

¿Debemos cambiar la estrategia de vacunación en pediatría?

Jesús Ruiz Contreras



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OURENSE, 14 Y 15 DE ABRIL DE 2023



Razones para cambiar la estrategia (no vacunación sistemática a partir de los 5 años)

- Enfermedad menos grave en la era ómicron ¿o en los inmunes por infección o vacunación?
- El virus evolucionará hacia variantes menos virulentas
- El PIMS es menos frecuente en la era ómicron
- El long COVID en adultos y niños es menos frecuente en la era ómicron
- Pocos niños mueren por COVID
- Las vacunas frente a COVID tienen efectos secundarios importantes





5 Benefits COVID-19 Vaccination



1 Boost the immunity by creating an antibody



3 Reduce the risk of death from COVID-19



2 Prevent & Reduce the risk of severe illness



4 Reduce the risk of spreading



5 Reconnect with society

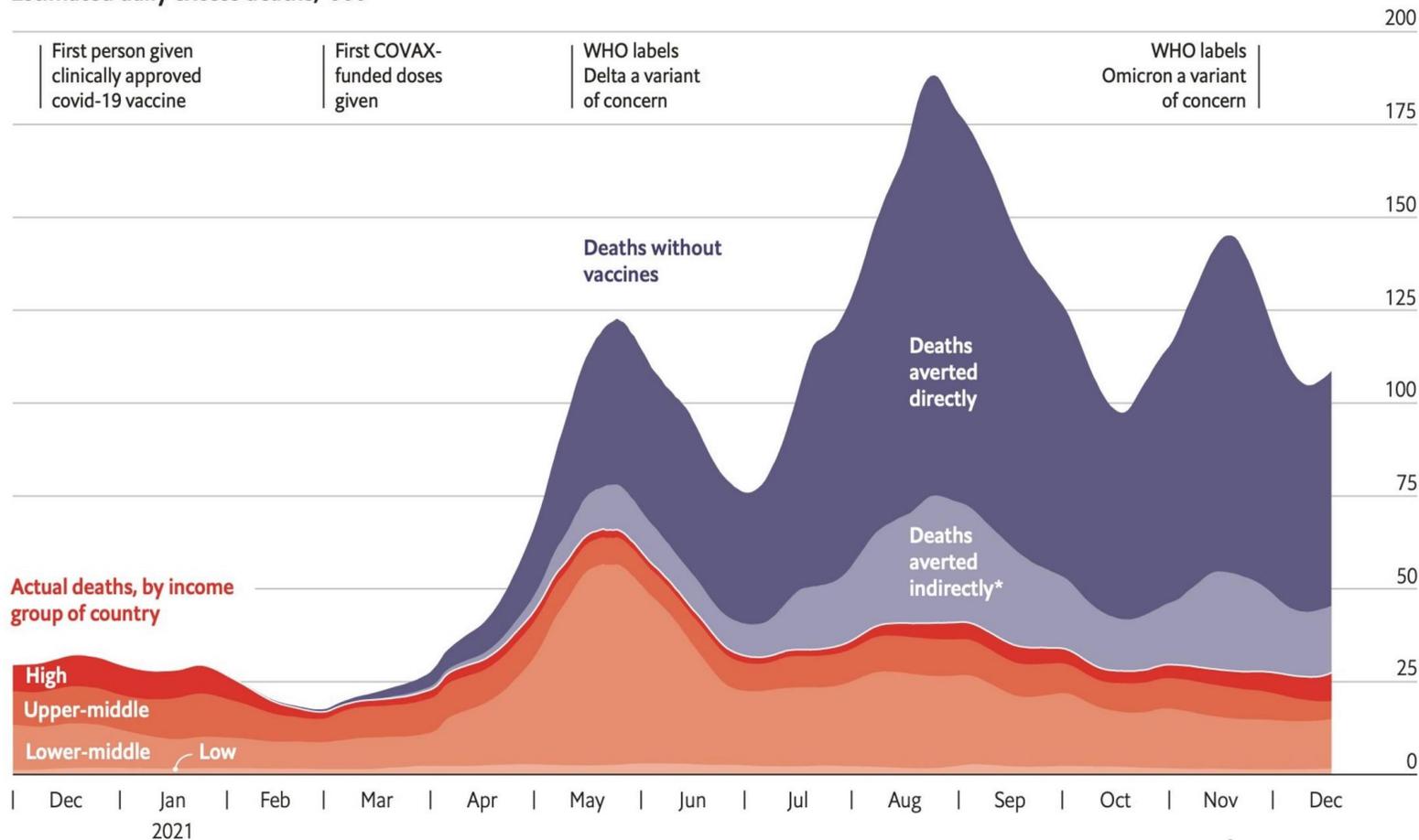
<https://www.vejthani.com/2021/05/5-benefits-of-covid-19-vaccination/>



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> 20 MILLION LIVES SAVED BY VACCINES in 1st YEAR

Estimated daily excess deaths, '000



Watson O, Lancet Inf Dis, Sept 2022



Interpretaciones que enturbian la realidad



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SARS-CoV-2, new and familiar.

3/29/2023

[0 Comments](#)

SARS-CoV-2, the coronavirus that is the cause of COVID-19, is new but also familiar. What we have seen in the past 3 years is virology and immunology in real time unfolding.

SARS-CoV-2 has behaved much as we expected it to behave. The route of infection, the cells it infects, its transmission, replication, in large part its evolutionary path, its selection criteria, the epidemiology, the way the immune system detects it and responds, the antibodies that bind it and wane, the T cell response that stays, the reinfections, how to detect it, and how to target it with a vaccine, did not hold much mystery. We knew much, expected most, but certainly not everything was and is understood!

Let's start with some statements to avoid confusion:

1. Pathogens, such as viruses, parasites, fungi or bacteria, can cause disease and kill people
2. Getting infected with a pathogen is never "good"
3. Infections can result in damage, including to organs and immunity
4. There are many poorly understood ways infections can cause problems
5. The result of an infection is person-dependent and can range from totally asymptomatic to severe illness and death
6. Endemic does not mean mild or "nothing to worry about"
7. Seasonal also does not mean mild, not does it exclude transmission at other times.



Professor [Marc Veldhoen](#) is an immunology expert and leads the [MVeldhoen lab](#) at the Instituto de Medicina Molecular (iMM) in Lisbon, Portugal.

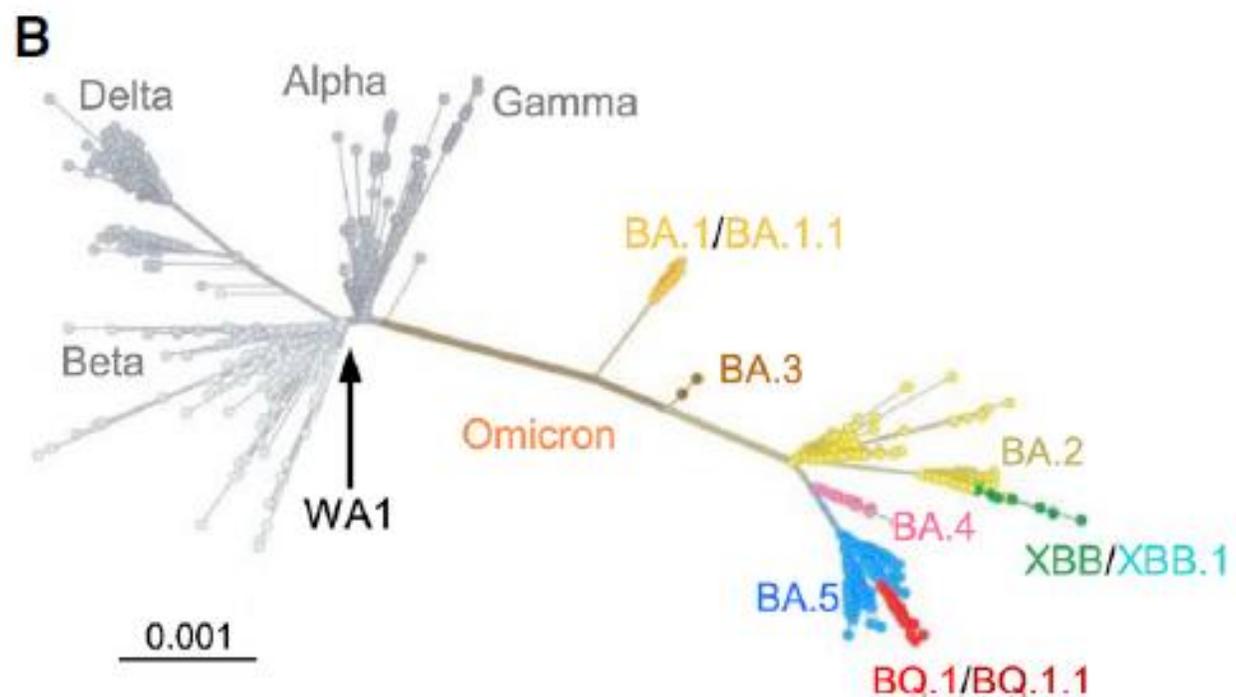
Twitter:
[@marc_veld](#)

[Google Scholar](#) profile

[Contact Prof. Marc Veldhoen](#)



Árbol genético de las variantes y subvariantes de SARS-CoV-2



Wang Q, et al. Cell 2022;

World view



By Aris
Katzourakis

COVID-19: endemic doesn't mean harmless

In other words, a disease can be endemic and both widespread and deadly. Malaria killed more than 600,000 people in 2020. Ten million fell ill with tuberculosis that same year and 1.5 million died. Endemic variants. Third, we must use – globally – the formidable weapons available: effective vaccines, antiviral medications, diagnostic tests and a better understanding of how to stop an airborne virus through mask wearing, distancing, and air ventilation and filtration. Fourth, we must invest in vaccines that protect against a broader range of variants.

