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, 2016–2017

COMMITTEE ON INFECTIOUS DISEASES

abstract

The purpose of this statement is to update recommendations for the routine use of seasonal influenza vaccine and antiviral medications for the prevention and treatment of influenza in children. The AAP recommends annual seasonal influenza immunization for *everyone* 6 months and older, including children and adolescents. Highlights for the upcoming 2016–2017 season include the following:

1. Annual universal influenza immunization is indicated with either a trivalent or quadrivalent (no preference) inactivated vaccine.

2. The 2016–2017 influenza A (H3N2) vaccine strain differs from that contained in the 2015–2016 seasonal vaccines. The 2016–2017 influenza B vaccine strain (Victoria lineage) included in the trivalent vaccine differs from that contained in the 2015–2016 seasonal trivalent vaccines (Yamagata lineage).

   a. Trivalent vaccine contains an A/California/7/2009 (H1N1)pdm09–like virus, an A/Hong Kong/4801/2014 (H3N2)–like virus, and a B/Brisbane/60/2008-like virus (B/Victoria lineage).

   b. Quadrivalent vaccine contains an additional B virus (B/Phuket/3073/2013-like virus [B/Yamagata lineage]).

3. Quadrivalent live attenuated influenza vaccine (LAIV4) should not be used in any setting during the 2016–2017 influenza season in light of the evidence for poor effectiveness of LAIV4 in recent seasons, particularly against influenza A (H1N1)pdm09 viruses.

4. All children with egg allergy can receive influenza vaccine with no additional precautions from those of routine vaccinations.

5. All HCP should receive an annual influenza vaccine, a crucial step in preventing influenza and reducing health care–associated influenza infections. Because HCP may care for or live with people at high risk of influenza-related complications, it is especially important for them to get vaccinated annually.

6. Pediatricians should attempt to promptly identify children suspected of having influenza for rapid antiviral treatment, when indicated, to reduce morbidity and mortality.

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INTRODUCTION

The American Academy of Pediatrics (AAP) recommends annual seasonal influenza vaccination for *everyone* 6 months and older, including children and adolescents, during the 2016–2017 influenza season. Special effort should be made to vaccinate people in the following groups:

- all children, including infants born preterm, aged 6 months and older (based on chronologic age) with conditions that increase the risk of complications from influenza (eg, children with chronic medical conditions, such as asthma, diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, or neurologic and neurodevelopmental disorders);
- all household contacts and out-of-home care providers of children with high-risk conditions and those younger than 5 years, especially infants younger than 6 months;
- American Indian/Alaska Native children;
- 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.

KEY POINTS RELEVANT FOR THE 2016–2017 INFLUENZA SEASON

1. **Annual seasonal influenza vaccine is recommended for everyone 6 months and older, including children and adolescents, during the 2016–2017 influenza season.** It is important that household contacts and out-of-home care providers of children younger than 5 years, especially infants younger than 6 months, and children of any age at high risk of complications from influenza (eg, children with chronic medical conditions, such as asthma, diabetes mellitus, hemodynamically significant cardiac disease, immunosuppression, or neurologic and neurodevelopmental disorders) receive annual influenza vaccine. In the United States, more than two-thirds of children younger than 6 years and almost 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. Children younger than 2 years are at increased risk of hospitalization and complications attributable to influenza. 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. Reducing influenza virus transmission (eg, by using appropriate hand hygiene and respiratory hygiene/cough etiquette) among children who attend out-of-home child care or school has been shown to decrease the burden of childhood influenza and the transmission of influenza virus to household contacts and community members of all ages.

2. The 2015–2016 influenza season was moderate overall, with lower levels of influenza activity, outpatient illness, influenza-associated hospitalization, and pediatric deaths compared with the previous season. Although the start of the season was typical in the United States, with increasing activity noted in January 2016, activity peaked in mid-March, which was later than in the previous 3 seasons. The influenza A (H1N1)pdm09 viruses predominated overall, influenza A (H3N2) viruses were more commonly identified from October through early December, and influenza B viruses were more commonly identified from mid-April through mid-May. The majority of circulating strains matched vaccine strains well. Pediatric hospitalizations and deaths caused by influenza vary by the predominant circulating strain and from 1 season to the next (Table 1). Historically, 80% to 85% of pediatric deaths have occurred in unvaccinated children aged 6 months and older. In the past 10 seasons, the rates of hospitalization for children younger than 5 years have always exceeded the rates for children 5 through 17 years of age. As of August 20, 2016, the following data were reported by the Centers for Disease Control and Prevention (CDC) during the 2015–2016 influenza season: 85 laboratory-confirmed influenza-associated pediatric deaths occurred; 53 of these were associated with influenza A viruses, 28 of these were associated with influenza B viruses, and 3 of these were associated with an undetermined type of influenza virus.Although children with certain conditions are at higher risk of complications, 59.7% of the deaths occurred in children with no high-risk underlying medical condition. Among children hospitalized with influenza and for whom medical chart data were available, approximately 50% had no recorded underlying condition, whereas approximately 21% had underlying asthma or reactive airway disease (Fig 1).

3. In light of the evidence for poor effectiveness of quadrivalent

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TABLE 1 Pediatric Deaths and Hospitalizations by Season and Predominant Strain

Influenza Season	Predominant Strain	Pediatric Deaths, *n*	Hospitalizations, per 100 000	
			0–4 years old	5–17 years old
2015–2016 (preliminary data)	H1N1	85	42.5	9.4
2014–2015[a]	H3N2	148	57.3	16.6
2013–2014	pH1NI	111	47.3	9.4
2012–2013	H3N2	171	67	14.6
2011–2012[a]	H3N2	37	16	4
2010–2011	H3N2	123	49.5	9.1
2009–2010	pH1NI	288	77.4	27.2
2008–2009	H1N1	137	28	5
2007–2008	H3N2	88	40.3	5.5
2006–2007	H1N1	77	34.6	2.3

Source: CDC (FluView 2015–2016 data as of August 20, 2016; available at: www.cdc.gov/flu/weekly/fluviewinteractive.htm).
[a] Vaccine strains did not change from previous influenza season.

live attenuated influenza vaccine (LAIV4) documented during the past 3 seasons, particularly against influenza A (H1N1) pdm09 viruses, LAIV4 should not be used in any setting during the 2016–2017 season. In the 2015–2016 influenza season, vaccine effectiveness of any vaccine (inactivated influenza vaccine [IIV] or live attenuated influenza vaccine [LAIV]) against influenza A and B was 47% (95% confidence interval

