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Recommendations for Prevention and Control of Influenza in Children, 2019–2020

COMMITTEE ON INFECTIOUS DISEASES

abstract

This statement updates the recommendations of the American Academy of Pediatrics for the routine use of influenza vaccines and antiviral medications in the prevention and treatment of influenza in children during the 2019–2020 season. The American Academy of Pediatrics continues to recommend routine influenza immunization of all children without medical contraindications, starting at 6 months of age. Any licensed, recommended, age-appropriate vaccine available can be administered, without preference of one product or formulation over another. Antiviral treatment of influenza with any licensed, recommended, age-appropriate influenza antiviral medication continues to be recommended for children with suspected or confirmed influenza, particularly those who are hospitalized, have severe or progressive disease, or have underlying conditions that increase their risk of complications of influenza.

The following updates for the 2019–2020 influenza season are discussed in this document:

1. Both inactivated influenza vaccine (IIV) and live attenuated influenza vaccine (LAIV) are options for influenza vaccination in children, with no preference.
2. The composition of the influenza vaccines for 2019–2020 has been updated. The A(H1N1)pdm09 and A(H3N2) components of the vaccine are new for this season. The B strains are unchanged from the previous season.
3. All pediatric influenza vaccines will be quadrivalent vaccines. The age indication for some pediatric vaccines has been expanded; therefore, there are now 4 egg-based quadrivalent inactivated influenza vaccines (IIV4s) licensed by the US Food and Drug Administration (FDA) for administration to children 6 months and older, 1 inactivated cell-based quadrivalent inactivated influenza vaccine (cIIV4) for children 4 years and older, and 1 quadrivalent live attenuated influenza vaccine (LAIV4)

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for children 2 years and older. No trivalent vaccines are expected to be available for children this season.

4. New formulations of licensed influenza vaccines with a volume of 0.5 mL per dose have been approved for children 6 through 36 months of age. Children 6 through 35 months of age may now receive either the 0.25- or 0.5-mL dose, with no preference, and children ≥36 months of age (3 years and older) continue to receive a 0.5-mL dose.
5. Children 6 months through 8 years of age who are receiving influenza vaccine for the first time or who have received only 1 dose before July 1, 2019, should receive 2 doses of influenza vaccine ideally by the end of October, and vaccines should be offered as soon as they become available. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination ideally by the end of October.
6. A new antiviral medication has been licensed for treatment of influenza in children.

Children often have the highest attack rates of influenza in the community during seasonal influenza epidemics. They play a pivotal role in the transmission of influenza virus infection to household and other close contacts and can experience morbidity, including severe or fatal complications from influenza infection.[1] Children younger than 5 years, especially those younger than 2 years, and children with certain underlying medical conditions are at increased risk of hospitalization and complications attributable to influenza.[1] School-aged children bear a large influenza disease burden and are more likely to seek influenza-related medical care compared with healthy adults.[1,2] Reducing influenza virus transmission among children decreases the burden of childhood influenza and transmission of influenza virus to household contacts and community members of all ages.[1,2] Routine influenza vaccination and antiviral agents for the treatment and prevention of influenza are recommended for children.[1,2]

SUMMARY OF RECENT INFLUENZA ACTIVITY IN THE UNITED STATES

2017–2018 Influenza Season

The 2017–2018 influenza season was the first classified as a high-severity season for all age groups, with high levels of outpatient clinic and emergency department visits for influenzalike illness, high influenza-related hospitalization rates, and high numbers of deaths.[3–5] Influenza A(H3N2) viruses predominated through February 2018; influenza B viruses predominated from March 2018 onward. Although hospitalization rates for children that season did not exceed those reported during the 2009 pandemic, they did surpass rates reported in previous high-severity A(H3N2)-predominant seasons. Excluding the 2009 pandemic, the 186 pediatric deaths reported during the 2017–2018 season (approximately half of which occurred in otherwise healthy children) were the highest reported since influenza-associated pediatric mortality became a nationally notifiable condition in 2004.[3–5] Among pediatric deaths of children 6 months and older who were eligible for vaccination and for whom vaccination status was known, approximately 80% had not received the influenza vaccine during the 2017–2018 season.[3]

Overall vaccine effectiveness (VE) against both influenza A and B viruses during the 2017–2018 season was estimated to be 38%, with higher VE (64%) in children 6 months to 8 years of age compared with those 9 to 17 years of age (28%).[4] Overall VE against influenza A(H1N1) was 65% (87% in those 6 months through 8 years of age; 70% in those 9 through 17 years of age), 25% against A(H3N2) (54% in those 6 months through 8 years of age; 18% in those 9 through 17 years of age), and 48% against influenza B (B/Yamagata predominant) (77% in those 6 months through 8 years of age; 28% in those 9 through 17 years of age).

2018–2019 Influenza Season

The 2018–2019 influenza season was the longest-lasting season reported in the United States in the past decade, with elevated levels of influenzalike illness activity for a total duration of 21 consecutive weeks (compared to the average duration of 16 weeks).[6] Influenza A(H1N1)pdm09 viruses predominated from October to mid-February, and influenza A(H3N2) viruses were identified more frequently from February to May. Influenza B (B/Victoria lineage predominant) represented approximately 5% of circulating strains. The majority of characterized influenza A(H1N1)pdm09 and influenza B viruses were antigenically similar to the viruses included in the 2018–2019 influenza vaccine, but most characterized influenza A(H3N2) viruses were antigenically distinct from the A(H3N2) component of the 2018–2019 vaccine. Co-circulation of multiple genetically diverse clades and/or subclades of A(H3N2) was documented. Circulating viruses identified belonged to clade 3C.2a, subclade 3C.2a1, or clade 3C.3a, with 3C.3a viruses accounting for >70% of the A(H3N2) in the United States. The 2018–2019 vaccine's A(H3N2) virus belonged to subclade 3C.2a1. This likely contributed to an overall lower VE against influenza A(H3N2) for that influenza season and supported the recommendation to change the A(H3N2) virus strain for the upcoming season's vaccine.

The 2018–2019 season was of moderate severity, with similar

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hospitalization rates in children as seen during the 2017–2018 season, which were higher than in those observed in previous seasons from 2013–2014 to 2016–2017. The cumulative hospitalization rates per 100 000 population were 72.0 among children 0 through 4 years old and 20.4 among children 5 through 17 years old.[6] Among 1132 children hospitalized with influenza and for whom data were available, 45% had no recorded underlying condition, and 55% had at least 1 underlying medical condition; the most commonly reported underlying conditions were asthma or reactive airway disease (27.1%), neurologic disorders (17.7%), and obesity (11.4%).[7]

As of June 21, 2019, the following data were reported by the Centers for Disease Control and Prevention (CDC):

- There were 116 laboratory-confirmed influenza-associated pediatric deaths. Most (66%) of those children died after being admitted to the hospital. The median age of the pediatric deaths was 6.1 years (range: 2 months–17 years).
  - A total of 107 were associated with influenza A viruses: 43 with influenza A(H1N1)pdm09, 25 with A(H3N2), and 39 with an influenza A virus for which no subtyping was available.
  - Eight were associated with influenza B viruses.
  - One was associated with an undetermined type of influenza virus.
- Among the 104 children with known medical history, 51% of deaths occurred in children who had at least 1 underlying medical condition recognized by the Advisory Committee on Immunization Practices (ACIP) to increase the risk of influenza-attributable disease severity. Therefore, nearly half had no known underlying medical conditions.
- Among 89 children who were 6 months or older at the time of illness onset and, therefore, would have been eligible for vaccination and for whom vaccination status was known, most (70%) were unvaccinated. Only 30 (34%) had received at least 1 dose of influenza vaccine (25 had complete vaccination, and 5 had received 1 of 2 ACIP-recommended doses).

Preliminary estimates of the VE of the 2018–2019 seasonal influenza vaccines (not based on specific products) against medically attended influenza illness from the US Influenza VE Network reveal an overall adjusted VE of 47% (95% confidence interval [CI], 34% to 57%) for people of all ages against any type of influenza (A or B).[7] The overall VE against any type of influenza for children 6 months through 17 years was 61% (95% CI, 44% to 73%). Virus-specific preliminary VE data available for influenza A(H1N1) viruses reveal overall VE of 45% (95% CI, 30% to 58%) in people of all ages and 63% (95% CI, 40% to 75%) for children 6 months to 17 years. Preliminary VE for influenza A(H3N2) in people of all ages is 44% (95% CI, 13% to 64%). No data are yet available for children within this network for A(H3N2) or B strains.

Preliminary estimates of influenza VE against hospitalization in children, from the CDC's New Vaccine Surveillance Network, which is focused on surveillance in children, reveal an overall adjusted (for age, site, and month) VE in children of 31% (95% CI, 5% to 51%) against any influenza A or B virus, with 26% (95% CI, −6% to 49%) in children 6 months through 8 years of age and 53% (95% CI, 5% to 77%) among those 9 through 17 years of age.[1] The overall adjusted VE against pediatric hospitalization by virus subtype was 48% (95% CI, 14% to 68%) for A(H1N1)pdm09 and 13% (95% CI, −31% to 43%) for A(H3N2). These are preliminary data and not vaccine specific.

INFLUENZA MORBIDITY AND MORTALITY IN CHILDREN

Pediatric hospitalizations and deaths caused by influenza vary from one season to the next. Historically, up to 80% of pediatric deaths have occurred in unvaccinated children 6 months and older. Influenza vaccination is associated with reduced risk of laboratory-confirmed influenza-related pediatric death.[8] In 1 case-cohort analysis comparing vaccination uptake among laboratory-confirmed influenza-associated pediatric deaths with estimated vaccination coverage among pediatric cohorts in the United States from 2010 to 2014, Flannery et al[8] found that only 26% of children had received the vaccine before illness onset compared to an average vaccination coverage of 48%. Overall VE against influenza-associated death in children was 65% (95% CI, 54% to 74%). More than half of children in this study who died of influenza had ≥1 underlying medical condition associated with increased risk of severe influenza-related complications; only 1 in 3 of these at-risk children had been vaccinated; yet, VE against death in children with underlying conditions was 51% (95% CI, 31% to 67%). Similarly, influenza vaccination reduces by three quarters the risk of severe, life-threatening laboratory-confirmed influenza in children requiring admission to the ICU.[9] The rates of influenza-associated hospitalization for children younger than 5 years exceed the rates for children 5 through 17 years of age. The influenza virus type might also affect the severity of disease. In a recent study of hospitalizations for influenza A versus B, the odds of mortality were significantly greater with influenza B than with influenza A and not entirely explained by underlying health conditions.[10]

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HIGH-RISK GROUPS IN PEDIATRICS

Children and adolescents with certain underlying medical conditions have a high risk of complications from influenza, as described in Table 1. Although universal influenza vaccination is recommended for everyone starting at 6 months of age, emphasis should be placed on ensuring that people in high-risk groups and their household contacts and caregivers receive an annual influenza vaccine.[11]

SEASONAL INFLUENZA VACCINES

Table 2 summarizes information on the types of influenza vaccines licensed for children and adults during the 2019–2020 season. More than 1 product may be appropriate for a given patient, and vaccination should not be delayed to obtain a specific product.

