X Jornadas de Actualización en Vacunas

Las Vacunas en la Sociedad Actual

¿Qué ha pasado en el último año en vacunas y cómo aplicarlo en la práctica diaria?

GRIPE y VARICELA

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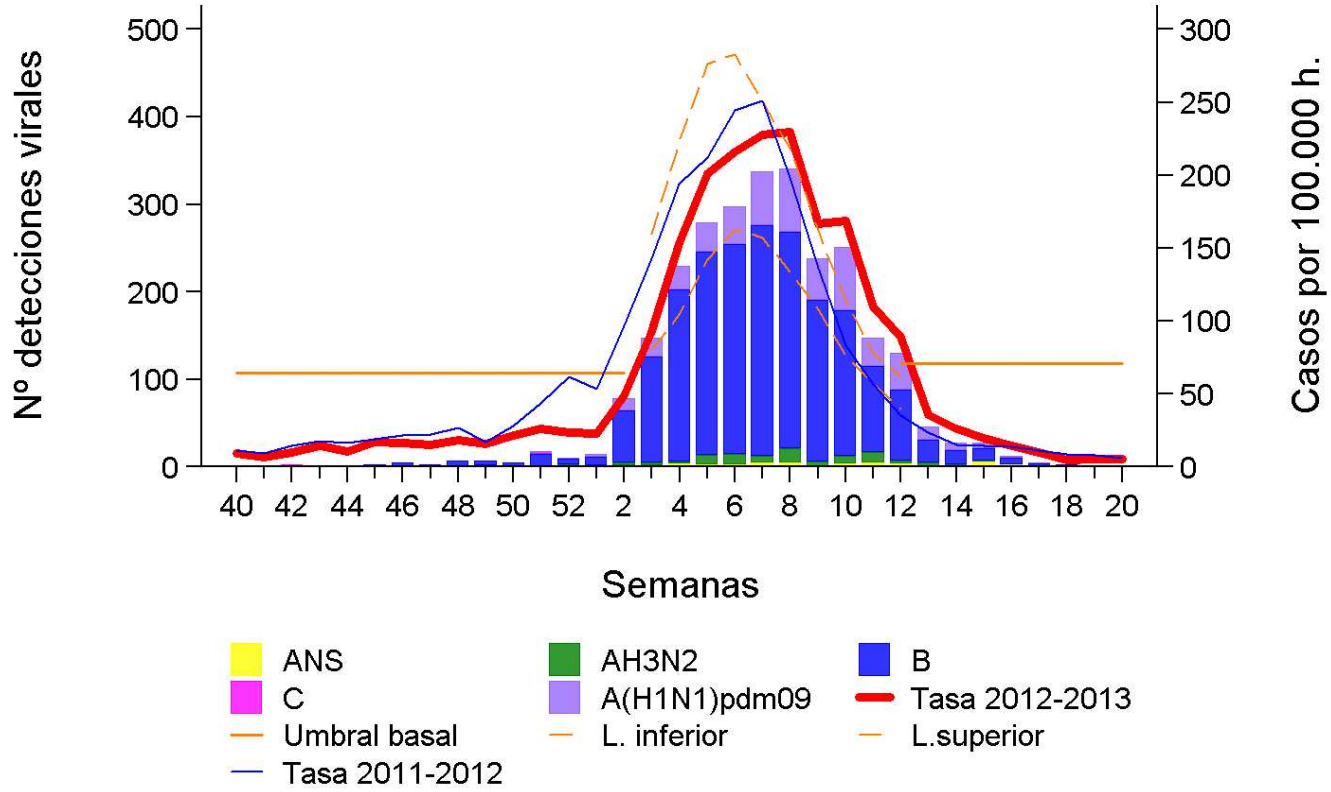
Almería, 25 de octubre de 2013

ibv
Instituto Balmis de Vacunas

COLEGIO DE MÉDICOS
DE ALMERÍA

CIRCULACIÓN PREDOMINANTE DE GRIPE B EN ESPAÑA Y EUROPA

Figura 1. Tasa de incidencia semanal de gripe y número de detecciones virales. Temporada 2012-13. Sistemas centinela. España



Fuente: CNE. Sistema de Vigilancia de Gripe en España

CIRCULACIÓN DE NUEVOS VIRUS GRIPALES

31/03/2013: CHINA: Nuevo virus de gripe A (H7N9)

RSI: Evento de Salud Pública de Importancia Internacional

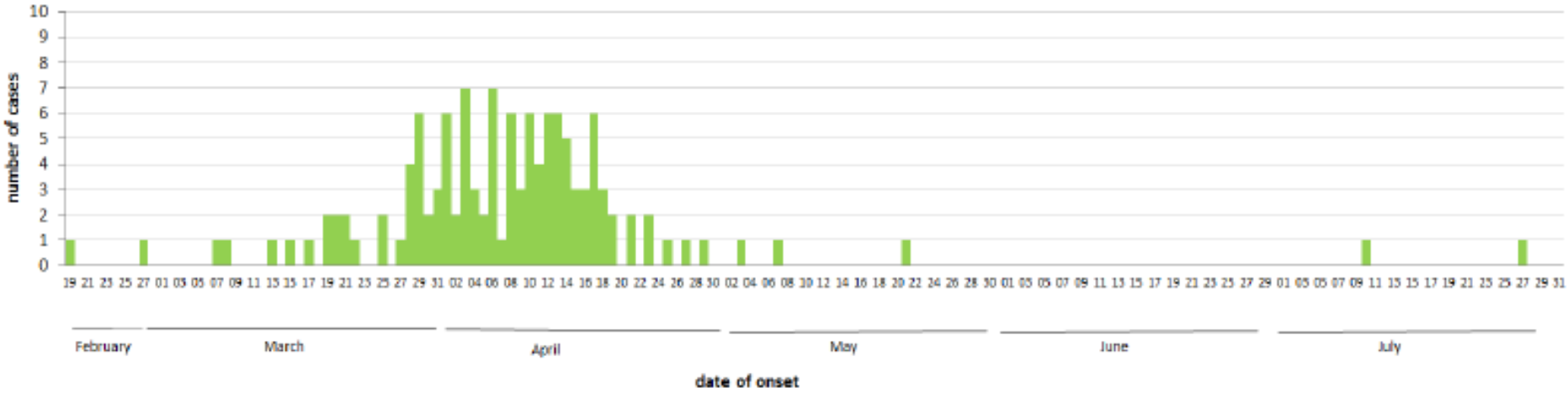
Evaluación del Riesgo (OMS / ECDC):

