

Live Attenuated Influenza Vaccine (LAIV)

The UK experience - England

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Spanish Association of Paediatrics, Toledo, 23 April 2016

UK routine immunisation schedule for children

Age

2 months

3 months

4 months

12–13 months

2–6 years (and at risk \geq 6 months)

3.5 years

12–13 years (girls only)

13–14 years

14–15 years

19–25 years (university entrants)

Vaccine

DTaP/IPV/Hib; MenB; PCV; Rotavirus

DTaP/IPV/Hib; MenC; Rotavirus

DTaP/IPV/Hib; MenB; PCV

Hib/MenC; MenB; PCV; MMR1

Influenza

DTaP/IPV; MMR2

HPV

Td/IPV

MenACWY

MenACWY



Epidemiology: pandemics

A(H1N1)

1918:
'Spanish Flu'
40 million
(severe)^{1,2}



A(H2N2)

1957:
'Asian Flu'
1 million
(moderate)¹



A(H3N2)

1968:
'Hong Kong Flu'
4 million
(severe)¹



A(H1N1)

2009
'H1N1 Swine Flu'
~18,000*
pig/bird/man^{3,4}



***2009: affected younger ages; greater impact in terms of 'years lost'**

1. World Health Organization. Influenza fact sheet 2011. March 2003. Available at: <http://www.who.int/mediacentre/factsheets/2003/fs211/en/> (last accessed 5 August 2015).
2. Pan American Health Organization. Press release. May 2006. Available at: <http://www.paho.org/English/DD/PIN/pr060526.htm> (last accessed 5 August 2015).
3. World Health Organization. Pandemic (H1N1) 2009: frequently asked questions. Available at: http://www.who.int/csr/disease/swineflu/frequently_asked_questions/en/ (last accessed 5 August 2015).
4. Pan American Health Organization. Press release. August 2010. Available at: http://new.paho.org/sur/index.php?option=com_content&task=view&id=195&Itemid=400 (last accessed 5 August 2015).

Burden of influenza in England and Wales¹

- 779,000–1,164,000 GP consultations
- 19,000–31,200 hospital admissions
- 18,500–24,800 deaths attributable to influenza
- Influenza infections affect up to almost 10% of children aged birth to 14 years in England in an average season²
- **Influenza:** the most common cause of lower respiratory illness in children aged 6 months to 12 years presenting to GPs, even in non-epidemic years³
 - significant risk of secondary bacterial infection³



1. Pitman RJ, et al. *J Infect* 2007;54:530–538.
2. Paget WJ, et al. *Eur J Pediatr* 2010;169:997–1008.
3. Harnden A, et al. *Arch Dis Child* 2007;92:594–597.

Influenza immunisation for children UK considerations



Rationale for vaccinating children

- Children are recognised as playing a key role in the transmission of influenza virus¹
- Targeting children with influenza vaccine would:
 - Not only reduce infection in immunised children themselves (**direct programme impact**)
 - But also reduce influenza-related disease in other age groups, including elderly people, and individuals in high-risk groups (**indirect programme impact**)^{2,3}



1. Petrie JG, et al. *PLoS One* 2013;8:e75339.
2. Baguelin M, et al. *PLoS Med* 2013;10:e1001527.
3. Rose MA, et al. *BMC Infect Dis* 2014;14:40.

Joint Committee on Vaccinations and Immunisations (JCVI), April 2012

- Discussed potential extension of the influenza vaccination programme to children:
 - ↓ impact of flu by directly averting many cases in children
 - ↓ many cases of severe flu and flu-related deaths in older adults and people with clinical risk factors
- Review of the (then unpublished) HPA/LSHTM study²:
 - Cost effectiveness of the vaccination programme
 - Range of possible extensions
- Followed NICE criteria
- Chosen vaccine: the Live Attenuated Influenza Vaccine (LAIV)
- Vaccine adverse effects not considered in cost effectiveness analysis
 - Reasonable, “*given the safety profile of chosen vaccine*”

1. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Friday 13 April 2012. Available at: <http://webarchive.nationalarchives.gov.uk/20130402145952/http://media.dh.gov.uk/network/261/files/2012/05/jcvi-minutes-13-april-2012-meeting.pdf> (last accessed 5 August 2015).

2. Baguelin M, et al. *PLoS Med* 2013;10:e1001527.

HPA, Health Protection Agency; LSHTM, London School of Hygiene & Tropical Medicine; NICE, National Institute for Health and Care Excellence.

Increasing vaccine uptake to 50% is cost saving – cost effective¹

Mathematical model exploring the effect of increasing the annual paediatric uptake rate of LAIV in children aged 2–18 years

Scenario	QALYs lost (millions)	Cost (millions)	Incremental QALYs (millions)	Incremental cost (millions)	ICER
Current policy	7.73	£18,304			
LAIV uptake rate					
10%	5.56	£17,818	2.17	–£486	Cost saving
30%	2.26	£18,040	5.46	–£264	Cost saving
50%	1.07	£19,973	6.65	£1,669	£251
70%	0.60	£22,511	7.13	£4,207	£590
90%	0.39	£25,275	7.33	£6,971	£951

ICER; incremental cost-effectiveness ratio; LAIV, live attenuated influenza vaccine; QALY, quality-adjusted life year.

1. Pitman R, et al. *Vaccine* 2013;31:927–942.

JCVI choice of vaccine: LAIV¹

- Significantly more effective than inactivated flu vaccines currently used
- Licensed for use in children aged 2–17 years
 - Suitable for use in a programme to vaccinate children
- Identified contraindications and precautions would need to be managed in the design of the programme
- Central procurement would be the most practicable approach to securing the quantities that would be required
 - *“it would take some time to set up and agree contacts for the supply, storage and distribution of the very large quantities of vaccine that would be needed”*
- Application for market authorisation of adjuvanted inactivated Fluad paediatric[®] (Novartis) has been withdrawn
 - No alternative vaccine



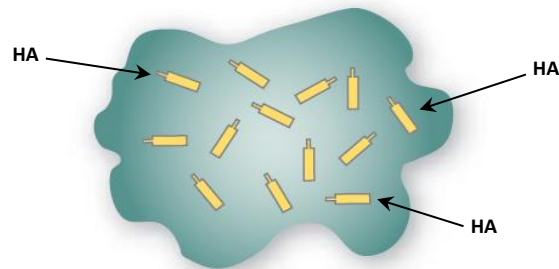
1. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Friday 13 April 2012. Available at: <http://webarchive.nationalarchives.gov.uk/20130402145952/http://media.dh.gov.uk/network/261/files/2012/05/jcvi-minutes-13-april-2012-meeting.pdf> (last accessed 5 August 2015).

