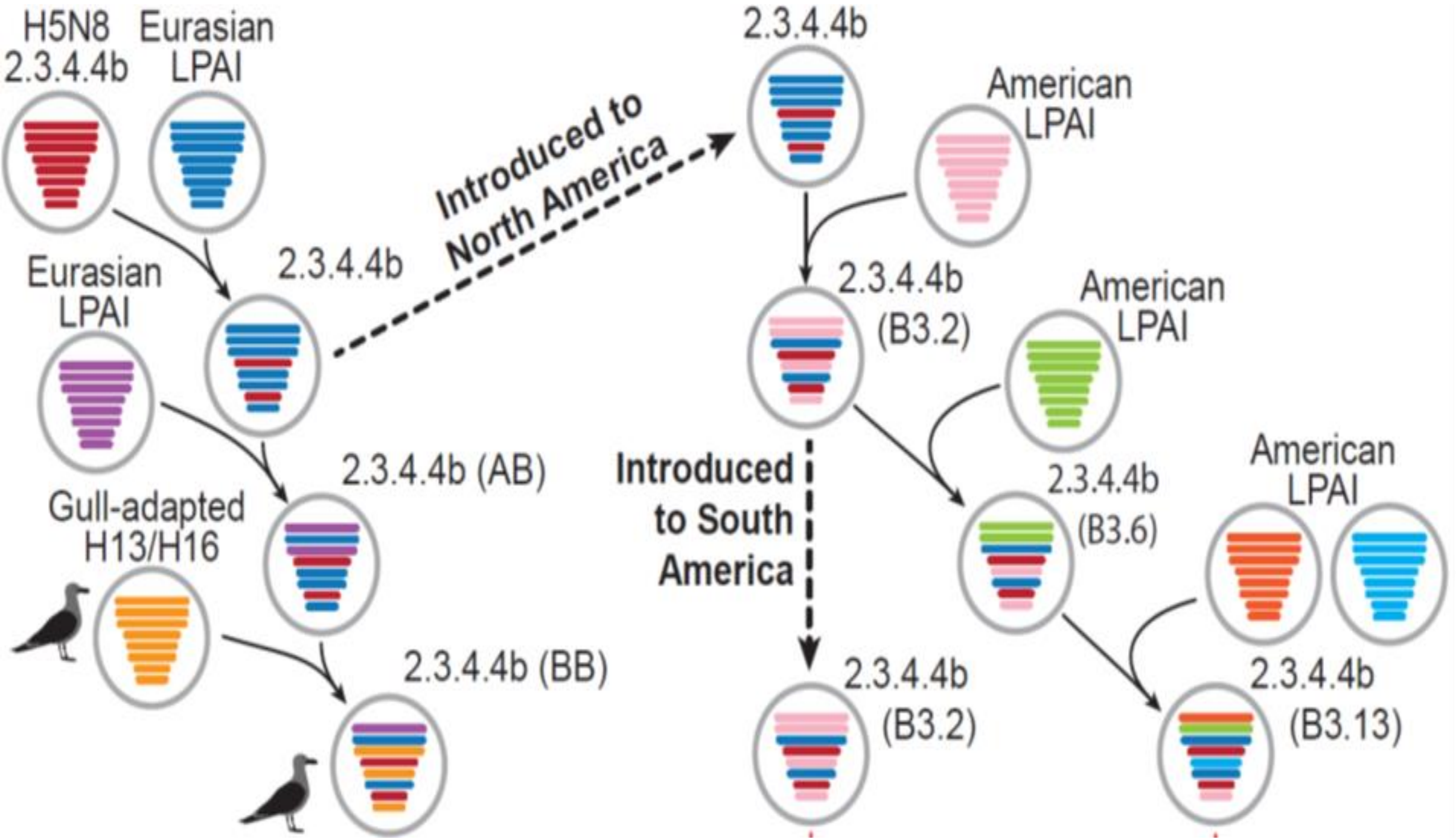
Wild bird species affected by Gs/Gd H5Nx HPAI Since 2021

Anseriformes (n=40)
Amazonetta brasiliensis (Brazilian Teal)*
Anas cyanoptera (Cinnamon Teal)
Anas discors (Blue-winged Teal)
Anas flavirostris (Andean Teal)
Anas formosa (Baikal Teal)*
Anas fulvigula (Mottled Duck)
Anas rhynchotis (Australasian Shoveler)
Anas rubripes (American Black Duck)
Anser cygnoides (Swan Goose)*
Anser rossii (Ross's Goose)
Aythya affinis (Lesser Scaup)
Aythya americana (Redhead Duck)
Aythya baeri (Baer's pochard)*
Aythya valisineria (Canvasback)
Branta ruficollis (Red breasted goose)
Branta sandvicensis (Nene)*
Bucephala albeola (Bufflehead)
Bucephala islandica (Barrow's goldeneye)*
Chloephaga melanoptera (Andean Goose)
Chloephaga picta (Upland Goose)
Cygnus bewickii (Tundra swan)
Cygnus buccinator (Trumpeter Swan)
Cygnus melancoryphus (black-necked swan)
Dendrocygna bicolor (Fulvous whistling Duck)
Dendrocygna viduata (White-faced Whistling-Duck)
Lophodytes cucullatus (Hooded Merganser)
Mareca falcata (Falcated Duck)
Marmaronetta angustirostris (Marbled Teal)
Melanitta fusca (Velvet Scoter)
Melanitta nigra (Common Scoter)
Melanitta perspicillata (Surf Scoter)
Mergellus albellus (Smew)*
Mergus serrator (Red-breasted merganser)
Mergus squamatus (Scaly-sided merganser)*
Oxyura jamaicensis (Ruddy Duck)
Spatula cyanoptera (Cinnamon Teal)
Spatula puna (Puna Teal)*
Spatula querquedula (Garganey)
Tachyeres pteneres (Magellanic Steamerduck)
Tadorna ferruginea (Ruddy Shelduck)
Gaviiformes (n=3)
Gavia immer (Common Loon)
Gavia pacifica (Pacific Loon)
Gavia stellata (Red-throated Loon)
Sphenisciformes (n=3)
Eudyptes chrysocome (Southern Rockhopper Penguin)
Spheniscus humboldti (Humboldt Penguin)
Spheniscus magellanicus (Magellanic Penguin)
Ciconiiformes (n=3)
Ciconia boyciana (Oriental Stork)
Ciconia nigra (Black Stork)
Mycteria americana (American Wood Stork)
Procellariiformes (n=13)
Ardenna gravis (Great Shearwater)
Ardenna grisea (Sooty Shearwater)
Ardenna tenuirostris (Short-tailed Shearwater)
Fulmarus glacialis (Northern Fulmar)
Fulmarus glacialoides (Southern Fulmar)
Macronectes giganteus (Southern Giant Petrel)
Macronectes halli (Northern Giant Petrel)
Pachyptila desolata (Antarctic Prion)
Phoebastria irrorata (Waved Albatross)
Procellaria aequinoctialis (White-chinned Petrel)
Pterodroma macroptera (Great-winged Petrel)
Puffinus puffinus (Manx Shearwater)
Thalassarche melanophris (Black-browed Albatross)
Suliformes (n=18)
Fregata magnificens (Magnificent Frigatebird)
Fregata minor (Great Frigatebird)
Leucocarbo atriceps (Imperial Shag)
Morus capensis (Cape Gannet)
Nannopterum brasilianum (Neotropic Cormorant)
Phalacrocorax auritus (Double-crested Cormorant)
Phalacrocorax bougainvillii (Guanay Cormorant)
Phalacrocorax brasilianus (Neotropical Cormorant)
Phalacrocorax gaimardi (Red-legged Cormorant)
Phalacrocorax lucidus (White-breasted Cormorant)
Phalacrocorax magellanicus (Rock Shag)
Phalacrocorax neglectus (Bank Cormorant)
Phalacrocorax punctatus (Spotted Shag)
Sula leucogaster (Brown Booby)
Sula nebouxii (Blue-footed Booby)
Sula sula (Red-footed Booby)
Sula variegata (Peruvian Booby)
Urile penicillatus (Brandt's Cormorant)
Pelecaniformes (n=13)
Ajaja ajaja (Roseate Spoonbill)
Ardea herodias (Great Blue Heron)
Bostrychia hagedash (Hadada Ibis)
Egretta caerulea (Little Blue Heron)
Egretta intermedia (Intermediate Egret)
Egretta thula (Snowy Egret)
Eudocimus ruber (Scarlet Ibis)*
Geronticus eremita (Northern Bald Ibis)
Pelecanus erythrorhynchos (American White Pelican)
Pelecanus occidentalis (Brown Pelican)
Pelecanus rufescens (Pink-backed Pelican)
Pelecanus thagus (Peruvian Pelican)
Plegadis chihi (White-faced Ibis)*