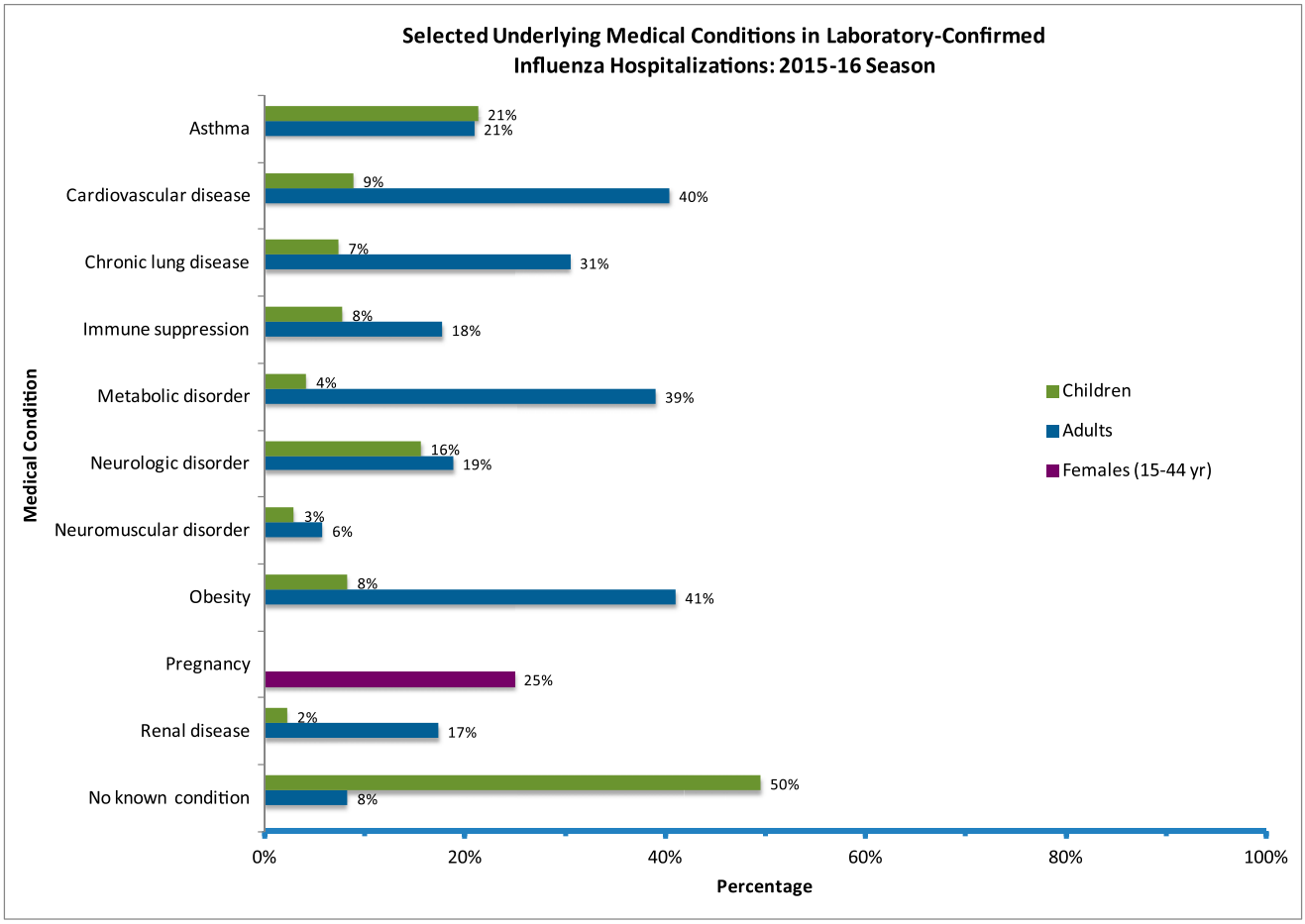

FIGURE 1
Selected underlying medical conditions in patients hospitalized with laboratory-confirmed influenza: FluSurv-NET 2015–2016. Asthma includes a medical diagnosis of asthma or reactive airway disease. Cardiovascular diseases include conditions such as coronary heart disease, cardiac valve disorders, congestive heart failure, pulmonary hypertension, and aortic stenosis (does not include hypertension disease only). 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, and HIV/AIDS and individuals taking immunosuppressive medications. Metabolic disorders include conditions such as diabetes mellitus and thyroid dysfunction. Neuromuscular disorders include conditions such as multiple sclerosis and muscular dystrophy. Obesity was assigned if indicated in the patient's medical chart or if BMI >30. Pregnancy percentages were calculated by using the number of female cases aged between 15 and 44 years 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 did not have any known underlying medical condition indicated in the medical chart at the time of hospitalization. Source: CDC (FluView 2015–2016 preliminary data as of August 20, 2016; available at: gis.cdc.gov/grasp/fluview/FluHospChars.html).

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[CI]: 39% to 53%) according to observational data from the US Influenza Vaccine Effectiveness Network. However, relative vaccine effectiveness against both influenza A (H1N1)pdm09 viruses (the predominant influenza strain this season) and influenza B viruses strongly favored IIV over LAIV4 among children 2 through 17 years of age. LAIV4 was not significantly effective against any influenza (all A and B viruses combined) among children 2 through 17 years of age (Table 2). In all pediatric age groups for all 3 seasons, LAIV4 did not have any statistically significant benefit in preventing influenza (all 95% CIs cross zero), whereas IIV provided statistically significant protection, albeit to differing degrees by season (Table 2). Children who received LAIV4 had more than 2.5 times higher odds of developing influenza attributable to any virus type compared with children who received IIV. For influenza A (H1N1)pdm09 viruses in particular, LAIV4 had an adjusted vaccine effectiveness of –21% (95% CI: –108% to 30%) compared with 65% for IIV (95% CI: 49% to 76%). The adjusted odds ratio was 3.67, indicating that children who received LAIV4 were almost 4 times more likely to get influenza than those who received IIV. In the 2014–2015 influenza season, data from the US Influenza Vaccine Effectiveness Network indicated that vaccine effectiveness of both IIV and LAIV4 was reduced against influenza A (H3N2) viruses for all age groups because of antigenic drift of the predominantly circulating A (H3N2) viruses. During the 2013–2014 season, observational data from the US Influenza Vaccine Effectiveness Network and 2 additional studies showed that LAIV4 was not effective against the predominantly circulating influenza A (H1N1)pdm09 viruses when compared with IIV in children aged 2 through 8 years. Additional research will help determine whether the interim recommendation that LAIV4 should not be used in any setting will continue for subsequent influenza seasons. Current focus should be on the administration of IIV for all children and adolescents, particularly those with underlying medical conditions associated with an elevated risk of complications from influenza.

