20ª edición

POSTCROI

Una actualización de la "30th Conference on Retroviruses and Opportunistic Infections"

20ª POST-CROI-2023

Barcelona, 2 de Marzo del 2023

FLS SCIENCE

Actualización en la epidemiología y respuesta de las vacunas frente a la COVID-19

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IDIBAPS Institut D'Investigacions Biomèdiques August Pi i Sunyer

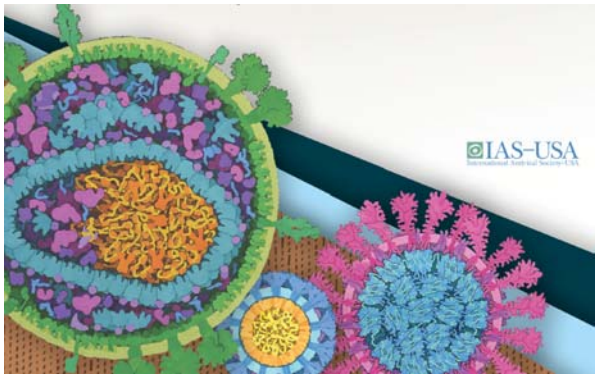
Potential conflict of interest

Dr. José M Miró has received honoraria for speaking or participating in Advisory Boards and/or research grants from the following Pharmaceutical Companies:

- Abbvie
- Angelini-Allergan
- Bristol-Myers Squibb
- Contrafect
- Genentech
- Gilead Sciencies
- Jansen
- Merck
- Medtronic
- Novartis
- Pfizer
- Roche
- Theravance
- ViiV Healthcare

30th CROI 2023
Conference on Retroviruses and Opportunistic Infections
February 19-22 | Seattle, WA

COVID-19 Abstracts at CROI



Statistics for Abstracts

General Abstracts Submitted	1051
General Abstracts Accepted	658
Late-Breaking HIV, SARS-CoV-2, or mpox Abstracts Submitted	558
Late-Breaking HIV, SARS-CoV-2, or mpox Abstracts Accepted	347
Total Abstracts Submitted	**1609**
Total Abstracts Accepted	**949**
Oral Abstract Presentations	115
Themed Discussion Presentations*	56
Poster Presentations	834

Abstracts Related to SARS-CoV-2 or Special Study Populations

SARS-CoV-2	228
Mpox	61
Adolescents	76
Men Who Have Sex With Men (MSM)	152
People Who Inject Drugs (PWID)	51
Transgender Men or Women	55
Women or Girls	155

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Update on the Epidemiology and Response of Vaccines against COVID-19

- **Current epidemiology in a vaccinated world**
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- Some clinical pearls
- Some therapeutic pearls
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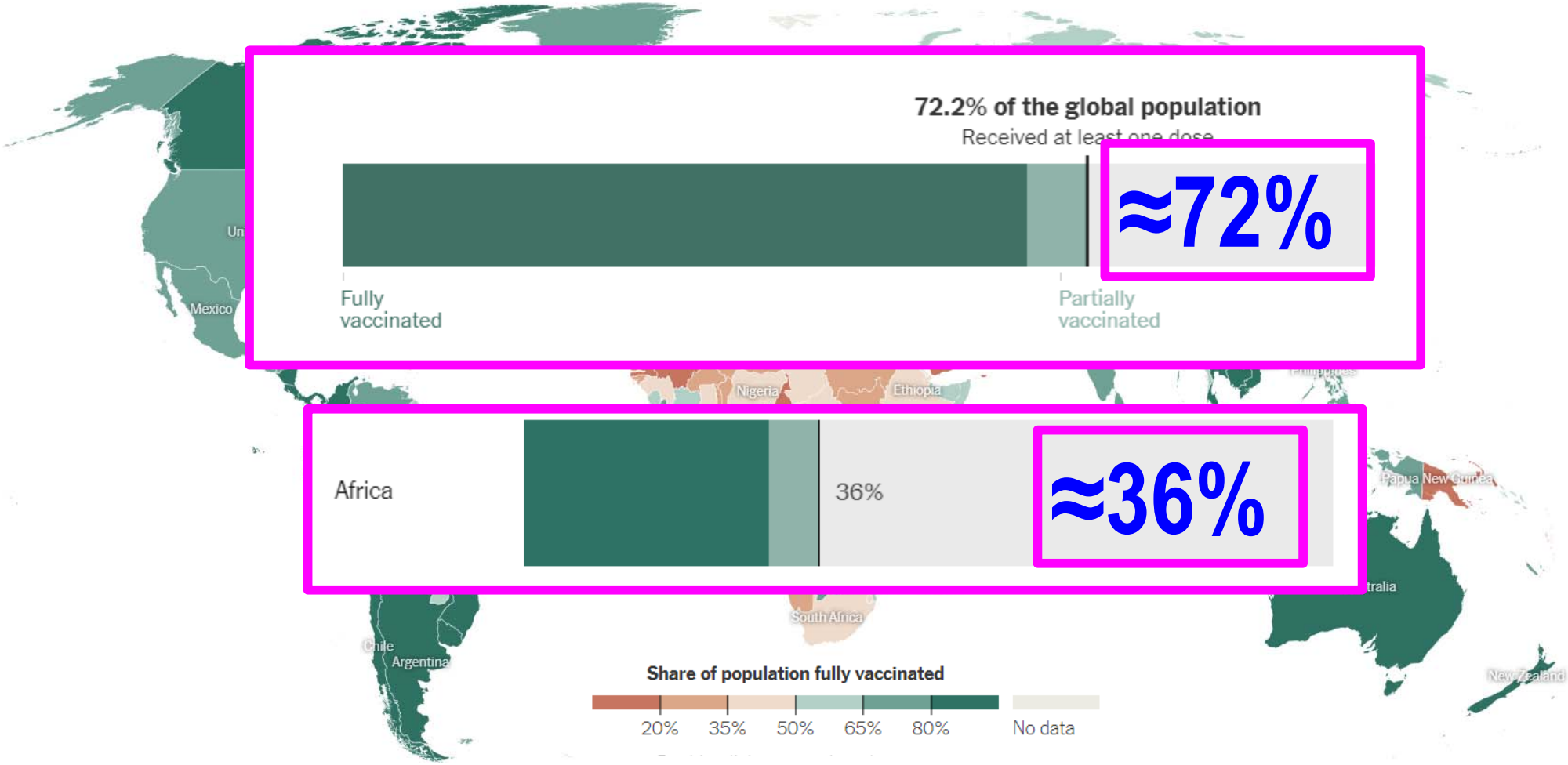
- Take-home messages

March 2nd 2023

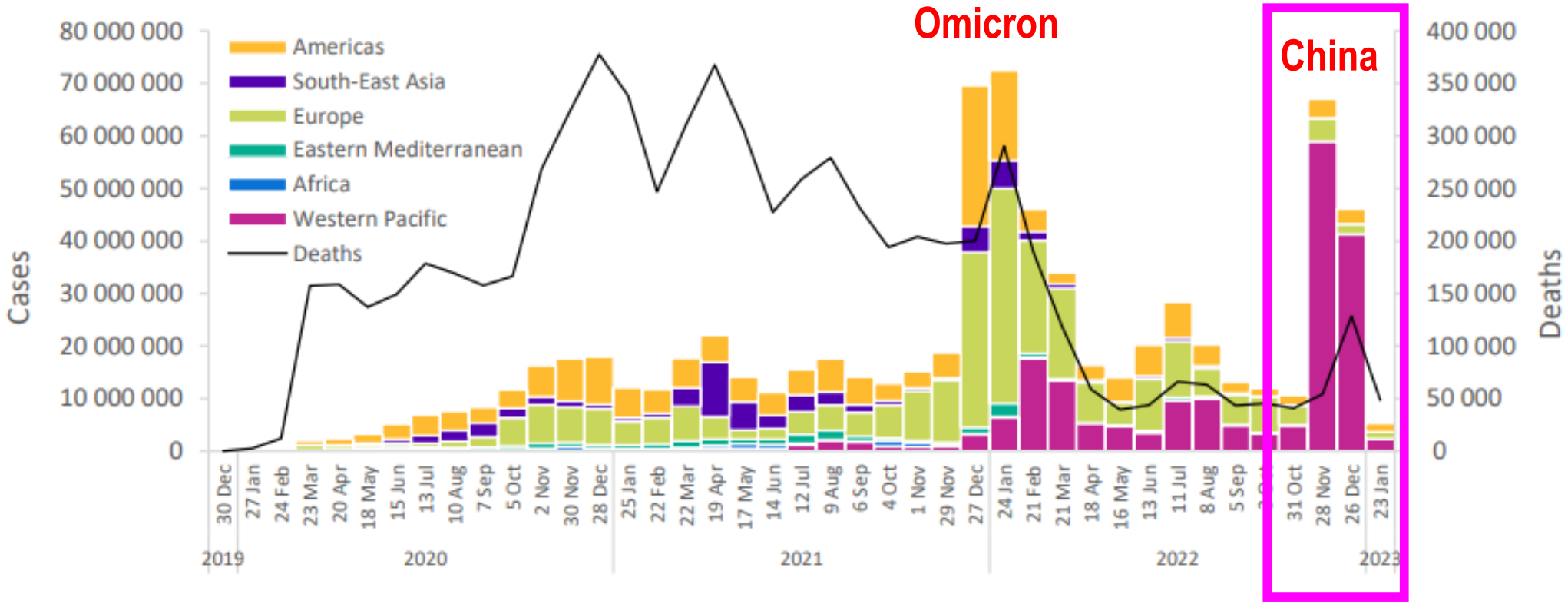
High rates of COVID-19 vaccination in high/upper-middle income countries



https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html with access February 19th 2023; Hunter DJ, et al. N Engl J Med. March 24 2022; 386:1176-1179.

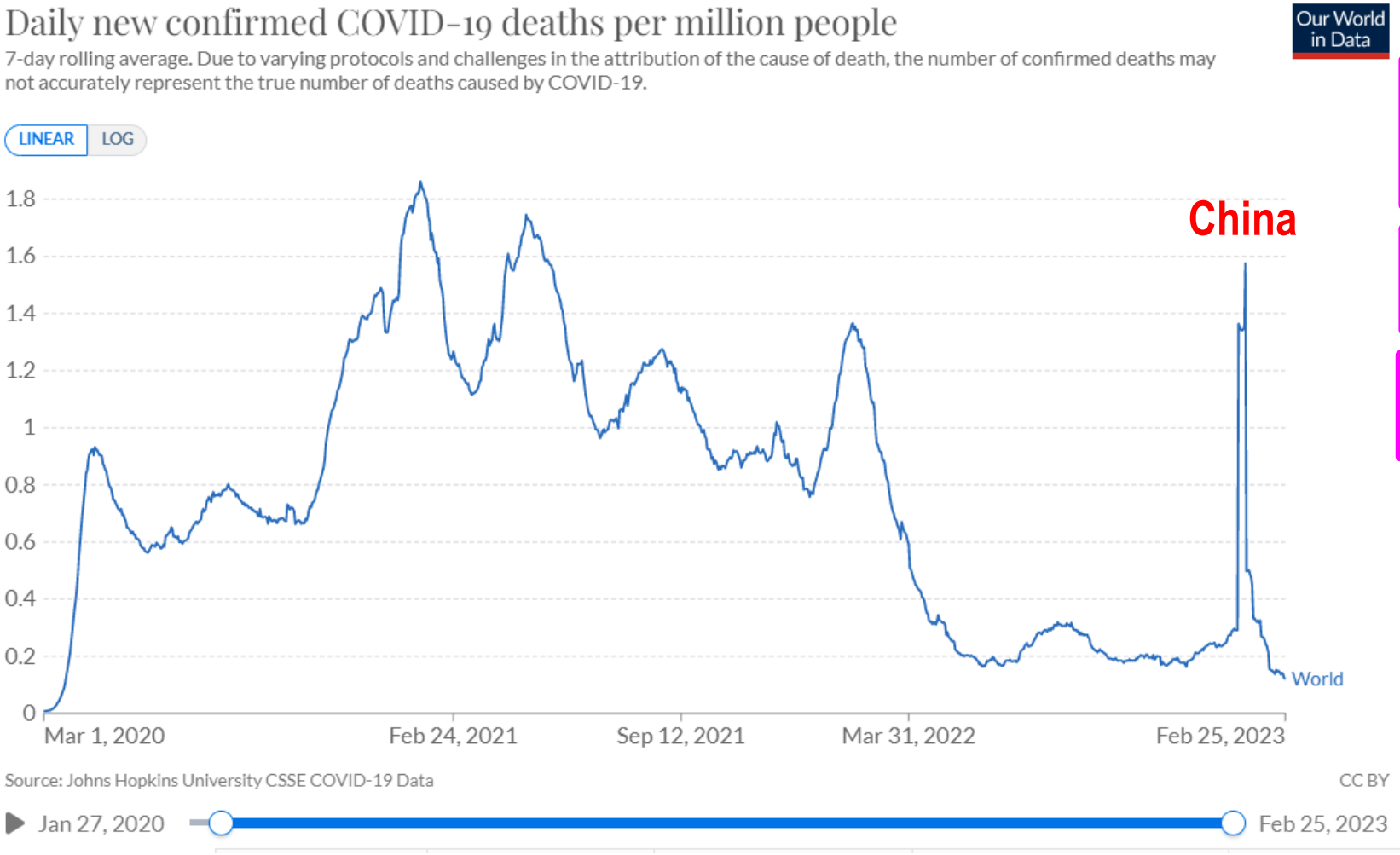
WHO COVID-19 Weekly Epidemiological Update

Figure 1. COVID-19 cases reported by WHO Region, and global deaths by 28-day intervals, as of 19 February 2023**



file:///C:/Users/JMMIRO/Downloads/20230222_Weekly_Epi_Update_131%20(1).pdf February 22nd 2023

Global COVID-19: ≈ 960 daily deaths!



