Estudios de efectividad de la vacunación en EE. UU. con vacunas de gripe atenuadas

2017 - Jornadas de Oviedo,

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Potencial conflicto de intereses

Investigador Principal en 2 ensayos clínicos I+D (fases II-III) con vacuna antigripal atenuada intranasal (MedImmune) en el año 2004

ORIGINAL STUDIES

Superior Relative Efficacy of Live Attenuated Influenza Vaccine Compared With Inactivated Influenza Vaccine in Young Children With Recurrent Respiratory Tract Infections

Shai Ashkenazi, MD, MSc, Andre Vertruyen, MD,† Javier Aristegui, MD,‡ Susanna Esposito, MD,§ David Douglas McKeith, MBChB, MRCGP,¶ Timo Klemola, MD,‖ Jiri Biolek, MD,# Joachim Kühr, MD,** Tadeusz Bujnowski, MD, PhD,†† Daniel Desgrandchamps, MD,‡‡ Shean-Mei Cheng, PhD,§§ Jonathan Skinner, PhD,§§ William C. Gruber, MD,§§ and Bruce D. Forrest, MB, BS, MD,§§ for the CAIV-T Study Group*

Background: Young children have a high incidence of influenza and influenza-related complications. This study compared the efficacy and safety of cold-adapted influenza vaccine, trivalent (CAIV-T) with trivalent inactivated influenza vaccine (TIV) in young children with a history of recurrent respiratory tract infections (RTIs).

Methods: Children 6 to 71 months of age were randomized to receive 2 doses of CAIV-T (n = 1161) or TIV (n = 1686), 35 ± 7 days apart before the start of the 2002–2003 influenza season and were followed up for culture-co... outcomes, reactogenicity, and adv...

Results: Overall, 52.7% (95% co... 72.2%) fewer cases of influenza ca... similar to vaccine were observed i... Greater relative efficacy for CAIV... cally similar A/H1N1 (100.0%; 9... (68.0%; 95% CI = 37.3%–84.8%... cally similar A/H3N2 strains (–... 31.5%). Relative to TIV, CAIV-... related healthcare provider visits f... and missed days of school, kinderg... CI = 16.8%–21.6%). Rhinitis a... decreased appetite were the only ... frequently in CAIV-T subjects. T... groups in the incidence of wheezi...

Conclusions: CAIV-T was well tolerated in these children with RTIs and demonstrated superior relative efficacy compared with TIV in preventing influenza illness.

Key Words: influenza, respiratory tract infection, cold-adapted influenza vaccine, trivalent, children

(*Pediatr Infect Dis J* 2006;25: 870–879)

adolescents and is ... complications,[1,2] par... itable trivalent inac... ...lly approved in the ...s of age and older.[5] ...r than 5 years of age ...o 83%.[6–8] ...e (LAIV; FluMist; ...rozen, cold-adapted, ... vaccine approved in ...nfluenza in healthy ...f age and in healthy ...y children 15 to 85 ...o reduce the rate of ...o reduce episodes of ...0%, compared with ...blished report of the ...r wheezing,[12] and a ...t of asthma in young ...recurrent respiratory ...zing illness. Such a ... significantly from a ... but also might be ...ciated with an atten...

Accepted for publication July 14, 200... From the *Schneider Children's Medic... Vincentius Hospital, Antwerp, Bel... Spain; ‡Institute of Paediatrics, Un... **Dapedale Maugiore Policlinico, ... Italy; ¶Vocational Surgery, Irvine; ... Helsinki, Espoo, Finland; #Hosp... **Clinic for Paediatric and Ado... Karlsruhe, Karlsruhe, Germany; ... Poland; ‡‡Children's Hospital, Lu... cines Research, Pearl River, NY.

This study was funded by Wyeth Vac...

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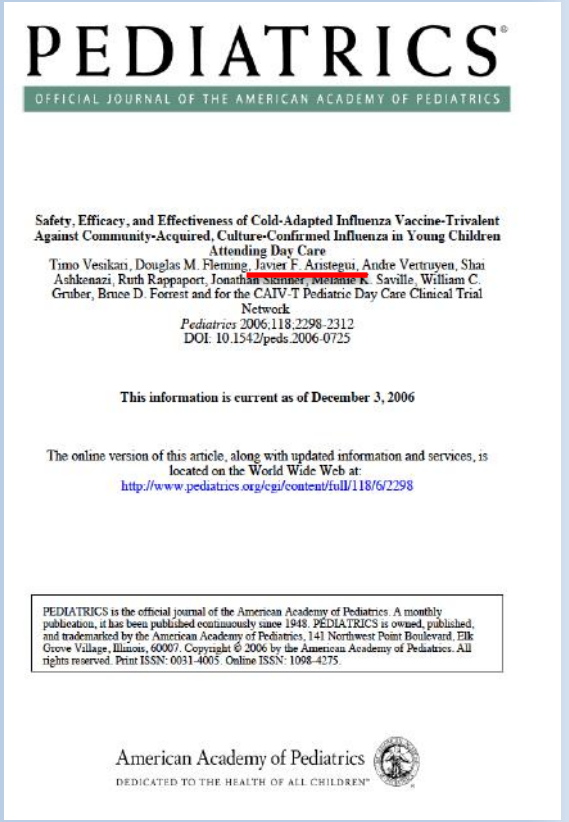
DOI: 10.1097/01.inf.0000237829.66110.85

compare the efficacy ... vaccine, trivalent ...-stable formulation ...-confirmed influenza during the 2002–2003 influenza season in children aged 6 to 71 months with a history of recurrent respiratory tract infections (RTIs).

870 *The Pediatric Infectious Disease Journal* • Volume 25, Number 10, October 2006

The Pediatric Infectious Disease Journal



PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Safety, Efficacy, and Effectiveness of Cold-Adapted Influenza Vaccine-Trivalent Against Community-Acquired, Culture-Confirmed Influenza in Young Children Attending Day Care

Timo Vesikari, Douglas M. Fleming, Javier F. Aristegui, Andre Vertruyen, Shai Ashkenazi, Ruth Rappaport, Jonathan Skinner, Melanie R. Saville, William C. Gruber, Bruce D. Forrest and for the CAIV-T Pediatric Day Care Clinical Trial Network

Pediatrics 2006;118;2298-2312
DOI: 10.1542/peds.2006-0725

This information is current as of December 3, 2006

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://www.pediatrics.org/cgi/content/full/118/6/2298

American Academy of Pediatrics
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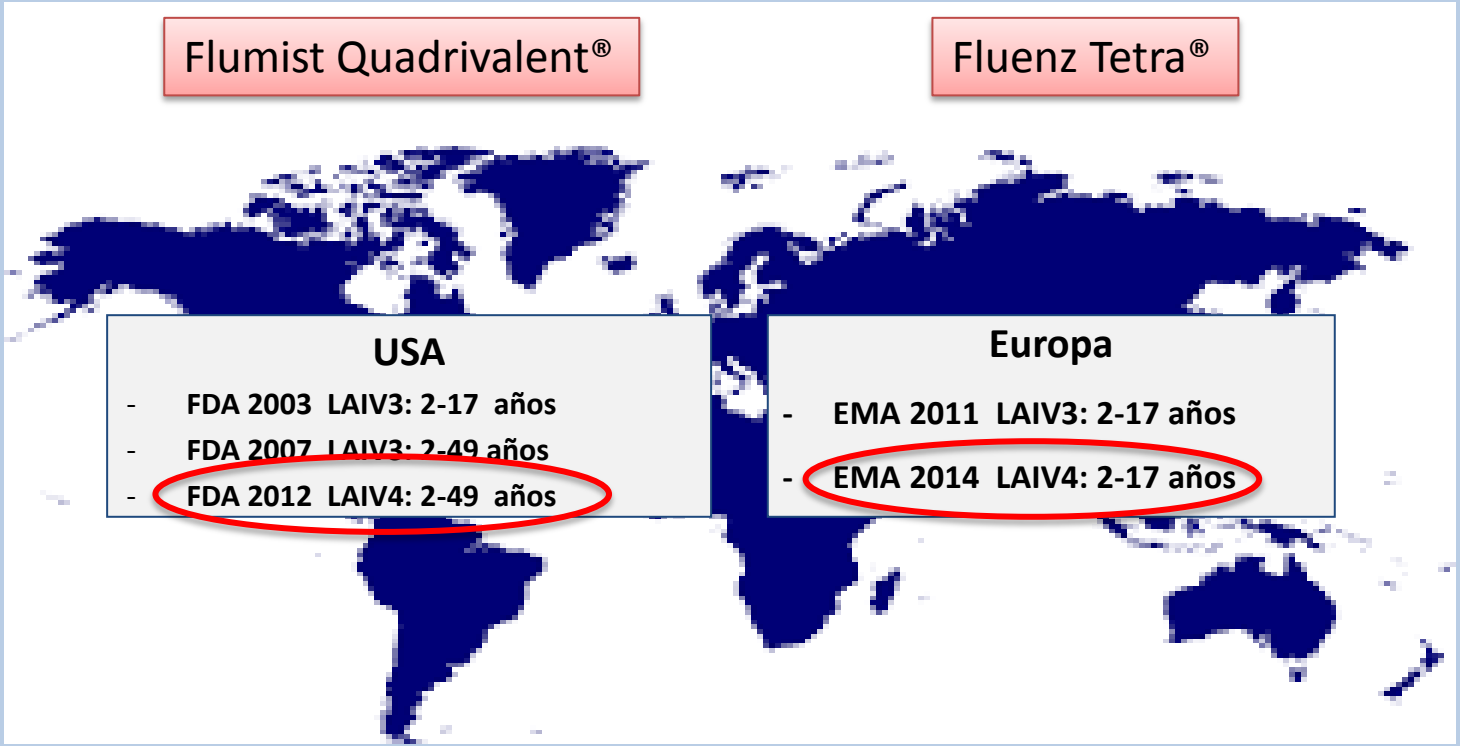
Live Attenuated Influenza Vaccine (LAIV)