Types of influenza vaccine approved in the EU

TIV

Trivalent inactivated influenza vaccine, intramuscular

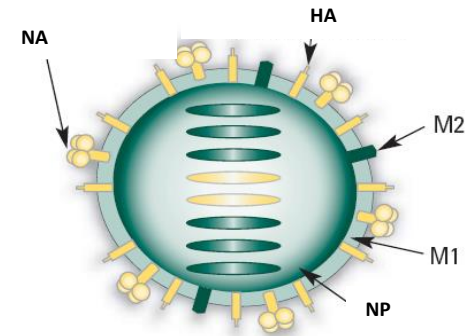
HA is the only standardised component; other antigens may be present^{1,2*}



LAIV

Live attenuated influenza vaccine, intranasal

Attenuated vaccine with multiple antigens^{3,4*}



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

*Image adapted from: Clinical Virology. 6th ed. 1997:911–942.⁴

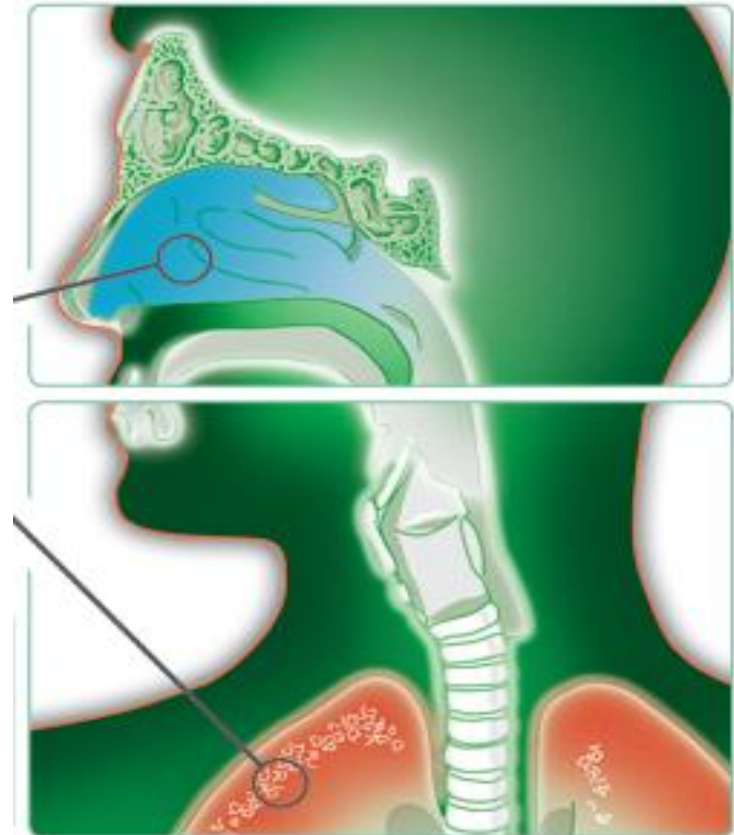
1. 1. Fluarix [Summary of Product Characteristics]. GlaxoSmithKline plc.
2. 2. Fluvirin [Summary of Product Characteristics]. Novartis Vaccines and Diagnostics Ltd.
3. 3. FLUENZ [Summary of Product Characteristics]. AstraZeneca Ltd.
4. 4. Hayden FG et al. Clinical Virology. 6th ed. 1997;911–942.

LAIV

Attenuated virus: disease-causing properties removed so as not to cause illness¹

Cold-adapted: replicates efficiently only in the cooler areas of the nasopharynx¹

Temperature-sensitive: does not replicate efficiently in warmer areas of the lower respiratory tract where influenza viruses typically replicate¹



JCVI choice of vaccine: LAIV¹



USA



Canada



Hong Kong



Israel



South Korea



UK



Germany



Nordics (SE, FI, DK)



France



Spain

2003–2010

2003

2012



1. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Friday 13 April 2012. Available at: <http://webarchive.nationalarchives.gov.uk/20130402145952/http://media.dh.gov.uk/network/261/files/2012/05/jcvi-minutes-13-april-2012-meeting.pdf> (last accessed 5 August 2015).

JCVI, Joint Committee on Vaccinations and Immunisations; LAIV, live attenuated influenza vaccine.

JCVI, April 2012 – children not previously vaccinated¹

- Not previously vaccinated (*naïve*) children under 9 years normally receive two doses of any flu vaccine:
 - Evidence of the effectiveness of a single dose of the LAIV in these children
 - Additional resources and increased complexity of implementation to provide two doses
- JCVI advised: one dose only to ‘*naïve*’ children under 9 years

Children aged 2–17 years in the ‘groups at risk’

- Consideration should be given to the preferential use of the LAIV in the current programme for children in most clinical risk groups (except severe asthma and some with immunosuppression)
 - in their case, naïve children received two doses, 1 month apart

1. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Friday 13 April 2012. Available at: <http://webarchive.nationalarchives.gov.uk/20130402145952/http://media.dh.gov.uk/net/work/261/files/2012/05/jcvi-minutes-13-april-2012-meeting.pdf> (last accessed 5 August 2015).

JCVI, Joint Committee on Vaccinations and Immunisations; LAIV, live attenuated influenza vaccine.

Influenza vaccination campaign: a stepwise approach to implementation

2013/14¹

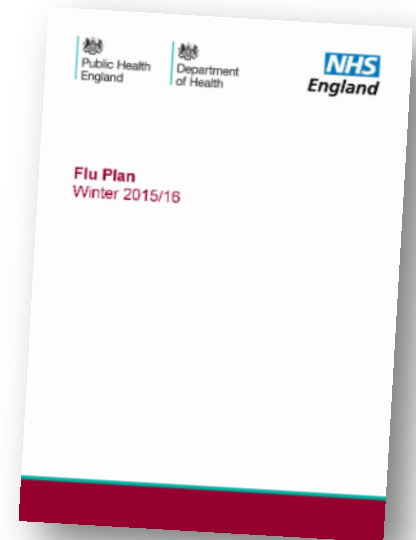
- GPs: all children aged **2 and 3 years**
- GPs: all children **from 6 months of age in 'at-risk groups'**
 - £7.60 (€11.00) per child vaccinated in the above groups
 - Vaccine supplied by the government
- **Pilots in primary schools**

2014/15¹

- As above but:
 - GPs: extended to all children aged **4 years**
 - **Pilots extended further to secondary schools**

2015/16²

- GPs: all children **aged 2–4 years**
- Local NHS to commission from local providers (including GPs) but predominantly school services: children **aged 5–6 years**



1. Public Health England. Correspondence. 15 July 2014. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/331045/2014-15_update_and_roll-out_schedule_letter.pdf (last accessed 5 August 2015).
2. Public Health England. Flu plan: Winter 2015 to 2016. March 2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/418038/Flu_Plan_Winter_2015_to_2016.pdf (last accessed 5 August).

