



COVID 19 in 2022, towards endemicity

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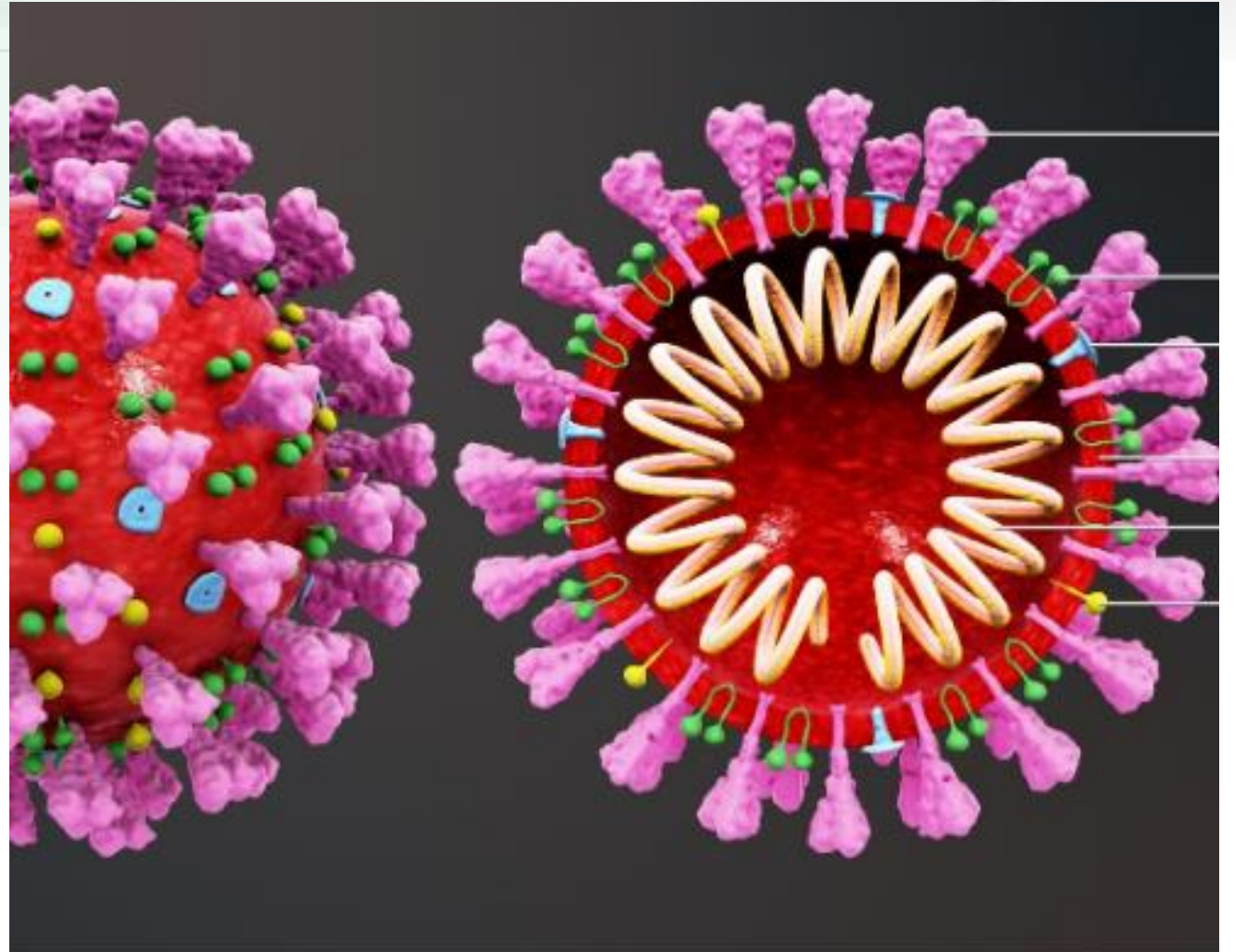
Eun Mi Chun

