Germans Trias i Pujol Hospital

UAB Universitat Autònoma de Barcelona

Vacuna antigripal tetravalente

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Virus de la gripe

Tipo A

- Infecta tanto a humanos como animales
- Dividido en subtipos, en función de dos proteínas de superficie: **hemaglutinina (H1-H15)** y **neuraminidasa (N1-N9)**
- Las principales cepas circulantes son H1N1 y H3N2

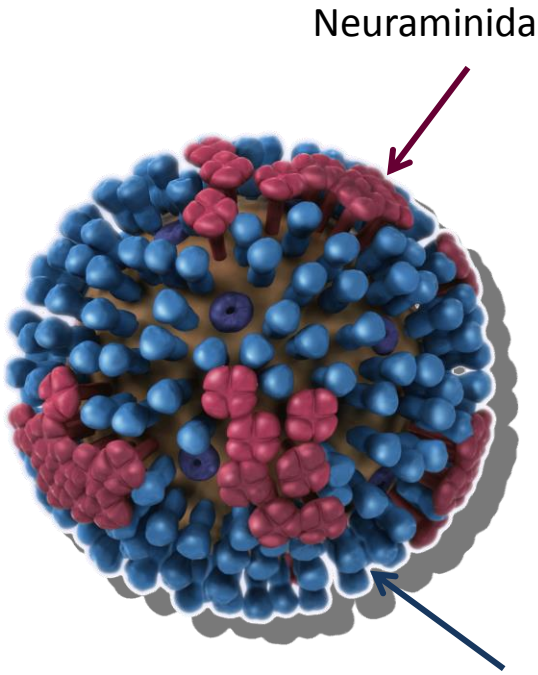
Tipo B

- Infecta predominantemente a humanos
- No está dividido en subtipos, sino en linajes: **Victoria** y **Yamagata**

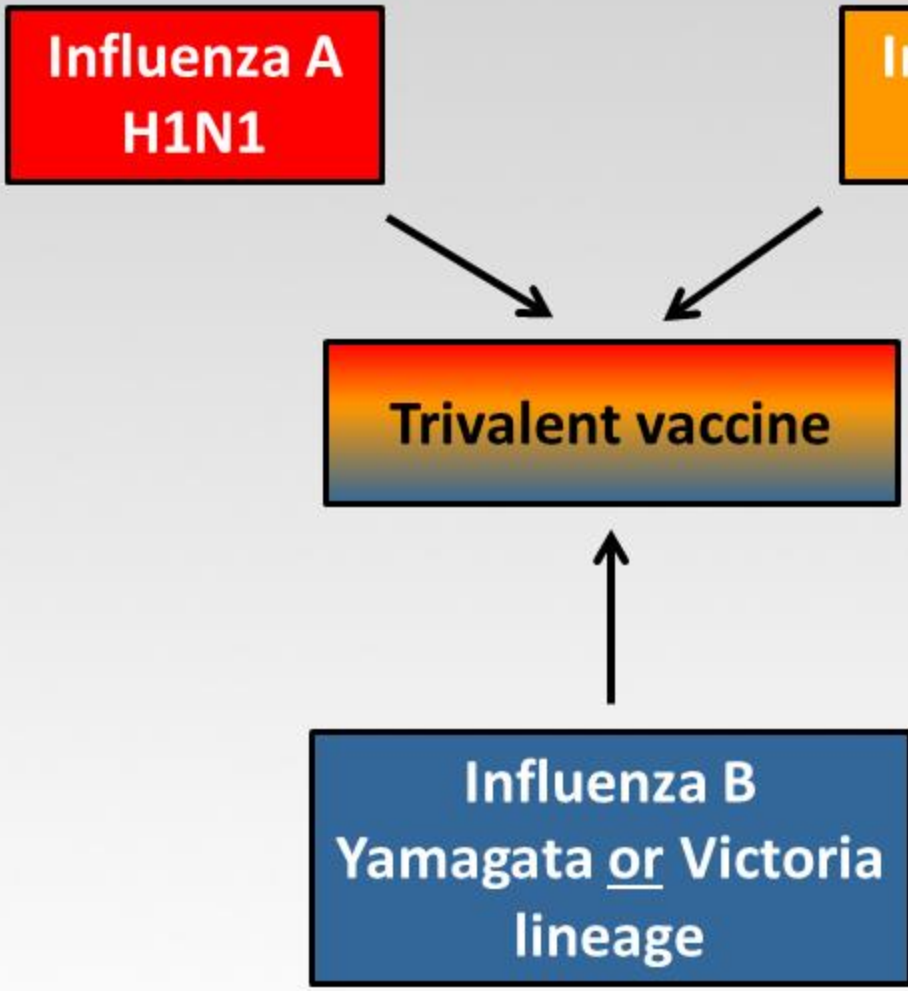
Tipo C

- Poco frecuente en humanos. La mayoría de los casos son subclínicos

Virus de la gripe mostrando las dos glucoproteínas mayores de superficie



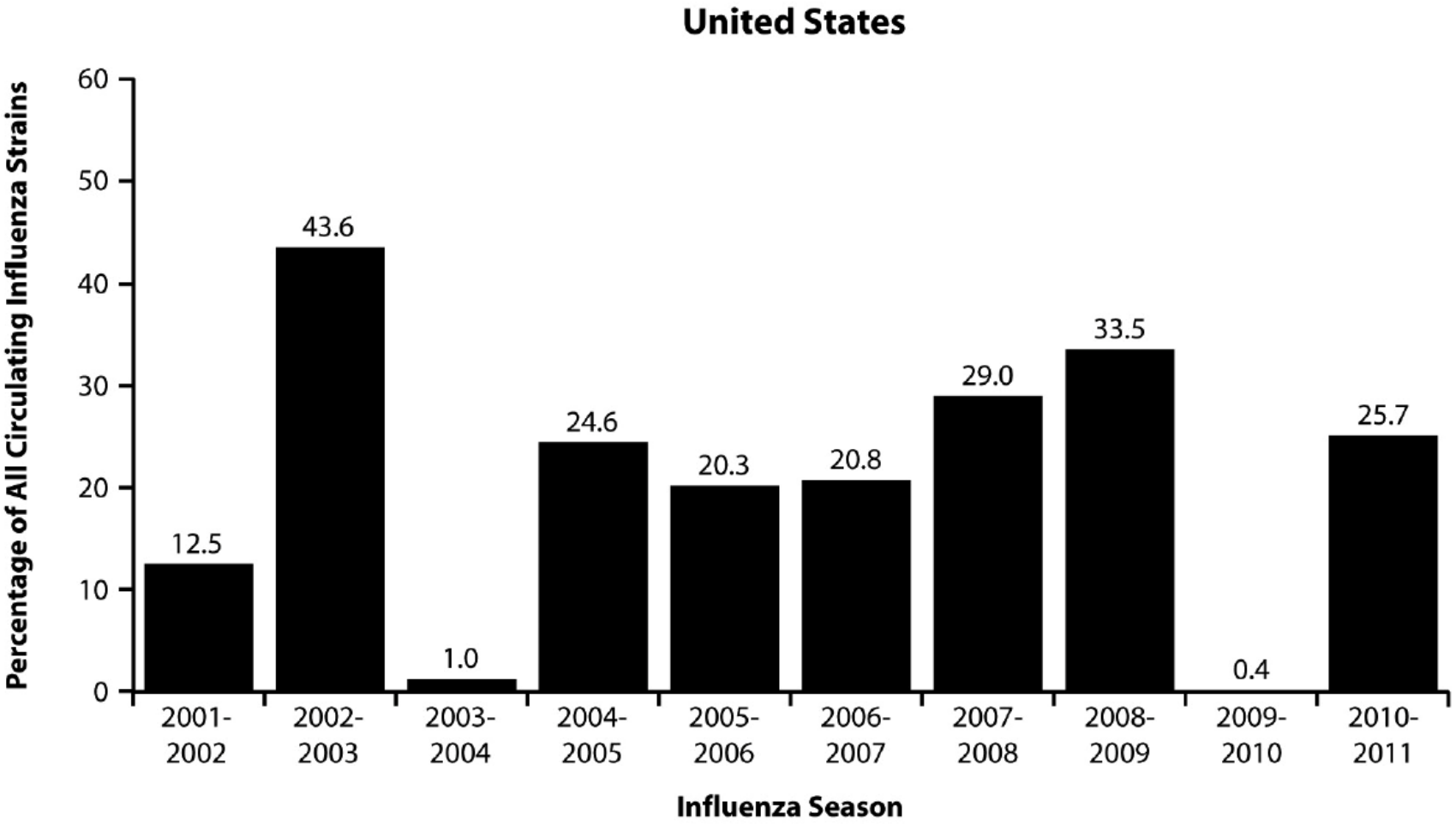
Traditional Trivalent Influenza Vaccines



