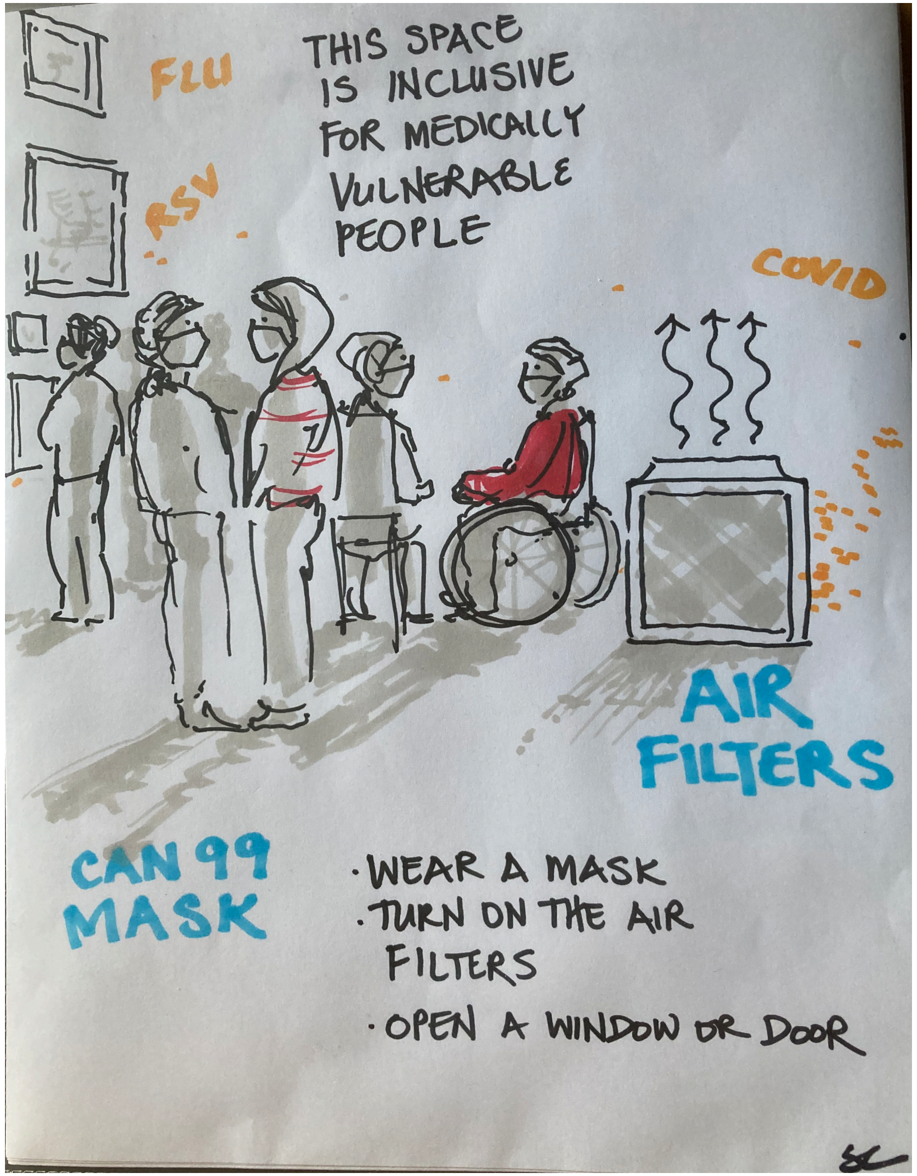
A New Mutated Influenza A H3N2 virus

Why you should care?

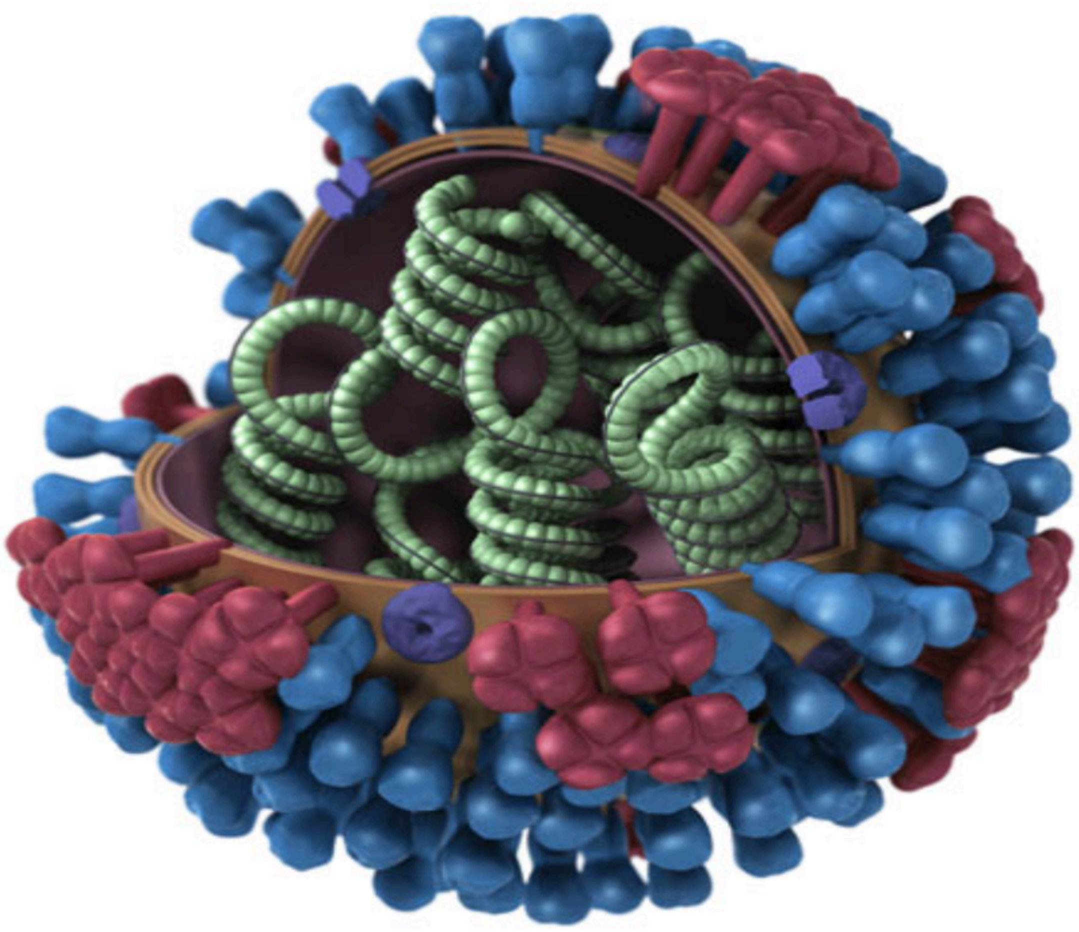


Lyne Filiatrault, MD retired

November 17, 2025

Outline

- Influenza Basics
- Influenza A H3N2 new mutations
- H3N2 mutations & Vaccine Effectiveness
- H3N2 in Japan & UK
- What’s happening in Canada?
- Virus-Host-Environment

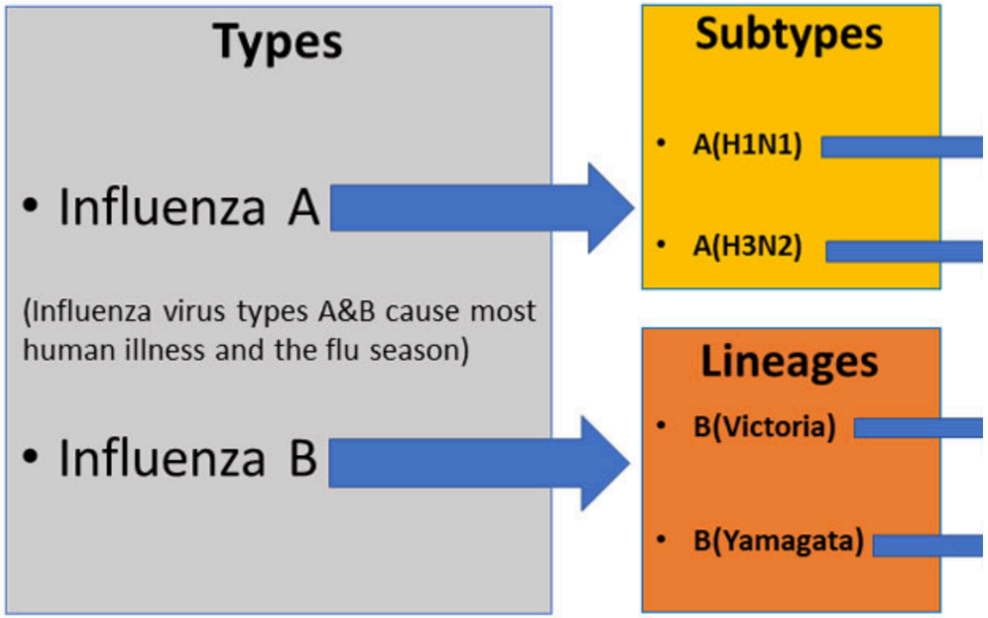


https://www.cdc.gov/flu/about/viruses-types.html

Influenza A virus

Classified by subtypes based on properties of Hemagglutinin and Neuraminidase surface proteins.

