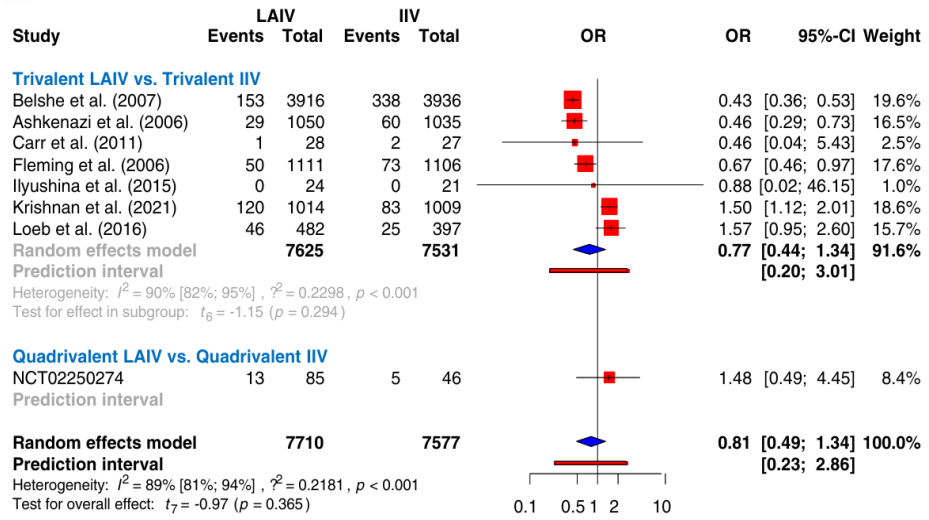
GRADE table: Comparison of live-attenuated influenza vaccine (LAIV; FluMist) with inactivated influenza vaccine (IIV) for prevention of influenza in children aged 2–17 years (PICO 2)

NCIRS is conducting GRADE assessments in support of the Australian Technical Advisory Group on Immunisation (ATAGI) and making pilot results available on the Centre's website. Please read this material as a supplement to the Australian Immunisation Handbook Influenza (flu) chapter.

Patient or population: Children aged 2–17 years
Intervention: LAIV (FluMist)
Comparison: Inactivated influenza vaccine (IIV)

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Laboratory-confirmed influenza infection (LCI)	LCI by vaccine valency 	15,287 (8 studies contributed to outcome; within 1 SR/MA)[1]	⊕⊕⊕◯ Moderate[a]	LAIV likely results in little to no difference in LCIs compared to IIV.

Patient or population: Children aged 2–17 years
Intervention: LAIV (FluMist)
Comparison: Inactivated influenza vaccine (IIV)

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Serious adverse events (SAEs)	Number of events Random effects model OR: 1.17 (95%CI: 1.06-1.29) Number of affected people Random effects model OR: 0.90 (95%CI: 0.23-3.51) Vaccine-related Random effects model OR: 1.05 (95%CI: 0.77-1.43)	17,444 (11 studies contributed to outcome; assessed by number of events) 12,613 (11 studies contributed to outcome; assessed by number of affected people) 17,833 (13 studies contributed to outcome; assessed by vaccine-related events) (all within 1 SR/MA)[1]	⊕⊕⊕◯ Moderate[a]	LAIV likely results in little to no difference in SAEs compared to IIV. Note: the SR/MA included several large studies of children with respiratory disease which contributed to these outcomes.