There is a widespread, rosy misconception that viruses evolve over time to become more benign. This is not the case: there is no predestined evolutionary outcome for a virus to become more benign, especially ones, such as SARS-CoV-2, in which most transmission happens before the virus causes severe disease. Consider that Alpha and Delta are more virulent than the strain first found in Wuhan, China. The second wave of the 1918 influenza pandemic was far more deadly than the first.

Nature 2022; 601: 485



High Death Rate in Hong Kong Shows Importance of Vaccinating the Elderly

Covid has surged in a number of Asian countries that had once held the virus at bay. Vaccination levels have largely determined how deadly those waves would be.



2019冠狀病毒病死亡個案報告初步數據分析

(2021年12月31日至2023年1月29日00:00)

Provisional Data Analysis on COVID-19 Reported Death Cases

(from 31 Dec 2021 up till 29 Jan 2023 00:00)

資料來源：衛生署衛生防護中心 Source: Centre for Health Protection of the Department of Health

特別感謝醫院管理局提供進一步資料以協助分析 Special thanks to the Hospital Authority for provision of further information to facilitate analysis



版本日期:2023年2月1日
Version date: 1 Feb 2023

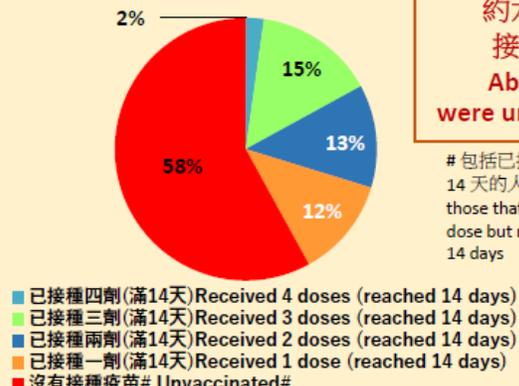
新冠疫苗能保護個人，預防2019冠狀病毒病的嚴重疾病和併發症。在本港，接種兩或三劑新冠疫苗個案的死亡率遠低於未接種的個案。就此，政府強烈建議合資格人士（尤其是12歲以下及60歲以上人士）應盡快接種疫苗。

COVID-19 vaccines can protect individuals from severe illnesses and complications from COVID-19. Locally, cases vaccinated with 2 or 3 doses have much lower fatality rate than the unvaccinated. With that, the Government strongly recommended eligible persons (especially those aged under 12 as well as those aged 60 and above) to get vaccinated as soon as possible.

第5波死者個案 Deceased in the 5th Wave®

累計數目 Cumulative number	13,115
年齡範圍 Age range	0 - 112
年齡中位數 Median	86
男性與女性比例 Male to female ratio	1.37

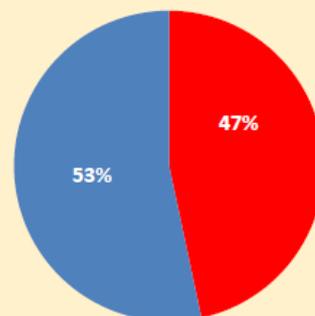
疫苗接種史* Vaccination History



約六成沒有
接種疫苗#
About 60%
were unvaccinated#

包括已接種一劑但未滿14天的人士 Including those that have received 1 dose but not yet reached 14 days

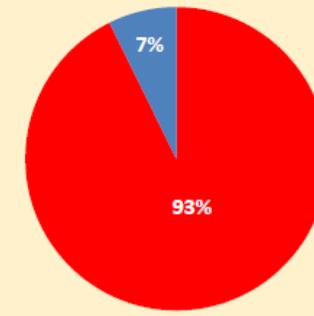
居住院舍情況* Residential Care Home (RCH) Status



■ 院舍人士 RCH Residents
■ 非院舍人士 Non-RCH Residents

超過四成為居於院舍人士
More than 40% were
RCH residents

長期病患歷史情況* History of Known Chronic Diseases

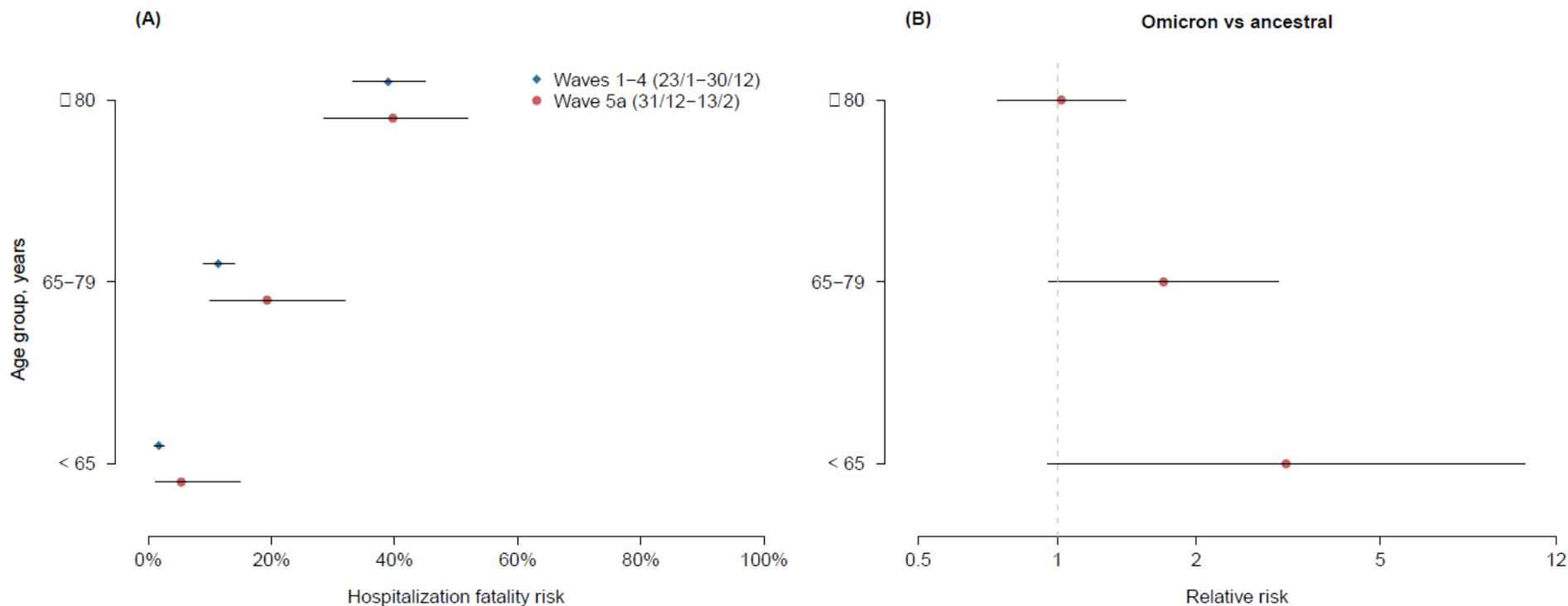


■ 已知有長期病患 With known chronic diseases
■ 沒有長期病患歷史 No history of chronic diseases

超過九成有已知長期病患情況
More than 90% were
with known chronic diseases

@ 不包括輸入個案 Excluding imported cases * 不包括待個案 Excluding pending cases

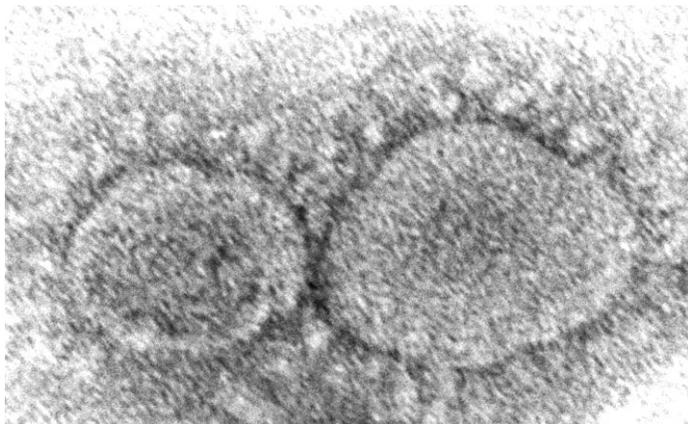
Letalidad intrínseca de ómicron vs ancestral en pacientes ingresados en Hong Kong no vacunados