Galliformes (n=8)
Alectoris rufa (Red legged partridge)*
Bonasa umbellus (Ruffed grouse)
Callipepla californica (California Quail)
Centrocercus urophasianus (Greater sage-grouse)
Coturnix coturnix (Common Quail)*
Cracidae (Incognita)*
Lagopus lagopus (Willow Grouse)
Perdix perdix (Grey Partridge)*
Charadriiformes (n=78)
Alca torda (Razorbill)
Alle alle (Little auk)
Arenaria interpres (Ruddy Turnstone)
Arenaria melanocephala (Black turnstone)
Calidris alba (Sanderling)
Calidris alpina (Dunlin)
Calidris fuscicollis (White-rumped Sandpiper)
Calidris maritima (Purple sandpiper)
Calidris pusilla (Semipalmated sandpiper)
Cepphus grylle (Black Guillemot)
Charadrius hiaticula (Common ringed plover)
Charadrius mongolus (Lesser Sand Plover)
Charadrius nivosus (Snowy plover)
Chlidonias hybrida (Whiskered Tern)
Chroicocephalus maculipennis (Brown-hooded gull)
Chroicocephalus ridibundus (Black-headed Gull)
Fratercula arctica (Atlantic Puffin)
Gallinago gallinago (Common Snipe)
Gallinago stenura (Pin-tailed Snipe)
Gelochelidon nilotica (Common Gull-billed Tern)
Haematopus ater (Blackish Oystercatcher)
Haematopus ostralegus (Eurasian oystercatcher)
Haematopus palliatus (American oystercatcher)
Hydroprogne caspia (Caspian Tern)
Ichthyaetus melanocephalus (Mediterranean Gull)
Larosterna inca (Inca tern)
Larus atricilla (Laughing Gull)
Larus audouinii (Audouin's Gull)
Larus belcheri (Belcher's Gull)
Larus brachyrhynchus (Short-billed Gull)
Larus brunnicephalus (Brown-headed Gull)
Larus cachinnans (Caspian Gull)
Larus californicus (California Gull)
Larus crassirostris (Black-tailed Gull)
Larus delawarensis (Ring-billed Gull)
Larus dominicanus (Kelp Gull)
Larus genei (Slender-billed Gull)
Larus glaucescens (Glaucous-winged Gull)
Larus glaucoides (Iceland Gull)
Larus hyperboreus (Glaucous Gull)
Larus michahellis (Yellow-legged Gull)
Larus novaehollandiae (Silver Gull)
Larus occidentalis (Western Gull)
Larus philadelphia (Bonaparte's Gull)
Larus pipixcan (Franklin's Gull)
Larus schistisagus (Slaty-backed Gull)
Larus scopulinus (Silver Gull)
Larus smithsonianus (Arctic Herring Gull)
Larus thayeri (Thayer's gull)
Leucophaeus modestus (Grey gull)
Numenius phaeopus (Whimbrel)
Phalaropus lobatus (Red-necked phalarope)
Pluvialis dominica (American Golden Plover)
Pluvialis squatarola (Grey Plover/Black-bellied Plover)
Rissa tridactyla (Black-legged Kittiwake)
Rynchops niger (Black skimmer)
Scolopax rusticola (Eurasian Woodcock)
Stercorarius antarcticus (Brown skua)
Stercorarius chilensis (Chilean Skua)
Stercorarius parasiticus (Arctic Skua)
Stercorarius skua (Great Skua)
Sterna dougallii (Roseate Tern)
Sterna forsteri (Forster's Tern)
Sterna hirundinacea (South American Tern)
Sterna paradisaea (Arctic Tern)
Sternula albifrons (Little Tern)
Thalasseus acuflavidus (Cabot's Tern)
Thalasseus elegans (Elegant Tern)
Thalasseus maximus (Royal Tern)
Tringa flavipes (Lesser Yellowlegs)
Tringa melanoleuca (Greater Yellowlegs)
Tringa semipalmata (Willet)
Tringa totanus (Common Redshank)
Uria aalge (Common Murre)
Uria lomvia (Thick-billed Murre)
Vanellus chilensis (Southern Lapwing)
Vanellus vanellus (Northern Lapwing)
Xema sabini (Sabine's Gull)
Podicipediformes (n=8)
Aechmophorus occidentalis (Western Grebe)
Podiceps auritus (Horned Grebe)
Podiceps grisegena (Red-necked Grebe)
Podiceps major (Great Grebe)
Podilymbus podiceps (Pied-billed Grebe)
Spilornis cheela (Crested Serpent Eagle)
Spizaetus nipalensis (Mountain hawk-eagle)
Vultur gryphus (Andean condor)*
Cathartiformes (n=2)
Gymnogyps californianus (California Condor)
Sarcoramphus papa (King Vulture)

Phoenicopteriformes (n=2)
Phoenicopterus chilensis (Chilean flamingo)*
Phoenicopterus ruber (American Flamingo)*
Gruiformes (n=7)
Anthropoides virgo (Demoiselle Crane)
Balearica regulorum (Crowned crane)
Fulica americana (American coot)
Fulica armillata (Red-gartered Coot)
Grus canadensis (Sandhill Crane)
Grus leucogeranus (Siberian crane)*
Rallus aquaticus (Water Rail)
Psittaciformes (n=10)
Amazona farinosa (Southern mealy amazon)*
Amazona ochrocephala (Yellow-crowned Parrot)*
Amazona oratrix (Yellow-headed amazon)*
Ara militaris (Military macaw)*
Brotogeris versicolurus (White-winged Parakeet)*
Cyanoliseus patagonus (Burrowing Parrot)
Enicognathus ferrugineus (Austral Parakeet)
Enicognathus leptorhynchus (Slender-billed Parakeet)
Loriculus spp. (Hanging Parrot)*
Pycnonotus zeylanicus (Straw-headed bulbul)*
Falconiformes (n=8)
Caracara cheriway (Northern Crested Caracara)
Caracara plancus (Southern Caracara)
Falco biarmicus (Lanner Falcon)
Falco columbarius (Merlin)
Falco mexicanus (Prairie falcon)
Falco sparverius (American Kestrel)
Falco vespertinus (Red-footed Falcon)
Milvago chimango (Chimango Caracara)
Accipitriformes (n=30)
Accipiter brachyurus (New Britain Sparrowhawk)
Accipiter gularis (Japanese Sparrowhawk)
Accipiter striatus (Sharp-shinned Hawk)
Aquila audax (Wedge-tailed Eagle)
Aquila chrysaetos (Golden Eagle)
Aquila fasciata (Bonelli's eagle)
Aquila rapax (Tawny Eagle)*
Buteo lagopus (Rough-legged Hawk)
Buteo lineatus (Red-shouldered Hawk)
Buteo magnirostris (Roadside Hawk)
Buteo platypterus (Broad-winged Hawk)
Buteo polyosoma (Red-backed Hawk)*
Buteo regalis (Ferruginous Hawk)
Buteo swainsoni (Swainson's Hawk)
Buteogallus urubitinga (Great Black Hawk)
Cathartes aura (Turkey Vulture)
Circus assimilis (Spotted Harrier)
Circus cyaneus (Hen Harrier)
Circus pygargus (Montagu's Harrier)
Coragyps atratus (Black Vulture)
Geranoaetus melanoleucus (Black-chested buzzard-eagle)
Gypaetus barbatus (Bearded vulture)
Gyps africanus (White-backed vulture)*
Haliaeetus pelagicus (Steller's Sea Eagle)
Haliaeetus vocifer (African Fish Eagle)
Milvus migrans (Black Kite)
Milvus milvus (Red Kite)
Pandion haliaetus (Osprey)
Parabuteo unicinctus (Harris's Hawk)
Sagittarius serpentarius (Secretary Bird)
Strigiformes (n=6)
Aegolius acadicus (Northern Saw-whet Owl)
Megascops asio (Eastern Screech Owl)
Megascops choliba (Tropical Screech-owl)
Megascops kennicottii (Western Screech-Owl)
Strix nebulosa (Great gray owl)
Strix varia (Barred owl)
Caprimulgiformes (n=1)
Caprimulgus fossii (Mozambique Nightjar)
Columbiformes (n=2)
Columbina inca (Inca Dove)
Streptopelia turtur (European Turtle-dove)
Piciformes (n=3)
Dendrocopos major (Great spotted woodpecker)
Pteroglossus castanotis (Chestnut-eared aracari)*
Ramphastos cuvieri (white-throated toucan)*
Trogoniformes (n=1)
Harpactes erythrocephalus (Red-headed Trogon)
Passeriformes (n=22)
Agelaius phoeniceus (Red-winged Blackbird)
Carduelis carduelis (European goldfinch)
Carduelis chloris (European Greenfinch)
Corvus brachyrhynchos (American Crow)
Corvus caurinus (Northwestern Crow)
Corvus corone (Carrion Crow)
Corvus monedula (Western Jackdaw)
Corvus ossifragus (Fish Crow)
Cyanocitta cristata (Blue Jay)
Cyanocorax chrysops (Plush-crested Jay)
Garrulus glandarius (Eurasian Jay)
Junco hyemalis (Dark-eyed Junco)
Passer montanus (Eurasian Tree Sparrow)
Phylloscopus trochilus (Willow warbler)
Pica hudsonia (Black-billed Magpie)
Pygochelidon cyanoleuca (Blue-and-white Swallow)
Pyrrhula pyrrhula (Eurasian Bullfinch)
Quiscalus mexicanus (Great-tailed grackle)
Quiscalus quiscula (Common Grackle)
Tachycineta bicolor (Tree Swallow)
Turdus iliacus (Redwing)
Turdus migratorius (American Robin)

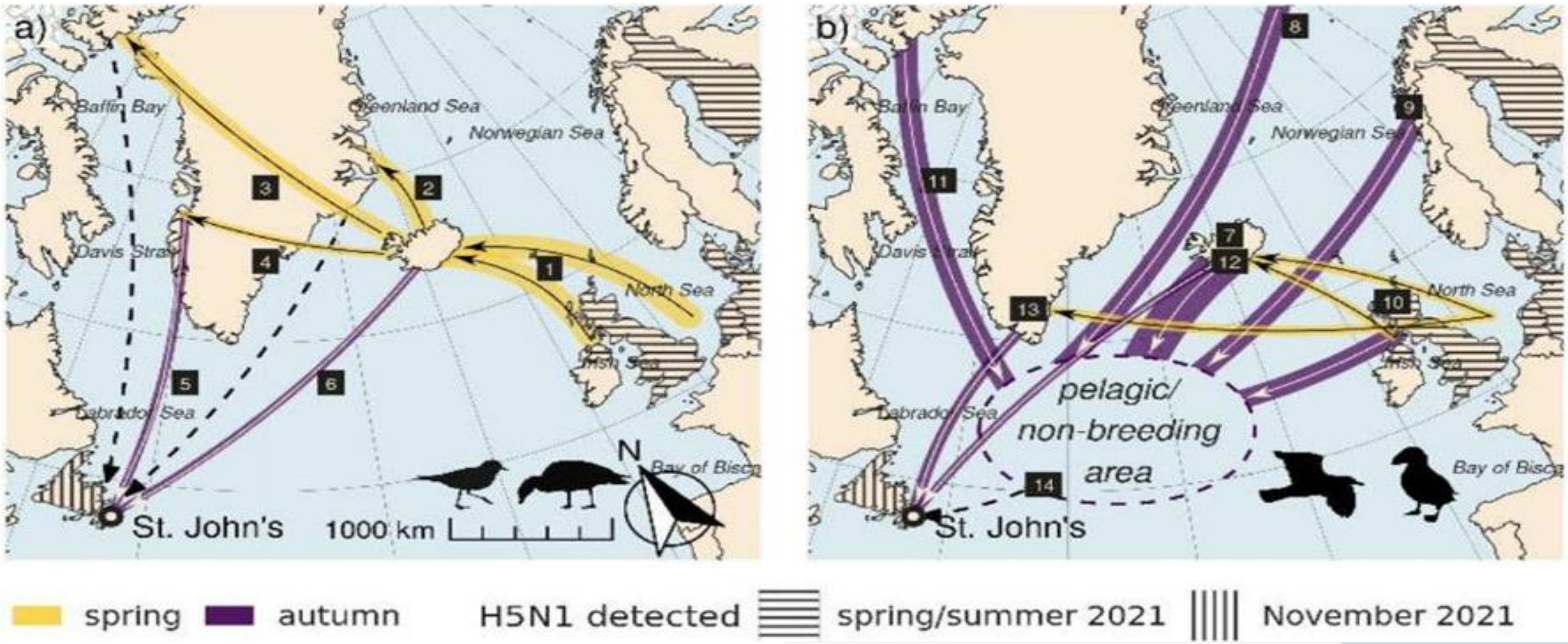
Iterative reassortment drove the emergence and propagation of the H5N1 panzootic



