CHEST®

Community-Acquired Pneumonia:

Using the Guidelines to Improve Our Outcomes

Prevention of CAP

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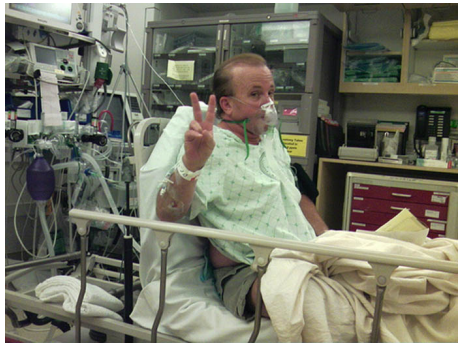
Disclosure: Nothing to disclose

Lesson Objectives

- To know the vaccine efficacy and effectiveness of influenza, pneumococcal and SARS-CoV-2 vaccines
- To explore the limitations of vaccines and their causes
- To know the vaccination indications in certain risk groups

Clinical case



Mr. García is an 80-year-old patient who presented a 2-day fever (39ºC), cough with mucous expectoration and dyspnea class 4 mMRC

Past history

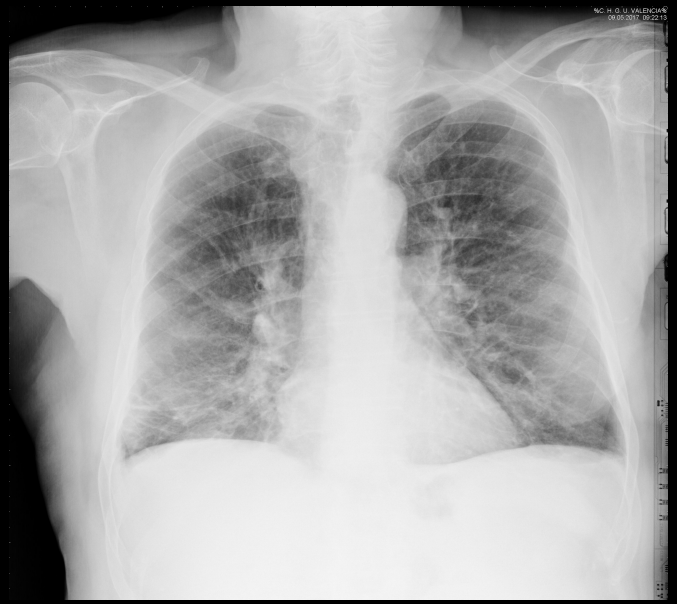
Multiple Myeloma. Hypertension

Vaccination status

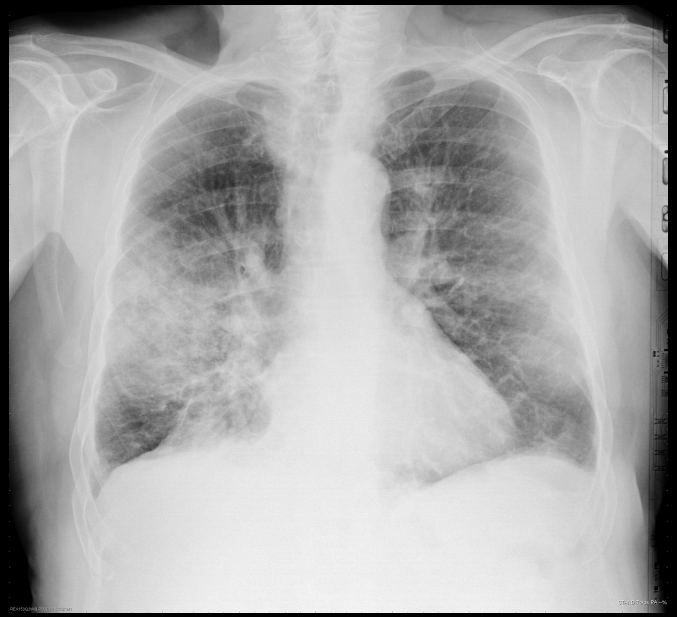
Influenza vaccine (8 months ago), PPVS23 7 years ago, and SARS-CoV-2 vaccine (BNT162b2) 6 months ago

Vital signs

SpO2 88% (FiO2 0.31) BP 100/50 Tª38,6ºC
HR 110 bpm RR 26 bpm



2 days later…



RT-PCR Influenza virus A

POSITIVE

Pneumococcal urinary antigen test

POSITIVE

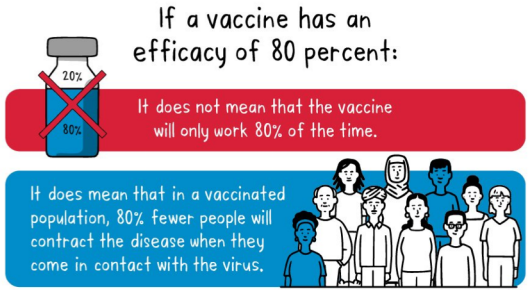
Have **vaccination strategies** failed in this patient?

Influenza vaccine

Vaccine efficacy and effectiveness

Vaccine efficacy

How the vaccine perform in **ideal conditions**: How much a vaccine lowers the risk of an outcome