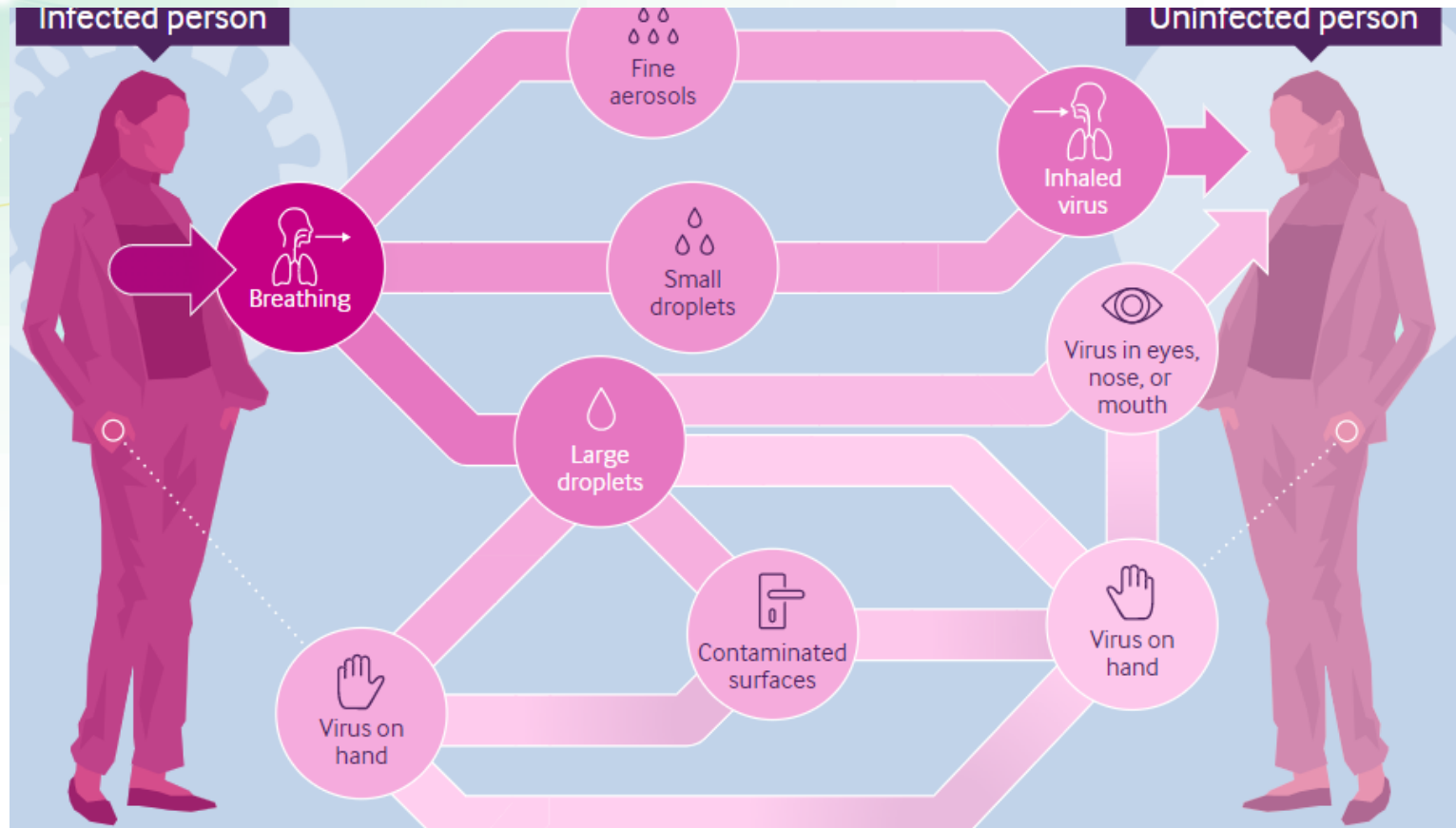




SARS CoV 2

- ① **Transmission route**
- ② **Natural immunity**
- ③ **Prevention methods**
- ④ **Multiple Variants**
- ⑤ **mRNA Vaccines**
- ⑥ **Anti- viral Drugs**
- ⑦ **Reinfection/Post COVID**
- ⑧ **Requirements for endemicity**





SARS-CoV-2 transmission routes

Long-Distance Airborne SARS-CoV-2 Transmission: Not Just Droplets

- Airborne transmission over longer distances may occur via virus-containing **aerosols** with much smaller particle size than droplets.
- Distances up to **15 m**. At the time of transmission, most of the index cases were **asymptomatic or presymptomatic.**
- Strengthen the need for mitigation measures in indoor settings, particularly the use of **adequate ventilation.**