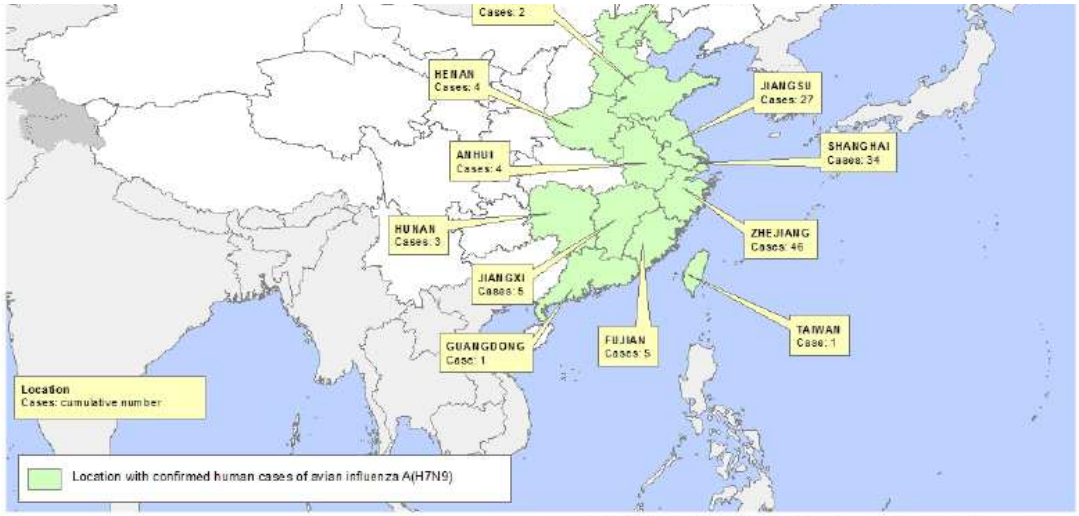
- No se ha evidenciado transmisión persona a persona.
- Riesgo de extensión internacional bajo.

16/10/2013: 136 casos / 45 muertes (letalidad=33,1%)

	February		March		April		May		June		July		unknown month of onset		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Total	2	2	30	12	88	7	3	0	0	0	2	0	10	23	**136**	**45**

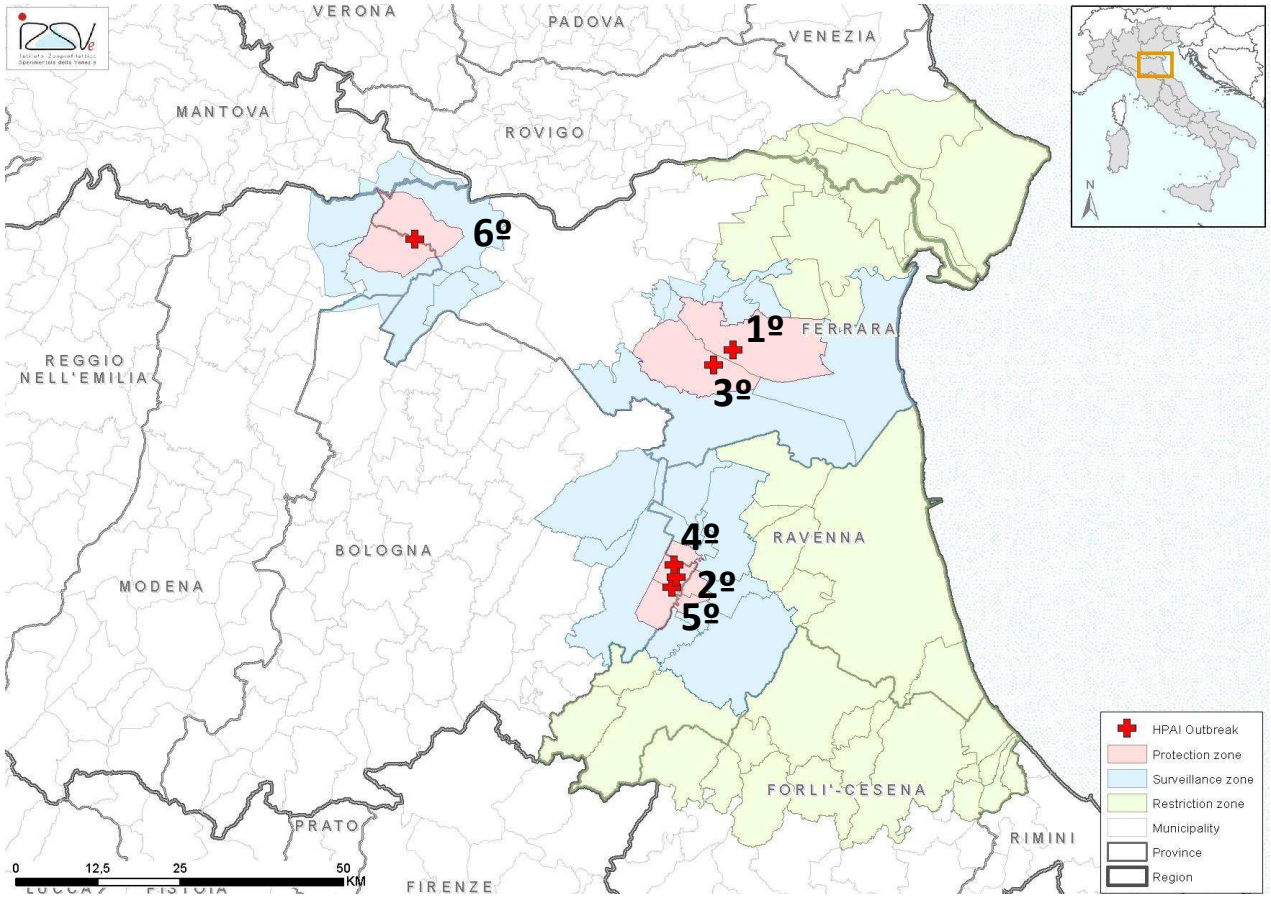
N = 125 confirmed cases for whom date of onset is known





GRIPE A (H7N9)

Report 9 - data in WHO/HQ as of 12 August 2013



Gripe aviar A (H7N7)
Italia (Emiglia Romana)

1º brote: 14-ago
2º brote: 21-ago
3º brote: 23-ago
4º brote: 28-ago
5º brote: 04-sep
6º brote: 06-sep

3 casos de infección humana por virus H7N7 en tres trabajadores que participaron en los procedimientos de erradicación de los brotes 1 y 2:

- 28-ago: 1º caso humano de conjuntivitis
- 31-ago: 2º caso de conjuntivitis e ILI
- 04-sep: 3º caso de conjuntivitis
- No hay transmisión de humano a humano

GRIPE A (H7N7)

GRIPE A (H5N1)

País	Año	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
Azerbaijan	Casos				8								8
	Defunciones				5								5
Banglasdesh	Casos						1			2	3	1	7
	Defunciones						0			0	0	1	1
Camboya	Casos			4	2	1	1	1	1	8	3	13	34
	Defunciones			4	2	1	0	0	1	8	3	9	28
China	Casos	1		8	13	5	4	7	2	1	2	2	45
	Defunciones	1		5	8	3	4	4	1	1	1	2	30
Djibuti	Casos				1								1
	Defunciones				0								0
Egipto	Casos				18	25	8	39	29	39	11	4	173
	Defunciones				10	9	4	4	13	15	5	3	63
Indonesia	Casos			20	55	42	24	21	9	12	9	1	193
	Defunciones			13	45	37	20	19	7	10	9	1	161
Irak	Casos				3								3
	Defunciones				2								2
Laos	Casos					2							2
	Defunciones					2							2
Myanmar	Casos					1							1
	Defunciones					0							0
Nigeria	Casos					1							1
	Defunciones					1							1
Pakistan	Casos					3							3
	Defunciones					1							1
Tailandia	Casos		17	5	3								25
	Defunciones		12	2	3								17
Turquía	Casos				12								12
	Defunciones				4								4
Vietnam	Casos	3	29	61		8	6	5	7		4	2	125
	Defunciones	3	20	19		5	5	5	2		2	1	62
Total	Casos	4	46	98	115	88	44	73	48	62	32	23	633
	Defunciones	4	32	43	79	59	33	32	24	34	20	17	377
	Letalidad	100%	70%	44%	69%	67%	75%	44%	50%	55%	63%	74%	60%

