

USDA Animal and Plant Health Inspection Service U.S. DEPARTMENT OF AGRICULTURE

U.S. HPAI Update (H5 2.3.4.4b)

USDA APHIS VS D&B National Veterinary Services Laboratories, Diagnostic Virology Laboratory SEPTEMBER 2023 Mia Kim Torchetti and Kristina Lantz NVSL.DVL.Heads@USDA.GOV

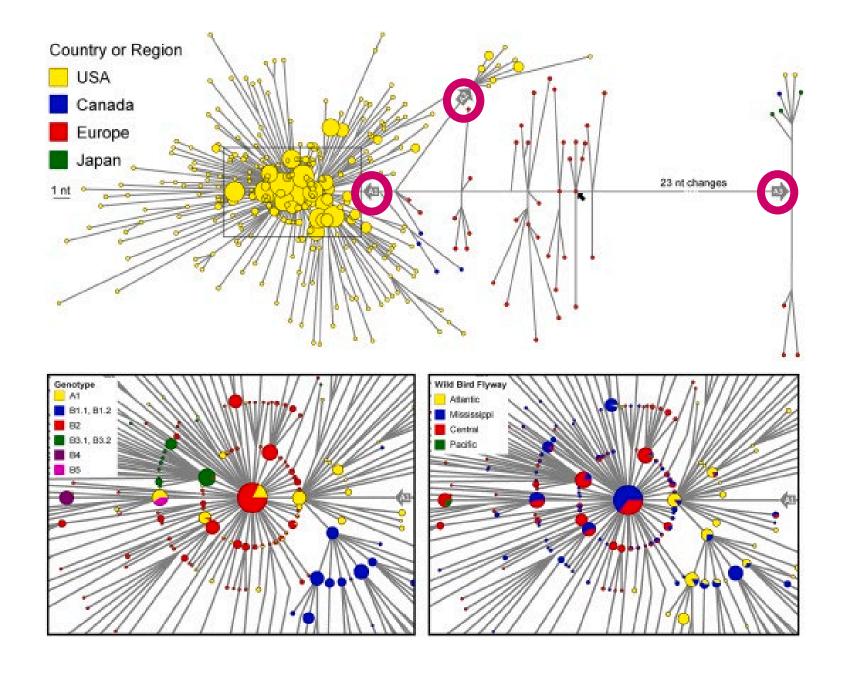
2022-2023 U.S. H5N1 clade 2.3.4.4b Event

Summary

This work is being conducted in collaboration with APHIS Wildlife Services and ARS Southeast Poultry Research Laboratory Near real-time analysis of over 7000 full genome sequences; poultry, mammal, and representative wild bird sequences uploaded to public databases The H5N1 clade 2.3.4.4b genotype A1 was first identified in wild birds collected December 2021. This virus spread across all four flyways and has reassorted with North American (AM) wild bird avian influenza viruses. Several introductions have since been identified: genotype A2 was detected in February 2022 in the northeastern US; A3 was likely introduced via the Pacific flyway April 2022; and three additional introductions have since been identified in wild bird samples collected from October through December of 2022 (A4 via the Pacific flyway in wild birds in Alaska, and A5 and A6 via Atlantic flyway [of note, A6 is a fully Eurasian virus with a reassorted neuraminidase (H5N5)].

Introductions into North American flyways

H5N1 highly pathogenic avian influenza clade 2.3.4.4b in wild and domestic birds: Introductions into the United States and reassortments, December 2021–April 2022 -ScienceDirect

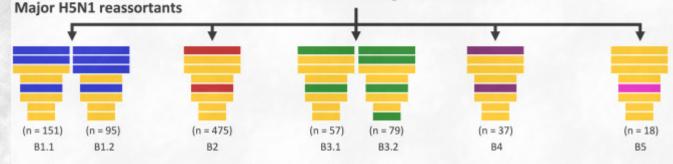


Reassortment of H5N1 2022 (A1) with North American lineage wild bird influenza A viruses

H5N1 highly pathogenic avian influenza clade 2.3.4.4b in wild and domestic birds: Introductions into the United States and reassortments, December 2021–April 2022 -ScienceDirect