- Both influenza A subtypes included
- Only 1 B lineage included
- Difficult to predict which B lineage to include each year

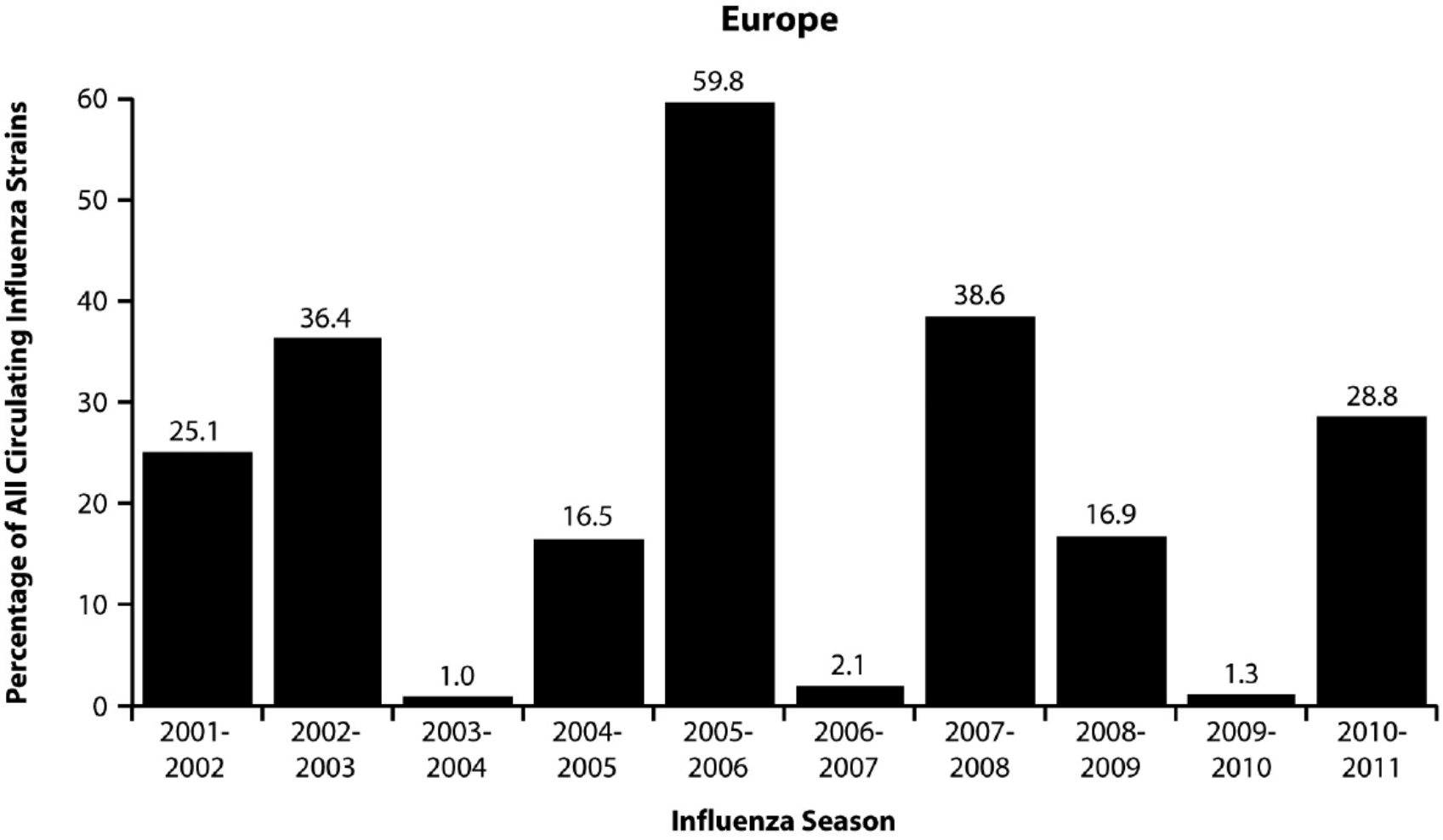
Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.

