Avances en la vacunación frente a Herpes zoster. Nuevas dianas

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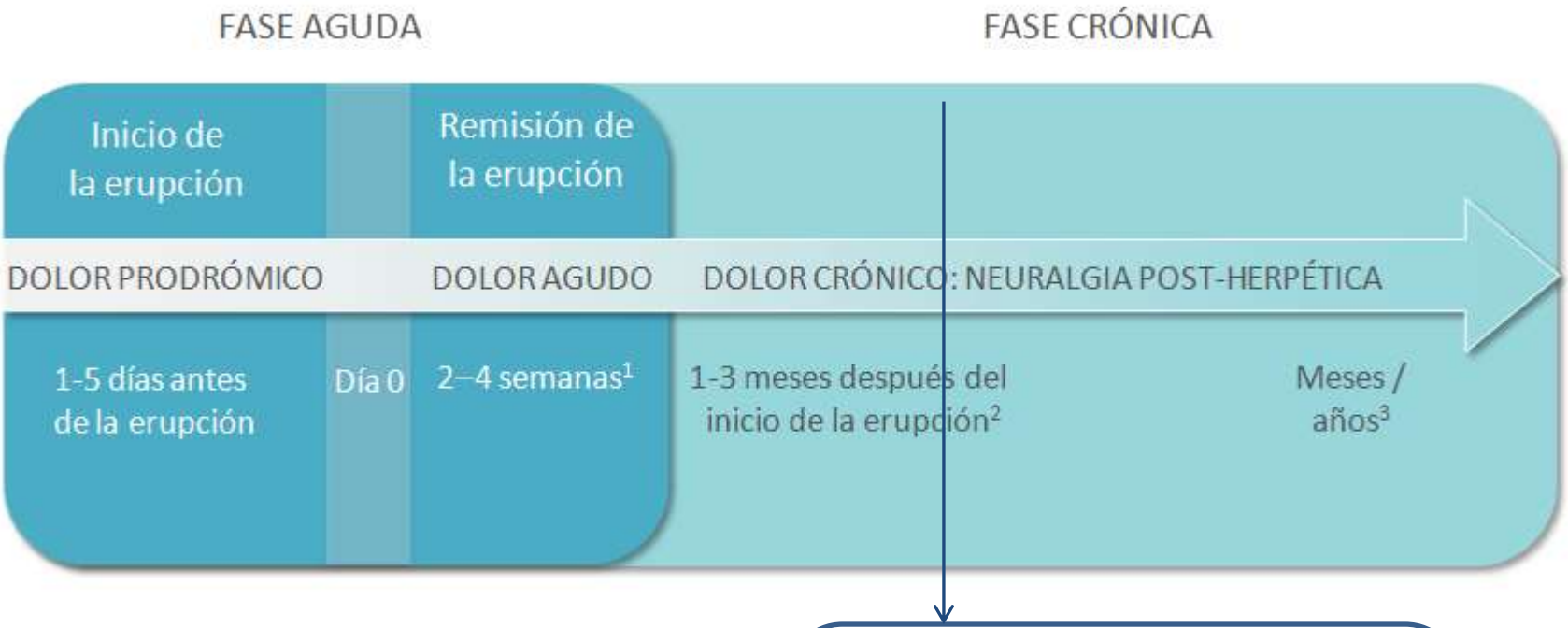
VIRUS DE HZ- PATOGÉNESIS:

- El HZ se asocia a una **disminución en la inmunidad celular.**
- **Adultos ≥ 50 años de edad, 98% seropositivos para varicela.**
- **1 de cada 4 personas desarrollará un HZ en su vida, el riesgo aumenta con la edad, sobre todo después de los 50 años de edad.**

CLÍNICA Y COMPLICACIONES: NEURALGIA POSTHERPÉTICA (NPH)

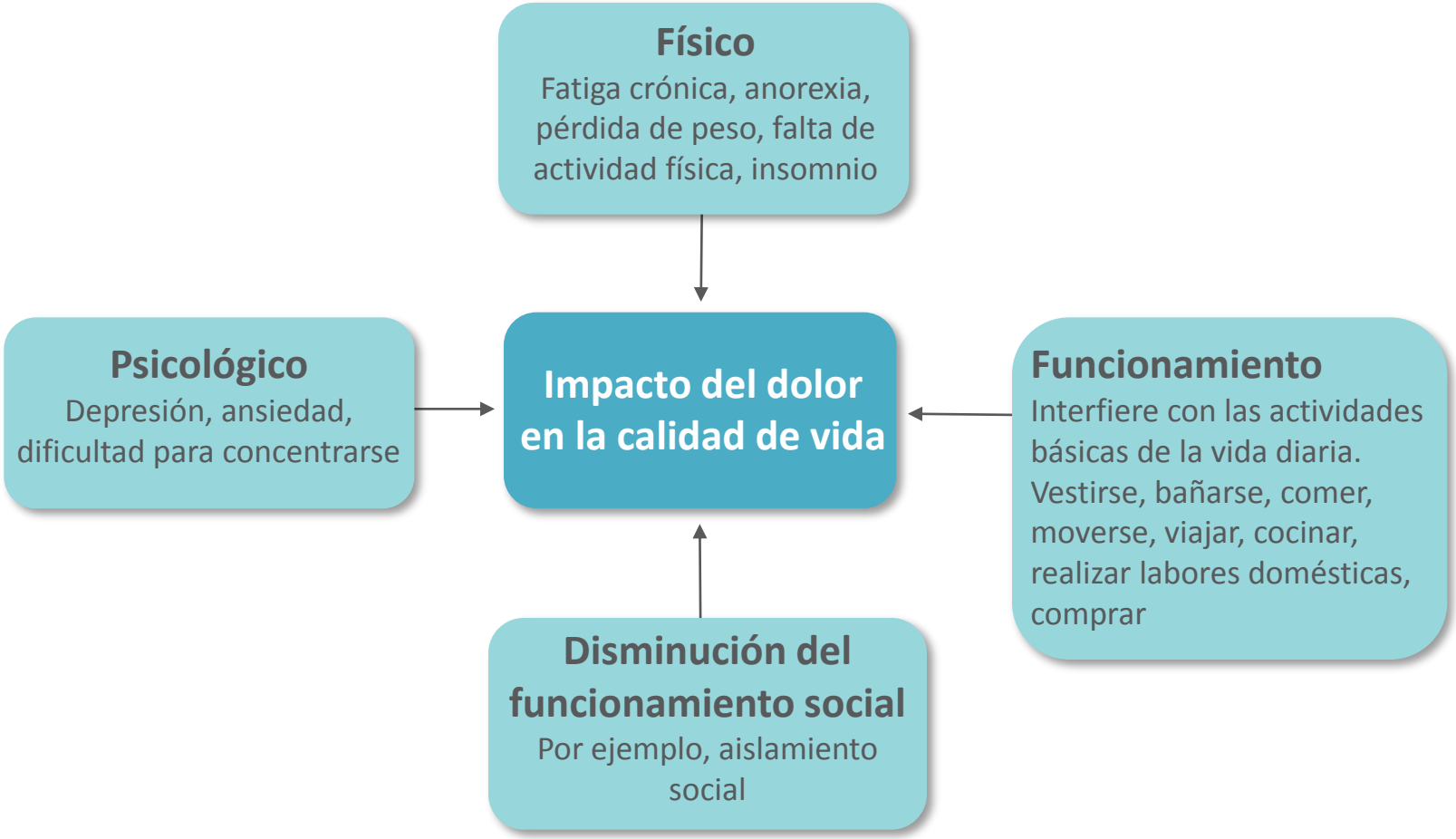


Neuralgia Post-Herpética (NPH) la complicación principal (15% de los casos).
Incidencia: 3 -5 casos por cada 1.000 habitantes.

1. *Gnann JW. 2002.*
2. *Opstelten W et al. 2002.*
3. *Dworkin RH et al 2003.*

Picazo de la Garza JJ, Abad Cervero P, Moya Mir M. Estudio epidemiológico nacional sobre herpes zóster en España. Incidencia, manifestaciones clínicas y evolución. Madrid: TCC; 1999

Impacto del dolor del Herpes Zóster en la calidad de vida relacionada con la salud



Schmader CID. 2001. Johnson B. 2011.

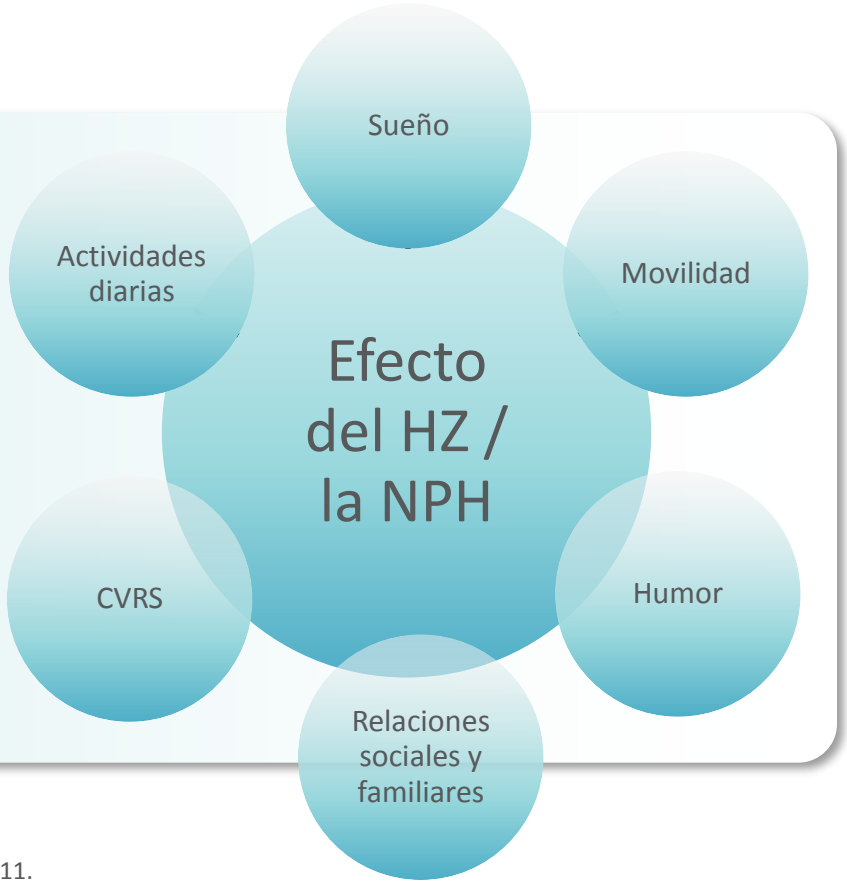
Calidad de vida relacionada con la salud

EL HZ Y LA NPH TIENEN UN EFECTO NEGATIVO EN LA CVRS DE LOS PACIENTES EN GENERAL, ASÍ COMO EN LOS ÁMBITOS ESPECÍFICOS DE LA CVRS.

