



Interim Estimates of 2018- 2019 Seasonal Influenza Vaccine Effectiveness

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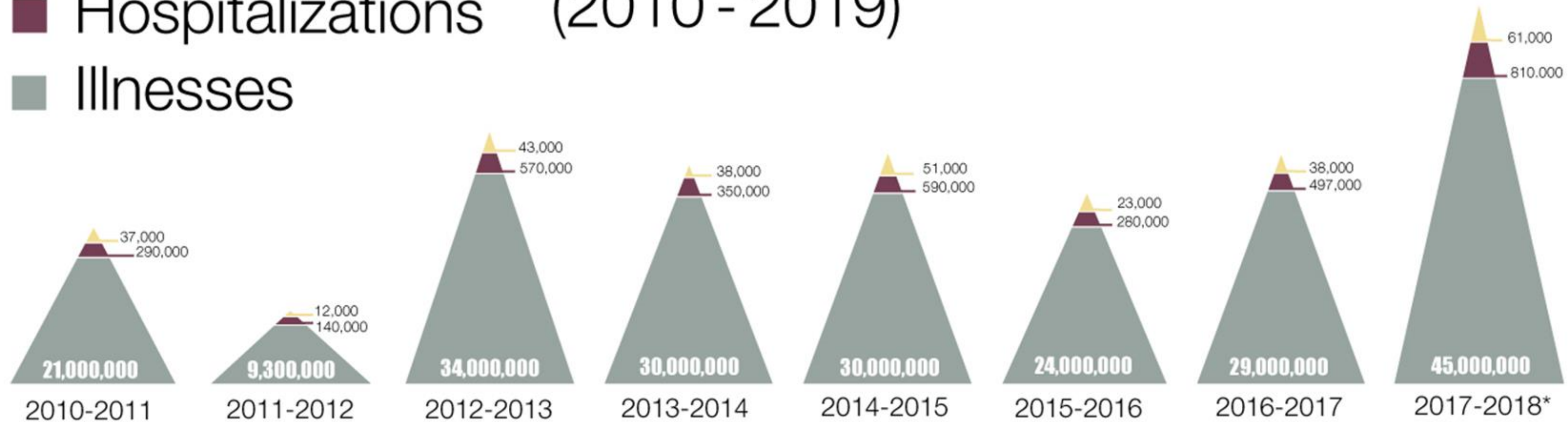
Agenda

- Background and Subtypes
- 2018-2019 Interim
- Compare and Contrast
 - 2018-2019 Year End
- Looking forward: the Flu and COVID-19

Overview

■ Deaths
■ Hospitalizations
■ Illnesses

Estimated U.S. Influenza Burden, By Season (2010 - 2019)



*Estimates for these seasons are preliminary and may change as data are finalized.

TYPES OF FLU

There are four main types of flu: A, B, C, and D.

A B C DA

Influenza A is the culprit behind headline-making pandemics of flu. Its ability to mutate and create new subtypes makes it hard to predict.

B

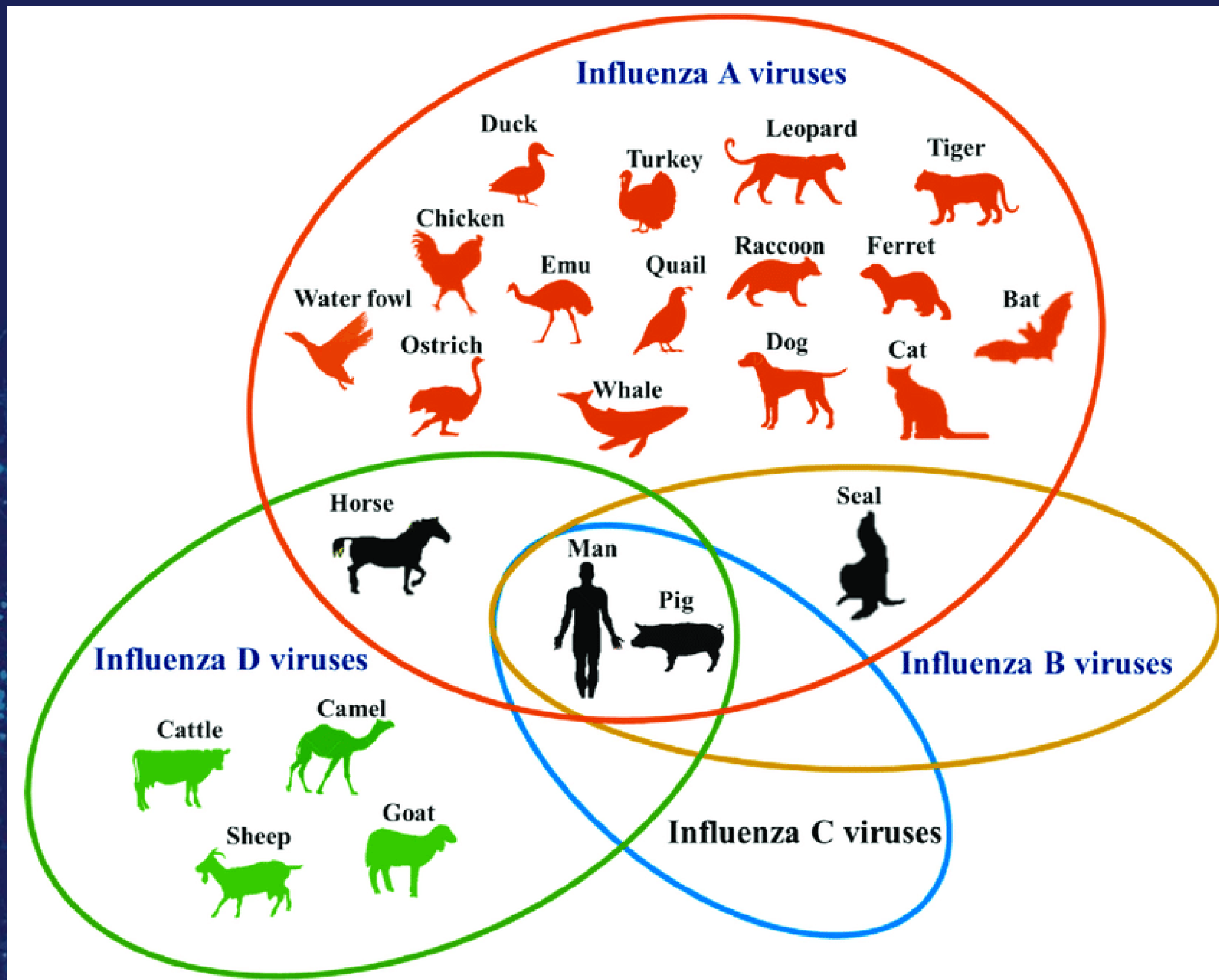
Along with Influenza A, Influenza B is a main driver of seasonal flu outbreaks.

C D

Influenza C causes mild upper respiratory infections, and Influenza D mainly affects cattle.

