FactSheet

Influenza vaccines

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

FREQUENTLY ASKED QUESTIONS

This fact sheet provides responses to common questions about influenza viruses and seasonal influenza vaccines, including the new influenza vaccine programs in 2019. More detailed information about influenza viruses and the available influenza vaccines can be found in the NCIRS factsheet Influenza vaccines for Australians: information for vaccination providers.

Questions about the 'enhanced' influenza vaccines

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Questions about the 'enhanced' influenza vaccines

Q1. I've heard there are 'enhanced' influenza vaccines available. How are they different from other influenza vaccines and who are they for?

The highest disease burden from influenza occurs in the elderly in terms of serious complications and death rates.[1] The elderly do not respond as well to the influenza vaccine as healthy adults do, as the immune system weakens with age. The level of protection they get from the influenza vaccine is usually less than that of a younger person. The effectiveness of influenza vaccines is particularly poor against the A/H3N2 strain, which is more severe and is the most common type of influenza in the elderly. This underpins the need for 'enhanced' influenza vaccines for people aged ≥65 years to better protect them from influenza infection.

Two 'enhanced' influenza vaccines (Fluzone High-Dose and Fluad) are available for people aged ≥65 years. Fluzone High-Dose and Fluad are specifically designed to increase the immune system's response to the vaccine, especially against the influenza A/H3N2 strain. Fluzone High-Dose contains 4 times the amount of antigen (the part of the vaccine that prompts the body to generate an immune response) than that in a standard dose influenza vaccine. Fluad contains the standard amount of antigen but with an adjuvant – a compound that stimulates a higher immune response to a vaccine. Fluzone High-Dose and Fluad are only licensed for use in people aged ≥65 years, as the effectiveness and safety of these two vaccines in younger populations have not been adequately examined.

Fluzone High-Dose and Fluad contain 3 strains of influenza virus – 2 influenza A strains and 1 influenza B strain (i.e. trivalent influenza vaccines or TIVs). Other influenza vaccines available in Australia contain 4 influenza virus strains – the same strains in a TIV and an additional influenza B strain (i.e. quadrivalent influenza vaccines or QIVs).

Although the 'enhanced' vaccines contain one less influenza B strain, the benefits of better protection among those aged ≥65 years against the strains included, especially against the A/H3N2 strain, are likely to outweigh the potential loss of protection against the missing alternative B strain. Research studies have shown that older people tend to have some level of immunity to B strains because of exposure to these strains in prior seasons.

In contrast to this, influenza B contributes to a more substantial portion of disease burden in infants and children than in older adults.[2,3] Therefore, infants and children will benefit more from the broader protection from the inclusion of a second B virus strain in QIVs than older adults.

Both vaccines are latex-free and safe in people with latex allergy.

While both of the enhanced vaccines are recommended in preference over QIV among people aged ≥65 years, in 2019, only Fluad is available free of charge via the National Immunisation Program (NIP).[4]

Q2. How well do the two 'enhanced' influenza vaccines work? Are they better than the standard dose vaccine? Is one better than the other?

Results from a clinical trial suggest Fluzone High-Dose is 24% more effective in preventing influenza infection than standard TIVs.[5] Unlike Fluzone High-Dose, there are no clinical trials on Fluad that demonstrated greater effectiveness against influenza infection. However, Fluad is estimated to be 25% more effective in preventing hospitalisation for influenza or pneumonia than standard TIVs.[6]

Fluzone High-Dose and Fluad are preferentially recommended over quadrivalent influenza vaccines (QIVs) for people aged ≥65 years. There is a lack of evidence comparing the two enhanced vaccines directly to each other. On the basis of currently available evidence, there is no preference for use between Fluzone High-Dose and Fluad. If either 'enhanced' vaccine is not available, vaccination should not be delayed and a suitable QIV should be used instead.

Q3. If I have received one of the 'enhanced' influenza vaccines, should I also receive a quadrivalent influenza vaccine (QIV) to cover the missing alternative B strain?

