Vaccination update: Childhood influenza immunisation

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This symposium has been sponsored by AstraZeneca UK
Prescribing information can be found at the end of this presentation
Contents

• Overview of influenza and vaccination
• The national influenza vaccination programme
• Use of flu vaccine for children
What is flu? ¹

• Influenza is an acute viral infection of the respiratory tract
• Three types of influenza virus: A, B and C. Influenza A and influenza B are responsible for most clinical illness
• Characterised by the sudden onset of fever, chills, headache, myalgia and extreme fatigue. Other common symptoms include a dry cough, sore throat and stuffy nose
• Risk of serious illness is higher:
  • children under six months of age
  • older people
  • those with underlying health conditions
  • pregnant women

¹. PHE. Influenza: the green book, chapter 19
The burden of seasonal influenza

- Seasonal influenza usually affects 5–15% of the global population\textsuperscript{1}
- Paediatric attack rates are between 20% and 35%\textsuperscript{1}
- Annual epidemics result in
  - \( \sim 3–5 \) million cases of severe illness worldwide\textsuperscript{2}
  - \( \sim 250,000–500,000 \) deaths worldwide\textsuperscript{2}
  - Up to 40,000 excess deaths in a moderate-to-severe season in the EU\textsuperscript{2}
  - Cumulative morbidity is greater for seasonal influenza epidemics than for pandemics\textsuperscript{2}
- The medical and economic burden associated with influenza-related HCP visits, prescriptions, hospitalisations and loss of productivity is significant\textsuperscript{2}

Role of immunisation

- Vaccination is the most effective way of preventing illness from influenza\(^1\)
- Antiviral drugs are not a substitute for vaccination\(^1\)
- Influenza immunisation has been recommended in the UK since the late 1960s\(^2\)

1. NICE. Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza
2. PHE. Influenza: the green book, chapter 19
Flu immunisation programme

The previous public vaccination programme was based on a risk approach with groups recommended to receive flu vaccine:

- All people aged 65 years and over
- Health & social care workers
- Carers
- Long-stay care patients

Clinical risk groups:
- Chronic respiratory disease
- Chronic heart disease
- Chronic kidney disease
- Chronic liver disease
- Chronic neurological disease
- Diabetes
- Immunosuppression

Children aged 6 months to less than 9 years:
- One dose influenza vaccine

Those aged 9 to less than 65 years:
- One dose influenza vaccine

Has the child received influenza vaccine previously?

- Yes:
  - One dose influenza vaccine

- No:
  - Two doses influenza vaccine at least 4 weeks apart

1. PHE. Influenza: the green book, chapter 19
### Seasonal influenza vaccination uptake by target group, UK, 2011/12 and 2012/13 seasons

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<thead>
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<td>Healthcare workers</td>
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<td>30.9</td>
<td>35.5</td>
<td>20.8</td>
<td>20.4</td>
</tr>
</tbody>
</table>

1. PHE Annual Report. [www.hpa.org.uk](http://www.hpa.org.uk)
JCVI recommendations – July 2012

- Annual influenza vaccination programme be extended to include school-aged children (spanning ages five to less than 17 years)
- AstraZeneca’s live attenuated intranasal influenza vaccine (Fluenz® live attenuated influenza vaccine (LAIV)) should be the vaccine of choice
- Highly likely to be cost-effective and well within accepted cost effectiveness thresholds
  - Low risk children aged six months to less than 17 years – cost effective but small additional benefit

Rationale for childhood flu programme changes\textsuperscript{1,2}

1. **Direct protection** - lowering the impact of influenza on children

2. **Indirect protection** - lowering influenza transmission from children to other children, adults and those in the clinical risk groups of any age

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Childhood flu immunisation programme
Roll out to two and three year olds - England¹

• Age group includes two and three year olds – but not four years or older – i.e. date of birth on or after 2 September 2009 and on or before 1 September 2011)

• GP practices are encouraged to ensure that uptake of flu vaccine in two and three year old children is as high as possible

• The vaccine should be offered on either
  – a proactive call basis, if not considered at-risk, or
  – a proactive call and recall basis, if considered at risk

Geographical pilots

- Cross section of urban, rural and inner city settings
- In England, geographical pilots four to ten year olds (up to and including pupils in school year 6)
- Assess issues such as workload, uptake and logistics of delivery in a variety of settings
- Testing of vaccine coverage monitoring systems in order to evaluate the programme in the longer term

Responsibility of healthcare professionals

- Practices are encouraged to ensure that uptake of flu vaccine in two and three year old children is as high as possible
- Responsibility of health visitors, school nurses and other relevant health professionals to encourage flu vaccination and to promote coverage of the vaccine, especially in the under-served groups