Influenza mortality in 2017-18 season: ≈ 1,500 cases/day*

TB mortality in 2020 ≈ 4,000 cases/day**

HIV mortality in 2020 ≈ 1,800 cases/day**

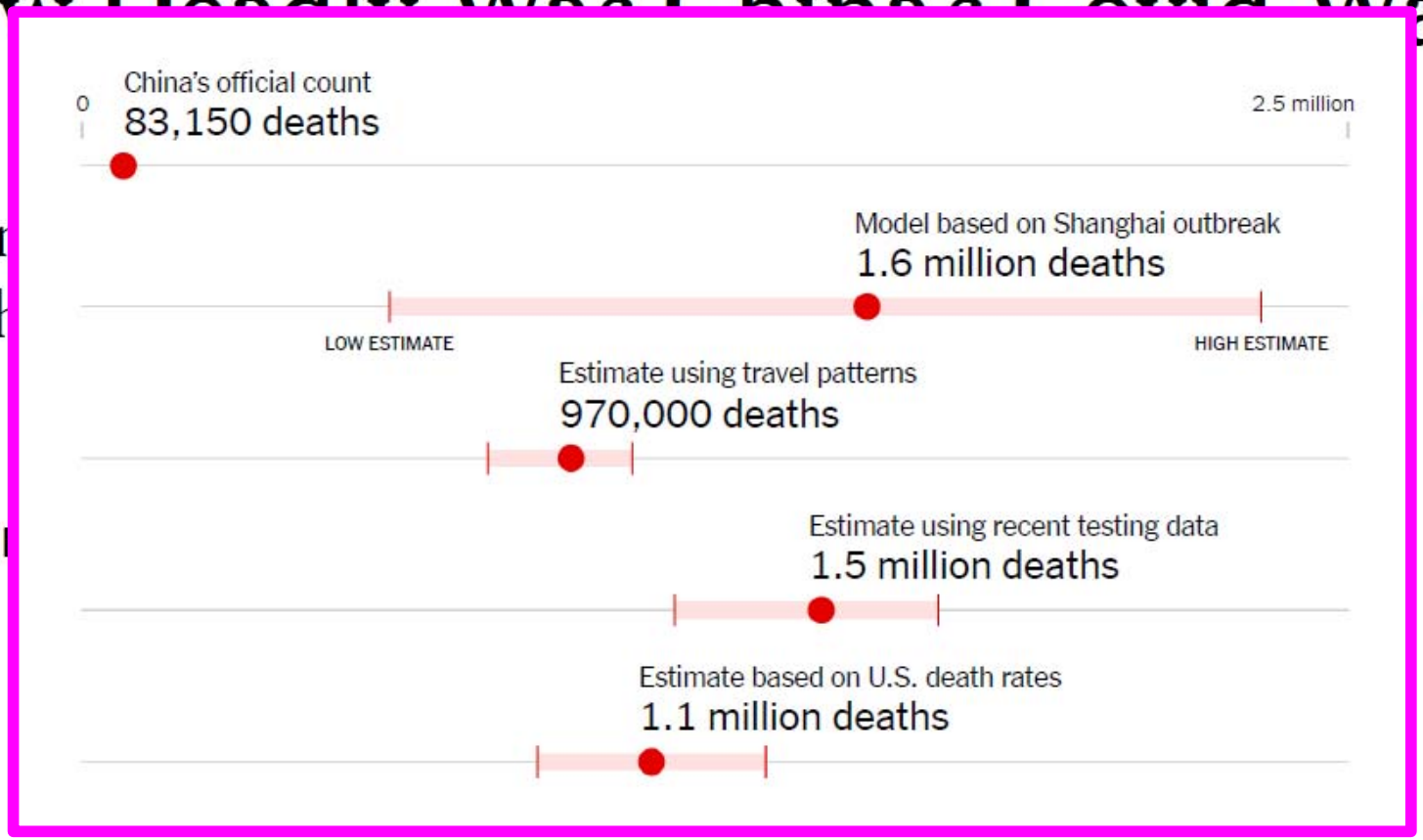
960!

https://ourworldindata.org/covid-cases – February 26th 2023

The New York Times | https://nyti.ms/3E8p0iv

How Deadly Was China's Covid Wave?

Two mor
suggest th



https://www.nytimes.com/interactive/2023/02/15/world/asia/china-covid-death-estimates.html

nature

NEW

W al
en

But others think that the pandemic has already moved beyond the legal criteria used to define an infectious-disease outbreak as a PHEIC (pronounced 'fake'). The WHO's decision came on the same day that President Joe Biden announced that the United States would end its own COVID-19 emergency declarations on 11 May.

The World Health Organization has decided the crisis isn't over yet – but it's at a transition point.

PHEIC = Public Health Emergency of International Concern

Adam D. Nature. February 1st 2023

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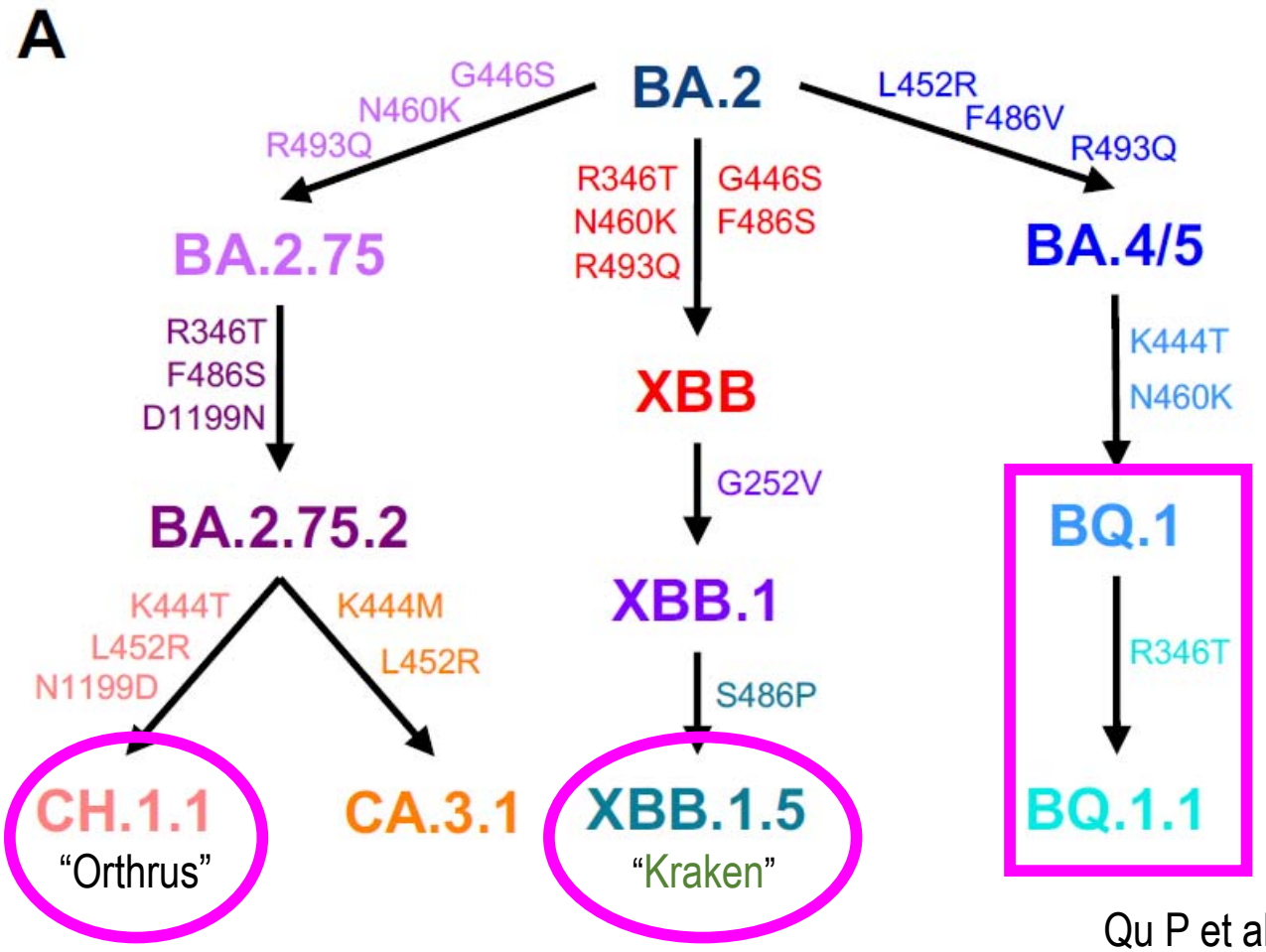
March 2nd 2023

Aims of the SARS-CoV-2 Phylogenetic Evolution

- First, mutating to transmit faster
- Second, evading accumulated specific immunity
- And third, without losing pathogenicity

Relationships between different Omicron subvariants with key lineage-defining amino acid mutations for each displayed



Qu P et al. bioRxiv, January 17th 2023

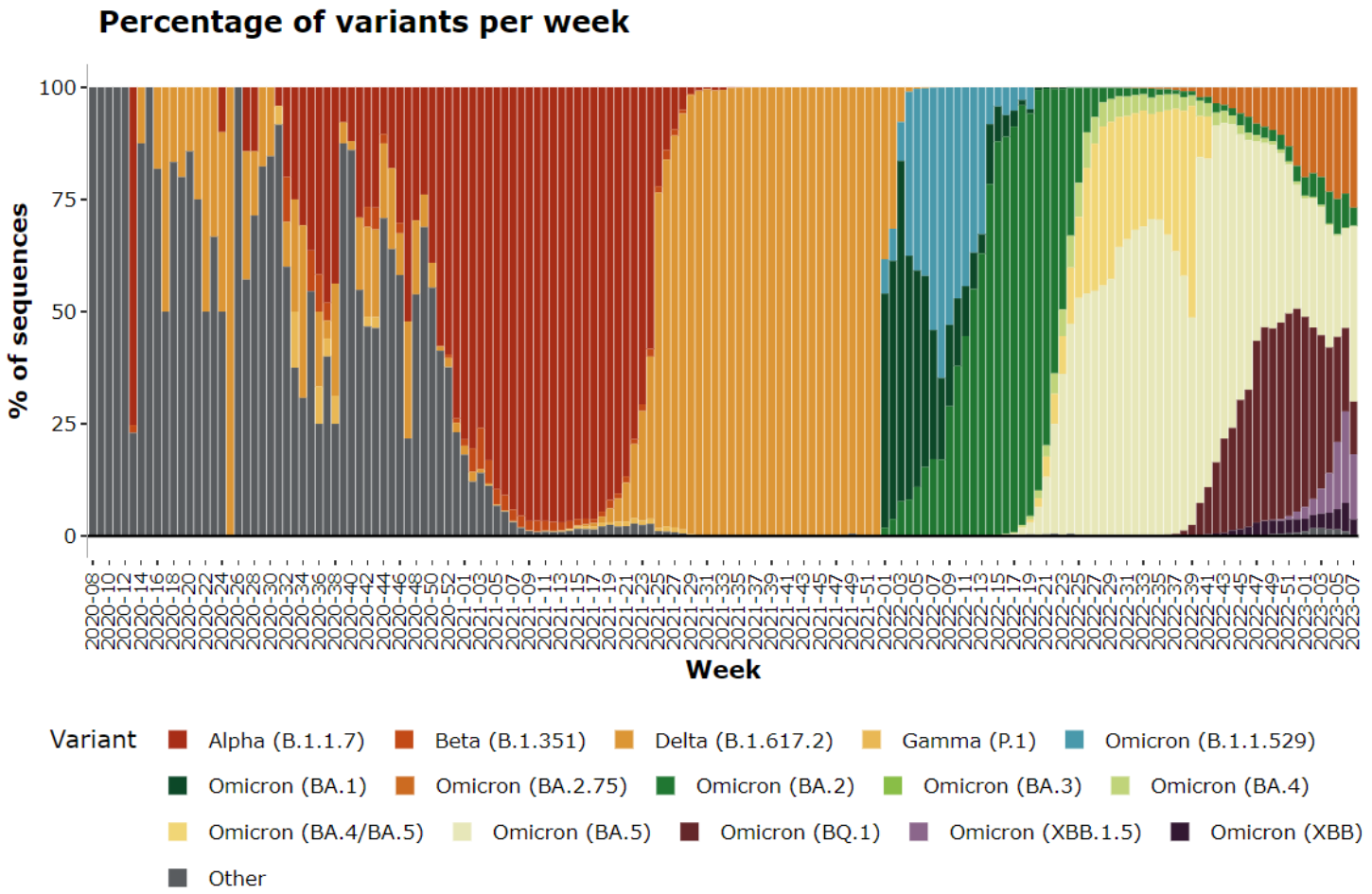
Omicron XBB.1.5 predominates in USA = 85%

USA

WHO label	Lineage #	US Class	%Total	95%PI
Omicron	XBB.1.5	VOC	85.0%	79.8-89.1%
	BQ.1.1	VOC	9.4%	6.8-12.8%
	BQ.1	VOC	2.6%	1.9-3.6%
	XBB	VOC	1.2%	0.9-1.6%
	CH.1.1	VOC	0.9%	0.7-1.3%
	BN.1	VOC	0.4%	0.3-0.6%
	BA.5	VOC	0.1%	0.1-0.2%
	BF.7	VOC	0.1%	0.1-0.2%
	BA.2	VOC	0.0%	0.0-0.1%
	BA.5.2.6	VOC	0.0%	0.0-0.1%
	BF.11	VOC	0.0%	0.0-0.0%
	BA.2.75	VOC	0.0%	0.0-0.0%
	BA.2.75.2	VOC	0.0%	0.0-0.0%
	BA.4.6	VOC	0.0%	0.0-0.0%
	B.1.1.529	VOC	0.0%	0.0-0.0%
	BA.2.12.1	VOC	0.0%	0.0-0.0%
	BA.4	VOC	0.0%	0.0-0.0%
	BA.1.1	VOC	0.0%	0.0-0.0%
Delta	B.1.617.2	VBM	0.0%	0.0-0.0%
Other	Other*		0.1%	0.0-0.1%

Source: https://covid.cdc.gov/covid-data-tracker/#variant-proportions, with access February 25th 2023