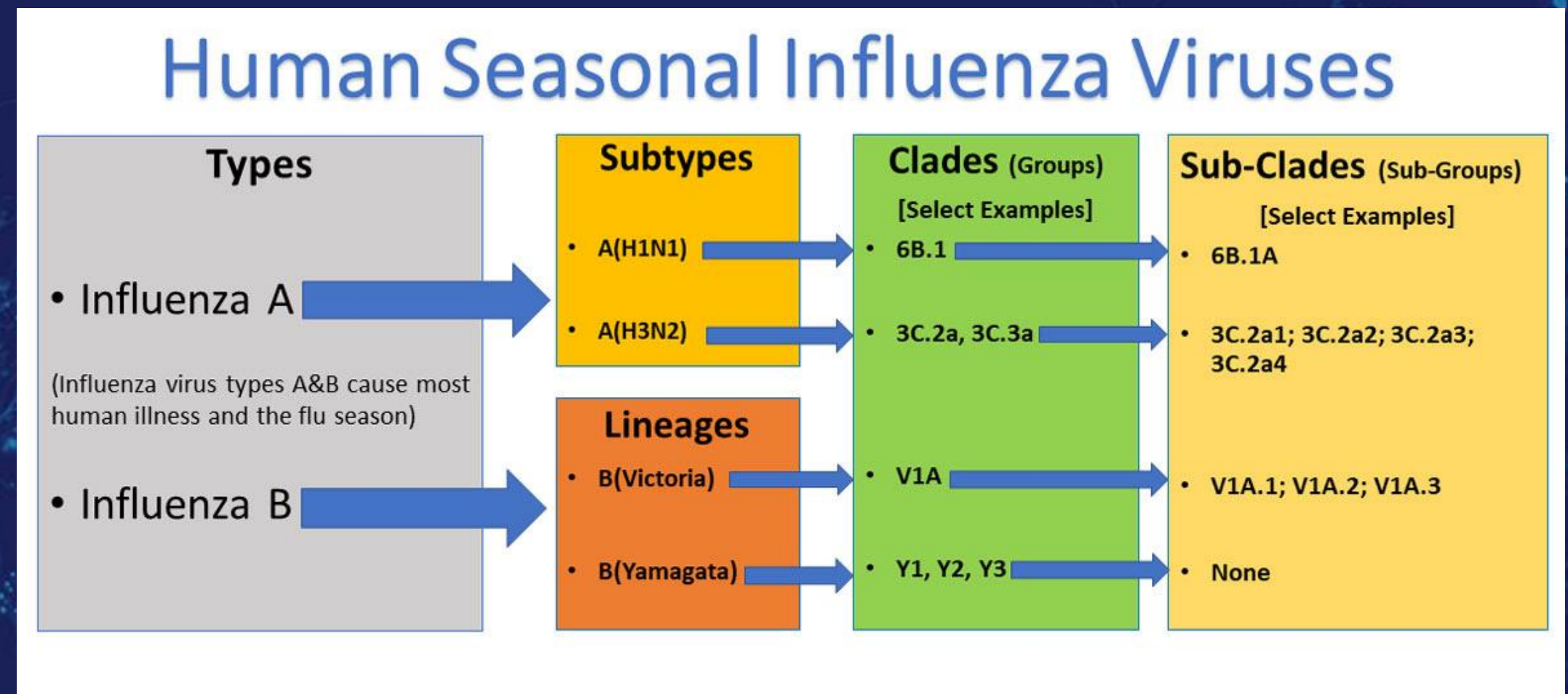
A B

The annual flu vaccine contains the two A and two B strains experts think will be the ones that get people sick that year.