Patient or population: Children aged 2–17 years
Intervention: LAIV (FluMist)
Comparison: Inactivated influenza vaccine (IIV)

<table>
<tr><th>Outcomes</th><th>Impact</th><th>№ of participants (studies)</th><th>Certainty of the evidence (GRADE)</th><th>Interpretation</th></tr>
<tr><td>Adverse events of special interest (AESI): asthma/wheeze in healthy children</td><td><u>Asthma exacerbation</u>
Random effects model OR: 1.08 (95%CI: 0.87–1.33)

<u>Wheezing</u>
Random effects model OR: 0.95 (95%CI: 0.75–1.20)

<u>Significant wheeze</u>
Random effects model OR: 1.11 (95%CI: 0.76–1.82)</td><td>10,704 (3 studies contributed to outcome of asthma exacerbation)

17,557 (7 studies contributed to outcome of wheezing)

13,273 (5 studies contributed to outcome of significant wheeze)

(all within 1 SR/MA)[1]</td><td>⊕⊕⊕◯
Moderate[a]</td><td>LAIV likely results in little to no difference in asthma/wheeze in healthy children compared to IIV.

Note: the SR/MA included several large studies of children with respiratory disease which contributed to these outcomes.</td></tr>
<tr><td>Adverse events of special interest (AESI) in children with asthma/history of wheeze (wheeze/medically attended wheeze) assessed with: MedDRA coded</td><td>
<table>
<tr><th>STUDY 1 (6-59 mo)</th><th colspan="2">Wheeze</th><th colspan="2">Medically attended wheeze</th></tr>
<tr><th></th><th>LAIV</th><th>TIV</th><th>LAIV</th><th>TIV</th></tr>
<tr><td>Any history of asthma/wheeze</td><td>9.3%</td><td>10.3%</td><td>7.2%</td><td>8.6%</td></tr>
<tr><td>Any history of asthma/wheeze - no wheeze in past 12 months</td><td>6.1%</td><td>5.0%</td><td>3.8%</td><td>4.4%</td></tr>
<tr><td>Any history of asthma/wheeze - wheeze in past 12 months</td><td>13.1%</td><td>16.0%</td><td>11.2%</td><td>13.1%</td></tr>
<tr><td>Diagnosis of asthma</td><td>15.3%</td><td>14.5%</td><td>12.1%</td><td>9.9%</td></tr>
<tr><th>STUDY 2 (6-71 mo)</th><th colspan="2">Wheeze</th><th colspan="2">Medically documented wheeze</th></tr>
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<tr><td>Any history of asthma/wheeze - wheeze in past 12 months</td><td>23.0%</td><td>25.4%</td><td>17.4%</td><td>18.3%</td></tr>
<tr><td>Diagnosis of asthma</td><td>23.9%</td><td>27.9%</td><td>18.2%</td><td>22.3%</td></tr>
</table>
</td><td>1145 (Study 1)
795 (Study 2)
(1 integrated analysis of 2 RCTs assessed individually)[2,c,d]</td><td>⊕⊕⊕◯
Moderate[b]</td><td>LAIV likely results in little to no difference in wheeze/medically attended/documented wheeze in children with asthma/history of wheeze compared to IIV.</td></tr>
</table>

Patient or population: Children aged 2–17 years
Intervention: LAIV (FluMist)
Comparison: Inactivated influenza vaccine (IIV)

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)	Interpretation
Adverse events (AEs)	Number of events Random effects model OR: 0.51 (95%CI: 0.05-5.09) Number of affected people Random effects model OR: 1.26 (95%CI: 1.14-1.40)	9,331 (3 studies contributed to outcome; assessed by number of events) 4,763 (3 studies contributed to outcome; assessed by number of affected people) (all within 1 SR/MA)[1]	⨁⨁⨁◯ Moderate[a]	LAIV likely results in fewer adverse events compared to IIV. Note: the studies contributing to the number of affected people outcome included children with respiratory disease.

Explanations

a. This systematic review/meta-analysis combined studies for some outcomes which included both healthy children and children with respiratory disease.
b. This study was an integrated, post-hoc analysis of two randomised controlled trials conducted in children with asthma/history of wheeze. One of the studies was open label.
c. In Ambrose et al 2012, two randomised controlled trials are summarised separately. Study 1 included the 2004-2005 influenza season and Study 2 included the 2002–2003 season.
d. Follow-up for wheeze outcomes: 0–42 days.