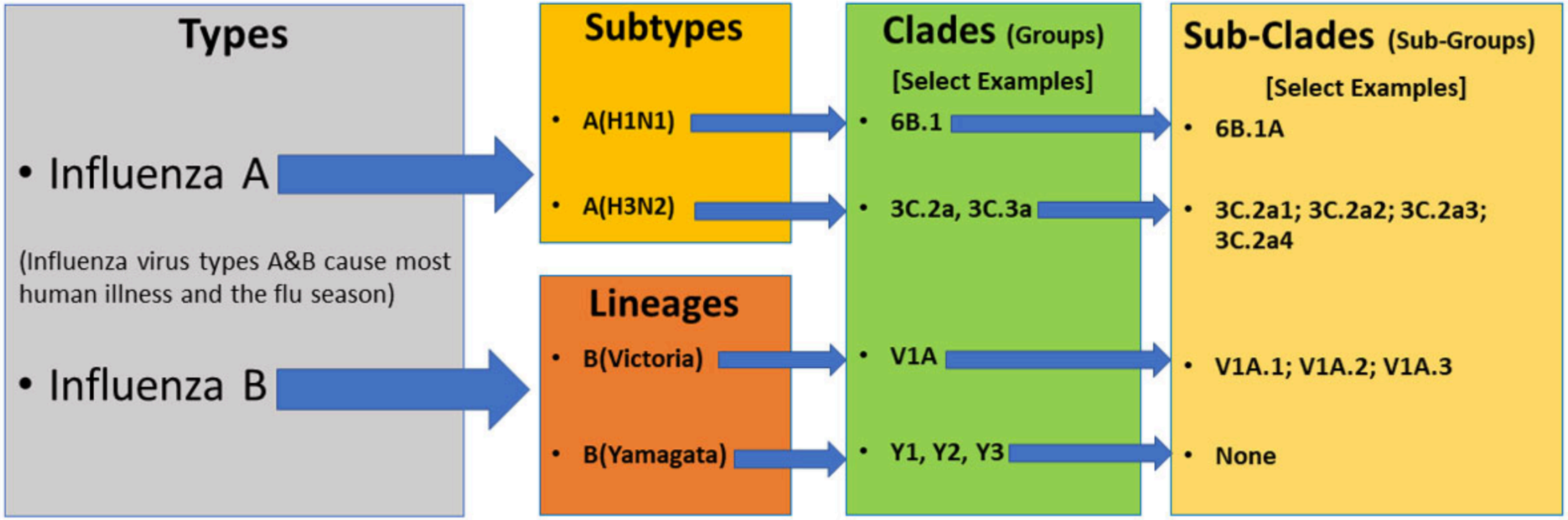
Human Seasonal Influenza Viruses



Influenza Viruses Types Cause Flu Season Influenza A (Influenza virus types responsible for most human illness and the flu season) Influenza B Influenza C (Not significant for public health) Influenza D (Mainly infect cows) Subtypes A(H1N1) A(H3N2) L...

https://www.cdc.gov/flu/about/viruses-types.html

Human Seasonal Influenza Viruses



→ **Sub-clade K**

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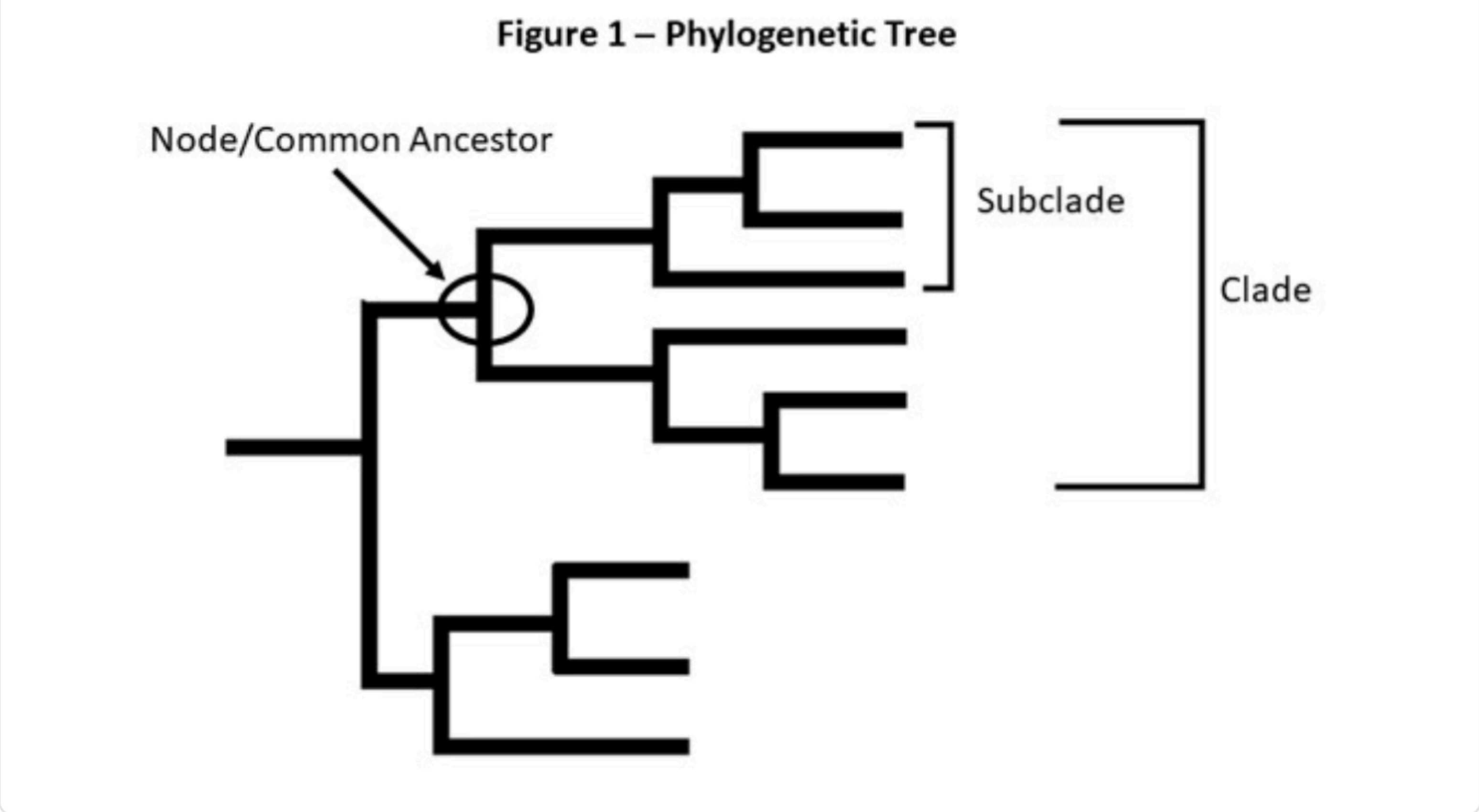
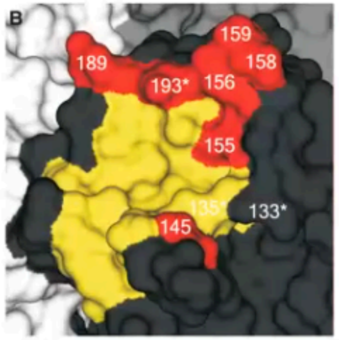


Figure 1 – This is a picture of a phylogenetic tree. Phylogenetic trees show how closely related viruses are to one another. Phylogenetic trees of influenza viruses usually show how similar the viruses' hemagglutinin (H or HA) or neuraminidase (N or NA) genes are to one another. Each sequence of specific influenza viruses have their own branches on the tree. The degree of genetic differences between viruses is represented by the length of the horizontal lines (branches) in the phylogenetic tree. The further apart viruses are on the horizontal axis of a phylogenetic tree, the more genetically different the viruses are from one another.

