



# Recommendations for Prevention and Control of Influenza in Children, 2020–2021

Committee on Infectious Diseases

This statement updates the recommendations of the American Academy of Pediatrics for the routine use of influenza vaccine and antiviral medications in the prevention and treatment of influenza in children during the 2020–2021 season.

The American Academy of Pediatrics (AAP) recommends routine influenza immunization of all children without medical contraindications, starting at 6 months of age. Influenza vaccination is an important intervention to protect vulnerable populations and reduce the burden of respiratory illnesses during the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pandemic. Any licensed, recommended, age-appropriate vaccine available can be administered, without preference for one product or formulation over another. Antiviral treatment of influenza with any licensed, recommended, age-appropriate influenza antiviral medication is recommended for children with suspected or confirmed influenza who are hospitalized, have severe or progressive disease, or have underlying conditions that increase their risk of complications of influenza. Antiviral treatment may be considered for any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom an influenza diagnosis is confirmed or suspected, if treatment can be initiated within 48 hours of illness onset, and for children whose siblings or household contacts either are younger than 6 months or have a high-risk condition that predisposes them to complications of influenza.

## UPDATES FOR THE 2020–2021 INFLUENZA SEASON

1. The composition of the influenza vaccines for 2020–2021 has been updated. The recommended influenza A(H1N1)pdm09 and A(H3N2) components and the influenza B/Victoria component of the vaccine are new for this season. The B/Yamagata component is unchanged from the previous season. All quadrivalent influenza vaccines include these 4 components. The trivalent vaccines do not include influenza B/Yamagata.

## abstract

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2. All pediatric vaccines are quadrivalent. There are no trivalent vaccines available for children.
3. The vaccine formulations available for children 6 through 35 months of age have been updated. Afluria Quadrivalent will be the only vaccine for children 6 through 35 months of age with a dosing volume of 0.25 mL. Fluzone Quadrivalent, which is licensed in a 0.25-mL and a 0.5-mL dosing volume, will likely be available only in a 0.5-mL dosing volume for this age group this season. The dosing volume for the 2 other vaccines available for this age group, Fluarix and FluLaval, is 0.5 mL. The AAP has no preference for one product over another.
4. Children 6 months through 8 years of age who are receiving influenza vaccine for the first time, who have received only 1 dose ever before July 1, 2020, or whose vaccination status is unknown should be offered vaccination as soon as influenza vaccines become available and should receive 2 doses of vaccine, ideally by the end of October. Children needing only 1 dose of influenza vaccine, regardless of age, should also receive vaccination ideally by the end of October.
5. The contraindications for live attenuated influenza vaccine (LAIV) have been updated to harmonize with recommendations of the Advisory Committee on Immunization Practices (ACIP). Although there are no reports of additional safety risks for LAIV in children with immunodeficiencies, anatomic or functional asplenia, cochlear implants, or active cerebrospinal fluid leaks, because the vaccine is a live attenuated product, it is not recommended in these populations.
6. The importance of influenza vaccination during the SARS-CoV-2 pandemic is discussed.

## INTRODUCTION

Children consistently 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 substantial morbidity, including severe or fatal complications from influenza infection.<sup>1</sup> 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.<sup>1</sup> School-aged children bear a large influenza disease burden and are more likely to seek influenza-related medical care compared with healthy adults.<sup>1,2</sup> 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.<sup>1,2</sup> Influenza vaccination is particularly important during the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pandemic to reduce the burden of respiratory illnesses and hospitalizations and preserve the capacity of the health care infrastructure. The American Academy of Pediatrics (AAP) recommends routine influenza vaccination and antiviral agents for the prevention and treatment of influenza in children, respectively.

## SUMMARY OF RECENT INFLUENZA SEASONS IN THE UNITED STATES

### 2017–2018 and 2018–2019 Influenza Seasons

The 2017–2018 influenza season had an important impact in pediatric patients. It was the first classified as a high-severity season for all age groups, with high levels of outpatient clinic and emergency department visits for influenza-like illness, high

rates of influenza-related hospitalization, and high mortality.<sup>3–5</sup> Influenza A (H3N2) predominated early, followed by a second wave of influenza B/Yamagata 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 188 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.<sup>3–5</sup> 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 influenza vaccine during the 2017–2018 season.<sup>3</sup> Influenza vaccine effectiveness (VE) for the 2017–2018 season in children is shown in Table 1.<sup>4</sup>

The 2018–2019 season was of moderate severity, with similar hospitalization rates in children as during the 2017–2018 season (71/100 000 among children 0 through 4 years old and 20.4/100 000 among children 5 through 17 years old), which were higher than those observed in previous seasons from 2013–2014 to 2016–2017.<sup>7</sup> Among 1132 children hospitalized with influenza and for whom data were available, 55% had at least 1 underlying medical condition; the most commonly reported underlying conditions were asthma or reactive airway disease (26%), neurologic disorders (15.6%), and obesity (11.6%).<sup>8</sup> A total of 144 influenza-associated pediatric deaths were reported. The 2017–2018 influenza season was the longest-lasting season reported in the United States in the past decade, with elevated levels of

**TABLE 1** Adjusted Vaccine Effectiveness (VE) in Children in the United States, by Season, as Reported by the Centers for Disease Control and Prevention (CDC), US Influenza Vaccine Effectiveness Network

Influenza Type/Age Group	2017–2018	2018–2019	2019–2020 <sup>a</sup>
	H3N2 and B/Yamagata VE% (95% CI)	H1N1 and H3N2 VE% (95% CI)	B/Victoria and H1N1 VE% (95% CI)
<b>Influenza A and B</b>			
Overall all ages	38 (31 to 43)	29 (21 to 35)	45 (36 to 53)
6 mo–17 y	Not reported	Not reported	55 (42 to 65)
6 mo–8 y	68 (55 to 77)	48 (37 to 58)	NA
9–17 y	32 (16 to 44)	7 (–20 to 28)	NA
<b>Influenza A(H1N1)pdm09</b>			
Overall all ages	62 (50 to 71)	44 (37 to 51)	37 (19 to 52)
6 mo–17 y	Not reported	Not reported	51 (22 to 69)
6 mo–8 y	87 (71 to 95)	59 (47 to 69)	Not reported
9–17 y	70 (46 to 67)	24 (–18 to 51)	Not reported
<b>Influenza A(H3N2)</b>			
Overall all ages	22 (12 to 31)	9 (–4 to 20)	NA
6 mo–17 y	Not reported	Not reported	NA
6 mo–8 y	54 (33 to 69)	24 (1 to 42)	NA
9–17 y	18 (–6 to 36)	3 (–30 to 28)	NA
<b>Influenza B Victoria</b>			
Overall all ages	76 (45 to 89)	Not reported	50 (39 to 50)
6 mo–17 y	Not reported	Not reported	56 (42 to 67)
6 mo–8 y	Not reported	Not reported	Not reported
9–17 y	Note reported	Not reported	Not reported
<b>Influenza B yamagata</b>			
Overall all ages	48 (39 to 55)	Not reported	NA
6 mo–17 y	Not reported	Not reported	NA
6 mo–8 y	77 (49 to 90)	Not reported	NA
9–17 y	28 (1 to 48)	Not reported	NA

Vaccine effectiveness is estimated as  $100\% \times (1 - \text{odds ratio})$  [ratio of odds of being vaccinated among outpatients with CDC's real-time RT-PCR influenza-positive test results to the odds of being vaccinated among outpatients with influenza-negative test results]; odds ratios were estimated using logistic regression. Adjusted for study site, age group, sex, race/ethnicity, self-rated general health, number of days from illness onset to enrollment, and month of illness using logistic regression.

<sup>a</sup> Interim results as of February 21, 2020.<sup>6</sup>

influenza-like illness activity for a total duration of 21 consecutive weeks (compared with an average duration of 16 weeks).<sup>7</sup> Variations in circulating strains affected vaccine efficacy. 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. Most characterized influenza A(H3N2) viruses were antigenically distinct from the A(H3N2) component of the 2018–2019 vaccine. The vaccine's A(H3N2) virus belonged to subclade 3C.2a1. Cocirculation of multiple genetically diverse subclades of A(H3N2) was documented.