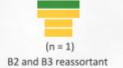
PB2 PB1 PA HA NP NA M NS (n = 395) First Atlantic inbound H5N1 Genotype A1

Reassortment with AM lineage wild birds AIVs



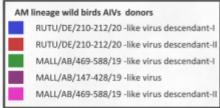
Minor H5N1 reassortants - subsets of the major reassortants





Minor H5N1 reassortants – episodic reassortants

					AM lineage wild b
					RUTU/DE/210
					RUTU/DE/210
					MALL/AB/469
(- 1)	(- 2)	(((n 1)	MALL/AB/147
(n = 1)	(n = 2)	(n = 4) 1 group)	(n = 2) PB2 and NP	(n = 1) Northeastern wild bird AIV-like	MALL/AB/469



Major genotypes as determined by GenoFlu

Genotype				Segm	ent group			
Genotype	PB2	PB1	РА	НА	NP	NA	M	NS
A1	ea1	ea1	ea1	ea1	ea1	ea1	ea1	ea1
B1.1	am1.1	am1.1	ea1	ea1	am1.2	ea1	ea1	ea1
B1.2	am1.1	am1.1	am1	ea1	am1.2	ea1	ea1	ea1
B2	am1.2	ea1	ea1	ea1	am1.1	ea1	ea1	ea1
B3.1	am2.1	ea1	ea1	ea1	am1.4.1	ea1	ea1	ea1
B3.2	am2.1	am1.2	ea1	ea1	am1.4.1	ea1	ea1	am1.1
B4	am2.2	ea1	ea1	ea1	am1.3	ea1	ea1	ea1
B5	ea1	ea1	ea1	ea1	am1.4.2	ea1	ea1	ea1

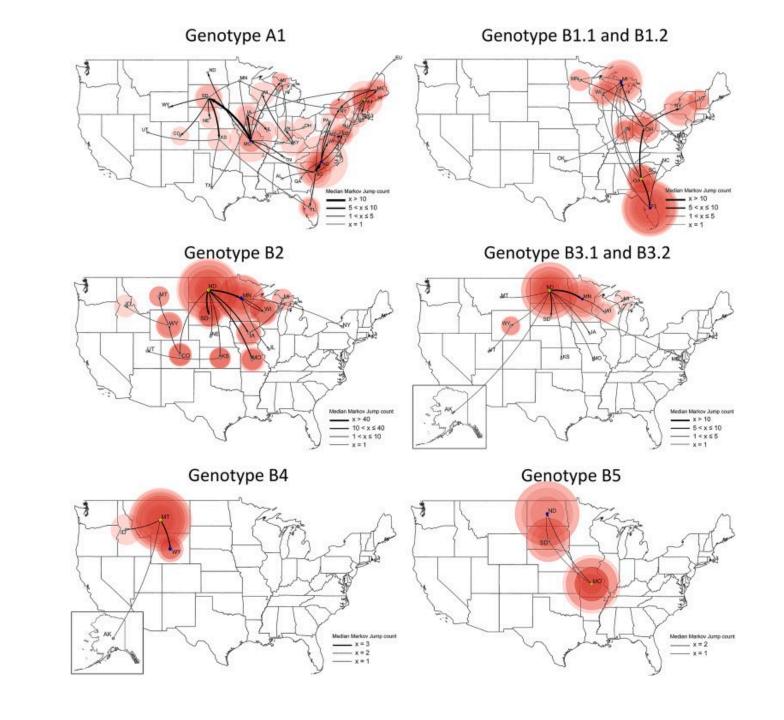
"A" genotypes are unreassorted or fully Eurasian (EA)