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

Transatlantic transmission

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



viruses
MDPI

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,†], Megan E. B. Jones [3,4], Benjamin C. Mollett [2], Laura Bourque [3], Oliver Lung [1], Joe James [2,5], Carmencita Yason [4], Ashley C. Banyard [2,5], Daniel Sullivan [1], Anthony V. Signore [1], Andrew S. Lang [6], Meghan Baker [7], Beverly Dawe [7], Ian H. Brown [2,5,*] and Yohannes Berhane [1,8,9,*]

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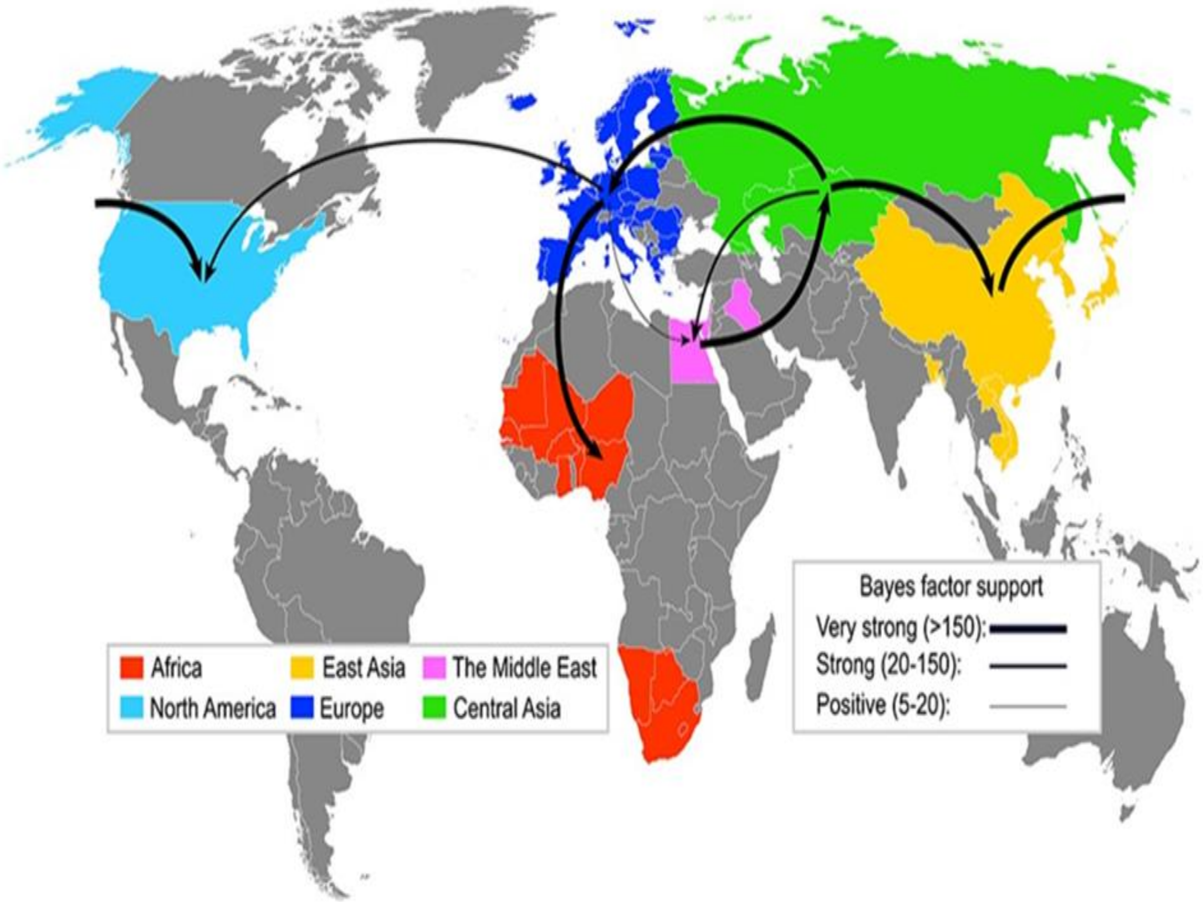
Transatlantic spread of highly pathogenic avian influenza H5N1 by wild birds from Europe to North America in 2021

V. Caliendo[1,16], N. S. Lewis[2,4,16], A. Pohlmann[3,16], S. R. Baillie[11,15], A. C. Banyard[4], M. Beer[3], I. H. Brown[4], R. A. M. Fouchier[1], R. D. E. Hansen[4], T. K. Lameris[14], A. S. Lang[6], S. Laurendeau[7], O. Lung[7], G. Robertson[8], H. van der Jeugd[5], T. N. Alkie[7], K. Thorup[12,13], M. L. van Toor[9], J. Waldenström[9], C. Yason[10], T. Kuiken[1,17] & Y. Berhane[7,17]

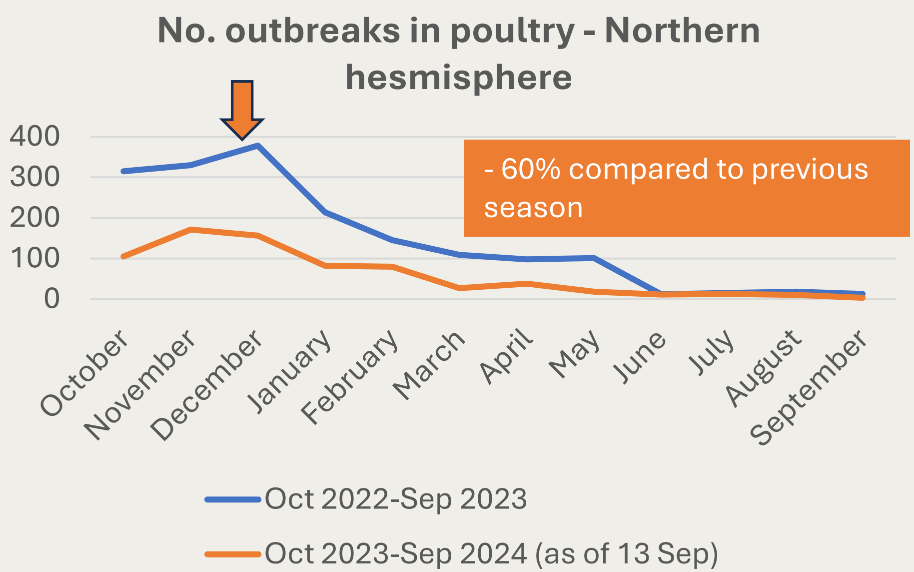
Global migration rates among the geographic regions of clade 2.3.4.4b (2020-2022)

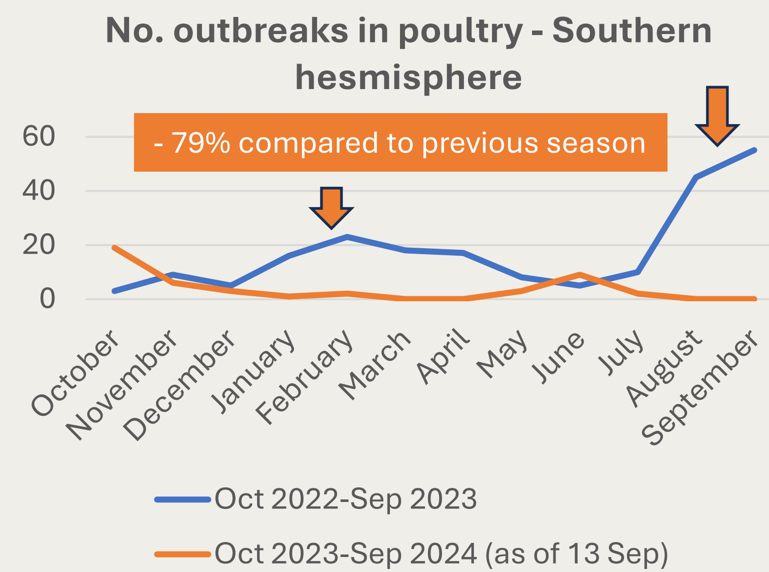


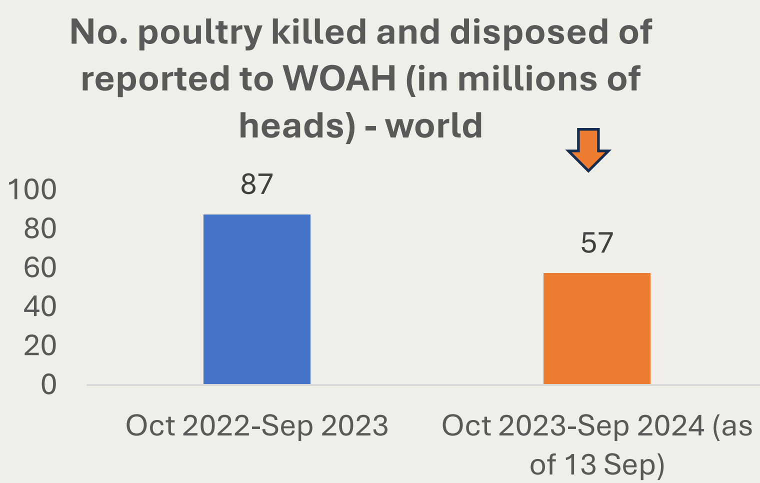
Fusaro et al High pathogenic avian influenza A(H5) viruses of clade 2.3.4.4b in Europe—Why trends of virus evolution are more difficult to predict, Virus Evolution, Volume 10, Issue 1, 2024, veae027, https://doi.org/10.1093/ve/veae027