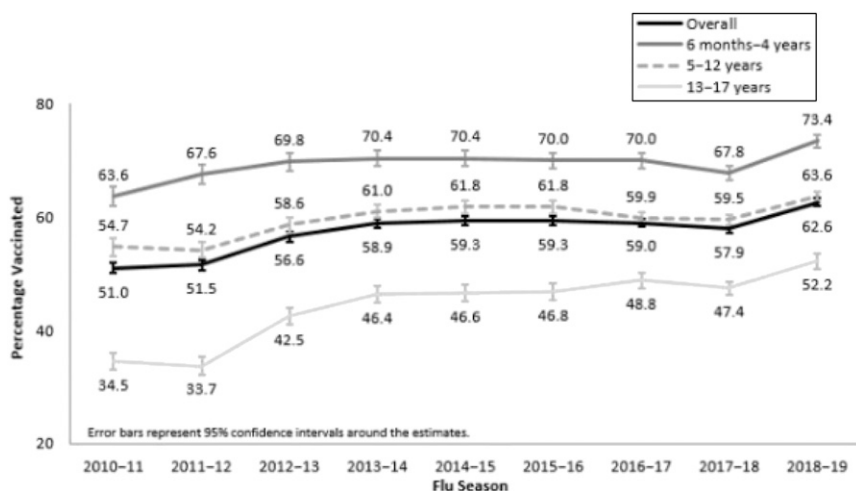
Circulating viruses identified belonged to subclade 3C.2a1 or clade 3C.3a, with 3C.3a viruses accounting for >70% of the A(H3N2) in the United States. This likely contributed to an overall lower vaccine effectiveness (VE) against influenza A(H3N2) this season, despite achieving the highest vaccination coverage reported in the last decade in children (62.6% overall) (Table 1 and Fig 1).<sup>7,9</sup>

### 2019–2020 Influenza Season

The 2019–2020 influenza season was unusual and complicated by the emergence of the SARS-CoV-2 pandemic in early 2020. Influenza activity began early in October 2019, continuing through mid-March 2020, with an abrupt decline after the

implementation of social distancing measures for mitigation of the pandemic. Although influenza B/Victoria viruses predominated early in the season, influenza A(H1N1)pdm09 viruses were the most predominant circulating strain this season. Influenza A(H3N2) and B/Yamagata lineage represented approximately 4.1% and 0.8% of circulating strains, respectively. The majority of characterized influenza A(H1N1)pdm09 (82.5%) and influenza B/Victoria (59.7%) viruses were antigenically similar to the viruses included in the 2019–2020 influenza vaccine. Less than half (46.5%) of influenza A(H3N2) viruses were antigenically similar to the A(H3N2) component of the 2019–2020 vaccine. During this season, the predominant A(H3N2) circulating clade was 3C.2a, subclade 3C.2a1, with cocirculation of a small proportion of 3C.3a, in contrast to the 2018–2019 season, when 3C.3a strains predominated. Preliminary estimates of the effectiveness of the 2019–2020 seasonal influenza vaccines against medically attended influenza illness from the US Flu VE Network are shown in Table 1.<sup>6</sup> These are preliminary data and are not vaccine specific. Susceptibility to available antiviral agents remains greater than 99% for all circulating strains, but 0.5% of A(H1N1)pdm09 isolates tested by the Centers for Disease Control and Prevention (CDC) exhibited highly reduced inhibition to oseltamivir and peramivir. Reduced susceptibility to baloxavir has not been reported in the United States to date.

The 2019–2020 season was of moderate severity, although 3 peaks of influenza-like illness activity and the highest hospitalization rates in children, 68.2 per 100 000 population overall, were reported this season. The first peak of activity occurred in early January, likely associated with influenza B circulation; the second peak occurred in February, when



**FIGURE 1**

Influenza vaccination coverage in children 6 months to 17 years of age in the United States, 2010 to 2019. Source: Centers for Disease Control and Prevention (<https://www.cdc.gov/flu/fluview/coverage-1819estimates.htm>).

influenza A(H1N1)pdm09 became predominant; and the third peak in March is thought to be associated with cocirculation of influenza and SARS-CoV-2. The CDC has now established a separate surveillance report for novel coronavirus disease 2019 (COVID-19)-like illness.<sup>10</sup> The cumulative influenza hospitalization rates per 100 000 population were 95.1 among children 0 through 4 years old, and 24.8 among children 5 through 17 years old. Hospitalization rates in children 0 to 4 years old were higher than those seen for this age group during the 2009 influenza pandemic, higher than the rate in adults 50 to 64 years old this season (91.8/100 000), and the highest on record for this age group. Among 168 children hospitalized with influenza and for whom data were available, 57.1% had no recorded underlying condition, and 42.9% had at least 1 underlying medical condition; the most commonly reported underlying conditions were asthma or reactive airway disease (19.7%), neurologic disorders (17.0%), and obesity (11.9%).

As of June 6, 2020, the following data were reported by the CDC:

- There were 182 laboratory-confirmed influenza-associated pediatric deaths. Most (63.0%) of those children died after being admitted to the hospital. The median age of the pediatric deaths was 6.1 years (range, 2 months to 17 years).
  - Seventy of the pediatric deaths were associated with influenza A viruses, and 112 were associated with influenza B viruses.
- Among the 168 children with known medical history, 42.9% 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, most (57.1%) had no known underlying medical conditions.
- The majority of the deaths occurred in children between 2 through 12 years of age: 37.4% were 5- through 11-year-olds, 20.9% were 2- through 4-year-olds, 20.3% were 12- through 17-year-olds, 15.9% were 6- through

23-month-olds, and 5.5% were younger than 6 months.

- Among 63 children who died and were tested, 46.0% had a bacterial coinfection.
- Among 141 children who were 6 months or older at the time of illness onset, and therefore, would have been eligible for influenza vaccination and for whom vaccination status was known, most (74%) were unvaccinated. Only 37 (26%) had received at least 1 dose of influenza vaccine (30 had complete vaccination, and 7 had received 1 of 2 ACIP-recommended doses).

## INFLUENZA MORBIDITY AND MORTALITY IN CHILDREN

Influenza viruses are a common cause of acute lower respiratory tract infection (ALRTI) in children. Pediatric hospitalizations and deaths caused by influenza can be substantial. A recent study estimated that globally, influenza virus accounts for 7% of all ALRTIs, 5% of ALRTI hospitalizations, and 4% of ALRTI deaths in children younger than 5 years.<sup>11</sup> In the United States, the rates of influenza-associated hospitalization for children younger than 5 years consistently exceed the rates for children 5 through 17 years of age, and during the 2019–2020 season, they exceeded the hospitalization rates of adults 50 to 64 years of age.<sup>8</sup> Children 5 through 17 years of age also experienced higher than usual hospitalization rates during the 2019–2020 season. The impact of the anticipated SARS-CoV-2 cocirculation with influenza in the 2020–2021 season is unknown at this time. Elevated rates of influenza-like illness hospitalization and mortality were observed toward the end of the 2019–2020 season, suggesting the possibility of comorbidity. It is, therefore, particularly important that children are protected against influenza

through timely vaccination in the 2020–2021 influenza season.

### HIGH-RISK GROUPS IN PEDIATRICS

Children and adolescents with certain underlying medical conditions have a high risk of complications from influenza (Table 2). While universal influenza vaccination is recommended for everyone starting at 6 months of age, emphasis should be placed in ensuring that people in high-risk groups and their household contacts and caregivers receive annual influenza vaccine.

