POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
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Recommendations for Prevention and Control of Influenza in Children, 2018–2019

COMMITTEE ON INFECTIOUS DISEASES

abstract

The authors of this statement update 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. Highlights for the upcoming 2018–2019 season include the following:

1. Annual influenza immunization is recommended for everyone 6 months and older, including children and adolescents.

2. The American Academy of Pediatrics recommends an inactivated influenza vaccine (IIV), trivalent or quadrivalent, as the primary choice for influenza vaccination in children because the effectiveness of a live attenuated influenza vaccine against influenza A(H1N1) was inferior during past influenza seasons and is unknown for this upcoming season.

3. A live attenuated influenza vaccine may be used for children who would not otherwise receive an influenza vaccine (eg, refusal of an IIV) and for whom it is appropriate because of age (2 years of age and older) and health status (ie, healthy and without any underlying chronic medical condition).

4. All 2018–2019 seasonal influenza vaccines contain an influenza A(H1N1) vaccine strain similar to that included in the 2017–2018 seasonal vaccines. In contrast, the influenza A(H3N2) and influenza B (Victoria lineage) vaccine strains included in the 2018–2019 trivalent and quadrivalent vaccines differ from those in the 2017–2018 seasonal vaccines.

    a. Trivalent vaccines contain an influenza A(Michigan/45/2015[H1N1]) pdm09–like virus, an influenza A(Singapore/INFIMH-16-0019/2016[H3N2])–like virus (updated), and an influenza B (Colorado/60/2017)–like virus (B/Victoria lineage; updated).

    b. Quadrivalent vaccines contain an additional B virus (Phuket/3073/2013–like virus; B/Yamagata lineage).

5. All children with egg allergy of any severity can receive an influenza vaccine without any additional precautions beyond those recommended for all vaccines.

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6. Pregnant women may receive an influenza vaccine (IIV only) at any time during pregnancy to protect themselves as well as their infants, who benefit from the transplacental transfer of antibodies. Postpartum women who did not receive vaccination during pregnancy should be encouraged to receive an influenza vaccine before discharge from the hospital. Influenza vaccination during breastfeeding is safe for mothers and their infants.

7. The vaccination of health care workers is a crucial step 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.

8. Pediatricians should attempt to promptly identify their patients who are suspected of having an influenza infection for timely initiation of antiviral treatment when indicated and on the basis of shared decision-making between each pediatrician and child caregiver to reduce morbidity and mortality. Although best results are seen when a 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 (see Table 2 in the full policy statement).

KEY POINTS RELEVANT TO THE 2018–2019 INFLUENZA SEASON

1. The American Academy of Pediatrics (AAP) recommends annual influenza vaccination for everyone 6 months and older, including children and adolescents, during the 2018–2019 influenza season. Special effort should be made to vaccinate individuals in the following groups:

- all children, including infants born preterm, 6 months and older (based on chronologic age) with chronic medical conditions that increase the risk of complications from influenza, such as pulmonary diseases (eg, asthma), metabolic diseases (eg, diabetes mellitus), hemoglobinopathies (eg, sickle cell disease), hemodynamically significant cardiac disease, immunosuppression, renal and hepatic disorders, or neurologic and neurodevelopmental disorders;
- all household contacts and out-of-home care providers of children with high-risk conditions or younger than 5 years, especially infants younger than 6 months;
- children and adolescents (6 months–18 years of age) receiving an aspirin- or salicylate-containing medication, which places them at risk for Reye syndrome after influenza virus infection;
- children who are American Indians and/or Alaskan natives;
- all health care personnel (HCP);
- all child care providers and staff; and
- all women who are pregnant, are considering pregnancy, are in the postpartum period, or are breastfeeding during the influenza season.

Children often have the highest attack rates of influenza in the community during seasonal influenza epidemics, play a pivotal role in the transmission of influenza infection to household and other close contacts, and experience relatively elevated morbidity, including severe or fatal complications from influenza infection.[1] In the United States, almost two-thirds of children younger than 6 years and nearly all children 6 years and older spend significant time in child care or school settings outside the home. Exposure to groups of children increases the risk of contracting infectious diseases.[2] Children younger than 2 years are at increased risk of hospitalization and complications attributable to influenza.[1] School-aged children bear a large influenza disease burden and have a significantly higher chance of seeking influenza-related medical care compared with healthy adults.[1] Reducing influenza virus transmission (eg, by using appropriate hand hygiene and respiratory hygiene and/or cough etiquette) among children who attend out-of-home child care or school has been shown to decrease the burden of childhood influenza and transmission of influenza virus to household contacts and community members of all ages.[2]

2. The 2017–2018 influenza season was a high-severity season, with high levels of outpatient clinic and emergency department

Highlights for the 2018–2019 Influenza Season

- Vaccination remains the best available preventive measure to prevent influenza illness.
- Annual influenza vaccine is recommended for everyone 6 months and older.
- ACIP reintroduced LAIV4 as an option for the 2018–2019 influenza season.
- The AAP recommends an IIV (IIV3 or IIV4) as the primary choice for all children because the effectiveness of LAIV4 was inferior against influenza A (/H1N1) during past seasons and is unknown against influenza A (/H1N1) for this upcoming season.
- LAIV4 may be used for children who would not otherwise receive an influenza vaccine (eg, refusal of an IIV) and for whom it is appropriate according to age (ie, 2 years of age and older) and health status (ie, healthy and without any underlying chronic medical condition).
- As always, families should receive counseling on these revised recommendations for the 2018–2019 season.
- Children should receive the influenza vaccine as soon as possible after it is available in their community, preferably by the end of October.
- The No. recommended doses of an influenza vaccine depends on a child's age at the time of the first administered dose and vaccine history.
- All children with egg allergy of any severity can receive either an IIV or LAIV without any additional precautions beyond those recommended for any vaccine.
- Pregnant women may receive an IIV at any time during pregnancy. Postpartum women who did not receive vaccination during pregnancy should be encouraged to receive the vaccine before discharge from the hospital. Vaccination is safe during breastfeeding for mothers and their infants.
- All HCP should receive an annual influenza vaccine, which is a crucial step in preventing influenza and reducing health care–associated influenza infections.
- Antiviral medications are important in the control of influenza but are not a substitute for influenza vaccination.

visits for influenza-like illness (ILI), high influenza-related hospitalization rates, high numbers of pediatric deaths, and elevated and geographically widespread influenza activity across the country for an extended period.[3,4] Influenza A(H3N2) viruses predominated overall for the season through February 2018; influenza B viruses predominated from March 2018 onward. The 2017–2018 season ranks as the third most severe since the 2003–2004 season and was the first to be classified as high severity for all age groups.[3] The peak percentage of outpatient visits for ILI was the third highest recorded since the 1997–1998 season. Although the hospitalization rates for children this season did not exceed the rates reported during the 2009 pandemic, hospitalization surpassed rates reported in previous high-severity influenza A(H3N2)–predominant seasons. Excluding the 2009 pandemic, the 179 pediatric deaths reported through August 18, 2018, during the 2017–2018 season (approximately half of which occurred in otherwise healthy children) are the highest reported since influenza-associated pediatric mortality became a nationally notifiable condition in 2004. Analyses of the influenza A(H1N1)pdm09, influenza A(H3N2), and influenza B (Yamagata lineage) viruses showed that circulating viruses were antigenically and genetically similar to the cell-grown reference viruses representing the 2017–2018 Northern Hemisphere influenza vaccine viruses. Although the overall number of circulating influenza B (Victoria lineage) viruses was low, a substantial amount of antigenic drift from the vaccine reference virus influenza B(Brisbane/60/2008) was observed.[3]

Pediatric hospitalizations and deaths caused by influenza vary by the predominant circulating strain and from one season to the next (Table 1). Historically, 80% to 85% of pediatric deaths have occurred in unvaccinated children 6 months and older. Among pediatric deaths of children 6 months and older who were eligible for influenza vaccination and for whom vaccination status was known, only 22% had received at least 1 dose of an influenza vaccine during the 2017–2018 season.[3] Influenza vaccination is associated with reduced risk of laboratory-confirmed influenza-related pediatric death.[5] In one case cohort analysis in which researchers compared 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[5] found that only 26% of case patients received a vaccine before illness onset compared with average vaccination coverage of 48%. The overall vaccine

TABLE 1 Pediatric Deaths and Hospitalizations by Season and Predominant Strain

Influenza Season	Predominant Strain	Pediatric Deaths	Hospitalizations (0–4 y Old) per 100 000	Hospitalizations (5–17 y Old) per 100 000
2017–2018 (preliminary data)	H3N2	179	71.4	19.7
2016–2017	H3N2	101	43.7	16.7
2015–2016	pH1N1	92	42.4	9.7
2014–2015[a]	H3N2	148	57.2	16.6
2013–2014	pH1N1	111	47.2	9.4
2012–2013	H3N2	171	67	14.6
2011–2012[a]	H3N2	37	16	4
2010–2011	H3N2	124	49.4	9.1
2009–2010	pH1N1	288	77.4	27.2
2008–2009	H1N1	137	28	5
2007–2008	H3N2	88	40.3	5.5

Adapted from Centers for Disease Control and Prevention. FluView 2017–2018 data as of August 18, 2018. Available at: www.cdc.gov/flu/weekly/fluviewinteractive.htm.
[a] Vaccine strains did not change from previous influenza season.

effectiveness against influenza-associated death in children was 65% (95% confidence interval [CI] 54% to 74%). More than one-half of pediatric deaths in this study had ≥1 underlying medical condition with increased risk of severe influenza-related complications; notably, only 1 in 3 of these at-risk children had been vaccinated, yet vaccine effectiveness against death in children with underlying conditions was 51% (95% CI 31% to 67%). Similarly, influenza vaccination reduces by three-fourths the risk of severe, life-threatening laboratory-confirmed influenza in children requiring admission to the ICU.[6] During the past 11 seasons, the rates of influenza-associated hospitalization for children younger than 5 years have always exceeded the rates for children 5 through 17 years of age.