There is no recommendation to give a QIV to people who have received an 'enhanced' influenza vaccine, and the use of multiple types of vaccines in one season has not yet been studied. While not recommended, administration of both vaccine types to an individual is not contraindicated and there are no serious safety concerns.

Q4. Are the 'enhanced' influenza vaccines equally safe?

Swelling, redness and pain at the injection site are more common after vaccination with Fluzone High-Dose and Fluad than with standard TIV. The majority of the reactions are mild or moderate in severity. Despite a higher rate of injection

site reactions, severe or serious adverse events are not expected at a higher frequency following administration of Fluzone High-Dose and Fluad.[7-9]

Questions about influenza virus and influenza vaccines

Q5. What's the difference between influenza and the common cold?

Influenza is a respiratory illness that occurs following an infection with influenza viruses.[10] Influenza is often referred to as 'the flu'. Sometimes the term 'the flu' is used incorrectly to describe the common cold, other respiratory viruses or even gastrointestinal illnesses. This is because their symptoms can be similar to those caused by influenza. There are many different viruses and some bacteria that can cause these symptoms. The influenza vaccine will only protect you from the influenza virus.[11]

The following table compares symptoms from the common cold and influenza and shows on average how frequently the symptoms affect people. Usually influenza is more severe and lasts longer than a cold or other viral respiratory illness.

Cold	Symptom	Influenza
☹	Fever	☹☹☹
☹	Headache	☹☹☹
☹☹	General aches and pains	☹☹☹
☹☹	Tired and weak	☹☹☹
☹	Extreme fatigue	☹☹☹
☹☹☹	Runny, stuffy nose	☹☹
☹☹☹	Sneezing	☹☹
☹☹☹	Sore throat	☹☹☹
☹☹	Chest discomfort, coughing	☹☹☹

☹ = rarely; ☹☹ = sometimes; ☹☹☹ = often

Table adapted from: Immunize Canada, 2010. Is it a cold or influenza? Available from: www.immunize.ca/sites/default/files/resources/176e.pdf (Accessed March 2019)

Q6. Is it worth getting the influenza vaccine? I'm a healthy person and have heard that influenza isn't serious.

Most Australians who get influenza are quite sick for a few days with fever, aches and pains, and sore throat, and then recover without lasting effects (***see*** Q5). However, influenza can be very serious in some people, causing hospitalisation or even death. It is not possible to predict who will be severely affected by influenza; each year, previously healthy people are hospitalised and die from the virus. Although around 100 deaths and 5,100 hospitalisations due to influenza are reported each year,[1] many cases don't get identified, so the true impact of influenza is much greater.

Even if a person does not get severely ill from influenza, it's still a big inconvenience to their lives. For example, influenza can cause people to miss time from childcare, school or work because either they are too sick to attend or they have to take time off to care for a sick child. They may need to buy medications and visit the doctor or even the hospital. One study has shown that parents of children younger than 3 years of age missed an average of 3 days of work to stay home and care for their sick child.[12] The estimated cost to the Australian healthcare system for GP visits and hospitalisations was $115 million per year for each year between April 2000 and March 2006.[13]

In addition to protecting you from influenza, vaccination also helps to protect people around you. If you don't catch influenza, then you can't spread the infection. It is particularly important to protect vulnerable people who can't receive the vaccine themselves, such as young babies less than 6 months old and those who have low immunity.[14,15]

You can think of the influenza vaccine as a seatbelt. When used properly, a seatbelt reduces the likelihood that you'd be injured in a car accident. However, they aren't perfect and won't prevent all injuries. Like a seatbelt, the influenza vaccine isn't perfect because the flu strain chosen to be in the vaccine each year needs to match the one that is circulating in the community. However, the vaccine will reduce the chance of getting influenza and its potentially serious complications, including death.

Q7. Why do healthy young children need an influenza vaccine?

Compared with older children and adults, infants and children <5 years of age, including those without pre-existing medical conditions, are more likely to get severe influenza infection, resulting in hospitalisation.[1,16] In 2017, approximately 1 in 400 children were diagnosed with laboratory-confirmed influenza. Previously healthy children can be severely ill and suffer from influenza-associated complication such as pneumonia and encephalitis.[17-19]

Q8. If the influenza vaccine is recommended for everyone then why can only certain people get it for free?