Wong JY, et al

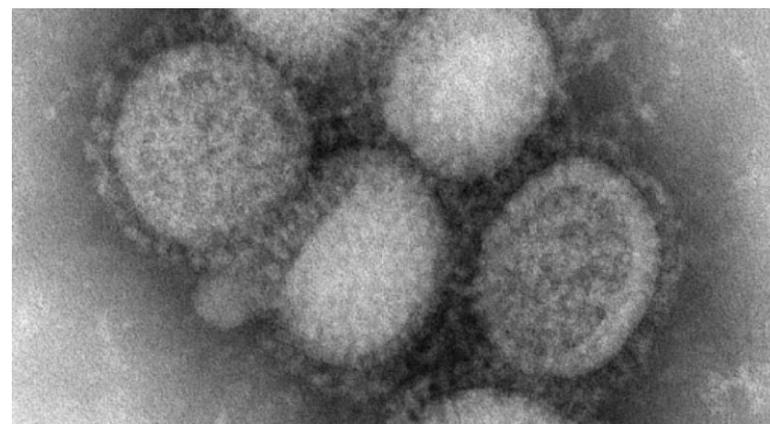
medRxiv preprint doi: <https://doi.org/10.1101/2023.02.13.23285848>

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SARS-CoV-2

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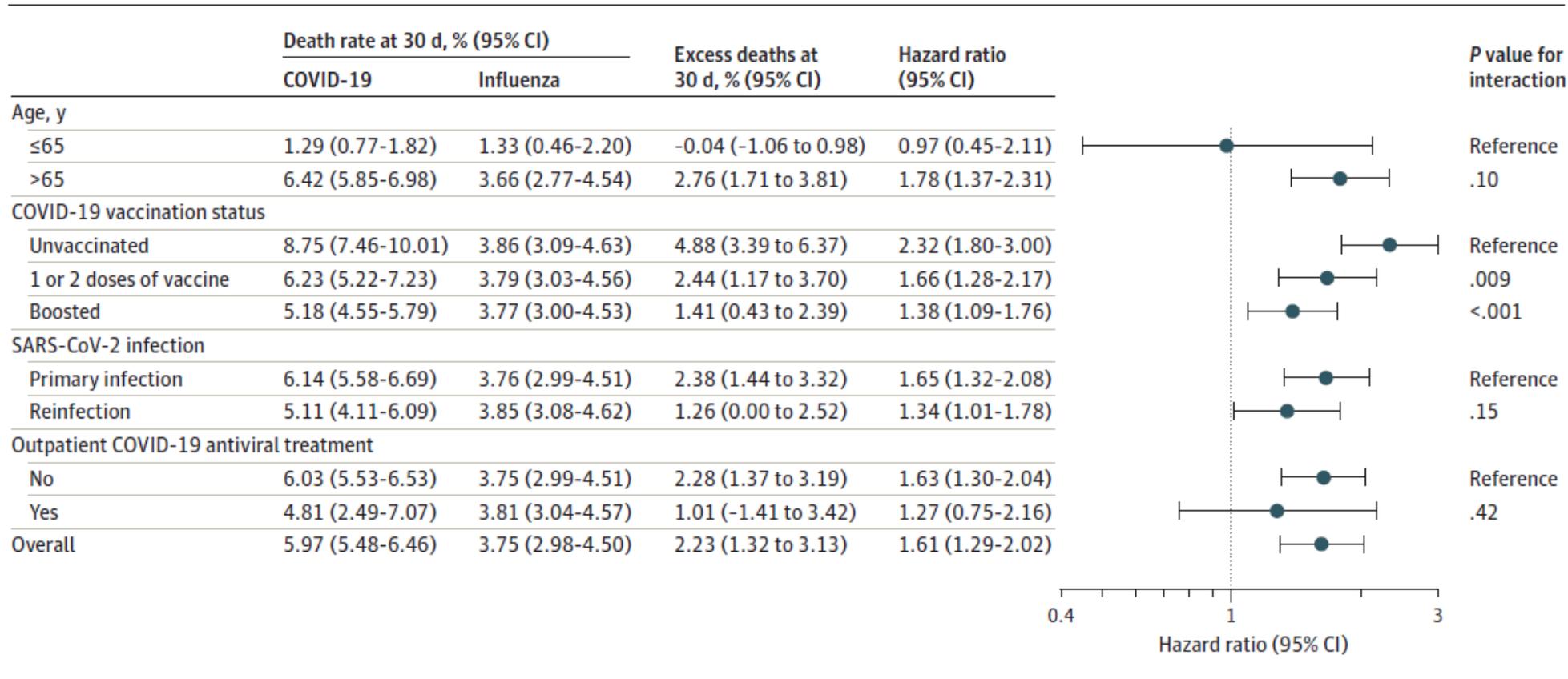


Gripe



Letalidad de la COVID 19 comparada con la gripe

Figure. Hazard Ratio, Death Rates, and Percentage of Excess Deaths in COVID-19 Compared With Seasonal Influenza



Hospital Outcomes of Community-Acquired SARS-CoV-2 Omicron Variant Infection Compared With Influenza Infection in Switzerland

Lea Portmann, BSc; Marlieke E. A. de Kraker, PhD; Georg Fröhlich, MD; Amaury Thiabaud, PhD; Maroussia Roelens, PhD; Peter W. Schreiber, MD; Nicolas Troillet, MD, MSc; Anne Iten, MD; Andreas Widmer, MD, MSc; Stephan Harbarth, MD, MSc; Rami Sommerstein, MD; for the CH-SUR study group

[59-83] years; $P < .001$). Overall, 214 patients with the SARS-CoV-2 Omicron variant (7.0%) died during hospitalization vs 95 patients with influenza (4.4%; $P < .001$). The final adjusted subdistribution hazard ratio (sdHR) for in-hospital death for SARS-CoV-2 Omicron variant vs influenza was 1.54 (95% CI, 1.18-2.01; $P = .002$). Overall, 250 patients with the SARS-CoV-2 Omicron

Portmann L, et JAMA Network Open. 2023;6(2):e2255599. doi:10.1001/jamanetworkopen.2022.55599



Feature



ROUELLE UMALIN/UNA/EVERETT

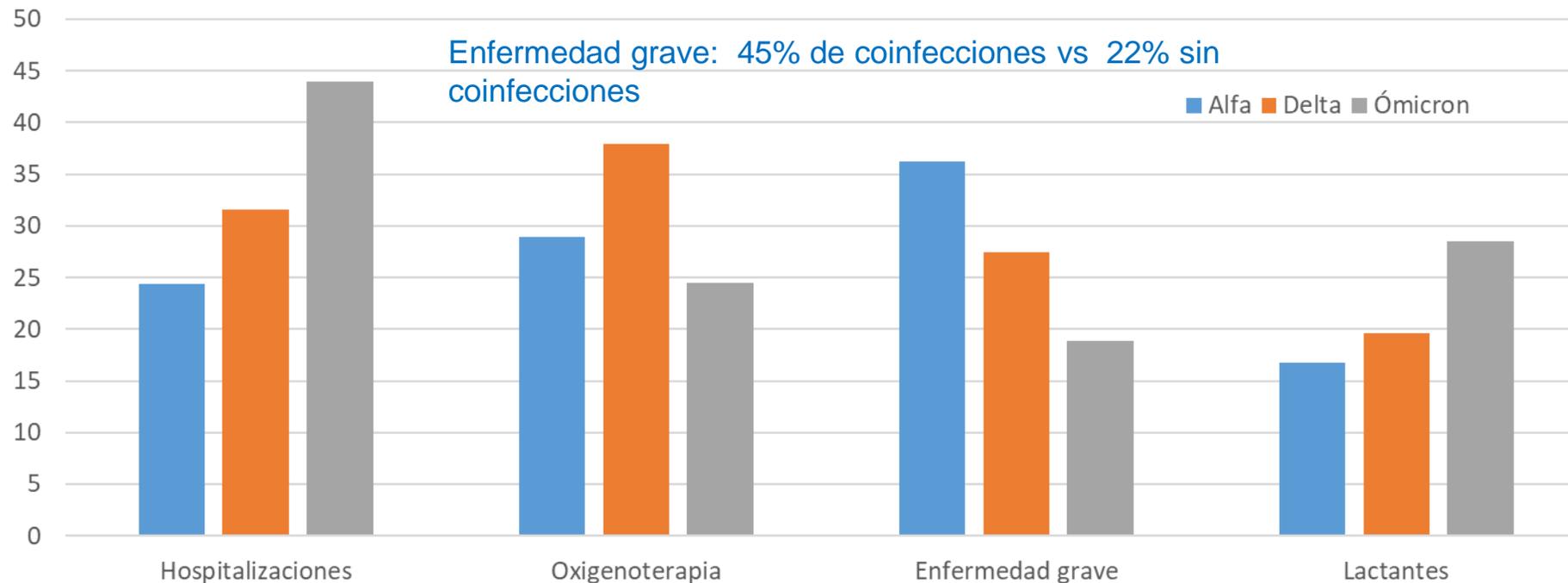
A girl receives a COVID-19 vaccination at a mall in the Philippines in February, on the first day of eligibility for children aged 5-11.