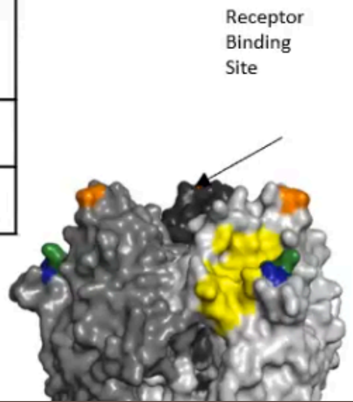
https://www.cdc.gov/flu/about/viruses-types.html

A(H3N2) viruses have picked up important mutations

- Vaccine and virtually all circulating viruses are 2a.3a.1
  - In subclade nomenclature, vaccine is subclade “J” but majority of circulating descendant viruses are “J.2”
    - J.2 viruses distinguished by N122D leading to loss of glycosylation in antigenic site A present since 1998
- Additionally, 3 antigenic cluster transition site mutations in **~50% of 2a.3a.1 viruses**



Substitution	Importance	% Overall (N=469)	% weeks 44-3 (N=148)	% weeks 4-9 (N=321)
S145N	Major antigenic cluster transition site A	23%	21%	23%
T135K	Accessory antigenic cluster transition site A, removes another sugar at N133 present since 1998	21%	18%	22%
S145N + **T135K/A**	As above	2%	—	2%
S145N + **N158K**	Major antigenic cluster transition site B	5%	2%	6%



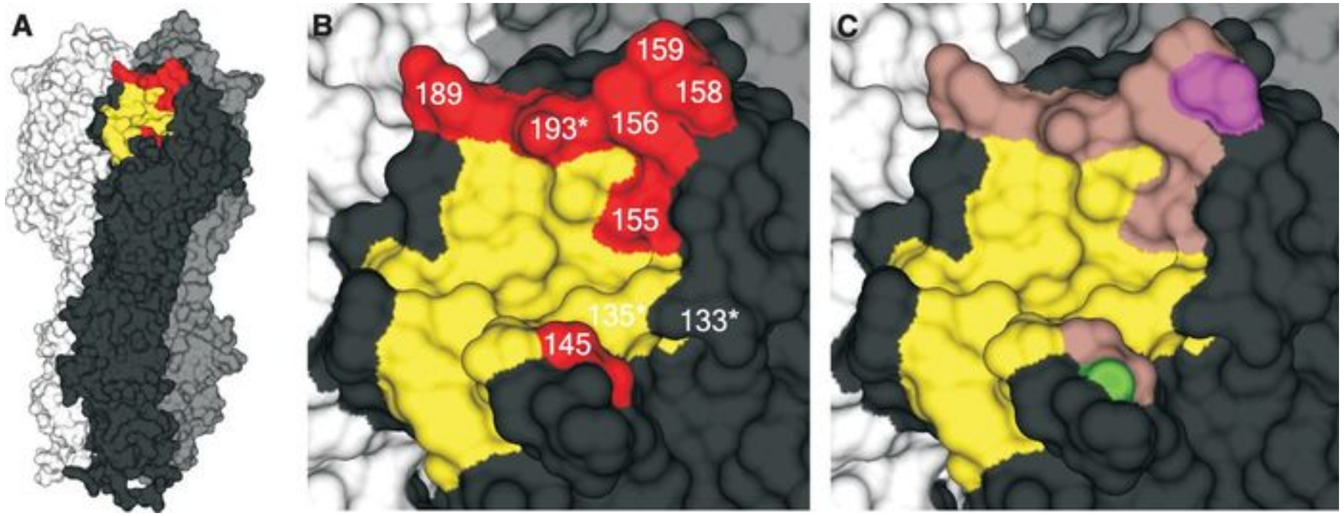
Source: Danuta Skowronski, BC
CDC Grand Rounds. April 1, 2025

Science | AAAS

Substitutions Near the Receptor Binding Site Determine Major Antigenic Change During Influenza Virus Evolution

Bjorn F Koel et al

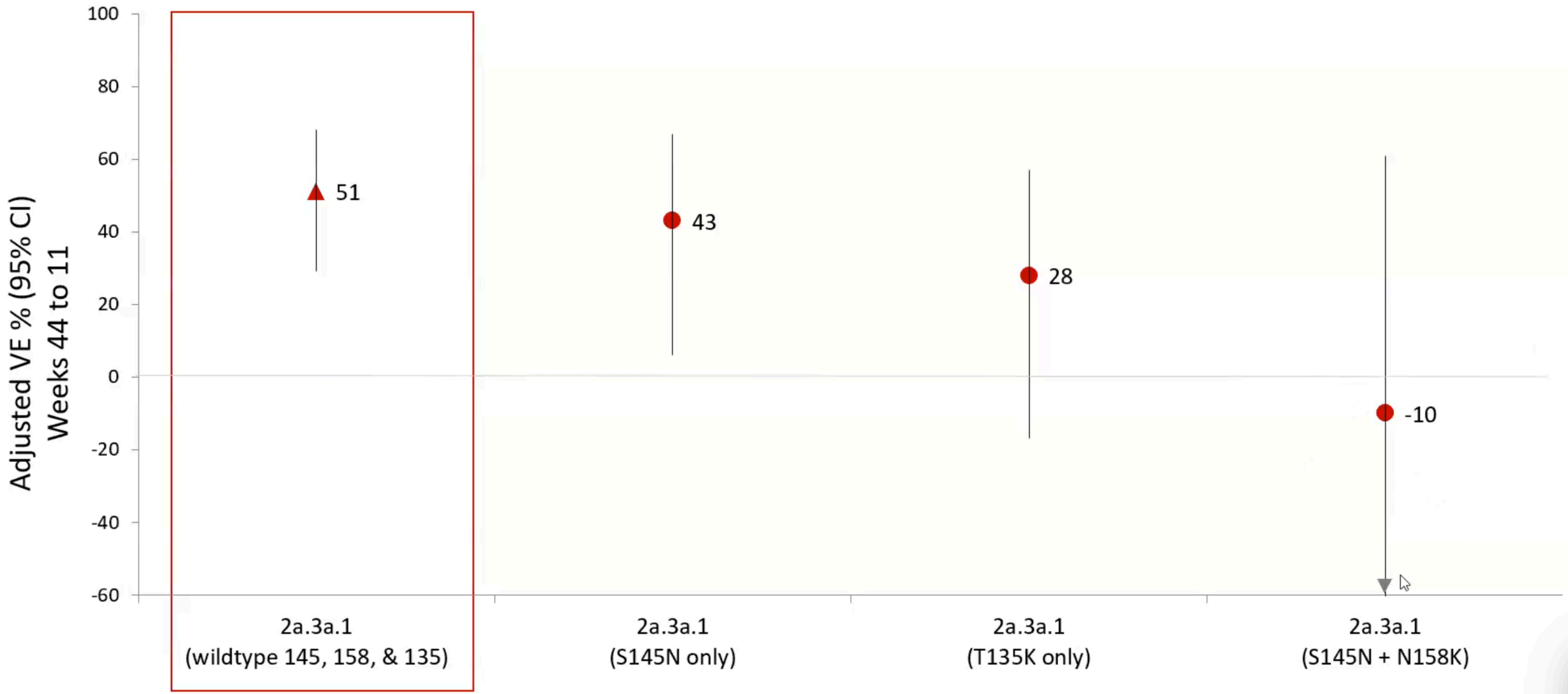
Science 22 Nov. 2013



10.1126/science.1244730

A(H3N2) VE by variant

27 Oct 2024 – 15 Mar 2025 (weeks 44-11)
(n=6,753)



2024/25 influenza findings, thus far:

- In mid-season analysis through mid-January, influenza vaccine approximately **halved** the risk of attended respiratory illness due to influenza A
  - VE of 53% against influenza A(H1N1)pdm09 and 54% against A(H3N2)

- Thereafter through mid-March 2025, VE estimated by SPSN decreased substantially
  - Associated with increased circulation of influenza A variants
    - H1N1 (T216X, -CHO)
    - H3N2 (**S145N**, **T135K, -CHO, N158K**) [major antigenic cluster transition sites affected]

- Contributions to VE are multi-factorial and may include potential agent-host influences/interactions
  - Agent: genetic and antigenic drift, glycosylation effects and immune evasion
  - Host: pre-existing immunity, repeat vaccination effects, imprinting, I-REV

- Regional variation needs to be taken into account when comparing VE findings

Source: Danuta Skowronski, BC CDC Grand Rounds. April 1, 2025

World Health Organization

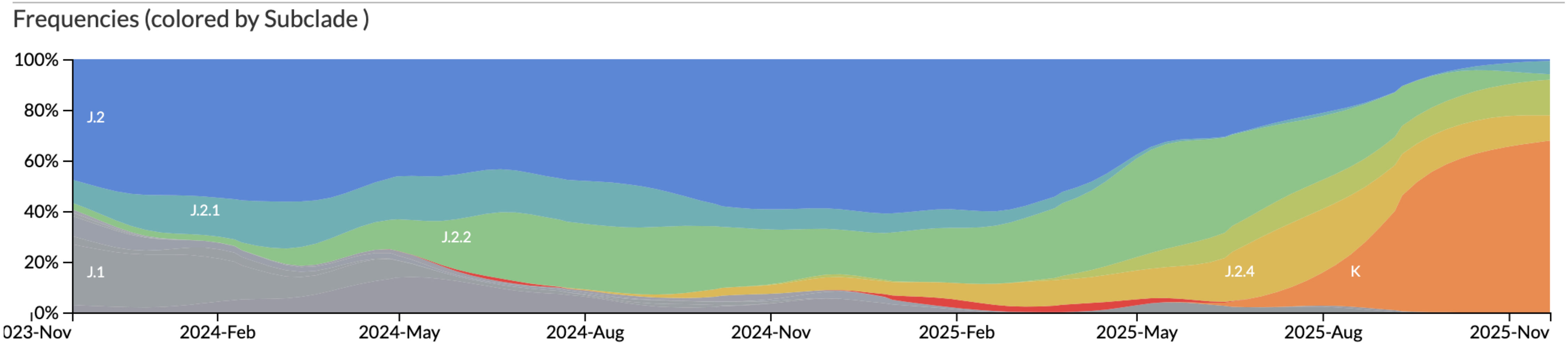
February strain selection for the Northern Hemisphere

	A(H1N1)pdm09	A(H3N2)	B/Victoria*	B/Yamagata
2023-24	A/Victoria/4897/2022	A/Darwin/9/2021	B/Austria/1359417/2021	B/Phuket/3073/2013
Clade**	"5a.2a.1" or "D"	"2a" or "G.1"	"3a.2" or "C"	Y3
2024-25	–	A/Thailand/8/2022	–	–
Clade**	–	"2a.3a.1" or "J"	–	–
2025-26	–	A/Croatia/10136RV/2023	–	–
Clade**	–	"2a.3a.1" or "J.2" (with **S145N**)	–	–

*recommended component of trivalent vaccine whereas quadrivalent vaccine includes both B/Victoria and B/Yamagata lineages

Source: Danuta Skowronski, BC
CDC Grand Rounds. April 1, 2025

Next-Strain: Real-time tracking of influenza A/H3N2 evolution



2025-11-20
nextstrain.org/seasonal-flu/h3n2/ha/2y

Next-Strain: Real-time tracking of influenza A/H3N2 evolution

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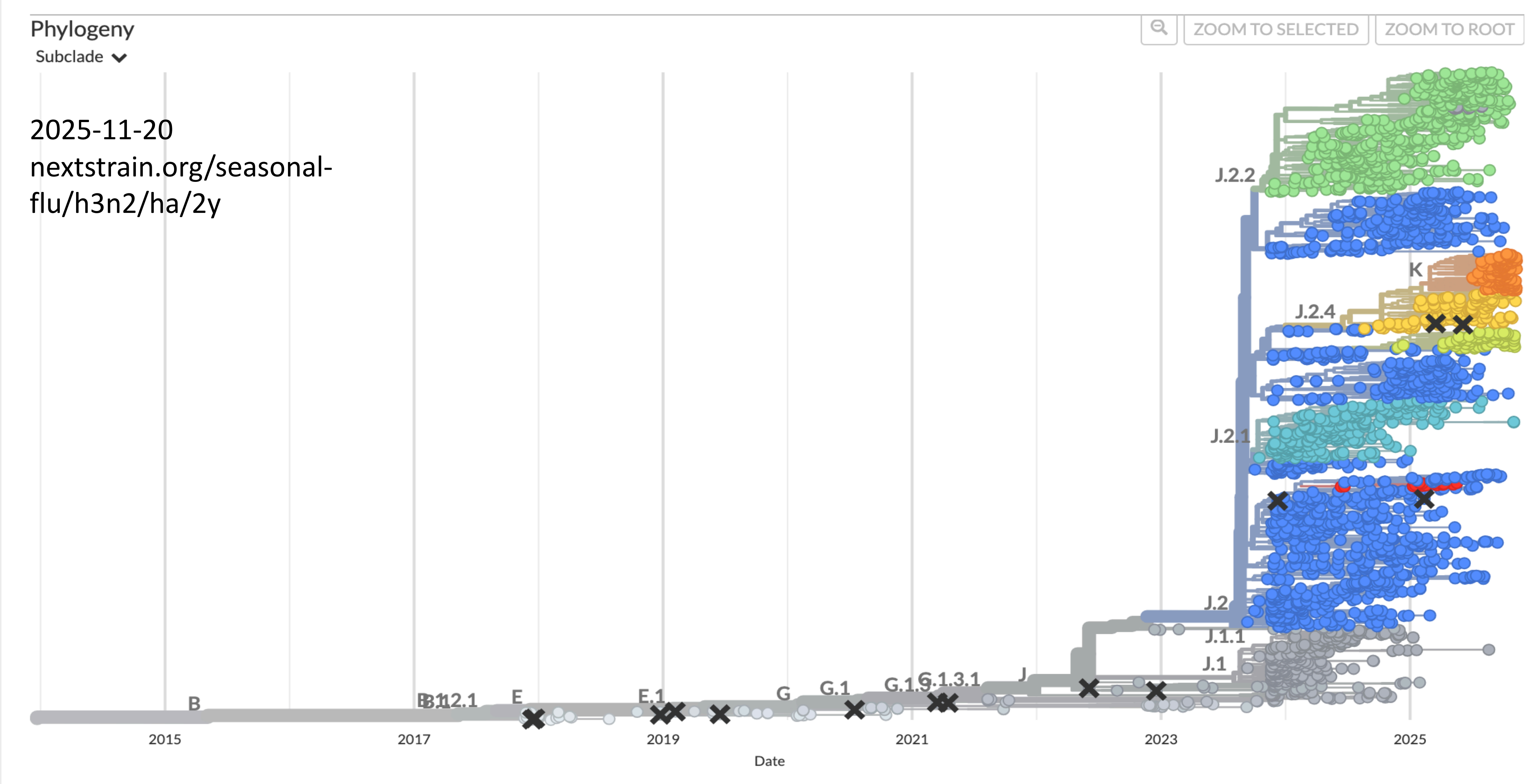


OPEN ACCESS | Research Article | 31 October 2025

Emergence of seasonal influenza A(H3N2) variants with immune escape potential warrants enhanced molecular and epidemiological surveillance for the 2025–2026 season

Authors: Suzana Sabaiduc, Samantha E Kaweski, Lea Separovic, Ruimin Gao, Charlene Ranadheera, Nathalie Bastien, and Danuta M Skowronski | AUTHOR INFORMATION AND AFFILIATIONS

