VACUNA GRIPE INTRANASAL

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Pediatría. Hospital Materno-Infantil, Málaga

CONFLICTOS DE INTERESES POTENCIALES:

- He recibido honorarios por actividades docentes subvencionadas por: GlaxoSmithKline, Novartis, Sanofi y Pfizer

- He colaborado como consultor en Advisory Boards de: AstraZeneca, Novartis y Pfizer

- He trabajado como investigador en ensayos clínicos de: GlaxoSmithKline y Novartis

VACUNACION GRIPE INTRANASAL

1. Introducción
2. ¿Qué es LAIV?
3. Ensayos clínicos: eficacia y seguridad
4. Recomendaciones oficiales
5. Efectividad
6. Perspectivas futuras y mensajes finales

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La gripe es una infección muy prevalente con un enorme impacto en la población

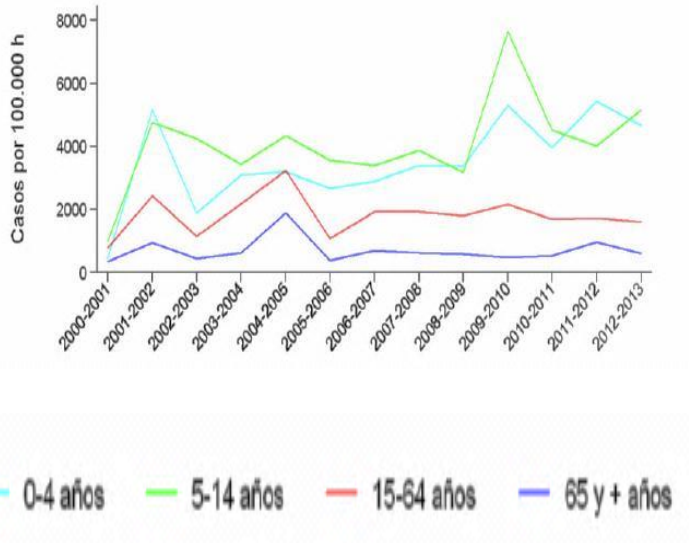
- ✓ **En EE. UU. cada año:**
  - ✓ Hasta 50 millones de casos de gripe al año
  - ✓ 225.000 hospitalizaciones
  - ✓ Hasta 50.000 fallecimientos

Ruf Br, et al. Eur J Pediatr 2014

Los niños son la fuente de contagio más importante en la comunidad

- ✓ Los niños son la fuente de transmisión más importante de la comunidad
- ✓ Tasa de ataque anual en niños pequeños de 20-40%

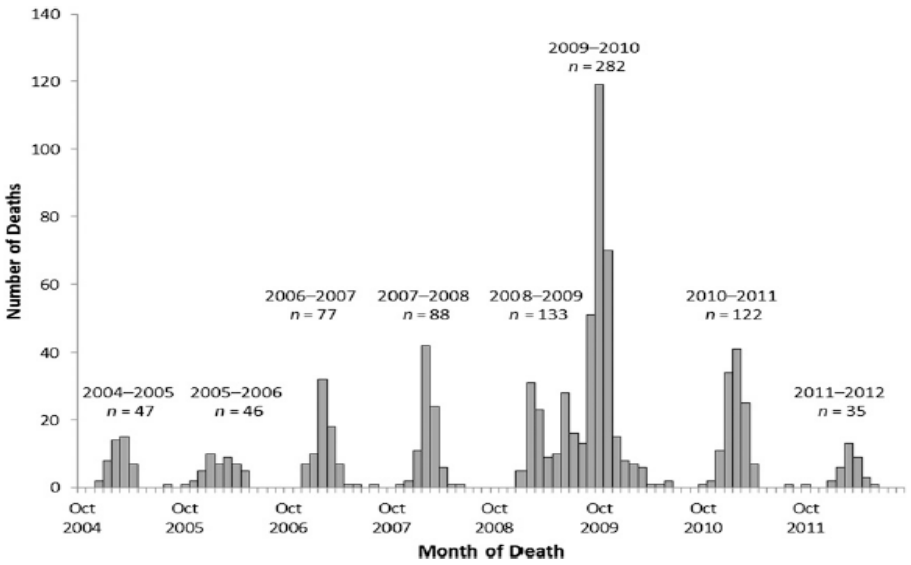
Figura 4. Tasas de incidencia acumulada de gripe por grupos de edad y temporada. Temporadas 2000-2001/2012-2013. Sistemas centinela. España.



Fuente: Instituto de Salud Carlos III (último acceso: 11/Mar/2015)

La gripe es una infección muy prevalente con un enorme impacto en la población

Influenza-Associated Pediatric Deaths in the United States, 2004–2012



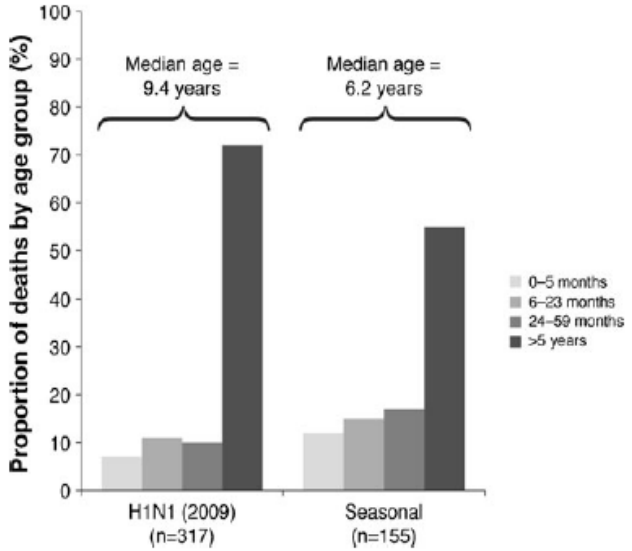


FIGURE 1
Number of influenza-associated pediatric deaths by month of death (N = 830): United States, October 2004 through September 2012.

Centers for Disease Control (CDC). Pediatrics 2013

Cox CM, et al. Clin Infect Dis 2011

La gripe es una infección muy prevalente con un enorme impacto en la población

Influenza-Associated Pediatric Deaths in the United States, 2004–2012

RESULTS: From October 2004 through September 2012, 830 pediatric influenza–associated deaths were reported. The median age was 7 years (interquartile range: 1–12 years). Thirty-five percent of children died before hospital admission. Of 794 children with a known medical history, 43% had no high-risk medical conditions, 33% had neurologic disorders, and 12% had genetic or chromosomal disorders. Children without high-risk medical conditions were more likely to die before hospital admission (relative risk: 1.9; 95% confidence interval: 1.6–2.4) and within 3 days of symptom onset (relative risk: 1.6; 95% confidence interval: 1.3–2.0) than those with high-risk medical conditions.

Centers for Disease Control (CDC). Pediatrics 2013

La gripe es una infección muy prevalente con un enorme impacto en la población

FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

CDC

2014-2015 Influenza Season Week 8 ending February 28, 2015

HHS Surveillance Regions*	Data for Current Week			Data Cumulative Since September 28, 2014 (Week 40)				
	Out-patient ILI†	Number of jurisdictions reporting regional or widespread activity§	% Respiratory specimens positive for flu‡	A(H1N1)pdm09	A (H3)	A(Subtyping not performed)	B	Pediatric Deaths
Nation	Elevated	45 of 54	10.9%	179	44,943	49,354	7,797	97
Region 1	Elevated	6 of 6	19.0%	7	2,591	2,605	222	1
Region 2	Elevated	4 of 4	17.1%	53	3,737	4,962	360	6
Region 3	Normal	3 of 6	12.1%	6	5,977	4,676	426	8
Region 4	Elevated	8 of 8	10.0%	9	3,577	12,140	2,189	18
Region 5	Normal	5 of 6	8.2%	12	7,898	7,787	764	19
Region 6	Elevated	5 of 5	14.5%	28	4,411	7,713	1,857	20
Region 7	Elevated	4 of 4	9.7%	8	1,735	2,359	394	7
Region 8	Elevated	4 of 6	10.9%	26	4,428	3,409	743	6
Region 9	Normal	4 of 5	19.4%	22	6,505	3,021	601	11
Region 10	Elevated	2 of 4	8.6%	8	4,084	682	240	1

Disponible en: http://www.cdc.gov/flu/weekly/
(último acceso: 13 marzo 2015)

Gripe en niños
Cuestiones para la comunidad científica…

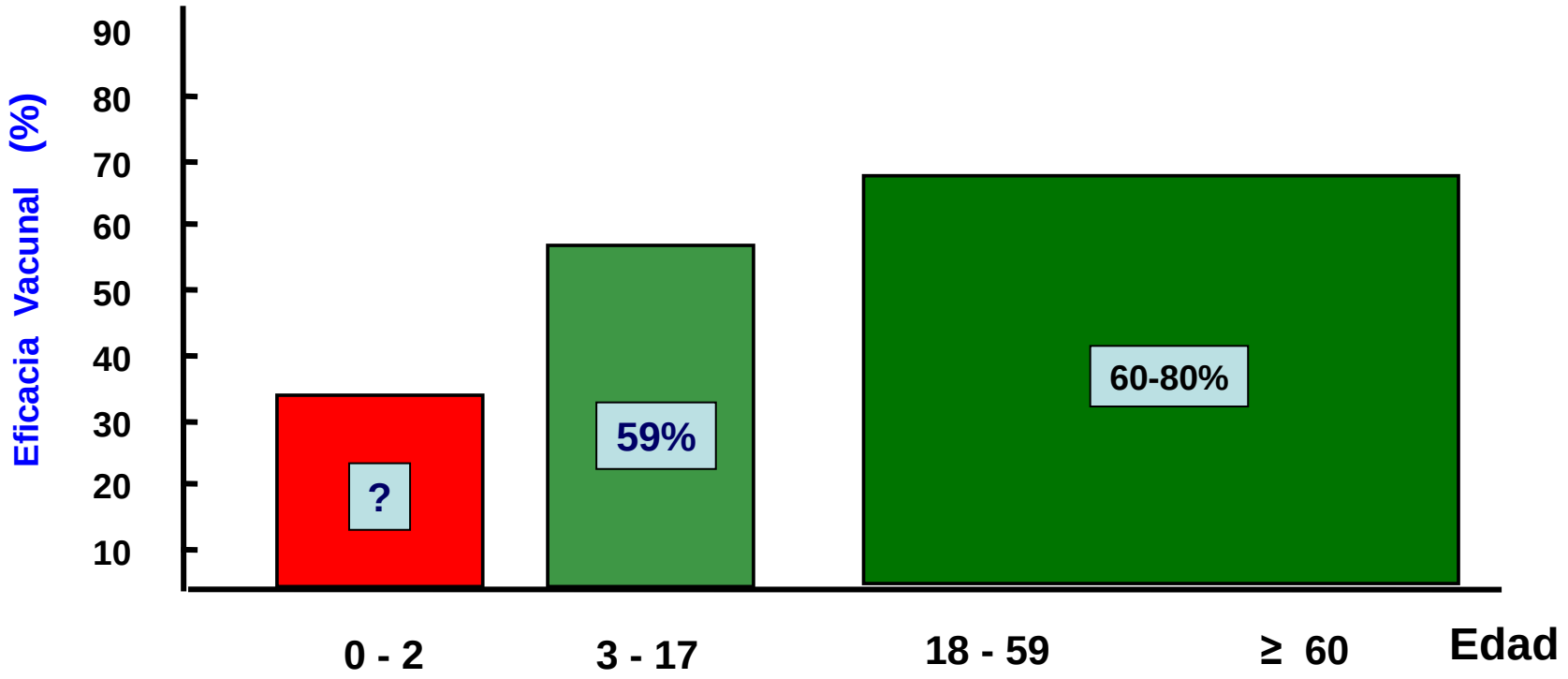
Gripe: enorme impacto sanitario en la comunidad

Niños: fuente de contagio más importante; puede ser grave, incluso en sanos

Niños: los vacunamos?

Niños: los vacunamos a todos?

Vacunas antigripales inactivadas
¿Eficacia en niños?



Necesidad médica no cubierta en pediatría

Jefferson T. Metanálisis Cochrane 2005, 2009, 2012.

Jefferson T, et al. Metanálisis adultos. Cochrane 2014.

Vacunas antigripales
Eficacia de TIV – LAIV en niños (Cochrane)

		2005	2008	2012
Estudios (total)		23	51	75
Estudios: EC		14	16	17
Estudios: Cohortes		8	18	19
Estudios: C/C		1		11
Eficacia (gripe confirmada)	TIV	65% (47-76%)	59% (47-71%)	59% (41-71%)
	LAIV	79% (48-92%)	82% (71-89%)	80% (78-87%)
Efectividad (sdr gripal)	TIV	28% (22-33%)	36% (24-46%)	36% (24-46%)
	LAIV	38% (33-43%)	33% (28-38%)	33% (28-38%)

Jefferson T, et al. Metanálisis niños. Cochrane 2005, 2009, 2012.

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Estudios: C/C		1		11
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Efectividad (sdr gripal)	TIV	28% (22-33%)	36% (24-46%)	36% (24-46%)
	LAIV	38% (33-43%)	33% (28-38%)	33% (28-38%)

Solo un EC randomizado en < 2 años

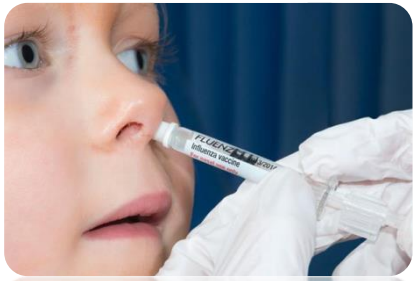
Efectividad de TIV en <2a similar a placebo !!

No diferencias en OMA, IVRBs y hospitalización !!

Jefferson T, et al. Metanálisis niños. Cochrane 2005, 2009, 2012.

NECESIDAD DE VACUNAS ANTIGRIPALES MAS EFICACES / EFECTIVAS - EN NIÑOS

ATENUADAS



TETRAVALENTES

ADYUVADAS

INTRADÉRMICAS

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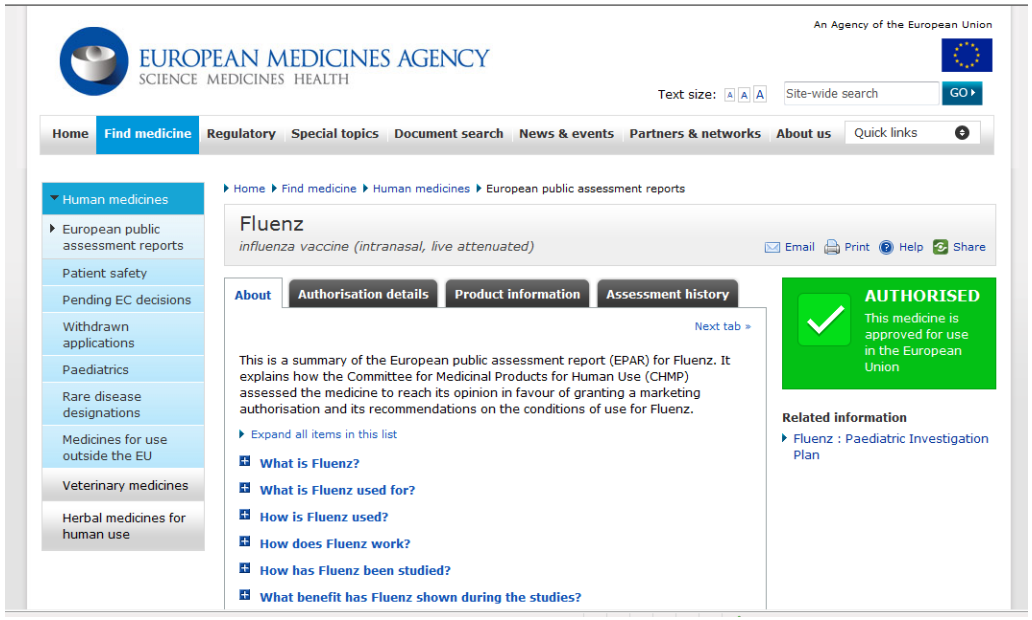
Vacuna atenuada intranasal
LAIV: Live Attenuated Influenza Vaccine

✓ Vacunas antigripales atenuadas (LAIV):

- **Flumist ™** - MedImmune (USA, jun 2003)
  - 2 – 49 años
- **Fluenz ®** - Astra-Zeneca (Europa, marzo 2011)
  - 2 - 18 años

Fluenz ®
(Ficha técnica EMA / AEMPS)



Vacuna atenuada intranasal
LAIV: Live Attenuated Influenza Vaccine

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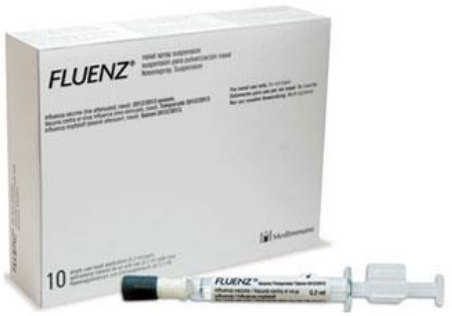
- **Flumist** ™ - MedImmune (USA, jun 2003)
  - 2 – 49 años
- **Fluenz** ® - Astra-Zeneca (Europa, marzo 2011)
  - 2 - 18 años

✓ Trivalente → Tetravalente 2014-2015:

- **A/ H1N1:** California/7/2009 (H1N1)pmd09
- **A/ H3N2:** A/Texas/50/2012 (H3N2)
- **B:** B/Massachusetts/2/2012 (linaje Yamagata)
- **B:** B/Brisbane/60/2008 (linaje Victoria)