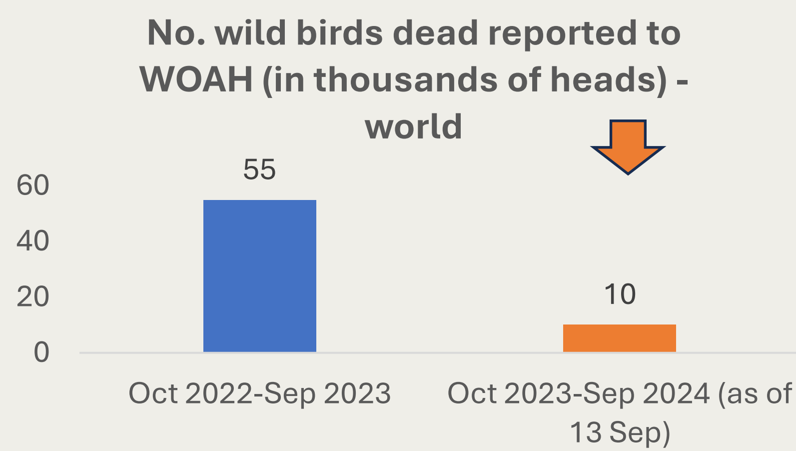
Impacts on biodiversity

Reducing trend of disease burden in last 2 years









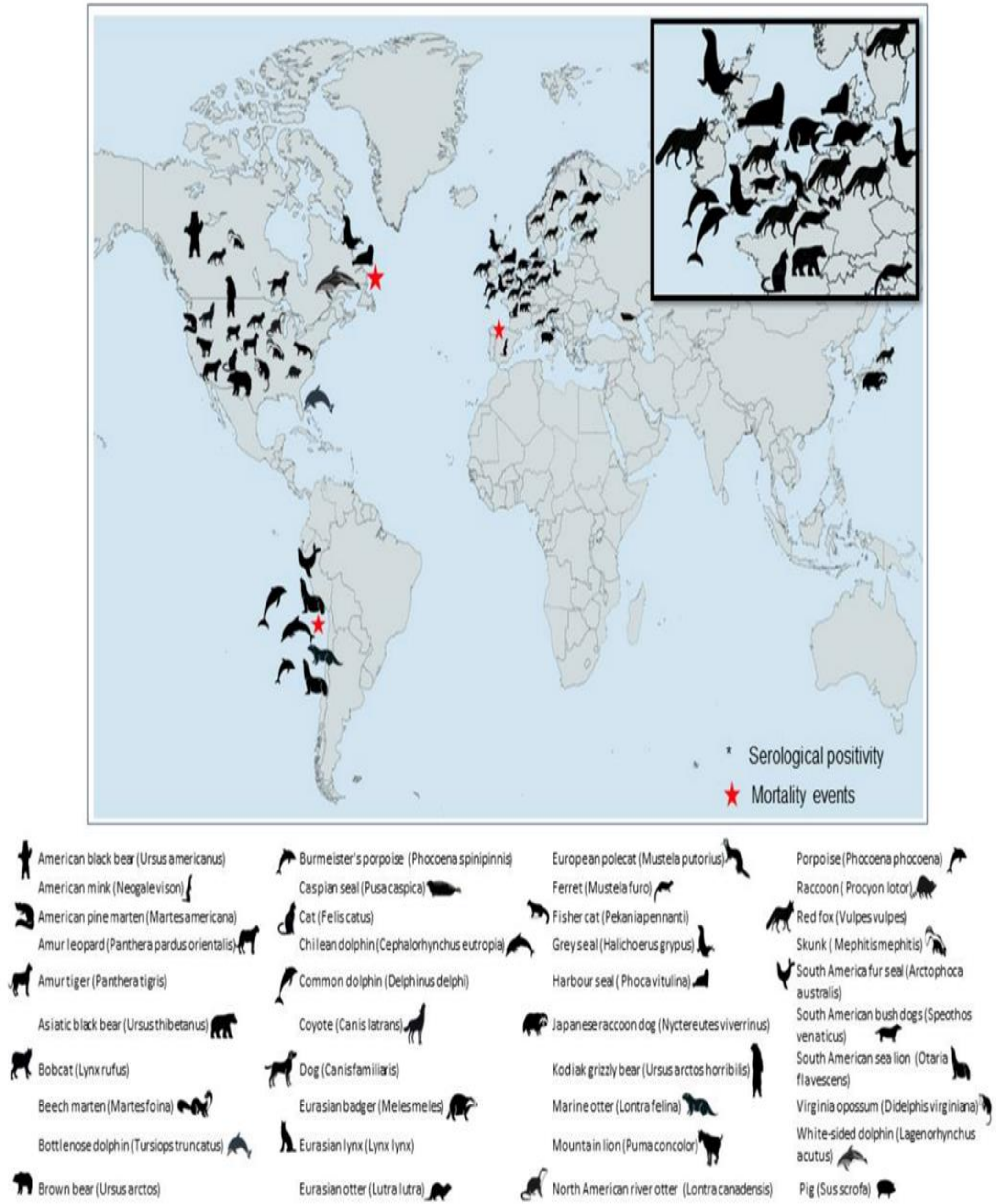
- 34% compared to previous season

- 82% compared to previous season
(caution : many dead birds go undetected & unreported)

Spread to mammals

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

Avian influenza overview March - April 2023



HPAI in mammals - impact on biodiversity

Mass mortality events (biodiversity)

More than **51,000** mammals died in South America (Oct-22 Nov-23)

More than 10,000 dead South American sea lions in Peru

offlu

WOAH FAO

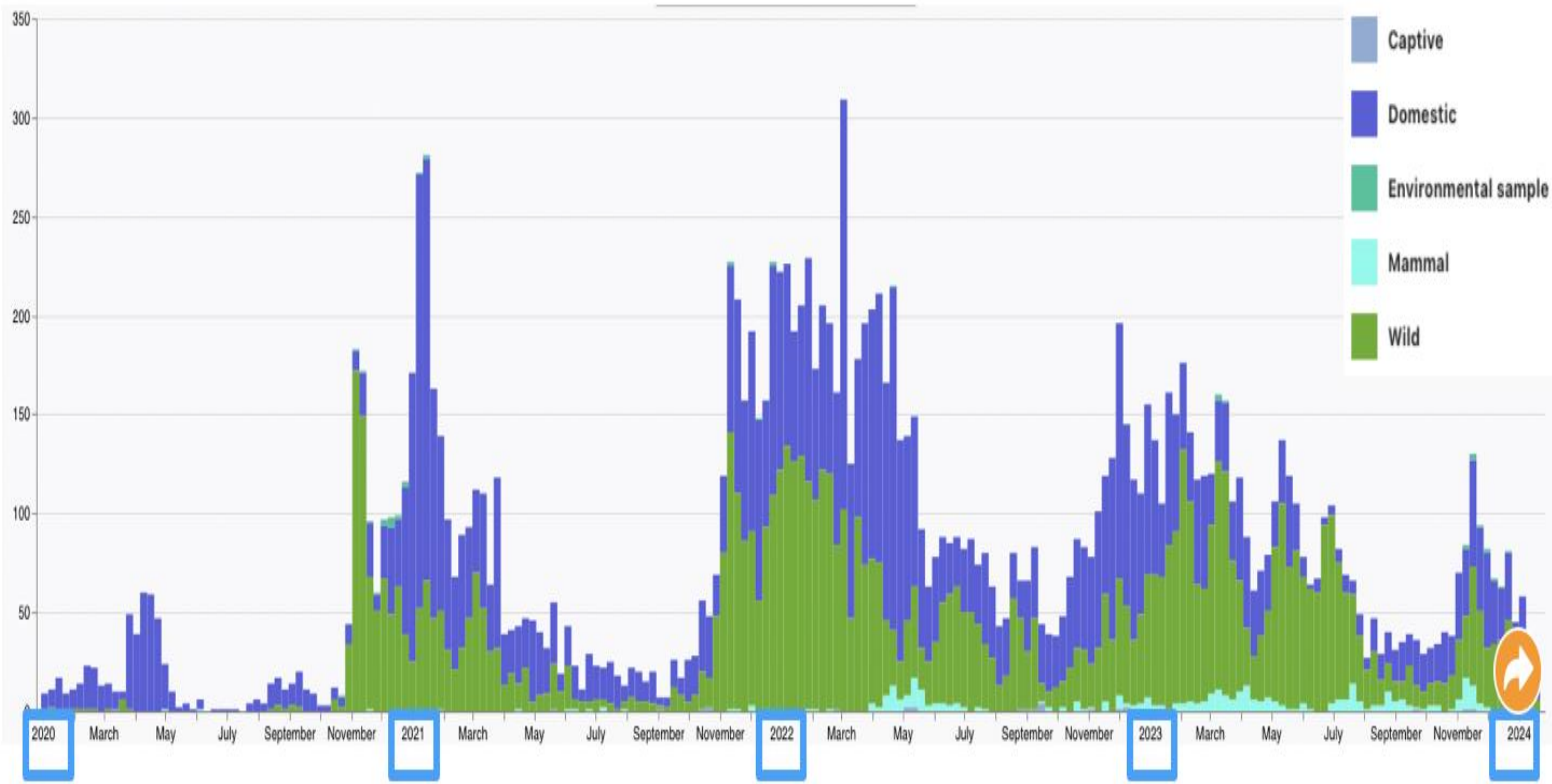
network of expertise on animal influenza

21 December, 2023

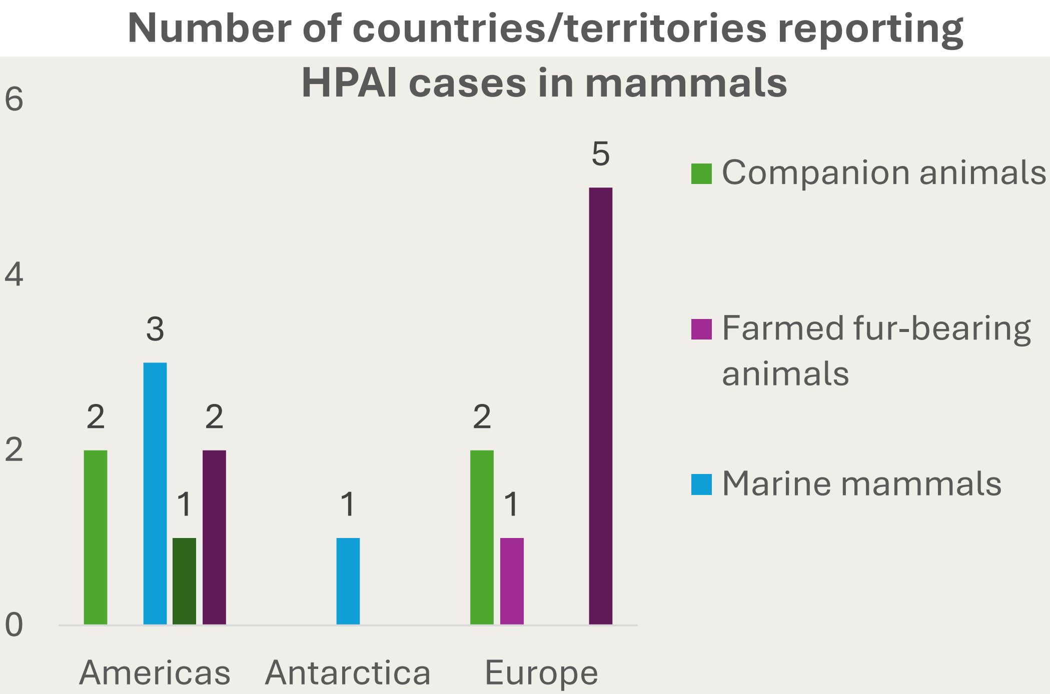
Continued expansion of high pathogenicity avian influenza H5 in wildlife in South America and incursion into the Antarctic region