As of August 18, 2018, the following data were reported by the Centers for Disease Control and Prevention (CDC) during the 2017–2018 influenza season:

179 laboratory-confirmed influenza-associated pediatric deaths occurred;

106 were associated with influenza A viruses, 68 were associated with influenza B viruses;

3 were associated with an undetermined type of influenza virus; and

2 were associated with both influenza A and influenza B viruses.

Among the 154 children with known medical history, 51% of the deaths occurred in children with at least one underlying medical condition that is recognized by the Advisory Committee on Immunization Practices (ACIP) to increase the risk of influenza-attributable disease severity. Among children hospitalized with influenza and for whom medical record data were available, approximately 43% had no recorded underlying condition, whereas 26.2% had asthma or a reactive airway disease, 16.8% had a neurologic disorder, and 10.5% had obesity (Fig 1).[3] In a recent study of hospitalizations for influenza A versus influenza B, the odds of mortality were significantly greater with influenza B than with influenza A and were not entirely explained by underlying health conditions.[7]

3. Vaccination remains the best available preventive measure against influenza illness. The universal administration of a seasonal vaccine to everyone 6 months and older is the best strategy available for preventing illness from influenza. Any licensed and age-appropriate inactivated influenza vaccine (IIV) available should be used to vaccinate children. There is notable room for improvement in influenza vaccination because overall influenza vaccination rates have been suboptimal during past seasons in both children and adults. Children's likelihood of being immunized according to recommendations appears to be associated with the immunization practices of their parents. One study revealed that children were 2.77 times (95% CI 2.74 to 2.79) more likely to also be immunized for seasonal influenza if their parents were immunized.[8] 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 an influenza vaccine.

4. The AAP recommends a trivalent inactivated influenza vaccine (IIV3) or quadrivalent inactivated influenza vaccine (IIV4) as the primary choice for influenza vaccination in children because the effectiveness of quadrivalent live attenuated influenza vaccine (LAIV4) against influenza A(H1N1) was inferior during past influenza seasons, and effectiveness is unknown for this upcoming season. Both the AAP Committee on Infectious Diseases and the ACIP of the CDC have reviewed and carefully considered all influenza vaccine efficacy data available to date as well as new information regarding the

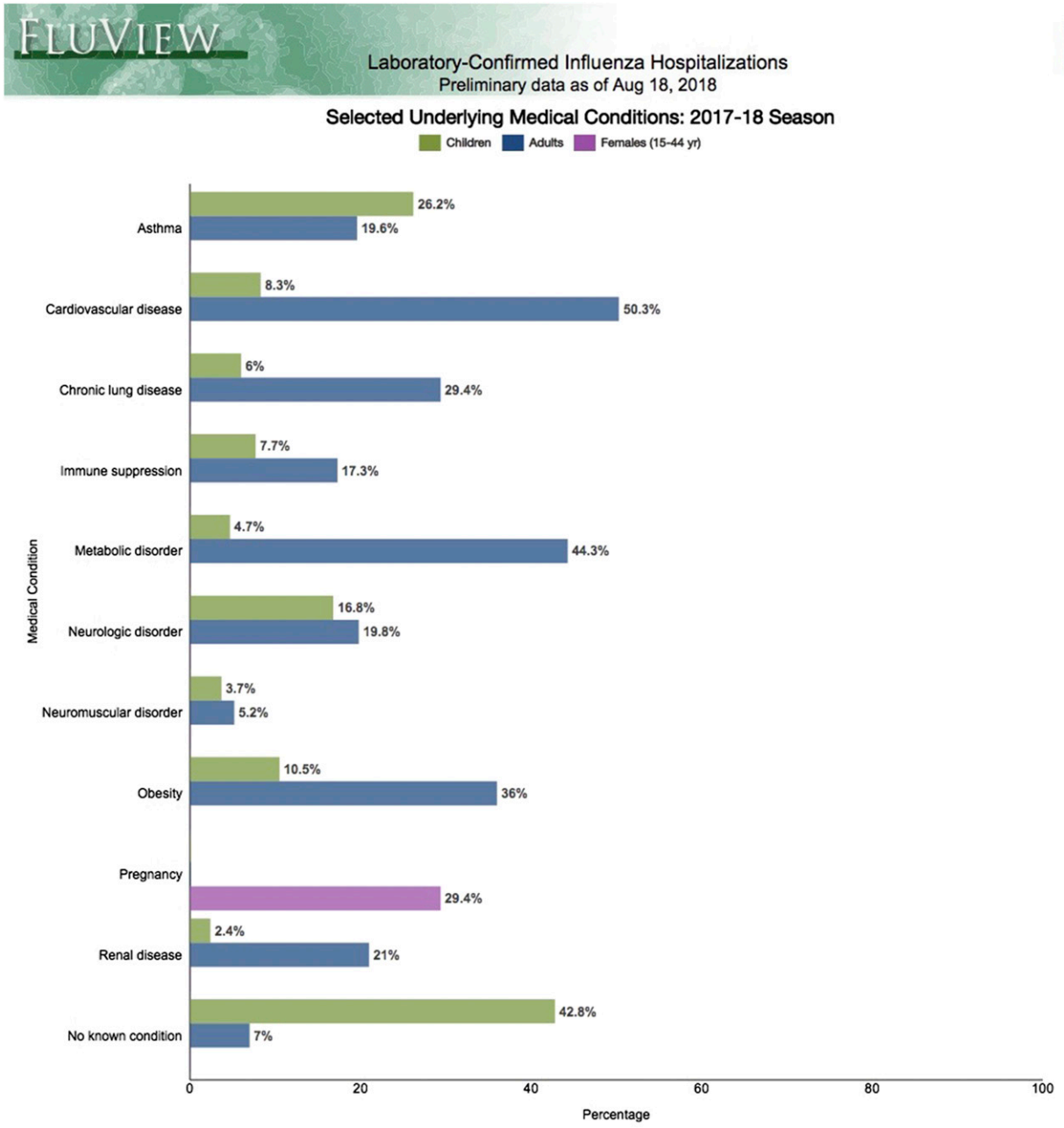

FIGURE 1

Selected underlying medical conditions in patients hospitalized with laboratory-confirmed influenza (Influenza Hospitalization Surveillance Network 2017–2018). Asthma includes a medical diagnosis of asthma or a reactive airway disease. Cardiovascular diseases include conditions such as coronary heart disease, cardiac valve disorders, congestive heart failure, pulmonary hypertension, and aortic stenosis; hypertension disease alone is not included. Chronic lung diseases include conditions such as chronic obstructive pulmonary disease, bronchiolitis obliterans, chronic aspiration pneumonia, and interstitial lung disease. Immune suppression includes conditions such as immunoglobulin deficiency, leukemia, lymphoma, HIV and/or AIDS, and individuals taking immunosuppressive medications. Metabolic disorders include conditions such as diabetes mellitus, thyroid dysfunction, adrenal insufficiency, and liver disease. Neurologic disorders include conditions such as seizure disorders, cerebral palsy, and cognitive dysfunction. Neuromuscular disorders include conditions such as multiple sclerosis and muscular dystrophy. Obesity was assigned if indicated in a patient's medical chart of if BMI was >30. Pregnancy percentage was calculated by using the number of female case patients between 15 and 44 years of age as the denominator. Renal diseases include conditions such as acute or chronic renal failure, nephrotic syndrome, glomerulonephritis, and impaired creatinine clearance. No known condition indicates that the case patient did not have any known underlying medical condition indicated in the medical chart at the time of hospitalization. (Reprinted from Centers for Disease Control and Prevention. FluView 2017–2018 preliminary data as of August 18, 2018. Available at: gis.cdc.gov/grasp/fluview/FluHospChars.html.)

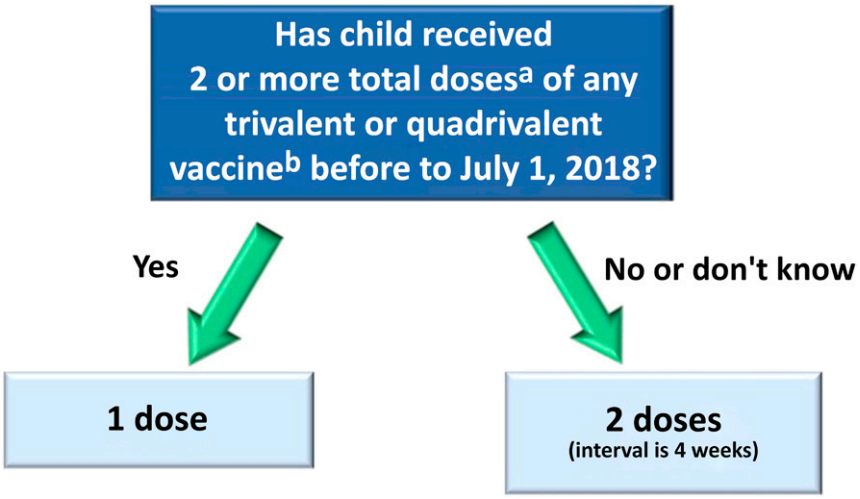

FIGURE 2

The number of 2018–2019 seasonal influenza vaccine doses for children 6 months through 8 years of age. [a] The 2 doses need not have been received during the same season or consecutive seasons. [b] Receipt of LAIV4 in the past is still expected to have primed a child's immune system despite recent evidence for poor effectiveness. There currently are no data that suggest otherwise.

updated LAIV4 formulation available for the 2018–2019 season to provide their latest recommendations. Although the AAP and CDC each support the use of LAIV4 for the 2018–2019 influenza season with the aim of achieving adequate vaccination coverage and optimal protection in children of all ages, the AAP recommends vaccination with IIV3 or IIV4 for all children and LAIV4 for children who would not otherwise receive an influenza vaccine (eg, refusal of an IIV) and for whom it is appropriate according to age (ie, 2 years of age and older) and health status (ie, healthy and without any underlying chronic medical condition).

