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**2018-2019 Recommendations for Influenza Prevention and
Treatment in Children: An Update for Pediatric Providers**

**Clinician Outreach and Communication Activity (COCA)
Webinar**

September 27, 2018



Continuing Education for this COCA Call

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- ❑ **Dr. Lisa Grohskopf would like to disclose that ACIP recommends that egg allergic persons should receive influenza vaccine, though egg allergy is a labeled contraindication to influenza vaccination for most influenza vaccine.**
- ❑ **Dr. Flor Munoz would like to disclose that the use of influenza antivirals in hospitalized, severely ill patients is off-label; the use of influenza vaccine in pregnant women is off label; however, these are recommended by CDC and AAP.**
- ❑ **CDC did not accept commercial support for this continuing education activity.**

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**At the conclusion of the session,
participants will be able to accomplish
the following:**

- **Summarize data from the 2017-2018 US influenza season and the 2018 Southern Hemisphere season to inform preparations for the 2018-2019 US influenza season.**
- **List key recommendations in the AAP influenza policy statement, “Recommendations for Prevention and Control of Influenza in Children, 2018–2019” and in the CDC Advisory Committee on Immunization Practices’ document, “Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices—United States, 2018-2019 Influenza Season.”**
- **Outline background information about updated recommendations for the use of intranasal live attenuated influenza vaccine (LAIV4) in children.**
- **List recommendations for influenza antiviral use in children.**

Today's First Presenter

Lisa Grohskopf, MD, MPH

Medical Officer, Influenza Division
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention



Today's Second Presenter



Flor Munoz, MD, MSc, FAAP
Associate Professor
Pediatric Diseases
Baylor College of Medicine
Member, AAP Committee on Infectious Diseases



National Center for Immunization & Respiratory Diseases



2018-2019 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers

Lisa Grohskopf

Influenza Division, CDC

Clinician Outreach and Communication Activity (COCA) Call/Webinar
September 27, 2018

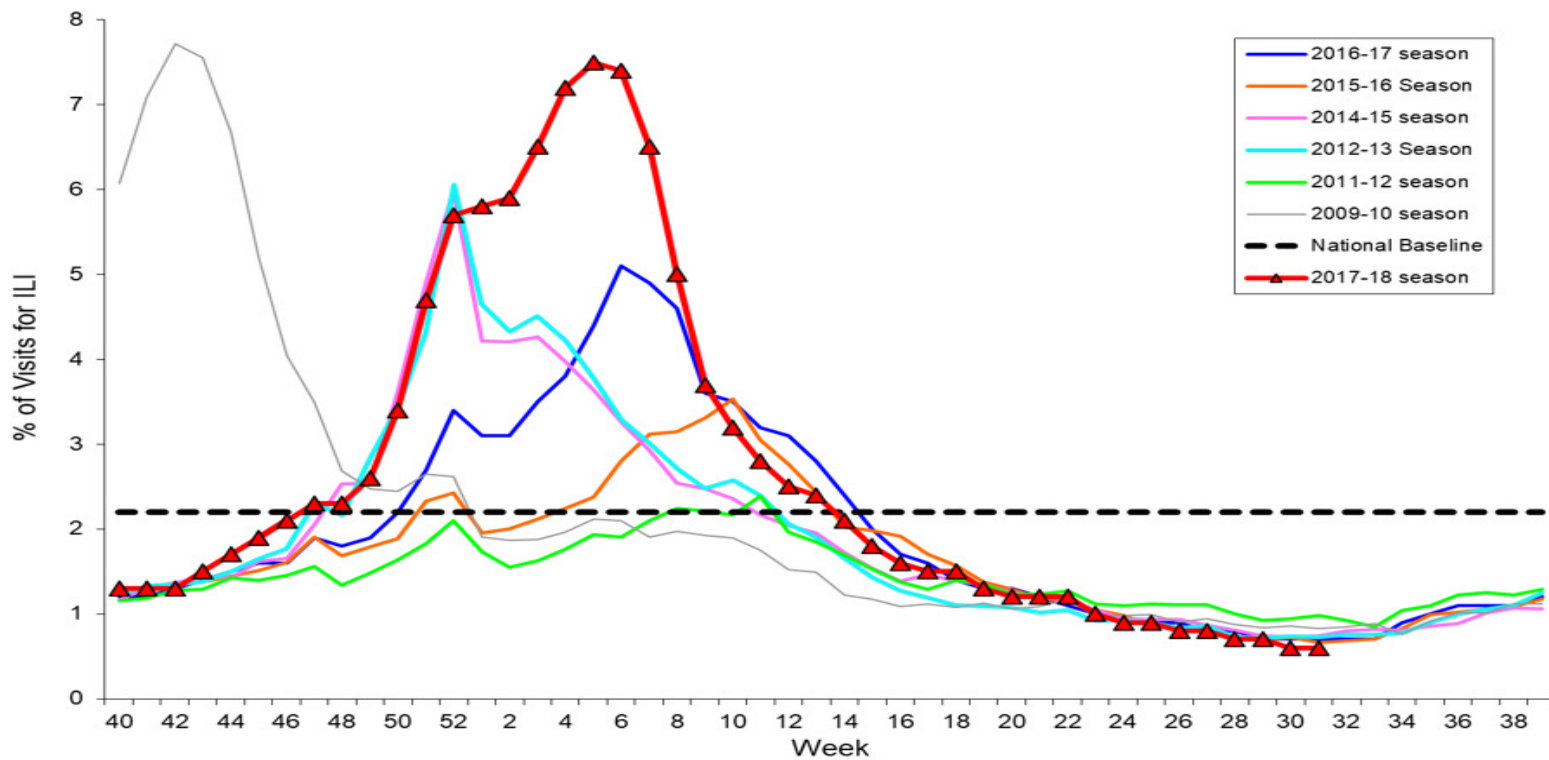
A Review of Last Season...

- High severity season
 - High levels of outpatient clinic and emergency department visits for ILI
 - High influenza-related hospitalization rates
 - Elevated and geographically widespread activity across the country for an extended period
- Activity began increasing in November and reached an extended period of high activity during January and February
- Influenza A(H3N2) viruses predominated overall
 - Influenza B viruses were reported more frequently than influenza A viruses from early March until mid-June
- The majority of circulating viruses were similar to the cell-grown reference viruses representing the 2017-18 influenza vaccine viruses



Percentage of Visits for Influenza-like Illness (ILI)

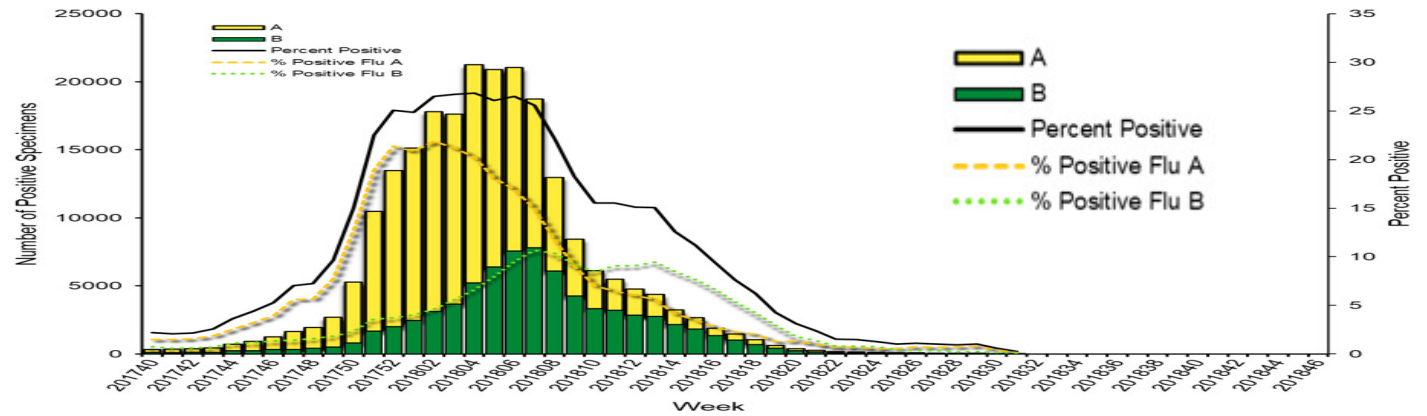
Weekly National Summary, 2017-18 & Selected Previous Seasons