"B" genotypes are A1 reassortments with North American (AM) lineage viruses

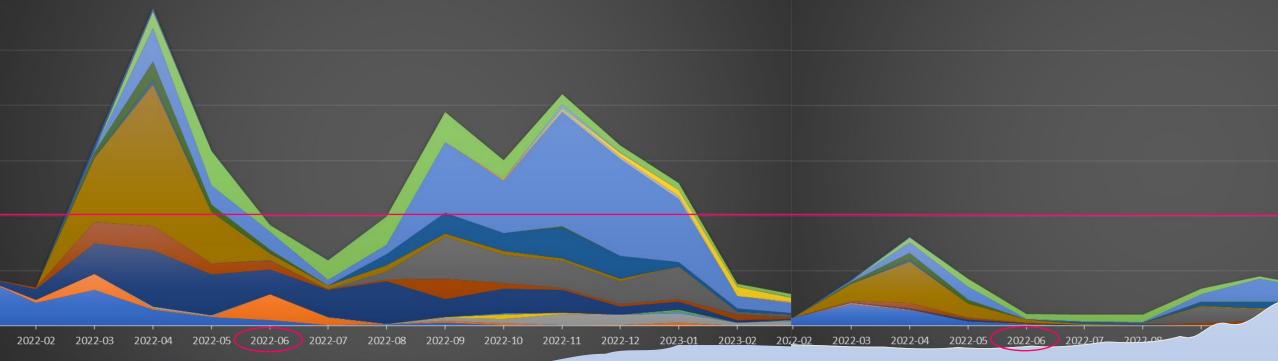
GitHub - USDA-VS/GenoFLU: Influenza data pipeline to automate genotyping assignment

Spatial diffusion of US H5N1 clade 2.3.4.4b viruses by genotype

H5N1 highly pathogenic avian influenza clade 2.3.4.4b in wild and domestic birds: Introductions into the United States and reassortments, December 2021–April 2022 -ScienceDirect



Wild Birds by Genotype



■A1 ■A2 ■A3 ■A4 ■A5 ■A6 ■B1.1 ■B1.2 ■B1.3 ■B2.1 ■B2.2 ■B3.1 ■B3

Mammals by Genotype

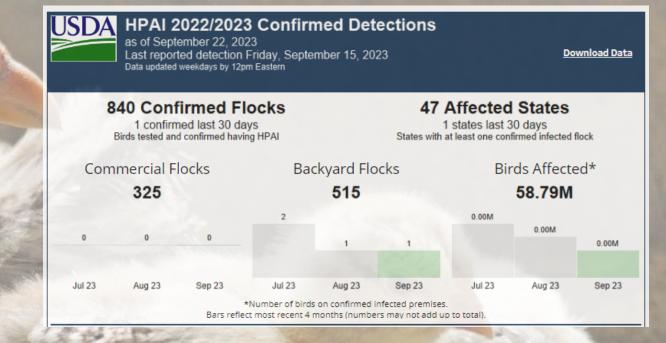
Genotype Distribution December 2021 to May 2023

(same scale across wild birds, poultry and mammals)

Counts are per virus; marker set at 200 viruses

2022-02 2022-03 2022-04 2022-05 2022-06 2022-07 2022-08 2022-09 2022-10 2022-11 2022-12 2023-01 2023-02 2022-02 2022-02 2022-02 2022-02 2022-02 2022-02 2022-02 2022-02 2022-0