5. Both trivalent and quadrivalent influenza vaccines are available in the United States for the 2018–2019 season. To vaccinate as many people as possible for this influenza season, neither vaccine formulation is preferred over the other. Although manufacturers anticipate an adequate supply of the quadrivalent vaccine, pediatricians should administer whichever formulation is available in their communities. The trivalent vaccine contains an influenza A(Michigan/45/2015[H1N1]) pdm09–like virus, an influenza A(Singapore/INFIMH-16-0019/2016[H3N2])–like virus, and an influenza B(Colorado/60/2017)–like virus (B/Victoria lineage). The influenza A(H3N2) virus component is updated because the egg-propagated influenza A (Singapore) vaccine virus is antigenically more similar to circulating viruses. The influenza B component is updated because of the increasing global circulation of an antigenically drifted influenza B (Victoria lineage) virus. The quadrivalent vaccine contains an additional influenza B(Phuket/3073/2013)–like virus (B/Yamagata lineage), which is the same as last season.

6. The number of seasonal influenza vaccine doses to be administered in the 2018–2019 influenza season remains the same and depends on a child's age at the time of the first administered dose and vaccine history (Fig 2)**:**

- Influenza vaccines are not licensed for administration to infants younger than 6 months.
- Children 9 years and older need only 1 dose.
- Children 6 months through 8 years of age need the following:
  - 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or live attenuated influenza vaccine [LAIV]) before July 1, 2018. The interval between the 2 doses should be at least 4 weeks; or
  - 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, 2018. The 2 previous doses do not need to have been received during the same influenza season or consecutive influenza seasons.

Vaccination should not be delayed to obtain a specific product for either dose. Any available age-appropriate trivalent or quadrivalent vaccine can be used. A child who receives only 1 of the 2 doses as a quadrivalent formulation is likely to be less primed against the additional influenza B virus.

7. 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.[1] Medical liability issues and medical record documentation requirements need to be considered before a pediatrician begins immunizing adults.[9] (see risk management guidance associated with adult immunizations at http://pediatrics.aappublications.org/content/129/1/e247). Pediatricians are reminded to document the recommendation for adult vaccination in the child's medical record. In addition, adults should still be encouraged to have a medical home and communicate their vaccination status to their primary care providers. Offering adult vaccinations in the pediatric

TABLE 2 People at High Risk of Influenza Complications and Thus Recommended for Antiviral Treatment of Suspected or Confirmed Influenza

Children <5 years and especially <2 years
Adults ≥50 years
People with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), or metabolic disorders (including diabetes mellitus) or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury)
People with immunosuppression, including that caused by medications or by HIV infection
All women who are pregnant, are considering pregnancy, or are in the postpartum period during the influenza season
People <19 years old who are receiving long-term aspirin therapy
American Indian and/or Alaskan native people
People with extreme obesity (ie, BMI ≥40)
Residents of nursing homes and other chronic care facilities
Hospitalized patients at high risk of influenza complications

Adapted from Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 influenza season. *MMWR Recomm Rep.* 2018;67(3):1–20.

practice setting would not be intended to undermine the adult medical home model but could serve as an additional venue for parents and other care providers of children to receive influenza vaccines. 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 the influenza vaccine.

8. Pregnant women who are immunized against influenza at any time during their pregnancy can provide protection for infants during their first 6 months of life, when they are too young to receive the influenza vaccine themselves, through transplacental passage of antibodies. Postpartum women who did not receive an influenza vaccination during pregnancy should be encouraged to discuss with their obstetricians receipt of the vaccine before discharge from the hospital. Vaccination during breastfeeding is safe for mothers and their infants. Pregnant women are a population of special concern because they are at increased risk for complications from influenza. Influenza vaccination is recommended by the ACIP and the American College of Obstetricians and Gynecologists for all women at any trimester of gestation for the protection of mothers against influenza and its complications.[1,10] Substantial evidence has been 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.[11–17] Infants born to women who receive an influenza vaccination during pregnancy can have a risk reduction of 72% (95% CI 39% to 87%) for laboratory-confirmed influenza hospitalization in the first few months of life.[18]

Any licensed, recommended, and age-appropriate trivalent or quadrivalent inactivated vaccine may be used to vaccinate pregnant women, including quadrivalent recombinant inactivated vaccine (RIV4).[1] However, experience with the use of RIVs in pregnant women 18 years and older is limited because RIVs have been available only since the 2013–2014 influenza season. Substantial data indicate that an IIV does not cause fetal harm when administered to a pregnant woman, although data on the safety of influenza vaccination in the early first trimester are limited.[19] A cohort study from the Vaccines and Medications in Pregnancy Surveillance System of vaccine exposure during the 2010–2011 through 2013–2014 seasons revealed no significant association of spontaneous abortion with influenza vaccine exposure in the first trimester or within the first 20 weeks of gestation.[20] Although researchers in previous studies have not noted any association between influenza vaccination and adverse pregnancy outcomes, one recent observational Vaccine Safety Datalink (VSD) study conducted during the 2010–2011 and 2011–2012 influenza seasons noted an association between the receipt of an IIV containing H1N1pdm09 and early spontaneous abortion when an H1N1pdm-09–containing vaccine had also been received the previous season.[21] A follow-up study is in progress. The ACIP influenza vaccine recommendations for pregnant women have not been changed for this coming season.

9. As soon as a seasonal influenza vaccine becomes available locally, pediatricians or vaccine administrators should encourage immunization of HCP, notify parents and caregivers of vaccine availability and the importance of annual vaccination, and immunize children 6 months and older per recommendations, especially those at high risk of complications from influenza. This strategy is particularly important for children who need 2 doses of the influenza vaccine to achieve optimal protection before the circulation of influenza viruses in the

community. Children should receive the first dose as soon as possible after a vaccine becomes available to allow sufficient time for receipt of the second dose ≥4 weeks later, preferably by the end of October. The onset and duration of influenza circulation is unpredictable. To effectively protect children, prompt initiation of influenza vaccination and continuing to vaccinate throughout the influenza season, regardless of whether influenza is circulating (or has circulated) in the community, are important components of an effective vaccination strategy. Protective immune responses generally persist in children throughout the influenza season. Although there is limited evidence that waning immunity from early administration of the vaccine increases the risk of infection in children, authors of recent reports raise the possibility that early vaccination of adults, particularly the elderly, might contribute to reduced protection later in the influenza season. Older adults are recognized as having a less robust immune response to influenza vaccines. A multiseason analysis from the US Influenza Vaccine Effectiveness Network revealed that vaccine effectiveness declined by approximately 7% per month for H3N2 and influenza B and by 6% to 11% per month for H1N1pdm09 in individuals 9 years and older.[22] Vaccine effectiveness remained greater than zero for at least 5 to 6 months after vaccination. Further evaluation is needed before any policy change in timing is made. An early onset of the influenza season is another concern about delayed vaccination. Until there are definitive data that can be used to determine whether waning immunity influences vaccine effectiveness in children, the administration of the influenza vaccine should not be delayed to a later date because this increases the likelihood of missing influenza vaccination altogether.

10. To effectively protect children, providers may continue to offer the vaccine until June 30 of each year, when the seasonal influenza vaccine expires, because the duration of influenza circulation is unpredictable. Although peak influenza activity in the United States tends to occur from January through March, influenza activity can occur in early fall (October) or late spring (end of May) and may have more than one disease peak. Similarly, although influenza activity in the United States is typically low during the summer, influenza cases and outbreaks also can occur. Furthermore, this approach also allows for optimal ability to immunize travelers, particularly international travelers, who may be exposed to influenza yearround depending on their destinations.

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

- Plan to make influenza vaccination easily accessible for all children. Examples include sending alerts to families that a vaccine is available (eg, e-mails, texts, letters, and patient portals); creating walk-in influenza vaccination clinics; extending hours beyond routine times during peak vaccination periods; administering an influenza vaccine during both well-child examinations and sick visits as well as to patients who are hospitalized, especially those at high risk of influenza complications, before discharge from the hospital (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)[9] at the same time in the same office setting 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 emergency departments, to expand venues for administering the vaccine. If a child receives the 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 appropriately prioritize distribution to the primary care office setting and patient-centered medical homes before other venues, especially when vaccine supplies are delayed or limited. Similar efforts should be made to assuage the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children Program.
- Public health will benefit from pediatricians' discussions about vaccine safety, effectiveness, and indications. Pediatricians can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children, emphasizing when a second dose of the vaccine is indicated, and explaining why the intranasal formulation is not recommended for routine use in all children. The AAP and CDC have created communication resources to convey these important messages and help the public understand influenza

recommendations. Resources will be available in the *Red Book Online* (https://redbook.solutions.aap.org/selfserve/ssPage.aspx?SelfServeContentId=influenza-resources).[23]

- The AAP supports mandatory influenza vaccination programs for all HCP in all settings, including outpatient settings. HCP should act as role models for both their patients and colleagues by receiving influenza vaccination annually and letting others know that they have received the vaccine, highlighting the safety and effectiveness of annual influenza vaccination. Influenza vaccination programs for HCP benefit the health of employees, their patients, and members of the community. Mandatory influenza immunization for all HCP is considered to be ethical, just, and necessary to improve patient safety. Employees of health care institutions are asked to act in the best interests of the health of their patients and to honor the requirement of causing no harm.

12. Antiviral medications are important in the control of influenza but are not a substitute for influenza vaccination. The neuraminidase inhibitors (NAIs) oral oseltamivir (Tamiflu) and inhaled zanamivir (Relenza) are the best-studied antiviral medications recommended for chemoprophylaxis or the treatment of influenza in children during the 2018–2019 season.[24] Intravenous peramivir (Rapivab), a third NAI, was approved in September 2017 as a treatment of acute uncomplicated influenza in children 2 years and older who are not hospitalized and have been symptomatic for no more than 2 days. Intravenous zanamivir is not approved in the United States and is not available for compassionate use.[25] Intravenous formulations are especially important as the only treatment option for serious influenza infection in those children who cannot absorb orally or enterally administered oseltamivir or tolerate inhaled zanamivir.