KIDS AND COVID VACCINES: WHAT THE DATA SAY

Mallapaty S, et al. Nature 2022; 610: 647-48

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Gravedad de la COVID en niños en las diferentes ondas epidémicas



Bahl, A et al. Lancet Regional Health Americas 2023; 18: 100 - 405



Grupo de edad	Hospitalizados ¹		UCI ¹		Defunciones ¹	
	Desde el inicio*	Desde el 28/03/2022	Desde el inicio*	Desde el 28/03/2022	Desde el inicio*	Desde el 28/03/2022
<5	8380	3731	353	123	15	2
5-9	1951	652	100	23	12	1
10-19	6348	1346	382	68	34	7

Tabla 4. Número promedio por temporada de casos de gripe confirmada estimados por grupo de edad y nivel de gravedad. Temporadas 2013/14 a 2019/20.

Grupo edad	Sistema de vigilancia	ScVGE	Chosp	CGHCG		
	Atención Primaria	Hospitalizados	Hospitalizados graves	Ingreso en UCI	Defunción	
0-4 años	58.640	4.239	822	249	8	
5-14 años	126.390	2.028	268	90	4	

	Hospitalizaciones anuales	Ingreso en UCIP	Muertes
Gripe	6267	339	12
COVID 19	3336	281	20



COVID-19 Vaccines in Young Children—Reassuring Evidence for Parents

Paul A. Offit, MD

were licensed within the past 30 years.⁹ Every year, prior to the availability of a vaccine, 3 children died of hepatitis A virus,¹⁰ 8 children died of meningococcus,⁹ 16 children died of varicella,¹¹ 17 people of all ages died of rubella,¹² and 20 children died of rotavirus.¹³ Between October 2020 and October 2021, 66 children aged 5 to 11 years died of SARS-CoV-2 infection.⁹ Now, we had a vaccine that would likely prevent those COVID-19 deaths.

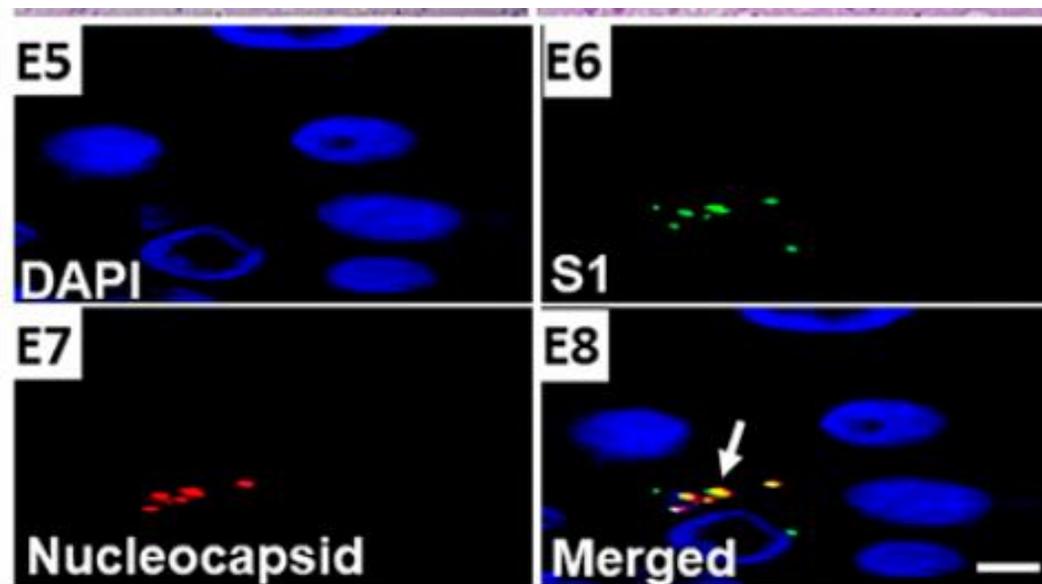
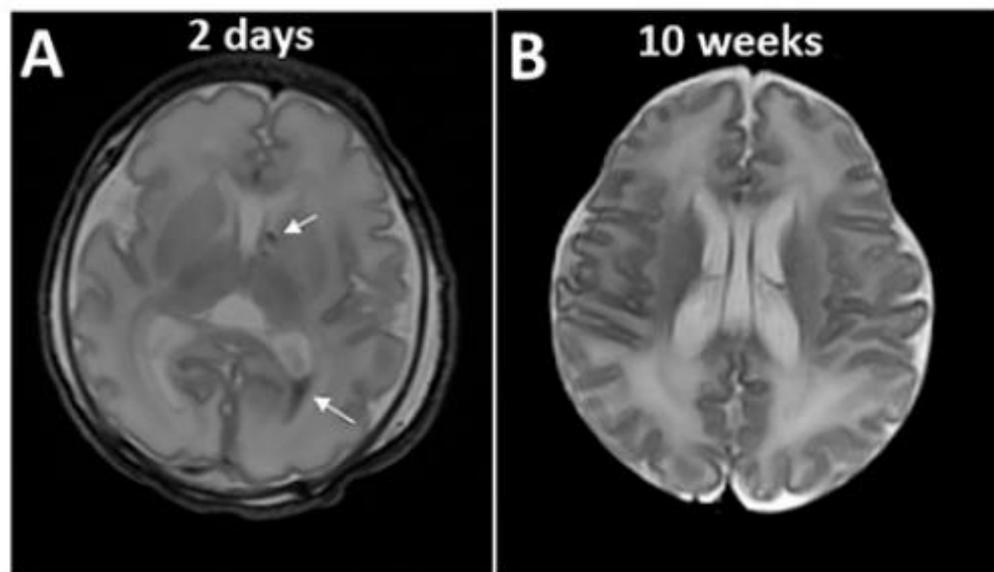


¿Conocemos todo acerca
de la covid en los niños?

Maternal SARS-CoV-2, Placental Changes and Brain Injury in 2 Neonates

Merline Benny, MD,^a Emmalee S. Bandstra, MD,^a Ali G. Saad, MD,^b Roberto Lopez-Alberola, MD,^c Gaurav Saigal, MD,^d Michael J. Paidas, MD,^e Arumugam R. Jayakumar, PhD,^e Shahnaz Duara, MD^a