Abbreviations: AE=adverse event; AESI=adverse event of special interest=CI: confidence interval=IIV: inactivated influenza vaccine; LAIV=live attenuated influenza vaccine; MA=meta-analysis; OR=odds ratio; SR=systematic review

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: We have limited confidence in the effect estimate: the true effect may be substantially different from the estimate of the effect.
Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE evidence profile

Evidence profile: LAIV (FluMist) compared with inactivated influenza vaccine (IIV) for prevention of influenza in children aged 2–17 years old (PICO 2)

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Laboratory-confirmed influenza infection									
1[1]	Systematic review/meta-analysis (SA/MA)	Not serious	N/A	Serious[a]	Not serious	None	The overall random effects model odds ratio (OR) (across trivalent and quadrivalent head-to-head studies) suggested a **small but insignificant reduction in laboratory-confirmed influenza infections in those receiving LAIV compared to IIV (8 studies; 0.81; 95%CI: 0.49–1.34).** This reduction was more pronounced for trivalent LAIV vs trivalent IIV (7 studies; 0.77; 95%CI: 0.44–1.34) but the result was still insignificant. Only one small quadrivalent-quadrivalent study was included for this outcome in this SR/MA, which demonstrated an OR of 1.48 (1 study; 95%CI: 0.49–4.45).	⊕⊕⊕◯ Moderate[a]	CRITICAL
Serious adverse events (SAEs)									
1[1]	Systematic review/meta-analysis	Not serious	N/A	Serious[a]	Not serious	None	Random effects model ORs varied depending on the outcome being reported but suggested **little or no difference in SAEs for those receiving LAIV vs IIV**. The only significant outcome was when SAEs were assessed by **number of events (1.17; 95%CI: 1.06–1.29)**, which suggested a slight increase in the odds of an SAE being reported after LAIV compared with IIV. Results were lower when SAEs were assessed either by **number of affected people (0.90; 95%CI: 0.23–3.51)** or **vaccine-related (1.05; 95%CI: 0.77–1.43)** but neither was statistically significant. For all three outcomes, results suggested slightly more SAEs after trivalent LAIV compared with trivalent IIV. No SAEs were reported for any quadrivalent vaccines (3 or 4 small studies). Several studies included in the assessment of each of the three outcomes included children with respiratory disease. Overall, the SR/MA assessed several studies contributing to the safety outcomes to be of low or very low quality.	⊕⊕⊕◯ Moderate[a]	CRITICAL

<table>
<tr><th colspan="7">Certainty assessment</th><th rowspan="2">Impact</th><th rowspan="2">Certainty</th><th rowspan="2">Importance</th></tr>
<tr><th>№ of studies</th><th>Study design</th><th>Risk of bias</th><th>Inconsistency</th><th>Indirectness</th><th>Imprecision</th><th>Other considerations</th></tr>
<tr><td colspan="10">Adverse event of special interest: asthma/wheeze in healthy children</td></tr>
<tr><td>1[1]</td><td>Systematic review/meta-analysis</td><td>Not serious</td><td>N/a</td><td>Serious[a]</td><td>Not serious</td><td>None</td><td>Random effects model ORs suggested little or no difference in asthma or wheeze outcomes in healthy children:
asthma exacerbation: 1.08 (95%CI: 0.87–1.33)
wheezing: 0.95 (95%CI: 0.75–1.20)
significant wheeze: 1.11 (95%CI: 0.76–1.82).
No outcomes were statistically significant. Several studies included in the assessment of each of the three outcomes included children with respiratory disease. Overall, the SR/MA assessed several studies contributing to the safety outcomes to be of low or very low quality.</td><td>⨁⨁⨁◯
Moderate[a]</td><td>CRITICAL</td></tr>
<tr><td colspan="10">Adverse events in children with asthma/history of wheeze (assessed with: MedDRA coded)</td></tr>
<tr><td>1[2]</td><td>Integrated analysis of two randomised control trials</td><td>Not serious</td><td>N/A</td><td>Serious[b]</td><td>Not serious</td><td>None</td><td>Results suggested that children with asthma or a history of wheeze may experience wheeze or medically attended wheeze; however, there is little difference between LAIV and IIV in terms of these outcomes. Those with no wheeze in the past 12 months had fewer reports of wheeze and medically attended wheeze compared with those with recent wheeze or those with asthma diagnosis. Note: study 1 included 1,145 participants and study 2 included 795 participants.
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Moderate[b]</td><td>CRITICAL</td></tr>
</table>