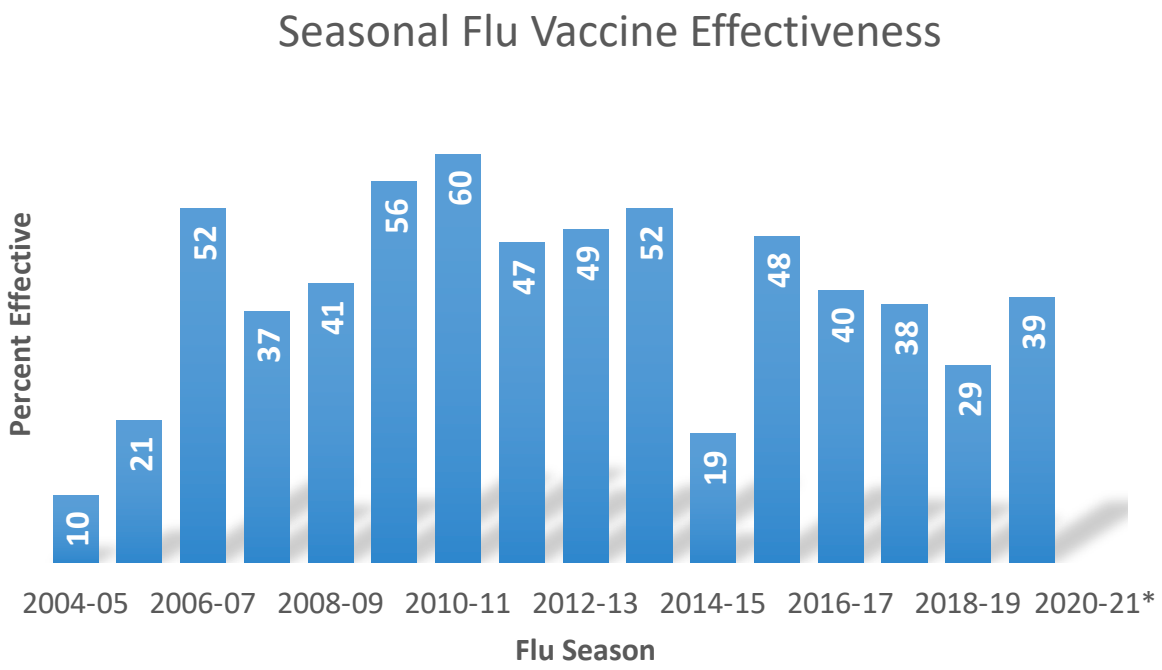


Vaccine effectiveness

How the vaccine performs in the **wider population**

Vaccine effectiveness

2005 – 2021 Flu seasons



Mean effectiveness

2005-2021

40%

Vaccine effectiveness

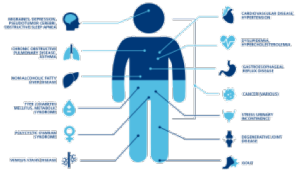
Vaccine effectiveness

VIRAL FACTORS

Antigen drift / shift

HOST FACTORS

Older age



Underlying medical conditions

History of prior flu illness

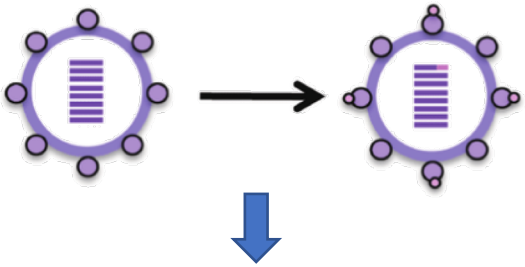
Prior flu vaccination

Vaccine effectiveness

Viral factors

Antigenic drift

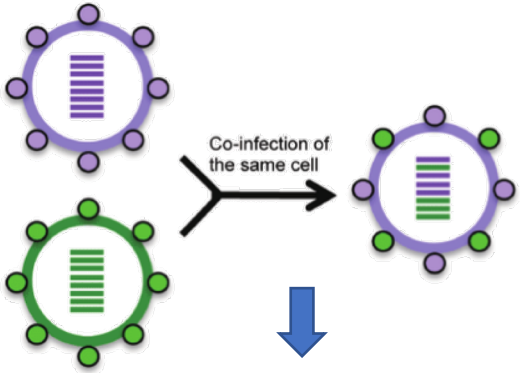
Small mutations in the hemagglutinin and neuraminidase genes



Epidemic

Antigenic shift

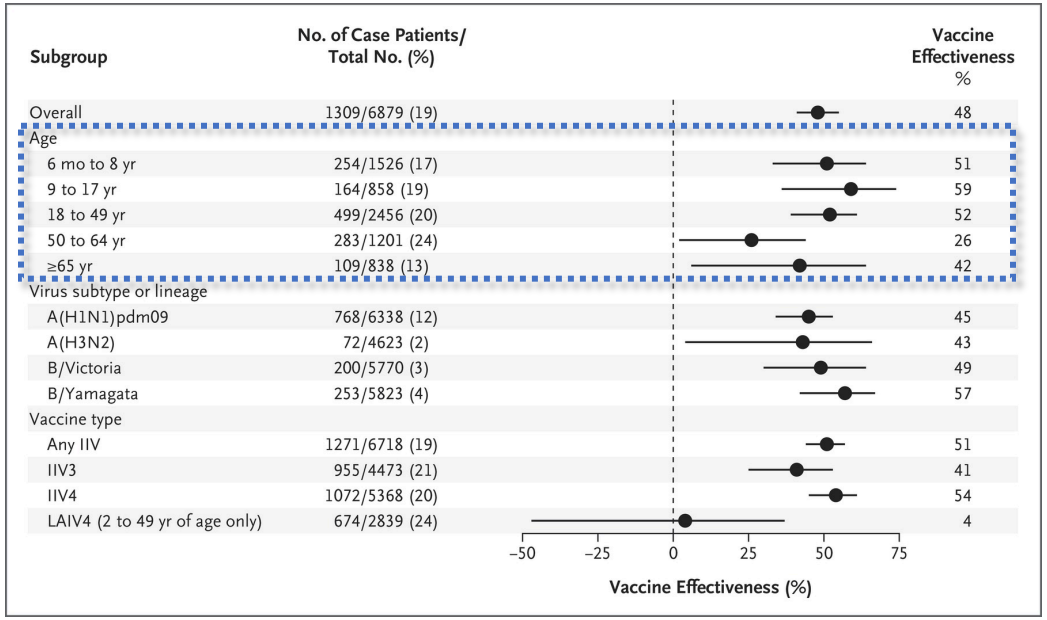
Major change in an influenza A virus, resulting in new HA and/or new HA and NA proteins



Pandemic

Vaccine effectiveness

Host factors



Vaccine effectivenes varies with age

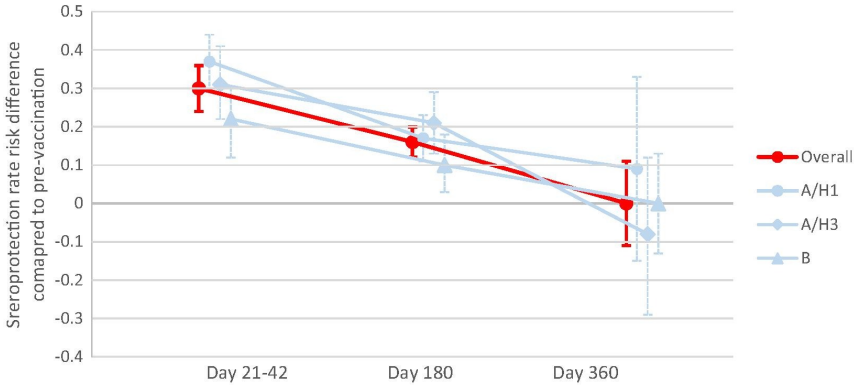
NEJM 2017;2017:377:534-43

Vaccine effectiveness

Host factors

Immune response

- Seroprotection declined linearly from Day 21–42 to Day 360



Serological protection falls 6-11% **each month**

- The wane of immune response depens on specific Influenza virus

Outcome	ΔVE (95% CI)	VE (95% CI), by Time After Vaccination	
		15–90 d	91–180 d
Influenza A(H3)	-33 (-57 to -12)	45 (34 to 54)	13 (-10 to 31)
Influenza B	-19 (-33 to -6)	62 (52 to 70)	43 (33 to 52)
Influenza A(H1)	-8 (-27 to 21)	62 (35 to 78)	54 (43 to 63)

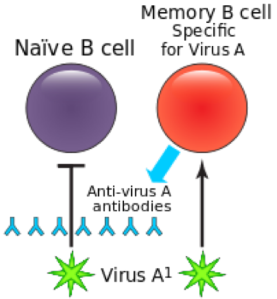
Vaccine 2017;35:212–221

Vaccine effectiveness

Host factors

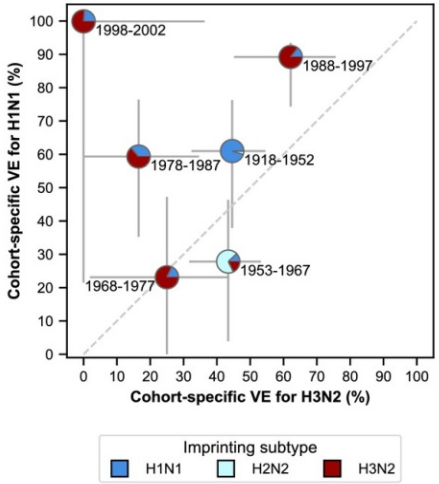
Immune response

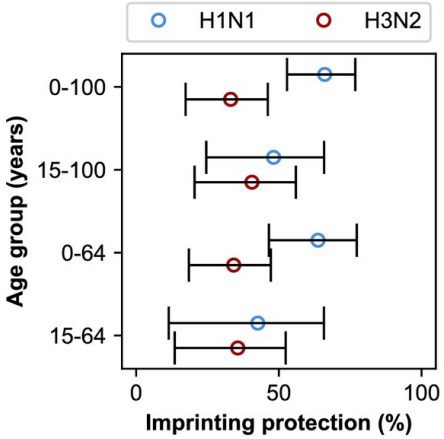
Original antigenic sin



Is the tendency of the body's immune system to preferentially use immune memory based on a previous infection when a second slightly different version of a virus is encountered

VE depens on year of birth



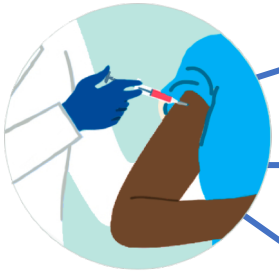


J Autoimmunity 2017;83:12-21 eLife 2020;9:e50060

How can vaccine effectiveness affect our patient **outcomes**?

Would it be beneficial for Mr. García to be vaccinated **against the flu**?