Omicron BQ.1 & XBB.1.5 are the predominant variants in Europe

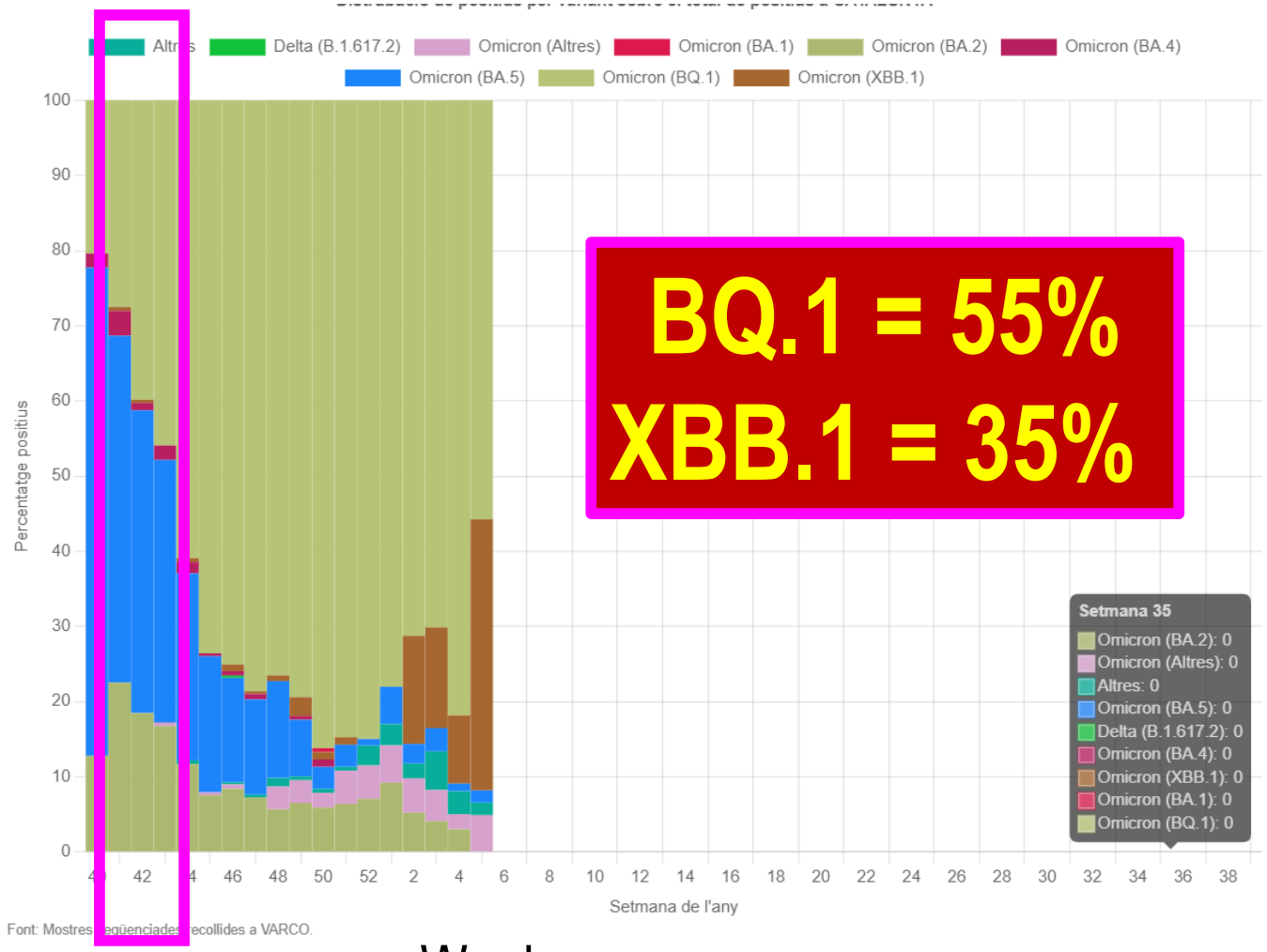


BQ.1 = 35.8%
XBB.1.5 = 22.2%
BA.2.75 = 20.2%
BA.5 = 10.3%
XBB = 2.6%
BA.2. = 1.0%
BA.4 = 0.5%

https://worldhealthorg.shinyapps.io/euro-covid19/ February 26th 2023.

Omicron BQ.1 & XBB.1 are predominating in Catalonia

%

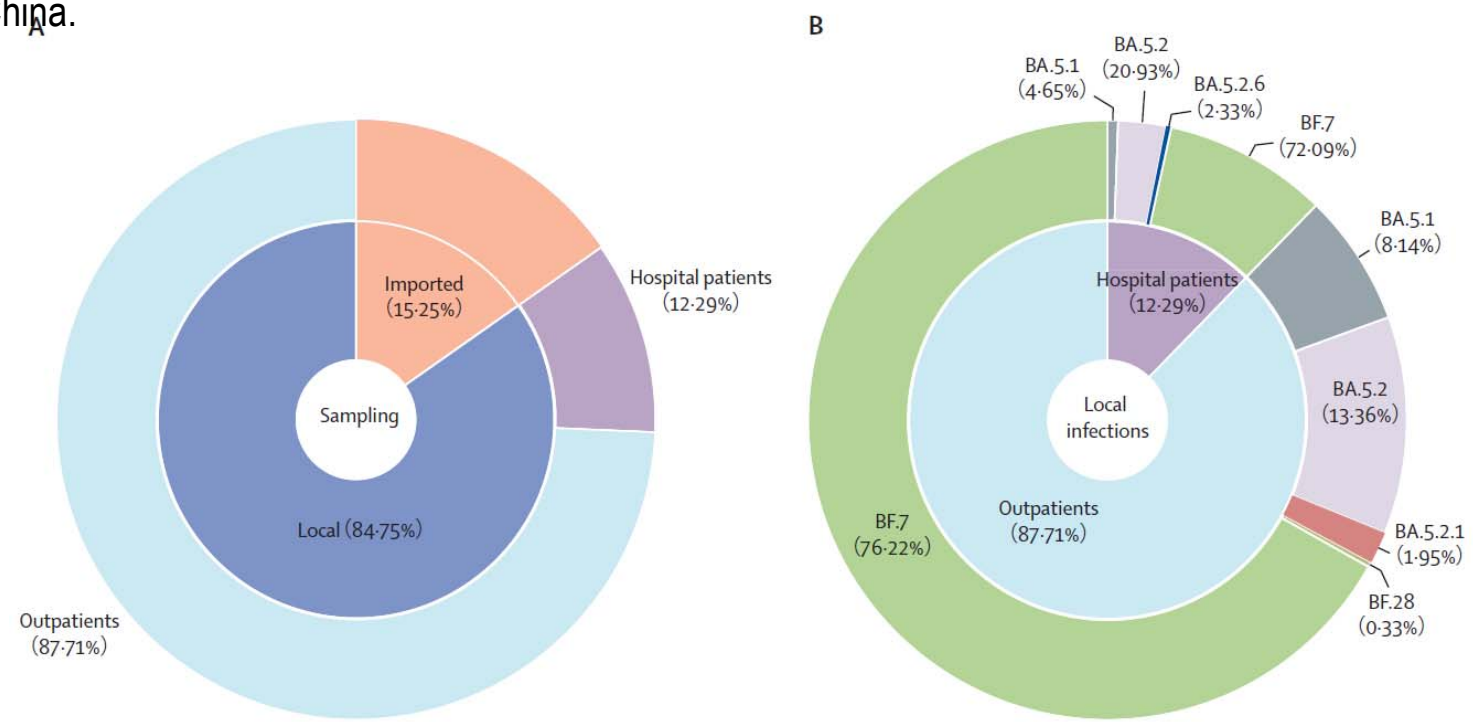


Weeks

https://sivic.salut.gencat.cat/covid_sequenciacio December 26th 2022.

Characterization of SARS-CoV-2 variants in Beijing during 2022 outbreak: BF.7 and BA.5.2 & no new VoC

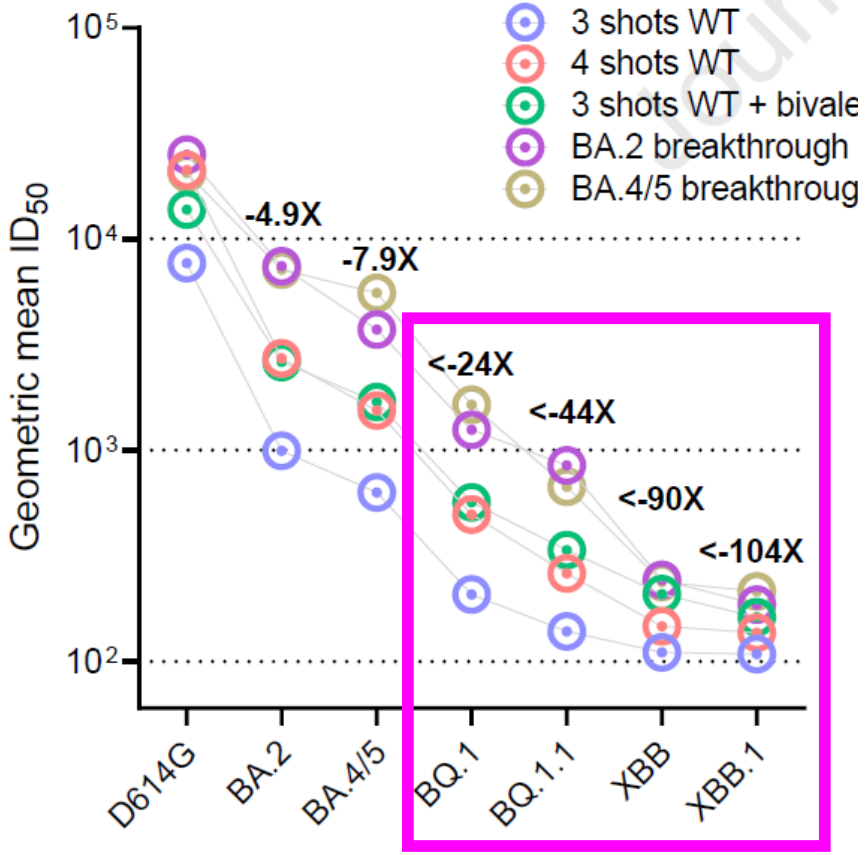
- 2,881 SARS-CoV-2 genome sequences were studied.
- The epidemiological and phylogenetic analysis concluded that the co-circulation of **BF.7 and BA.5.2 (90%)** was present in the current outbreak since Nov 14, 2022 in Beijing, and **there is no evidence that novel VoC emerged**. This results could be considered a snapshot of China.



Pan Y et al. Lancet. Feb 8th 2023

Immune evasion of BQ.1 and XBB.1.5 Omicron subvariants

Neutralization by sera from 5 cohorts



Neutralization by monoclonal Abs

Abs impaired (>3X, >10X, >100X)		BQ.1	BQ.1.1	BA.4/5-R346T	BA.4/5-K444T	BA.4/5-N460K	XBB	XBB.1	BA.2-Q183E
NTD	C1520								
NTD-SD2	C1717								
RBD class 1	S2K146								
	Omi-3								
	BD-515								
RBD class 2	XGv051								
	XGv347								
	ZCB11								
RBD class 3	Bebtelovimab								
	XGv289								
	P2G3								
	SP1-77								
	BD55-5840								
	XGv282								
	BD-804								
Evusheld									

A

	B.1	XBB.1
Single mAbs		
Casirivimab	7	>50000
Imdevimab	7	>50000
Bamlanivimab	11	>50000
Etesevimab	20	>50000
Cilgavimab	12	>50000
Tixagevimab	3	>50000
Amubarvimab	57	>50000
Romlusevimab	979	>50000
Sotrovimab	101	1169
Bebtelovimab	2	>50000
S2H97	2378	26610
Regdanvimab	1	>50000
mAb cocktails		
Casirivimab–imdevimab	6	>50000
Bamlanivimab–etesevimab	11	>50000
Cilgavimab–tixagevimab	5	>50000
Amubarvimab–romlusevimab	69	>50000
	EC_{50} (ng/ml)	

Wang Q et al. bioRxiv. Nov 28th 2022; Arora P et al. Lancet ID January 5th 2023

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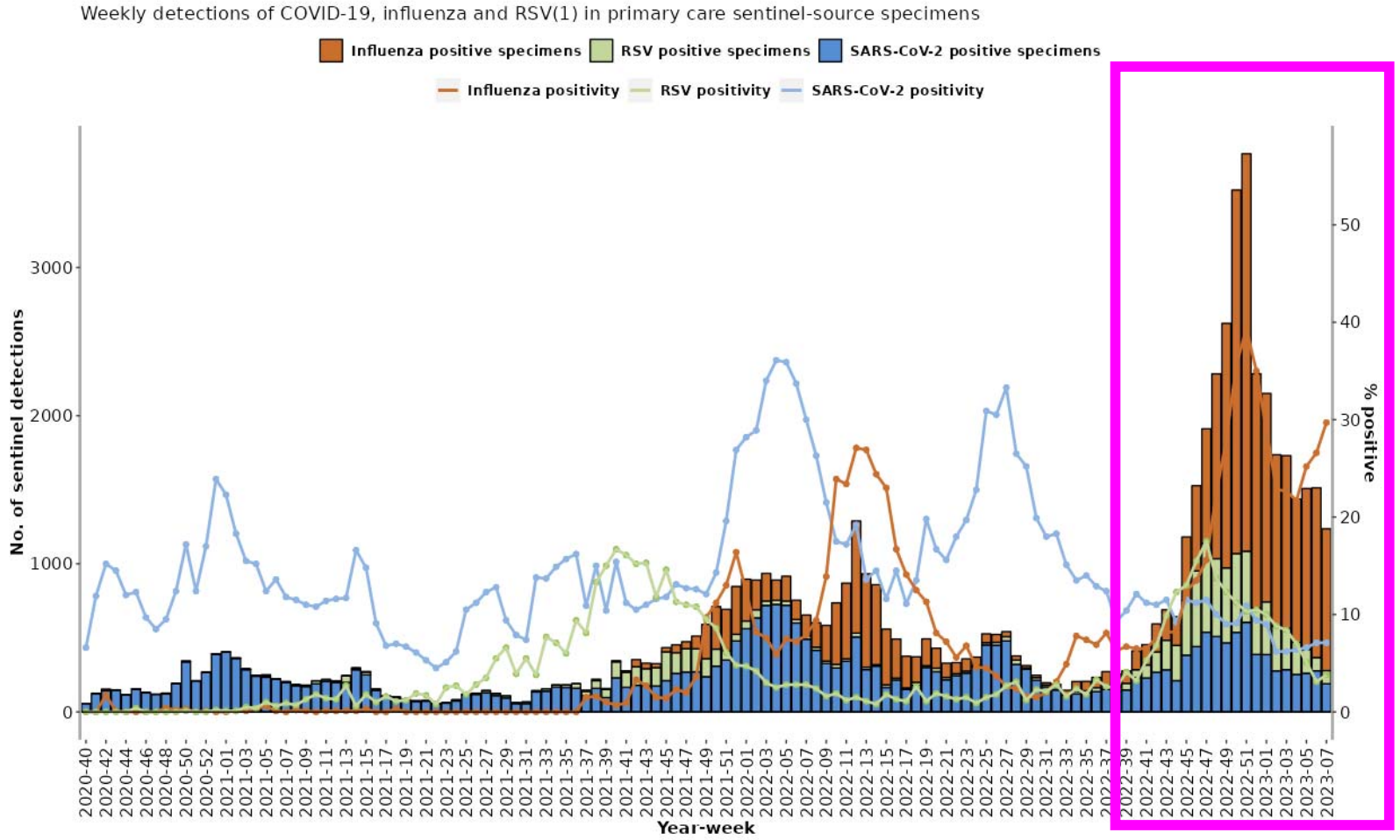
SARS-CoV-2 *vs.* Flu *vs.* RSV Sentinel Surveillance in Europe

