

# **Influenza Work Group: Updates, Considerations, and Proposed Recommendations for the 2020-21 Season**

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Advisory Committee on Immunization Practices

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# Acknowledgements

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# Overview

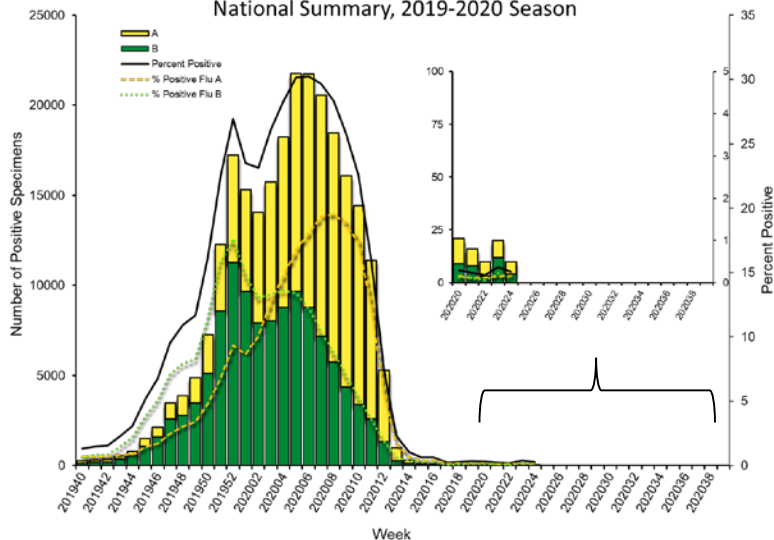
- Updates
  - 2019-20 influenza activity
  - Preliminary 2019-20 influenza vaccine effectiveness
  - 2019-20 influenza vaccine safety update
- WG considerations and proposed recommendations

# **2019-20 Influenza Activity**

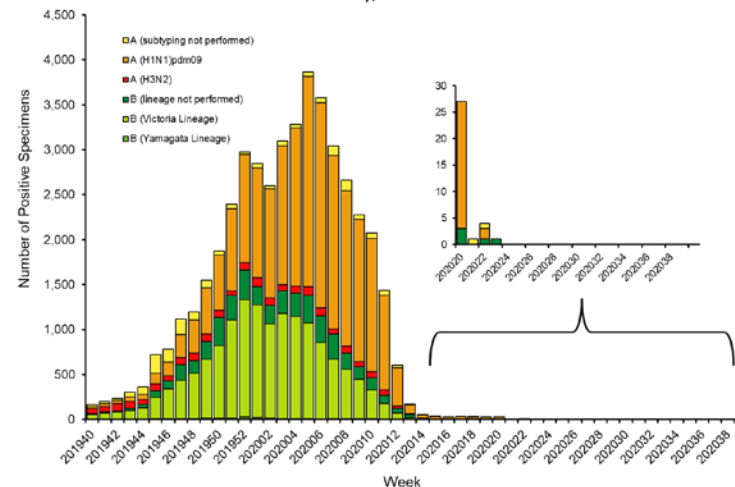
Slides courtesy of Lynnette Brammer and colleagues

# Influenza Virologic Surveillance, 2019-2020 Season

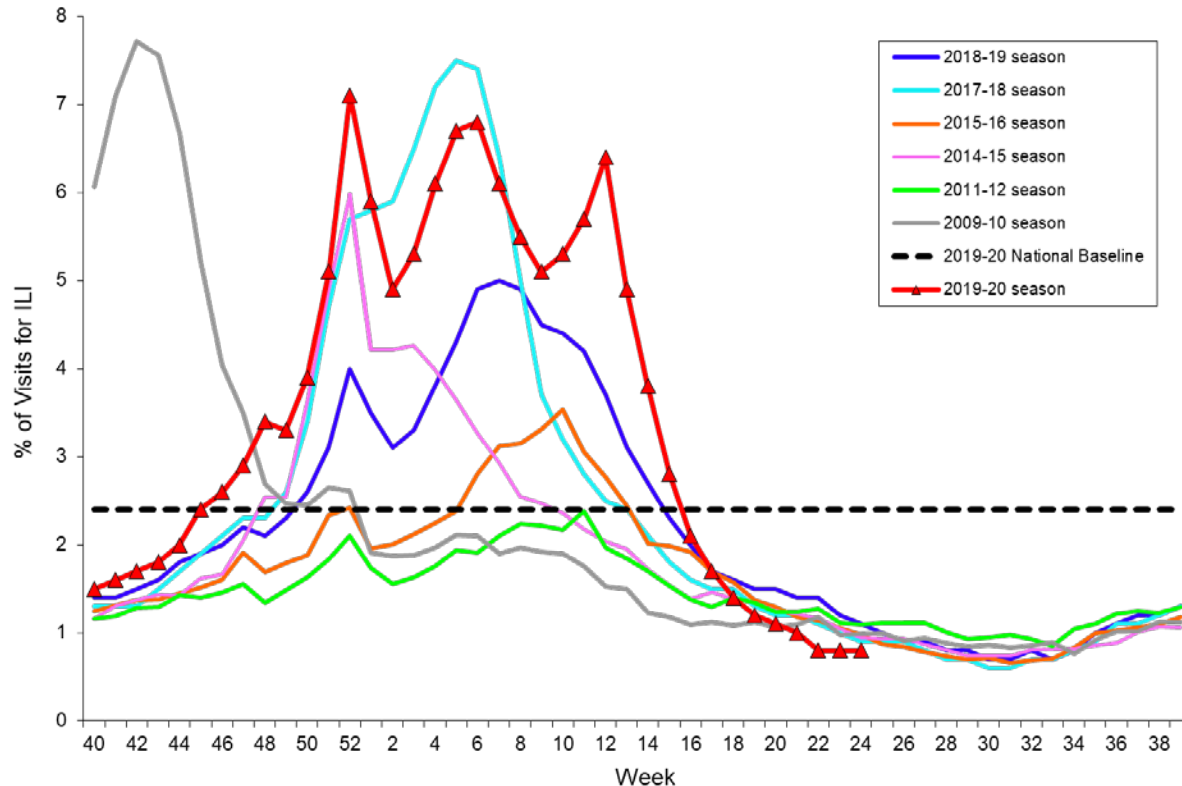
Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories,  
National Summary, 2019-2020 Season