Fluenz Tetra® composición 2016-2017

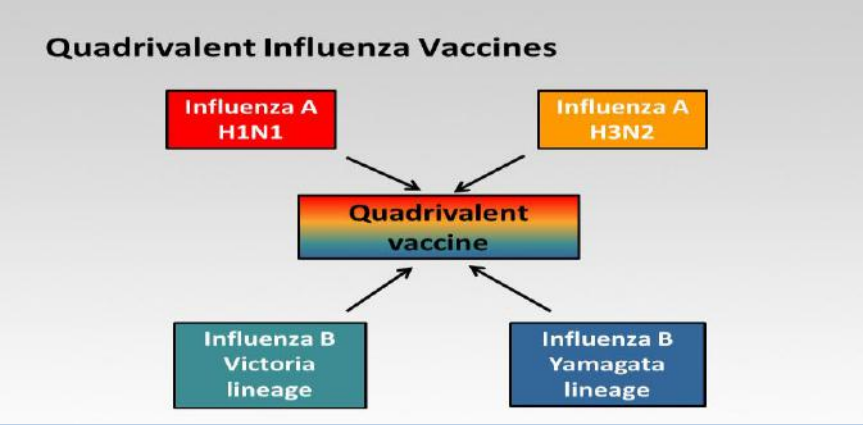
Antígenos:

A/California/7/2009 (H1N1)pdm09-like virus

A/Hong Kong/4801/2014 (H3N2)-like virus

B/Brisbane/60/2008-like virus (linaje Victoria)

B/Phuket/3073/2013-like virus (linaje Yamagata)



2016, 91, 121-132 No 10

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

11 MARCH 2016, 91th YEAR / 11 MARS 2016, 91e ANNÉE
No 10, 2016, 91, 121-132
http://www.who.int/wer

It is recommended that trivalent vaccines for use in the 2016-2017 northern hemisphere influenza season contain the following:

– an A/California/7/2009 (H1N1)pdm09-like virus;

– an A/Hong Kong/4801/2014 (H3N2)-like virus;

– a B/Brisbane/60/2008-like virus.

It is recommended that quadrivalent vaccines containing 2 influenza B viruses contain the above 3 viruses and a B/Phuket/3073/2013-like virus.

Il est recommandé que les vaccins antigrippaux trivalents destinés à être utilisés pendant la saison 2016-2017 (hiver dans l'hémisphère Nord) contiennent:

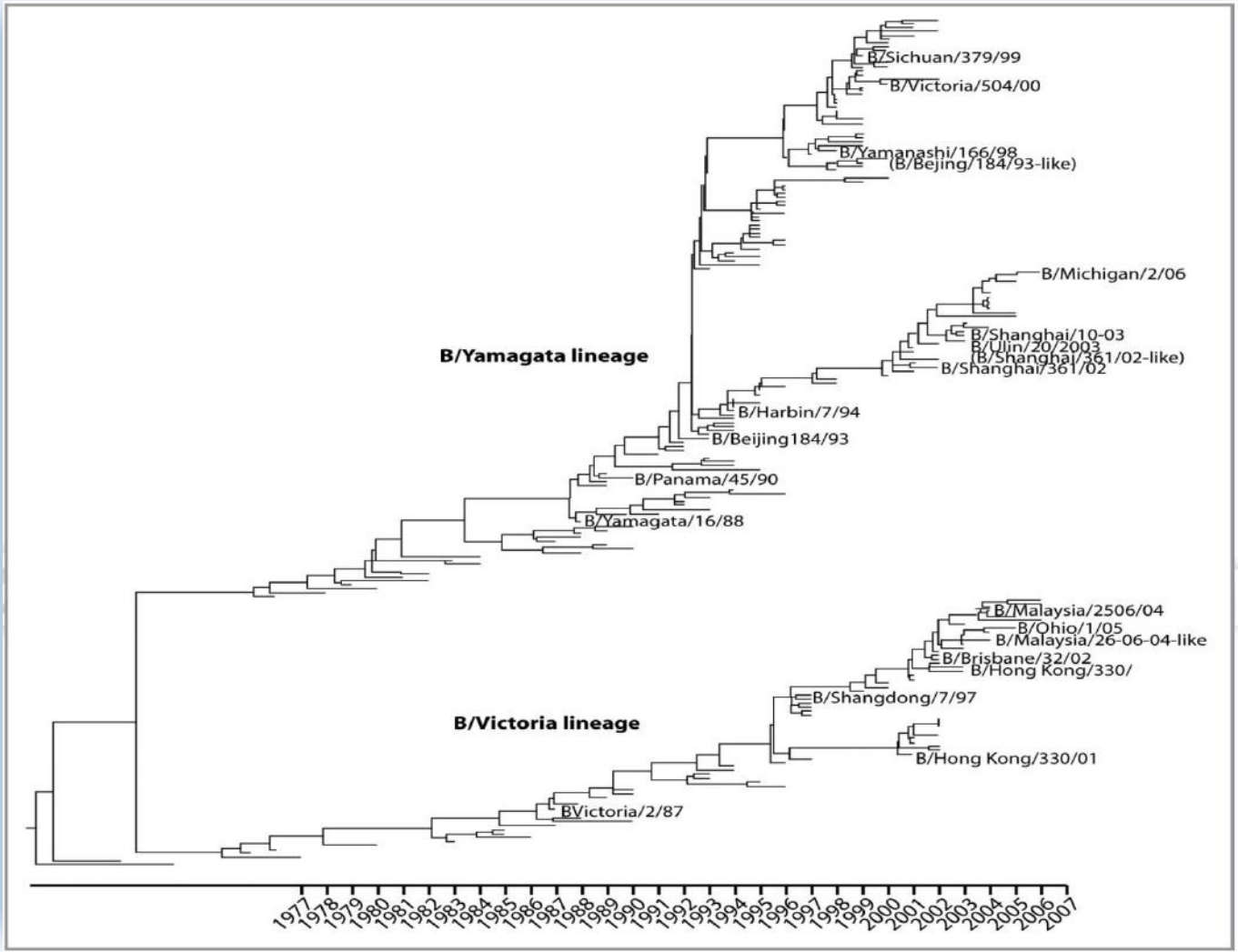
- un virus de la souche A/California/7/2009 (H1N1)pdm09;

- un virus de la souche A/Hong Kong/4801/2014 (H3N2);