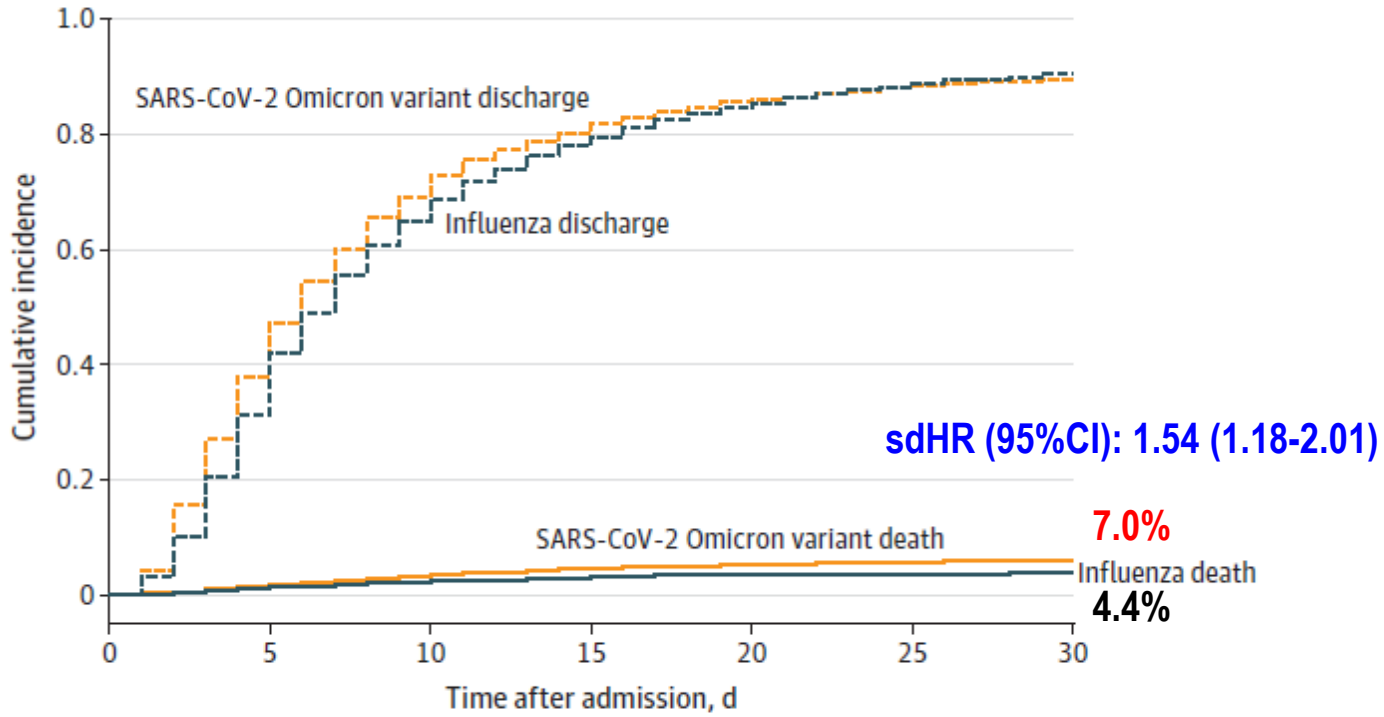


1-RSV: Respiratory Syncytial Virus

https://worldhealthorg.shinyapps.io/euro-covid19/ – February 26th 2023

Hospital COVID-19 *vs.* Influenza Outcomes in Switzerland

Figure 2. Cumulative Incidence Plot for Mortality



sdHR (95%CI): 1.54 (1.18-2.01)

7.0%

4.4%

No. at risk

SARS-CoV-2 Omicron variant	3066	1853	848	468	280	187	144
Influenza	2146	1447	705	410	260	175	125

Portmann L et al. JAMA Network Open. 2023;6(2):e2255599 February 15th 2023

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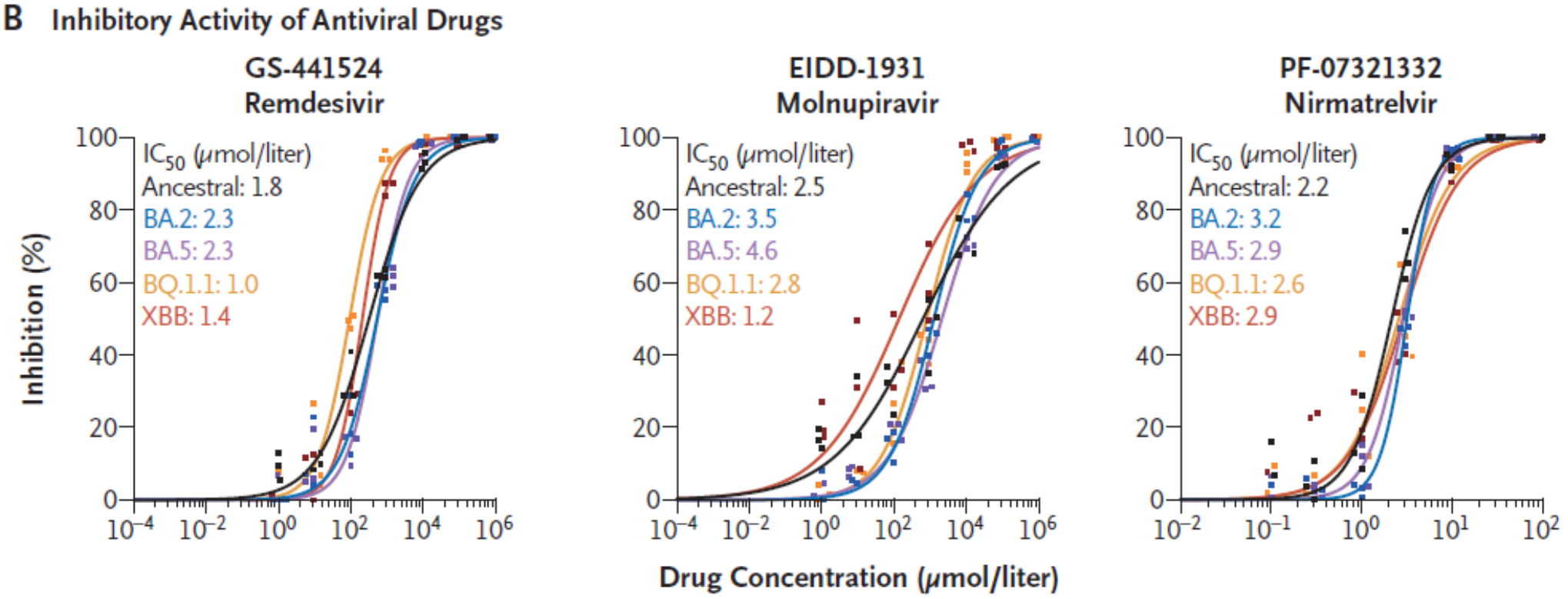
Antiviral Agents are active against Omicron Subvariants BQ.1.1 and XBB



Imai M et al. NEJM. January 5th 2023; 388:89-91.

Antiviral efficacy in non-vaccinated individuals

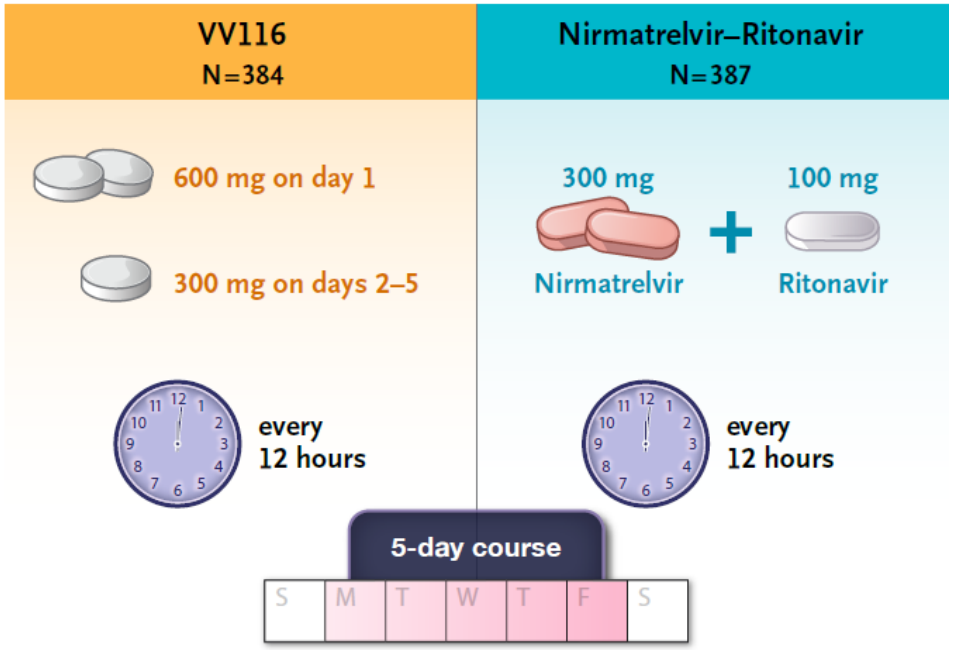
	Remdesivir PINETREE	Molnupiravir MOVE-OUT	Nirmatrelvir/rtv EPIC-HR
Efficacy	**87%**	**30-65%**	**87%**
Administration	**Intravenous (IV), 3 d.**	Oral, 5 d. (40 tablets)	Oral, 5 d. (30 tablets)
Advantages	Highly efficacious Studied in pregnancy Few/No DDI	No DDI	Highly efficacious Ritonavir safe in pregnancy
Disadvantages	**IV infusion** for 3 days	**Lowest efficacy** Not recommended in pregnancy/children	Important **DDI**
NNT	**18**	**31/36**	**18**

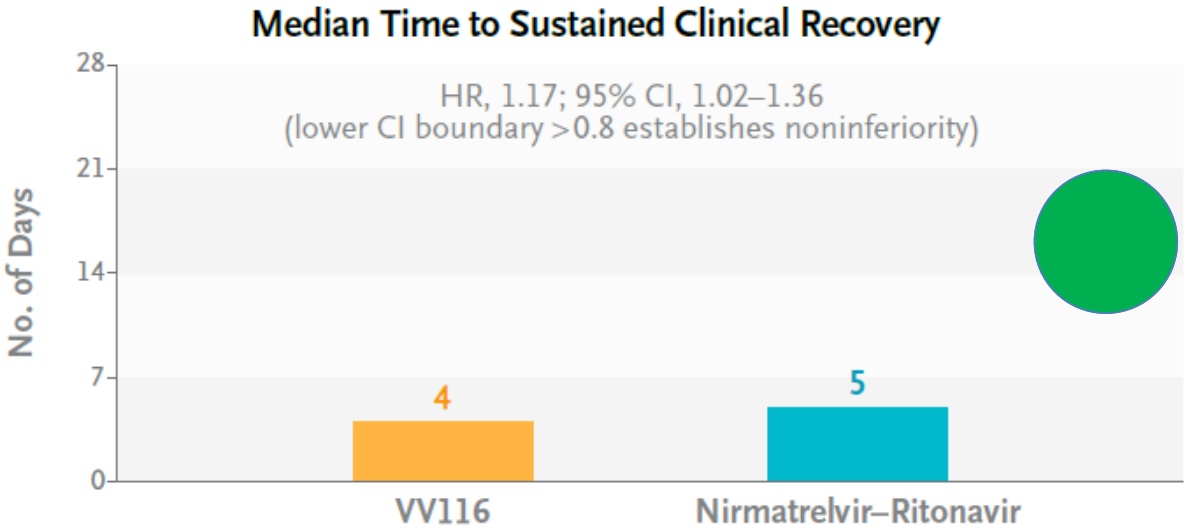
*Relative risk reduction hospitalization/death; NNT=Number needed to treat; DDI = Drug-drug interactions; rtv = ritonavir

Adapted from Gandhi RT et al. JAMA. 2022; 327:617-618; Bernal AJ et al, N Engl J Med. Dec 16, 2021; Gottlieb RL, et al. NEJM. Dec 22 2021; Hammond J, et al. N Engl J Med. Feb 16 2022.

VV116 (oral remdesivir analogue) *vs.* Nirmatrelvir–Ritonavir for Oral Treatment of Covid-19

- A **phase 3 multicenter, open-label, randomized, noninferiority trial assessed the efficacy and safety of VV116** as compared with nirmatrelvir–ritonavir in adults hospitalized with Covid-19 during an outbreak of SARSCoV-2 dominated by the B.1.1.529 (omicron) variant.
- The **primary efficacy end point** was the **time from randomization to sustained clinical recovery** (alleviation of all Covid-19–related target symptoms for 2 consecutive days) through day 28. ClinicalTrials.gov number, NCT05341609; Chinese Clinical Trial Registry number, ChiCTR2200057856





Cao Z et al. N Engl J Med. Feb 2 2023; 388: 406-417.

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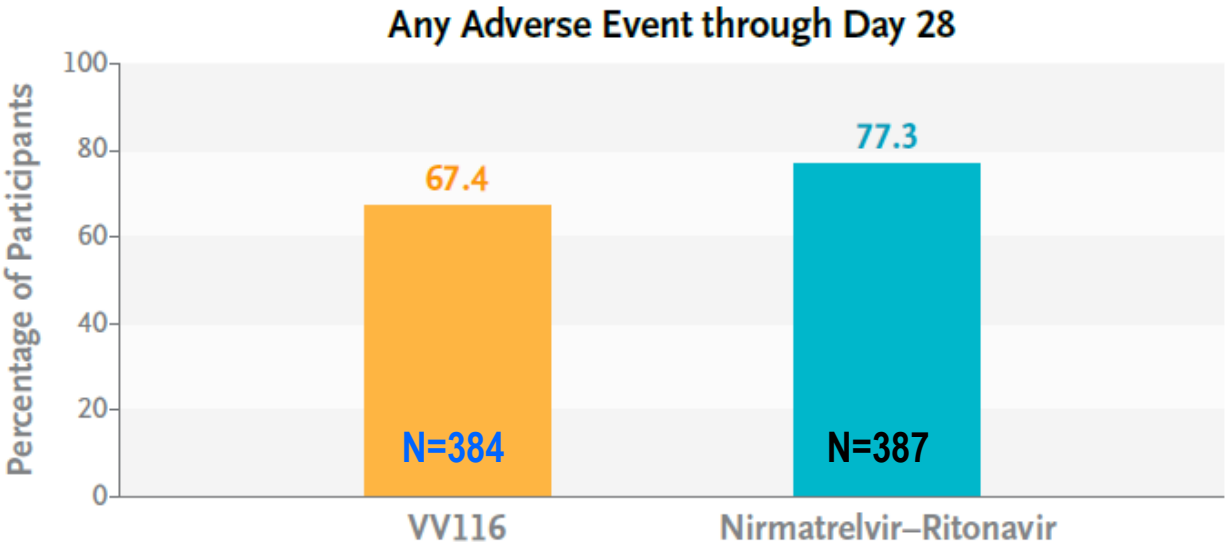


- In symptomatic adults hospitalized with mild-to-moderate Covid-19 and at risk for disease progression, **a 5-day course of VV116 was noninferior to nirmatrelvir–ritonavir** with **respect to the time to sustained clinical recovery** and **was associated with fewer adverse events**.