All 2019–2020 seasonal influenza vaccines contain the same influenza strains as recommended by the World Health Organization (WHO) as well as the FDA Vaccines and Related Biological Products Advisory Committee for the Northern Hemisphere[6,14]:

1. Trivalent vaccines contain the following:
   a. A/Brisbane/02/2018 (H1N1) pdm09-like virus (new this season);
   b. A/Kansas/14/2017 (H3N2)-like virus (new this season); and
   c. B/Colorado/60/2017-like virus (B/Victoria/2/87 lineage) (unchanged).
2. Quadrivalent vaccines contain a second B virus:
   a. B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) (unchanged).

IIV

For the 2019–2020 season, all IIVs for children in the United States will be quadrivalent vaccines, with specific age indications for available formulations (Table 2). All licensed inactivated vaccines for children in the United States are unadjuvanted; 4 are egg-based (seed strains grown in eggs), 1 is cell culture-based (seed strains grown in Madin-Darby canine kidney cells), and all are available in single-dose, thimerosal-free prefilled syringes as well multidose vial presentations. With the FDA approval of the expansion of the age indication for Afluria Quadrivalent[15] to children 6 months and older (previously approved for children 5 years and older) in October 2018, all egg-based IIV4s (Afluria, Fluarix, Flulaval, and Fluzone) are now licensed for children 6 months and older, and the cell culture–based vaccine (Flucelvax) is licensed for children 4 years and older.

The licensure of the expanded age indication for Afluria quadrivalent was supported by a single randomized, double-blind safety and immunogenicity study in children 6 through 59 months of age who received Afluria quadrivalent or a comparator licensed quadrivalent vaccine.[15] The vaccine was found to have a similar safety profile and noninferior immunogenicity as the comparator vaccine. Importantly, there were no febrile seizures in the 7 days after vaccination. The trivalent formulation is no longer expected to be available. The dose volume for Afluria quadrivalent is 0.25 mL for children 6 through 35 months of age and 0.5 mL for those 36 months and older. This vaccine should only be administered by needle and syringe in children, whereas administration via jet injector is an option for individuals 18 through 64 years of age.

A quadrivalent recombinant baculovirus-expressed hemagglutinin influenza vaccine (RIV4; Flublok) is licensed only for people 18 years and older. The high-dose trivalent inactivated influenza vaccine (IIV3; Fluzone High-Dose), containing 4 times the amount of antigen for each virus strain than the standard-dose vaccines, is licensed only for people 65 years and older. A trivalent MF59 adjuvanted IIV (Fluad) licensed

TABLE 1 Persons at High Risk of Influenza Complications

Children <5 years and especially those <2 years,[a] regardless of the presence of underlying medical conditions
Adults ≥50 years and especially those ≥65 years
Children and adults with chronic pulmonary (including asthma and cystic fibrosis), hemodynamically significant cardiovascular disease (except hypertension alone), or renal, hepatic, hematologic (including sickle cell disease and other hemoglobinopathies), or metabolic disorders (including diabetes mellitus)
Children and adults with immunosuppression attributable to any cause, including that caused by medications or by HIV infection
Children and adults with neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy, stroke, intellectual disability, moderate-to-severe developmental delay, muscular dystrophy, or spinal cord injury)
Children and adults with conditions that compromise respiratory function or handling of secretions (including tracheostomy and mechanical ventilation)[12]
Women who are pregnant or postpartum during the influenza season
Children and adolescents <19 years who are receiving long-term aspirin therapy or salicylate-containing medications (including those with Kawasaki disease and rheumatologic conditions) because of increased risk of Reye syndrome
American Indian and Alaskan native people
Children and adults with extreme obesity (ie, BMI ≥40 for adults and based on age for children)
Residents of chronic care facilities and nursing homes

[a] The 2019–2020 CDC recommendations state that "Although all children younger than 5 years old are considered at higher risk for complications from influenza, the highest risk is for those younger than 2 years old, with the highest hospitalization and death rates among infants younger than 6 months old."

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TABLE 2 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2019–2020 Influenza Season

Vaccine	Trade Name	Manufacturer	Presentation HA Antigen Content (IIVs and RIV4) or Virus Count (LAIV4) per Dose for Each Vaccine Virus	Thimerosal Mercury Content, μg of Hg/0.5-mL Dose	Age Group	CPT Code
Inactivated						
Trivalent						
IIV3	Fluzone High-Dose	Sanofi Pasteur	0.5-mL prefilled syringe (60 μg/0.5 mL)	0	≥65 y	90662
aIIV3	Fluad MF59 adjuvanted	Seqirus	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥65 y	90653
Quadrivalent						
Egg based						
IIV4	Fluzone Quadrivalent	Sanofi Pasteur	0.25-mL prefilled syringe (7.5 μg/0.25 mL)	0	6–35 mo	90685
			0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥6 mo	90686
			0.5-mL single-dose vial (15 μg/0.5 mL)	0	≥6 mo	90686
			5.0-mL multidose vial[a] (7.5 μg/0.25 mL) (15 μg/0.5 mL)	25	≥6 mo	90687, 90688
IIV4	Fluarix Quadrivalent	GlaxoSmithKline	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥6 mo	90686
IIV4	FluLaval Quadrivalent	ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline)	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥6 mo	90686
			5.0-mL multidose vial (15 μg/0.5 mL)	<25	≥6 mo	90688
IIV4	Afluria Quadrivalent	Seqirus	0.25-mL prefilled syringe (7.5 μg/0.25 mL)	0	6–35 mo	90685
			0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥36 mo	90686
			5.0-mL multidose vial[a] (7.5 μg/0.25 mL) (15 μg/0.5 mL)	24.5	≥6 mo (needle/syringe) 18–64 y (jet injector)	90687, 90688
Cell based						
ccIIV4	Flucelvax Quadrivalent	Seqirus	0.5-mL prefilled syringe (15 μg/0.5 mL)	0	≥4 y	90674
			5.0 mL multidose vial (15 μg/0.5 mL)	25	≥4 y	90756
Recombinant						
RIV4	Flublok Quadrivalent	Protein Sciences Corporation (distributed by Sanofi Pasteur)	0.5-mL prefilled syringe (45 μg/0.5 mL)	0	≥18 y	90682
Live attenuated						
LAIV4	FluMist Quadrivalent	AstraZeneca	0.2-mL prefilled intranasal sprayer (virus dose: $10^{6.5–7.5}$ FFU/0.2 mL)	0	2–49 y	90672

Implementation guidance on supply, pricing, payment, CPT coding, and liability issues can be found at www.aapredbook.org/implementation. Data sources are from references[1] and[13]. aIIV3, adjuvanted trivalent inactivated influenza vaccine; ccIIV4, quadrivalent cell culture–based inactivated influenza vaccine; CPT, *Current Procedural Terminology*; FFU, focus-forming unit; —, not applicable.

[a] For vaccines that include a multidose vial presentation and a 0.25-mL dose, a maximum of 10 doses can be drawn from a multidose vial.

for people 65 years and older is the first adjuvanted influenza vaccine marketed in the United States. Adjuvants may be included in a vaccine to elicit a more robust immune response, which could lead to a reduction in the number of doses required for children. In a study in children, the relative vaccine efficacy of an MF59 adjuvanted influenza vaccine was significantly greater than nonadjuvanted vaccine in the 6- through 23-month age group.[16] Adjuvanted seasonal influenza vaccines are not licensed for children at this time.

Children 36 months (3 years) and older can receive any age-appropriate licensed IIV, administered at a 0.5-mL dose and containing 15 μg of hemagglutinin (HA) from each strain in the vaccine. Children 6 through 35 months of age may receive any licensed IIV at either 0.25 or 0.5 mL per dose, without preference over one or the other.

The only IIV products licensed for children 6 through 35 months of age before 2016 were the 0.25-mL (containing 7.5 μg of HA for each vaccine virus) dose formulations of Fluzone (IIV3) and Fluzone Quadrivalent (IIV4). The recommendation for use of a reduced dose and volume for children in this age group (half that recommended for people 3 years and older) was based on increased reactogenicity noted among younger children after receipt of whole-virus inactivated vaccines, which have since been replaced with split virus and subunit IIV. Several vaccines have been licensed for children 6 through 35 months of age since 2017, which are less reactogenic (Table 2).[17,18] All are quadrivalent, but the dose volume

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and, therefore, the antigen content vary among different IIV products. In addition to the 0.25-mL (7.5 μg of HA per vaccine virus) Fluzone Quadrivalent vaccine, Fluzone Quadrivalent containing 15 μg of HA per vaccine virus per 0.5-mL dose was licensed in January 2019[19,20] after these 2 formulations were compared in a single randomized, multicenter safety and immunogenicity study. Both products are expected to be available this season because no direct comparison data are available to demonstrate superiority of one over the other. In addition, 2 other vaccines, Fluarix Quadrivalent[21] and FluLaval Quadrivalent,[22] have been licensed for a 0.5-mL dose in children 6 through 35 months of age. These 2 vaccines do not have a 0.25-mL dose formulation.

Given that different formulations of IIV for children 6 through 35 months of age are available, care should be taken to administer the appropriate volume and dose for each product. In each instance, the recommended volume may be administered from an appropriate prefilled syringe, a single-dose vial, or multidose vial, as supplied by the manufacturer. For vaccines that include a multidose vial presentation and a 0.25-mL dose, a maximum of 10 doses can be drawn from a multidose vial. Importantly, dose volume is different from the number of doses needed to complete vaccination. Children 6 months through 8 years of age who require 2 doses of vaccine for the 2019–2020 season should receive 2 separate doses at the recommended dose volume specified for each product.

IIVs can be used in healthy children as well as those with underlying chronic medical conditions. IIV is well tolerated in children. The most common injection-site adverse reactions after administration of IIV in children are injection-site pain, redness, and swelling. The most common systemic adverse events are drowsiness, irritability, loss of appetite, fatigue, muscle aches, headache, arthralgia, and gastrointestinal tract symptoms.

