

Paediatric Influenza Vaccination: individual protection and herd immunity

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Outline

- The burden of influenza in children
- Influenza vaccine efficacy in children
 - Trivalent inactivated vaccine (TIV)
 - Live-attenuated influenza vaccine (LAIV)
- Herd immunity

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THE EFFECT OF INFLUENZA ON HOSPITALIZATIONS, OUTPATIENT VISITS, AND COURSES OF ANTIBIOTICS IN CHILDREN

- Retrospective cohort study
- Children <15 years of age in Tennessee
- 19 years of observation
- 2,035,143 person years observation

Neuzil et al NEJM 2000;342:225

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AGE	NO. OF PERSON- YEARS	NO. OF HOSPITALIZATIONS FOR ACUTE CARDIOPULMONARY CONDITIONS PER 10,000 PERSON-YEARS		NO. OF INFLUENZA- ATTRIBUTABLE HOSPITALIZATIONS PER 10,000 PERSON-YEARS*	
		INFLUENZA SEASON	PERI-INFLUENZA SEASON	CRUDE	STANDARDIZED†
<6 mo	68,959	1779	1207	572	538
6 to <12 mo	48,651	1023	730	293	227
1 to <3 yr	197,334	441	336	105	101
3 to <5 yr	184,860	247	194	53	55
5 to <15 yr	759,063	127	112	15	25