Cao Z et al. N Engl J Med. Feb 2 2023; 388: 406-417.

PANORAMIC trial: Molnupiravir fails to prevent COVID-19 hospitalization in vaccinated patients in UK

- **Same design, criteria and dosage as in the MOVE-OUT RCT** but this was an open-label trial: **oral Molnupiravir for 5 days** *vs.* Standard of Care (SoC)
  → **93% of individuals had received a booster COVID-19 vaccine; 99% at least one dose.**
- **The primary efficacy endpoint hospitalization or all-cause death by day 29**.
- Median age 57 yr., 58% females; any comorbidity, 69% of participants; **median (IQR) time between symptoms onset to molnupiravir/SoC: 3 days (3-5).**

Outcomes at 29 days	Molnupiravir N=12,774	SoC N=12,934	*P*-value
- Hospitalization/Death	105 (0.8%)	98 (0.8%)	0.33
- Mortality	3	5	
- Severe adverse events	77 (0.6%)	64 (0.5%)	

→ **Molnupiravir did not reduce hospitalization/death in COVID-19 vaccinated individuals. No differences in subgroup analysis**

Molnupiravir is not approved by the EMA, it is in the review phase.

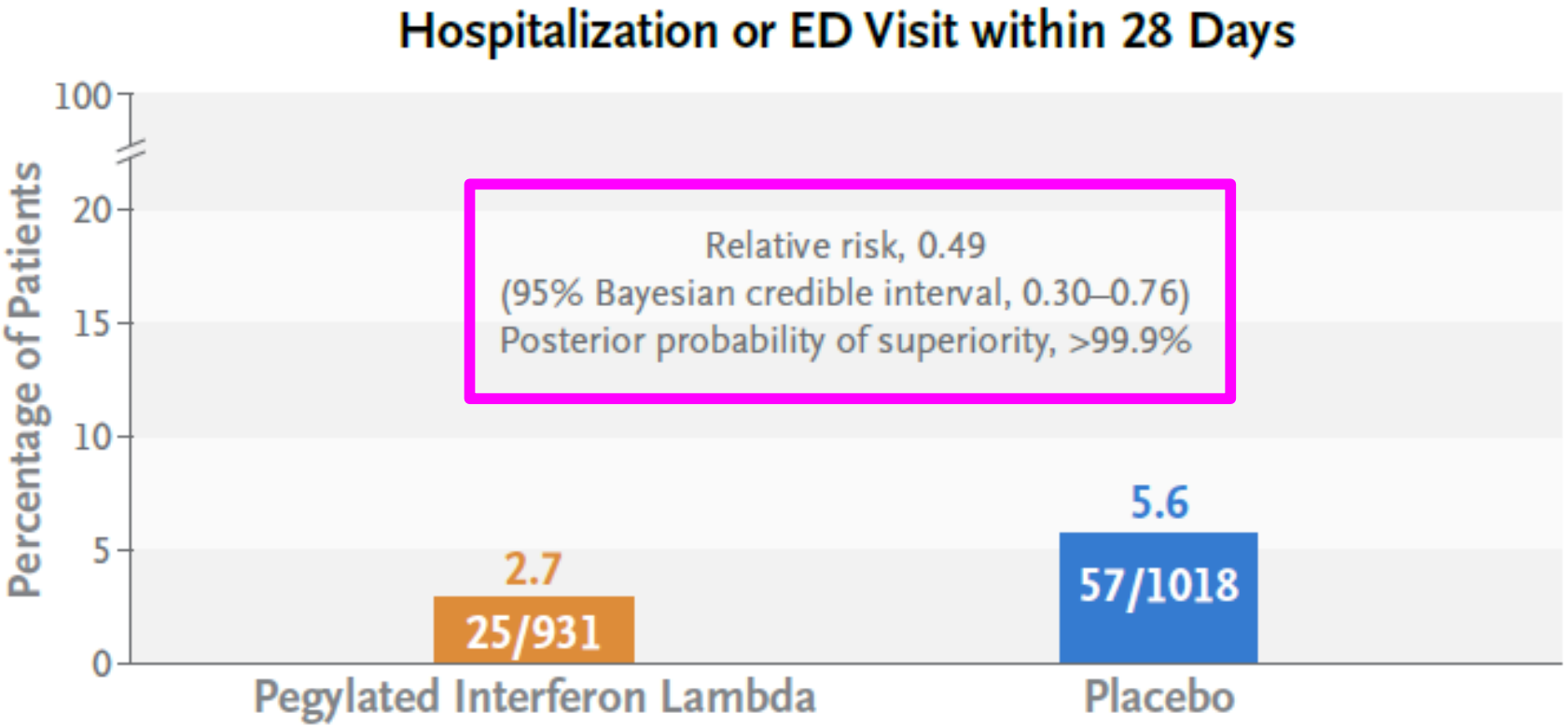
Butler CC on behalf the PANORAMIC Trial Investigators. Lancet. December 22nd 2022

Early Treatment with Pegylated Interferon Lambda for Covid-19 in vaccinated individuals

- A phase 3, adaptive platform, **randomized, placebo-controlled trial** assessed the efficacy and safety of pegylated interferon lambda in adult outpatients in **Brazil and Canada** who were at high risk for severe illness soon after they received a diagnosis of Covid-19.
- 1,949 adults presenting within 7 days after symptom onset with a positive rapid test for SARS-CoV-2 and with at least one high-risk criterion (e.g., age ≥50 years, diabetes mellitus, and hypertension leading to the use of medication) were assigned to receive a **single subcutaneous injection of pegylated interferon lambda (180 µg) or placebo**. **Most patients (85%) had received at least one dose of Covid-19 vaccine.**
- The primary outcome was a composite of Covid-19–related hospitalization (or referral to a tertiary hospital) or admission to an emergency department (ED) (observation for >6 hours) within 28 days after randomization. **TOGETHER ClinicalTrials.gov number, NCT04727424**

Reis G et al. N Engl J Med. Feb 9th 2023;388(6):518-528; Reis G et al. CROI Feb 19-22 2023; Abstract #167.

Early Treatment with Pegylated Interferon Lambda for Covid-19 in vaccinated individuals



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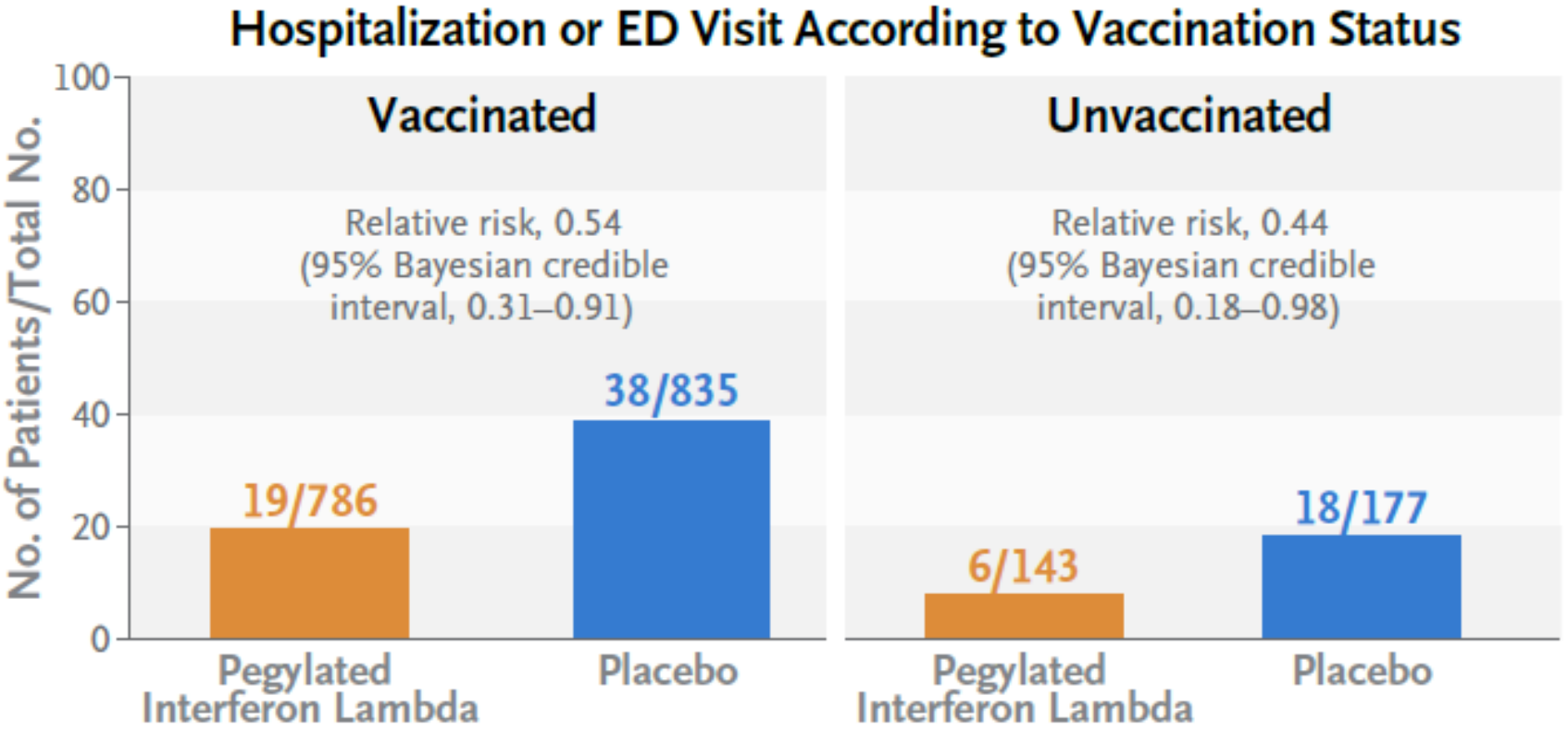

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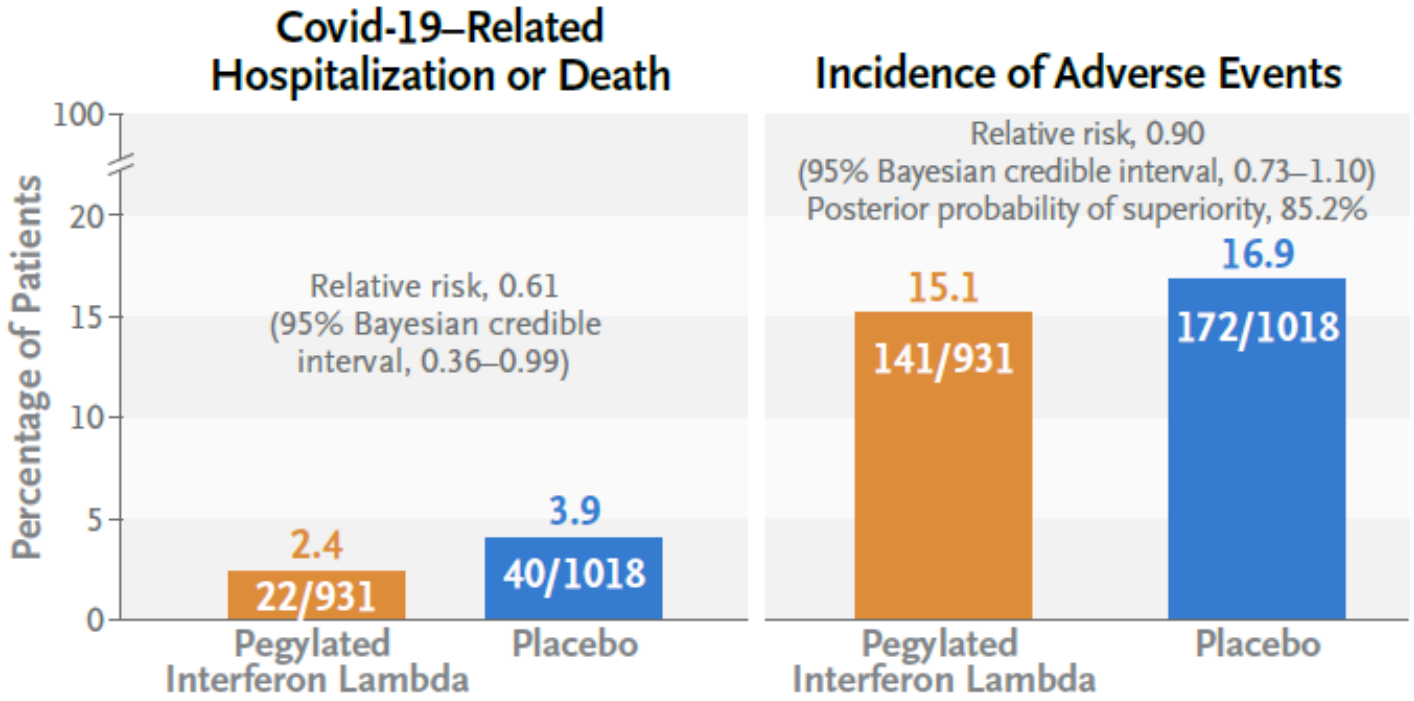


- Among high-risk, symptomatic, largely vaccinated outpatients with a recent diagnosis of Covid-19, those who received **a single subcutaneous injection of pegylated interferon lambda had a lower risk of Covid-19–related hospitalization or an ED visit within 28 days** than those who received placebo.

Reis G et al. N Engl J Med. Feb 9th 2023;388(6):518-528; Reis G et al. CROI Feb 19-22 2023; Abstract #167.