TABLE 2 Vaccine Effectiveness Against Any Influenza in Children, by Age and Vaccine Type

Season (Predominant Strain) and Age Range	Adjusted Vaccine Effectiveness, % (95% CI)	
	LAIV4	IIV3/IIV4
2013–2014 (H1N1pdm09)		
2–17 years	2 (–53 to 37)	61 (42 to 74)
2–8 years	–39 (–156 to 25)	60 (32 to 76)
9–17 years	36 (–31 to 69)	62 (30 to 80)
2014–2015 (H3N2)		
2–17 years	9 (–18 to 29)	31 (16 to 44)
2–8 years	9 (–28 to 35)	26 (2 to 44)
9–17 years	17 (–27 to 46)	33 (9 to 51)
2015–2016 (H1N1pdm09)		
2–17 years	3 (–49 to 37)	63 (52 to 72)
2–8 years	–3 (–76 to 40)	58 (40 to 70)
9–17 years	20 (–78 to 64)	71 (52 to 82)

Source: CDC.

4. **Vaccination remains the best available preventive measure against influenza.** Given the unpredictable nature of influenza each season, *any* licensed and age-appropriate IIV available should be used. The vaccine strains are predicted to be well matched to circulating strains with the intent of providing optimal protection. Vaccination is effective in reducing outpatient medical visits for illness caused by circulating influenza viruses by 50% to 75%. The universal administration of seasonal vaccine to everyone 6 months and older is still the best strategy available for preventing illness from influenza.

5. Both trivalent and quadrivalent IIVs are available in the United States for the 2016–2017 season. To vaccinate as many people as possible for this influenza season, neither *inactivated* vaccine formulation is preferred over the other. Although manufacturers anticipate an increasing amount of quadrivalent vaccine, pediatricians should give whichever formulation is available in their communities. Both formulations contain an A/California/7/2009 (H1N1)pdm09–like virus, an A/HongKong/4801/2014 (H3N2)–like virus, and a B/Brisbane/60/2008-like virus (B/Victoria lineage). Quadrivalent influenza vaccines contain the B/Phuket/3073/2013-like virus (B/Yamagata lineage) as well. The influenza A (H3N2) virus in both formulations differs from that contained in the 2015–2016 seasonal vaccines. The influenza B virus in the trivalent formulation is the opposite lineage from that in last season's trivalent vaccine.

6. The number of seasonal influenza vaccine doses to be administered in the 2016–2017 influenza season depends on the

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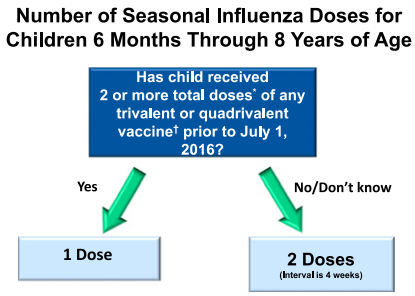

FIGURE 2
Number of 2016–2017 seasonal influenza vaccine doses for children 6 months through 8 years of age. *The 2 doses need not have been received during the same season or consecutive seasons. †Receipt of LAIV4 in the past is still expected to have primed a child's immune system, despite recent evidence for poor effectiveness. There currently are no data that suggest otherwise.

TABLE 3 People at High Risk of Influenza Complications and Therefore Recommended for Antiviral Treatment of Suspected or Confirmed Influenza

Children aged <2 years
Adults aged ≥65 years
Persons 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)
Persons with immunosuppression, including that caused by medications or by HIV infection
Women who are pregnant or postpartum (within 2 weeks after delivery)
Persons aged <19 y who are receiving long-term aspirin therapy
American Indian/Alaska Native persons
Residents of nursing homes and other chronic care facilities

Adapted from the CDC. 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.

child's age at the time of the first administered dose and his or her vaccine history (Fig 2):

- Influenza vaccines are not licensed for administration to infants younger than 6 months.
- Children aged 9 years and older need only 1 dose.
- Children 6 months through 8 years of age:
  - Need 2 doses if they have received fewer than 2 doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2016. The interval between the 2 doses should be at least 4 weeks.
  - Require only 1 dose if they have previously received 2 or more total doses of any trivalent or quadrivalent influenza vaccine (IIV or LAIV) before July 1, 2016. The 2 previous doses do not need to have been received during the same influenza season or consecutive influenza seasons. Despite recent evidence for poor effectiveness of LAIV4, receipt of LAIV4 in the past is still expected to have primed a child's immune system. There currently are no data that suggest otherwise. Therefore, children who received 2 or more doses of LAIV4 before July 1, 2016 may receive only 1 dose of IIV for the 2016–2017 season. Given the continuing circulation of H1N1pdm09 viruses as the predominant influenza A (H1N1) strain since 2009 and its inclusion in all seasonal influenza vaccines since the 2010–2011 season, this virus is no longer believed to be antigenically novel; therefore, special consideration with respect to vaccine policy is no longer necessary. Vaccination should not be delayed to obtain a specific product for either dose. Any available, age-appropriate trivalent or quadrivalent inactivated 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 B virus.

7. Pediatric offices may choose to serve as an alternate 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 (see details at www.aapredbook.org/implementation). 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 provider. Offering adult vaccinations in the pediatric 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 3) is intended to reduce their risk of contagion (ie, "cocooning"). The practice of cocooning also will help protect infants younger than 6 months who are too young to be immunized with influenza vaccine.

8. Pregnant women can receive influenza vaccine safely at any time during pregnancy. Pregnant women are of special concern because they are at high risk of complications from influenza. Vaccination of pregnant women

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also provides protection for their infants, potentially for as long as 6 months through the transplacental transfer of antibodies. For example, 1 recent study documented that infants born to women reporting influenza vaccination during pregnancy had risk reductions of 70% for laboratory-confirmed influenza and 81% for influenza hospitalizations in their first 6 months.

9. Once seasonal influenza vaccine is 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. HCP should ideally provide vaccination by the end of October, if possible. This is particularly important for children who need 2 doses of influenza vaccine to achieve optimal protection before the circulation of influenza viruses in the community. Provider endorsement plays a major role in patient acceptance and vaccine uptake. Prompt initiation of influenza vaccination and continuing to vaccinate throughout the influenza season, whether influenza is circulating (or has circulated) in the community, are important components of an effective vaccination strategy. Although there is no evidence that waning immunity from administering the vaccine early increases the risk of infection in children, recent literature raises the possibility that very early vaccination of adults, particularly the elderly, might contribute to reduced protection later in the influenza season. Until there is definitive information that determines whether waning immunity influences vaccine effectiveness, the influenza vaccine should not be delayed until a later date, because this increases the likelihood of missing influenza vaccination altogether. Further evaluation is needed before any policy change in timing is made.

10. Providers may continue to offer vaccine until June 30th of each year, marking the end of the influenza season, because influenza is so unpredictable. Protective immune responses generally persist in children throughout the influenza season. Although peak influenza activity in the United States tends to occur in January through March, influenza activity can occur in early fall (October) or in late spring (end of May) and may have more than 1 disease peak. This approach also provides ample opportunity to administer a second dose of vaccine to children 6 months through 8 years of age when indicated, as detailed previously in key point 6. This approach also allows for optimal ability to immunize international travelers, who may be exposed to influenza year-round, depending on destination.