Benefits of Influenza vaccine



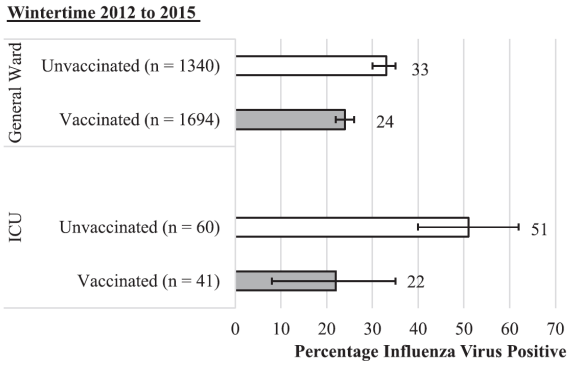
Vaccine effectiveness among vaccinated adults

23%

36%-42%

18-65 y	51%	*A H1N1*	51%
>65 y	37%	*A H3N2*	37%
>80 y	34%	*B*	34%

82%



J Infect. 2017 Nov;75(5):381-394

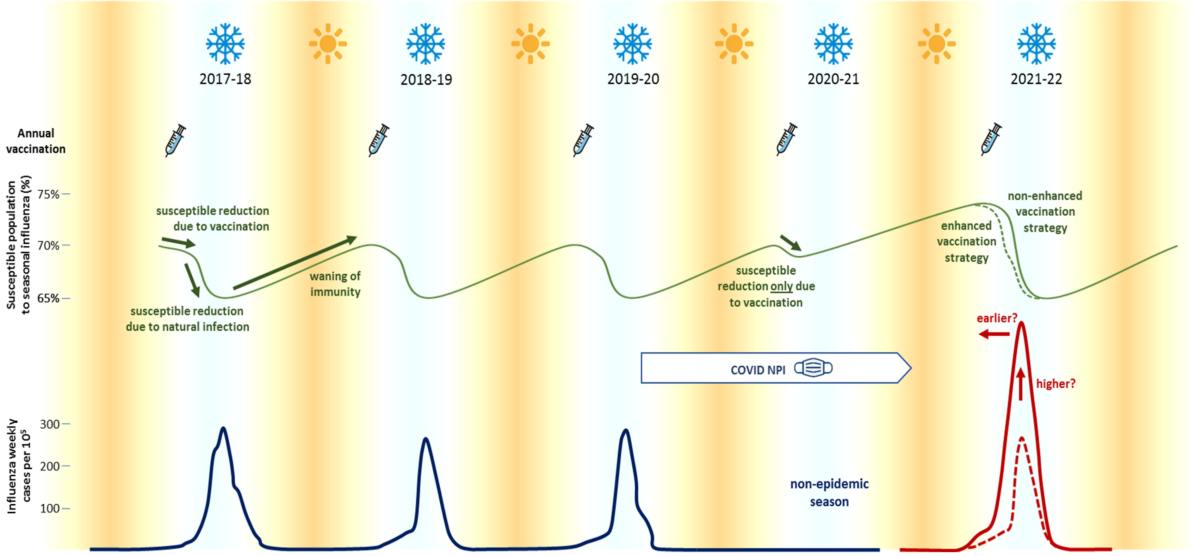
¿Qué pasará con la gripe?

vaccines MDPI

Communication

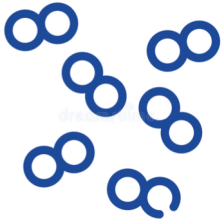
Social Distancing, Lockdown and the Wide Use of Mask; A Magic Solution or a Double-Edged Sword for Respiratory Viruses Epidemiology?

Ivan Sanz-Muñoz [1,*], Sonia Tamames-Gómez [1,2], Javier Castrodeza-Sanz [1,3], José María Eiros-Bouza [1,4] and Raul Ortiz de Lejarazu-Leonardo [1]



Vaccine 2021;9:595

Pneumococcal vaccine

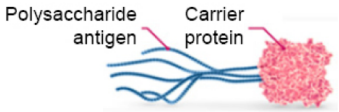


Types of pneumococcal vaccines

Polysaccharide vaccines (PPSV23)

Serotypes: **1**, 2, **3**, **4**, **5**, **6B**, **7F**, 8, 9N, **9V**, 10A, 11A, 12F, **14**, 15B, 17F, **18C**, **19F**, 19A, 20, 22F, **23F**, and 33F

Conjugate vaccines (PCV13)



Serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 18C, and 23F

Vaccine effectiveness

PPSV23

Vaccine efficacy and effectiveness
Vaccine-type
Invasive Pneumococcal Disease

69.9%
(95%CI 24.8-88)

73% (RCT)

Vaccine efficacy and effectiveness
Any-serotype
Invasive Pneumococcal Disease

57.4%
(95%CI 19.4-77.5)
[65-74 y]

73% (RCT)
59% (Case-control)
45% (cohort studies)

Vaccine efficacy and effectiveness
Pneumococcal pneumonia

64% (RCT)
37-53% (cohort studies)

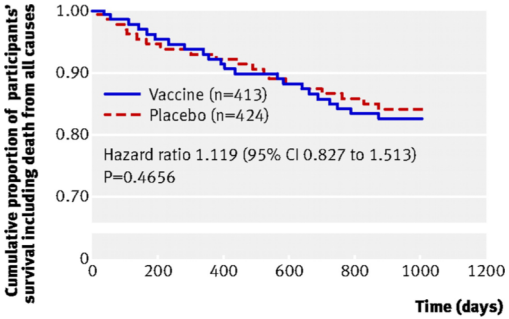
PLoS One. 2017 Jan 6;12(1):e0169368
Expert Rev Vaccines 2021;20(3):243-256

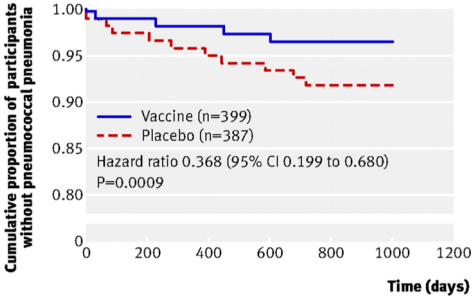
Vaccine effectiveness

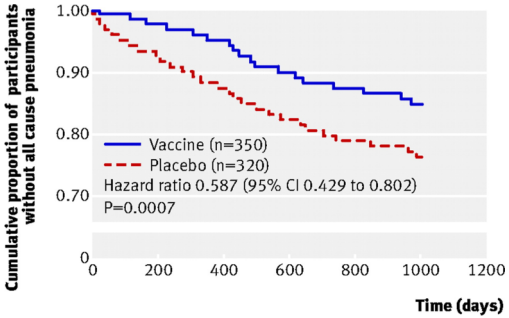
PPV23 NURSING HOME

Table 2 | Incidence and reduction of primary end points in Japanese nursing home residents assigned to 23-valent pneumococcal polysaccharide vaccine or placebo

End point	Incidence (per 1000 person years)		% reduction in incidence (95% CI)	P value
	Vaccine group (n=502)	Placebo group (n=504)		
Pneumococcal pneumonia	12	32	63.8 (32.1 to 80.7)	0.0015
Non-pneumococcal pneumonia	43	59	29.4 (−4.3 to 52.3)	0.0805
All cause pneumonia	55	91	44.8 (22.4 to 60.8)	0.0006







BMJ 2010 Mar 8;340:c1004

Vaccine effectiveness

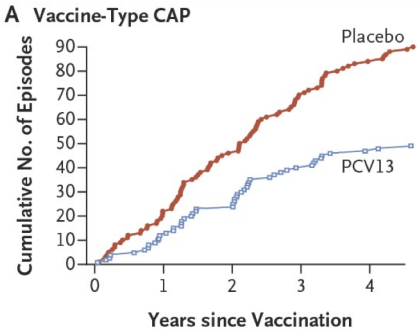
PCV13

CAPITA Study

42,237 PCV13 vs 42,255 placebo (adults > 65 y)

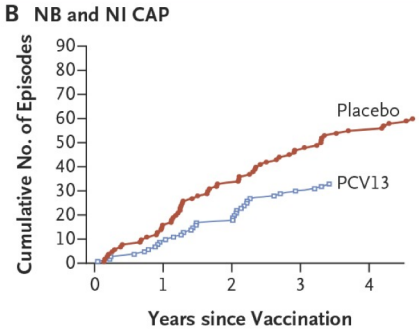
VE 45.6%

(95% CI 21.8%-62.5%)