Ensitrelvir (protease inhibitor): effective and safe in mild/moderate COVID-19 in vaccinated patients in Asia

- Ensitrelvir fumaric acid (Xocova®), an investigational, **3CL protease inhibitor**, administered within first three days for 5 days, was evaluated as an antiviral treatment for COVID-19, achieved the primary endpoint in the Phase 3 part of a Phase 2/3 study conducted in Asia.
- This study was conducted in **1,821 patients with mild/moderate symptoms of COVID-19** and assessed clinical symptom resolution with ensitrelvir (high dose and low dose), orally administered once daily for five days, compared to placebo. **The majority of patients were previously vaccinated**.
- **The primary endpoint:** time to resolution of five key COVID-19 symptoms (stuffy or runny nose, sore throat, cough, feeling hot or feverish, and low energy or tiredness)

Outcomes	Ensitrelvir 125 mg; n=336	Ensitrelvir 250 mg; n=329	PBO n=321	*P*-value
- Time to resolution (hours)	168	171	192	0.04
- ↓ Viral load (log10 copies/mL) on day 4	-2.48	ND	-1.01	<.0001

- **Safety**: ensitrelvir were well tolerated, and there were no serious adverse events or deaths in this study. The most common treatment-related adverse events were decreased high-density lipoprotein (HDL) and increased blood triglycerides.
- **NIAID** is evaluating this antiviral in the outpatient population **(ACTIV-2 SCORPIO-HR clinical trial).**

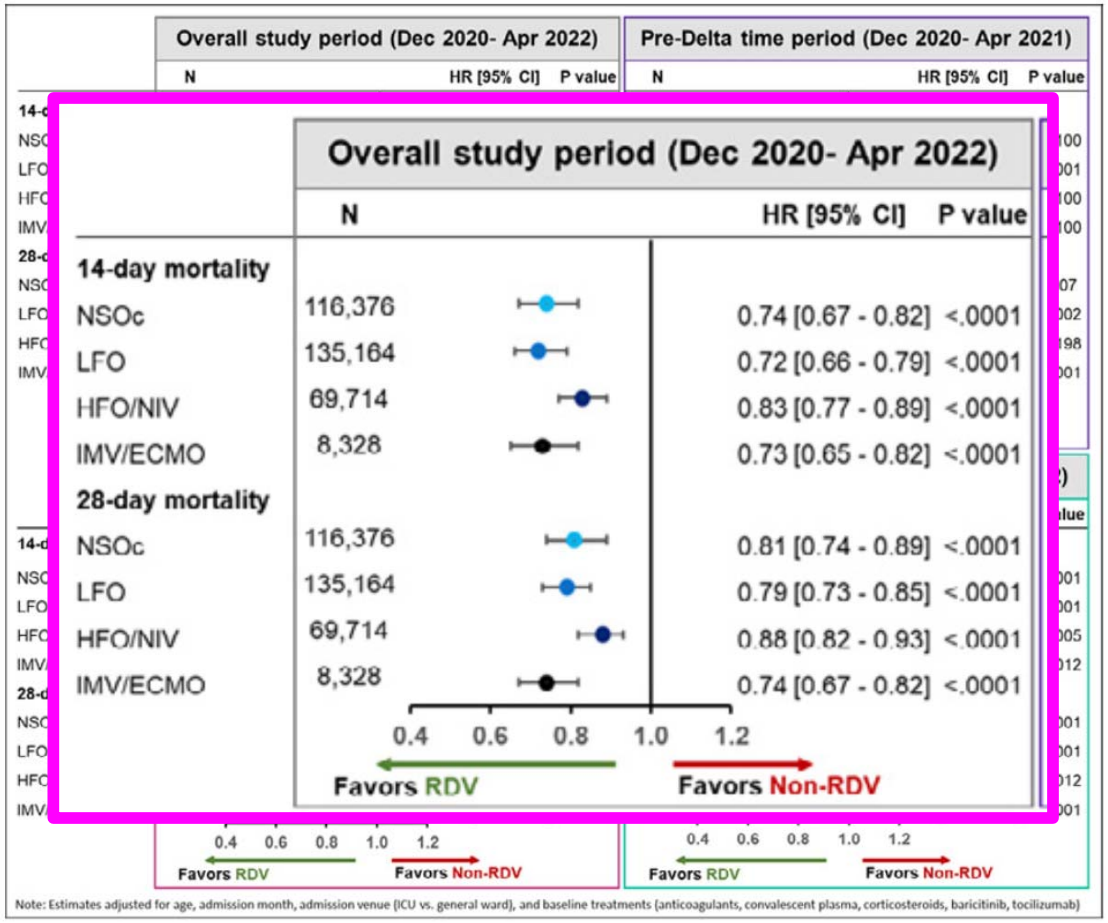
Shionogi press release, OSAKA, Japan, September 28, 2022; Ichihashi G et al. et al. CROI Feb 19-22 2023; Abstract #166.

Remdesivir Reduces Mortality in Hospitalized Covid-19 Patients Across Variant SARS-CoV-2 Eras

Figure: Time to 14- and 28-day mortality across the COVID-19 variant periods (adjusted Cox Proportional Hazards model)

- **Pre-Delta**
- **Delta**
- **Omicron**

Time to mortality was examined for 164,791 RDV-treated patients that were matched to 48,473 unique non-RDV patients with no supplemental oxygen charges (NSOc), low-flow oxygen (LFO), high-flow oxygen/non-invasive ventilation (HFO/NIV) and invasive mechanical ventilation/ECMO (IMV/ECMO) at baseline. Baseline was defined as first 2 days of hospitalization.

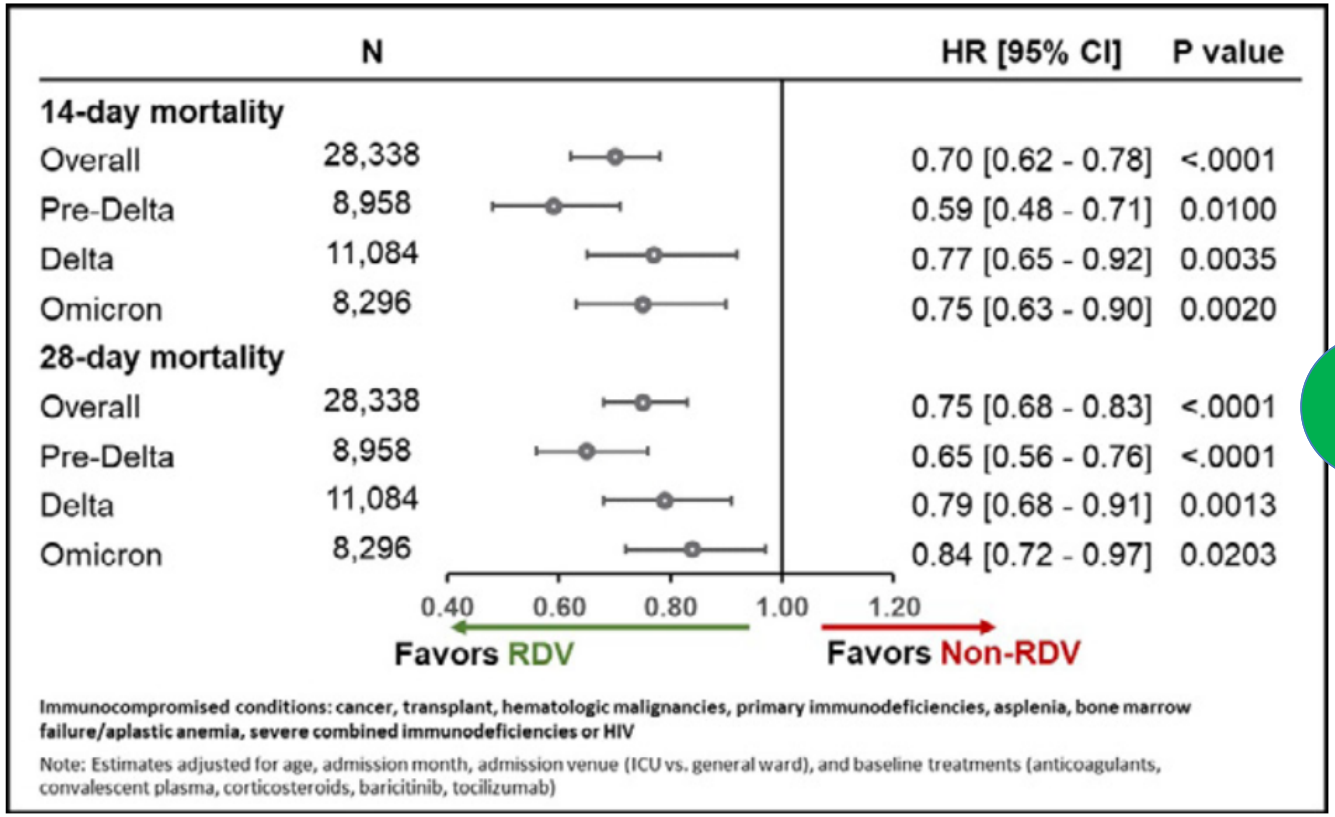


Mozaffari E et al. CROI Feb 19-22 2023; Abstract #556.

Remdesivir Reduces Mortality in Immunocompromised Patients Hospitalized for Covid-19

Figure: Time to 14- and 28-day mortality across the COVID-19 variant periods (adjusted Cox Proportional Hazards model)

14,169 RDV-treated patients with an immunocompromised condition (cancer, solid organ and hematopoietic stem cell transplant, hematologic malignancies, primary immunodeficiencies, asplenia, bone marrow failure/aplastic anemia, severe combined immunodeficiencies or HIV) hospitalized with a primary diagnosis of COVID-19 were matched to 5,341 unique non-RDV patients. Baseline was defined as first 2 days of hospitalization.



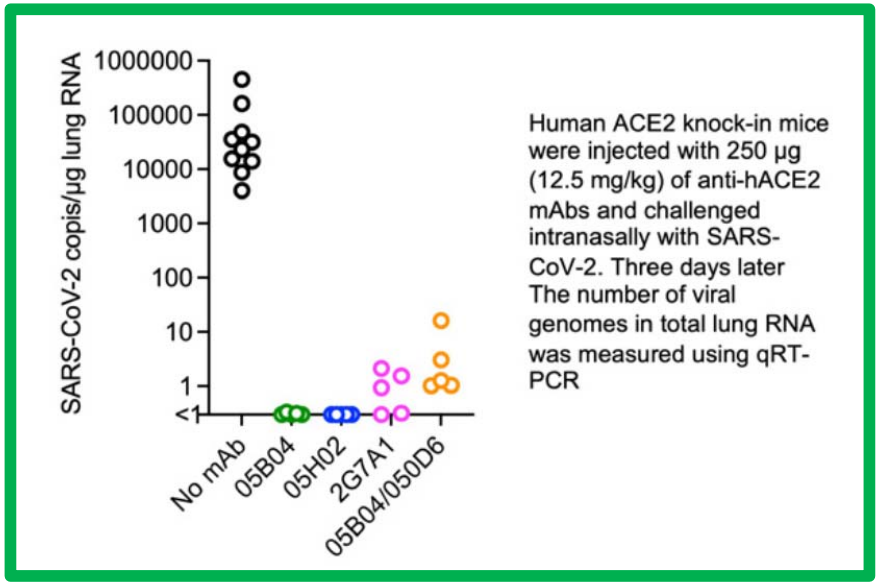
Mozaffari E et al. CROI Feb 19-22 2023; Abstract #557.

Other therapeutic pearls

- **Metformin reduced SARS-CoV-2 VL[1]**
  Antiviral potency ≈ nirmatrelvir/ritonavir
- **Inhaled Interferon-β1A does not work in outpatients with mild/moderate COVID-19[2]**
- **Remdesivir, no dose adjustment is recommended in patients with eGFR<30 mL/min regardless the need of dialysis[3]**
- **Zinc adjuvant treatment during acute pase reduced severity and increased faster recovery hospitalized COVID-19 patients[4]**

- **Human anti-ACE2 mAbs as Pan-Sarbecovirus agents in mice[5]**

The antibodies do not inhibit hACE2 enzymatic activity, nor do they induce ACE depletion from cell surfaces.



1.- Boulware DR et al. et al. CROI Feb 19-22 2023; Abstract #170; 2.- Jagannathan P et al. CROI Feb 19-22 2023; Abstract #169; 3.-Humeniuk R et al. CROI Feb 19-22 2023; Abstract #514; 4.-Gómez-Zorrilla S et al. CROI Feb 19-22 2023; Abstract #542; 5.- Zhang F et al. CROI Feb 19-22 2023; Abstract #109.