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

- Plan to make seasonal influenza vaccine easily accessible for all children. Examples include sending alerts to families that 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 influenza vaccine during both well and sick visits; considering how to immunize parents, adult caregivers, and siblings at the same time in the same office setting as children[1]; 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 vaccine. If a child receives an influenza vaccine outside of his or her medical home, such as at a pharmacy, retail-based clinic, or another practice, appropriate documentation of vaccination should be provided to the patient for his or her medical home and entered into the state or regional immunization registry as required by state law.

- Concerted efforts among the aforementioned groups, plus vaccine manufacturers, distributors, and payers, also are necessary to prioritize distribution appropriately to the primary care office setting and patient-centered medical home before other venues, especially when vaccine supplies are delayed or limited. Similar efforts should be made to assuage the vaccine supply discrepancy between privately insured patients and those eligible for vaccination through the Vaccines for Children program. Without an intranasal influenza vaccine recommended for this 2016–2017 season, the AAP is working closely with manufacturers to make available an adequate supply with geographically wide and timely distribution of inactivated vaccine products for pediatric-aged patients.

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- Public health will benefit from pediatricians' discussions about vaccine safety, effectiveness, and indications, particularly since LAIV4 should not be used during the 2016–2017 season because of its poor effectiveness against influenza A (H1N1) pdm09 viruses during the 2013–2014 and 2015–2016 influenza seasons in the United States. Pediatricians can influence vaccine acceptance by explaining the importance of annual influenza vaccination for children, emphasizing when a second dose of vaccine is indicated, and explaining why the intranasal formulation is not available this season. The AAP and CDC are developing communication resources to convey these important messages and to help the public understand this influenza recommendation. Resources will be available on *Red Book* Online (www.aapredbook.org/flu).
- HCP should act as role models for both their patients and colleagues by receiving influenza vaccination annually and by letting others know that they have received 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 ethical, just, and necessary to improve patient safety.[2] Employees of health care institutions are obligated to act in the best interests of the health of their patients and to honor the requirement of causing no harm.

12. Antiviral medications also are important in the control of influenza but are not a substitute for influenza vaccination. The neuraminidase inhibitors (NAIs) oral oseltamivir (Tamiflu; Roche Laboratories, Nutley, NJ) and inhaled zanamivir (Relenza; GlaxoSmithKline, Research Triangle Park, NC) are the only antiviral medications that are recommended for chemoprophylaxis or treatment of influenza in children during the 2016–2017 season. Peramivir (Rapivab; BioCryst Pharmaceuticals, Durham, NC), a third NAI, was licensed on December 19, 2014, for use in adults 18 years or older and is being studied in children. Intravenous use of peramivir is approved for adults. Intravenous zanamivir remains investigational but can be used in consultation with infectious diseases specialists, and it may also be obtained on a compassionate-use basis for seriously ill children, as currently supported by the US Food and Drug Administration (FDA) through the manufacturer, GlaxoSmithKline. This information is especially important for those who are immunocompromised or who cannot tolerate or absorb orally or enterically administered oseltamivir. Intravenous zanamivir is being studied in pediatric patients, but the manufacturer has not publicly released any information regarding any plans to file for licensure in adults or children. Recent viral surveillance and resistance data from the CDC and the World Health Organization (WHO) indicate that the majority of currently circulating influenza viruses likely to cause influenza in North America during the 2016–2017 season continue to be susceptible to oseltamivir, zanamivir, and peramivir. If a newly emergent oseltamivir- or peramivir-resistant virus is a concern, the use of intravenous zanamivir may be feasible. Amantadine and rimantadine (adamantanes that block M2 proton channels) should not be used to treat influenza in 2016–2017, because circulating influenza A viruses continue to have extremely high levels of resistance to these drugs, which also are not effective against influenza B viruses. Because resistance characteristics can change over the duration of a treatment course, especially in severely immunocompromised people who may receive prolonged courses, pediatricians can verify susceptibility data for circulating strains at the start of the influenza season and monitor the data throughout the season. Up-to-date information can be found on the AAP Web site (www.aap.org or www.aapredbook.org/flu), through state-specific AAP chapter Web sites, or on the CDC Web site (www.cdc.gov/flu/index.htm).

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 B viral lineage confers little cross-protection against the other 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 B lineage will predominate during a given influenza season. Therefore, a quadrivalent influenza vaccine with influenza B strains of *both* lineages would be predicted to offer additional protection, but there is no evidence

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TABLE 4 Recommended Seasonal Influenza Vaccines for Different Age Groups: United States, 2016–2017 Influenza Season

Vaccine	Trade Name	Manufacturer	Presentation	Thimerosal Mercury Content, μg Hg/0.5-mL dose	Age Group
Inactivated					
IIV3	Fluzone High-Dose	Sanofi Pasteur	0.5-mL prefilled syringe	0	≥65 years
IIV3	Fluvirin	Seqirus	0.5-mL prefilled syringe	≤1.0	≥4 years
			5.0-mL multidose vial	25	≥4 years
IIV3	Afluria	Seqirus	0.5-mL prefilled syringe	0	≥9 years[a]
			5.0-mL multidose vial	24.5	≥9 years[a] via needle/syringe 18–64 years via jet injector
aIIV3	Fluad	Seqirus	0.5-mL prefilled syringe	0	≥65 years
ccIIV4	Flucelvax	Seqirus	0.5-mL prefilled syringe	0	≥4 years
IIV4	Fluzone	Sanofi Pasteur	0.25-mL prefilled syringe	0	6–35 months
			0.5-mL prefilled syringe	0	≥36 months
			0.5-mL vial	0	≥36 months
			5.0-mL multidose vial	25	≥6 months
IIV4	Fluzone Intradermal	Sanofi Pasteur	0.1-mL prefilled microinjection	0	18–64 years
IIV4	Fluarix	GlaxoSmithKline	0.5-mL prefilled syringe	0	≥3 years
IIV4	FluLaval	ID Biomedical Corporation of Quebec (distributed by GlaxoSmithKline)	0.5-mL prefilled syringe	0	≥3 years
			5.0-mL multidose vial	<25	≥3 years
Recombinant					
RIV3	Flublok	Protein Sciences	0.5-mL vial	0	≥18 years

Sources: AAP Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2015–2016. *Pediatrics*. 2015;136(4):792–808; Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2016-2017 influenza season. *MMWR Recomm Rep*. 2016;65(RR-3):1-54. Implementation guidance on supply, pricing, payment, Current Procedural Terminology (CPT) coding, and liability issues can be found at www.aapredbook.org/implementation. aIIV, adjuvanted inactivated influenza vaccine.