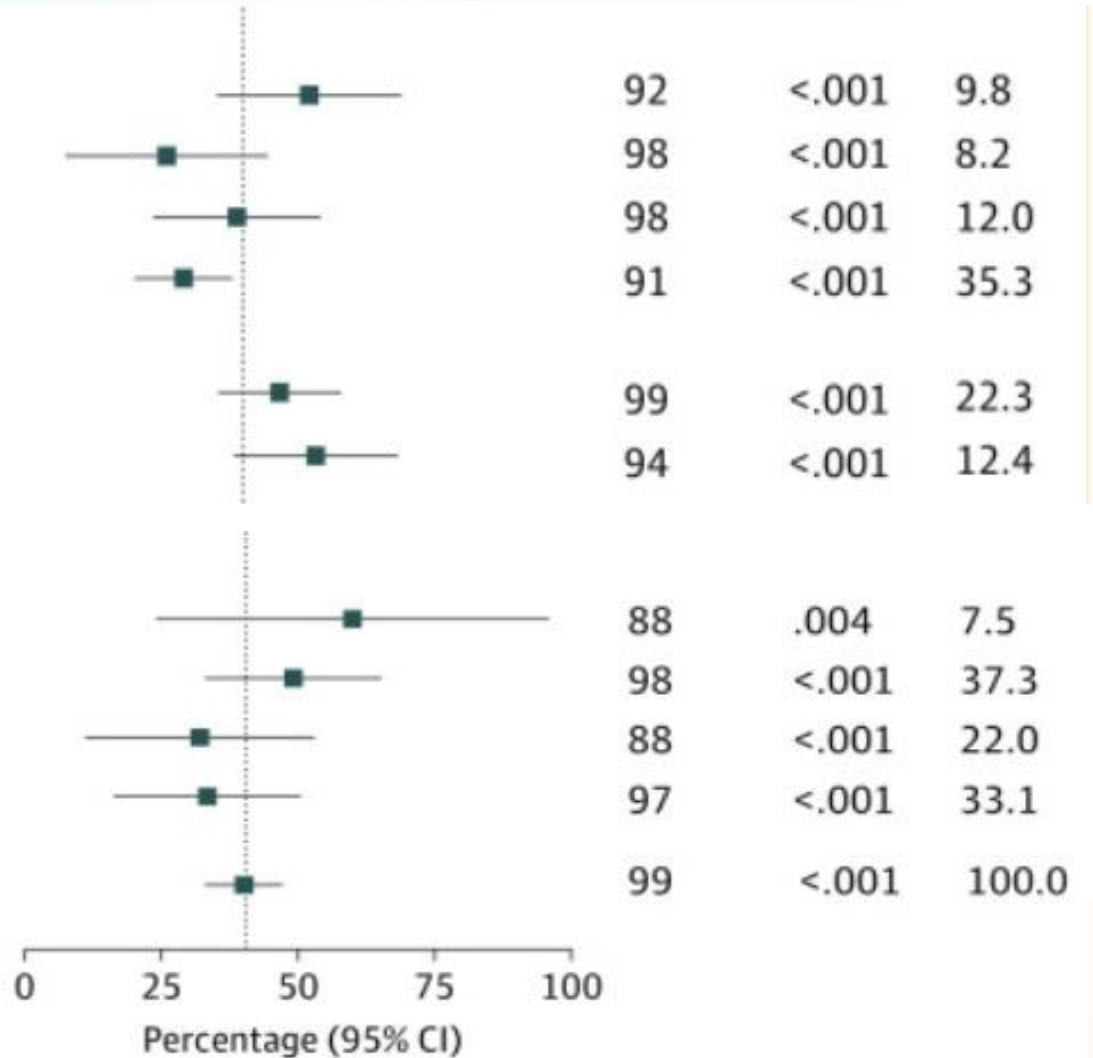
Global Percentage of Asymptomatic SARS-CoV-2 Infections Among Individuals With Confirmed COVID-19 Diagnosis

Study population

Air/cruise travel	8	52.91 (36.08-69.73)
Close contact	6	26.94 (8.50-45.38)
Community residents	9	39.74 (24.50-54.98)
Health care workers/ in-hospital patients	27	30.01 (21.13-38.88)
Nursing home residents/staff	17	47.53 (36.36-58.70)
Pregnant women	10	54.11 (39.16-69.05)

Average age, y

<20	2	60.21 (24.51-95.91)
20-39	9	49.49 (33.48-65.50)
40-59	5	32.48 (11.63-53.34)
≥60	8	33.83 (16.83-50.82)
Combined percentage	77	40.50 (33.50-47.50)