IIV can be administered concomitantly with other inactivated or live vaccines. During the 2 influenza seasons spanning 2010–2012, there were increased reports of febrile seizures in the United States in young children who received IIV3 and the 13-valent pneumococcal conjugate vaccine (PCV13) concomitantly. Subsequent retrospective analyses of past seasons revealed a slight increase in the risk of febrile seizures in children 6 through 23 months of age when PCV13s were administered concomitantly with IIV.[23] The concomitant administration of IIV3, PCV13, and diphtheria-tetanus-acellular pertussis vaccine was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated compared to the administration of the vaccines on separate days. In contrast, data from the Post-Licensure Rapid Immunization Safety Monitoring program of the FDA, the largest vaccine safety active surveillance program in the United States, revealed that there was no significant increase in febrile seizures associated with concomitant administration of these 3 vaccines in children 6 through 59 months of age during the 2010–2011 season.[24] In a subsequent sentinel Center for Biologics Evaluation and Research–Post-Licensure Rapid Immunization Safety Monitoring surveillance report evaluating influenza vaccines and febrile seizures in the 2013–2014 and 2014–2015 influenza seasons, there was no evidence of an elevated risk of febrile seizures in children 6 through 23 months of age after IIV administration during the 2013–2014 and 2014–2015 seasons. It was concluded that the risk of seizures after PCV13 or concomitant PCV13 and IIV is low compared to a child's lifetime risk of febrile seizures from other causes.[25] Although the possibility of increased risk for febrile seizures cannot be ruled out, simultaneous administration of IIV with PCV13 and/or other vaccines for the 2019–2020 influenza season continues to be recommended when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of IIV and PCV13 or diphtheria-tetanus-acellular pertussis vaccine outweigh the risk of febrile seizures. Vaccine-proximate febrile seizures rarely have any long-term sequelae, similar to non–vaccine-proximate febrile seizures.

Thimerosal-containing vaccines are not associated with an increased risk of autism spectrum disorder in children.[1] Thimerosal from vaccines has not been linked to any neurologic condition. The American Academy of Pediatrics (AAP) supports the current WHO recommendations for use of thimerosal as a preservative in multiuse vials in the global vaccine supply. Concerns about the residual, trace amount of thimerosal in some IIV formulations may arise. Despite the lack of evidence of harm, some states, including California, Delaware, Illinois, Missouri, New York, and Washington, have legislation restricting the use of vaccines that contain even trace amounts of thimerosal. The benefits of protecting children against the known risks of influenza are clear. Therefore, to the extent permitted by state law, children should receive any available formulation of IIV rather than delaying vaccination while waiting for reduced thimerosal-content or thimerosal-free vaccines. IIV formulations that are free of even trace amounts of thimerosal are widely available (Table 2).

Live Attenuated (Intranasal) Influenza Vaccine

The intranasal LAIV was initially licensed in the United States in 2003 for people 5 through 49 years of age as a trivalent live attenuated influenza vaccine (LAIV3)

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formulation. The approved age group was extended to 2 years of age in 2007. The quadrivalent formulation (LAIV4) has been licensed in the United States since 2012 and was first available during the 2013–2014 influenza season, replacing the LAIV3. The most commonly reported reactions in children are runny nose or nasal congestion, headache, decreased activity or lethargy, and sore throat. The safety of LAIV in people with a history of asthma, diabetes mellitus, or other high-risk medical conditions associated with an elevated risk of complications from influenza (see Contraindications and Precautions) has not been firmly established. In postlicensure surveillance of LAIV (including LAIV3 and LAIV4), the Vaccine Adverse Event Reporting System, jointly sponsored by the FDA and CDC, did not identify any new or unexpected safety concerns, including in people with a contraindication or precaution. Although the use of LAIV in young children with chronic medical conditions, including asthma, has been implemented outside of the United States, data are considered insufficient to support an expanded recommendation in the United States.

The CDC conducted a systematic review of published studies evaluating the effectiveness of LAIV3 and LAIV4 in children from the 2010–2011 to the 2016–2017 seasons, including data from US and European studies.[1,26] The data suggested that the effectiveness of LAIV3 or LAIV4 for influenza strain A(H1N1) was lower than that of IIV in children 2 through 17 years of age. LAIV was similarly effective against influenza B and A(H3N2) strains in some age groups compared to IIV.

For the 2017–2018 season, a new A(H1N1)pdm09-like virus (A/Slovenia/2903/2015) was included in LAIV4, replacing A/Bolivia/559/2013. A study conducted by the LAIV4 manufacturer evaluated viral shedding and immunogenicity associated with the LAIV4 formulation containing the new A(H1N1)pdm09-like virus among US children 24 months through 3 years of age.[27] Shedding and immunogenicity data provided by the manufacturer suggested that the new influenza A(H1N1)pdm09-like virus included in its latest formulation had improved replicative fitness over previous LAIV4 influenza A(H1N1) pdm09-like vaccine strains, resulting in an improved immune response comparable to that of LAIV3 available before the 2009 pandemic. Shedding and replicative fitness are not known to correlate with efficacy, and no published effectiveness estimates for this revised formulation of the vaccine against influenza A(H1N1) pdm09 viruses were available before the start of the 2018–2019 influenza season because influenza A(H3N2) and influenza B viruses predominated during the 2017–2018 northern hemisphere season. Therefore, for the 2018–2019 season, the AAP recommended IIV4 or IIV3 as the primary choice for influenza vaccination in children, with LAIV4 use reserved for children who would not otherwise receive an influenza vaccine and for whom LAIV use was appropriate for age (2 years and older) and health status (ie, healthy, without any underlying chronic medical condition).

After the ACIP meeting in February 2019, the AAP convened a meeting of its Committee on Infectious Diseases to discuss the influenza vaccination recommendations for the 2019–2020 season. The group reviewed available data on influenza epidemiology and VE for the 2018–2019 season and agreed that harmonizing recommendations between the AAP and CDC for the use of LAIV in the 2019–2020 season is appropriate as more information becomes available. Despite the early predominance of A(H1N1) circulation, low use of LAIV4 in the US population limited evaluation of product-specific VE, and no additional US data on LAIV4 VE was anticipated at the end of the 2018–2019 season. The information reviewed by the Committee on Infectious Diseases included the following:

- The epidemiology of the 2018–2019 influenza season in the United States and worldwide, showing an early predominance of A(H1N1)pdm09 virus circulation, followed by A(H3N2) (https://www.cdc.gov/flu/weekly/index.htm).
- Interim VE for 2018–2019 influenza season showing overall influenza VE against medically attended illness for influenza A(H1N1)pdm09 in children of approximately 60% (not product specific, but most vaccine used was IIV), approximately 40% for influenza A(H3N2) overall (given small numbers of H3N2 cases, no pediatric data), and no data for influenza B.[28]
- Influenza vaccine coverage rates in children, demonstrating an increase to ~45% compared with ~38% at the same time point in 2017–2018 season (interim estimate in November 2018; https://www.cdc.gov/flu/fluvaxview/nifs-estimates-nov2018.htm).
- VE data from the European surveillance networks for which uninterrupted use of LAIV continued during the 2016–2017 and 2017–2018 seasons (when it was not used in the United States) and through the 2018–2019 season. In this network, the only country with interim estimates, the United Kingdom, reported VE against medically attended influenza in children and adolescents 2 through 17 years of age for 2017–2018 and 2018–2019 (same vaccine formulation) of >85% for A(H1N1)pdm09. Estimates were based on a small number of cases and were preliminary but consistent with the previous season.[29]
- Other countries that use LAIV (Canada, Finland) may have LAIV4-

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specific VE at the end of the season, but this is not certain. Small case numbers and low LAIV use may also limit accurate VE calculations in these countries. In general, as long as use of LAIV is low relative to IIV, it will be difficult to estimate LAIV VE accurately. Furthermore, variability in VE for other strains (A [H3N2] and B strains) remains for both IIV and LAIV.

- The committee noted that LAIV is licensed in the United States and recommended by the CDC.

Influenza VE varies from season to season and is affected by many factors, including age and health status of the recipient, influenza type and subtype, existing immunity from previous infection or vaccination, and degree of antigenic match between vaccine and circulating virus strains. It is possible that VE also differs among individual vaccine products; however, product-specific comparative effectiveness data are lacking for most vaccines. Additional experience spanning multiple influenza seasons will help to determine optimal use of the available vaccine formulations in children. The AAP will continue to monitor annual influenza surveillance and VE reports to update influenza vaccine recommendations if necessary.

CONTRAINDICATIONS AND PRECAUTIONS

Children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate. An anaphylaxis reaction after receipt of any influenza vaccine (IIV or LAIV) may be a contraindication to influenza vaccination. LAIV has specific contraindications (see below). Minor illnesses, with or without fever, are not contraindications to the use of influenza vaccines, including among children with mild upper respiratory infection symptoms or allergic rhinitis. In children with a moderate-to-severe febrile illness (eg, high fever, active infection, requiring hospitalization, etc), on the basis of the judgment of the clinician, vaccination should be deferred until resolution of the illness. Similarly, children with an amount of nasal congestion that would notably impede vaccine delivery into the nasopharyngeal mucosa should have LAIV vaccination deferred until resolution.

History of Guillain-Barré syndrome (GBS) after influenza vaccine is considered a precaution for the administration of influenza vaccines. Data on the risk of GBS after vaccination with seasonal influenza vaccine are variable and have been inconsistent across seasons. If there is an increased risk, it is likely small and primarily in adult patients. GBS is rare, especially in children, and there is a lack of evidence on risk of GBS after influenza vaccine in children. Nonetheless, regardless of age, a history of GBS <6 weeks after a previous dose of influenza vaccine is a precaution for administration of influenza vaccine. The benefits of influenza vaccination might outweigh the risks for certain people who have a history of GBS (particularly if not associated with previous influenza vaccination) and who also are at high risk for severe complications from influenza. Additional precautions for LAIV include a diagnosis of asthma in children older than 5 years and the presence of an underlying medical condition that increases the risk to severe illness with wild-type influenza virus (Table 1). Persons who should not receive LAIV are listed below.

Persons in Whom LAIV Is Contraindicated

- children younger than 2 years;
- children 2 through 4 years of age with a diagnosis of asthma or history of recurrent wheezing or a medically attended wheezing episode in the previous 12 months because of the potential for increased wheezing after immunization. In this age range, many children have a history of wheezing with respiratory tract illnesses and are eventually diagnosed with asthma;
- children who have known or suspected immunodeficiency disease or who are receiving immunosuppressive or immunomodulatory therapies;
- close contacts and caregivers of those who are severely immunocompromised and require a protected environment;
- children and adolescents receiving aspirin or salicylate-containing medications;
- children who have received other live-virus vaccines within the previous 4 weeks (except for rotavirus vaccine); however, LAIV can be administered on the same day with other live-virus vaccines if necessary;
- children taking an influenza antiviral medication and until 48 hours (oseltamivir, zanamivir, peramivir) and up to 2 weeks (baloxavir) after stopping the influenza antiviral therapy. If a child recently received LAIV but has an influenza illness for which antiviral agents are appropriate, the antiviral agents should be given. If antiviral agents are necessary for treatment within 5 to 7 days of LAIV immunization, reimmunization is indicated because of the potential effects of antiviral medications on LAIV replication and immunogenicity; and
- pregnant women.

