



SPANISH ASSOCIATION OF PAEDIATRICS

Vaccination against seasonal flu in childhood and adolescence. Recommendations of the Advisory Committee on Vaccines and Immunizations of the Spanish Association of Pediatrics (CAV-AEP) for the 2024–2025 season



Javier Álvarez Aldeán^a, Franciso José Álvarez García^{b,*}, María Garcés-Sánchez^c, Elisa Garrote Llanos^d, Antonio Iofrío de Arce^e, Marisa Luisa Navarro Gómez^f, Valentín Pineda Solas^g, Irene Rivero Calle^h, Jesús Ruiz-Contrerasⁱ, Ignacio Salamanca de la Cueva^j, Pepe Serrano Marchuet^k, en representación del Comité Asesor de Vacunas de la Asociación Española de Pediatría (CAV-AEP)

^a Servicio de Pediatría, Hospital Costa del Sol, Marbella, Málaga, Spain

^b Centro de Salud de Llanera, Lugo de Llanera; Departamento de Medicina, Universidad de Oviedo, Oviedo, Spain

^c Centro de Salud Nazaret, FISABIO, Valencia, Spain

^d Sección de Infectología, Hospital Universitario Basurto, Facultad de Medicina, Universidad del País Vasco, UPV-EHU, Bilbao, Spain

^e Centro de Salud El Ranero, Murcia, Spain

^f Servicio de Pediatría, Hospital Universitario Gregorio Marañón; Departamento de Pediatría, Facultad de Medicina, Universidad Complutense de Madrid, CIBER ISCIII y IISGM, Madrid, Spain

^g Sección de Infectología Pediátrica, Hospital Universitario Parc Taulí; Universidad Autónoma de Barcelona, Sabadell, Barcelona, Spain

^h Sección de Pediatría Clínica, Infectológica y Traslacional, Hospital Clínico Universitario de Santiago de Compostela; Sociedad Española de Infectología Pediátrica (SEIP), Grupo Genética, Vacunas, Infecciones y Pediatría (GENVIP), Spain

ⁱ Pediatra, Madrid, Spain

^j Unidad de Investigación, Instituto Hispalense de Pediatría, Sevilla, Spain

^k Pediatra, Barcelona, Spain

Received 25 April 2024; accepted 25 April 2024

Available online 8 June 2024

KEYWORDS

Flu vaccine;
Child;

Abstract The flu is a constant threat that can sometimes cause severe forms of disease. The highest incidence rates by age group occur in children under 15 years of age, especially in those under 5 years, in whom the rate of hospitalization is also similar to the population aged 65 years and older. In addition, children are the main transmitters of the infection. In Spain, 5 influenza

DOI of original article: <https://doi.org/10.1016/j.anpede.2024.04.012>

* Corresponding author.

E-mail address: pacoalvarez1959@yahoo.es (F.J. Álvarez García).

2341-2879/© 2024 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Adolescent;
Pregnant;
Health worker;
CAV-AEP

vaccines are authorized for the paediatric age group: three inactivated tetravalent vaccines harvested from fertilised eggs, one tetravalent inactivated vaccine obtained from cell cultures and one attenuated tetravalent vaccine for intranasal administration, which will become trivalent in the 2024–2025 season by excluding the B Yamagata lineage as recommended by the WHO. The CAV-AEP recommends systematic vaccination in children aged 6–59 months, children and adolescents belonging to risk groups, people who can transmit the flu to groups at risk of complicated flu, and household contacts or close family of infants under 6 months. From 2 years of age, the intranasal attenuated vaccine is preferred due to its greater acceptability and thus contribution to greater vaccination coverage. The CAV-AEP also considers that vaccination against influenza of healthy children and adolescents aged 5–18 years is advisable, as it provides individual protection and promotes protection at the family and community levels. It is especially important to vaccinate all health care professionals against influenza as well as pregnant women at any time during pregnancy.

© 2024 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

Vacuna de la gripe;
Niño;
Adolescente;
Embarazada;
Profesional sanitario;
CAV-AEP

Vacunación frente a la gripe estacional en la infancia y la adolescencia. Recomendaciones del Comité Asesor de Vacunas e Inmunizaciones de la Asociación Española de Pediatría (CAV-AEP) para la temporada 2024–2025

Resumen La gripe es una amenaza constante, que en ocasiones puede producir cuadros clínicos graves. Las mayores tasas de incidencia por grupos de edad ocurren en los menores de 15 años, especialmente en los menores de 5 años, en los que además las tasas de hospitalización son similares a las de las personas de 65 años en adelante. Además, los niños son los principales vectores de transmisión de la enfermedad. En España, están autorizadas cinco vacunas antigripales en la edad pediátrica: tres inactivadas tetravalentes procedentes de cultivos en huevos embrionados, una inactivada tetravalente procedente de cultivos celulares, y una atenuada tetravalente de administración intranasal, que para la temporada 2024–2025 pasará a ser trivalente, al no incluir el linaje B Yamagata como recomienda la OMS. El CAV-AEP recomienda la vacunación sistemática en: niños de 6 a 59 meses, niños y adolescentes pertenecientes a grupos de riesgo, personas que puedan transmitir la gripe a los grupos que tienen riesgo de gripe complicada, y convivientes o entorno familiar de menores de 6 meses. A partir de los 2 años de edad, se recomienda preferentemente la vacuna atenuada intranasal por su mayor aceptabilidad y facilitar la mejora de las coberturas. El CAV-AEP considera también que la vacunación antigripal de niños y adolescentes de 5–18 años sanos es una medida recomendable, por cuanto le proporciona protección individual y favorece la protección familiar y comunitaria. Es especialmente importante la vacunación antigripal de todos los profesionales sanitarios y la vacunación de las gestantes en cualquier momento del embarazo.

