Istituto Zooprofilattico Sperimentale delle Venezie

The 2024-2025 clade 2.3.4.4b epidemic wave - a genetic overview -

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20th November 2025

Genetic diversity, 2020-2025

W1 - 2020-2021

	PB2	PB1	PA	HA	NP	NA	MP	NS
A	20	20	20	20	20	20	20	20
B	35	28	1	20	1	30	20	20
C	1	1	1	20	1	1	20	1
D	20	20	20	20	20	27	20	20
E	20	20	29	20	20	27	20	20
F	27	20	29	20	37	27	20	20
G	31	31	32	20	12	17	20	1
H	20	31	29	20	27	63	20	20
I	25	14	25	20	26	13	20	28
J	31	23	5	20	26	2	20	28
L	25	1	1	20	1	13	20	1
M	20	20	14	20	20	20	20	20
N	12	33	20	20	36	64	20	20
O	20	29	14	20	20	20	20	20
P	31	23	3	20	26	2	20	28
Q	20	20	20	20	26	20	20	20
R	20	20	29	20	56	27	20	20
S	20	20	29	20	20	20	20	20
V	34	1	1	20	1	1	20	1
X	20	9	14	20	16	61	20	20

W2 - 2021-2022

	PB2	PB1	PA	HA	NP	NA	MP	NS
A	20	20	20	20	20	20	20	20
C	1	1	1	20	1	1	20	1
I	25	14	25	20	26	13	20	28
AA	1	1	1	20	26	1	20	1
AB	31	1	3	20	38	1	20	1
AC	4	1	1	20	1	1	20	1
AD	4	27	1	20	31	1	20	1
AE	4	1	1	20	54	1	20	1
AF	12	6	1	20	50	1	20	29
AG	12	1	1	20	50	1	20	1
AH	12	1	1	20	1	1	20	1
AI	7	1	8	20	37	1	20	29
AJ	10	1	1	20	1	1	20	1
AK	10	1	3	20	38	1	20	1
AL	1	1	1	20	11	1	20	1
AM	1	1	1	20	12	1	20	1
AN	31	1	1	20	1	1	20	1
AO	13	1	1	20	38	1	20	1
AP	45	31	32	20	32	1	20	28
AQ	31	1	8	20	37	1	20	27
AR	1	18	14	20	16	62	16	27
AS	1	1	3	20	38	1	20	1
AT	12	1	1	20	37	1	20	1
AU	19	1	14	20	21	22	20	1
AV	1	1	3	20	1	1	20	1
AW	4	23	1	20	11	1	20	27
AX	31	1	1	20	38	1	20	1
AY	31	1	24	20	38	1	20	1
AZ	1	31	1	20	12	1	20	1
BA	13	1	1	20	1	1	20	1
BB	31	1	43	20	43	1	20	43
BC	45	1	43	20	37	1	20	27
BD	31	31	8	20	26	1	20	1
BE	4	1	14	20	26	1	20	1
BF	13	1	1	20	11	1	20	1

W3 - 2022-2023

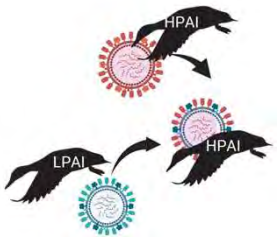
	PB2	PB1	PA	HA	NP	NA	MP	NS
C	1	1	1	20	1	1	20	1
I	25	14	25	20	26	13	20	28
AB	31	1	3	20	38	1	20	1
AF	12	6	1	20	50	1	20	29
BB	31	1	43	20	43	1	20	43
CA	31	1	3	20	16	1	16	1
CB	32	1	3	20	38	1	20	1
CC	12	1	8	20	38	1	20	1
CD	31	1	3	20	37	1	20	29
CE	44	1	3	20	38	1	20	1
CF	31	1	3	20	X	1	20	1
CG	4	1	3	20	26	1	20	1
CH	31	1	3	20	26	1	20	1
CI	10	1	12	20	38	1	20	1
CJ	46	6	32	20	26	22	47	1
CK	4	1	3	20	38	1	20	1
CL	31	1	48	20	38	1	20	1
CM	31	49	3	20	38	1	20	1
CN	31	31	3	20	26	1	20	1
CP	31	31	3	20	38	1	20	1
CQ	31	1	3	20	37	1	20	1
CR	31	1	3	20	38	1	20	28
CS	34	1	3	20	38	1	20	51
CU	xxxx	29	xxxx	20	37	1	20	27

W4 - 2023-2024

	PB2	PB1	PA	HA	NP	NA	MP	NS
AB	31	1	3	20	38	1	20	1
AF	12	6	1	20	50	1	20	29
BB	31	1	43	20	43	1	20	43
CH	31	1	3	20	26	1	20	1
CK	4	1	3	20	38	1	20	1
I	25	14	25	20	26	13	20	28
DA	4	52	3	20	38	1	20	27
DB	31	53	3	20	38	1	20	1
DC	41	53	32	20	36	1	20	1
DD	41	1	3	20	26	1	20	56
DE	41	53	3	20	26	1	20	56
DF	4	52	3	20	50	1	20	27
DG	57	1	14	20	38	1	20	1
DH	4	52	3	20	11	1	20	27
DI	14	14	3	20	38	1	20	27
DJ	31	52	3	20	26	1	20	58
DK	4	1	12	20	26	1	20	1
DL	31	1	1	20	38	1	20	1
DM	31	52	3	20	11	1	20	27
DN	4	60	3	20	26	1	20	27
DO	57	1	14	20	26	1	20	1
DP	31	1	65	20	26	1	20	1
DQ	31	1	14	20	38	1	20	1
DR	57	53	3	20	16	1	20	27
DS	57	53	3	20	16	66	20	27
DT	31	43	43	20	43	1	20	43

W5 - 2024-2025

	PB2	PB1	PA	HA	NP	NA	MP	NS
BB	31	1	43	20	43	1	20	43
DI	14	14	3	20	38	1	20	27
I	25	14	25	20	26	13	20	28
DA	4	52	3	20	38	1	20	27
AF	12	6	1	20	50	1	20	29
DT	31	43	43	20	43	1	20	43
EA	4	14	3	20	38	1	20	27
EB	31	14	3	20	11	1	20	29
EC	14	52	3	20	38	1	20	27
ED	14	31	3	20	38	1	20	27
EE	14	14	3	20	26	1	20	27
EF	14	14	3	20	54	1	20	27
EG	4	14	3	20	11	1	20	27
EI	31	14	3	20	38	1	20	27
EJ	14	52	3	20	59	1	20	27
EK	14	55	3	20	38	1	20	27
EL	41	53	43	20	26	1	20	43