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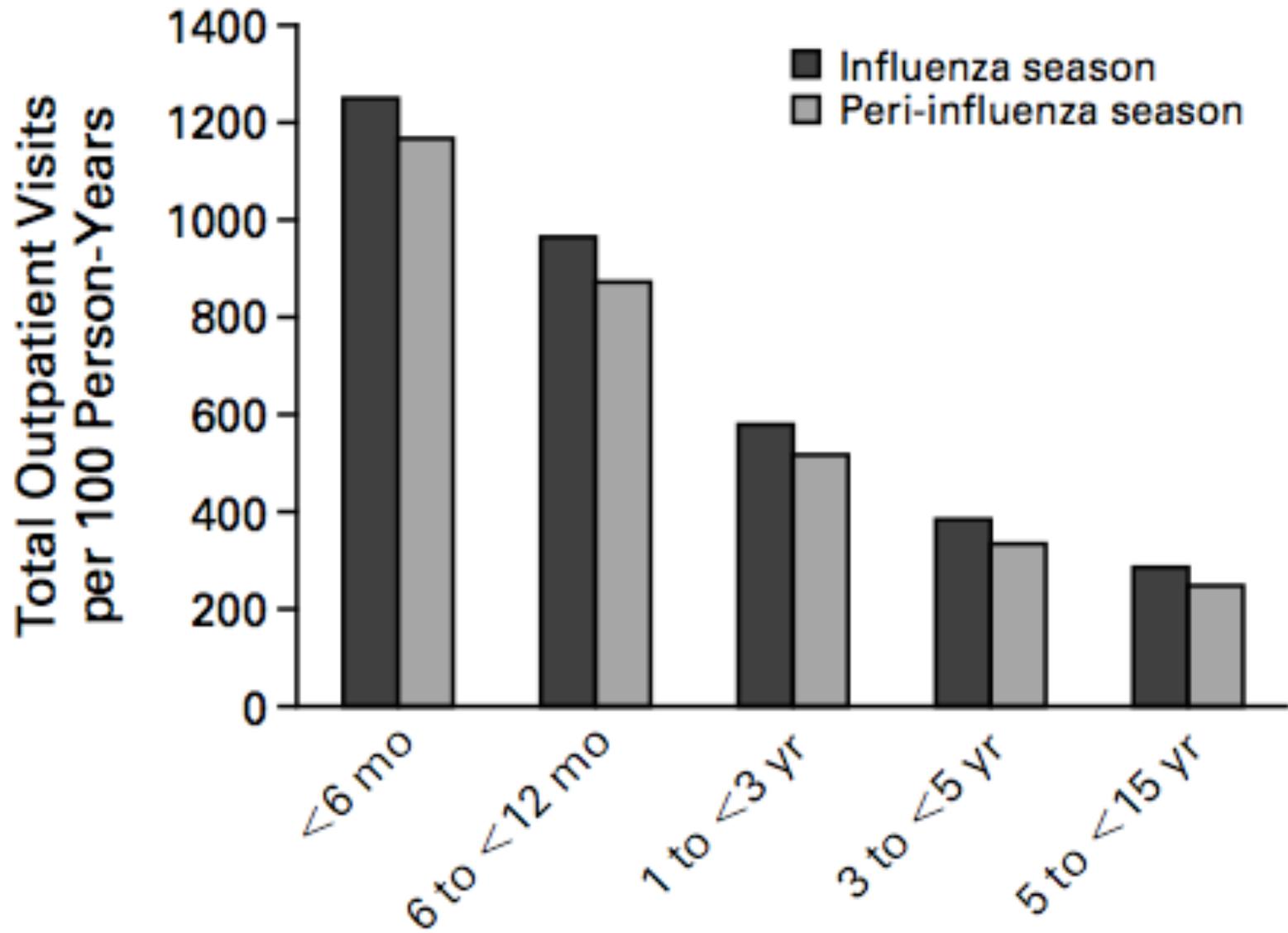
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