### EFFECTIVENESS OF INFLUENZA VACCINATION ON HOSPITALIZATION AND MORTALITY

Several studies demonstrate that influenza vaccination can effectively decrease hospitalization in children where universal pediatric immunization has been implemented. In a study during the 2015–2016 season conducted by the United

States New Vaccine Surveillance Network (NVSN), among 1653 children enrolled from 7 pediatric hospitals, the adjusted VE in children with complete influenza immunization against any influenza-associated hospitalization was 56% (95% confidence interval [CI], 34% to 71%), against A(H1N1)pdm09 was 68% (95% CI, 36% to 84%), and against B viruses was 44% (95% CI, –1% to 69%).<sup>17</sup> A study in children 6 months to 8 years of age conducted in Israel over 3 influenza seasons from 2015 to 2017 demonstrated that over all seasons, fully vaccinated children had a VE against hospitalization of 53.9% (95% CI, 38.6% to 68.3%), while partial vaccination was not effective (25.6%; 95% CI, –3% to 47%).<sup>18</sup> In this study, a VE against hospitalization as high as 60% to 80% was observed when circulating and vaccine influenza A and B strains matched. After establishing free vaccination for preschool children and children at risk because of comorbid medical

conditions in Australia in 2018, VE of influenza vaccine in preventing influenza hospitalization was estimated to be 78.8% (95% CI, 66.9% to 86.4%).<sup>19</sup> In the United Kingdom, during the 2018–2019 season, the overall adjusted VE against influenza-confirmed hospitalization was reported to be 53% (95% CI, 33.3% to 66.8%), with protection varying by strain. Protection was 63.5% (95% CI, 34.4% to 79.7%) against influenza A(H1N1)pdm09, but there was no protection against influenza A(H3N2).<sup>20</sup> Finally, a systematic review and meta-analysis of 28 studies conducted by Kalligeros et al<sup>21</sup> concluded that influenza vaccine offered significant protection against any type of influenza-related hospitalization in children 6 months through 17 years of age, with VE of 57.5% (95% CI, 54.8% to 65.5%). Strain-specific VE was higher for influenza A(H1N1)pdm09 (75.1%; 95% CI, 54.8% to 93.3%) and influenza B (50.9%; 95% CI, 41.7% to 59.9%), compared with influenza A(H3N2) (40.8%; 95% CI, 25.6% to 55.9%). As expected, children who were fully vaccinated were better protected (VE 61.8%; 95% CI, 54.4% to 69.1%) compared with those who were partially vaccinated (VE 33.91%; 95% CI, 21.1% to 46.7%). Notably, VE was higher in children younger than 5 years of age (61.7%; 95% CI, 49.3% to 74.1%) than in children 6 to 17 years old (54.4%; 95% CI, 35.1% to 73.6%). In the United States, the CDC estimates that during the 2018–2019 season, influenza vaccination prevented 20% of projected hospitalizations associated with infection with A(H1N1)pdm09 virus among children 5 through 17 years, and 43% among children 6 months through 4 years.<sup>22</sup>

Historically, up to 80% of influenza-associated pediatric deaths have occurred in unvaccinated children 6 months and older. Influenza vaccination is associated with

**TABLE 2** People at High Risk of Influenza Complications

Children <5 y, and especially those <2 y, <sup>a</sup> regardless of the presence of underlying medical conditions
Adults ≥50 y, and especially those ≥65 y
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) <sup>12</sup>
Women who are pregnant or postpartum during the influenza season
Children and adolescents <19 y 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/Alaska Native people <sup>b</sup>
Children and adults with extreme obesity (ie, BMI [BMI] ≥40 for adults, and based on age for children)
Residents of chronic care facilities and nursing homes

Source: Adapted from Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2020–21 influenza season. *MMWR Recomm Rep*. 2020; in press.

<sup>a</sup> The 2019–2020 CDC recommendations state: 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.

<sup>b</sup> American Indian/Alaska Native (AI/AN) children have higher rate of influenza complications.<sup>15–16</sup> Most at-risk AI/AN children will also qualify in other high-risk categories to receive appropriate antiviral treatment. In the setting of a shortage, AI/AN children should be prioritized to receive influenza vaccine or anti-viral medications according to local public health guidelines.

reduced risk of laboratory-confirmed influenza-related pediatric death.<sup>23</sup> In one 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<sup>23</sup> found that only 26% of children had received vaccine before illness onset, compared with 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  $\geq 1$  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.<sup>24</sup> The influenza virus type might also affect the severity of disease. In a 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.<sup>25</sup>

## SEASONAL INFLUENZA VACCINES

The seasonal influenza vaccines licensed for children and adults for the 2020–2021 season are shown in Table 3. More than one product may be appropriate for a given patient, and vaccination should not be delayed to obtain a specific product.

All 2020–2021 seasonal influenza vaccines contain the same influenza strains as recommended by the World Health Organization (WHO) and the US Food and Drug Administration (FDA)'s Vaccines and Related Biological Products Advisory

Committee (VRBPAC) for the Northern Hemisphere.<sup>26</sup> Both influenza A(H1N1) and A(H3N2) and the B/Victoria components are different in this season's vaccine. The B/Yamagata component is unchanged. The influenza A strains are different for egg-based versus cell- or recombinant-based vaccines this year on the basis of their optimal characteristics for each platform, but all are matched to the strains expected to circulate in the 2020–2021 season.

1. Quadrivalent vaccines contain:
  - a. Influenza A(H1N1) component:
    - i. Egg-based vaccines: A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09-like virus (new this season)
    - ii. Cell- or recombinant-based vaccines: A/Hawaii/70/2019 (H1N1) pdm09-like virus (new this season)
  - b. Influenza A(H3N2) component:
    - i. Egg-based vaccines: A/Hong Kong/2671/2019 (H3N2)-like virus (new this season)
    - ii. Cell- or recombinant-based vaccines: A/Hong Kong/45/2019 (H3N2)-like virus (new this season)
  - c. B/Victoria component:
    - i. All vaccines: B/Washington/02/2019-like virus (B/Victoria/2/87 lineage) (new this season)
  - d. B/Yamagata component:
    - i. All vaccines: B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) (unchanged).
2. Trivalent vaccines do not include the B/Yamagata component.

## Inactivated Influenza Vaccine

For the 2020–2021 season, all licensed inactivated influenza vaccines (IIVs) for children in the United States are quadrivalent unadjuvanted vaccines, with specific age indications for available

formulations (Table 3). Four are egg-based (seed strains grown in eggs), and one is cell culture-based (seed strains grown in Madin-Darby canine kidney cells). All inactivated egg-based vaccines (Afluria Quadrivalent, Fluarix Quadrivalent, Flulaval Quadrivalent, and Fluzone Quadrivalent) are licensed for children 6 months and older and available in single-dose, thimerosal-free, prefilled syringes. The only pediatric cell culture-based vaccine (Flucelvax Quadrivalent) is licensed for children 4 years and older.<sup>1</sup>

A quadrivalent recombinant baculovirus-expressed hemagglutinin influenza vaccine (RIV4, Flublok Quadrivalent) is licensed only for people 18 years and older. A new quadrivalent high-dose inactivated influenza vaccine (HD-IIV4, Fluzone High Dose Quadrivalent) 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 high-dose formulation is no longer available. Both trivalent and quadrivalent MF-59 adjuvanted inactivated vaccines (aIIV3 Fluad and aIIV4 Fluad Quadrivalent) are now licensed for people 65 years and older. The quadrivalent formulation is new this year (licensed in February 2020).<sup>1</sup> 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 one pediatric study, the relative vaccine efficacy of a MF-59 adjuvanted influenza vaccine was significantly greater than nonadjuvanted vaccine in the 6- through 23-month age group.<sup>27</sup> Adjuvanted seasonal influenza vaccines are not licensed for children in the United States.