Case-1 Brain MRI

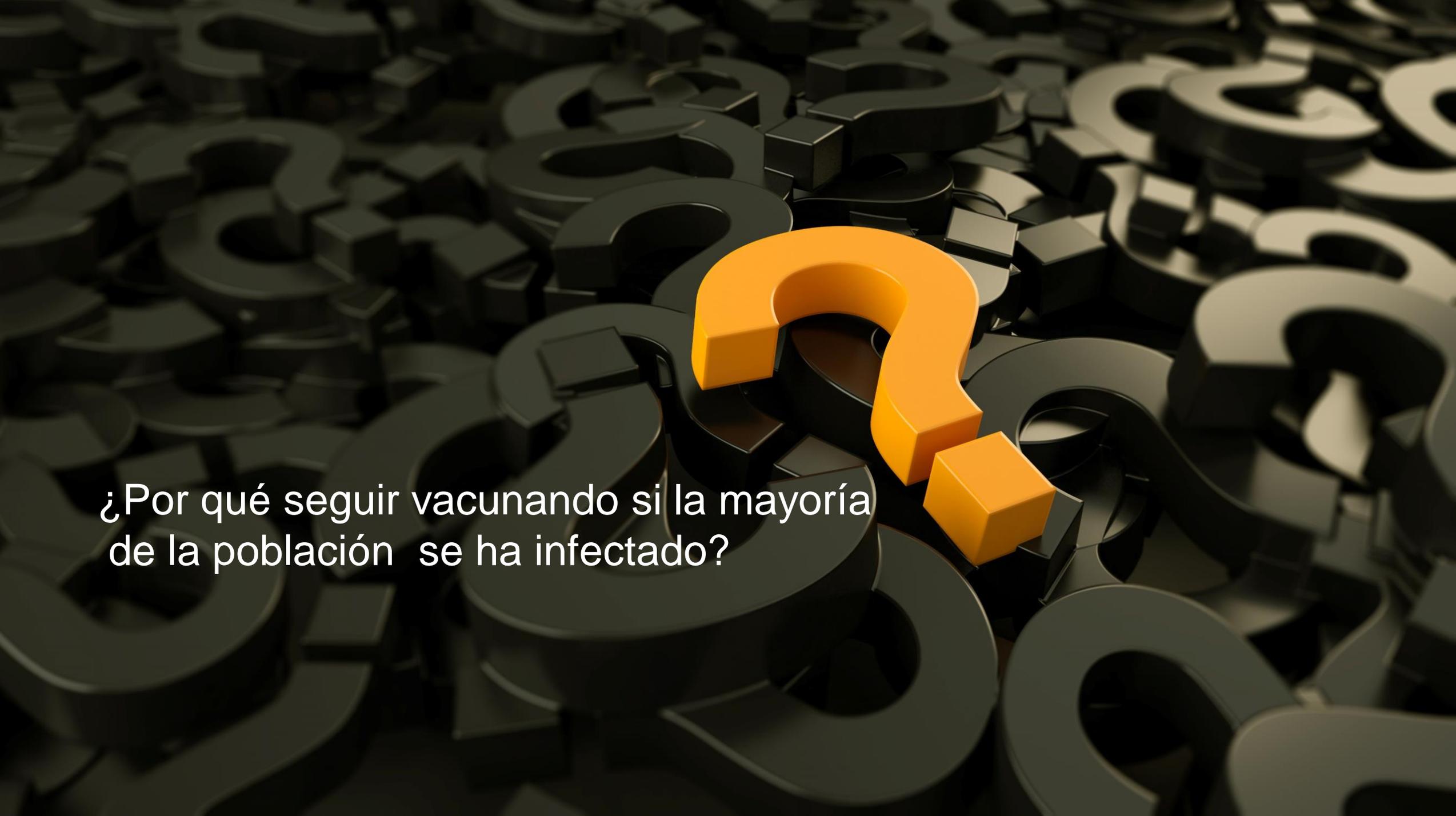


Benny M, et al. Pediatrics 2023



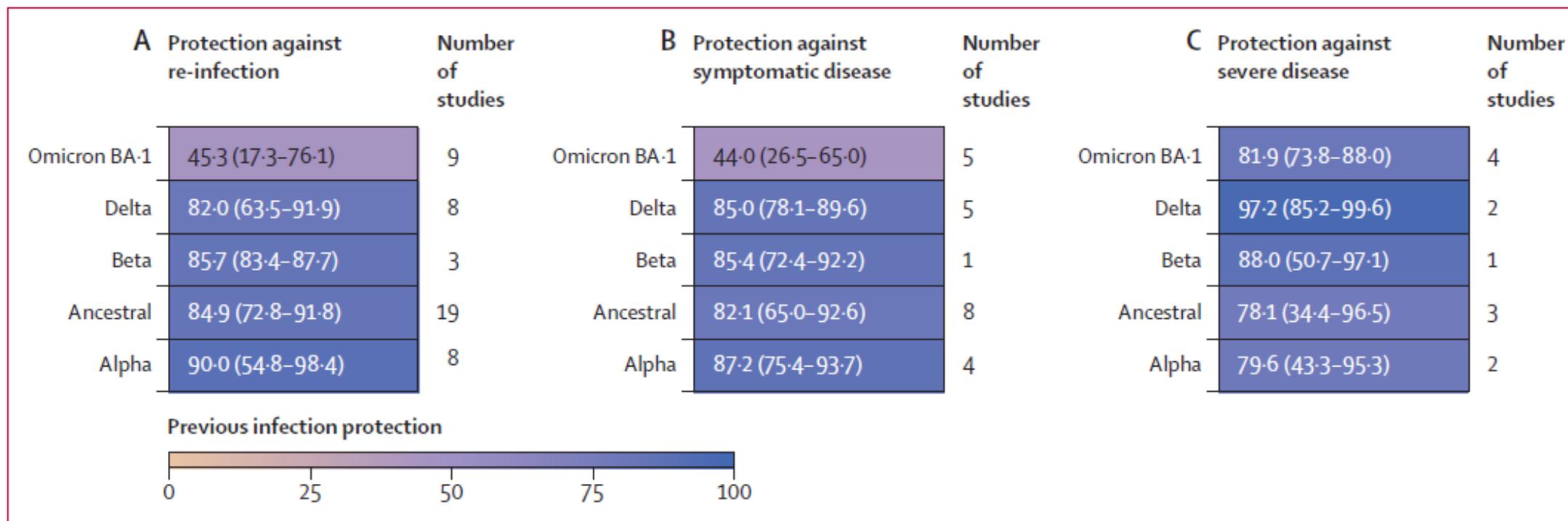
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¿Por qué seguir vacunando si la mayoría de la población se ha infectado?

Eficacia de la infección previa frente a la re-infección por cepas diferentes



COVID-19 Forecasting Team. Lancet 2023; 401: 833-42

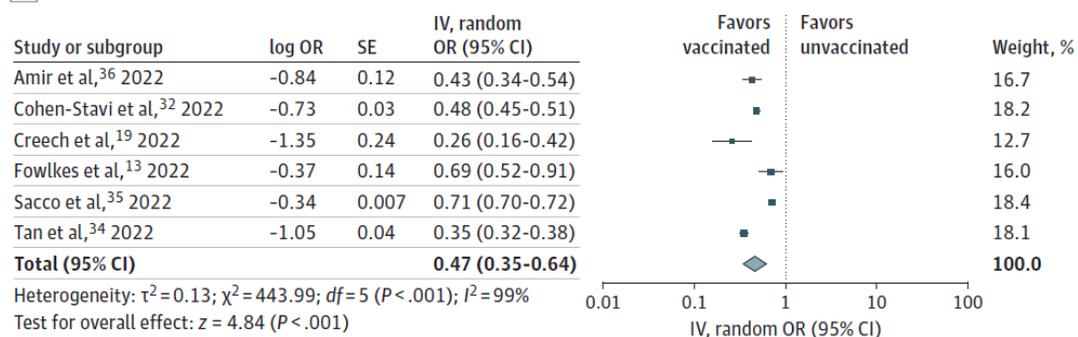


Efectividad de las vacunas frente a COVID-19 en niños de 5-11 años frente a infecciones de cualquier tipo e infecciones sintomáticas por SARS-CoV-2

Infecciones de cualquier tipo

EV: 53% (36-65%)

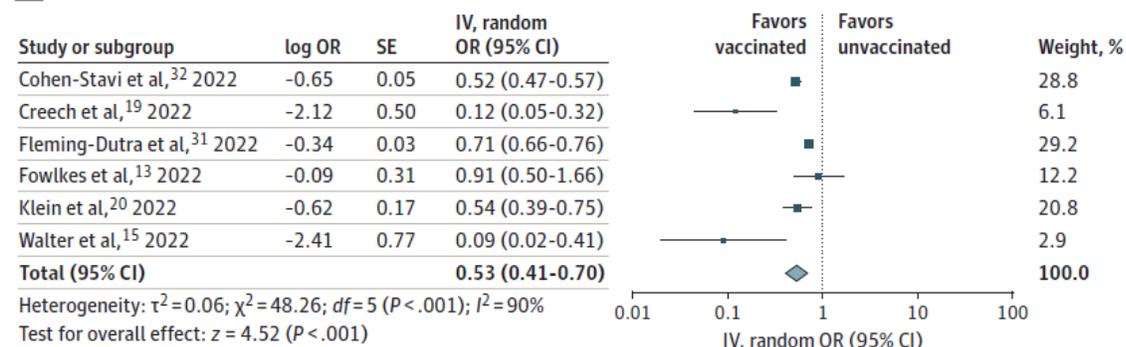
A SARS-CoV-2 infections with or without symptoms



Infecciones sintomáticas

EV: 47% (30-59%)

B Symptomatic SARS-CoV-2 infections



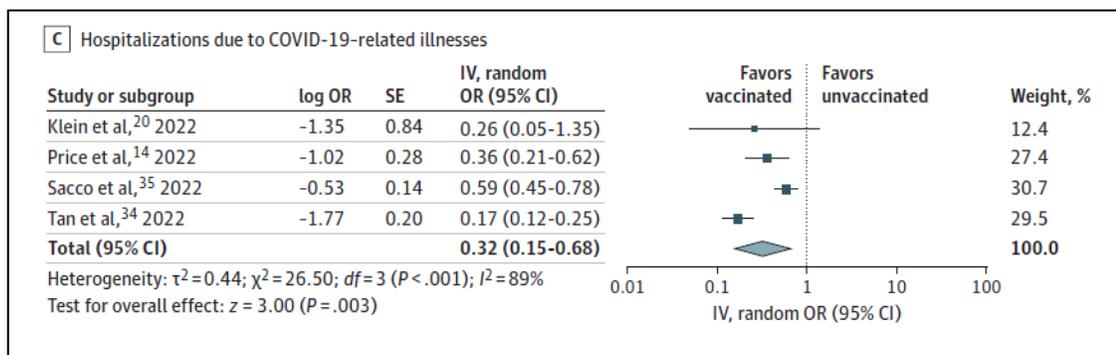
Watanabe JAMA Pediatr. 2023 Jan 23:e226243. doi: 10.1001/jamapediatrics.2022.6243.