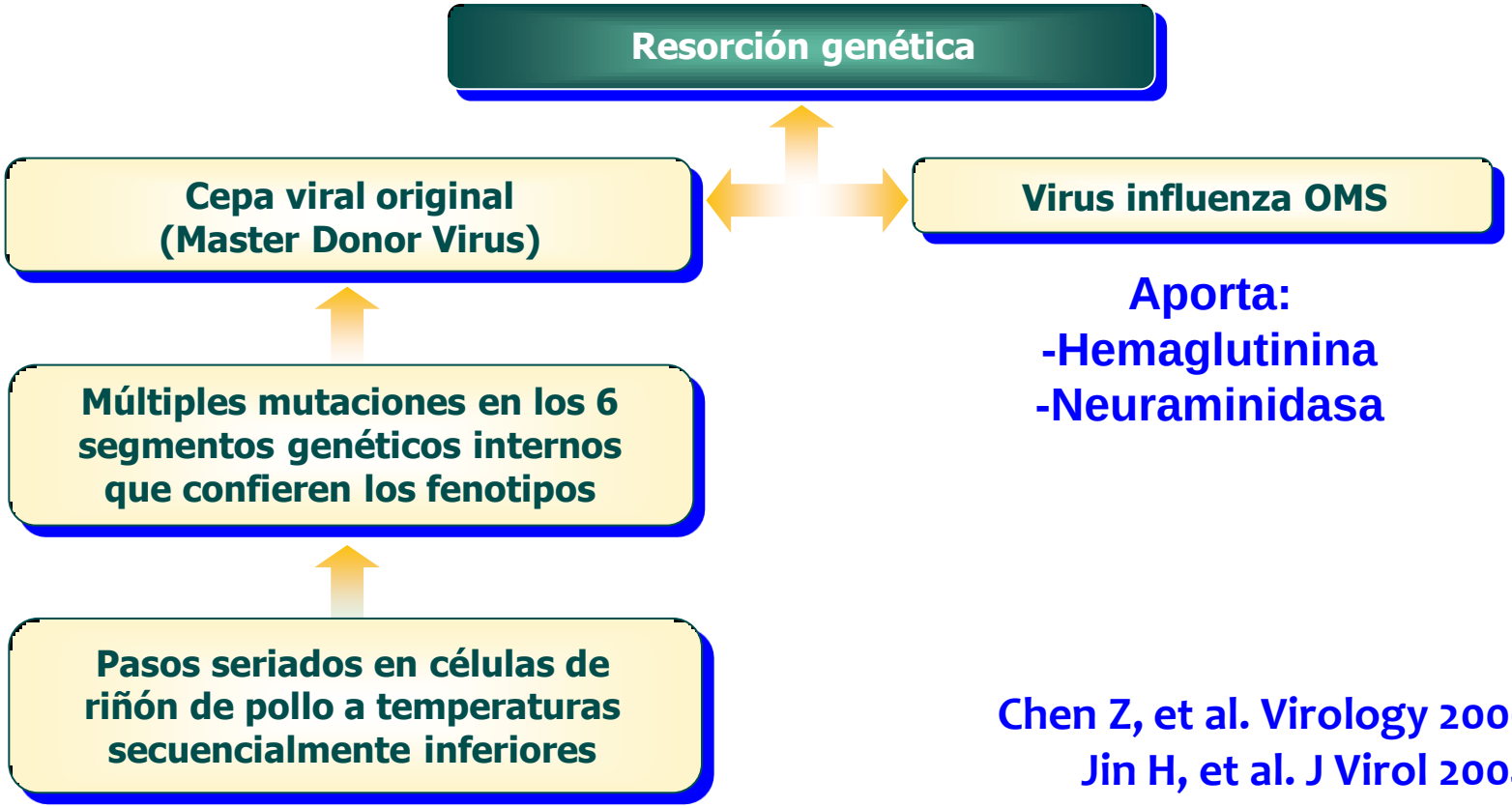


Flumist (Ficha técnica FDA)
Fluenz (Ficha técnica EMA / AEMPS)

Vacuna atenuada intranasal
LAIV: Live Attenuated Influenza Vaccine

✓ Vacuna atenuada

✓ Virus atenuados reasortantes – mutantes



Chen Z, et al. Virology 2006
Jin H, et al. J Virol 2004

Vacuna atenuada intranasal
LAIV: Live Attenuated Influenza Vaccine

- **Vacuna atenuada**
  - **Virus atenuados reasortantes – mutantes**
    - No pueden producir gripe
    - Adaptados al frío (cold-adapted):
      - se replican a 25ºC
      - pero no >37ºC: no pueden replicarse en pulmón
    - Simulación de infección natural.
    - Estimulación directa de la inmunidad mucosa:
      - IgA mucosa + inmunidad celular

Chen Z, et al. Virology 2006
Jin H, et al. J Virol 2004

Vacuna atenuada intranasal
LAIV: Live Attenuated Influenza Vaccine

✓ Administración intranasal:

→ 0,1 ml por cada narina

	Dosis	Num dosis
<23 meses	No autorizada	-
2 - 8 años	0,2 mL (0,1 ml por cada narina)	1 (2 si 1er año)
9 - 17 años	0,2 mL (0,1 ml por cada narina)	1

Fluenz (Ficha técnica EMA / AEMPS)

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Vacuna gripe atenuada intranasal
Eficacia (ensayos clínicos)

¿cuál es la **eficacia** de la vacuna antigripal atenuada intranasal

frente a otras intervenciones, incluido placebo?

¿y en niños con HRB-asma?

Vacuna gripe atenuada intranasal
Ensayos clínicos realizados en adultos

	Population (dates)	Patients randomly allocated to receive LAIV and placebo	Vaccine efficacy (95% CI)	Reported antigenic match
Adults (≥60 years)				
De Villiers et al (2010)[37]	Community-dwelling ambulatory adults aged ≥60 years (2001–02)	3242	Overall 42% (21 to 57); 31% (−3 to 53) for patients aged 60–69 years; 57% (29 to 75) for patients aged ≥70 years	Type A: similar H3N2; type B: lineage match
Adults (18–49 years)				
Ohmit et al (2006)[24]	Healthy adults aged 18–46 years (2004–05)	725	48% (−7 to 74)	Type A: drifted H3N2; type B: mixed lineage
Ohmit et al (2008)[25]	Healthy adults aged 18–48 years (2005–06)	1191	8% (−194 to 67)	Type A: drifted H3N2; type B: lineage mismatch (1 isolate)
Monto et al (2009)[28]*	Healthy adults aged 18–49 years (2007–08)	1138	36% (0 to 59)	Type A: drifted H3N2; type B: lineage mismatch
Children (6 months–7 years)				
Belshe et al (1998)[32]	Healthy children aged 15–71 months (1996–97)	1602	93% (88 to 96)	Type A: similar H3N2; type B: lineage match
Belshe et al (2000)[33]	Healthy children aged 26–85 months (1997–98)	1358	87% (78 to 93)	Type A: drifted H3N2; type B: not reported (1 isolate)
Vesikari et al (2006)[34]	Healthy children aged 6–<36 months attending day care (2000–01)	1784	84% (74 to 90)	Type A: similar H3N2 and H1N1; type B: lineage match
Vesikari et al (2006)[34]	Healthy children aged 6–<36 months attending day care (2001–02)	1119	85% (78 to 90)	Type A: similar H3N2 and H1N1; type B: mixed lineage
Bracco Neto et al (2009)[38]	Healthy children aged 6–<36 months (2000–01)	1886	72% (62 to 80)	Majority of strains were similar (not reported by type)
Tam et al (2007)[35]	Healthy children aged 12–<36 months (2000–01	3174	68% (59 to 75)	Type A: similar H3N2 and H1N1; type B: lineage match
Tam et al (2007)[35]	Healthy children aged 12–<36 months (2001–02	2947	57% (30 to 74)	Type A: similar H3N2 and H1N1; type B: mixed lineage
Lum et al (2010)[36]	Healthy children aged 11–<24 months (2002–03	1233	64% (40 to 79)	Type A: similar H1N1 and mixed H3N2; type B: mixed lineage

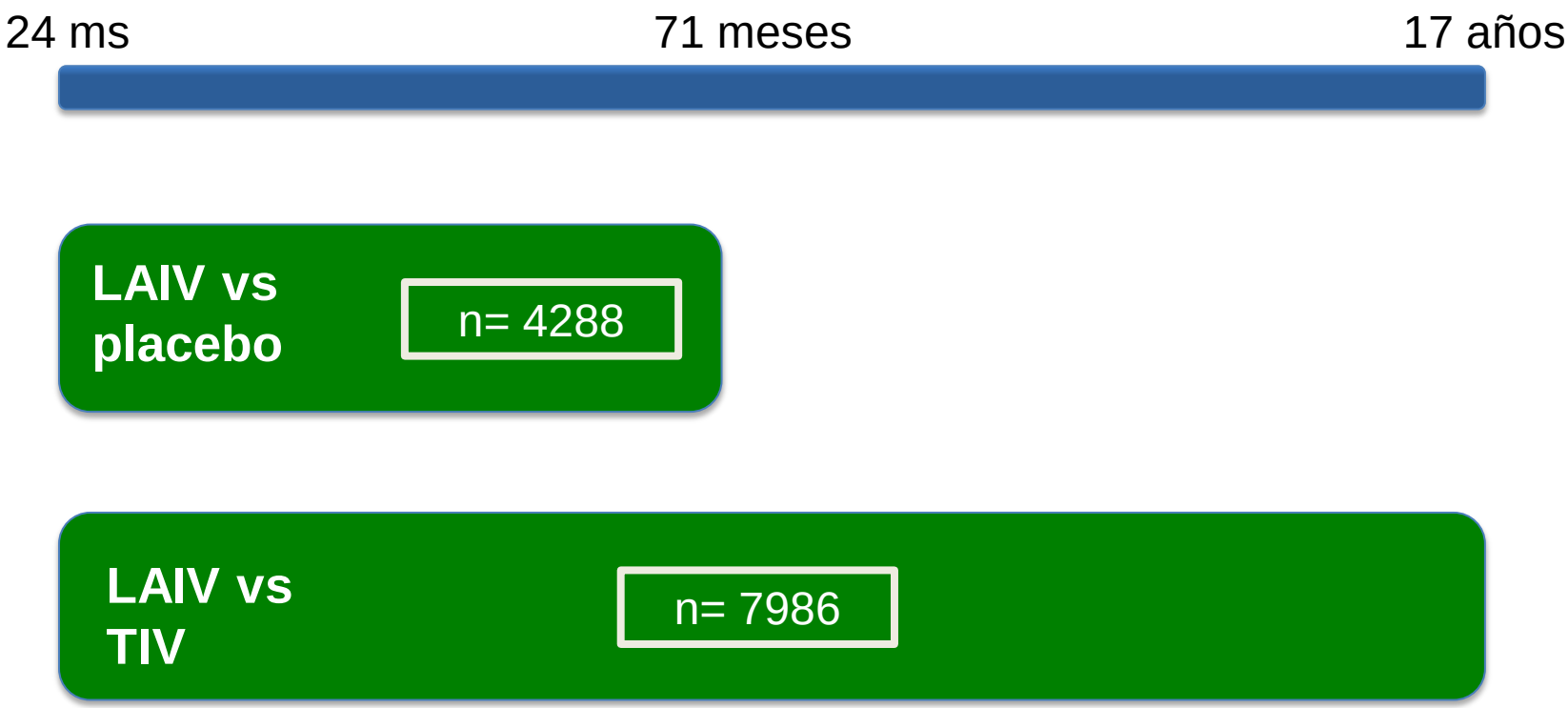
Osterholm MT, et al. Lancet Infect Dis 2012

Vacuna gripe atenuada intranasal
Estudios de eficacia: 6 meses – 17 años

	Sanos / HRB-asma	LAIV vs Placebo	LAIV vs TIV	Conclusiones principales
< 6 ms		NO estudios	NO estudios	---
6 ms a 7 años	- **Sanos**: 7 RCT (10 temporadas) - **HRB-asma**: 2 RCT (2 temporadas)	**LAIV > placebo**	**LAIV > TIV**	LAIV de elección: Evidencia alta
8 a 17 años	- Sanos: 0 RCT - **Asmáticos:** 1 RCT (1 temporada)	NO estudios	**LAIV > TIV**	LAIV de elección en asmáticos: Evidencia moderada

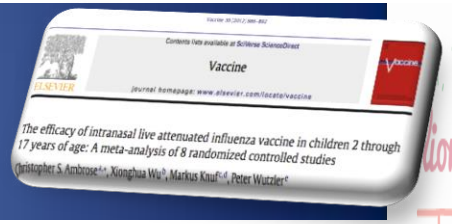
Andersohn F, et al. GMS Health Technology Assessment 2014

Vacuna gripe atenuada intranasal
Metanálisis 8 estudios eficacia: 24 ms - 17 años



Ambrose CS, et al. Vaccine 2012

Vacuna gripe atenuada intranasal
Eficacia LAIV vs placebo: 24 - 71 ms



LAIV vs placebo n= 4288

AÑO 1

AÑO 2 (revac)

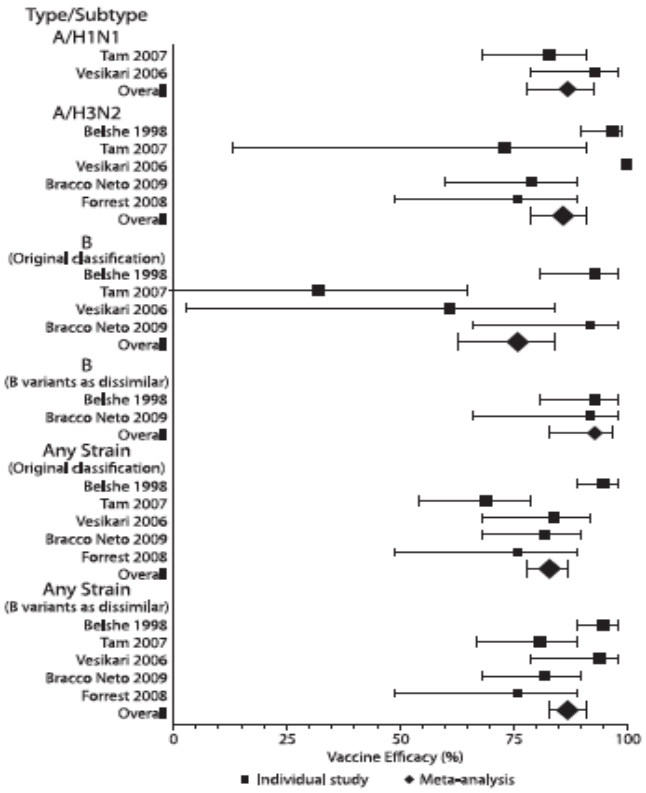


Fig. 1. LAIV efficacy versus placebo (year 1; 2 doses) for antigenically similar strains by type/subtype and study. LAIV, live attenuated influenza vaccine. Symbol sizes are relative to the study population sizes. See Table 1 for details of each study.

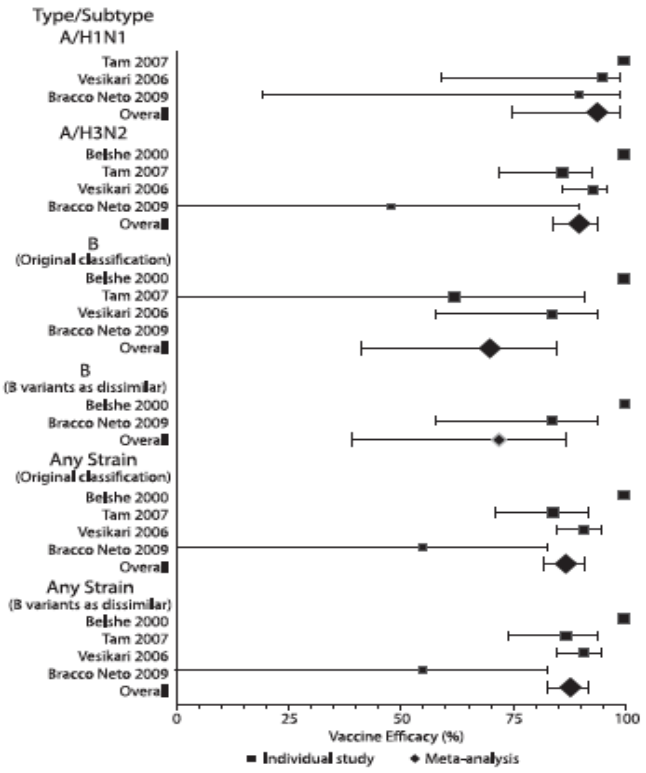
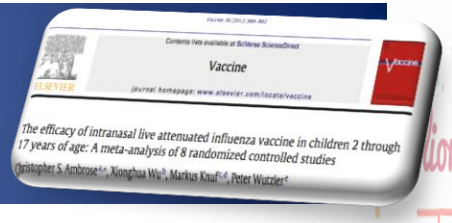


Fig. 2. Live attenuated influenza vaccine efficacy versus placebo (year 2; 1 revaccination dose) for antigenically similar strains by type/subtype and study. Symbol sizes are relative to the study population sizes. See Table 1 for details of each study.