95 studies with 29 776 306 individuals

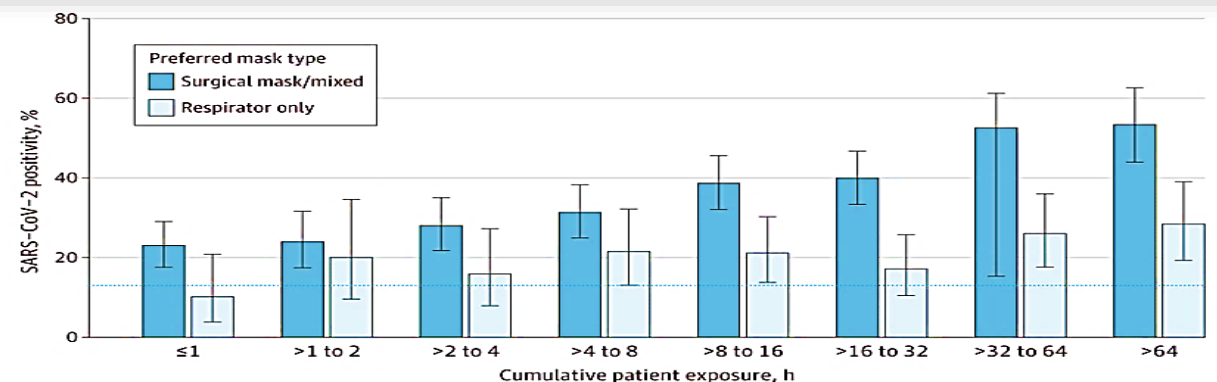


3. Risk of SARS-CoV-2 Acquisition in Health Care Workers According to Cumulative Exposure and Preferred Mask Type

Cumulative patient contact (OR per category), h						
0	720 (33.2)	110 (14.7)				
>0-1	230 (10.6)	59 (7.9)				
>1-2	150 (6.9)	45 (6.0)				
>2-4	189 (8.7)	63 (8.4)				
>4-8	198 (9.1)	79 (10.5)	1.22 (1.18-1.26)	<.001	1.20 (1.14-1.26)	<.001
>8-16	212 (9.8)	104 (13.9)				
>16-32	218 (10.0)	105 (14.0)				
>32-64	135 (6.2)	96 (12.8)				
>64	118 (5.4)	88 (11.7)				
Always respirator (vs surgical/mixed mask use) ^b	506 (23.3)	132 (17.6)	0.57 (0.45-0.73)	<.001	0.56 (0.43-0.74)	<.001
Working ≥80% FTE	1130 (52.1)	430 (57.4)	1.30 (1.07-1.50)	.007	1.39 (1.10-1.77)	.006
Working in intensive care	189 (8.7)	67 (8.9)	1.05 (0.78-1.41)	.75	0.82 (0.57-1.16)	.26
Hospital canteen visit once weekly or more (vs less)	1418 (65.3)	490 (65.4)	1.01 (0.85-1.21)	.88	1.15 (0.91-1.45)	.23
Nonwork-related factors						
SARS-CoV-2 vaccination	1915 (88.2)	577 (77.0)	0.49 (0.39-0.60)	<.001	0.55 (0.41-0.74)	<.001
Positive household contact	165 (7.6)	314 (41.9)	8.82 (7.09-11.0)	<.001	7.79 (5.98-10.15)	<.001

OR:1.2

OR:7.79



Evolution of SARS-CoV-2 Shedding in Aerosols

- **Omicron BA.1** is **three times** more transmissible than Delta
- **Omicron BA.2** is estimated to be **30-40%** more transmissible than BA.1
- The viral RNA load in the **fine fraction was on average five times greater** than in the coarse fraction

Risk of SARS-CoV-2 Transmission Among Healthcare Workers Dining in Hospital Staff Cafeterias

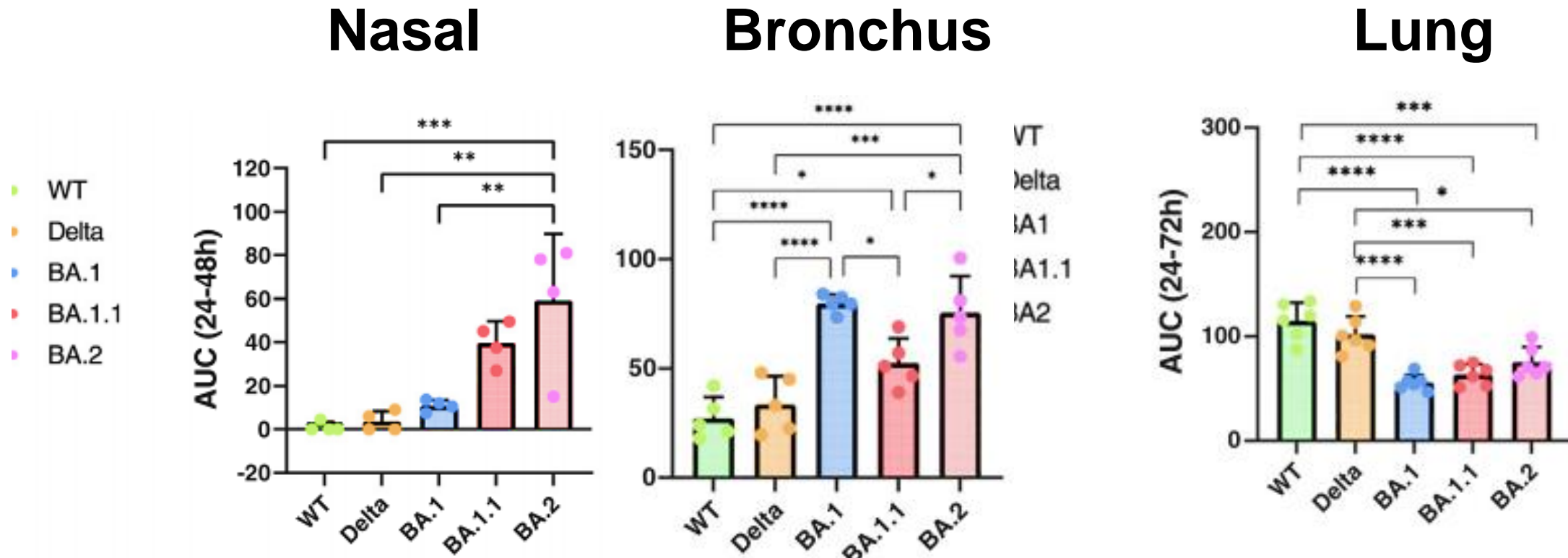
- Setting: A tertiary care hospital with 14,751 healthcare workers (HCWs)
- Cafeterias had good ventilation (air change rate, 13-14 air change/h). Distance between seats was 30 cm. Seats were arranged so the HCWs sit either side without facing each other.