Influenza B circulation as a proportion of circulating influenza strains: US data for 2001 to 2011



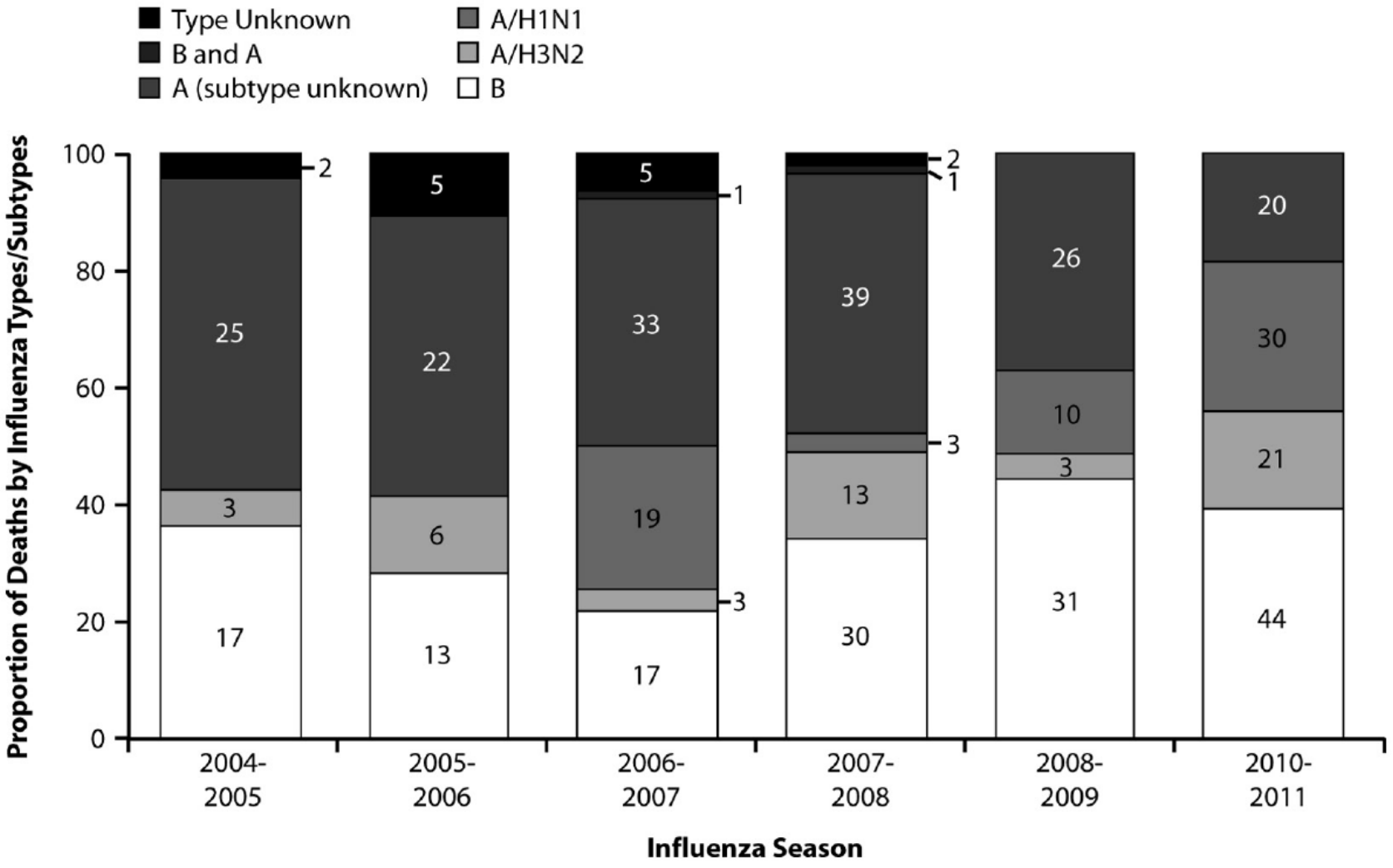
Ambrose CS et al. Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012

Influenza B circulation as a proportion of circulating influenza strains: European data for 2001 to 2011



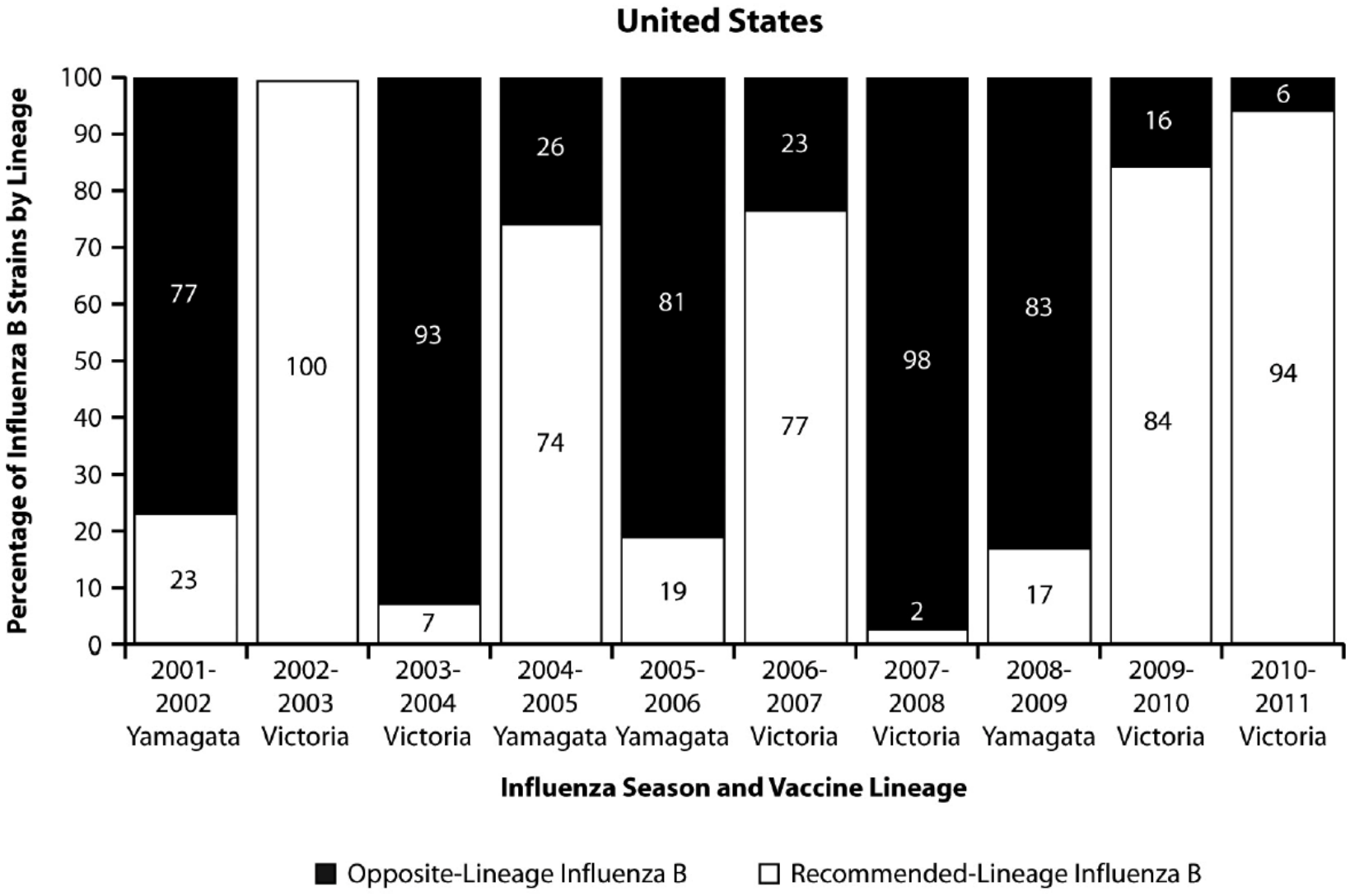
Ambrose CS et al. Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012