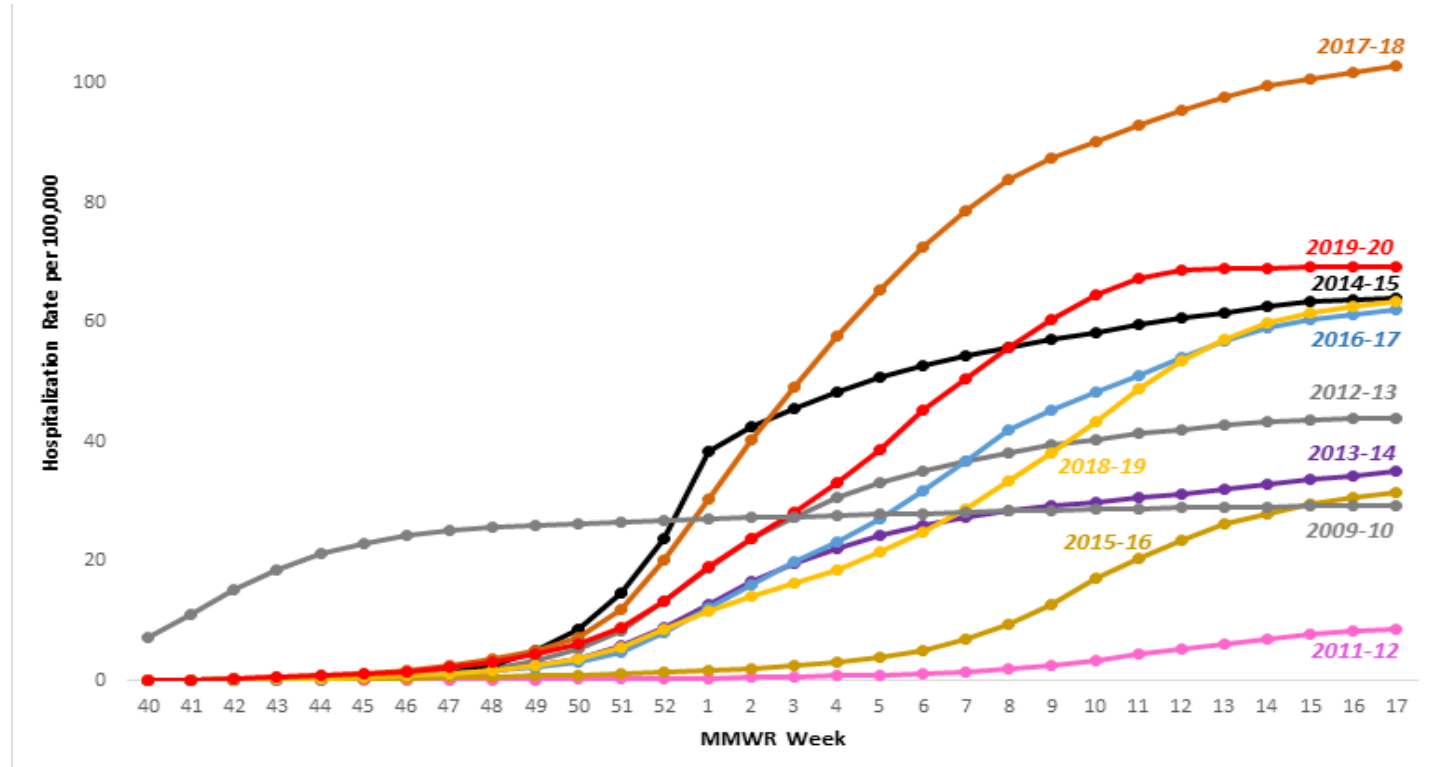
Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories,  
National Summary, 2019-2020 Season



# Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2019-2020 and Selected Previous Seasons

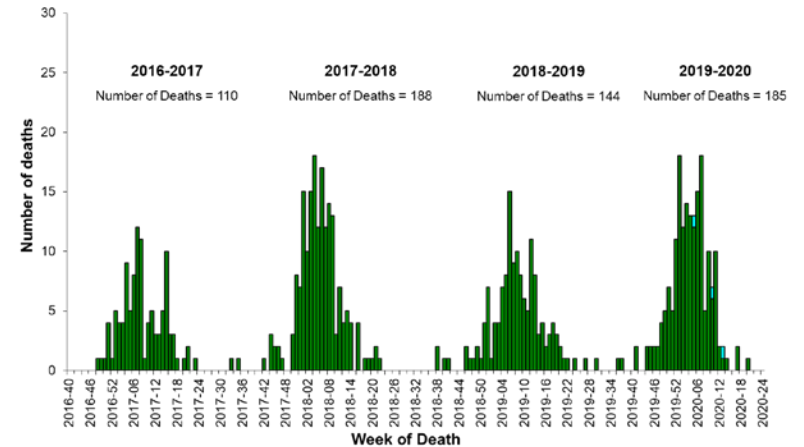
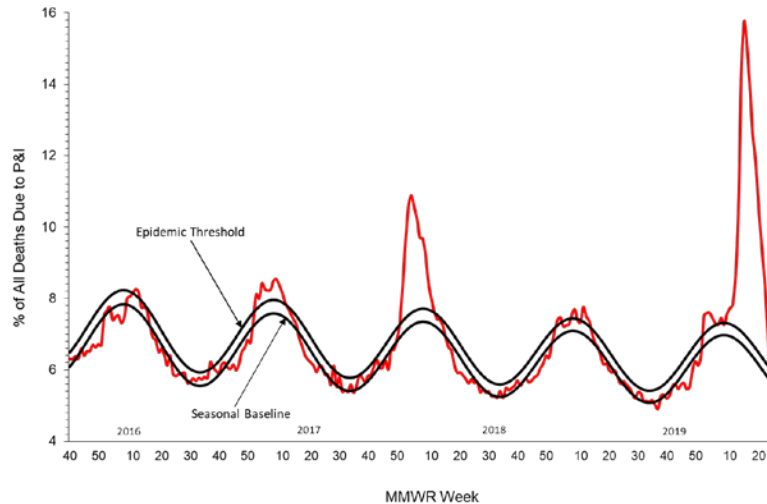


# Cumulative Rate of Laboratory Confirmed Influenza-Associated Hospitalizations, FluSurvNet, 2009-10 - 2019-20



# Influenza-Associated Mortality

Pneumonia and Influenza Mortality from  
the National Center for Health Statistics Mortality Surveillance System  
Data through the week ending June 13, 2020, as of June 18, 2020





# 2019-20 Flu Season: Preliminary Burden Estimates

CDC estimates\* that, from October 1, 2019, through April 4, 2020, there have been:

39,000,000 – 56,000,000  
flu **illnesses**



18,000,000 – 26,000,000  
flu **medical visits**



410,000 – 740,000  
flu **hospitalizations**



24,000 – 62,000  
flu **deaths**



# **Preliminary 2019-20 U.S. VE Estimates**

## **U.S. Flu VE Network—Data as of June 9, 2020**

Slides courtesy of Jessie Chung, Brendan Flannery, Manish Patel and colleagues

# Preliminary Estimates of 2019–20 Seasonal Influenza Vaccine Effectiveness

for the US Flu VE Network

**DATA AS OF JUNE 9, 2020**

Advisory Committee on Immunization Practices

June 2020

# US Flu VE Network sites and principal investigators

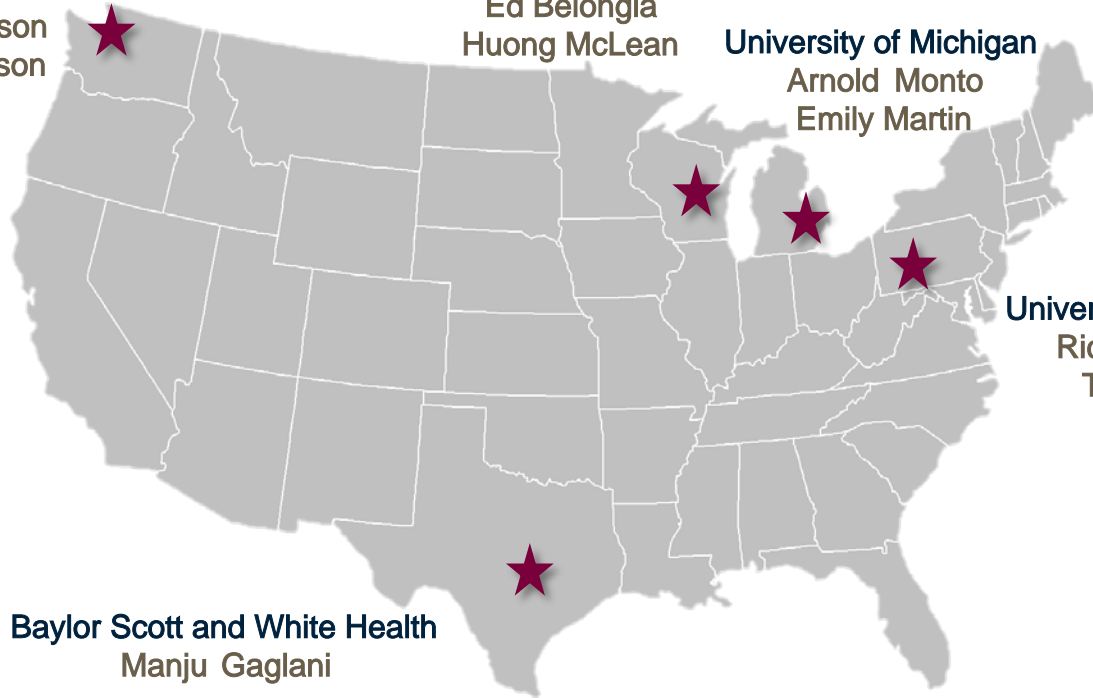
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# US Flu VE Network Methods

**Enrollees:** Outpatients aged  $\geq 6$  months with acute respiratory illness with cough  $\leq 7$  days duration

**Dates of enrollment:** October 29, 2019–March 26, 2020

**Design:** Test-negative design

- Comparing vaccination odds among influenza RT-PCR positive cases and RT-PCR negative controls
- Vaccination status: receipt of at least one dose of any 2019–20 seasonal flu vaccine according to medical records, immunization registries, and/or self-report

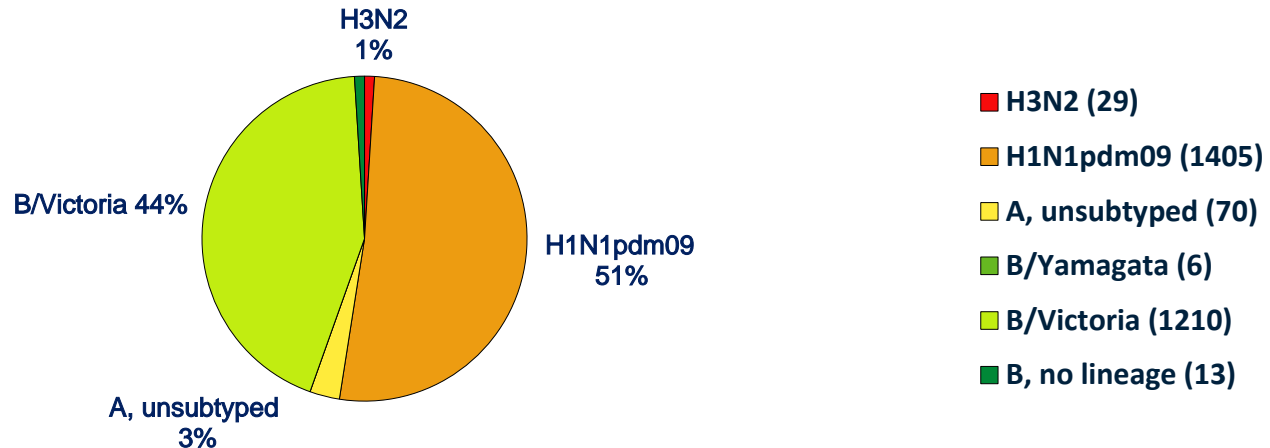
**Analysis:**  $VE = (1 - \text{adjusted OR}) \times 100\%$

- Adjustment for study site, age, sex, self-rated general health status, race/Hispanic ethnicity, interval from onset to enrollment, and calendar time