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Adverse events									
1[1]	Systematic review/meta-analysis	Not serious	N/A	Serious[a]	Not serious	None	The random effects model OR assessing AEs by number of events suggested **decreased odds of reporting an AE after LAIV compared with IIV (0.51; 95%CI: 0.05–5.09).** When assessing AEs by number of affected people, the OR was 1.26 (95%CI: 1.14–1.40), suggesting a decreased odds for those receiving IIV. However, studies included in the assessment of number of affected people included children with respiratory disease which may have impacted the results. Overall, the SR/MA assessed several studies contributing to the safety outcomes to be of low or very low quality.	⊕⊕⊕◯ Moderate[a]	IMPORTANT

Explanations

a. This systematic review/meta-analysis combined studies for some outcomes which included both healthy children and children with respiratory disease.

b. This study was a post-hoc, "integrated analysis" of two RCTs conducted in children with asthma/wheeze. Each study was presented individually but results combined in this one manuscript. One of the studies was open label. Proportions of children with and without history of wheeze and with diagnosis of asthma varied across the two studies. For the purposes of risk of bias, domains were assessed for each of the two studies individually, where appropriate, with one overall combined risk of bias judgement presented for each domain.

Abbreviations: AE=adverse event; AESI=adverse event of special interest; CI=confidence interval; MA=meta-analysis; OR=odds ratio; SAE=serious adverse event; SR=systematic review

References

1. Garai R, Jánosi Á, Krivácsy P, et al. Head-to-head comparison of influenza vaccines in children: a systematic review and meta-analysis. Journal of Translational Medicine 2024; 22(1):903.

2. Ambrose CS, Dubovsky F, Yi T, et al. The safety and efficacy of live attenuated influenza vaccine in young children with asthma or prior wheezing. European Journal of Clinical Microbiology & Infectious Diseases 2012;31(10):2549-57.

Evidence to decision framework

Evidence to decision framework: LAIV (FluMist) compared with inactivated influenza vaccine (IIV) for prevention of influenza in children aged 2–17 years old (PICO 2)