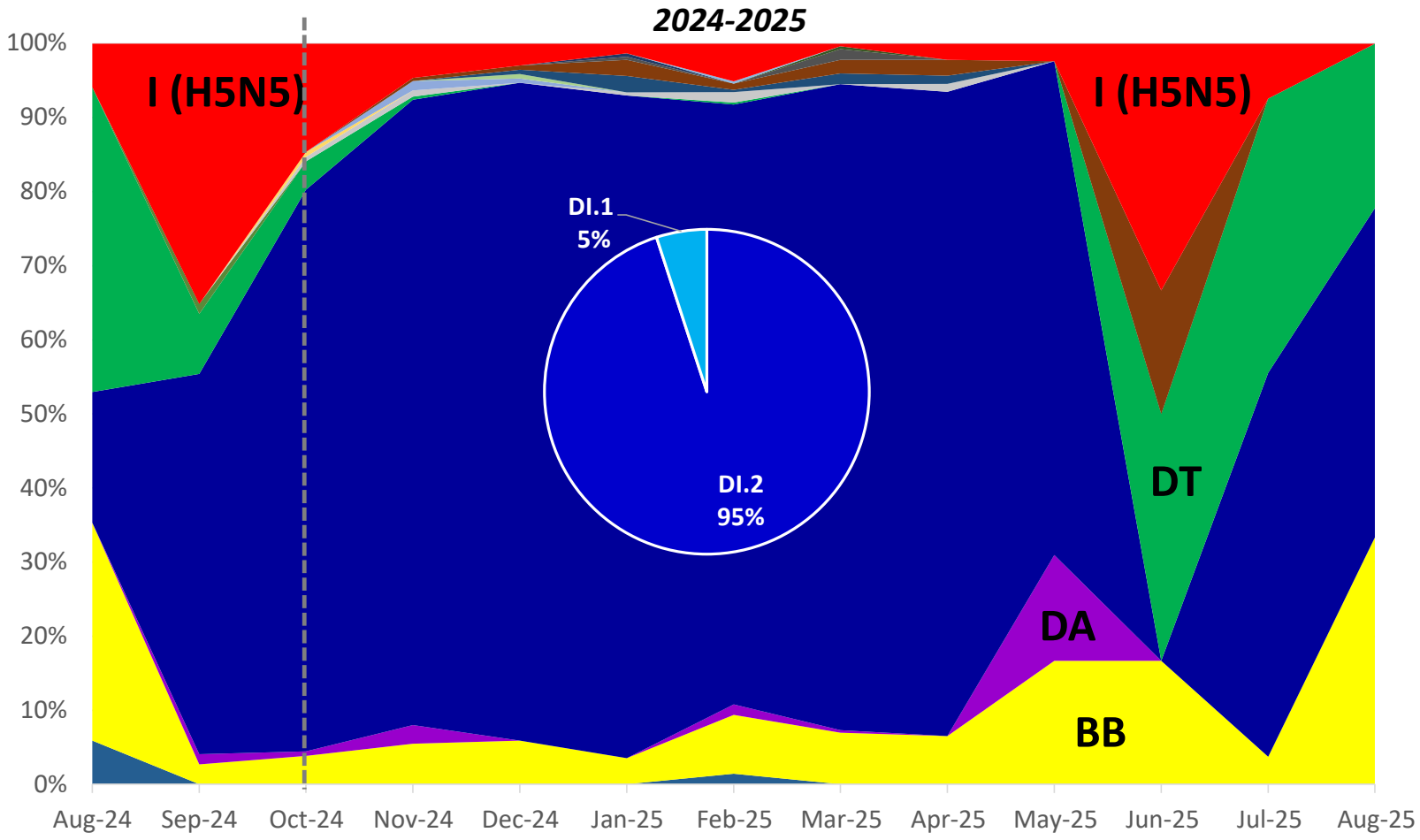
The characterized viruses during the 2024-2025 epidemiological year belong to **three major genotypes**:

- 2 H5N1 genotypes EA-2024-DI, EA-2022-BB
- 1 H5N5 genotype (EA-2021-I)

Occasional detections of novel genotypes generated from reassortments of the genotype EA-2024-DI

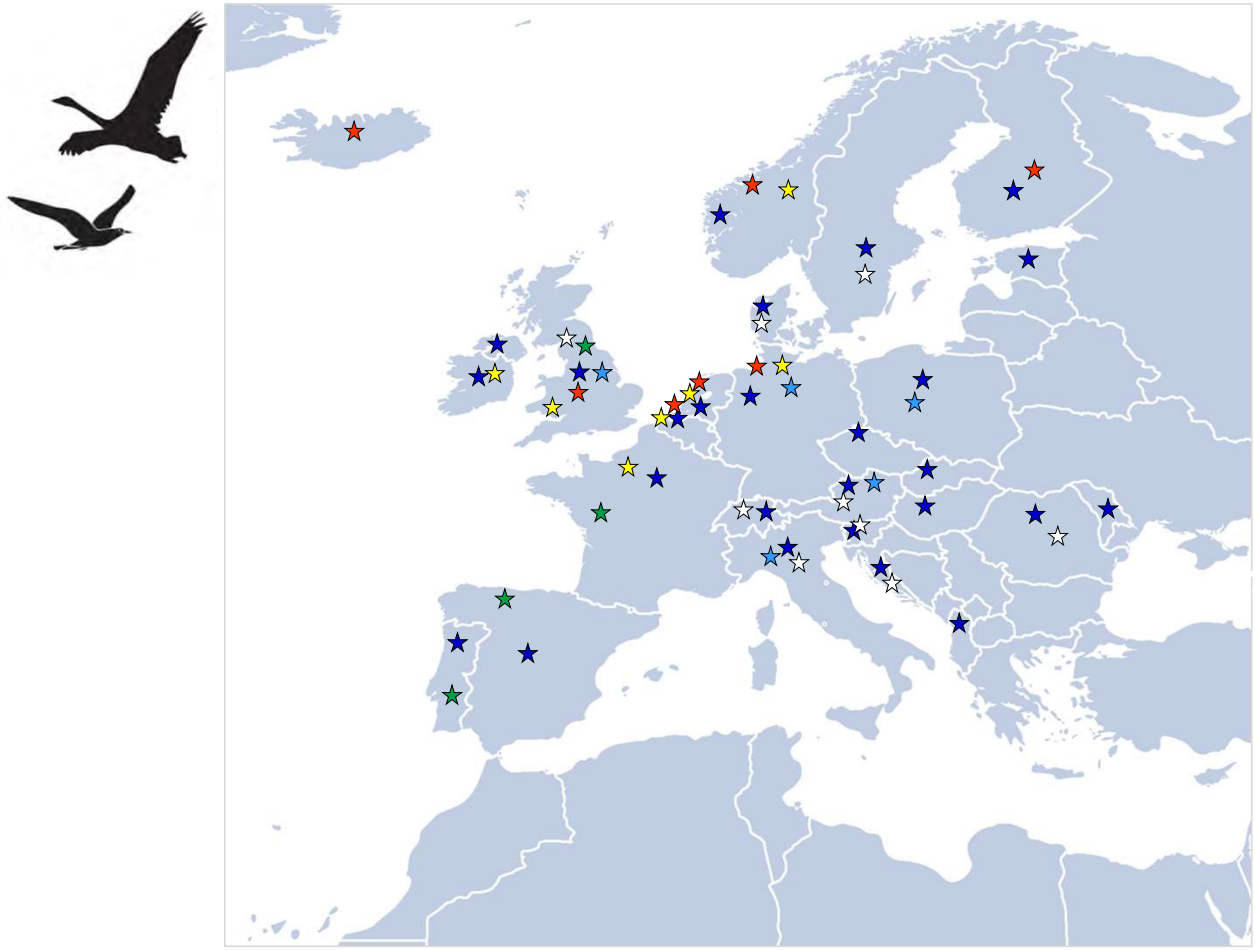
Fusaro A., Zecchin B., et al. High pathogenic avian influenza A(H5) viruses of clade 2.3.4.4b in Europe – why trends of virus evolution are more difficult to predict, Virus Evolution, 2024; https://doi.org/10.1093/ve/veae027

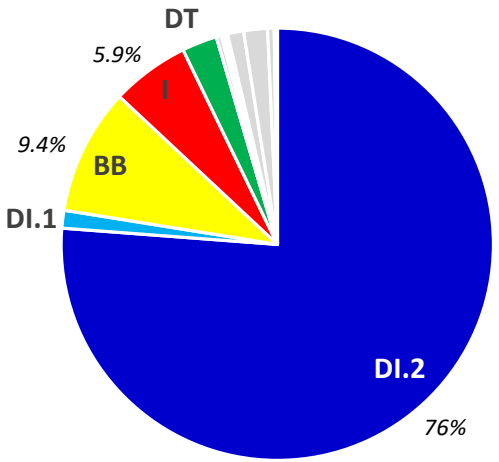
Temporal dynamics of the virus genotypes in Europe: 2024-2025