Influenza vaccine uptake data

- **Vaccine uptake information** is reported by Public Health England for the following groups:
 - People aged 65 years and over
 - People aged under 65 years with specific clinical conditions
 - All pregnant women
 - All children aged 2, 3 and 4 years
 - Healthcare workers with direct patient contact
 - Carers
 - Children at school aged 5 and 6 years
- Uptake data collected via the web-based ImmForm system
- Over 90% of GP practices reporting weekly – electronically via *ImmForm*
<https://www.gov.uk/government/collections/immform>

Influenza vaccine uptake: 2013/14 and 2014/15

England	2-year-olds	3-year-olds	4-year-olds
2013/14 ¹	42.6%	39.6%	NR
2014/15 ²	38.5%	41.3%	32.9%

NR, not reported

Pilots	Setting	Age group	Uptake
2013/14 ³	Primary school	5–10 years	36–72%
2014/15 ⁴	Primary and secondary schools	5–13 years	53%

Modelling suggests that reaching levels of 30% vaccine coverage in children would start to produce substantial benefits⁵



1. Department of Health. The national flu immunisation programme 2014/15. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/316007/FluImmunisationLetter2014_accessible.pdf (last accessed 5 August).
2. Public Health England. The national flu immunisation programme 2015 to 2016: supporting letter. 27 March 2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/418428/Annual_flu_letter_24_03_15__FINALv3_para9.pdf (last accessed 5 August 2015).
3. Pebody RG, et al. *Euro Surveill* 2014;19:pii: 20823.
4. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Wednesday 3 June 2015. Available at: <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#minutes> (last accessed 5 August 2015).
5. Public Health England. Surveillance of influenza and other respiratory viruses in the United Kingdom: Winter 2013/14. June 2014. Available at: http://webarchive.nationalarchives.gov.uk/20140714084352/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317141339421 (last accessed 5 August 2015).

The school pilots¹

- Testing a variety of delivery methods
- Mostly in primary schools
- Some working through general practice and community pharmacists
- Determine the best approach to implement efficiently and sustainably the programme for school-aged children, without putting pressure on essential services²

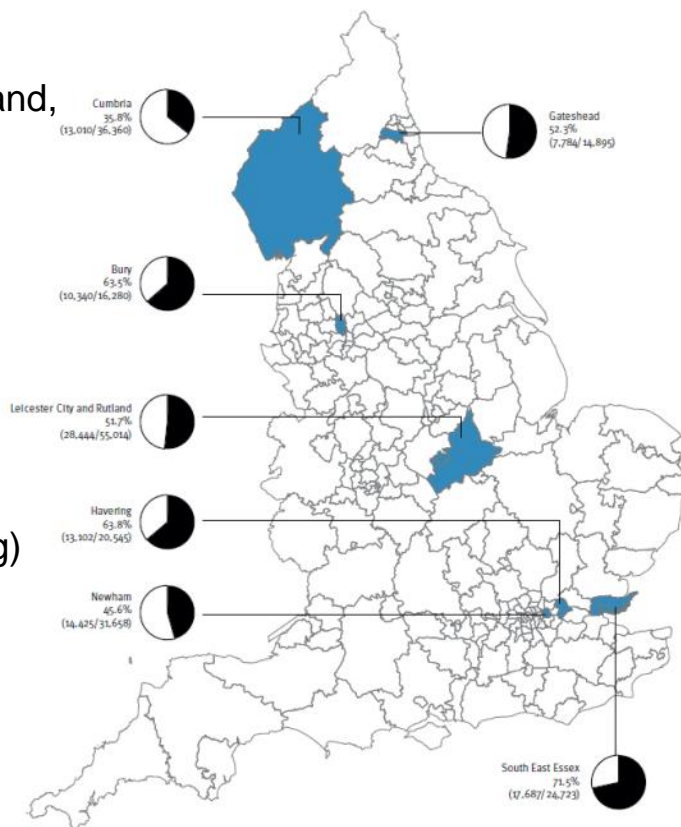


1. Public Health England. Flu plan: Winter 2015 to 2016. March 2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/418038/Flu_Plan_Winter_2015_to_2016.pdf (last accessed 5 August 2015).
2. Public Health England. Flu Vaccination in Pilot Areas 2014/15. Stakeholder briefing. August 2014. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/343878/Stakeholder_briefing_14-15_F.pdf (last accessed 5 August 2015).

England's geographical pilot regions^{1,2}

Primary school (age 5–10 years)

- Cumbria, Northumberland, Tyne and Wear
- Greater Manchester
- Essex
- Leicestershire and Lincolnshire
- Shropshire and Staffordshire
- London (Newham and Havering)



Secondary school (age 11–13 years)

- Greater Manchester
- Lancashire
- North Yorkshire and Humber
- Sheffield, Rotherham, Doncaster and Bassetlaw
- West Yorkshire
- Arden, Herefordshire and Worcestershire
- Birmingham, Solihull and The Black Country
- East Anglia and Essex
- Leicestershire and Lincolnshire
- Shropshire and Staffordshire
- London (Newham and Havering) (children aged 11 years only); all special schools across London

1. Public Health England. Press release. 28 July 2014. Available at: <http://www.gov.uk/government/news/child-flu-vaccine-pilots-announced-for-second-year> (last accessed 5 August 2015).

2. Department of Health. The national flu immunisation programme 2014/15. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/316007/FluImmunisationLetter2014_accessible.pdf (last accessed 25 August 2015).