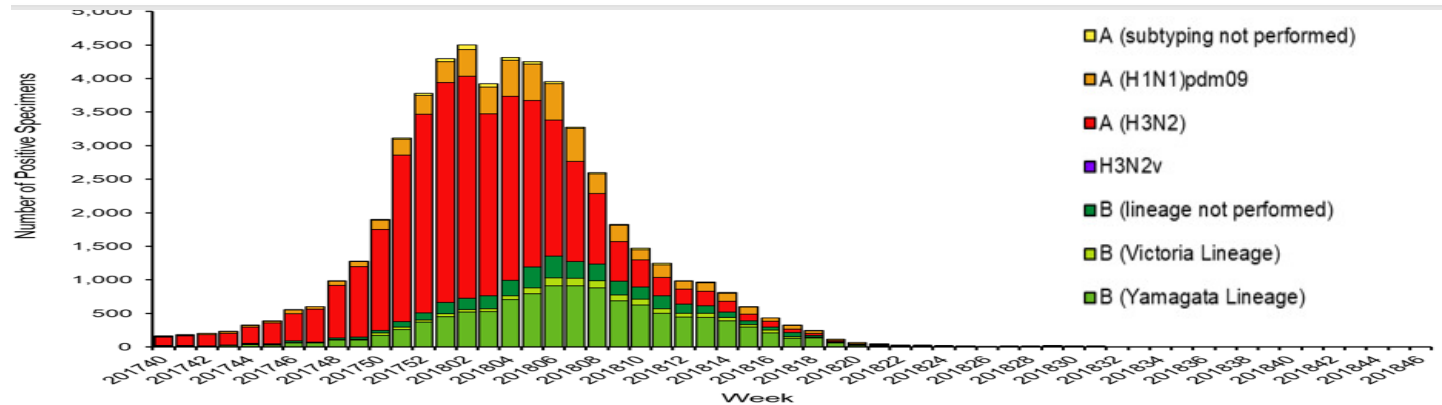
ILINet; data as of week 31 ending August 4, 2018

Influenza Positive Tests Reported to CDC by U.S. Clinical and Public Health Laboratories

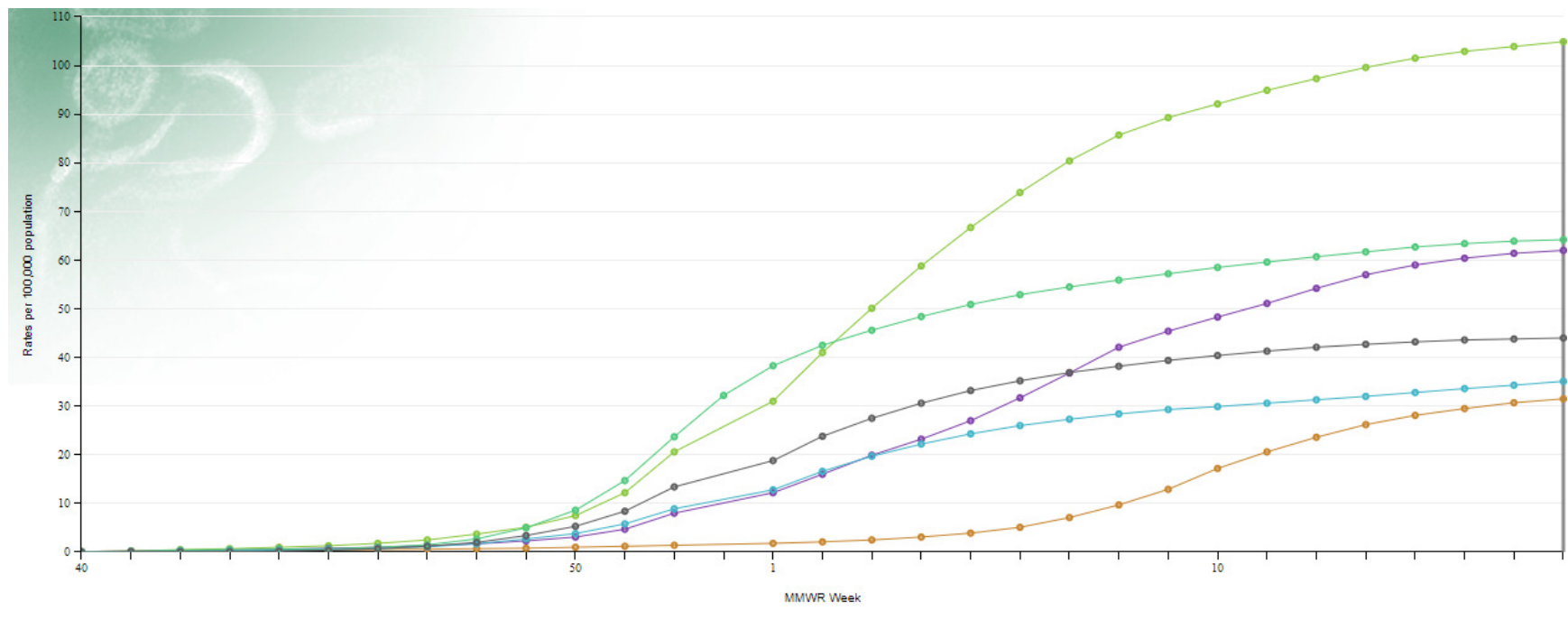
Clinical Laboratories



Public Health Laboratories



Laboratory-Confirmed Influenza-Associated Hospitalizations, Cumulative Rate, 2017-18 and Previous 5 Seasons



Age group: Overall, Week: 17

Rates per 100,000 by Age Group

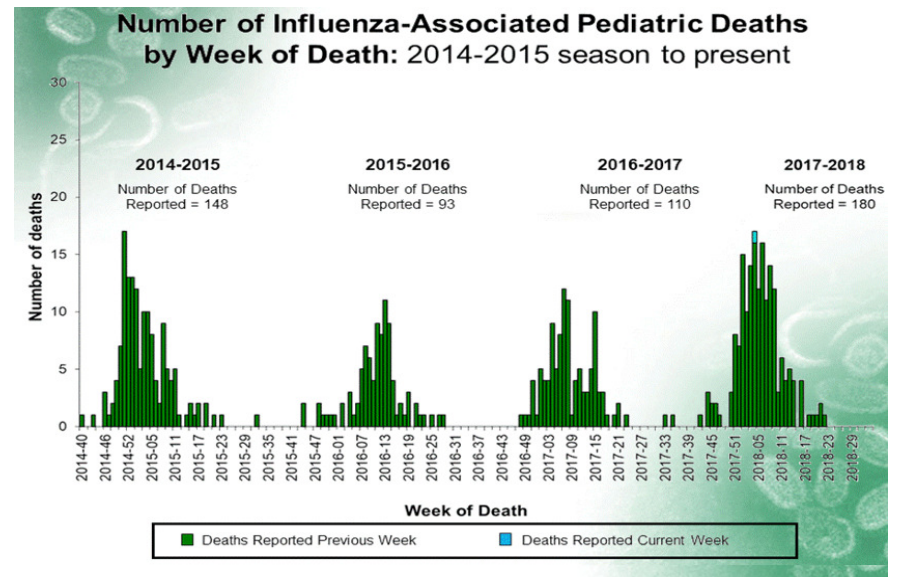
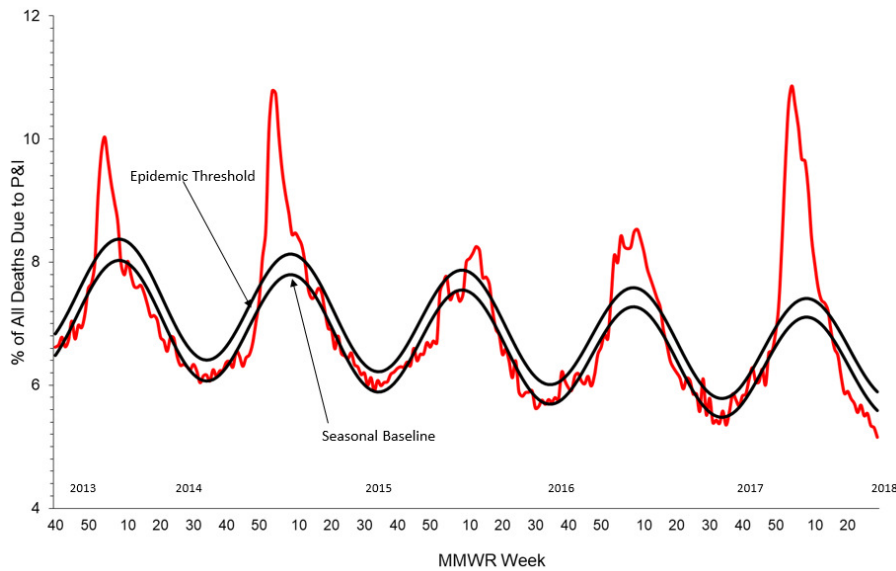
- 2017-18 **104.9**
- 2016-17 **62**
- 2015-16 **31.5**
- 2014-15 **64.2**
- 2013-14 **35.1**
- 2012-13 **44**