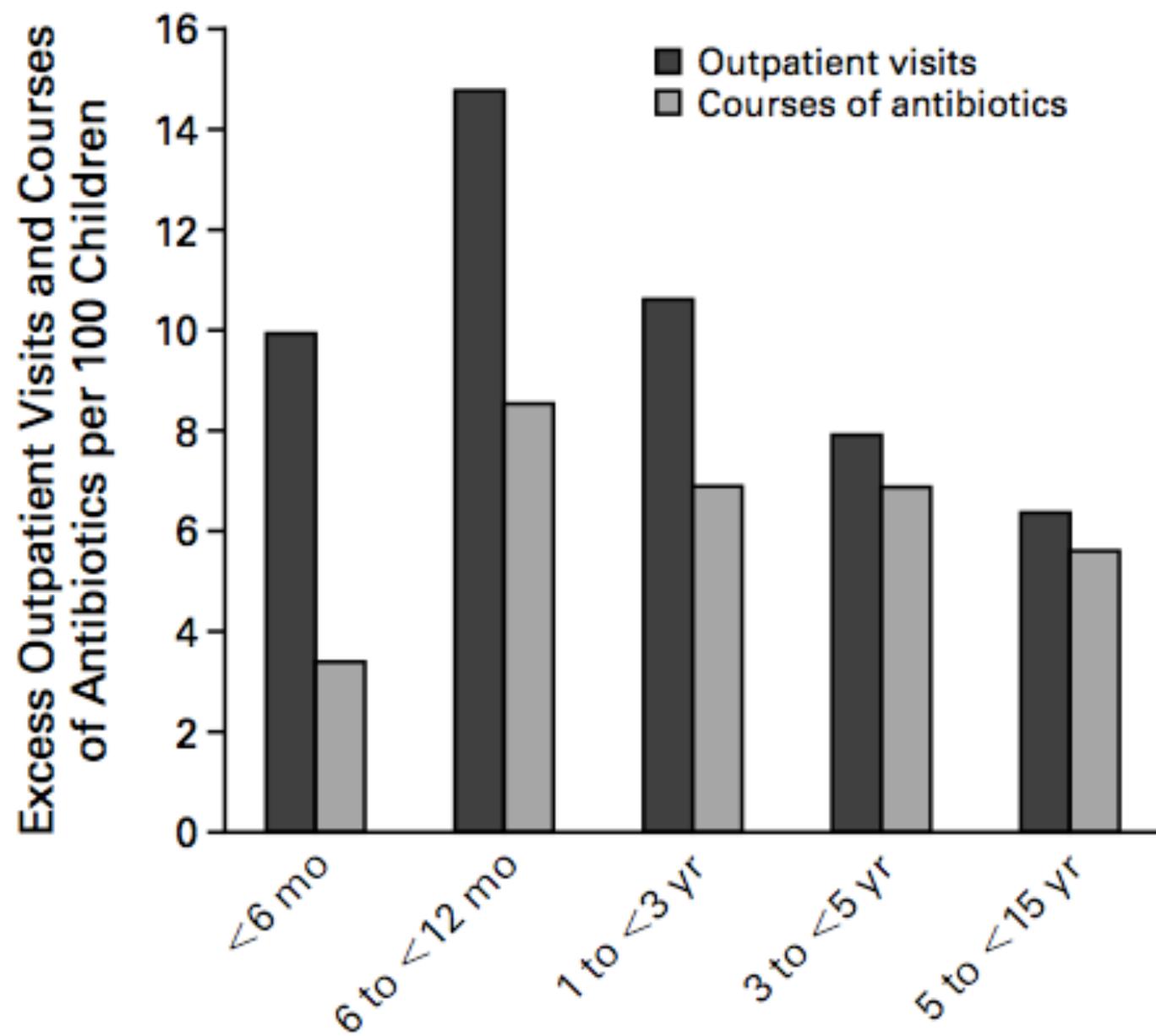
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Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS)