CAMBIO EN LA COMPOSICIÓN DE LA VACUNA FRENTE A LA GRIPE

Temporada 2011-2012

- Virus similar a **A/California/7/2009 (H1N1)**
- Virus similar a **A/Perth/16/2009 (H3N2)**
- Virus similar a **B/Brisbane/60/2008**

Temporada 2012-2013

- Virus similar a **A/California/7/2009 (H1N1)pdm09**
- Virus similar a **A/Victoria/361/2011 (H3N2)**
- Virus similar a **B/Wisconsin/1/2010**

Temporada 2013-2014

- Virus similar a **A/California/7/2009 (H1N1)pdm09**
- Virus similar a **A/Victoria/361/2011**
- Virus similar a **B/Massachusetts/2/2012**

ESPAÑA: RECOMENDACIONES DE VACUNACIÓN ANTIGRIPAL, 2013-2014

- Grupos de riesgo: niños a partir de los 6 meses y adolescentes con diferentes enfermedades de base

- Niños sanos a partir de los 6 meses y adolescentes sanos que convivan con pacientes de riesgo

- Adultos en contacto con niños y adolescentes pertenecientes a grupos de riesgo

- Vacunación del personal sanitario

USA, ACIP

Mantienen su recomendación de vacunación frente a la gripe estacional de toda la población desde los 6 meses de edad.

Nuevas vacunas antigripales:

Tetravalente: Añaden una segunda cepa de virus B

- Atenuada
- Inactivada

A/California/7/2009 (H1N1)
A/Victoria/361/2011 (H3N2)
B/Massachusetts/2/2012
B/Brisbane/60/2008

Recombinante (sin proteínas de huevo)

Influenza Vaccines United States, 2013–14 Influenza Season

Vaccine	Trade name	Manufacturer	Presentation	Age indications	Route
Inactivated Influenza Vaccine, Quadrivalent (IIV4)	**Fluarix® Quadrivalent**	GSK	0.5 mL single-dose prefilled syringe	≥3 yrs.	IM
	FluLaval® Quadrivalent	ID Biomedical Corporation of Quebec (distributed by GSK)	5.0 mL multi-dose vial	≥3 yrs.	IM
	Fluzone® Quadrivalent	Sanofi Pasteur	0.25 mL single-dose prefilled syringe	6-35 mos.	IM
			0.5 mL single-dose prefilled syringe	≥36 mos.	IM
			0.5 mL single-dose vial	≥36 mos.	IM
Recombinant Influenza Vaccine, Trivalent (RIV3)	**FluBlok®**	Protein Sciences	0.5 mL single-dose vial	18-49 yrs.	IM
Live-attenuated Influenza Vaccine, Quadrivalent (LAIV4)	**FluMist® Quadrivalent §§**	MedImmune	0.2 mL prefilled intranasal sprayer	2-49 yrs.***	IN

IIV4=Inactivated Influenza Vaccine, Quadrivalent; RIV=Recombinant Influenza Vaccine LAIV=Live-Attenuated Influenza Vaccine; IM=intramuscular; IN=intranasal.

§§ Children 2-4 yrs who have asthma or who had a wheezing episode noted in the medical record within the past 12 months should not receive FluMist®.

*** Flumist® is indicated for healthy, non-pregnant persons aged 2-49 years. Individuals who care for severely immunosuppressed persons who require a protective environment should not receive FluMist given the theoretical risk of transmission of the live attenuated vaccine virus.

Contents lists available at ScienceDirect

Vaccine

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

Cochrane re-arranged: Support for policies to vaccinate elderly people against influenza☆

Walter E.P. Beyer[a], Janet McElhaney[b], Derek J. Smith[c,d,a], Arnold S. Monto[e], Jonathan S. Nguyen-Van-Tam[f], Albert D.M.E. Osterhaus[a,*]

ABSTRACT

The 2010 Cochrane review on efficacy, effectiveness and safety of influenza vaccination in the elderly by Jefferson et al. covering dozens of clinical studies over a period of four decades, confirmed vaccine safety, but found no convincing evidence for vaccine effectiveness (VE) against disease thus challenging the ongoing efforts to vaccinate the elderly.

However, the Cochrane review analyzed and presented the data in a way that may itself have hampered the desired separation of real vaccine benefits from inevitable 'background noise'. The data are arranged in more than one hundred stand-alone meta-analyses, according to various vaccine types, study designs, populations, and outcome case definitions, and then further subdivided according to virus circulation and antigenic match. In this way, general vaccine effects could not be separated from an abundance of environmental and operational, non vaccine-related variation. Furthermore, expected impacts of changing virus circulation and antigenic drift on VE could not be demonstrated.

We re-arranged the very same data according to a biological and conceptual framework based on the basic sequence of events throughout the 'patient journey' (exposure, infection, clinical outcome, observation) and using broad outcome definitions and simple frequency distributions of VE values. This approach produced meaningful predictions for VE against influenza-related fatal and non-fatal complications (average ~30% with large dispersion), typical influenza-like illness (~40%), disease with confirmed virus infection (~50%), and biological vaccine efficacy against infection (~60%), under conditions of virus circulation. We could also demonstrate a VE average around zero in the absence of virus circulation, and decreasing VE values with decreasing virus circulation and increasing antigenic drift.

We regard these findings as substantial evidence for the ability of influenza vaccine to reduce the risk of influenza infection and influenza-related disease and death in the elderly.