The influenza vaccine is available free of charge via the government-funded Australian NIP for certain groups of people who are at the greatest risk of severe influenza or more likely to get complications from influenza than the general population.[4] This includes the elderly, Aboriginal and Torres Strait Islander Australians, pregnant women and people with certain underlying medical conditions. In addition, because young children experience the highest hospitalisation rates from influenza and are just as likely as adults to be admitted to ICU, all states and territories are providing free influenza vaccine for children aged 6 months to <5 years in 2019.

Since 2005, decisions on what vaccines are provided for free, and for whom, are made following a process that involves the Pharmaceutical Benefits Advisory Committee.[20] This ensures any government spending on a health intervention is cost-effective. This is important as there is a limited amount of money that is available for healthcare in Australia and these funds need to be used to bring about the greatest benefit for the whole population.

However, people who are not eligible for influenza vaccine on the NIP will still benefit from vaccination (***see*** Q6). *The Australian Immunisation Handbook*, the national clinical guideline advising on the safest and most effective use of vaccines in Australia, recommends the influenza vaccine from 6 months of age.[21] Influenza vaccines can be purchased for around $10–$20 each.

Q9. I'm travelling to the northern hemisphere and it is influenza season at my destination. How do I protect myself from influenza while travelling? What should I do if I have been travelling/living overseas and am coming back to Australia?

Depending on the time of year and destination, travellers may be exposed to the influenza virus at any time throughout the year. The influenza season in the southern hemisphere is mostly during the months of April to September; in the northern hemisphere, influenza activity occurs during October to April. Influenza activity has been reported throughout the year in the tropics.

Travellers may be exposed to the influenza virus while travelling regardless of their destination. Travellers in large tourist groups or involving travel in confined circumstances for days to weeks, such as on a cruise ship, are at particular risk of influenza.[22,23] Infection can be acquired either before departure or from travel to areas of the world where influenza is currently circulating.

Influenza vaccination is recommended if travelling during the influenza season, especially if it is known before travel that influenza is circulating in the destination region. Some brands of current southern hemisphere influenza vaccine are available from March through to February the following year (when the vaccine expires). A northern hemisphere formulation of influenza vaccine may be preferred if travelling in the northern hemisphere during their influenza season (usually October to May), but is generally unavailable in Australia. The southern hemisphere formulation is considered as an acceptable alternative and a second dose late in the season may be given even if the person has previously received this vaccine earlier in the current season.

Similarly, if a person has been travelling to or living in the northern hemisphere and is returning to Australia during the southern hemisphere influenza season, influenza vaccination can be considered even if the person has received the northern hemisphere influenza vaccine. The decision to vaccinate should take into account personal risk factors, risk of disease, currently circulating virus strains and differences in the strains included in the northern and southern hemisphere vaccine formulations.

Q10. Does the influenza vaccine work? I've had the vaccine before and I still got sick that year.

There have been many research studies that have shown the effectiveness of the influenza vaccine. It takes 2 weeks for the vaccine to become effective and for immunity to develop after vaccination. However, how well the influenza vaccine works can vary among different people and in different years, as it depends on several factors.

For example, the age and health of the person receiving the influenza vaccine can impact how effective it is. Influenza vaccination can prevent illness in about 50–60% of healthy adults under the age of 65 years, although this figure varies year by year.[24] Similar levels of protection occur in young children.[25] However, people with an underlying medical condition, such as those with low immunity or the elderly, may not respond as well to the influenza vaccine as healthy adults do and so the level of protection they get from the vaccine may be less. Importantly, among high-risk individuals such as nursing home residents, the vaccine prevents pneumonia and hospitalisation due to influenza.[26] Because of the higher risk of severe influenza in the elderly, any protection provided by vaccination against influenza is worthwhile.