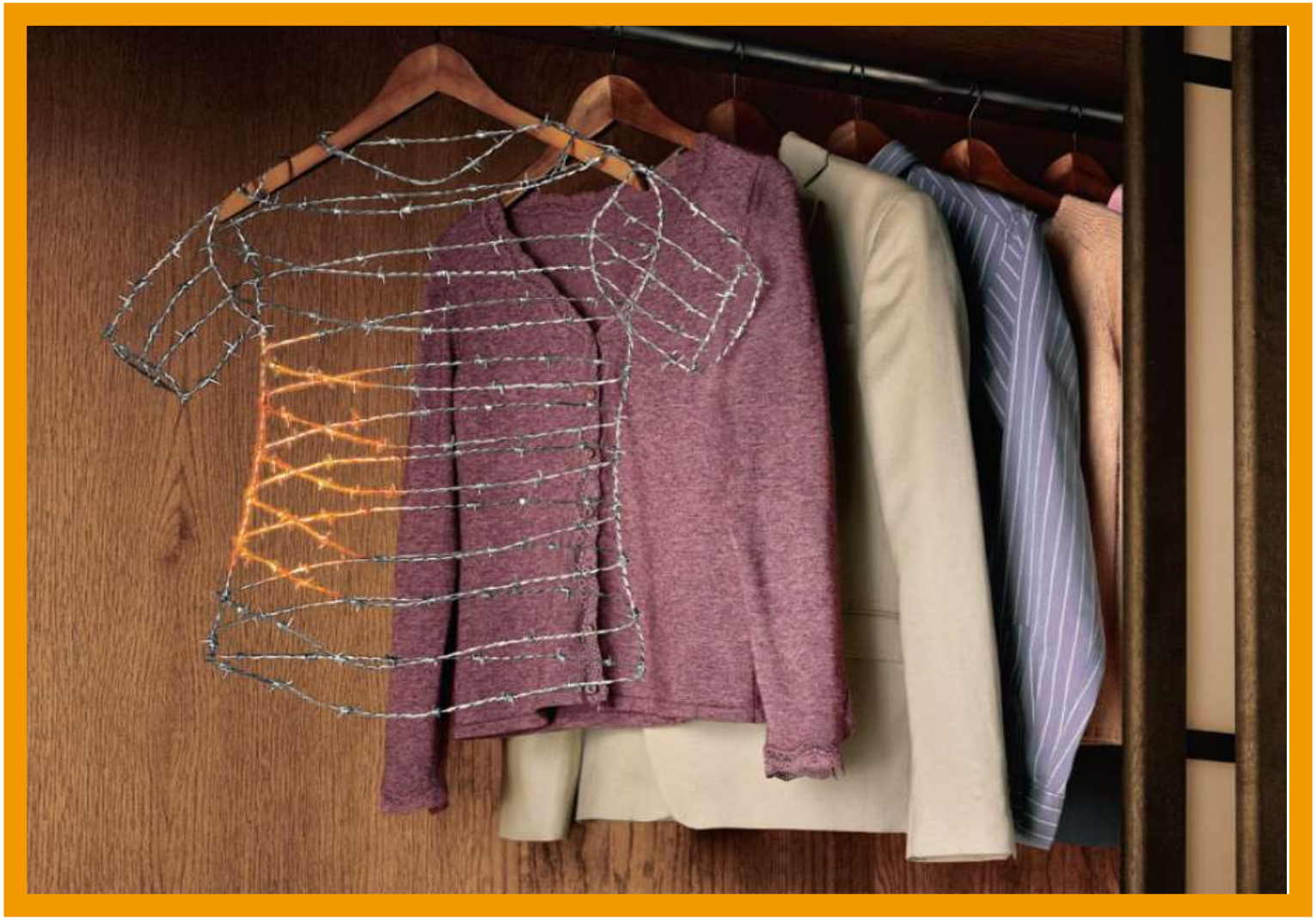
Se observó que el efecto que tienen el HZ y la NPH en la CVRS, se asociaba principalmente a:

- **La presencia de la NPH**
  Los pacientes con NPH, experimentaron un efecto mayor en la mayoría de los ámbitos de la CVRS, en comparación con los pacientes con HZ[1–3]

- **El nivel del dolor experimentado**
  En general, la CVRS está inversamente relacionada con los niveles del dolor reportado[4–5]



1. Weinke 2010. 2. Lukas 2012. 3. Carroll 2011. 4. Van Sventer 2006. 5. Pickering 2011.



Indicación en FT

ZOSTAVAX ® está indicado para la prevención del herpes zóster (“zóster” o culebrilla) y la neuralgia post-herpética (NPH) relacionada con herpes zóster.

La primera vacuna con indicación de prevención de HZ y NPH en adultos de más de 50 años

- Zostavax® polvo y disolvente para suspensión inyectable en jeringa precargada
- Después de su reconstitución, una dosis (0,65 ml) contiene:
  - **Virus de la varicela-zóster,** cepa OKA/Merck **(vivos, atenuados)**
  - **19.400 unidades** formadoras de placas (UFP) como mínimo
  - **Obtenidos en células diploides humanas (MRC-5).**
  - **Se debe administrar una sola dosis por vía subcutánea./im**
  - **Actualmente se desconoce si es necesaria una segunda dosis**

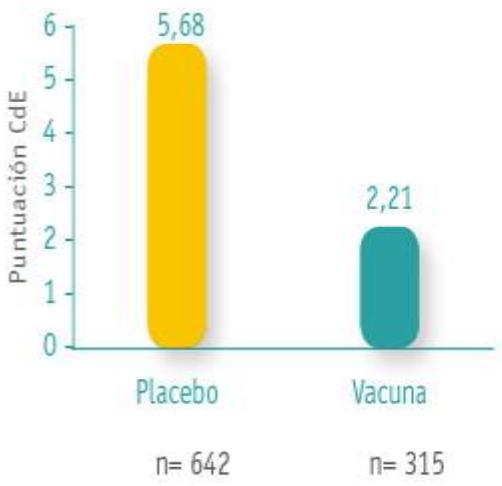
Ficha Técnica Zostavax. 2013

Desarrollo clínico de la Vacuna

Eficacia de Zostavax®: estudio SPS

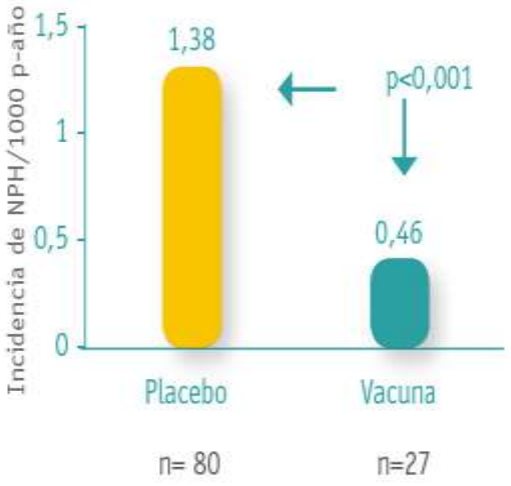
✓ Resultados:

Variable Principal: Carga de enfermedad asociada a HZ



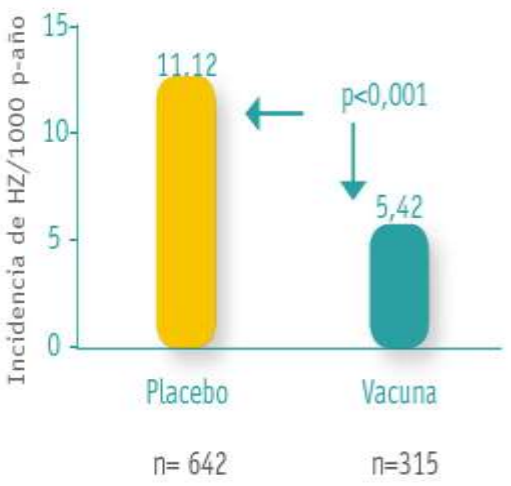
EVCdE = 61,1%
(IC 95%: 51,1–69,1%)

Variable Secundaria: reducción de la incidencia de NPH



EVNPH = 66,5%
(IC 95%: 47,5–79,2%)

Variable secundaria: Reducción de la incidenica de HZ



EVHZ = 51,3%
(IC 95%: 44,2–57,6%)

cátedra de investigación en vacunas

1. Oxman MN et al. 2005

Eficacia a largo plazo: estudio STPS

- ✓ **El estudio STPS evalúa la eficacia de la vacuna hasta 7 años desde su administración, mostrando una eficacia duradera.**

	EV HZ	EV NPH	EV CdE
SPS[1]	51,3%	66,5%	61,1%
0,0 - 4,0 años	(44,2 - 57,6)	(47,5 - 79,2)	(51,1 - 69,1)
Eficacia duradera hasta 4 años después de la vacunación			
STPS[2]	39,6%	60,1 %	50,1%
3,5 - 7,0 años	(18,2 - 55,5)	(-9,8 - 86,7)	(14,1 - 71,0)
SPS + STPS agrupados[2]	48,7%	64,9 %	50,1%
0,0 - 7,0 años	(42,0 - 54,7)	(47,4 - 77,0)	(48,6 - 66,6)
Eficacia duradera hasta 7 años después de la vacunación			

1. Oxman MN et al. 2005 I, 2. Schmader KE 201

Seguridad de la vacuna frente al Herpes Zóster

La vacuna frente al HZ tiene un perfil de tolerabilidad y seguridad bien establecido, con datos clínicos y experiencias reales que lo apoyan, con más de 27 millones de dosis administradas desde 2006[1,2]

Los efectos adversos más comunes son reacciones en el lugar de inyección y dolor de cabeza[2]

1. *Baxter R, Tran TN, Hansen J, et al . Safety of Zostavax ™ a cohort study in amanaged care organization. Vaccine 2012; 19;30(47):6636-41.*
2. *MacIntyre CR, Egerton T, McCaughey M, et al. Concomitant administration of zoster and pneumococcal vaccines in adults≥60 years old. Human Vaccine 2015*

CRITERIO DE RECOMENDACIÓN	
EDAD	**Adultos mayores de 60 años[1]**
PATOLOGÍA DE BASE	
Grupos prioritarios de vacunación	
- Mayor frecuencia y/o gravedad del HZ y sus complicaciones respecto a la población sana - El HZ y sus complicaciones pueden afectar negativamente el curso clínico o el tratamiento de la patología de base	- Pacientes con diabetes mellitus (tipo I o II) - Pacientes con EPOC avanzada en tratamiento con corticoides Inhalados - Pacientes con Insuficiencia Cardiaca Crónica clases funcionales II, III y IV de la NYHA - Personas inmunocompetentes en las que está previsto un periodo de inmunosupresión programada o posible en un futuro [2]
Otros grupos recomendables (2º nivel de prioridad de vacunación)	
- Algunos datos sugieren una mayor frecuencia de HZ respecto a la población general - En algunos casos, el HZ y sus complicaciones pueden afectar negativamente el curso clínico o el tratamiento de la patología de base	- Pacientes con enfermedad crónica, no incluidos en los grupos anteriores [3] - Cirugía mayor programada (antes de la intervención) - Depresión mayor

1 *Edad de recomendación, de acuerdo con organismos como el ACIP y sociedades de geriatría europeas.* ***2*** *Pacientes que estén esperando un trasplante, pacientes que van a recibir quimioterapia o terapia inmunosupresora (incluyendo altas dosis de corticoesteroides orales) frente a cáncer, artritis reumatoide, lupus u otras enfermedades autoinmunes. El inicio de la terapia inmunosupresora debe retrasarse al menos hasta 14 días después de la administración de la vacuna.* ***3*** *Enfermedad crónica respiratoria, cardíaca, neurológica, metabólica, hepática y/o renal siempre y cuando no impliquen precaución o contraindicación.*

- La DM puede afectar a la inmunidad celular y puede facilitar la reactivación del VVZ con independencia de la edad y del sexo **(nivel de evidencia: 2b).**
- El de riesgo de HZ asociado a la DM2 está condicionada por la edad de los individuos y la presencia de comorbilidades. Aumento de riesgo en los pacientes diabéticos más jóvenes (40 y 64 años) **(nivel de evidencia: 2b).**
- Las tasas de NPH en el paciente con DM son similares a olas de la población general **(nivel de evidencia: 1b).**
- El riesgo de HZ en la diabetes aumenta significativamente en los pacientes con comorbilidades macro y microvasculares **(nivel de evidencia: 3b).**
- Los diabéticos tratados en monoterapia con metformina o sulfonilureas tienen **menor riesgo** de desarrollar HZ que las que reciben tiazolidinedionas, inhibidores de la alfa-glucosidasa o insulina **(nivel de evidencia: 3b).**

Chronic Medical Conditions as Risk Factors for Herpes Zoster

Riduan M. Joesoef, MD, PhD; Rafael Harpaz, MD, MPH; Jessica Le
and Stephanie R. Bialek, MD, MPH

Mayo Clin Proc. 2

Infection (2011) 39:537–544
DOI 10.1007/s15010-011-0162-0

CLINICAL AND EPIDEMIOLOGICAL STUDY

Risk of Herpes zoster in patients with underlying diseases: a retrospective hospital-based cohort study

Incidencia de herpes zóster en pacientes diabéticos

Herpes zoster incidence in diabetic patients

An. Sist. Sanit. Navar. 2013; 36 (1): 57-62

Osacáriz[1,3], J. Castilla[6,7]

Infection (2014) 42:729–735
DOI 10.1007/s15010-014-0645-x

CLINICAL AND EPIDEMIOLOGICAL STUDY

Risk of herpes zoster among diabetics: a matched cohort study in a US insurance claim database before introduction of vaccination, 1997–2006

A. P. Guignard · M. Greenberg · C. Lu · D. Rosillon · V. Vannappagari

Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study

CMAJ 2011. DOI:10.1503/cmaj.101137

n-Yi Wang MD, Hui-Wen Lin PhD

J Pediatr. 2013 September ; 163(3): 816–821. doi:10.1016/j.jpeds.2013.03.010.