Children 36 months (3 years) and older can receive any age-appropriate licensed IIV, administered at a 0.5-mL dose containing 15  $\mu$ g of hemagglutinin (HA) from each strain. Children 6

**TABLE 3** Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2020–2021 Influenza Season

Vaccine	Trade Name (Manufacturer)	Age Group	Presentation Hemagglutinin Antigen Content (IIVs and RIV4) or Virus Count (LAIV4) per dose for Each Antigen	Thimerosal Mercury Content (µg Hg/0.5-mL dose)	CPT Code
Quadrivalent standard dose – egg-based vaccines					
IIV4	Afluria Quadrivalent (Seqirus)	6–35 mo	0.25-mL prefilled syringe <sup>a</sup> (7.5 µg/0.25 mL)	0	
		≥36 mo	0.5-mL prefilled syringe (15 µg/0.5 mL)	0	90686
IIV4	Fluarix Quadrivalent (GlaxoSmithKline)	≥6 mo	5.0-mL multidose vial <sup>b</sup> (15 µg/0.5 mL)	24.5	90688
IIV4	FluLaval Quadrivalent (GlaxoSmithKline)	≥6 mo	0.5-mL prefilled syringe (15 µg/0.5 mL)	0	90686
IIV4	Fluzone Quadrivalent (Sanofi Pasteur)	≥6 mo	0.5-mL prefilled syringe (15 µg/0.5 mL) <sup>c</sup>	0	90686
		≥6 mo	0.5-mL single-dose vial (15 µg/0.5 mL)	0	90687
		≥6 mo	5.0-mL multidose vial <sup>b</sup> (15 µg/0.5 mL)	25	90688
Quadrivalent standard dose – cell-based vaccines					
ccIIV4	Flucelvax Quadrivalent (Seqirus)	≥4 y	0.5-mL prefilled syringe (15 µg/0.5 mL)	0	90674
		≥4 y	5.0 mL multidose vial (15 µg/0.5 mL)	25	90756
Standard dose – egg-based with adjuvant vaccines					
aIIV3 MF-59 adjuvanted	Fluad Trivalent Seqirus	≥65 y	0.5-mL prefilled syringe (15 µg/0.5 mL)	0	90653
aIIV4 MF-59 adjuvanted	Fluad Quadrivalent Seqirus	≥65 y	0.5-mL prefilled syringe (15 µg/0.5 mL)	0	90653
Quadrivalent high dose – egg-based vaccine					
IIV4	Fluzone High-dose (Sanofi Pasteur)	≥65 y	0.7-mL prefilled syringe (60 µg/0.7 mL)	0	90662
Recombinant vaccine					
RIV4	Flublok Quadrivalent (Sanofi Pasteur)	≥18 y	0.5-mL prefilled syringe (45 µg/0.5 mL)	0	90682
Live attenuated vaccine					
LAIV4	FluMist Quadrivalent (MedImmune)	2–49 y	0.2-mL prefilled intranasal sprayer (Virus dose: 10 6.5–7.5 FFU/0.2 mL)	0	90672

Data sources: Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2020–2021 influenza season. *MMWR Recomm Rep*. 2020; in press. Implementation guidance on supply, pricing, payment, CPT coding, and liability issues can be found at [www.aapredbook.org/implementation](http://www.aapredbook.org/implementation). (Table has been reformatted and updated).

<sup>a</sup> For Afluria Quadrivalent, children 6 through 35 months of age should receive 0.25 mL per dose; people ≥36 months (≥3 years) of age should receive 0.5 mL per dose.

<sup>b</sup> For vaccines that include a multidose vial presentation a maximum of 10 doses can be drawn from a multidose vial.

<sup>c</sup> The 7.5-µg/0.25-mL dosing volume is no longer available this season.

through 35 months of age may receive any age-appropriate licensed IIV without preference for one over another. Several vaccines have been licensed for children 6 through 35 months of age since 2017 (Table 3). All are quadrivalent, but the dose volume and, therefore, the antigen content vary among different IIV products. In addition to a 0.25-mL (7.5 µg of HA per vaccine virus) Fluzone Quadrivalent vaccine, a 0.5-mL formulation of Fluzone Quadrivalent containing 15 µg of HA per vaccine virus per dose was licensed in January 2019 after these 2 formulations were shown to have comparable safety and

immunogenicity in a single randomized, multicenter study.<sup>28–30</sup> Only the 0.5-mL Fluzone product is expected to be available this season. In addition, 2 other vaccines, Fluarix Quadrivalent<sup>31</sup> and FluLaval Quadrivalent,<sup>32</sup> are 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. Afluria Quadrivalent is the only pediatric vaccine that has a 0.25-mL (7.5 µg of HA per vaccine virus) presentation for children 6 through 35 months of age. Afluria Quadrivalent 0.5 mL (15 µg of HA per vaccine virus) is licensed for children 3 years and older only.<sup>33</sup>

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, 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

2020–2021 season should receive 2 separate doses at the recommended dose volume specified for each product.

Inactivated influenza vaccines are well tolerated in children and can be used in healthy children as well as those with underlying chronic medical conditions. The most common injection site adverse reactions following 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 trivalent IIV (IIV3) and the 13-valent pneumococcal conjugate vaccine (PCV13) concomitantly. Subsequent retrospective analyses of past seasons demonstrated a slight increase in the risk of febrile seizures in children 6 through 23 months of age when PCV13 vaccines were administered concomitantly with IIV.<sup>34</sup> The concomitant administration of IIV3, PCV13, and diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated, compared with the administration of the vaccines on separate days. In contrast, data from the Post-Licensure Rapid Immunization Safety Monitoring (PRISM) program of the FDA, 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 influenza season.<sup>35</sup>

Similarly, in a subsequent sentinel CBER/PRISM surveillance report evaluating influenza vaccines and febrile seizures, there was no evidence of an elevated risk of febrile seizures in children 6 through 23 months of age following IIV administration during the 2013–2014 and 2014–2015 seasons, noting that the risk of seizures after PCV13 or concomitant PCV13 and IIV was low compared with a child's lifetime risk of febrile seizures from other causes.<sup>36</sup> Using a self-controlled interval study design, Baker et al<sup>37</sup> further evaluated the relative risk of febrile seizures following IIV or PCV13 in children 6 through 23 months, using the PRISM health care claims during those same 2 influenza seasons. When the febrile seizure rate was compared in a risk interval (0–1 days post vaccination) versus a control interval (14–20 days after vaccination), adjusting by age, calendar time, and concomitant administration of the other vaccine, an elevated risk of febrile seizures was identified after vaccination with PCV13 (incidence rate ratio [IRR], 1.80; 95% CI, 1.29 to 2.52), but not after IIV (IRR, 1.12; 95% CI, 0.80 to 1.56). Furthermore, in a study of children 12 to 16 months of age vaccinated during the 2017–2018 season, no difference was observed in the occurrence of fever when IIV administration was delayed for 2 weeks after PCV13 and DTaP vaccination (9.3%) compared with PCV13, DTaP and IIV given on the same day (8.1%) (adjusted risk ratio [aRR], 0.87; 95% CI, 0.36 to 2.19).<sup>38</sup> On the basis of these findings, simultaneous administration of IIV with PCV13 and/or other vaccines continues to be recommended for the 2020–2021 influenza season when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of IIV and PCV13 or DTaP outweigh the risk of febrile seizures. Vaccine-proximate febrile seizures rarely have any long-term sequelae, similar to

nonvaccine-proximate febrile seizures.

Thimerosal-containing vaccines are not associated with an increased risk of autism spectrum disorder in children. 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.<sup>39</sup> Despite the lack of evidence of harm, some states 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 3).

### **Live Attenuated (Intranasal) Influenza Vaccine**

The intranasal live attenuated influenza vaccine (LAIV) was initially licensed in the United States in 2003 for people 5 through 49 years of age as a trivalent formulation (LAIV3), and the approved age group was extended to 2 years of age in 2007. The quadrivalent formulation (LAIV4) licensed in 2012 was first available during the 2013–2014 influenza season, replacing LAIV3. The most commonly reported reactions of LAIV in children are runny nose or nasal congestion, headache, decreased activity or lethargy, and sore throat.

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 influenza seasons, including data from United States and European studies.<sup>40</sup> The data suggested that the



effectiveness of LAIV3 or LAIV4 for influenza A(H1N1)pdm09 strain 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 with IIV. LAIV was not recommended by the CDC or AAP for use in children during the 2016–2017 and 2017–2018 seasons, given concerns about its effectiveness against A(H1N1)pdm09. For the 2017–2018 season, a new A(H1N1)pdm09-like virus strain (A/Slovenia/2903/2015) was included in LAIV4, replacing the prior A/Bolivia/559/2013 strain. 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 to 48 months of age.<sup>41</sup> Shedding and immunogenicity data 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 with that of the LAIV3 available prior to 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 prior to 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 influenza 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 utilization was appropriate for age (2 years and older) and health status

(ie, healthy, without any underlying chronic medical condition).