Proportion of US pediatric influenza deaths by viral type (2004 to 2011, excluding 2009–2010 pandemic). Values in columns represent the number of deaths in each category for each season



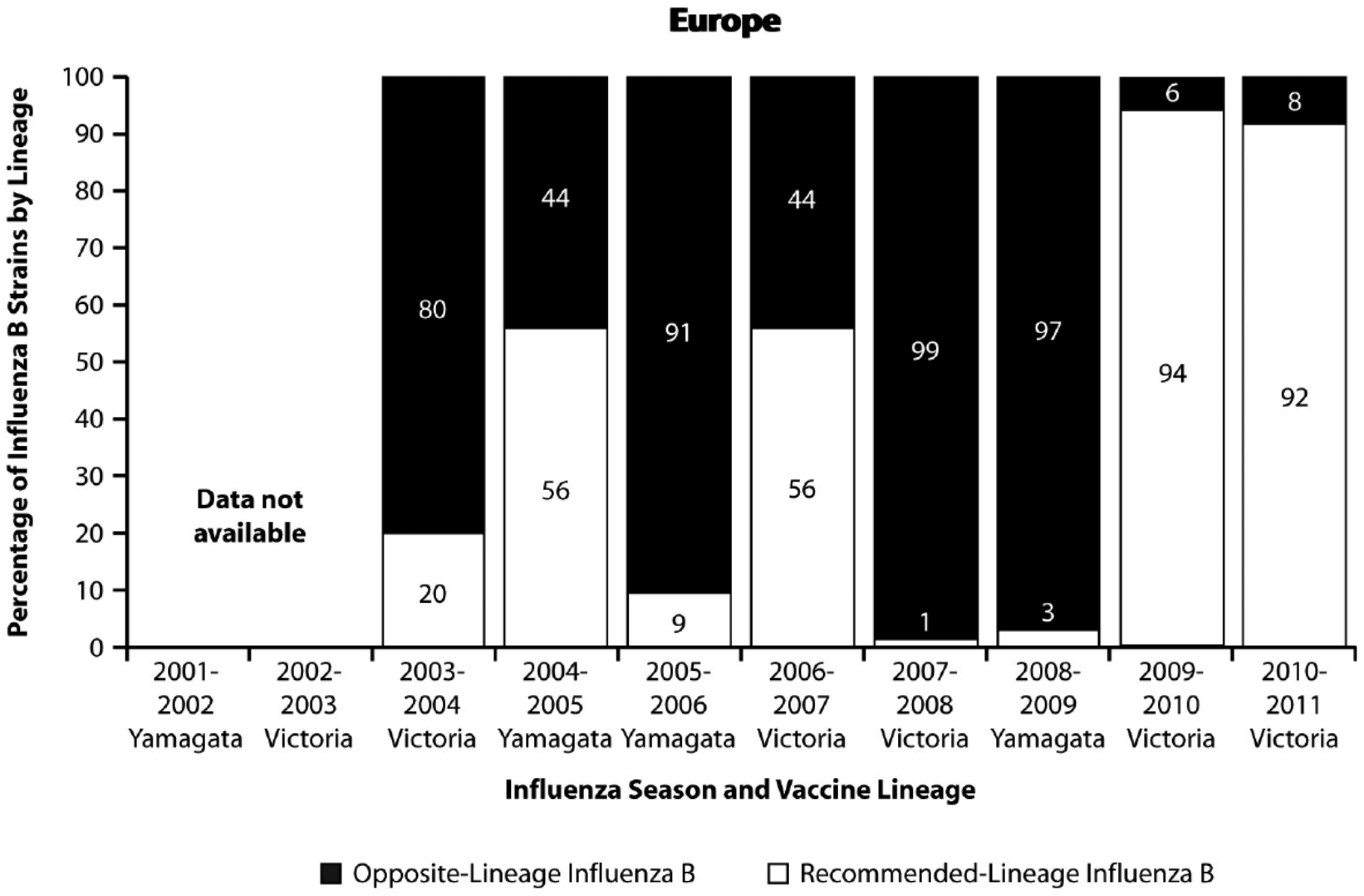
Ambrose CS et al. Human Vaccines & Immunotherapeutics 8:1, 81–88; January 2012

Influenza B circulation by lineage: US data for 2001 to 2011



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

Influenza B circulation by lineage: European data for 2001 to 2011



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

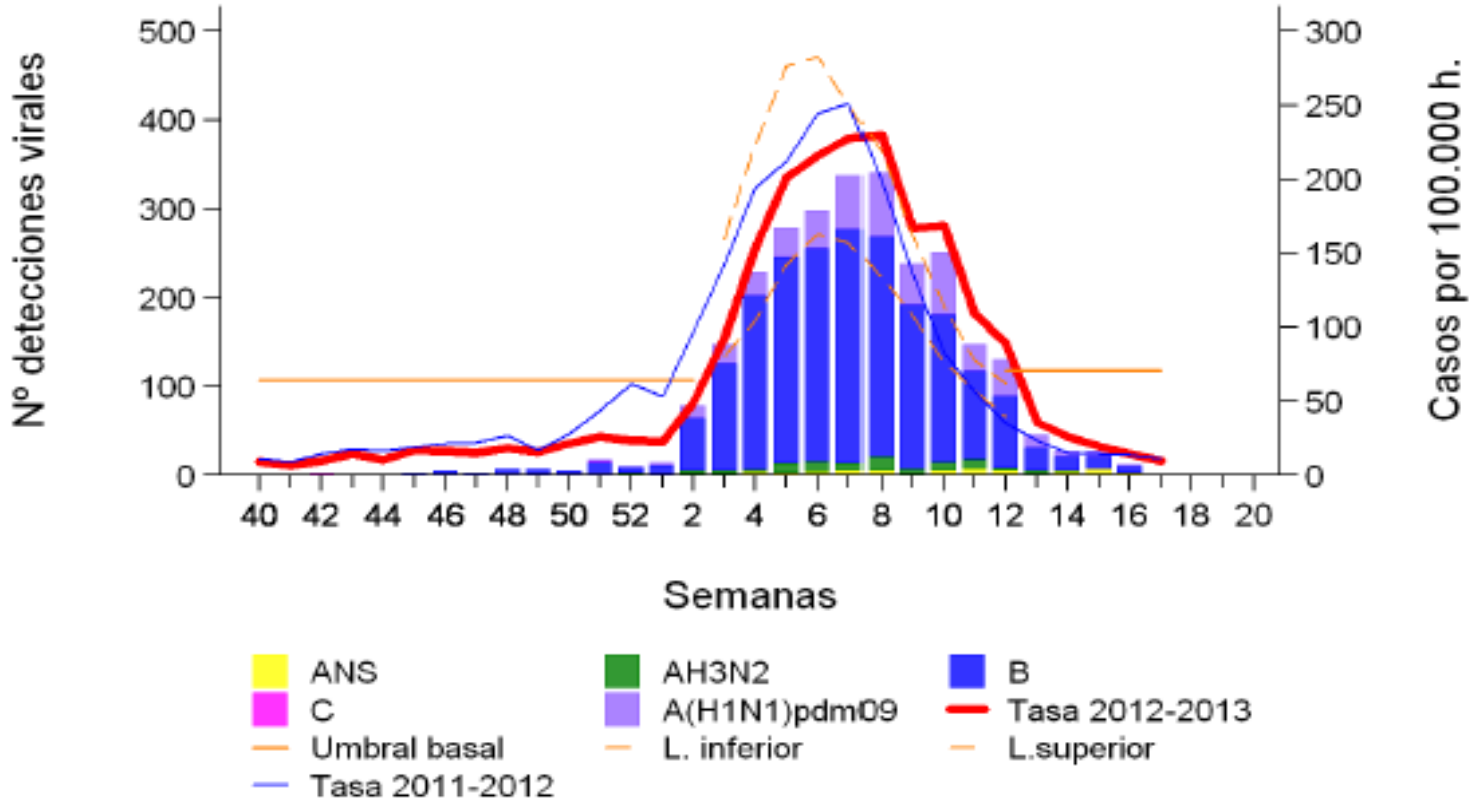
Detecciones de los diferentes tipos de virus de la gripe. Redes centinelas y no centinelas de España 2005-2013