Information materials and resources

• An updated patient leaflet will be available from the GOV.uk immunisation page before the start of the flu immunisation programme

• Leaflets and a poster have been prepared and tested with parent groups for children’s flu immunisation for pilot regions and the two and three year old cohort

• Printed copies can be ordered by GP surgeries through Publications Order
  www.orderline.dh.gov.uk/ecom_dh/public/home.jsf

• The Green Book Immunisation against Infectious Disease provides guidance for healthcare workers on administering the flu vaccine

USE OF FLU VACCINE FOR CHILDREN
### Types of influenza vaccine approved in the EU

<table>
<thead>
<tr>
<th>TIV</th>
<th>LAIV</th>
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<tbody>
<tr>
<td>Trivalent inactivated influenza vaccine, intramuscular</td>
<td>Live attenuated influenza vaccine, intranasal</td>
</tr>
<tr>
<td><strong>HA</strong> is the only standardised component; other antigens may be present$^{1,2*}$</td>
<td>Attenuated vaccine with multiple antigens$^{3,4*}$</td>
</tr>
</tbody>
</table>

HA: haemagglutinin; M1, M2: matrix proteins; NA: neuraminidase; NP: nucleoprotein.


Please refer to the specific prescribing information for each manufacturer’s influenza vaccine as not all influenza vaccines are indicated for all ages.

2. Fluvirin [Summary of Product Characteristics]. Novartis Vaccines and Diagnostics Ltd.
3. FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd.
LAIv - vaccine of choice for the extended programme

- More effective in children than other inactivated influenza vaccines
- Good safety profile in children aged two years and older
  - More than 70 clinical studies were conducted worldwide
    - Africa, Europe, Asia, Latin America and US
- May provide protection against influenza strains that are not well matched to the vaccine strains as recommended annually by the WHO
- Established history of use – available in U.S since 2003
LAIV is engineered to prevent influenza infection

**Attenuated virus**: disease-causing properties removed so as not to cause illness\(^1\)

**Cold-adapted**: replicates efficiently only in the cooler areas of the nasopharynx\(^1\)

**Temperature-sensitive**: does not replicate efficiently in warmer areas of the lower respiratory tract where influenza viruses typically replicate\(^1\)
CLINICAL EXPERIENCE
Efficacy relative to placebo
5 Randomized studies; matched strains

- 87% reduction (95% CI: 83, 91)
- 88% reduction (95% CI: 83, 92)

1. Adapted from Ambrose et al., Vaccine, 30:886-892, 2012.
Incidence of Culture-Confirmed Influenza

- 24-59 mos: 1.2% TIV, 0.1% LAIV
- 24-71 mos with RTIs: 4.8% TIV, 2.4% LAIV
- 6-17 yrs with asthma: 6.4% TIV, 4.1% LAIV

Efficacy Relative to TIV
3 Randomized Studies; Matched Strains

92% reduction (95% CI: 68, 98)
49% reduction (95% CI: 13, 71)
35% reduction (95% CI: 6, 55)

TOLERABILITY PROFILE
Comparable safety to placebo in children aged 2–17 years of age†

Solicited reactogenicity events days 0–10 post-vaccination in year 1 of placebo-controlled studies

†Data available from 14 placebo-controlled studies.
*Statistically significant difference (p<0.05)

Adapted from Ambrose CS et al, 2011
Summary of LAIV safety in children 2-17 years of age

- LAIV has an established safety profile based on data derived from >20,000 children and adolescents
- Common post-vaccination adverse events
  - Runny nose/nasal congestion, headache, decreased activity, decreased appetite and low grade fever (>100°F/37.8°C)
- Post-marketing safety surveillance has confirmed the safety profile observed in clinical trials
Undesirable effects

• Hypersensitivity reactions (facial oedema, urticaria, very rarely anaphylaxis)
• Decreased appetite
• Headache
• Nasal congestion/rhinorrhoea, uncommonly epistaxis
• Rash
• Myalgia, malaise
• Pyrexia
• Very rarely Guillain-Barré syndrome
Contraindications and precautions\textsuperscript{1,2}

- Age less than two years and \( \geq 18 \) years
- Pregnancy
- Hypersensitivity to the active substances, excipients, gentamicin, eggs or egg proteins
- Children and adolescents who are:
  - clinically immunodeficient due to conditions or immunosuppressive therapy. Examples: acute & chronic leukaemia; lymphoma; HIV infection not receiving stable antiretroviral therapy
  - receiving salicylate therapy (aspirin) – association with Reye’s syndrome with salicylates & wild-type influenza infection
- Not contraindicated if: receiving topical/inhaled steroids, low dose systemic steroids, or as a replacement therapy, e.g. for adrenal insufficiency\textsuperscript{3}