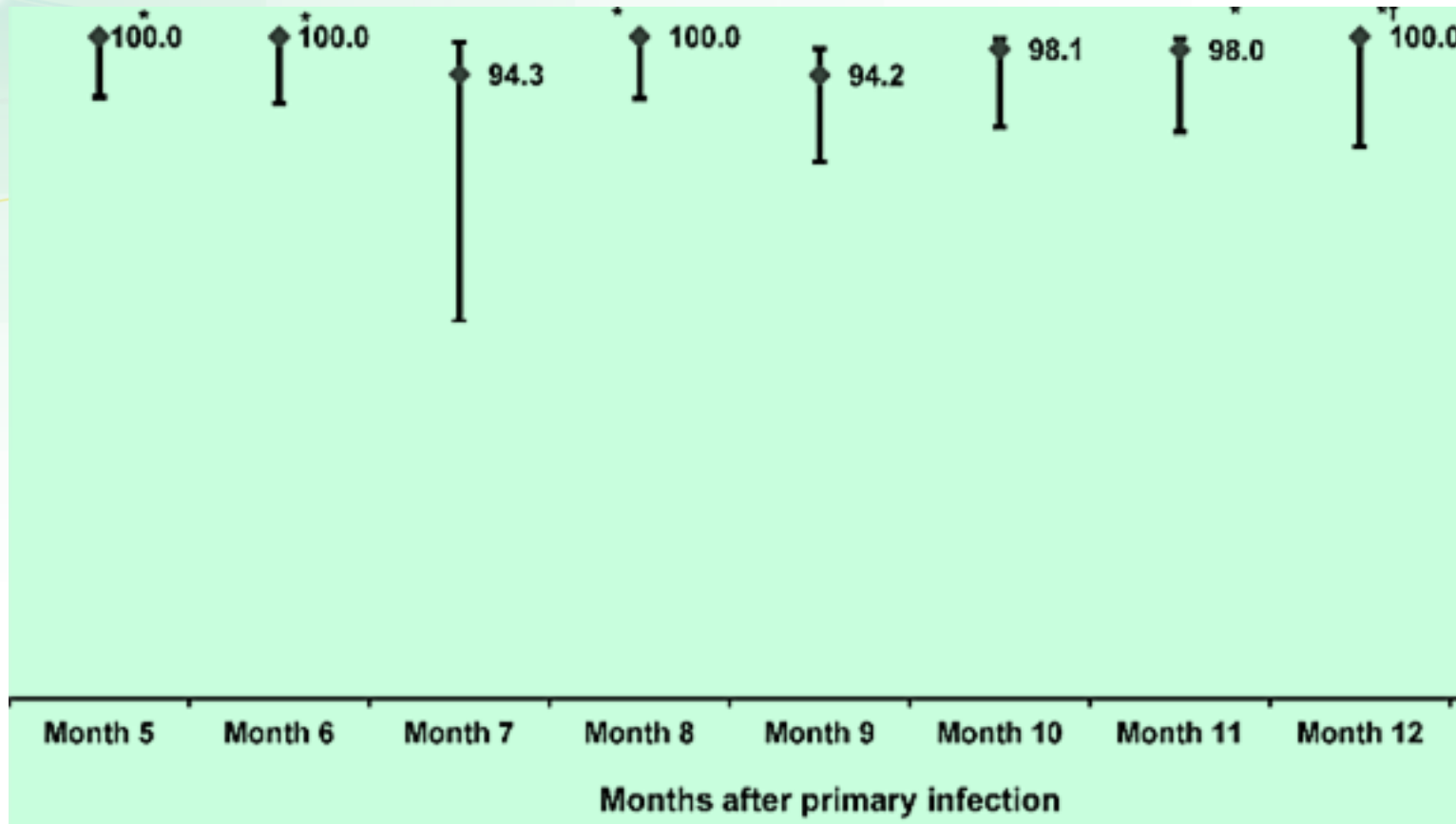
- Of the 119 individuals who ate the seat next to the 33 indexes, 3 (2.5% [95% CI, 0.5-7.4%]) were diagnosed with COVID-19.
- When the indexes had conversations during mealtime, transmission risk was 12.5% (3/24), while transmission risk was 0% (0/74) when the index did not have conversations ($P = 0.01$).