Because the vaccine is not 100% effective, it means a small proportion of people may catch the virus after getting the vaccine. However, in many instances, people may think they have caught influenza after being vaccinated but that is not the case. For example, often people catch influenza before getting the influenza vaccine but their symptoms don't appear until shortly after being vaccinated, making them think the vaccine didn't work, or even (mistakenly) that the vaccine made them sick (***see*** Q11).

Similarly, a person who is vaccinated against influenza may catch a different virus that is mistaken for influenza (***see*** Q5). For instance, respiratory syncytial virus (RSV) and parainfluenza are viruses that cause symptoms similar to those of influenza, spread in the community at the same time influenza does and can cause severe illness and complications just like influenza.[27]

Q11. When should I get the influenza vaccine and when is it too late in the season to get it?

Annual influenza vaccination is recommended before the influenza season starts.

The peak of influenza activity in Australia can vary from season to season. Typically it occurs between June and September, but infections can still occur year round, particularly in tropical areas where influenza peaks can commonly occur outside of the typical winter epidemics. The influenza vaccine can therefore be effective in preventing infection whenever it is given. However, recent evidence suggests optimal protection occurs in the 3–4 months following vaccination and so vaccination before the expected winter peak is advisable.[28,29]

Women who are in their first trimester in the first quarter of a calendar year may wish to wait until that year's influenza vaccine becomes available (approximately March), rather than receiving the previous season's influenza vaccine. For women who received an influenza vaccine late in the previous influenza season, revaccinate if the new season influenza vaccine becomes available before the end of pregnancy. If not already given at an earlier opportunity, pregnant women can receive influenza vaccine at the same time as pertussis vaccine.

There is no time when it is considered too late to be vaccinated against influenza. Vaccination should continue to be offered throughout the influenza season, as long as unexpired vaccine is available.

Q12. Is the influenza vaccine available all year round?

The influenza vaccine is available from March through to February the following year (when the vaccine expires). This means there is a gap of about 1 month where no influenza vaccine is available.

Questions about the safety of influenza vaccines

Q13. I've heard one of the side effects after having the vaccine is getting sick with influenza. Is that true?

It is not possible for the influenza vaccine to give you influenza. This is because all influenza vaccines in use in Australia are 'inactivated' which means the vaccine is only made with the outside 'shell' of the influenza virus, and it is not alive or functioning like a whole virus.[30] Think of it as like the outside shell of a car without the motor – it looks like a car but doesn't actually run.

Sometimes the normal responses the body has to getting the vaccine (i.e. side effects) are similar to the early signs of influenza which can make people think they have gotten influenza from the vaccine. For example, the expected side effects of the vaccine are swelling, redness and pain at the injection site but also fever, tiredness and muscle aches which also occur when you get influenza (***see*** Q5, Q10). However, these side effects are a sign that the vaccine is triggering an immune response, which is what it is designed to do. The symptoms can start within a few hours of being vaccinated, last 1–2 days, and are generally much milder than an actual influenza infection. These symptoms go away on their own once your body has successfully made an immune response to the vaccine which will protect you from influenza virus.[31]

Q14. I've heard influenza vaccine causes seizures or convulsions in young children. Is that true?

Febrile seizures (or convulsions) can be triggered by fever of any cause. A small proportion of children (2–4%) are susceptible to febrile seizures until 6 years of age.[32] The seizures themselves usually last around 1 or 2 minutes with loss of consciousness. Nearly all children who have a febrile seizure, regardless of the cause, will recover quickly. Studies have shown that academic outcomes and behaviour in children who have febrile seizures are the same as children without seizures.[33] The risk of epilepsy after a simple febrile seizure is only slightly higher than the general population and likely related to underlying genetic predisposition.[34]

Influenza infection itself can cause fever and results in many more febrile seizures than vaccination. Influenza is one of the most common infectious causes of febrile seizures in children hospitalised in the winter in Australia.[35] In one study 6% of children hospitalised with influenza suffered a febrile seizure.[36] Compare this with febrile seizures related to fever after influenza vaccination which occurred in approximately 1 in every 20,000 children who receive the vaccine.[37]

In Australia in 2010, higher than expected numbers of fever and febrile convulsions following influenza vaccination were detected in children under 5 years of age, particularly children under 3 years of age.[38] Upon investigation, the reports were linked to only one manufacturer's influenza vaccine (Seqirus [previously bioCSL] Fluvax and Fluvax Junior). The use of this vaccine in Australia was suspended while further investigations by the Therapeutic Goods Administration (TGA) were undertaken. The investigations revealed that the issue was likely caused by the manufacturing process used by bioCSL at the time.[39-41] This vaccine is no longer available in Australia.