\textsuperscript{1} FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd

\textsuperscript{2} Department of Health. The flu immunisation programme 2013/14 – extension to children. July 2013

\textsuperscript{3} British Thoracic Society, British Guideline on the Management of Asthma.
Contraindications and precautions

• Should not be administered to children and adolescents with:
  - active wheezing
  - severe asthma BTS SIGN step 4 or above
    - Under 5 y: child referred to Respiratory Physician
    - 5 to 12 years: inhaled steroid 800 mcg/day (step 4) or requiring oral steroids (step 5)
    - 13 to 18 years (as in adults): inhaled steroid above 800 mcg/day and/or addition of 4th drug (already on inhaled β2 agonist, inhaled steroid, inhaled long-acting β2 agonist) e.g. leukotriene receptor antagonist, SR theophylline, β2 agonist tablet

1. FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd
2. DH. Green Book Ch 19
For those who are contra-indicated to LAIV

<table>
<thead>
<tr>
<th>Supplier</th>
<th>Name of product</th>
<th>Type</th>
<th>Age indication</th>
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<tbody>
<tr>
<td><em>Abbott Healthcare</em></td>
<td>Influvac Desu®</td>
<td>Surface antigen, inactivated</td>
<td>From 6 months</td>
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<tr>
<td></td>
<td>Imuvac®</td>
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<td><em>GlaxoSmithKline</em></td>
<td>Fluarix®</td>
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<td>FluarixTM Tetra</td>
<td>Split virion inactivated virus</td>
<td>From 3 years</td>
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<td><em>Janssen-Cilag Ltd</em></td>
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<td>Surface antigen, inactivated</td>
<td>From 6 months</td>
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<td><em>MASTA</em></td>
<td>Imuvac®</td>
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<td>Inactivated Influenza Vaccine (Split Virion) BP</td>
<td>Split virion, inactivated virus</td>
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<td></td>
<td>Fluarix®</td>
<td>Split virion inactivated virus</td>
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<td>Agrippal®</td>
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<td>From 6 months</td>
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<td>Fluvirin®</td>
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<td>CSL Inactivated Influenza Vaccine</td>
<td>Split virion Inactivated virus</td>
<td>From 5 years</td>
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<td></td>
<td>Enzira®</td>
<td>Split virion Inactivated virus</td>
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<tr>
<td><em>Sanofi Pasteur MSD</em></td>
<td>Inactivated Influenza Vaccine (Split Virion) BP</td>
<td>Split virion, inactivated virus</td>
<td>From 6 months</td>
</tr>
</tbody>
</table>

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Shedding and transmission\textsuperscript{1,2}

LAIV: potential for transmission

- 1 to 2 weeks following vaccination (peak incidence 2 to 3 days post vaccination)
- Most at risk: the severely immunocompromised e.g. bone marrow transplant patients requiring isolation
  - close contacts (such as household members)
  \(\Rightarrow\) should receive an inactivated influenza vaccine

1. FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd
Overview

• LAIV => 0.2 ml suspension in a single-use nasal applicator with nozzle & a dose-divider clip

• Administered by the intranasal route and is supplied in an applicator that allows a divided dose to be administered in both nostrils

• Neither divided dose needs to be repeated if the child
  – Sneezes
  – Blows their nose following administration

• Postpone if child very snuffly on the day of vaccination

• Can be given at the same time as all other vaccines (incl. live vac)
Dosing\textsuperscript{1,2}

- SPC recommends two doses for children vaccine naïve (after an interval of at least 4 weeks)

- JCVI: most children only one dose of Fluenz\textsuperscript{®}

- JCVI: children two to nine years, not had the influenza vaccine before
  - Two doses if child in ‘at-risk’ group or receiving the TIV (four weeks apart)

\textsuperscript{1} FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd
\textsuperscript{2} Department of Health. The flu immunisation programme 2013/14 – extension to children. July 201
Shelf life & storage

- Pack size: $10^1$ (16 cm L, 12 cm W, 4 cm H)
- Store in refrigerator ($+2^\circ$C to $+8^\circ$C) \(^1\)
- Maximum time out of refrigerator at temperature not higher than $25^\circ$C => 12 hours \(^2\)
- *Advice can be sought from AstraZeneca directly about temperature excursions*
- Shelf life: 18 weeks => check nasal spray applicator for expiry date (DH: 2013 supplies will expire by 16 January 2014) \(^1,2\)

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1. FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd
QUESTIONS
FLUENZ® nasal spray suspension Influenza vaccine (live attenuated, nasal)

PRESCRIBING INFORMATION. Consult Summary of Product Characteristics before prescribing.