Ambrose CS, et al. Vaccine 2012

Vacuna gripe atenuada intranasal
Eficacia LAIV vs placebo: 24 - 71 ms



LAIV vs placebo n= 4288

Influenza strain	LAIV *n/N* (%)	Placebo *n/N* (%)	Vaccine efficacy (95% CI)
Following year 1 vaccination, antigenically similar strains			
A/H1N1	14/1272 (1.1)	78/890 (8.8)	87 (78, 93)
A/H3N2	26/2542 (1.0)	135/1746 (7.7)	86 (79, 91)
B (original classification)	30/2333 (1.3)	82/1564 (5.2)	76 (63, 84)
B (variants as dissimilar)	6/1061 (0.6)	52/674 (7.7)	93 (83, 97)
Any strain (original classification)	70/2542 (2.8)	281/1746 (16.1)	83 (78, 87)
Any strain (B variants as dissimilar)	46/2542 (1.8)	260/1764 (14.5)	87 (83, 91)
Following year 1 vaccination, all strains regardless of antigenic similarity			
A/H1N1	14/1272 (1.1)	85/890 (9.6)	88 (80, 93)
A/H3N2	32/2542 (1.3)	143/1746 (8.2)	84 (77, 89)
B	47/2542 (1.8)	102/1746 (5.8)	68 (55, 77)
Any strain	94/2542 (3.7)	311/1746 (17.8)	79 (73, 83)
Following year 2 revaccination, antigenically similar strains			
A/H1N1	2/1606 (0.1)	27/1173 (2.3)	94 (75, 99)
A/H3N2	20/2354 (0.8)	137/1535 (8.9)	90 (84, 94)
B (original classification)	12/2354 (0.5)	28/1535 (1.8)	70 (41, 85)
B (variants as dissimilar)	9/1583 (0.6)	23/1041 (2.2)	72 (39, 87)
Any strain (original classification)	33/2354 (1.4)	183/1535 (11.9)	87 (82, 91)
Any strain (B variants as dissimilar)	30/2354 (1.3)	179/1535 (11.7)	88 (83, 92)
Following Year 2 Revaccination, All Strains Regardless of Antigenic Similarity			
A/H1N1	2/1606 (0.1)	27/1173 (2.3)	94 (75, 99)
A/H3N2	35/2354 (1.5)	186/1535 (12.1)	88 (84, 92)
B	55/2354 (2.3)	76/1535 (5.0)	43 (19, 59)
Any strain	91/2354 (3.9)	275/1535 (17.9)	78 (72, 82)

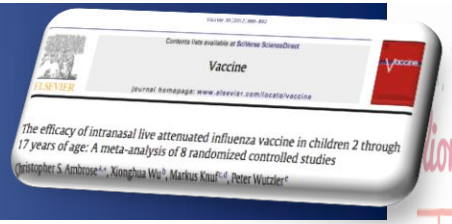
LAIV, live attenuated influenza vaccine; NE, not estimable.

AÑO 1

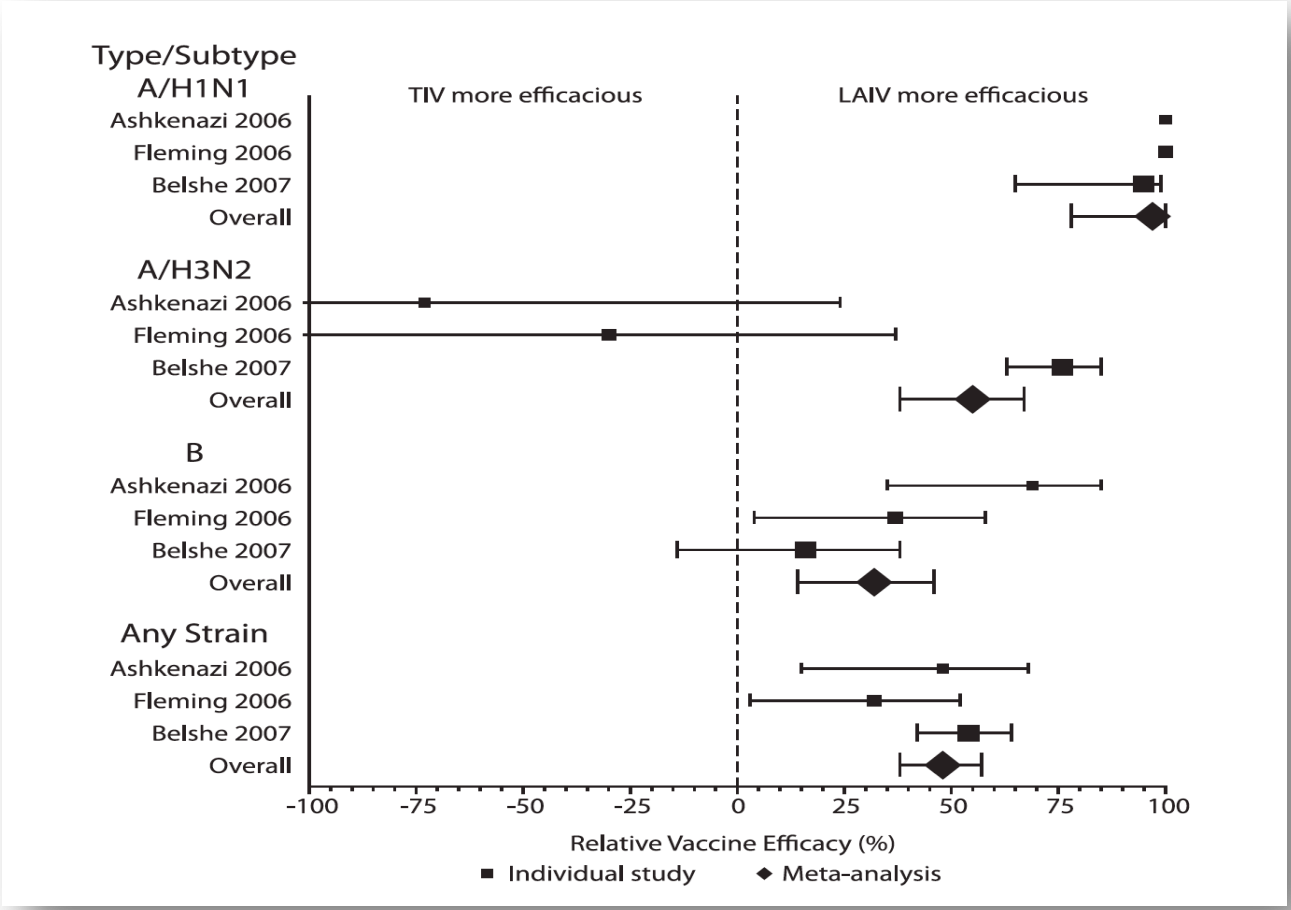
AÑO 2

Ambrose CS, et al. Vaccine 2012

Vacuna gripe atenuada intranasal
Eficacia LAIV vs TIV: 2-17 años



LAIV vs TIV n= 7986



Ambrose CS, et al. Vaccine 2012

Vacuna gripe atenuada intranasal
Eficacia LAIV vs TIV: 2-17 años

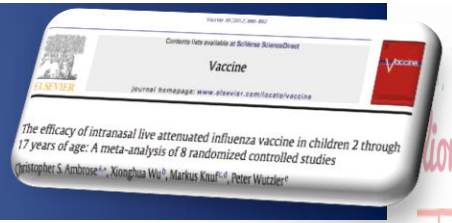


Table 3
Relative efficacy of LAIV versus TIV.

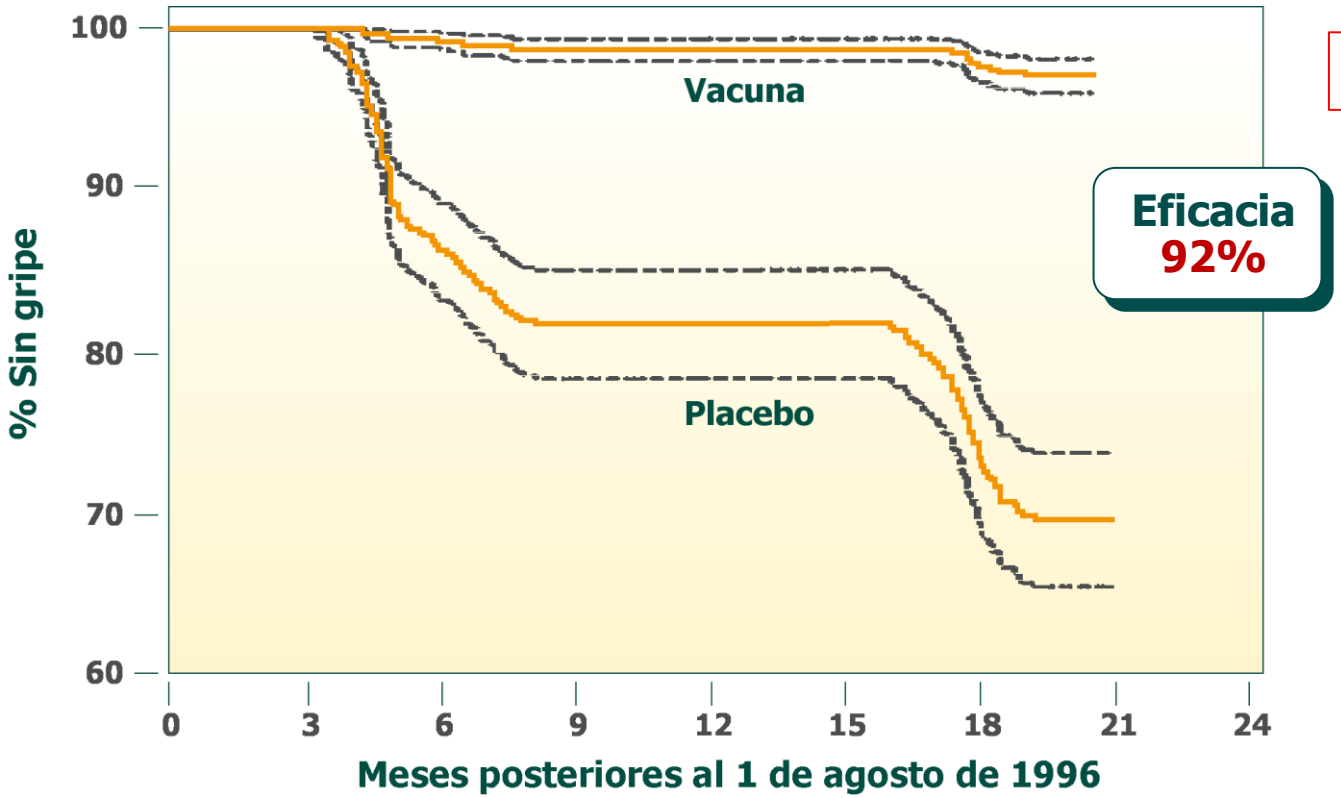
Influenza strain	Study	LAIV *n*/*N* (%)	TIV *n*/*N* (%)	Relative vaccine efficacy (95% CI)
Antigenically similar strains				
A/H1N1	Ashkenazi (2006)	0/790 (0.0)	6/819 (0.7)	100 (NE, 100)
	Fleming (2006)	0/1109 (0.0)	5/1102 (0.5)	100 (NE, 100)
	Belshe (2007)	1/2083 (0.0)	21/2083 (1.0)	95 (65, 99)
	Meta-analysis	1/3982 (0.0)	32/4004 (0.8)	97 (77, 100)
A/H3N2	Ashkenazi (2006)	10/790 (1.3)	5/819 (0.6)	−107 (−504, 29)
	Fleming (2006)	12/1109 (1.1)	12/1102 (1.1)	1 (−120, 55)
	Meta-analysis	22/1899 (1.2)	17/1921 (0.9)	−31 (−145, 30)
B (original classification)	Ashkenazi (2006)	9/790 (1.1)	29/819 (3.5)	68 (32, 85)
	Fleming (2006)	34/1109 (3.1)	53/1102 (4.8)	36 (3, 58)
	Belshe (2007)	29/2083 (1.4)	40/2083 (1.9)	27 (−16, 55)
	Meta-analysis	72/3982 (1.8)	122/4004 (3.0)	41 (21, 56)
B (variants as dissimilar)	Ashkenazi (2006)	9/790 (1.1)	29/819 (3.5)	68 (32, 85)
	Fleming (2006)	34/1109 (3.1)	53/1102 (4.8)	36 (3, 58)
	Belshe (2007)	1/2083 (0.0)	5/2083 (0.2)	80 (−71, 98)
	Meta-analysis	44/3982 (1.1)	87/4004 (2.2)	49 (27, 64)
Any strain (original classification)	Ashkenazi (2006)	19/790 (2.4)	39/819 (4.8)	49 (13, 71)
	Fleming (2006)	46/1109 (4.1)	70/1102 (6.4)	35 (6, 55)
	Belshe (2007)	30/2083 (1.4)	61/2083 (2.9)	51 (24, 68)
	Meta-analysis	95/3982 (2.4)	170/4004 (4.2)	44 (28, 56)
Any strain (B variants as dissimilar)	Ashkenazi (2006)	19/790 (2.4)	39/819 (4.8)	49 (13, 71)
	Fleming (2006)	46/1109 (4.1)	70/1102 (6.4)	35 (6, 55)
	Belshe (2007)	2/2083 (0.1)	26/2083 (1.2)	92 (68, 98)
	Meta-analysis	67/3982 (1.7)	135/4004 (3.4)	50 (33, 62)
All strains regardless of antigenic similarity				
A/H1N1	Ashkenazi (2006)	0/790 (0.0)	7/819 (0.9)	100 (NE, 100)
	Fleming (2006)	0/1109 (0.0)	6/1102 (0.5)	100 (NE, 100)
	Belshe (2007)	1/2083 (0.0)	21/2083 (1.0)	95 (65, 99)
	Meta-analysis	1/3982 (0.0)	34/4004 (0.8)	97 (78, 100)
A/H3N2	Ashkenazi (2006)	15/790 (1.9)	9/819 (1.1)	−73 (−293, 24)
	Fleming (2006)	17/1109 (1.5)	13/1102 (1.2)	−30 (−166, 37)
	Belshe (2007)	24/2083 (1.2)	102/2083 (4.9)	76 (63, 85)
	Meta-analysis	56/3982 (1.4)	124/4004 (3.1)	55 (38, 67)
B	Ashkenazi (2006)	9/790 (1.1)	30/819 (3.7)	69 (35, 85)
	Fleming (2006)	35/1109 (3.2)	55/1102 (5.0)	37 (4, 58)
	Belshe (2007)	72/2083 (3.5)	86/2083 (4.1)	16 (−14, 38)
	Meta-analysis	116/3982 (2.9)	171/4004 (4.3)	32 (14, 46)
Any	Ashkenazi (2006)	23/790 (2.9)	46/819 (5.6)	48 (15, 68)
	Fleming (2006)	50/1109 (4.5)	73/1102 (6.6)	32 (3, 52)
	Belshe (2007)	94/2083 (4.5)	205/2083 (9.8)	54 (42, 64)
	Meta-analysis	167/3982 (4.2)	324/4004 (8.1)	48 (38, 57)

LAIV, live attenuated influenza vaccine; NE, not estimable, TIV, trivalent inactivated influenza vaccine.

Ambrose CS, et al. Vaccine 2012

Vacuna gripe atenuada intranasal vs placebo
Eficacia independiente de cepa (26 – 85 ms)

Eficacia durante dos años de la vacuna viva atenuada intranasal contra la gripe, expresada según una representación de Kaplan Meier (líneas continuas) de la probabilidad de mantener un cultivo negativo del virus influenza. En el año 1 se produjo una epidemia de gripe A (meses 3-4) y de gripe B (meses 4-6). En el año 2, la mayoría de los casos de gripe estuvieron producidos por el virus influenza A/Sydney (meses 16-18). Líneas discontinuas = IC del 95%



N=1110

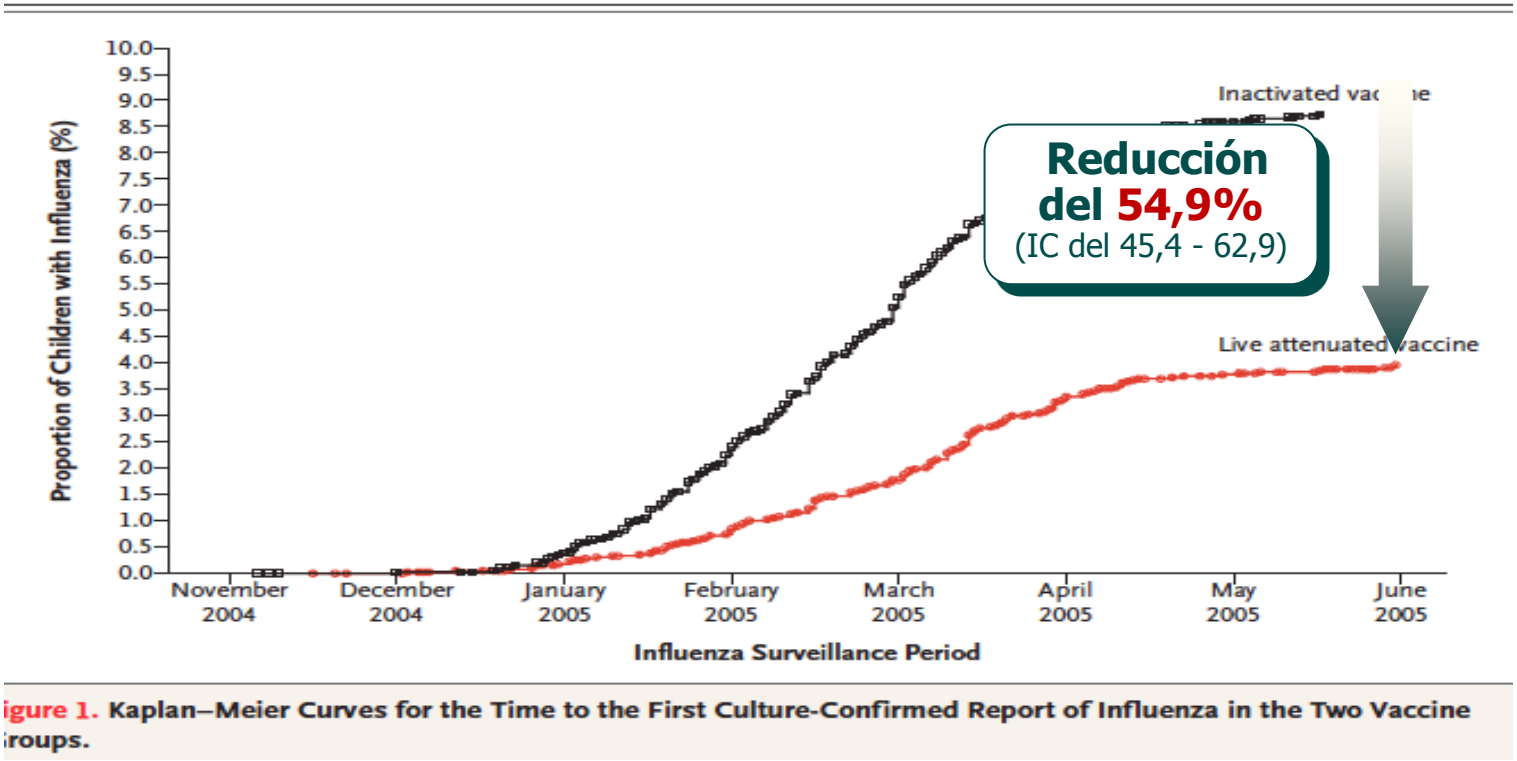
Belshe RB, et al. J Pediatr 2000

Vacuna gripe atenuada intranasal vs TIV
Eficacia niños sanos 24 – 59 meses

Estudio CP111: Niños (24 a 59 años)