Genotype distribution in wild birds

October 2024 – August 2025



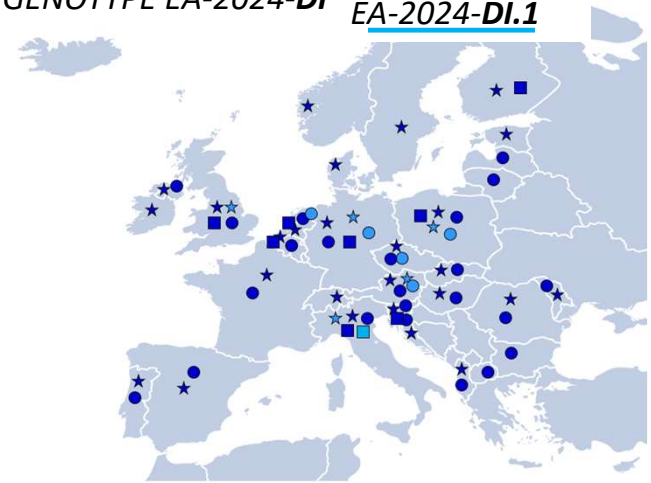


= DI.1
= DI.2
= I (H5N5)
= BB
= DT
= DA
= other genotypes

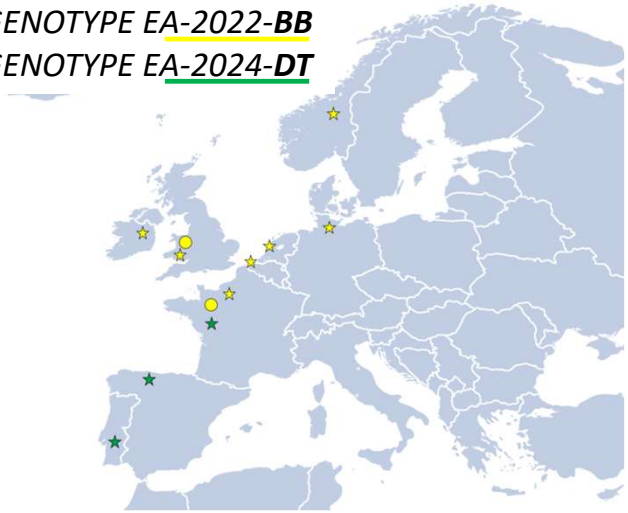
Geographic and host distribution of the genotypes, 2024-2025

☆ = wild birds ○ = poultry □ = mammal

GENOTYPE EA-2024-**DI** EA-2024-**DI.2** EA-2024-**DI.1**

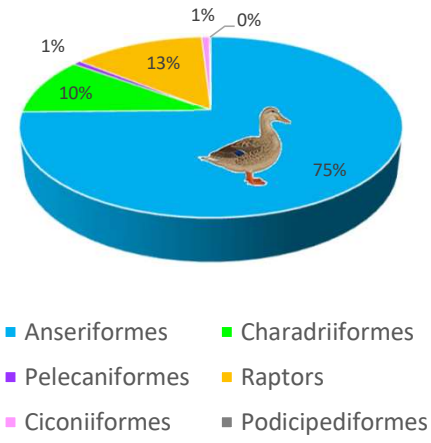


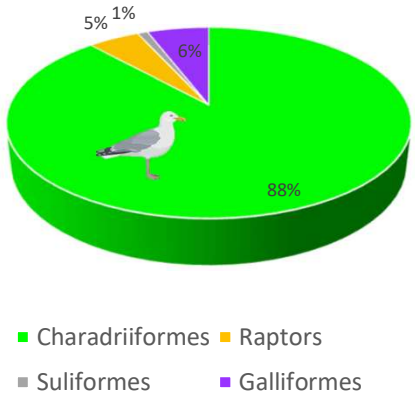
GENOTYPE EA-2022-**BB** GENOTYPE EA-2024-**DT**