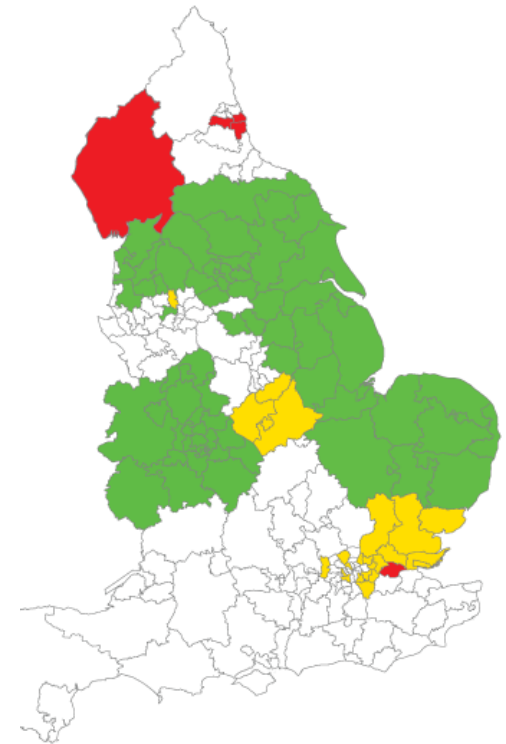
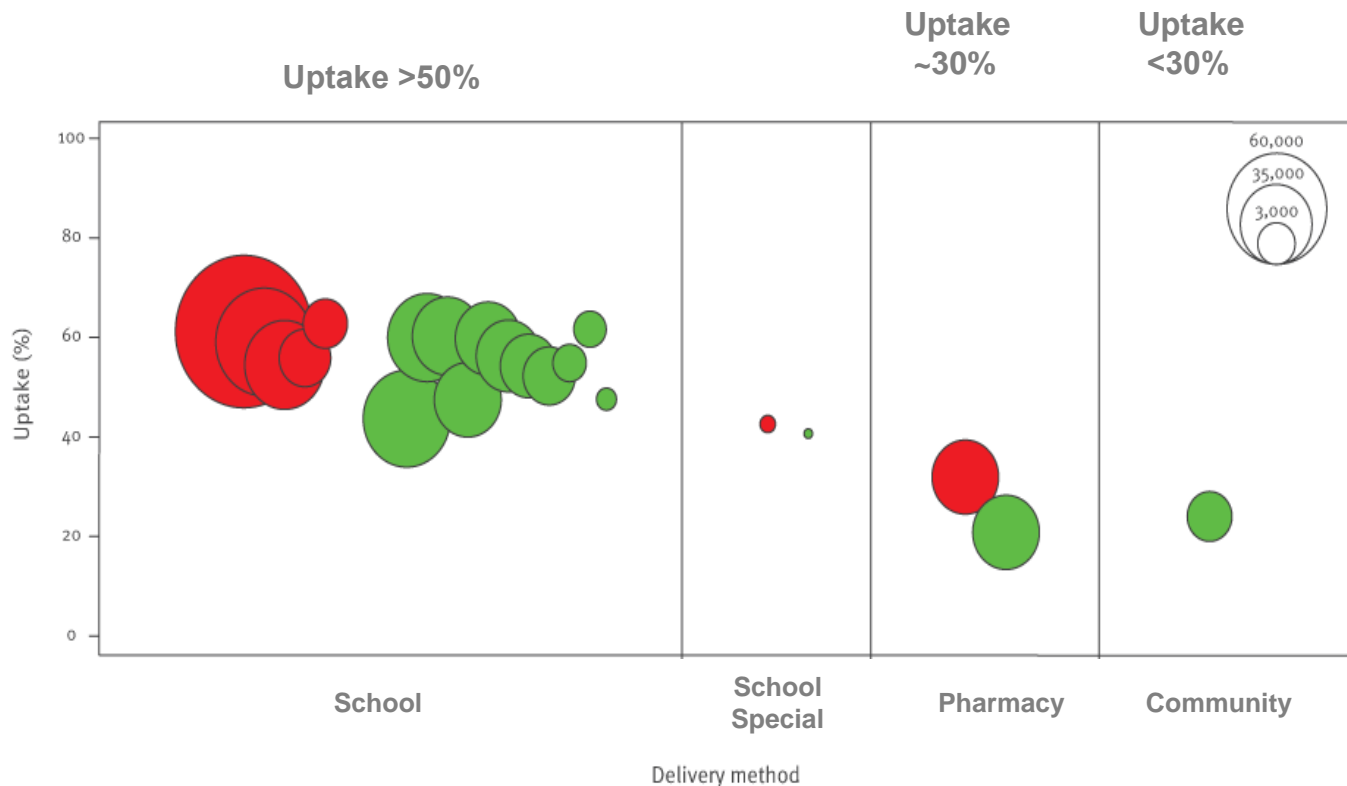
England regional school pilots (age 5–10 years)¹

Site	Cohort	Vaccinated	% uptake	Model	Provider
Bury	16,280	10,340	63.5	School-based	Private
Cumbria	36,360	13,010	35.8	Community	Pharmacy/GP
Gateshead	14,895	7,784	52.3	School-based	School nursing service
Havering	20,545	13,102	63.8	School-based	Trust immunisation team
Leicester	55,014	28,444	51.7	School-based	Trust immunisation team
Newham	31,658	14,425	45.6	School-based	Trust immunisation team
SE Essex*	24,723	17,687	71.5	School-based	Trust immunisation team
Total	199,475	104,792	52.5		

*SE Essex additionally piloted self-administration by 10-year-old pupils and vaccination by healthcare support workers.



England's geographical pilot regions: average coverage rates in 2014–2015^{1–3}



- Primary school pilot (age 5–11 years)
- Secondary school pilot (age 11–13 years)
- Primary and secondary school pilot

¹Public Health England. Press release. 28 July 2014. ²Department of Health. The national flu immunisation programme 2014/15.

³Pebody RG, et al, *Euro Surveill*, 2015; 20(39):pii=30029. *full weblinks in notes

Experience from the pilots in primary schools (age 5–10 years)

2 administrators plus 2 nurses per 100 children

1 additional nurse for every additional 100 children

Significant administrative burden

Utilise staff in existing posts

Temporary staff contracts problematic

Self-administration by children aged 10 years:

- Well received by pupils (65% self-administered)

- More time-consuming than nurse administration

80% of vaccines given in the community and not by GPs:

- Given by pharmacies instead

- Contracting with multiple pharmacy providers is time-consuming

- Vaccine distribution to multiple providers introduces potential for increased wastage

Impact data England

Number of children in the Pilots 2014/2015

Primary schools: 197,000

- All offered the vaccine (5-10 y)
- Flu virus bigger spreaders

Secondary schools: 185,000

- Offered only to 11-13 y (two cohorts)
- Flu virus moderate spreaders



Impact of the 2014/15 school pilots

Number of influenza cases in non-pilot areas vs pilot areas¹

School	Influenza swab-negative	Influenza B cases	Influenza A(H1N1) cases	Influenza A(H3N2) cases
	n (%)	n (%)	n (%)	n (%)
Non-pilot	725 (65.8)	91 (8.3)	28 (2.5)	253 (22.9)
Pilot	1,272 (71.1)	91 (5.1)	32 (1.8)	368 (20.6)
Missing information	32	2	0	8

- Significantly lower influenza positivity in areas where school-aged children were vaccinated compared with non-pilot areas ($p=0.002$)