- Funding from US Centers for Disease Control (5 years)
- Led by the Institute for Environmental Science and Research, Principle Investigator Dr. Sue Huang



- Collaborating organisations:



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THE SHIVERS PROJECT

SOUTHERN HEMISPHERE INFLUENZA AND VACCINE EFFECTIVENESS RESEARCH & SURVEILLANCE

Southern Hemisphere Influenza and Vaccine Effectiveness Research and Surveillance (SHIVERS)

Dr. Sue Huang

Principal investigator of the SHIVERS project

Director, WHO National Influenza Centre

**Institute of Environmental Science and Research,
Wellington, New Zealand**

SOUTHERN HEMISPHERE INFLUENZA AND VACCINE EFFECTIVENESS RESEARCH & SURVEILLANCE

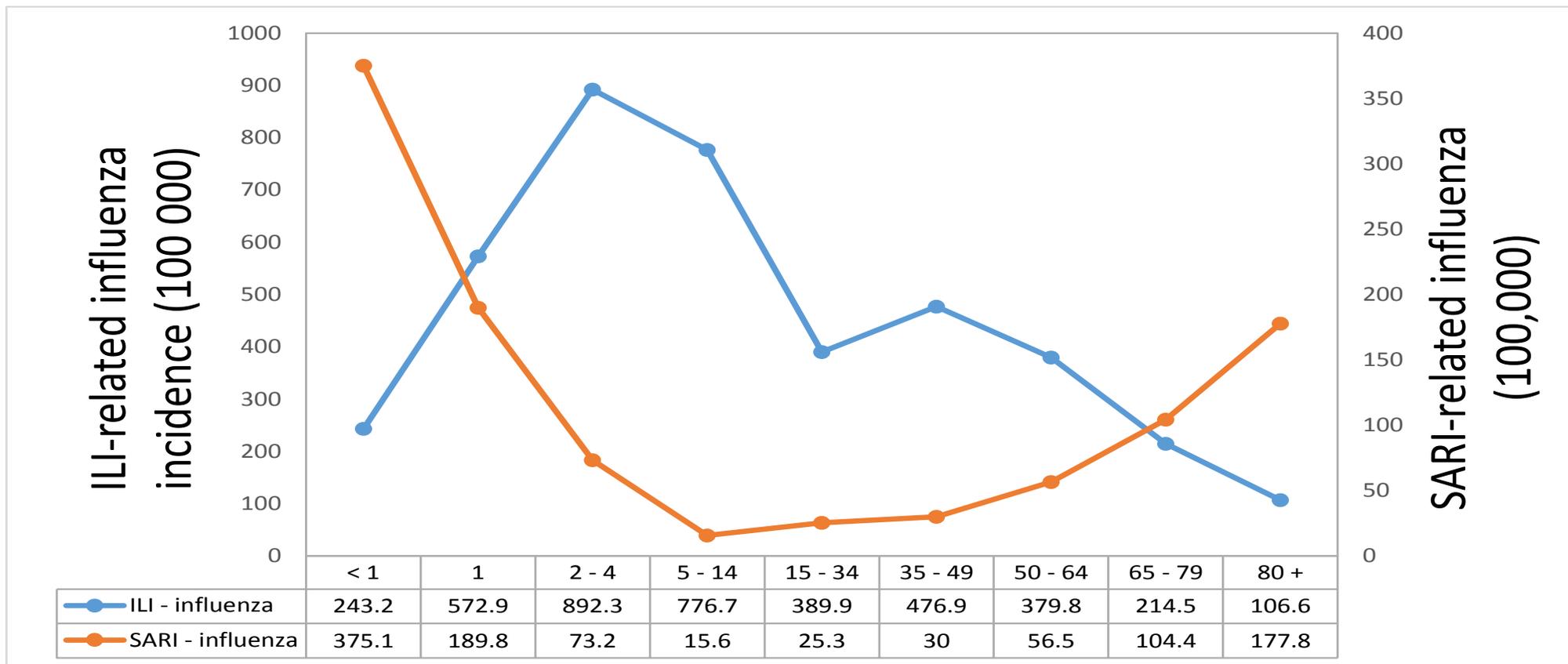




- Influenza surveillance in New Zealand
 - PCR confirmation of all cases
- Prospective study children and adults
- Hospital based
 - Severe Acute Respiratory Illness (SARI)
- Community based
 - Influenza-like illness (ILI)

THE SHIVERS PROJECT

SOUTHERN HEMISPHERE INFLUENZA AND VACCINE EFFECTIVENESS RESEARCH & SURVEILLANCE



Vaccine efficacy in children



Maternal immunisation

- The benefits for the mother
 - Norway study showed 70% reduction in flu-like illness in immunised mothers
- The benefits for the infant
 - May be associated with increased birth weight
 - Lower rates of low birth weight
 - 3rd trimester vaccination reduces hospitalisation with influenza by 90% up to 6 months of age

Is annual influenza vaccination effective in children?



CDC's Advisory Committee on Immunization Practices (ACIP) Recommends Universal Annual Influenza Vaccination

A panel of immunization experts voted today (February 24, 2010) to expand the recommendation for annual influenza vaccination to include all people aged 6 months and older.....

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[JCVI statement on the annual influenza vaccination programme – extension of the programme to children](#)

...despite the high cost, extending the influenza vaccination programme to low risk children is highly likely to be cost effective.... 25 July 2012



Trivalent
inactivated
vaccine
(TIV)

Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis

Michael T Osterholm, Nicholas S Kelley, Alfred Sommer, Edward A Belongia

	Number of trials
Trivalent inactivated vaccine	
6–23 months	1
2–17 years	0
18–64 years	6
≥65 years	0

Table 1: Number of RCTs showing significant vaccine efficacy

Effectiveness of Inactivated Influenza Vaccine in Preventing Acute Otitis Media in Young Children

A Randomized Controlled Trial

- Healthy children aged 6-24 months
- Two doses (0.25mls) TIV
- 1999-2000 - VE 66% (CI 34 to 82%)
- 2000-2001 - VE -7% (CI -247 to 67%)

Protective Efficacy Against Pandemic Influenza of Seasonal Influenza Vaccination in Children in Hong Kong: A Randomized Controlled Trial

Benjamin J. Cowling,¹ Sophia Ng,¹ Edward S. K. Ma,² Vicky J. Fang,¹ Hau Chi So,¹ Winnie Wai,¹ Calvin K. Y. Cheng,¹ Jessica Y. Wong,¹ Kwok-Hung Chan,³ Dennis K. M. Ip,¹ Susan S. Chiu,⁴ J. S. Malik Peiris,^{1,2,a} and Gabriel M. Leung^{1,a}

¹School of Public Health, ²Centre for Influenza Research, and Departments of ³Microbiology, and ⁴Pediatrics and Adolescent Medicine, Li Ka Shing Faculty of Medicine, University of Hong Kong, Pokfulam, China

(See the Editorial Commentary by Monto and Ohmit, on pages 703–5.)