© 2024 Asociación Española de Pediatría. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Influenza continues to be a constant threat and an enormous public health problem, and vaccination is the most effective preventive measure. In 2012, the World Health Organization (WHO) recommended giving children aged 6–59 months priority group status for vaccination against influenza. Since 2005, the Advisory Committee on Vaccines and Immunizations (CAV) of the Asociación Española de Pediatría (AEP, Spanish Association of Paediatrics) publishes annual recommendations for vaccination against influenza in children and adolescents, judging that in children aged more than 6 months who do not belong to any established risk groups, vaccination is advisable to grant the child individual pro-

tection and to contribute to the protection of the family and the community, and has recommended routine vaccination of children aged 6–59 months from the 2021–2022 season. In December 2022, the Interterritorial Council of the National Health System of Spain (known as CISNS) included routine vaccination against influenza for all children aged 6–59 months in its unified immunization schedule for the lifespan for 2023, a measure that was implemented by all the autonomous communities in Spain in 2023–2024, although three of them (Andalusia, Galicia and the Region of Murcia) had already started implementing it in the previous season.

Priority is given to vaccination against influenza of individuals older than 6 months who belong to any risk group for severe influenza, including pregnant women, household

Table 1 Summary of the recommendations of the CAV-AEP for vaccination against influenza for the 2024–2025 season.

The CAV-AEP recommends vaccination against influenza in the following groups:

- All children aged 6–59 meses (universal recommendation)
 - Children and adolescents aged 5 and 18 years (individualized recommendation)^a
 - Risk groups: individuals aged 6 months or older in specific situations or with underlying diseases associated with an increased risk of developing complications of influenza
 - Household contacts aged 6 months or older of individuals at risk
 - Household contacts aged 6 months or older of infants aged less than 6 months
 - All health care professionals
 - Pregnant woman, for their own protection and the protection of their future children, at any point of pregnancy
- In children aged less than 2 years, use of the intranasal attenuated vaccine is preferred

^a The CAV-AEP considers that the health care authorities should include routine vaccination of children and adolescents aged 6 months to 18 years in the vaccination schedule, especially children aged 6–59 months, but given the discouraging vaccination coverage against influenza in this age group, it is our opinion that all possible efforts should be made by the public health system, health care professionals and scientific societies to pursue, as the chief objective, an increase in vaccination coverage in this group, and that, once this is achieved, efforts should be made not only to maintain an adequate coverage but also to increase routine vaccination against influenza in children and adolescents aged 6–18 years.

contacts of individuals at risk and health care workers. Unfortunately, the vaccination coverages achieved in these groups and in healthy children included in seasonal campaigns have been low, generally falling short of established objectives. Health care authorities, health care professionals, scientific societies and patient associations need to get involved more actively to succeed in increasing them.

In this article, we present the recommendations of the CAV-AEP for vaccination against influenza in the 2024–2025 season (summarised in Table 1), and discuss other related aspects, such as the effectiveness and safety of these vaccines in the paediatric population.

Epidemiology of influenza in the 2023–2024 season

Every year, there are approximately 1000 million cases of seasonal flu, including 3–5 million severe cases and 290 000–650 000 deaths.¹ The proportion of the paediatric population affected during the annual influenza outbreaks ranges between 30% and 40%, with nearly 1 million severe cases in children under 5 years worldwide and 99% of flu-related deaths occurring in developing countries.

Each season, children aged less than 15 years, especially those age less than 5 years, are the age group with the highest incidence of influenza. In Spain, the disease activity data for the 2023–2024 season (through week 15 of 2024) reported by the acute respiratory tract infection surveillance system (SIVIRA)² show that the incidence at the primary care level peaked on week 52/2023, a very high and intense peak compared to previous seasons, while the value below the threshold that marks the end of the season occurred in week 06/2024. By age group, once again the highest incidence occurred in infants aged less than 1 year, followed by children aged 1–4 years and children and adolescents aged 5–14 years. As regards hospital admission due to influenza, following the group aged more than 65 years, infants aged less than 1 year were the group with the highest hospitalization rate. In Europe, in the 2023–2024 season influenza activity also started around mid-November, peaking in the second or third week of December

and gradually decreasing until the early weeks of January. The main circulating strain was A(H1N1)pdm09, followed by a lower proportion of A(H3N2) and a few isolated cases of B/Victoria.³

Vaccination against influenza for the 2024–2025 season

Every year, the WHO issues recommendations regarding the composition of the seasonal influenza vaccines for each hemisphere to aim at achieving an adequate match between the components of the vaccines and the viruses expected to be circulating during the season based on epidemiological surveillance data and the characterization of the circulating viruses in the previous season. For the first time in years, the WHO⁴ has recommended the use of trivalent vaccines for the upcoming season excluding the B/Yamagata lineage on account of the lack of detection of viruses of this lineage since 2020 (Table 2).

In Spain, seven vaccine formulations will be distributed for the upcoming season, of which 5 (4 inactivated and 1 live attenuated) are authorised for use in children and adolescents (Table 3). The attenuated vaccine, following the recommendation of the WHO, will have a trivalent composition excluding the Yamagata lineage. The inactivated vaccines will continue to be quadrivalent.

Of the 4 inactivated vaccines, 3 are manufactured using fertilised chicken eggs in a regulated process, allowing the viruses to replicate in the eggs prior to inactivation, and the remaining one is a cell culture-based vaccine manufactured by inoculating virus into cultured mammalian cells and allowing them to replicate, after which the viral antigen is purified. In theory, the cell culture method could offer better results compared to the egg-based method, as adaptive mutations may affect viral synthesis in the latter, although the current evidence⁵ is not consistent enough due to the lack of comparative clinical studies spanning several seasons.