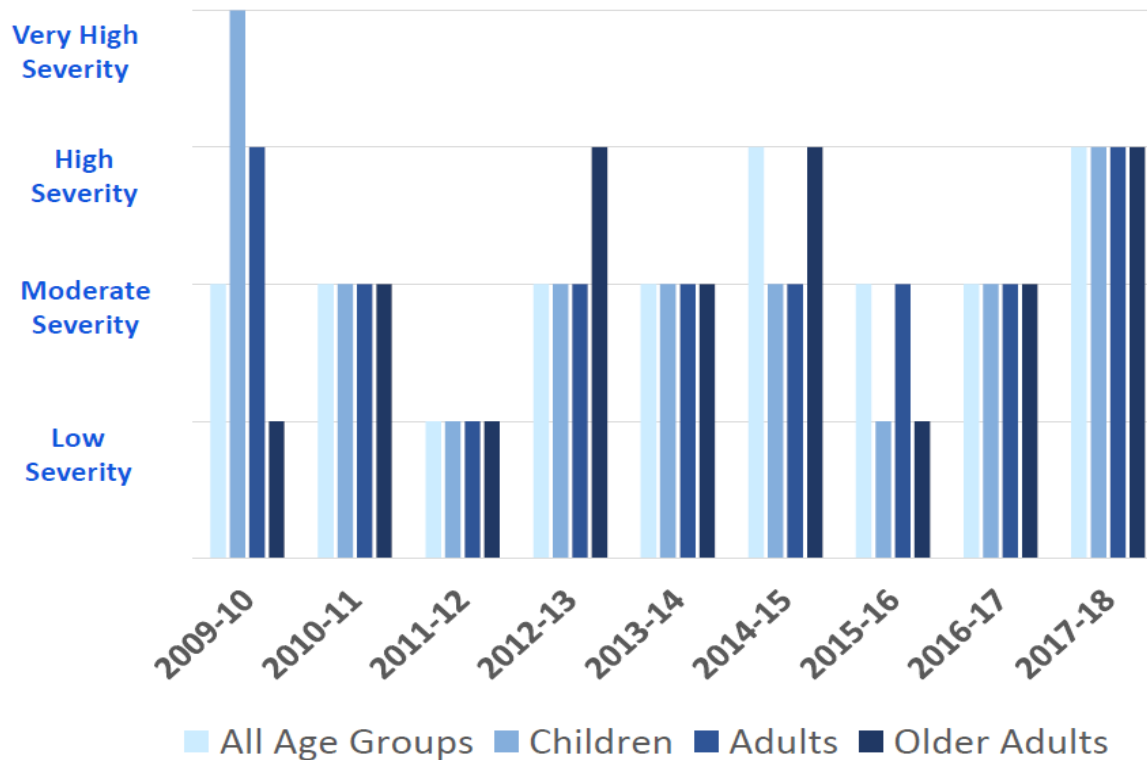
Mortality Surveillance: 2017-18 and Previous Seasons

- Pneumonia and Influenza Mortality, National Center for Health Statistics

- Deaths in Children with Laboratory Confirmed Influenza



Season Severity Assessment – By Age Group and Season, 2009-10 through 2017-18



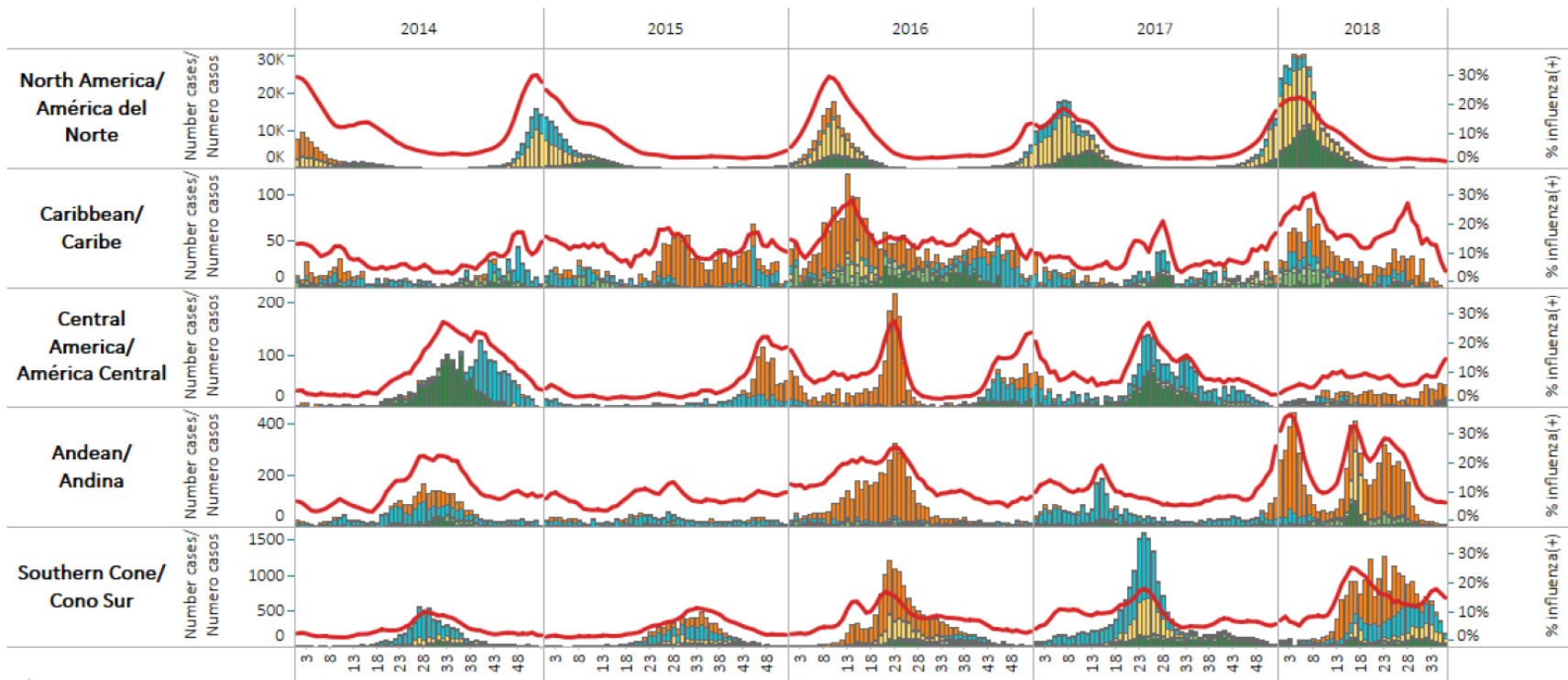
2017-18 was High Severity based on outpatient visits, hospitalizations, and deaths