Use  Prophylaxis of influenza in individuals 24 months to less than 18 years of age.  Presentation  Nasal spray, suspension.  Dosage and administration  0.2ml (administered as 0.1ml per nostril). Children not previously vaccinated against seasonal influenza should be given a second dose after an interval of at least 4 weeks.  FLUENZ should not be used in individuals below 24 months of age because of safety concerns.  Method of administration: Nasal administration only.  Do not inject FLUENZ.

Contraindications  Hypersensitivity to the active substances, any of the excipients (e.g. gelatin), gentamicin (a possible trace residue), eggs or to egg proteins (e.g. ovalbumin).  Children and adolescents who are clinically immunodeficient due to conditions or immunosuppressive therapy: (acute and chronic leukaemias; lymphoma; symptomatic HIV infection; cellular immune deficiencies; and high-dose corticosteroids).  Not contraindicated for use in individuals with asymptomatic HIV infection; or individuals who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids or those receiving corticosteroids as replacement therapy, e.g. for adrenal insufficiency.  Contraindicated in children and adolescents younger than 18 years of age receiving salicylate therapy because of the association of Reye’s syndrome with salicylates and wild-type influenza infection.  Precautions  Medical treatment and supervision should always be readily available in case of an anaphylactic event following administration.  FLUENZ should not be administered to children and adolescents with severe asthma or active wheezing because these individuals have not been adequately studied in clinical studies.  Do not administer to infants and toddlers younger than 12 months.  Not recommended to administer to infants and toddlers 12-23 months of age.  In a clinical study, an increase in hospitalisations was observed in infants and toddlers younger than 12 months after vaccination and an increased rate of wheezing was observed in infants and toddlers 12-23 months of age after vaccination.
Vaccine recipients should be informed that FLUENZ is an attenuated live virus vaccine and has the potential for transmission to immunocompromised contacts. Vaccine recipients should attempt to avoid close association with severely immunocompromised individuals (e.g. bone marrow transplant recipients requiring isolation) for 1-2 weeks following vaccination. Where contact is unavoidable, the potential risk of transmission of the influenza vaccine virus should be weighed against the risk of acquiring and transmitting wild-type influenza virus. No data exists regarding the safety in children with unrepaired craniofacial malformations. **Interactions:** Salicylates must not be used for 4 weeks following vaccination unless medically indicated. Co-administration of FLUENZ with the live attenuated vaccines: No clinically meaningful changes in immune responses to measles, mumps, varicella, orally-administered poliovirus or FLUENZ have been observed. Immune response to rubella vaccine was significantly altered. This might not be of clinical relevance with the two dose immunisation schedule of the rubella vaccine. Co-administration of FLUENZ with inactivated vaccines has not been studied. Concurrent use of FLUENZ with antiviral agents active against influenza A and/or B viruses has not been evaluated. However, based upon the potential for influenza antiviral agents to reduce the effectiveness of FLUENZ, it is recommended not to administer the vaccine until 48 hours after the cessation of influenza antiviral therapy. Administration of influenza antiviral agents within two weeks of vaccination may affect the response of the vaccine. If influenza antiviral agents and FLUENZ are administered concomitantly, revaccination should be considered when appropriate. **Pregnancy and Lactation:** Not recommended during pregnancy. Should not be used during breastfeeding. **Undesirable effects** Very common: decreased appetite, headache, nasal congestion/rhinorrhoea, malaise. Common: myalgia, pyrexia. Uncommon: hypersensitivity reactions (including facial oedema, urticaria and very rare anaphylactic reactions), epistaxis, rash. Very rare reports of Guillain-Barré syndrome and exacerbation of symptoms of Leigh syndrome (mitochondrial encephalomyopathy) have also been observed in the post-marketing setting. **Consult SmPC for a full list of adverse events.**
Consult SmPC for a full list of adverse events.

**Legal category**  POM.

**Marketing authorisation number**  EU/1/10/661/001-002

**Basic NHS cost**  Pack of 10: £140.00

**Further information is available from AstraZeneca on behalf of the Marketing Authorisation Holder**

**MedImmune**  AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, UK.

MedImmune is the Global biologics business for AstraZeneca

FLUENZ is a trade mark of the AstraZeneca group of companies.

02/2012

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to AstraZeneca on 0800 783 0033