Current Status for U.S. Poultry



Choose variable

Choose time period

Birds Affected

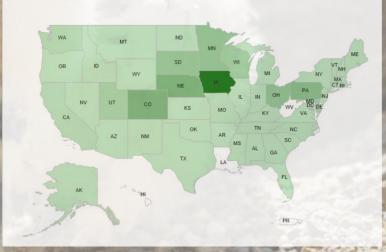
Total Outbreak

Legend



Choose variable

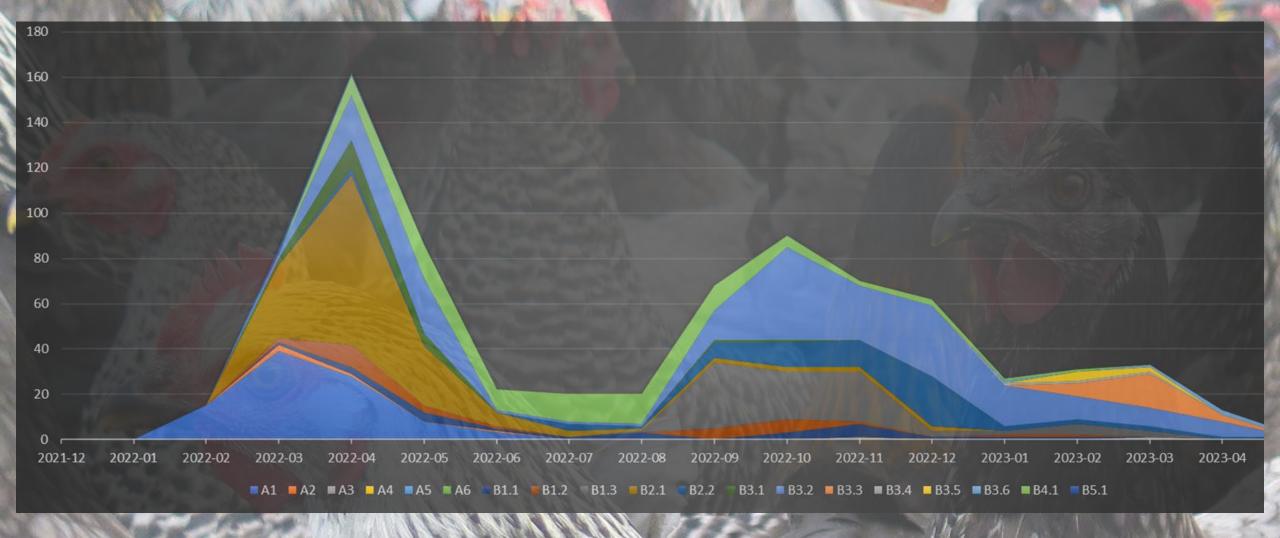
Choose time period



Birds Affected by State

Legend

15,951,72



Genotype Distribution for Poultry December 2021 to May 2023

Genomic analysis

The outcomes of phylogenetic analysis should be interpreted in context of all available virus and epidemiologic information and should not be used directly to infer transmission

- The entire genome is used for analysis (not only HA gene)
- Single Nucleotide Polymorphism (SNP)
 - A single genetic change in the virus, compared to other related viruses
- Ancestral genotype/common ancestor
 - The (often theoretical) virus that is the last common ancestor between two viruses
- Directionality
 - Once a SNP is acquired and fixed in a population it is unlikely to revert
 - Stepwise acquisition of SNPs may indicate directionality (e.g., movement of virus from one population to another)

Independent Introduction Example (at least 83% of U.S. poultry detections) Genotype B3.2 – PB2 PB1 NP NS

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Independent But Related Example Genotype B4 – PB2 NP