Período	Tipo A	Tipo B	Tipo C	Total	% Tipo B
2012-2013	1135	3373	3	4511	**74,77%**
2011-2012	4967	412	7	5386	7,65%
2010-2011	3413	1320	4	4747	27,81%
2009-2010	10600	151	10	10761	1,40%
2008-2009	1492	553	2	2047	27,02%
2007-2008	828	946	2	1776	**53%**
2006-2007	1522	152	0	1674	9,08%
2005-2006	552	374	0	926	**40,39%**

Adaptada de: Instituto de Salud Carlos III. Informes anuales y semanales de Vigilancia de la Gripe en España. Sistema de Vigilancia de la Gripe en España. Disponible en: http://vgripe.isciii.es/gripe/inicio.do Acceso: diciembre 2014

Predominio del virus de la gripe B en España durante la temporada 2012-2013

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



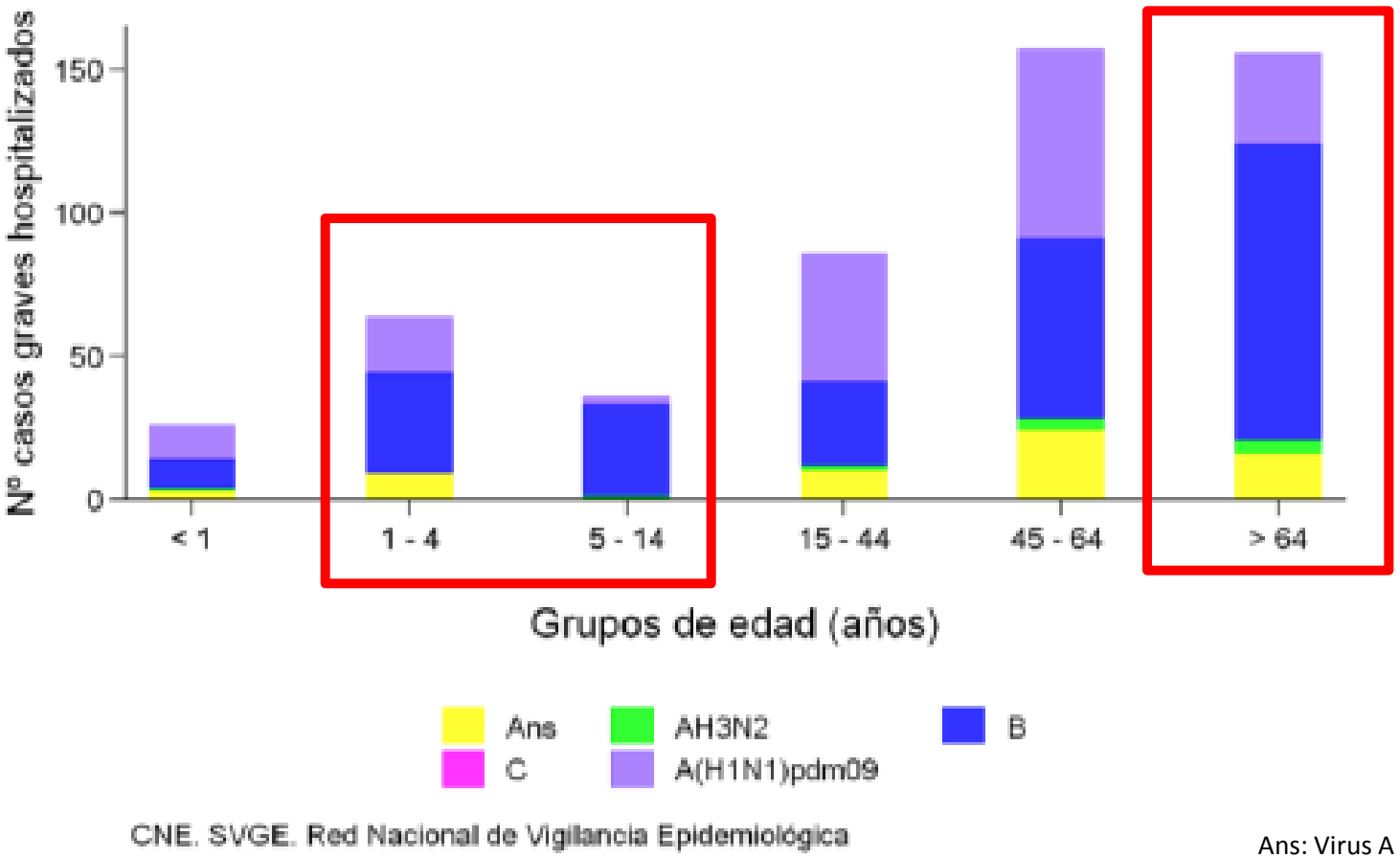
Fuente: CNE. Sistema de Vigilancia de Gripe en España

Ans: Virus A no tipado

Adaptada de :Instituto de Salud Carlos III. Informe de Vigilancia de la Gripe en España. Temporada 2012-2013 (Desde la semana 40/2012 hasta la semana 20/2013).

Sistema de Vigilancia de la Gripe en España. Disponible en: http://vgripe.isciii.es/gripe/documentos/20122013/InformesAnuales/Informe_Vigilancia_GRIPE_2012-13_18sep2013.pdf

Detecciones virales en casos graves hospitalizados y confirmados de gripe, por grupo de edad en España. Temporada 2012-2013



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Sistema de Vigilancia de la Gripe en España. Disponible en: http://vgripe.isciii.es/gripe/documentos/20122013/InformesAnuales/Informe_Vigilancia_GRIPE_2012-13_18sep2013.pdf

Influenza B Disease

- Influenza B strains are not associated with pandemics
- Perceived as causing only mild disease
- But influenza B can cause severe disease
- Burden of infection mainly on children and young adults
- B lineages responsible for seasonal epidemics every 2-4 years
- B lineages have been responsible for ≥25% of influenza epidemics

Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.
Thompson WW, et al. *JAMA.* 2003;289(2):179-186.