Publication: Journal of the Association of Medical Microbiology and Infectious Disease Canada • Advance Access
https://doi.org/10.3138/jammi-2025-0025

PDF

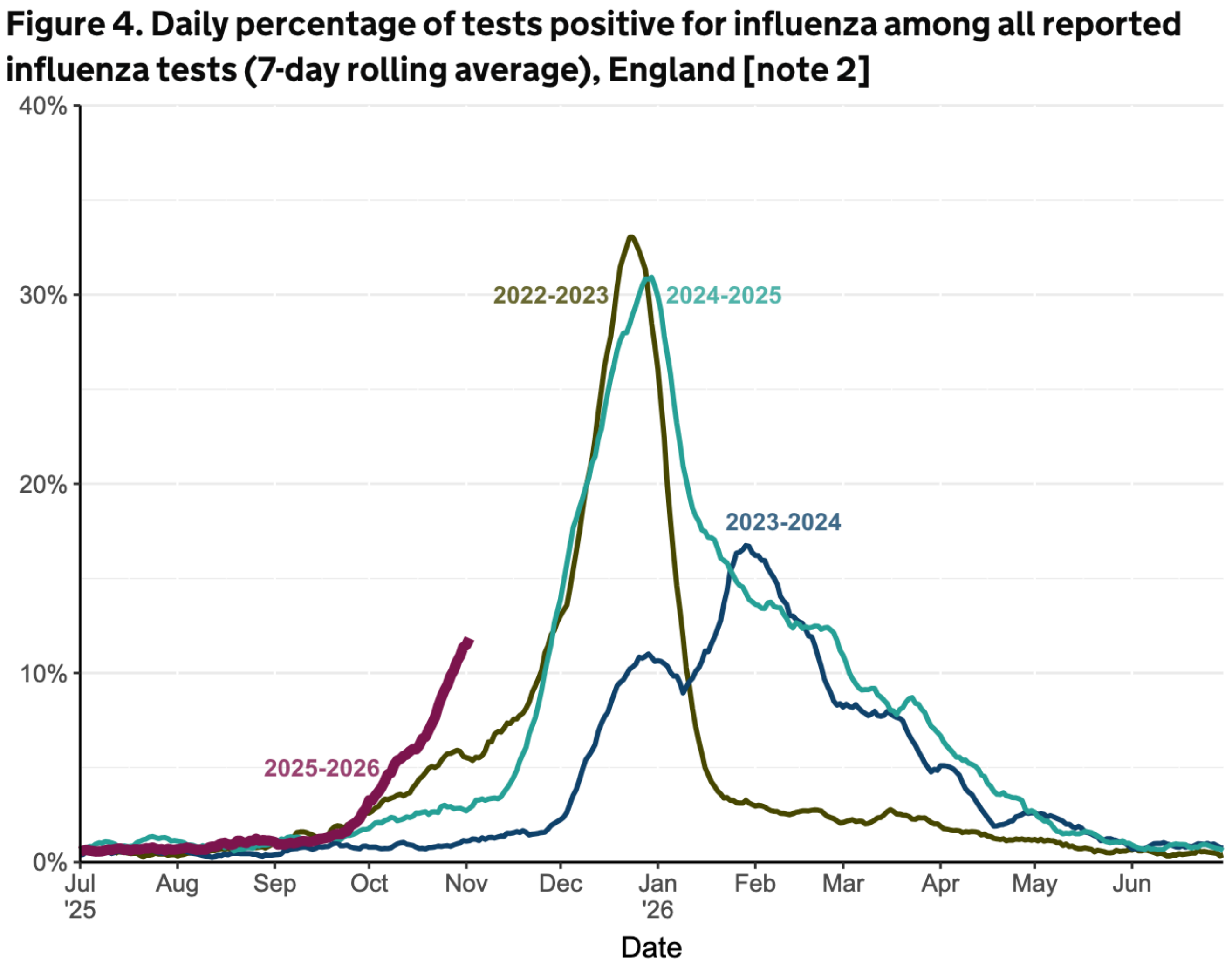
2025 FLU SEASON OVERSEAS

- UK CASES:
  3x HIGHER THAN LAST YEAR
- JAPAN CASES:
  6x HIGHER THAN LAST YEAR
- NEW STRAIN:
  H3N2 SUBCLADE K

U.K.'S NHS & JAPAN'S MHLW

UKHSA data for England

Up to week 44: Oct.27 –Nov.2, 2025



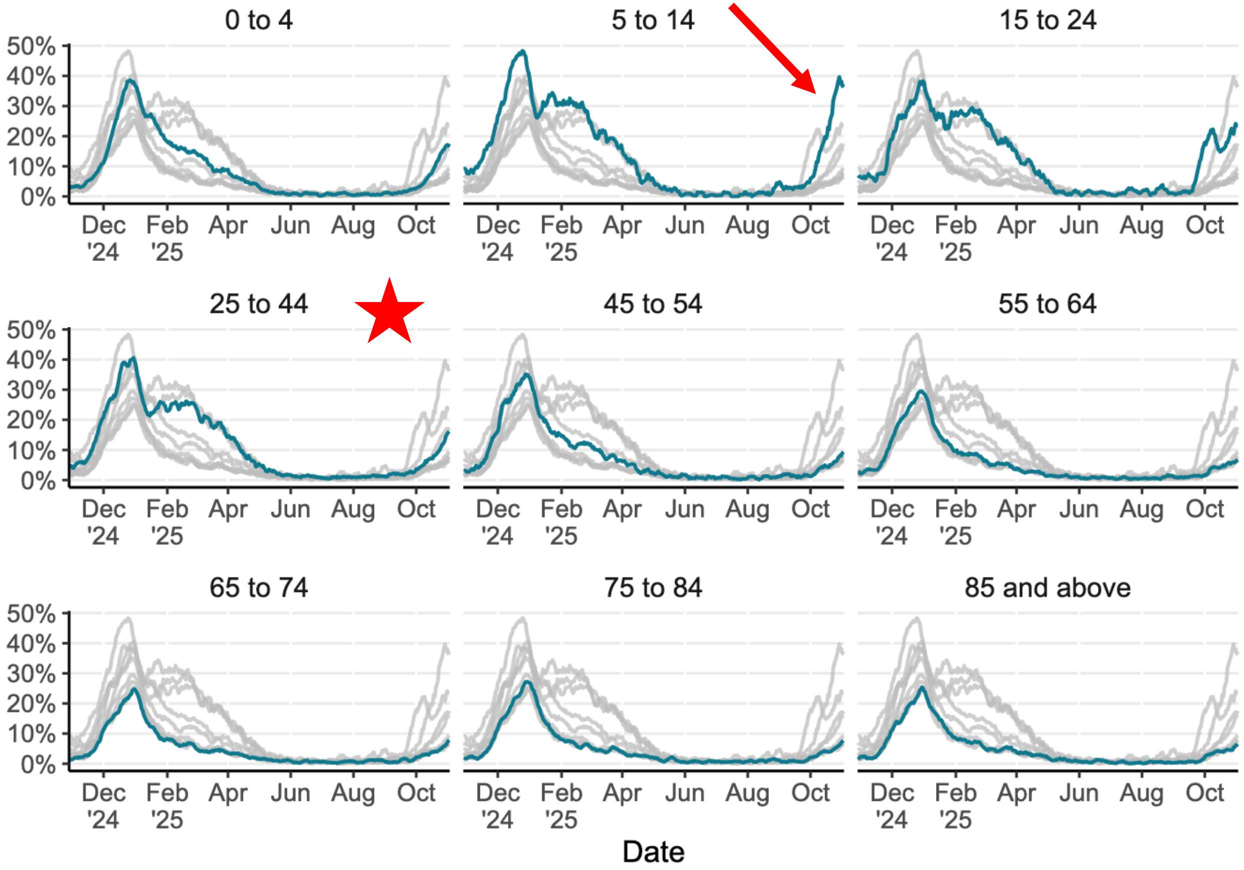
Note 2: data from previous seasons is aligned by day.

https://www.gov.uk/government/statistics/influenza-in-the-uk-annual-epidemiological-report-winter-2024-to-2025