Eficacia Total durante la estación de gripe 2004-2005[1]

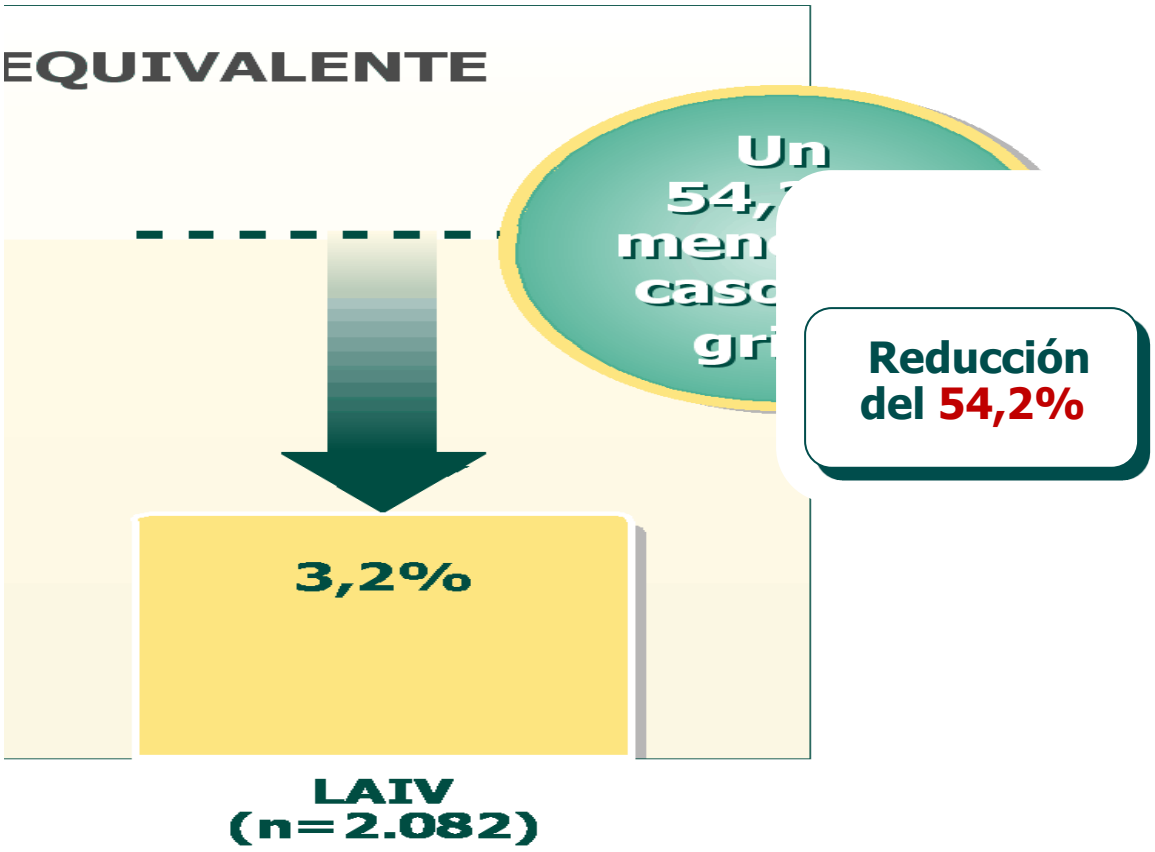
N=4166



igure 1. Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine roups.

Belshe RB, et al. N Engl J Med 2007

Vacuna gripe atenuada intranasal vs TIV
Eficacia cepas no concordantes (24 – 59 ms)



Belshe RB, et al. N Engl J Med 2007

Vacuna gripe atenuada intranasal
Duración de eficacia (segundo año)

- La protección en el año 2 de una cohorte vacunada en el año 1, pero **no revacunada en el año 2,** se ha valorado en 3 estudios.

Estudio	Edad de los sujetos	Cepas dominantes	Eficacia (IC del 95%)
D153-P501[1]	12-36 meses	A/H3N2	**56%** (IC del 95%: 31, 73)
D153-P504[2]	6-36 meses	A/H1N1	**57%** (IC del 95%; 6, 82)
AV012[3,4]	1,5-18 años	A/H1N1[a], B[a]	**62%** (IC del 95%: 9, 85)[b]

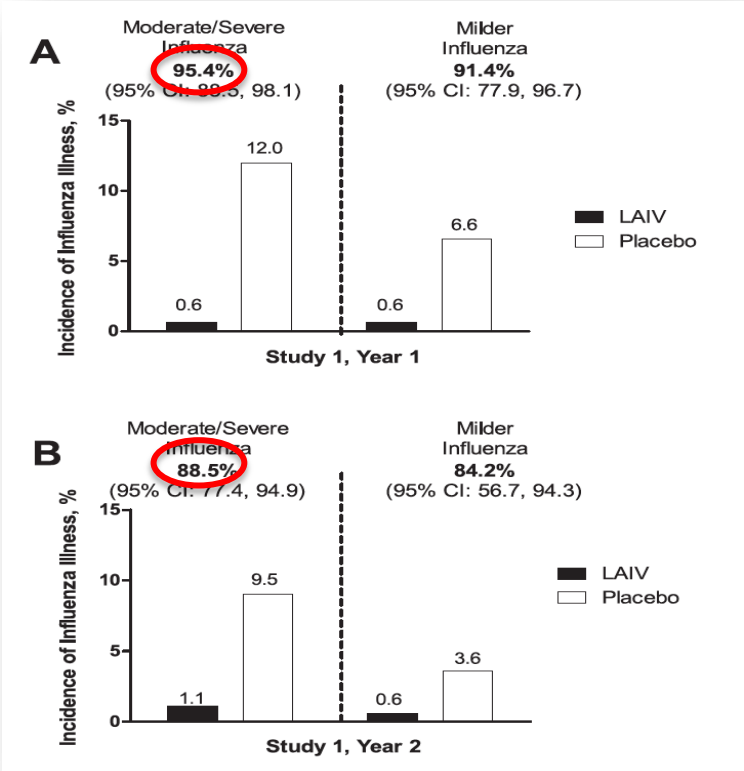
[a]Antigénicamente distinto de la cepa de la vacuna
[b]Eficacia estimada según los datos de efectividad y los cultivos durante la vigilanc

Tam JS, et al. Pediatr Infect Dis J Med 2007
Halloran ME, et al. Am J Epidemiol 2003

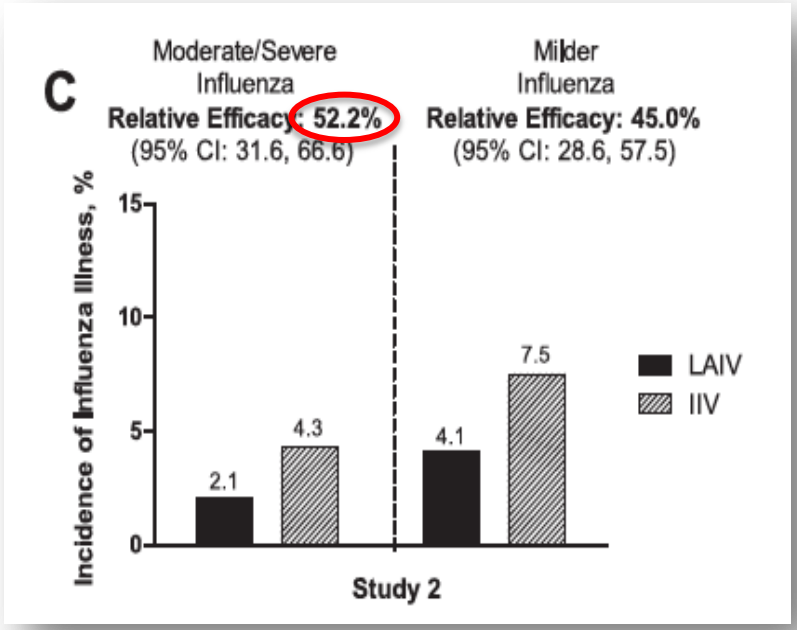
Vacuna gripe atenuada intranasal
Eficacia para gripe moderada-grave en >24 ms

Metanálisis 2 ensayos clínicos	>24 meses: n= 6854	Gripe moderada-grave: >39ºC, OMA, afectación respiratoria inferior

15 – 71 ms. LAIV vs placebo



6 – 59 ms. LAIV vs TIV



Ambrose CS, et al. Vaccine 2014

Vacuna gripe atenuada intranasal
Eficacia para OMA relacionada con gripe

Metanálisis
6 EC LAIV-placebo
2 EC LAIV-TIV

6 – 83 meses:
n= 24046

LAIV vs placebo

TABLE 1. Rate of AOM Associated With Culture-confirmed Influenza* in 6 Placebo-controlled Trials

Age Group	LAIV, n/N (%)	Placebo, n/N (%)	Efficacy, %	95% CI
AOM attack rate in all subjects				
6–23 mo	25/4075 (0.61)	82/2972 (2.76)	77.8	64.8, 86.4
24–83 mo	11/4278 (0.26)	83/2784 (2.98)	91.4	83.8, 95.6
All ages	36/8353 (0.43)	165/5756 (2.87)	85.0	78.3, 89.8

LAIV vs TIV

TABLE 2. Rate of AOM Associated With Culture-confirmed Influenza* in 2 TIV-controlled Trials

Age Group	LAIV, n/N (%)	TIV, n/N (%)	Efficacy, %	95% CI
AOM attack rate in all subjects				
6–23 mo	17/2094 (0.81)	32/2068 (1.55)	47.5	2.7, 72.7
24–83 mo	11/2872 (0.38)	29/2903 (1.00)	61.7	20.9, 82.7
All ages	28/4966 (0.56)	61/4971 (1.23)	54.0	27.0, 71.7

Block SL, et al. Pediatr Infect Dis J 2011

Resumiendo… eficacia LAIV en niños

1. **VACUNA ATENUADA INTRANASAL en niños de 2 a 17 años:**

– **Es más eficaz que placebo para:**

- Prevenir la gripe confirmada: **80%**
- Prevenir la gripe moderada-grave: **88-95%**
- Prevenir la OMA asociada a gripe: **85%**

– **Es más eficaz que vacuna inactivada:**

- Prevenir la gripe confirmada: **50%**
- Prevenir la gripe moderada-grave: **52%**
- Prevenir la OMA asociada a gripe: **54%**

VACUNACION GRIPE INTRANASAL

1. Introducción
2. ¿Qué es LAIV?
3. Ensayos clínicos: eficacia y seguridad
4. Recomendaciones oficiales
5. Efectividad
6. Perspectivas futuras y mensajes finales

Vacuna gripe atenuada intranasal
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Ambrose CS, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV en niños < 2 años

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Live Attenuated versus Inactivated Influenza Vaccine in Infants and Young Children

Robert B. Belshe, M.D., Kathryn M. Edwards, M.D., Timo Vesikari, M.D., Steven V. Black, M.D., Robert E. Walker, M.D., Micki Hultquist, M.S., George Kemble, Ph.D., and Edward M. Connor, M.D., for the CAIV-T Comparative Efficacy Study Group*

Table 1. Characteristics and Follow-up of Subjects Included in the Safety Population.*

Variable	Live Attenuated Vaccine	Inactivated Vaccine	Total
No. of subjects	4179	4173	8352
History of influenza vaccination — no. (%)	933 (22.3)	947 (22.7)	1880 (22.6)
Mean age at first vaccination — mo	25.7	25.6	25.6
Age distribution — no. (%)			
6–23 mo	1992 (47.7)	1975 (47.3)	3967 (47.5)
6–11 mo	684 (16.4)	683 (16.4)	1367 (16.4)
12–23 mo	1308 (31.3)	1292 (31.0)	2600 (31.1)

Table 3. Incidence in the Safety Population of Medically Significant Wheezing within 42 Days after Receiving Vaccine.*

Variable	Live Attenuated Vaccine	Inactivated Vaccine	Adjusted Rate Difference (95% CI)†
	no./total no. of cases (%)		
All children (6–59 mo of age)			
Previously vaccinated			
After dose 1	19/933 (2.0)	17/947 (1.8)	0.03 (−1.24 to 1.38)
Not previously vaccinated			
After dose 1	74/3246 (2.3)	48/3226 (1.5)	0.77 (0.12 to 1.46)
After dose 2	73/3002 (2.4)	67/3034 (2.2)	0.20 (−0.56 to 0.97)
Children <24 mo‡			
Previously vaccinated			
After dose 1	7/267 (2.6)	3/269 (1.1)	1.34 (−1.11 to 4.30)
Not previously vaccinated			
After dose 1	55/1725 (3.2)	34/1706 (2.0)	1.18 (0.13 to 2.29)
After dose 2	57/1578 (3.6)	39/1595 (2.4)	1.15 (−0.04 to 2.38)

Belshe RB, et al. N Engl J Med 2007

Vacuna gripe atenuada intranasal
Seguridad LAIV en niños < 2 años

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12–23 mo	1308 (31.3)	1292 (31.0)	2600 (31.1)

Table 4. Medically Significant Wheezing, Serious Adverse Events, and Rates of Hospitalization According to Age Group, through 180 Days after the Last Dose of Vaccine.*

Age	Event	Live Attenuated Vaccine	Inactivated Vaccine
		no./total no. (%)	
6–11 mo	Medically significant wheezing	93/684 (13.6)	71/683 (10.4)
	Any serious adverse event	44/684 (6.4)	23/683 (3.4)
	Hospitalization for any cause	42/684 (6.1)	18/683 (2.6)
12–59 mo	Medically significant wheezing	272/3495 (7.8)	255/3490 (7.3)
	Any serious adverse event	92/3495 (2.6)	105/3490 (3.0)
	Hospitalization for any cause	88/3495 (2.5)	101/3490 (2.9)
6–59 mo	Medically significant wheezing	365/4179 (8.7)	326/4173 (7.8)
	Any serious adverse event	136/4179 (3.3)	128/4173 (3.1)
	Hospitalization for any cause	130/4179 (3.1)	119/4173 (2.9)

P=0,002

Belshe RB, et al. N Engl J Med 2007

La mayoría >6 sem después de la vacunación

Vacuna gripe atenuada intranasal
Seguridad LAIV 2-17 años

DOI:10.1111/j.1750-2659.2011.00243.x
www.influenzajournal.com

Original Article

An integrated, multistudy analysis of the safety of Ann Arbor strain live attenuated influenza vaccine in children aged 2–17 years

Christopher S. Ambrose, Tingting Yi, Judith Falloon

Ambrose C, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV 2-17 años metanálisis


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6 EC
LAIV vs TIV

14 EC
LAIV vs PB

Table 1. Number of subjects in safety populations from TIV- and placebo-controlled clinical studies

AE and reactogenicity event populations (refrigerated LAIV)	Year 1		Year 2
	Dose 1	Dose 2	
TIV-controlled studies			
Reactogenicity event population: LAIV	4108	2187	NA
Reactogenicity event population: TIV	4118	2223	NA
AE population: LAIV	4147	2230	NA
AE population: TIV	4182	2270	NA
Placebo-controlled studies			
Reactogenicity event population: LAIV	3245	2503	2287
Reactogenicity event population: Placebo	1994	1702	1248
AE population: LAIV	3278	2533	2295
AE population: Placebo	2026	1734	1256

4 EC
LAIV vs PB

SAE populations (Frozen & Refrigerated LAIV)	Year 1		Year 2	
	Days 0–42 PLD	Days 0–180 PLD	Days 0–42 PLD	Days 0–180 PLD
TIV-controlled studies				
LAIV	4245	4130	NA	NA
TIV	4278	4163	NA	NA
Placebo-controlled studies				
LAIV	10 693	2408	3212	2295
Placebo	5667	1546	1697	1256

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Vacuna gripe atenuada intranasal
Seguridad LAIV 2-17 años metanálisis


Original Article

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Table 2. Demographics of subjects by study type and vaccine received