Enhanced safety monitoring systems for influenza vaccines introduced in recent years, such as AusVaxSafety (***see*** Q15), have confirmed that influenza vaccine is safe in children younger than 5 years, reporting low rates of fever and medical attendance after vaccination.[32]

Q15. What is being done in Australia to make sure vaccines are safe to give to the public?

Reviewing and monitoring the safety of vaccines is included at all stages of the vaccine development process, from initial lab-based research, vaccine registration including authorities for use, recommendations on use of the vaccine to ongoing surveillance once the vaccine is being used in the population.

The TGA is responsible for registering vaccines for use in Australia. To ensure their safety and efficacy, vaccines are evaluated using the most up-to-date research and testing information available. Independent medical and scientific advice on the safety, quality and efficacy of vaccines is provided by experts who make up the Advisory Committee on Vaccines (ACV).[42] Once vaccines are registered and in use, the TGA continues to monitor their safety and effectiveness through a national monitoring system. The system includes reporting of adverse events by health authorities, immunisation providers, doctors, consumers and vaccine manufacturers. If the TGA receives information that there are

safety concerns about a vaccine, the issue is investigated immediately. As part of the investigation, the TGA seeks vaccine safety advice from the ACV.[43]

Another important vaccine safety initiative in Australia is AusVaxSafety, a national, active sentinel-based vaccine safety surveillance program. AusVaxSafety collects patient-reported outcomes following a vaccination encounter via an SMS-based survey. Data are collected in near real-time and collated for analysis and monitoring for safety signals.

Another important body is the Australian Technical Advisory Group on Immunisation (ATAGI).[44] This group advises the government on existing, new and emerging vaccines in relation to their effectiveness and use in Australian populations. ATAGI produces *The Australian Immunisation Handbook*, the national clinical guideline advising on the safest and most effective use of vaccines in Australia. ATAGI and the ACV work together with other bodies on matters relating to the implementation of immunisation policies, procedures and vaccine safety.

Q16. I've been told to get the influenza vaccine when pregnant to protect me and my baby. Is this safe?

Influenza can cause severe disease in pregnant women and young babies. Getting sick with influenza while pregnant can lead to complications such as premature delivery and even perinatal death.[45] Young children, especially those younger than 6 months, are more likely to be hospitalised or die from influenza than older children.

Influenza vaccine is recommended with every pregnancy and at any stage of pregnancy to protect both the mother and her unborn child against complications from influenza. Babies born to women vaccinated against influenza while pregnant are less likely to be born prematurely or have a low birth weight.[46,47]

Influenza vaccination protects babies after birth. During pregnancy, protective antibodies are transferred through the placenta from the mother to the baby. Maternal vaccination is estimated to reduce the risk of influenza in infants <6 months of age by 48%.[48-50] However, the protection wears off as babies get to 6 months of age, at which time babies can start to receive the vaccine themselves.[51]

Influenza vaccine is safe during pregnancy. A systematic review combining data from multiple studies found no increase in fetal death, spontaneous abortion or congenital malformation after maternal influenza vaccination in pregnancy.[46] Expected adverse events after vaccination, like injection site reactions, do not occur any more frequently in pregnant women than in non-pregnant women. Influenza vaccine is also safe when given to mothers who are breastfeeding, and can provide protection to the baby through antibodies that are transferred to the baby in breastmilk.[52]

Women who are in their first trimester in the first quarter of 2019 may wish to wait until the 2019 influenza vaccine becomes available, rather than receiving the 2018 influenza vaccine. For women who received an influenza vaccine late in the 2018 influenza season, revaccinate if the 2019 influenza vaccine becomes available before the end of pregnancy. If not already given at an earlier opportunity, pregnant women can receive influenza vaccine at the same time as pertussis vaccine.