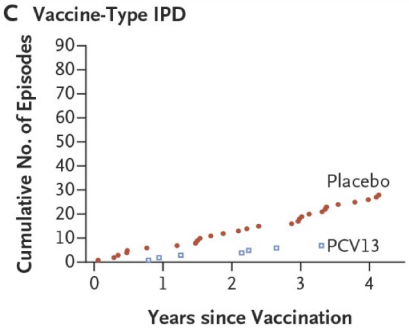
VE 45%

(95% CI 14.2%-65.3%)



VE 75%

(95% CI 41.4%-90.8%)



Post-licensure studies	VE 38-70%	VE 47-59%

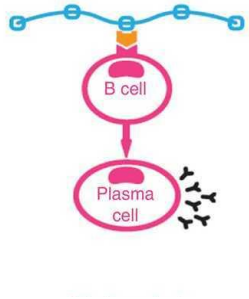
* The efficacy of PCV13 persisted for at least **4 years**

* PCV13 **do not prevent** CAP from **any** cause

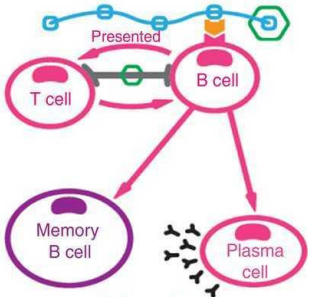
NEJM 2015;372:1114-25 I Vaccine 2019;37(38):5777-5787 I Hum Vaccin Immunother 2017;13(9):2065-2071

Immunological response

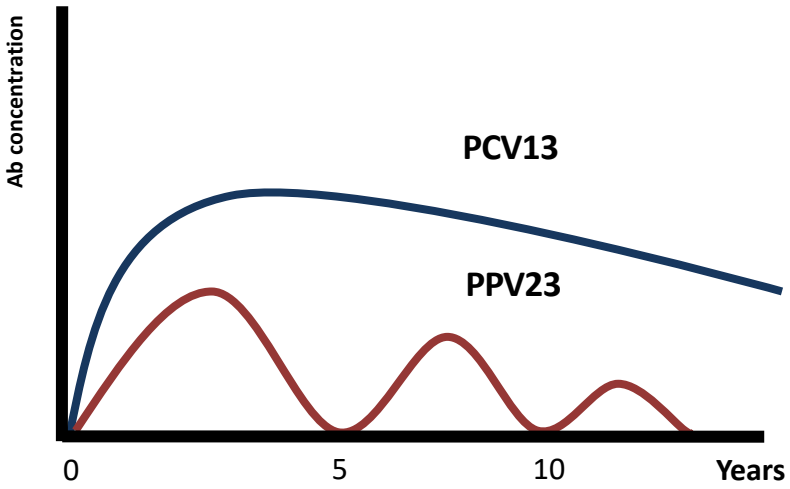
Polysaccharide vaccine



Conjugate vaccine



Contain polysaccharide antigens	Contain polysaccharide antigens covalently linked to carrier protein
T-cell-independent immunoresponse	T-cell-dependent immunoresponse
Stimulate B cells to produce antibodies	Stimulate T cells to help B cells produce antibodies a generate immune memory Provide improved immunological responses Prevent nasopharyngeal carriage



J Chron Obstruct Pulmon Dis 2017;12:3457-3468

CDC ACIP

CENTERS FOR DISEASE CONTROL AND PREVENTION

ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES

Sequential vaccination

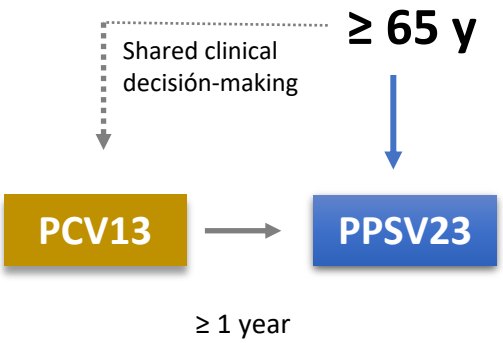
PPSV23 All adults ≥ 65 y

PCV13 Adults ≥ 19 y +

- Immunocompromising condition
- Cerebrospinal fluid leak
- Cochlear implant

All adults ≥ 65 y

- Shared clinical decisión-making



MMWR 2019;68(46);1069–1075

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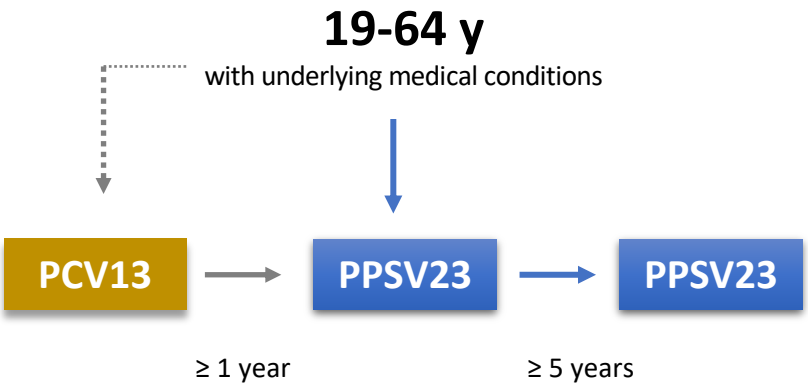

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- Immunocompromising condition
- Cerebrospinal fluid leak
- Cochlear implant