Antigenic Mutation Among Influenza Viruses

- Influenza A viruses undergo antigenic shift due to large domestic animal reservoir.
- Influenza B viruses do not have a domestic animal reservoir; they mutate more slowly.
- Drift variants of both B lineages have been circulating concurrently in recent influenza seasons.
- Strains/lineages in vaccine need to be reviewed each year.
- It is better to include all 4 strains/lineages in vaccine.

Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.
WHO. http://www.who.int/influenza/vaccines/virus/recommendations/2014_15_north/en/

Antigenic Cross-Reactivity Between Influenza Viruses

- Effectively no cross-reactivity:
  - Between influenza A and B viruses
  - Between influenza A subtypes
  - Between influenza B lineages
- Vaccines need to include all 4 strains/lineages to provide optimal protection against influenza.
- Vaccine needs to be given each year to take into account antigenic drift and waning immunity.

Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.
Belshe RB, et al. *Vaccine.* 2010;28(9):2149-2156.
WHO. http://www.who.int/influenza/vaccines/virus/recommendations/2014_15_north/en/

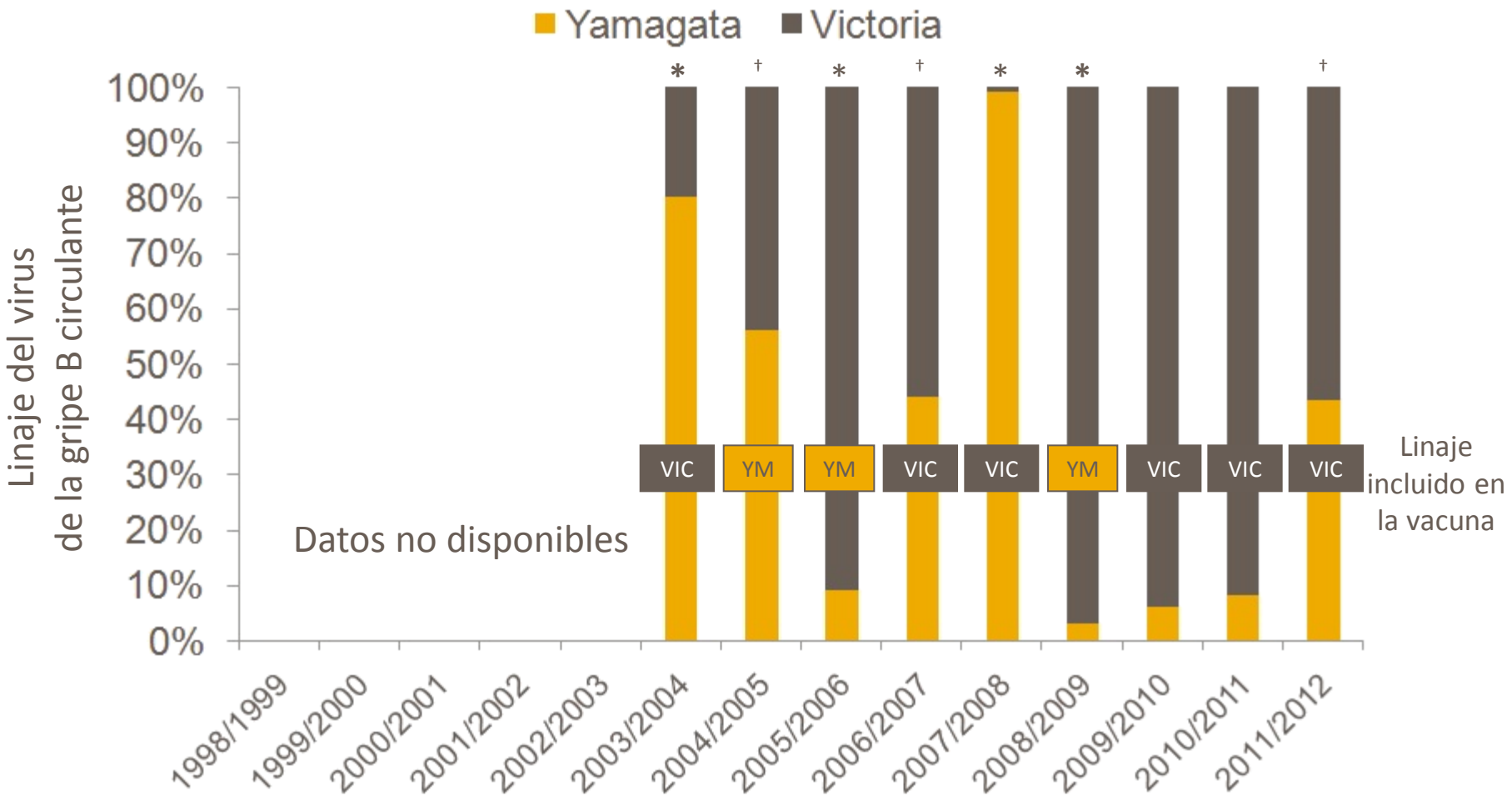
Antigenic Mismatch

- The closer the match between circulating virus strains/lineages and the vaccine, the better the protection it offers.
- If there is a mismatch between the circulating strains and the vaccine, protection is reduced.*
- Including both influenza B lineages provides optimal protection against influenza.
- The quadrivalent vaccine includes both B lineages.

* Mismatches are rare; most years, the vaccines match the circulating strains very well.

Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.
Jefferson T, et al. *Cochrane Database Syst Rev.* 2010;(7):CD001269.
Reed C, et al. *Vaccine.* 2012;30(11):1993-1998.