2018: Southern Hemisphere

Influenza circulation by subregion, 2014-18

Distribution of influenza viruses by subregion, 2012-18
Distribución de virus de influenza por subregión, 2012-18

- Influenza viruses/Virus influenza**
- Influenza A(H3N2)
 - Influenza A(H1N1)pdm09
 - Influenza A Not Subtyped/No subtipificado
 - Influenza B
 - Influenza A not subtypeable/no subtipifica..
 - % Influenza



Data as of September 10, 2018

https://www.paho.org/hq/index.php?option=com_content&view=article&id=3352:influenza-situation-report&Itemid=2469&lang=pt

Sources of 2018–19 Influenza Season Data

- Updated surveillance information is available each Friday
 - FluView, static report: <https://www.cdc.gov/flu/weekly/>
 - FluView Interactive, online application: <https://www.cdc.gov/flu/weekly/fluviewinteractive.htm>
- Vaccine effectiveness estimates
 - Morbidity and Mortality Week Report (MMWR) updates: <https://www.cdc.gov/mmwr/index.html>
 - Advisory Committee on Immunization Practices (ACIP) meetings: <https://www.cdc.gov/vaccines/acip/meetings/index.html>

CDC Antiviral Treatment Recommendations

- Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is:
 - Hospitalized
 - Has severe, complicated, or progressive illness
 - Is at high risk for influenza complications

People at High Risk for Influenza Complications for Whom Antiviral Treatment is Recommended

- Children <2 years old (although all children <5 years old are considered at high risk for complications, highest risk is for children <2 years old)
- Adults age 65 years and over
- Pregnant/postpartum women
- Children <18 years old receiving long-term aspirin therapy
- American Indians/Alaska Natives
- People with underlying medical conditions (e.g., pulmonary, cardiac, immunosuppression, neurologic and neurodevelopment conditions)
- Residents of nursing homes/chronic care facilities

CDC Antiviral Treatment Recommendations

- Antiviral treatment is recommended as early as possible for any patient with confirmed or suspected influenza who is:
 - Hospitalized
 - Has severe, complicated, or progressive illness
 - Is at high risk for influenza complications
- Antiviral treatment can be considered for any previously healthy, symptomatic outpatient not at high risk with confirmed or suspected influenza on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset
- Clinical benefit is greatest when antiviral treatment is administered early
- Three FDA-approved antivirals are recommended for use in the United States: oral oseltamivir, inhaled zanamivir, and intravenous peramivir,,

On the Horizon...

- Baloxavir = targets polymerase (new mechanism of action)
- Oral, single dose
- New Drug Application filed with FDA and Priority Review granted; potential approval date 12/24/2018
 - Treatment of acute, uncomplicated influenza in patients >12-64 years
- Baloxavir was associated with:
 - Significantly shorter time to alleviation of symptoms than placebo
 - Significantly more rapid declines in infectious viral load, RNA viral levels, and shorter duration of infectious virus detection than oseltamivir or placebo

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Baloxavir Marboxil for Uncomplicated Influenza
in Adults and Adolescents

Frederick G. Hayden, M.D., Norio Sugaya, M.D., Nobuo Hirotsu, M.D., Ph.D., Nelson Lee, M.D.,
Menno D. de Jong, M.D., Ph.D., Aeron C. Hurt, Ph.D., Tadashi Ishida, M.D., Ph.D., Hisakuni Sekino, M.D., Ph.D.,
Kota Yamada, M.D., Simon Portsmouth, M.D., Keiko Kawaguchi, M.Sc., Takao Shishido, Ph.D.,
Masatsugu Arai, M.Sc., Kenji Tsuchiya, M.Sc., Takeki Uehara, Ph.D., and Akira Watanabe, M.D., Ph.D.,
for the Baloxavir Marboxil Investigators Group*

Hayden, et al. NEJM 2018

Greatest clinical benefit when initiated early after illness onset

National Center for Immunization & Respiratory Diseases



2018-19 ACIP Influenza Vaccination Recommendations Update

Groups Recommended for Vaccination

- Routine annual influenza vaccination is recommended for all persons **≥6 months of age** who do not have contraindications
- While vaccination is recommended for everyone in this age group, there are some for whom it is particularly important—
 - People aged ≥6 months who are at increased risk of complications and severe illness due to influenza
 - Contacts and caregivers of persons
 - <5 years of age
 - ≥50 years of age
 - with medical conditions that put them at higher risk for severe complications from influenza

Groups at Increased Risk for Influenza Complications and Severe Illness

- Children aged 6 through 59 months and adults aged ≥ 50 years (children under 6 months of age are also at high risk, but cannot be vaccinated);
- Persons with chronic pulmonary (including asthma) or cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);
- Immunosuppressed persons;
- Women who are or will be pregnant during the influenza season;
- Children and adolescents (aged 6 months–18 years) who are receiving aspirin- or salicylate-containing medications (who might be at risk for Reye syndrome after influenza virus infection);
- Residents of nursing homes and other long-term care facilities;
- American Indians/Alaska Natives; and
- Persons who are extremely obese (BMI ≥ 40).

2018-19 ACIP Influenza Statement—Updates

- Principal changes and updates for 2018-19
 - Influenza vaccine composition for 2018-19
 - LAIV4 an option for 2018-19
 - Vaccines for egg-allergic persons
 - Two labeling changes for existing vaccines

2018-19 Influenza Vaccine Composition

- Trivalent vaccines:
 - an A/Michigan/45/2015 (H1N1)pdm09-like virus;
 - an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus--*updated*;
 - a B/Colorado/06/2017-like virus (Victoria lineage)--*updated*.
- Quadrivalent vaccines:
 - The above three viruses, and
 - a B/Phuket/3073/2013-like virus (Yamagata lineage).

ACIP LAIV4 Recommendations for 2018-19 (1)

- Can choose any appropriate vaccine (IIV, RIV4*, or LAIV4)
(*RIV4 not licensed for children <18 years)
 - LAIV had not been recommended for 2016-17 or 2017-18
 - Low effectiveness vs. influenza A(H1N1)pdm09 among children 2 through 17 yrs during 2013-14 and 2015-16
 - Thought due to poor fitness of the H1N1pdm09 virus in the vaccine
 - In February 2018, ACIP reviewed additional data
 - Two analyses of previous seasons' data from observational studies
 - Manufacturer data on shedding and immunogenicity of new H1N1pdm09 vaccine virus indicating improved fitness
 - For 2018-19, LAIV4 is an option for those for whom it is appropriate
 - No U.S. VE data yet on new formulation with the new H1N1pdm09

ACIP LAIV4 Recommendations for 2018-19 (2)

- Difference in ACIP and American Academy of Pediatrics (AAP) recommendations:
 - ACIP makes no preferential recommendations for any one vaccine type when more than one is appropriate;
 - AAP recommends IIV as the primary choice for children.
- Recommendations share the same principle that influenza vaccination is an important preventive strategy for children

Who Shouldn't Receive LAIV4

- **Persons aged <2 years or >49 years (for whom not licensed by FDA)**
- **Labeled contraindications in package insert:**
 - History of severe allergic reaction to any vaccine component* or to a previous dose of influenza vaccine (like other influenza flu vaccines)
 - *Note though* that ACIP recommends vaccination of persons with egg allergy: this differs from FDA-approved labeling for most influenza vaccines)
 - Concomitant aspirin- or salicylate-containing therapy in children or adolescents (risk of Reye syndrome)
- **ACIP also recommends LAIV not be used in these situations:**
 - Pregnancy
 - Immunocompromised persons
 - Children <5 with a history of asthma or wheezing
 - Caregivers and contacts of persons requirement a protected environment
 - Persons who have received influenza antivirals within previous 48 hours