Increased Risk of Herpes Zoster in Children with Asthma: A Population-Based Case-Control Study

Bong-Seong Kim, MD[1,5], Sonia Mehra, MD[1], Barbara Yawn, MD, MSc[2], Charles Grose, MD[3], Robert Tarrell, BS[4], Brian Lahr, MS[4], and Young J. Juhn, MD, MPH[1,*]

Risk of Stroke Following Herpes Zoster: A Self-Controlled Case-Series Study

Clinical Infectious Diseases 2014;58(11):1497–503

Sinéad M. Langan,[a] Caroline

The Short- and Long-Term Risk of Stroke after Herpes Zoster - A Nationwide Population-Based Cohort Study

Nandini Sreenivasan[1], Saima Basit[1], Jan Wohlfahrt[1], Björn Pasternak[1]*, Tina N. Munch[1], Lars P. Nielsen[2],

July 2013 | Volume 8 | Issue 7 | e69156

Herpes zoster as a risk factor for stroke and TIA

A retrospective cohort study in the UK

Judith Breuer, MD
Maud Pacou, BSc
Aline Gauthier, BSc

Arthritis Care Res (Hoboken). 2013 June ; 65(6): 854–861. doi:10.1002/acr.21928.

Incidence and time trends of Herpes zoster in rheumatoid arthritis: a population-based cohort study

edova, MD, PhD[1,2], Eric L. Matteson, MD, Green, BA[2], and Cynthia S. Crowson,

The use, safety, and effectiveness of herpes zoster vaccination in individuals with inflammatory and autoimmune diseases: a longitudinal observational study

Jie Zhang[1], Elizabeth Delzell[1], Fenglong Xie[2], John W Baddley[3], Claire Spettell[4], Raechele M Mcmahan[5], Joaquim Fernandes[4], Lang Chen[2], Kevin Winthrop[6] and Jeffrey R Curtis[1,2*]

Zhang *et al. Arthritis Research & Therapy* 2011, **13**:R174
http://arthritis-research.com/content/13/5/R174

Quantification of risk factors for herpes zoster: population based case-control study

BMJ

Table 3| Relative risk of zoster in patients with key risk factors of interest and other covariates

	No (%)		Odds ratio (99% CI)		
	Cases (n=144 959)	Controls (n=549 336)	Model 1*	Model 2†	Model 3‡
Key risk factors of interest					
Rheumatoid arthritis	3111 (2.1)	8029 (1.5)	1.52 (1.43 to 1.60)	1.46 (1.38 to 1.55)	1.22 (1.15 to 1.30)
Systemic lupus erythematosus	387 (0.3)	818 (0.1)	1.85 (1.58 to 2.17)	1.72 (1.45 to 2.04)	1.60 (1.35 to 1.90)
Inflammatory bowel disease	1851 (1.3)	5118 (0.9)	1.38 (1.29 to 1.48)	1.36 (1.26 to 1.46)	1.28 (1.18 to 1.38)
Chronic obstructive pulmonary disease	6815 (4.7)	20 201 (3.7)	1.34 (1.29 to 1.39)	1.32 (1.27 to 1.37)	1.22 (1.17 to 1.28)
Asthma	10 243 (7.1)	31 865 (5.8)	1.24 (1.20 to 1.28)	1.21 (1.17 to 1.25)	1.11 (1.06 to 1.16)
Chronic kidney disease	8724 (6.0)	29 437 (5.4)	1.20 (1.16 to 1.24)	1.14 (1.09 to 1.18)	1.12 (1.08 to 1.17)
Depression	6830 (4.7)	22 052 (4.0)	1.19 (1.15 to 1.24)	1.15 (1.10 to 1.20)	1.15 (1.10 to 1.19)
Diabetes	11 430 (7.9)	41 320 (7.5)	1.07 (1.04 to 1.10)	1.02 (0.99 to 1.05)	1.02 (0.99 to 1.05)
Diabetes type:§					
No diabetes	133 529 (92.1)	508 016 (92.5)	1.00 (1.00 to 1.00)	1.00	1.00
Type 1	396 (0.3)	1054 (0.2)	1.37 (1.18 to 1.60)	1.27 (1.07 to 1.50)	1.26 (1.06 to 1.49)
Type 2	10 359 (7.1)	38 136 (6.9)	1.05 (1.02 to 1.09)	1.01 (0.98 to 1.04)	1.01 (0.98 to 1.04)
Unknown	675 (0.5)	2130 (0.4)	1.20 (1.07 to 1.35)	1.13 (1.00 to 1.27)	1.12 (0.99 to 1.27)

Forbes HJ et al. BMJ 2014; 348: g2911 doi:10.1136/bmj.g2911

Quantification of risk factors for herpes zoster: population based case-control study

BMJ

Table 3| Relative risk of zoster in patients with key risk factors of interest and other covariates

	No (%)		Odds ratio (99% CI)		
	Cases (n=144 959)	Controls (n=549 336)	Model 1*	Model 2†	Model 3‡
Other covariates					
Inhaled corticosteroids	12 996 (9.0)	38 902 (7.1)	1.31 (1.28 to 1.35)	—	1.13 (1.08 to 1.18)
Severe immunosuppression:					
HIV	128 (0.09)	97 (0.02)	4.74 (3.34 to 6.73)	5.07 (3.41 to 7.54)	5.07 (3.41 to 7.54)
Leukaemia	205 (0.14)	368 (0.07)	2.14 (1.71 to 2.68)	1.78 (1.39 to 2.28)	1.77 (1.38 to 2.27)
Lymphoma	444 (0.31)	386 (0.07)	4.41 (3.68 to 5.28)	3.90 (3.21 to 4.74)	3.89 (3.20 to 4.73)
Myeloma	492 (0.34)	816 (0.15)	2.35 (2.03 to 2.73)	2.16 (1.84 to 2.53)	2.13 (1.82 to 2.51)
Haematopoietic stem cell transplantation	26 (0.02)	3 (0.00)	32.82 (6.80 to 158.44)	13.46 (2.68 to 67.60)	13.71 (2.73 to 68.94)
Other unspecified cellular immune deficiencies	95 (0.07)	190 (0.03)	1.90 (1.37 to 2.63)	1.57 (1.10 to 2.22)	1.49 (1.05 to 2.12)
Oral corticosteroids	2164 (1.49)	3822 (0.70)	1.82 (1.58 to 2.10)	—	1.48 (1.27 to 1.72)
Other immunosuppressive treatment	502 (0.35)	1058 (0.19)	2.20 (2.05 to 2.36)	—	1.82 (1.67 to 1.98)

Forbes HJ et al. BMJ 2014; 348: g2911 doi:10.1136/bmj.g2911

Quantification of risk factors for herpes zoster: population based case-control study

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Table 5| Association of various risk factors with herpes zoster, stratified by age

Key risk factors of interest	Adjusted odds ratio (99% CI)*				P value †
	<50 years	50-59 years	60-69 years	≥70 years	
Rheumatoid arthritis	1.69 (1.38 to 2.06)	1.45 (0.93 to 2.28)	1.49 (0.97 to 2.29)	1.41 (0.93 to 2.15)	0.203
Systemic lupus erythematosus	3.04 (2.14 to 4.31)	1.98 (0.86 to 4.58)	1.23 (0.52 to 2.89)	1.29 (0.56 to 2.93)	<0.001
Inflammatory bowel disease	1.73 (1.47 to 2.03)	1.40 (0.95 to 2.07)	1.30 (0.88 to 1.90)	1.18 (0.81 to 1.70)	<0.001
Chronic obstructive pulmonary disease	1.11 (0.80 to 1.54) *	1.29 (0.65 to 2.53)	1.37 (0.71 to 2.66)	1.30 (0.68 to 2.51)	0.228
Asthma	1.24 (1.17 to 1.32)	1.19 (1.02 to 1.39)	1.22 (1.05 to 1.42)	1.18 (1.02 to 1.37)	0.465
Chronic kidney disease	1.63 (1.37 to 1.95)	1.26 (0.85 to 1.87)	1.14 (0.78 to 1.65)	1.10 (0.77 to 1.57)	<0.001
Depression	1.24 (1.16 to 1.33)	1.12 (0.94 to 1.33)	1.08 (0.90 to 1.30)	1.10 (0.93 to 1.30)	0.002
Diabetes	1.28 (1.15 to 1.43)	1.11 (0.87 to 1.42)	1.01 (0.80 to 1.28)	0.97 (0.77 to 1.22)	<0.001
Diabetes type:					
Type 1	1.51 (1.22 to 1.88)	1.16 (0.62 to 2.18)	0.98 (0.46 to 2.08)	0.62 (0.23 to 1.65)	<0.001
Type 2	1.22 (1.05 to 1.42)	1.09 (0.79 to 1.52)	1.02 (0.74 to 1.40)	0.97 (0.71 to 1.32)	
Unknown	1.20 (0.95 to 1.50)	1.30 (0.71 to 2.36)	1.02 (0.57 to 1.81)	1.07 (0.62 to 1.82)	

Forbes HJ et al. BMJ 2014; 348: g2911 doi:10.1136/bmj.g2911

Diabetes Mellitus (DM)

Incidencia de herpes zóster en pacientes diabéticos

An Sist Sanit Navar 2013; 36 (1): 57-62

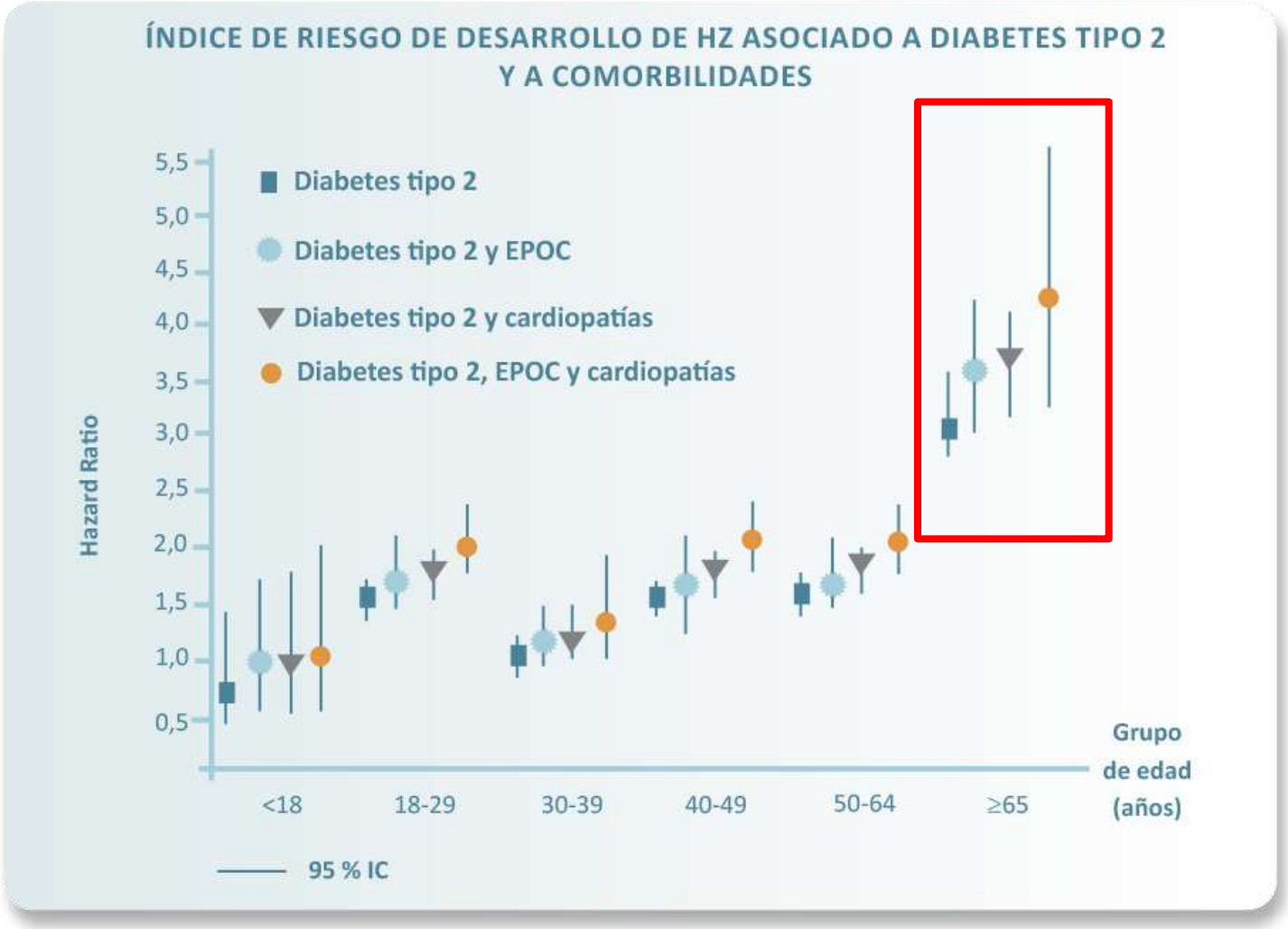
Herpes zoster incidence in diabetic patients