	SAE population						Reactogenicity event/AE population					
	TIV-controlled		Placebo-controlled				TIV-controlled		Placebo-controlled			
	Year 1		Year 1		Year 2		Year 1		Year 1		Year 2	
	LAIV	TIV	LAIV	Placebo	LAIV	Placebo	LAIV	TIV	LAIV	Placebo	LAIV	Placebo
Number of subjects	4245	4278	10 693	5677	3212	1697	4147	4182	3278	2026	2295	1256
Age, year Mean (SD)	4·9 (3·9)	4·8 (3·8)	5·8 (4·3)	5·7 (4·4)	3·0 (1·1)	2·9 (1·0)	4·9 (3·9)	4·8 (3·8)	2·4 (2·0)	2·7 (2·7)	2·6 (0·6)	2·6 (0·6)
Range	2–17	2–17	2–17	2–17	2–7	2–7	2–17	2–17	2–17	2–17	2–4	2–4
Age, 24–35 month, *n*	1650	1647	4117	2383	1223	660	1650	1647	3149	1900	1063	574
Age, 36–59 month, *n*	1219	1247	1636	790	1615	866	1219	1247	11	4	1232	682
Age, 5–17 year, *n*	1376	1384	4940	2504	374*	171*	1278	1288	118	122	0	0
Gender, % Male	53·8	55·5	50·0	50·0	51·1	49·4	53·9	55·7	52·3	51·2	53·0	49·5
Region, %												
USA	22·1	22·4	68·7	63·4	28·5	26·0	20·3	20·6	0·5	0·8	0·0	0·0
Asia/Oceania†	3·1	3·1	14	17·5	25·4	31·2	3·2	3·2	45·7	48·9	35·5	42·1
Latin America	0·0	0·0	7·8	6·5	15·7	9·8	0·0	0·0	25·0	17·8	22·0	13·2
Africa‡	0·0	0·0	2·7	2·7	11·6	8·0	0·0	0·0	8·8	7·7	16·2	10·8
Europe§	74·8	74·5	6·7	9·9	18·8	25·0	76·5	76·2	19·9	24·8	26·4	33·8

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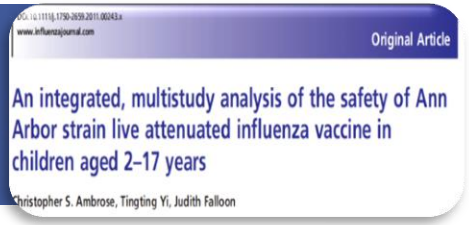
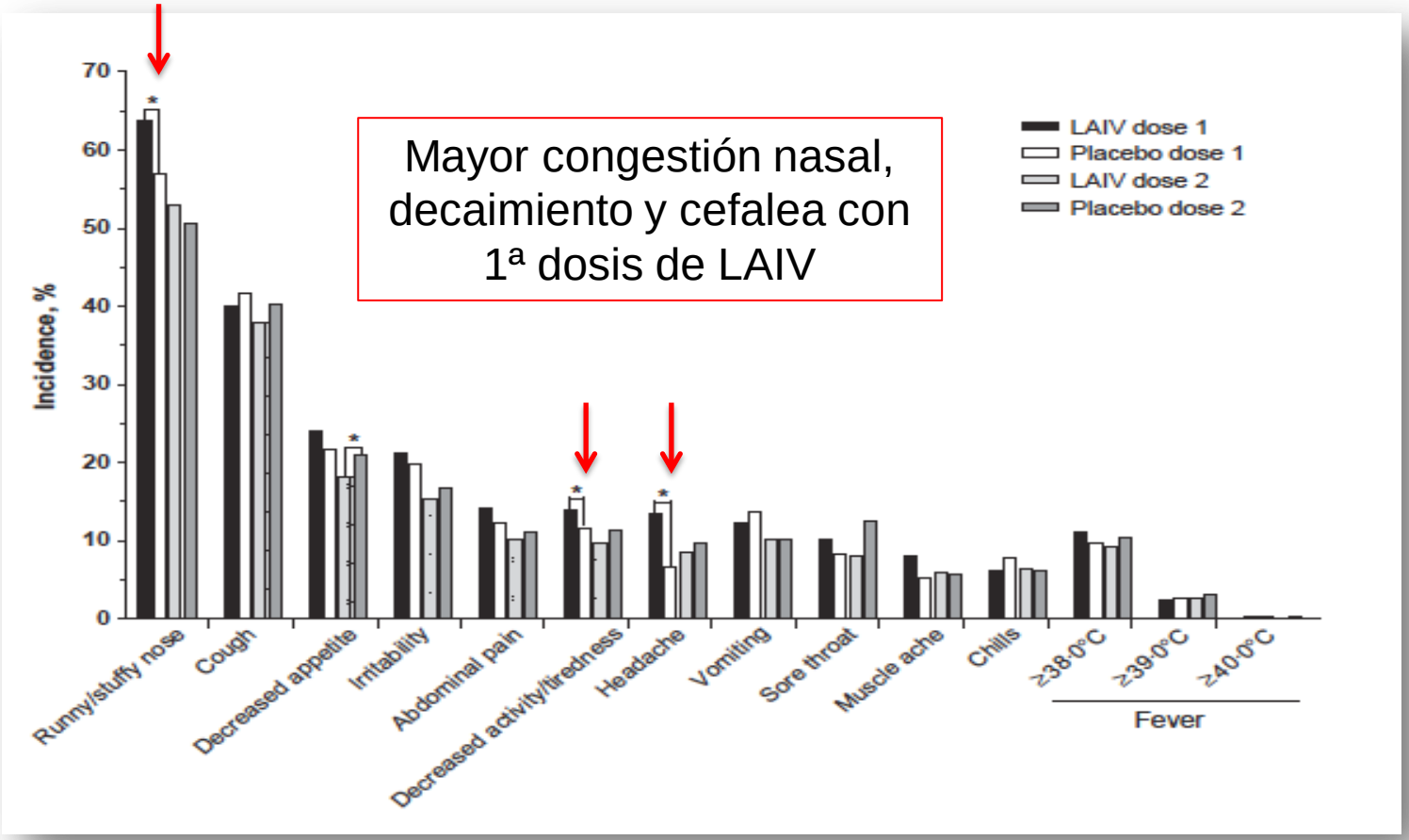
Vacuna gripe atenuada intranasal

Reactogenicidad LAIV vs placebo (1er año)



14 EC LAIV vs PB



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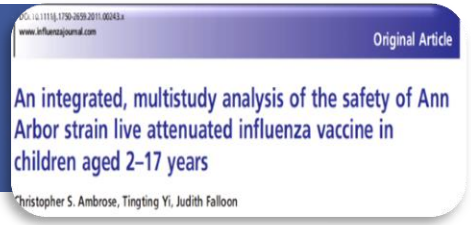
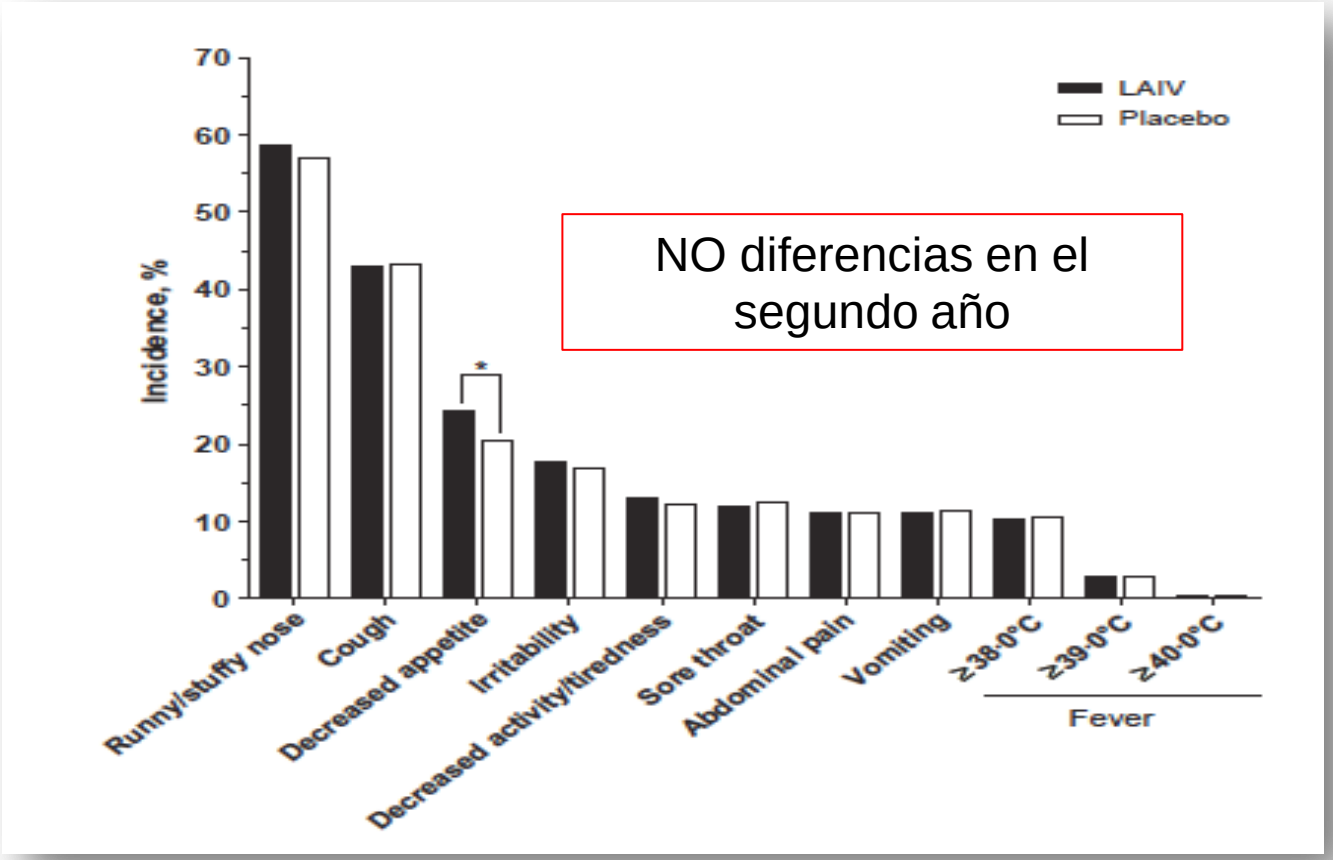
Vacuna gripe atenuada intranasal
Reactogenicidad LAIV vs placebo (2º año)



14 EC LAIV vs PB



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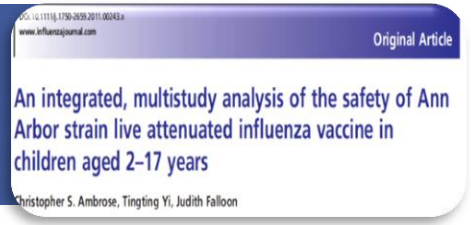
Vacuna gripe atenuada intranasal
Reactogenicidad LAIV vs TIV (2-17 años)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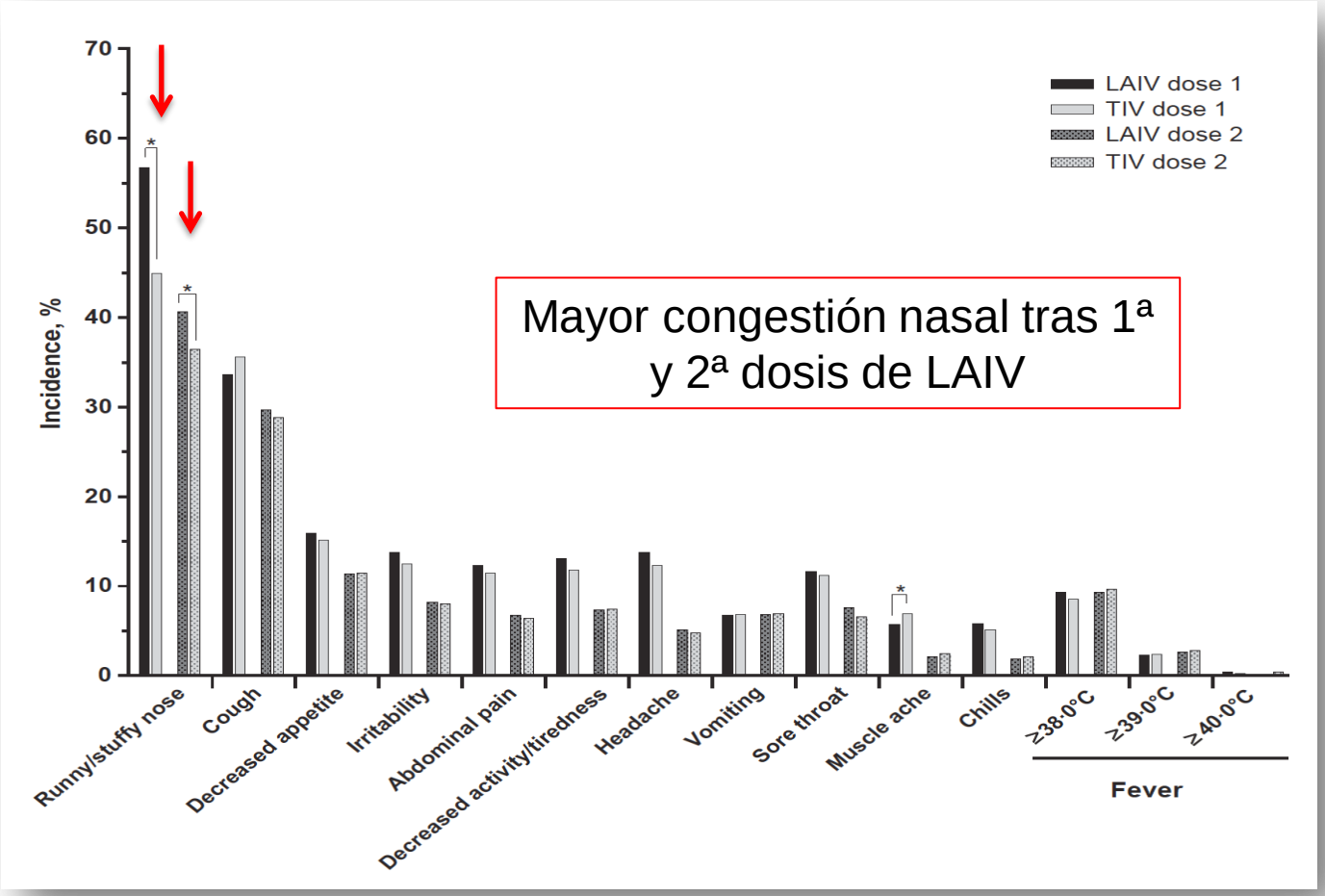
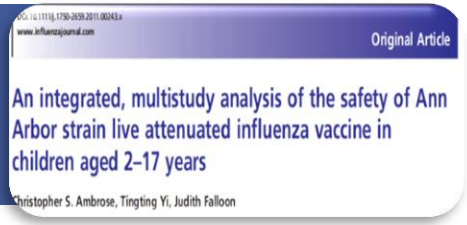


Mayor congestión nasal tras 1ª y 2ª dosis de LAIV

Ambrose C, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV vs placebo (2-17 años)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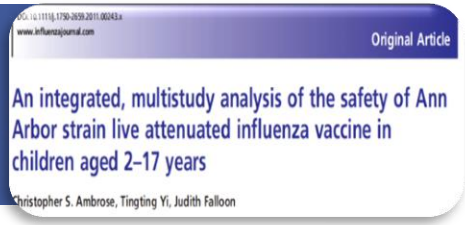
14 EC LAIV vs PB

Table 4. Adverse events (AEs) after LAIV and placebo administration in placebo-controlled studies

AEs	Year 1, dose 1			Year 1, dose 2			Year 2		
	LAIV, *n* (%)	Placebo, *n* (%)	Rate difference*	LAIV, *n* (%)	Placebo, *n* (%)	Rate difference*	LAIV, *n* (%)	Placebo, *n* (%)	Rate difference*
Total number of events	1380	841		893	657		955	482	
Subjects reporting ≥1 event	975 (29·7)	559 (27·6)	2·2	616 (24·3)	460 (26·5)	−2·2	624 (27·2)	336 (26·8)	0·4
Events by organ class with absolute rate difference ≥0·10%									
General disorders and administration site conditions	318 (9·7)	152 (7·5)	2·2†	147 (5·8)	119 (6·9)	−1·1	206 (9·0)	97 (7·7)	1·3
Injury, poisoning and procedural complications	25 (0·8)	8 (0·4)	0·4	13 (0·5)	6 (0·3)	0·2	4 (0·2)	5 (0·4)	−0·2
Psychiatric disorders	30 (0·9)	12 (0·6)	0·3	15 (0·6)	9 (0·5)	0·1	21 (0·9)	6 (0·5)	0·4
Nervous system disorders	13 (0·4)	4 (0·2)	0·2	5 (0·2)	2 (0·1)	0·1	4 (0·2)	0 (0·0)	0·2
Reproductive system and breast disorders	5 (0·2)	0 (0·0)	0·2	2 (0·1)	0 (0·0)	0·1	1 (0·0)	0 (0·0)	0·04
Metabolism and nutrition disorders	11 (0·3)	6 (0·3)	0·04	13 (0·5)	8 (0·5)	0·1	15 (0·7)	3 (0·2)	0·4
Immune system disorders	3 (0·1)	2 (0·1)	−0·01	0 (0·0)	2 (0·1)	−0·1	0 (0·0)	0 (0·0)	
Ear and labyrinth disorders	7 (0·2)	5 (0·2)	−0·03	1 (<0·1)	6 (0·3)	−0·3†	6 (0·3)	6 (0·5)	−0·2
Infections and infestations	388 (11·8)	243 (12·0)	−0·2	288 (11·4)	228 (13·1)	−1·8	230 (10·0)	124 (9·9)	0·1
Eye disorders	14 (0·4)	13 (0·6)	−0·2	18 (0·7)	5 (0·3)	0·4	8 (0·3)	3 (0·2)	0·1
Skin and subcutaneous tissue disorders	17 (0·5)	16 (0·8)	−0·3	15 (0·6)	11 (0·6)	−0·04	13 (0·6)	2 (0·2)	0·4
Gastrointestinal disorders	98 (3·0)	67 (3·3)	−0·3	70 (2·8)	34 (2·0)	0·8	46 (2·0)	30 (2·4)	−0·4
Respiratory, thoracic and mediastinal disorders	285 (8·7)	188 (9·3)	−0·6	198 (7·8)	137 (7·9)	−0·1	255 (11·1)	135 (10·7)	0·4
Events of interest									
Lower respiratory illness	58 (1·8)	37 (1·8)	−0·1	48 (1·9)	51 (2·9)	−1·0†	40 (1·7)	19 (1·5)	0·2
Wheezing illness	22 (0·7)	14 (0·7)	0·0	16 (0·6)	18 (1·0)	−0·4	17 (0·7)	7 (0·6)	0·2