Precautions to use of LAIV4

- **Some similar to other influenza vaccines:**
 - Moderate or severe illness with or without fever
 - Guillain-Barré syndrome within 6 weeks following a previous dose of influenza vaccine
- **Additional precautions specific to LAIV4**
 - Asthma in persons aged 5 and older
 - Other medical conditions that predispose to increased risk of severe influenza illness e.g., other chronic pulmonary diseases; cardiovascular disease (excluding isolated hypertension); renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);

Influenza Vaccination of Persons with Egg Allergy

- Mostly unchanged, except that LAIV4 is an option
- Egg allergic persons can receive any licensed, recommended vaccine that is otherwise appropriate (IIV, RIV4, or LAIV4)—for children, IIV or LAIV4
- With history of severe allergic reaction to egg (any symptom other than hives), vaccine should be administered in an inpatient or outpatient medical setting, supervised by a health care provider able to recognize and manage severe allergic conditions.
 - **NOTE:** Here ACIP differs from FDA-approved labeling for most IIVs and LAIV, for which severe egg allergy is a contraindication
- No specific post-vaccination observation period recommended
 - ACIP General Best Practices guidelines: providers should consider observing recipients of any vaccine for 15 minutes to avoid injury due to syncope

Licensure Changes Since Publication of 2017-18 ACIP Statement

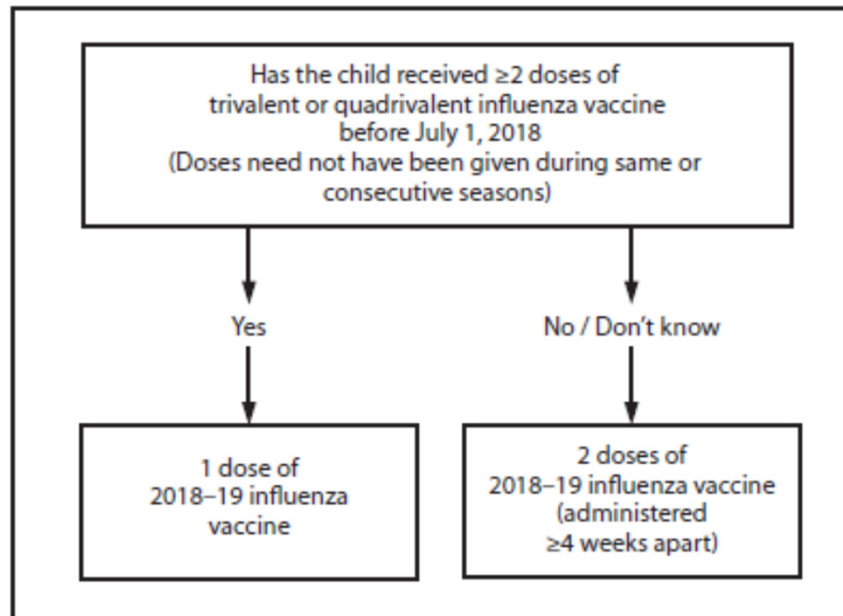
- **Afluria Quadrivalent (Standard-dose IIV4, Seqirus)**
 - Licensed in August 2016, for ≥ 18 years
 - In August 2017, expanded to ≥ 5 years
 - Like Afluria (IIV3, also available this season), can be administered via jet injector (the Pharmajet Stratis), but only for ages 18 through 64 years
- **Fluarix Quadrivalent (Standard-dose IIV4, GSK)**
 - Previously licensed for ≥ 3 years; in January 2018 expanded to ≥ 6 months
 - One of three IIVs approved for children 6 through 35 months of age
 - Dose volume is same for all ages (0.5mL)

Inactivated Influenza Vaccines (IIVs) for 6- through 35-month-olds

- **Two potential points of confusion**
 - Three licensed products, but the **dose volumes differ**:
 - Fluarix Quadrivalent: **0.5mL**
 - FluLaval Quadrivalent: **0.5 mL**
 - Fluzone Quadrivalent: **0.25 mL**
 - ***Dose volume* is distinct from *number of doses* needed**:
 - A child aged 6 months through 8 years who needs 2 doses—
 - (for example, if a first-time vaccinee)—
 - and who gets 0.5mL FluLaval Quadrivalent for a first dose—
 - *Still* needs a second dose of influenza vaccine, ≥ 4 weeks later

Number of Doses for Ages 6 Months through 8 Years

FIGURE. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2018–19 influenza season



- Approach is same as last season
- Children in this age group who have not had ≥ 2 doses of trivalent or quadrivalent vaccine before July 1, 2018 need two doses in 2018-19.
- Previous doses can be from different/non-consecutive seasons.
- If two doses needed for 2018-19, should be given ≥ 4 weeks apart.

Additional CDC Resources

- CDC Influenza homepage: <https://www.cdc.gov/flu/>
- Influenza surveillance: <https://www.cdc.gov/flu/weekly/fluactivitysurv.htm>
- Influenza vaccination coverage: <https://www.cdc.gov/flu/fluview/index.htm>
- For Professionals: <https://www.cdc.gov/flu/professionals/index.htm>
 - Vaccination homepage:
<https://www.cdc.gov/flu/professionals/vaccination/index.htm>
 - 2017-18 ACIP Influenza Recommendations:
<https://www.cdc.gov/mmwr/volumes/66/rr/rr6602a1.htm>
 - Antiviral homepage:
<https://www.cdc.gov/flu/professionals/antivirals/index.htm>
- For Children (created by CDC and endorsed by the AAP): activity book
 - https://www.cdc.gov/phpr/readywrigley/documents/ready_wrigley_flu.pdf



Thank You

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



2018-19 Recommendations for Influenza Prevention and Treatment in Children: An Update for Pediatric Providers

COCA, 27 SEPT 2018

Flor M. Munoz, MD, MSc, FAAP

Baylor
College of
Medicine

American Academy of Pediatrics
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THE COMMITTEE ON INFECTIOUS DISEASES (COID) OF THE AAP

- Reviews influenza epidemiology, vaccines, antivirals
- Provides recommendations for influenza prevention, diagnosis and treatment in children

Recommendations reviewed and approved by

- COID
- 9 AAP Committees
- 6 Councils
- 17 Sections
- AAP Board



The Authority on
Pediatric Infectious Diseases.



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2018-2019 AAP INFLUENZA PREVENTION RECOMMENDATIONS

- Aligned with CDC ACIP recommendations
- IIV is recommended as primary choice for children this season, with LAIV as an option for those would not receive IIV
- Affirm vaccination in egg-allergic patients
- Update recommendations for treatment of influenza with antivirals for children



2018-2019 AAP INFLUENZA PREVENTION RECOMMENDATIONS



Everyone starting at 6 months of age

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Special Populations at Risk for Complications with Influenza



Children < 5 years



Persons > 65 years



Health Care Personnel



Pregnant Women

Underlying Medical Conditions

- *Asthma and other chronic lung diseases*
- *Cardiovascular disease*
- *Immune suppression*
- *Diabetes and other metabolic disorders*
- *Hemoglobinopathies*
- *Chronic renal disease*
- *Neuromuscular dysfunction or aspiration risk*
- *Aspirin use*



Household Contacts and caregivers of High Risk Persons and Children

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AAP COID APRIL 2018

- Based on review of available information
- **The AAP recommends inactivated influenza vaccine (IIV), trivalent [IIV3] or quadrivalent [IIV4], as the primary choice for influenza vaccination in children,** because the effectiveness of live attenuated influenza vaccine (LAIV4) against influenza A/H1N1 was inferior during past influenza seasons and is unknown for this upcoming season.
- **Quadrivalent LAIV4 may be used for children who would not otherwise receive an influenza vaccine** (e.g., refusal of IIV) and for whom it is appropriate by age and health status (i.e., >2 years of age and healthy, without any underlying chronic medical condition).