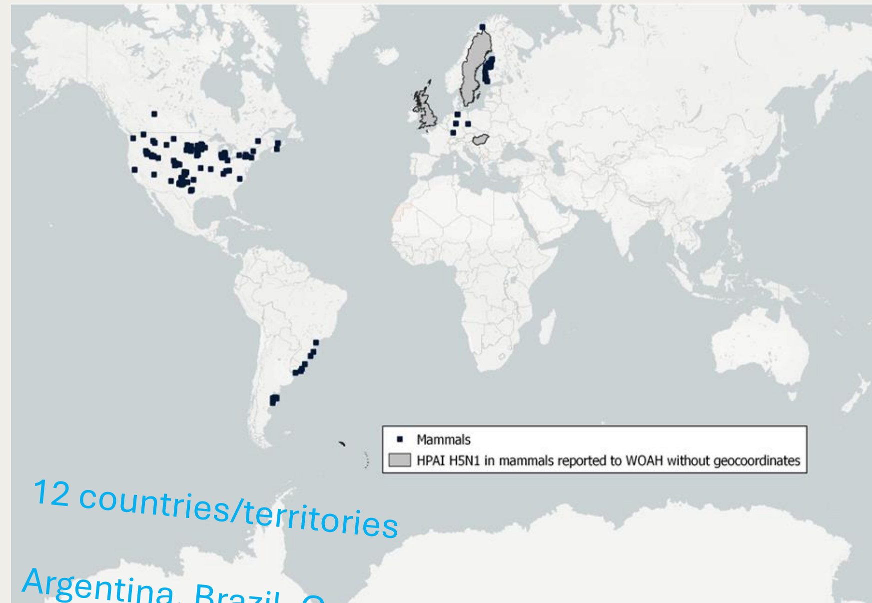
H5 detections: Expanded host range

Timeline of number of outbreaks of HPAI from 2020 to present



Reporting by mammal category October 2023 –September 2024



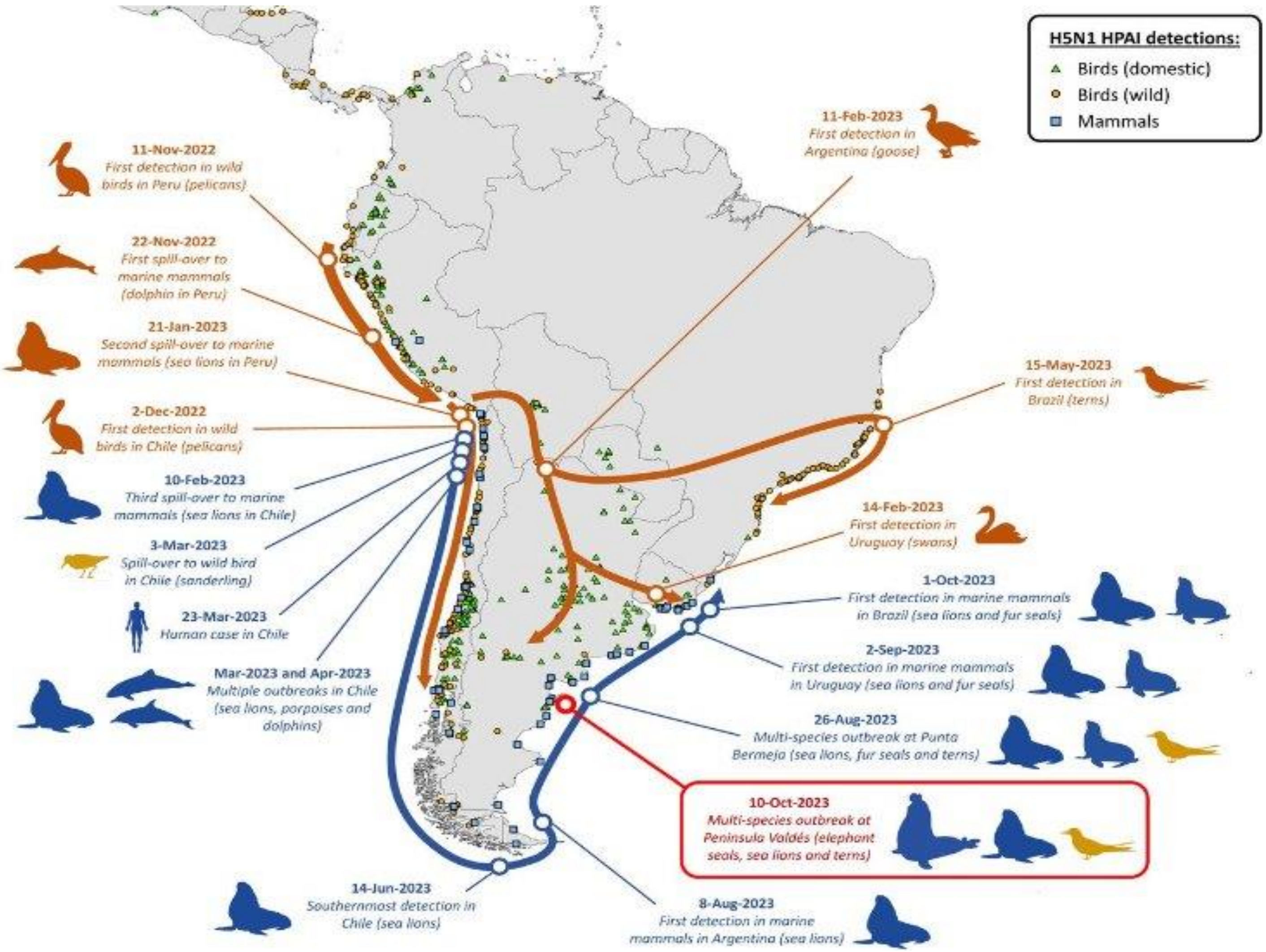


12 countries/territories

Argentina, Brazil, Canada, Finland, Germany, Hungary, Norway, United Kingdom, United States of America, South Georgia, Sweden, Uruguay

- **Companion animals** : cats and dogs
- **Farmed fur-bearing mammals** : 4 species *(American mink, Arctic fox, raccoon dog, sable)*
- **Marine mammals** : 4 species *(Antarctic fur seal, South American fur seal, South American sea lion, Southern elephant seal)*
- **Other domestic mammals** : 3 species *(alpaca, bovine, goat)*
- **Terrestrial wild mammals:** 13 species (e.g. raccoon, red fox, Eurasian otter)

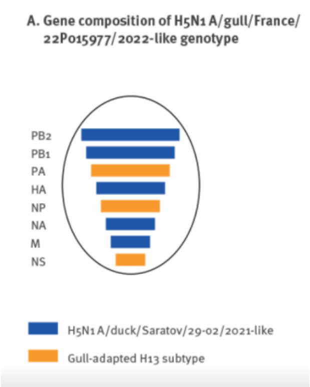
Semi-aquatic mammals in South America
Mammal to mammal transmission

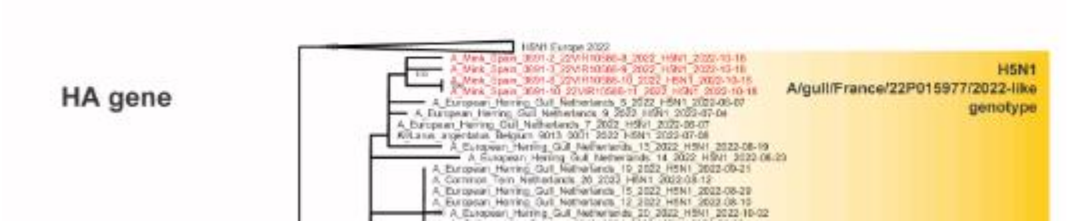


Uhart et al, bioRxiv, 2024

Outbreaks in captive bred mammals

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

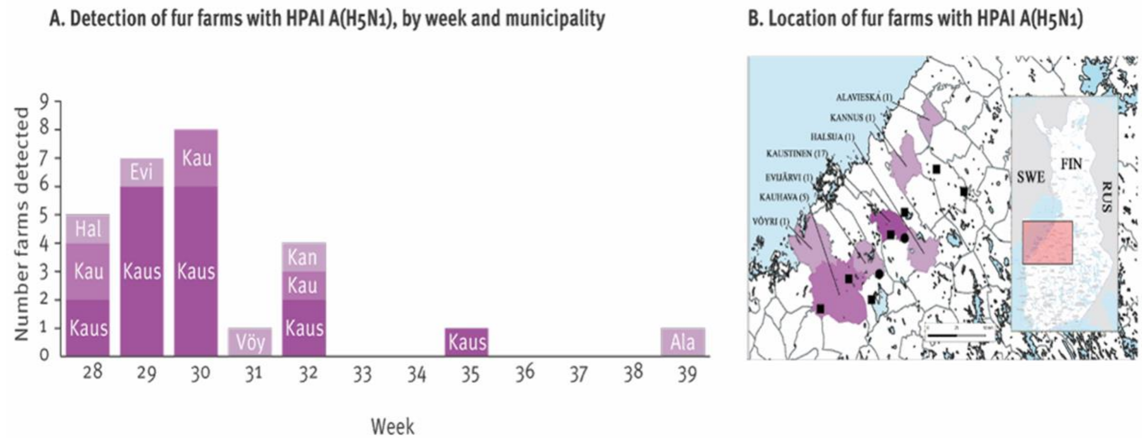




Limited adaptive genetic changes in the virus (T271A in the PB2 gene)