All adults ≥ 65 y

- Shared clinical decisión-making

Immunocompromised
CSF leak
Cochlear implant

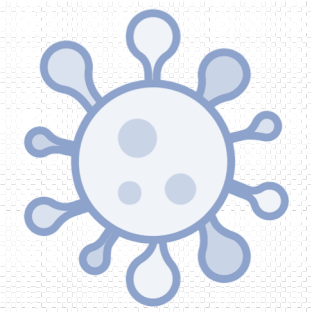
↓

PCV13 → **PPSV23** → **PPSV23**

≥ 8 weeks ≥ 5 years

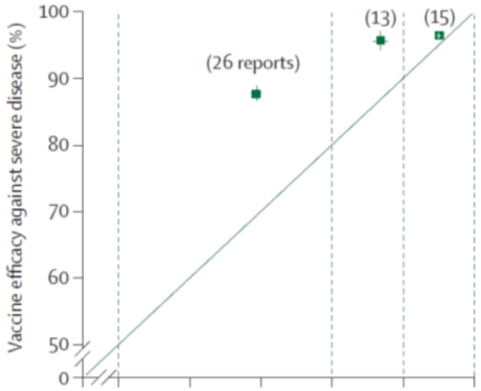
MMWR 2019;68(46);1069–1075

SARS-CoV-2 vaccine

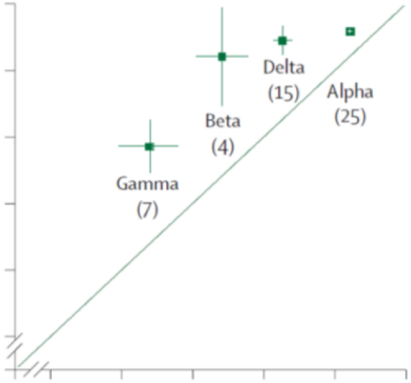


Vaccine effectiveness

VE against severe disease



VE against viral variants



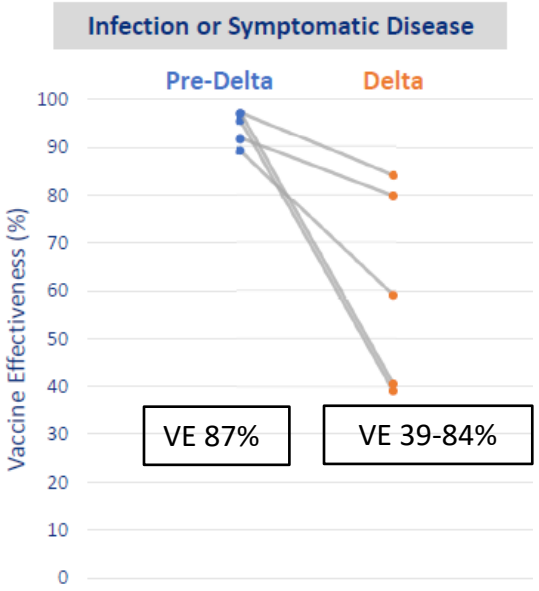
OPEN QUESTIONS

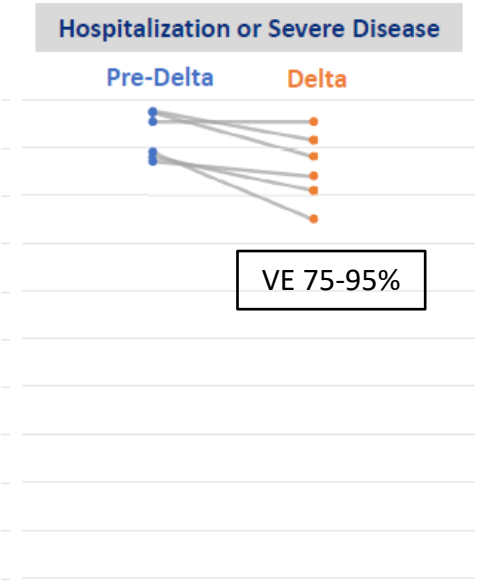
- Is vaccine effectiveness waning over the time?
- Is VE reduced for the Delta variant?
- Does the VE vary in certain populations?

Lancet 2021 Sep 14:S0140-6736(21)02046-8

Viral variants

Vaccine effectiveness in the pre-Delta and Delta periods

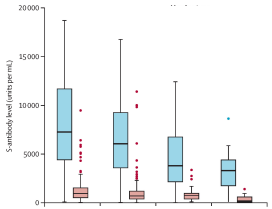




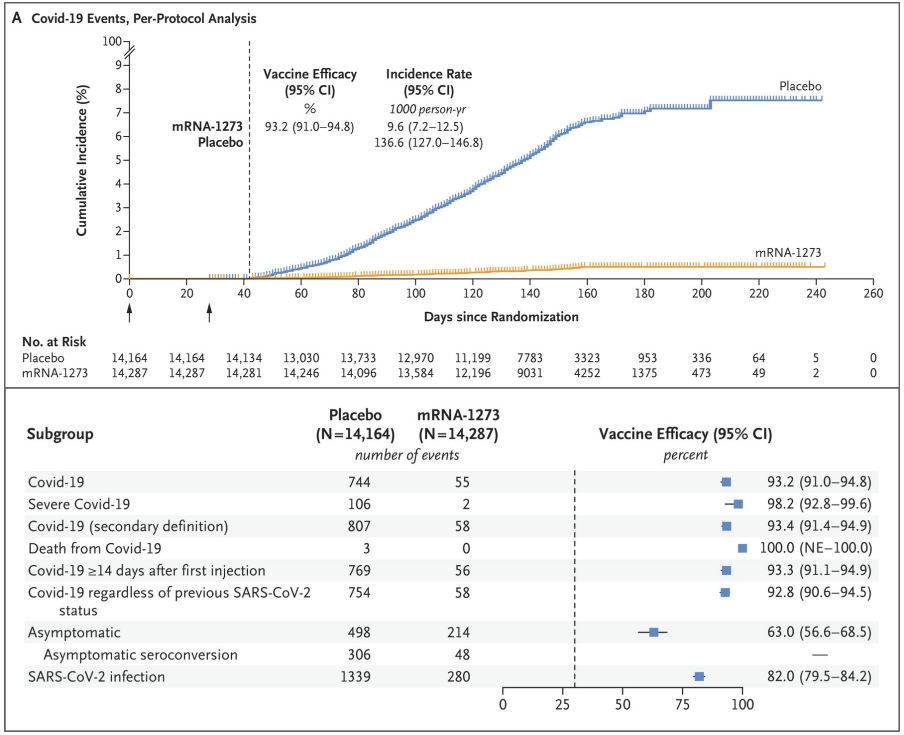
Duration of immunity

SARS-CoV-2
Vaccine effectiveness

Immunogenicity



Viral variants

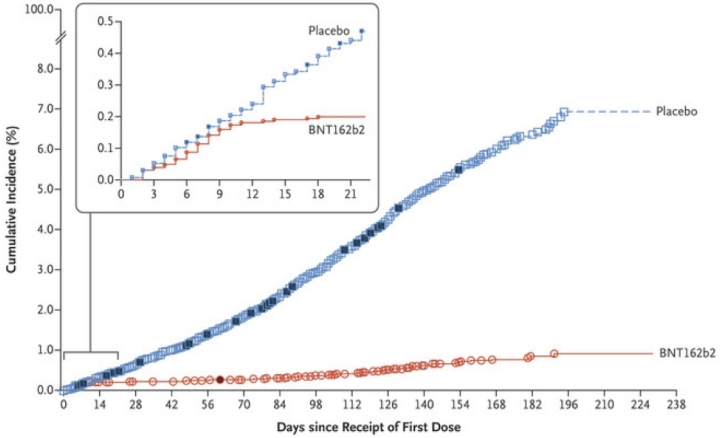


NEJM 2021 Sep 22. doi: 10.1056/NEJMoa2113017

Duration of immunity

Among the participants with or without evidence of previous infection, cases of Covid-19 were observed in 46 vaccine recipients and in 110 placebo recipients from receipt of the first dose up to receipt of the second dose, corresponding to a vaccine efficacy of 58.4% (95% CI, 40.8 to 71.2) (Figure 2). During the interval from the approximate start of observed protection at 11 days after receipt of the first dose up to receipt of the second dose, vaccine efficacy increased to 91.7% (95% CI, 79.6 to 97.4). From its peak after the second dose, observed vaccine efficacy declined. From 7 days to less than 2 months after the second dose, vaccine efficacy was 96.2% (95% CI, 93.3 to 98.1); from 2 months to less than 4 months after the second dose, vaccine efficacy was 90.1% (95% CI, 86.6 to 92.9); and from 4 months after the second dose to the data cutoff date, vaccine efficacy was 83.7% (95% CI, 74.7 to 89.9).

Average decline of approximately
6% every 2 months



Efficacy End Point	BNT162b2 (N=23,040)			Placebo (N=23,037)			Vaccine Efficacy
	No. of cases	Surveillance time	No. at risk	No. of cases	Surveillance time	No. at risk	
		1000 person-yr			*1000 person-yr*		*% (95% CI)*
Overall: first occurrence of Covid-19 after receipt of first dose	131	8.412	22,505	1034	8.124	22,434	87.8 (85.3 to 89.9)
After receipt of first dose up to receipt of second dose	46	1.339	22,505	110	1.331	22,434	58.4 (40.8 to 71.2)
<11 Days after receipt of first dose	41	0.677	22,505	50	0.675	22,434	18.2 (−26.1 to 47.3)
≥11 Days after receipt of first dose up to receipt of second dose	5	0.662	22,399	60	0.656	22,369	91.7 (79.6 to 97.4)
After receipt of second dose to <7 days after	3	0.424	22,163	35	0.422	22,057	91.5 (72.9 to 98.3)
≥7 Days after receipt of second dose	82	6.649	22,132	889	6.371	22,001	91.2 (88.9 to 93.0)
≥7 Days after receipt of second dose to <2 mo after	12	2.923	22,132	312	2.884	22,001	96.2 (93.3 to 98.1)
≥2 Mo after receipt of second dose to <4 mo after	46	2.696	20,814	449	2.593	20,344	90.1 (86.6 to 92.9)
≥4 Mo after receipt of second dose	24	1.030	12,670	128	0.895	11,802	83.7 (74.7 to 89.9)

NEJM 2021 September 15
DOI: 10.1056/NEJMoa2110345

Duration of immunity

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Waning Immune Humoral Response to BNT162b2 Covid-19 Vaccine over 6 Months