RATIONALE FOR RECOMMENDATIONS

Morbidity and Mortality Weekly Report

June 8, 2018

Update: ACIP Recommendations for the Use of Quadrivalent Live Attenuated Influenza Vaccine (LAIV4) — United States, 2018–19 Influenza Season

Lisa A. Grohskopf, MD¹; Leslie Z. Sokolow, MSc, MPH^{1,2}; Alicia M. Fry, MD¹; Emmanuel B. Walter, MD³; Daniel B. Jernigan, MD¹



THE OFFICIAL NEWSMAGAZINE OF THE AMERICAN ACADEMY OF PEDIATRICS

AAP News

News Articles, Influenza

AAP influenza immunization recommendations revised for 2018-'19 season

by Flor M. Munoz-Rivas M.D., FAAP; Henry H. Bernstein D.O., M.H.C.M., FAAP

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RATIONALE FOR RECOMMENDATIONS DATA REVIEWED BY AAP AND ACIP

- 1) 5 U.S. observational studies – pooled data analysis of the effectiveness of LAIV4 and IIV vaccines for the 2013–14 through 2015–16 seasons among children aged 2-17 years
- 2) A systematic review (meta-analysis) of published literature regarding the effectiveness of LAIV3 and LAIV4 among children during the 2010–11 through 2016–17 seasons
- 3) A study conducted by the manufacturer of LAIV that evaluated viral shedding and immunogenicity associated with LAIV4 containing a new influenza A(H1N1)pdm09-like virus (A/Slovenia/2903/2015) among U.S. children aged 24 months through <4 years.



SUMMARY OF CDC US OBS STUDIES AND VE META-ANALYSIS (2011-2016 SEASONS)

A(H1/N1)pdm09

- LAIV was better than no vaccine for 2-17 yr olds in pooled US studies; but only in non-US studies in metaanalysis
- IIV better than LAIV for all age groups in the US
- A/Slovenia is in LAIV4 since 2017-18 (use in UK, Finland, Canada)
- No US VE data for LAIV since 2015, or with A/Slovenia

H3N2

- LAIV = IIV, except for 2-4 yr olds where IIV better in US-pooled

B strains

- LAIV might be better than IIV (not significant)

There are 13 licensed influenza vaccines. Recommendations for individual influenza vaccines are not generally based upon comparative effectiveness data.

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ACOG APRIL 2018

- Influenza vaccination is an **essential element** of pre-pregnancy, prenatal and post-partum care.
- ACOG recommends annual influenza vaccine for all women who are or will be pregnant during influenza season, as soon as the vaccine is available.
- **Any of the licensed, recommended, age appropriate inactivated influenza vaccines can be given safely during any trimester.**



ACOG COMMITTEE OPINION

Number 732 • April 2018

(Replaces Committee Opinion Number 608, September 2014)

Committee on Obstetric Practice

This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' Immunization and Emerging Infections Expert Work Group and the Committee on Obstetric Practice in collaboration with Neil S. Silverman, MD, and Richard Beigi, MD.

Influenza Vaccination During Pregnancy

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AAFP JULY 2018

July 31st, 2018 AAFP voted on preferential recommendation for IIV for 2018-2019

“For the 2018-2019 influenza season, the AAFP recommends routine annual influenza vaccination for all persons age six months and older who do not have contraindications. **The AAFP recommends Inactivated Influenza Vaccine (IIV) as preferred to Live Attenuated Influenza Vaccine (LAIV4) for non-pregnant persons 2-49 years of age. LAIV4 may still be used to vaccinate non-pregnant persons 2-49 years of age, who would not otherwise be vaccinated.**”



AAFP JULY 2018

July 31st, 2018 AAFP voted on preferential recommendation for IIV for 2018-2019

“For the 2018-2019 influenza season, the AAFP recommends routine annual influenza vaccination for all persons age six months and older who do not have contraindications. **The AAFP recommends Inactivated Influenza Vaccine (IIV) as preferred to Live Attenuated Influenza Vaccine (LAIV4) for non-pregnant persons 2-49 years of age. LAIV4 may still be used to vaccinate non-pregnant persons 2-49 years of age, who would not otherwise be vaccinated.**”



Influenza Vaccination

ACIP / AAP Recommendations 2018-2019

- Annual **universal influenza immunization**
- **IIV or LAIV** can be used during 2018-2019 season*
- No Preference for **trivalent or quadrivalent** influenza vaccine
- LAIV approved for otherwise healthy children (no underlying medical conditions) 2 years of age or older
- **Contraindication** all vaccines: Severe allergic reaction
- **Precaution:** Acute febrile illness, History of GBS

*AAP: LAIV use in children who otherwise will not receive flu shot (e.g. refuse IIV) and appropriate age (2-18 yr) and health status (healthy, without contraindications).

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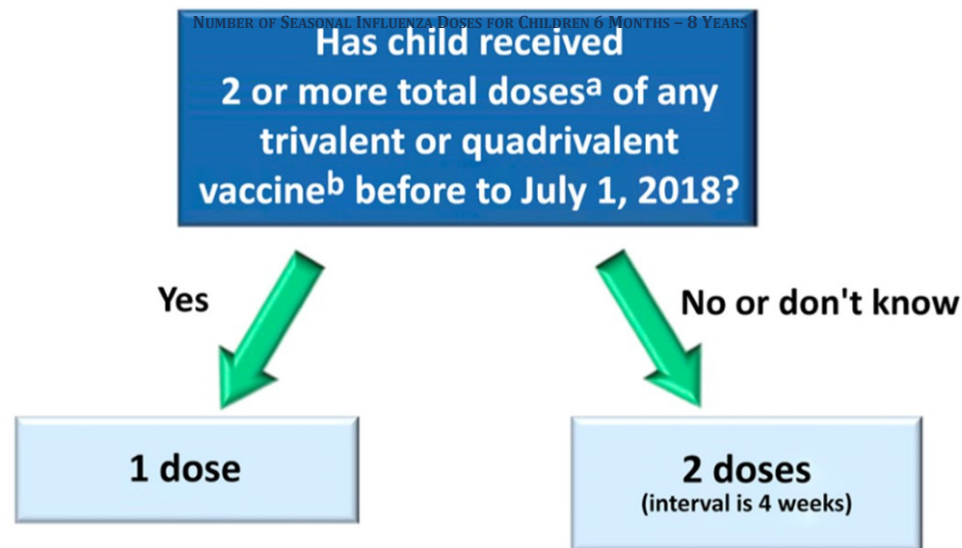
CONTRAINDICATIONS AND PRECAUTIONS OF IIV/LAIV

TABLE 2. Contraindications and precautions to the use of influenza vaccines — United States, 2018–19 influenza season*

Vaccine type	Contraindications	Precautions
IIV	History of severe allergic reaction to any component of the vaccine [†] or after a previous dose of any influenza vaccine	Moderate or severe acute illness with or without fever History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine
RIV	History of severe allergic reaction to any component of the vaccine	Moderate or severe acute illness with or without fever History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine
LAIV	<p>History of severe allergic reaction to any component of the vaccine[†] or after a previous dose of any influenza vaccine</p> <p>Concomitant aspirin- or salicylate-containing therapy in children and adolescents</p> <p>Children aged 2 through 4 years who have received a diagnosis of asthma or whose parents or caregivers report that a health care provider has told them during the preceding 12 months that their child had wheezing or asthma or whose medical record indicates a wheezing episode has occurred during the preceding 12 months</p> <p>Children and adults who are immunocompromised due to any cause (including immunosuppression caused by medications or by HIV infection)</p> <p>Close contacts and caregivers of severely immunosuppressed persons who require a protected environment</p> <p>Pregnancy</p> <p>Receipt of influenza antiviral medication within the previous 48 hours</p>	<p>Moderate or severe acute illness with or without fever</p> <p>History of Guillain-Barré syndrome within 6 weeks of receipt of influenza vaccine</p> <p>Asthma in persons aged ≥5 years</p> <p>Other underlying medical conditions that might predispose to complications after wild-type influenza infection (e.g., chronic pulmonary, cardiovascular [except isolated hypertension], renal, hepatic, neurologic, hematologic, or metabolic disorders [including diabetes mellitus])</p>

Source: MMWR, AUG 24, 2018

Number of Seasonal Influenza Doses for Children 6 Months – 8 Years



* 2 doses need not have been received during the same season or consecutive seasons

† Receipt of LAIV4 in the past is still expected to have primed a child's immune system, despite recent evidence for poor effectiveness. There currently are no data that suggest otherwise.