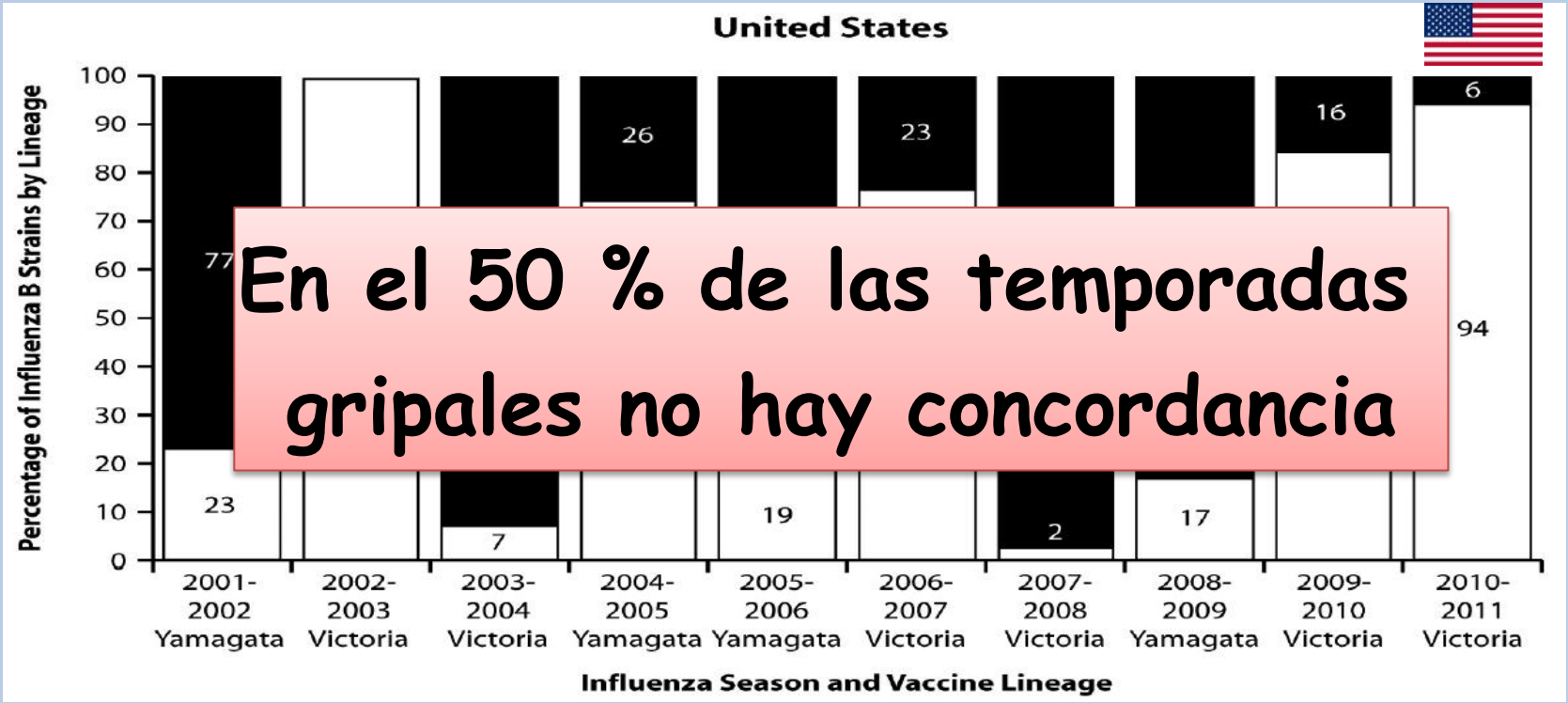
- un virus de la souche B/Brisbane/60/2008.

Il est recommandé que les vaccins quadrivalents contenant 2 virus de la grippe B renferment aussi les 3 virus ci-dessus et un virus de la souche B/Phuket/3073/2013.

Evolución de los 2 linajes antigénicamente distintos del virus influenza B (1970 – 2006)



Circulación de Influenza B según linaje: datos en EE.UU., desde 2001 a 2011



En el 50 % de las temporadas gripales no hay concordancia

Ambrose CS et al. Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012

Vaccine 30 (2012) 1993–1998

Contents lists available at SciVerse ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Public health impact of including two lineages of influenza B in a quadrivalent seasonal influenza vaccine☆

Carrie Reed[a,*], Martin I. Meltzer[b], Lyn Finelli[a], Anthony Fiore[a]

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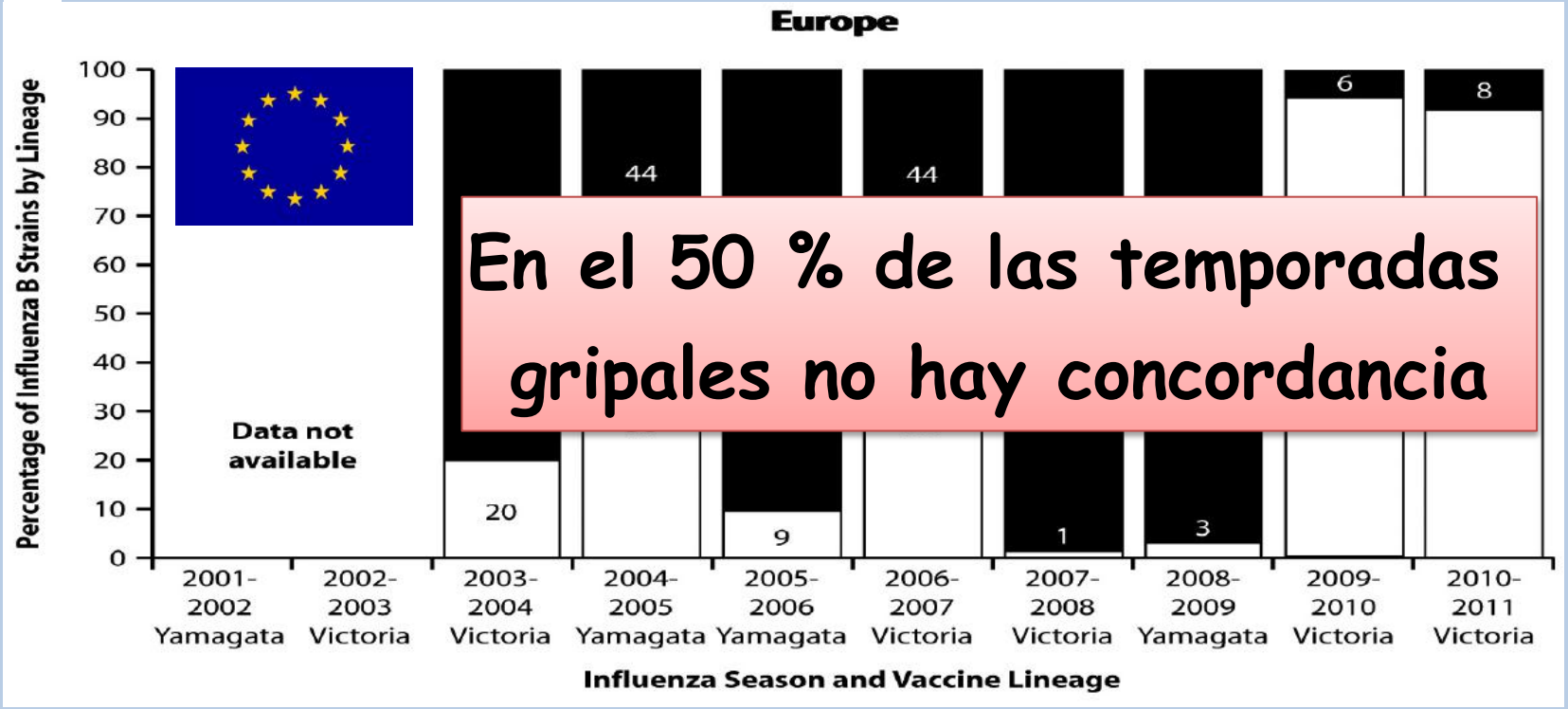
[b] Division of Emerging Infections and Surveillance Systems, National Center for Preparedness, Detection and Control of Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, United States

La sustitución de la vacuna antigripal TV por la CV, en el periodo 2001-2009, hubiera evitado entre 2.200 - 970.000 casos de gripe, entre 14 y 8.200 hospitalizaciones, y entre 1 y 485 fallecimientos asociados a la propia gripe