The intranasal live attenuated vaccine is developed using embryonated chicken eggs. It has the capacity to simulate natural infection and thus induce a humoral and

Table 2 Vaccine composition recommendations for the 2024–2025 season in the northern hemisphere (WHO).^{13,14}

| Trivalent vaccines | Fertilized chicken egg-based vaccines | | Recombinant or cell culture-based vaccines |
|-----------------------|---|--|---|
| | Inactivated | Attenuated | |
| | <ul style="list-style-type: none"> • A H1N1: an A/Victoria/4897/2022 (H1N1)pdm09-like virus • A H3N2: A/Thailand/8/2022 (H3N2)-like virus • B/Victoria lineage: /Austria/1359417/2021-like virus | <ul style="list-style-type: none"> • A H1N1: A/Norway/31694/2022 (H1N1)pdm09 • A H3N2: an A/Thailand/8/2022/(H3N2)-like virus • B/Victoria lineage: cepa similar a B/Austria/1359417/2021 | <ul style="list-style-type: none"> • A H1N1: an A/Wisconsin/67/2022 (H1N1)pdm09-like virus • A H3N2: A/Massachusetts/18/2022 (H3N2)-like virus • B, Victoria lineage: B/Austria/1359417/2021 (B/Victoria lineage)-like virus |
| Quadrivalent vaccines | [0.2-4]Same composition, with addition of a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus | | |

Table 3 Influenza vaccines available for individuals aged less than 18 years distributed in Spain for the 2024–2025 season.

| Influenza vaccines for use in paediatrics. 2024–2025 season | | | | | |
|---|-----------------------------------|--------------|------------|------------------------------------|------------|
| Preparation (manufacturer) | Virus | Vaccine type | Age | Dose | Route |
| Flucelvax Tetra (Seqirus) | Quadrivalent (cell culture-based) | Inactivated | ≥2 years | 0.5 mL | IM |
| Influvac Tetra (Mylan) | Quadrivalent (egg-based) | Inactivated | ≥6 months | 0.5 mL | IM/SC |
| Fluarix Tetra (GSK) | Quadrivalent (egg-based) | Inactivated | ≥6 months | 0.5 mL | IM |
| Vaxigrip (Sanofi) | Quadrivalent (egg-based) | Inactivated | ≥6 months | 0.5 mL | IM/SC |
| Fluenz (AstraZeneca) | Trivalent (egg-based) | Attenuated | 2–17 years | 0.2 mL (0.1 mL in each nostril) | Intranasal |

IM, intramuscular; SC, deep subcutaneous injection.

Source: <https://vacunasaep.org/profesionales/fichas-tecnicas-vacunas/resultados?diseases=148> (CAV-AEP/April 2024).

cell-mediated immune response that also involves mucosal immunity.

Dosage and administration

In concordance with the recommendations approved on September 12, 2023 by the Public Health Committee of the CISNS,⁶ in September 2023 the CAV-AEP updated its recommendations for the 2023–2024 vaccination season so that the schedule for healthy children aged 6–59 months would include a single dose with inactivated or intranasal attenuated vaccine. The one exception corresponds to children aged less than 9 years in risk groups who are getting vaccinated against influenza for the first time, in whom the schedule consists of 2 doses given 4 weeks apart in their first influenza season (Table 4).

For inactivated vaccines, the recommended dose is 0.5 mL for every age group, while for the intranasal attenuated vaccine the dose is 0.2 mL (0.1 mL in each nostril).

Egg-based inactivated vaccines are authorised for use in children aged more than 6 months, while the cell culture-based vaccine and the intranasal attenuated vaccine are

authorised from age 2 years. In Europe, the intranasal vaccine is authorised for use through age 17 years, while in the United States it is approved for use through age 49 years.

Effectiveness of the influenza vaccine in the paediatric age group

The vaccine effectiveness (VE) of influenza vaccines varies widely based on the vaccinated population, the vaccine used, the viruses circulating in the season and the match with the viruses contained in the vaccines, among other factors,⁷ and whether the outcomes considered include efficacy against confirmed influenza, emergency department visits, hospital admission or prevented deaths.

When it comes to VE in the paediatric population, a recent review estimated it ranged between 25.6% and 78.8%.⁸ A Cochrane review of 41 studies and more than 200 000 individuals, most aged more than 2 years, concluded that universal vaccination of individuals aged 3–16 years reduced the risk of influenza infection, both with attenuated vaccines (relative risk [RR], 0.22; 95% confidence interval [CI], 0.11–0.41) and with inactivated vaccines (RR, 0.36;

Table 4 Recommended dosage of vaccines against seasonal influenza for the 2024–2025 season based on age, risk factors and previous vaccination history.

| Vaccine | Age | Number of doses based on patient category |
|---------------------|----------------------|---|
| Inactivated vaccine | 6 months–8 years | <ul style="list-style-type: none"> • General population: one dose each season, independently of history of vaccination against influenza in previous seasons • Risk groups: <ul style="list-style-type: none"> – One or no dose of vaccine received in the past: 2 doses at least 4 weeks apart – Two or more doses of vaccine or more received in the past (the 2 previous doses need not have been administered in consecutive seasons): 1 dose |
| | ≥9 years | <ul style="list-style-type: none"> • One dose per season, independently of history of vaccination against influenza in previous seasons and risk conditions |
| Attenuated vaccine | 24 months to 8 years | <ul style="list-style-type: none"> • General population: one dose each season, independently of history of vaccination against influenza in previous seasons • Risk groups (without contraindication for attenuated vaccines): <ul style="list-style-type: none"> – One or no dose of vaccine received in the past: 2 doses at least 4 weeks apart – Two or more doses of vaccine or more received in the past (the 2 previous doses need not have been administered in consecutive seasons): 1 dose |
| | ≥9 years | <ul style="list-style-type: none"> • One dose per season, independently of history of vaccination against influenza in previous seasons and risk conditions |

95% CI, 0.28–0.48).⁹ Another systematic review found a VE for prevention of any type influenza-related hospitalization of 57.48% (95% CI, 49.46–65.49), with a higher VE against H1N1 (74.07%; 95% CI, 54.85–93.30) compared to influenza B (50.87%; 95% CI, 41.75–59.98), and a moderate VE against H3N2 (40.77%; 95% CI, 25.65–55.89). The VE was highest in children under 5 years (61.71%; 95% CI, 49.29–74.12) and children aged 6–17 years (54.37%; 95% CI, 35.14–73.60).¹⁰

An interim report of data for 10 European countries, including Spain, showed that the 2023–2024 VE against influenza A for all ages was 51% (95% CI, 41–59) in primary care settings, with a VE of 71% (95% CI, 55–82) in the group aged 0–17 years that was even greater against A(H1N1)pdm09 (85%; 95% CI, 71–93). When it came to preventing hospitalization, the overall VE was 38% (95% CI, 27–48), with no figures given for the group aged less than 18 years.¹¹

In the United States, interim estimates for the 2023–2024 season showed a VE in the group aged 6 months to 17 years of 52%–67%, of 46%–59% for influenza A and of 64%–89% for influenza B.¹²

Vaccine safety, contraindications and precautions in immunization against influenza

Influenza vaccines have a high safety profile with an overall favourable risk-benefit ratio.