WHEN IS IT TOO EARLY TO ADMINISTER INFLUENZA VACCINE?

- Influenza vaccine can be administered as soon as available and **complete vaccination** (one or two doses, as pertinent) **should be achieved by end of October**
- Influenza circulation is unpredictable, but most seasons peak in February
- Protection through vaccination BEFORE influenza begins to circulate is recommended, but important **continue to vaccinate through the season**
- Programmatic issues need to be considered



WANING INFLUENZA IMMUNITY

- Waning of influenza immunity after vaccination is expected based on natural antibody decay, starting approximately 2 months after vaccination
- Waning immunity has been reported mostly in adults
- Waning antibodies have not been associated with increased risk of disease in pediatrics

See MMWR 2018 recommendations.

Ferdinands JM, Fry AM, Reynolds S, et al. Intraseason waning of influenza vaccine protection: Evidence from the US Influenza Vaccine Effectiveness Network, 2011–12 through 2014–15. *Clin Infect Dis* 2017;64:544–50.

Castilla J, Martínez-Baz I, Martínez-Artola V, et al.; Primary Health Care Sentinel Network; Network for Influenza Surveillance in Hospitals of Navarre. Decline in influenza vaccine effectiveness with time after vaccination, Navarre, Spain, season 2011/12. *Euro Surveill* 2013;18:20388. <https://doi.org/10.2807/ese.18.05.20388-en>

Belongia EA, Sundaram ME, McClure DL, Meece JK, Ferdinands J, VanWormer JJ. Waning vaccine protection against influenza A (H3N2) illness in children and older adults during a single season. *Vaccine* 2015;33:246–51. <https://doi.org/10.1016/j.vaccine.2014.06.052>

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OPTIONS TO IMPROVE INFLUENZA VACCINATION IN PEDIATRICS

- Make vaccine easily accessible for all children (send alerts when vaccine is available, accept walk-ins, set up vaccination clinics, extended hours, vaccination at well-checks, prior to discharge from hospitalization)
- Standing orders
- Cover all family members/parents
- Work with other venues
- Document administration
- Vaccination of contacts and health care workers



EGG ALLERGY AND FLU VACCINES

- Egg allergy **does not increase risk** of anaphylactic reaction to vaccination with inactivated influenza vaccines*
- Children with egg allergies can receive any licensed, recommended vaccine that is age appropriate, with **no special precautions than those recommended for routine vaccines.**
- Children with a history of *severe* allergic reaction to egg (anaphylaxis)
 - “Vaccine administration should be supervised by a health care provider who is able to recognize and manage severe allergic conditions.”

*Based on 28 studies evaluating 4,315 egg-allergic subjects (656 with severe allergies)



DIAGNOSIS OF INFLUENZA

- Most reliable through laboratory confirmation with molecular detection assays (PCR)
- Rapid influenza molecular assays now available, some CLIA certified – point of care
- Consider influenza activity in the community and consistent clinical presentation



Comparison of Types of Influenza Diagnostic Tests Ordered by Typical Processing Time

Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity	Distinguishing Subtype Strains of Influenza A	Cost
Rapid influenza diagnostic tests¹	Antigen detection	Wide	<15 minutes	10-70%	No	\$
Rapid influenza molecular assays²	RNA detection	Wide	<20 minutes	86-100%	No	\$\$\$
Nucleic Acid Amplification Tests (including RT-PCR)	RNA detection	Limited	1-8 hours	86-100%	Yes	\$\$\$
Direct and indirect Immunofluorescence assays	Antigen detection	Wide	1-4 hours	70-100%	No	\$
Rapid cell culture (shell vials and cell mixtures)	Virus isolation	Limited	1-3 days	100%	Yes	\$\$
Viral cell culture	Virus isolation	Limited	3-10 days	100%	Yes	\$\$

1- Some rapid influenza molecular assays are CLIA-waived, depending on the specimen

2- Commercial rapid immunoassay diagnostic tests are CLIA-waived

Adapted from the Centers for Disease Control and Prevention (CDC) Guidance for clinicians on the use of rapid influenza diagnostic tests. http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm.

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Clinical Presentation of Influenza in Children

Sign/Symptom	Children	Adults	Elderly
Cough (nonproductive)	++	++++	+++
Fever	+++	+++	+
Myalgia	+	+	+
Headache	++	++	+
Malaise	+	+	+++
Sore throat	+	++	+
Rhinitis/nasal congestion	++	++	+
Abdominal pain/diarrhea	+	-	+
Nausea/vomiting	++	-	+

++++ Most frequent sign/symptom; + Least frequent; - Not found

Cox NJ. *Lancet*. 1999;354:1277-1282.

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	Cold	Flu
Respiratory Virus?	Yes	Yes
Symptoms	Mild (runny/stuffy nose)	More intense (fever, body aches, and more)
Can lead to hospitalization or death?	No	Yes
Vaccine Available?	No	Yes
Can identify with a test?	No	Yes

INFLUENZA COMPLICATIONS IN CHILDREN

- **Primary influenza pneumonia:** Sudden onset of fever, chills/rigors, headache, malaise, myalgia, non-productive cough, sore throat, congestion, rhinitis
- Acute **myositis**, otitis media, croup, bronchiolitis, pneumonia
- **Myocarditis**
- **Encephalopathy, febrile seizures**, seizures, post-infectious encephalitis, Guillain Barre syndrome
- Invasive **secondary bacterial infections** with Staph aureus (MRSA, MSSA), Pneumococcus, Group A Streptococcus, H. influenzae
- **Sepsis like syndrome** in neonates
- **Exacerbation of asthma (CLD) or heart disease**
- Reye syndrome if combined with aspirin
- Death