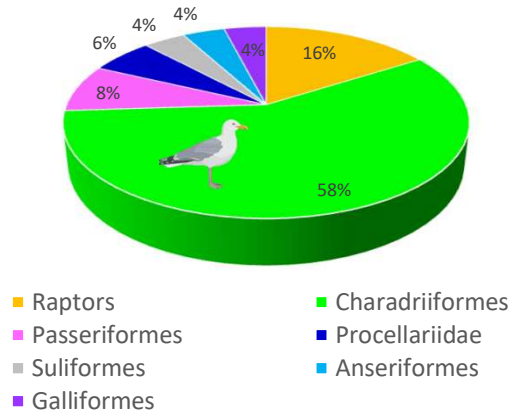


GENOTYPE EA-2021-**I**

WILD BIRDS

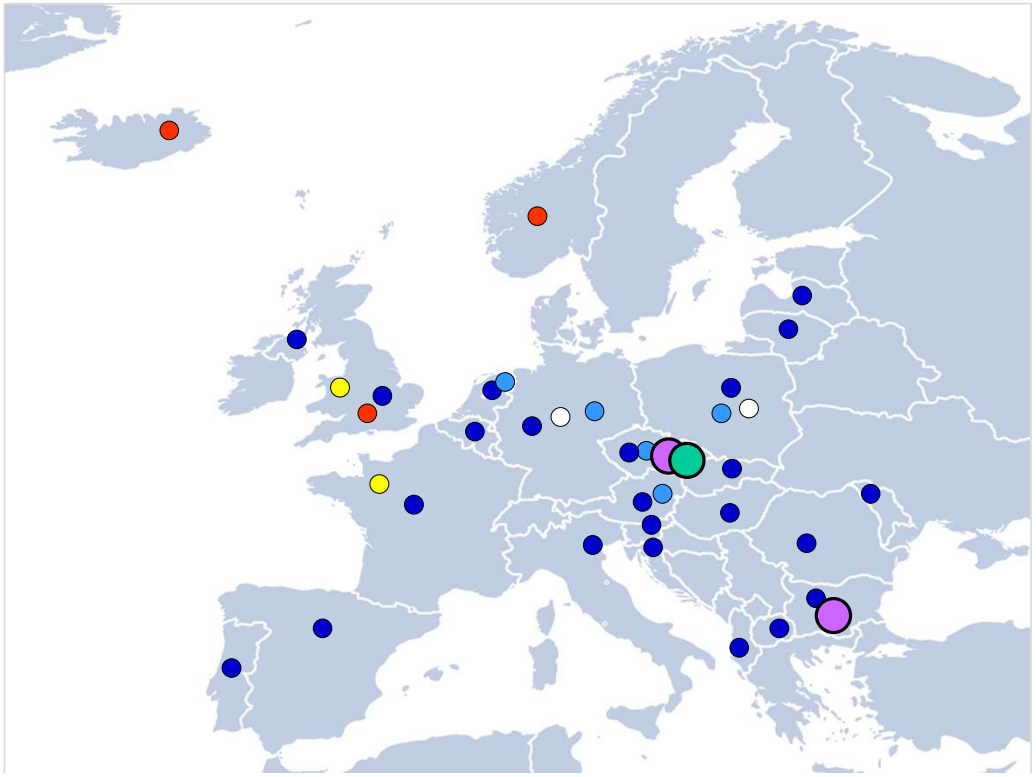


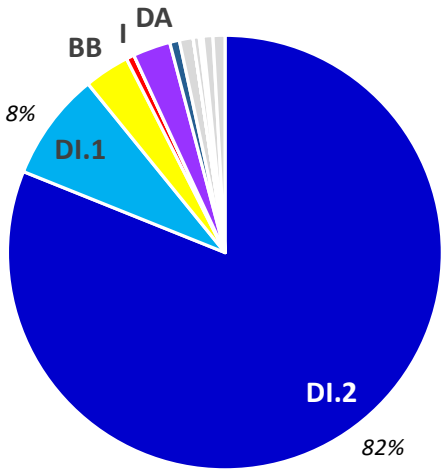


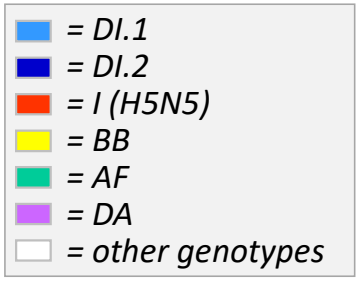


Genotype distribution in domestic birds

October 2024 – August 2025

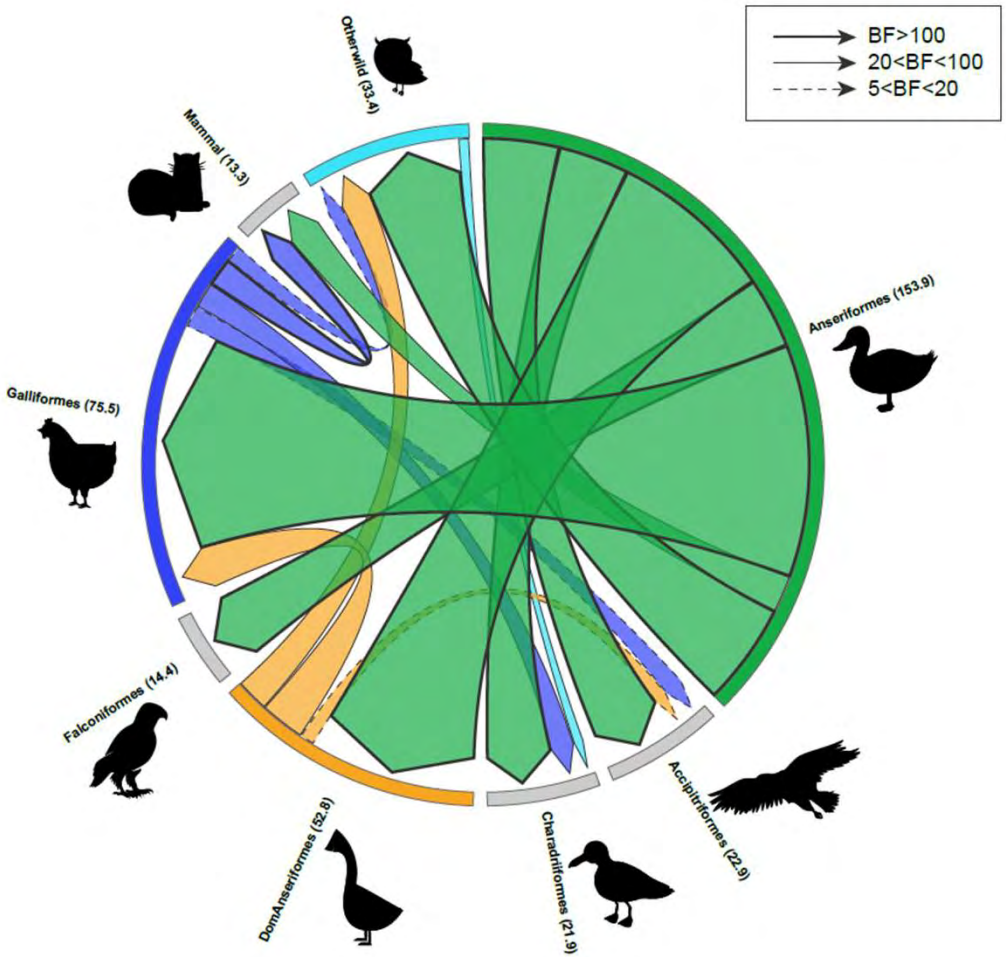


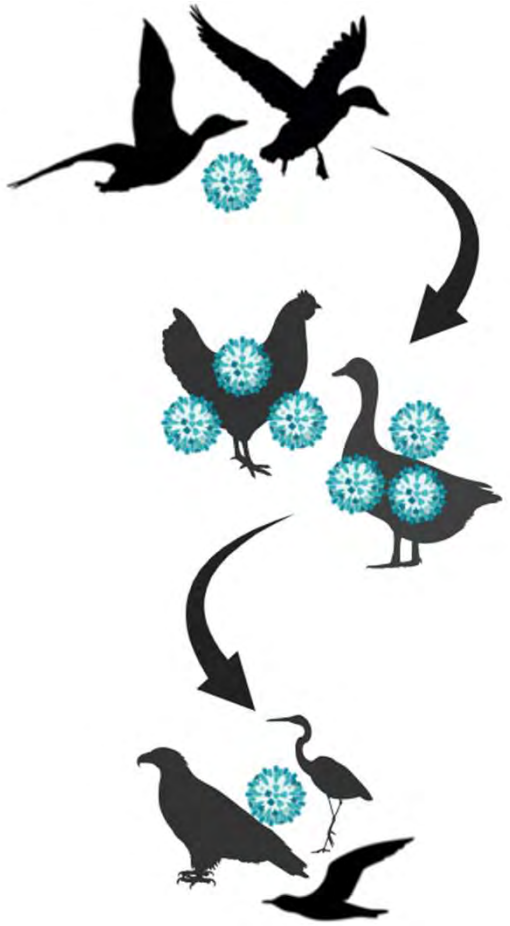


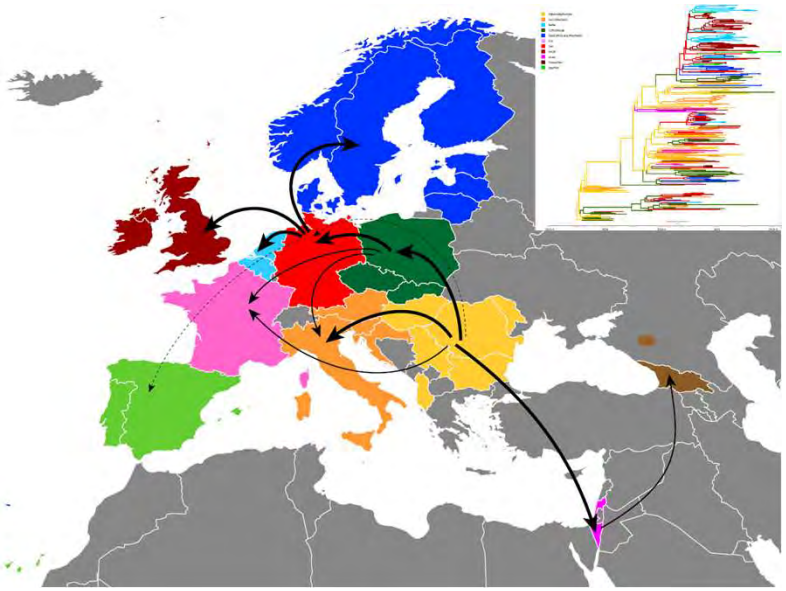


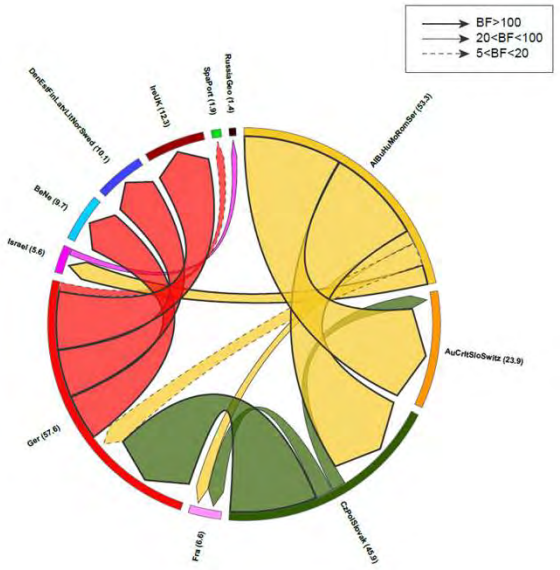
Identification in poultry in Eastern countries of two old genotypes (EA-2023-DA and EA-2020-AF), which were not detected in wild birds during the current epidemiological year in or outside other regions of Europe, suggesting undetected persistent circulation of these genotypes in an unknown ecological or domestic niche.