HA:517 3/2021_NP:240	PB1:1202 3/2021_NP:556	(39/2020_PB2:1475 MS:570		3/2021_NP:1332 HA:976	M:415	HA:IbII HA:I588	33/2020_PB2:335 PB1:153	PB1:492	HA:1604 HA:490	PA:634	(39/2020_PB2:888 PA:168		M:9 NS:278		.3/2021_NP:425 PB1:726	39/2020_PB2:76	39/2020_ A:1219	HA:1261	(39/2020_PB2:1337 (39/2020_PB2:1467	981:1515	HA:1579 /39/2020 PB2:1737		HA:1078 NA:1202	PA:879	HA:295 NA:815	PB1:663	M:364 3/2021 NP:837		'39/2020_PB2:1113 HA:358	NA:373	NA:902 NA:572	3/2021_NP:705	PA:726 NA:1106		PB1:1368	PA:1409 PB1:1551	39/2020_PB2:1812	9_02.02/65	39/2020_PB2:941	PB1:855	39/2020_PB2:1002	PB1:1416 3/2021 NP:468	NA:419	'39/2020_PB2:2013 PA:1238	PA:1362	PB1:2016 PB1:2142	HA:1678 20-1410	3 o	39/2020_PB2:1011 HA:773	PB1:1062	NA:329 HA:583	
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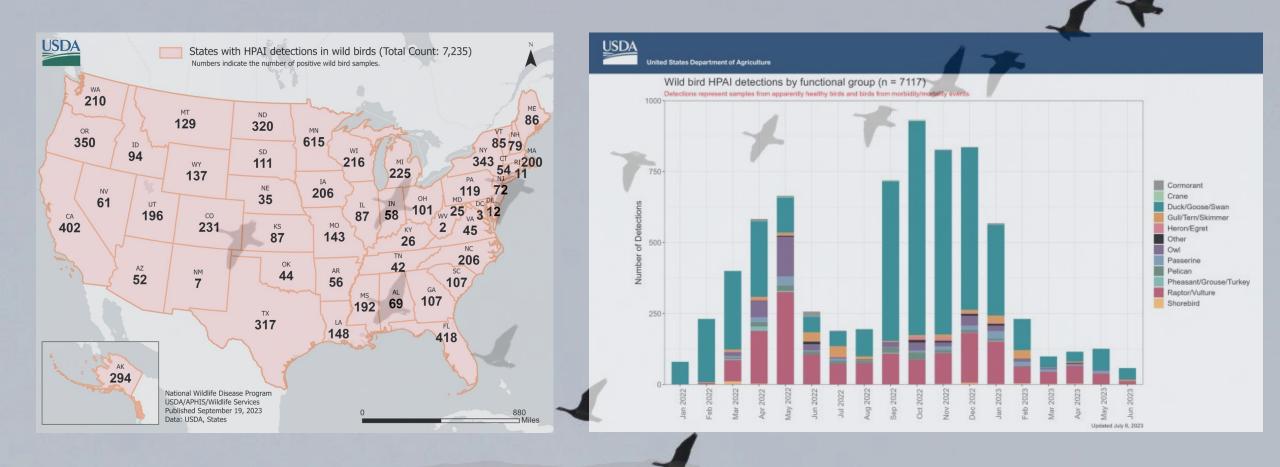
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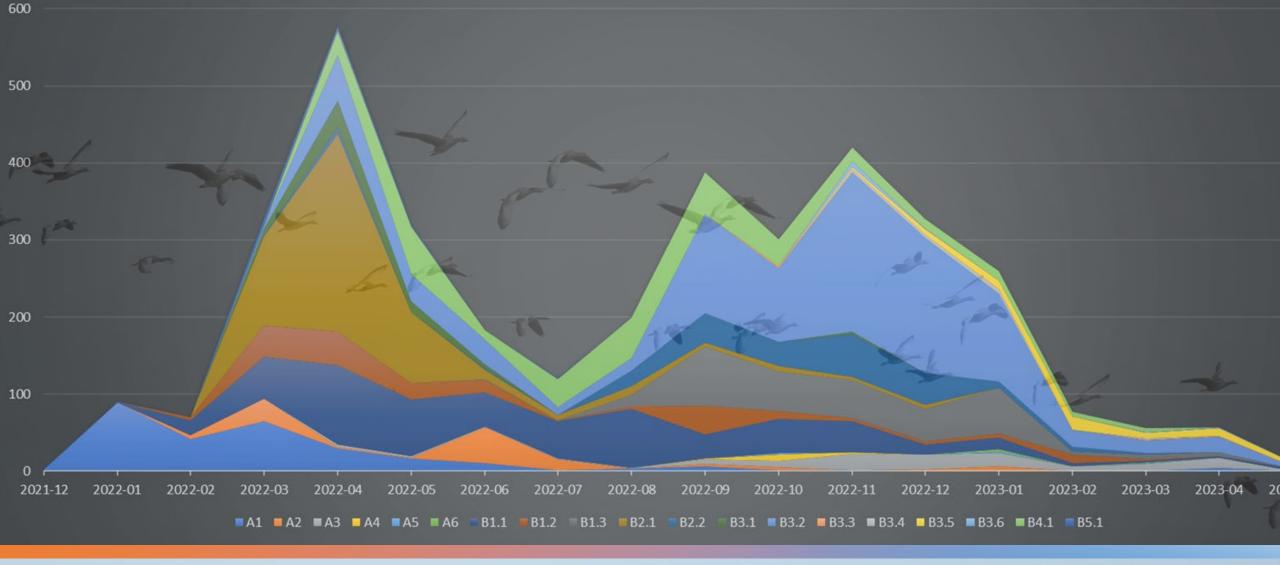
Common Source/ Lateral Transmission Example Genotype B3.3 PB2 PB1 NP NS