P. Aldaz[1,2,3], J.A. Díaz[4], J.R. Loayssa[5], M.J. Dronda[1], M. Osacáriz[1,3], J. Castilla[6,7]

Tabla 1. Incidencia de herpes zóster en población con y sin diagnóstico de diabetes mellitus. Navarra, 2006

Sexo y edad	Sin diagnóstico de diabetes			Con diagnóstico de diabetes			Comparación		
	N	Casos	Tasa por 10^3	N	Casos	Tasa por 10^3	Riesgo relativo	IC 95%	P
Hombres									
30-44	76.475	143	1,9	981	6	6,1	3,3	1,5-7,4	0,012
45-59	53.773	186	3,5	3.650	26	7,1	2,1	1,4-3,1	0,002
60-74	32.222	221	6,9	6.340	85	13,4	2,0	1,5-2,5	<0,001
≥ 75	16.575	151	9,1	3.554	63	17,7	2,0	1,5-2,6	<0,001
Total	179.045	701	3,9	14.525	180	12,4	3,2	2,7-3,7	<0,001
Mujeres									
30-44	70.094	135	1,9	588	5	8,5	4,4	1,8-10,8	0,007
45-59	53.798	299	5,6	1.795	23	12,8	2,3	1,5-3,5	<0,001
60-74	36.868	334	9,1	4.657	77	16,5	1,8	1,4-2,3	<0,001
≥ 75	27.387	243	8,9	5.228	124	23,7	2,7	2,2-3,3	<0,001
Total	188.147	1011	5,4	12.268	229	18,7	3,5	3,0-4,0	<0,001
Ambos sexos									
30-44	146.569	278	1,9	1.569	11	7,0	3,7	2,0-6,8	<0,001
45-59	107.571	485	4,5	5.445	49	9,0	2,0	1,5-2,7	<0,001
60-74	69.090	555	8,0	10.997	162	14,7	1,8	1,5-2,2	<0,001
≥ 75	43.962	394	9,0	8.782	187	21,3	2,4	2,0-2,8	<0,001
Total	367.192	1712	4,7	26.793	409	15,3	3,3	2,9-3,7	<0,001

Riesgo aumentado de Herpes Zóster en pacientes diabéticos en presencia de otras comorbilidades



1. Guignard AP, Greenberg M, Lu C, et al. Risk of herpes zoster among diabetics: a matched cohort study in a US insurance claim database before introduction of vaccination, 1997-2006. Infection. 2014 Aug;42(4):729-35.

EPOC

Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study

CMAJ 2011. DOI:10.1503/cmaj.101137

Ya-Wen Yang MD MS, Yi-Hua Chen PhD, Kuo-Hsien Wang MD MS, Chen-Yi Wang MD, Hui-Wen Lin PhD

- Las alteraciones inmunológicas encontradas en EPOC podrían poner a los pacientes en un riesgo incrementado de desarrollar HZ

Tras 3 años de seguimiento, se observan diferencias significativas en la proporción de HZ en pacientes con EPOC comparado con la población general ($p < 0.001$).

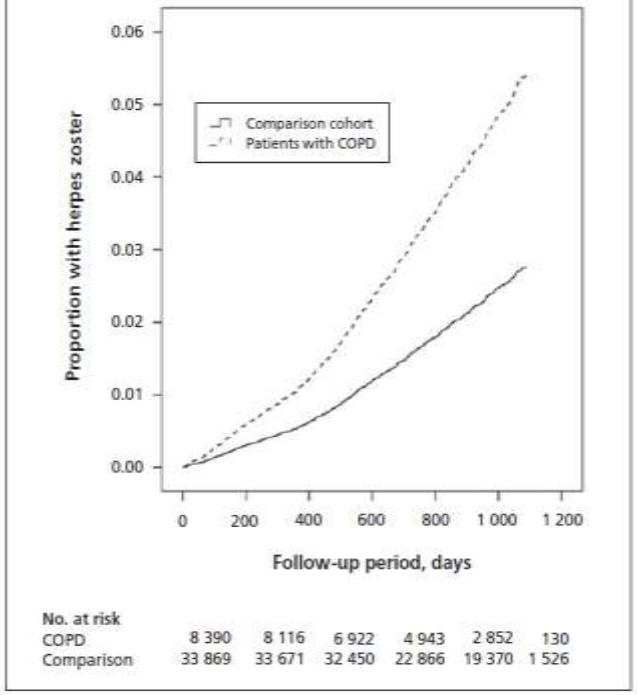


Figure 1: Herpes zoster event rates for patients with chronic obstructive pulmonary disease and comparison patients from 2004 to 2006. Log-rank test: $p < 0.001$

EPOC

Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study

CMAJ 2011. DOI:10.1503/cmaj.101137

Ya-Wen Yang MD MS, Yi-Hua Chen PhD, Kuo-Hsien Wang MD MS, Chen-Yi Wang MD, Hui-Wen Lin PhD

- En todos los grupos de edad los pacientes con EPOC presentaron > riesgo de padecer HZ que el grupo control

Table 2: Crude and adjusted hazard ratios for herpes zoster during the follow-up period for patients with chronic obstructive pulmonary disease and patients in the comparison group, stratified by age

Age, yr	Had herpes zoster	Person-years at risk	Incidence per 1000 person-years	Crude HR (95% CI)	Adjusted HR* (95% CI)
50–59					
COPD	44	2 941.47	14.26	1.81 (1.27–2.56)	1.85 (1.27–2.70)
Comparison	112	13 089.16	8.56	1.00	1.00
60–69					
COPD	84	5 269.45	15.94	1.77 (1.38–2.28)	1.65 (1.24–2.20)
Comparison	220	23 540.40	9.35	1.00	1.00
≥ 70					
COPD	193	11 073.02	17.43	2.10 (1.77–2.49)	1.68 (1.38–2.04)
Comparison	427	49 668.80	8.60	1.00	1.00

Note: CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio.
*Adjusted for sex, age (as a continuous variable), diabetes mellitus, rheumatic diseases, cancer, Charlson comorbidity index score, use of corticosteroids, monthly income, geographic region and urbanization level.

EPOC

Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study

CMAJ 2011. DOI:10.1503/cmaj.101137

Ya-Wen Yang MD MS, Yi-Hua Chen PhD, Kuo-Hsien Wang MD MS, Chen-Yi Wang MD, Hui-Wen Lin PhD

- Los corticoides (inhalados, orales) pueden generar cierto grado de alteración de la inmunidad celular específica y se asocian a una mayor frecuencia y/o gravedad de HZ

Table 3: Crude and adjusted hazard ratios for herpes zoster for patients without steroid therapy, with inhaled corticosteroid therapy only and with oral steroid therapy, compared to control patients

Patient group	Had herpes zoster	Person-years at risk	Incidence per 1000 person-years	Crude HR (95% CI)	Adjusted HR* (95% CI)
Comparison	759	86 298.37	8.80	1.00	1.00
Patients with COPD					
No use of corticosteroids	209	14 643.74	14.27	1.69 (1.45–1.97)	1.67 (1.43–1.96)
Inhaled corticosteroids	23	1 251.90	18.37	2.11 (1.39–3.19)	2.09 (1.38–3.16)
Oral corticosteroids	89	3 388.80	26.26	3.03 (2.43–3.77)	3.00 (2.40–3.75)

Note: CI = confidence interval, COPD = chronic obstructive pulmonary disease, HR = hazard ratio.
*Adjusted for sex, age (as a continuous variable), diabetes mellitus, rheumatic diseases, cancer, Charlson comorbidity index score, use of corticosteroids, monthly income, geographic region and urbanization level.

Insuficiencia cardiaca crónica
Clases funcionales II, III y IV de la NYHA

- Estos pacientes están en tratamiento con múltiples fármacos y en muchas ocasiones presentan patologías concomitantes
- Objetivo principal de salud ➔ evitar descompensaciones
- El HZ o NPH y/o su tratamiento serían potenciales causas de descompensación y por tanto suponen un riesgo adicional
  - ↑ demanda metabólica por infecciones, estrés, fármacos que retienen Na (corticoides, AINE)
- De acuerdo con los criterios clínicos, se debería priorizar la vacunación frente a HZ en aquellos pacientes con ICC sintomática de las clases funcionales II, III y IV de la NYHA

The Short- and Long-Term Risk of Stroke after Herpes Zoster - A Nationwide Population-Based Cohort Study

Nandini Sreenivasan[1], Saima Basit[1], Jan Wohlfahrt[1], Björn Pasternak[1]*, Tina N. Munch[1], Lars P. Nielsen[2], Mads Melbye[1]

PLOS ONE | July 2013 | Volume 8 | Issue 7 | e69156

- Riesgo alto de accidente cerebrovascular tras los primeros meses después de padecer HZ.
- Aunque el riesgo a corto plazo fue particularmente alto, no pueden descartar la posibilidad de un pequeño, pero importante, riesgo a largo plazo.

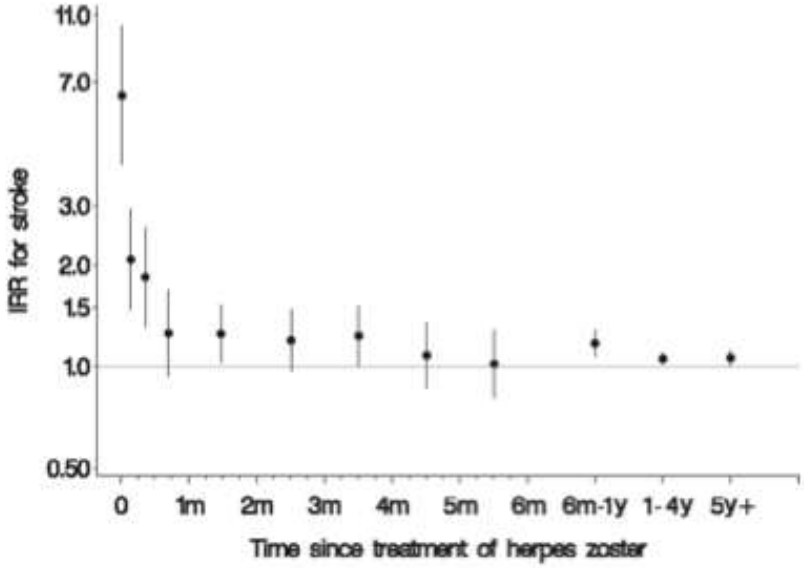


Figure 1. Incidence rate ratio (IRR) of stroke with 95% confidence intervals in individuals receiving antiviral treatment for herpes zoster by time since treatment compared with individuals with no antiviral treatment in Danish adults 1995–2008. The 12 dots represent point estimates for days 0 and 1–6; weeks 1 and 2–3; months (m) 1, 2, 3, 4, and 5; and the intervals 6 months to just below 1 year (y), 1 to 4 years, and 5 years or more.
doi:10.1371/journal.pone.0069156.g001

Pacientes con enfermedad crónica

- No está claramente documentada la mayor frecuencia de HZ en los paciente crónicos en general
- El HZ y la NPH tienen consecuencias clínicas que pueden ser graves en estos pacientes
- ACIP (EE.UU.) incluye entre las recomendaciones de vacunación frente a HZ a las personas con enfermedades crónicas (respiratorias, cardiacas, neurológicas, metabólicas, hepáticas y/o renales) en ausencia de precauciones o contraindicaciones.