JCVI, August 2015²

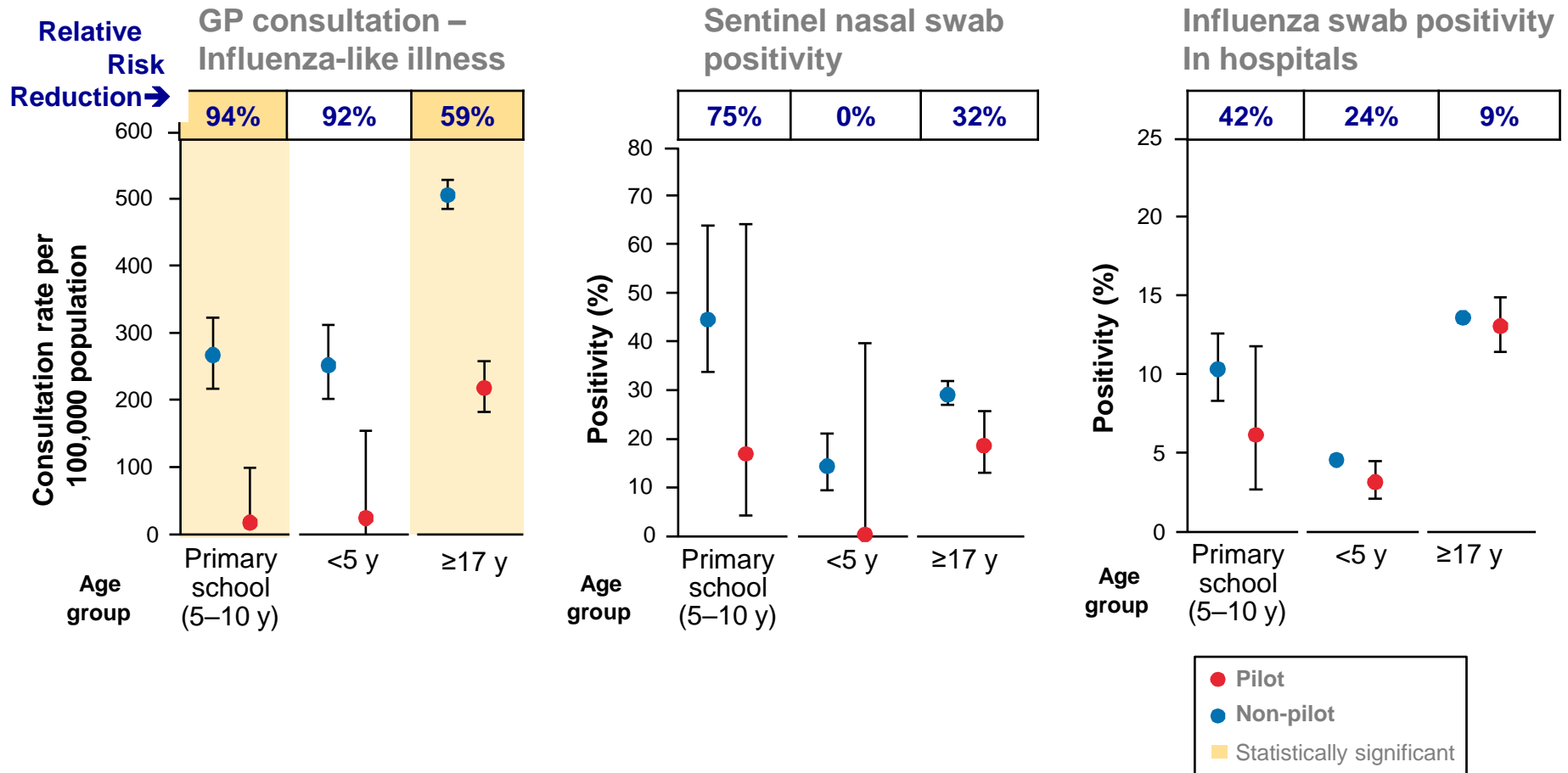
- *The Committee was encouraged by the evidence emerging from the UK childhood influenza programmes, which indicated that **LAIV appeared to offer protection with some herd protection in primary school pilots in England**, despite moderate levels of uptake*

JCVI, Joint Committee on Vaccinations and Immunisations; LAIV, live attenuated influenza vaccine.

1. Pebody RG, et al. *Euro Surveill* 2015;20:pii:30013.
2. Joint Committee on Vaccination and Immunisation. Minutes of the meeting held on Wednesday 3 June 2015. Available at: <https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#minutes> (last accessed 5 August 2015).

Impact of the programme – season 2014-2015

Reduction in surveillance indicators in primary school pilot areas compared with non-pilot areas



ILI, influenza-like illness; GP, general practitioner

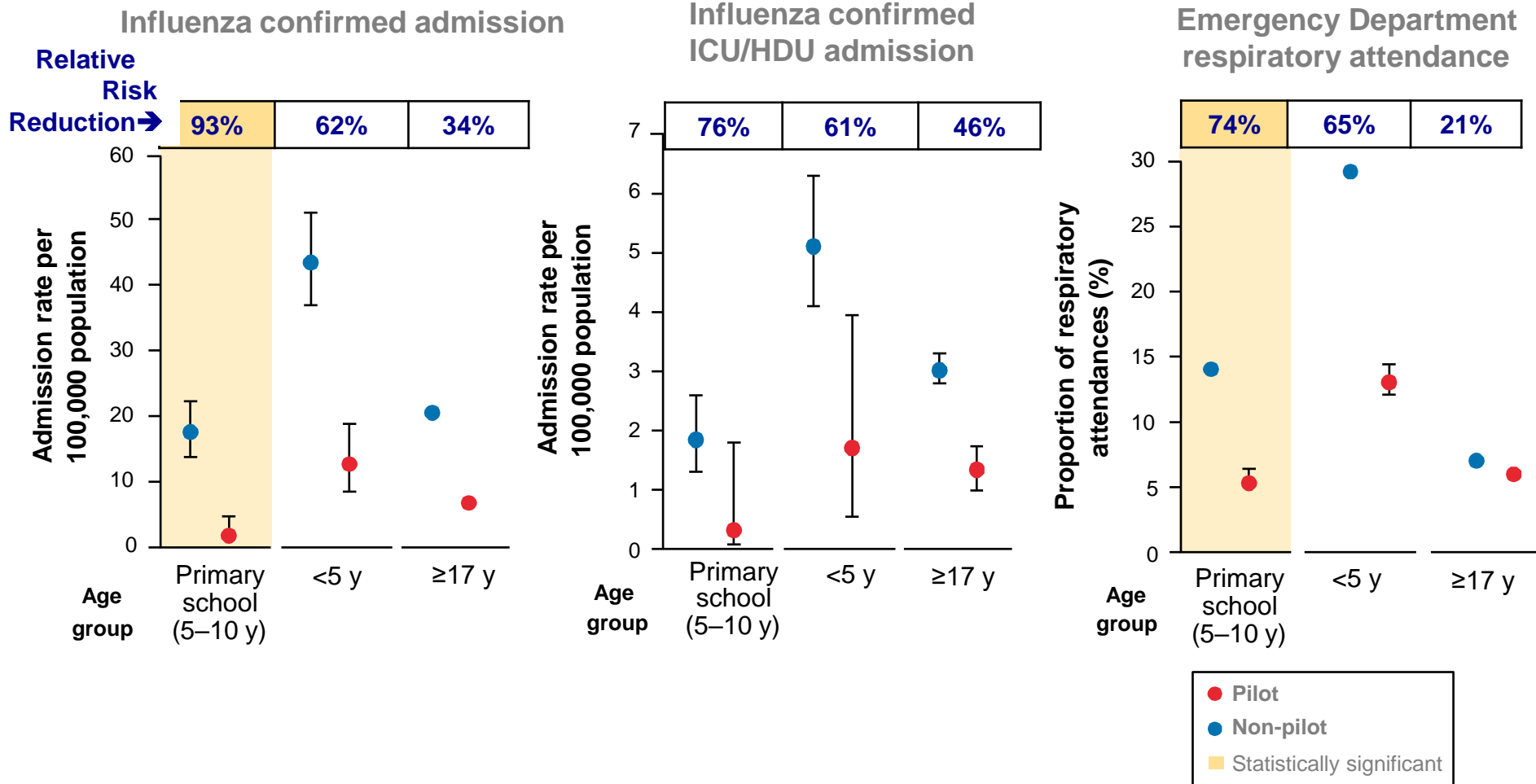
Pebody RG, et al. *Euro Surveill.* 2015; 20(39):pii=30029.