[a] Age indication per the package insert is ≥5 years; however, the Advisory Committee on Immunization Practices recommends Afluria not be used in children 6 months through 8 years of age because of increased reports of febrile reactions noted in this age group. If no other age-appropriate, licensed inactivated seasonal influenza vaccine is available for a child 5 through 8 years of age who has a medical condition that increases the child's risk of influenza complications, Afluria can be used; however, pediatricians should discuss with the parents or caregivers the benefits and risks of influenza vaccination with Afluria before administering this vaccine.

at this time that quadrivalent vaccine is more effective.

IIVs

For the 2016–2017 season, IIVs will be available for intramuscular injection in both trivalent (IIV3) and quadrivalent (IIV4) formulations. IIVs do not contain live virus. The available intramuscular formulations and age groups for which use is approved are presented in Table 4. The intramuscular formulations can be used in children with and without 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 administration of IIV3.

Intramuscular formulations of IIV4 are available from several manufacturers. Different formulations have different age indications, but there are brands licensed for use in children as young as 6 months of age. In children, the most common injection site adverse reactions were pain, redness, and swelling. The most common systemic adverse events were drowsiness, irritability, loss of appetite, fatigue, muscle aches, headache, arthralgia, and gastrointestinal tract symptoms. These events were reported with comparable frequency among participants receiving the licensed comparator IIV3. IIV4 is an acceptable vaccine for people 6 months or older when otherwise appropriate and may offer broader protection against circulating influenza B strains than IIV3.

An intradermal formulation of IIV4 is licensed and available for use in persons 18 through 64 years of age. Intradermal vaccine administration involves a microinjection with a shorter needle than needles used for intramuscular administration. The most common adverse events are redness, induration, swelling, pain, and itching, which occur at the site of administration. There is no preference for intramuscular or intradermal immunization with IIV4 in persons 18 through 64 years of age. Therefore, pediatricians may choose to use either the intramuscular or intradermal product for their young adult patients and for any adults they are vaccinating in their office.

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During the 2 influenza seasons spanning 2010–2012, there were increased reports of febrile seizures in the United States in young children who received IIV3 and the 13-valent pneumococcal conjugate vaccine (PCV [PCV13]) concomitantly. Subsequent retrospective analyses of past seasons have revealed a slight increase in the risk of febrile seizures in children 6 through 23 months of age when vaccines are given concomitantly with IIV. For example, although 1 study found that IIV3 was not independently associated with a risk of febrile seizures, an increased risk of febrile seizures was noted when IIV3 was administered on the same day as either PCV or diphtheria-tetanus-acellular pertussis (DTaP) vaccine. Data on which dose in the series for either of these vaccines were not documented. The concomitant administration of IIV3, PCV, and DTaP was associated with the greatest relative risk estimate, corresponding to a maximum additional 30 febrile seizure cases per 100 000 children vaccinated, compared with the administration of the vaccines on separate days. In contrast, data from the FDA's Postlicensure Rapid Immunization Safety Monitoring (PRISM) program, the largest vaccine safety surveillance program in the United States, revealed that there was no significant increase in febrile seizures associated with concomitant administration of these 3 vaccines in children 6 to 59 months of age during the 2010–2011 season. Although the possibility of increased risk of febrile seizures cannot be ruled out, simultaneous administration of IIV with PCV13 and/or other vaccines for the 2016–2017 influenza season continues to be recommended when these vaccines are indicated. Overall, the benefits of timely vaccination with same-day administration of IIV and PCV or DTaP outweigh the risk of febrile seizures, which rarely have any long-term sequelae, with simultaneous administration.

Two trivalent influenza vaccines manufactured with the use of newer technologies will also be available for people 18 years or older during the 2016–2017 season: trivalent recombinant hemagglutinin influenza vaccine (RIV3) and trivalent cell culture–based inactivated influenza vaccine (ccIIV3), both administered intramuscularly. RIV3 is a recombinant baculovirus-expressed hemagglutinin vaccine produced in cell culture. The most frequently reported adverse events after the administration of RIV3 and ccIIV3 are pain, headache, myalgia, and fatigue. RIV3 and ccIIV3 have been shown to be efficacious against influenza disease in randomized controlled efficacy trials. A quadrivalent cell culture–based inactivated influenza vaccine (ccIIV4), administered intramuscularly, also will be available for people 4 years and older during the 2016–2017 season. Studies showed noninferiority of ccIIV4 compared with ccIIV3; ccIIV4 elicited a robust immune response in both children and adults. ccIIV4 has a similar safety profile to ccIIV3 and other licensed trivalent influenza vaccines. In children aged 4 through 17 years, injection site tenderness and erythema were the most common (≥10%) local reactions, and the most common (≥10%) systemic reactions included sleepiness/fatigue and irritability/headache.

In November 2015, the FDA licensed a trivalent, MF-59–adjuvanted IIV for people 65 years and older. This vaccine is the first adjuvanted influenza vaccine marketed in the United States. Adjuvants elicit a more robust immune response, which could lead to a reduction in the number of doses required for children. The vaccine is currently being studied in children.

Table 4 summarizes information on the types of IIVs licensed for children and adults during the 2016–2017 season. More than 1 product may be appropriate for a given patient. Vaccination should not be delayed to obtain a specific product.

A large body of scientific evidence shows that thimerosal-containing vaccines are not associated with an increased risk of autism spectrum disorders in children. Thimerosal from vaccines has not been linked to any other medical condition. As such, the AAP extends its strongest support to the current WHO 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 minute amounts of thimerosal in some IIV formulations (Table 4), and in some states, including California, Delaware, Illinois, Missouri, New York, and Washington, there is 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 IIV rather than delaying vaccination while waiting for reduced-thimerosal-content or thimerosal-free vaccines. Although some formulations of IIV contain a trace amount of thimerosal, thimerosal-free IIV products can be obtained (Table 4). Vaccine manufacturers are delivering increasing amounts of thimerosal-free influenza vaccine each year.

Vaccine Effectiveness and LAIV

The AAP supports the decision by the CDC that LAIV4 not be used in any setting during the 2016–2017 influenza season. This interim recommendation follows 3 influenza seasons during which observational data from the US Influenza Vaccine

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Effectiveness Network revealed that LAIV performed poorly (see Table 2). The 2015–2016 influenza season was the first season in which an updated influenza A (H1N1) pdm09 LAIV virus strain was used in response to unexpectedly low vaccine effectiveness for LAIV against influenza A (H1N1)pdm09 viruses in the 2013–2014 influenza season. Despite this virus strain adjustment, LAIV was not effective against influenza A (H1N1)pdm09 and influenza B viruses among children 2 through 17 years of age. Results of relative vaccine effectiveness favored IIV over LAIV for both influenza A (H1N1)pdm09 viruses among children in this age range.