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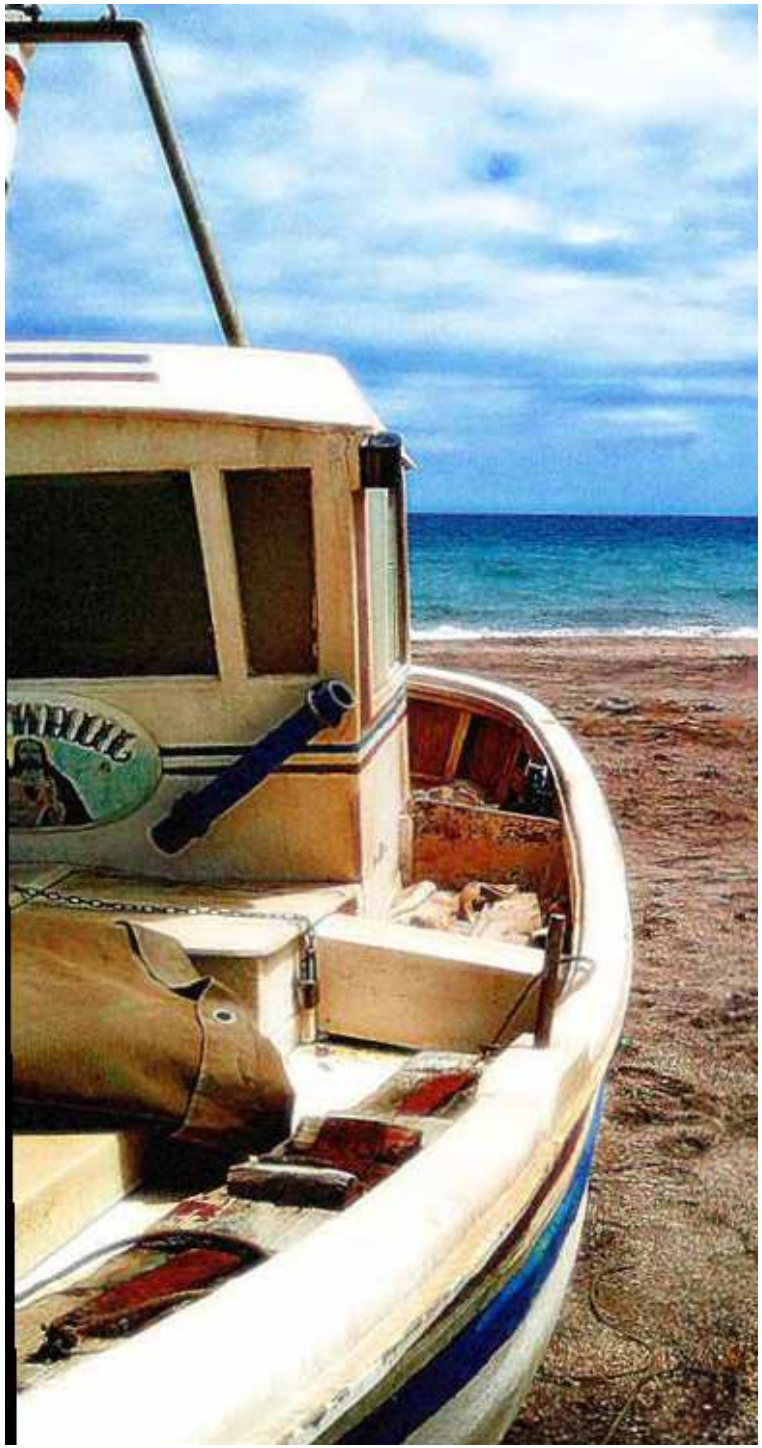

VACUNA DE LA VARICELA

Impact of universal two-dose vaccination on varicella epidemiology in Navarre, Spain, 2006 to 2012

M García Cenoz (mgcenoz@navarra.es)[1,2], J Castilla[1,2], J Chamorro[3], I Martínez-Baz[1,2], V Martínez-Artola[3], F Irisarri[1,2], M Arriazu[1,2], C Ezpeleta[3], A Barricarte[1,2]

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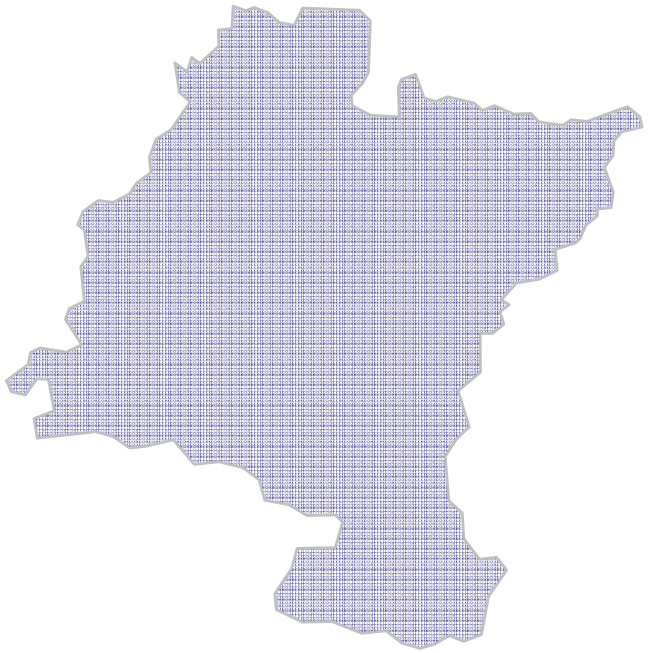
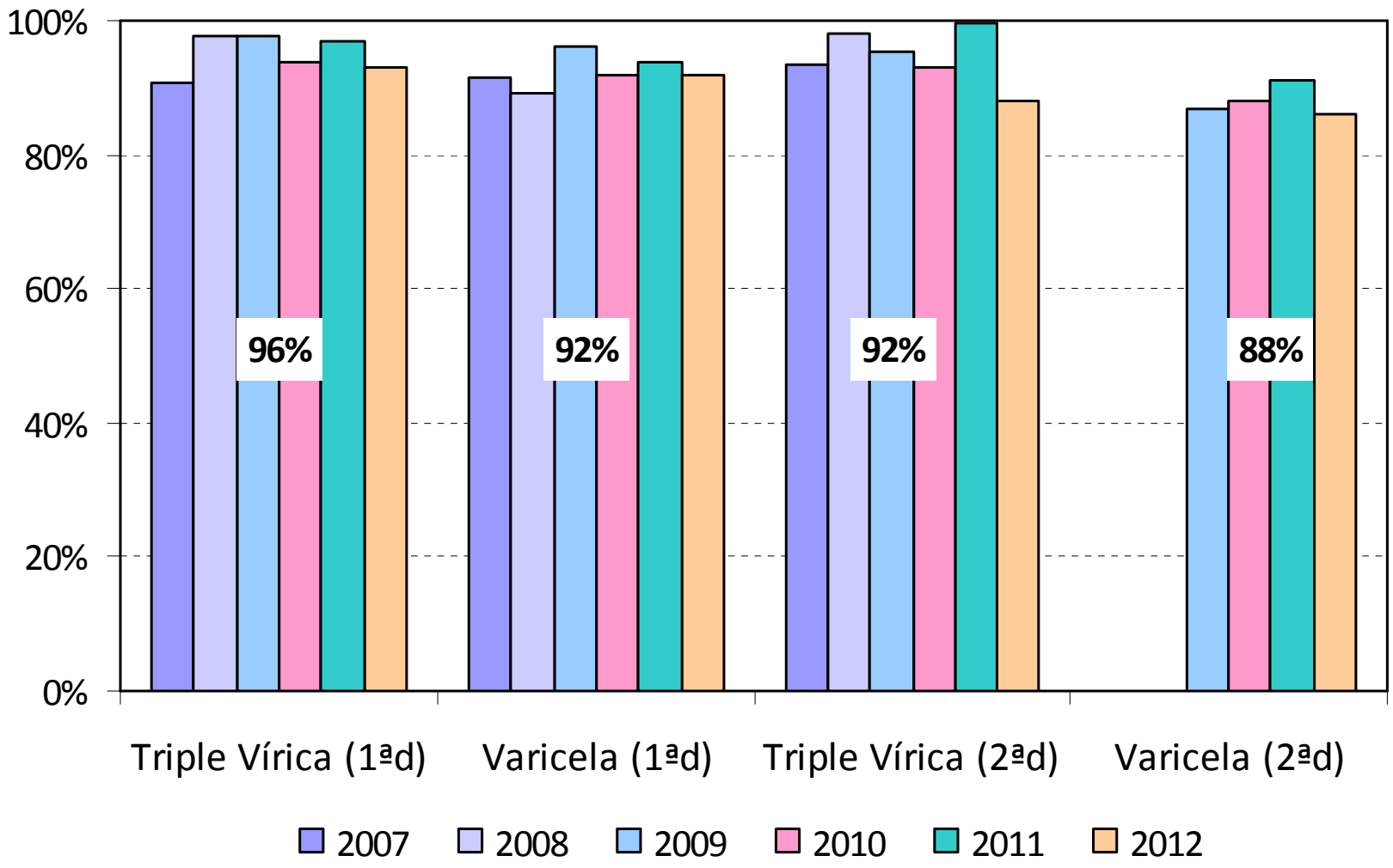
García Cenoz M, Castilla J, Chamorro J, Martínez-Baz I, Martínez-Artola V, Irisarri F, Arriazu M, Ezpeleta C, Barricarte A. Impact of universal two-dose vaccination on varicella epidemiology in Navarre, Spain, 2006 to 2012. Euro Surveill. 2013;18(32):pii=20552. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20552