UKHSA data for England

Up to week 44: Oct.27 –Nov.2, 2025

Figure 5. Daily percentage of tests positive for influenza among all reported influenza tests by age group (7-day rolling average), England [note 4]



Note 4: the highlighted line corresponds to the age group in the subplot title, grey lines correspond to all other age groups.

https://www.gov.uk/government/statistics/national-flu-and-covid-19-surveillance-reports-2025-to-2026-season

Tokyo Metropolitan Institute of Public Health

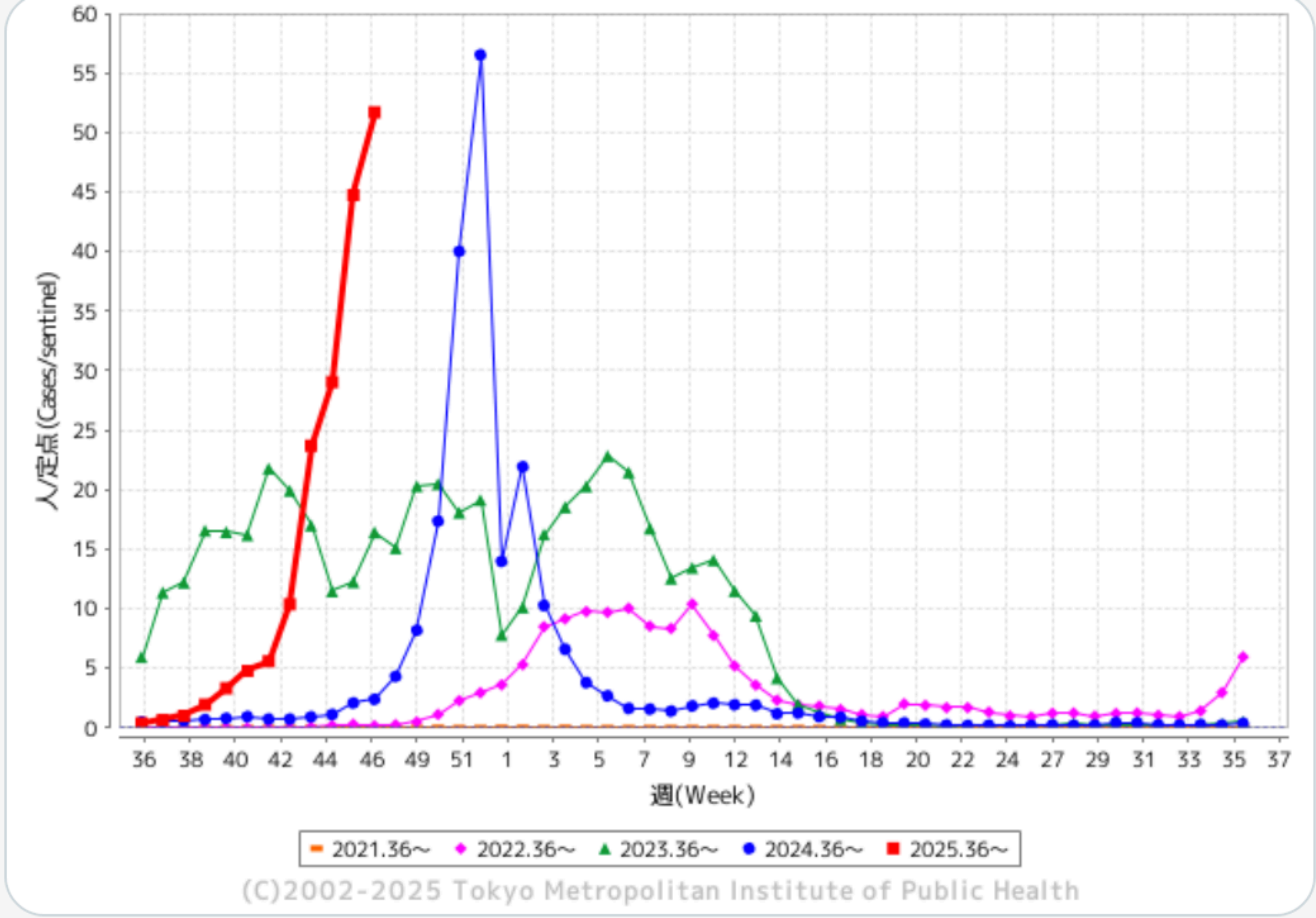
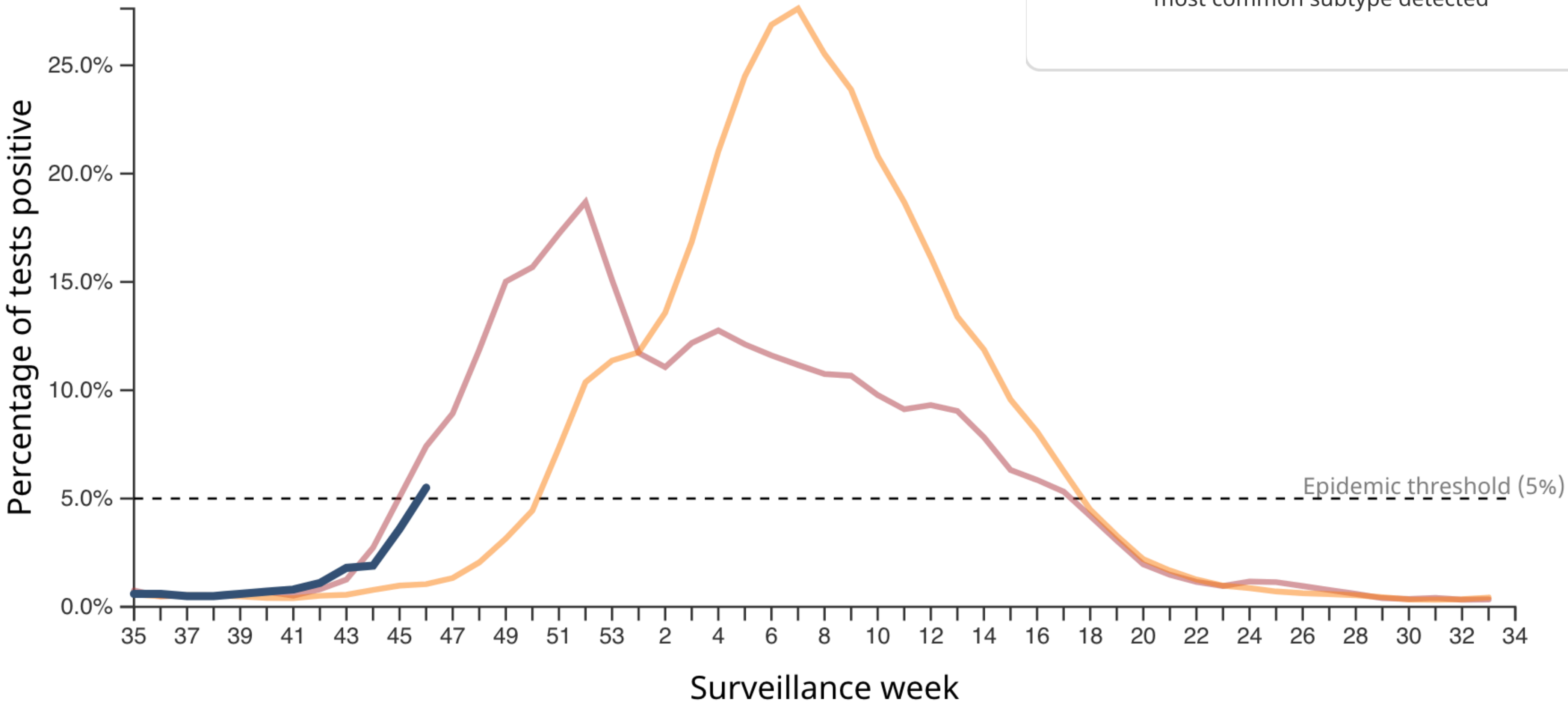


Figure 3: Percentage of tests positive for influenza in Canada for surveillance period 2025-2026 compared to previous periods