During the 2014–2015 influenza season, the predominant circulating influenza A (H3N2) viruses were antigenically distinct from the influenza A (H3N2) vaccine viruses, resulting in reduced vaccine effectiveness against influenza A (H3N2) viruses in all ages. In contrast to what had been anticipated from previous studies, LAIV did not offer greater protection than IIV against the drifted H3N2 viruses. During the 2013–2014 season, observational data from the US Influenza Vaccine Effectiveness Network and 2 additional studies showed that LAIV was not effective against the predominantly circulating influenza A (H1N1) pdm09 viruses when compared with IIV in children 2 through 8 years of age.

INFLUENZA VACCINES AND EGG ALLERGY

Although most IIV vaccines are produced in eggs and contain measurable amounts of egg protein, recent data have shown that IIV administered in a single, age-appropriate dose is well tolerated by recipients with a history of egg allergy of any severity. Recent literature has shown that egg allergy does not impart an increased risk of anaphylactic reaction to vaccination with IIV. A 2012 review of published data found no instances of anaphylaxis among 4172 egg-allergic patients, 513 of whom had a history of severe egg allergy, after vaccination with influenza vaccine; some did have milder reactions. According to a Vaccine Safety Datalink study, the rate of anaphylaxis after IIV3 administration is about 1 per 1 000 000 doses (10 cases in almost 7.5 million doses given alone from 2009 to 2011). This rate is not different from those of other vaccines, including ones that do not contain egg. Although a waiting period of 30 minutes after vaccination for patients with egg allergy was previously recommended, this study also found that the onset of symptoms of anaphylaxis after receiving any vaccine began more than 30 minutes later in 21 of 29 cases. In addition, ccIIV4 is anticipated to be available for people 4 years and older during the 2016–2017 season.

The Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma, and Immunology and the American College of Allergy, Asthma, and Immunology, states that special precautions regarding medical setting and waiting periods after the administration of IIV to egg-allergic recipients beyond those recommended for any vaccine are no longer warranted. Therefore, the algorithm used beginning in the 2011–2012 influenza season to guide vaccination precautions on the basis of the severity of the allergic reaction to eggs is not necessary. The recommended waiting period for influenza vaccine, as for any vaccine, is 15 minutes after vaccination for all vaccine recipients to decrease the risk of injury should they faint. Standard vaccination practice should include the ability to respond to acute hypersensitivity reactions.[3]

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). 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° to 8°C (36°–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. The volume of vaccine is age dependent; infants and toddlers 6 months through 35 months of age should receive a dose of 0.25 mL, and all persons 3 years (36 months) and older should receive a dose of 0.5 mL. 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.

Intradermal Vaccine

IIVs for intradermal injection are shipped and stored at 2° to 8°C (36°–46°F). These vaccines are administered intradermally only to people 18 through 64 years of age, preferably over the deltoid muscle, and only using the device included in the vaccine package. Vaccine is supplied in a single-dose, prefilled

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microinjection system (0.1 mL) for adults. The package insert contains the full administration details of this product.

CURRENT RECOMMENDATIONS

Seasonal influenza vaccination with IIV is recommended for all children 6 months and older. LAIV should *not* be used. Children and adolescents with certain underlying medical conditions have an elevated risk of complications from influenza, which include 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, including juvenile idiopathic arthritis or Kawasaki disease;
- chronic renal dysfunction;
- chronic metabolic disease, including diabetes mellitus;
- any condition that can compromise respiratory function or handling of secretions or that can increase the risk of aspiration, such as neurodevelopmental disorders, spinal cord injuries, seizure disorders, or neuromuscular abnormalities; and
- pregnancy.

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

- Household contacts and out-of-home care providers of children younger than 5 years and of at-risk children of all ages
- Any woman who is pregnant or considering pregnancy, is in the postpartum period, or is breastfeeding during the influenza season. Studies have shown that infants born to immunized women have better influenza-related health outcomes compared with infants of unimmunized women. However, according to Internet-based panel surveys conducted by the CDC, only approximately 50% of pregnant women reported receiving an influenza vaccine during the 2014–2015 season, even though both pregnant women and their infants are at higher risk of complications. In addition, data from some studies suggest that influenza vaccination in pregnancy may decrease the risk of preterm birth and infants being small for gestational age. Breastfeeding also is recommended to protect against influenza viruses by activating innate antiviral mechanisms, specifically type 1 interferons. In addition, the breast milk of mothers vaccinated during the third trimester contains higher levels of influenza-specific immunoglobulin A. Greater exclusivity of breastfeeding in the first 6 months of life decreases the episodes of respiratory illness with fever in infants of vaccinated mothers. Pregnant women can receive influenza vaccine safely during any trimester.
- American Indian/Alaska Native children and adolescents
- HCP or health care volunteers. Despite the AAP recommendation for mandatory influenza immunization for all health care personnel,[2] many remain unvaccinated. With an increasing number of organizations mandating influenza vaccine, coverage among HCP increased to 77% in the 2014–2015 season. The 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.[2] Mandating influenza vaccine for all HCP is ethical, just, and necessary to 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 put the health and safety of patients first.
- Close contacts of immunosuppressed people

CONTRAINDICATIONS AND PRECAUTIONS

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 moderate to severe febrile illness, based on the judgment of the clinician, should not be vaccinated with IIV until resolution of the illness. Infants younger than 6 months should also not be vaccinated with IIV. A previous severe allergic reaction (ie, anaphylaxis involving cardiovascular changes, respiratory or gastrointestinal tract symptoms, or reactions that necessitate the use of epinephrine) to influenza vaccine, regardless of the component suspected of being responsible for the reaction, continues to be a contraindication to future receipt of the vaccine.

The estimated risk of Guillain-Barré syndrome (GBS) is low, especially in children. As a precaution, people who are not at high risk of severe

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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 and who also are at high risk of severe complications from influenza.

SURVEILLANCE

Information about influenza surveillance is available through the CDC Voice Information System (influenza update: 888-232-3228) or at www.cdc.gov/flu/index.htm. Although current influenza season data on circulating strains do not necessarily predict which and in what proportion strains will circulate in the subsequent season, it is instructive to be aware of 2015–2016 influenza surveillance data and use them as a guide to empirical therapy until current seasonal data are available from the CDC. Information is posted weekly on the CDC Web site (www.cdc.gov/flu/weekly/fluactivitysurv.htm). The AAP offers "What's the Latest With the Flu" (http://www.aap.org/disasters/flu) messages to highlight those details most relevant for AAP members and child care providers on a monthly basis during influenza season.

VACCINE IMPLEMENTATION

These updated recommendations for the prevention and control of influenza in children may have considerable operational and fiscal effects on pediatric practice. Therefore, the AAP has developed implementation guidance on supply, payment, coding, and liability issues; these documents can be found at http://redbook.solutions.aap.org/ss/vaccine-policy-guidance.aspx.