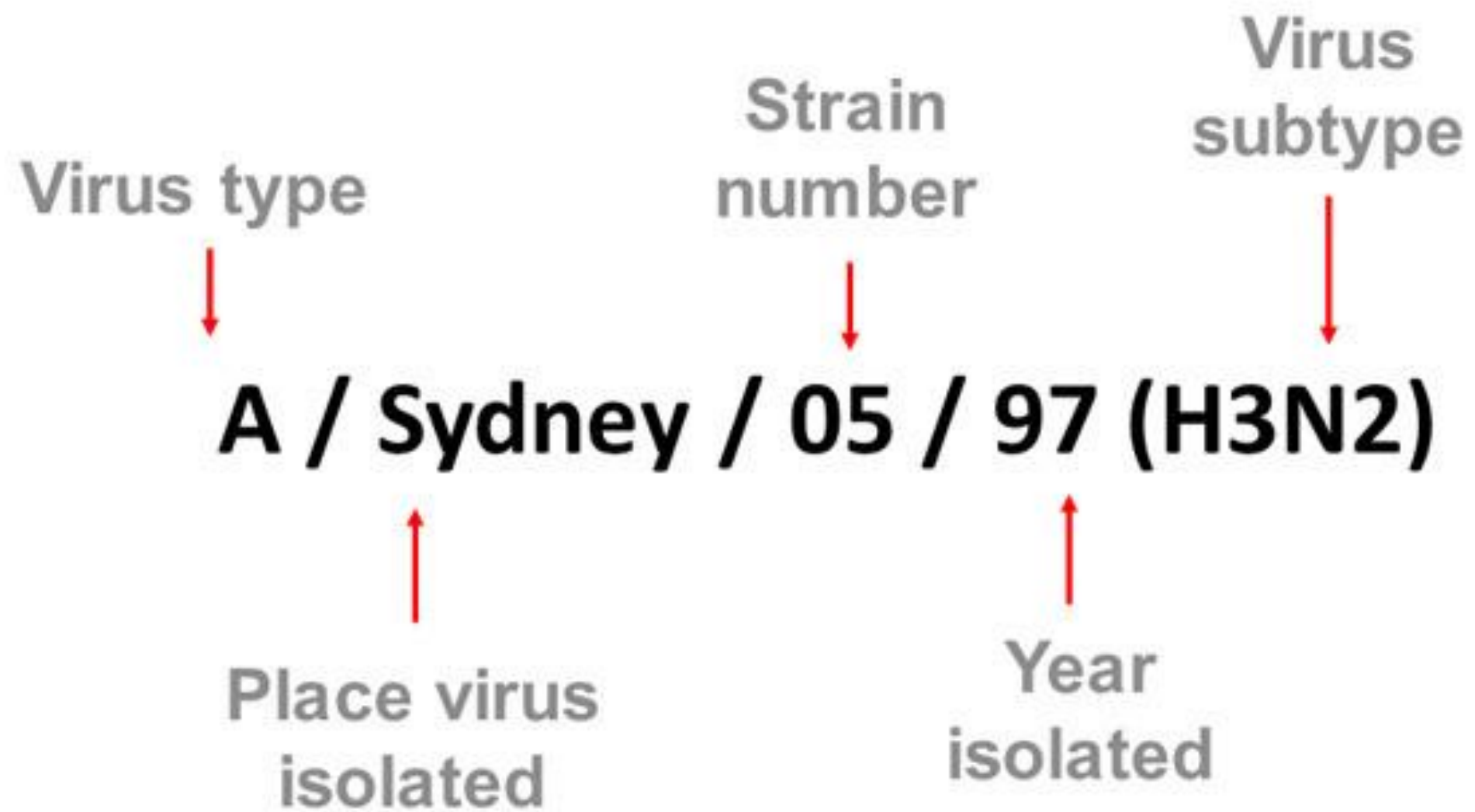


Classification

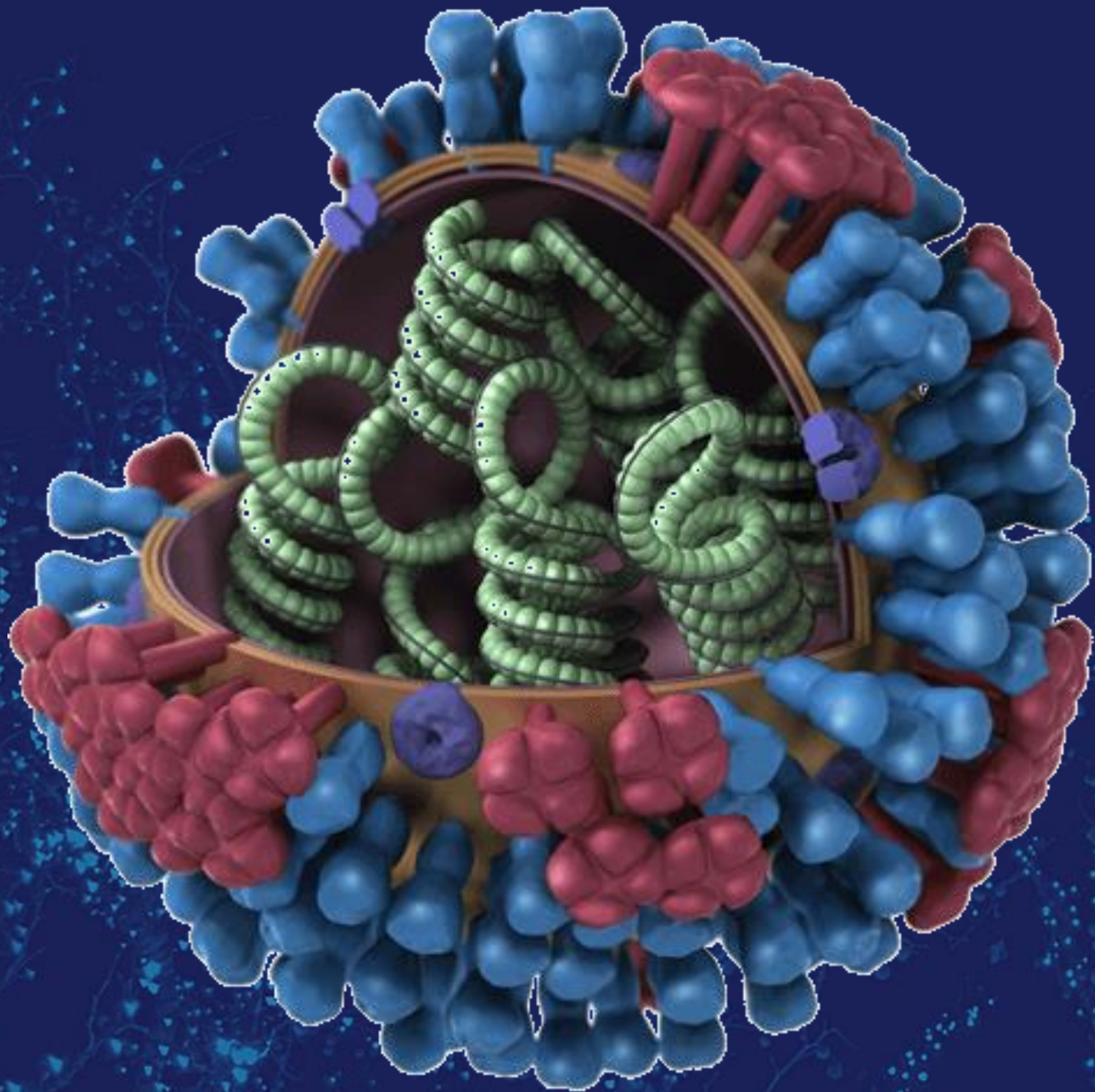
- Type A
 - Based on surface proteins
 - 18 H subtypes and 11 N subtypes
- Type B
 - By lineage and HA glycoprotein



Understanding the naming of flu viruses



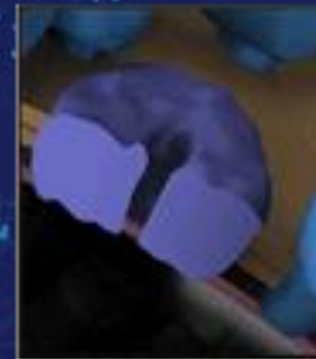
Influenza A Virus



Hemagglutinin



Neuraminidase



M2 Ion Channel

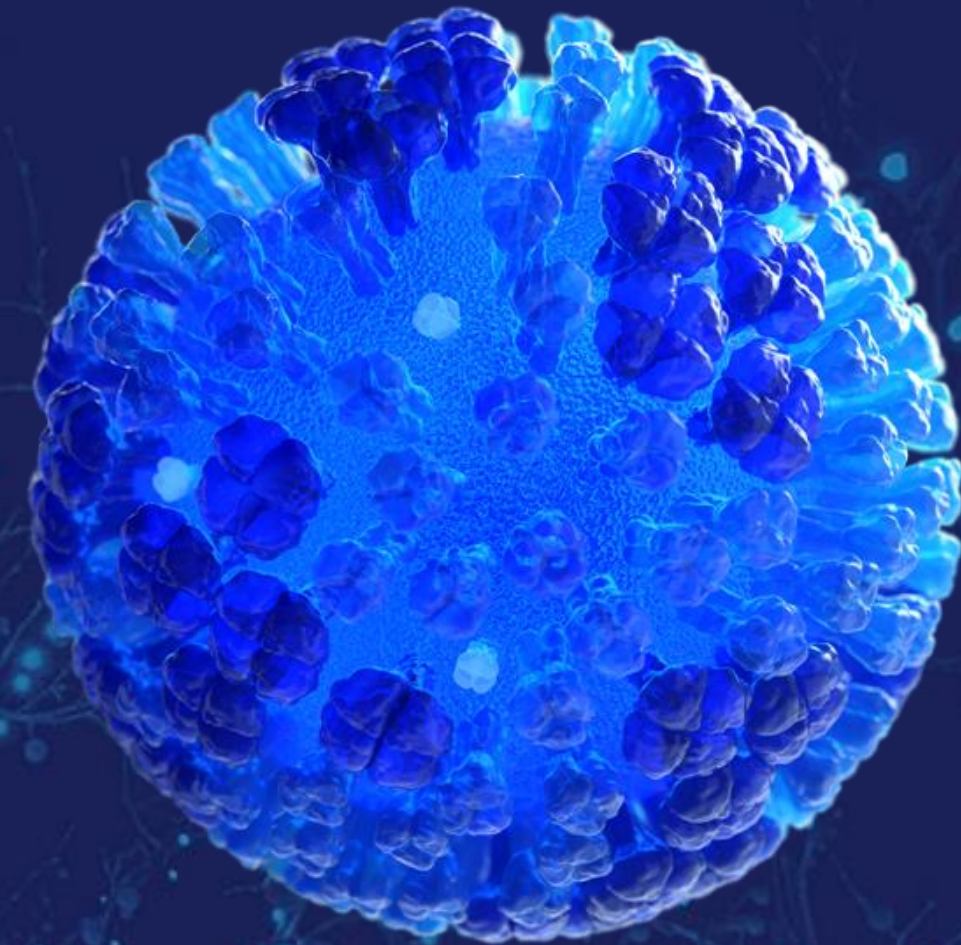


RNP

- Seasonal epidemics
- Pandemic potential
 - Drift and Shift
- 198 different subtype combos
 - 113 detected
- A(H1N1) and A(H3N2)