In February 2019, the AAP Committee of Infectious Diseases (COID) reviewed available data on influenza epidemiology and vaccine effectiveness 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 was appropriate. After the February 2020 ACIP meeting, the AAP COID reviewed available epidemiologic and effectiveness data for the previous and current seasons to inform recommendations for the 2020–2021 season. Despite the early circulation of A(H1N1)pdm09 during the 2018–2019 season and its predominance during the 2019–2020 season, low utilization of LAIV4 in the United States population has limited the evaluation of product-specific vaccine effectiveness, and no additional US data on LAIV4 VE are available. Although the proportion of LAIV used for vaccination is unknown, interim overall VE (not specific to a type of vaccine) for the 2019–2020 influenza season shows reassuring protection in children against circulating influenza A and B strains (Table 1).<sup>6</sup> Furthermore, influenza vaccine coverage rates in children are stable.<sup>9</sup> In European surveillance networks where uninterrupted utilization of LAIV has continued from the 2016–2017 through the 2019–2020 seasons, the only country with LAIV VE estimates, the United Kingdom, reported final VE against medically attended influenza for the 2018–2019 season in children 2 through 17 years of age of 49.9% (95% CI, –14.3% to 78.0%) for A(H1N1)pdm09 and of 27.1% (95% CI, –130.5% to 77%) for A(H3N2).<sup>42</sup> The final adjusted VE in the United States (where mostly IIV was used) for 2018–2019 against A(H1N1)pdm09 was 59% (95% CI, 47% to 69%) for children 6 months through 8 years of age but only 24%

(95% CI, –18% to 51%) for children 9 through 17 years and for A(H3N2) 24% (95% CI, 1% to 42%) in children 6 months through 8 years of age, and 3% (95% CI, –30% to 28%) in children 9 through 17 years of age.<sup>43</sup> Direct comparisons cannot be made given differences in reporting of VE for various age groups. Other countries that use LAIV (Canada, Finland) have not reported LAIV4-specific VE in past several seasons. 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, important variability in VE against all strains is reported for both IIV and LAIV.

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 over multiple influenza seasons will help to determine optimal utilization 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

Anaphylactic reactions to any vaccine are considered a contraindication to vaccination. The AAP recommends that 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. Similarly, consultation

with an infectious disease specialist may be sought to assess potential contraindications and precautions and to determine which influenza vaccine is most appropriate to ensure immunization in special circumstances.

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. Children with confirmed COVID-19 can receive influenza vaccine when the acute illness has resolved. Children with an amount of nasal congestion that would notably impede vaccine delivery into the nasopharyngeal mucosa should have LAIV vaccination deferred until resolution.

A precaution for vaccination is a condition in a recipient that might increase the risk or seriousness of a possible vaccine-related adverse reaction. A precaution also may exist for conditions that might compromise the ability of the host to develop immunity after vaccination. Vaccination may be recommended in the presence of a precaution if the benefit of protection from the vaccine outweighs the potential risks.

History of Guillain-Barré syndrome (GBS) following influenza vaccine is considered a precaution for the administration of influenza vaccines. GBS is rare, especially in children, and there is a lack of evidence on risk of GBS following influenza vaccine in children. Nonetheless, regardless of age, a history of GBS less than 6 weeks after a previous dose of influenza vaccine is a precaution for administration of influenza vaccine. GBS may occur

after influenza infection. The benefits of influenza vaccination might outweigh the risks for certain people who have a history of GBS (particularly if not associated with prior influenza vaccination) and who also are at high risk for severe complications from influenza.

Specific precautions for LAIV include a diagnosis of asthma in children 5 years and older and the presence of certain chronic underlying medical conditions, including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies. Although the safety of LAIV has not been definitely established in these situations, IIV can be considered. In a study comparing a large cohort of children 2 through 17 years old with asthma who received LAIV instead of IIV under established practice guidelines from 2007 to 2016, the occurrence of asthma exacerbation within 21 to 42 days of vaccination was not higher compared with children who received IIV.<sup>44</sup> In a prospective open-label phase IV study conducted in the United Kingdom, 478 children aged 2 to 18 years with physician-diagnosed asthma or recurrent wheezing received LAIV, with no significant change in asthma symptoms or exacerbation in the 4 weeks after vaccination.<sup>45</sup> However, 14.7% of patients eventually reported a severe asthma exacerbation after vaccination, requiring treatment. In post-licensure surveillance of LAIV (including LAIV3 and LAIV4), the Vaccine Adverse Event Reporting System (VAERS), jointly sponsored by the FDA and CDC, has not identified any new or unexpected safety concerns, including in people with a contraindication or precaution (<https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/>).

People who should not receive LAIV are listed below.

### People 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 with new cochlear implants or active cerebrospinal fluid leaks.
- Children who have a known or suspected primary or acquired immunodeficiency or who are receiving immunosuppressive or immunomodulatory therapies.
- Children with anatomic or functional asplenia, including from sickle cell disease.
- 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) and up to 2 weeks (peramivir and 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.

- Pregnant women.

### **LAIV and Immunocompromised Hosts**

The inactivated influenza vaccine 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 very 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.<sup>46,47</sup> 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 (ACOG), and the American Academy of Family Physicians (AAFP) for all women, during any trimester of gestation, for the protection of mothers against influenza and its complications.<sup>1,48</sup> 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.<sup>48-53</sup> 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.<sup>50-58</sup> Infants born to women who receive influenza vaccination during pregnancy can have a risk reduction of up to 72% (95% CI, 39% to 87%) for laboratory-

confirmed influenza hospitalization in the first few months of life.<sup>56</sup>

It is safe to administer inactivated influenza vaccine 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 support the safety of influenza immunization during pregnancy.<sup>48,50-55,59</sup> 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.<sup>60</sup> 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.<sup>61</sup> Assessments of any association with influenza vaccination and preterm birth and small-for-gestational-age infants have yielded inconsistent results, with most studies reporting a protective effect or no association against these outcomes.<sup>62,63</sup> A cohort study from the Vaccines and Medications in Pregnancy Surveillance System (VAMPSS) of vaccine exposure during the 2010-2011 through 2013-2014 influenza seasons found no significant association of spontaneous abortion with influenza vaccine exposure in the first trimester or within the first 20 weeks of gestation.<sup>64</sup> One observational Vaccine Safety Datalink (VSD) study conducted during the 2010-2011 and 2011-2012 influenza seasons indicated 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.<sup>65</sup> A follow-up study conducted by the same investigators with a larger population and stricter outcome measures did not show this association and further supported the safety of influenza vaccine during pregnancy.<sup>66</sup>

Women in the postpartum period who did not receive influenza vaccination during pregnancy should be encouraged to discuss with their obstetrician, family physician, nurse midwife, or other trusted provider receiving influenza 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 (IgA).<sup>67</sup> 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 illness. 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 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](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 ([www.aap.org/disasters](http://www.aap.org/disasters)). During the COVID-19 pandemic, the AAP recommends that influenza vaccine administration follow CDC guidance for administration of immunizations (<https://www.cdc.gov/vaccines/pandemic-guidance/index.html>). Vaccination in the medical home is ideal to ensure that pediatric patients receive other vaccinations and routine care in a timely manner and receive catch-up immunizations if delays have occurred because of the pandemic. In general, infection-prevention measures should be in place for all patient encounters, including screening for symptoms, physical distancing, respiratory and hand hygiene, and surface decontamination. In addition to standard precautions and hand hygiene, during the COVID-19 pandemic, it is recommended that vaccine administrators wear a surgical face mask (not N95 or respiratory) at all times and eye protection if the level of community spread is moderate or elevated. Administration of LAIV intranasally is

not an aerosol-generating procedure; however, vaccine administrators are advised to wear gloves when injecting LAIV given the potential to coming in contact with respiratory secretions. Gloves used for intranasal or intramuscular vaccine administration should be changed with every patient. Gowns are not required.

#### **Inactivated Influenza Vaccines**

IIVs for intramuscular (IM) 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 according to its approved age indication, dosing, and volume of administration (Table 3). 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 only approved for adults, the dose should be counted as valid.

#### **Live Attenuated Influenza Vaccine**

The cold-adapted, temperature-sensitive LAIV4 formulation 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 2020–2021 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 2.