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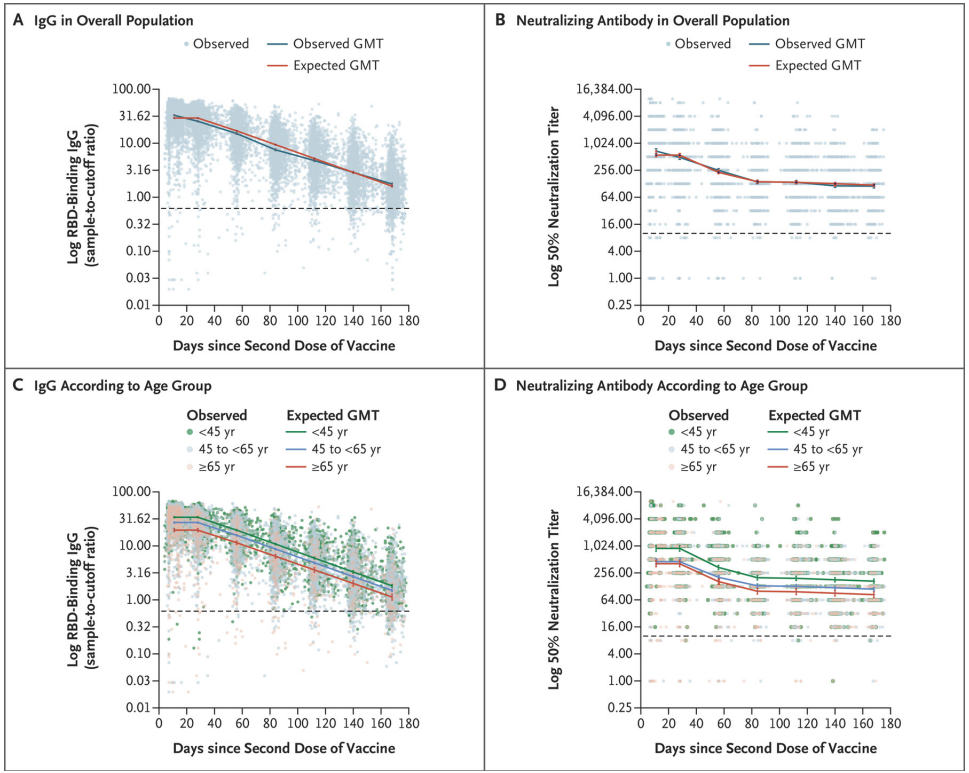
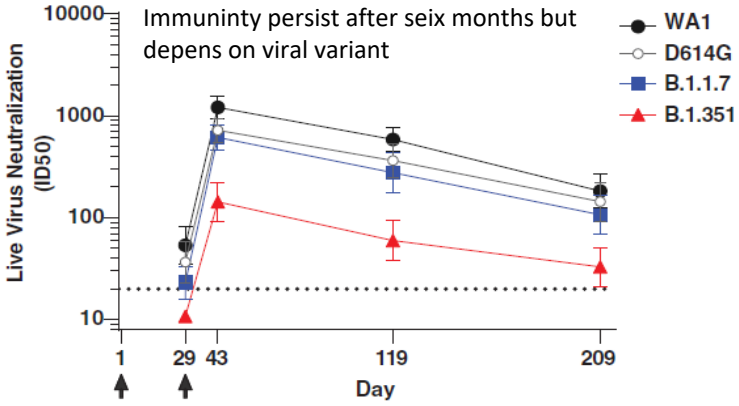
3808 trabajadores sanitarios

Mayor declinar en:
- -Edad avanzada
- -Inmunodepresión
- -Obesidad



NEJM 2021; Oct 6. doi: 10.1056/NEJMoa2114583

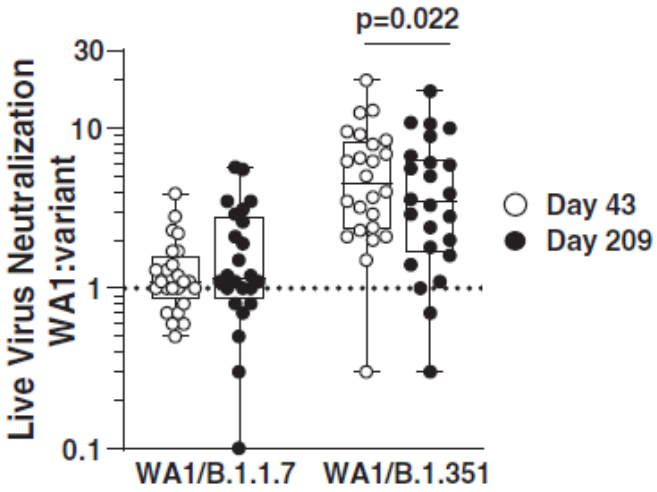
Duration of immunity



Assay	Variant	% of sera with detectable antibodies			
		Day 29	Day 43	Day 119	Day 209
Pseudovirus Neutralization	WA1	25%	100%	100%	88%
	D614G	83%	100%	100%	100%
	B.1.1.7	33%	100%	100%	96%
	B.1.351	8%	100%	71%	54%
	P.1	*not tested*	100%	*not tested*	85%
	B.1.429	*not tested*	100%	*not tested*	100%
	B.1.526	*not tested*	100%	*not tested*	88%
	B.1.617.2	*not tested*	100%	*not tested*	96%

Antibodies decay faster

(new variants)