- 2009-10 school-aged children
- Vaccine efficacy TIV 66% (CI 31-83%) against Influenza B
- No effect against seasonal influenza A (H3N2)
- 47% efficacy(CI 15-67%) against pandemic Influenza A(H1N1)

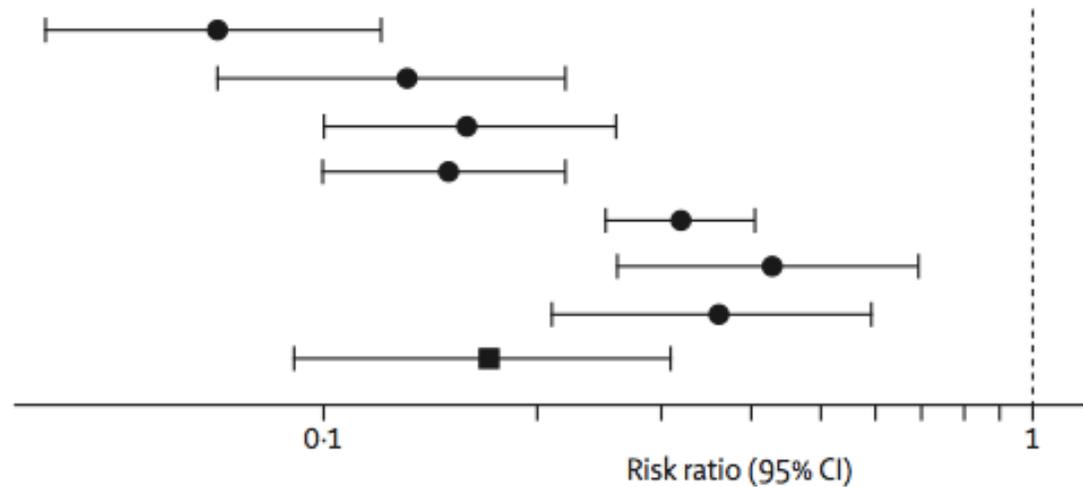
Live-attenuated influenza vaccine

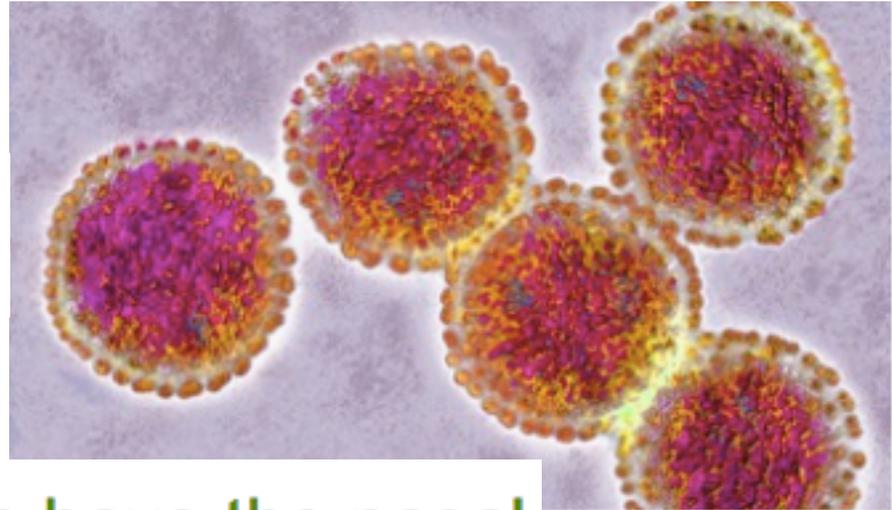


Efficacy of LAIV in children

B

Belshe (1998) ³²	14/1070	94/532
Belshe (2000) ³³	15/917	56/441
Vesikari (2006) ³⁴	23/1059	97/725
Vesikari (2006) ³⁴	31/658	148/461
Tam (2007) ³⁵	98/1900	204/1274
Tam (2007) ³⁵	26/503	59/494
Lum (2010) ³⁶	28/819	39/413
Pooled	235/6926	697/4340





At what age should children have the nasal spray flu vaccine?