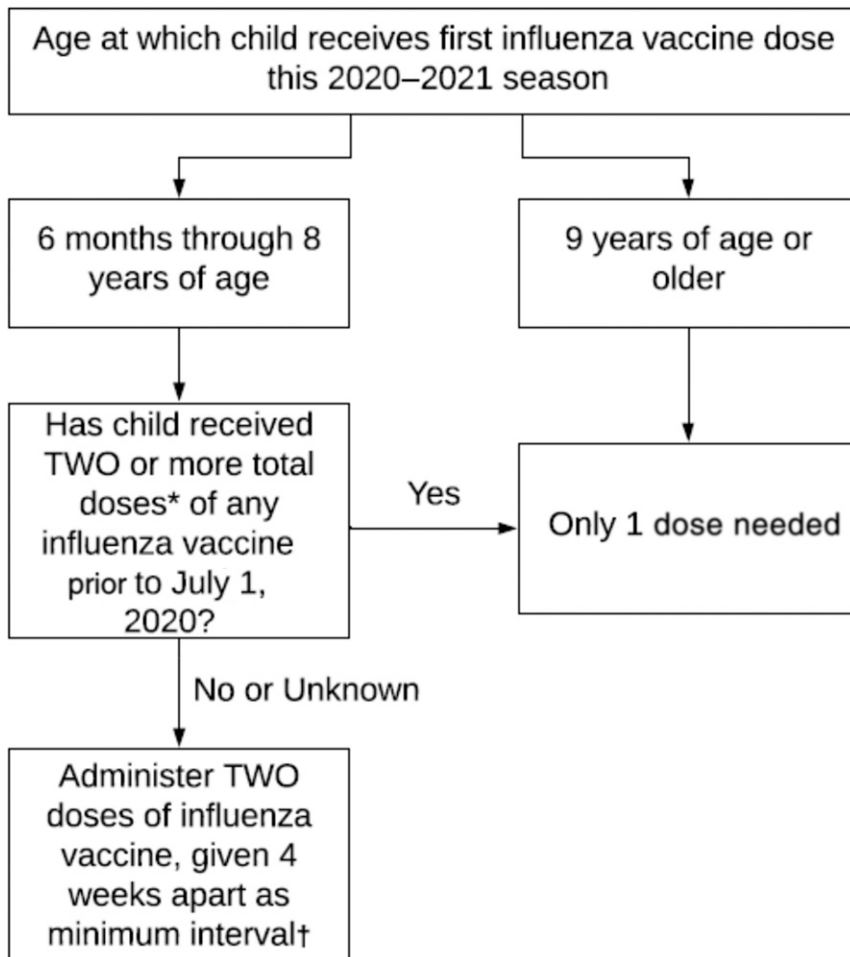
- Influenza vaccines are not licensed for administration to infants younger than 6 months and should not be used in this age group.
- Children 9 years and older need only 1 dose, regardless of previous vaccination history.
- Children 6 months through 8 years of age:
  - Need 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2020, or if their vaccination status is unknown. The interval between the 2 doses should be at least 4 weeks. Two doses should be administered to children who receive their first dose before their ninth birthday, even if their ninth birthday occurs during the same season.
  - 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, 2020. 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 one or more disease peaks. Predicting the onset and duration or the severity of the influenza season with accuracy 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, particularly this season, when circulation of SARS-CoV-2 is expected to continue.

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 vaccine becomes available, to allow sufficient time for receipt of the second dose  $\geq 4$  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) suggests that very early vaccination (July or August) might be associated with suboptimal immunity



**FIGURE 2** Number of 2020–2021 seasonal influenza vaccine doses for children based on age and prior vaccination history. \* The 2 doses need not have been received during the same season or consecutive seasons. † 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.

before the end of the influenza season.

Although the evidence is limited in children, recent reports raise the possibility that early vaccination might contribute to reduced protection later in the influenza season.<sup>68-79</sup> In these studies, vaccine effectiveness 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<sup>71,73</sup> and with influenza A(H3N2) viruses more than influenza A(H1N1) or B viruses.<sup>72,75,77</sup> A multiseason analysis from the US Influenza Vaccine Effectiveness 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.<sup>70</sup> VE remained greater than 0 for at least 5 to 6 months after vaccination. A more recent study including children older than 2 years also found evidence of declining vaccine effectiveness with an odds ratio increasing approximately 16% with each additional 28 days from vaccine administration.<sup>80</sup> In another study evaluating VE from the 2011–2012 through the 2013–2014 influenza seasons demonstrated 54% to 67% protection from 0 to 180 days after vaccination.<sup>74</sup> Finally, a multiseason study in Europe from 2011–2012 through 2014–2015 showed a steady decline in VE down to 0% protection by 111 days after vaccination.<sup>75</sup>

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 whether 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.<sup>81</sup> Providers may continue to offer vaccine until June 30th of each year when the seasonal influenza vaccine expires, because the duration of influenza circulation is unpredictable. Furthermore, a person may experience more than one influenza infection during a given season because of the various cocirculating strains. 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 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](http://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](http://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. For example, pediatricians can play a key role in educating and assisting early childhood education centers and schools in educating parents on the importance of influenza immunization. Resources for effective communication and messaging strategies are available on the AAP

Web site – promoting vaccinations and providing resources for pediatricians to communicate with patients, families, and the communities they serve (<https://www.aap.org/en-us/about-the-aap/aap-press-room/campaigns/immunizations/Pages/default.aspx> and <https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Influenza-Implementation-Guidance/Pages/Patient-Family-and-Community.aspx>).

Pediatricians and other pediatric health care providers should plan to make influenza vaccine easily accessible for all children. Examples include sending alerts to families that 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 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. Payers should eliminate remaining “patient responsibility” cost barriers to influenza vaccine where they still exist. Similar efforts should be made to eliminate the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children (VFC) program. American Indian/Alaska Native children, who are eligible for vaccines through the VFC program, are at higher risk for influenza complications and should be prioritized in a vaccine shortage (Table 2).

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. 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. Vaccine coverage among HCP was 81.1% during the 2018–2019 season, up from 78.4% the previous year.<sup>82</sup> 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.

### INFLUENZA VACCINE COVERAGE

Although national influenza vaccination coverage among children has not declined in the past several seasons, overall vaccination coverage remains suboptimal (Fig 1). Achieving high coverage rates of influenza vaccine in infants and children is a priority to protect them against influenza disease and its complications. Timely influenza vaccination is particularly important during the 2020–2021 influenza season, given the concurrent SARS-CoV-2 pandemic.

The AAP and CDC recommend vaccine administration at any visit to the medical home before and 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. The CDC has developed guidance for the planning of vaccination clinics during the COVID-19 pandemic (<https://www.cdc.gov/vaccines/>

[hcp/admin/mass-clinic-activities/index.html?deliveryName=USCDC\\_7\\_3-DM33813](https://www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/)). It is important that 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 crucial to maintain 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 2-dimensional barcodes can be found at [www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/](https://www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/).

Children’s likelihood of being immunized according to recommendations appears to be associated with the immunization practices of their parents. One 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.<sup>49</sup> 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 and payment issues along with 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, where 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 2) 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](http://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 2019–2020 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](http://www.cdc.gov/flu/weekly/fluactivitysurv)).

htm). The AAP offers "What's the Latest with the Flu" messages to highlight those details most relevant for AAP members and child care providers on a monthly basis during influenza season (<https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Pages/What's-the-Latest-with-the-Flu.aspx>).