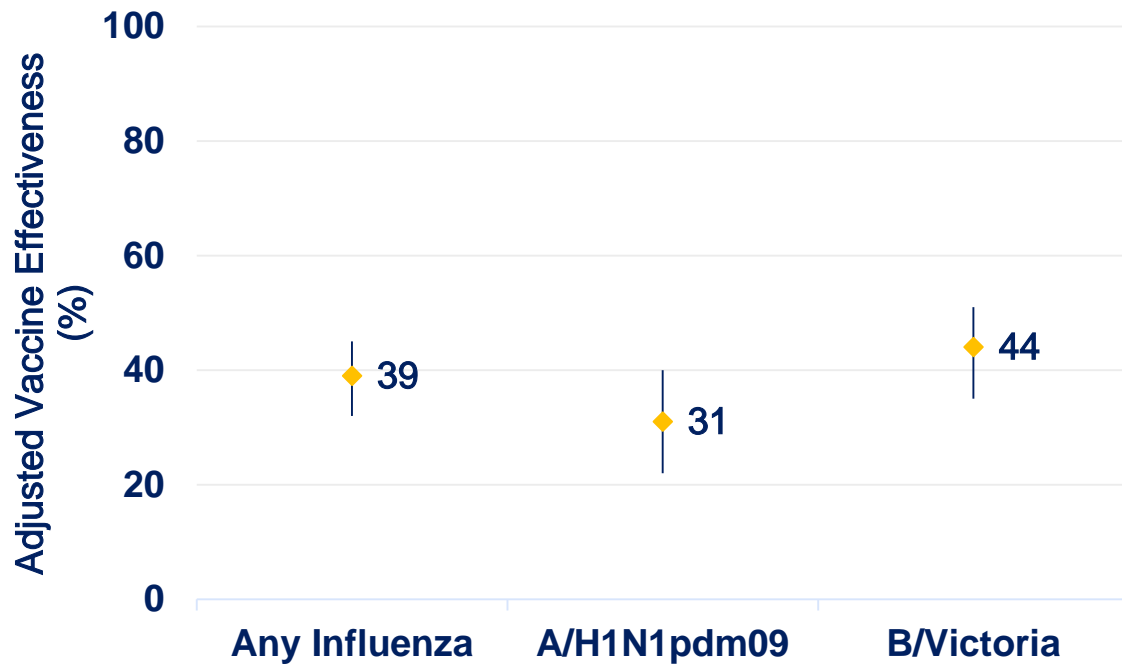
# Preliminary End-of-Season Results, US Flu VE Network

- 8,844 enrolled from Oct 29, 2019–March 26, 2020 at 5 sites
- 2,743 (31%) influenza RT-PCR positive
- 6,121 (69%) influenza RT-PCR negative