- GOLD shaded viruses are closely related to BLUE and RED shaded viruses that are ancestral
 - Three mixed/fixed SNPs in the ancestral viruses are fixed in the GOLD viruses
 - Additionally, there are 2-5 more SNPs in GOLD, moderate diversity may be indicative of longer circulation or a diverse virus source
 - Potential for lateral transmission from either the RED or BLUE premises or a common source to all three

	A A/Fancy_Ck/NL/FAV33/2021_M:853	A/Fancy_Ck/NL/FAV33/2021_HA:687	C C A/Blue-Winged_Teal/Alberta/39/2020_PB2:20	A A AF ancy_Ck/NL/FAV33/2021_PB1:564	A/Blue-Winged_Teal/Alberta/39/2020_PB2:27:	Ο Ο Ο A/Blue-Winged_Teal/Alberta/39/2020_PB2:15	A A MFancy_CK/NL/FAV33/2021_PB1:1773	のののの4453/2021_PA:1272 、	
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Wild Bird Detections (slides courtesy of APHIS-WS)



Genotype Distribution for Wild Birds December 2021 to May 2023

AZ: California Condors Genotype A3

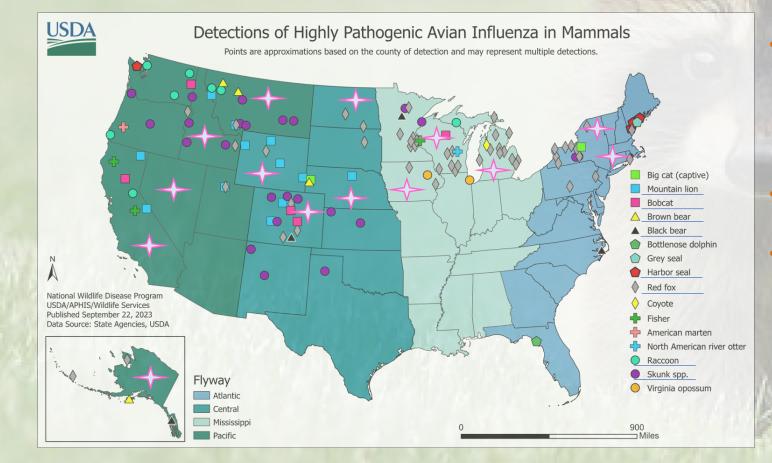
- A3 is fully Eurasian, no AM genes
- Pacific flyway introduction, initially detected in AK
- Spread to lower 48 in fall 2022
- Located on a branch of A3 with other detections in the Southeastern US

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	22-039756-001-2w WILD_BIRD_GHOW_2022-12-05 WY 22-039756-001-3w_WILD_BIRD_GHOW_2022-12-05 WY 23-003666-004_WILD_BIRD_CORA_2023-01-30_MT 23-010132-001_WILD_BIRD_CORA_2023-03-21_CA 23-007052-007_BYF-CHICKEN_2023-03-02_Douglas-01_NV 23-007052-009_BYF-CHICKEN_2023-03-02_Douglas-01_NV 23-007052-005-r_BYF-CHICKEN_2023-03-02_Douglas-01_NV 23-007052-005-r_BYF-CHICKEN_2023-03-02_Douglas-01_NV 23-007052-005-r_BYF-CHICKEN_2023-03-02_Douglas-01_NV 22-040683-006_WILD_BIRD_RTHA_unknown_MT 22-037636-003_WILD_BIRD_AMCR_2022-11-15_WA 22-038528-001_WILD_BIRD_SNGO_2022-10-26_CA 22-041956-001_RACCCON_2022-12-19_Curry_OR 22-041956-001_RACCCON_2022-12-19_Curry_OR 22-034430-001_WILD_BIRD_BAEA_2022-10-09_CO 23-000337-001_WILD_BIRD_RTHA_2023-01-03_WY 23-000337-001_WILD_BIRD_RTHA_2023-01-03_WY 23-0005384-001_WILD_BIRD_RTHA_2023-01-03_WY 23-0005384-001_WILD_BIRD_RTHA_2023-01-03_WY 23-001191-001_California-Condor_2023-03-27_AZ 23-010191-001_California-Condor_unknown_AZ 22-034931-001_WILD_BIRD_BAEA_2022-11-28_CO 23-010191-001_California-Condor_unknown_AZ 22-031916-001_WILD_BIRD_BAEA_2022-10-01_AK 22-031916-001_WILD_BIRD_GLGU_Unknown_AK 22-013831-001_WILD_BIRD_BAEA_2022-01-01_AK 22-031916-001_WILD_BIRD_GLGU_Unknown_AK
L PB2:2152 PB1:2580 L PB1:2580 L PA:189 L PA:181 L PA:185 L PB2:1787 L PA:185 L PB2:1787 L PA:185 L PB2:1185 L NA:209 L NA:201	LP3288 LP3288 LP3288 LP3288 LP4263 LP4268 LP41366 LP41366 LP41368 LP42064 LP42064 LP42064 LP4278 LP42859 LP4285555 LP42855555 LP4285555555 LP428555555555555555555555555555555555555