Should LAIV be used in children aged 2–17 years for the prevention of influenza?					
Population	Children aged 2–17 years				
Intervention	LAIV				
Comparison	IIV				
Main outcomes	Efficacy, effectiveness and safety				
Setting	A range of countries spanning lower-middle, middle- and high-income were included in the systematic review which informed most outcomes in this PICO.				
ASSESSMENT					
Problem *Is the problem a priority?*					
Don't know	Varies	No	Probably no	Probably yes	Yes
Children experience high influenza notification and hospitalisation rates and are significant transmitters of disease. Further exacerbating the impact of influenza on children, influenza vaccination coverage is the lowest among children compared to other age groups and has been trending downward. *Burden and transmission* • Influenza notifications among children dropped during the COVID-19 pandemic years of 2020–2021 but were substantially increased in 2022–2024. • During 2022-2024, notification rates were highest among those aged <5 years at 2543.8 per 100,000 followed by those aged 5-17 years at 2164.0 per 100,000. Rates were substantially lower in those aged 18–64 years, and lowest among those aged ≥65 years at 619.1 per 100,000. • In 2022-2024, within the 5–17-year age group, notification rates were highest for those aged 5–9 years at 2,912.1 per 100,000. • Hospitalisation rates were moderately higher in 2022 compared to rates in 2015–2019 (216.9 per 100,00 among children aged <5 years). • Among older children aged 5–19 years, hospitalisation rates were estimated at 49.6 per 100,000 and similar to rates among those aged 20–64 years. Rates among older adults aged ≥65 years were estimated at 169.0 per 100,000. • Children are known to shed influenza virus a day or two before becoming symptomatic and shed virus for longer than adults,[1] making them significant transmitters of influenza virus. A 2010–2011 study demonstrated that households with a younger average age of members were more likely to have influenza viral transmission events.[2] • In addition to disease burden, influenza is responsible for significant economic burden related to disease in children due to the indirect costs of parents or carers having to take time off from work to care for sick children.[3] *Vaccination coverage* • Cumulative influenza vaccine coverage (AIR data; doses given) reached a high of 45% in 2020 for those aged 6 months to <5 years. In 2025, coverage in this age group was approximately 25.7%. • For those aged 5–<15 years, 2020 coverage was approximately 27%; coverage has declined over time: 16% in 2023, 14% in 2024, and 14.5% in 2025.[4]					

Desirable effects

How substantial are the desirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- Overall, the evidence indicates that, among healthy children aged 2–17 years, LAIV is likely similar in effectiveness to IIV. Evidence on the effectiveness of LAIV in preventing other influenza-related outcomes is insufficient to make a judgement in favour of or against LAIV.
- One systematic review and meta-analysis from 2024 included results for lab-confirmed influenza by vaccine valency, comparing head-to-head randomised controlled trials (RCTs) comparing LAIV to inactivated influenza vaccine (IIV). Eight studies with more than 15,000 participants contributed to the assessment and some studies included at risk populations like children with respiratory disease. The overall random effects model odds ratio (across trivalent and quadrivalent head-to-head studies) suggested a small but insignificant reduction in lab-confirmed influenza infections in those receiving LAIV compared to IIV (0.81; 95% confidence interval (CI): 0.49–1.34).[5]
- A study of real-world effectiveness including 20 years of effectiveness data in children and adolescents broken down by time period (2003/04–2008/09; 2010/11–2016/17; 2017/18–2022/23) showed that absolute vaccine effectiveness of LAIV and IIV were comparable at approximately 50% in each of the three time periods.[6]
- There is some additional evidence suggesting that LAIV may be more effective than IIV in preventing influenza infection. A network meta-analysis including 24 RCTs encompassing 60,502 children aged <18 years and 5 vaccines found that trivalent LAIV was more efficacious than trivalent IIV (RR=0.52, 95%CI: 0.32–0.82) in preventing lab-confirmed influenza.[7]
- There is limited evidence on the effectiveness of LAIV relative to IIV in individuals at higher risk for severe influenza infection.
- In the UK, significant indirect benefits were observed in adults not targeted for vaccination with LAIV, including a 59% reduction in GP ILI consultations in pilot vs non-pilot areas; non-significant reductions were observed for emergency department respiratory attendances, influenza confirmed hospitalisations, and influenza ICU admissions. LAIV coverage ranged from 32.3% to 63.1% (average 56.8%) in pilot areas.[8]

Undesirable effects

How substantial are the undesirable anticipated effects?