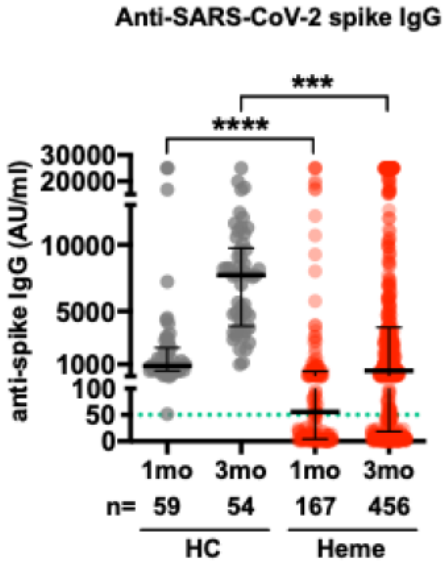


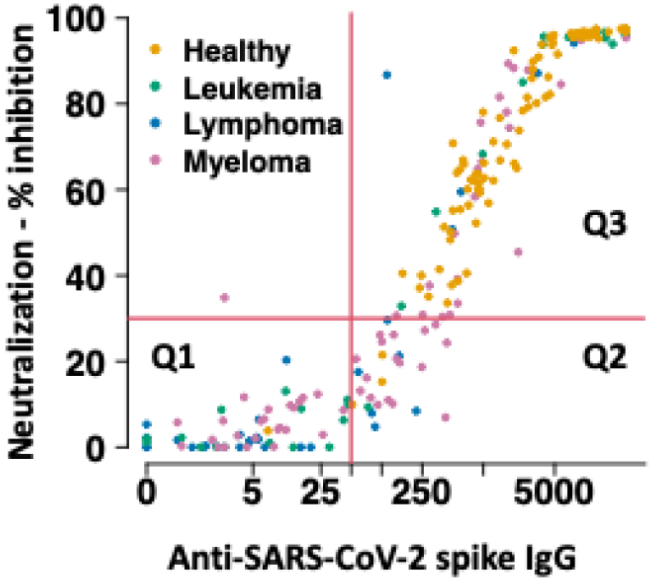
Science 2021;373:1372-7

Special situations

Hematologic malignancy

Healthy vs hematologic malignancy



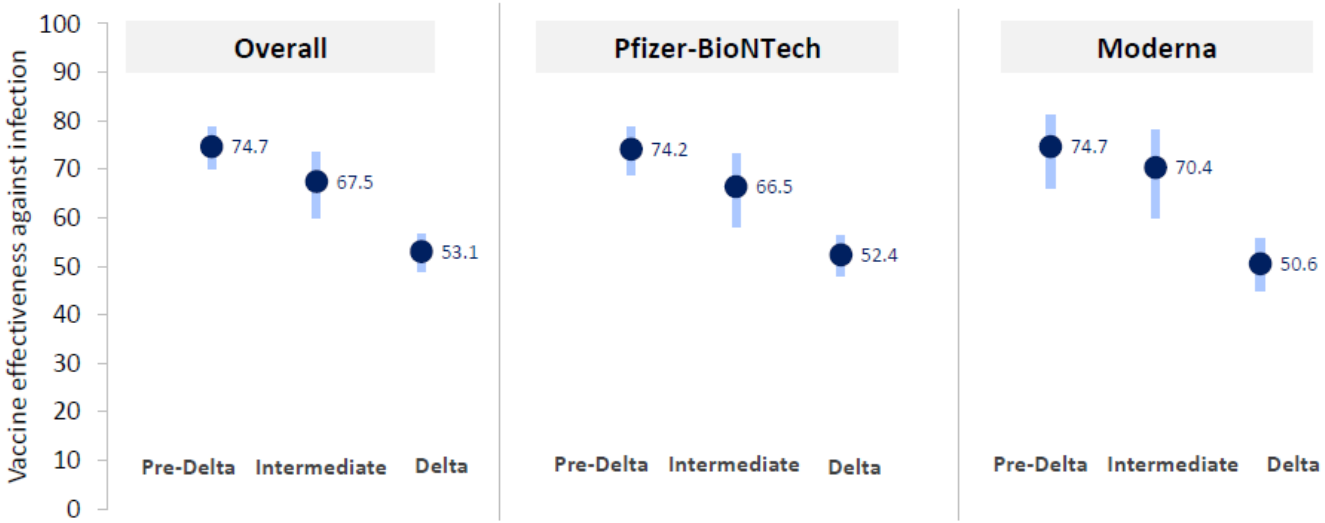


Blood Cancer Discov September 13
2021 DOI: 10.1158/2643-3230.BCD-21-0139

Special situations

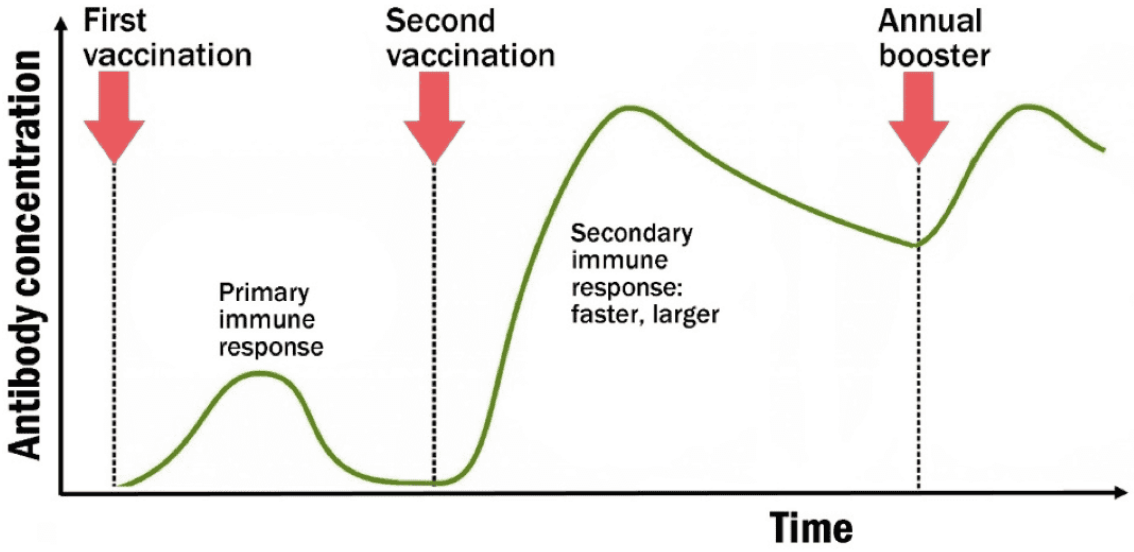
Long-term care facility residents

VE against infection among long-term care facility residents differed significantly from pre-Delta period to Delta period



MMWR 2021;70

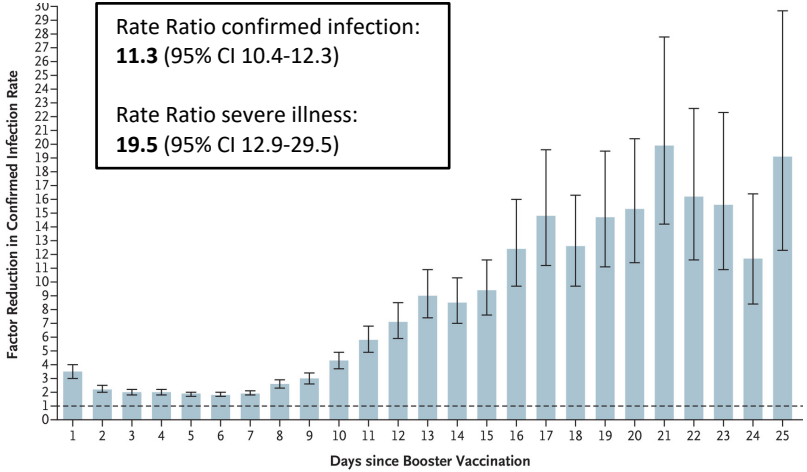
Vaccine booster



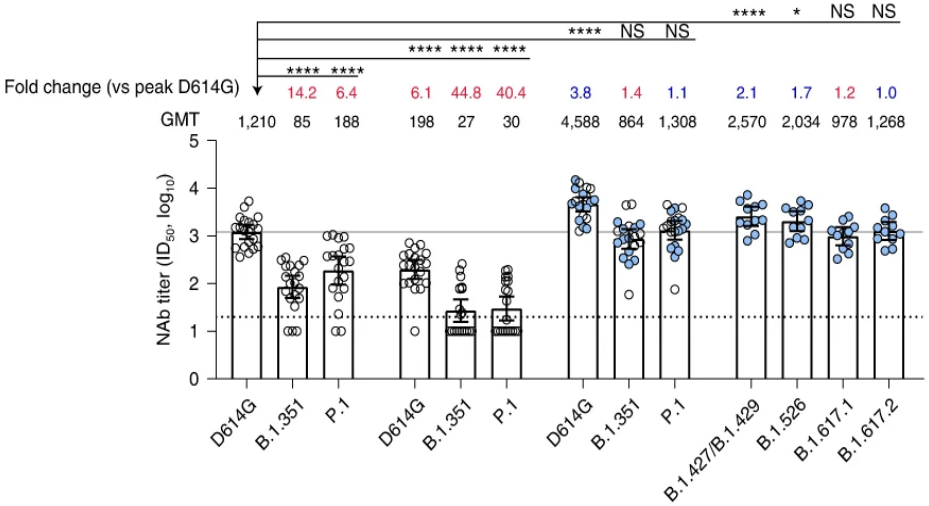
Vaccine booster

BNT162b2 BOOSTER

Reduction in rate of confirmed infection



mRNA-1273 BOOSTER



NEJM 2021 Sep 15. doi: 10.1056/NEJMoa2114255
Nat Med. 2021 Sep 15. doi: 10.1038/s41591-021-01527-y

U.S. FOOD & DRUG ADMINISTRATION

FDA NEWS RELEASE

FDA Authorizes Booster Dose of Pfizer-BioNTech COVID-19 Vaccine for Certain Populations

September 22, 2021

- Individuals **65 years of age and older**
- Individuals **18 through 64 years** of age at **high risk** of severe COVID-19
- Individuals **18 through 64 years** of age whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk os serious complications
- **Special populations**: health care workers, teachers and day care staff, grocery workers and those in homeless shelters or prisions

4 de octubre 2021

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Comirnaty and Spikevax: EMA recommendations on extra doses and boosters

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News 04/10/2021

EMA's human medicines committee (CHMP) has concluded that an extra dose of the COVID-19 vaccines Comirnaty (BioNTech/Pfizer) and Spikevax (Moderna) may be given to people with severely weakened immune systems, at least 28 days after their second dose.