With inactivated vaccines, local reactions are the most frequent type of adverse event (redness and tenderness), and the most common systemic adverse events are fever, myalgia and fatigue, with a frequency that ranges between 5% and 20%. These events are usually mild and do not require medical care.¹³

When it comes to the attenuated vaccine, many clinical trials and postmarketing surveillance studies support its good safety profile. The most frequent adverse reactions are nasal congestion and fever. In a prospective observational study,¹⁴ the adverse events observed most frequently were lower respiratory tract infection and wheezing, although there was not an increase in hospital admissions compared to the unvaccinated group.

A history of anaphylactic reaction to any vaccine component, with the exception of egg,¹⁵ or to a previous dose of influenza vaccine is considered an absolute contraindication for the influenza vaccine.

The intranasal influenza vaccine is also contraindicated in¹⁶:

- Immunocompromised individuals, with the exception of children with stable HIV infection receiving antiretroviral therapy and with adequate immune function.
- Household contacts of severely immunocompromised individuals. If they receive this vaccine, contact needs to be avoided for 1–2 weeks following vaccination.
- Children aged 2–17 years currently taking aspirin or other treatment containing acetylsalicylic acid due to the association with Reye syndrome.
- Pregnant women, due to the lack of safety data.

The attenuated vaccine must be used with caution in individuals with severe asthma or active wheezing, as these conditions were not studied during clinical trials.¹⁷ The Centers for Disease Control and Prevention (CDC) of the United States consider it contraindicated in children aged 2–4 years with asthma or who have had a wheezing episode in the past 12 months, while they recommend precaution in children aged 5 or more years with asthma.¹⁸ When this vaccine

has been used in children with asthma aged 5–17 years, there have been no significant differences in the frequency of asthma symptoms or changes in pulmonary function tests in the 14 days following vaccination.¹⁹

There is no evidence in children that vaccination against influenza is a risk factor for Guillain-Barré syndrome (GBS). In addition, it is estimated that the risk of developing GBS after an influenza infection is greater than the risk associated with vaccination.^{20,21} Although it is not a contraindication but a precaution,¹⁸ the CDC recommends against administering additional doses to healthy children who developed GBS within 6 weeks of receiving the influenza vaccine. However, vaccination in subsequent seasons should still be considered in children with underlying diseases, in whom its benefits of vaccination exceed the hypothetical risk.¹⁶

Caution must be exerted in children who developed immune thrombocytopenic purpura in the week following receipt of the inactivated influenza vaccine. Given the risk of recurrence, the appropriateness of vaccination should be determined on a case-by-case basis.¹⁶

The intranasal vaccine can be administered at the same time as other parenteral or oral attenuated vaccines or as apart as desired.

Vaccination in special situations

Individuals with egg allergies

According to a study of the Vaccine Safety Datalink, the rate of anaphylaxis for seasonal flu vaccines was 1.35 per million doses (95% CI, 0.65–2.47),²² and this event is very rare in individuals with egg allergy, in whom it is usually related to components other than ovalbumin, since the amount of this protein contained in influenza vaccines ($\leq 1 \mu\text{g}/\text{mL}$)²³ is considered completely safe. Acting based on previous clinical manifestations is recommended²⁴:

- 1 Individuals with mild reactions to egg, such as urticaria, can be vaccinated against influenza with any of the available vaccines.
- 2 Individuals who have developed serious reactions after egg consumption, such as angioedema, respiratory distress or symptoms requiring adrenaline, may be vaccinated with any of the available vaccines but should be vaccinated in facilities, not necessarily hospitals, with adequately trained staff and with the experience and resources to manage potential serious reactions, and need to remain in observation for 30²⁵ to 60 min²⁶ after receiving the vaccine.
- 3 A severe allergic reaction to the influenza vaccine, independently of the component that causes the reaction, is an absolute contraindication for receiving any future doses of vaccine.

Immunocompromised individuals or individuals with chronic diseases

Vaccination against influenza in individuals who are immunocompromised or have chronic diseases is indicated yearly from age 6 months, as the morbidity and mortality are higher

in these individuals when they have the flu compared to their healthy counterparts. A study conducted in Spain should that up to 45% of children with influenza-related hospitalizations have an underlying condition associated with an increased risk, so vaccination is indicated in this group, in spite of which a remarkable 74% go unvaccinated.²⁷ Vaccination of household and other close contacts of these patients, including health care professionals, is of vital importance.²⁸

Vaccination against seasonal flu during pregnancy

Pregnant women are at increased risk of severe disease, complications and hospitalization due to influenza compared to women of reproductive age who are not pregnant,²⁹ which is why since 2012 the WHO has recommended that pregnant woman be given the highest priority.³⁰ Vaccination not only protects the pregnant woman but also the foetus and the future child in the first months of life. A large number of studies support the safety of vaccination against influenza at any time of pregnancy.^{31,32} Non-adjuvanted inactivated vaccines should be used for vaccination in pregnancy.