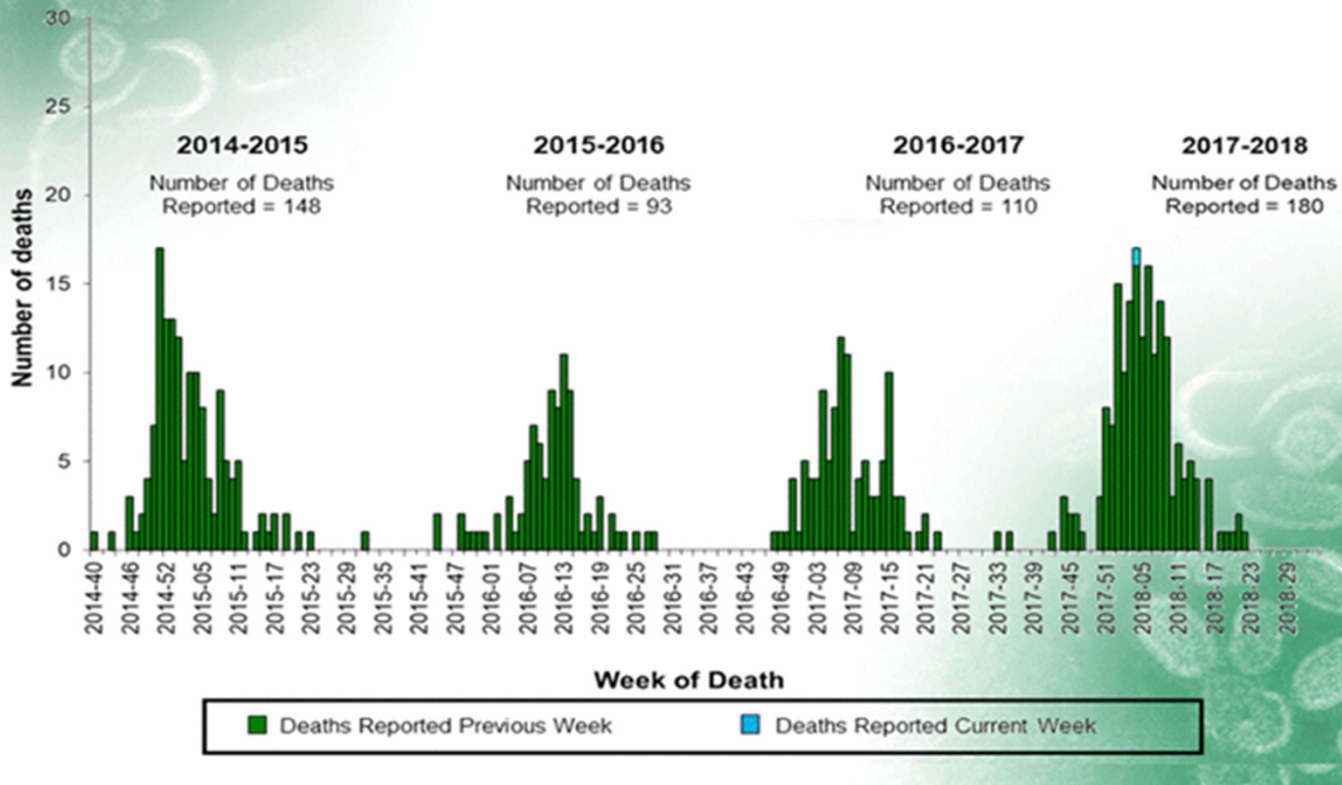


COMPLICATIONS OF INFLUENZA

- Among children aged <5 years, influenza-related illness is a common cause of visits to medical practices and emergency departments
- Rates of influenza-associated hospitalization are highest among children aged <2 years- similar to the elderly and other high risk groups
- In the US, approximately 1% of influenza illnesses result in hospitalization
- Deaths among children due to co-infection with influenza and *Staphylococcus aureus*, particularly MRSA, have increased. Antibiotic treatment is recommended in cases of pneumonia or sepsis.



Number of Influenza-Associated Pediatric Deaths by Week of Death: 2014-2015 season to present



Source: CDC.gov

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Pediatric influenza deaths 2017-18

- ~ 21% associated with infection with A(H3N2) virus, 18% with A(H1N1)pdm09, 21% with an influenza A virus for which no subtyping was performed, 37% with an influenza B virus
- The mean was 7.1 years (range = 8 weeks–17 years)
- 97 (57%) children died after admission to the hospital
- Among children with known medical history, 51% had at least one underlying medical condition placing them at high risk for influenza-related complications; 49% did not and were previously healthy.
- Among the children who were eligible for influenza vaccination (age ≥ 6 mo at date of onset) and for whom vaccination status was known, 78% were NOT vaccinated.



INFLUENZA VACCINATION CAN PROTECT AGAINST SEVERE INFLUENZA AND DEATH

- **PICU Hospitalization**
 - 44 cases, 172 PICU controls, 93 community controls among children 6 mo-17 yrs, in 21 PICUs in US, 2010-2012 (PALISI)
 - Vaccinated children were **74%** (95% CI 19-91%) **or 82%** (95% CI 23-96%) **less likely to be admitted to PICU for influenza** vs. PICU or community controls
 - 1 dose only (when 2 needed), was NOT protective
- **Death**
 - 359 influenza associated deaths among children 6 mo to 17 years
 - 26% received flu vaccine vs. 48% in comparative survey cohort
 - **Overall VE against death: 65%** (95% CI 54%-74%)
 - **Children with high-risk conditions VE: 51%** (95% CI 31%-67%)
 - **Children without high risk conditions VE: 65%** (95% CI 47% to 78%)



TREATMENT OF INFLUENZA IN CHILDREN

- Does not require laboratory confirmation*
- Offer antiviral treatment ASAP to children:
 - Hospitalized for suspected influenza
 - Hospitalized with severe, complicated, or progressive illness attributable to influenza regardless of duration
 - Suspected influenza of any severity and at high risk for complications
- Consider treatment ASAP
 - In any healthy child with suspected influenza
 - Healthy children with suspected influenza who live with high risk persons at home

* Efforts should be made to minimize treatment in patients who are not infected with influenza



CHILDREN AT HIGH RISK OF INFLUENZA COMPLICATIONS – TREATMENT OF SUSPECTED OR CONFIRMED INFLUENZA

- Children < 5 years, especially if < 2 yr
- Children with chronic pulmonary, cardiovascular, renal, hepatic, hematologic, or metabolic disorders, neurologic or eurodevelopmental conditions
- Immunosuppression, including meds/HIV
- Pregnant women or postpartum during flu
- Long term aspirin therapy
- Am Indian and/or Alaskan native
- Extreme obesity (BMI > 40)
- Residents of chronic facilities or nursing homes
- Hospitalized patients at high risk of complications



ANTIVIRALS FOR INFLUENZA

Drug (Trade Name)	Virus	Route	Treatment ^{a,b}	Chemoprophylaxis ^d	Adverse Effects
Oseltamivir (Tamiflu)	A and B	Oral	Birth or older ^c	3 mo of age or older	Nausea, vomiting
Zanamivir (Relenza)	A and B	Inhalation	7 y of age or older	5 y of age or older	Bronchospasm
Peramivir (Rapivab)	A and B	Intravenous	2 y of age and older	N/A	Diarrhea; some reports of skin reactions. Neuropsychiatric events

- Treatment within 48 hr of onset of illness has greatest effect in reduction of symptoms and duration of illness
- No antiviral is specifically approved for severe influenza, but observational studies support effect on reduction of complications, and most experts support use
- FDA approved for children 2 wk of age and older but AAP supports use from birth in term and preterm infants
- Chemoprophylaxis: High risk children who cannot get vaccinated or may not respond to vaccine; within 2 weeks after vaccination if circulation of influenza, contacts of HR patients, control of outbreaks



CONCLUSIONS

- AAP recommends influenza vaccine for **everyone \geq 6 months of age**
- Two doses recommended for first time or previously incomplete immunization in children 6 months to 8 years of age
- Groups at risk for complications of influenza need to be immunized
- Complete vaccination by end of October, continue to vaccinate through season
- Trivalent and quadrivalent inactivated influenza vaccines can be administered, no preference
- **IIV is primary vaccine choice**, LAIV for healthy children > 2 yr who would not receive IIV this season
- No special precautions for egg allergy
- Previous allergic reaction to *any* component of the vaccine is contraindication



CONCLUSIONS

- Neuraminidase inhibitors are available in different formulations (PO, Inhaled, IV) and recommended for treatment of influenza in:
 - Hospitalized
 - High risk conditions
 - Severe and progressive influenza
 - Contacts of high risk persons
 - Healthy children who could benefit from treatment based on clinician's assessment
- Avoid use of antivirals in children who do not have influenza



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- Type your question in the Q&A box (please do not submit questions via the “chat” button, as it will not be seen by the moderator).
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- CDC Media: media@cdc.gov or 404-639-3286.
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When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

https://emergency.cdc.gov/coca/calls/2018/callinfo_092718.asp

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Upcoming COCA Call

Topic: Multi-state Hepatitis A Outbreak





Date: TBD

Time: 2:00-3:00pm ET



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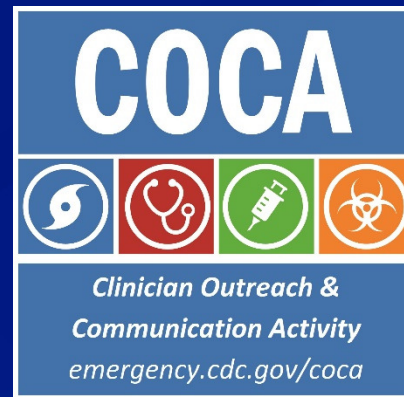


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