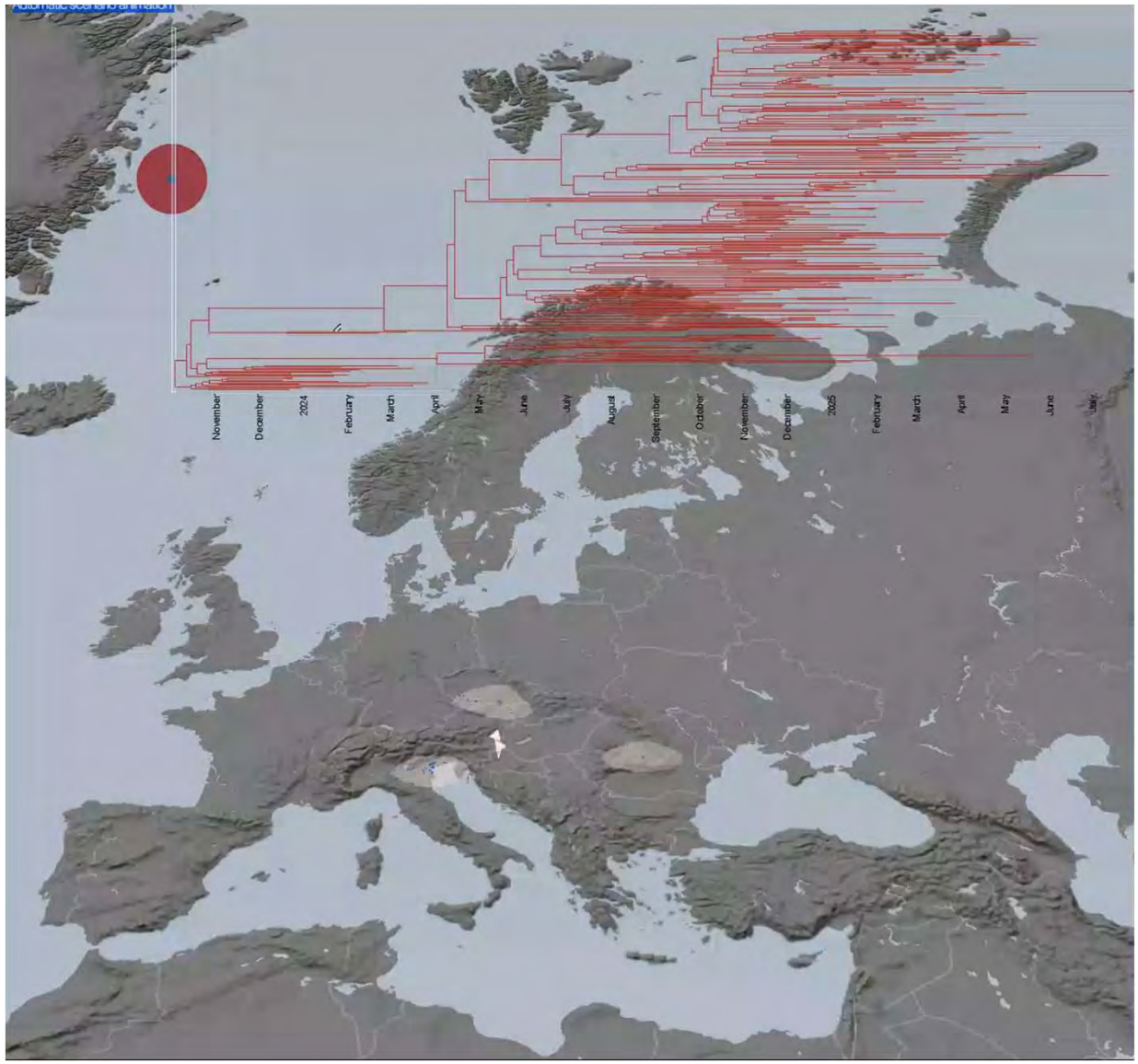
Host jumps and geographic spread of the genotype EA-2024-DI