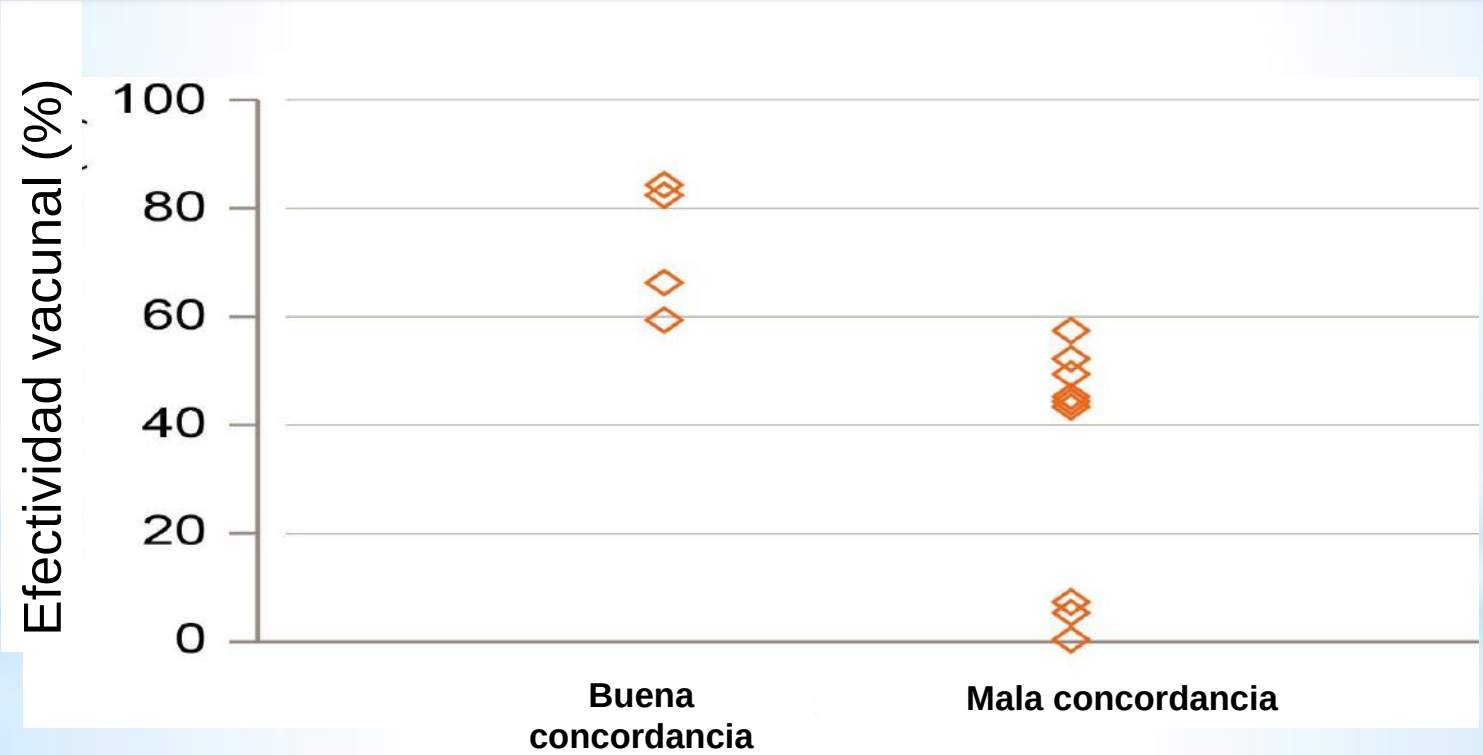
Circulación de Influenza B según linaje: datos europeos desde 2003 a 2011



En el 50 % de las temporadas gripales no hay concordancia

Ambrose CS et al. Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012

Estimación de la efectividad de la vacuna inactivada de gripe de acuerdo a la concordancia de la vacuna



1. Heikkinen & Heinonen. *Vaccine* 2011:29:7529– 3754; 2. Tricco *et al*. *BMC Med* 2013;11:153; 3. DiazGranados *et al*. *Vaccine* 2012; 31: 49– 57; 4. Belshe RB. *Vaccine* 2010; 28:2 149–2156; 5. Belshe RB. *Vaccine* 2010; 28(Suppl 4): D45–D53.

Estudios de efectividad de la vacuna LAIV en los EE. UU

- Temporadas gripales 2000 - 2009
- Temporadas gripales 2010 – 2014
- Temporadas gripales 2015 - 2016

Temporadas gripales

2000 - 2009

Eficacia de LAIV3 frente a placebo (2000-2009)

Frente a la gripe producida por **cepas equivalentes**, con una reducción del **62% - 100%**

Frente a la gripe producida por todas las cepas, con **independencia de equivalencia** antigénica, con una reducción del **48% - 93%**

NÚMERO DEL ESTUDIO	REGIÓN	INTERVALO DE EDAD[a]	NÚMERO DE PARTICIPANT.[b]	TEMPORADA DE GRIPE	EFICACIA (IC DEL 95%)[c]	
					CEPAS COINCIDENTES	TODAS LAS CEPAS INDEPENDIENTEMENTE DE LA COINCIDENCIA
D153 P502	Europa	6 a 35 M	1.616	2000- 2001 2001-2002	**85,4%** (74,3; 92,2) **88,7%** (82,0; 93,2)	**85,9%** (76,3; 92,0) **85,8%** (78,6; 90,9)
D153 P504	África, Latinoamérica	6 a 35 M	1.886	2001 2002	**73,5%** (63,6; 81,0)[d] **73,6%** (33,3; 91,2)	**72,0%** (61,9; 79,8)[d] **46,6%** (14,9; 67,2)
D153 P513	Asia/Oceanía	6 a 35 M	1.041	2002	**62,2%** (43,6; 75,2)	**48,6%** (28,8; 63,3)
D153 P522	Europa, Asia/Oceanía, Latinoamérica	11 a 24 M	1.150	2002-2003	**78,4%** (50,9; 91,3)	**63,8%** (36,2; 79,8)
D153 P501	Asia/Oceanía	12 a 35 M	2.764	2000- 2001 2001-2002	**72,9%** (62,8; 80,5) **84,3%** (70,1; 92,4)[e]	**70,1%** (60,9; 77,3) **64,2%** (44,2; 77,3)[e]
AV006	EE.UU.	15 a 71 M	1.259	1996-1997 1997-1998	**93,4%** (87,5; 96,5) **100%** (63,1; 100)	**93,4%** (87,5; 96,5) **87,1%** (77,7; 92,6)[f]

a M = meses.
b Número de participantes en el estudio para el análisis de eficacia en el año 1.
c Reducción de la enfermedad de gripe confirmada por cultivo con respecto al placebo.
d Los datos presentados para el ensayo clínico D153 P504 son de participantes en el estudio que recibieron dos dosis de la vacuna en estudio. En los participantes en el estudio sin vacunación anterior que recibieron una dosis en el año 1, la eficacia fue del 57,7% (IC al 95%: 44,7; 67,9) y del 56,3% (IC al 95%: 43,1; 66,7), respectivamente, lo cual respalda la necesidad de dos dosis de vacuna en niños sin vacunación anterior.
e En los participantes en el estudio que recibieron 2 dosis en el año 1 y placebo en el año 2, la eficacia en el año 2 fue del 56,2% (IC al 95%: 30,5; 72,7) y del 44,8% (IC al 95%: 18,2; 62,9), respectivamente, en D153 P501, respaldando así la necesidad de la revacunación en la segunda temporada.
f La principal cepa circulante era antigénicamente diferente de la cepa H3N2 vacunal; la eficacia contra la cepa no coincidente A/H3N2 fue del 85,9% (IC al 95%: 75,3; 91,9).

[1]Ficha técnica de Fluenz Tetra® Disponible en: http://www.ema.europa.eu/docs/es_ES/document_library/EPAR_-_Product_Information/human/002617/WC500158412.pdf. 2013.