Influenza B Virus

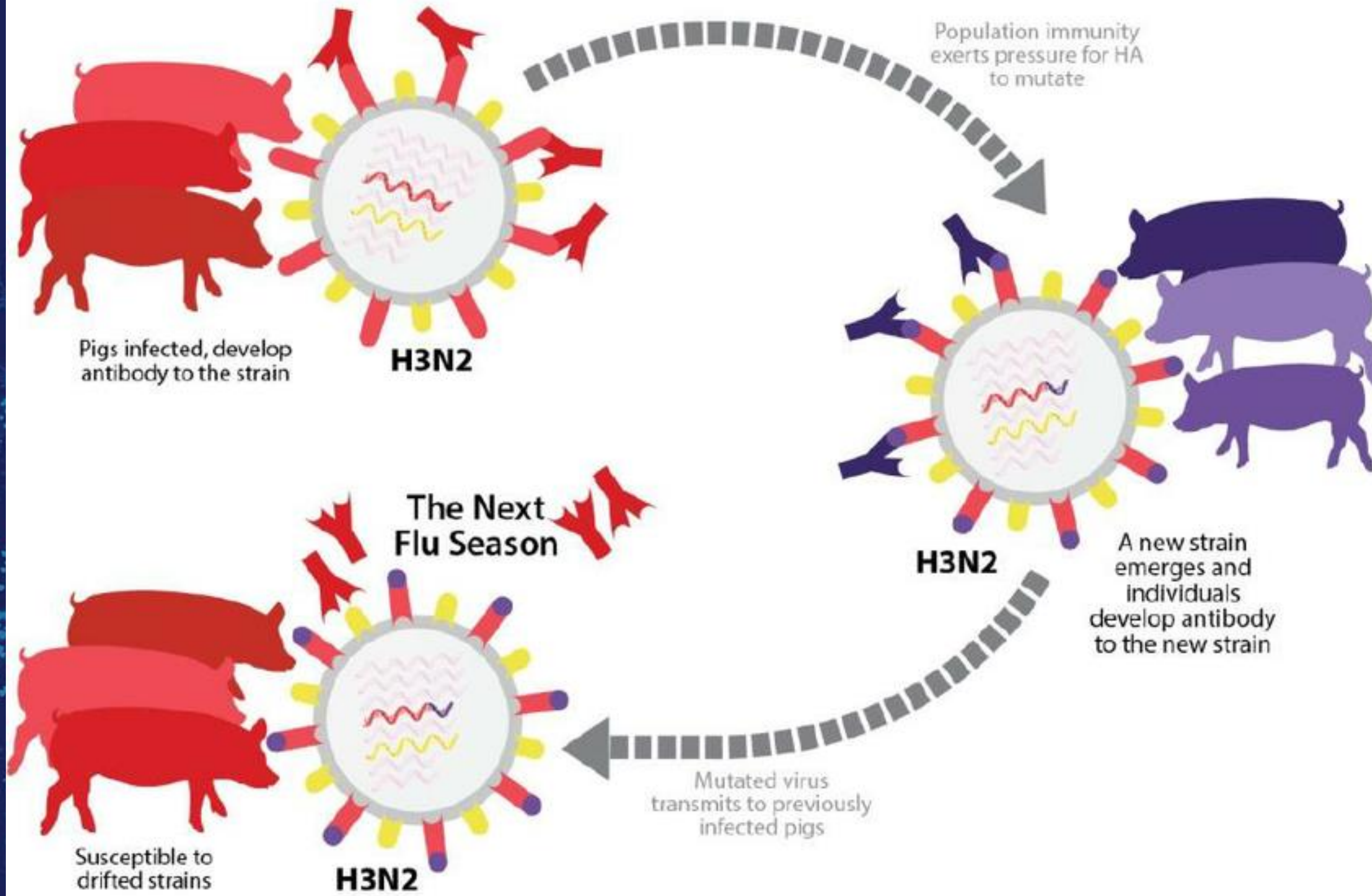
- Almost exclusive to humans
- Slower genetic/antigenetic change
 - Immunity implications?
- Co-circulating lineages



Antigenetic Drift

- Small mutations that alter surface proteins (antigens)
 - Vaccine targets
- Happen continually over time
- Reason for seasonal vaccines