Ambrose C, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV vs TIV (2-17 años)


Original Article

An integrated, multistudy analysis of the safety of Ann Arbor strain live attenuated influenza vaccine in children aged 2–17 years

Christopher S. Ambrose, Tingting Yi, Judith Falloon

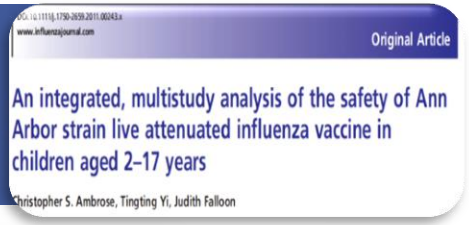
4 EC LAIV vs TIV

Table 3. Adverse events (AEs) during days 0–10 after LAIV and TIV administration in TIV-controlled studies

AEs	Year 1, dose 1			Year 1, dose 2		
	LAIV, *n* (%)	TIV, *n* (%)	Rate difference*	LAIV, *n* (%)	TIV, *n* (%)	Rate difference*
Total number of events, *n*	1292	1103		528	519	
Subjects reporting ≥1 events	860 (20·7)	755 (18·1)	2·7	359 (16·1)	363 (16·0)	0·1
Events by organ class with absolute rate difference ≥0·10%						
Infections and infestations	329 (7·9)	267 (6·4)	1·5†	192 (8·6)	175 (7·7)	0·9
Respiratory, thoracic and mediastinal disorders	270 (6·5)	209 (5·0)	1·5†	92 (4·1)	97 (4·3)	−0·1
Nervous system disorders	79 (1·9)	55 (1·3)	0·6†	5 (0·2)	7 (0·3)	−0·1
Eye disorders	44 (1·1)	32 (0·8)	0·3	16 (0·7)	12 (0·5)	0·2
Psychiatric disorders	27 (0·7)	16 (0·4)	0·3	4 (0·2)	8 (0·4)	−0·2
General disorders and administration site conditions	112 (2·7)	109 (2·6)	0·1	61 (2·7)	67 (3·0)	−0·2
Skin and subcutaneous tissue disorders	55 (1·3)	55 (1·3)	0·01	23 (1·0)	15 (0·7)	0·4
Surgical and medical procedures	5 (0·1)	7 (0·2)	−0·05	1 (0·0)	9 (0·4)	−0·4†
Immune system disorders	1 (0·0)	5 (0·1)	−0·1	1 (0·0)	1 (0·0)	0·0
Ear and labyrinth disorders	10 (0·2)	16 (0·4)	−0·1	9 (0·4)	8 (0·4)	0·1
Events of interest						
Lower respiratory illness	93 (2·2)	110 (2·6)	−0·4	51 (2·3)	60 (2·6)	−0·4
Wheezing illness	59 (1·4)	68 (1·6)	−0·2	19 (0·9)	30 (1·3)	−0·5

Ambrose C, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV 24-35 meses


Original Article

An integrated, multistudy analysis of the safety of Ann Arbor strain live attenuated influenza vaccine in children aged 2–17 years

Christopher S. Ambrose, Tingting Yi, Judith Falloon

Table 5. Adverse Events (AEs) and SAEs because of lower respiratory illness and wheezing in children 24–35 months of age

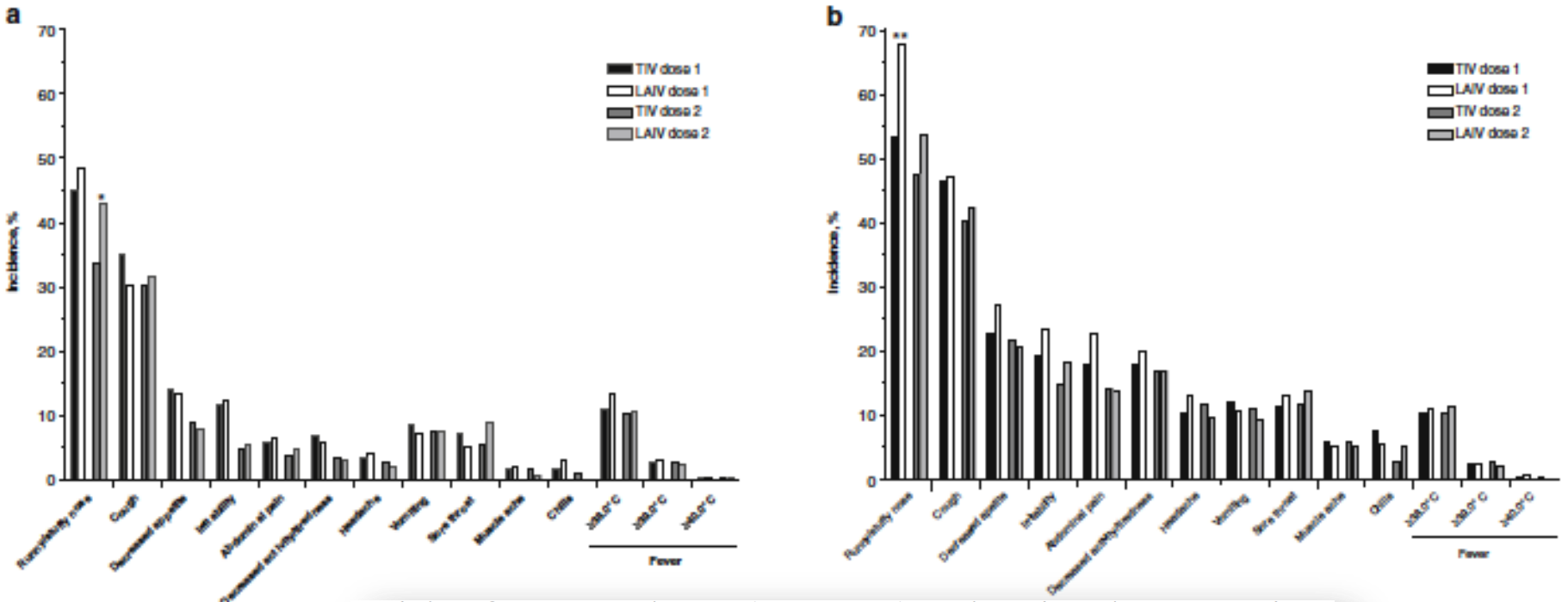
	Year 1						Year 2		
	Dose 1			Dose 2					
AEs, days 0–10	LAIV, *n* (%)	Comparator, *n* (%)	Rate difference*	LAIV, *n* (%)	Comparator, *n* (%)	Rate difference*	LAIV, *n* (%)	Comparator, *n* (%)	Rate difference*
TIV-controlled studies									
Lower respiratory illness	33 (2·0)	45 (2·7)	−0·7	27 (2·5)	28 (2·6)	−0·1	NA	NA	NA
Wheezing ill									
Placebo-contro									
Lower respir									
Wheezing ill									
SAEs									
TIV-controlled studies, days 0–42									
Lower respiratory illness	9 (0·55)	9 (0·55)	0·00			NA	NA	NA	
Wheezing illness	3 (0·18)	2 (0·12)	0·06			NA	NA	NA	
TIV-controlled studies, days 0–180									
Lower respiratory illness	29 (1·29)	19 (1·17)	0·12			NA	NA	NA	
Wheezing illness	6 (0·37)	3 (0·18)	0·18			NA	NA	NA	
Placebo-controlled studies, day 0–42									
Lower respiratory illness	13 (0·41)	8 (0·42)	−0·01			4 (0·38)	3 (0·52)	−0·15	
Wheezing illness	7 (0·22)	4 (0·21)	0·01			1 (0·09)	0 (0·00)	0·09	
Placebo-controlled studies, day 0–180									
Lower respiratory illness	28 (1·17)	15 (0·97)	0·20			7 (0·66)	4 (0·70)	−0·04	
Wheezing illness	9 (0·38)	5 (0·32)	0·05			2 (0·19)	0 (0·00)	0·19	

Subgroup analyses

For children aged 24–35 months, similar rates of lower respiratory and wheezing illness were observed among LAIV recipients and their corresponding TIV or placebo

Ambrose C, et al. Influenza Other Resp Vir 2011

Vacuna gripe atenuada intranasal
Seguridad LAIV HRB – asmáticos (2 EC; 6-71 ms)



trials of LAIV and TIV (N=1,940). Wheezing, lower respiratory illness, and hospitalization were not significantly in-

Increased upper respiratory symptoms and irritability were observed among LAIV recipients ($p<0.05$). Relative effica-

Ambrose CS, et al. Eur J Clin Microbiol Infect Dis 2012

Seguridad LAIV: asmáticos <5 años
Estudios post-comercialización

Table 3
Number of emergency department visits or hospitalizations for lower respiratory conditions among children with asthma or wheezing within 42 days of vaccination, season 3 (2009–2010).

Condition	LAIV (n = 8308) Events,[a] n	Rate[b] (95% CI)	TIV (n = 39,407) Events,[a] n	Rate[b] (95% CI)
Asthma	37	4.5 (3.1–6.1)	373	9.5 (8.5–10.5)
Bronchiolitis	2	0.2 (0.0–0.9)	29	0.7 (0.5–1.1)
Croup	23	2.8 (1.8–4.2)	144	3.7 (3.1–4.3)
Influenza[c]	23	2.8 (1.8–4.2)	150	3.8 (3.2–4.5)
Pneumonia	27	3.2 (2.1–4.7)	139	3.5 (3.0–4.2)
Any LRI[d]	110	13.2 (10.9–15.9)	806	20.5 (19.1–21.9)
Any hospitalization or ED visit	444	53.4 (48.6–58.7)	2657	67.4 (64.9–70.0)

Menor tasa de complicaciones respiratorias en siguientes 42 días post-vacunación que con TIV

Tennis P, et al. Vaccine 2012

Seguridad LAIV: <24 meses
Estudios post-comercialización

Table 2
Number of emergency department visits or hospitalizations for lower respiratory conditions among children <24 months of age within 42 days of vaccination, season 3 (2009–2010).

Condition	LAIV (n = 686)		TIV (n = 190,618)	
	Events,[a] n	Rate[b] (95% CI)	Events,[a] n	Rate[b] (95% CI)
Asthma	3	4.4 (0.9–12.7)	245	1.3 (1.1–1.5)
Bronchiolitis	1	1.5 (0.0–8.1)	407	2.1 (1.9–2.4)
Croup	2	2.9 (0.4–10.5)	701	3.7 (3.4–4.0)
Influenza[c]	2	2.9 (0.4–10.5)	476	2.5 (2.3–2.7)
Pneumonia	3	4.4 (0.9–12.7)	389	2.0 (1.8–2.3)
Total[d]	10	14.6 (7.0–26.6)	2153	11.3 (10.8–11.8)
Any hospitalization or ED visit	40	58.3 (41.7–79.4)	10,807	56.7 (55.6–57.8)

Discreto aumento complicaciones respiratorias

No diferencias hospitalizaciones o visitas a urgencias

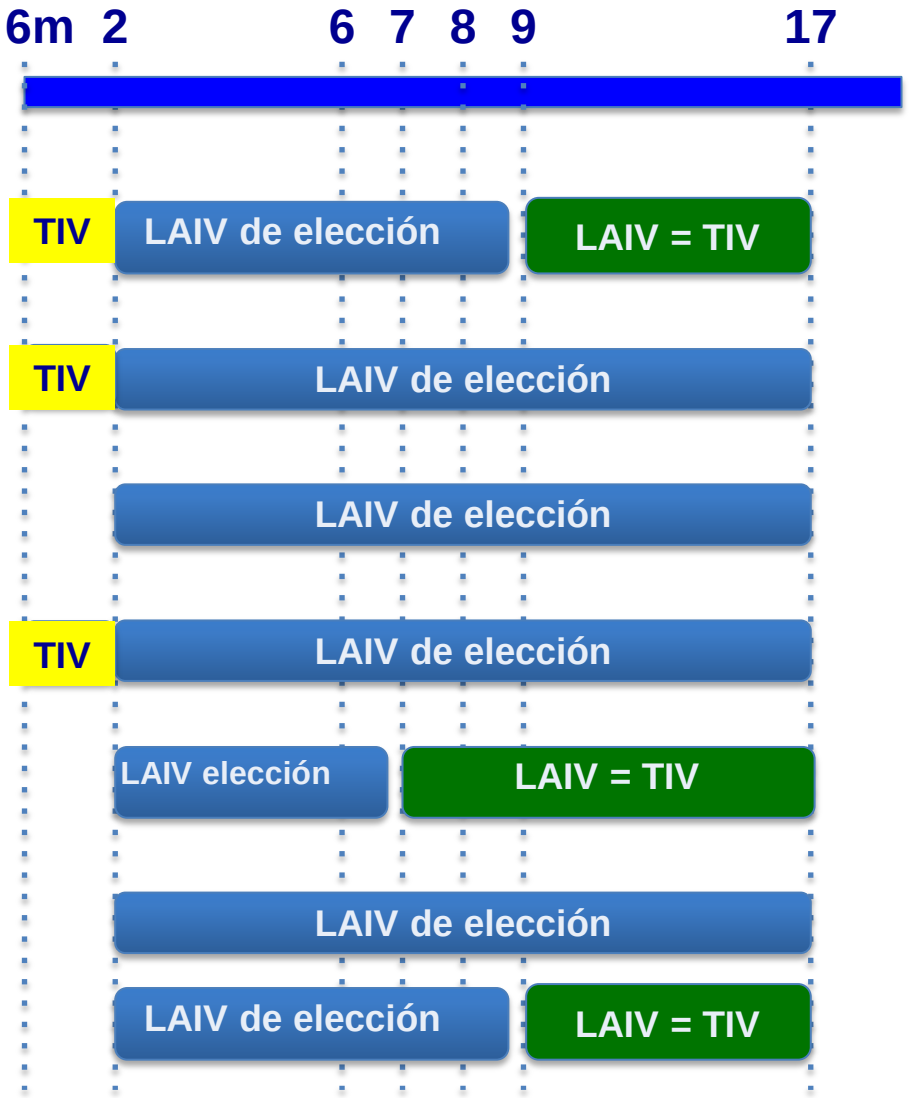
Tennis P, et al. Vaccine 2012

VACUNACION GRIPE INTRANASAL

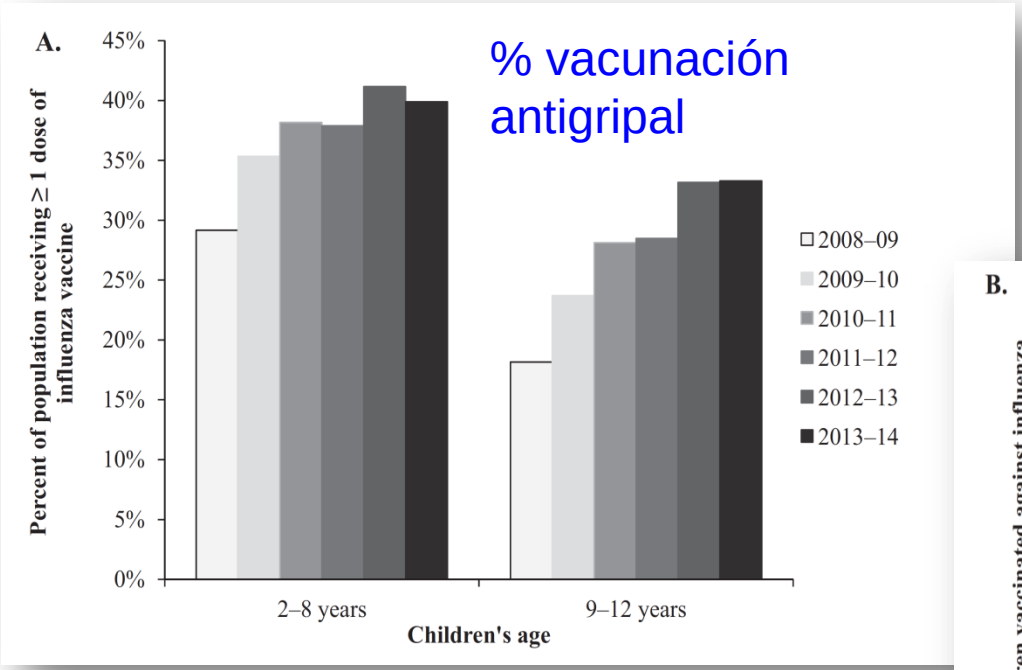
1. Introducción
2. ¿Qué es LAIV?
3. Ensayos clínicos: eficacia y seguridad
4. Recomendaciones oficiales
5. Efectividad
6. Perspectivas futuras y mensajes finales

Vacuna atenuada intranasal
Recomendaciones oficiales 2014 - 2015

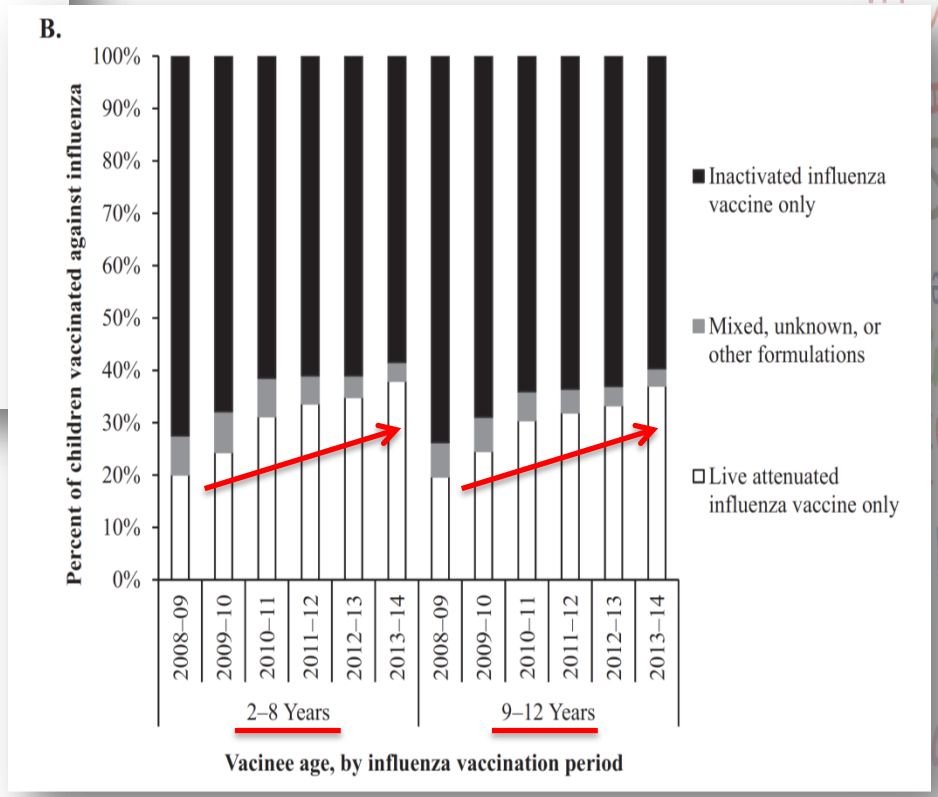
	País	Población
	USA	Niños sanos*
	Canadá	Niños sanos*
	UK	Niños sanos*
	Israel	Niños sanos*
	Alemania	Niños de grupos de riesgo
	Suecia	Niños de grupos de riesgo
	Noruega	Niños de grupos de riesgo



Vacuna gripe atenuada intranasal
Aceptabilidad en USA



% vacunación antigripal



Rodgers L, et al. Vaccine 2015

Vacuna gripe atenuada intranasal
Vacunación universal niños en UK

The childhood flu immunisation programme 2014/15

Information for schools participating in the pilot programmes

Public Health England

In July 2012, the JCVI recommended extending the programme to healthy children. This programme will lower the potentially serious impact of influenza on those children but should also have a more profound effect on influenza transmission. Children are the main source of transmission in the population, and this programme will therefore reduce the spread of infection from children to other children, to adults and to those in clinical risk groups of any age. The Secretary of State accepted this recommendation, and the implementation of the extension commenced in September 2013 with a general practice roll-out to children aged two and three years and seven geographic pilots in children aged 5-11 years.