The safety of LAIV in some high-risk populations has not been definitively established. These conditions are not contraindications but are listed under the "Warnings and Precautions"

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section of the LAIV package insert, including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies. A precaution is a condition in a recipient that might increase the risk or seriousness of an adverse reaction or complicate making another diagnosis because of a possible vaccine-related reaction. A precaution also may exist for conditions that might compromise the ability of the vaccine to produce immunity. Vaccination may be recommended in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk.

LAIV and Immunocompromised Hosts

IIV is the vaccine of choice for anyone in close contact with a subset of severely immunocompromised people (ie, those in a protected environment). IIV is preferred over LAIV for contacts of severely immunocompromised people because of a theoretical risk of infection attributable to LAIV strain in an immunocompromised contact of an LAIV-immunized person. Available data indicate a low risk of transmission of the virus from both children and adults vaccinated with LAIV. Health care personnel (HCP) immunized with LAIV may continue to work in most units of a hospital, including the NICU and general oncology ward, using standard infection control techniques. As a precautionary measure, people recently vaccinated with LAIV should restrict contact with severely immunocompromised patients for 7 days after immunization, although there have been no reports of LAIV transmission from a vaccinated person to an immunocompromised person. In the theoretical scenario in which symptomatic LAIV infection develops in an immunocompromised host, LAIV strains are susceptible to antiviral medications.

INFLUENZA VACCINES AND EGG ALLERGY

There is strong evidence that egg-allergic individuals can safely receive influenza vaccine without any additional precautions beyond those recommended for any vaccine.[1,30,31] The presence of egg allergy in an individual is not a contraindication to receive IIV or LAIV. Vaccine recipients with egg allergy are at no greater risk for a systemic allergic reaction than those without egg allergy. Therefore, precautions such as choice of a particular vaccine, special observation periods, or restriction of administration to particular medical settings are not warranted and constitute an unnecessary barrier to immunization. It is not necessary to inquire about egg allergy before the administration of any influenza vaccine, including on screening forms. Routine prevaccination questions regarding anaphylaxis after receipt of any vaccine are appropriate. Standard vaccination practice for all vaccines in children should include the ability to respond to rare acute hypersensitivity reactions. Children who have had a previous allergic reaction to the influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.

INFLUENZA VACCINES DURING PREGNANCY AND BREASTFEEDING

Influenza vaccine is recommended by the ACIP, the American College of Obstetrics and Gynecology, and the American Academy of Family Physicians for all women during any trimester of gestation for the protection of mothers against influenza and its complications.[1,32] Substantial evidence has accumulated regarding the efficacy of maternal influenza immunization in preventing laboratory-confirmed influenza disease and its complications in both mothers and their infants in the first 2 to 6 months of life.[14,32–37] Pregnant women who are immunized against influenza at any time during their pregnancy provide protection to their infants during their first 6 months of life (when they are too young to receive influenza vaccine themselves) through transplacental passage of antibodies.[38,39] Infants born to women who receive influenza vaccination during pregnancy can have a risk reduction of 72% (95% CI, 39% to 87%) for laboratory-confirmed influenza hospitalization in the first few months of life.[40]

It is safe to administer IIV to pregnant women during any trimester of gestation and postpartum. Any licensed, recommended, and age-appropriate influenza vaccine may be used, although experience with the use of RIV4 in pregnant women is limited. LAIV is contraindicated during pregnancy. Data on the safety of influenza vaccination at any time during pregnancy continues to accumulate and support the safety of influenza immunization during pregnancy. In a 5-year retrospective cohort study from 2003 to 2008 with more than 10 000 women, influenza vaccination in the first trimester was not associated with an increase in the rates of major congenital malformations.[41] Similarly, a systematic review and meta-analysis of studies of congenital anomalies after vaccination during pregnancy, including data from 15 studies (14 cohort studies and 1 case-control study), did not show any association between congenital defects and influenza vaccination in any trimester, including the first trimester of gestation.[42] Assessments of any association with influenza vaccination and preterm birth and infants who are small for gestational age have yielded inconsistent results, with most studies reporting a protective effect or no association against these outcomes. Authors of a cohort study from the Vaccines and Medications in Pregnancy Surveillance System of vaccine exposure during the 2010–2011

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through 2013–2014 seasons found no significant association of spontaneous abortion with influenza vaccine exposure in the first trimester or within the first 20 weeks of gestation.[43] One recent observational Vaccine Safety Datalink study conducted during the 2010–2011 and 2011–2012 seasons noted an association between receipt of IIV containing H1N1pdm09 and risk of spontaneous abortion when an H1N1pdm-09-containing vaccine had also been received the previous season.[44] A follow-up study conducted by the same investigators with a larger population did not reveal this association and further supported the safety of influenza vaccine during pregnancy.

Postpartum women who did not receive influenza vaccination during pregnancy should be encouraged to discuss with their obstetrician, family physician, nurse midwife, or other trusted provider receipt of the vaccine before discharge from the hospital. Vaccination during breastfeeding is safe for mothers and their infants.

Breastfeeding is strongly recommended to protect infants against influenza viruses by activating innate antiviral mechanisms, specifically type 1 interferons. Human milk from mothers vaccinated during the third trimester also contains higher levels of influenza-specific immunoglobulin A.[45] Greater exclusivity of breastfeeding in the first 6 months of life decreases the episodes of respiratory illness with fever in infants of vaccinated mothers. For infants born to mothers with confirmed influenza illness at delivery, breastfeeding is encouraged, and guidance on breastfeeding practices can be found at https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/maternal-or-infant-illnesses/influenza.html and https://www.cdc.gov/flu/professionals/infectioncontrol/peri-post-settings.htm. Breastfeeding should be encouraged even if the mother or infant has influenza. The mother should pump and feed expressed milk if she or her infant are too sick to breastfeed. If the breastfeeding mother requires antiviral agents, treatment with oral oseltamivir is preferred. The CDC does not recommend use of baloxavir for treatment of pregnant women or breastfeeding mothers. There are no available efficacy or safety data in pregnant women, and there are no available data on the presence of baloxavir in human milk, the effects on the breastfed infant, or the effects on milk production.

VACCINE STORAGE AND ADMINISTRATION

The AAP Vaccine Storage and Handling Tip Sheet provides resources for practices to develop comprehensive vaccine management protocols to keep the temperature for vaccine storage constant during a power failure or other disaster (https://www.aap.org/en-us/Documents/immunization_disasterplanning.pdf). The AAP recommends the development of a written disaster plan for all practice settings. Additional information is available at www.aap.org/disasters.

IIVs

IIVs for intramuscular injection are shipped and stored at 2°C to 8°C (36°F–46°F); vaccines that are inadvertently frozen should not be used. These vaccines are administered intramuscularly into the anterolateral thigh of infants and young children and into the deltoid muscle of older children and adults. Given that various IIVs are available, careful attention should be used to ensure that each product is used for its approved age indication, dosing, and volume of administration (Table 2). A 0.5-mL unit dose of any IIV should not be split into 2 separate 0.25-mL doses. If a lower dose than recommended is inadvertently administered to a child 36 months or older (eg, 0.25 mL), an additional 0.25-mL dose should be administered to provide a full dose of 0.5 mL as soon as possible. The total number of full doses appropriate for age should be administered. If a child is inadvertently vaccinated with a formulation approved for adults, the dose should be counted as valid.

LAIV

The cold-adapted, temperature-sensitive LAIV4 formulation currently licensed in the United States is shipped and stored at 2°C to 8°C (35°F–46°F) and administered intranasally in a prefilled, single-use sprayer containing 0.2 mL of vaccine. A removable dose-divider clip is attached to the sprayer to facilitate administration of 0.1 mL separately into each nostril. If the child sneezes immediately after administration, the dose should not be repeated.

VACCINE DOSING RECOMMENDATIONS

The number of seasonal influenza vaccine doses recommended for children during the 2019–2020 influenza season depends on the child's age at the time of the first administered dose and vaccine history. The recommendations are unchanged from previous years, as shown in Fig 1.

1. Influenza vaccines are not licensed for administration to infants younger than 6 months and should not be used in this age group.
2. Children 9 years and older need only 1 dose, regardless of previous vaccination history.
3. Children 6 months through 8 years of age:
   a. Need 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2019. The interval between the 2 doses should be at least 4 weeks. Two

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doses should be administered to children who receive their first dose before their ninth birthday, even when they turn 9 years old during the same season.

b. Require only 1 dose if they have previously received 2 or more total doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2019. The 2 previous doses do not need to have been received during the same influenza season or consecutive influenza seasons.

TIMING OF VACCINATION AND DURATION OF PROTECTION

Although peak influenza activity in the United States tends to occur from January through March, influenza can circulate from early fall (October) to late spring (May), with 1 or more disease peaks. Predicting the onset and duration or the severity of the influenza season is impossible. It is also challenging to balance public health strategies needed to achieve high vaccination coverage with achieving optimal individual immunity for protection against influenza at the peak of seasonal activity, knowing that the duration of immunity after vaccination can wane over time. Initiation of influenza vaccination before influenza is circulating in the community and continuing to vaccinate throughout the influenza season are important components of an effective influenza vaccination strategy.

Complete influenza vaccination by the end of October is recommended by the CDC and AAP. Children who need 2 doses of vaccine should receive their first dose as soon as possible when the vaccine becomes available to allow sufficient time for receipt of the second dose ≥4 weeks after the first before the onset of the influenza season. Children who require only 1 dose of influenza vaccine should also ideally be vaccinated by end of October; however, recent data (mostly in adults) suggest that early vaccination (July or August) might be associated with suboptimal immunity before the end of the influenza season.