In addition, the AAP's Partnership for Policy Implementation has developed a series of definitions with the use of accepted health information technology standards to assist in the implementation of this guideline in computer systems and quality measurement efforts. This document is available at www2.aap.org/informatics/PPI.html.

The interim recommendation that LAIV should not be used in any setting during the 2016–2017 season could have supply and financial effects on health care settings that have already preordered their influenza vaccines. The AAP is advocating with the manufacturer to appropriately address reimbursement for LAIV. In response to a decrease in overall influenza vaccine supply (ie, LAIV represented approximately 8% of an anticipated 171–176 million doses), manufacturers may adjust their production capacities of IIV.

USE OF ANTIVIRAL MEDICATIONS

Oral oseltamivir remains the antiviral drug of choice for the management of influenza infections. Inhaled zanamivir is an equally acceptable alternative for patients who do not have chronic respiratory disease. However, it is more difficult to administer. Antiviral resistance to either drug can emerge, necessitating continuous population-based assessment that is conducted by the CDC. If local or national influenza surveillance data indicate the emergence of an influenza strain with a known antiviral resistance profile, then empirical treatment can be directed toward that strain with an effective antiviral agent. During the 2015–2016 season, the great majority of influenza strains were susceptible to oseltamivir, zanamivir, and peramivir. In contrast, high levels of resistance to amantadine and rimantadine exist, so these drugs should not be used in the upcoming season unless resistance patterns change significantly.

- Current treatment guidelines for antiviral medications (Table 5) are unchanged for the 2016–2017 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 commercially manufactured liquid formulation has a concentration of 6 mg/mL. If the commercially manufactured oral suspension is not available, the capsule may be opened and the contents mixed with simple syrup or Ora-Sweet SF (sugar-free) by retail pharmacies to a final concentration of 6 mg/mL (Table 5).
- Continuous monitoring of the epidemiology, change in severity, and resistance patterns of influenza strains may lead to new guidance.

Regardless of influenza vaccination status and whether the onset of illness has been <48 hours, treatment should be *offered* as early as possible for the following individuals (Table 6):

- any hospitalized child clinically presumed to have influenza disease or with severe, complicated, or progressive illness attributable to influenza; and
- influenza infection of any severity in children at high risk of complications of influenza infection (Table 3).

Treatment should be *considered* for the following individuals (Table 6):

- any otherwise healthy child clinically presumed to have influenza disease (the greatest effect on outcome will occur if treatment can be initiated within 48 hours of illness onset but still should be considered if later in the course of illness); and
- children clinically presumed to have influenza disease and whose siblings or household contacts either are younger than 6 months or who have underlying medical conditions that predispose them to complications of influenza.

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TABLE 5 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2016–2017 Influenza Season: United States

Medication	Treatment (5 Days)	Chemoprophylaxis (10 Days)
Oseltamivir[a]		
Adults	75 mg twice daily	75 mg once daily
Children aged ≥12 months		
Body weight		
≤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 aged 9–11 months[b]	3.5 mg/kg per dose twice daily	3.5 mg/kg per dose once daily
Term infants aged 0–8 months[b]	3 mg/kg per dose twice daily	3 mg/kg per dose once daily for infants 3–8 months; not recommended for infants <3 months old unless situation is judged critical, because of limited safety and efficacy data in this age group
Preterm infants	See details[c]	
Zanamivir[d]		
Adults	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily
Children (≥7 years for treatment, ≥5 years for chemoprophylaxis)	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily

Sources: CDC. 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; 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.

[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 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 is also 6 mg/mL), based on instructions that are present 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 of 10–30 mL/min: 75 mg, once daily, for 5 d. For chemoprophylaxis of patients with creatinine clearance of 10–30 mL/min: 30 mg, once daily, for 10 d after exposure or 75 mg, once every other day, for 10 d after exposure (5 doses). See www.cdc.gov/flu/professionals/antivirals/antiviral-drug-resistance.htm.

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

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

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

Reviews of available studies by the CDC, the WHO, and independent investigators have consistently found that timely oseltamivir treatment can reduce the duration of fever and illness symptoms and the risks of complications, including those resulting in hospitalization and death. However, treatment efficacy has not yet been evaluated among hospitalized children or children with comorbid conditions in randomized trials. Although no prospective comparative data exist to date, multiple retrospective studies and meta-analyses have been conducted to determine the role of NAIs in treating severe influenza. Most experts support use of NAIs to reduce complications and hospitalizations, but less agreement exists on the use of NAIs in low-risk populations in whom the benefits are likely modest.

Importantly, treatment with oseltamivir for children with serious, complicated, or progressive disease 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, and Infectious Diseases Society of America. Earlier treatment provides better clinical responses. However, treatment after 48 hours of symptoms in adults and children with moderate to severe disease or with progressive disease has been shown to provide some benefit and should be strongly considered. In previous years, the use of double-dose oseltamivir, particularly for those hospitalized with severe illness caused by influenza A (H1N1)pdm09, was believed to provide better outcomes compared with standard dosing. However, published data from a randomized prospective trial with 75% of subjects younger than 15 years documented no benefit of double-dose therapy over standard-dose therapy.

Dosages of antiviral agents for both treatment and chemoprophylaxis in children are shown in Table 5

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TABLE 6 Summary of Antiviral Treatment of Clinical Influenza During the 2016–2017 Season

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

(for 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). Children younger than 2 years are at an increased risk of hospitalization and complications attributable to influenza. The FDA has licensed oseltamivir for children as young as 2 weeks of age. Given preliminary pharmacokinetic data and limited safety data, the AAP believes that oseltamivir can be used to treat influenza in both term and preterm infants from birth because benefits of therapy 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 placebo when studied in children aged 1 through 12 years (ie, 15% of treated vs 9% receiving placebo). In addition, after reports from Japan of oseltamivir-attributable neuropsychiatric adverse effects, a review of controlled clinical trial data and ongoing surveillance failed to establish a link between this drug and neurologic or psychiatric events. Information is available at www.gene.com/download/pdf/tamiflu_prescribing.pdf and www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/pediatricadvisorycommittee/ucm302449.pdf.

Clinical judgment (on the basis of underlying conditions, disease severity, time since symptom onset, and local influenza activity) is an important factor in treatment decisions for pediatric patients who present with influenza-like illness. Antiviral treatment should be started as soon as possible after illness onset and should not be delayed while waiting for a definitive influenza test result, because early therapy provides the best outcomes. Influenza diagnostic tests vary by method, availability, processing time, sensitivity, and cost (Table 7), all of which should be considered in making the best clinical judgment. 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 be used in a similar fashion because of the suboptimal sensitivity and potential for false-negative results. Positive results of rapid influenza tests are helpful, because they may reduce additional testing to identify the cause of the child's influenza-like illness. Available FDA-approved rapid molecular assays are highly sensitive and specific diagnostic tests performed in less than 20 minutes with the use of RNA detection. These molecular assays or polymerase chain reaction (PCR) test confirmation are preferred in hospitalized patients because they are more sensitive compared with antigen detection. Presumptive antiviral treatment in high-risk and hospitalized patients should be started before receiving rapid test, molecular assay, or PCR results. 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.