Concordancia/discordancia entre el virus B circulante y la cepa B incluida en la vacuna antigripal trivalente (Europa)



*Falta de concordancia con la vacuna (falta de concordancia >60%);
†Falta de concordancia parcial con la vacuna (concordancia <80%)

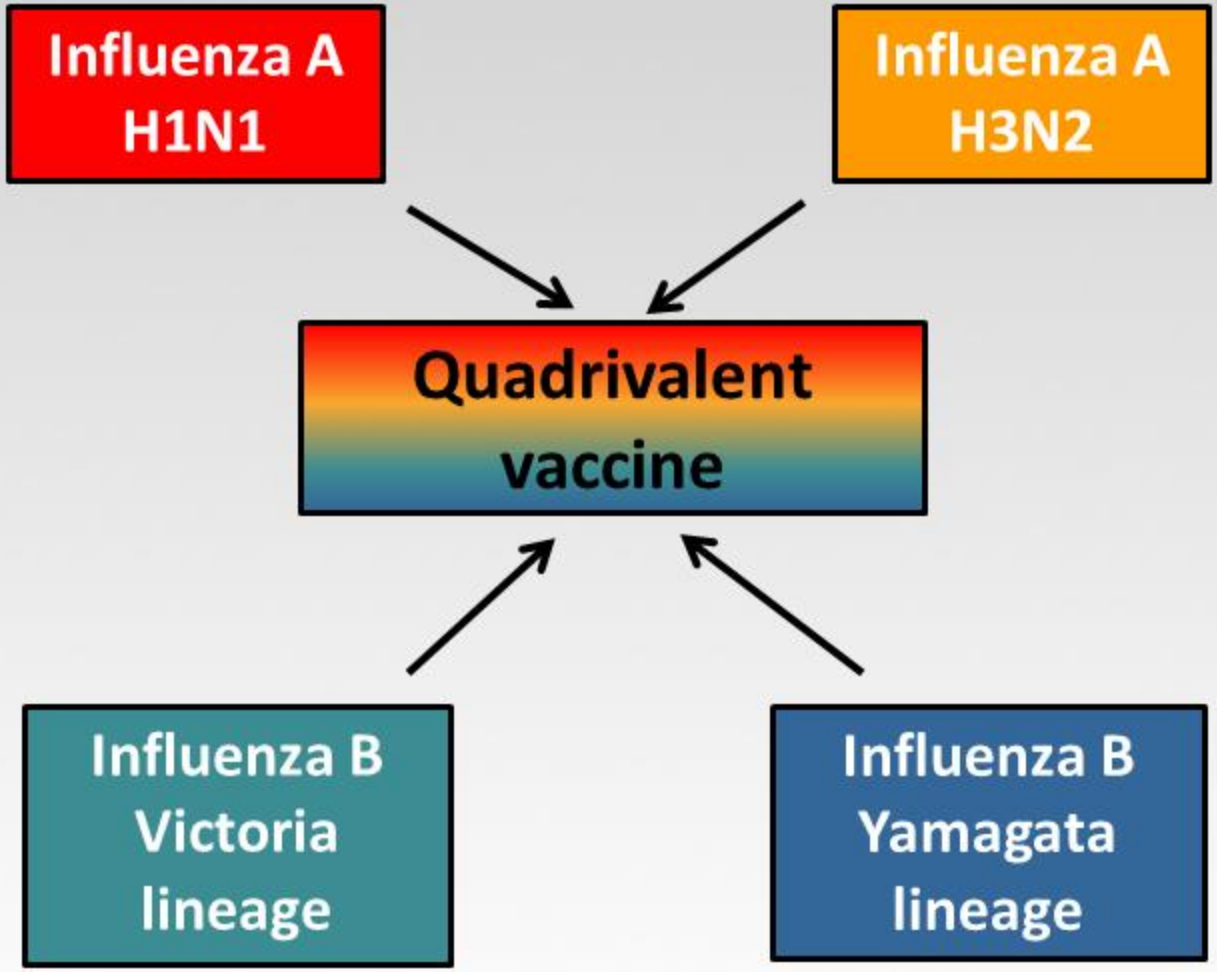
Ambrose CS, Levin MJ. Hum Vaccin Immunother 2012;8:81–88
ECDC. Seasonal influenza 2011–2012 in Europe.
www.ecdc.europa.eu/

Concordancia/discordancia entre el virus de la gripe B circulante y la cepa B incluida en la vacuna antigripal trivalente (España)

Temporada	Cepas principales circulantes	Linaje	Nº caracte-rizaciones	% del total	Cepa vacunal	Cepa vacunal y linaje
2012/2013	B/Estonia/55669/2011 B/Wisconsin/1/2010 B/Brisbane/60/2008	Yamagata Yamagata Victoria	111 110 46	22,4 22,2 9,3	No Sí No	Yamagata B/Wisconsin/1/2010
2011/2012	B/Brisbane/3/2007 B/Bangladesh/3333/2007 B/Brisbane/60/2008	Yamagata Yamagata Victoria	4 32 11	0,8 6,8 2,3	No No Sí	**Victoria** B/Brisbane/60/08
2010/2011	B/Brisbane/60/2008 B/Bangladesh/3333/2007	Victoria Yamagata	119 5	27,2 1,1	Sí No	Victoria B/Brisbane/60/08
2009/2010	B/Brisbane/60/2008	Victoria	-	1,4	Sí	Victoria B/Brisbane/60/08
2008/2009	B/Brisbane/60/2008 B/Malaysia/2506/04	Victoria Victoria	88 10	25,2 2,9	No No	**Yamagata** B/Florida/4/2006
2007/2008	B/Florida/4/2006 B/Malaysia/2506/04	Yamagata Victoria	118 4	40,1 1,4	No Sí	**Victoria** B/Malaysia/2506/2004
2006/2007	B/Jiangsu/10/2003 B/Malaysia/2506/04	Yamagata Victoria	8 1	5,5 0,7	No Sí	Victoria B/Malaysia/2506/2004
2005/2006	B/Malaysia/2506/04 B/Shanghai/361/02	Victoria Yamagata	38 6	55,9 8,9	No No	**Yamagata** B/Florida/4/2006