≥17 y → age 17 and over (includes the over 65s)

– does not differentiate between <65 & >65 years

Impact of the programme – season 2014-2015

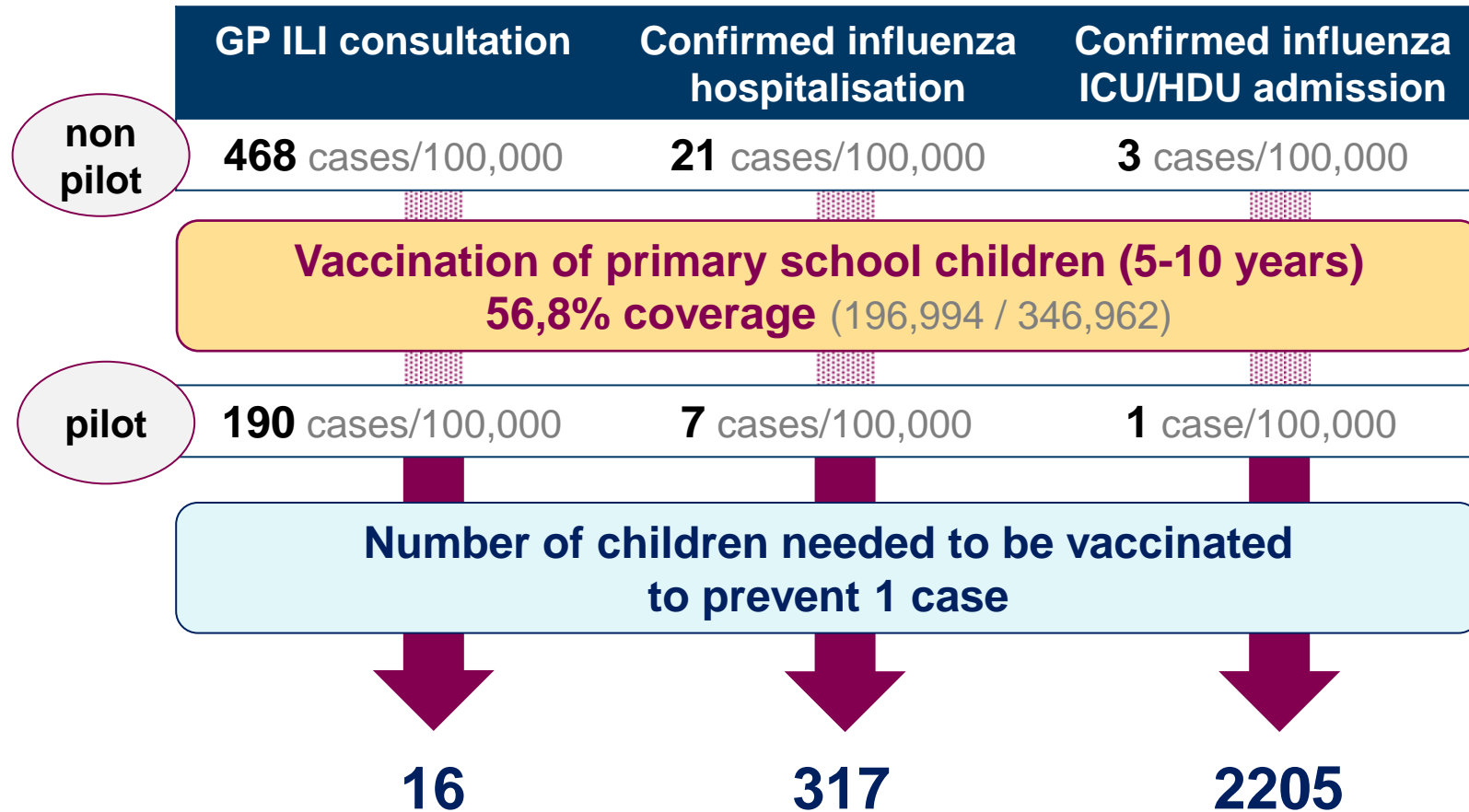
Reduction in surveillance indicators in primary school pilot areas compared with non-pilot areas



ED, emergency department; ILI, influenza-like illness; GP, general practitioner;
USISS, UK Severe Influenza Sentinel Surveillance System
Pebody RG, et al. *Euro Surveill.* 2015; 20(39):pii=30029.

≥17 y → age 17 and over (includes the over 65s)
– does not differentiate between <65 & >65 years