Efectividad de las vacunas frente a COVID-19 en niños de 5-11 años frente a hospitalizaciones por COVID y PIMS

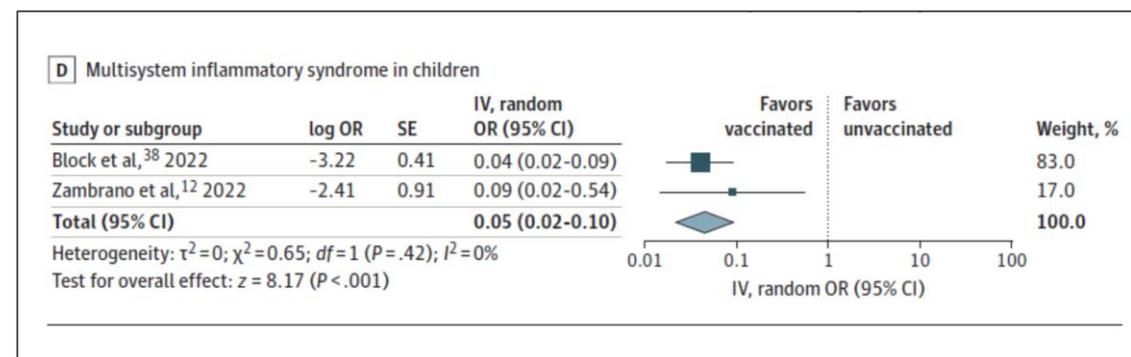
Hospitalizaciones

EV: 68% (32-85%)



PIMS

EV: 95% (90-98%)



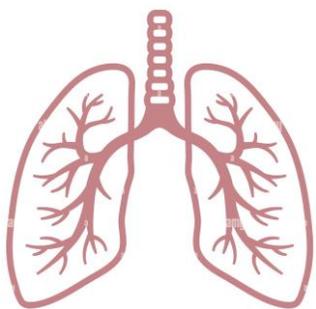
Watanabe JAMA Pediatr. 2023 Jan 23:e226243. doi: 10.1001/jamapediatrics.2022.6243.



Inmunidad híbrida vs inmunidad vacunal



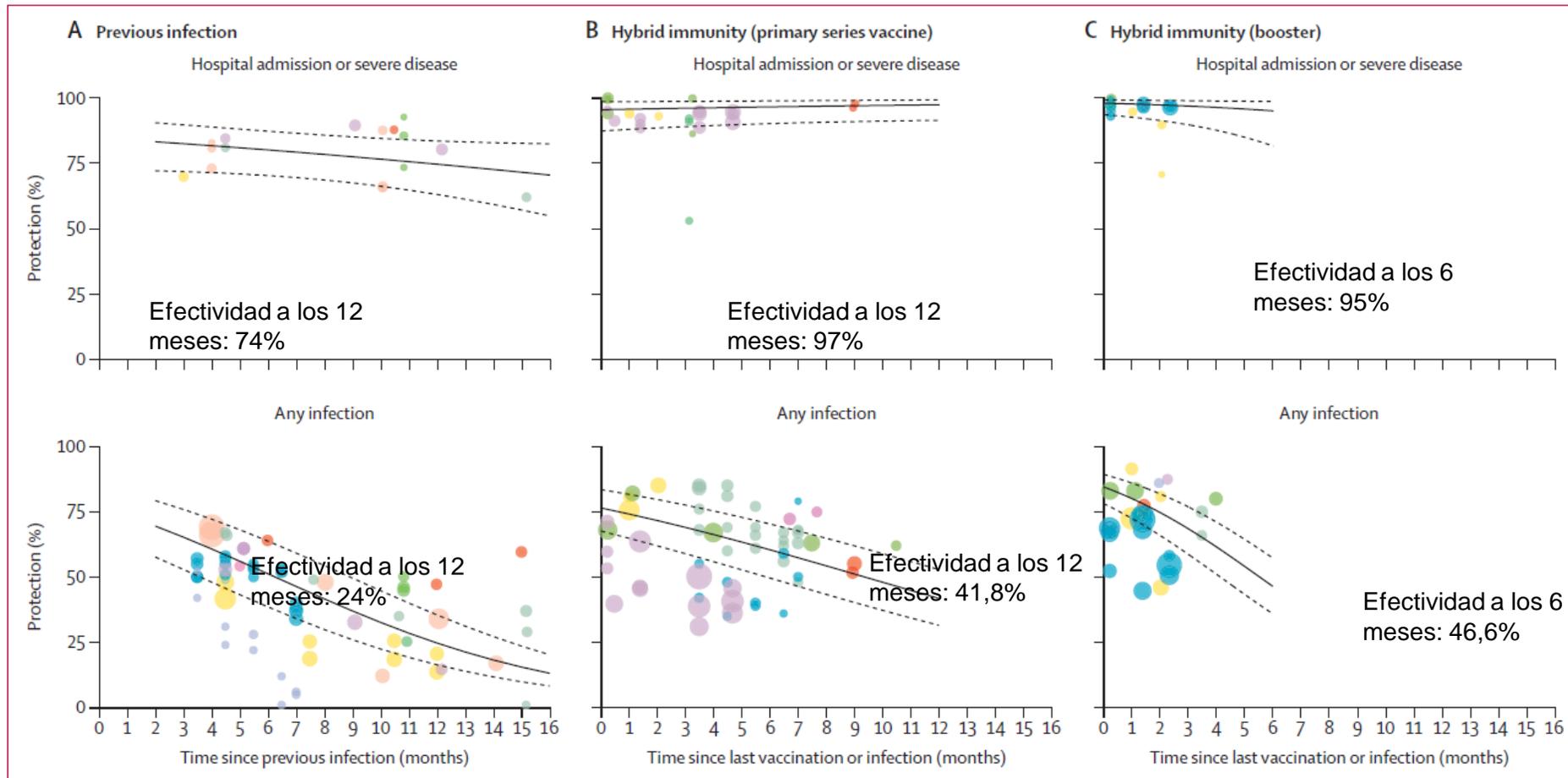
	Solo vacuna	Infección + vacuna
IgG anti-S	+++	++++ (significativo)
IgG-anti-RBD	+++	++++ (significativo)
CBM anti-S	++	++
CD4+ anti S	++	+++ (no significativo)
CD8+ anti-S	+	+++ (no significativo)



IgG anti-S	+++	++++ (significativo)
IgG-anti-RBD	+++	++++ (significativo)
IgA-anti-S	0	++ (significativo)
CBM anti-S	?	+++
CD4+ anti-S	+	+++ (significativo)
CD8+ anti-S	+	+++ (significativo)



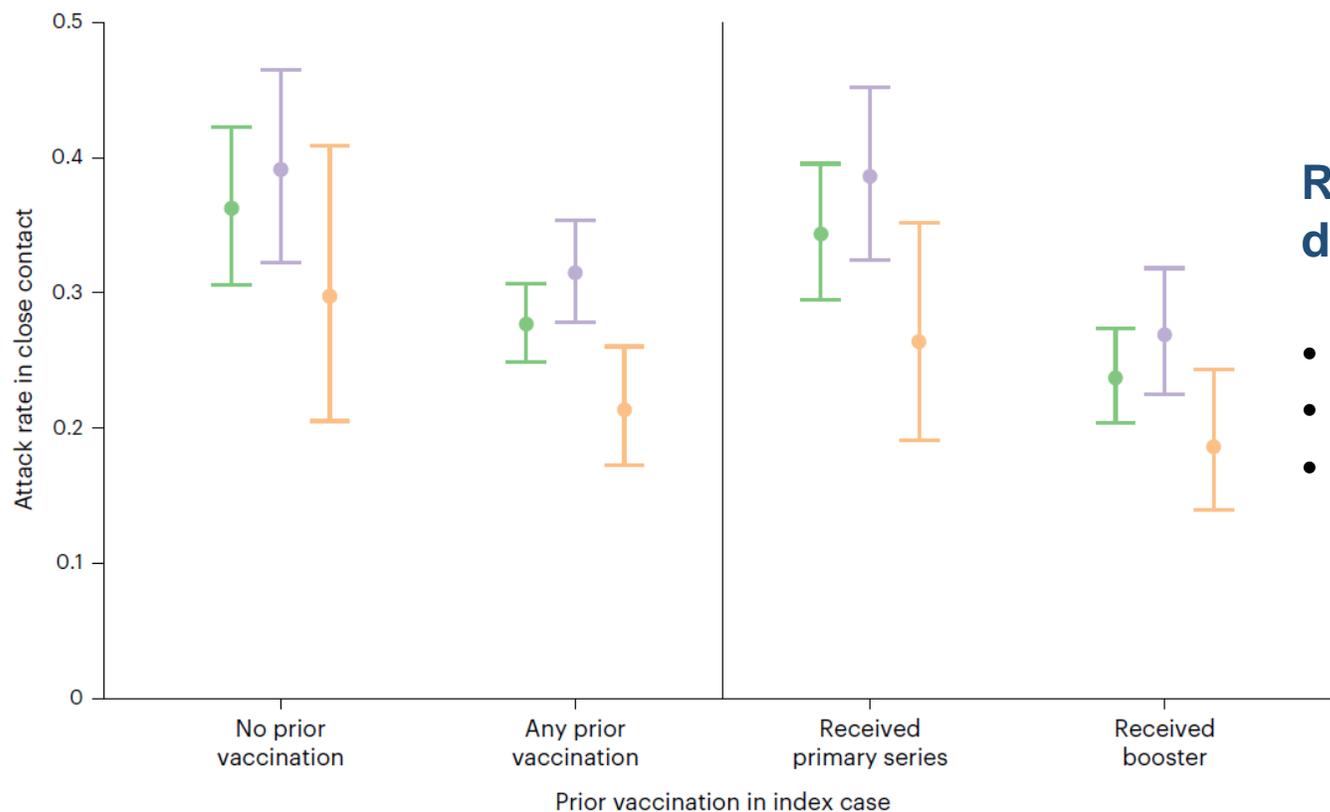
Efectividad de la Inmunidad híbrida



Bobrovitz N, et al. Lancet Infect Dis 2023; [https://doi.org/10.1016/S1473-3099\(22\)00801-5](https://doi.org/10.1016/S1473-3099(22)00801-5)



Transmisibilidad de la infección de brecha en vacunados e infectados a contactos estrechos



Reducción del riesgo de transmisión desde el caso índice

- Cualquier vacunación: 22% (6-36%)
- Infección previa: 23% (3-39%)
- Infección previa y vacunación: 40% (20-55%)

● Overall ● No prior infection ● Prior infection

¿Por qué no seguir vacunando?