Replication of SARS-CoV-2 Omicron BA.2 variant in ex vivo cultures of the human upper and lower respiratory tract

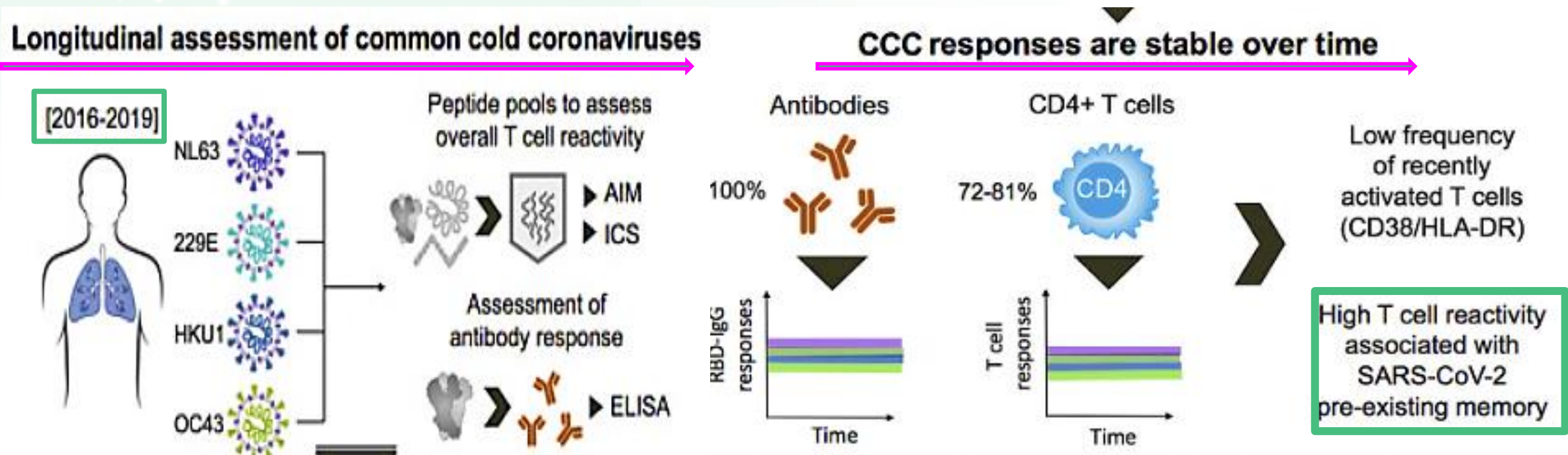


Omicron BA.2 replicates better than the BA.1 and previous strains in the upper respiratory tract but less efficiently in the lung parenchyma than wild-type and Delta.