Although the evidence is limited that waning immunity from early administration of the vaccine increases the risk of infection in children, authors of recent reports raise the possibility that early vaccination might contribute to reduced protection later in the influenza season.[46–55] These observational studies and a post hoc analysis from a randomized controlled trial (RCT) were reviewed by the ACIP influenza working group and are summarized in the CDC recommendations for 2019–2020 influenza prevention.[1] In these studies, VE decreased within a single influenza season, and this decrease was correlated with increasing time after vaccination. However, this decay in VE was not consistent across different age groups and varied by season and virus subtypes. In some studies, waning VE was more evident among older adults and younger children,[47,49] and with influenza A(H3N2) viruses more than influenza A(H1N1) or B viruses.[48,51,53] A multiseason analysis from the US Influenza VE Network found that VE declined by approximately 7% per month for influenza A(H3N2) and influenza B and by 6% to 11% per month for influenza A(H1N1)pdm09 in individuals 9 years and older.[46] VE remained greater than 0 for at least 5 to 6 months after vaccination. A more recent study including children older than 2 years of age also found evidence of declining VE with an odds ratio increasing approximately 16% with each additional 28 days from vaccine administration.[52] Another study evaluating VE from the 2011–2012 through the 2013–2014 seasons demonstrated 54% to 67% protection from 0 to 180 days after vaccination.[50] Finally, a multiseason study in Europe from 2011–2012 through 2014–2015 revealed a steady decline in VE down to 0% protection by 111 days after vaccination.[48,53]

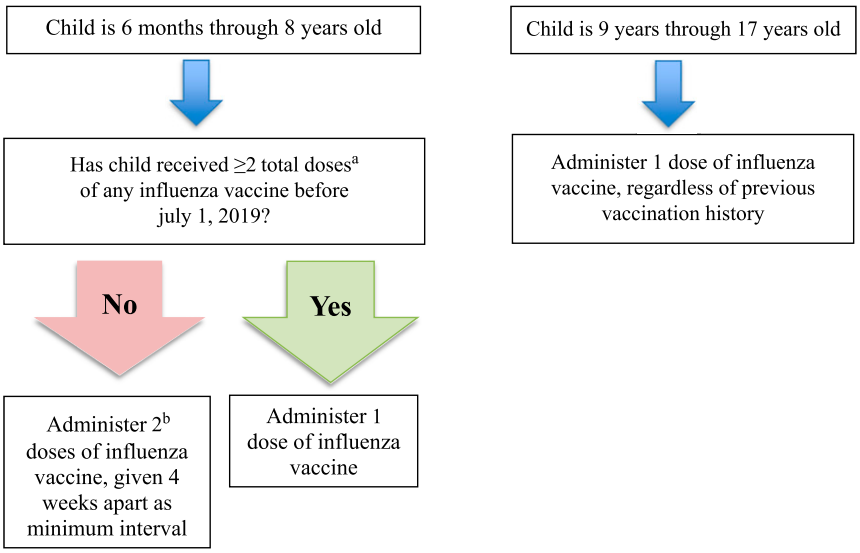

FIGURE 1
Number of 2019–2020 seasonal influenza vaccine doses for children based on age and previous vaccination history and recommendations for prevention and control of influenza in children, 2019–2020. [a] The 2 doses need not have been received during the same season or consecutive seasons. [b] Administer 2 doses based on age at receipt of the first dose of influenza vaccine during the season. Children who receive the first dose before their ninth birthday should receive 2 doses, even if they turn 9 years old during the same season.

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Further evaluation is needed before any policy change in timing of influenza administration is made. An early onset of the influenza season is a concern when considering delaying vaccination. Until there are definitive data that determine if waning immunity influences VE in children, administration of influenza vaccine should not be delayed to a later date because this increases the likelihood of missing influenza vaccination altogether.[56,57] Providers may continue to offer the vaccine until June 30 of each year when the seasonal influenza vaccine expires because the duration of influenza circulation is unpredictable. Although influenza activity in the United States is typically low during the summer, influenza cases and outbreaks can occur, particularly among international travelers, who may be exposed to influenza year-round, depending on the destination.

VACCINE IMPLEMENTATION

The AAP Partnership for Policy Implementation has developed a series of definitions using accepted health information technology standards to assist in the implementation of vaccine recommendations in computer systems and quality measurement efforts. This document is available at www2.aap.org/informatics/PPI.html. In addition, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at www.aapredbook.org/implementation.

HCP, influenza campaign organizers, and public health agencies are encouraged to collaborate to develop improved strategies for planning, distribution, communication, and administration of vaccines.

- Plan to make influenza vaccine easily accessible for all children. Examples include sending alerts to families that the vaccine is available (eg, e-mails, texts, letters, patient portals, practice-specific websites or social media platforms); creating walk-in influenza vaccination clinics; extending hours beyond routine times during peak vaccination periods; administering the influenza vaccine during both well-child examinations and sick visits as well as in hospitalized patients, especially those at high risk of influenza complications, before hospital discharge (unless medically contraindicated); implementing standing orders for influenza vaccination; considering how to immunize parents, adult caregivers, and siblings (see risk management guidance associated with adult immunizations at http://pediatrics.aappublications.org/content/129/1/e247) at the same time as children; and working with other institutions (eg, schools, child care programs, local public health departments, and religious organizations) or alternative care sites, such as pharmacies and hospital emergency departments, to expand venues for administering vaccine. If a child receives influenza vaccine outside of his or her medical home, such as at a pharmacy, retail-based clinic, or another practice setting, appropriate documentation of vaccination should be provided to the patient to be shared with his or her medical home and entered into the state or regional immunization information system (ie, registry).
- Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, are necessary to prioritize distribution appropriately to the primary care office setting and patient-centered medical home before other venues, especially when vaccine supplies are delayed or limited. Similar efforts should be made to mitigate the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children program.
- Population health can benefit from pediatricians' discussions about vaccine safety and effectiveness. Pediatricians and their office staff can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children and emphasizing when a second dose of vaccine is indicated. The AAP and CDC have created communication resources to convey these important messages and to help the public understand influenza recommendations. Resources will be available on *Red Book Online* (https://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=influenza-resources).
- The AAP supports mandatory influenza vaccination programs for all HCP in all settings, including outpatient settings.[58] Optimal prevention of influenza in the health care setting depends on the vaccination of at least 90% of HCP, which is consistent with the national Healthy People 2020 target for annual influenza vaccination among HCP. Early-season 2018–2019 vaccine coverage among HCP was 67.6%. Influenza vaccination programs for HCP benefit the health of employees, their patients, and members of the community, especially because HCP frequently come into contact with patients at high risk of influenza illness in their clinical settings. Mandatory influenza immunization for all HCP is considered to be ethical, just, and necessary to improve patient safety. For the prevention and control of influenza, HCP must prioritize the health and safety of their patients, honor the requirement of causing no harm, and act as role models for both their patients and colleagues by receiving influenza vaccination annually.

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INFLUENZA VACCINE COVERAGE

Although national influenza vaccination coverage among children has not declined in the past 3 seasons, overall vaccination coverage remains suboptimal. Additional options for vaccination of children may provide a means to improve coverage, particularly in pharmacies and child care and school-based settings. Achieving high coverage rates of influenza vaccine in infants and children is a priority to protect them against influenza disease and its complications.

Children's likelihood of being immunized according to recommendations appears to be associated with the immunization practices of their parents.[59–63] Authors of 1 study found that children were 2.77 times (95% CI, 2.74 to 2.79) more likely to be immunized against seasonal influenza if their parents were immunized.[33] When parents who were previously not immunized had received immunization for seasonal influenza, their children were 5.44 times (95% CI, 5.35 to 5.53) more likely to receive influenza vaccine.

Pediatric offices may choose to serve as a venue for providing influenza vaccination for parents and other care providers of children if the practice is acceptable to both pediatricians and the adults who are to be vaccinated. Medical liability issues and medical record documentation requirements need to be considered before a pediatrician begins immunizing adults (see risk management guidance associated with adult immunizations at http://pediatrics.aappublications.org/content/129/1/e247). Pediatric practices should be aware of payment implications, including nonpayment or having the parent inappropriately attributed by a payer as a patient of the pediatrician's office. The AAP supports efforts to overcome these payment barriers with insurance payers to maximize influenza immunization rates. To avoid errors in claims processing and payment and in the exchange of immunization data, pediatricians are reminded that parents should have their own basic medical record in which their influenza vaccination should be documented. Adults should be encouraged to have a medical home and communicate their vaccination status to their primary care provider. Offering adult vaccinations in the pediatric practice setting should not undermine the adult medical home model. Vaccination of close contacts of children at high risk of influenza-related complications (Table 1) is intended to reduce children's risk of exposure to influenza (ie, "cocooning"). The practice of cocooning also may help protect infants younger than 6 months who are too young to be immunized with influenza vaccine.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (influenza update at 1-800-232-4636) or at www.cdc.gov/flu/index.htm. Although current influenza season data on circulating strains do not necessarily predict which and in what proportion strains will circulate in the subsequent season, it is instructive to be aware of 2018–2019 influenza surveillance data and use them as a guide to empirical therapy until current seasonal data are available from the CDC. Information is posted weekly on the CDC Web site (www.cdc.gov/flu/weekly/fluactivitysurv.htm). The AAP offers "What's the Latest with the Flu" (https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Pages/What's-the-Latest-with-the-Flu.aspx) messages to highlight those details most relevant for AAP members and child care providers on a monthly basis during influenza season.

INFLUENZA VACCINATION RECOMMENDATIONS

1. The AAP recommends annual influenza vaccination for everyone 6 months and older, including children and adolescents, during the 2019–2020 influenza season.
2. For the 2019–2020 season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. IIV and LAIV are options for children for whom these vaccines are appropriate. This recommendation is based on review of current available data on LAIV and IIV VE. The AAP will continue to review VE data as they become available and update these recommendations if necessary.
3. The AAP does not have a preference for any influenza vaccine product over another for children who have no contraindication to influenza vaccination and for whom more than 1 licensed product appropriate for age and health status is available. Pediatricians should administer whichever formulation is available in their communities to achieve the highest possible coverage this influenza season.
4. Children 6 through 35 months of age may receive either a 0.25- or 0.5-mL dose of the licensed, age-appropriate IIVs available this season. No product or formulation is preferred over another for this age group. Children 36 months (3 years) and older should receive a 0.5-mL dose of any available, licensed, age-appropriate inactivated vaccine.
5. The number of seasonal influenza vaccine doses recommended to

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be administered to children in the 2019–2020 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 1).

6. Children 6 months through 8 years of age who are receiving the influenza vaccine for the first time or who have received only 1 dose before July 1, 2019, should receive 2 doses of influenza vaccine ideally by the end of October, and vaccines should be offered as soon as they become available. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive the vaccination ideally by the end of October.
7. Efforts should be made to ensure vaccination for children in high-risk groups (Table 1) and their contacts unless contraindicated.
8. Product-specific contraindications must be considered when selecting the type of vaccine to administer. Children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.
9. Children with egg allergy can receive influenza vaccine without any additional precautions beyond those recommended for all vaccines.
10. Pregnant women may receive IIV at any time during pregnancy to protect themselves and their infants who benefit from the transplacental transfer of antibodies. Postpartum women who did not receive vaccination during pregnancy should be encouraged to receive influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants.
11. The AAP supports mandatory vaccination of HCP as a crucial element in preventing influenza and reducing health care–associated influenza infections because HCP often care for individuals at high risk for influenza-related complications.