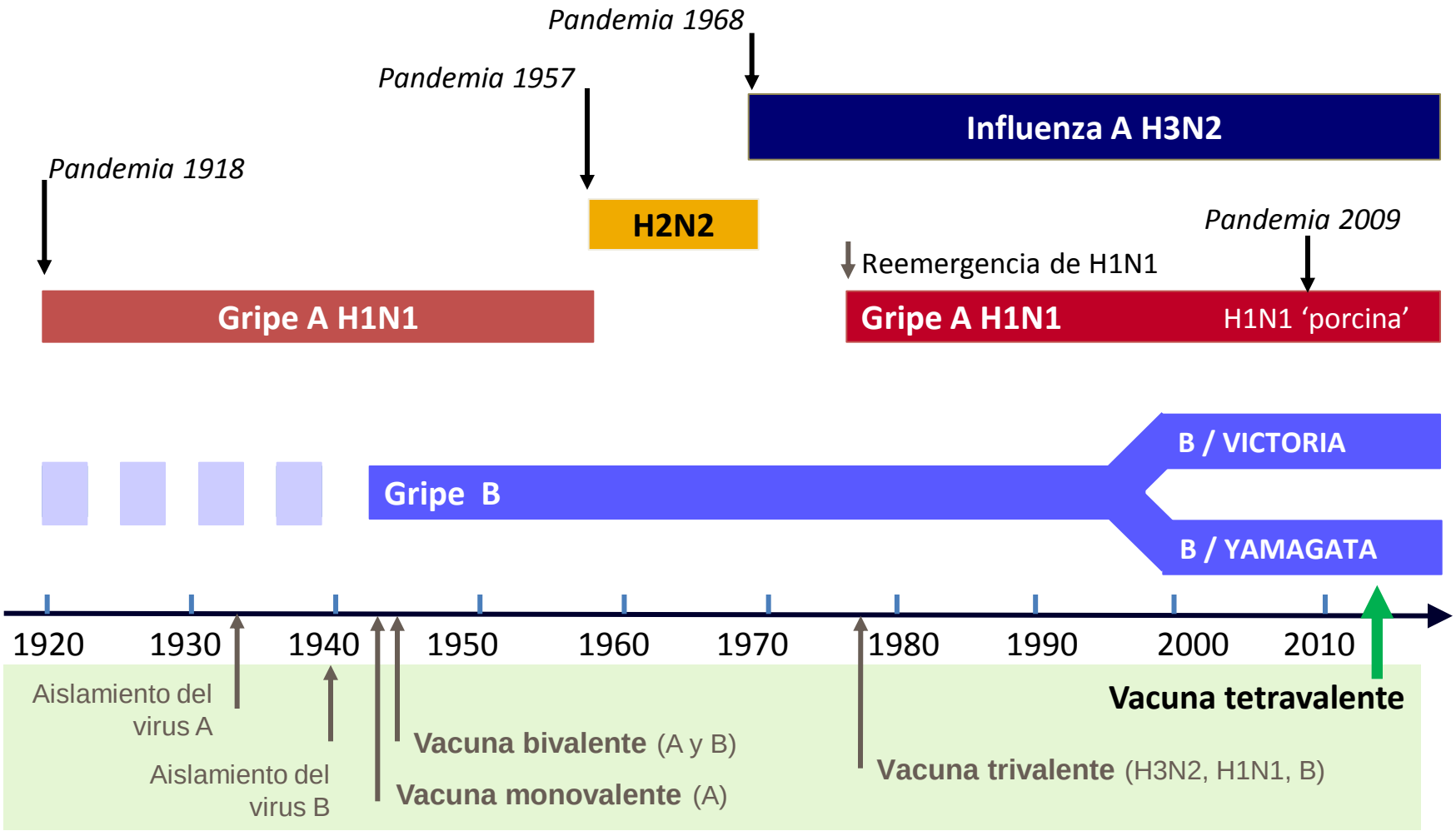
Instituto de Salud Carlos III. Informes anuales y semanales de Vigilancia de la Gripe en España. Sistema de Vigilancia de la Gripe en España

Quadrivalent Influenza Vaccines



Beran J, et al. *BMC Infect Dis.* 2013;13:224.
Belshe RB. *Vaccine.* 2010;28(Suppl 4):D45-D53.
Reed C, et al. *Vaccine.* 2012;30(11):1993-1998.

Historia de las vacunas de gripe



McCullers JA, Huber MC. Hum Vaccin Immunother. 2012;8:34-44

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Vacunas autorizadas en menores de 18 años en España

Nombre comercial	Laboratorio	Características	Presentación	Dosificación	Vía de Admón.	Edad autorizada
Chiroflu®	Novartis	Subunidades inactivadas Trivalente Sin adyuvante	Jeringa con 0,5 ml precargada	- Mayores de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml	IM	≥ 6 meses
Fluarix®	GSK	Virus fraccionados e inactivados Trivalente Sin adyuvante	Jeringa con 0,5 ml precargada	- Mayores de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml	IM	≥ 6 meses
Fluarix Tetra®	GSK	Virus fraccionados e inactivados Tetravalente Sin adyuvante	Jeringa con 0,5 ml precargada	- A partir de 36 meses: 0,5 ml	IM	≥ 36 meses
Fluenz Tetra®	AstraZeneca	Virus vivos atenuados Tetravalente	Aplicador nasal con 0,2 ml Envases multidosis	- 0,2 ml a razón de 0,1 ml en cada fosa nasal	Intranasal	2-17 años
Inflexal V®	Crucell	Subunidades inactivadas Trivalente Adyuvante / transportador: virosomas	Jeringa con 0,5 ml precargada	- A partir de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml	IM	≥ 6 meses
Influvac®	Abbott	Subunidades inactivadas Trivalente Sin adyuvante	Jeringa con 0,5 ml precargada	- A partir de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml	IM	≥ 6 meses
Mutagrip®	Sanofi Pasteur MSD	Virus fraccionados e inactivados Trivalente Sin adyuvante	Jeringa con 0,5 ml precargada	- A partir de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml	IM	≥ 6 meses
Vaxigrip®	Sanofi Pasteur MSD	Virus fraccionados e inactivados Trivalente Sin adyuvante	Jeringa con 0,5 ml precargada	- Mayores de 36 meses: 0,5 ml - Niños de 6-35 meses: experiencia limitada. Se han administrado dosis de 0,25 ml o 0,5 ml.	IM	≥ 6 meses

Recomendaciones de la OMS para la temporada 2014-2015

World Health Organization

Recommended composition of influenza virus vaccines for use in the 2014-2015 northern hemisphere influenza season

February 2014

It is recommended that vaccines for use in the 2014-2015 influenza season (northern hemisphere winter) contain the following:

– an A/California/7/2009 (H1N1)pdm09-like virus;
– an A/Texas/50/2012 (H3N2)-like virus;
– a B/Massachusetts/2/2012-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.

FDA Advisers Recommend Total Overhaul of 2015 Flu Vaccine

Alicia Ault | March 05, 2015

A panel of US Food and Drug Administration (FDA) advisers has recommended all new components for the influenza vaccine for the 2015-16 season.

The influenza vaccine has included the exact same strains for the last two flu seasons, but data indicate that this year's vaccine was largely ineffective and that those strains are no longer circulating.

The Vaccines and Related Biological Products Advisory Committee recommended a total overhaul of both the trivalent and quadrivalent vaccines that are available in the United States.

http://www.medscape.com/viewarticle/840944

For the winter of 2014-15, the vaccine has proven to be very ineffective, reducing the chances that someone needs to seek medical help for influenza by 19% — compared with 60% or more in most years — according to an interim analysis by the Centers for Disease Control and Prevention (CDC).

This season's vaccine mostly failed to protect against the predominant A strain, A/Switzerland/9715293/2013-like virus (H3N2). The H3N2 strains are associated with worse illness and higher mortality.

The Switzerland strain was barely in circulation — comprising only 1% of viruses detected — when FDA advisers formulated US vaccine recommendations in February 2014. It was not until late summer that it became apparent that the Switzerland strain was the main illness-causing agent, Lisa Grohskopf, MD, medical officer with the CDC's Influenza Division, told the FDA panel.

The latest data from the World Health Organization (WHO), the Department of Defense, and the CDC indicate that the Switzerland strain continues to be dominant worldwide.

In September 2014, the WHO recommended that an inactivated form of that strain be included in the northern hemisphere vaccine for 2015-16. It also recommended inclusion of a new H1N1 A strain, A/California/7/2009 pandemic09-like virus, and a new B strain, B/Phuket/3073/2013-like virus. For quadrivalent vaccines, the recommendation was to add B/Brisbane/60/2008-like virus.

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