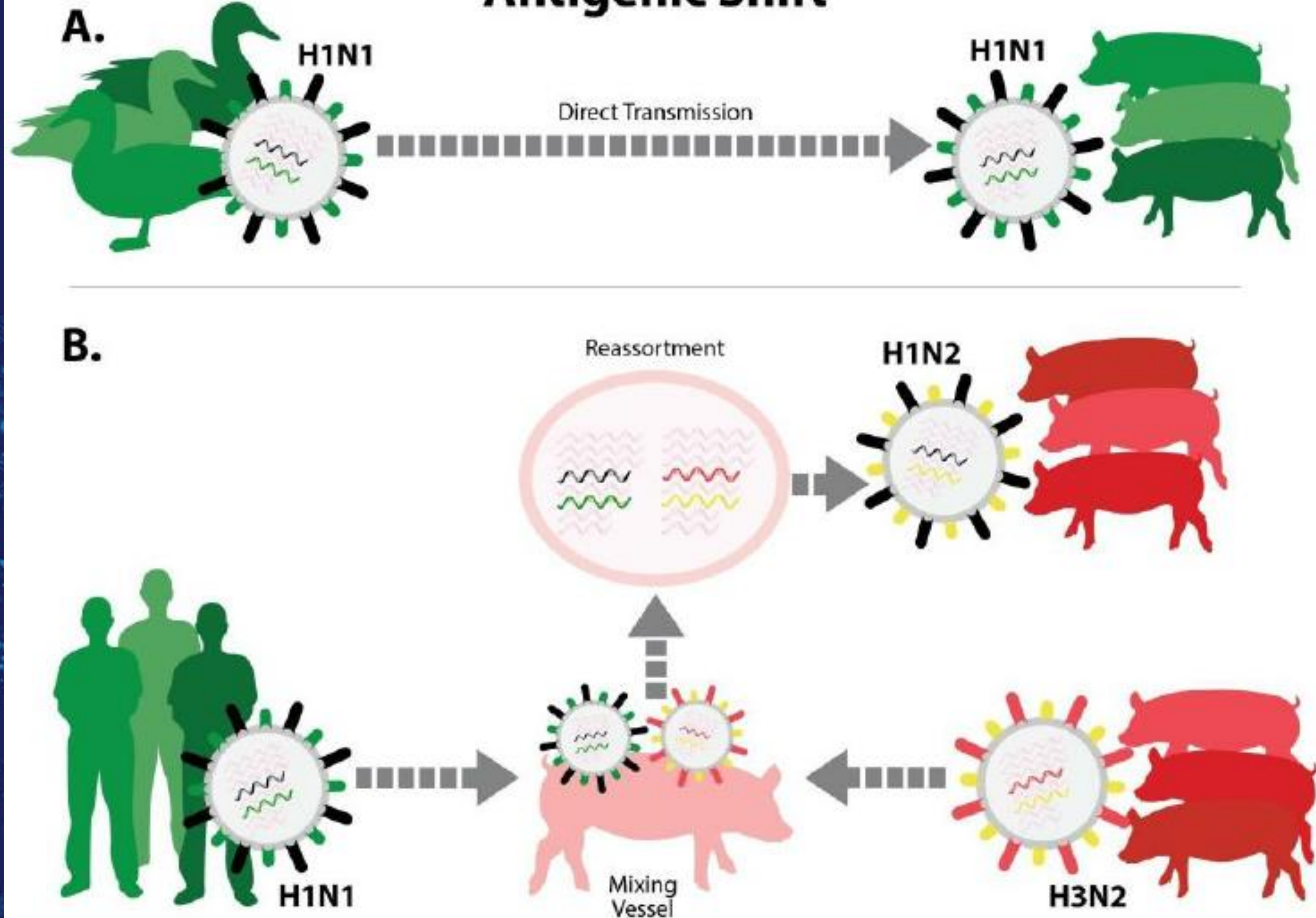
Antigenic Drift



Antigenetic Shift

- Major change in Influenza A
- Abrupt, not over time
- NEW surface proteins introduced
 - Pandemic potential
- Less frequent

Antigenic Shift



CASE STUDY: 2009 H1N1

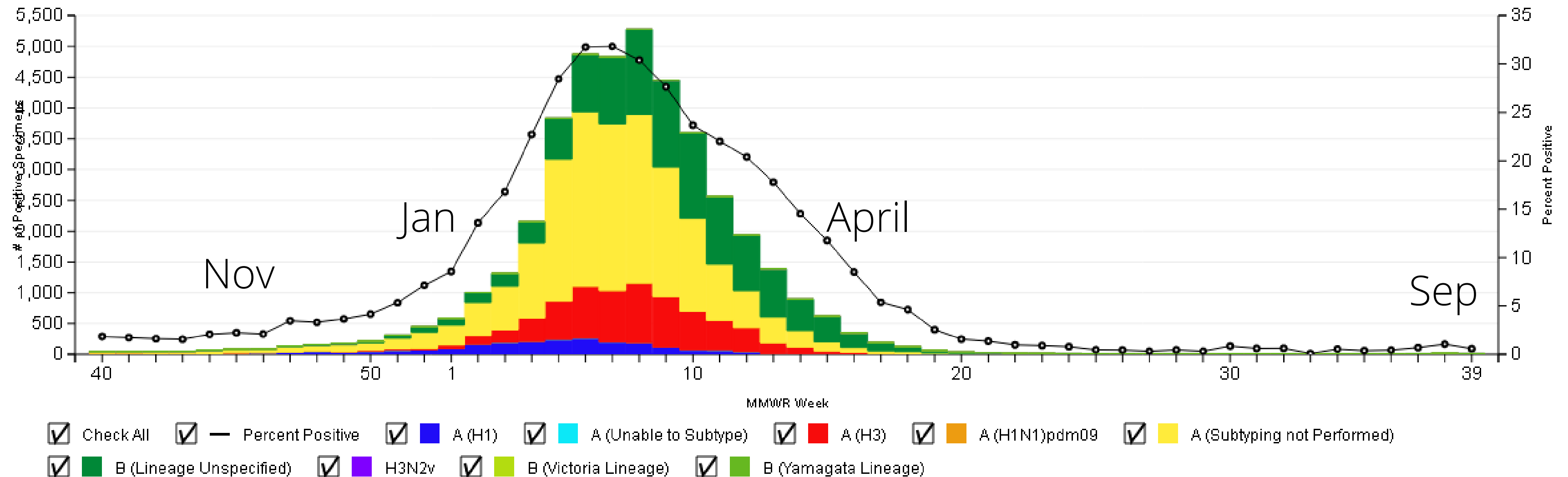


Influenza in the U.S.: 2007-2008 Season

FLUVIEW
interactive



Influenza Positive Tests Reported to CDC, National Summary,
2007-08 Season, week ending Sep 27, 2008
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet