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



- 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 farm workers

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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 Check for updates

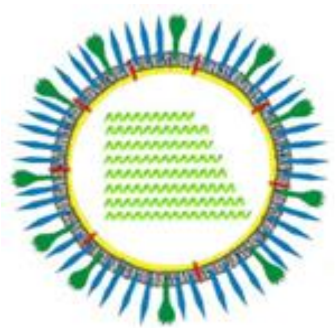
Lauri Kareinen[1], Niina Tammiranta[1], Ari Kauppinen[1], Bianca Zecchin[2], Ambra Pastori[2], Isabella Monne[2], Calogero Terregino[2], Edoardo Giussani[2], Riikka Kaarto[3], Veera Karkamo[1], Tanja Lähteinen[1], Hanna Lounela[1], Tuija Kantala[1], Ilona Laamanen[1], Tiina Nokireki[1], Laura London[1], Otto Helve[4], Sohvi Kääriäinen[4], Niina Ikonen[4], Jari Jalava[4], Laura Kalin-Mänttäri[4], Anna Katz[4], Carita Savolainen-Kopra[4], Erika Lindh[4], Tarja Sironen[5], Essi M Korhonen[5], Kirsi Aaltonen[5], Monica Galiano[6], Alice Fusaro[2], Tuija Gadd[1]

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, contaminated feed or in the milking parlour!
- Captivity die offs ie Large cats in zoos

- Dogs susceptible
- Very infrequent reports

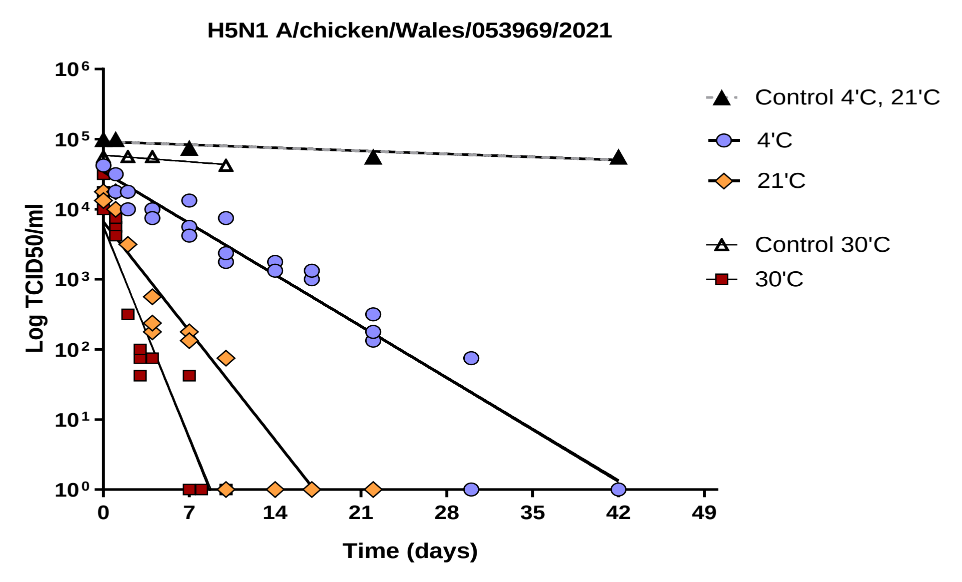
The virus driving the impact!

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

Multiple evolved traits

H5N1 HPAI viruses have enhanced survival kinetics in the environment



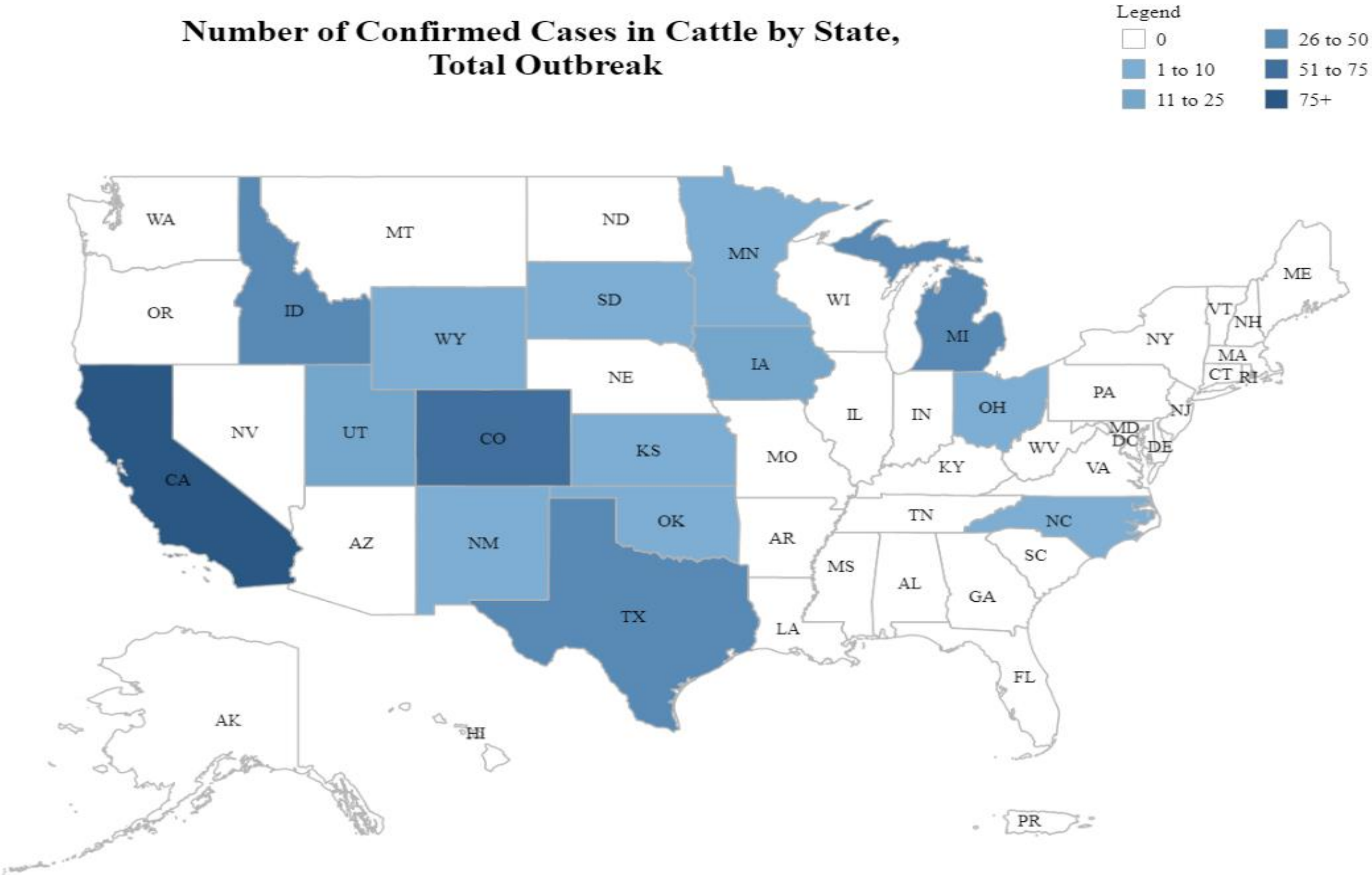
- D_t is time taken in days for a 90% reduction in viral infectivity, (a 1 log_{10} decrease) at temperature t.
- Survival of H5N1-2021 at 4˚C is 43.2 days dose adjusted

- **H5N1-2021 at 4˚C** **D_4 of 9.5 days** (R^2 0.93, to 6 weeks) X=0 at 43.2 days
- **H5N1-2021 at 20˚C** **D_{20} of 4.5 days** (R^2 0.87, to 3 weeks) X=0 at 17.2 days
- **H5N1-2021 at 30˚C** **D_{30} of 2.3 days** (R^2 0.88, to 2 weeks) X=0 at 8.7 days

Warren et al (2024) Assessment of Survival Kinetics for Emergent Highly Pathogenic Clade 2.3.4.4 H5Nx Avian Influenza Viruses. Viruses 2024, 16, 889. https://doi.org/10.3390/v16060889