In the autumn/winter of 2016-17, the vaccine will be available free on the NHS for eligible children, including:

- children aged two, three and four on August 31 2016 – that is, children born between September 1 2011 and August 31 2014
- children in school years one, two and three
- in some parts of the country, all primary school-aged children will be offered the vaccine as part of a test programme
- children aged 2 to 17 with long-term health conditions

July 2016

Business

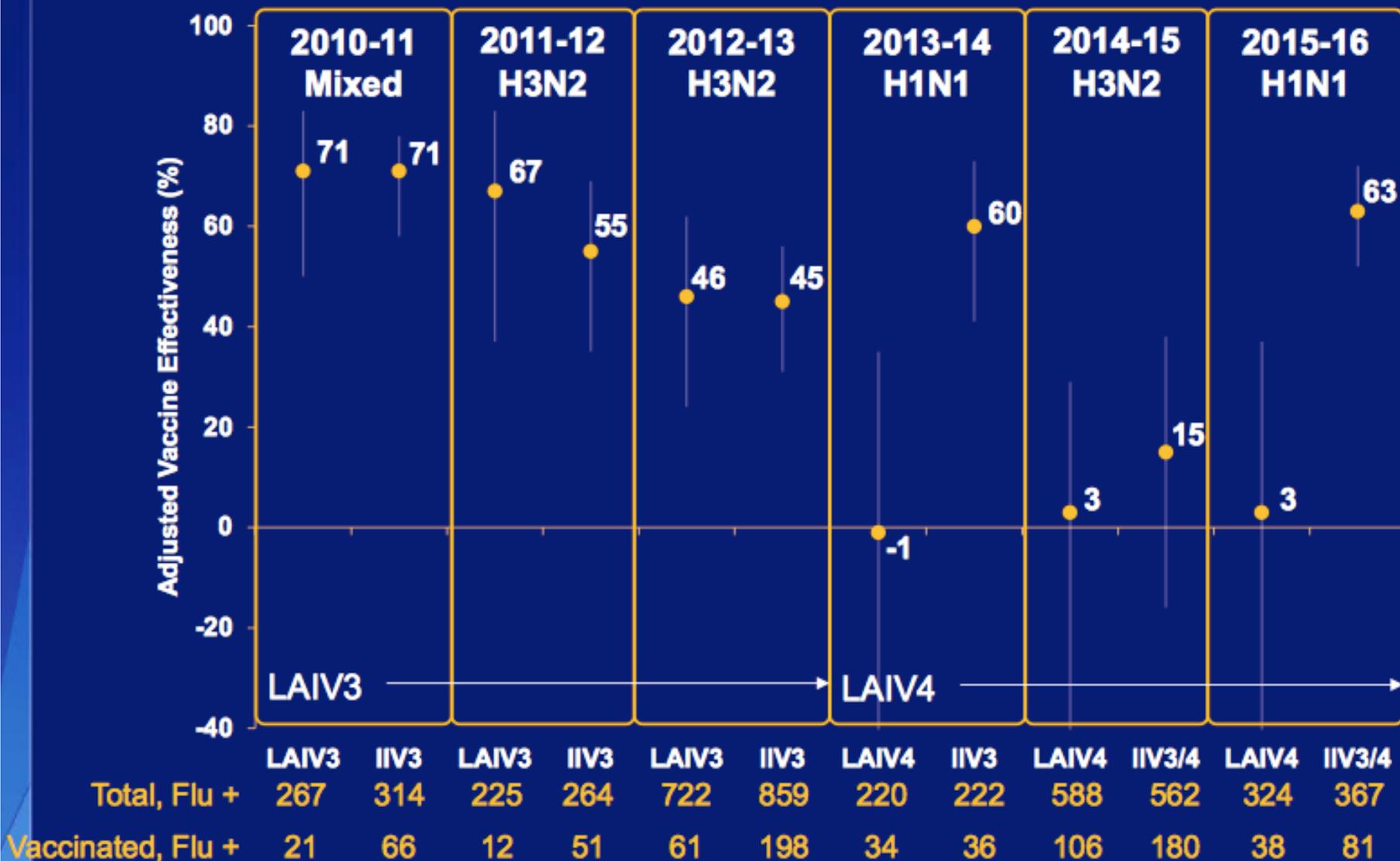
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AstraZeneca's nasal spray flu vaccine knocked by US health officials for having 'no protective benefit'