Cirugía mayor programada

- Los traumatismos mecánicos pueden ser un factor de riesgo para el HZ
  - La estimulación del nervio podría desencadenar la reactivación del VVZ desde el ganglio dorsal
- A

Case-control study of the effect of mechanical trauma on the risk of herpes zoster

S L Thomas, J G Wheeler, Andrew J Hall

BMJ, doi:10.1136/bmj.37991.511829.F7 (published 23 January 2004)

Depresión mayor

- Pacientes > 60 años con depresión mayor ➔ Disminución de la inmunidad celular específica frente a VVZ, comparados con personas de la misma edad sin esa patología
- Los eventos vitales negativos se asocian a > riesgo de HZ
- El dolor del HZ afecta negativamente a las actividades diarias de los pacientes y a su salud psico-emocional ➔ Descompensación
- Pacientes polimedicados, difíciles de controlar y que tienen una alta sensibilidad a los cambios de dosis de medicación

ELSEVIER

BIAM British Infection Association

www.elsevierhealth.com/journals/jinf

Temporal trends in incidence rates of herpes zoster among patients treated in primary care centers in Madrid (Spain), 2005–2012

M.D. Esteban-Vasallo [a,*], R. Gil-Prieto [b], M.F. Domínguez-Berjón [a], J. Astray-Mochales [a], A. Gil de Miguel [b]

[a] *Subdirectorate for Health Promotion and Prevention, Madrid Regional Health Authority, C/San Martín de Porres, 6, 28035 Madrid, Spain*
[b] *Department of Preventive Medicine and Public Health and Medical Immunology and Microbiology, Rey Juan Carlos University, Avda. de Atenas, s/n, 28922 Alcorcón, Madrid, Spain*

Accepted 30 September 2013
Available online 16 November 2013

KEYWORDS
Herpes zoster;
Incidence;
Primary health care;
Temporal trend

Summary *Objectives:* This study aimed to estimate total and age-specific incidence rates of HZ with data from electronic clinical records in primary care (ECRPC) and to analyze trends by sex and age.
Methods: Descriptive cross-sectional study covering the incident HZ episodes registered in the ECRPC of the Madrid Regional Public Health System in 2005–2012. Annual crude and age-adjusted incidence rates were calculated. Differences by sex and age were assessed by poisson regression. The annual percentage of change (APC) of incidence rates and 'breakthrough points' of the time trends were determined with the Joinpoint Regression Program.
Results: 211,650 episodes of HZ were identified (60.6% women, 52.2% > 55 years). The incidence rate increased from 363.21 to 481.92 per 100,000 person-year in 2005–2012. Rates were higher among women and increased with age. The APC for the period was 3.59% in men and 3.67% in women ($p < 0.05$). Age-specific rates increased in patients over 14 years. The APC in the 25–44 age group was 7.4% since 2007. The incidence rate ratio (women/men) was highest in this group.
Conclusions: The incidence of HZ presents an upward trend in 2005–2012 in adults and the elderly. Monitoring the incidence and age-specific rates, will help to detect changes in trends.

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ELSEVIER

www.elsevierhealth.com/journals/jinf

Temporal trends in herpes zoster-related hospitalizations in Madrid (Spain), 2003—2013

María D. Esteban-Vasallo [a,*], M. Felicitas Domínguez-Berjón [a], Ruth Gil-Prieto [b], Jenaro Astray-Mochales [a], Ángel Gil de Miguel [b]

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[b] *Area of Preventive Medicine and Public Health, Rey Juan Carlos University, Avda. de Atenas, s/n, 28922 Alcorcón, Madrid, Spain*

Accepted 30 January 2015
Available online ■ ■ ■

KEYWORDS
Epidemiology;
Herpes zoster;
Hospitalization;
Incidence;
Spain;
Trends;
Varicella zoster virus

Summary *Objectives:* This study aimed to estimate herpes zoster (HZ) related hospitalization rates in the Autonomous Community of Madrid (Spain), considering both total and complicated cases, and to analyze their temporal trends by sex and age.
Methods: Population based cross-sectional study of all hospital admissions with an HZ diagnosis in any position from 2003 to 2013. Annual crude, age-adjusted and age-specific hospitalization rates were calculated by sex and year. Joinpoint Regression models were used to analyze time trends.
Results: The incidence of hospitalizations with HZ increased significantly during the study period from 10.81 to 16.97 per 100,000 person-year, with an average annual rise of 2.80%. The rate of hospitalization of complicated HZ increased from 4.67 to 8.99 per 100,000 person-year. No 'breakthrough points' of the time trends were detected. The proportion of complicated HZ was similar in both sexes, and increased from 43.2% to 53.0%. By age and sex significant increases affecting women from age 85 and men from age 75 and in the group of 45—64 years were observed.
Conclusions: Hospitalizations related to HZ are increasing, with a significant rise of complicated cases. Long term and more detailed studies are required to monitor HZ.

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E-mail address: maria.estebanv@salud.madrid.org (M.D. Esteban-Vasallo).

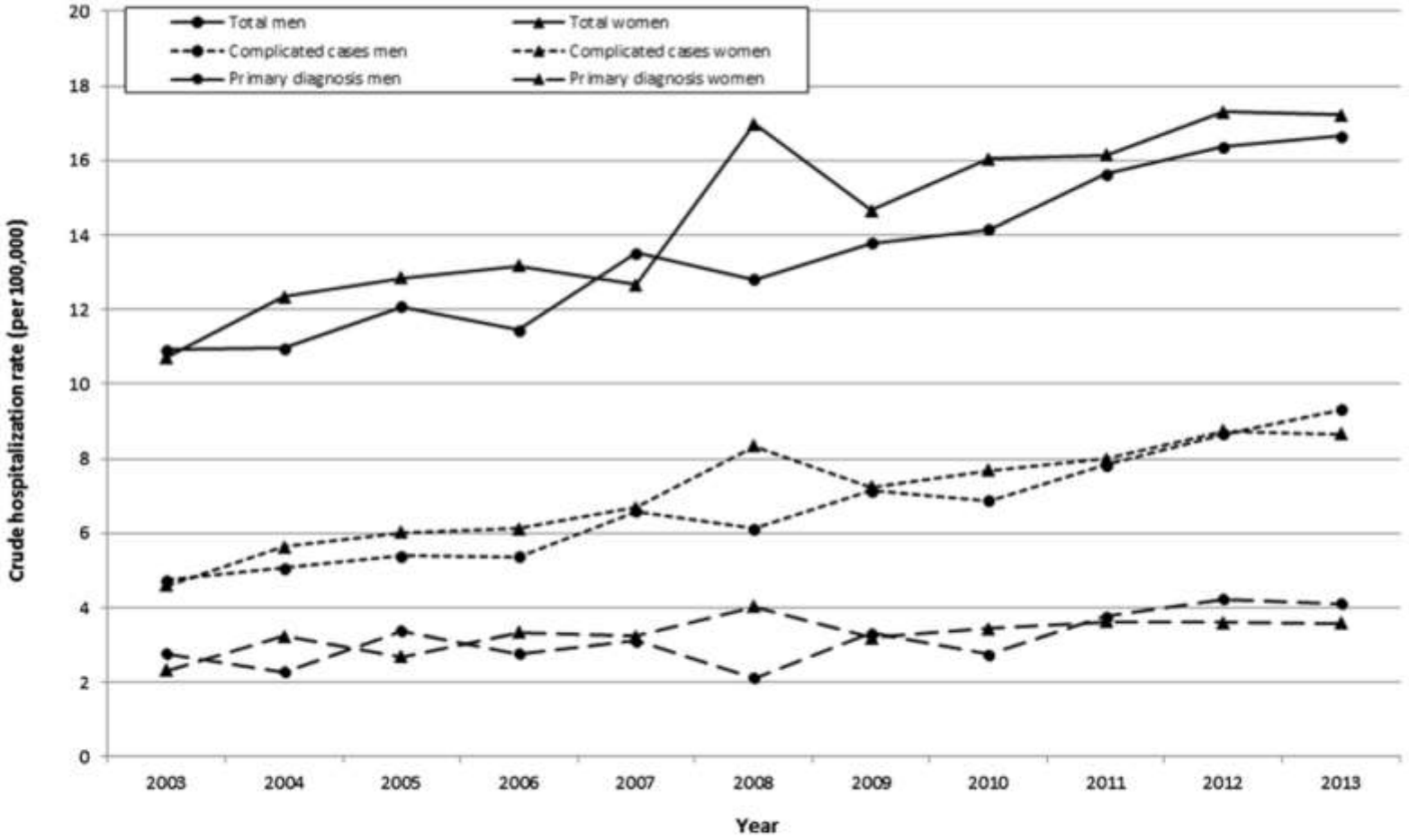
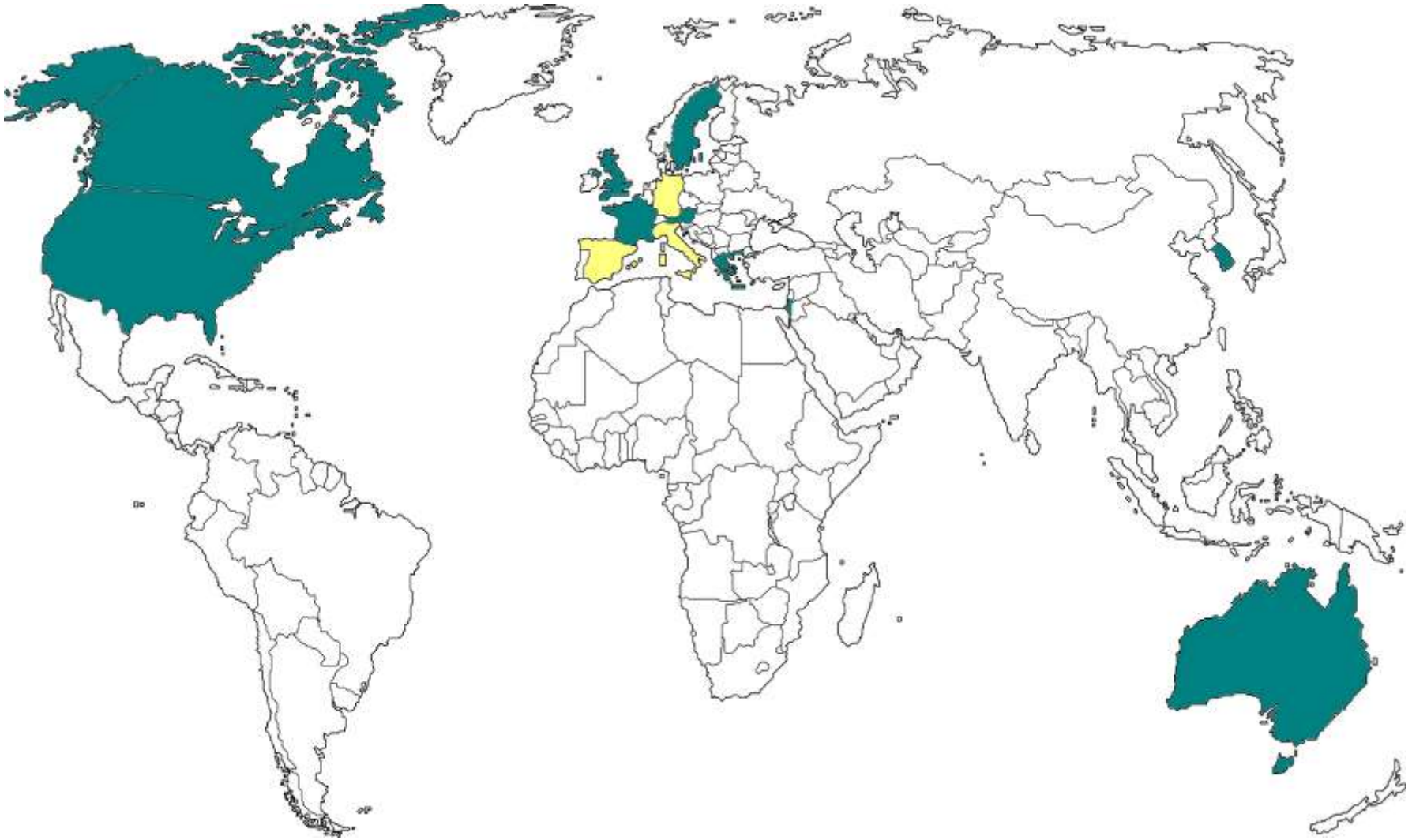


Figure 1 Crude annual rates of herpes zoster-related hospitalizations per 100,000 person-year, total and as primary diagnosis, by sex, Autonomous Community of Madrid, 2003–2013.

SITUACIÓN DE LA VACUNACIÓN FRENTE AL HZ



- CANADA:

- La vacuna contra herpes zoster se puede administrar a adultos de 50 a 59 años de edad y se recomienda habitualmente para adultos de 60 años de edad o más.

- No se recomienda realizar pruebas de rutina de adultos mayores de 50 años para detectar anticuerpos del virus varicela zoster antes de la vacunación

- La administración concomitante de la vacuna neumocócica 23-valente polisacárido (Pneu-P-23) y la vacuna HZ no presenta una disminución de la eficacia y por lo tanto las dos vacunas pueden administrarse concomitantemente.

Fuente: http://healthycanadians.gc.ca/publications/healthy-living-vie-saine/3-canadian-immunization-guide-canadien-immunisation/index-eng.php?page=2#p3c1t1

- CDC:
- Se recomienda una dosis única de vacuna contra el zoster para adultos de 60 años o más, independientemente de si reportan un episodio previo de herpes zóster.
- ACIP recomienda que la vacunación comience a la edad de 60 años.
- Las personas de 60 años de edad o mayores con condiciones médicas crónicas pueden ser vacunadas a menos que su condición constituya una contraindicación, como embarazo o inmunodeficiencia grave.

Immunisation recommendations for adults in Australia

Summary of vaccine recommendations for adults from the 10th edition *Australian Immunisation Handbook*,[a] including the circumstances that may indicate their use. Shaded cells represent adult vaccinations funded under the National Immunisation Program (NIP).[a] More detail is provided in the corresponding footnote(s).