Vacuna de gripe atenuada intranasal (LAIV3)
Estudios de eficacia frente a placebo (2000-2009)

	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)[74]	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)[75]	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)[76]	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

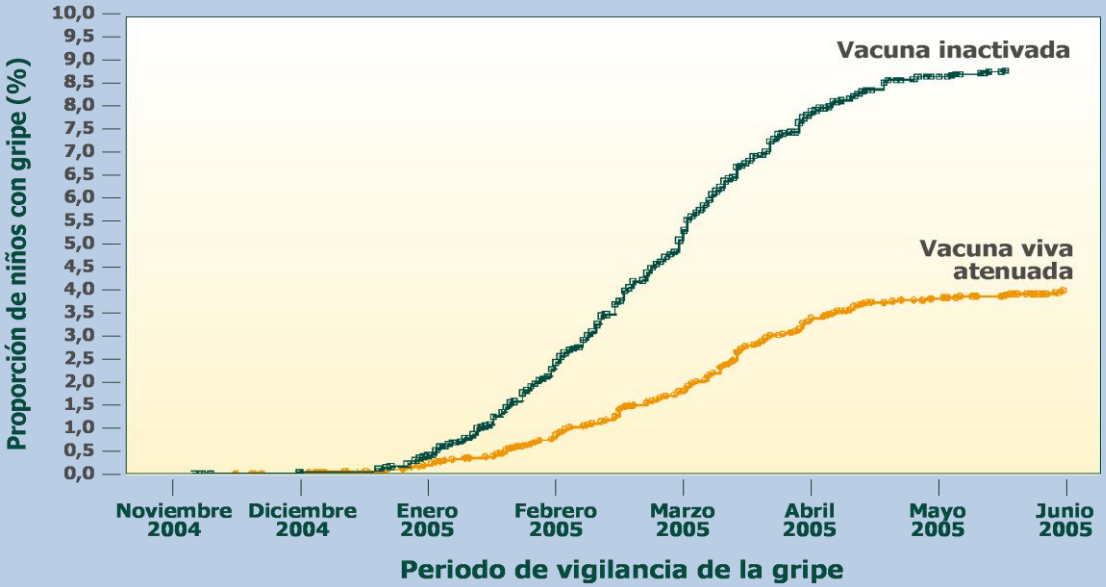
Tabla 1 Eficacia de Fluenz en estudios pediátricos controlados con placebo

Número del estudio	Región	Intervalo de edad[a]	Número de participantes en el estudio[b]	Temporada de gripe	Eficacia (IC al 95%) [c] Cepas coincidentes	Eficacia (IC al 95%)[c] Todas las cepas independientemente de la coincidencia
D153-P502	Europa	6 a 35 M	1.616	2000 – 2001	85,4% (74,3; 92,2)	85,9% (76,3; 92,0)
				2001 – 2002	88,7% (82,0; 93,2)	85,8% (78,6; 90,9)
D153-P504	África, Latinoamérica	6 a 35 M	1.886	2001	73,5% (63,6; 81,0)[d]	72,0% (61,9; 79,8)[d]
				2002	73,6% (33,3; 91,2)	46,6% (14,9; 67,2)
D153-P513	Asia/Oceanía	6 a 35 M	1.041	2002	62,2% (43,6; 75,2)	48,6% (28,8; 63,3)
D153-P522	Europa, Asia/Oceanía, Latinoamérica	11 a 24 M	1.150	2002 – 2003	78,4% (50,9; 91,3)	63,8% (38,2; 79,8)
D153-P501	Asia/Oceanía	12 a 35 M	2.764	2000 – 2001	72,9% (62,8; 80,5)	70,1% (60,9; 77,3)
				2001 – 2002	84,3% (70,1; 92,4)[e]	64,2% (44,2; 77,3)[e]
AV006	EE. UU.	15 a 71 M	1.259	1996 – 1997	93,4% (87,5; 96,5)	93,4% (87,5; 96,5)
				1997 – 1998	100% (63,1; 100)	87,1% (77,7; 92,6)[f]

Ficha Técnica de Fluenz Tetra.
Disponible en: http://www.ema.europa.eu/docs/es_ES/document_library/EPAR_-_Product_Information/human/002617/WC500158412.pdf.

Eficacia pediátrica: LAIV3 *vs* IIV

Curvas de Kaplan-Meier del periodo de tiempo hasta el primer episodio de gripe confirmado por cultivo en los dos grupos vacunados



Reducción del 54,9%
(IC del 45,4 - 62,9)

Belshe RB, et al. Live attenuated versus inactivated influenza vaccine in infants and young children. New Engl J Med 2007; 356: 685-696

Tabla 2 **Eficacia relativa de Fluenz en estudios pediátricos controlados con tratamiento activo con vacuna inyectable contra la gripe**

Número del estudio	Región	Intervalo de edad[a]	Número de participantes en el estudio	Temporada de gripe	Eficacia mejorada (IC al 95%)[b] Cepas coincidentes	Eficacia mejorada (IC al 95%)[b] Todas las cepas independientemente de la coincidencia
MI-CP111	EE. UU., Europa, Asia/Oceanía	6 a 59 M	7.852	2004 – 2005	44,5% (22,4; 60,6) menos casos que el inyectable	54,9% (45,4; 62,9)[c] menos casos que el inyectable
D153-P514	Europa	6 a 71 M	2.085	2002 – 2003	52,7% (21,6; 72,2) menos casos que el inyectable	52,4% (24,6; 70,5)[d] menos casos que el inyectable
D153-P515	Europa	6 a 17 A	2.211	2002 – 2003	34,7% (3,9; 56,0) menos casos que el inyectable	31,9% (1,1; 53,5) menos casos que el inyectable

Ficha Técnica de Fluenz Tetra.
Disponible en: http://www.ema.europa.eu/docs/es_ES/document_library/EPAR_-_Product_Information/human/002617/WC500158412.pdf.

En resumen: ↑↑ eficacia LAIV3 en niños de 2 a 17 años (2000-2009)

– LAIV3 es más eficaz que el placebo para:

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

– LAIV es más eficaz que la vacuna inactivada (IIV):

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

Temporadas gripales 2010 – 2015

- Pandemia de gripe A (H1N1) en 2009
- Circulación de la cepa A/California/H1N1/pdm09
- LAIV3 → LAIV4

Recomendaciones del ACIP (CDC)

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 62 / No. 7
September 20, 2013

Temporada gripal 2013-2014

Prevention and Control of Seasonal Influenza with Vaccines

Recommendations of the Advisory Committee on Immunization Practices — United States, 2013–2014

Prepared by
Lisa A. Grohskopf, MD[1]

One LAIV4 product, FluMist Quadrivalent (MedImmune), is expected to be available during the 2013–14 influenza season. **No preference is indicated for LAIV versus other vaccines appropriate for this group of age.**

Live Attenuated Influenza Vaccine

One LAIV4 product, FluMist Quadrivalent (MedImmune), is expected to be available during the 2013–14 influenza season. Flumist is indicated for nonpregnant persons aged 2 through 49 years who do not have a medical condition that predisposes them to medical complications from influenza. No preference is indicated for LAIV versus other vaccines appropriate for this group.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 63 / No. 32
August 15, 2014

Temporada gripal 2014-2015

Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP) — United States, 2014–15 Influenza Season

Lisa A. Grohskopf, MD[1], Sonja J. Olsen, PhD[1], Leslie Z. Sokolow, MSc, MPH[1], Joseph S. Bresee, MD[1], Nancy J. Cox, PhD[1], Karen R. Broder, MD[2], Ruth A. Karron, MD[3], Emmanuel B. Walter, MD[4] (Author affiliations at end of text)

In 2014, following review of evidence on the relative efficacy of LAIV compared with IIV for healthy children, ACIP recommended that **LAIV should be used for healthy children aged 2 through 8 years** who have no contraindications or precautions.

2. When immediately available, LAIV should be used for healthy children aged 2 through 8 years who have no contraindications or precautions (Category A). If LAIV is not immediately available, IIV should be used. Vaccination should not be delayed to procure LAIV. The age of 8 years

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 64 / No. 30
August 7, 2015

Temporada gripal 2015-2016

Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015–16 Influenza Season

Lisa A. Grohskopf, MD[1]; Leslie Z. Sokolow, MSc, MPH[1,2]; Sonja J. Olsen, PhD[1]; Joseph S. Bresee, MD[1]; Karen R. Broder, MD[3]; Ruth A. Karron, MD[4]

Analysis of data from 3 observational studies of LAIV4 vaccine effectiveness for the 2013–14 season revealed poor effectiveness of LAIV4 against influenza A(H1N1)pdm09 among children aged 2 through 17 years .