## INFLUENZA VACCINATION RECOMMENDATIONS

1. The AAP recommends annual influenza vaccination for *everyone* 6 months and older, including children and adolescents, during the 2020–2021 influenza season.
2. For the 2020–2021 influenza season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. Inactivated influenza vaccine (IIV) and live attenuated vaccine (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 vaccine efficacy (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 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 any licensed, age-appropriate IIV available this

season, at the dose indicated for the vaccine. No product 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 2020–2021 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 2).
6. 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, 2020, or whose vaccination status is unknown 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 2) 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 inactivated influenza vaccine at



any time during pregnancy, to protect themselves and their infants, who benefit from the transplacental transfer of antibodies. Women in the postpartum period 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 health care personnel as a crucial element in preventing influenza and reducing health care-associated influenza infections, because health care personnel 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 4 (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](http://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), all of which have activity against influenza A and B viruses.<sup>83</sup>

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.<sup>83</sup> IV zanamivir is not approved in the United States and has not been available for compassionate use since the 2017–2018 season.<sup>68,69</sup> 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.<sup>84</sup> This antiviral agent for influenza has a different mechanism of action (cap-endonuclease inhibitor) than NAIs and requires only a single oral dose for treatment of uncomplicated influenza. A clinical trial of baloxavir treatment of influenza in hospitalized patients 12 years and older is ongoing (<https://clinicaltrials.gov/ct2/show/NCT03684044?cond=baloxavir&rank=6>).

## INFLUENZA TREATMENT

Randomized controlled trials (RCTs) conducted to date to evaluate the efficacy of influenza antiviral medications among outpatients with uncomplicated influenza have found that timely treatment can reduce the duration of influenza symptoms and fever in pediatric populations.<sup>85–89</sup> Observational studies in pediatric and adult populations suggest that antiviral agents could reduce the risk of certain influenza complications, including hospitalization and death.<sup>90–93</sup> 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 involving treatment of 2356 children with clinically diagnosed influenza, of whom 1255 had laboratory-confirmed influenza, showed that in children with laboratory-confirmed influenza, oral oseltamivir and inhaled zanamivir reduced median duration of illness by 36 hours (26%;  $P < .001$ ) and 1.3 days (24%,  $P < .001$ ), respectively.<sup>89</sup> Among the studies reviewed, 1 trial of oseltamivir in children with asthma who had laboratory-confirmed influenza showed 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 [RD],  $-0.14$ ; 95% CI,  $-0.24$  to  $-0.04$ ).<sup>89</sup> Another Cochrane review of RCTs in adults and children, which included 20 oseltamivir (9623 participants) and 26 zanamivir trials (14 628 participants),<sup>86</sup> found no effect of oseltamivir in reducing the duration of illness in asthmatic children, but in otherwise healthy 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, this review did not find a significant effect of NAIs on reducing hospitalizations, pneumonia, bronchitis, otitis media, or sinusitis in children.<sup>86</sup> More recently, a meta-analysis of 5 new RCTs that included 1598 children with laboratory-confirmed influenza showed 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).<sup>87</sup> 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.

**TABLE 4** Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis in Children for the 2020–2021 Influenza Season: United States

Medication	Treatment (5 Days)	Chemoprophylaxis (10 Days) <sup>a</sup>
<b>Oseltamivir<sup>b</sup></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 kg–23 kg (33 lb–51 lb)	45 mg, twice daily	45 mg, once daily
>23 kg–40 kg (>51 lb–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 <sup>c</sup>	3.5 mg/kg per dose, twice daily	3.5 mg/kg per dose, once daily
Term infants 0–8 mo <sup>c</sup>	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
<b>Preterm infants<sup>d</sup></b>		
<38 wks' postmenstrual age	1.0 mg/kg per dose, twice daily	
38 through 40 wks' postmenstrual age	1.5 mg/kg per dose, twice daily	
>40 wks' postmenstrual age	3.0 mg/kg per dose, twice daily	
<b>Zanamivir<sup>e</sup></b>		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
≥7 y for treatment		
≥5 y for chemoprophylaxis		
<b>Peramivir</b>		
Adults	One 600-mg intravenous infusion, given over 15–30 min	Not recommended
Children (2–12 y)	One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for 15–30 min	Not recommended
Children (13–17 y)	One 600 mg dose, via intravenous infusion for 15–30 min	Not recommended
<b>Baloxavir</b>		
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<sup>78</sup> and <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm>.

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

<sup>b</sup> 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 oral suspension, a 60-mg dose is given with 10 mL oral suspension, and a 75-mg dose is given with 12.5 mL 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), based on 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 days. For chemoprophylaxis of patients with creatinine clearance 10–30 mL/min: 30 mg, once daily, for 10 days after exposure or 75 mg, once every other day, for 10 days after exposure (5 doses). See <https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm> and IDSA Guidelines.<sup>85</sup>

<sup>c</sup> Approved by the FDA for children as young as 2 weeks 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/dose, twice daily, for all infants <12 months old; the IDSA guidelines<sup>83</sup> include both AAP and CDC recommendations.

<sup>d</sup> Oseltamivir dosing for preterm infants. The weight-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 full-term infants may lead to very 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.

<sup>e</sup> 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.

Overall, efficacy outcomes are best demonstrated in patients with laboratory confirmed influenza. All these studies confirmed vomiting as an occasional adverse 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 to determine the efficacy of influenza antiviral medications in

hospitalized patients or pediatric patients with comorbidities have not been conducted, and prospectively collected data 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.<sup>88,90-94</sup> An observational epidemiologic study conducted in adult patients hospitalized with severe laboratory-confirmed influenza in Spain over 6 influenza seasons (2010–2016) evaluated the effectiveness of NAIs, concluding that when started early after the onset of symptoms ( $\leq 48$  hours or  $\leq 5$  days), NAI treatment was associated with a reduction in influenza-associated deaths (adjusted odds ratio [aOR], 0.37; 95% CI, 0.22 to 0.63; and aOR, 0.50; 95% CI, 0.32 to 0.79, respectively).<sup>90</sup> 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 from prospectively conducted trials, 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, is recommended by the AAP, CDC, Infectious Diseases Society of America (IDSA),<sup>83</sup> 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.<sup>95-97</sup> In a retrospective study of 653 PICU admissions from 2009 to 2012, the estimated risk of death was reduced in NAI treated cases (OR 0.36, 95% CI: 0.16 to 0.83).<sup>95</sup> No additional

benefit exists for double-dose NAI therapy on reduction of mortality or virologic clearance, compared with standard-dose therapy, on the basis of a recent systematic review and meta-analysis of 10 published studies<sup>98</sup> (4 RCT and 6 observational studies) involving 20 947 adult and pediatric patients.

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 benefits of therapy of neonatal influenza are likely to outweigh 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 with placebo when studied in children 1 through 12 years of age (ie, 15% of treated children versus 9% receiving placebo). In addition, following reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, a review of controlled clinical trial data and ongoing surveillance has failed to establish a link between this drug and neurologic or psychiatric events.<sup>99,100</sup>

## ANTIVIRAL TREATMENT AND INFLUENZA TESTING CONSIDERATIONS

Clinical judgment (on the basis of 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 influenza-like 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 5), all of which should be considered in making the best clinical decision. Positive and negative predictive values of influenza test results are influenced by the level of influenza activity in the population being tested, the characteristics of a test compared with 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. Given the similarities in clinical presentation, testing for influenza and for SARS-CoV-2 infection should be offered to patients with a febrile respiratory illness or influenza-like illness.

Although decisions on treatment and infection control can be made on the basis of positive rapid influenza diagnostic test (RIDT) results, negative results should not always be used in a similar fashion because of the suboptimal sensitivity and potential for false-negative results. An updated list of RIDTs is available at: <https://www.cdc.gov/flu/professionals/diagnosis/table-ridt.html>. Positive results of RIDTs are helpful, because they may reduce additional testing to identify

**TABLE 5** 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 device); 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 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 with reverse transcriptase-polymerase chain reaction (RT-PCR). FDA-cleared rapid influenza diagnostic tests are CLIA-waived; most FDA-cleared rapid influenza molecular assays are CLIA-waived, depending on the specimen. Source: Uyeki.<sup>85</sup>

alternative causes of the child's influenza-like illness, provide the opportunity for early antiviral treatment, promote appropriate antimicrobial stewardship, and allow the timely implementation of appropriate strategies to prevent transmission. Available FDA-approved rapid molecular assays based on nucleic acid detection are highly sensitive and specific diagnostic tests that can provide rapid results. An updated list of these tests is available here: <https://www.cdc.gov/flu/professionals/diagnosis/table-nucleic-acid-detection.html>. Molecular assays are preferred in hospitalized patients, because they are more sensitive compared with 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. This containment strategy is particularly relevant during the SARS-CoV-2 pandemic.