Select seasons 2025-2026 | 2024-2025 | 2023-2024 | 2022-2023 | Select all

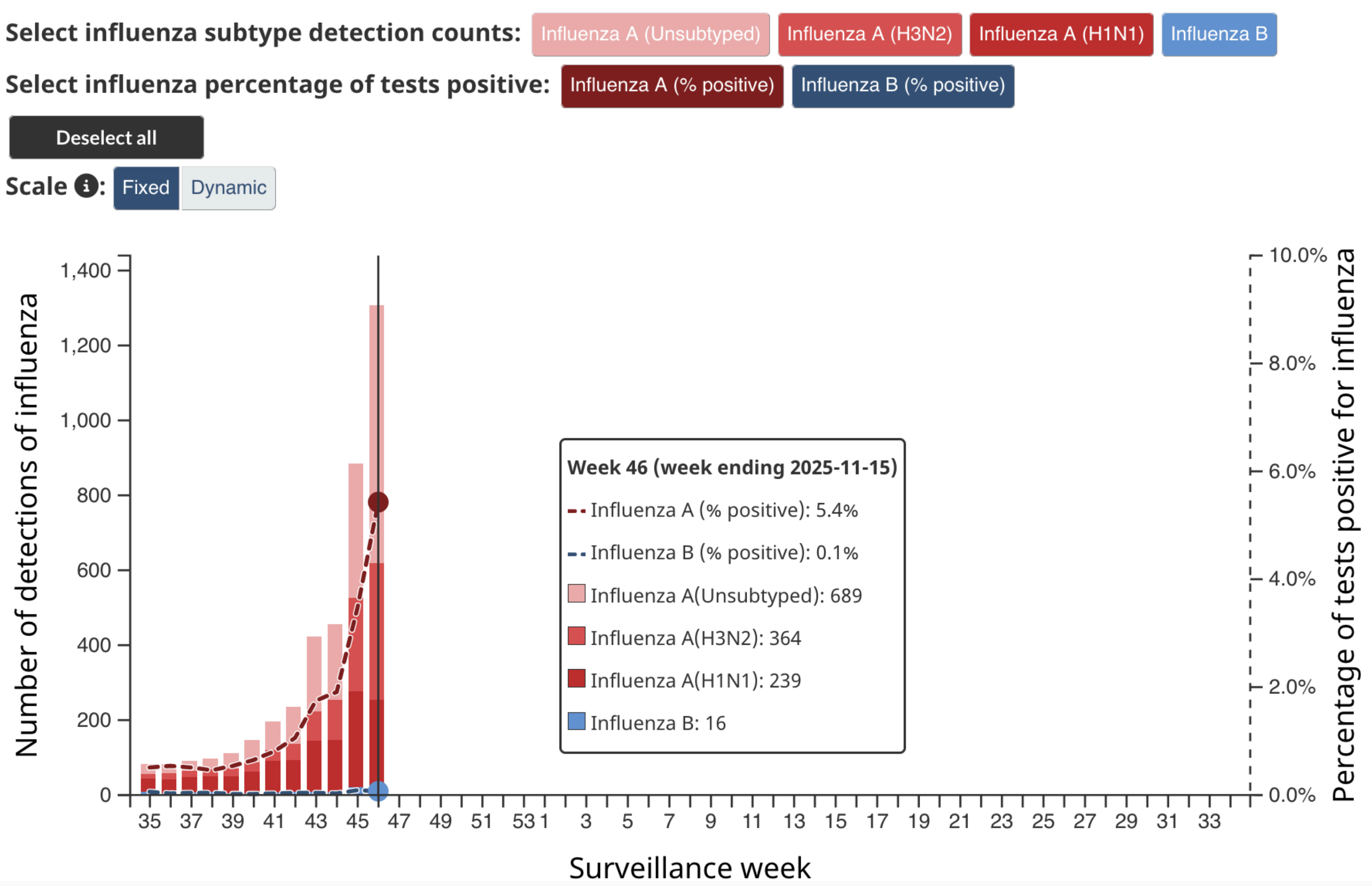
Dominant subtype

Influenza A(H3N2)
most common subtype detected



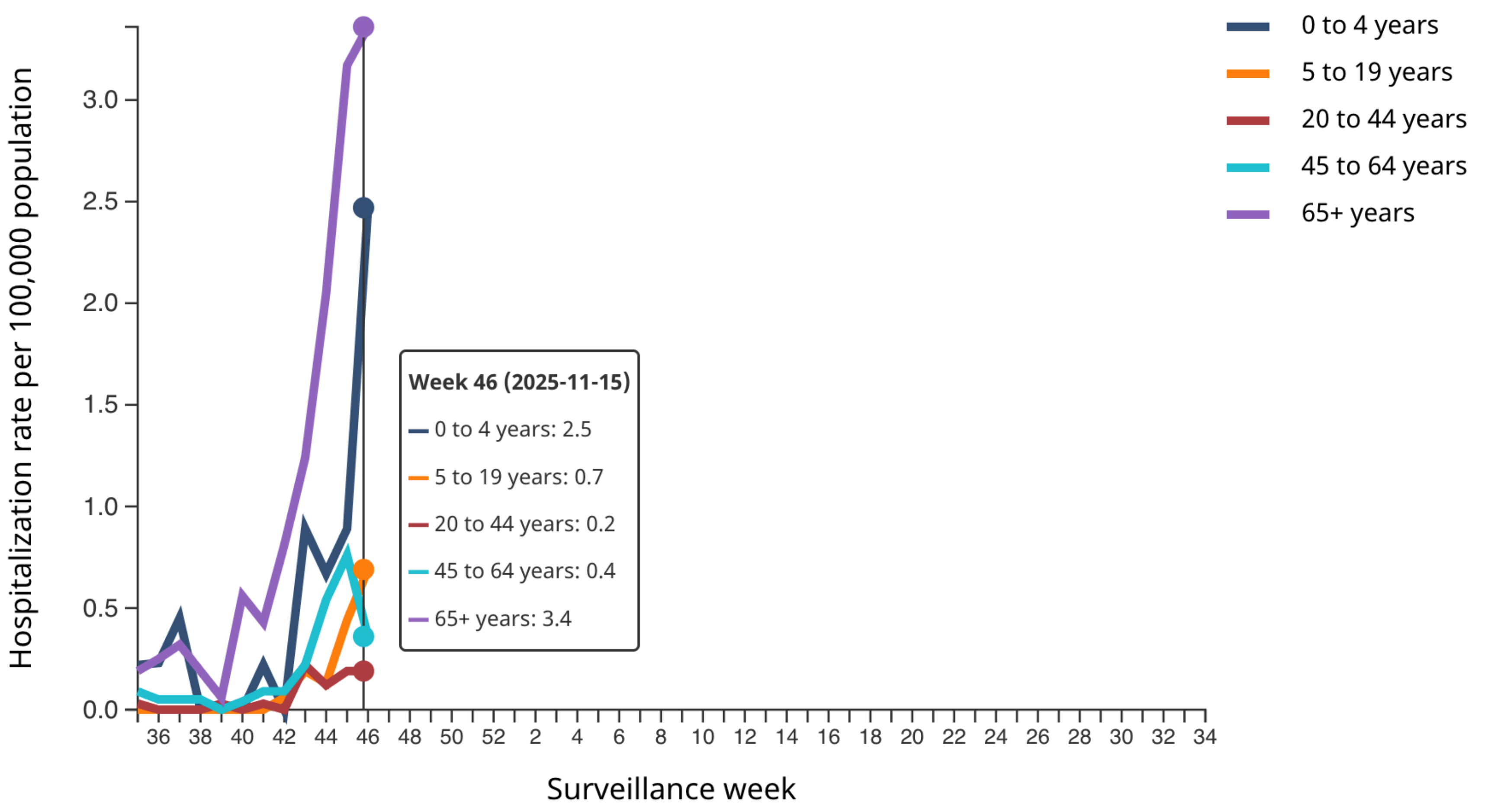
https://health-infobase.canada.ca/respiratory-virus-surveillance/influenza.html

Figure 2: Number of reported influenza detections and percentage of tests positive in Canada, by type, subtype, and report week



https://health-infobase.canada.ca/respiratory-virus-surveillance/influenza.html

Figure 8: Crude weekly rates (per 100,000 population) ⌄ of influenza-associated hospitalizations by age group and by surveillance week, Canada, participating provinces and territories, 2025-2026 surveillance period