This table does NOT include vaccinations used in the context of response to and control of a disease outbreak, or specifically for travel outside of Australia.

Disease/vaccine antigen	Abbrev.	All adults	Elderly	Indigenous	At-risk			Pregnancy	
					Medical	Behavioural	Occupational	During	Planning or postpartum
Influenza (annual)	TIV	✓[b]	✓ ≥65 years	✓ ≥15 years	✓[c]		✓[d]	✓[e]	✓[e]
Pneumococcal	23vPPV		✓ 65 years[f]	✓ ≥50 years[f]	✓[f]				
	13vPCV				✓[f]				
Measles, mumps, rubella	MMR	✓[g]					✓[h]		✓[i]
Varicella (chickenpox)	VV	✓[j]				✓[j]	✓[j]		✓[j]
Herpes zoster	HZ		✓ ≥60 years						

- Se recomienda una dosis única para todos los adultos ≥60 años de edad, a menos que hayan recibido previamente una dosis. No financiado
- A partir de noviembre de 2016, se financiará una dosis única en el NIP para adultos a los 70 años de edad (con un programa de recuperación a corto plazo para adultos de entre 71 y 79 años) ya que se espera que la vacunación rutinaria de este grupo de edad obtenga el mayor beneficios contra el herpes zoster y sus complicaciones.

Estrategias de utilización de la vacuna HZ en Salud Pública: situación en países de nuestro entorno

Recomendaciones y Financiación de la vacuna contra el HZ en Europa

España: recien comercializada en farmacias, con receta médica.

UK (JCVI) Financiada para 70-79años desde 2010.

Suecia (TLV): financiado en >50 años desde 2012

Francia (HCPH): recomendación y financiación 2013, personas entre 65-74 años y para mayores de 74 a 79 años de edad, durante el primer año

Alemania (SIKO): Recomendada por SP en región de Sajonia en >50 años, no financiada

Austria: recomendación de vacunación desde 2007 sin financiación pública

Grecia: recomendación de vacunación en >60 años, . Financiada solo para grupos de riesgo.

BUNDESMINISTERIUM FÜR GESUNDHEIT

Erwachsene

Erwachsene mit vorliegender Grundimmunisierung gemäß den Empfehlungen*

Alter→ ↓Impfung	18.-20. Jahr	30. Jahr	40. Jahr	50. Jahr	60. Jahr	65. Jahr	70. Jahr	75. Jahr	80. Jahr usw.
Diphtherie (dip) **Tetanus** (TET) **Pertussis** (PEA) **Poliomyelitis** (IPV)	alle 10 Jahre auffrischen				alle 5 Jahre auffrischen				
Hepatitis B (HBV)	gegebenenfalls nachholen								
Humane Papillomaviren (HPV)	gegebenenfalls nachholen								
Mumps **Masern** (MMR) **Röteln**	gegebenenfalls nachholen								
FSME	alle 5 Jahre auffrischen				alle 3 Jahre auffrischen				
Pneumokokken				siehe Kapitel Pneumokokken					
Herpes Zoster (HZV)				einmalige Gabe					
Varizellen (VZV)	bei seronegativen Personen ggf. nachholen								
Influenza (IV)	IV jährlich								

* Für Personen, bei denen die Grundimmunisierung ganz oder teilweise fehlt, siehe auch Kapitel „Nachhol-Empfehlungen“.

Kostenfrei

Nicht kostenfrei

Public Health England

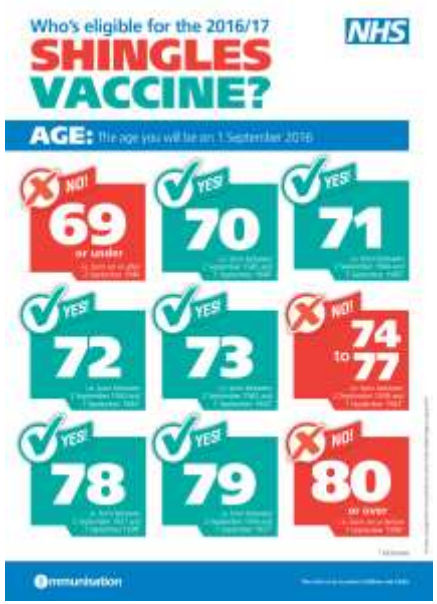
Shingles vaccination programme

OBJETIVO: Reducir tanto la incidencia como la severidad del zóster en los adultos de 70 a 79 años de edad.

INICIO: **1 de septiembre de 2013**

- Cohorte a vacunar: nacidos entre el 02/09/1942 y el 01/09/1943 (**70 años**)
- Catch-up: Nacidos entre el 02/09/1933 y el 01/09/1934 (**79 años**)

Año 2016-2017



- Inició en 2016
- Vacunación sistemática contra el herpes zóster para las personas **65 a 74** años de edad.
- Catch-up a las personas entre **75 y 79** años (hasta 2017)

- CASTILLA Y LEÓN
- 2015: Personas entre 60 y 64 años con EPOC en tto con corticoides inhalados
- 2016: Ampliación indicación: Personas entre 60 y 69 años con:
    - EPOC en tto con corticoides inhalados
    - Diabéticos

- Islas Baleares:
- Recomendada desde el 1 enero de 2016 a todos los adultos a partir de los 50 años, siempre que no esté contraindicada
- RECOMENDADA, NO FINANCIADA

- La Rioja:
- Cohorte de edad de 65 años (diabéticos)
- Fecha inicio probable: Enero 2017

MURCIA:

Recomendada en pacientes > 50 años, que vayan a a someterse a un TOS (PRETRASPLANTE)

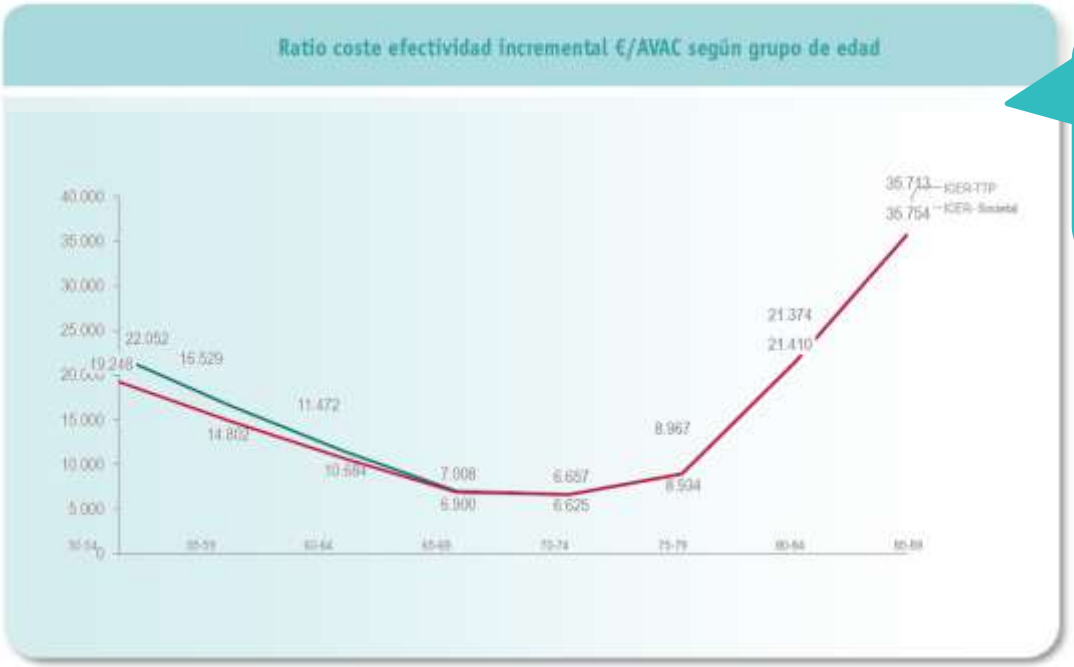
Se realizarán anticuerpos prevacunales

- Si el resultado es negativo se vacunará frente a la varicela, antes del TOS.
- Si el resultado es positivo y el paciente es mayor de 50 años se vacunará frente al Herpes Zóster antes del TOS.

http://www.murciasalud.es/recursos/ficheros/345241-Protocolo.pdf

Resultados del caso base

- Zostavax® es una alternativa eficiente al obtener un RCEI frente a la no vacunación de HZ, considerando todas las cohortes de edad, de 12.659€/AVAC y 11.926€/AVAC según la perspectiva del SNS y Social, respectivamente



El escenario más eficiente sería la vacunación de la cohorte de edad de 65 a 79 años, que supondría un RCEI de 6.657 €/AVAC

JOURNAL OF MEDICAL ECONOMICS, 2016
http://dx.doi.org/10.3111/13696998.2016.1146726
Article 0149.R1/1146726

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

The use of Zostavax in Spain: the economic case for vaccination of individuals aged 50 years and older

Juan Luis Lopez-Belmonte[a], Ramón Cisterna[b], Angel Gil de Miguel[c], Caroline Guilmet[d], Florence Bianic[d] and Mathieu Uhart[e]

[a]Sanofi Pasteur MSD, Madrid, Spain; [b]Clinical Microbiology and Infection Control OSI Bilbao Basurto, UPV/EHU Bilbao, Spain; [c]Health Sciences and Public Healthcare Department, Universidad Rey Juan Carlos, Madrid, Spain; [d]Mapi Group, Nanterre, France; [e]Sanofi Pasteur MSD, Lyon, France

ABSTRACT

Background Population aging brings up a number of health issues, one of which is an increased incidence of herpes zoster (HZ) and its complication, post-herpetic neuralgia (PHN). Zostavax vaccine has recently become available to prevent HZ and PHN. This study evaluates the cost-effectiveness of vaccination against HZ in Spain considering a vaccination of the population aged 50 years and older and comparing this to the current situation where no vaccination is being administered.

Methods An existing, validated, and published economic model was adapted to Spain using relevant local input parameters and costs from 2013.

Results Vaccinating 30% of the Spanish population aged 50 years and older resulted in €16,577/QALY gained, €2025/HZ case avoided, and €5594/PHN case avoided under the third-party payer perspective. From a societal perspective, the ICERs increased by 6%, due to the higher price of the vaccine. The number needed to vaccinate to prevent one case was 20 for HZ, and 63 for PHN3. Sensitivity analyses showed that the model was most sensitive to the HZ and PHN epidemiological data, the health state utilities values, and vaccine price used.

Conclusion Considering an acceptable range of cost-effectiveness of €30,000–€50,000 per QALY gained, vaccination of the 50+ population in Spain against HZ with a new vaccine, Zostavax, is cost-effective and makes good use of the valuable healthcare budget.

ARTICLE HISTORY
Received 15 October 2015
Revised 21 January 2016
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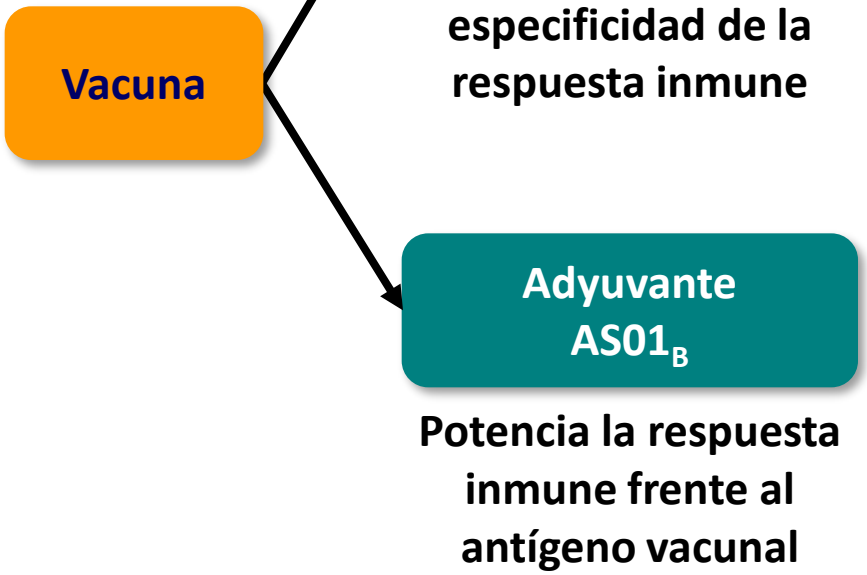
Published online 1 March 2016

KEYWORDS
Cost-effectiveness; Spain; VZV; Zostavax; 50 years; Vaccination

SHINGRIX. Vacuna HZ/su (gE/AS01B), GSK



- Glicoproteína más abundante del VVZ
- Se expresa en las lesiones cutáneas y ganglios durante los episodios de zóster
- Esencial para la replicación viral y la propagación celular
- Objetivo primario de la repuesta inmune específica frente al VZV

- Liposomas: dos inmunomoduladores: **MPL + QS21** (*Quillaja saponaria* Molina, fracción 21)
- Induce una potente respuesta inmune celular y humoral

Garçon et al. Expert Rev Vaccines 2007;6:723–39

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

This article was published on April 28, 2015, at NEJM.org.