INFLUENZA ANTIVIRALS

Antiviral agents available for both influenza treatment and chemoprophylaxis in children of all ages can be found in Table 3 (including doses for preterm infants that have not been evaluated by the FDA) and on the CDC Web site (www.cdc.gov/flu/professionals/antivirals/index.htm). These include the neuraminidase inhibitors (NAIs) (oseltamivir, zanamivir, peramivir) and a selective inhibitor of influenza cap-dependent endonuclease (baloxavir),[64] all of which have activity against influenza A and B viruses.

Oral oseltamivir remains the antiviral drug of choice for the management of illness caused by influenza virus infections. Although more difficult to administer, inhaled zanamivir (Relenza) is an equally acceptable alternative for patients who do not have chronic respiratory disease. Options are limited for children who cannot absorb orally or enterally administered oseltamivir or tolerate inhaled zanamivir. Intravenous (IV) peramivir (Rapivab), a third NAI, was approved in September 2017 as treatment of acute uncomplicated influenza in nonhospitalized children 2 years and older who have been symptomatic for no more than 2 days. The efficacy of peramivir in patients with serious influenza requiring hospitalization has not been established.[65] A prospective, open-label pediatric clinical trial was conducted to investigate pharmacokinetics and the clinical and virological response to treatment with IV zanamivir for children aged 6 months or older with severe influenza and who could not tolerate oral or inhaled NAIs.[66] IV zanamivir is not approved in the United States. IV zanamivir for compassionate use has not been available in the United States since the 2017–2018 season.[67] The FDA licensed baloxavir marboxil in 2018 for the early treatment of uncomplicated influenza in outpatients 12 years and older who have been ill for no more than 2 days. This antiviral agent for influenza works by a different mechanism than NAIs and requires only a single oral dose for treatment of uncomplicated influenza.[68] A clinical trial of baloxavir treatment of influenza in hospitalized patients is ongoing (https://clinicaltrials.gov/ct2/show/NCT03684044?cond=baloxavir&rank=6).

INFLUENZA TREATMENT

In RCTs conducted to date to evaluate the efficacy of influenza antiviral medications among outpatients with uncomplicated influenza, researchers have found that timely treatment can reduce the duration of influenza symptoms and fever, as well as the risk of certain complications, including hospitalization and death in pediatric and adult populations.[30,31,41,42,45,69,70] The number of published RCTs in children is limited, and interpretation of the results of these studies needs to take into consideration the size of the study (the number of events might not be sufficient to assess specific outcomes in small studies), the variations in the case definition of influenza illness (clinically diagnosed versus laboratory confirmed), the time of treatment administration in relation to the onset of illness, and the child's age and health status as important variables. A Cochrane review of 6 RCTs[2,3,71] involving treatment of 2356 children with clinical influenza,[1,2,72] of whom 1255

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TABLE 3 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis in Children for the 2019–2020 Influenza Season: United States

Medication	Treatment (5 d)	Chemoprophylaxis (10 d)[a]
Oseltamivir[b]		
Adults	75 mg, twice daily	75 mg, once daily
Children ≥12 mo (based on body wt)		
≤15 kg (≤33 lb)	30 mg, twice daily	30 mg, once daily
>15–23 kg (33–51 lb)	45 mg, twice daily	45 mg, once daily
>23–40 kg (>51–88 lb)	60 mg, twice daily	60 mg, once daily
>40 kg (>88 lb)	75 mg, twice daily	75 mg, once daily
Infants 9–11 mo[c]	3.5 mg/kg per dose, twice daily	3.5 mg/kg per dose, once daily
Term infants 0–8 mo[c]	3 mg/kg per dose, twice daily	3 mg/kg per dose, once daily for infants 3–8 mo Not recommended for infants <3 mo old because of limited safety and efficacy data in this age group
Preterm infants[d]		
<38 wk' postmenstrual age	1.0 mg/kg per dose, twice daily	—
38 through 40 wk' postmenstrual age	1.5 mg/kg per dose, twice daily	—
>40 wk' postmenstrual age	3.0 mg/kg per dose, twice daily	—
Zanamivir[e]		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children ≥7 y for treatment ≥5 y for chemoprophylaxis	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Peramivir		
Adults	One 600-mg IV infusion, given over 15–30 min	Not recommended
Children (2–12 y)	One 12 mg/kg dose, up to 600 mg maximum, via IV infusion for 15–30 min	Not recommended
Children (13–17 y)	One 600 mg dose, via IV infusion for 15–30 min	Not recommended
Baloxavir		
People ≥12 y who weigh more than 40 kg	40–80 kg: one 40-mg dose, orally ≥80 kg: one 80-mg dose, orally	Not recommended

Sources: 2018 IDSA Guidelines[65] and https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm. —, not applicable.

[a] CDC recommends for 7 days and 10 days only if part of institutional outbreak (https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm).

[b] Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30-, 45-, and 75-mg capsules and as a powder for oral suspension that is reconstituted to provide a final concentration of 6 mg/mL. For the 6-mg/mL suspension, a 30-mg dose is given with 5 mL of oral suspension, a 45-mg dose is given with 7.5 mL of oral suspension, a 60-mg dose is given with 10 mL of oral suspension, and a 75-mg dose is given with 12.5 mL of oral suspension. If the commercially manufactured oral suspension is not available, a suspension can be compounded by retail pharmacies (final concentration also 6 mg/mL) on the basis of instructions contained in the package label. In patients with renal insufficiency, the dose should be adjusted on the basis of creatinine clearance. For treatment of patients with creatinine clearance 10–30 mL/min: 75 mg, once daily, for 5 d. For chemoprophylaxis of patients with creatinine clearance 10–30 mL/min: 30 mg, once daily, for 10 d after exposure or 75 mg, once every other day, for 10 d after exposure (5 doses). See https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm and IDSA guidelines.[65]

[c] Approved by the FDA for children as young as 2 wk of age. Given preliminary pharmacokinetic data and limited safety data, oseltamivir can be used to treat influenza in both term and preterm infants from birth because benefits of therapy are likely to outweigh possible risks of treatment. Of note, the CDC recommends a 3 mg/kg per dose, twice daily, for all infants <12 mo old; the IDSA guidelines[65] include both AAP and CDC recommendations.

[d] Oseltamivir dosing for preterm infants. The wt-based dosing recommendation for preterm infants is lower than for term infants. Preterm infants may have lower clearance of oseltamivir because of immature renal function, and doses recommended for term infants may lead to high drug concentrations in this age group. Limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provides the basis for dosing preterm infants using their postmenstrual age (gestational age + chronologic age). For extremely preterm infants (<28 wk), please consult a pediatric infectious disease physician.

[e] Zanamivir is administered by inhalation using a proprietary "Diskhaler" device distributed together with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered using nebulizers, ventilators, or other devices typically used for administering medications in aerosolized solutions. Zanamivir is not recommended for people with chronic respiratory diseases, such as asthma or chronic obstructive pulmonary disease, which increase the risk of bronchospasm.

had laboratory-confirmed influenza, revealed that in children with laboratory-confirmed influenza, oral oseltamivir and inhaled zanamivir reduced the median duration of illness by 36 hours (26%; $P < .001$) and 1.3 days (24%, $P < .001$), respectively.[68] Among the studies reviewed, 1 trial of oseltamivir in children with asthma who had laboratory-confirmed influenza revealed only a nonsignificant reduction in illness duration (10.4 hours; 8%; $P = .542$). Oseltamivir significantly reduced acute otitis media in children 1 through 5 years of age with laboratory-confirmed influenza (risk difference, −0.14; 95% CI, −0.24 to −0.04).[73] Authors of another Cochrane review of RCTs in adults and children, which included 20 oseltamivir (9623 participants) and 26 zanamivir trials (14 628 participants),[74] found no effect of oseltamivir in reducing the duration of illness in asthmatic children, but in otherwise healthy

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children, there was a reduction by a mean difference of 29 hours (95% CI, 12 to 47 hours; P = .001). No significant effect was observed with zanamivir. Regarding complications, the authors of this review did not find a significant effect of NAIs on reducing hospitalizations, pneumonia, bronchitis, otitis media, or sinusitis in children.[75] More recently, a meta-analysis of 5 new RCTs that included 1598 children with laboratory-confirmed influenza revealed that treatment with oseltamivir significantly reduced the duration of illness in this population by 17.6 hours (95% CI, −34.7 to −0.62 hours), and when children with asthma were excluded, this difference was larger (−29.9 hours; 95% CI, −53.9 to −5.8 hours). The risk of otitis media was 34% lower in this group as well.[31] Overall, efficacy outcomes are best demonstrated in patients with laboratory-confirmed influenza. All these studies confirmed vomiting as an occasional side effect of oseltamivir, occurring in approximately 5% of treated patients. The balance between benefits and harms should be considered when making decisions about the use of NAIs for either treatment or chemoprophylaxis of influenza.

Although prospective comparative studies used to determine the efficacy of influenza antiviral medications in hospitalized patients or pediatric patients with comorbidities have not been conducted, and prospectively collected data used to determine the role of antiviral agents in treating severe influenza are limited, on the basis of information obtained from retrospective observational studies and meta-analyses conducted to date in both adults and children, most experts support the use of antiviral medications as soon as possible to treat pediatric patients with severe influenza, including hospitalized patients.[76–79] In an observational epidemiological study conducted in adult patients hospitalized with severe laboratory-confirmed influenza in Spain spanning 6 influenza seasons (2010–2016), authors evaluated the effectiveness of NAIs, concluding that when started early after the onset of symptoms (≤48 hours or ≤5 days), NAI treatment was associated with a reduction in influenza-associated deaths (adjusted odds ratio, 0.37; 95% CI, 0.22 to 0.63l, and adjusted odds ratio, 0.50; 95% CI, 0.32 to 0.79, respectively).[80,81] However, treatment initiation more than 5 days after the onset of influenza symptoms was not associated with reduction in mortality in hospitalized adults.

Importantly, and despite limited evidence for efficacy, treatment with oseltamivir for children with serious, complicated, or progressive disease presumptively or definitively caused by influenza, irrespective of influenza vaccination status (the circulating strains may not be well matched with vaccine strains) or whether illness began greater than 48 hours before admission, continues to be recommended by the AAP, CDC, Infectious Diseases Society of America (IDSA),[65] and Pediatric Infectious Diseases Society (PIDS). Earlier treatment provides better clinical responses. However, treatment after 48 hours of symptoms in adults and children with moderate-to-severe disease or with progressive disease has been shown to provide some benefit and should be offered. No benefit exists for double-dose NAI therapy, compared to standard-dose therapy, on the basis of published data from a randomized prospective trial enrolling 75% of subjects younger than 15 years.[1]

Children younger than 2 years are at an increased risk of hospitalization and complications attributable to influenza. The FDA has approved oseltamivir for treatment of children as young as 2 weeks. Given preliminary pharmacokinetic data and limited safety data, the CDC and AAP support the use of oseltamivir to treat influenza in both term and preterm infants from birth because the benefits of therapy of neonatal influenza are likely to outweigh the possible risks of treatment.