IN DEPTH

A teen receives a dose of the new Omicron-specific COVID-19 booster in a Pennsylvania pharmacy last month. Data on boosters' benefits for young people are lacking.

COVID-19

Heart risks fuel debate over COVID-19 boosters

With benefits unclear, some scientists question new round of shots for young people

Moutinho S, et al. *Science*, 378 (6617), • DOI: 10.1126/science.adf3945



Miocarditis en niños tras la vacunación frente al SARS-CoV-2

Estudio	Vacuna	Edad (años)	Sexo	Frecuencia /100.000
Buchan, SA. JAMA Pediatr 2023	Comirnaty	12-17	V y M	4,6
Watanabe, JAMA Pediatrics	Cualquier Vacuna ARNm	5-11 años	V y M	0,18
Oster ME, JAMA 2022	Comirnaty	12-15 años 16-17 años	V V	1ª dosis: 0,7; 2ª dosis: 7 1ª dosis: 0,7; 2ª dosis: 10,5
Block JP, MMWR 2022	Comirnaty	5-11 años 12-17 años	V V	0 casos 2,2- 1ª dosis; 22- 2ª dosis
Grinberg NEJM 2022	Comirnaty	12-15 años	V y M	4,8



Reporting rates of myocarditis (per 1 million doses administered) after Pfizer-BioNTech COVID-19 vaccination, 7-day risk interval*

Age group	Males		Females	
	Dose 1	Dose 2	Dose 1	Dose 2
5–11 years	0.0	4.3	Not calculated [†]	2.0
12–15 years	4.8	45.7	1.0	3.8
16–17 years (included for reference)	6.1	70.2	0.0	7.6

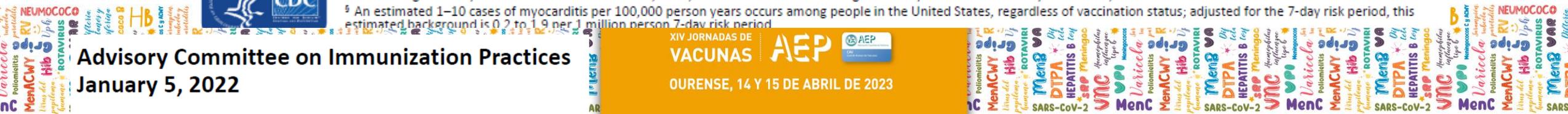
- 37,810,998 total doses 1 and 2 of vaccine administered[‡]
- Reporting rates exceed background incidence (peach shaded cells)[§]
 - Males: after dose 1 (ages 12–15 and 16–17 years) and after dose 2 (ages 5–11, 12–15, and 16–17 years)
 - Females: after dose 2 (ages 12–15 and 16–17 years)
 - Reporting rates among males substantially lower among ages 5–11 vs. 12–15 and 16–17 years

* Reports of myocarditis after doses 1 and 2 of Pfizer-BioNTech COVID-19 vaccine during a 7-day risk interval after vaccination (as of Dec 19, 2021); reports verified to meet case definition by healthcare provider interview and/or medical record review.

[†] Too few reports of females ages 5–11 years to calculate a stable rate.

[‡] Children ages 5–11 years vaccinated Nov 3–Dec 19, 2021, children and adolescents ages 12–15 years vaccinated May 12–Dec 19, 2021.

[§] An estimated 1–10 cases of myocarditis per 100,000 person years occurs among people in the United States, regardless of vaccination status; adjusted for the 7-day risk period, this estimated background is 0.2 to 1.9 per 1 million person 7-day risk period.





mRNA COVID-19 vaccine safety of primary series vaccination in children ages 6 months–5 years



U.S. reports to VAERS among children after primary series Pfizer-BioNTech (ages 6 months–4 years) or Moderna (ages 6 months–5 years) vaccination* (as of August 21, 2022)

Manufacturer	Doses admin [†]	Total reports	Median age	Male [‡] n (%)	Female [‡] n (%)	Non-serious n (%)	Serious [§] n (%)	Myocarditis reports (n)
Pfizer-BioNTech	890,378	496	3 years	249 (50)	245 (49)	486 (98)	10 (2)	0
Moderna	664,484	521	2 years	272 (52)	240 (46)	512 (98)	9 (2)	0
Total	1,554,862	1,017	3 years	521 (51)	485 (48)	998 (98)	19 (2)	0

* Among children ages 6 months–4 years after Pfizer-BioNTech, and among children ages 6 months–5 years after Moderna, vaccinated during June 18–August 21, 2022; reports received and processed as of August 23, 2022

[†] Dose 1 and dose 2 administered among children described in previous footnote during June 16–August 18, 2022.

[‡] 2 reports after Pfizer-BioNTech and 9 reports after Moderna did not have sex reported

[§] Based on the Code of Federal Regulations if one of the following is reported: death, life-threatening illness, hospitalization or prolongation of hospitalization, permanent disability, congenital anomaly or birth defect



Circulation

ORIGINAL RESEARCH ARTICLE

Circulating Spike Protein Detected in Post-COVID-19 mRNA Vaccine Myocarditis

Lael M. Yonker^{ID}, MD*; Zoe Swank, PhD*; Yannic C. Bartsch, PhD*; Madeleine D. Burns^{ID}, MS; Abigail Kane^{ID}, MD;

RESULTS: Extensive antibody profiling and T-cell responses in the individuals who developed postvaccine myocarditis were essentially indistinguishable from those of vaccinated control subjects, despite a modest increase in cytokine production. A notable finding was that markedly elevated levels of full-length spike protein (33.9 ± 22.4 pg/mL), unbound by antibodies, were detected in the plasma of individuals with postvaccine myocarditis, whereas no free spike was detected in asymptomatic vaccinated control subjects (unpaired *t* test; $P < 0.0001$).

Yonker LM et al. Circulation 2023; 147: 867-876



Intervalos prolongados entre las dosis de primoinfección

- Aumento de inmunogenicidad
- Mayor título de Ac neutralizantes
- Respuestas específicas de células T más potentes
- Mayor efectividad
- Menor riesgo de miocarditis



Effectiveness of BNT162b2 after extending the primary series dosing interval in children and adolescents aged 5–17

Received: 6 January 2023

Francisco Tsz Tsun Lai ^{1,2,7}, Min Fan ^{1,7}, Caige Huang¹, Celine Sze Ling Chui^{2,3,4}, Eric Yuk Fai Wan ^{1,2,5}, Xue Li ^{1,2,6}, Carlos King Ho Wong ^{1,2,5}, Ching-Lung Cheung ¹, Ian Chi Kei Wong ^{1,8}  & Esther Wai Yin Chan ^{1,2,8} 

Accepted: 21 March 2023

August 15, 2022, 5396 Covid-19 cases and 202 Covid-19 related hospitalizations were identified and matched with 21,577 and 808 controls, respectively. For vaccine recipients with extended intervals [≥ 28 days, adjusted odds ratio 0.718, 95% Confidence Interval: 0.619, 0.833] there was a 29.2%-reduced risk of Covid-19 infection compared to those with regular intervals (21–27 days). If the threshold was set at eight weeks, the risk reduction was estimated at 43.5% (aOR 0.565, 95% CI: 0.456, 0.700). In conclusion, longer dosing intervals for children and adolescents should be considered.



Maternal third dose of BNT162b2 mRNA vaccine and risk of infant COVID-19 hospitalization

according to maternal vaccination status at delivery. Among 48,868 live-born infants included in the analysis, rates of COVID-19 hospitalization were 0.4%, 0.6% and 0.7% in the third-dose, second-dose and unvaccinated groups, respectively. Compared to the second dose, the third dose was associated with reduced infant hospitalization with estimated effectiveness of 53% (95% CI: 36–65%). Greater protection was associated with a shorter interval between vaccination and delivery. A third maternal dose during



Sex-Specific Neurodevelopmental Outcomes Among Offspring of Mothers With SARS-CoV-2 Infection During Pregnancy

Andrea G. Edlow, MD, MSc; Victor M. Castro, MS; Lydia L. Shook, MD; Sebastien Haneuse, PhD; Anjali J. Kaimal, MD, MAS; Roy H. Perlis, MD, MSc

ethnicity, insurance status, hospital type (academic center vs community), maternal age, and preterm status, maternal SARS-CoV-2 positivity was associated with a statistically significant elevation in risk for neurodevelopmental diagnoses at 12 months among male offspring (adjusted OR, 1.94 [95% CI 1.12-3.17]; $P = .01$) but not female offspring (adjusted OR, 0.89 [95% CI, 0.39-1.76]; $P = .77$). Similar effects were identified using matched analyses in lieu of regression. At 18 months, more modest effects were observed in male offspring (adjusted OR, 1.42 [95% CI, 0.92-2.11]; $P = .10$).