2009 (H1N1)pdm09 Pandemic



April 15, 2009 → April 25, 2009 → April 28, 2009 → May 2009

Index case

WHO Emergency

FDA Test
Approval

Peak #1

October 5, 2009 → Late Oct 2009 → Late Dec 2009

1st Vaccine
Administered in US

Peak #2

Vaccine widely
available

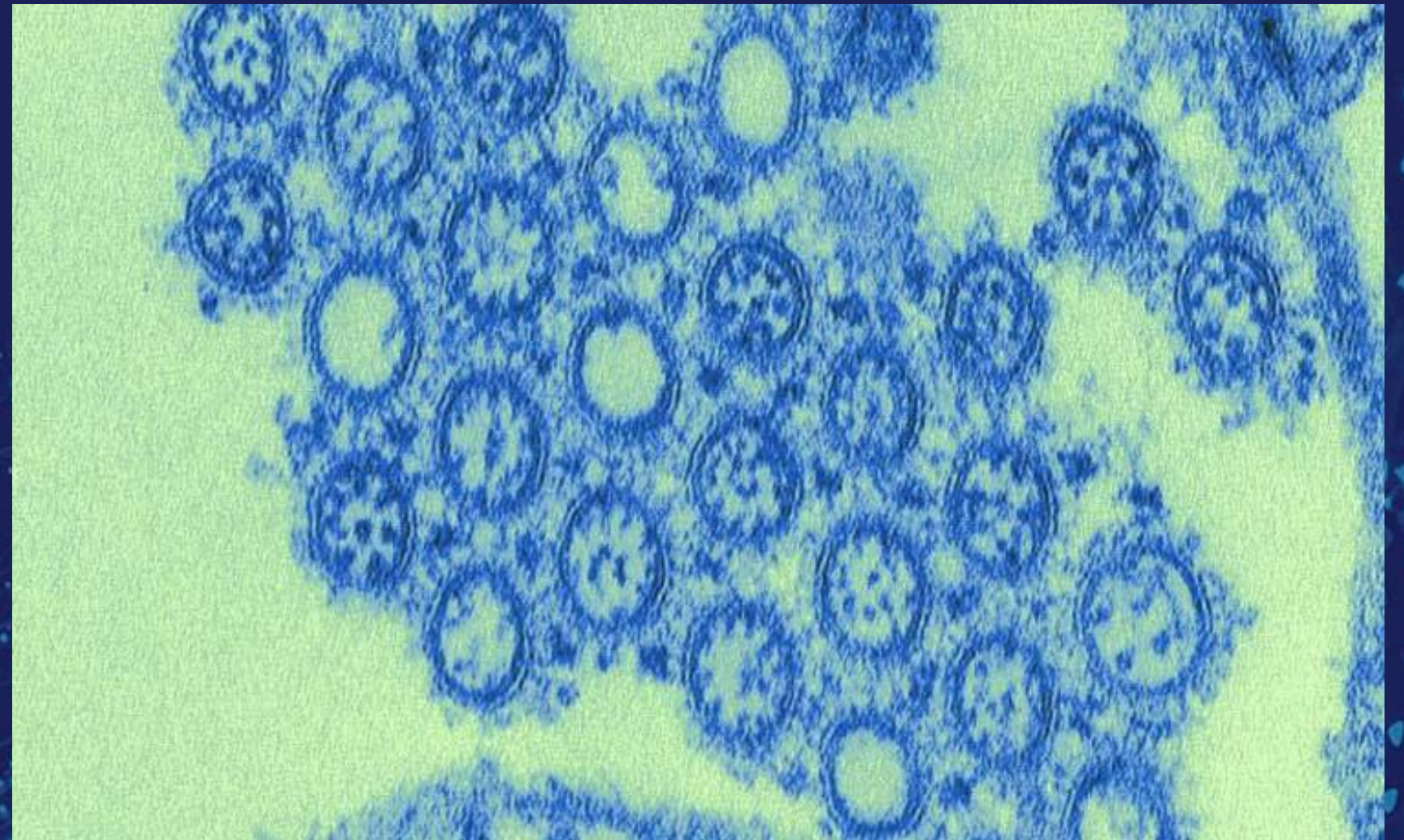
January 2010 → August 11, 2010

Activity drops
below baseline

WHO declares
end of
pandemic

The Aftermath

- 151,700 - 575,400 deaths worldwide (estimate)
- 80% <65 years old
 - Normally 70%-90% in >65
 - 0.001%-0.007% mortality



Vaccine Development

- 3 types of production, 2 types of vaccines:
 - Egg-based (most common), Cell-based, Recombinant (synthetic)
 - Inactivated (shot), live attenuated (nasal spray)
- Based on surveillance of previous seasons and forecasting
- Is there a good vaccine virus available?

The 2018-2019 Vaccine

- Trivalent:
 - A/Michigan/45/2015 (H1N1)pdm09-like virus
 - A/Singapore/INFIMH-16-0019/2016 A(H3N2)-like virus (updated)
 - B/Colorado/06/2017-like (Victoria lineage) virus (updated)
- Quadrivalent:
 - + B/Phuket/3073/2013-like (Yamagata lineage) virus

Interim Estimates of 2018–19 Seasonal Influenza Vaccine Effectiveness

- Criteria for start:
 - Increasing ILI activity or 1+ confirmed cases per week for 2 weeks
- Five study sites
 - Michigan, Pennsylvania, Texas, Washington, Wisconsin
- Recruitment based on seeking outpatient care for ARI

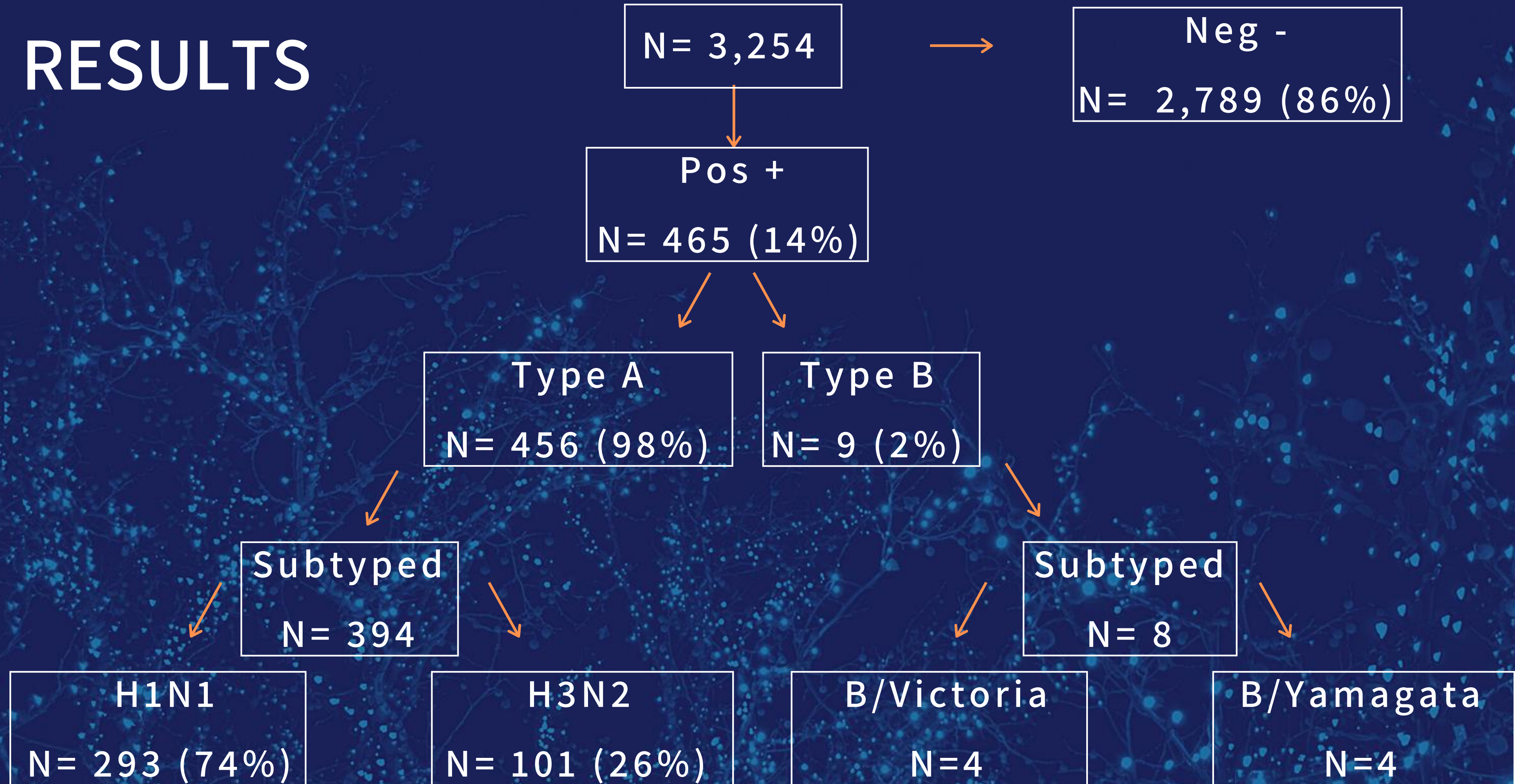
Eligibility

- ≥ 6 months old on September 1, 2018
 - Reported ARI with cough
 - Onset < 7 days ago
- Not treated with influenza antivirals

METHODS

- Nov 23, 2018 - February 2, 2019
- Interview component
- Nasal and oropharyngeal swabs
 - RT-PCR
- "Vaccinated" = >1 dose >14 days before onset
- Vaccine effectiveness =
 - $100 \times (1 - OR)$

RESULTS



RESULTS

- 1,789 (55%) of cohort vaccinated
 - Strong significant trends by state, age, race/ethnicity
 - Illness onset to enrollment time span ($p=0.01$)
- 57% of negative results vs 43% of positive results had received vaccine

RESULTS: VACCINE EFFECTIVENESS

- Adjusted vaccine effectiveness against ARI for all types: 47% [34%-57%]*
 - Slightly lower for ONLY A(H1N1)pdm09 and ONLY A(H3N2)
 - Highest effectiveness in 6 mos-17 yrs for both subtypes

LIMITATIONS

- Sample size
 - Interim estimate
- Self-report of vaccination status at 4/5 sites
- Observational study design
- Outcome = outpatient care