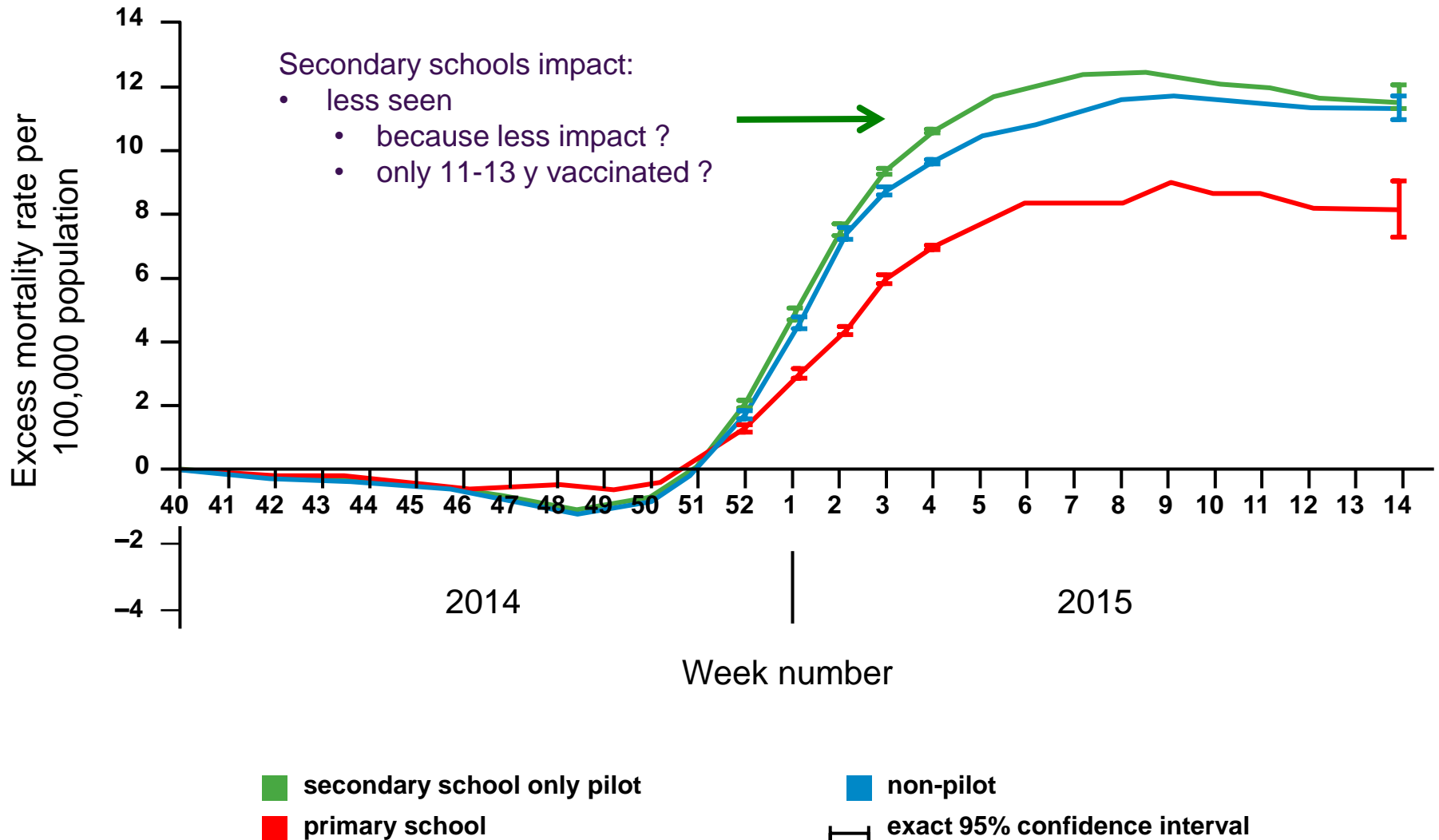
Number of primary school age children needed to be vaccinated to prevent selected surveillance indicators in the pilot population



GP, general practitioner, ILI, influenza-like illness, ICU, intensive care unit, HDU, high dependency unit

Pebody RG, et al, *Euro Surveill*, 2015; 20(39):pii=30029.

Significant reduction in respiratory excess mortality in primary school pilot areas (2014-2015 season)



2014-2015 season

- Uptake levels were similar or higher compared with the previous season
- Significant reduction in incidence for a range of surveillance indicators, both in children and adults, in pilot areas vaccinating primary school age children (**aged 5-10 years**) compared to non-pilot areas:
 - GP ILI consultations (94%↓, $p=0.018$), Emergency Department Respiratory attendances (74%↓, $p=0.035$), Confirmed Influenza hospital admissions (93%↓, $p=0.012$)
- Indirect impact in **children <5 years** was over and above any direct impact expected by vaccinating these children across the whole England, in pilot areas where primary school children were vaccinated with LAIV
 - Consistent with 2013–2014 findings and support the on-going roll out of the national LAIV programme for children of primary school age
- Vaccinating secondary school age children needs further consideration – perhaps extension to all cohorts

Lower effectiveness of the 2014–2015 influenza vaccine¹

UK end-of-season results (September 2015)

- Overall adjusted VE against **all strains: 34.3%** (95% CI 17.8–47.5)
 - VE against A(H3N2) strain: **29.3%** (95% CI: 8.6–45.3)
 - VE against B strain: **46.3%** (95% CI: 13.9–66.5)
- For those aged under 18 years receiving **QLAIV**
 - VE against A(H3N2) strain: **35.0%** (95% CI: –29.9–67.5)
 - VE against B strain: **100%** (95% CI: 17.0–100.0)

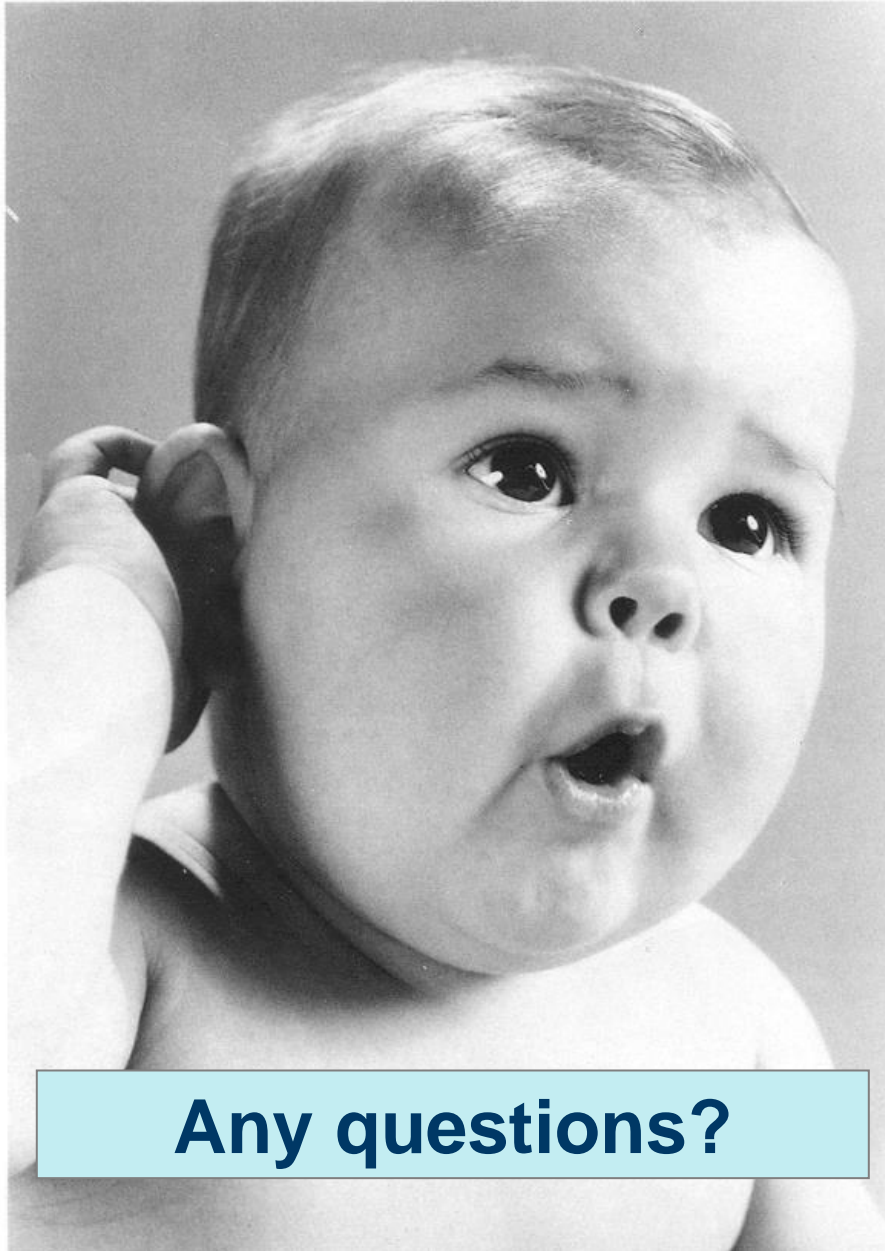
“Although the VE against influenza A(H3N2) infection was low, there was still evidence of significant protection, together with moderate, significant protection against *drifted* circulating influenza B viruses.