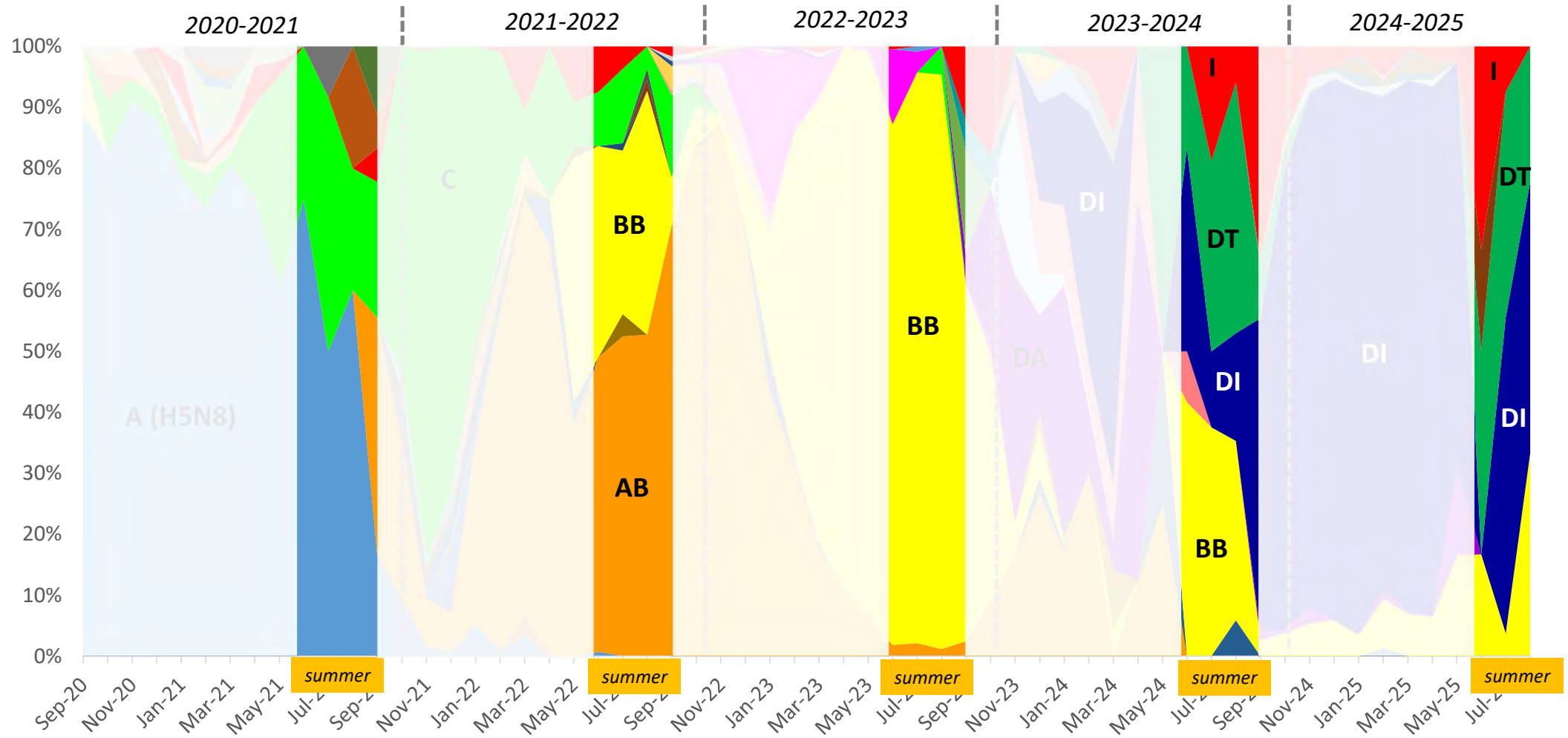




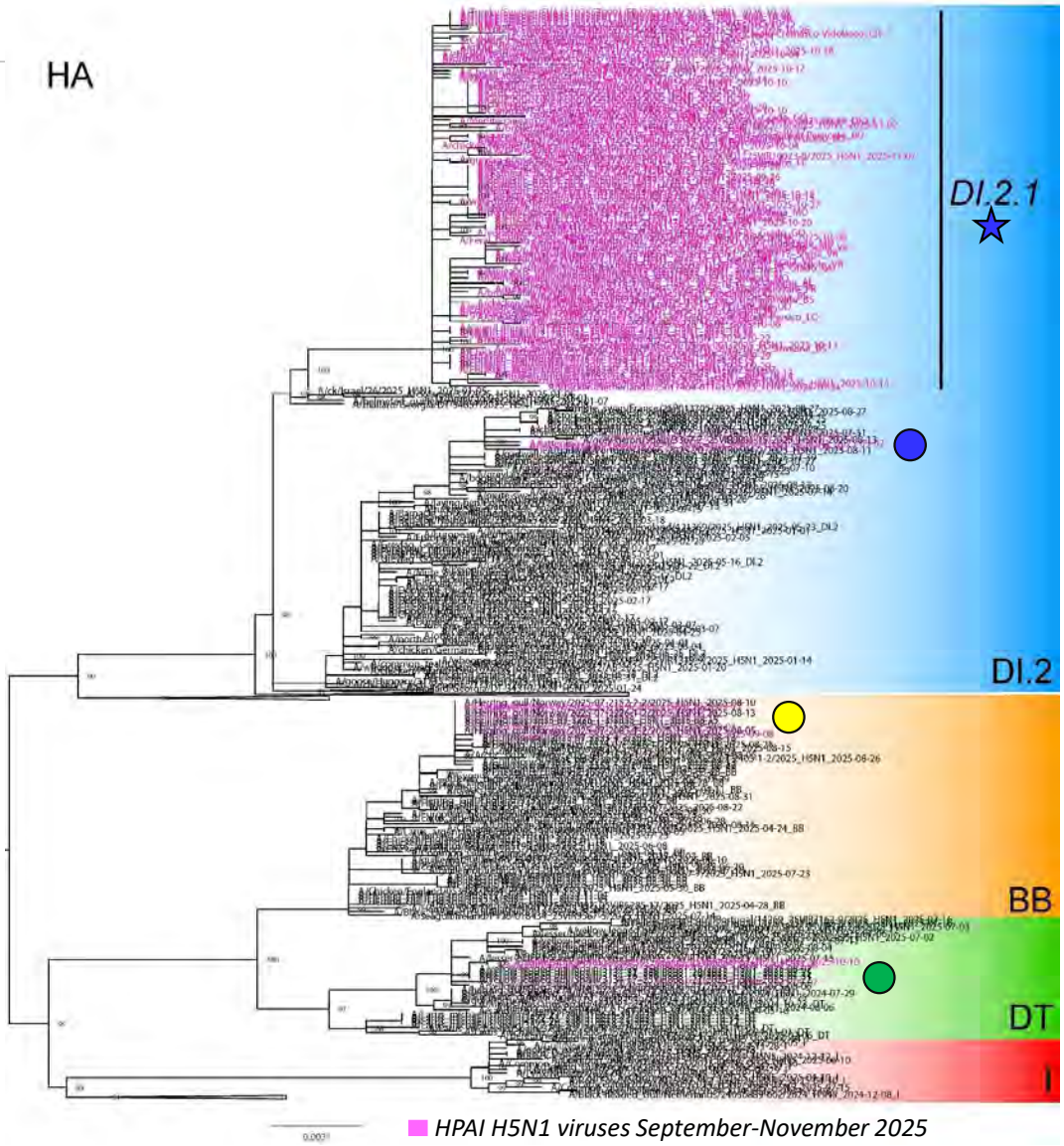

BF>100
20<BF<100
5<BF<20
DenEstFinLatLitNorSwed (10.1)
IreUK (13.3)
SpaPort (1.9)
RussiaSwe (1.4)
ABHuMoRomSer (33.3)
BaMe (0.7)
Israel (5.6)
AuCrtSloSwitz (23.9)
Ger (57.6)
Fra (6.6)
CzeSloSlovA (49.8)

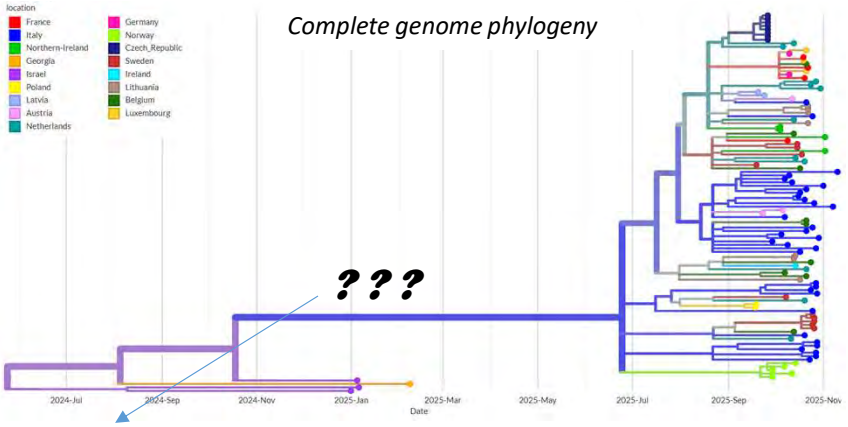

November
December
2024
February
March
April
May
June
July
August
September
October
November
December
2025
February
March
April
May
June
July