30th CROI 2023
Conference on Retroviruses and Opportunistic Infections
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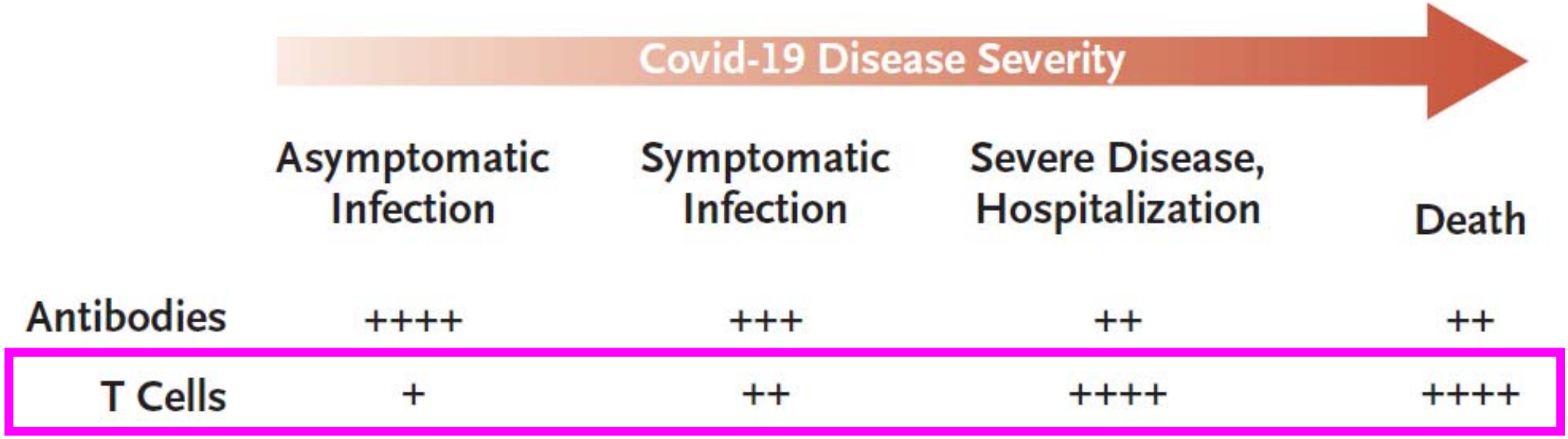
Update on the Epidemiology and Response of Vaccines against COVID-19

- Current epidemiology in a vaccinated world
- New Omicron variants: BQ.1 & XBB.1.5 / China
- Some clinical pearls
- Some therapeutic pearls
- **Response to vaccines in the Omicron era**
- Take-home messages

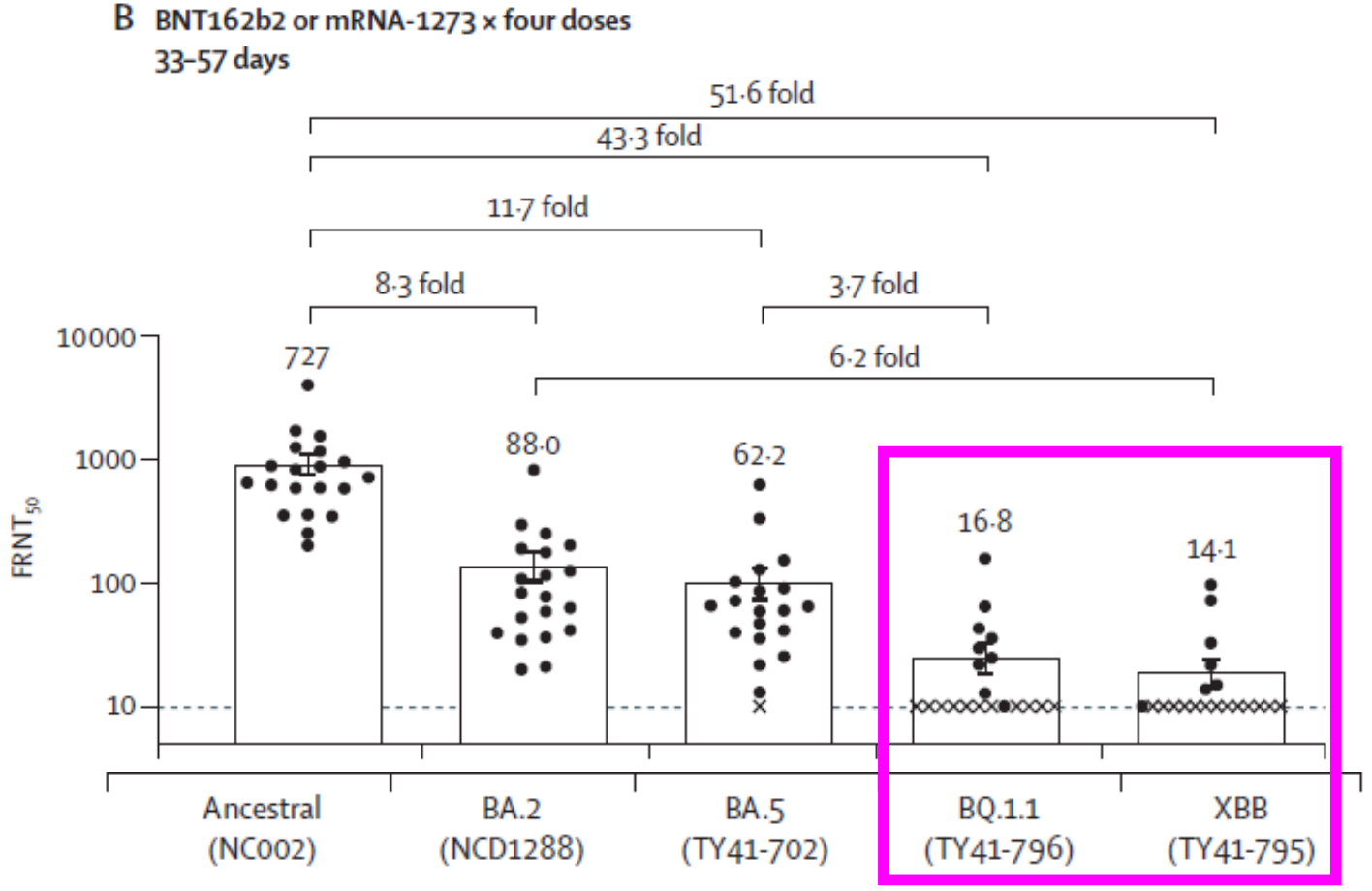
March 2nd 2023

Immune Responses for Protection against Severe SARS-CoV-2



Barouch DH. N Engl J Med. Sep 15, 2022; 387:1011-1020.

Humoral immune evasion of the omicron subvariants BQ.1.1 and XBB after four mRNA monovalent doses



PLHIV with hybrid immunity and a fourth COVID-19 vaccine dose had the highest neutralization of Omicron-BA.5 and BQ.1 variants

Uraki R et al. Lancet ID. Dec 7th 2022; Cheung PK et al. CROI Feb 19-22 2023; Abstract #366.

Rationale for New Bivalent Booster Vaccines

Goals of new bivalent booster vaccines[1,2]

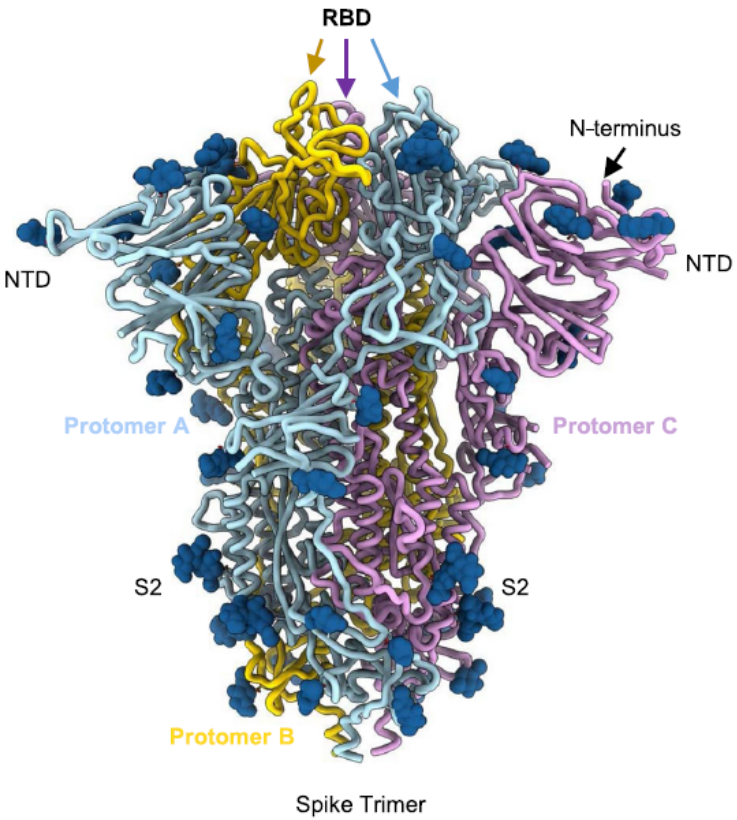
- Retain neutralization for Original SARS-CoV-2
- Stronger immune response against current omicron variants
- Broader cross-neutralization against future variants
- Provide broad protection and sterilizing mucosal immunity
- Extend durability of protection

1. FDA Briefing Document for June 26, 2022 VRBPAC Meeting.
2. WHO Interim Statement on the Composition of Current COVID-19 Vaccines, June 17, 2022.

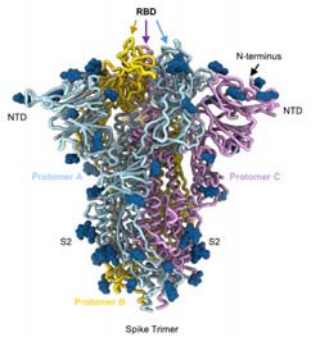
Pfizer and Moderna Bivalent Vaccines against Covid-19

Monovalent mRNA vaccines
Original SARS-CoV-2 Spike

D614G, 30/50 µg



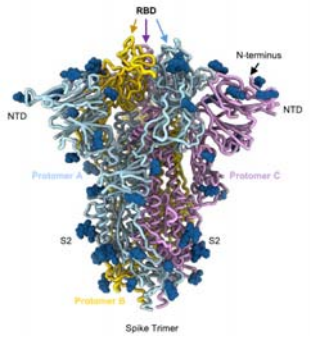
Bivalent mRNA vaccines



Original SARS-CoV-2

D614G, 15/25 µg

+



Omicron variants

Pfizer: BA4/5, 15 µg

Moderna: BA1, BA4/5 25 µg

Kleanthous H et al. NPJ Vaccines. Oct 28, 2021; 6:128.

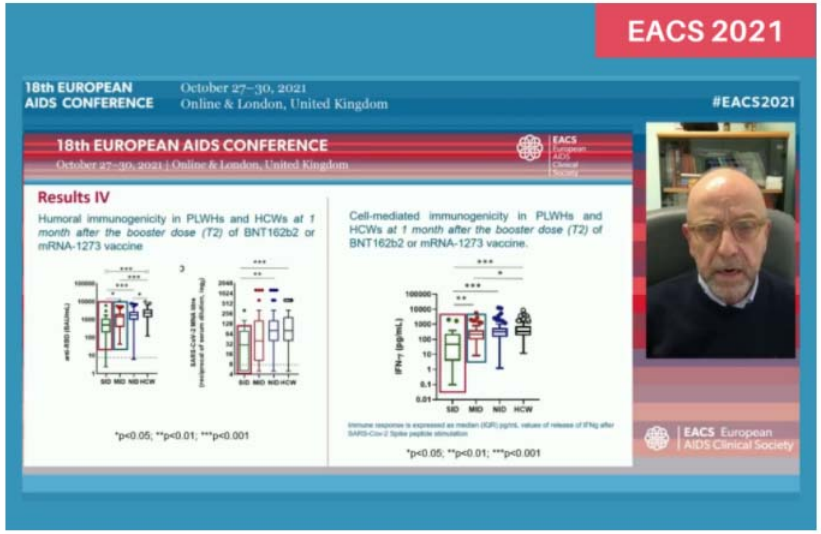
PLHIV with CD4 counts below 200 showed weaker responses to COVID-19 Vaccines and are Candidates to 3rd Dose

Vaccinations & immunisations

People with HIV with CD4 counts below 200 show weaker responses to COVID-19 vaccines

Findings reinforce advice on third vaccine dose for people with low CD4 counts

Keith Alcorn | 1 November 2021



Dr Andrea Antinori presenting to EACS 2021.

People with CD4 counts below 200 were significantly less likely to generate strong antibody and cellular immune responses to the Pfizer or Moderna mRNA COVID-19 vaccines compared to people with better immune function, Italian researchers reported on Friday at the 18th European AIDS Conference (EACS 2021) in London.

Coronavirus

Some people with HIV may have weaker response to COVID-19 vaccines

Liz Highleyman | 14 October 2021

Dr Matthew Spinelli presenting to IDWeek 2021

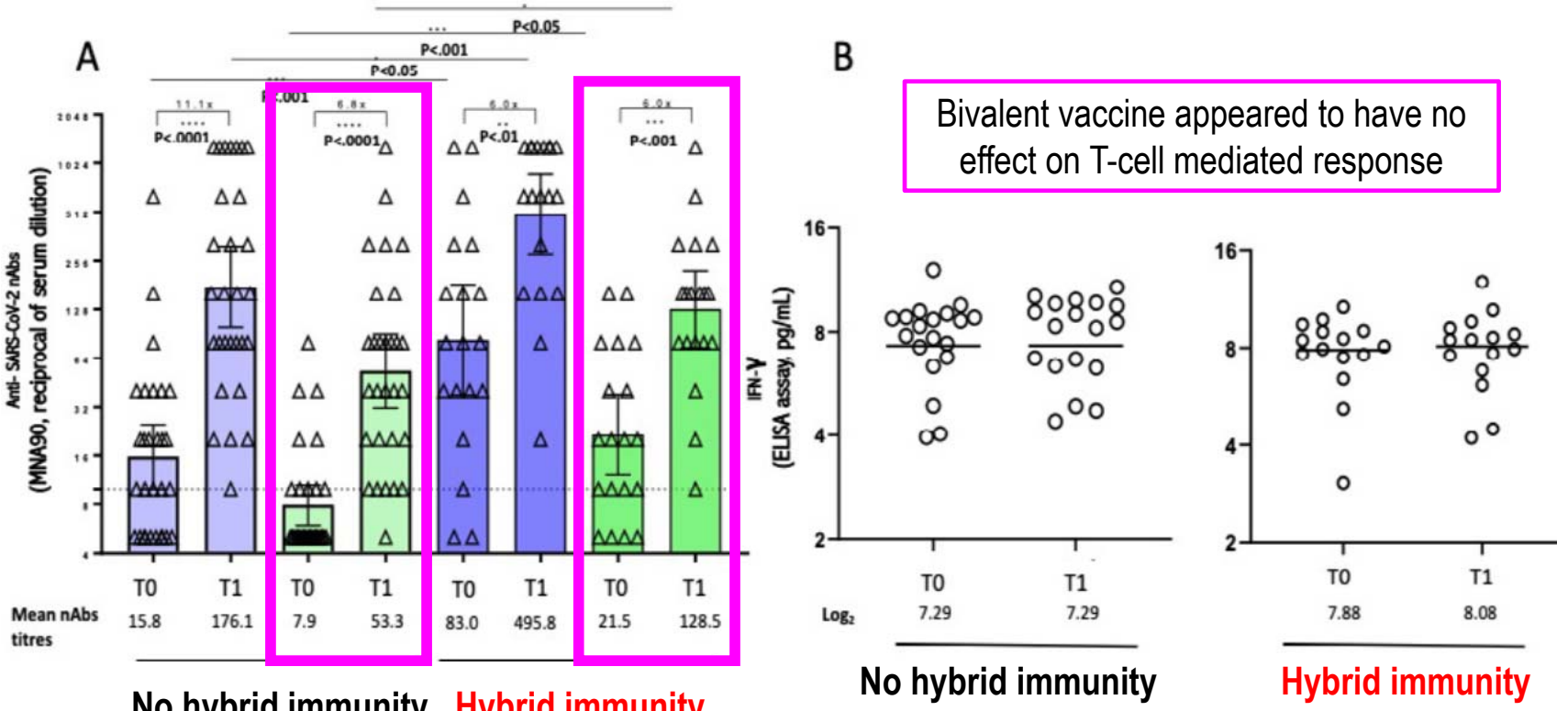
People living with HIV had lower than expected antibody levels after receiving the Pfizer or Moderna COVID-19 vaccines, according to study results presented last week at the virtual IDWeek meeting. Those with a detectable viral load or a low CD4 T-cell count were at greater risk for diminished response, supporting a third vaccine dose for these individuals.