immune protection of SARS-CoV-2 natural infection

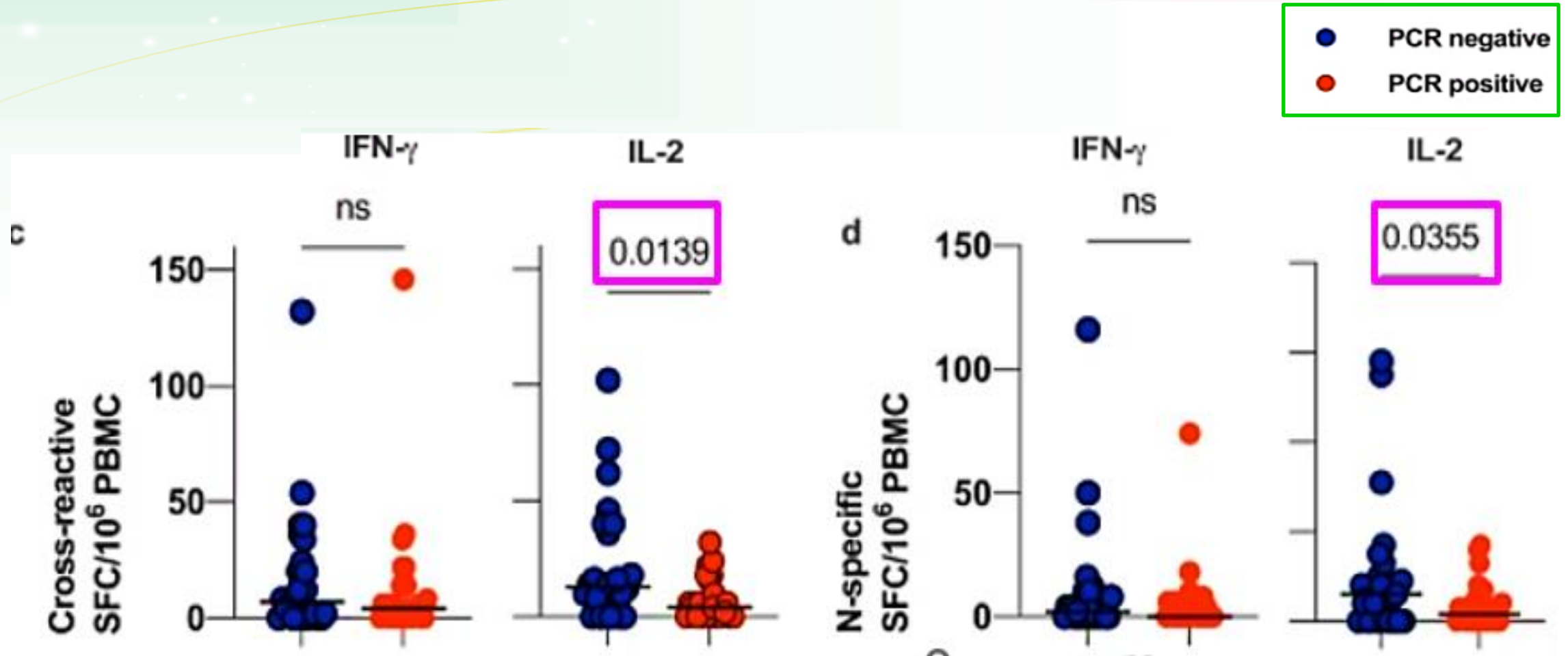
2. Immunological memory to common cold coronaviruses assessed longitudinally pre-COVID19 pandemic



High CCC-specific T cell reactivity was associated with pre-existing SARS-CoV-2 immunity

Immune memory to CCC might influence SARS-CoV-2 disease severity and/or vaccine responses

Cross-reactive memory T cells associate with protection against SARS-CoV-2 infection in COVID-19 contacts