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23-000337-001_WILD_BIRD_HAWK_2022-12-29_WY	A	т	т	GT	Δ	Δ	C I		T	c	T	Δ Δ	Ċ	G	G	АТ	G	G	s c	c	Δ	ст	· c	Ť	Δ	36	ς Α	G	c	Δ 4	A C	T	T	G	A 4	c	c	G	ΔΔ	Δ	c
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23-010191-001 California-Condor 2023-03-27 AZ	G		C	ΔΔ	G	-	A	A C	C	т	c	GC	т	G	G	A T	G	G	G C	C	Δ	CI	C	т	A		G	Δ	T	G	-	c	C	A	G d		Δ	Δ	GG	G	Δ
23-010194-001_California-Condor_unknown_AZ	G		C	ΔΔ	G	-	A	A C	C	T	C	GO	T	G	G	A T	G	G	G C	c	A	СТ	- C	т	A	3 6	G	A	т	G	а т		c	A	G C	A	Δ	Δ	GG	G	С
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Mammal Detections (Sept 2023)

USDA APHIS | 2022-2023 Detections of Highly Pathogenic Avian Influenza

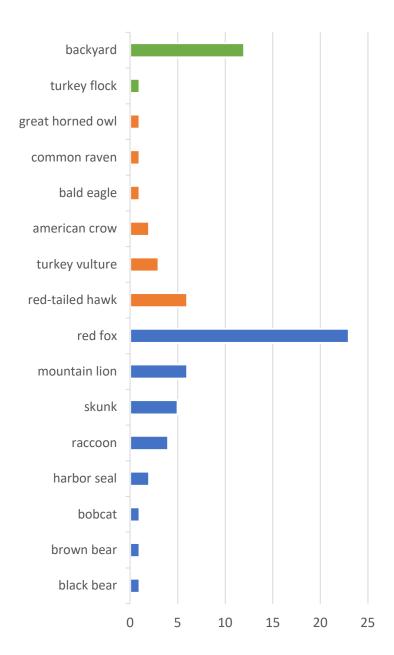


- Over **200** animals across **18** species (terrestrial and marine) in **26** states have been confirmed including a Florida dolphin that was collected in March 2022.
- The confirmations include several domestic/outdoor cats in 3 states.
- A molecular marker (E627K) previously associated with adaptation in mammals has been identified in ~19% (37/200) across all 4 flyways and multiple genotypes. NVSL continues to monitor viruses for known mammalian mutations.