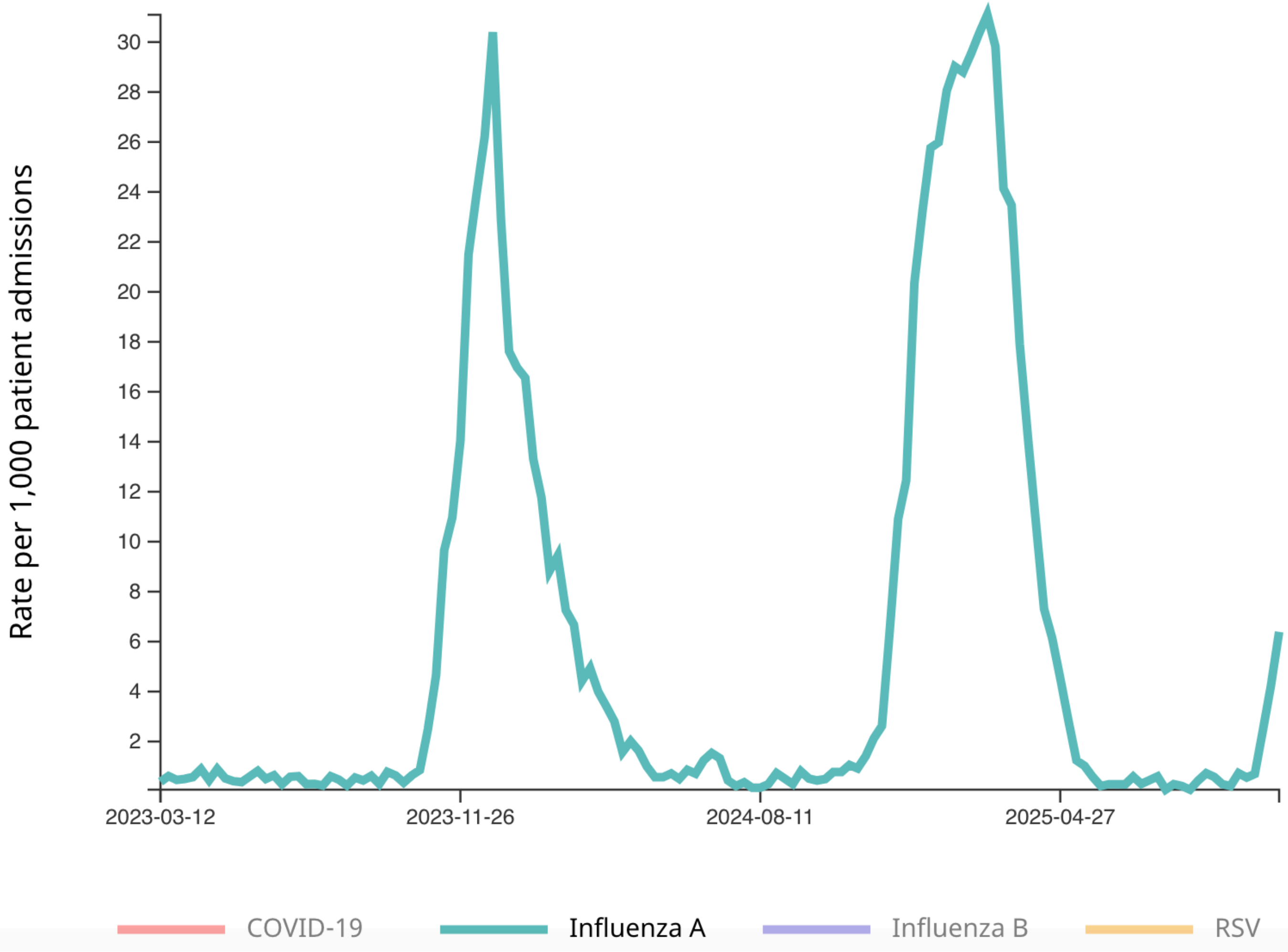


https://health-infobase.canada.ca/respiratory-virus-surveillance/influenza.html

Figure 1. Weekly incidence of patients hospitalized with a VRI per 1,000 patient admissions for

All ages

Data collection for Influenza A, Influenza B, and RSV began on January 1, 2023.



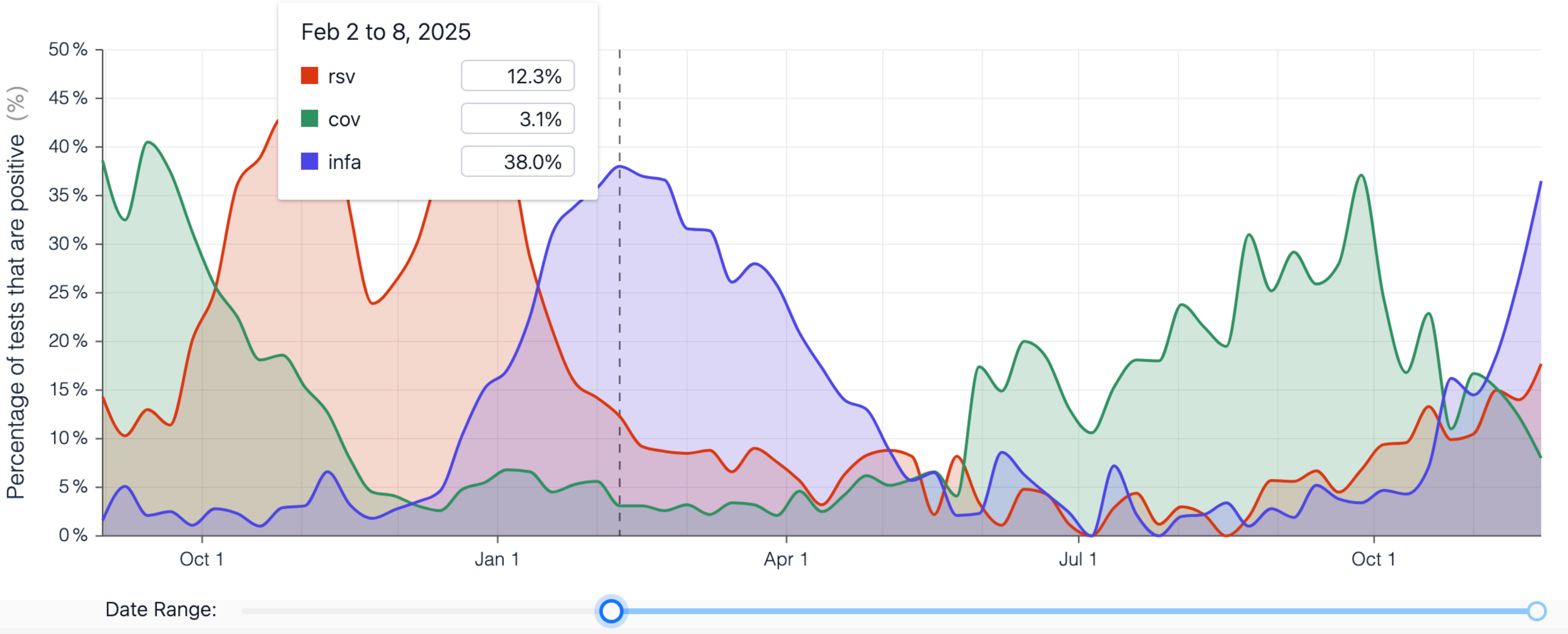
https://health-infobase.canada.ca/cnisp/viral-respiratory-infections.html

SPRINT-KIDS Dashboard

Show the percentage of tests that are positive for

patients with Influenza A × SARS-CoV-2 × RSV ×

including everyone in Canada aged 0 to 18 years old



https://dashboard.sprint-kids.ca/

What will happen this flu season?

Influenza A H3N2 (subclade K):
Vaccine Immunity Evading + more transmissible
Other viruses co-circulating

Host: Age-Cohorts & Imprinting
Immune System Dysfunction after Repeated Covid Infections
Immune Amnesia post Measles

Environment: Strained Canadian Healthcare
Misinformation Rampant
Vaccine Uptake?
Resistance to Masking
No Clean Indoor Air
Public Health leaders are MIA

What would applying the Precautionary Principle look like?

FLU
RSV
COVID
wildfire smoke
CAN 99
WEAR A CAN 99