LAIV provided non-significant positive protection against influenza A, with significant protection against B.”

CI, confidence interval; LAIV, live attenuated influenza vaccine; QLAIV, quadrivalent live attenuated influenza vaccine; VE, vaccine effectiveness.

Summary

- Children are recognised as playing a key role in the transmission of influenza virus
 - Targeting children with influenza vaccine reduces the number of cases in children directly and offers herd protection to others
- LAIV chosen by the UK JCVI for children as a more effective vaccine than the inactivated influenza vaccines
- The programme has had a significant impact by reducing GP consultations, emergency room visits, and hospitalisations
- Over the coming years, the programme will be extended to children of older age groups



Any questions?

Back-up slides if specifically asked about contraindications, asthma, shedding and transmission, Egg allergy or porcine gelatine for the influenza program vaccine.



Contraindications and precautions^{1,2}



- Age less than 2 years and 18 years & over
- Pregnancy & Lactation
- Hypersensitivity to the active substances, to any of the excipients, to gentamicin, to eggs or to egg proteins, or previous dose of this vaccine
- Children and adolescents who are clinically immunodeficient due to conditions or immunosuppressive therapy. Examples: acute & chronic leukaemias; lymphoma; HIV infection not receiving stable antiretroviral therapy (*OK if they do – consult treating Physician*); cellular immune deficiencies; high doses of corticosteroids [prednisolone (or its equivalent) , orally or rectally, at a daily dose of 2mg/kg/day for at least one week, or 1mg/kg/day for one month] [DoH²: Prednisolone ≥ 20 mg per day or children < 20 kg $\Rightarrow \geq 1$ mg/Kg body weight, taken for ≥ 1 month]
Not contraindicated if: receiving topical steroids, low dose systemic steroids, or as a replacement therapy, e.g. for adrenal insufficiency
- Receiving salicylate therapy (aspirin) – association with Reye's syndrome with salicylates & wild-type influenza infection
- Within 48h following cessation of use of influenza antiviral agents
- LAIV effectiveness may be \downarrow if influenza antiviral agents used within 2/52

1. Fluenz Tetra SmPC.section 4.3 and 4.4.

2. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/306646/FluImmunisationLetter2014_accessible.pdf

Severe asthma, recommendations UK influenza vaccination program



• *Influenza: The Green Book:*

QLAIV is not recommended for children with:

- who are currently taking or have been prescribed oral steroids in the last 14 days
- who are currently taking a high dose inhaled steroid – Budesonide >800 mcg/day or equivalent* (e.g. Fluticasone >500 mcgs/day)
 - ➔ other than on the advice of a specialist

Defer vaccination if:

- Active wheezing at the time of vaccination or previous 72 h (until at least 72 hours after wheezing has stopped)
- Increased use of bronchodilators in the previous 72 h
 - ➔ use TIV if still a problem after waiting for 72h

Shedding and transmission

- QLAIV: potential for transmission
- 1 to 2 weeks following vaccination
(vaccine virus recovery 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)
should receive an inactivated influenza vaccine



Egg Allergy - JCVI 4 February 2015

- QLAIV Ovalbumin content: ≤ 0.12 mcgs/ml
- QLAIV can be safely administered to children with an egg allergy

EXCEPT:

- past severe anaphylaxis to egg requiring intensive care (refer to a Specialist)

Egg allergy

The SNIFFLE study¹

- Prospective, multicentre, open-label, phase IV intervention study involving 11 secondary/tertiary centres in the UK
- LAIV administered to 282 children with egg allergy*
 - 67% had a diagnosis of asthma/recurrent wheezing

Key findings

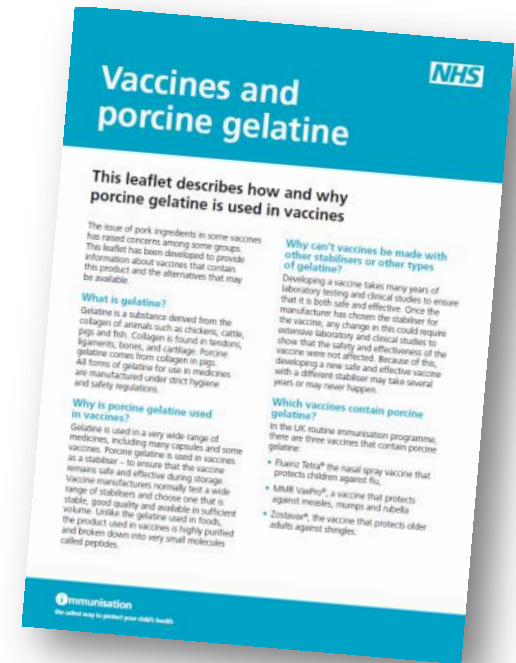
- No systemic allergic reactions (upper 95% CI for population, 1.3%).
- Mild self-limiting symptoms, which might have been due an IgE-mediated allergic reaction, were reported by 8 (0.3%) children
- LAIV appears to be safe for use in children with egg allergy
- LAIV was well tolerated in children with a diagnosis of asthma or recurrent wheeze

*Defined as positive food challenge result to egg within the last 12 months performed under medical supervision.

Concerns about porcine gelatine¹

“With all this concern about porcine gelatine in the nasal flu vaccine, does it actually contain any DNA from pigs?”²

- No, as shown by very sensitive scientific tests
- The gelatine is so degraded that the original source cannot be identified
- Broad acceptance from faith groups for the use of porcine gelatine in non-oral medicines^{3–7}
 - There is still some uncertainty amongst some groups
 - Vaccine not compulsory – cannot request an alternative vaccine (except at-risk groups)



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