Q17. Can I get the influenza vaccine if I have an egg or latex allergy?

Reactions such as hives, angioedema (a skin reaction with swelling similar to hives) or anaphylaxis (severe allergic reaction) are rare side effects following vaccination for influenza. They can be due to an allergic response to something in the vaccines, such as egg protein.

Although influenza vaccines in Australia are grown in eggs, because of new vaccine manufacturing methods, the amount of material from the egg in the influenza vaccine is small (usually less than 1 microgram of egg protein per dose). Recent studies have shown that people with egg allergy, including egg-induced anaphylaxis, have safely received the influenza vaccine.[53,54] Although the risk of anaphylaxis or an adverse event is very low, people with this type of allergy should be vaccinated by healthcare providers experienced in recognising and treating anaphylaxis.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) guidelines should be referred to for additional information on influenza vaccination of individuals with an allergy to eggs, including risk, dosage and observation period.[55]

Influenza vaccines used in Australia are latex-free and safe for use by people with a latex allergy or sensitivity. Although the product information for Fluad and Fluarix Tetra states that some presentations of the vaccine cannot be considered latex-free, these presentations are not supplied in Australia.

Q18. Can the influenza vaccine be given to someone who has had Guillain-Barré syndrome?

Guillain-Barré syndrome (GBS) is a rare disorder in which the immune system damages nerve cells, causing muscle weakness and sometimes paralysis. The symptoms usually last for a few weeks followed by a full or partial recovery. In very rare cases people have died of GBS. The risk of the syndrome increases with age and is greatest for those aged 50 years or older. Diagnosis of GBS is complex and must be made by a doctor.

A small increased risk of GBS was found in people given a specific influenza vaccine in the United States in 1976.[56] Since then, close monitoring has shown that GBS has occurred at a very low rate of less than 1 in 1 million doses of influenza vaccine.[57] Studies suggest that a person is more likely to get GBS from infection with the influenza virus than from the influenza vaccine.[58]

People with a history of GBS whose first episode was not after vaccination have an extremely low risk of recurrence of GBS after vaccination.[59-61] Vaccination is recommended for these people.

Vaccination is generally not recommended for people with a history of GBS whose first episode occurred within 6 weeks of influenza vaccination. There are limited data in people where the first episode occurred within 6 weeks of influenza vaccination (i.e. the first episode was possibly triggered by the vaccine). In these people, discuss the potential for GBS recurrence if vaccinated, the potential for exacerbation following influenza infection, and other protective strategies (e.g. vaccination of household members). Vaccination can be considered in special circumstances.

Q19. Can the influenza vaccine be given to someone taking immune checkpoint inhibitors?

Immune checkpoint inhibitors are a class of monoclonal antibodies currently used in the treatment of a number of cancers, including metastatic melanoma, renal clear cell carcinoma, non-Hodgkin lymphoma, non-small cell lung cancer and other solid organ tumours.

Checkpoint inhibitors include:

- CTLA-4 inhibitors (such as ipilimumab)
- PD-1 and PD-L1 inhibitors (such as nivolumab or pembrolizumab)

People taking checkpoint inhibitors may have a higher risk of immune-related adverse events following immunisation with influenza vaccine.[62] Consult the person's treating oncologist about the risks and benefits of influenza vaccination in people taking treatments.

Additional resources for primary medical care/vaccination providers

- National Centre for Immunisation Research and Surveillance (NCIRS) influenza fact sheet
  http://ncirs.org.au/ncirs-fact-sheets-faqs/influenza-vaccines-australians
- Australian Technical Advisory Group on Immunisation (ATAGI) advice for immunisation providers regarding the administration of seasonal influenza vaccines in 2019
  https://beta.health.gov.au/resources/publications
- Australian Government Department of Health immunisation website
  https://beta.health.gov.au/health-topics/immunisation
- National Immunisation Program schedule
  https://beta.health.gov.au/health-topics/immunisation/immunisation-throughout-life/national-immunisation-program-schedule

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