- **INCIDENCIA**
- **HOSPITALIZACIONES**
- **FALLOS VACUNALES**
- **EFECTIVIDAD**

COBERTURA DE VACUNACIÓN DE TRIPLE VÍRICA Y VARICELA
Navarra, 2007-2012

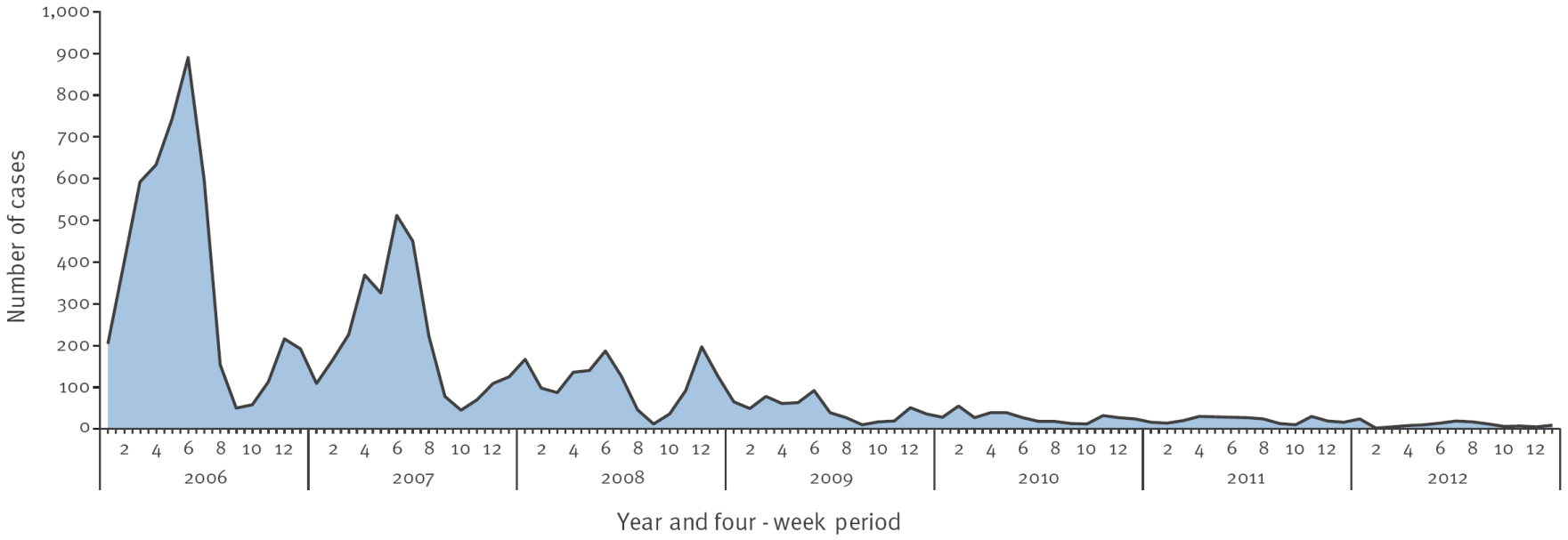


IMPACTO DE LA VACUNACIÓN FRENTE A LA VARICELA

Casos de varicela declarados al SVE en Navarra por cuatrisemanas, 2006-2012

FIGURE 1

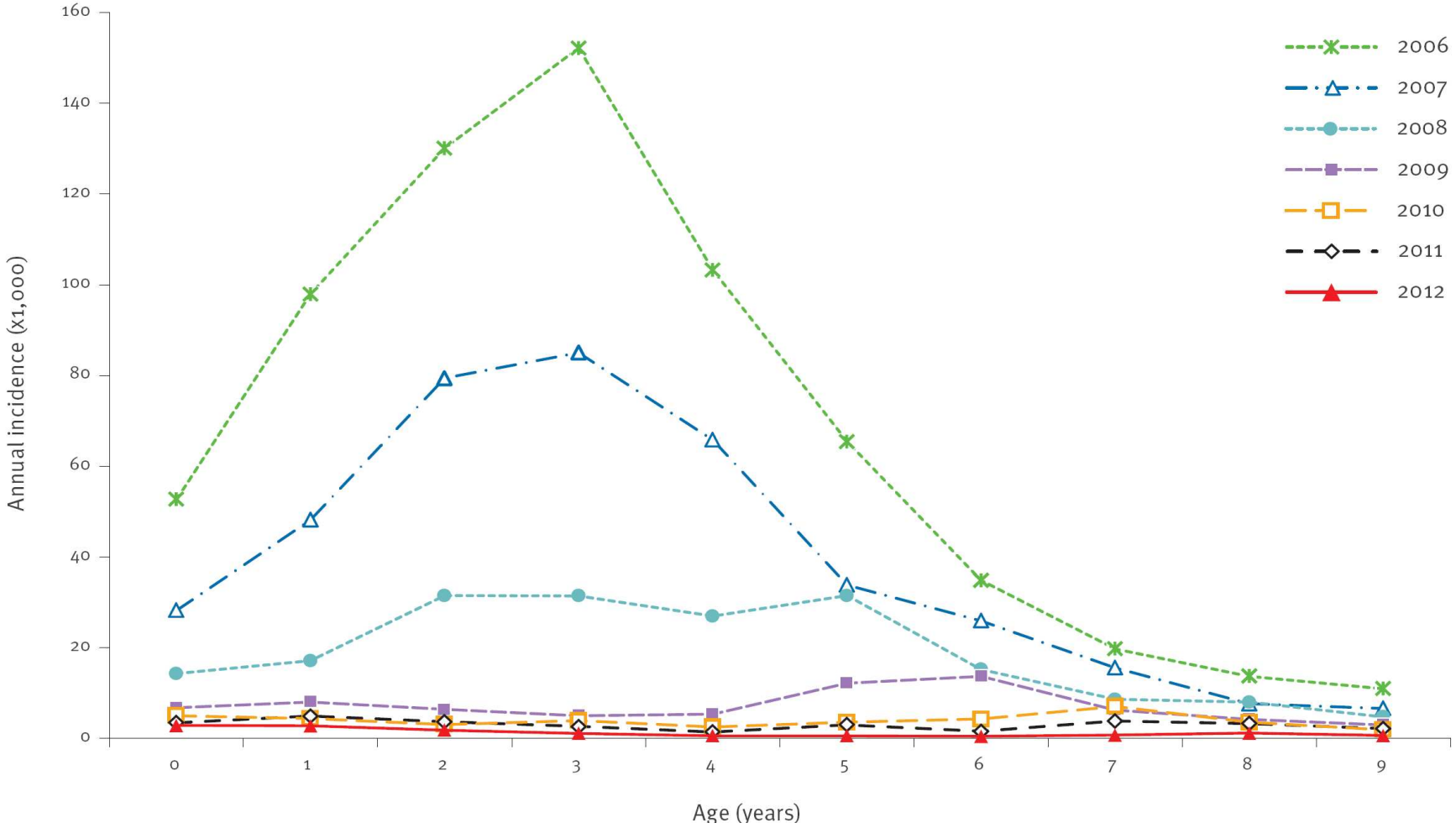
Notified varicella cases, by four-week period, Navarre, 2006–2012 (n=10,477)



Incidencia anual de varicela por 1000 hab. en población < 10 años, según edad año a año, 2006-2012.