23 June 2016

US Flu VE Network: LAIV and IIV VE age 2-17 yrs Any Influenza A or B



2015-16 Season: Data from Other Countries

□ UK test-negative VE study

- Significant adjusted VE for LAIV against any influenza A or B among children aged 2-17 years (58% [25, 76])

□ National cohort study from Finland

- Significant unadjusted VE against flu A (mainly H1N1pdm09) for LAIV in 2-year old children (47% [20, 65]); higher point estimates for IIV (78% [46, 91])



Effectiveness of Influenza Vaccination of Day Care Children in Reducing Influenza-Related Morbidity Among Household Contacts

Eugene S. Hurwitz, MD

Michael Haber, PhD

Albert Chang, MD

Timothy Shope, MD

Siew Teo, MS

Context A growing proportion of young children in the United States participate in day care, and these children are considered to be at high risk for influenza infection. Whether vaccinating day care children reduces household transmission of influenza is not known.

Objective To evaluate the effect of vaccinating day care children on reducing influenza-related morbidity among their household contacts.

- RCT in US Navy daycare centres
- Outcomes – parent reports of respiratory illness
- Vaccine effectiveness in unvaccinated:
 - 50% for any respiratory illness (p=0.007)
 - 80% for respiratory illness with fever (p=0.01)
 - 80% with temp >38°C (p=0.01)

JAMA 2000;248:1677

Household contacts

Table 4. Respiratory-Related Morbidity Among Unvaccinated 5- to 17-Year-Old Household Contacts of Study Children*

Event	Control Children Contacts, No. (Attack Rate)† (n = 31)	Vaccinated Children Contacts, No. (Attack Rate)† (n = 28)	Vaccine Effectiveness, %‡	P Value
Missed school	12 (0.39)	3 (0.11)	72	.02
Adult missed work	7 (0.23)	0 (0.00)	100	.04
Physician visits	12 (0.39)	1 (0.04)	91	.007
Earache	9 (0.29)	1 (0.04)	88	.02
Antibiotics prescribed	9 (0.29)	1 (0.04)	88	.02
Over-the-counter medications used	18 (0.58)	9 (0.32)	45	.03

*Morbidity was measured for the respiratory illness with the highest reported temperature. Household contacts did not receive influenza vaccine.

†Attack rate equals rate of illness divided by total population.

‡Vaccine effectiveness equals 1 minus attack rate among household contacts of vaccinated children divided by attack rate among household contacts of unvaccinated children.

Effect of Influenza Vaccination of Children on Infection Rates in Hutterite Communities