- Public health authorities in the United States and Europe already recommend a third dose of a vaccine against SARS-CoV-2 for PLHIV with immune suppression but there is still a lack of clarity about below which CD4 threshold a 3rd dose is needed.
- Antibody levels and neutralization responses were significantly lower in **PLHIV with CD4 counts below 200** compared to people with CD4 counts above 200, one month after the second dose.

Antinori A et al, 18th EACS. London. 2021.

Neutralizing Activity and T Cell Response After Bivalent mRNA Third Booster Dose in PLHIV

Mean values of MNA90 and IFN-γ from T0 to T1 according to hybrid immunity



Blue plots represent nAbs against **BA.5**,
Green plots represent nAbs against **BQ.1.1.**

Vergori A et al. CROI Feb 19-22 2023; Abstract #364.

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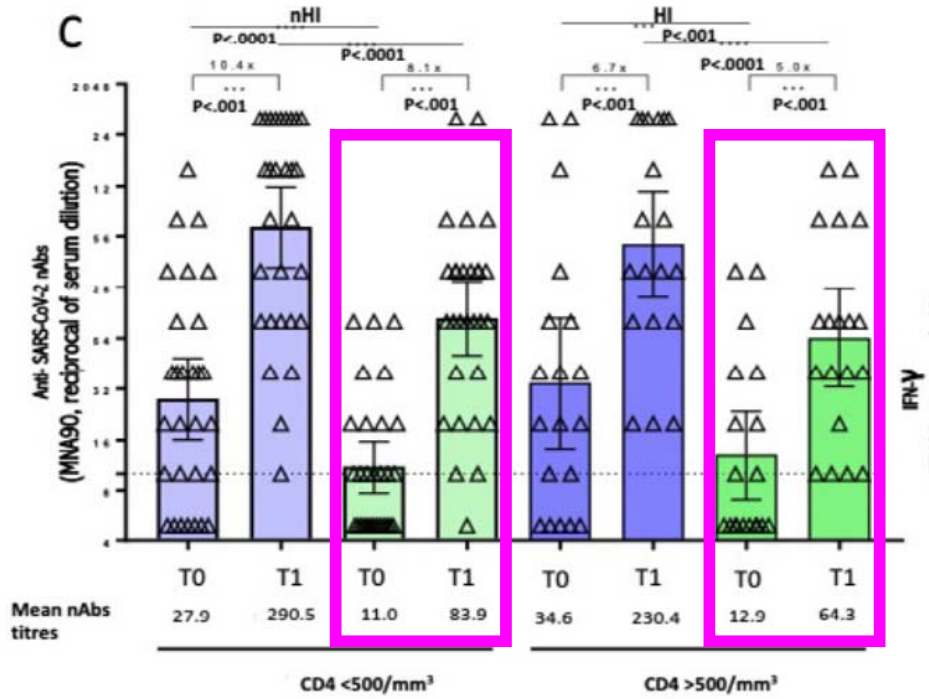
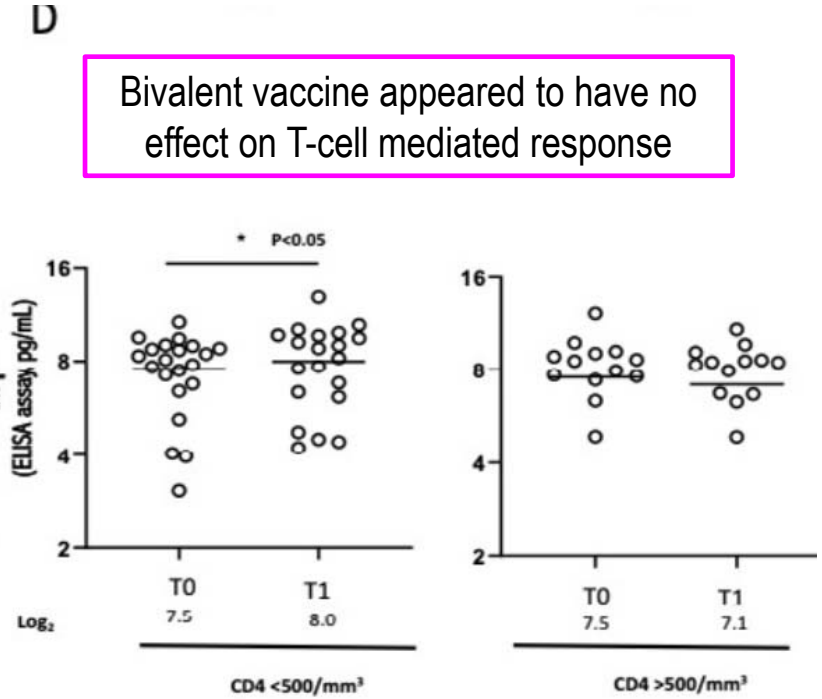


CD4<500/mm3 CD4≥500/mm3



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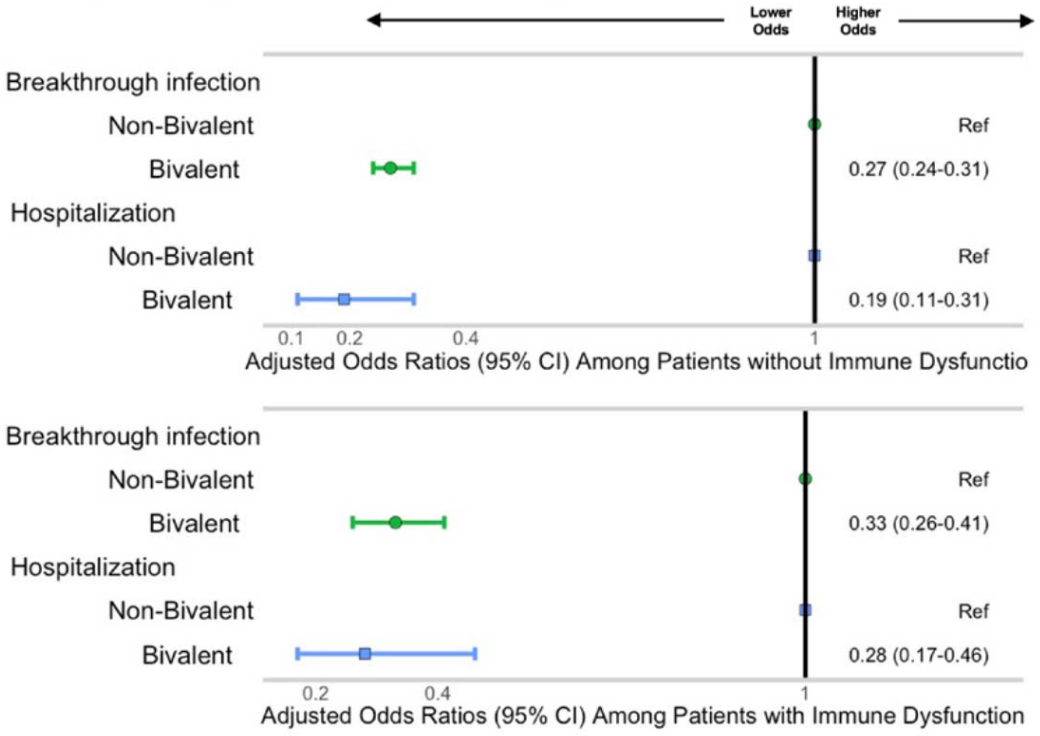
Vergori A et al. CROI Feb 19-22 2023; Abstract #364.

COVID-19 Bivalent Booster Effectiveness in People with and without Immune Dysfunction (including PLHIV)

- We estimated **bivalent mRNA booster effectiveness** against breakthrough infection and hospitalization between 09/01/2022 to 12/15/2022 in **75,873 patients** among 2,414,904 patients had received 2+ doses of mRNA vaccination.
- At baseline, the median age was 52 (IQR 36-67) years, 40% male, 63% white, 10% Black, 12% Latin, 3.5% Asian American/Pacific Islander, and **14% were patients with immunosuppressed/compromised conditions (ISC; HIV infection, solid organ/bone marrow transplant, autoimmune diseases, and cancer).**



* All models controlled for age, sex, race/ethnicity, comorbidities, geographic region, prior SARS-CoV-2 infection, months since the last dose of non-bivalent vaccine, and prior non-bivalent booster.

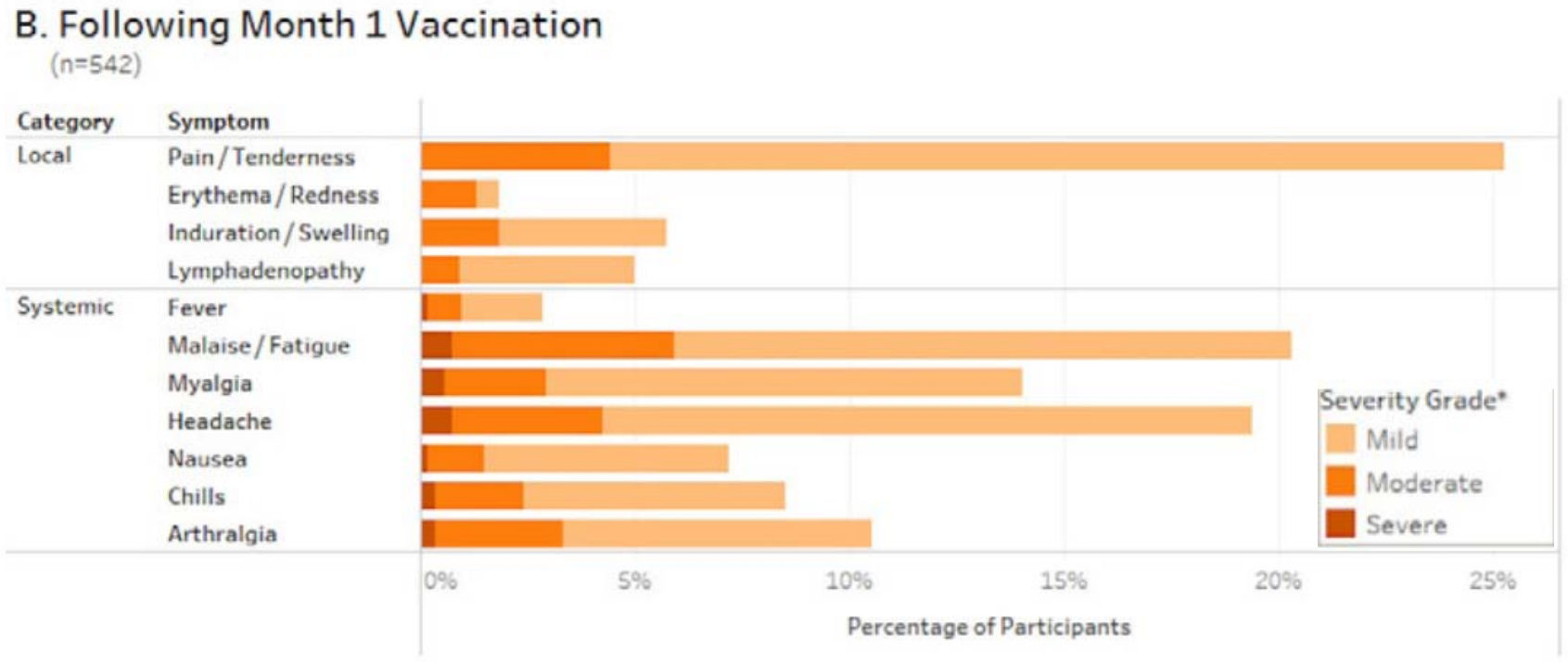
No Immune Dysfunction (HR [95%CI])
- **Infection 0.27 (0.24-0.31)**
- **Hospitalization 0.19 (0.11-0.31)**

With Immune Dysfunction (HR [95%CI])
- **Infection 0.33 (0.26-0.41)**
- **Hospitalization 0.28 (0.17-0.46)**

Sun J et al. CROI Feb 19-22 2023; Abstract #214.

Reactogenicity among PLHIV after mRNA-1273 vaccination Sub-Saharan Africa (N=14,002)

- Similar to observations in HIV-negative populations, mRNA-1273 was well tolerated by PLHIV with **more reactogenicity in females**.
- Impaired inflammatory responses among **PLHIV with CD4 counts < 500 cell/µL had less moderate/severe reactions**.



*Events were graded using the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (2017)

Spinelli MA, et al. CROI Feb 19-22 2023; Abstract #1011.

Factors Associated with SARS-CoV-2 Vaccine Hesitancy in PLHIV in USA – Prevalence 7%

Vaccine hesitancy was reported by approximately 7% of a USA multi-site cohort of PLHIV and decreased over time.

Factor	Adjusted Odds Ratio	95% Confidence Interval	p-value
Female sex at birth	2.04	1.48-2.81	<0.001
Black vs. White Race	1.78	1.28-2.49	0.001
Age< 30 years	2.79	1.49-5.24	0.001
Region vs. Northeast (ref): West	1.23	0.84-1.81	0.29
South/Midwest	1.73	1.23-2.44	0.002
Unsuppressed Viral Load (>200 copies/mL)	2.20	1.41-3.45	0.001
Years on ART (per 5 years)	0.79	0.69-0.86	<0.001
Study month	0.88	0.84-0.93	<0.001

Analyses were adjusted for age, birth sex, race/ethnicity, site, time on ART, viral suppression, and study month.

Spinelli MA, et al. CROI Feb 19-22 2023; Abstract #1011.

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March 2nd 2023

Take-home messages

- The **global epidemiological situation has improved** markedly thanks to **mass vaccination** and the appearance of **less SARS-CoV-2 Omicron pathogenic variants**.
- **BQ.1.1 and XBB.1.5** are the current predominating variants and they **escape the immunity generated by monovalent vaccination with the original strain or previous infection**.
- **Subcutaneous peg-interferon lambda** and **oral ensitrelvir** (protease inhibitor) may be effective for mild/moderate COVID-19 in vaccinated individuals.
- **Bivalent mRNA vaccines provide cross-neutralization** against multiple variants of concern, including Omicron subvariants **BA.1, BA.4/BA.5, BA.2.75, BQ.1.1, and XBB.1.5.**
- **Bivalent mRNA boosters must be given to PLHIV**. Preliminary results showed a good humoral response against new Omicron variants in non-immunocompromised patients, no safety concerns and prevention of SARS-CoV-2 infection and hospital admission.