DOI: 10.1056/NEJMoa1501184

Table 2. Vaccine Efficacy against the First or Only Episode of Herpes Zoster Infection.*

Cohort and Age Group	HZ/su Group				Placebo Group				Vaccine Efficacy†
	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period ‡ *person-yr*	Rate of Herpes Zoster *no./1000 person-yr*	No. of Participants	No. of Confirmed Cases	Cumulative Follow-up Period‡ *person-yr*	Rate of Herpes Zoster *no./1000 person-yr*	*% (95% CI)*
Modified vaccinated cohort									
All participants in cohort	7344	6	23,297.0	0.3	7415	210	23,170.5	9.1	97.2 (93.7–99.0)
50–59 yr	3492	3	11,161.3	0.3	3525	87	11,134.7	7.8	96.6 (89.6–99.3)
60–69 yr	2141	2	7,007.9	0.3	2166	75	6,952.7	10.8	97.4 (90.1–99.7)
70 yr or older	1711	1	5,127.9	0.2	1724	48	5,083.0	9.4	97.9 (87.9–100.0)
Total vaccinated cohort									
All participants in cohort	7698	9	25,584.5	0.4	7713	235	25,359.9	9.3	96.2 (92.7–98.3)
50–59 yr	3645	3	12,244.9	0.2	3644	95	12,162.5	7.8	96.9 (90.6–99.4)
60–69 yr	2244	5	7,674.1	0.7	2246	83	7,581.8	10.9	94.1 (85.6–98.1)
70 yr or older	1809	1	5,665.5	0.2	1823	57	5,615.6	10.2	98.3 (89.9–100.0)

2d

1d

* The total vaccinated cohort included all vaccinated participants for whom data related to efficacy end points were available. The modified vaccinated cohort excluded participants who did not receive the second dose of vaccine or who received a confirmed diagnosis of herpes zoster within 1 month after the second dose. Efficacy was calculated by means of the Poisson method.

† $P<0.001$ for all efficacy comparisons with placebo. Vaccine efficacy in each age group was adjusted for region. Overall vaccine efficacy was adjusted for age group and region.

‡ Data were censored at the time of the first confirmed diagnosis of herpes zoster.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 15, 2016 VOL. 375 NO. 11

Efficacy of the Herpes Zoster Subunit Vaccine in Adults 70 Years of Age or Older

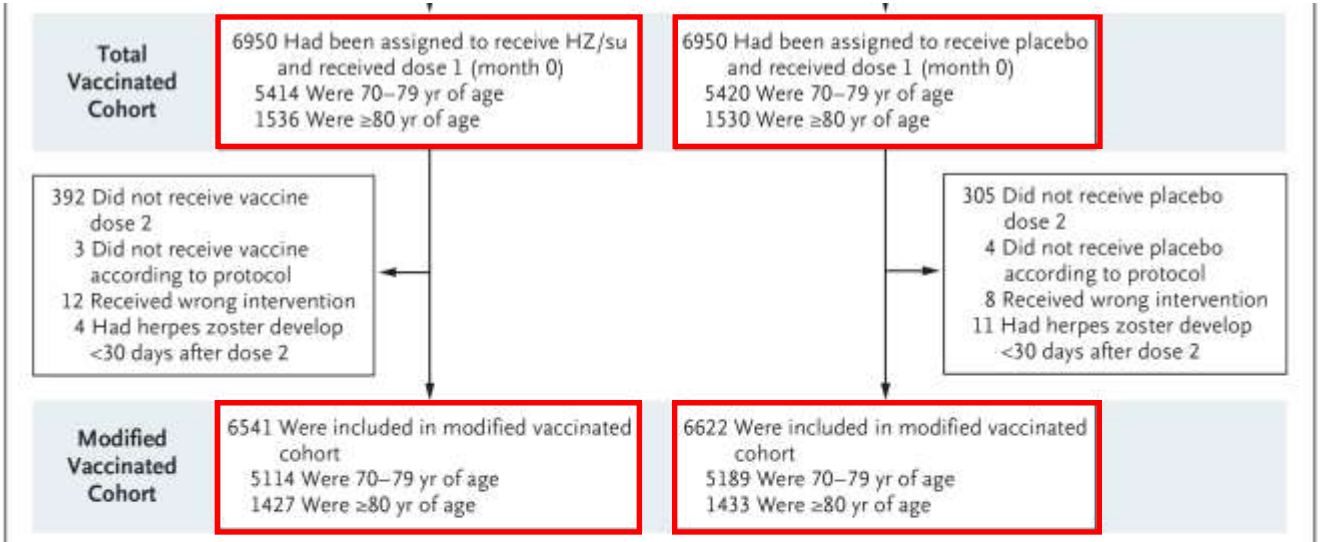


Figure 1. Enrollment and Randomization.

After enrollment, one study center was closed because of Good Clinical Practice violations, and one study center was closed for financial reasons (see the Supplementary Appendix). All participants who had been enrolled at these centers were excluded from all analyses. An additional four participants were excluded because of issues with informed consent. Some participants in the total vaccinated cohort had more than one reason for being excluded from the modified vaccinated cohort. HZ/su denotes herpes zoster subunit vaccine.

Table 1. Vaccine Efficacy against the First or Only Episode of Herpes Zoster and Postherpetic Neuralgia in the Modified Vaccinated Cohort.*

Condition and Cohort	HZ/su Group				Placebo Group				Vaccine Efficacy†
	Participants	Cases	Cumulative Follow-up Period‡	Incidence Rate	Participants	Cases	Cumulative Follow-up Period‡	Incidence Rate	
	number		*person-yr*	*cases/1000 person-yr*	*number*		*person-yr*	*cases/1000 person-yr*	*% (95% CI)*
Herpes zoster									
ZOE-70									
Age group									
Overall	6,541	23	24,405.1	0.9	6,622	223	24,167.8	9.2	89.8 (84.2 to 93.7)
70–79 yr	5,114	17	19,346.5	0.9	5,189	169	19,247.5	8.8	90.0 (83.5 to 94.4)
≥80 yr	1,427	6	5,058.5	1.2	1,433	54	4,920.3	11.0	89.1 (74.6 to 96.2)
Year§									
1	6,541	2	6,464.7	0.3	6,622	68	6,511.2	10.4	97.0 (88.8 to 99.7)
2	6,379	6	6,281.0	1.0	6,372	68	6,240.4	10.9	91.3 (79.9 to 96.9)
3	6,137	9	6,043.5	1.5	6,076	48	5,943.0	8.1	81.6 (61.9 to 92.1)
4	5,898	6	5,615.9	1.1	5,776	39	5,473.2	7.1	85.1 (64.4 to 94.9)
Pooled ZOE-70 and ZOE-50									
Age group									
Overall	8,250	25	30,725.5	0.8	8,346	284	30,414.7	9.3	91.3 (86.8 to 94.5)
70–79 yr	6,468	19	24,410.9	0.8	6,554	216	24,262.8	8.9	91.3 (86.0 to 94.9)
≥80 yr	1,782	6	6,314.6	1.0	1,792	68	6,151.9	11.1	91.4 (80.2 to 97.0)
Year§									
1	8,250	2	8,156.2	0.2	8,346	83	8,206.2	10.1	97.6 (90.9 to 99.8)
2	8,039	7	7,916.9	0.9	8,024	87	7,860.5	11.1	92.0 (82.8 to 96.9)
3	7,736	9	7,612.2	1.2	7,661	58	7,488.4	7.7	84.7 (69.0 to 93.4)
4	7,426	7	7,040.3	1.0	7,267	56	6,859.6	8.2	87.9 (73.3 to 95.4)
Postherpetic neuralgia									
Pooled ZOE-70 and ZOE-50									
≥70 yr¶	8,250	4	30,760.3	0.1	8,346	36	30,942.0	1.2	88.8 (68.7 to 97.1)
≥50 yr	13,881	4	53,171.5	0.1	14,035	46	53,545.0	0.9	91.2 (75.9 to 97.7)
Age group									
50–59 yr	3,491	0	13,789.7	0.0	3,523	8	13,928.7	0.6	100.0 (40.8 to 100.0)
60–69 yr	2,140	0	8,621.4	0.0	2,166	2	8,674.4	0.2	100.0 (−442.9 to 100.0)
70–79 yr	6,468	2	24,438.8	0.1	6,554	29	24,660.4	1.2	93.0 (72.4 to 99.2)
≥80 yr	1,782	2	6,321.5	0.3	1,792	7	6,281.6	1.1	71.2 (−51.6 to 97.1)

Table 2. Vaccine Reactogenicity and Safety Overall.

Time Period and Event	HZ/su Group		Placebo Group	
	no. of participants/ total no.	*% (95% CI)*	*no. of participants/ total no.*	*% (95% CI)*
Within 7 days after vaccination in the reactogenicity subgroup*				
Any reaction	399/505	79.0 (75.2–82.5)	149/505	29.5 (25.6–33.7)
Grade 3 reaction†	60/505	11.9 (9.2–15.0)	10/505	2.0 (1.0–3.6)
Injection-site reaction	374/505	74.1 (70.0–77.8)	50/505	9.9 (7.4–12.8)
Pain	347/505	68.7 (64.5–72.7)	43/505	8.5 (6.2–11.3)
Redness	198/505	39.2 (34.9–43.6)	5/505	1.0 (0.3–2.3)
Swelling	114/505	22.6 (19.0–26.5)	2/505	0.4 (0.0–1.4)
Grade 3 injection-site reaction†	43/505	8.5 (6.2–11.3)	1/505	0.2 (0.0–1.1)
Systemic reaction	267/504	53.0 (48.5–57.4)	127/505	25.1 (21.4–29.2)
Fatigue	166/504	32.9 (28.8–37.2)	77/505	15.2 (12.2–18.7)
Myalgia	157/504	31.2 (27.1–35.4)	41/505	8.1 (5.9–10.9)
Headache	124/504	24.6 (20.9–28.6)	55/505	10.9 (8.3–13.9)
Shivering	75/504	14.9 (11.9–18.3)	22/505	4.4 (2.7–6.5)
Fever	62/504	12.3 (9.6–15.5)	13/505	2.6 (1.4–4.4)
Gastrointestinal symptoms	55/504	10.9 (8.3–14.0)	40/505	7.9 (5.7–10.6)
Grade 3 systemic reaction†	30/504	6.0 (4.1–8.4)	10/505	2.0 (1.0–3.6)
Throughout the study period in the total vaccinated cohort‡				
Serious adverse event	1153/6950	16.6 (15.7–17.5)	1214/6950	17.5 (16.6–18.4)
Serious adverse event considered as related to vaccination §	12/6950	0.2 (0.1–0.3)	8/6950	0.1 (0.0–0.2)
Potential immune-mediated disease	92/6950	1.3 (1.1–1.6)	97/6950	1.4 (1.1–1.7)
Death	426/6950	6.1 (5.6–6.7)	459/6950	6.6 (6.0–7.2)

* Reports within 7 days after vaccination in the reactogenicity subgroup (a randomly selected subgroup of age-stratified participants) were solicited reports of injection-site reactions (pain, redness, and swelling) and systemic reactions (fatigue, fever, gastrointestinal symptoms, headache, myalgia, and shivering).

† Redness and swelling at the injection site were scored as 0 if the affected area was less than 20 mm in diameter, 1 if the affected area was 20 to 50 mm, 2 if the affected area was more than 50 to 100 mm, and 3 if the affected area was more than 100 mm. Fever was scored as 0 for a body temperature lower than 37.5°C, 1 for 37.5°C to 38.0°C, 2 for 38.1°C to 39.0°C, and 3 for higher than 39.0°C (the preferred route for recording temperature was oral). All other symptoms were scored as 0 for absent, 1 for easily tolerated, 2 for interferes with normal activity, and 3 for prevents normal activity. Serious adverse events were defined as events that resulted in death, were life-threatening, led to hospitalization or prolongation of existing hospitalization, resulted in disability or incapacity, or caused a congenital anomaly or birth defect in the child of a participant.

‡ Details are provided in Tables S5 through S8 in the Supplementary Appendix.