Recent viral surveillance and resistance data from the CDC and the World Health Organization reveal that the majority of currently circulating influenza viruses likely to cause influenza in North America during the 2018–2019 season continue to be susceptible to oseltamivir, zanamivir, and peramivir.[1] If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, recommendations for alternative system treatment, such as the use of intravenous zanamivir,[25,26] will be available from the CDC and AAP. Resistance characteristics can also change for an individual child over the duration of a treatment course, especially in those who are severely immunocompromised and may receive extended courses of antiviral medications because of prolonged viral shedding. Up-to-date information on current recommendations and therapeutic options can be found on the AAP Web site (www.aap.org) or in the *Red Book Online*, through state-specific AAP chapter Web sites, or on the CDC Web site.[27]

SEASONAL INFLUENZA VACCINES

Before the 2013–2014 influenza season, only trivalent influenza vaccines that included a single influenza B strain were available. Since the 1980s, 2 antigenically distinct lineages (ie, Victoria or Yamagata) of influenza B viruses have circulated globally. Vaccination against 1 influenza B viral lineage generally confers little cross-protection against the other influenza B viral lineage. Thus, trivalent vaccines offer limited immunity against circulating influenza B strains of the lineage not present in the vaccine. Furthermore, in recent years, it has proven difficult to predict consistently which influenza B lineage will predominate during a given influenza season. Therefore, a quadrivalent vaccine with influenza B strains of both lineages would be predicted to offer additional protection, but there is no evidence at this time that a quadrivalent vaccine is more effective. Table 3 includes a summary of information on the types of influenza vaccines licensed for children and adults during the 2018–2019 season. More than 1 product may be appropriate for a given patient. Vaccination should not be delayed to obtain a specific product.

IIVs

For the 2018–2019 season, an IIV will be available for intramuscular injection in both IIV3 and IIV4 formulations. IIVs do not contain a live virus. The available IIV formulations and age groups for which use is approved are presented in Table 4. IIV formulations can be used in healthy children as well as those with underlying chronic medical conditions. The most common adverse events after IIV3 administration are local injection site pain and tenderness. Fever occurs within 24 hours after immunization in approximately 10% to 35% of children younger than 2 years but rarely in older children and adults. Mild systemic symptoms, such as nausea, lethargy, headache, muscle aches, and chills, may occur after the administration of IIV3. Several formulations of IIV4 are now available with specific age indications, including brands licensed for use in children as young as 6 months. In children, the most common injection site adverse reactions after the administration of IIV4 are 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.

TABLE 3 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2018–2019 Influenza Season

Vaccine	Trade Name	Manufacturer	Presentation	Thimerosal Mercury Content (μm of Hg per 0.5 mL Dose)	Age Group	CPT Code
Inactivated						
IIV3	Fluzone high-dose	Sanofi Pasteur	0.5 mL prefilled syringe	0	≥65 y	90662
IIV3	Afluria	Seqirus	0.5 mL prefilled syringe	0	≥5 y	90656
			5.0 mL multidose vial	24.5	≥5 y	90658
aIIV3	Fluad	Seqirus	0.5 mL prefilled syringe	0	≥65 y	90653
ccIIV4	Flucelvax quadrivalent	Seqirus	0.5 mL prefilled syringe	0	≥4 y	90674
			5.0 mL multidose vial	25	≥4 y	90756
IIV4	Fluzone quadrivalent	Sanofi Pasteur	0.25 mL prefilled syringe	0	6–35 mo	90685
			0.5-mL prefilled syringe	0	≥36 mo	90686
			5.0 mL multidose vial	25	≥6 mo	90687, 90688
IIV4	Fluarix quadrivalent	GlaxoSmithKline	0.5 mL prefilled syringe	0	≥6 mo	90686
IIV4	FluLaval quadrivalent	ID Biomedical Corporation of Quebec	0.5 mL prefilled syringe	0	≥6 mo	90686
		Distributed by GlaxoSmithKline	5.0 mL multidose vial	<25	≥6 mo	90688
IIV4	Afluria quadrivalent	Seqirus	0.5 mL prefilled syringe	0	≥5 y	90686
			5.0 mL multidose vial	24.5	≥5 y	90688
Recombinant						
RIV4	Flublok quadrivalent	Protein Sciences Corporation (distributed by Sanofi Pasteur)	0.5 mL prefilled syringe	0	≥18 y	90682
Live attenuated						
LAIV4	FluMist quadrivalent	MedImmune	0.2 mL prefilled intranasal sprayer	0	2–49 y	90672

aIIV3, adjuvanted inactivated influenza vaccine trivalent; ccIIV4, quadrivalent cell culture–based inactivated influenza vaccine; CPT, *Current Procedural Terminology.* Implementation guidance on supply, pricing, payment, CPT coding, and liability issues can be found in the *Red Book Online*.[28] Adapted from American Academy of Pediatrics, Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2017–2018. *Pediatrics.* 2017;140(4):e20172550; and Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal in uenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 influenza season. MMWR Recomm Rep. 2018;67(3):1–20.

These events are reported with comparable frequency with IIV3s. Therefore, an IIV4 is available for people ≥6 months old when otherwise appropriate and may offer broader protection against circulating influenza B strains than an IIV3.

This is the first influenza season during which several vaccine products are licensed for children 6 through 35 months of age, as listed in Table 3. All of these vaccines are quadrivalent, but the dose volumes and antigen amounts vary among different IIV products. In addition to the 0.25 mL (7.5 μg of hemagglutinin per vaccine virus) Fluzone vaccine, 2 other IIV4 vaccines containing 15 μg of hemagglutinin per vaccine virus per 0.5 mL dose (Fluarix and FluLaval) are now available for children 6 through 35 months of age.

TABLE 4 Summary of Antiviral Treatment of Clinical Influenza During the 2018–2019 Season

Offer Treatment ASAP to Children	Consider Treatment ASAP for
Hospitalized with suspected influenza Hospitalized for severe, complicated, or progressive illness attributable to influenza regardless of duration of symptoms With suspected influenza (of any severity) and at high risk of complications	Any healthy child with suspected influenza Healthy children with suspected influenza who live at home with a sibling or household contact who is <6 months old or has a medical condition that predisposes to complications

ASAP, as soon as possible.

Before November 2016, the only IIV formulations licensed for children 6 through 35 months of age were the 0.25 mL (containing 7.5 μg of hemagglutinin per vaccine virus) dose formulations of Fluzone and Fluzone Quadrivalent. The recommendation for the use of a reduced dose and volume for children in this age group (half of that recommended for people ≥3 years of age) was based on the increased reactogenicity noted among children (particularly younger children) after older influenza vaccines, primarily whole-virus inactivated vaccines. Currently available split-virus inactivated products have demonstrated less reactogenicity.[1]

Given that the formulations of IIV4 vaccines for children 6 through 35 months of age are different, care should be taken to administer the appropriate, recommended 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 a multidose vial (a maximum of 10 doses can be withdrawn from a multidose vial) as supplied by the manufacturer. Note that for Fluzone, if a 0.5 mL single-use vial of Fluzone Quadrivalent is used for a child between 6 and 35 months of age, only half the volume (0.25 mL) should be administered to provide the currently approved dose for this product, and the other half should be discarded. A 0.5 mL unit dose of any IIV should not be split into 2 separate 0.25 mL doses because of safety concerns for lack of sterility, variance with the package insert, and potential compliance difficulties with vaccine excise taxes.

Children 36 months of age and older can receive any licensed IIV. All IIVs licensed for children of this age in the United States are split-product, egg-based, inactivated vaccines administered in a 0.5 mL dose and containing 15 μg of hemagglutinin from each strain in the vaccine.

Two quadrivalent influenza vaccines manufactured by using newer technologies will be available during the 2018–2019 season, 1 of which can be used in children. A recombinant baculovirus-expressed hemagglutinin influenza vaccine (RIV4) for people 18 years and older is produced in cell culture, and a quadrivalent cell culture–based IIV is available for individuals 4 years and older. Both of these vaccines are also administered intramuscularly. No preference is expressed for RIV4 versus IIVs within specified indications.

The US Food and Drug Administration (FDA) licensed a trivalent MF59 adjuvanted IIV for people 65 years and older in November 2015; it was the first adjuvanted influenza vaccine marketed in the United States. Adjuvants may be included in a vaccine to elicit a more robust immune response, which could lead to a reduction in the number of doses required for children. In 1 recent study of children, the relative vaccine efficacy of an MF-59 adjuvanted influenza vaccine was significantly greater than a nonadjuvanted vaccine in the 6- through 23-month age group.[29] However, adjuvanted seasonal influenza vaccines are not licensed for children at this time.

During the 2 influenza seasons spanning 2010 through 2012, there were increased reports of febrile seizures in the United States in young children who received an IIV3 and the 13-valent pneumococcal conjugate vaccine (PCV13) concomitantly. Subsequent retrospective analyses of past seasons revealed a slight increase in the risk of febrile seizures in children 6 through 23 months of age when PCV13 vaccines are administered concomitantly with an IIV.[30] The concomitant administration of an IIV3, PCV13, and the diphtheria-tetanus-acellular pertussis vaccine was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated compared 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, the largest vaccine safety surveillance program in the United States, revealed that there was no significant increase in febrile seizures associated with the concomitant administration of these 3 vaccines in children 6 to 59 months of age during the 2010–2011 season.[31] In a subsequent sentinel Center for Biologics Evaluation and Research–Post-Licensure Rapid Immunization Safety Monitoring surveillance report looking at influenza vaccines and febrile seizures in the 2013–2014 and 2014–2015 influenza seasons, there was no evidence of an elevated risk of febrile seizures in children 6 to 23 months of age after IIV vaccination during the 2013–2014 and 2014–2015 seasons. It was concluded that the risk of seizures after PCV13 or concomitant PCV13 and IIV administration is low compared with a child's lifetime risk of febrile seizures due to other causes.[32] Although the possibility of increased risk for febrile seizures cannot be ruled out, the simultaneous administration of an IIV with PCV13 and/or other vaccines for the 2018–2019 influenza season continues to be recommended when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of an IIV and PCV13 or the diphtheria-tetanus-acellular pertussis vaccine outweigh the risk of febrile seizures, which rarely have any long-term sequelae.