Spread of H5N1 HPAI to dairy cattle

H5N1 HPAI dairy cattle outbreak 10th March 2024 to present
Cases 492/15 states

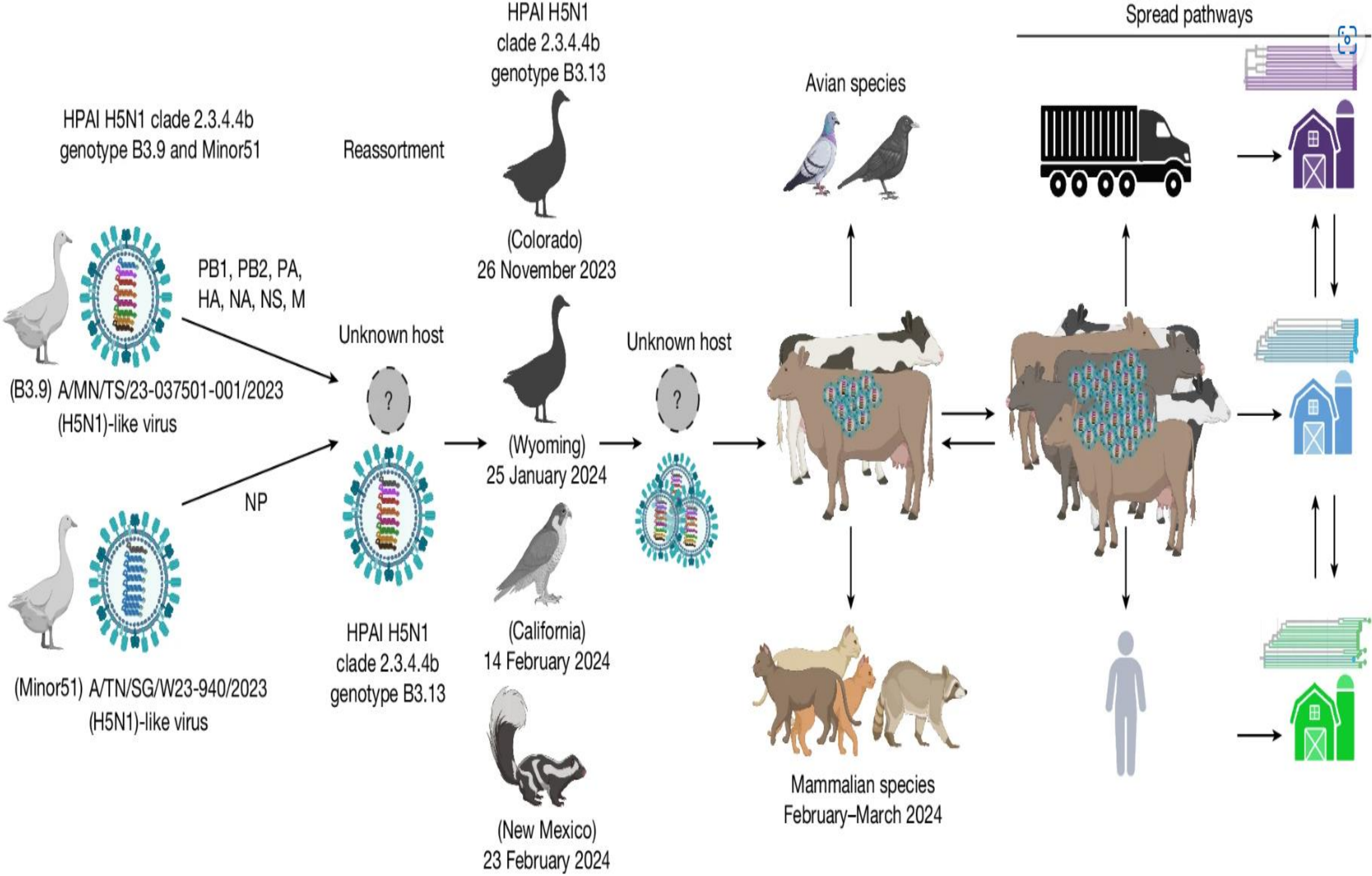


Dairy cattle; infection and epidemiology

- Single spill over of H5N1 HPAI (B3.13 genotype)
- 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
- More in older animals

- Replication largely in mammary gland
- Respiratory infection at best transient

- Spread pathways mechanical ie via fomite, or movement of infected animals but high uncertainties
- Substantial opportunities for human exposure ie in milking parlours
    - 46 human cases in USA since March 24
    - PPE use/compliance limited



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

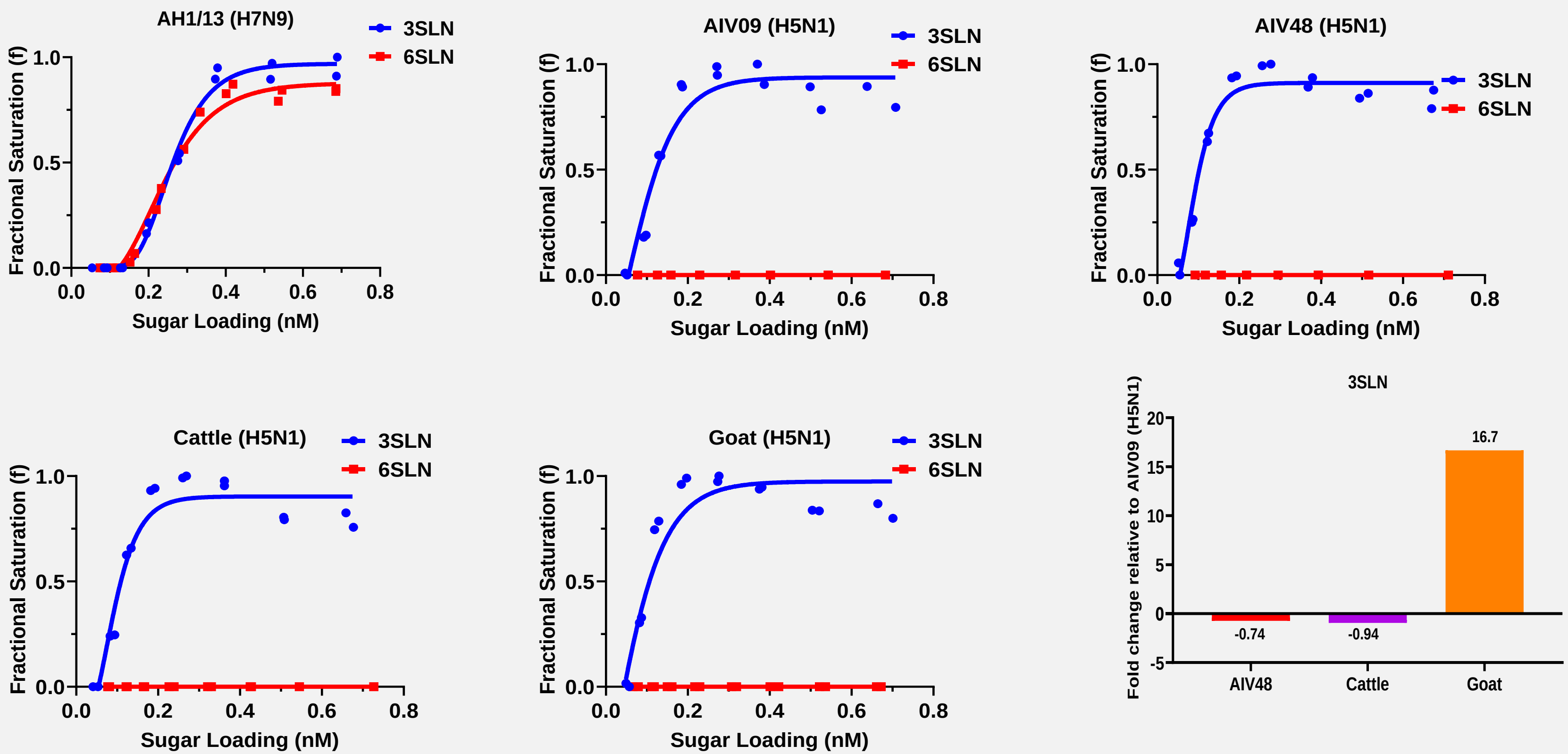
Human case summary associated with dairy cattle epidemic (16/10/24)

State	Cattle	Poultry	Unknown	State Total
California	21	0	0	21
Colorado	1	9	0	10
Michigan	2	0	0	2
Missouri	0	0	1	1
Texas	1	0	0	1
Washington	0	11	0	11
Source Total	**25**	**20**	**1**	**46**

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

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



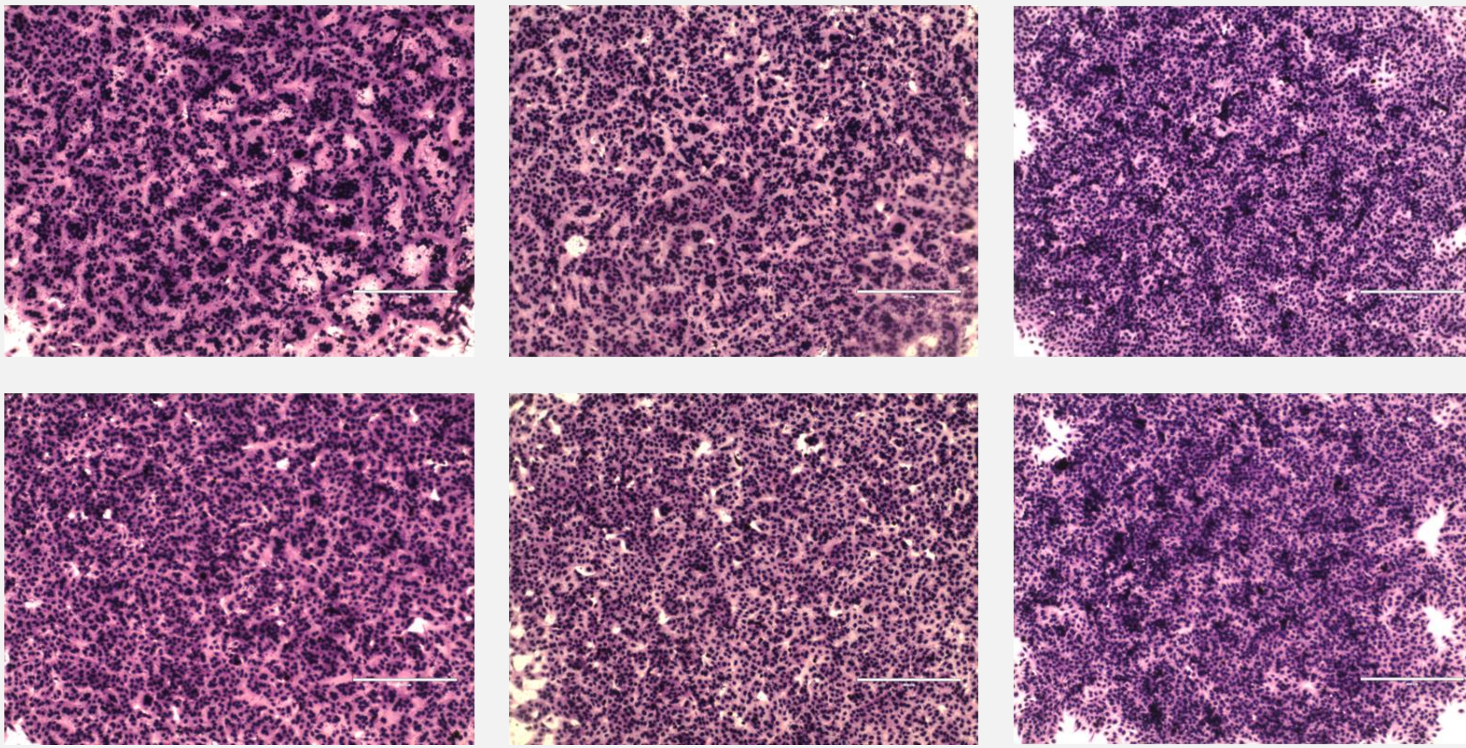
Cattle and goat H5N1 viruses retain affinity for avian-like receptor analogue 3SLN.