A Randomized Trial

Mark Loeb, MD, MSc

Margaret L. Russell, MD, PhD

Lorraine Moss, BSc

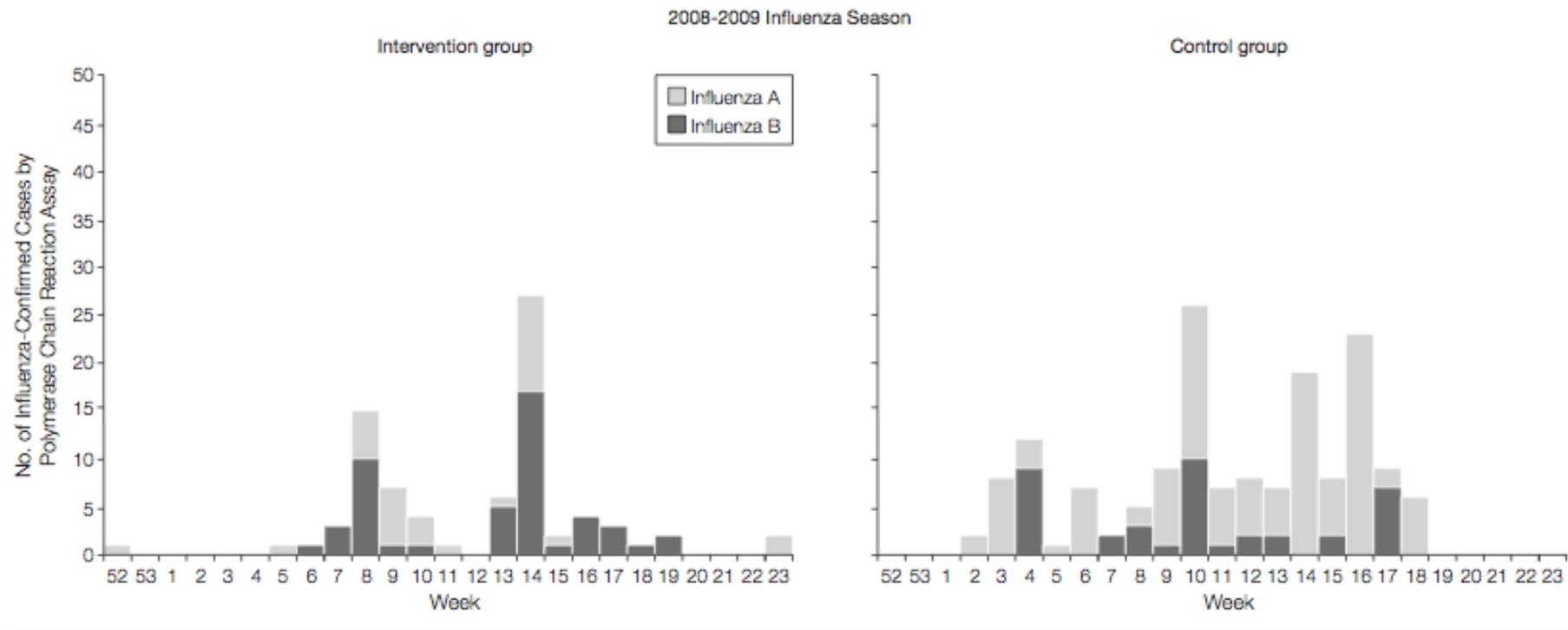
Kevin Fonseca, PhD

Context Children and adolescents appear to play an important role in the transmission of influenza. Selectively vaccinating youngsters against influenza may interrupt virus transmission and protect those not immunized.

Objective To assess whether vaccinating children and adolescents with inactivated influenza vaccine could prevent influenza in other community members.

- Blinded, cluster randomised trial
- Children aged 36 months to 15 years vaccinated with TIV or placebo
- Influenza A and B confirmed with PCR

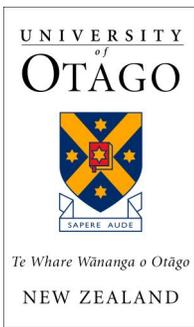
Figure 2. Epidemic Curve of Influenza A and B in Enrolled Colonies



Protective effectiveness

Table 2. Protective Effectiveness on Nonrecipients of Immunizing Children and Adolescents With Influenza Vaccine

Study Group	Nonrecipients in Vaccine Colony		Protective Effectiveness of Influenza Vaccine (95% CI), %	P Value
	Influenza (n = 1271)	Hepatitis (n = 1055)		
Influenza detected by PCR, No. (%)	39 (3.1)	80 (7.6)		
Person-day of follow-up, No. (%)	182 866	151 902		
No. of cases/10 000 person-days	2.13	5.27	Simple, 61 (8-83) ^a	.03
			Adjusted, 61 (8-83) ^b	.03



Summary



- Highest incidence rates of influenza disease
 - Infants and young children
- Influenza vaccine efficacy
 - Moderately efficacious vaccine in children
- Vaccinating young children will reduce the rates of disease in unvaccinated contacts
 - Likely need high rates of coverage

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