A large body of scientific evidence reveals that thimerosal-containing vaccines are not associated with increased risk of autism spectrum disorders in children.[1] Thimerosal from vaccines has not been linked to any medical condition. As such, the AAP extends its strongest support to the current World Health Organization recommendations to retain the use of thimerosal as a preservative in multiuse vials in the global vaccine supply. Some people may still raise concerns about the trace amount of thimerosal in some IIV vaccine formulations (Table 3), and in some states, including California, Delaware, Illinois, Missouri, New York, and Washington, there is a legislated restriction on the use of thimerosal-containing vaccines. The benefits of protecting children against the known risks of influenza are clear. Therefore, to the extent authorized by state law, children should receive any available formulation of an IIV rather than delay vaccination while waiting for reduced thimerosal content or thimerosal-free vaccines. Although some IIV formulations contain a trace amount of thimerosal, thimerosal-free IIV products can be obtained (Table 3). To respond to consumer

requests, vaccine manufacturers are delivering increasing amounts of thimerosal-free influenza vaccines each year.

Live Attenuated (Intranasal) Influenza Vaccine

For the 2018–2019 influenza season, the AAP recommends LAIV4 to be used for children who would not otherwise receive an influenza vaccine (eg, refusal of an IIV) and for whom it is appropriate according to age (ie, 2 years of age and older) and health status (ie, healthy and without any underlying chronic medical condition). This recommendation represents a change from the 2016–2017 and 2017–2018 influenza seasons, when intranasal LAIV4 was not recommended in any setting in light of the evidence of its poor effectiveness in previous seasons against influenza A(H1N1)pdm09 viruses. After reviewing studies on the effectiveness of LAIV4 during past seasons, the ACIP of the CDC recommended that LAIV4 be an option for influenza vaccination in people for whom it is appropriate for the 2018–2019 season.[1] Although the AAP and the CDC each support the use of LAIV4 for the 2018–2019 season with the aim of achieving adequate vaccination coverage and optimal protection in children of all ages and both acknowledge that efficacy data are not available for the current LAIV4 formulation, the AAP recommends IIV3 or IIV4 as the primary choice of influenza vaccine for all children.

LAIV was initially licensed in the United States in 2003 as a trivalent formulation. LAIV4 has been licensed in the United States since 2012 and was first available during the 2013–2014 influenza season, replacing trivalent live attenuated influenza vaccine (LAIV3). Recommended for people 2 through 49 years of age, LAIV4 is administered intranasally. The most commonly reported reactions in children were runny nose or nasal congestion, headache, decreased activity or lethargy, and sore throat. LAIV4 should not be administered to people with notable nasal congestion because that can impede vaccine delivery. The safety of LAIV in people with a history of asthma, diabetes mellitus, or other high-risk medical conditions associated with an elevated risk of complications from influenza (see the section on contraindications and precautions) has not been firmly established. In postlicensure surveillance of LAIV over 7 seasons, the Vaccine Adverse Event Reporting System, jointly sponsored by the FDA and CDC, did not identify any new or unexpected safety concerns, although there were reports of the use of LAIV in people with a contraindication or precaution. Although the use of LAIV in young children with chronic medical conditions, including asthma, has been implemented outside of the United States, data are considered insufficient to support an expanded recommendation in the United States.

The CDC conducted a systematic review of all published studies evaluating the effectiveness of LAIV3 and LAIV4 in children from the 2010–2011 to the 2016–2017 seasons, including data from United States and European studies.[1,33] The data revealed that the effectiveness of LAIV3 or LAIV4 for influenza strain A (H1N1) was lower than that of an IIV in children 2 to 17 years of age. A LAIV was more effective against influenza B strains and similarly effective against influenza A(H3N2) in some age groups compared with an IIV.

For the 2017–2018 season, a new influenza A(/H1N1) pdm09–like virus, influenza A/Slovenia/2903/2015, was included in LAIV4, replacing influenza A/Bolivia/559/2013. In a study conducted by the LAIV4 manufacturer, researchers evaluated viral shedding and immunogenicity associated with the LAIV4 formulation containing the new influenza A(/H1N1)pdm09–like virus among US children 24 months through 3 years of age. Shedding and immunogenicity data provided by the manufacturer reveal that the new influenza A(H1N1)pdm09–like virus included in its latest formulation has improved replicative fitness over previous LAIV4 influenza A(H1N1) pdm09–like vaccine strains, resulting in an improved immune response comparable to that of the LAIV3 available before the 2009 pandemic. Shedding and replicative fitness are not known to be correlated with efficacy, and no published effectiveness estimates for this formulation of the vaccine against influenza A(H1N1)pdm09 viruses are available because influenza A(H3N2) and influenza B viruses predominated during the 2017–2018 Northern Hemisphere season.

The effectiveness of influenza vaccines varies and is affected by many factors, including age and health status of the recipient, influenza type and subtype, previous vaccinations, and degree of antigenic match between the vaccine and circulating viruses. It is possible that vaccine effectiveness also differs among different individual vaccine products (for example, different IIVs); however, product-specific comparative effectiveness data are lacking for most vaccines. Although national influenza vaccination coverage among children did not decline during the past 2 seasons, when LAIV was not recommended in the United States, overall vaccination coverage remains suboptimal. Additional options for the vaccination of children may provide a means to improve coverage, particularly in school-based settings.

Particular focus should be placed on the administration of an IIV in

all children and adolescents with underlying medical conditions associated with an elevated risk of complications from influenza. Achieving high coverage rates of influenza vaccine in infants and children is a priority to protect them against influenza disease and its complications. Additional experience over multiple influenza seasons will help to determine optimal use of the available vaccine formulations in children.

INFLUENZA VACCINES AND EGG ALLERGY

It is not necessary to inquire about egg allergy before the administration of any influenza vaccine, including on screening forms. There is strong evidence that individuals with egg allergy can safely receive an influenza vaccine without any additional precautions beyond those recommended for any vaccine.[1,34,35] The presence of egg allergy in an individual is not a contraindication to receive an IIV or LAIV. Influenza vaccine recipients with egg allergy are at no greater risk for a systemic allergic reaction than those without egg allergy. 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. Standard vaccination practice for all vaccines in children should include the ability to respond to rare acute hypersensitivity reactions. Patients who refuse to receive an egg-based vaccine may be vaccinated with an age-appropriate recombinant or cell-cultured product. Children who have had a previous allergic reaction to any component of the influenza vaccine, for any reason, should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate.

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).[36] The AAP recommends the development of a written disaster plan for all practice settings. Additional information is available on the AAP Web site.[37]

Any of the influenza vaccines can be administered at the same visit with all other recommended routine vaccines.

Intramuscular Vaccine

IIVs for intramuscular injection are shipped and stored at 2°C to 8°C (36°F–46°F); frozen vaccines 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. Most vaccines have variable immune responses in young children. This is the first influenza season for which 3 vaccine products are available for children 6 through 35 months of age, as listed in Table 3. The dose volume of the available vaccines, 2 of which contain twice the amount of antigen in this young age group, varies for these different brands, so care should be taken by clinicians to administer the correct dose. Clinical data reveal comparable immunogenicity and reactogenicity for these vaccines with the one used in this age group in recent seasons and administered as 0.25 mL per dose (Table 3). Although the amount of antigen differs, the number of doses required with either vaccine for this age group is the same. A 0.5 mL unit dose of any IIV should not be split into 2 separate 0.25 mL doses because of safety concerns for lack of sterility, variance with the package insert, and potential compliance difficulties with vaccine excise taxes.

LAIV4

The cold-adapted, temperature-sensitive LAIV4 formulation currently licensed in the United States is shipped and stored at 2°C to 8°C (35°F–46°F) and administered intranasally in a prefilled, single-use sprayer containing 0.2 mL of the vaccine. A removable dose-divider clip is attached to the sprayer to facilitate the administration of 0.1 mL separately into each nostril. After the administration of any live virus vaccine, at least 4 weeks should pass before another live-virus vaccine is administered.

CURRENT AAP RECOMMENDATIONS

Seasonal influenza vaccination is recommended for all children 6 months and older. The AAP recommends an IIV (IIV3 or IIV4) as the primary influenza vaccine choice for all children because the effectiveness of LAIV4 was inferior against influenza A(H1N1) during past seasons, and effectiveness is unknown against influenza A(H1N1) for this upcoming season. LAIV4 may be used for children who would not otherwise receive an influenza vaccine (eg, refusal of an IIV) and for whom it is appropriate according to age (ie, 2 years of age and older) and health status (ie, healthy and without any underlying chronic medical condition). Additional details on the contraindications and precautions for the use of all influenza vaccines are listed below.

Children and adolescents with certain underlying medical conditions have an elevated risk of complications from influenza, including the following:

- asthma or other chronic pulmonary diseases, including cystic fibrosis;

- hemodynamically significant cardiac disease;
- immunosuppressive disorders or therapy;
- HIV infection;
- sickle cell anemia and other hemoglobinopathies;
- diseases that necessitate long-term aspirin therapy or salicylate-containing medication, including juvenile idiopathic arthritis or Kawasaki disease, that may place a child at increased risk of Reye syndrome if infected with influenza;
- chronic renal dysfunction;
- chronic metabolic disease, including diabetes mellitus;
- any condition that can compromise respiratory function or handling of secretions or increase the risk of aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities; and
- pregnancy.