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

The Pirbright Institute

pH stability

	Cattle	Goat	Control
pH 5.9			
pH 6.0			



Optimum pH fusion for human cells: <5.5

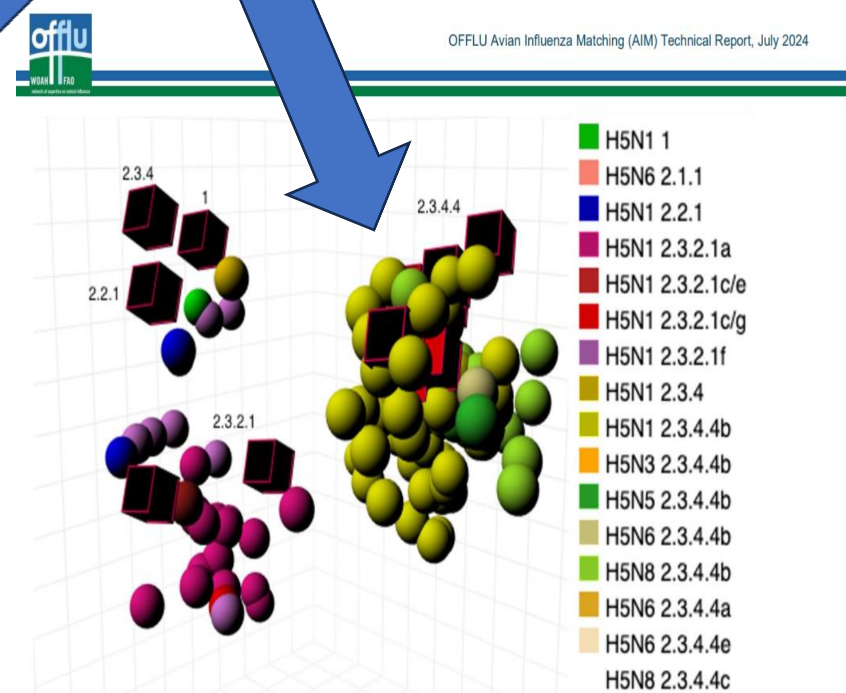
Optimum pH fusion for Avian cells: >5.5

Cattle and goat H5N1 viruses retained avian-like phenotype and showed membrane fusion at pH5.9.

Have the viruses changed antigenically in last two years :relevance for vaccines?

				A/Vietnam/1194/2004/1 A/chicken/Vietnam/C58/04	A/Turkey/turkey/2005 A/swan/Hungary/4999/2006	A/Anhui/1/2005 A/Duck/Anhui/1/2006	A/chicken/Nepal/T360/2014 A/duck/Guangdong/S1322/2010	A/mynah/Indonesia/13064792-010/201[illegible] A/duck/Sukoharjo/BBVW-1428- 9/2012	A/duck/Cambodia/f4k241D3/2021 A/whooper swan/Shanxi/4-1/2020	A/mallard/Georgia/DT09382/2017 A/chicken/ME-2018	A/Mute_Swan/Croatia/102/2016 A/green-winged teal/Egypt/877/2016	A/gyrfalcon/Washington/41088/6/2014 A/Gyrfalcon/WA/41088-6/2014
			Subtype	H5N1	H5N1	H5N1	H5N1	H5N1	H5N8	H5N8	H5N8	H5N[illegible]
Year	Clade	Subtype	Region / Clade	*1*	*2.2*	*2.3.4*	*2.3.2.1a*	2.3.2.1c[1]/g[2]	*2.3.4.4b*	*2.3.4.4b*	*2.3.4.4b*	[illegible]
2023	2.3.2.1a	H5N1	South Asia	4.8	4.8	5.6	3.9	2.7	7.5	6.6	7.2	[illegible]
2023	2.3.2.1a	H5N1	South Asia	6.3	6.4	7.2	5.0	3.8	8.3	7.5	8.0	[illegible]
2023	2.3.2.1a	H5N1	South Asia	5.3	4.8	5.8	2.9	2.3	7.3	6.5	[illegible]	[illegible]
2023	2.3.2.1a	H5N1	South Asia	4.5	3.9	4.8	2.5	1.1	4.9	4[illegible]	[illegible]	4.0
2023	2.3.4.4b	H5N1	Africa	5.1	5.1	5.3	5.5	4.1	1.1	0[illegible]	[illegible]	1.1
2023	2.3.4.4b	H5N1	Africa	5.9	5.9	6.5	5.4	3.3	3.7	3[illegible]	[illegible]	2.8
2023	2.3.4.4b	H5N1	Africa	6.2	5.8	6.1	6.0	5.2	2.0	2[illegible]	[illegible]	2.9
2023	2.3.4.4b	H5N1	Africa	6.0	6.3	6.9	6.0	3.7	4.0	3[illegible]	4.7	2.9
2023	2.3.4.4b	H5N1	Africa	4.8	4.9	5.5	4.3	2.0	4.3	3.5	4.3	3.1
2023	2.3.4.4b	H5N1	Americas	5.1	5.7	6.1	6.0	3.6	4.0	3.3	5.1	2.6
2023	2.3.4.4b	H5N1	Americas	4.7	4.9	5.4	4.8	2.6	3.4	2.6	3.8	2.2
2023	2.3.4.4b	H5N1	Americas	5.0	5.3	5.7	5.7	3.7	2.4	1.7	3.6	1.1
2023	2.3.4.4b	H5N1	Americas	5.2	5.5	5.9	5.8	3.8	2.3	1.7	3.5	1.2
2023	2.3.4.4b	H5N1	Europe	5.0	5.3	5.7	5.5	3.5	2.4	1.7	3.4	1.2
2023	2.3.4.4b	H5N1	Europe	5.1	5.1	5.7	4.9	3.0	2.8	2.1	3.0	1.8
2023	2.3.4.4b	H5N1	Europe	4.7	4.8	5.1	5.3	3.7	1.5	0.7	2.4	0.7
2023	2.3.4.4b	H5N1	Europe	5.5	5.8	6.2	5.9	3.9	2.6	2.0	3.6	1.5
2023	2.3.4.4b	H5N1	Europe	4.9	5.0	5.4	5.2	3.4	2.0	1.3	2.6	1.1
2023	2.3.4.4b	H5N1	Europe	5.1	5.3	5.8	5.2	3.1	3.1	2.4	3.7	1.9
2023	2.3.4.4b	H5N1	Europe	5.0	5.1	5.4	5.6	4.0	1.3	0.6	2.5	0.6
2023	2.3.4.4b	H5N1	Europe	4.9	5.1	5.5	5.2	3.2	2.4	1.7	3.2	1.3
2023	2.3.4.4b	H5N1	Europe	5.0	5.4	5.8	5.6	3.5	2.7	2.0	3.8	1.4
2023	2.3.4.4b	H5N1	Europe	5.1	5.1	5.3	5.5	4.1	1.1	0.6	1.9	1.1
2023	2.3.4.4b	H5N1	Europe	5.1	5.3	5.7	5.6	3.7	2.1	1.4	3.1	1.0
2023	2.3.4.4b	H5N1	Europe	5.3	5.4	5.8	5.2	3.3	2.6	2.0	3.1	1.7
2023	2.3.4.4b	H5N1	Europe	4.5	4.6	4.9	5.2	3.6	1.5	0.7	2.3	0.8
2023	2.3.4.4b	H5N1	South Asia	4.6	4.4	4.9	4.3	2.7	2.6	1.8	2.3	1.8
2023	2.3.4.4b	H5N1	Southeast Asia	4.8	4.4	4.7	4.7	3.9	2.2	1.9	0.9	2.4
2023	2.3.4.4b	H5N1	Southeast Asia	4.9	5.5	5.6	6.2	4.2	2.1	1.5	3.8	0.8
2023	2.3.4.4b	H5N5	Europe	5.6	5.7	6.1	5.5	3.6	2.6	2.0	3.2	1.7

‘Relatively’ stable given established across the world



Multiple clades circulating; antigenic heterogeneity

- Despite transmission between hosts dominant 2.3.4.4b relatively stable
- Host specific adaptive changes not altering antigenic phenotype YET!
- Variation on how each host see's virus antigenically?
- Creates an environment for ease of vaccine strain selection
  - Regional variations
  - Multiple clades = multivalent
- 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

General recommendations

The animal health sector

Biosecurity to reduce spillover or spillback of AI into poultry, livestock value chains and mammals including humans

- Surveillance in wild and domestic birds including whole genome sequencing where economically feasible
- Sensitisation of stakeholders to increase understanding of the risks associated with HPAI
- Emergency preparedness and contingency planning for HPAI including capacity building and fitness for purpose of diagnostic testing

Recommendations

OFFLU urges the scientific community to continue to

- Monitor HPAI events in animals and report to WOAH. Include HPAI in differential diagnosis in non-avian species, including cattle and other livestock populations with high risk of exposure to HPAI viruses.
- Timely deposition and sharing genetic sequence data in publicly available databases in order to monitor viral evolution and potential transmission pathways.
- Coordinate studies to better understand pathogenesis, transmission and adaptation of virus lineages and share the results with OFFLU.
- Provide support to national risk managers.

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 (15 states); vaccination in future?
- H5 HPAI virus evolving with high fitness traits
- Antigenically clade 2.3.4.4b moderately stable

- Vaccination remains an important tool for prevention/control in some countries/regions

Acknowledgements

- OFFLU AIM project team (APHA, IZSVe)
- Ash Banyard, Joe James and Caroline Warren, APHA; Munir Iqbal and Jiayun Yang, Pirbright Institute
- Lina Awada, WOAH for some graphics
- International partners sharing data

Thank you for your attention

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Passion
Reliability
Innovation
Dignity
Excellence

Preventing and controlling viral diseases

Ian.Brown@pirbright.ac.uk

Food and Agriculture Organization of the United Nations | World Health Organization | World Organisation for Animal Health Founded as OIE

Updated joint FAO/WHO/WOAH assessment of recent influenza A(H5N1) virus events in animals and people
Assessment based on data as of 18 July 2024

14 August 2024

Key points
At the present time, based on available information, FAO-WHO-WOAH assess the global public health risk of influenza A(H5N1) viruses to be low, while the risk of infection for occupationally exposed persons is low to moderate depending on the risk mitigation measures in place. Transmission between animals continues to occur and, to date, a limited number of human infections have been reported. Although additional human infections associated with exposure to infected animals or contaminated environments are likely to continue to occur, the overall public health impact of such infections at a global level is minor.

90th General Session World Organisation for Animal Health | World Assembly Paris, 21-25 May 2023 | GS

Resolution 28: Strategic Challenges in the Global Control of High Pathogenicity Avian Influenza

World Health Organization

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Updated joint FAO/WHO/WOAH assessment of recent influenza A(H5N1) virus events in animals and people

14 August 2024 | Emergency Situational Updates

Food and Agriculture Organization of the United Nations | World Organisation for Animal Health Founded as OIE

Global strategy for the prevention and control of highly pathogenic avian influenza (2024-2033)