Don't know	Varies	Large	Moderate	Small	Trivial

- Evidence suggests little or no difference in the frequency of serious adverse events after vaccination with LAIV compared with IIV.[5]
- In healthy children, including those aged <2 years, exacerbation of wheeze or asthma frequency appeared similar between LAIV and IIV.[5,9]
- In an analysis of two RCTs assessing children with a history of asthma or wheeze, results demonstrated that those with wheeze in the past 12 months and those with an asthma diagnosis experienced wheeze or medically attended or documented wheeze. However, there was little difference between LAIV and IIV in regards to these outcomes.[10]
- In one systematic review, pooled analysis suggested that there was a decreased odds of reporting an adverse event after LAIV compared with IIV (0.51; 95%CI: 0.05–5.09).[5]
- Studies have demonstrated that the most common adverse events reported after LAIV administration are nasal symptoms including rhinitis and runny/blocked nose and that these symptoms occur more commonly after LAIV compared to IIV.[5,9,10]
- Children with egg allergy can safely receive LAIV – a phase IV study in the UK including approximately 780 children aged 2–18 years with egg allergy did not experience systemic allergic reactions; 9 children had mild symptoms consistent with a local, IgE mediated allergic reaction.[11]
- Studies examining the safety profiles of LAIV in children with specific conditions, including data from large passive safety surveillance systems in the US and phase IV studies in the UK, suggest LAIV is well-tolerated in children with asthma, cardiovascular conditions, diabetes, obesity, liver, renal disease, and other conditions that increase the risk of severe influenza.[12–16] All studies (including one with more than 387,000 immunisations) demonstrated no evidence of asthma exacerbation among children with asthma who received LAIV.[12–16] LAIV vaccination was also tolerated well among children who were mildly immunocompromised, specifically children with cystic fibrosis, HIV infection and those receiving cancer treatment; while some mild adverse events occurred more frequently relative to healthy children (mostly nasal symptoms), vaccine-related serious adverse events were not increased.[17–19] These studies also

demonstrated absence of prolonged shedding in children with mildly immunocompromising conditions. Studies of the safety profiles of LAIV in children with at-risk conditions suggest LAIV is well-tolerated.

- As a precaution, IIV is preferred over LAIV in pregnancy as it is a live attenuated vaccine. However, there is no evidence of risk with LAIV use during pregnancy. A 2011 study from the US identified within a health insurance claims database women who had received LAIV. Among this cohort, there was no evidence of adverse maternal outcomes and all adverse outcomes identified occurred at similar rates to those in unvaccinated women.[20] Data from case reports and spontaneous reports to the US Vaccine Adverse Event Reporting System (VAERS) have not identified any increased risk of adverse foetal outcomes following LAIV administration to pregnant women.[20]
- Because LAIV is a live attenuated vaccine, it is contraindicated in the following populations:
  - those who have experienced anaphylaxis with a previous dose of any influenza vaccine or after any component of an influenza vaccine
  - moderately and severely immunocompromised persons
  - children receiving salicylate therapy.

Certainty of evidence
What is the overall certainty of the evidence of effects?

No included studies	Very low	Low	Moderate	High

- The evidence for LAIV compared to IIV consisted largely of one systematic review and meta-analysis, which synthesised evidence from head-to-head RCTs.[5] This was the only source of evidence for lab-confirmed influenza infection, serious adverse events, the AESI of asthma/wheeze in healthy children and any adverse event. The certainty of evidence was assessed as moderated, downgraded because the systematic review combined both studies with healthy children and studies of children with underlying medical conditions. Some of the safety studies included in the systematic review were assessed by the review authors as being of low quality.
- One integrated analysis of two RCTs which included children with a history of asthma or wheeze was used for the outcome of exacerbation of asthma/wheeze in children with a history of asthma or wheeze.[10] The certainty of evidence for this study was assessed as moderate, downgraded because it was an ad hoc analysis and because one of the two RCTs was open-label.

Values
Is there important uncertainty about or variability in how much people value the main outcomes?

Important uncertainty	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability

- Overall, there is probably no important uncertainty or variability in how much parents/carers value protecting their children from influenza infection. However, due to widespread belief that influenza is not serious and that the influenza vaccine may not be effective, combined with increasing vaccine scepticism and hesitancy following the COVID-19 pandemic, this has meant that some parents/carers may not value vaccinating their children against influenza.
- In a quantitative and qualitative assessment of community attitudes towards influenza vaccination in 2021, parents of children aged 0–5 years were significantly less likely than most other subgroups to see influenza as a very serious disease, and viewed influenza vaccine as being significantly less important than a range of other vaccines included on the childhood immunisation schedule.[21] This has been evident in decreased influenza vaccine coverage rates in children.[22]

Balance of effects
Does the balance between desirable and undesirable effects favour the intervention or the comparison?

