UK paediatric influenza vaccine programme

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UK has had a long-standing annual seasonal trivalent inactivated vaccine (TIV) programme

All high risk groups under 65 years, including pregnant women
All 65+ year olds

Aim→ to provide direct protection to target groups

Problems:
• effectiveness of TIV in elderly and very young is moderate at best
• most vulnerable groups are elderly and very young
Influenza vaccine uptake (GP Patient survey) by year for England

% Vaccine Uptake

- 65 and Over
- Under 65 at Risk

WHO 2010 target
Deaths / 1000 influenza admissions by age and risk group, 2000/1 – 2007/8
Incidence of influenza admission by age and risk group/100,000 (2000/01 to 2007/08)
Flu vaccination of children – a new paradigm?

- Evidence to suggest children are main drivers of influenza transmission

- Intra-nasally administered cold adapted live attenuated influenza recently licensed in Europe
Effectiveness of flu vaccine: meta-analysis

Figure 2. Vaccine efficacy compared with placebo (Mantel-Haenszel random-effects model). (A) Trivalent inactivated influenza vaccine in adults aged 18–64 years. (B) Live attenuated influenza vaccine in children aged 6 months to 7 years. Studies were prospective (risk ratio) which are equivalent to case-control (odds ratio). n=cases of influenza, N=group size.

Lancet ID Osterholm 2012
Flu vaccination of children – a new paradigm?

- Evidence to suggest children are main drivers of influenza transmission

- Intra-nasally administered cold adapted live attenuated influenza recently licensed in Europe

- Vaccination of healthy children has potential to provide:
  - *Direct protection to children themselves*
  - *Indirect protection to other vulnerable persons in population (by reduction in transmission)*
Modelling and economic evaluation of current and extended flu programme in the United Kingdom

Estimate current burden of influenza

Built transmission model to estimate:

•  impact of current selective programme

•  direct and indirect effects of various programme extensions

•  costs of different programme extensions

•  savings in health care costs and QALYs
Cost-effectiveness of various additions to current flu programme

All additions involving vaccination of children were cost-effective even at low uptake (30%)

Little additional benefit by adding older age groups but big increase in programme costs

Baguelin M BMC Med 2015  Cost in £ per QALY gained
Recommended introduction of flu vaccination of healthy children aged 2 to 16 years of age with newly licensed live attenuated influenza vaccine

Based on the predicted direct and indirect impact of such a programme
Roll-out of Childhood Live Attenuated Influenza Vaccination (LAIV) Programme

**UK**
- 2-3 year olds
- 2-4 year olds
- 2-4 year olds and year 1 & 2
- Ultimate objectives

**Pilots (England)**
- 4-11 year olds
- 5-11 year olds and year 7 & 8
- 4-11 year olds
- 2013-14 season
  - Recommended a single dose of LAIV intranasal
  - Selected geographical pilot areas
  - Offered through GPs and schools
- 2014-15 season
  - Selected geographical pilot areas
  - Delivered through GPs and schools
- 2015-16 season
  - Selected geographical pilot areas
  - Delivered through schools, GPs and/or pharmacies

- To offer vaccination to all healthy children 2-16 years old
UK surveillance plans for childhood flu vaccine programme

1. To measure **uptake** of the new programme;
2. To measure **vaccine effectiveness**
3. To obtain an estimate of the population **impact (indirect and overall)** of vaccinating school age children for range of influenza indicators
LAIV uptake
Pre-school uptake for childhood flu programme, England, 2013/14 – 15/16

Influenza vaccine uptake (%) in GP patient groups for 2013/14 to 2015/16

*The universal childhood vaccines were only extended to all 4 year olds in 2014/15*
School-age LAIV pilot areas and uptake in 13/14, 14/15 and 15/16

13/14

14/15

15/16

UPTAKE  56%  53.2%  57.9%
First year of vaccinating in all primary schools
Total of >1.3 million children Y1 & 2 targeted in >15,000 schools