Oseltamivir is available in capsule and oral suspension formulations. The available capsule doses are 30, 45, and 75 mg, and the commercially manufactured liquid formulation has a concentration of 6 mg/mL in a 60-mL bottle. If the commercially manufactured oral suspension is not available, the capsule may be opened and the contents mixed with simple syrup or Ora-Sweet SF (sugar free) by retail pharmacies to a final concentration of 6 mg/mL.

In adverse event data collected systematically in prospective trials, vomiting was the only adverse effect reported more often with oseltamivir compared to placebo when studied in children 1 through 12 years of age (ie, 15% of treated children vs 9% receiving placebo). In addition, after reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, authors of a review of controlled clinical trial data and ongoing surveillance have failed to establish a link between this drug and neurologic or psychiatric events.[66,82]

Clinical judgment (based on underlying conditions, disease severity, time since symptom onset, and local influenza activity) is an important factor in treatment decisions for pediatric patients who present with influenzalike illness. Antiviral treatment should be started as soon as possible after illness onset and should not be delayed while waiting for a definitive influenza test result because early therapy provides the best outcomes. Influenza diagnostic tests vary by method, availability, processing time, sensitivity, and cost (Table 4), all of which should be considered in making the best clinical decision. Positive and negative predictive values of influenza test results are

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influenced by the level of influenza activity in the population being tested, the characteristics of a test compared to a gold standard, pretest probability, whether the influenza virus is actively replicating in the person, proper collection and transport of specimens, and proper test procedures. Testing should be performed when timely results will be available to influence clinical management or infection control measures. Although decisions on treatment and infection control can be made on the basis of positive rapid antigen test results, negative results should not always be used in a similar fashion because of the suboptimal sensitivity and potential for false-negative results. Positive results of rapid influenza tests are helpful, because they may reduce additional testing to identify the cause of the child's influenzalike illness and promote appropriate antimicrobial stewardship. Available FDA-approved rapid molecular assays are highly sensitive and specific in diagnostic tests performed in <20 minutes using RNA detection. These and other FDA-approved influenza molecular assays or reverse transcription polymerase chain reaction (RT-PCR) test confirmation are preferred in hospitalized patients because they are more sensitive compared to antigen detection. Early detection, prompt antiviral treatment, and infection control interventions can lead to improved individual patient outcomes and allow for effective cohorting and disease containment.

People with suspected influenza who are at higher risk of influenza complications should be offered treatment with antiviral medications (Table 1). Efforts should be made to minimize treatment of patients who are not infected with influenza. Otherwise healthy children who have suspected influenza with an uncomplicated presentation should be considered for antiviral medication, particularly if they are in contact with other children who either are younger than 6 months (because they are not able to receive influenza vaccine) or have high-risk conditions (including young age) that predispose them to complications of influenza, when influenza viruses are known to be circulating in the community. If there is a local shortage of antiviral medications, local public health authorities should be consulted to provide additional guidance about testing and treatment. In previous years, local shortages of oseltamivir suspension have occurred because of uneven drug distribution, although national shortages have not occurred since 2009, particularly given the availability of the capsule formulation that can be made into a suspension for young children if needed (Table 3).

INFLUENZA CHEMOPROPHYLAXIS

Randomized placebo-controlled studies revealed that oral oseltamivir and inhaled zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza.[1,41] There are no data on IV peramivir or oral baloxavir for chemoprophylaxis. During the 2009 pandemic, the emergence of oseltamivir resistance was noted rarely among people receiving postexposure chemoprophylaxis, highlighting the need to be aware of the possibility of emerging resistance in this population. Decisions on whether to administer antiviral chemoprophylaxis should take into

TABLE 4 Comparison of Types of Influenza Diagnostic Tests

Testing Category	Method	Influenza Viruses Detected	Distinguishes Influenza A Virus Subtypes	Time to Results	Performance
Rapid molecular assay	Nucleic acid amplification	Influenza A or B viral RNA	No	15–30 min	High sensitivity; high specificity
Rapid influenza diagnostic test	Antigen detection	Influenza A or B virus antigens	No	10–15 min	Low-to-moderate sensitivity (higher with analyzer devise); high specificity
Direct and indirect immunofluorescence assays	Antigen detection	Influenza A or B virus antigens	No	1–4 h	Moderate sensitivity; high specificity
Molecular assays (including RT-PCR)	Nucleic acid amplification	Influenza A or B viral RNA	Yes, if subtype primers are used	1–8 h	High sensitivity; high specificity
Multiplex molecular assays	Nucleic acid amplification	Influenza A or B viral RNA, other viral or bacterial targets (RNA or DNA)	Yes, if subtype primers are used	1–2 h	High sensitivity; high specificity
Rapid cell culture (shell vial and cell mixtures)	Virus isolation	Influenza A or B virus	Yes	1–3 d	High sensitivity; high specificity
Viral culture (tissue cell culture)	Virus isolation	Influenza A or B virus	Yes	3–10 d	High sensitivity; high specificity

Negative test results may not rule out influenza. Respiratory tract specimens should be collected as close to illness onset as possible for testing. Clinicians should consult the manufacturer's package insert for the specific test for the approved respiratory specimen(s). Specificities are generally high (>95%) for all tests compared to RT-PCR. FDA-cleared rapid influenza diagnostic tests are waived by the Clinical Laboratory Improvement Amendments of 1988; most FDA-cleared rapid influenza molecular assays are waived by the Clinical Laboratory Improvement Amendments of 1988, depending on the specimen. Adapted from Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. *Clin Infect Dis*. 2019;68(6):e13.

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account the exposed person's risk of influenza complications, vaccination status, the type and duration of contact, recommendations from local or public health authorities, and clinical judgment. Optimally, postexposure chemoprophylaxis should only be used when antiviral agents can be started within 48 hours of exposure; the lower once-daily dosing for chemoprophylaxis with oral oseltamivir or inhaled zanamivir should not be used for the treatment of children symptomatic with influenza. Early, full treatment doses (rather than chemoprophylaxis doses) should be used in high-risk symptomatic patients without waiting for laboratory confirmation.

Chemoprophylaxis should not be considered a substitute for vaccination. Influenza vaccine should always be offered before and throughout the influenza season when not contraindicated. Antiviral medications are important adjuncts to influenza vaccination for the control and prevention of influenza disease. Toxicities may be associated with antiviral agents, and indiscriminate use might limit availability. Pediatricians should inform recipients of antiviral chemoprophylaxis that the risk of influenza is lowered but still remains while taking the medication, and susceptibility to influenza returns when the medication is discontinued. Oseltamivir use is not a contraindication to vaccination with IIV, although LAIV effectiveness will be decreased for the child receiving oseltamivir.[66] No data are available on the impact of inhaled zanamivir or oral baloxavir on the effectiveness of LAIV, but it is likely that all antiviral medication will have some impact on effectiveness of LAIV. Among some high-risk people, both vaccination with IIV and antiviral chemoprophylaxis may be considered. Updates will be available at www.aapredbook.org/flu and www.cdc.gov/flu/professionals/antivirals/index.htm.

ANTIVIRAL RESISTANCE

Antiviral resistance to any drug can emerge, necessitating continuous population-based assessment that is conducted by the CDC. During the 2018–2019 season, >99% of influenza A(/H1N1)pdm09 viruses tested were susceptible to oseltamivir and peramivir, and all of the tested influenza virus strains were susceptible to zanamivir. All tested influenza A(H3N2) viruses were susceptible to oseltamivir, zanamivir, and peramivir. Influenza B virus strains were all susceptible to oseltamivir and zanamivir, and >99% were susceptible to peramivir. Decreased susceptibility to baloxavir has been reported in Japan where use has been more common,[83–85] and surveillance for resistance among circulating influenza viruses is ongoing in the United States.[83,86] In contrast, high levels of resistance to amantadine and rimantadine persist among the influenza A viruses currently circulating. Adamantane medications are not recommended for use against influenza unless resistance patterns change.[1]

Recent viral surveillance and resistance data from the CDC and WHO indicate that the majority of currently circulating influenza viruses likely to cause influenza in North America during the 2019–2020 season continue to be susceptible to oseltamivir, zanamivir, peramivir, and baloxavir.[1] If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, recommendations for alternative treatment, such as use of IV zanamivir,[87,88] will be available from the CDC and AAP. Resistance characteristics can change for an individual child over the duration of a treatment course, especially in those who are severely immunocompromised and may receive extended courses of antiviral medications because of prolonged viral shedding. Up-to-date information on current recommendations and therapeutic options can be found on the AAP Web site (www.aap.org or www.aapredbook.org/flu), through state-specific AAP chapter websites, or on the CDC Web site (www.cdc.gov/flu/).

INFLUENZA ANTIVIRALS RECOMMENDATIONS

Treatment recommendations for antiviral medications for the 2019–2020 season are applicable to infants and children with suspected influenza when influenza viruses are known to be circulating in the community or when infants or children are tested and confirmed to have influenza. Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza virus strains by the CDC may lead to new guidance. Oseltamivir (oral), zanamivir (inhaled), peramivir (IV), and baloxavir (oral) are FDA approved for treatment of uncomplicated influenza virus infection in pediatric outpatients; published data exist to support the use of oseltamivir (oral) for hospitalized children and children at high risk. For more serious influenza virus infections, particularly in immune compromised children, seeking the advice of an infectious diseases specialist is suggested.

ANTIVIRAL TREATMENT RECOMMENDATIONS

Regardless of influenza vaccination status, antiviral treatment should be offered as early as possible to the following individuals:

- any hospitalized child with suspected or confirmed influenza disease, regardless of the duration of symptoms;
- any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to

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influenza, regardless of the duration of symptoms; and

- children with influenza virus infection of any severity who are at high risk of complications of influenza, as listed in Table 1, regardless of the duration of symptoms.

Antiviral treatment may be considered for the following individuals:

- any previously healthy, symptomatic outpatient not at high risk for influenza complications who is diagnosed with confirmed or suspected influenza, on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset; and
- children with suspected or confirmed influenza disease whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them to complications of influenza as listed in Table 1.

Efforts should be made to minimize treatment of patients who are not infected with influenza viruses.