In the absence of data demonstrating consistent greater relative effectiveness of the current quadrivalent formulation of LAIV**, preference for LAIV over IIV is no longer recommended for any person aged 2 through 49 years.**

ACIP. Summary Report: February 26, 2015. Meeting minutes http://www.cdc.gov/vaccines/acip/meetings/downloads/min-archive/min-2015-02.pdf

Effectiveness of live attenuated influenza vaccine and inactivated influenza vaccine in children 2–17 years of age in 2013–2014 in the United States

Herve Caspard [a,*], Manjusha Gaglani [b], Lydia Clipper [b], Edward A. Belongia [c],

Vaccine

Results. 1.033 children and adolescents were included. LAIV did not show significant effectiveness against A/H1N1pdm09 **(VE LAIV 13%)**. Inactivated influenza vaccine was effective against A/H1N1pdm09 **(VE IIV 74%)**.

Conclusions. LAIV not provided significant protection against A/H1N1pdm09 in children aged 2–17 years in 2013–2014, resulting in a proposed change of the 2015–2016 formulation with a new and more heat-stable A/H1N1pdm09 LAIV strain.

Influenza strain	LAIV effectiveness % (95% CI)		IIV effectiveness % (95% CI)	
	Crude	Adjusted[a]	Crude	Adjusted[a]
Any strain	47 (17–66)	32 (−13 to 59)	76 (62–85)	68 (47–81)
A/H1N1pdm09	36 (−6 to 61)	13 (−5 to 51)	81 (66–90)	74 (50–86)
A/H3N2	-	-	-	-
B/Yamagata	83 (26–96)	82 (12–96)	71 (28–89)	70 (18–89)
B/Victoria	-	-	-	-
B undetermined	-	-	-	-

Caspard H, et al. Vaccine 2016; 34: 77-82

Pediatrics
January 2016

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®

Seasonal Effectiveness of Live Attenuated and Inactivated Influenza Vaccine

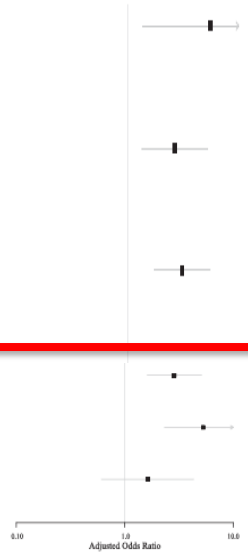
Jessie R. Chung, Brendan Flannery, Mark G. Thompson, Manjusha Gaglani, Michael L. Jackson, Arnold S. Monto, Mary Patricia

Results. In 2013–2014, odds of influenza were significantly higher among LAIV recipients compared with IIV recipients 2 to 8 years old (OR 5.36). LAIV recipients had greater odds of illness due to influenza A/H1N1pdm09 in 2010–2011 and 2013–2014.

Conclusions. We observed lower effectiveness of LAIV compared with IIV against influenza A/H1N1pdm09, suggesting poor performance related to the LAIV A/H1N1pdm09

Relative EV of LAIV and IIV, over 4 influenza seasons, US Flu VE Network

Influenza Type/ Subtype	Influenza Season	Vaccine Type	Total	No. (%) Positive	aOR
A/H1N1pdm09	2010–2011	LAIV	102	7 (9)	5.53
		IIV	420	9 (2)	REF
	2013–2014	LAIV	154	24 (16)	2.65
		IIV	459	27 (6)	REF
	Combined*	LAIV	256	31 (12)	3.08
		IIV	879	36 (4)	REF
2013–2014	2–17	LAIV	164	34 (21)	2.88
		IIV	468	36 (8)	REF
	2–8	LAIV	92	22 (24)	5.36
		IIV	305	21 (7)	REF
	9–17	LAIV	72	12 (17)	1.62
		IIV	163	15 (9)	REF



Chung JR, et al. Pediatrics. 2016; 137(2): e20153279

Resumen de la efectividad vacunal (EV) frente a la gripe durante la temporada 2013-2014 en los EE.UU.

La cepa H1N1 circuló en la comunidad, por primera vez desde la pandemia del 2009, de forma predominante durante la temporada 2013-2014. Los estudios de EV mostraron una baja efectividad en niños de la vacuna LAIV4 contra la cepa de gripe A/California/H1N1/pdm09, mientras que la efectividad vacunal de la vacuna IIV fue claramente superior y estadísticamente significativa.

Temporada gripal 2016 – 2017

Recomendaciones del ACIP (CDC)

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 5
August 26, 2016

Temporada gripal 2016-2017

Prevention and Control of Seasonal Influenza with Vaccines Recommendations of the Advisory Committee on Immunization Practices — United States, 2016–17 Influenza Season

Lisa A. Grohskopf, MD[1]
Leslie Z. Sokolow, MSc, MPH[1,2]

In light of low effectiveness of LAIV against influenza A/H1N1/pdm09 in the USA during the 2013–14 and 2015–16 seasons, for the 2016–17 season, ACIP makes the recommendation that **LAIV4 should not be used.**

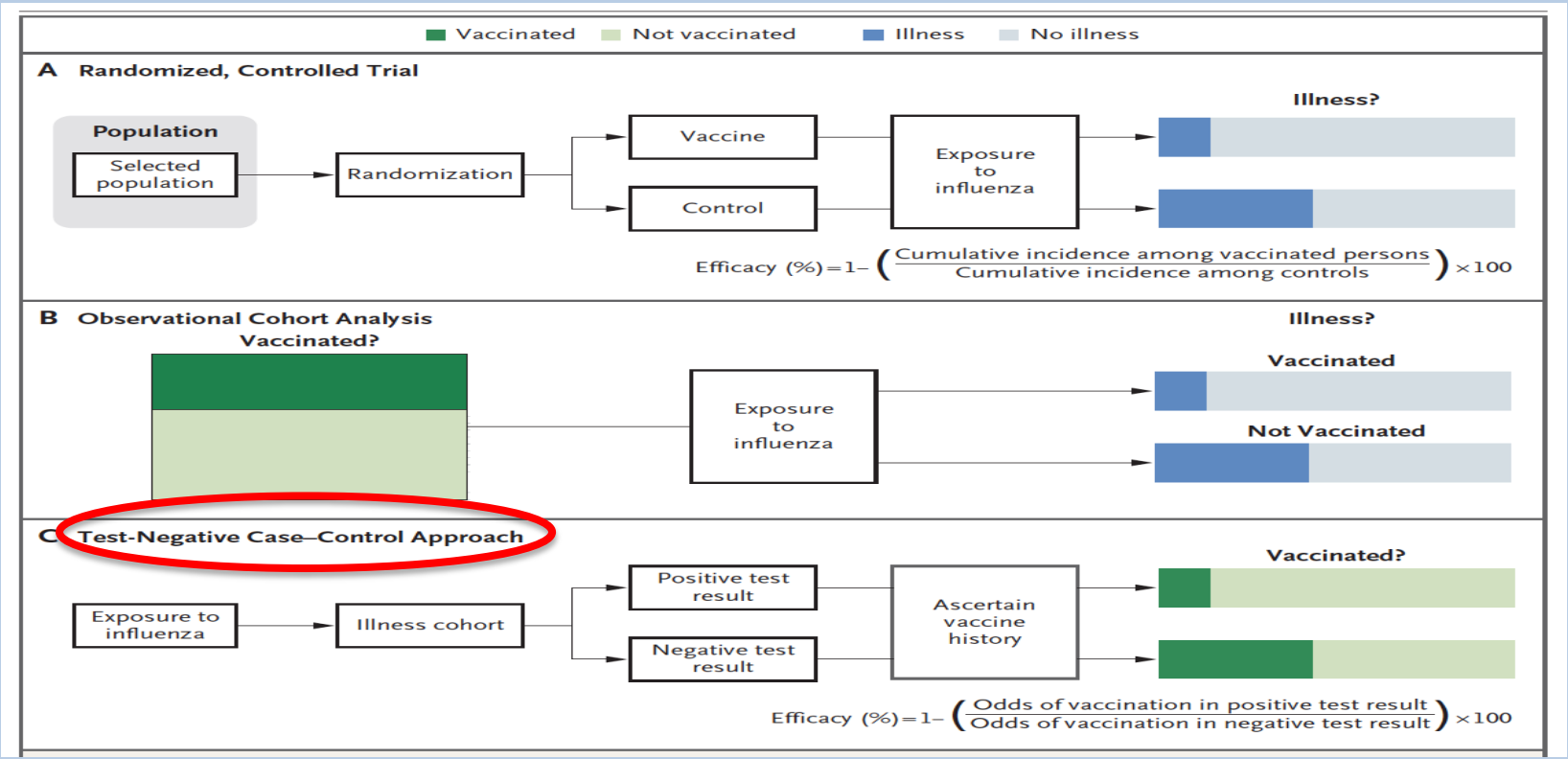
ACIP. Summary Report June, 22, 2015. Meeting minutes