People with suspected influenza who are at higher risk of influenza complications should be offered

treatment with antiviral medications (Table 2). 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 (as they are not able to receive influenza vaccine) or have high-risk conditions (including age <5 years) 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 4).

### INFLUENZA CHEMOPROPHYLAXIS

Randomized placebo-controlled studies showed that oral oseltamivir and inhaled zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza.<sup>83</sup> There are no data on IV peramivir or oral baloxavir for chemoprophylaxis. Decisions on whether to administer antiviral chemoprophylaxis should take into 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 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 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 risk of influenza is lowered but still remains while taking the medication, and susceptibility to influenza returns when medication is discontinued. Oseltamivir use is not a contraindication to vaccination with IIV, although LAIV effectiveness will be decreased for the child receiving oseltamivir.<sup>83</sup> No data are available on the impact of inhaled zanamivir, IV peramivir or oral baloxavir on effectiveness of LAIV, but it is likely that all antiviral agents 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](http://www.aapredbook.org/flu) and [www.cdc.gov/flu/professionals/antivirals/index.htm](http://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 2019–2020 season, >99% of influenza A(H1N1)pdm09 and B/Victoria viruses tested were susceptible to oseltamivir, peramivir, and zanamivir, and all were susceptible to baloxavir. All tested influenza A(H3N2) and B/Yamagata viruses were susceptible to these antiviral agents. Decreased susceptibility to baloxavir has been reported in Japan, where utilization has been more common,<sup>101–105</sup> and

surveillance for resistance among circulating influenza viruses is ongoing in Japan and the United States.<sup>106–108</sup> 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.<sup>83</sup>

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 2020–2021 influenza season continue to be susceptible to oseltamivir, zanamivir, peramivir, and baloxavir (<https://www.cdc.gov/flu/weekly/>). If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, recommendations for alternative treatment will be available from the CDC and AAP. Resistance characteristics can change for an individual patient over the duration of a treatment course, especially in those who are severely immunocompromised. Up-to-date information on current recommendations and therapeutic options can be found on the AAP Web site ([www.aap.org](http://www.aap.org) or [www.aapredbook.org/flu](http://www.aapredbook.org/flu)), through state-specific AAP chapter websites, or on the CDC Web site ([www.cdc.gov/flu/](http://www.cdc.gov/flu/)).

### INFLUENZA ANTIVIRALS RECOMMENDATIONS

Treatment recommendations for antiviral medications for the 2020–2021 influenza 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 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 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:

- Any hospitalized child with suspected or confirmed influenza disease, regardless of duration of symptoms.
- Any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to influenza, regardless of duration of symptoms.
- Influenza virus infection of any severity in children at high risk of complications of influenza, as listed in Table 2, regardless of duration of symptoms.

Antiviral treatment may be considered for the following individuals:

- Any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom an influenza diagnosis is confirmed or suspected on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
- 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 2.

Shared informed decision making between providers and parents/legally authorized caregivers is encouraged to initiate therapy and monitor children for safety and efficacy while receiving antiviral agents. 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 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:
  - 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 following 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.
- For children at high risk of complications and their family members and close contacts, as well as for 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. Children who have higher rates of influenza complications, including American Indian/Alaska Native children, should be prioritized to receive influenza antiviral agents in the setting of a shortage according to local public health guidelines (Table 2). 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 2020–2021 influenza season will be analyzed as they become available and reported by CDC as they are each season. Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccines, especially for at risk populations, is important. The duration of protection,

the potential role of previous influenza vaccination on overall vaccine effectiveness, and vaccine effectiveness 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. For the 2020–2021 influenza season, it will be particularly important to understand the effect of SARS-CoV-2 and influenza virus cocirculation on the epidemiology and morbidity of influenza in the pediatric population. Understanding how to better 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 in these populations are warranted. This is particularly relevant as new antiviral agents or new indications for existing antiviral agents become available. At this time, the FDA has accepted supplemental new drug applications for baloxavir marboxil. One application concerns the treatment of acute, uncomplicated influenza in pediatric patients from 1 year of age through 12 years of age. Another application addresses the use of baloxavir marboxil for postexposure prophylaxis (<https://www.biospace.com/article/releases/fda-accepts-genentech-s-new-drug-application-for-xofluza-for-the-treatment-of-influenza-in-children-/>).

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

Efforts should be made to create adequate outreach (eg, mobile integrated health care) and infrastructure to facilitate the optimal distribution of vaccine so that more people are immunized. Given the experience with COVID-19, pediatricians should become more involved in pandemic preparedness and disaster planning efforts. 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. Additional information can be found at [www.aap.org/disasters/resourcekit](http://www.aap.org/disasters/resourcekit) and <https://pediatrics.aappublications.org/content/pediatrics/early/2017/05/11/peds.2016-3690.full.pdf>.

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/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 universal influenza vaccines that induce broader protection and eliminate the need for annual vaccination. Understanding the

establishment of immunity against influenza in early life and the development of 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 are needed. Efforts to improve the vaccine development process to allow for a shorter interval between identification of vaccine strains and vaccine production continue. New antiviral drugs are in various development phases, given the need to improve options for the treatment and chemoprophylaxis of influenza.

Pediatricians can remain informed of advances and other updates during the influenza season by following the CDC Influenza page ([www.cdc.gov/flu](http://www.cdc.gov/flu)) and the AAP *Red Book Online* Influenza Resource Page ([www.aapredbook.org/flu](http://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 2020–2021 influenza season.
2. For the 2020–2021 influenza season, the AAP recommends that any licensed influenza vaccine appropriate for age and health status can be used for influenza vaccination in children. Inactivated influenza vaccine (IIV) and live attenuated vaccine (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 vaccine efficacy (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 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 any licensed, age-appropriate IIV available this season, at the dose indicated for the vaccine. No product 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 2020–2021 influenza season remains unchanged and depends on the child's age at the time of the first administered dose and vaccine history (Fig 2).
6. 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, 2020, or whose vaccination status is unknown, 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 2) 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 inactivated influenza vaccine at any time during pregnancy, to protect themselves and their infants, who benefit from the transplacental transfer of antibodies. Women in the postpartum period 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 health care personnel as a crucial element in preventing influenza and reducing health care-associated influenza infections, because health care personnel 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 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 duration of symptoms.
  - Any child, inpatient or outpatient, with severe, complicated, or progressive illness attributable to influenza, regardless of duration of symptoms.
  - Influenza infection of any severity in children at high risk of complications of influenza infection (Table 2), regardless of duration of symptoms.
14. Treatment may be considered for the following individuals:
  - Any previously healthy, symptomatic outpatient not at high risk for influenza complications in whom influenza is confirmed or suspected on the basis of clinical judgment, if treatment can be initiated within 48 hours of illness onset.
  - 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 2).
15. Antiviral chemoprophylaxis is recommended after known or suspected exposure to influenza 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 likely to have ongoing, close exposure to:
    - 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 vaccination among children at high risk, including children who are immunocompromised and may not respond with sufficient protective immune responses following 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.
  - 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.

## ADDITIONAL RESOURCES

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#### ABBREVIATIONS

AAP: American Academy of Pediatrics  
WHO: World Health Organization  
ACIP: Advisory Committee on Immunization Practices  
ANE: acute necrotizing encephalopathy  
ccIV4: quadrivalent cell culture-based inactivated influenza vaccine  
CDC: Centers for Disease Control and Prevention  
FDA: US Food and Drug Administration  
GBS: Guillain-Barré syndrome  
HA: hemagglutinin  
HCP: health care personnel  
IAE: influenza-associated encephalopathy  
IIV: inactivated influenza vaccine  
IIV3: trivalent inactivated influenza vaccine  
IIV4: quadrivalent inactivated influenza vaccine  
IM: intramuscular  
LAIV4: quadrivalent live attenuated influenza vaccine  
NAIs: neuraminidase inhibitors  
PCR: polymerase chain reaction  
PCV13: 13-valent pneumococcal conjugate vaccine  
RIV4: quadrivalent recombinant influenza vaccine  
SARS-CoV-2: severe acute respiratory syndrome-coronavirus 2  
VE: vaccine effectiveness

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