Don't Know	Varies	Favours comparison	Probably favours comparison	Does not favour either comparison or intervention	Probably favours intervention	Favours intervention

- LAIV is likely at least as efficacious against lab-confirmed influenza infection as IIV.
- The potential for increased mild-moderate nasal symptoms associated with LAIV likely balances against the potential for increased mild-moderate local reactions with IIV.
- Serious adverse events and adverse events of special interest appear similar between LAIV and IIV.

- Overall, comparing desirable and undesirable effects as outlined above suggest that LAIV is likely similar to IIV.

Acceptability
Is the intervention acceptable to key stakeholders?

Don't know	Varies	No	Probably no	Probably yes	Yes

- Data from a survey of 1,987 Australian parents indicated that 27% of children aged ≥4 years have an intense phobia of needles, and 13% have a phobia severe enough to stop them getting the influenza vaccine.[23] Intranasal administration avoids vaccination by injection, so LAIV may have greater acceptability by vaccine recipients and their parents compared with current influenza vaccinations available in Australia (i.e. intramuscular IIV).
- Studies of LAIV acceptability in other high-income countries show that parents have a preference for vaccinating their child with LAIV over intramuscularly administered IIV.[24–26] In a study of pilot implementation in schools in Canada, nurses administering vaccines perceived that children were calmer after LAIV administration compared with IIV administration.[27]
- Factors that may possibly adversely impact acceptability include perceptions of increased risk associated with being a live vaccine and objections to porcine gelatin contents of LAIV (particularly among some faith-based communities).
- Intranasal administration may be challenging in very young children; current IIVs as an alternative are still required.
- Providers' willingness to stock and administer LAIV may be affected by the shorter shelf life of LAIV compared to currently available seasonal influenza vaccines, increased complexity in managing stock and predicting demand, additional storage requirements to stock both LAIV and IIV, increased time for consultations and shared decision-making with children and parents, and requirements for training on correct administration.
- England uses LAIV with delivery via schools and GPs and has achieved higher coverage than Australia. In 2023-2024, 55.1% of primary school children (through year 6) and 42.8% of secondary school children (years 7–11) were vaccinated.[28] In England in the 2024-2025 season, coverage of 2–4 year olds was 37.2%.[29]

Equity
What would be the impact on health inequities?

Don't know	Varies	Increased	Probably increased	Probably no impact	Probably reduced	Reduced

- The potential for easier administration via the intranasal route may mean that additional cadres of healthcare providers can administer vaccine, which can potentially increase access to influenza vaccination. This may help increase access to influenza vaccination and reduce inequities, including for high-risk groups.
- Intranasal administration of LAIV may assist in vaccinating specialised population groups who have traditionally been more challenging to vaccinate using intramuscular injections, such as those with needle phobia and people with intellectual and other disabilities including those living in disability accommodation settings. This can reduce inequities in vaccination.
- Despite the benefits of LAIV, some individuals are contraindicated to receive LAIV (particularly those with severe immunocompromising conditions) so continued access to currently available inactivated influenza vaccines is necessary to avoid any inadvertent difficulties in accessing influenza vaccination for these high-risk groups.
- As LAIV will not yet be available through the NIP, there may be potential inequities in access to LAIV for parents who will need to pay out-of-pocket. However, IIV is still available to these people.
- LAIV's shorter shelf life (relative to current influenza vaccines) may cause access issues for people living in rural or regional areas if few or no local providers can maintain adequate stock level.

Feasibility
Is the intervention feasible to implement?