This year, the programme in general practice will continue and there will be further pilots in primary and secondary schools designed to help us understand how best to vaccinate large numbers of children in a very short period of time. Using this information, it may prove possible to offer the vaccination to all children aged two to 16. Exactly how the programme will roll out year by year, and for how long, will be guided by the experience of the previous years' programmes.

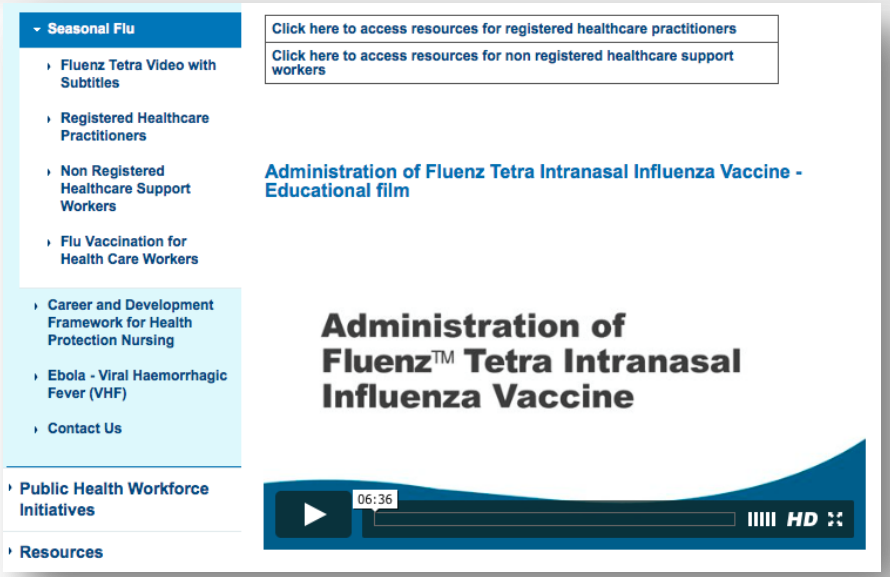
Disponible en:
https://www.gov.uk/government/collections/annual-flu-programme

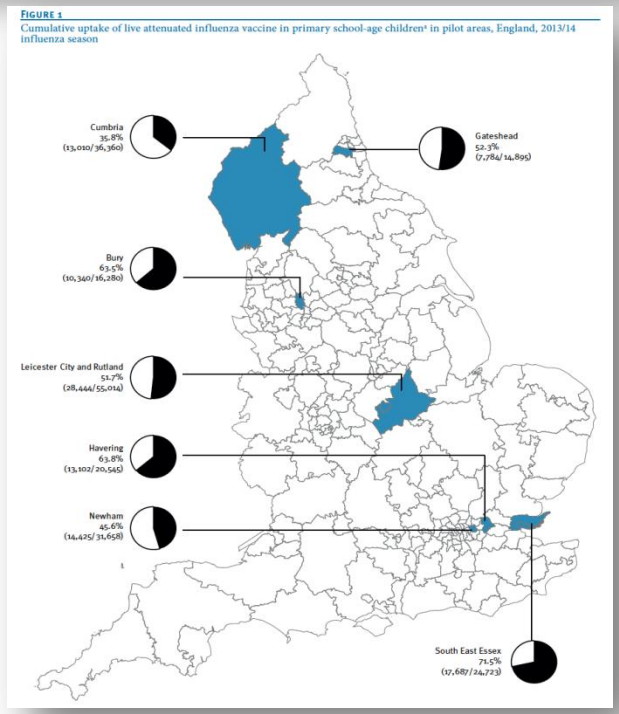
Vacuna gripe atenuada intranasal
Vacunación universal niños en UK

The children's flu immunisation programme 2013/14

There are two elements to the children's flu immunisation programme this year:

- a routine offer of vaccination to all two and three year olds (but not four years or older) on the 1 September 2013; and
- geographical pilots for four to ten year olds (up to and including pupils in school year 6).





Disponible en:
https://www.gov.uk/government/collections/annual-flu-programme

VACUNACION GRIPE INTRANASAL

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6. Perspectivas futuras y mensajes finales

Vacuna gripe atenuada intranasal
Efectividad en UK

SURVEILLANCE AND OUTBREAK REPORTS

Uptake and impact of a new live attenuated influenza vaccine programme in England: early results of a pilot in primary school-age children, 2013/14 influenza season

R G Pebody (Richard.Pebody@phe.gov.uk)[1], H K Green[1], N Andrews[1], H Zhao[1], N Boddington[1], Z Bawa[1], H Durnall[2], N Singh[1], A Sunderland[1], L Letley[1], J Ellis[1], A J Elliot[1], M Donati[1], G E Smith[1], S de Lusignan[2,3], M Zambon[1]

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Citation style for this article:
Pebody RG, Green HK, Andrews N, Zhao H, Boddington N, Bawa Z, Durnall H, Singh N, Sunderland A, Letley L, Ellis J, Elliot AJ, Donati M, Smith GE, de Lusignan S, Zambon M. Uptake and impact of a new live attenuated influenza vaccine programme in England: early results of a pilot in primary school-age children, 2013/14 influenza season. Euro Surveill. 2014;19(22):pii=20823. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20823

Article submitted on 12 May 2014 / published on 05 June 2014

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Statistics

Weekly national flu reports

From: Public Health England
First published: 19 June 2014
Last updated: 5 March 2015 , see all updates
Part of: Pandemic flu: public health response, Respiratory syncytial virus (RSV): guidance, data and analysis and Seasonal influenza: guidance, data and analysis

National influenza reports for winter 2013 onward, tracking seasonal flu and other seasonal respiratory illnesses in the UK.

Documents

Pre-release access: 2014 to 2015 weekly influenza surveillance report
PDF, 88.9KB, 1 page
This file may not be suitable for users of assistive technology.
Request a different format.

National flu report: 5 March 2015 (week 10)
PDF, 613KB, 11 pages
This file may not be suitable for users of assistive technology.
Request a different format.

National flu report surveillance: 5 March 2015 (week 10)
PDF, 439KB, 34 pages

RAPID COMMUNICATIONS

Low effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: 2014/15 mid–season results

R G Pebody (Richard.Pebody@phe.gov.uk)[1], F Warburton[1], J Ellis[2], N Andrews[1], C Thompson[2], B von Wissmann[3], H K Green[1], S Cottrell[4], J Johnston[5], S de Lusignan[6], C Moore[7], R Gunson[8], C Robertson[9,10], J McMenamin[3], M Zambon[2]

1. Public Health England Centre of Infectious Disease Surveillance and Control, London, United Kingdom
2. Public Health England Operations Directorate, Microbiology Services, Colindale, London, United Kingdom
3. Health Protection Scotland, Glasgow, United Kingdom
4. Public Health Wales, Cardiff, United Kingdom
5. Public Health Agency Northern Ireland, Belfast, United Kingdom
6. Royal College of General Practitioners Research and Surveillance Centre, United Kingdom
7. Public Health Wales Molecular Diagnostics Unit, Cardiff, United Kingdom
8. West of Scotland Specialist Virology Centre, Glasgow, United Kingdom
9. University of Strathclyde, Glasgow, United Kingdom
10. International Prevention Research Institute, Lyon, France

Citation style for this article:
Pebody RG, Warburton F, Ellis J, Andrews N, Thompson C, von Wissmann B, Green HK, Cottrell S, Johnston J, de Lusignan S, Moore C, Gunson R, Robertson C, McMenamin J, Zambon M. Low effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza in primary care in the United Kingdom: 2014/15 mid–season results. Euro Surveill. 2015;20(5):pii=21025. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21025

Article submitted on 30 January 2015 / published on 05 February 2015

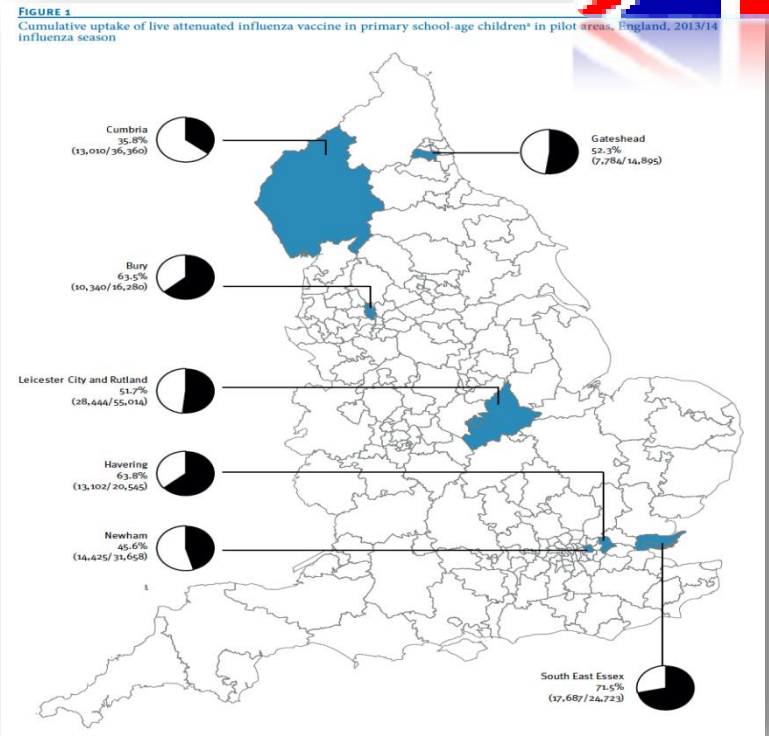
https://www.gov.uk/government/collections/annual-flu-programme

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)

- Desde 2013-2014
- En todo UK
- **Vacunación universal**
  LAIV niños 2-3 años

Cobertura media:

- **2 años: 42,6 %**
  (308.925 / 724.747)
- **3 años: 39,6 %**
  (285.616 / 722.048)



- Programa piloto en 7 áreas de UK (5 %)
- Vacunación universal LAIV niños 4-11 años

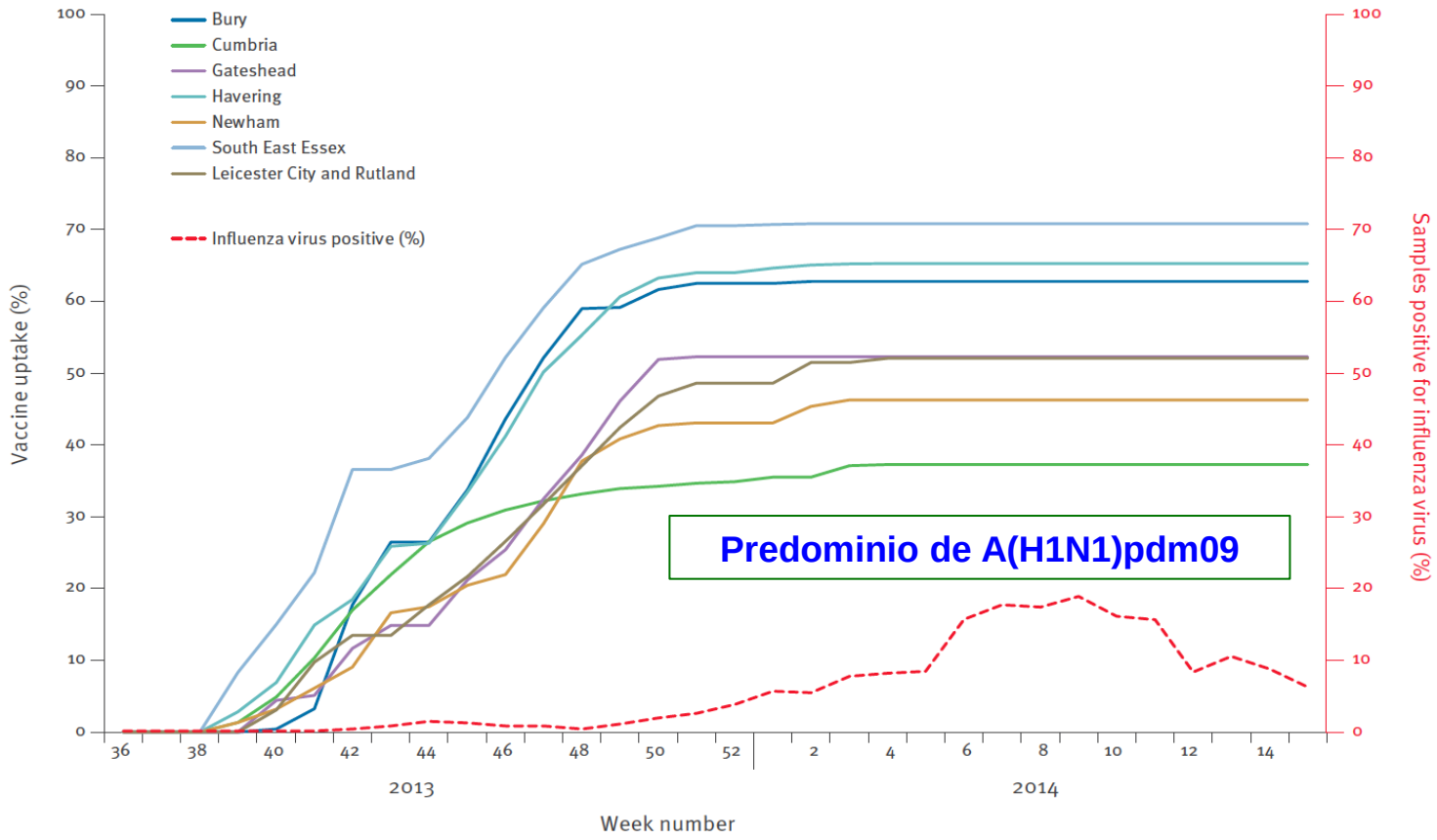
Cobertura : 52,5 % (36-72 %)
(104.792 / 199.475)

Pebody RG, et al. Eurosurveillance 2014

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)