In Spain, influenza vaccination coverage in pregnant women continues to be suboptimal. According to data published by the SIVAMIN,³³ the coverage in pregnant women increased progressively between 2017 (29.6%) and 2020 (62.3%), the year when the target coverage threshold was met ($\geq 60\%$), probably due to the indirect effect of the COVID-19 pandemic and the uncertainties surrounding the potential coinfection by influenza and SARS-CoV-2. In 2021, the increasing trend stopped, as coverage declined to 55.2% to decrease further to 53.5% in 2022, although the coverage still remained a bit higher compared to the prepandemic period. One of the factors that poses a barrier to increasing vaccination coverage is the lack of awareness of the professionals that deliver care to pregnant women of the efficacy and safety of the influenza vaccine. The development of a multidisciplinary strategy involving all those professionals to inform pregnant women about the importance of vaccination against influenza should be made a priority.³⁴

As regards VE, a previous study demonstrated that vaccination against influenza in pregnant women reduced the risk of influenza-related hospitalization by approximately 40%,³⁵ while a more recent study found a VE in preventing hospitalization in infants under 3 months of 53% and in infant of mothers vaccinated in the third trimester of 52%.³⁶ Furthermore, other studies have found a decreased probability of preterm birth (odds ratio [OR] 0.75) and low birth weight (OR 0.73).^{32,37}

Health care professionals

Vaccination of health care professionals is particularly relevant, not only for their personal protection but also for collective protection, as they are in contact with vulnerable individuals, in addition to reducing sickness absence in staff, which would decrease the burden experienced by health care teams when demand peaks.³⁸ However, the adherence to vaccination against influenza among health care professionals is pretty low.³⁹

The CAV-AEP recommends annual vaccination against influenza in the following groups:

- Staff of health care facilities, in primary care or hospitals, in the public or private system, or in emergency services, as well as staff of pharmacies and day centres and students doing internships or practicums in health care facilities or community or day centres. Special emphasis should be placed on vaccination of staff in contact with patients at high risk of complicated influenza.
- Staff of nurseries, geriatric facilities or chronic disease care facilities.
- Household contacts or individuals providing home care to individuals at high risk or aged 65 years or older.

Recommendations for vaccination against influenza of the CAV-AEP for the 2024–2025 season

The CAV-AEP recommends vaccination against influenza in the following groups (Table 5):

- 1 Children aged 6–59 months (routine vaccination).
- 2 Children and adolescents aged 5–18 years, based on individual indications^a.
- 3 Individuals at risk of complicated influenza due to their age or risk factors.
- 4 Individuals who could transmit influenza to groups at risk of complicated disease, including household contacts of infants aged less than 6 months.
- 5 Other cases. In general, essential workers and individuals exposed to influenza at work.

The intranasal vaccine offers the advantages of greater acceptability,⁴⁰ easy administration, superior effectiveness compared to inactivated vaccines and a low reactogenicity, so, from age 2 years, the minimum age from which it can be administered according to the summary of product characteristics, it is the vaccine recommended for preferential use by the CAV-AEP.

Funding

The development of these recommendations (analysis of the published data, debate, consensus and publication) has not been supported by any funding source outside of the logistic support provided by the AEP.

^a The CAV-AEP considers that the health care authorities should include routine vaccination of children and adolescents aged 6 months to 18 years in the vaccination schedule, especially children aged 6–59 months, but given the discouraging vaccination coverage against influenza in this age group, it is our opinion that all possible efforts should be made by the public health system, health care professionals and scientific societies to pursue, as the chief objective, an increase in vaccination coverage in this group, and that, once this is achieved, efforts should be made not only to maintain an adequate coverage but also to increase routine vaccination against influenza in children and adolescents aged 6–18 years.

Conflicts of interest (last 5 years)

Javier Álvarez Aldeán has collaborated in educational activities funded by AstraZeneca, GlaxoSmithKline, MSD, Pfizer, Sanofi and Seqirus; as a researcher in clinical trials for GlaxoSmithKline and Sanofi, and as a consultant in AstraZeneca, GlaxoSmithKline, MSD, Pfizer and Sanofi advisory boards.

Francisco José Álvarez García has collaborated in educational activities funded by Alter, AstraZeneca, GlaxoSmithKline, MSD, Pfizer and Sanofi, and as a consultant in GlaxoSmithKline, MSD, Pfizer and Sanofi advisory boards.

María Garcés-Sánchez has collaborated in educational activities funded by Astra, GlaxoSmithKline, MSD, Pfizer and Sanofi, as a researcher in clinical trials for GlaxoSmithKline, Janssen, MSD, Pfizer and Sanofi, and as a consultant in GlaxoSmithKline, Novartis and Pfizer advisory boards.

Elisa Garrote Llanos has received funding to attend domestic educational activities and has participated in educational activities funded by GlaxoSmithKline, MSD, Pfizer and Sanofi, as a researcher in studies for GlaxoSmithKline and MSD, and as a consultant in GlaxoSmithKline advisory boards.

Antonio Iofrío de Arce has collaborated in educational activities funded by AstraZeneca and GlaxoSmithKline, MSD and Pfizer, and as a consultant in GlaxoSmithKline and Pfizer advisory boards. He has received financial support from GlaxoSmithKline, MSD and Pfizer to attend domestic educational activities.

Marisa Luisa Navarro Gómez has collaborated in educational activities funded by Gilead, GlaxoSmithKline, Janssen, MSD, Pfizer and ViiV, as a consultant in Abbott, AstraZeneca, Novartis and ViiV advisory boards and in clinical trials funded by GlaxoSmithKline, Pfizer, Roche and Sanofi.

Valentín Pineda Solas has received funding from MSD, Pfizer and Sanofi to attend domestic and international educational activities, has collaborated in educational activities funded by AstraZeneca, GlaxoSmithKline, MSD, Pfizer and Sanofi, and as a consultant in GlaxoSmithKline, Pfizer and Sanofi advisory boards.