## Cases enrolled by (sub)type, N=2743

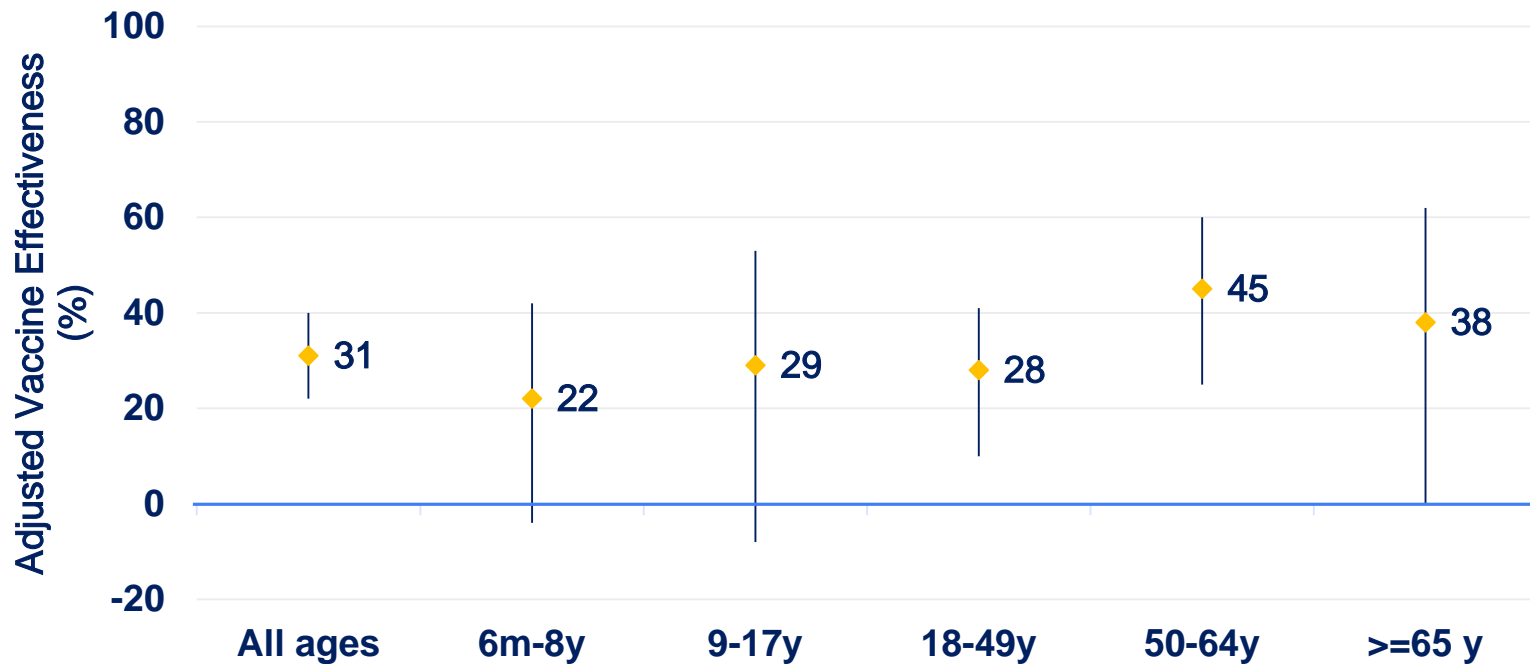


# **PRELIMINARY** Adjusted vaccine effectiveness against medically attended influenza, US Flu VE Network, 2019–20



\* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

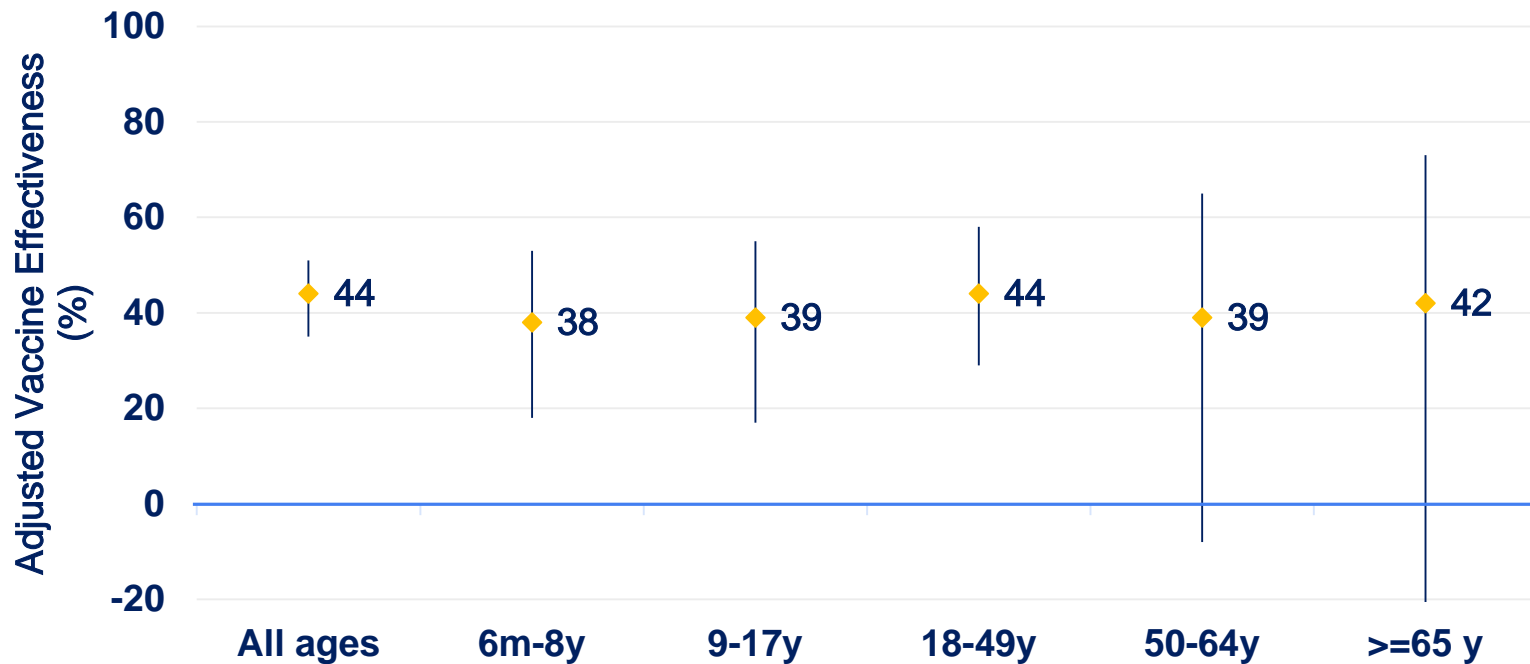
# PRELIMINARY Adjusted vaccine effectiveness against influenza A/H1N1pdm09 by age group, US Flu VE Network, 2019–20



\* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.



## **PRELIMINARY** Adjusted vaccine effectiveness against influenza B/Victoria by age group, US Flu VE Network, 2019–20



\* Multivariable logistic regression models adjusted for site, age, sex, race/ethnicity, self-rated general health status, interval from onset to enrollment, and calendar time.