Live-attenuated vaccine sCPD9 elicits superior mucosal and systemic immunity to SARS-CoV-2 variants in hamsters

Nouailles G, et al. Nature Microbiology 2023

<https://doi.org/10.1038/s41564-023-01352-8>

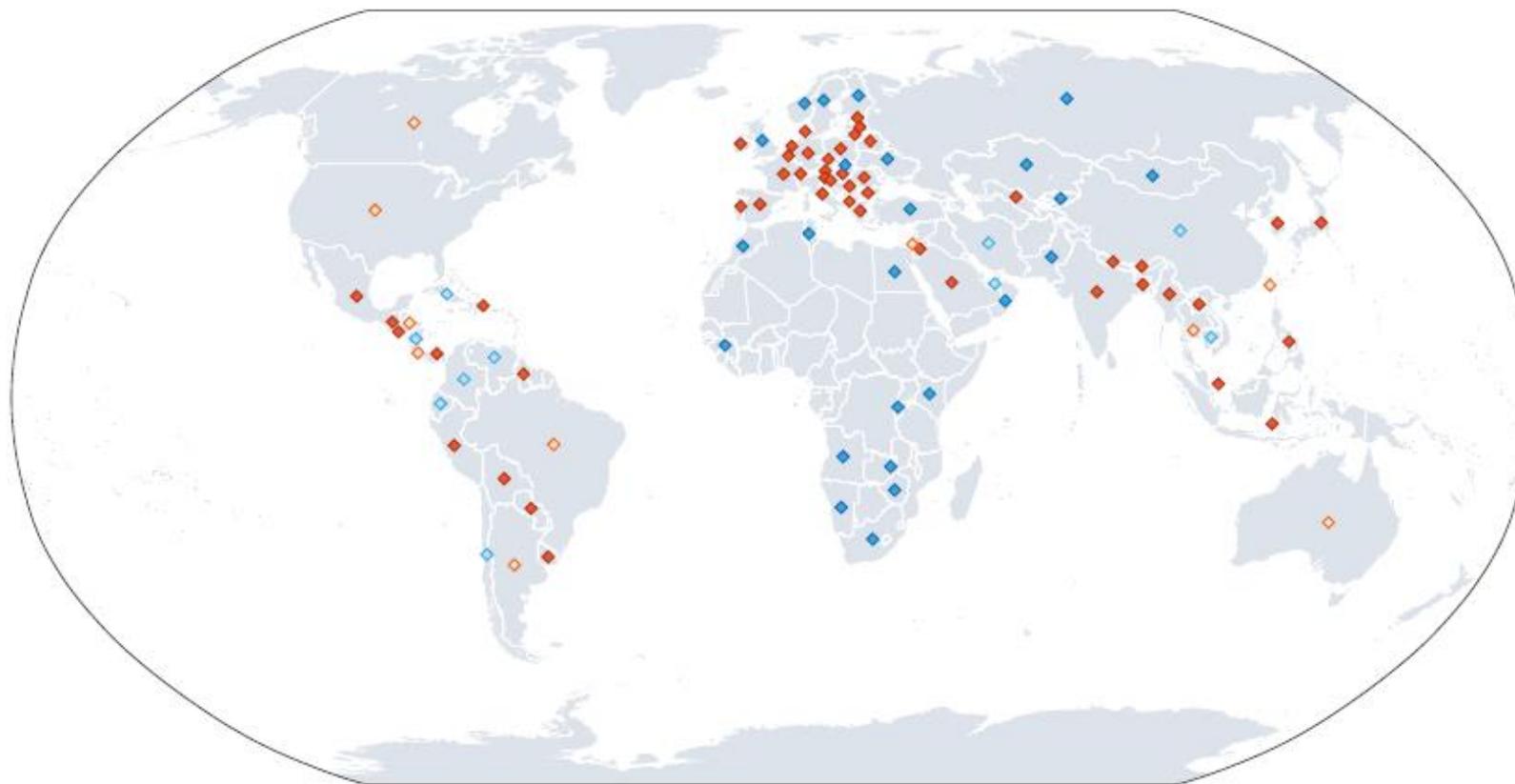
OURENSE, 14 Y 15 DE ABRIL DE 2023



APPROVALS BY AGE

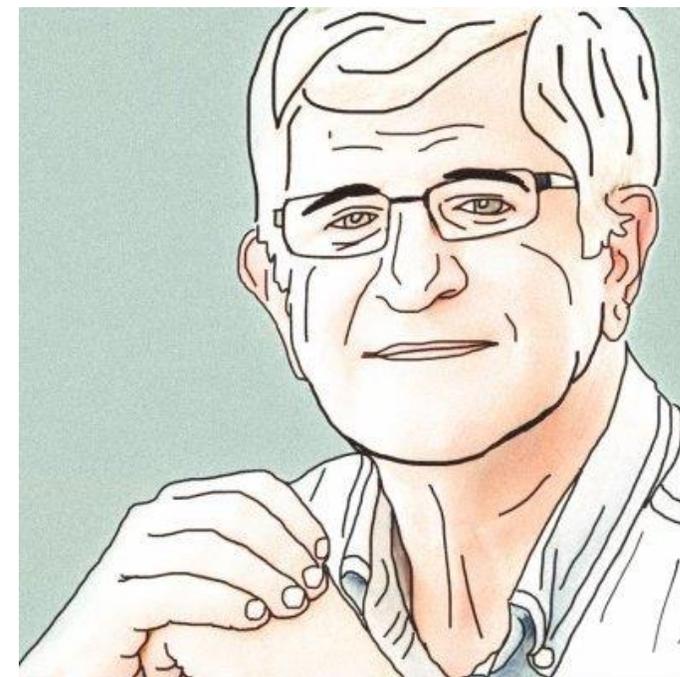
About 120 countries have approved COVID-19 vaccines for children, but at different ages. Some nations, such as the United States, Brazil, Costa Rica and Israel, offer an mRNA vaccine to children as young as six months.

Minimum age ◆ 6 months ◆ 2 or 3 ◆ 5 or 6 ◆ 12 or 15



El SAGE actualiza la guía de vacunación contra la COVID-19

El grupo de prioridad baja incluye a los niños y adolescentes sanos de entre 6 meses y 17 años. Las dosis primarias y de refuerzo son seguras y eficaces en los niños y adolescentes. Sin embargo, teniendo en cuenta la baja carga de morbilidad de este grupo de edad, el SAGE insta a los países que estén considerando su vacunación a que fundamenten sus decisiones en factores contextuales, entre ellos, la mencionada carga de morbilidad y la relación costoeficacia, así como otras prioridades sanitarias o programáticas y los costos de oportunidad.



Paul Offit



En espera de nuevas vacunas, mantener las indicaciones vacunales actuales es la opción más adecuada, haciendo hincapié en la vacunación de las personas de alto riesgo

Es primordial seguir las indicaciones del Ministerio de Sanidad



Recomendación de vacunación frente a la covid en España

		Inmunocompetentes		Inmunodeprimidos	
Dosis	Edad	Serie primaria	Refuerzo	Serie primaria	Refuerzo
3 µg	6 – 4 años	3 dosis (3-8 semanas entre dosis 1ª y 2ª; ≥ 8 semanas entre dosis 2ª y 3ª)	No aprobado	3 dosis (3 semanas entre dosis 1ª y 2ª; ≥ 8 semanas entre dosis 2ª y 3ª)	No aprobado
10 µg	5-11 años	2 dosis (8 semanas entre dosis 1ª y 2ª)	No recomendado	3 dosis (3 semanas entre dosis 1ª y 2ª; ≥ 4 semanas entre dosis 2ª y 3ª)	≥ 5 meses tras la serie primaria
30 µg	12-17 años	2 dosis (8 semanas entre dosis 1ª y 2ª)	No recomendado	3 dosis (3 semanas entre dosis 1ª y 2ª; ≥ 4 semanas entre dosis 2ª y 3ª)	≥ 5 meses tras la serie primaria



Vacunación de 6 meses a 4 años

- Prematuros
- Inmunodeprimidos (grupo 7 del Ministerio de Sanidad)
- Cardiopatías complejas
- Anomalías de la vía aérea o enfermedad pulmonar crónica
- Enfermedades metabólicas o mitocondriales
- Enfermedades neurológicas o neuromusculares crónicas
- Síndrome de Down
- Obesidad
- Asma



Muchas gracias



XIV JORNADAS DE
VACUNAS **AEP**
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