FIGURE 2

Annual incidence of varicella per 1,000 inhabitants by age, Navarre, 2006–2012



EVOLUCIÓN DE LA INCIDENCIA DE VARICELA EN LAS COHORTES VACUNADAS

Table 1

Annual incidence of varicella per 1,000 inhabitants among age groups included in universal vaccination (1–8 years) and vaccination of susceptibles (10–21 years), Navarre, 2006–2012

Age groups	2006	2007	2008	2009	2010	2011	2012	% reduction 2006–2012
Universal vaccination								
1 year	70.1	32.8	19.2	8.5	5.3	5.1	2.9	95.9%[c]
2 years	117.9	67.3	11.3	7.3	3.8	3.6	2.7	97.7%[c]
3 years	133.0	78.0	46.7	5.2	3.6	3.5	1.4	99.0%[c]
4 years	142.8	86.3	15.3	5.4	3.3	1.3	0.7	99.5%[c]
5 years	94.9	49.3	43.0	4.5	2.8	2.2	0.3	99.7%[c]
6 years	51.7	30.0	21.4	21.7	3.5	2.5	0.7	98.6%[c]
7 years	28.3	19.7	9.5	7.4	6.3	1.6	0.3	99.0%[c]
8 years	14.4	12.5	9.8	5.2	5.9	5.0	0.7	94.9%[c]
Total 1–8 years	**92.1**	**52.6**	**23.9**	**8.5**	**4.1**	**2.8**	**1.2**	**98.5%[c]**
Vaccination of susceptibles								
10–16 years[a]	**7.3**	**2.0**	**1.6**	**1.5**	**0.6**	**0.4**	**7.3**	**95.6%[c]**
17–21 years[b]	**2.7**	**1.4**	**0.6**	**0.6**	**0.4**	**0.2**	**0.3**	**90.1%[c]**

[a] Vaccinated at 10 years of age.

[b] Vaccinated at 11, 12, 13 or 14 years of age.

[c] p value <0.001.

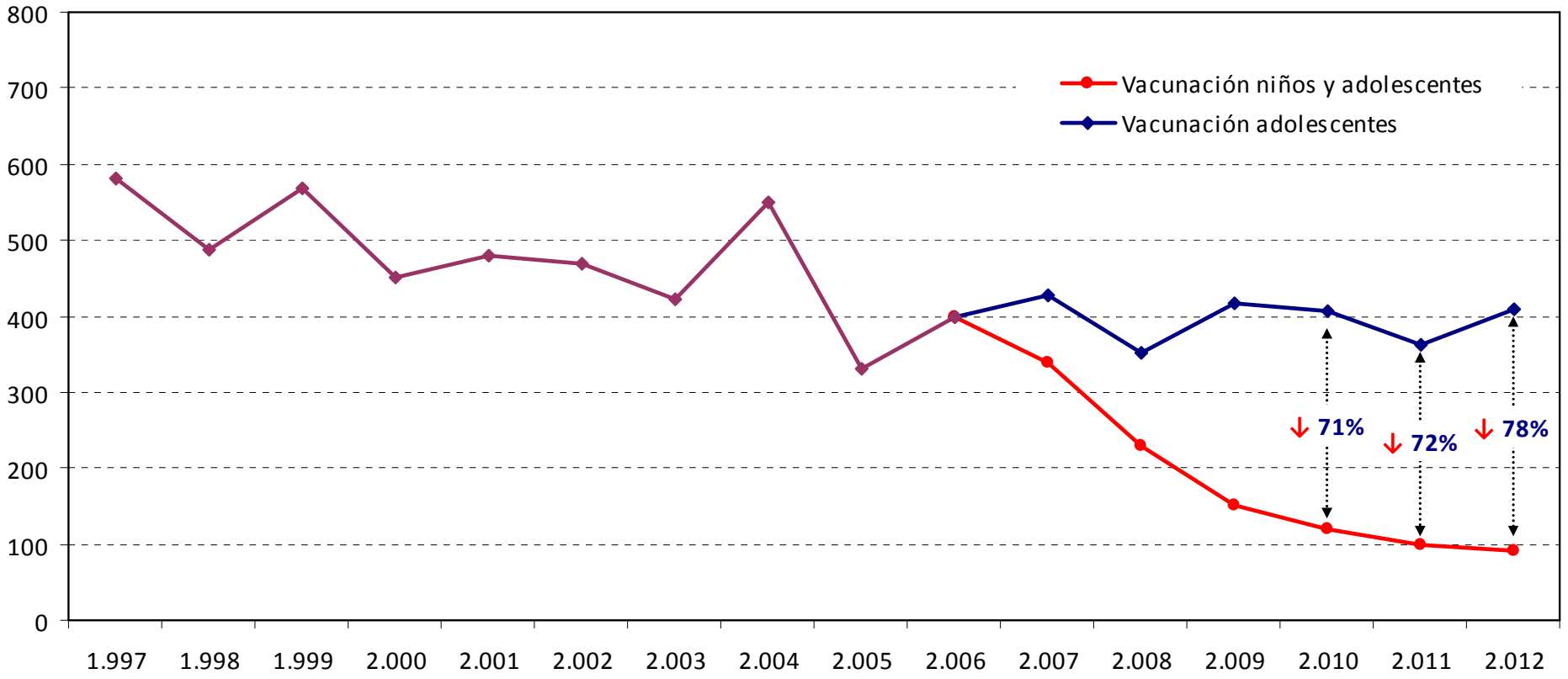
EVOLUCIÓN DE LA INCIDENCIA DE VARICELA EN LAS COHORTES NO VACUNADAS

Table 2

Annual incidence of varicella per 1,000 inhabitants in unvaccinated age groups (indirect effect), Navarre, Spain, 2006–2012

Age groups	2006	2007	2008	2009	2010	2011	2012	% reduction 2006–2012	p
< 1 year	**12.5**	**8.7**	**5.5**	**1.9**	**1.5**	**1.3**	**1.2**	**90.5%**	**<0.0001**
9 years	**11.7**	**6.3**	**5.9**	**3.0**	**2.4**	**2.9**	**1.2**	**89.4%**	**<0.0001**
22–24 years	1.6	1.2	0.6	0.4	0.3	0.1	0.1	96.8%	<0.0001
25–44 years	1.6	0.9	0.6	0.3	0.2	0.2	0.05	92.4%	<0.0001
45–64 years	0.2	0.2	0.1	0.08	0.06	0.07	0.04	84.6%	0.0015
≥65 years	0.1	0.07	0.04	0.03	0.02	0.02	0.01	91.7%	0.0526
Total ≥22 years	**0.8**	**0.5**	**0.3**	**0.2**	**0.1**	**0.1**	**0.06**	**92.4%**	**<0.0001**