# Summary

- Preliminary results for 2019–20 season indicate 39% (95%CI: 32, 45) vaccine effectiveness against medically attended influenza
- Important protection against influenza B virus given severity of 2019-20 season for children
- Protection against A/H1N1pmd09 virus lower than previous seasons
  - Investigation of contributing factors ongoing
- Preliminary end-of-season estimates use best available information on vaccination status; estimates will be revised as data are finalized
- Three vaccine components (A/H1N1pdm09, A/H3N2, and B/Victoria) updated for 2020–21 influenza vaccines

# 2019-20 Vaccine Safety Update

Slides courtesy of Karen Broder, Tom Shimabukuro, Frank DeStefano, and colleagues

## Disclaimer

- The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of CDC and FDA
- The use of product trade names is for identification purposes only

# Summary 2019-2020 Influenza Vaccine Safety Surveillance

- ~174.5 million doses of influenza vaccine distributed in the United States through February 28, 2020\*
- CDC and FDA analyzed spontaneous reports to the Vaccine Adverse Event Reporting System (VAERS)
  - No new safety concerns were identified for any influenza vaccine types
- CDC conducted near real-time sequential monitoring (Rapid Cycle Analysis [RCA]) in the Vaccine Safety Datalink (VSD)
  - ~5.8 million doses of influenza vaccine administered in VSD sites through March 7, 2020
  - No new safety concerns were identified for any influenza vaccine types

\* CDC Seasonal Influenza Vaccine Supply & Distribution: <https://www.cdc.gov/flu/prevent/vaccine-supply-distribution.htm>

# Clinical Immunization Safety Assessment (CISA) Project

## Safety of RIV4 vs. IIV4 in Pregnant Women: Study Design<sup>1</sup>

- Randomized clinical trial (observers and participants blinded)
  - Study population: Pregnant women aged  $\geq 18$  years
    - Gestational age  $\leq 34$  weeks at time of vaccination
  - Randomized 1:1 to receive RIV4 (Flublok<sup>®</sup> Quadrivalent) or IIV4 (Flulaval<sup>®</sup> Quadrivalent)
  - Maternal and Infant safety outcomes collected from enrollment through 90 days postpartum
    - Local and systemic reaction collected from vaccination day through 8 days after vaccination
  - Blood collected at baseline and 28 days after vaccination for immunogenicity
- Participants enrolled from 3 sites<sup>2</sup> during 2019-20 and 2020-21 influenza seasons (total goal: 430 participants)

<sup>1</sup>Official title: A Prospective, Randomized, Clinical Trial to Compare Adverse Birth Outcomes in Pregnant Women Receiving Quadrivalent Recombinant Influenza Vaccine (RIV4) Versus Quadrivalent Inactivated Influenza Vaccine (IIV4) of Quadrivalent Recombinant Influenza Vaccine (RIV4) versus Quadrivalent Inactivated Influenza Vaccine (IIV4) in Pregnant Women (ClinicalTrials.gov: NCT03969641)

<sup>2</sup>Duke University (Lead), Boston Medical Center, and Cincinnati Children's Hospital Medical Center

## Safety of RIV4 vs IIV4 in Pregnant Women: Interim Safety Review and Update First Season (2019-20)

- Enrolled and randomized **233** pregnant women participants during the 2019-20 season
- Safety review
  - Safety panel of three medical experts who are not study investigators reviewed interim safety data for serious adverse events on April 13, 2020
  - Each panel member concluded there were no substantial safety concerns observed
- Study plans to continue enrollment in 2020-2021 influenza season

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- CDC Immunization Safety Office staff
- FDA VAERS Staff
- Vaccine Safety Datalink (VSD) Investigators
- Clinical Immunization Safety Assessment (CISA) Project Investigators



# **WG Considerations and Proposed 2020-21 Recommendations**

## 2020-21 Core Recommendation (Unchanged)

- Annual influenza vaccination is recommended for all persons aged 6 months and older who do not have contraindications.

## 2020-21 Primary Updates

- U.S. influenza vaccine viral composition
- Inclusion of two recently licensed vaccines
  - Fluzone High-Dose Quadrivalent
  - Fluad Quadrivalent

# 2020-21 Influenza Vaccine Composition

- **Egg based** influenza vaccines will contain hemagglutinin derived from:
  - an A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus;
  - an A/Hong Kong/2671/2019 (H3N2)-like virus;
  - a B/Washington/02/2019 (Victoria lineage)-like virus; and
  - (for quadrivalent vaccines) a B/Phuket/3073/2013 (Yamagata lineage)-like virus.
- **Non-egg based** influenza vaccines will contain hemagglutinin derived from:
  - an A/Hawaii/70/2019 (H1N1)pdm09-like virus;
  - an A/Hong Kong/45/2019 (H3N2)-like virus;
  - a B/Washington/02/2019 (Victoria lineage)-like virus; and
  - a B/Phuket/3073/2013 (Yamagata lineage)-like virus.