E627K detections

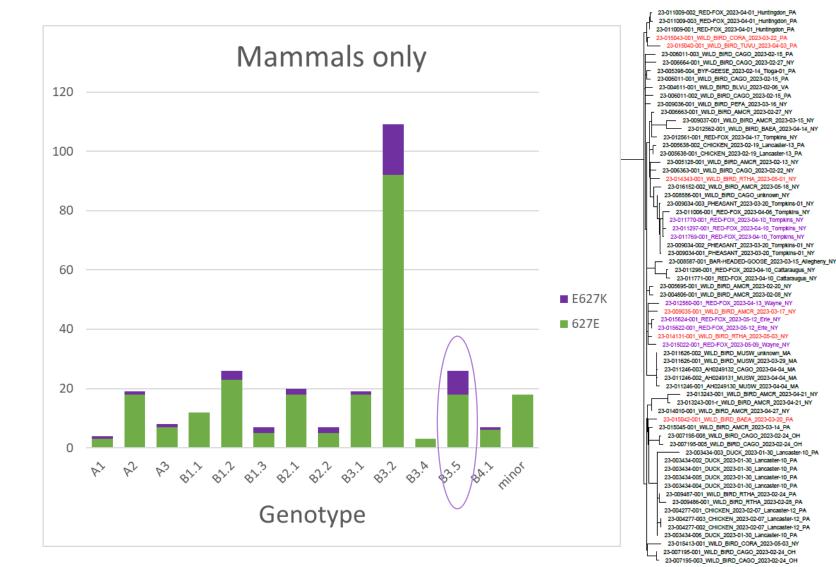
Findings span all four flyways, & represent multiple species and genotypes

- 12 backyard findings and one turkey flock across 10 states and several genotypes; no evidence of onward transmission
- Wild bird species affected are those that may predate or scavenge on small mammals
- Red fox are most frequently detected and also the most frequently sampled (nearly half of all mammals)
- D701N rare detections in pheasants, raptors, and single detections in cat, fox, mountain lion, and captive leopard



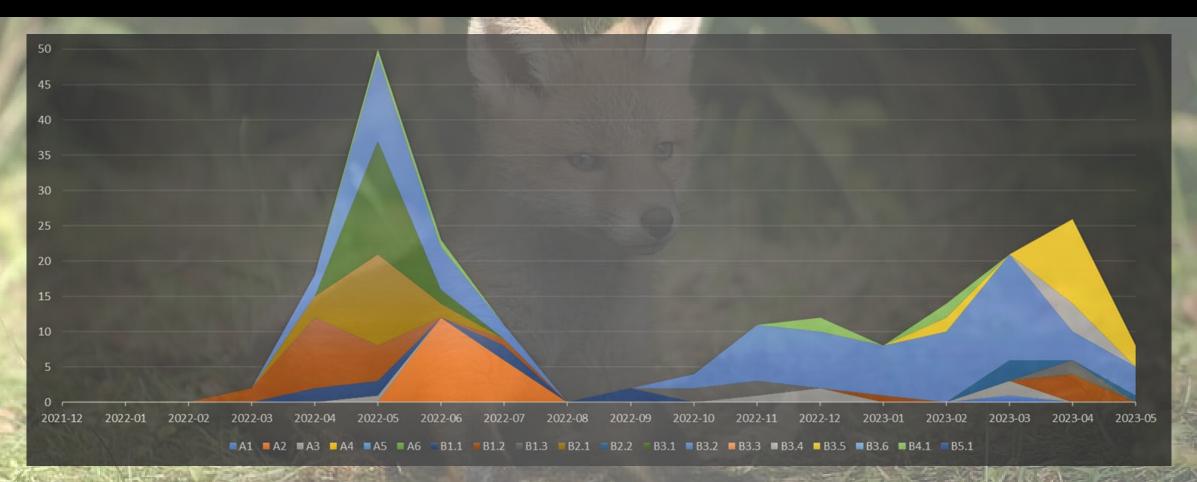
Genotype B3.5 Example

Spontaneous emergence of E627K



Mammal E627K Wild Bird E627K No E627K

Genotype Distribution for Mammals December 2021 to May 2023



2mail



Acknowledgments



- We are grateful for the dedicated people and institutions working hard to combat this virus including the DVL team!
- Many thanks to our NAHLN and state partners as well as other academic institutions and states that continue to contribute to surveillance in wildlife.
- This analysis is possible thanks to our collaboration with Wildlife Services, ARS Southeast Poultry Research Laboratory, and our colleagues at the Center for Epidemiology and Animal Health.











World Organisation for Animal Health ounded as OIE