2018-2019 YEAR END OUTCOMES

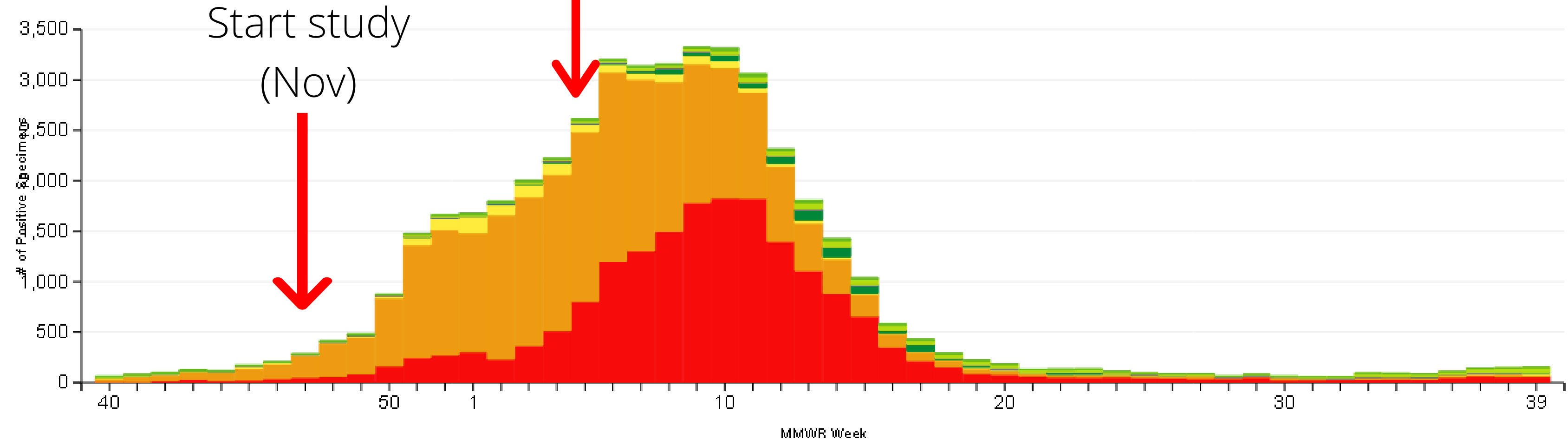
FLUVIEW
interactive

End study (Feb)



Influenza Positive Tests Reported to CDC by Public Health Laboratories, National Summary,
2018-19 Season, week ending Sep 28, 2019

Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet



- Check All
- A (H1)
- A (Unable to Subtype)
- A (H3)
- A (H1N1)pdm09
- A (Subtyping not Performed)
- B (Lineage Unspecified)
- H3N2v
- B (Victoria Lineage)
- B (Yamagata Lineage)

YEAR END RESULTS

- Total participants = 10,012
 - 72% Negative, 28% Positive
- Trend by study site remains
- Greater age group representation
- Vaccine effectiveness:
 - 44% A(H1N1)
 - 9% A(H3N2) overall
 - 3C.3a (5%), 3C.2a1 (46%)
 - 46% Influenza B

IMPLICATIONS

- Interim implies A(H1N1) was dominant
- Vaccine effectiveness
 - A(H1N1) similarity to reference
 - A/Michigan/45/2015
- A(H3N2) predominant after Feb
 - Shift in clade circulation: 3C.2a -> 3C.3a
- WHO 2019-2020 recommendations

The 2019-2020 Vaccine

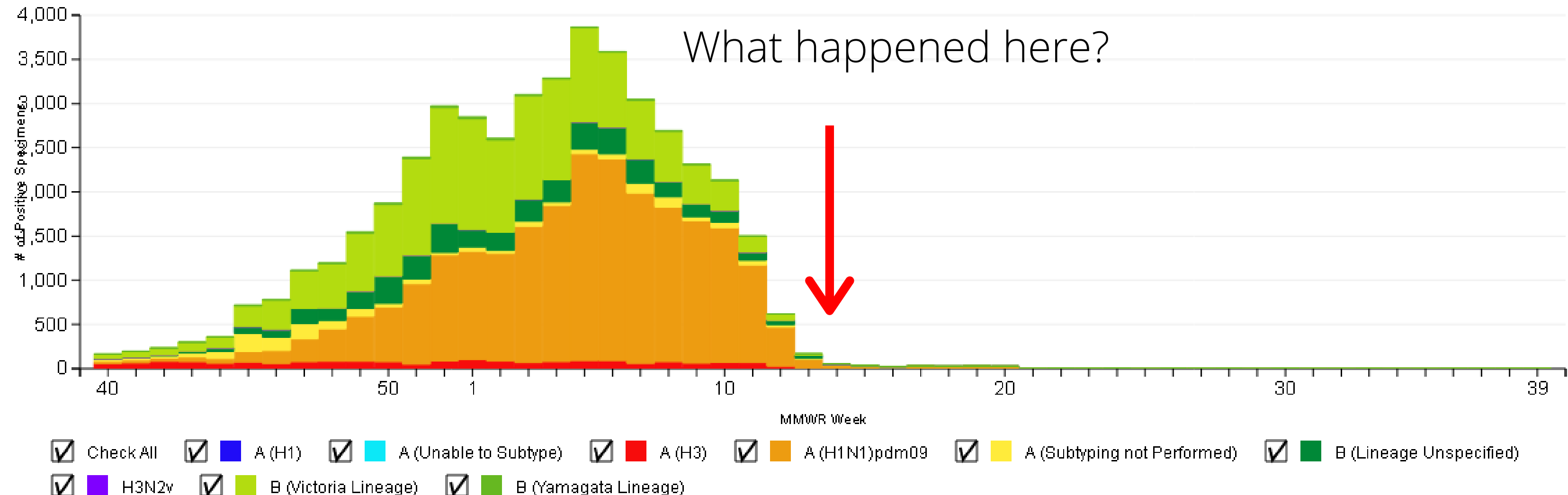
- Trivalent:
 - A/Brisbane/02/2018 (H1N1)pdm09-like virus (updated)
 - A/Kansas/14/2017 (H3N2)-like virus (updated)
 - B/Colorado/06/2017-like (Victoria lineage) virus
- Quadrivalent:
 - + B/Phuket/3073/2013-like (Yamagata lineage) virus

2019-2020 Season: COVID Impacts

FLUVIEW
interactive



Influenza Positive Tests Reported to CDC by Public Health Laboratories, National Summary,
2019-20 Season, week ending Sep 26, 2020
Reported by: U.S. WHO/NREVSS Collaborating Laboratories and ILINet