Persons 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 3). Any otherwise healthy child who has a similar uncomplicated presentation should be considered for antiviral medication, particularly if he or she is in contact with other children who either are younger than 6 months or who 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 provide additional guidance on testing and treatment. In past years, local shortages of oseltamivir suspension have occurred because of uneven drug distribution, although national shortages have not occurred since 2009, particularly given the availability of the capsule formulation that can be made into a suspension for young children (Table 5).

Randomized placebo-controlled studies showed that oseltamivir and zanamivir were efficacious when administered as chemoprophylaxis to household contacts after a family member had laboratory-confirmed influenza. During the 2009 pandemic, the emergence of oseltamivir resistance was noted among people

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TABLE 7 Comparison of Types of Influenza Diagnostic Tests Ordered by Test Accuracy and Time to Results

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

Adapted from the CDC. Guidance for clinicians on the use of rapid influenza diagnostic tests. Available at: www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm. Accessed June 8, 2016.

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 symptomatic children. Early, full-treatment doses provided to high-risk symptomatic patients 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), is recommended in the following situations:

- for children at high risk of complications from influenza for whom influenza vaccine is contraindicated;
- for children at high risk during the 2 weeks after influenza vaccination, when 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 who 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 persons are at high risk of complications from influenza; and
- for children at high risk 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 change on the basis of updated recommendations from the CDC in concert with antiviral availability, local resources, clinical judgment, recommendations from local or public health authorities, risk of influenza complications, type and duration of exposure contact, and change in epidemiology or severity of influenza. Chemoprophylaxis is not recommended for infants younger than 3 months unless the situation is judged critical because of limited efficacy data in this age group.

Chemoprophylaxis should not be considered a substitute for vaccination. Influenza vaccine should always be offered before and within the influenza season when not contraindicated, even after 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 may be associated with antiviral agents; indiscriminate use might limit availability. Pediatricians should inform recipients of antiviral chemoprophylaxis that the risk of influenza is lowered but still remains while taking the medication, and susceptibility to influenza returns when the medication is discontinued. Oseltamivir use is not

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a contraindication to vaccination with IIV. For recommendations on treatment and chemoprophylaxis against influenza, see Tables 5 and 6. Among some high-risk people, both vaccination and antiviral chemoprophylaxis may be considered. Updates will be available at www.aapredbook.org/flu and www.cdc.gov/flu/professionals/antivirals/index.htm.

FUTURE DIRECTIONS

For the 2016–2017 season, postmarketing safety and real-time vaccine effectiveness data will be analyzed as they become available. Continued evaluation of the safety, immunogenicity, and effectiveness of influenza vaccine, especially for children younger than 2 years, 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. In addition, with limited data on the use of NAIs in hospitalized children or in children with comorbid conditions, prospective randomized clinical trials in this population are warranted. In addition, to administer antiviral therapy optimally in hospitalized patients with influenza who cannot tolerate oral or inhaled antiviral agents, FDA-approved intravenous NAIs for children also are needed. A single-dose, intranasal drug, lananimivir octanoate, needs further research as a potential option for influenza prophylaxis in children.

The interim recommendation that LAIV4 not be used in children will be reevaluated for future influenza seasons, although it is recognized that analyses of LAIV effectiveness in the United States during the 2016–2017 influenza season will be limited. Data on the vaccine effectiveness of LAIV4 against a matched H3N2 virus strain are lacking. Analyses of LAIV effectiveness also differ somewhat between the CDC and other groups in the United States and abroad. This discrepancy may be attributable to varied sample sizes, dissimilar rates of vaccine exposure history in different populations, interference with the addition of the fourth vaccine antigen in the quadrivalent formulation, or other unknown factors. In addition, it recently has been documented that LAIV is well tolerated in children with a history of anaphylaxis after exposure to egg, similar to IIV. This finding could be clinically useful in the future.

Immunizing all HCP, 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 immunization of 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 important, 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 the identification of methods to enhance uptake.

Efforts should be made to create adequate outreach and infrastructure to facilitate the optimal distribution of vaccine so that more people are immunized. Pediatricians also might consider becoming more involved in pandemic preparedness and disaster-planning efforts. A bidirectional partner dialog between pediatricians and public health decision-makers assists efforts to address children's issues during the initial state, regional, and local plan-development stages. Additional information can be found at www.aap.org/disasters/resourcekit.

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 child care centers to provide influenza vaccine. If alternate venues, including pharmacies and other retail-based clinics, are used for vaccination, a system of patient record transfer is beneficial in maintaining the accuracy of immunization records. Immunization information systems should be used whenever available. Two-dimensional barcodes have been used to facilitate more efficient and accurate documentation of vaccine administration, with limited experience to date. Additional information concerning current vaccines shipped with two-dimensional barcodes can be found at www.cdc.gov/vaccines/programs/iis/2d-vaccine-barcodes/. Access to care issues, lack of immunization records, and questions regarding who can provide consent may be addressed by linking children (eg, those in foster care or refugee, immigrant, or homeless children) with a medical home, by using all health care encounters as vaccination opportunities, and more consistently by using immunization registry data. Innovative strategies of capturing those who usually

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prefer the intranasal formulation would be valuable given the recent recommendation to not use LAIV this season.

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. Finally, efforts to improve the vaccine development process to allow for a shorter interval between the identification of vaccine strains and vaccine production continue. Pediatricians can remain informed during the influenza season by following the AAP *Red Book* Online Influenza Resource Page (www.aapredbook.org/flu).

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ABBREVIATIONS

AAP: American Academy of Pediatrics
ccIIV3: trivalent cell culture-based inactivated influenza vaccine
ccIIV4: quadrivalent cell culture-based inactivated influenza vaccine
CDC: Centers for Disease Control and Prevention
CI: confidence interval
DTaP: diphtheria-tetanus-acellular pertussis
FDA: US Food and Drug Administration
GBS: Guillain-Barré syndrome
HCP: health care personnel
IIV: inactivated influenza vaccine
IIV3: trivalent inactivated influenza vaccine
IIV4: quadrivalent inactivated influenza vaccine
LAIV: live attenuated influenza vaccine
LAIV4: quadrivalent live attenuated influenza vaccine
NAI: neuraminidase inhibitor
PCR: polymerase chain reaction
PCV: pneumococcal conjugate vaccine
RIV3: trivalent recombinant influenza vaccine
WHO: World Health Organization

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