ANTIVIRAL CHEMOPROPHYLAXIS RECOMMENDATIONS

Although vaccination is the preferred approach to prevention of infection, chemoprophylaxis during an influenza season, as defined by the CDC (https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm), is recommended in the following situations:

- for children at high risk of complications from influenza for whom influenza vaccine is contraindicated;
- for children at high risk during the 2 weeks after IIV influenza vaccination, before optimal immunity is achieved (prophylaxis after LAIV may decrease vaccine efficacy);
- for family members or HCP who are unvaccinated and are likely to have ongoing, close exposure to the following:
  - unvaccinated children at high risk; or
  - unvaccinated infants and toddlers who are younger than 24 months;
- for control of influenza outbreaks for unvaccinated staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities);
- as a supplement to IIV vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses after influenza vaccination;
- as postexposure antiviral chemoprophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza; and
- for children at high risk of complications and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not well matched by seasonal influenza vaccine virus strains on the basis of current data from the CDC and state or local health departments.

These recommendations apply to routine circumstances, but it should be noted that guidance may change on the basis of updated recommendations from the CDC in concert with antiviral availability, local resources, clinical judgment, recommendations from local or public health authorities, risk of influenza complications, type and duration of exposure contact, and change in epidemiology (resistance, antigenic shift) or severity of influenza. Chemoprophylaxis is not routinely recommended for infants younger than 3 months given limited safety and efficacy data in this age group.

FUTURE DIRECTIONS

Safety and effectiveness data for influenza vaccines used during the 2019–2020 season will be analyzed as they become available and reported by the CDC as they are each season.[89] Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccine, especially for at-risk populations, is important. The duration of protection and the potential role of previous influenza vaccination on overall VE and VE by vaccine formulation, virus strain, timing of vaccination, and subject age and health status in preventing outpatient medical visits, hospitalizations, and deaths continue to be evaluated. Research to better understand how to educate parents about influenza symptoms and how to recognize when to seek medical attention would be informative. Additionally, with limited data on the use of antiviral agents in hospitalized children and in children with underlying medical conditions, prospective clinical trials to inform optimal timing and efficacy of antiviral treatment and in these populations are warranted.

There is also a need for more systematic health services research on influenza vaccine uptake and refusal as well as identification of methods to enhance uptake. Further investigation is needed about vaccine acceptance and hesitancy and methods to overcome parental concerns and improve coverage. This may include evaluating the strategy of offering to immunize parents and adult child care providers in the pediatric office setting and understanding the level of family contact satisfaction with this approach; how practices handle the logistic, liability, legal, and financial barriers that limit or complicate this service; and most importantly, how this practice may affect disease rates in children and adults. Furthermore, ongoing efforts should include broader implementation and

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evaluation of mandatory HCP vaccination programs in both inpatient and outpatient settings.

Efforts should be made to create adequate outreach and infrastructure to facilitate the optimal distribution of vaccine so that more people are immunized. Pediatricians should consider becoming more involved in pandemic preparedness and disaster planning efforts (especially in collaboration with schools and child care programs). A bidirectional partner dialogue between pediatricians and public health decision makers assists efforts to address children's issues during the initial state, regional, and local plan development stages. Pandemic influenza preparedness of directors of child care centers also needs to improve. Additional information can be found at www.aap.org/disasters/resourcekit and https://pediatrics.aappublications.org/content/pediatrics/early/2017/05/11/peds.2016-3690.full.pdf.

Pandemic influenza preparedness is of particular interest because of the increase in the number of human infections with Asian H7N9 virus reported in China (updates available at https://www.cdc.gov/flu/avianflu/h7n9-virus.htm). All cases of H7N0 virus infection identified outside of mainland China (eg, Taiwan, Malaysia, Canada) had exposure and were infected in China and were identified outside China after becoming ill. Although the current risk to the public's health from this virus is low, Asian H7N9 virus is among the nonhuman influenza viruses that are most concerning to public health officials because of their pandemic potential and ability to cause severe disease in infected humans. The current risk to public health from the virus remains low; however, the CDC is monitoring the situation carefully and taking routine preparedness measures, including testing candidate vaccines.

With the increased demand for vaccination during each influenza season, the AAP and CDC recommend vaccine administration at any visit to the medical home during influenza season when it is not contraindicated, at specially arranged vaccine-only sessions, and through cooperation with community sites, schools, and Head Start and child care facilities to provide influenza vaccine. It is important that the annual delivery of influenza vaccine to primary care medical homes should be timely to avoid missed opportunities. If alternate venues, including pharmacies and other retail-based clinics, are used for vaccination, a system of patient record transfer is beneficial in maintaining the accuracy of immunization records. Immunization information systems should be used whenever available and prioritized to document influenza vaccination. Two-dimensional barcodes have been used to facilitate more efficient and accurate documentation of vaccine administration with limited experience to date. Additional information concerning current vaccines shipped with two-dimensional barcodes can be found at www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/.

Access to care issues, lack of immunization records, and questions regarding who can provide consent may be addressed by linking children (eg, those in foster care or a juvenile justice system or refugee, immigrant, or homeless children) with a medical home, using all health care encounters as vaccination opportunities and more consistently using immunization registry data.

Development efforts continue for a universal influenza vaccine that induces broader protection and eliminates the need for annual vaccination. In addition, understanding the establishment of immunity against influenza in early life and developing a safe, immunogenic vaccine for infants younger than 6 months are essential. Studies on the effectiveness and safety of influenza vaccines containing adjuvants that enhance immune responses to influenza vaccines or that use novel routes of administration (such as microneedle patch) are ongoing.[90] Efforts to improve the vaccine development process to allow for a shorter interval between identification of vaccine strains and vaccine production continue. Many antiviral drugs are in various development phases, given the need to improve options for the treatment and chemoprophylaxis of influenza. Finally, pediatricians should remain informed during the influenza season by following the CDC influenza page (www.cdc/gov/flu) and the AAP *Red Book Online* Influenza Resource Page (www.aapredbook.org/flu).

SUMMARY OF RECOMMENDATIONS

1. The AAP recommends annual influenza vaccination for everyone 6 months and older, including children and adolescents, during the 2019–2020 influenza season.
2. For the 2019–2020 season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. IIV and LAIV are options for children for whom these vaccines are appropriate. This recommendation is based on review of current available data on LAIV and IIV VE. The AAP will continue to review VE data as they become available and update these recommendations if necessary.
3. The AAP does not have a preference for any influenza vaccine product over another for children who have no

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contraindication to influenza vaccination and for whom more than one licensed product appropriate for age and health status is available. Pediatricians should administer whichever formulation is available in their communities to achieve the highest possible coverage this influenza season.

4. Children 6 through 35 months of age may receive either a 0.25- or 0.5-mL dose of the licensed, age-appropriate IIVs available this season. No product or formulation is preferred over another for this age group. Children 36 months (3 years) and older should receive a 0.5-mL dose of any available, licensed, age-appropriate inactivated vaccine.
5. The number of seasonal influenza vaccine doses recommended to be administered to children in the 2019–2020 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 1).
6. Children 6 months through 8 years of age who are receiving an influenza vaccine for the first time or who have received only 1 dose before July 1, 2019, should receive 2 doses of influenza vaccine ideally by the end of October, and vaccines should be offered as soon as they become available. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination ideally by the end of October.
7. Efforts should be made to ensure vaccination for children in high-risk groups (Table 1) and their contacts, unless contraindicated.
8. Product-specific contraindications must be considered when selecting the type of vaccine to administer. Children who have had an allergic reaction after a previous dose of any influenza vaccine should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.
9. Children with egg allergy can receive influenza vaccine without any additional precautions beyond those recommended for all vaccines.
10. Pregnant women may receive an IIV at any time during pregnancy to protect themselves and their infants who benefit from the transplacental transfer of antibodies. Postpartum women who did not receive vaccination during pregnancy should be encouraged to receive an influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants.
11. The AAP supports mandatory vaccination of HCP as a crucial element in preventing influenza and reducing health care–associated influenza infections because HCP often care for individuals at high risk for influenza-related complications.
12. Antiviral medications are important in the control of influenza but are not a substitute for influenza vaccination. Pediatricians should promptly identify their patients suspected of having influenza infection for timely initiation of antiviral treatment, when indicated and based on shared decision-making between the pediatrician and child's caregiver, to reduce morbidity and mortality. Although the best results are observed when the child is treated within 48 hours of symptom onset, antiviral therapy should still be considered beyond 48 hours of symptom onset in children with severe disease or those at high risk of complications.
13. Antiviral treatment should be offered as early as possible to the following individuals, regardless of influenza vaccination status:
    - any hospitalized child with suspected or confirmed influenza disease, regardless of the duration of symptoms;
    - any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to influenza, regardless of the duration of symptoms; and
    - children with influenza infection of any severity who are at high risk of complications of influenza infection (Table 1), regardless of the duration of symptoms.
14. Treatment may be considered for the following individuals:
    - any previously healthy, symptomatic outpatient not at high risk for influenza complications who is diagnosed with confirmed or suspected influenza, on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset; and
    - children with suspected or confirmed influenza disease whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them to complications of influenza (Table 1).
15. Antiviral chemoprophylaxis is recommended in the following situations:
    - for children at high risk of complications from influenza for whom influenza vaccine is contraindicated.
    - for children at high risk during the 2 weeks after influenza vaccination, before optimal immunity is achieved.
    - for family members or HCP who are unvaccinated and are

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likely to have ongoing, close exposure to the following:

unvaccinated children at high risk; or

unvaccinated infants and toddlers who are younger than 24 months.

- for the control of influenza outbreaks for unvaccinated staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities);
- as a supplement to vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses after influenza vaccination;
- as postexposure antiviral chemoprophylaxis for family members and close contacts of an infected person if those people are at high risk of complications from influenza; and
- for children at high risk of complications and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not well matched by seasonal influenza vaccine virus strains on the basis of current data from the CDC and state or local health departments.

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ACIP: Advisory Committee on Immunization Practices
CDC: Centers for Disease Control and Prevention
CI: confidence interval
FDA: US Food and Drug Administration
GBS: Guillain-Barré syndrome
HA: hemagglutinin
HCP: health care personnel
IDSA: Infectious Diseases Society of America
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
IV: intravenous
LAIV: live attenuated influenza vaccine
LAIV3: trivalent live attenuated influenza vaccine
LAIV4: quadrivalent live attenuated influenza vaccine
NAI: neuraminidase inhibitor
PCV13: 13-valent pneumococcal conjugate vaccine
RCT: randomized controlled trial
RIV4: quadrivalent recombinant influenza vaccine
RT-PCR: reverse transcription polymerase chain reaction
VE: vaccine effectiveness
WHO: World Health Organization

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COMMITTEE ON INFECTIOUS DISEASES

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