Particular efforts should be made to ensure vaccination in the following groups to prevent the transmission of influenza to those at risk, unless contraindicated:

- household contacts and out-of-home care providers of children younger than 5 years and at-risk children of all ages;
- close contacts of people with immunosuppression;
- any woman who is pregnant or considering pregnancy, is in the postpartum period, or is breastfeeding during the influenza season. It is safe to administer an IIV to pregnant women during any trimester of gestation and postpartum. Any licensed, recommended, and age-appropriate trivalent or quadrivalent IIV or RIV4 may be used, although experience with the use of RIV4 in pregnant women is limited. LAIV is contraindicated during pregnancy. Studies have shown that infants born to women who are immunized have better influenza-related health outcomes compared with infants of women who are unimmunized. However, according to Internet-based panel surveys conducted by the CDC, only approximately 47% of pregnant women during the 2016–2017 influenza season and 35.6% of pregnant women during the 2017–2018 season (according to preliminary data) reported receiving an influenza vaccine, although both pregnant women and their newborn infants are at a higher risk of complications. More data on the safety of influenza vaccination in the early first trimester are becoming available. In a 5-year retrospective cohort study from 2003 to 2008 of more than 10 000 women, influenza vaccination in the first trimester was not associated with an increase in the rates of major congenital malformations.[18] 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 reveal any association between congenital defects and influenza vaccination in any trimester, including the first trimester of gestation.[38] 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 with these outcomes. A cohort study from the Vaccines and Medications in Pregnancy Surveillance System of vaccine exposure during the 2010–2011 through 2013–2014 seasons revealed no significant association of spontaneous abortion with influenza vaccine exposure in the first trimester or within the first 20 weeks of gestation.[20] Although researchers in most studies have not noted an association between influenza vaccination and adverse pregnancy outcomes, 1 recent observational Vaccine Safety Datalink study conducted during the 2010–2011 and 2011–2012 seasons revealed an association between receipt of an IIV containing H1N1pdm09 and risk of spontaneous abortion when an H1N1pdm-09–containing vaccine had also been received the previous season.[21] A follow-up study is in progress, and ACIP influenza vaccine recommendations for pregnant women have not been changed for this coming season;

- breastfeeding mothers. Breastfeeding is strongly recommended to protect against influenza viruses because it activates 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.[39] Greater exclusivity of breastfeeding in the first 6 months of life decreases the episodes of respiratory illness with fever in infants of mothers who are 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.[40,41] Breastfeeding should be encouraged even if the mother or infant has influenza. The mother should pump and feed expressed breast milk if she or her infant

TABLE 5 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis in Children for the 2018–2019 Influenza Season: United States

Medication	Treatment (5 d)	Chemoprophylaxis (10 d)
Oseltamivir[a]		
Adults	75 mg twice daily	75 mg once daily
Children ≥12 mo		
Body wt		
≤15 kg (≤33 lb)	30 mg twice daily	30 mg once daily
>15–23 kg (33–51 lb)	45 mg twice daily	45 mg once daily
>23–40 kg (>51–88 lb)	60 mg twice daily	60 mg once daily
>40 kg (>88 lb)	75 mg twice daily	75 mg once daily
Infants ages 9–11 mo[b]	3.5 mg/kg per dose twice daily	3.5 mg/kg per dose once daily
Term infants ages 0–8 mo[b]	3 mg/kg per dose twice daily	3 mg/kg per dose once daily for infants 3–8 mo old; not recommended for infants <3 mo old unless situation judged critical because of limited safety and efficacy data in this age group
Preterm infants	See details in footnote[c]	—
Zanamivir[d]		
Adults	10 mg (two 5 mg inhalations) twice daily	10 mg (two 5 mg inhalations) once daily
Children (≥7 y old for treatment; ≥5 y old for chemoprophylaxis)	10 mg (two 5 mg inhalations) twice daily	10 mg (two 5 mg inhalations) once daily
Peramivir		
Adults	600 mg intravenous infusion once given over 15–30 min	—
Children (2–12 y old)	One 12 mg/kg dose, up to 600 mg maximum, via intravenous infusion for 15–30 min	—
Children (13–17 y old)	One 600 mg dose via intravenous infusion for 15–30 min	—

Adapted from Centers for Disease Control and Prevention. Antiviral agents for the treatment and chemoprophylaxis of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(RR–1):1–24; and Kimberlin DW, Acosta EP, Prichard MN, et al; National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Oseltamivir pharmacokinetics, dosing, and resistance among children aged <2 y with influenza. *J Infect Dis*. 2013;207(5):709–720. — indicates not applicable.

[a] Oseltamivir is administered orally without regard to meals, although administration with meals may improve gastrointestinal tolerability. Oseltamivir is available as Tamiflu in 30 mg, 45 mg, 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) on the basis of instructions contained in the package label. In patients with renal insufficiency, the dose should be adjusted on the basis of creatinine clearance. For the treatment of patients with creatinine clearance 10 to 30 mL per min: 75 mg once daily for 5 days. For the chemoprophylaxis of patients with creatinine clearance 10 to 30 mL per min: 30 mg once daily for 10 days after exposure or 75 mg once every other day for 10 days after exposure (5 doses).

[b] Approved by the FDA for children as young as 2 wk of age. Given preliminary pharmacokinetic data and limited safety data, oseltamivir can be used to treat influenza in both term and preterm infants from birth because benefits of therapy are likely to outweigh possible risks of treatment.

[c] Oseltamivir dosing for preterm infants. The wt-based dosing recommendation for preterm infants is lower than for term infants. Preterm infants may have lower clearance of oseltamivir because of immature renal function, and doses recommended for term infants may lead to high drug concentrations in this age group. Limited data from the National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group provide the basis for dosing preterm infants by using their postmenstrual age (gestational age plus chronological age): 1.0 mg/kg per dose orally twice daily for those <38 wk postmenstrual age; 1.5 mg/kg per dose orally twice daily for those 38 through 40 wk postmenstrual age; and 3.0 mg/kg per dose orally twice daily for those >40 wk postmenstrual age. For extremely preterm infants (<28 wk), please consult a pediatric infectious diseases physician.

[d] Zanamivir is administered by inhalation by using a proprietary Diskhaler device distributed together with the medication. Zanamivir is a dry powder, not an aerosol, and should not be administered by 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.

are too sick to breastfeed. If the breastfeeding mother requires antiviral agents, treatment with oral oseltamivir is preferred. However, none of the antiviral agents are reasons to discontinue breastfeeding;

- American Indian and/or Alaskan native children and adolescents;
- HCP or health care volunteers. Despite the AAP recommendation for mandatory influenza immunization for all HCP, many HCP remain unvaccinated. With an increasing number of organizations mandating influenza vaccination, coverage among HCP was 78.6% for the 2016–2017 season, which is similar to the 79.0% in the 2015–2016 season. Early season 2017–2018 vaccine coverage among HCP was 67.6%, which is similar to the early season coverage during the 2016–2017 season. 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. However, overall vaccination rates for this group remain consistently below this goal. The AAP recently reaffirmed its support for a mandatory influenza vaccination policy for all HCP nationwide, including those in outpatient settings. Mandating influenza vaccination for all HCP is ethical, just, and necessary to

TABLE 6 Comparison of Types of Influenza Diagnostic Tests

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

Negative results may not be used to 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 RT PCR. FDA-cleared rapid influenza diagnostic tests are Clinical Laboratory Improvement Amendments waived; most FDA-cleared rapid influenza molecular assays are Clinical Laboratory Improvement Amendments waived depending on the specimen. RT, reverse transcriptase. Adapted from Uyeki T, Bernstein H, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America (IDSA): 2018 update: diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. Clin Infect Dis. 2018;67: in press.

improve patient safety, especially because HCP frequently come into contact with patients at high risk of influenza illness in their clinical settings. For the prevention and control of influenza, all HCP must continue to prioritize the health and safety of patients; and

- people with influenza-associated encephalopathy (IAE). One complication associated with influenza observed in young children is encephalopathy, the most severe category being acute necrotizing encephalopathy (ANE). During the 2009 pandemic, a large increase in pediatric IAE was observed in Japan, and there have been sporadic cases of influenza A(H1N1)pdm09–associated IAE in children reported in the United States and worldwide.[42] Studies support annual influenza vaccination for all children ≥6 months of age in the United States, and it might be especially important in survivors of ANE, their household contacts, and their caregivers. Because of the potential for ANE recurrence, it also is important to closely monitor children with a history of neurologic complications associated with respiratory illnesses and to promptly initiate antiviral treatment along with influenza testing.

CONTRAINDICATIONS AND PRECAUTIONS

An anaphylactic or serious allergic reaction to any component of the vaccine is the only medical contraindication to influenza vaccination. Children who have had a previous allergic reaction to any component of the influenza vaccine, for any reason, should be evaluated by an allergist to determine whether future receipt of the vaccine is appropriate. Minor illnesses, with or without fever, are not contraindications to the use of influenza vaccines, particularly among children with mild upper respiratory infection symptoms or allergic rhinitis. Children with a moderate-to-severe febrile illness, based on the judgment of the clinician, should not be vaccinated until resolution of the illness.

Specific to influenza vaccination, a history of Guillain-Barre syndrome (GBS) is considered to be a precaution for the administration of influenza vaccine. The estimated risk for GBS is low, especially in children. Although influenza infection is recognized to be associated with GBS, there is no elevated risk of GBS from influenza vaccination in children. As a precaution, people who are not at high risk for severe influenza and who are known to have experienced GBS within 6 weeks of influenza vaccination generally should not be vaccinated. However, the benefits of influenza vaccination might outweigh the risks for certain people who have a history of GBS (particularly if not associated with previous influenza vaccination) and who also are at high risk for severe complications from influenza.