Temporal dynamics of the virus genotypes in Europe: 2020-2025



A new virus incursion – EA-2024-DI.2.1

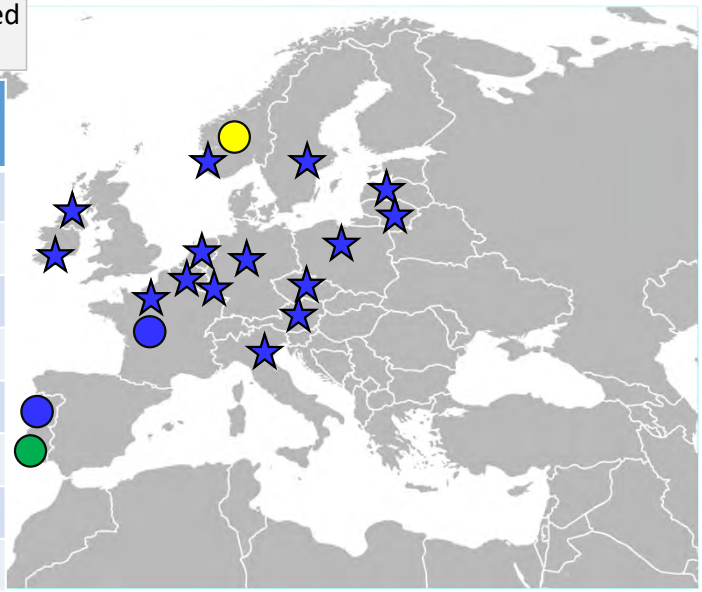




33 nt and 9 aa differences accumulated along the genome

	NT diff	AA diff
PB2	4	1
PB1	6	3
PA	7	1
HA	7	1
NP	3	0
NA	2	1
M	1	0
NS	3	2

September-November 2025

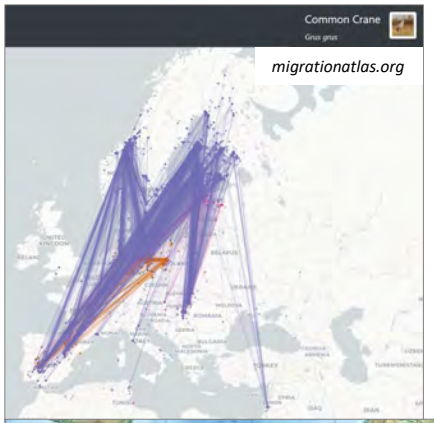


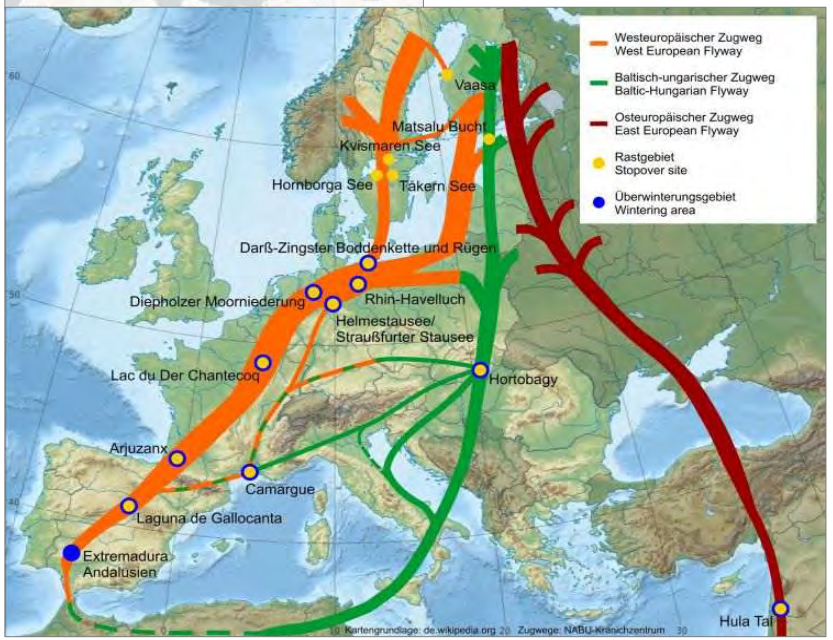
Common cranes: September-October 2025

Germany, France, Luxembourg and Belgium have reported increased mortality among cranes.

Preliminary data from Germany, France, Luxembourg and Belgium indicate that viruses belonging to the subcluster EA-2024-DI.2.1 of genotype EA-2024-DI were responsible for the mass mortality events reported in common cranes in these countries.

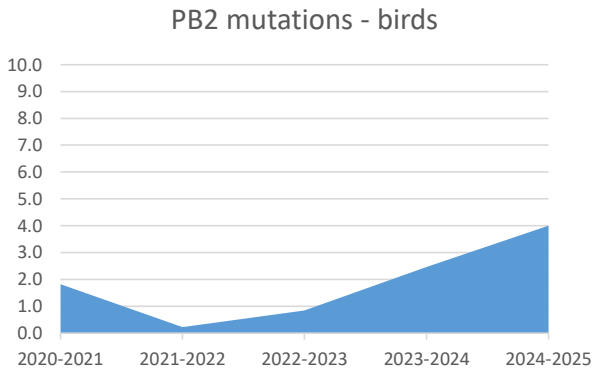
EURL Avian Flu Data Portal



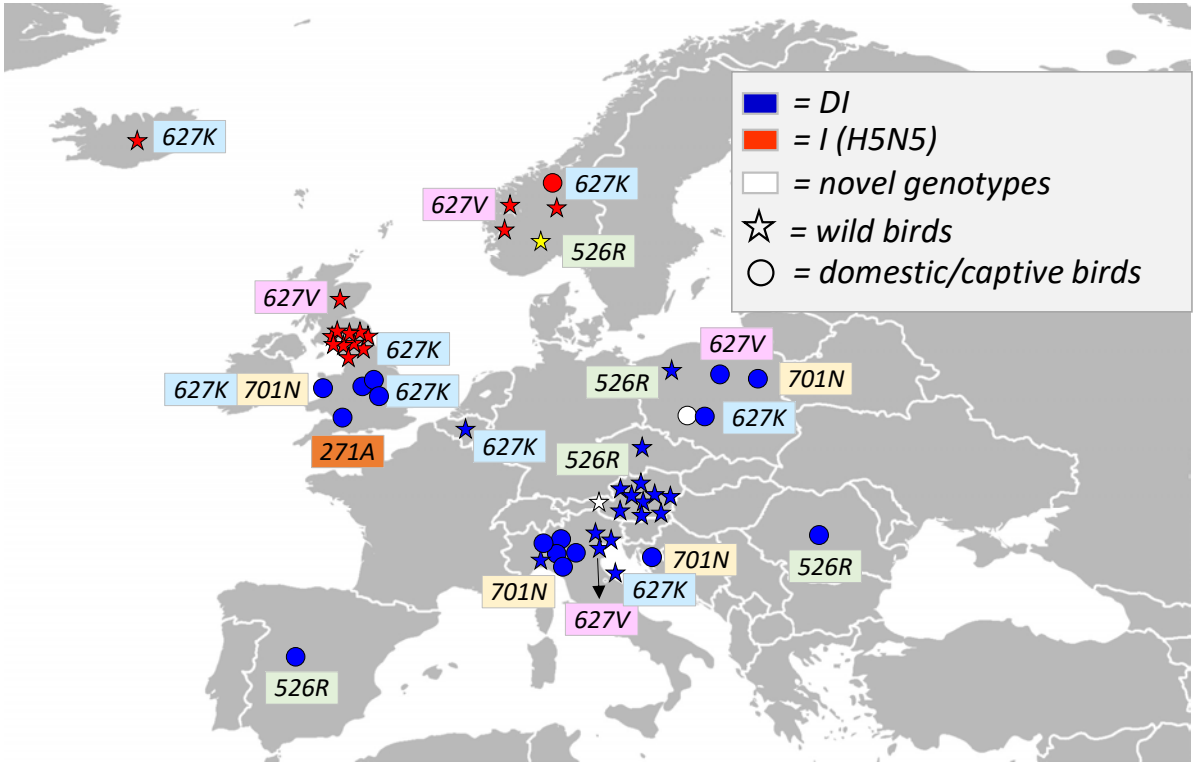


https://www.kraniche.de/en/crane-migration.html

Mutations of interest in birds, October 2024-August 2025



Geographic distribution in Europe of H5Nx viruses with molecular markers of mammalian adaptation PB2 E627K/V, K526R and D701N, 2024-2025



FLU MUT

https://izsvenezie-virology.github.io/FluMut

Mutations of interest in birds, October 2024-August 2025

DI

DI

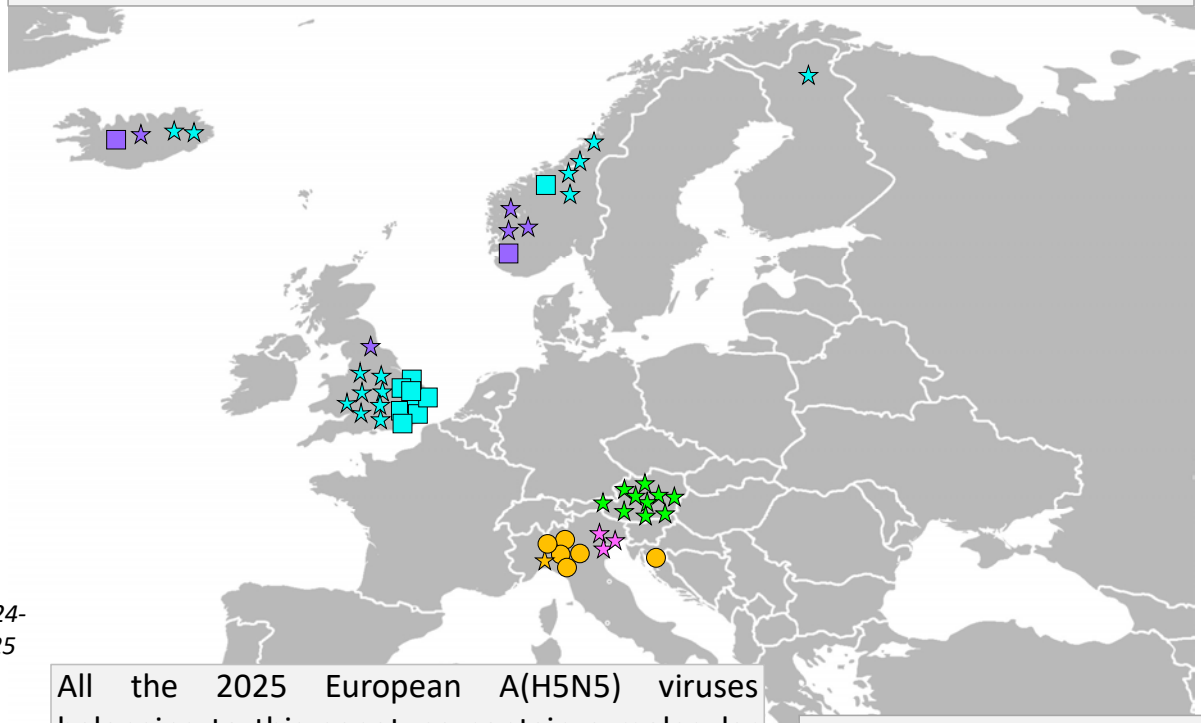
I

Nov 2024-July 2025

I

Nov 2024-July 2025

Geographic distribution in Europe of H5Nx viruses with molecular markers of mammalian adaptation PB2 E627K/V, K526R and D701N, 2024-2025