	CDC United States	DoD United States	ICICLE United States
VE against A(H1N1)pdm09 (95%CI)	−21%	15%	50%
Study design	Test-negative case–control	Test-negative case–control	Test-negative case–control
Source population / inclusion criteria	Children and adolescents aged 2–17 years*	adolescents (Military dependents) aged 2–17 years presenting to participating facilities	Children and adolescents aged 2–17 years
Inclusion criteria	MAARI, including cough, and onset of illness ≤ 7 days before enrolment	ILI (fever ≥ 38 °C AND cough and/or sore throat of < 72 hours duration)	ARI with fever ≥ 100.0°F (37.8 °C), duration < 5 days
Assessment of vaccination status	Current-season vaccination (at least one vaccine dose ≥ 14 days before illness onset; vaccine records obtained from electronic medical records and immunisation registries for children aged 2–8 years; with addition of reported vaccination for patients aged 9–17 years)*	Electronic medical records	Vaccination status was ascertained by medical record review and/or state or regional vaccine registries
Case definition	RT-PCR-positive subjects*	RT-PCR-positive subjects	RT-PCR positive subjects
Final sample size (number of vaccinated with LAIV / number of non-vaccinated)*	133/1,078*	93/338*	101/594
Adjusted for	Study site, age, self-rated general health status, race/hispanic ethnicity, interval (days) from onset to enrolment, and calendar time	Age groups, three time periods	Site, age group, visit date, outpatient visits in past 6 months, health insurance, and sex

Comparación de los 3 estudios de efectividad de la vacuna LAIV realizados en los EE.UU. durante la temporada gripal 2015-2016

Penttinen PM, et al. Euro Surveill. 2016

Métodos para determinar la efectividad de la vacuna de la gripe



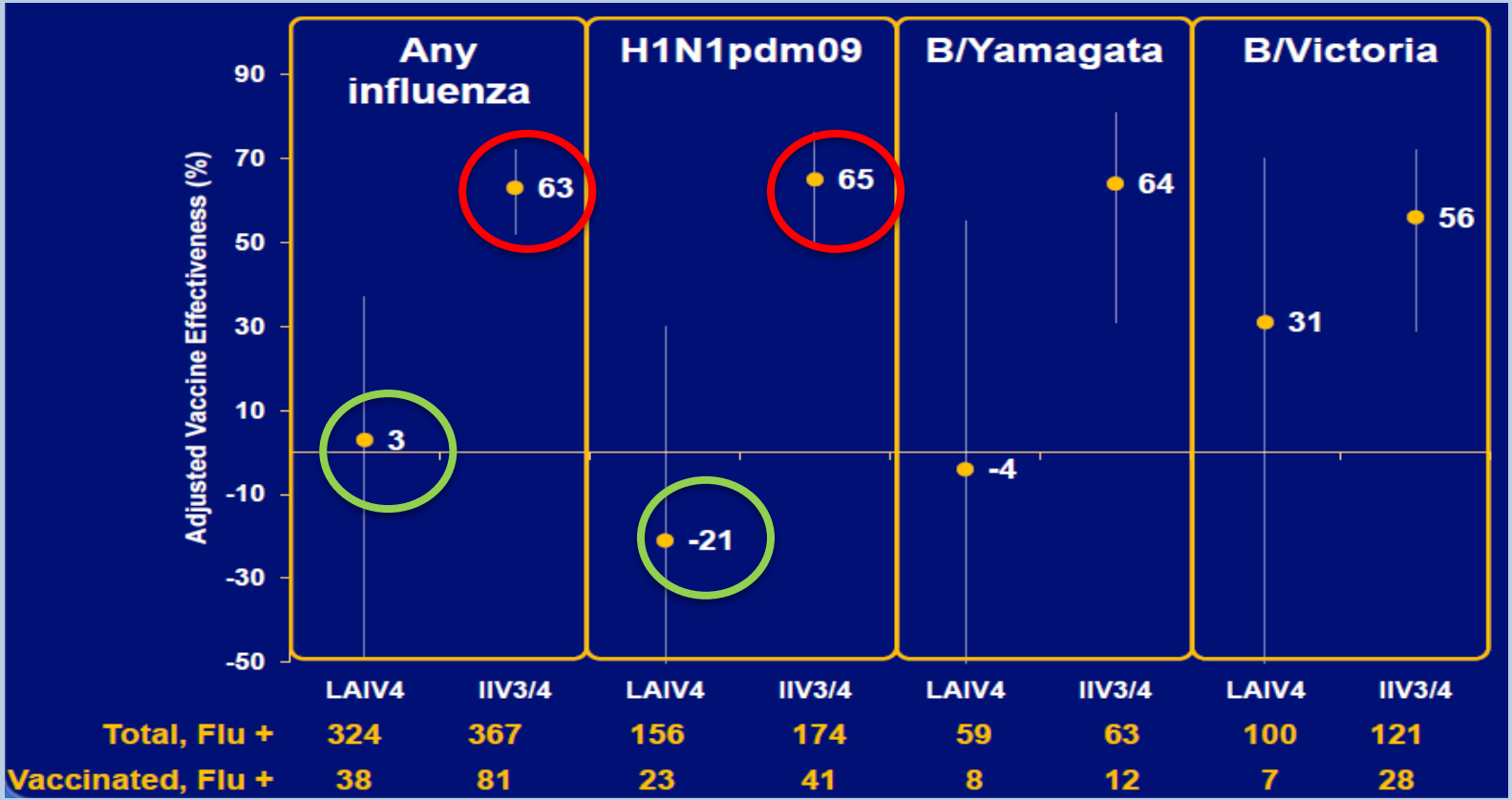
Treanor JJ. NEJM 2016; 375: 1261-1268

Estudios de test negativo

Los pacientes con síntomas gripales se reclutan en centros sanitarios, realizándose en ellos diagnóstico microbiológico molecular de gripe (RT-PCR). Se comparan el grupo de no vacunados y de vacunados (LAIV/IIV) entre los que tienen resultado de gripe (+) y resultado de gripe (-), obtiéndose una OR de la que se calcula la EV como (1-OR) X 100. La EV se calcula usando un diseño de **"test negativo"**, que compara proporciones (probabilidades) de vacunación contra la gripe entre los pacientes con y sin gripe.