Irene Rivero Calle has collaborated in educational activities funded by GlaxoSmithKline, MSD, Pfizer and Sanofi, as a researcher in vaccine clinical trials for Abbott, AstraZeneca, Enanta, Gilead, GlaxoSmithKline, HIPRA, Janssen, Medimmune, Merck, Moderna, MSD, Novavax, Pfizer, Reviral, Roche, Sanofi and Seqirus, and as a consultant in GlaxoSmithKline, MSD, Pfizer and Sanofi advisory boards.

Jesús Ruiz-Contreras has collaborated in educational activities funded by GlaxoSmithKline, MSD, Pfizer and Sanofi, and as a researcher in clinical trials for GlaxoSmithKline and Pfizer.

Ignacio Salamanca de la Cueva has collaborated in educational activities funded by GlaxoSmithKline, MSD, Moderna, Novavax, Pfizer, Sanofi Pasteur and Seqirus, as a researcher in vaccine clinical trials for Ablynx, Abbott, Almirall, Allergan, AstraZeneca, Biomedal, GlaxoSmithKline, Janssen, Lilly, Medimmune, Merck, MSD, Moderna, Nestlé, Novavax, Novartis, Nutricia, Pfizer, Roche, Regeneron, Sanofi Pasteur, Seqirus and Wyeth, and as a consultant in AstraZeneca, GSK, MSD, Moderna, Novavax, Pfizer and Sanofi Pasteur advisory boards.

Table 5 Recommendations for vaccination against influenza of the Advisory Committee on Vaccines and Immunizations of the AEP (CAV-AEP) that must be prioritised in the 2024–2025 influenza season.

1. All children aged 6–59 months (universal recommendation)
2. All children aged 5–18 years (individualised recommendation)^a
3. Children aged more than 6 months and adolescents at risk of complicated influenza due to the following circumstances or underlying diseases:
 - Chronic respiratory disease (cystic fibrosis, bronchopulmonary dysplasia, bronchiectasis, asthma and bronchial hyperresponsiveness, respiratory sequelae of severe COVID-19, etc)
 - Severe cardiovascular disease, including isolated systolic hypertension
 - Chronic metabolic disease (eg, diabetes mellitus, inborn errors of metabolism, etc)
 - Oncological disease
 - Rheumatic disease
 - Chronic neuromuscular disease and moderate or severe encephalopathy. Respiratory compromise and secretion management (tracheostomy, mechanical ventilation). Severe COVID-19 sequelae
 - Cochlear implant or awaiting implantation of one
 - Cerebrospinal fluid fistula
 - Moderate or severe undernutrition
 - Morbid obesity (BMI \geq 3 standard deviations above the mean)
 - Chronic renal or hepatic disease
 - Chronic inflammatory bowel disease
 - Coeliac disease
 - Immunodeficiency, congenital (excluding asymptomatic isolated IgA deficiency) or acquired (including HIV infection, treatment with sustained high-dose systemic corticosteroids, immunosuppressive drugs, eculizumab or ravulizumab, transplant recipients)
 - Functional or anatomical asplenia
 - Moderate to severe haematological disease (eg, clinically significant anaemia or haemoglobinopathy requiring blood products or transfusions, haemophilia and chronic bleeding disorders etc)
 - Preterm birth < 32 weeks of gestation. Age 6–24 months
 - Down syndrome and other genetic disorders associated with risk factors
 - Ongoing treatment with ASA
 - Institutionalised children or adolescents or children or wards of the state
 - Pregnant women (at any time of pregnancy, during the influenza season)
4. Individuals that could transmit influenza to individuals in risk groups:
 - Healthy children from age 6 months, healthy adolescents and adults who are close contacts (household contacts and carers) of individuals at risk^b
 - Household contacts of infants aged less than 6 months
5. Other. Essential workers or individuals exposed at work^c

^a The CAV-AEP considers that the health care authorities should include routine vaccination of children and adolescents aged 6 months to 18 years in the vaccination schedule, especially children aged 6–59 months, but given the discouraging vaccination coverage against influenza in this age group, it is our opinion that all possible efforts should be made by the public health system, health care professionals and scientific societies to pursue, as the chief objective, an increase in vaccination coverage in this group, and that, once this is achieved, efforts should be made not only to maintain an adequate coverage but also to increase routine vaccination against influenza in children and adolescents aged 6–18 years.

^b Special emphasis should be placed on vaccination against influenza of health care professionals in contact with patients, including pharmacy staff.

^c Including teachers and child care staff.

Pepe Serrano Marchuet has collaborated in educational activities funded by AstraZeneca, GlaxoSmithKline and MSD, as a researcher in clinical trials for Sanofi, and as a consultant in GlaxoSmithKline and Sanofi advisory boards. He has received funding from GlaxoSmithKline, MSD and Pfizer to attend domestic and international educational activities. He has also received grants with the support of GlaxoSmithKline.

Acknowledgments

We thank Javier Arístegui, M. José Cilleruelo Ortega, José María Corretger, Nuria García Sánchez, Ángel Hernández Merino, Manuel Merino Moína, Abián Montesdeoca Melián and Luis Ortigosa, for their in-house guidance in the development and writing of these recommendations.