2019-2020 Season: COVID Impacts

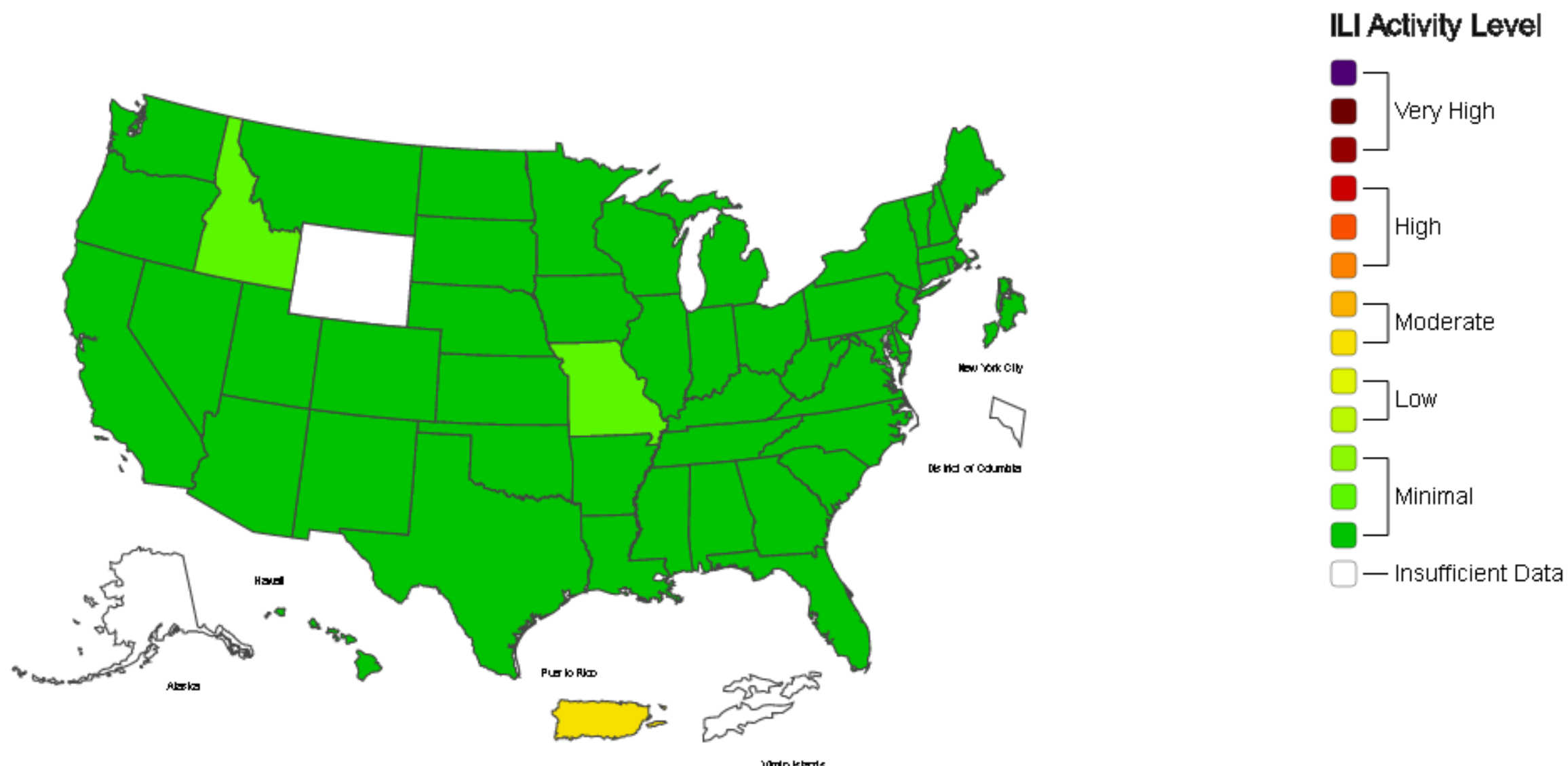
FLUVIEW
interactive



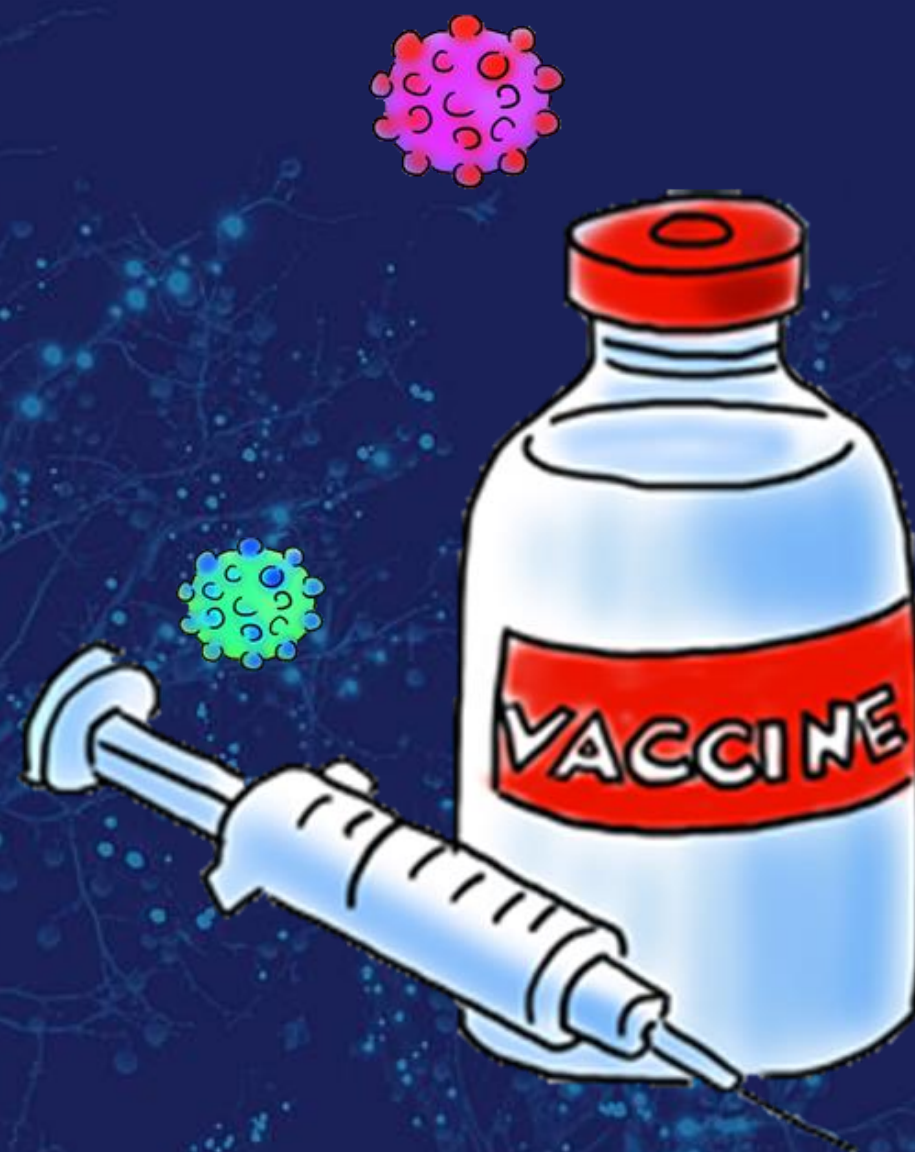
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINet

2019-20 Influenza Season Week 39 ending Sep 26, 2020



Takeaway: Get Your Flu Shot!



Sources

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Discussion Questions

- What factors might account for the dramatic rise in Influenza B subtypes in 2019-2020/should we expect this trend to persist?
- Why do you think only Influenza A undergoes antigenetic SHIFT?
- Given the relaxing of COVID-19 guidelines, how do you see this affecting the imminent flu season?