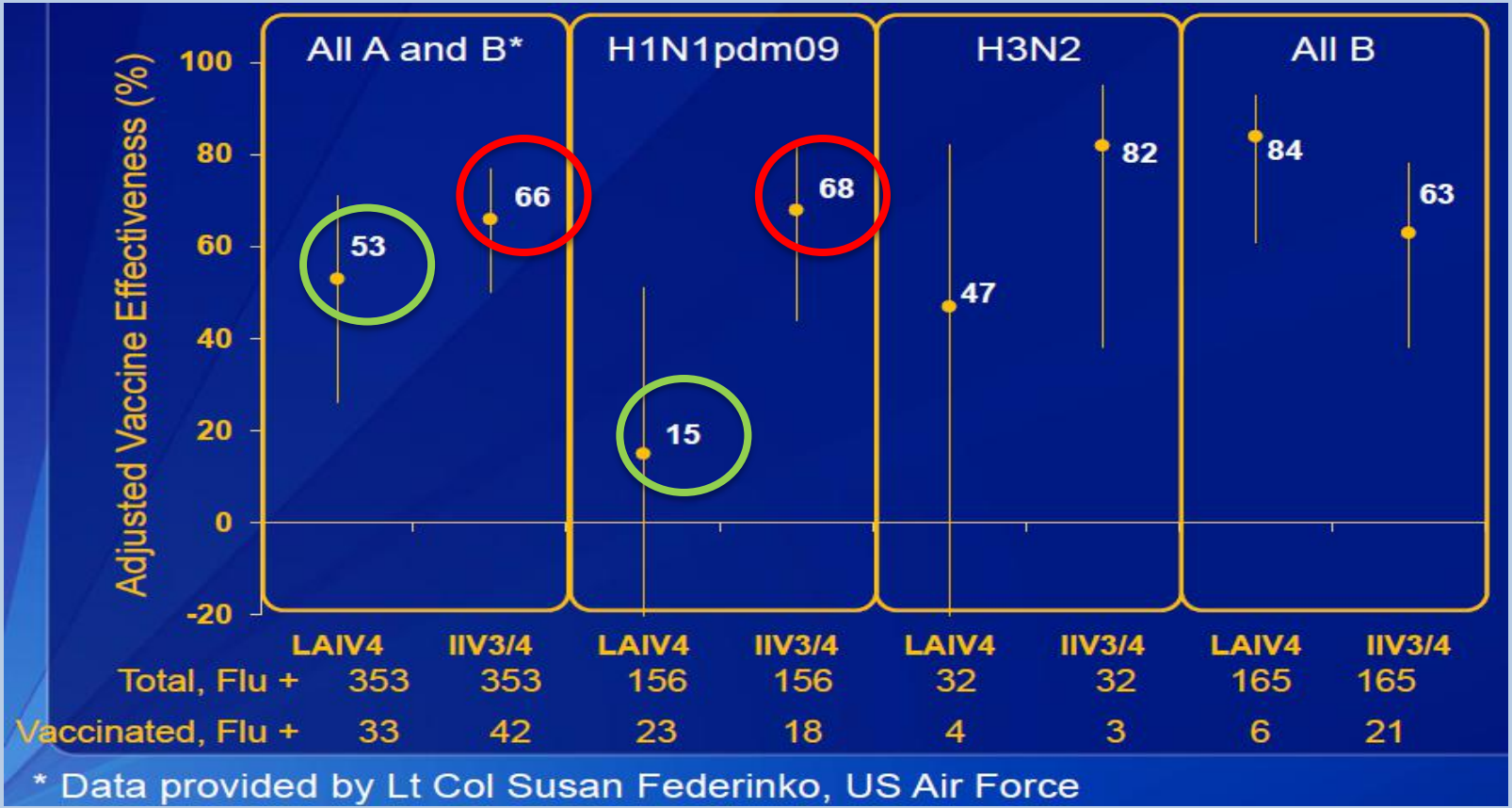
El diseño de **"test negativo"** es una variante de los estudios de caso-control, son muy eficientes y son los habitualmente utilizados en los estudios de efectividad de la vacuna antigripal. Como contrapartida, están sometidos a numerosos sesgos (nº de muestra, proporción de vacunados, criterios de diagnóstico clínico, aspectos (toma de muestra, técnica empleada, etc.) que afecten a la sensibilidad y especificidad del diagnóstico microbiológico.

2015-2016 US-CDC VE data for children 2-17 years (N=2286)



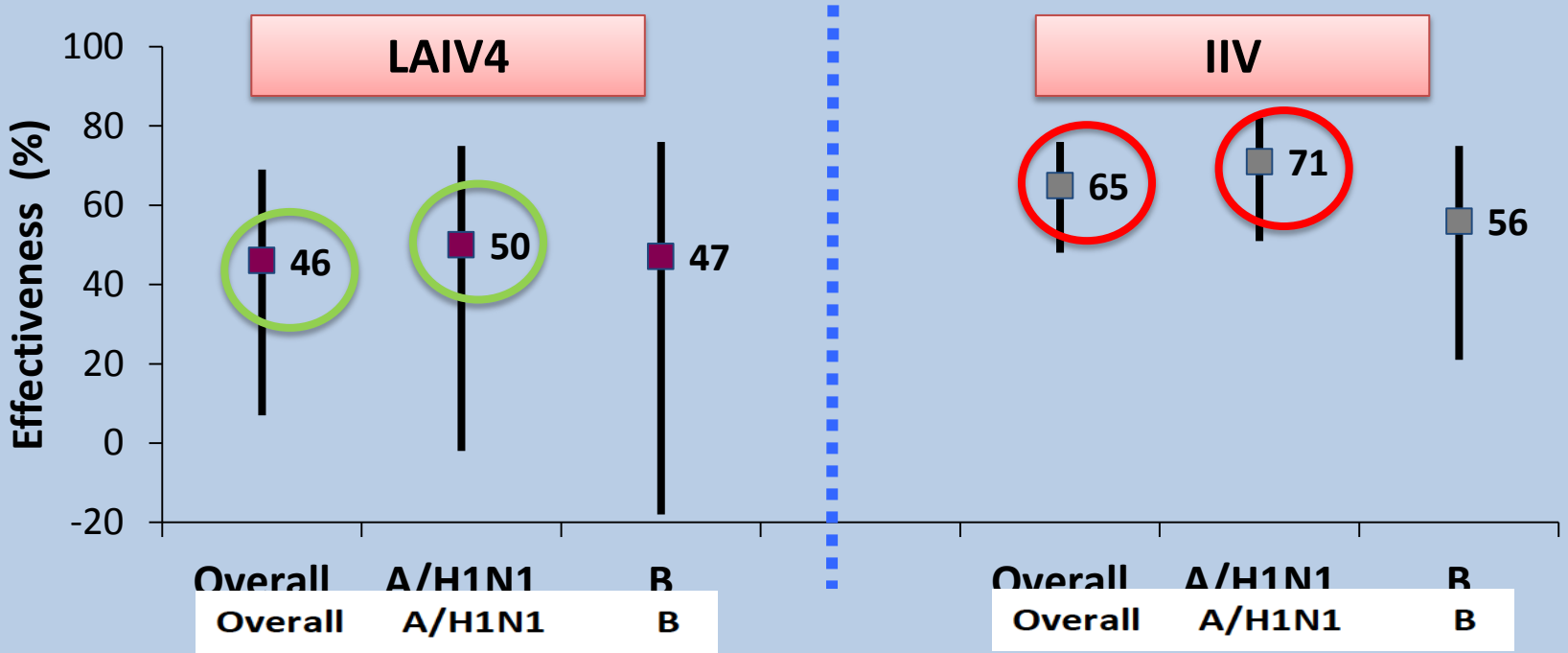
Flannery B, Chung J. Presented at ACIP meeting, June 22, 2016 (https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-05-flannery.pdf)

2015-2016 US-DoD VE data for military dependent children 2-17 years



Flannery B, Chung J. Presented at ACIP meeting, June 22, 2016 (https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-05-flannery.pdf)

ICICLE (US): 2015-16 Adjusted Estimates of Effectiveness



→ Results similar for 1) those fully vaccinated, 2) excluding those negative for any respiratory virus, and 3) excluding those with high-risk conditions

VE adjusted on site, age group, visit date, outpatient visits in past 6 months, health insurance, and sex

Ambrose Ch. Presented at ACIP meeting, June 22, 2016 (www.cdc.gov/vaccines/acip/meetings/downloads/slides-2016-06/influenza-06-ambrose.pdf)

Teorías sobre la menor efectividad vacunal de la cepa A/California/H1N1/pdm09 en la vacuna LAIV4

EDITORIAL

Decreased effectiveness of the influenza A(H1N1) pdm09 strain in live attenuated influenza vaccines: an observational bias or a technical challenge?

PM Penttinen [1], MH Friede [2]

Euro Surveill. 2016; 21(38): pii=30350

Publisher: European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Eurosurveillance 20 years 1996–2016
Europe's journal on infectious disease epidemiology, prevention and control

Letter to the editor: Potential causes of the decreased effectiveness of the influenza A(H1N1)pdm09 strain in live attenuated influenza vaccines

CS Ambrose [1], H Bright [2], R Mallory [1]

Euro Surveill. 2016; 21(45): pii=30394

Teorías sobre la pérdida de efectividad vacunal de la LAIV4 para la cepa Influenza A/California /H1N1/pdm09

1. **Termoestabilidad** reducida de la cepa A/H1N1/pdm09 contenida en la LAIV4

2. Capacidad reducida de replicación de las cepas virales que contiene la LAIV4 debido a la **"interferencia" entre cepas.** Paso de LAIV3 a LAIV4

3. Reducida capacidad de replicación de las cepas virales contenidas en la LAIV4 debido a la **pre-existencia de inmunidad** antigripal, como consecuencia de vacunaciones anteriores

4. Reducida **capacidad replicativa** de la cepa A/H1N1/pdm09 en las células epiteliales del tracto respiratorio humano

5. **Diseño inadecuado** de los estudios de EV ("test negativo") para la vacuna LAIV

Muchas gracias