References

- WHO. Fact sheets. Influenza (Seasonal). 3 Oct 2023. Available from: [https://www.who.int/news-room/factsheets/detail/influenza-\(seasonal\)](https://www.who.int/news-room/factsheets/detail/influenza-(seasonal)).
- Instituto de Salud Carlos III. Vigilancia centinela de Infección Respiratoria Aguda en Atención Primaria (IRAs) y en Hospitales (IRAG) en España. Gripe, COVID-19 y otros virus respiratorios. Informe n.º 178. Semana 15/2024 (del 8 al 14 de abril de 2024). Available from: https://docsivira.isciii.es/Informe_semanal_SiVIRA_202415_n178.html.
- ECDC. Influenza virus characterization - Summary report, Europe, enero de 2024. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/Euro-report_Jan24_corrected_150224.pdf.
- WHO. Global Influenza Programme. Recommendations for influenza vaccine composition. Available from: <https://www.who.int/teams/global-influenza-programme/vaccines/who-recommendations>.
- Imran M, Ortiz JR, McLean HQ, Fisher L, O'Brien D, Bonafede M, et al. Relative effectiveness of cell-based versus egg-based quadrivalent influenza vaccines in children and adolescents in the United States During the 2019-2020 influenza season. *Pediatr Infect Dis J*. 2022;41:769-74 <https://pubmed.ncbi.nlm.nih.gov/35797705/>
- Comisión de Salud Pública. Consejo Interterritorial del Sistema Nacional de Salud. Recomendaciones de vacunación frente a gripe y COVID-19 en la temporada 2023-2024 en España. 12 de septiembre de 2023 [accessed 30 Apr 2024]. https://www.sanidad.gob.es/areas/promocionPrevencion/vacunaciones/gripe_covid19/docs/Recomendaciones_Vacunacion-Gripe-Covid19.pdf.
- Trombetta CM, Kistner O, Montomoli E, Viviani S, Marchi S. Influenza viruses and vaccines: the role of vaccine effectiveness studies for evaluation of the benefits of influenza vaccines. *Vaccines (Basel)*. 2022;10:714 <https://pubmed.ncbi.nlm.nih.gov/35632470/>
- Orrico-Sánchez A, Valls-Arévalo Á, Garcés-Sánchez M, Álvarez Aldeán J, Ortiz de Lejarazu Leonardo R. Efficacy and effectiveness of influenza vaccination in healthy children. A review of current evidence. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2023;41:396-406 <https://pubmed.ncbi.nlm.nih.gov/36681572/>
- Jefferson T, Rivetti A, Di Pietrantonj C, Demicheli V. Vaccines for preventing influenza in healthy children. *Cochrane Database Syst Rev*. 2018;2:CD004879 <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004879.pub5/full>
- Kalligeros M, Shehadeh F, Mylona EK, Dapaah-Afryiyie C, van Aalst R, Chit A, et al. Influenza vaccine effectiveness against influenza-associated hospitalization in children: a systematic review and meta-analysis. *Vaccine*. 2020;38:2893-903 <https://pubmed.ncbi.nlm.nih.gov/32113808/>
- Maurel M, Howard J, Kissling E, Pozo F, Pérez-Gimeno G, Buda S, et al. European IVE group. Interim 2023/24 influenza A vaccine effectiveness: VEBIS European primary care and hospital multicentre studies, September 2023 to January 2024. *Euro Surveill*. 2024;29:2400089 <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.8.2400089>
- Frutos AM, Price AM, Harker E, Reeves EL, Ahmad HM, Murugan V, et al. Interim estimates of 2023-24 seasonal influenza vaccine effectiveness - United States. *MMWR Morb Mortal Wkly Rep*. 2024;73:168-74 <https://www.cdc.gov/mmwr/volumes/73/wr/mm7308a3.htm>
- Trombetta CM, Giancchetti E, Montomoli E. Influenza vaccines: evaluation of the safety profile. *Hum Vaccin Immunother*. 2018;14:657-70 <https://pubmed.ncbi.nlm.nih.gov/29297746/>
- Baxter R, Eaton A, Hansen J, Aukes L, Caspard H, Ambrose CS. Safety of quadrivalent live attenuated influenza vaccine in subjects aged 2-49 years. *Vaccine*. 2017;35:1254-8 <https://pubmed.ncbi.nlm.nih.gov/28162825/>
- Echeverría Zudaire L, Ortigosa del Castillo L, Alonso Lebrero E, Álvarez García FJ, Cortés Álvarez N, García Sánchez N, et al. Documento de consenso sobre la actitud ante un niño con una reacción alérgica tras la vacunación o alergia a componentes vacunales (SEICAP, CAV-AEP). *An Pediatr (Barc)*. 2015;83:63.e1-10 <https://www.analesdepediatria.org/es-documento-consenso-sobre-actitud-ante-articulo-S1695403314005244>
- Comité Asesor de Vacunas e Inmunizaciones (CAV-AEP). Gripe. Manual de inmunizaciones en línea de la AEP. Madrid: AEP; abril de 2024. Available from: <https://vacunasaep.org/documentos/manual/cap-26#11>.
- AEMPS/EMA. Fluenz Tetra. Ficha técnica [accessed 30 Apr 2024]. Available from: https://cima.aemps.es/cima/dochtml/ft/113887003/FT_113887003.html.
- CDC. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023-24 influenza season. Influenza vaccine contraindications and precautions. Last revision: 23 Aug 2023. Available from: <https://www.cdc.gov/flu/professionals/acip/summary/summary-recommendations.htm#table3>.
- Sokolow AG, Stallings AP, Kercksmar C, Harrington T, Jimenez-Truque N, Zhu Y, et al. Safety of live attenuated influenza vaccine in children with asthma. *Pediatrics*. 2022;149:e2021055432 <https://pubmed.ncbi.nlm.nih.gov/35342923/>
- Sanz Fadrique R, Martín Arias L, Molina-Guarneros JA, Jimeno Bulnes N, García Ortega P. Guillain-Barré syndrome and influenza vaccines: current evidence. *Rev Esp Quimioter*. 2019;32:288-95 <https://pubmed.ncbi.nlm.nih.gov/31232571/>
- Levison LS, Thomsen RW, Andersen H. Guillain-Barré syndrome following influenza vaccination: a 15-year nationwide population-based case-control study. *Eur J Neurol*. 2022;29:3389-94 <https://pubmed.ncbi.nlm.nih.gov/35913431/>
- CDC. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2023-24 influenza season. Flu vaccine and people with egg allergies. Last revision: 25 Aug 2023. Available from: <https://www.cdc.gov/flu/prevent/egg-allergies.htm#recommendations>.
- McKinney KK, Webb L, Petersen M, Nelson M, Laubach S. Ovalbumin content of 2010-2011 influenza vaccines. *J Allergy Clin Immunol*. 2011;127:1629-32 <https://pubmed.ncbi.nlm.nih.gov/21397313/>
- Comité Asesor de Vacunas de la AEP. Vacunación frente a la gripe estacional en la infancia y la adolescencia. Recomendaciones 2023-2024. AEP [accessed 30 Apr 2024]. Available from: <https://vacunasaep.org/profesionales/noticias/vacunacion-antigripal-recomendaciones-CAV-2023-24-sep2023>.
- Sgrulletti M, Ottaviano G, Sangerardi M, Chini L, Dellepiane RM, Martire B, et al. One step closer to influenza vaccine inclusiveness. *Pediatr Allergy Immunol*. 2020;31 Suppl 26:69-71 <https://pubmed.ncbi.nlm.nih.gov/33236432/>
- Canadian Immunization Guide. Chapter on influenza and statement on seasonal influenza vaccine for 2023-2024. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Available from: <https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-statement-seasonal-influenza-vaccine-2023-2024.html>.
- Aristegui Fernández J, González Pérez-Yarza E, Mellado Pena MJ, Gonzalo de Liria CR, Hernández Sampelayo T, García García JJ, et al. Grupo HOSPIGRIP. Hospitalizaciones infantiles asociadas a infección por virus de la gripe en 6 ciudades