§ The serious adverse events considered by the investigator to be related to the trial intervention were lymphadenitis, acute myocardial infarction, ulcerative colitis, acute pancreatitis, administration-site erythema, administration-site pain, chills, pyrexia, allergic granulomatous angiitis, bacterial arthritis, erysipelas, herpes zoster oticus, eczema, neutropenic sepsis, and acute myeloid leukemia in the HZ/su group and polymyalgia rheumatica, gastric adenocarcinoma, cerebral infarction, cerebrovascular accident, the Guillain–Barré syndrome, loss of consciousness, syncope, and glomerulonephritis in the placebo group. Some participants had more than one event.

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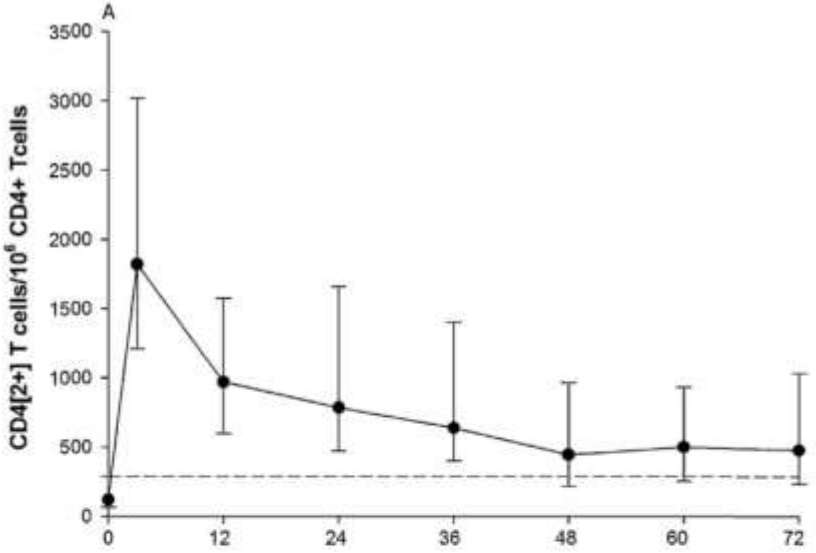
Long-term immunogenicity and safety of an investigational herpes zoster subunit vaccine in older adults

Roman Chlibek[a], Karlis Pauksens[b], Lars Rombo[c,d], Gini van Rijckevorsel[e], Jan H. Richardus[f], Georg Plassmann[g], Tino F. Schwarz[h], Grégory Catteau[i], Himal Lal[j,*], Thomas C. Heineman[j]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24
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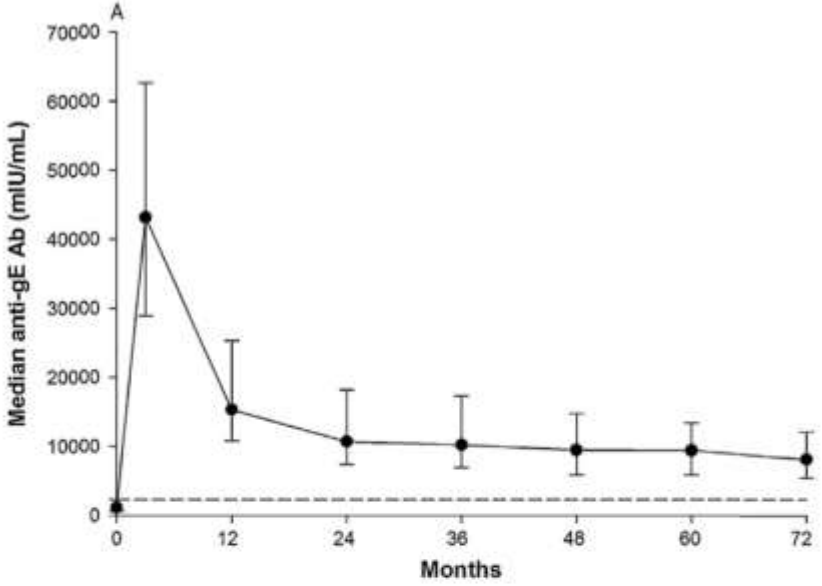
60
72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24
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48
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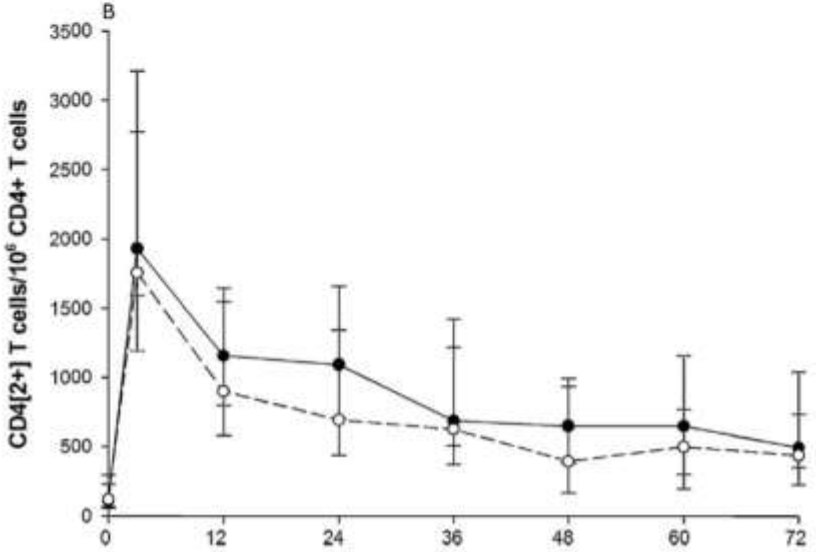
72
Months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0
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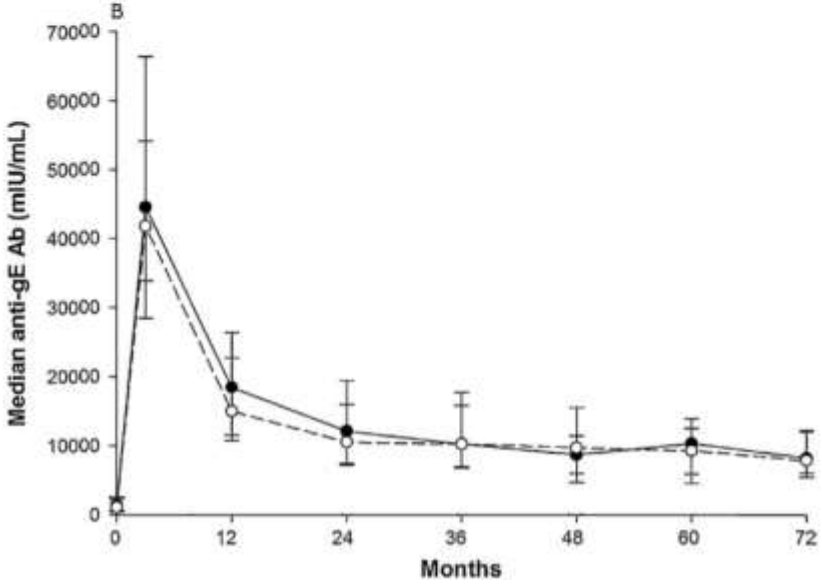
12
24
36
48
60
72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Median anti-gE Ab (mIU/mL)
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60000
50000
40000
30000
20000
10000
0
0
12
24
36
48
60
72
Months

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BRIEF REPORT

OPEN ACCESS

Comparative preclinical evaluation of AS01 versus other Adjuvant systems in a candidate herpes zoster glycoprotein E subunit vaccine

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ABSTRACT

The candidate vaccine HZ/su is being developed to prevent herpes-zoster disease (HZ). HZ occurrence is attributed to declines in varicella-zoster virus (VZV) specific T-cell immunity. HZ/su contains VZV antigen, gE, and Adjuvant System $AS01_B$ (liposome-based formulation of MPL and QS-21). In clinical trials, $AS01_B$ enhances $CD4^+$ T-cell responses to gE. In clinical trials of other vaccines, Adjuvant Systems AS03 and AS04 also enhance antigen-specific $CD4^+$ T-cell responses. Hence the purpose of this study was to evaluate gE formulated with $AS01_B$, $AS01_E$ (50% less MPL and QS-21 than $AS01_B$), AS03 or AS04 in C57BL6 mice primed with live-attenuated VZV. Four-weeks post-vaccination, the gE-specific $CD4^+$ T-cell response to gE/$AS01_B$ was 5.4, 2.8 and 2.2-fold greater than those to gE/AS03, gE/AS04 and gE/AS03, respectively ($p<0.001$). Therefore in the VZV-primed mouse model, $CD4^+$ T-cell responses to gE appeared most enhanced by $AS01_B$, and adds further support for the use of $AS01_B$ in the HZ/su formulation.

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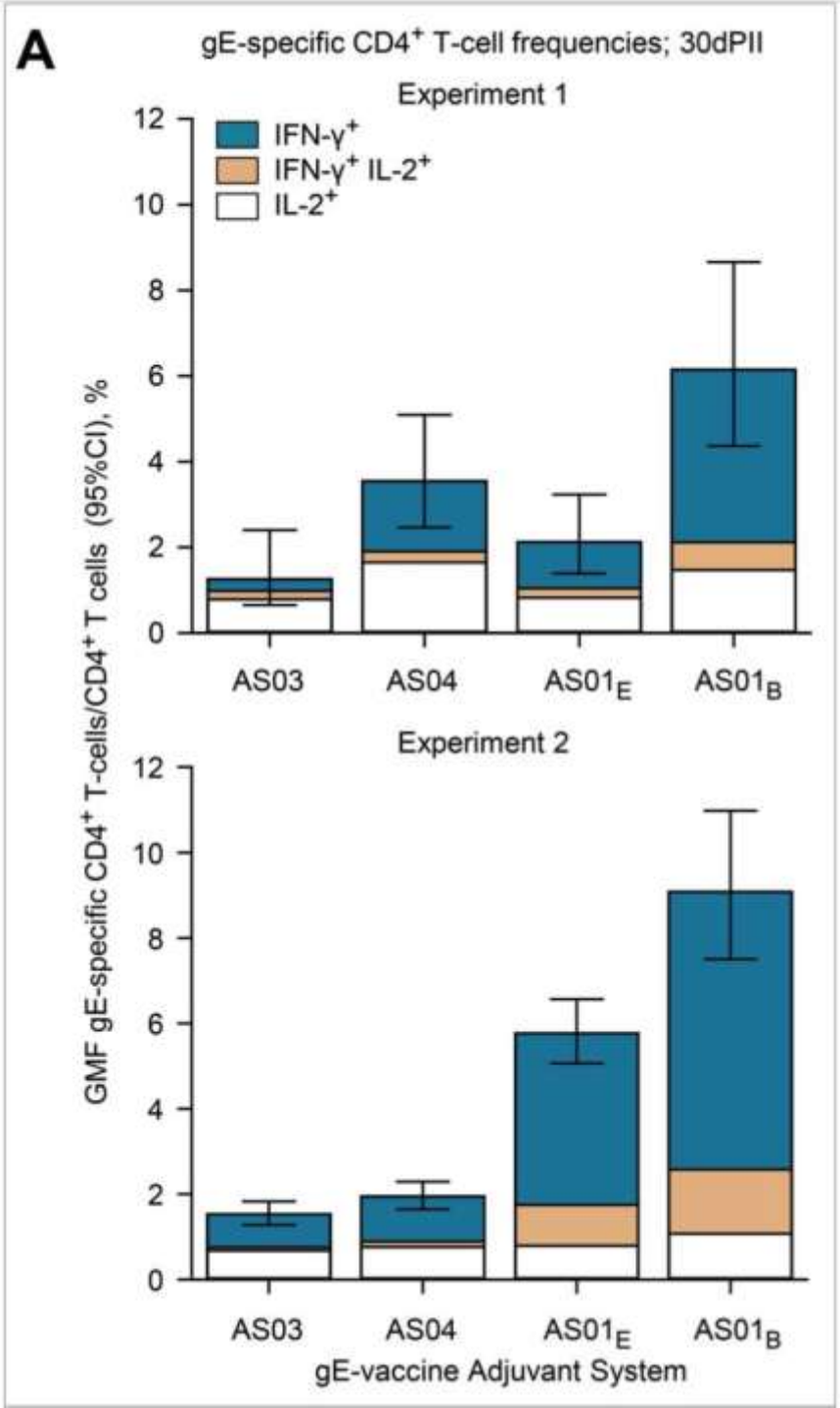
herpes zoster Adjuvant System; MPL; QS-21; Varicella-zoster virus; vaccine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IFN-γ+ IL-2+
IL-2+
GMF gE-specific CD4+ T-cells/CD4+ T cells (95%CI), %
0
2
4
6
8
10
12
AS03
AS04
AS01E
AS01B
Experiment 2
gE-vaccine Adjuvant System

Muchas gracias
por su atención