The recommendation comes after studies showed that an extra dose of these vaccines increased the ability to produce antibodies against the virus that causes COVID-19 in organ transplant patients with weakened immune systems.[1] [2]

Although there is no direct evidence that the ability to produce antibodies in these patients protected against COVID-19, it is expected that the extra dose would increase protection at least in some patients. EMA will continue monitoring any data that emerges on its effectiveness.

The product information of both vaccines will be updated to include this recommendation.

Booster doses

It is important to distinguish between the extra dose for people with weakened immune systems and booster doses for people with normal immune systems.

For the latter, the CHMP has evaluated data for Comirnaty showing a rise in antibody levels when a booster dose is given approximately 6 months after the second dose in people from 18 to 55 years old. On the basis of this data, the Committee concluded that booster doses may be considered at least 6 months after the second dose for people aged 18 years and older.

At national level, public health bodies may issue official recommendations on the use of booster doses, taking into account emerging effectiveness data and the limited safety data. The risk of inflammatory heart conditions or other very rare side effects after a booster is not known and is being carefully monitored. As for all medicines, EMA will continue to look at all data on the safety and effectiveness of the vaccine.

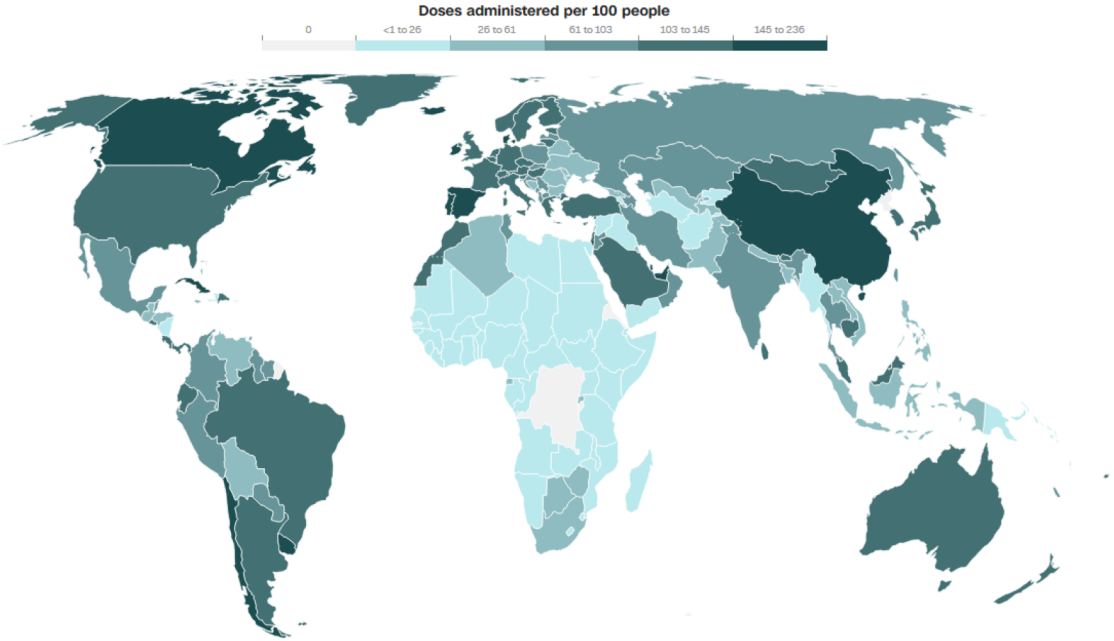
More information about the booster recommendations for Comirnaty will be available in the updated product information.

The Committee is currently evaluating data to support a booster dose for Spikevax. EMA will communicate the outcome when the evaluation is complete.

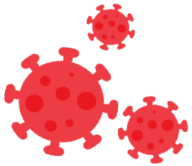
National immunisation campaigns

The implementation of vaccination campaigns in the EU remains the prerogative of the national immunisation technical advisory groups (NITAGs) guiding the vaccination campaigns in each EU Member State. These bodies are best placed to take into account the local conditions, including the spread of the virus (especially any variants of concern), the availability of vaccines and the capacities of national health systems.

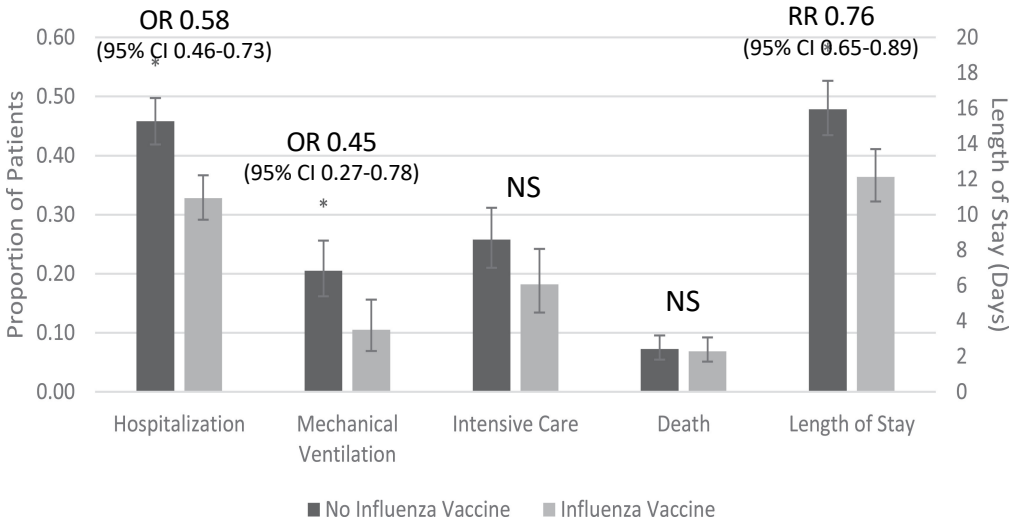
EMA will continue working closely with national authorities and the European Centre for Disease Prevention and Control (ECDC) to evaluate available data and provide recommendations to protect the public during the ongoing pandemic.



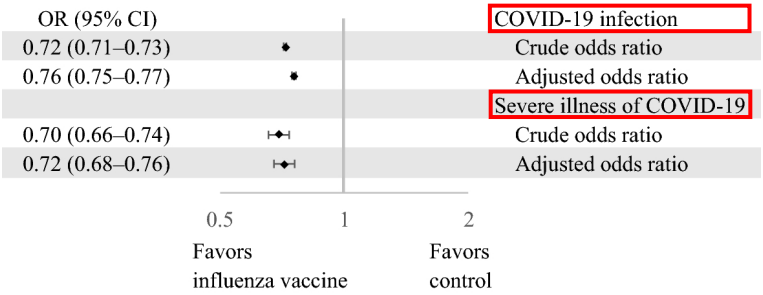
Last updated: October 5, 2021 at 4:49 p.m. ET
Source: Our World in Data



Effect of influenza vaccination status on clinical outcomes

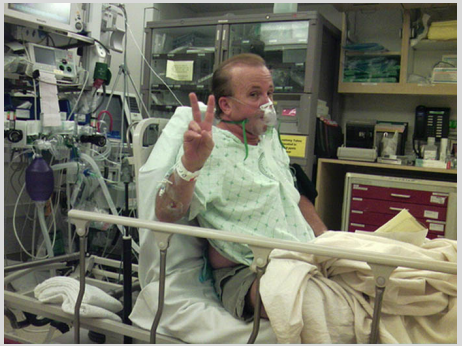


Influenza vaccination vs no influenza vaccination



Sci Rep. 2021 May 26;11(1):11025
Am J Infect Control 2021 Jun;49(6):694-700

But, what about Mr. García?



Does influenza vaccination fail to protect him?

MAYBE. Probably influenza vaccine could help to reduce disease severity. ¿Need for new formulations?

Does pneumoccocal vaccination fail to protect him?

YES, Because he should have received a dose of PCV13 and then PPVS23 eight weeks later

Does Mr. García will need an additional dose of SARS-CoV-2 vaccine?

YES. Current evidence would recommend that the patient receive a third dose from six months after the second injection.

Thank you very much!

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