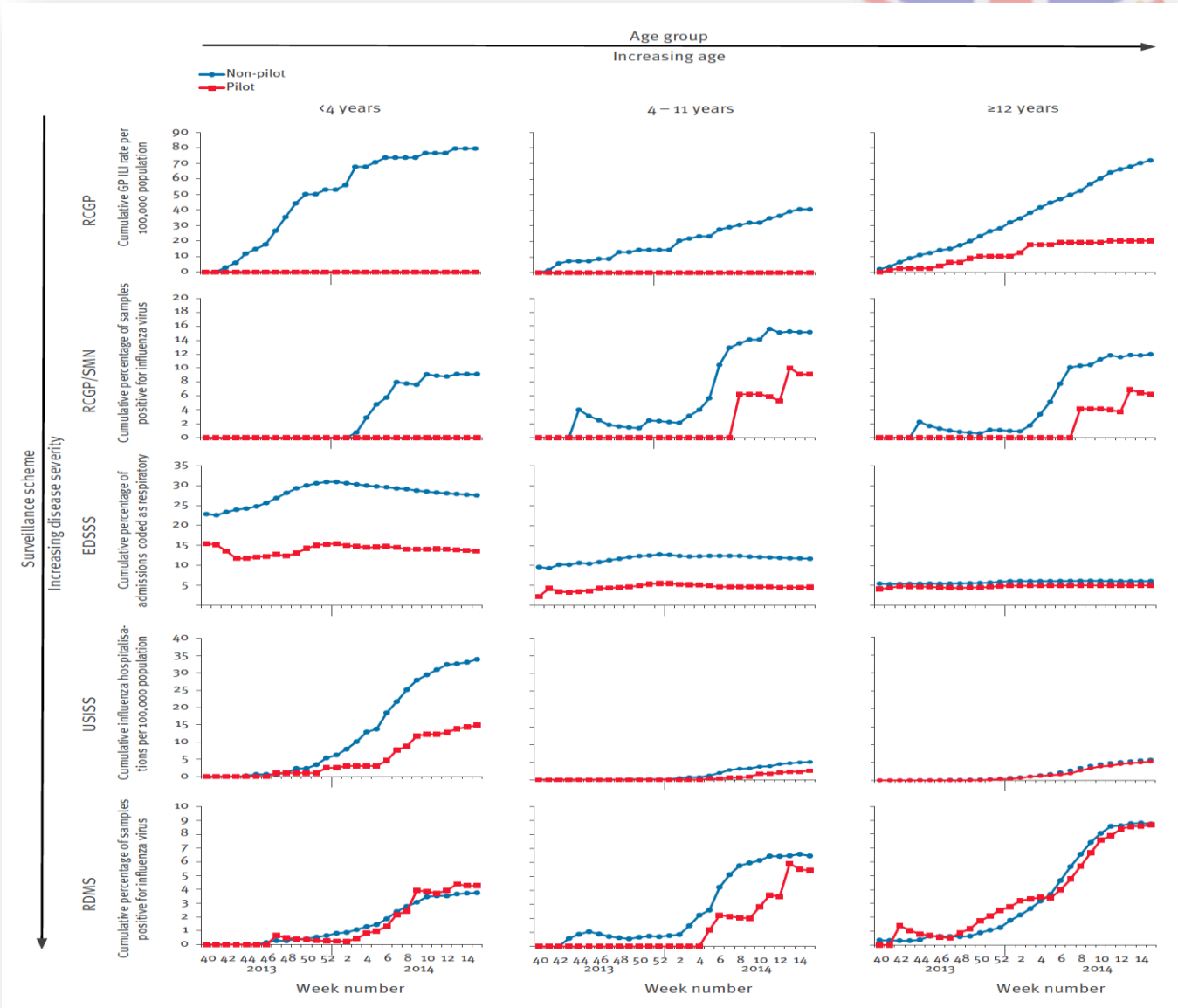
FIGURE 2

Estimated weekly proportion of uptake of live attenuated influenza vaccine in primary school-age children[a] by pilot area and weekly proportion of samples positive for influenza virus[b], England, 2013/14 influenza season[c]



Pebody RG, et al. Eurosurveillance 2014

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)



Pebody RG, et al.
Eurosurveillance 2014

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)

Surveillance scheme	Disease indicator	Age group (years)	Pilot areas	Non-pilot areas	Ratio[b] (95% CI)	p value
RCGP	Number of sentinel GPs		9	78		
	Cumulative GP ILI consultation rate per 100,000 population[c]	<4	0.0 (0/3,641)	73.6 (27/36,672)	0 (0–1.47)	0.170
		4–11	0.0 (0/7,809)	37.9 (28/73,957)	0 (0–1.33)	0.110
		≥12	20.3 (16/78,953)	66.8 (483/723,075)	0.38 (0.08–1.86)	0.232
		Total	17.7 (16/90,403)	64.5 (538/833,704)	0.34 (0.07–1.72)	0.194

Menor número de consultas por sdr gripal
en Atención Primaria
en niños <18 años
en las áreas del estudio piloto
17,7 / 100.000 versus 64,5 /100.000

Eficacia vacunal estimada: 66 %

Pebody RG, et al. Eurosurveillance 2014

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)

Surveillance scheme	Disease indicator	Age group (years)	Pilot areas	Non-pilot areas	Ratio[b] (95% CI)	p value
RCGP/SMN	Number of swabbing GPs		10	76		
	Cumulative proportion (%) of swabs positive for influenza (n/N)[d]	<4	NA	9.1	1 (0–4.58)	1.000
			(0/9)	(17/186)		
		4–11	9.1	15.1	0.49 (0.07–3.26)	0.462
			(2/22)	(23/152)		
		≥12	9.1	17.3	0.54 (0.28–1.04)	0.067
			(13/143)	(221/1,276)		
		Total	8.5	16.2	0.53 (0.28–1.01)	0.055
			(15/176)	(265/1,634)		

Menor número de muestras influenza positivas
en Atención Primaria
en niños <18 años
en las áreas del estudio piloto
8,5 / 100.000 versus 16,2 /100.000

Eficacia vacunal estimada: 47 %

Pebody RG, et al. Eurosurveillance 2014

Vacuna gripe atenuada intranasal
Efectividad en UK (2013-2014)

Surveillance scheme	Disease indicator	Age group (years)	Pilot areas	Non-pilot areas	Ratio[b] (95% CI)	p value
USISS	Number of sentinel NHS hospital trusts		9	26		
	Cumulative incidence of laboratory-confirmed influenza hospitalisations per 100,000 population[c]	<4	14.8 (29/195,379)	31.4 (146/465,442)	0.37 (0.11–1.25)	0.111
		4–11	2.6 (9/352,911)	5.0 (42/840,722)	0.28 (0.13–1.56)	0.203
		≥12	5.3 (174/3,293,487)	5.8 (452/7,845,918)	0.93 (0.43–2.04)	0.858
		Total	5.5 (212/3,841,777)	7.0 (640/9,152,082)	0.76 (0.33–1.75)	0.516

Menor número de ingresos por influenza confirmados
en Atención Hospitalaria
en niños <18 años
en las áreas del estudio piloto
5,5 / 100.000 versus 7,0 /100.000

Eficacia vacunal estimada: 24 %

Pebody RG, et al. Eurosurveillance 2014

Vacuna gripe atenuada intranasal Efectividad en UK (2013-2014)

Con una cobertura media del 52 % (36 – 72 %)

Aunque los resultados no son estadísticamente significativos

Menos gripe en <18 años en las áreas de vacunación universal con LAIV en niños 2-3 años

Resultados menos llamativos en niños mayores y para formas graves (hospitalizaciones)

Pebody RG, et al. Eurosurveillance 2014

Discussion

This pilot universal paediatric influenza vaccination programme achieved an overall uptake of 53% (ranging from 36 to 72% in individual pilot areas) in primary school-age children in the first year of implementation in England. Although the results were not statistically significant, the cumulative disease incidence was lower in pilot relative to non-pilot areas in both targeted and non-targeted age groups for a range of influenza indicators – both laboratory-confirmed and syndromic. These observed differences were smaller for more severe disease end-points.

Vacuna gripe atenuada intranasal Efectividad en UK (2013-2014)

LIMITACIONES POTENCIALES

Cepa predominante: A(H1N1) Virulencia leve-moderada

Memoria inmunitaria desde 2009-2010

Programa de reclutamiento de casos novedoso: infradiagnóstico potencial

Pebody RG, et al. Eurosurveillance 2014

There are several potential limitations to this study. Firstly, the 2013/14 influenza season in the UK was characterised by influenza A(H1N1)pdm09 virus circulation, the novel pandemic strain that first emerged in 2009: across surveillance schemes, only moderate influenza activity was seen predominately in the hospital-based surveillance systems and mainly in younger adults. There was little signal of influenza activity either in primary care or from syndromic surveillance, nor was there evidence of excess mortality in elderly people. Along with the small geographical coverage of the pilot areas, this will have limited the ability of the school-age pilot programme to detect evidence of direct and indirect impact. Secondly, older people, who are typically susceptible to severe disease following influenza virus infection, are recognised to have background immunity to influenza A(H1N1)pdm09 [23], hence the lack of impact in relation to excess mortality among elderly people and why so few lives are likely to have been saved by the LAIV programme in the 2013/14 influenza season. Thirdly, the potential indirect effects of the programme (through reduction in transmission) would be diluted through opportunities for populations (e.g. adult unvaccinated groups) to move back and forth into pilot areas, thus reducing the potential herd effects of vaccinated paediatric groups. This may also explain why the time to peak positivity was shorter for non-pilot compared with pilot areas for some indicators. Fourthly, we were very aware of the possibility of cluster effects, with the data being at the GP or hospital trust level. For this reason, we carefully examined each outcome indicator for evidence of overdispersion and as a consequence employed the more conservative negative binomial regression (rather than Poisson regression). Fifthly, a sample of GP practices and hospitals were newly recruited to surveillance

Vacuna gripe atenuada intranasal
Programa UK (2014-2015)

Vaccination

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- Provisional data from the fourth monthly collection of influenza vaccine uptake up to 31 January 2015 by targeted groups has been published. The report provides uptake at national, area team and CCG level. Up to the end of January 2015, the provisional proportion of people in England who had received the 2014/15 influenza vaccine in targeted groups was as follows:
  - 50.3% in under 65 years in a clinical risk group
  - 44.1% in pregnant women
  - 72.8% in 65+ year olds
  - 38.5% in all 2 year olds
  - 41.3% in all 3 year olds
  - 32.9% in all 4 year olds

Low effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza i… care in the United Kingdom: 2014/15 mid-s…

	Cases (vaccinated : unvaccinated)	Controls (vaccinated : unvaccinated)	Crude VE (95% CI)	Adjusted[a] VE (95% CI)
All influenza (A and B)	65 : 247	177 : 825	−26.7% (−74.0 to 7.8)	3.4% (−44.8 to 35.5)
All influenza A	64 : 232		−32.2% (−82.2 to 4.0)	−0.7% (−52.0 to 33.2)
Influenza A(H3N2) only	61 : 210		−39.8% (−94.1 to −0.7)	−2.3% (−56.2 to 33.0)

Weekly report HPA 2015
Pebody et al. Eurosurveillance 2015

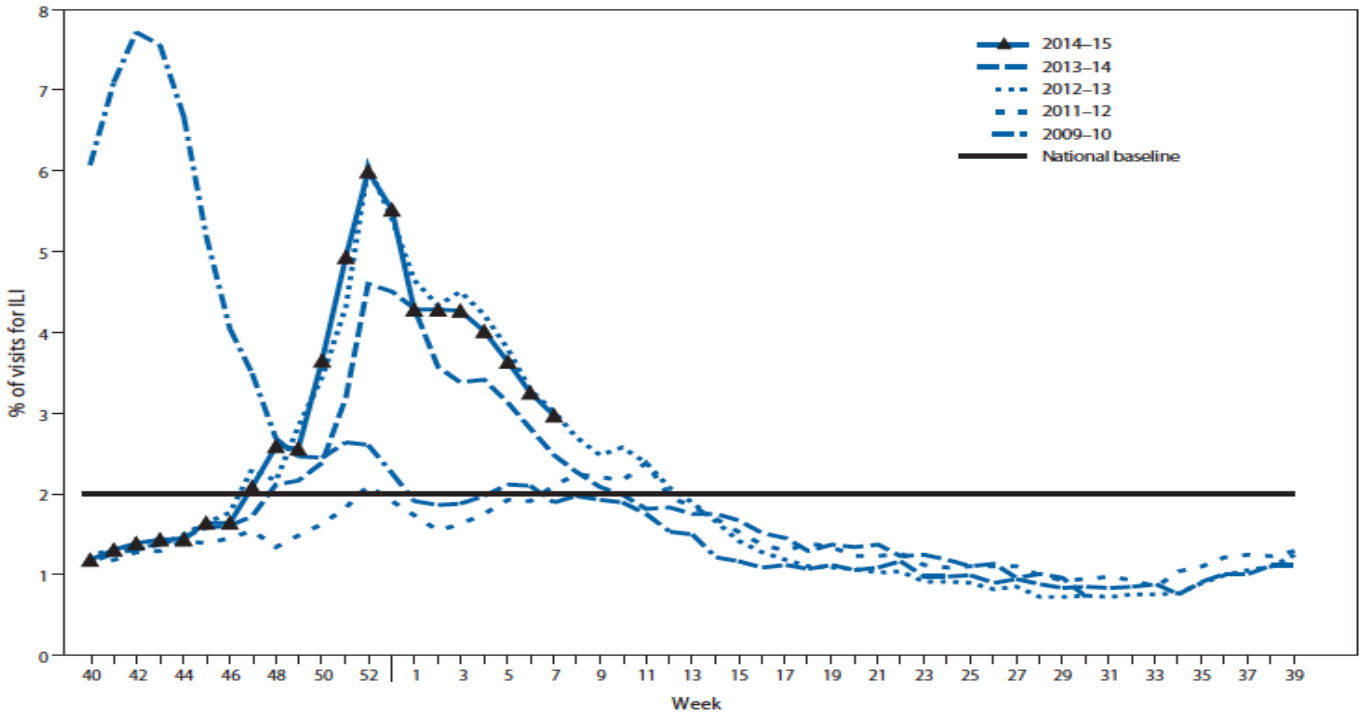
Vacuna gripe atenuada intranasal
Efectividad en USA

Morbidity and Mortality Weekly Report

MMWR / March 6, 2015 / Vol. 64 / No. 8

Update: Influenza Activity — United States, September 28, 2014–February 21, 2015

FIGURE 2. Percentage of visits for influenza-like illness (ILI)* reported to CDC, by surveillance week — Outpatient Influenza-Like Illness Surveillance Network, United States, 2014–15 influenza season and selected previous influenza seasons



CDC. MMWR - March 6, 2015

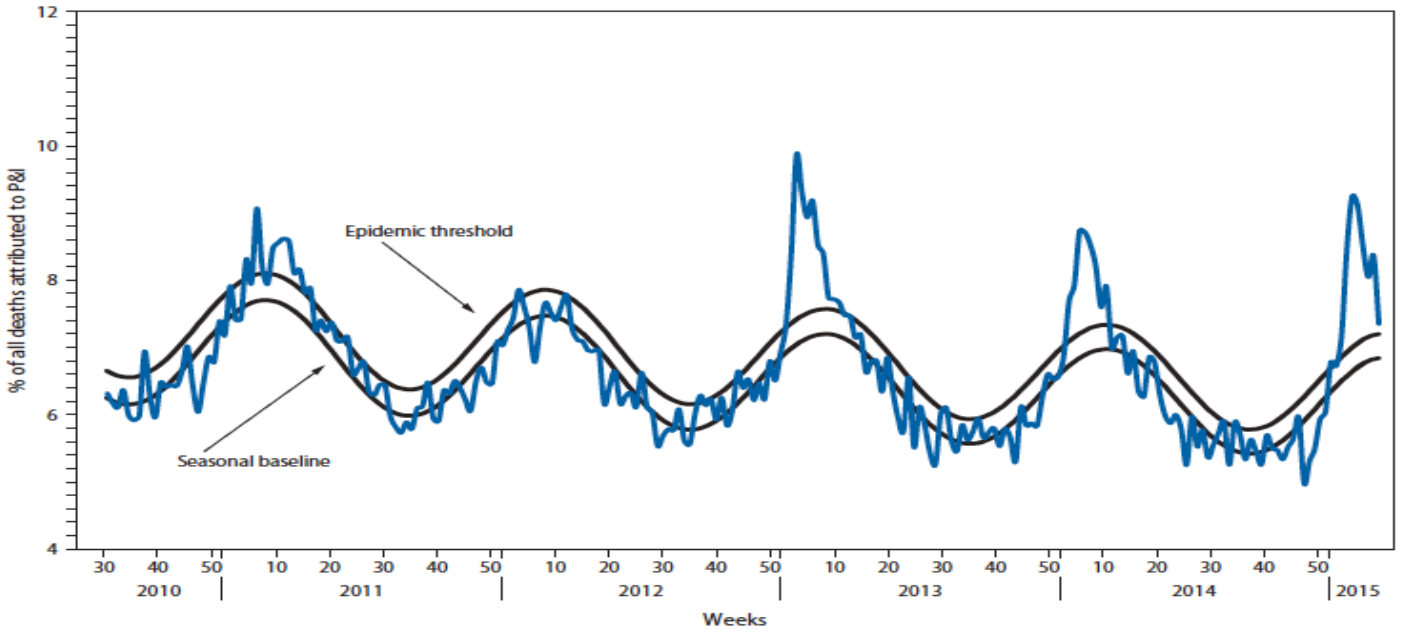
Vacuna gripe atenuada intranasal
Efectividad en USA

Morbidity and Mortality Weekly Report

MMWR / March 6, 2015 / Vol. 64 / No. 8

Update: Influenza Activity — United States, September 28, 2014–February 21, 2015

FIGURE 4. Percentage of all deaths attributable to pneumonia and influenza (P&I), by surveillance week and year* — 122 Cities Mortality Reporting System, United States, 2010–2015



* Data as of February 21, 2015.

CDC. MMWR - March 6, 2015

VACUNACION GRIPE INTRANASAL

1. Introducción
2. ¿Qué es LAIV?
3. Ensayos clínicos: eficacia y seguridad
4. Recomendaciones oficiales
5. Efectividad
6. Situaciones especiales
7. Perspectivas futuras y mensajes finales

Vacuna gripe atenuada intranasal
Perspectivas futuras en España

¿cuál puede ser el papel de LAIV en nuestro medio?

¿tendrá mayor aceptación que TIV?

¿será más efectiva que TIV?

¿podría ser incluida en los programas de vacunación de las CC.AA.?

¿podría desencadenar la recomendación de vacunación universal?

MENSAJES FINALES

1. LAIV tetra aprobada en España en 2 a 18 años

2. Ha demostrado ser más eficaz que las vacunas antigripales inactivadas

3. Ha demostrado ser segura en >2 años

4. Ha demostrado ser segura en asmáticos y otros enfermos crónicos. Contraindicada en asmáticos graves e inmunodeprimidos

MENSAJES FINALES

5. Incluida en calendarios sistemáticos relevantes: UK, USA, Canadá

6. Vacuna que podría tener perfil de sistemática en un futuro cercano

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Muchas gracias