- 53.6% in children school years 1 and 2 age in England
- 54.4% in children school years 1 age in England
- 52.9% in children school years 2 age in England
Recent epidemiology of influenza in UK
2013/14: low intensity activity dominated by A/H1N1pdm099

2014/15: moderate intensity dominated by drifted A/H3N2 & B

2015/16: moderate intensity dominated by A/H1N1pdm09 & B
LAIV effectiveness, UK
Annual estimation of flu VE in the UK

**Network:** ~200 GP practices across 5 sentinel networks in England, Scotland, Wales and Northern Ireland

**Study population:** patients consulting in primary care with an acute influenza-like illness consented to be swabbed

**Dates:** October – April each influenza season

**Design:** Test negative design

- compare odds of vaccination in RT-PCR confirmed influenza cases and RT-PCR negative controls

**Vaccination status:** at least one dose of influenza vaccine 14 or more days after onset of respiratory illness. Information collected on route of administration (injected, intranasal)

**End of season analysis:** including age-specific analysis in 2-17 year olds
ACIP votes down use of LAIV for 2016-2017 flu season

**Media Statement**

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CDC’s Advisory Committee on Immunization Practices (ACIP) today voted that live attenuated influenza vaccine (LAIV), flu vaccine, should **not** be used during the 2016-2017 flu season. ACIP continues to recommend annual flu vaccine, either inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV), for everyone 6 months and older.

ACIP is a panel of immunization experts that advises the Centers for Disease Control and Prevention (CDC). This page is publicly accessible to inform the general public about CDC’s recommendations for the 2016-2017 flu season.
Adjusted VE estimates by type of vaccine in 2-17 year olds, UK, October 2015–May 2016

*Adjusted for age-group, month of sample, pilot area, surveillance scheme
Pooled VE estimates by type of vaccine in 2-17 yr olds, 13/14 to 15/16

* Adjusted for age-group, month of sample, pilot area, surveillance scheme
LAIV impact
Influenza disease pyramid: sources of data for impact assessment

- Deaths
- Hospitalised cases
  - Community cases seen by a general practitioner
  - Community cases not seen by a general practitioner
- Excess mortality
- Flu + ICU admissions
- Flu + hospital admissions
- GP ILI consultation rates
- Flu swab positivity
- School absenteeism
- Social media (Twitter)
Methods – to measure overall and indirect impact

Compared disease incidence in targeted and non-targeted age-groups in pilot and non-pilot control areas

Recruited additional swabbing GP practices, emergency departments and hospitals in pilot areas;

Calculated cumulative incidence and positivity rates in pilot and control areas based upon place of residence/catchment population
Impact of vaccinating primary and/or secondary school age children on range of primary care indicators, 14-15

*Risk ratios calculated for rates with negative binomial regression. Odds ratios calculated for proportions with logistic regression, correcting for overdispersion.

Red – primary pilot area; Green – secondary pilot only area Blue – control area

Pebody Eurosurveillance 2015
Key findings

United Kingdom now completed third season of roll-out of paediatric live attenuated influenza vaccine programme

Uptake of LAIV programme in roll-out in school age-pilots achieved ~50% and ~40% in 2-4 year olds with lessons regarding delivery and risk factors for low uptake;

Evidence of effectiveness of LAIV, despite circulation of drifted H3 strain in 14/15. In 15/16, unlike the USA, overall LAIV VE was good, particularly against flu B, though lower against A/H1N1pdm09.

Evidence of impact (indirect & overall) of primary-school age vaccination:
- Consistent, decreases in disease incidence and influenza positivity in primary school age pilot vs control areas in targeted and non-targeted groups;
- Less clear impact for more severe end-points

JCVI has recently reviewed the programme in the light of US observations – and has strongly recommended continuation of the childhood LAIV programme

On-going enhanced surveillance and further studies planned as programme is rolled out to additional age-cohorts
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PHE SW Region laboratory
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Public Health Wales

ALL THE LAIV PILOT SITES responsible for delivery of programme

All contributing USISS and EDSSS NHS acute trusts and RCGP practices

Office for National Statistics for the mortality data