INCIDENCIA MEDIA ANUAL DE LA VARICELA EN ESPAÑA, 1997-2012



HOSPITALIZACIONES POR VARICELA, NAVARRA 2006-2012

Table 3

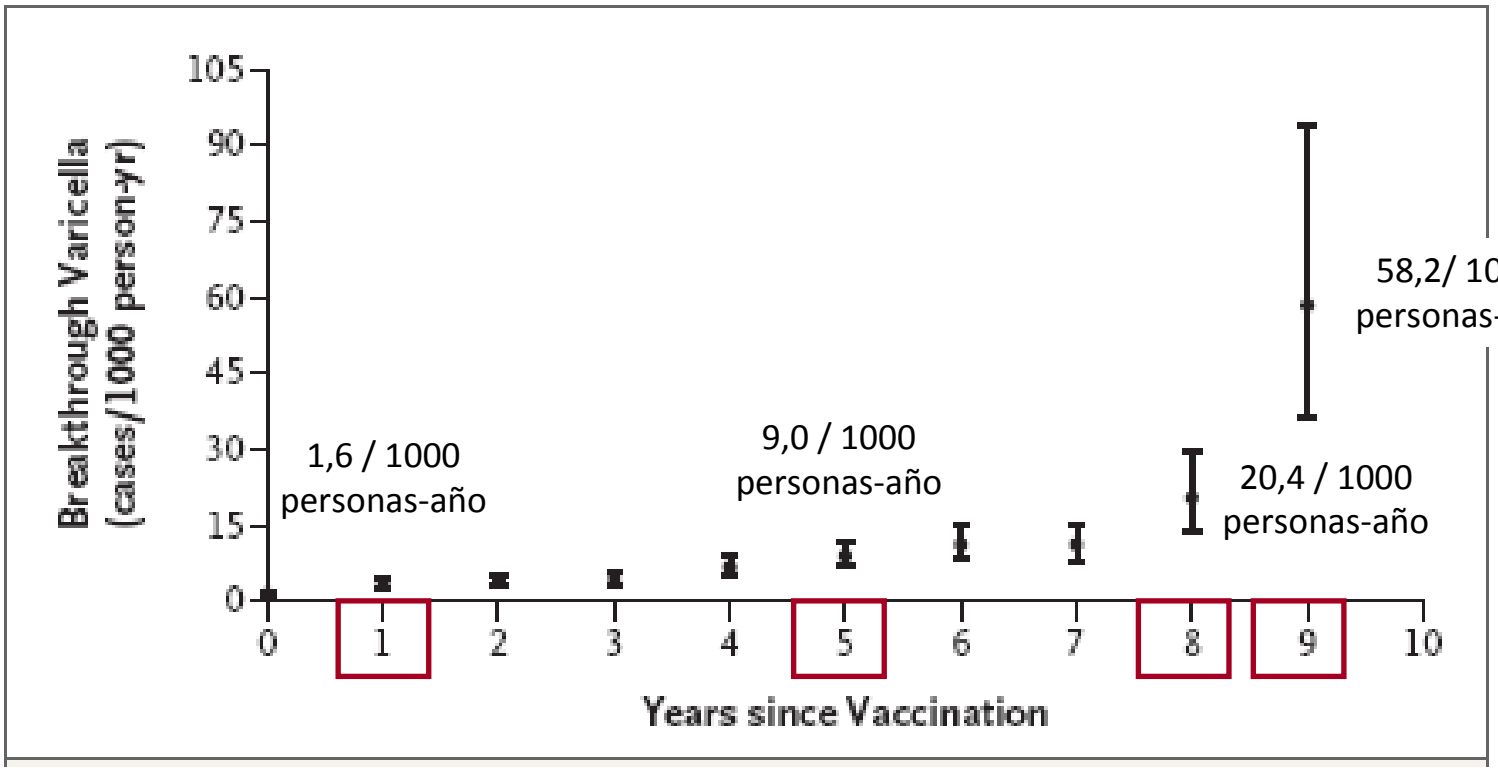
Hospital admissions with diagnosis of varicella (ICD-9-CM code 052.9) and varicella with complication (ICD-9-CM codes 052.0, 052.1, 052.7 and 052.8), Navarre, Spain, 2006–2012 (n=71)

	2006	2007	2008	2009	2010	2011	2012	% reduction 2006–2012
Total population								
Hospital admissions	25	22	11	7	1	2	3	88%
Average stay (days)	5.9	5.0	3.4	5.0	6.0	1.5	4.3	NA
Admissions per 100,000	4.2	3.6	1.8	1.1	0.3	0.3	0.5	89%[a]
Number of complicated varicella	10	10	2	3	0	0	0	NA
Children <15 years								
Hospital admissions	18	14	9	2	0	0	1	94%
Average stay (days)	5.9	4.6	3.2	4.0	NA	NA	3,0	NA
Admissions per 100,000	20.9	15.9	9.9	2.1	0	0	1,0	95%[a]
Number of complicated varicella	5	6	1	1	0	0	1	NA

NA: not applicable.

[a] p value =0.0001.

Tasas ajustadas de fallos vacunales en niños vacunados entre los 12 meses y 12 años, según los años desde la vacunación (1 dosis)



Fuente: Chaves SS et al. N Eng J Med 2007; 356: 1121-1129

EFECTIVIDAD DE LA VACUNACIÓN FRENTE A LA VARICELA

MAJOR ARTICLE

Effectiveness of 2 Doses of Varicella Vaccine in Children

JID 2011:203

Eugene D. Shapiro,[1,3,4] Marietta Vazquez,[1] Daina Esposito,[1] Nancy Holabird,[1] Sharon P. Steinberg,[5] James Dziura,[1,2] Philip S. LaRussa,[5] and Anne A. Gershon[5]

[1]Department of Pediatrics; [2]Department of Medicine; [3]Department of Epidemiology; [4]Department of Investigative Medicine, Yale University School of Medicine and Graduate School of Arts and Sciences, New Haven, Connecticut; and [5]Department of Pediatrics, Columbia University College of Physicians and Surgeons, New York, New York

La efectividad de 2 dosis de vacuna fue del 98,3%. La probabilidad de desarrollar varicela en los niños que recibieron 2 dosis fue un 95% menor que los que recibieron una dosis.