CHILDREN WHO SHOULD NOT BE VACCINATED WITH LAIV

The following should not be vaccinated with LAIV:

- children younger than 2 years;
- children who have a moderate-to-severe febrile illness as judged by the clinician;

- children with an amount of nasal congestion that would notably impede vaccine delivery;
- children 2 through 4 years of age with a 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. Therefore, when offering LAIV to children 24 through 59 months of age, pediatricians should screen them by asking the parents or guardians, "In the previous 12 months, has a health care professional ever told you that your child had wheezing?" If a parent answers "yes" to this question, an IIV, rather than LAIV, is recommended;
- children with a diagnosis of asthma;
- children who have received other live-virus vaccines within the previous 4 weeks; however, LAIV can be administered on the same day as other live-virus vaccines if necessary;
- children who have a known or suspected immunodeficiency disease or who are receiving immunosuppressive or immunomodulatory therapies;
- children who are receiving aspirin or other salicylates;
- women who are pregnant or considering pregnancy;
- children with any condition that can compromise respiratory function or the handling of secretions or can increase the risk for aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities;
- children taking an influenza antiviral medication (oseltamivir, zanamivir, or peramivir) until 48 hours 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 may be indicated because of the potential effects of antiviral medications on LAIV replication and immunogenicity; and
- children with chronic underlying medical conditions that may predispose them to complications after wild-type influenza infection, including metabolic disease, diabetes mellitus, other chronic disorders of the pulmonary or cardiovascular systems, renal dysfunction, or hemoglobinopathies. The safety of LAIV in these populations has not been established. These conditions are not contraindications but are listed under the warnings and precautions section of the LAIV package insert. A precaution is a condition in a recipient that might increase the risk or seriousness of an adverse reaction or complicate making another diagnosis because of a possible vaccine-related reaction. A precaution also may exist for conditions that might compromise the ability of the vaccine to produce immunity. Vaccination may be recommended in the presence of a precaution if the benefit of protection from the vaccine outweighs any risk.

An IIV is the vaccine of choice for anyone in close contact with a subset of severely immunocompromised people (ie, those in a protected environment). An IIV is preferred over LAIV for contacts of people who are severely immunocompromised because of a theoretical risk of infection attributable to the LAIV strain in an immunocompromised contact of a person who is LAIV immunized. Available data indicate a low risk of transmission of the virus in both children and adults vaccinated with LAIV. 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 patients who are severely immunocompromised for 7 days after immunization, although there have been no reports of LAIV transmission from a person who is vaccinated to a person who is immunocompromised. In the theoretical scenario in which symptomatic LAIV infection develops in an immunocompromised host, oseltamivir or zanamivir could be prescribed because LAIV strains are susceptible to these antiviral medications.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (for influenza updates, call 1-800-232-4636) or at www.cdc.gov/flu/index.htm.[29] Although current influenza season data on circulating strains can not necessarily be used to predict which and in what proportion strains will circulate in the subsequent season, it is instructive to be aware of 2018–2019 influenza surveillance data and use them as a guide for empirical therapy until current seasonal data are available from the CDC. Information is posted weekly on the CDC Web site (www.cdc.gov/flu/weekly/fluactivitysurv.htm).[43] The AAP offers "What's the Latest with the Flu" (www.aap.org/disasters/flu) messages[44] to highlight those details most relevant to AAP members and

child care providers on a monthly basis during influenza season.

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 these recommendations in computer systems and quality measurement efforts. This document is available at https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Influenza-Implementation-Guidance/Pages/default.aspx.[45] In addition, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found in the *Red Book Online*.[28]

USE OF ANTIVIRAL MEDICATIONS

Oral oseltamivir remains the antiviral drug of choice for the management of influenza infections. Although more difficult to administer, inhaled zanamivir 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 peramivir (Rapivab), a third NAI, was approved in September 2017 as treatment of acute uncomplicated influenza in children 2 years and older who are not hospitalized and have been symptomatic for no more than 2 days. Intravenous zanamivir is not approved in the United States. A prospective, open-label pediatric clinical trial was conducted to investigate pharmacokinetics and the clinical and/or virologic response to treatment with intravenous zanamivir for children 6 months or older with a serious influenza infection and who could not tolerate oral or inhaled NAIs.[25] Compassionate use was not available for the 2017–2018 season and is not likely to be available during the 2018–2019 influenza season.

Antiviral resistance to any drug can emerge, necessitating continuous population-based assessment that is conducted by the CDC. If local or national influenza surveillance data indicate emergence of an influenza strain with a known antiviral resistance profile, then according to the CDC, empirical treatment can be directed toward that strain with an effective antiviral agent. During the 2017–2018 season, 99% of the influenza A(H1N1)pdm09 viruses tested were susceptible to oseltamivir and peramivir, and all of the tested influenza strains were susceptible to zanamivir. All tested influenza A(H3N2) and influenza B viruses were susceptible to oseltamivir, zanamivir, and peramivir. In contrast, high levels of resistance to amantadine and rimantadine persist among the influenza A viruses currently circulating. Adamantane drugs are not recommended for use against influenza at this time unless resistance patterns change significantly.[1]

Current treatment guidelines for antiviral medications (Table 4) are unchanged for the 2018–2019 season and are applicable to both infants and children with suspected influenza when strains are known to be circulating in the community or when infants or children are tested and confirmed to have influenza.

Oseltamivir is available in capsule and oral suspension formulations. The available capsule doses are 30 mg, 45 mg, 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 for a final concentration of 6 mg/mL (Table 5).

Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza strains by the CDC may lead to new guidance.

Regardless of influenza vaccination status, antiviral treatment should be offered as early as possible to the following individuals (Table 4):

- Children hospitalized with suspected influenza;
- Children hospitalized for severe, complicated, or progressive illness attributable to influenza, regardless of duration of symptoms; and
- Children with suspected influenza (of any severity) and at high risk of complications (Table 2).

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

Treatment may be considered for the following individuals (Table 4):

- any otherwise healthy child suspected of having influenza disease. The greatest effect on outcome is expected to occur if treatment can be initiated within 48 hours of illness onset, but it still should be considered if later in the course of a progressive, symptomatic illness; and
- children suspected of having influenza disease and whose siblings or household contacts either are younger than 6 months or have underlying medical conditions that predispose them to complications of influenza.

Studies conducted to date to evaluate the efficacy of NAIs have revealed that timely treatment can reduce the duration of influenza symptoms and fever as well as the risk of certain complications, including hospitalization and death, in pediatric and adult populations.[24,46–51] The number of published randomized,

controlled clinical (RCT) studies 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 (clinical 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 of treatment involving 2356 children with clinical influenza, 1255 of whom had laboratory-confirmed influenza, revealed that in children with laboratory-confirmed influenza, oseltamivir and zanamivir reduced the median duration of illness by 36 hours (26%; $P < .001$) and 1.3 days (24%; $P < .001$), respectively.[52] Among the studies reviewed, 1 trial of oseltamivir in children with asthma who had laboratory-confirmed influenza revealed only a nonsignificant reduction in illness duration (10.4 hours [8%]; $P = .542$). Oseltamivir significantly reduced acute otitis media in children aged 1 to 5 years with laboratory-confirmed influenza (risk difference −0.14; 95% CI −0.24 to −0.04).[52] Another Cochrane review of RCTs of adult and children, which included 20 oseltamivir (9623 participants) and 26 zanamivir trials (14 628 participants),[53] revealed no effect of oseltamivir in reducing the duration of illness in children with asthma; 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, the authors of this review did not find a significant effect of NAIs on reducing hospitalizations, pneumonia, bronchitis, otitis media, or sinusitis in children.[53] More recently, in a meta-analysis of 5 new RCTs that included 1598 children with laboratory-confirmed influenza, treatment with oseltamivir significantly reduced the duration of illness in this population by 17.6 hours (95% CI −34.7 to −0.62 hours), and when children with asthma were excluded, this difference was larger (−29.9 hours; 95% CI −53.9 to −5.8 hours). The risk of otitis media was 34% lower in this group as well.[47] Overall, efficacy outcomes are best demonstrated in patients with laboratory-confirmed influenza. Researchers in all these studies confirmed vomiting as a frequent side effect of oseltamivir, occurring in approximately 5% of treated patients. The balance between benefits and harms should be considered when making decisions about the use of NAIs for either the treatment or prophylaxis of influenza.

Although prospective comparative studies to determine the efficacy of NAIs in patients who are hospitalized or pediatric patients with comorbidities have not been conducted and prospectively collected data to determine the role of NAIs 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 NAIs to treat pediatric patients with severe influenza, including patients who are hospitalized.

Importantly, treatment with oseltamivir for children with serious, complicated, or progressive diseases presumptively or definitively caused by influenza, irrespective of influenza vaccination status or whether illness began greater than 48 hours before admission, continues to be recommended by the AAP, CDC, Infectious Diseases Society of America, and Pediatric Infectious Diseases Society. Earlier treatment provides better clinical responses. However, treatment after 48 hours of symptoms in adults and children with a moderate-to-severe disease or progressive disease has been shown to provide some benefit and should be offered. No benefit exists for double-dose NAI therapy compared with standard-dose therapy based on published data from a randomized prospective trial enrolling 75% of subjects younger than 15 years.[1,54]

Dosages of antiviral agents for both treatment and chemoprophylaxis in children can be found in Table 5 (for children of all ages, 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).[55] Children younger than 2 years are at an increased risk of hospitalization and complications attributable to influenza. The FDA has approved oseltamivir for the treatment of children as young as 2 weeks. Given preliminary pharmacokinetic data and limited safety data, the AAP supports the use of oseltamivir to treat influenza in both term and preterm infants from birth because the benefits of therapy for neonatal influenza are likely to outweigh the possible risks of treatment.