Don't know	Varies	No	Probably no	Probably yes	Yes

- Implementation of an LAIV program, alongside the current influenza vaccination program with IIV, is considered feasible. Use of LAIV in a mass vaccination setting (e.g. school-based vaccination program) is also considered more feasible than the current intramuscularly administered IIV.

- Some individuals will continue to need access to currently used IIVs due to contraindication to LAIV or a preference for IIV over LAIV. Programmatic use of LAIV should complement the current influenza vaccination program utilising IIV.
- As LAIV is a new vaccine being introduced, a number of implementation considerations are necessary to ensure seamless implementation:
    - There are additional cold chain requirements and stock management challenges (such as forecasting demand and supply needs and additional refrigerator capacity) at all levels of the health system, due to the requirement to stock both IIV and LAIV
    - Additional trainings are required for immunisation providers on nasal spray administration and handling of LAIV across different settings (e.g. primary care, pharmacy, tertiary hospital etc.), especially as vaccinating very young children can be more challenging.
    - Providers may need to provide extra time for pre-vaccination screening and counselling.
    - Shorter shelf life of LAIV (approximately 4 months) relative to IIV may create complexities for stock handling and storage.[30]
    - Easier administration via the intranasal route increases the feasibility of using school-based vaccination delivery to increase vaccination coverage; however, this would be very resource intensive and require extensive planning and phased implementation over a period of several years.
    - Updates are needed to existing vaccine surveillance and monitoring systems to monitor adverse events and vaccine effectiveness for LAIV, including updates to existing immunisation registries and reporting tools.
    - LAIV is a live attenuated vaccine and contraindicated in some individuals. Processes to accurately identify contraindicated individuals are needed.
- Coadministration studies including LAIV are limited. Studies of LAIV co-administered with measles-mumps-rubella (MMR) vaccine, varicella vaccine and oral vaccine demonstrate similar immunogenicity compared to separate administration, and co-administration was well-tolerated.[31,32] Based on available evidence, there are no concerns about co-administering other routine vaccines with LAIV.
- There are no concerns about vaccinating children with LAIV across consecutive seasons. A systematic review of 4 placebo-controlled RCTs including 6,090 children investigating the efficacy of LAIV upon revaccination of children against lab-confirmed influenza infection in consecutive season found that there was no decrease in efficacy of LAIV when administered in 2 consecutive seasons.[33] A separate test-negative case-control study in the US including 3,369 children aged 2-17 years observed across 3 influenza seasons found that protection against influenza A(H3N2) was significantly improved among children who were repeatedly vaccinated with LAIV.[34]

ATAGI recommendation

- LAIV is recommended as an alternative to IIV for prevention of influenza in individuals aged 2–17 years.

Justification and considerations

- Influenza caused significant disease burden among children aged 2–17 years in Australia, including hospitalisations. Vaccination coverage among this age group remains low, despite a long-standing influenza vaccination program including NIP-funded vaccination for children aged <5 years.
- LAIV has been used widely for 2 decades in other countries (including in the USA since 2003 and the UK in a school-based program since 2013). A substantial body of evidence including RCTs and large observational studies of national-level programs demonstrate that LAIV is effective in preventing influenza infections and hospitalisations. Some evidence also suggests that herd protection to non-target populations is observed when high rates of coverage among children are achieved.
- Both RCTs and large observational studies indicate that LAIV is safe and has a similar safety profile to currently used IIVs and can be safely used in children with mild immunocompromising conditions and those with asthma. As a live vaccine, it is contraindicated in certain populations including moderate/severe immunocompromising conditions.
- LAIV is administered intranasally and may be more acceptable to intra muscularly administered IIVs, especially among children with needle phobia or others who are difficult to vaccinate due to pre-existing conditions. Therefore, use of LAIV may increase influenza vaccination coverage.
- LAIV has the potential to be used in mass vaccination programs in school-based settings to increase influenza vaccination coverage.

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