# Recent Influenza Vaccine Licensures

- November 2019: Fluzone High-Dose Quadrivalent (Sanofi Pasteur) licensed for  $\geq 65$  years
  - 60 mcg hemagglutinin per vaccine virus in a 0.7 mL dose (240mcg total)
  - Will replace previous trivalent Fluzone High-Dose for 2020-21
  - Pre-licensure data presented to the ACIP in October, 2019
- February 2020: Fluad Quadrivalent (Seqirus) licensed for  $\geq 65$  years
  - Contains MF59 adjuvant, similarly to the previously licensed trivalent formulation of Fluad
  - Pre-licensure data presented to the ACIP in February, 2020

# Changes to the Contraindications and Precautions Table (Table 2)

- Contraindications/precautions table:
  - “Contraindications and conditions for which use is not recommended” header changed to “Contraindications”
  - Text provides more detail concerning which contraindications are labeled contraindications in the package insert, and which are ACIP Recommendations.

# Vaccine Adverse Event Reporting System (VAERS): Review of Live Attenuated Influenza Vaccine (LAIV) in Special Populations

- Conducted targeted review in VAERS for LAIV reports in 2 special populations of interest
  - Asplenia or sickle cell disease
  - Cerebrospinal fluid leak or cochlear implant
- VAERS \*
  - United States spontaneous reporting surveillance system
  - Operating since 1990
  - Co-managed by CDC and FDA
  - Receives adverse event reports from manufacturers, medical providers, vaccine recipients and the general public

# VAERS Reports after LAIV in Special Populations: Methods

- Primary U.S. reports
- Time period: July 1990 – March 16, 2020
- Vaccines: LAIV (monovalent, trivalent or quadrivalent) with or without other vaccines
- Age: no restriction
- Search criteria: two different search methods used
  - Medical Dictionary for Regulatory Activities (MedDRA) preferred terms
  - Text string search
- Serious report definition: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect (based on the Code of Federal Regulations)



# VAERS Reports after LAIV in Special Populations: Results

- Asplenia or sickle cell disease: **2 reports**
  - Sickle cell anemia: 1 child, non-serious report
  - Asplenia/splenectomy: 1 adult, death report\*
- CSF Leak or cochlear implant: **3 reports**
  - CSF Leak: 0 reports
  - Cochlear implant: 3 children, non-serious reports

\* Person had history of splenectomy; cause of death reported as *Streptococcus pneumoniae* sepsis

# LAIV4 use in Settings of Asplenia, Cochlear Implant, and Active CSF Leaks

- Literature search
  - Terms based on “influenza vaccine” and “Cochlear implant”, “cerebrospinal fluid leak”, “CSF leak”, “anatomic asplenia”, “functional asplenia”, or “sickle-cell anemia”
  - 141 citations
  - No data related to use of LAIV in these populations

# LAIV4 use in Settings of Asplenia, Cochlear Implant, and Active CSF Leaks

- Work Group Discussion:
  - Insufficient data for use in these populations
  - Alternative vaccines are available
  - In the proposed document, these conditions have been added to list of contraindications for LAIV4 (previously only discussed in text)

# Influenza Antivirals and LAIV4

- Previously indicated that use of antivirals from 48 hours before to 2 weeks after administration of LAIV4 may interfere with vaccine
- Newer antivirals peramivir and baloxavir have longer half-lives than oseltamivir and zanamivir
- Insufficient data available on use of LAIVs in setting of antiviral use
- Based on half-lives, language added indicating prudent to assume interference possible if antivirals are administered within these intervals:

Antiviral	Interval
Oseltamivir and Zanamivir	48 hours before to 2 weeks after LAIV4
Peramivir	5 days before to 2 weeks after LAIV4
Baloxavir	17 days before to 2 weeks after LAIV4

# Vaccination of Persons with Egg Allergy

- Language concerning persons with a history of severe allergic reaction to egg (having had any symptom other than hives after egg ingestion) updated to reflect availability of two egg-free vaccines, the cell-culture based inactivated vaccine (cclIV4) and the recombinant influenza vaccine (RIV4).
- For these individuals, if a vaccine ***other than cclIV4 or RIV4*** is used, the selected vaccine should be administered in an inpatient or outpatient medical setting, supervised by a health care provider who is able to recognize and manage severe allergic reactions.

# Summary of Changes

- Principal changes:
  - 2020-21 U.S. Influenza vaccine composition
  - Inclusion of Fluzone High-Dose Quadrivalent and Flud Quadrivalent
- Other changes:
  - Table 2 now says “Contraindications” rather than “Contraindications and conditions for which use is not recommended”
  - Asplenia, cochlear implant, and active CSF leak included in contraindications in Table 2
  - Updated guidance concerning LAIV4 and influenza antivirals based on half-lives of the various agents
  - Updating of language concerning vaccination of persons with egg allergy to reflect availability of egg-free vaccines

# *Thank You!*

For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://www.cdc.gov)

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