- de España (2014-2016). *An Pediatr (Barc)*. 2019;90:86–93 [https://www.analesdepediatria.org/es-hospitalizaciones infantiles-asociadas-infeccion-por-articulo-5169540331830300X](https://www.analesdepediatria.org/es-hospitalizaciones-infantiles-asociadas-infeccion-por-articulo-5169540331830300X)
28. Ministerio de Sanidad, Consumo y Bienestar Social. Vacunación en grupos de riesgo de todas las edades y en determinadas situaciones. Madrid, septiembre de 2018. Available from: [https://www.sanidad.gob.es/areas/promocionPrevencion/vacunaciones/programasDeVacunacion/riesgo/Vac.Grupos Riesgo_todasEdades.htm](https://www.sanidad.gob.es/areas/promocionPrevencion/vacunaciones/programasDeVacunacion/riesgo/Vac.GruposRiesgo_todasEdades.htm).
 29. Mertz D, Lo CK, Lytvyn L, Ortiz JR, Loeb M, Flurisk-Investigators. Pregnancy as a risk factor for severe influenza infection: an individual participant data meta-analysis. *BMC Infect Dis*. 2019;19:683 <https://pubmed.ncbi.nlm.nih.gov/31375073/>
 30. WHO. Vaccines against influenza WHO position paper - November 2012. *Wkly Epidemiol Rec*. 2012;87:461–76 <https://pubmed.ncbi.nlm.nih.gov/23210147/>
 31. McMillan M, Porritt K, Kralik D, Costi L, Marshall HH. Influenza vaccination during pregnancy: a systematic review of fetal death, spontaneous abortion, and congenital malformation safety outcomes. *Vaccine*. 2015;33:2108–17 <https://pubmed.ncbi.nlm.nih.gov/25758932/>
 32. Mohammed H, Roberts CT, Grzeskowiak LE, Giles LC, Dekker GA, Marshall HS. Safety and protective effects of maternal influenza vaccination on pregnancy and birth outcomes: a prospective cohort study. *EclinicalMedicine*. 2020;26:100522 <https://pubmed.ncbi.nlm.nih.gov/32964200/>
 33. Ministerio de Sanidad. Portal Estadístico SIVAMIN. Sistema de información de Vacunaciones del Ministerio de Sanidad. Available from: <https://pestadistico.inteligenciadegestion.sanidad.gob.es/publicoSNS/S/sivamin>.
 34. McHugh L, O'Grady KF, Nolan T, Richmond PC, Wood N, Marshall HS, et al. National predictors of influenza vaccine uptake in pregnancy: the FluMum prospective cohort study, Australia, 2012–2015. *Aust N Z J Public Health*. 2021;45:455–61 <https://pubmed.ncbi.nlm.nih.gov/34411398/>
 35. Thompson MG, Kwong JC, Regan AK, Katz MA, Drews SJ, Azziz-Baumgartner E, et al. Influenza vaccine effectiveness in preventing influenza-associated hospitalizations during pregnancy: a multi-country retrospective test negative design study, 2010–2016. *Clin Infect Dis*. 2019;68:1444–53 <https://pubmed.ncbi.nlm.nih.gov/30307490/>
 36. Sahni LC, Olson SM, Halasa NB, Stewart LS, Michaels MG, Williams JV, et al. Maternal vaccine effectiveness against influenza-associated hospitalizations and emergency department visits in infants. *JAMA Pediatr*. 2024;178:176–84 <https://pubmed.ncbi.nlm.nih.gov/38109102/>
 37. Legge A, Dodds L, MacDonald NE, Scott J, McNeil S. Rates and determinants of season influenza vaccination in pregnancy and association with neonatal outcomes. *CMAJ*. 2014;186:E157–64 <https://pubmed.ncbi.nlm.nih.gov/24396098/>
 38. Pereira M, Williams S, Restrict L, Cullinan P, Hopkinson NS, London Respiratory Network. Healthcare worker influenza vaccination and sickness absence - an ecological study. *Clin Med (Lond)*. 2017;17:484–9 <https://pubmed.ncbi.nlm.nih.gov/29196347/>
 39. Guillari A, Polito F, Pucciarelli G, Serra N, Gargiulo G, Esposito MR, et al. Influenza vaccination and healthcare workers: barriers and predisposing factors. *Acta Biomed*. 2021;92 Suppl 2:e2021004 <https://pubmed.ncbi.nlm.nih.gov/33855983/>
 40. Zornoza Moreno M, Pérez-Martín J, Robles Mañueco M. Parents and teachers' perspectives on a school-located influenza vaccination program: a pilot study in the Region of Murcia, Spain. *Hum Vaccin Immunother*. 2024;20:2328406 <https://pubmed.ncbi.nlm.nih.gov/38573783/>