In adverse event data collected systematically in prospective trials, vomiting was the only adverse effect seen more often with oseltamivir compared with a placebo when studied in children 1 through 12 years of age (ie, 15% of treated children versus 9% receiving a placebo). In addition, following reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, reviewers of controlled clinical trial data and ongoing surveillance have failed to establish a link between this drug and neurologic or psychiatric events. Information is available through the FDA Web site.[56]

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 ILI. 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 6), all of which should be considered in making the best clinical judgment. 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. Although decisions on treatment and infection control can be made on the basis of positive rapid antigen test results, negative results should not always be used in a similar fashion because of the suboptimal sensitivity and potential for false-negative results. Positive results of rapid influenza tests are helpful because they may reduce additional testing to identify the cause of a child's ILI and promote appropriate antimicrobial stewardship. Available FDA-approved rapid molecular assays are highly sensitive and specific diagnostic tests performed in less than 20 minutes by using RNA detection. These molecular assays and polymerase chain reaction (PCR) test confirmation are preferred in patients who are hospitalized because they are more sensitive compared with antigen detection. Immunofluorescence assays may be an alternative to PCR testing, although the sensitivity is lower. Early detection, prompt antiviral treatment, and infection control interventions can lead to improved individual patient outcomes and allow for effective cohorting and disease containment.

People with suspected influenza who present with an uncomplicated febrile illness should be offered treatment with antiviral medications if they are at higher risk of influenza complications (Table 2). Efforts should be made to minimize treatment in 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 or have underlying medical conditions that predispose them to complications of influenza. 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 past years, local shortages of oseltamivir suspension have occurred because of uneven local 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 5).

Randomized placebo-controlled studies revealed that oral oseltamivir and inhaled zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza.[1, 24] During the 2009 pandemic, the emergence of oseltamivir resistance was noted rarely among people receiving postexposure prophylaxis, highlighting the need to be aware of the possibility of emerging resistance in this population. Decisions on whether to administer antiviral chemoprophylaxis should take into 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 dose for prophylaxis should not be used for the treatment of children symptomatic with influenza. Early, full treatment doses (rather than prophylaxis doses) provided to patients who are at high-risk and symptomatic without waiting for laboratory confirmation is an alternate strategy.

Although vaccination is the preferred approach to the prevention of infection, chemoprophylaxis during an influenza outbreak, as defined by the CDC (http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section11.html),[57] is recommended in the following situations:

- for children at high risk of complications from influenza for whom an 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 unimmunized and are likely to have ongoing, close exposure to unimmunized children at high risk or unimmunized infants and toddlers who are younger than 24 months;
- for control of influenza outbreaks for unimmunized staff and children in a closed institutional setting with children at high risk (eg, extended-care facilities);
- as a supplement to vaccination among children at high risk, including children who are

immunocompromised and may not respond with sufficient protective immune responses after vaccination;

- as postexposure prophylaxis for family members and close contacts of an infected person if those people are at high risk for complications from influenza; and
- for children at high risk of complications and their family members and close contacts, as well as HCP, when circulating strains of influenza virus in the community are not matched with seasonal influenza vaccine strains on the basis of current data from the CDC and local health departments.

These recommendations apply to routine circumstances, but it should be noted that guidance may be changed 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 and antigenic shift) or severity of influenza. Chemoprophylaxis is not routinely recommended for infants younger than 3 months given limited safety and efficacy data in this age group.

CHEMOPROPHYLAXIS SHOULD NOT BE CONSIDERED AS A SUBSTITUTE FOR VACCINATION

An influenza vaccine should always be offered before and during the influenza season when not contraindicated even after the influenza virus has been circulating in the community. Antiviral medications currently licensed are important adjuncts to influenza vaccination for the control and prevention of influenza disease. Toxicities are 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 an IIV, although LAIV effectiveness will be decreased for the children receiving oseltamivir. No data are available on the impact of inhaled zanamivir on the effectiveness of LAIV. For recommendations about treatment and chemoprophylaxis against influenza, see Table 5. Among some people at high risk, both vaccination and antiviral chemoprophylaxis may be considered. Updates will be available in the *Red Book Online*[58] and the CDC Web site.[55]

FUTURE DIRECTIONS

For the 2018–2019 season, the safety and effectiveness of influenza vaccines will be analyzed as they become available and reported by the CDC as it is each season.[59] The manufacturer of LAIV4 reported that it will employ additional vaccine virus evaluation techniques in its selection of candidate vaccine viruses for inclusion in LAIV4 with the expectation that this will result in improved effectiveness of the formulation for the 2018–2019 season. Continued evaluation of the safety, immunogenicity, and effectiveness of the influenza vaccine, especially for young children and pregnant women, is important. The potential role of previous influenza vaccination on overall vaccine effectiveness by vaccine formulation, virus strain, and subject age in preventing outpatient medical visits, hospitalizations, and deaths continues to be evaluated. Furthermore, complete analysis of quadrivalent vaccines is needed as the number of formulations of IIV4 increase. Additionally, with limited data on the use of NAIs in children who are hospitalized or in children with comorbid conditions, prospective randomized clinical trials in this population are warranted.

Immunizing all HCP, which is a crucial step in efforts to reduce health care–associated influenza infections, serves as an example to patients, highlighting the safety and effectiveness of annual vaccination. Ongoing efforts should include broader implementation and evaluation of mandatory vaccination programs in both inpatient and outpatient settings. Further investigation into the extent of offering to immunize parents and adult child care providers in the pediatric office setting; the level of family contact satisfaction with this practice; how practices handle the logistic, liability, legal, and financial barriers that limit or complicate this service; and most importantly, how this practice will affect disease rates in children and adults is needed. There is also a need for more systematic health services research on influenza vaccine uptake and refusal as well as for an identification of methods to enhance uptake.

Efforts should be made to create adequate outreach and infrastructure to facilitate the optimal distribution of vaccines so that more people are immunized. Pediatricians also might consider becoming 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. Pandemic influenza preparedness of directors of child care centers also needs to improve. Additional information can be found in the Pediatric Preparedness Resource Kit.[60]

Pandemic influenza preparedness is of particular interest because of the increase in the number of human infections with Asian lineage avian influenza A(H7N9) reported in China (updates are available at https://www.cdc.gov/flu/avianflu/h7n9-virus.htm). A few human infections of Asian lineage avian influenza A(H7N9) have been reported outside of mainland China, but most of these infections have occurred among people who had traveled to China before becoming ill. These Asian lineage avian influenza A(H7N9) viruses have not been detected in people or birds in the United States. Although the current risk to the public's health from this virus is low, Asian lineage avian influenza A(H7N9) virus is among the nonhuman influenza viruses that are most concerning to public health officials because of their pandemic potential and ability to cause severe disease in infected humans. The current risk to the public's health from the virus remains low; however, the CDC is monitoring the situation carefully and taking routine preparedness measures, including testing candidate vaccines.

With the increased demand for vaccination during each influenza season, the AAP and the CDC recommend vaccine administration at any visit to the medical home during influenza season when it is not contraindicated, at specially arranged vaccine-only sessions, and through cooperation with community sites, schools, and Head Start and child care facilities to provide the influenza vaccine. It is important that the annual delivery of influenza vaccines to primary care medical homes should be timely to avoid missed opportunities. If alternative venues, including pharmacies and other retail-based clinics, are used for vaccination, a system of patient record transfer is beneficial in maintaining the accuracy of immunization records. Immunization information systems should be used whenever available and prioritized to document influenza vaccination. Two-dimensional barcodes have been used to facilitate more efficient and accurate documentation of vaccine administration with limited experience to date. Additional information concerning current vaccines shipped with 2-dimensional barcodes can be found on the CDC Web site.[61]

Access to care issues, a lack of immunization records, and questions regarding who can provide consent may be addressed by linking children (eg, those in foster care and/or the juvenile justice system or who are refugees, immigrants, or homeless) with a medical home, using all health care encounters as vaccination opportunities, and more consistently using immunization registry data. One new strategy of interest is an IIV delivered by a dissolvable microneedle patch, which has the potential to improve vaccine acceptability and coverage and reduce costs. Data from the first phase 1 human clinical trial (n = 100) found that the microneedle patch immunization was well tolerated and generated robust antibody responses.[62]

Development efforts continue for a universal influenza vaccine that induces broader protection and eliminates the need for annual vaccination. In addition, the development of a safe, immunogenic vaccine for infants younger than 6 months is essential. Studies on the effectiveness and safety of influenza vaccines containing adjuvants that enhance immune responses to influenza vaccines are ongoing. Efforts to improve the vaccine development process to allow for a shorter interval between the identification of vaccine strains and vaccine production continue. Lastly, many antiviral drugs are in various development phases given the need to improve options for the treatment and chemoprophylaxis of influenza. One recent example, baloxavir marboxil, a new antiviral for influenza that works by a different mechanism than NAIs and requires only a single dose for the treatment of infection, has recently been approved in Japan for adults and children. The FDA recently granted a priority review of this new drug, for which impact on the treatment of influenza will be followed closely.[63] Finally, pediatricians should remain informed during the influenza season by following the CDC influenza page[64] (www.cdc/gov/flu) and the AAP *Red Book Online* influenza resource page (www.aapredbook.org/flu)[58].

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ACIP: Advisory Committee on Immunization Practices
ANE: acute necrotizing encephalopathy
CDC: Centers for Disease Control and Prevention
CI: confidence interval
FDA: Food and Drug Administration
GBS: Guillain-Barre syndrome
HCP: health care personnel
IAE: influenza-associated encephalopathy
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
ILI: influenza-like illness
LAIV: live attenuated influenza vaccine
LAIV3: trivalent live attenuated influenza vaccine
LAIV4: quadrivalent live attenuated influenza vaccine
NAI: neuraminidase inhibitor
PCR: polymerase chain reaction
PCV13: 13-valent pneumococcal conjugate vaccine
RCT: randomized controlled trial
RIV4: quadrivalent recombinant influenza vaccine

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