Table 4

Estimated vaccine effectiveness of any dose of varicella vaccine in vaccinated cohorts (children born between 2004 and 2010), Navarre, 2007–2012

Birth year	Population			Varicella cases			Vaccine effectiveness (95% confidence interval)	
	n	Vaccinated n (%)		n	Vaccinated n (%)			
2004	6,723	2,357	(35)	678	19	(3)	94.7	(91.6–96.6)
2005	6,612	3,104	(47)	819	23	(3)	96.7	(95.1–97.8)
2006	6,869	6,004	(87)	355	86	(24)	95.4	(94.2–96.3)
2007	6,881	6,207	(90)	271	47	(17)	97.7	(96.9–98.3)
2008	7,135	6,587	(92)	147	29	(20)	98.0	(97.0–98.6)
2009	6,917	6,434	(93)	87	24	(28)	97.1	(95.5–98.2)
2010	6,771	6,278	(93)	65	10	(15)	98.6	(97.2–99.3)
2004–2010	**47,908**	**36,971**	**(77)**	**2,422**	**238**	**(10)**	**96.8**	**(96.3–97.2)**

En las cohortes vacunadas entre 2007 y 2012, la efectividad de la vacuna fue ≈ 97%

Método de Screening (Farrington[1])

$$VE = 1 - \left[\frac{PCV}{1 - PCV} * \frac{1 - PPV}{PPV} \right]$$

[1] *Farrington CP. Estimation of vacccine effectiveness using the screening method. Int J. Epidemiol 1993; 22:742-746*

SHORT REPORT

Human Vaccines & Immunotherapeutics 9:5, 1–5; May 2013; © 2013 Landes Bioscience

Effectiveness of one and two doses of varicella vaccine in preventing laboratory-confirmed cases in children in Navarre, Spain

Manuel García Cenoz,[1,2] Víctor Martínez-Artola,[3] Marcela Guevara,[1,2] Carmen Ezpeleta,[3] Aurelio Barricarte[1,2] and Jesús Castilla[1,2,*]

[1]Instituto de Salud Pública de Navarra; Pamplona, Spain; [2]CIBER Epidemiología y Salud Pública (CIBERESP); Pamplona, Spain; [3]Servicio de Microbiología; Complejo Hospitalario de Navarra; Pamplona, Spain

Estudio de casos y controles apareado

Casos: Niños de 15 meses a 10 años con clínica de varicela confirmada mediante PCR de una lesión cutánea, residentes en Navarra, cubiertos por el SNS-0.

Controles: Niños sin diagnóstico previo de varicela, apareados por pediatra, distrito de residencia y año de nacimiento ±1 (8 por caso).

Periodo de estudio: 1 Mayo 2010 – 30 Junio 2012

Table 1. Characteristics of cases and controls

	Cases	Controls	p-value
	N (%)	N (%)	
Sex			0.067
Male	21 (39%)	225 (52%)	
Female	33 (61%)	207 (48%)	
Age			0.998
15–24 mo	6 (11%)	48 (11%)	
3–4 y	7 (13%)	59 (14%)	
5–6 y	9 (17%)	67 (16%)	
7–8 y	26 (48%)	214 (50%)	
9–10 y	6 (11%)	44 (10%)	
Major chronic condition			0.487
No	47 (87%)	360 (83%)	
Yes	7 (13%)	72 (17%)	
Other persons in the household			0.124
1	4 (7%)	41 (9%)	
2	5 (9%)	96 (22%)	
3	24 (44%)	164 (38%)	
4+	21 (39%)	131 (30%)	
Migrant parents			0.019
No	42 (78%)	384 (89%)	
Yes	12 (22%)	48 (11%)	

Table 1. Characteristics of cases and controls

	Cases	Controls	p-value
	N (%)	N (%)	
Visits to the pediatrician			0.050
0	3 (6%)	73 (17%)	
1–5	30 (56%)	239 (55%)	
6+	21 (39%)	120 (28%)	
Doses of varicella vaccine			< 0.001
0	48 (89%)	257 (59%)	
1	5 (9%)	112 (26%)	
2	1 (2%)	63 (15%)	
Doses of measles-mumps-rubella vaccine			0.766
0	2 (4%)	26 (6%)	
1	14 (26%)	103 (24%)	
2	38 (70%)	303 (70%)	
Total	54 (100%)	432 (100%)	

Tiempo desde la primera dosis

Table 3. Estimates of the effectiveness of one dose of varicella vaccine according to time since vaccination

Varicella vaccine status	Cases/controls	Crude vaccine effectiveness (95% CI)*	Adjusted vaccine effectiveness (95% CI)#	p-value
Unvaccinated	48/257	-	-	
< 12 mo after vaccination	1/30	89% (4%; 100%)	93% (34%; 100%)	0.011
12–35 mo after vaccination	1/47	93% (51%; 100%)	95% (62%; 100%)	< 0.001
≥ 36 mo after vaccination	3/35	64% (-42%; 94%)	61% (-64%; 94%)	0.271

*Result of the unadjusted conditional logistic regression model. #Result of the exact conditional logistic regression adjusted for migrant parents and visits to the pediatrician in the previous 12 mo.

waning immunity

La circulación del virus de la varicela-zóster se redujo con la consiguiente reducción del efecto de refuerzo de la exposición repetida al virus salvaje.

ESTIMACIÓN DE LA EFECTIVIDAD DE LA VACUNA

Table 2. Estimates of the effectiveness of varicella vaccine in different analyses

Varicella vaccine status	Cases/ controls	Crude vaccine effectiveness (95% CI)*	Adjusted vaccine effectiveness (95% CI)#	p-value
Unvaccinated	48/257	-	-	
Vaccinated (any dose)	6/175	90% (73%; 96%)	92% (77%; 97%)	< 0.001
Unvaccinated	48/257	-	-	
One dose	5/112	84% (53%; 95%)	87% (60%; 97%)	< 0.001
Two doses	1/63	97% (79%; 100%)	97% (80%; 100%)	< 0.001
Children aged < 3 y				
Unvaccinated	5/12	-	-	
One dose	1/36	93% (31%; 100%)	84% (-58%; 100%)	0.119
Children aged ≥ 3 y				
Unvaccinated	43/245	-	-	
One dose	4/76	78% (30%; 95%)	80% (37%; 95%)	0.003
Two doses	1/63	96% (78%; 100%)	97% (79%; 100%)	< 0.001

* Result of the unadjusted conditional logistic regression model. #Result of the exact conditional logistic regression adjusted for migrant parents and visits to the pediatrician in the previous 12 mo.

La efectividad incremental de la segunda dosis fue de un 74% (IC95%: -115% to 100%; *P* =0,231).

SEPTIEMBRE/2013

NOTICIAS

Varivax: una vacuna que no llega a las farmacias

25 septiembre 2013

Varivax es el nombre comercial de una vacuna de varicela que se vende en las farmacias. Se han denunciado problemas de "desabastecimiento" en varias comunidades autónomas. Pero descubrimos que se trata de algo intencionado para evitar su uso en edades tempranas.

La Aemps restringe el uso de Varivax más allá de lo establecido en su FT

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Sanidad bloquea por abuso la vacuna de la varicela en las farmacias

- El ministerio desliza posibles repercusiones de salud pública
- Tres sociedades científicas acusan al Gobierno de provocar el desabastecimiento del fármaco

2 de septiembre de 2013

DESABASTECIMIENTO DE VACUNAS DE LA VARICELA EN LAS OFICINAS DE FARMACIA ESPAÑOLAS

"Las Sociedades Científicas más vinculadas con el empleo de vacunas manifestamos nuestra extrañeza y preocupación ante el desabastecimiento de vacunas de la varicela que se está produciendo en numerosas oficinas de farmacia españolas…"

"…no tenemos conocimiento oficial, es decir, por parte del Ministerio de Sanidad o de la Agencia Española de Medicamentos y Productos Sanitarios (AEMPS), de ninguna circunstancia que explique este desabastecimiento, como podría ser un eventual problema de producción, de distribución o de seguridad."