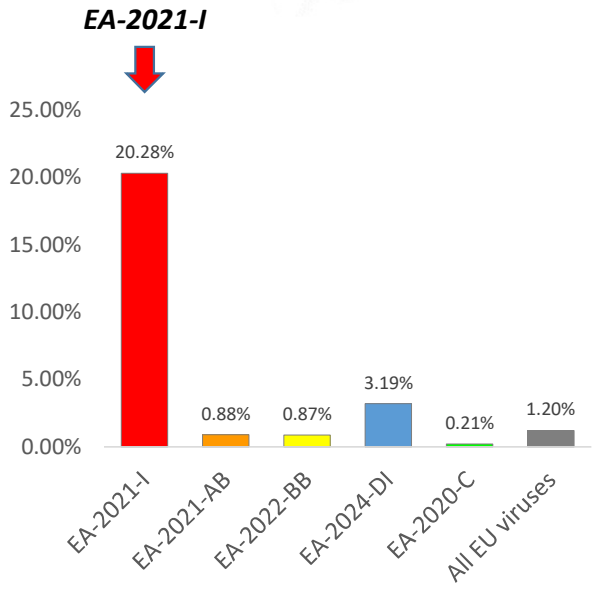
All the 2025 European A(H5N5) viruses belonging to this genotype contain a molecular marker of virus adaptation to mammals

□ = *mammal*
☆ = *wild birds*
○ = *domestic/captive birds*

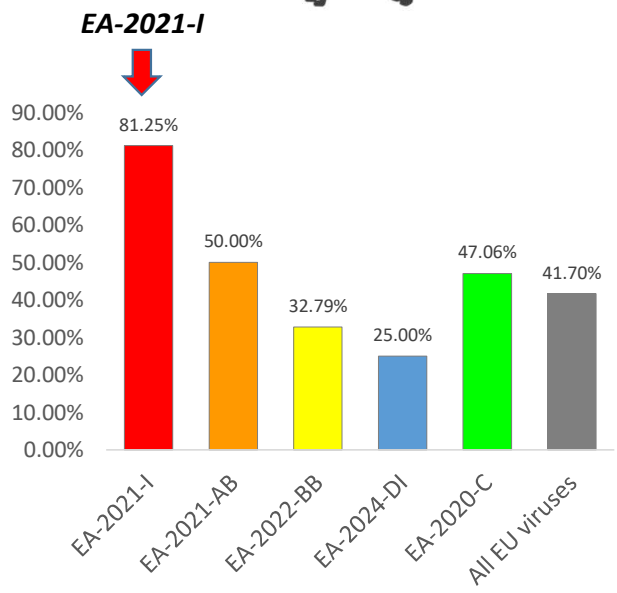
https://izsvenezie-virology.github.io/FluMut

Created in BioRender.com

Mammalian adaptive markers - A(H5N5) EA-2021-I



AVIAN: more than **20%** of the European A(H5N5) viruses of the **genotype EA-2021-I** (2021-2025) contains one of the PB2 mammalian adaptive markers, while this frequency drops to about 1% considering all the other European viruses of other genotypes.



MAMMAL: **80%** of the European A(H5N5) viruses of the **genotype EA-2021-I** (2021-2025) contains one of the PB2 mammalian adaptive markers, while this frequency drops to about 42% considering all the European viruses of other genotypes.

Conclusions

- Evidence of a predominance of the EA-2024-DI genotype in 2024-2025 in Europe and the circulation of the genotypes EA-2022-BB, EA-2023-DT and EA-2021-I in distinct ecological niches.
- Rapid westward diffusion of genotype EA-2024-DI at the beginning of the 2024-2025 epidemic wave, likely driven by *Anseriformes*.
- Poultry mainly acted as a sink host, but occasionally contributed to the virus spread to wildlife.
- Data collected so far indicates that the recent outbreaks in Europe are caused by a novel incursion of the EA-2024-DI.2 genotype, namely EA-2024-DI.2.1.
- To date, no key mutations associated to the switch in the virus binding preference from avian to human-type receptors have been identified in the H5 collected in Europe. However, we observed an increase in the frequency of viruses collected from birds with molecular markers of mammalian adaptation in the PB2 protein. Viruses containing such mutations may have a greater zoonotic potential.
- Surveillance and real-time genetic characterization are highly recommended to promptly identify viruses with mutations able to increase their zoonotic potential.

Acknowledgements

European National Reference Laboratories for AI

Aldin Lika (Albania); Sandra RevillaFernández, Irene Zimpernik (Austria); Mieke Steensels and Steven Van Borm (Belgium); Emiliya Ivanova (Bulgaria); Vladimir Savic (Croatia); Vasiliki Christodoulou (Cyprus); Alexander Nagy (Czechia); Charlotte Kristiane Hjulsager, Yuan Liang (Denmark); Tuija Gadd, Lauri Kareinen, Ari Kauppinen, Niina Tammiranta (Finland); François-Xavier Briand, Béatrice Grasland, Éric Niquex, , Audrey Schmitz (France); Timm Harder, Anne Pohlmann (Germany); Malik Peter (Hungary); Brigitte Brugger and Vilhjálmur Svansson (Iceland); Laura Garza Cuartero (Ireland); Simona Pileviciene, Egidijus Pumputis (Lithuania); Chantal Snoeck (Luxembourg); Igor Dzadzovski, Aleksandar Dodovski (Macedonia); Oxana Groza (Moldova); Monika Ballmann (Netherlands); Britt Gjerset (Norway); Anna Pikula, Katarzyna Domańska-Blicharz, Krzysztof Śmietanka and Edyta Swieton (Poland); Margarida Duarte, Teresa Fagulha, Margarida Henriques (Portugal); Iuliana Onita (Romania); Dejan Vidanovic (Serbia); Zuzana Dirbakova and Martin Tinak (Slovakia); Brigita Slavec (Slovenia); Montserrat Agüero García, María Teresa Barrios Zambrano and Azucena Sánchez (Spain); Siamak Zohari (Sweden); Claudia Bachofen (Switzerland);

Ron Fouchier from Erasmus Medical Center (Netherlands); Ashley Banyard and Holly Coombes from the Animal and Plant Health Agency (United Kingdom); Michael McMenamy from Agri-food and Biosciences Institute (Northern Ireland)

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The authors, originating and submitting laboratories of the sequences from GISAID's EpiFlu™ Database

Phylodynamics analyses were supported by:

KAPPA-FLU HORIZON-CL6-2022-FARM2FORK-02-03 (grant agreement No 101084171)

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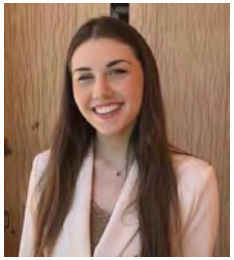

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Thank you
for your attention

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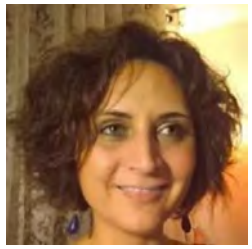

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