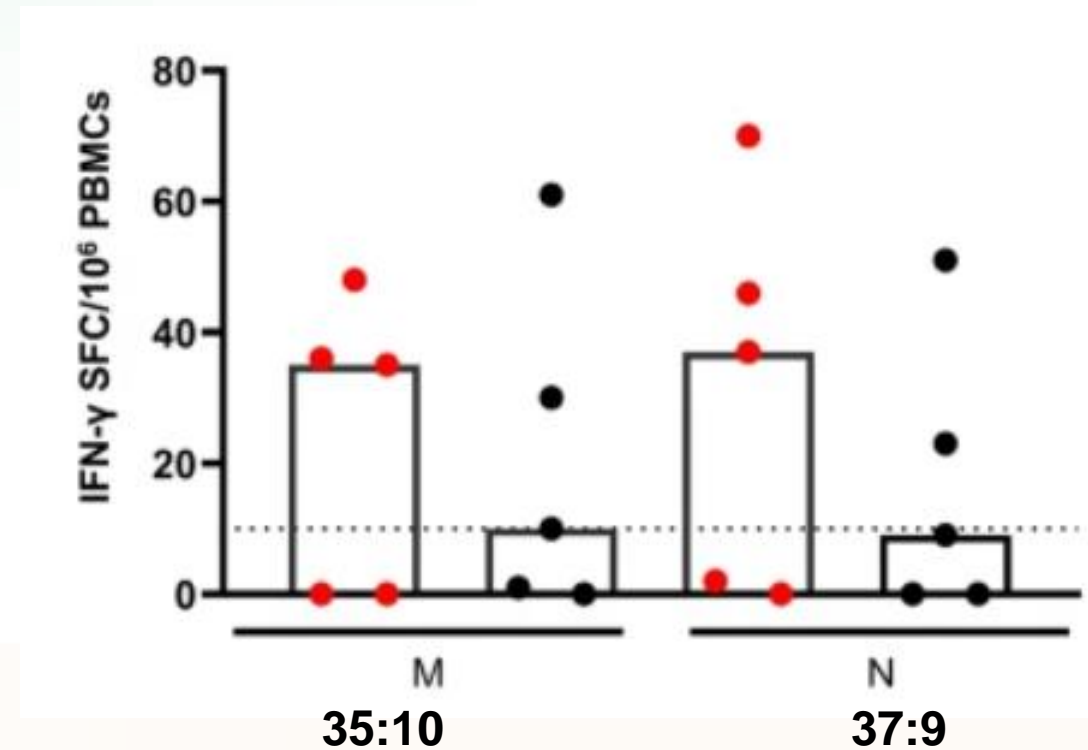
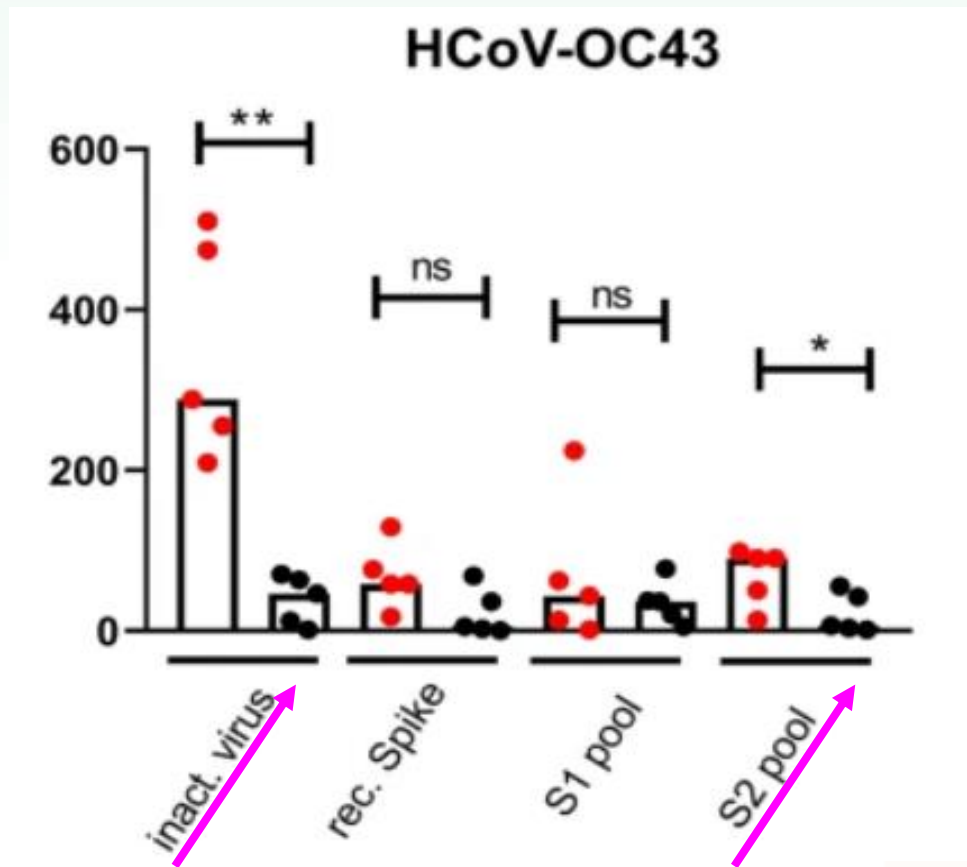




Older adults lack SARS CoV-2 cross-reactive T lymphocytes to human coronaviruses OC43 and NL63

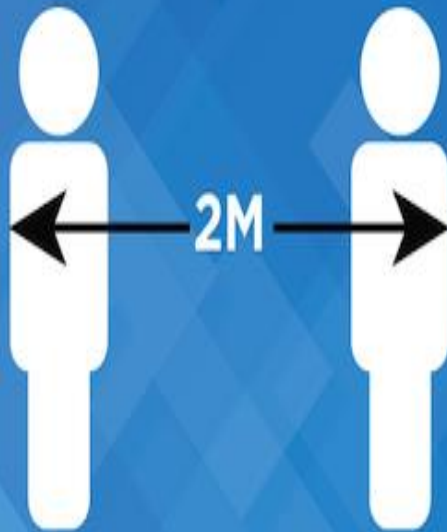
S protein-specific T cell immune responses in young and older subjects.

N and M peptide pools and frequency of IFN- γ producing T cells





ENJOY OUR BEACH, BUT STAY APART



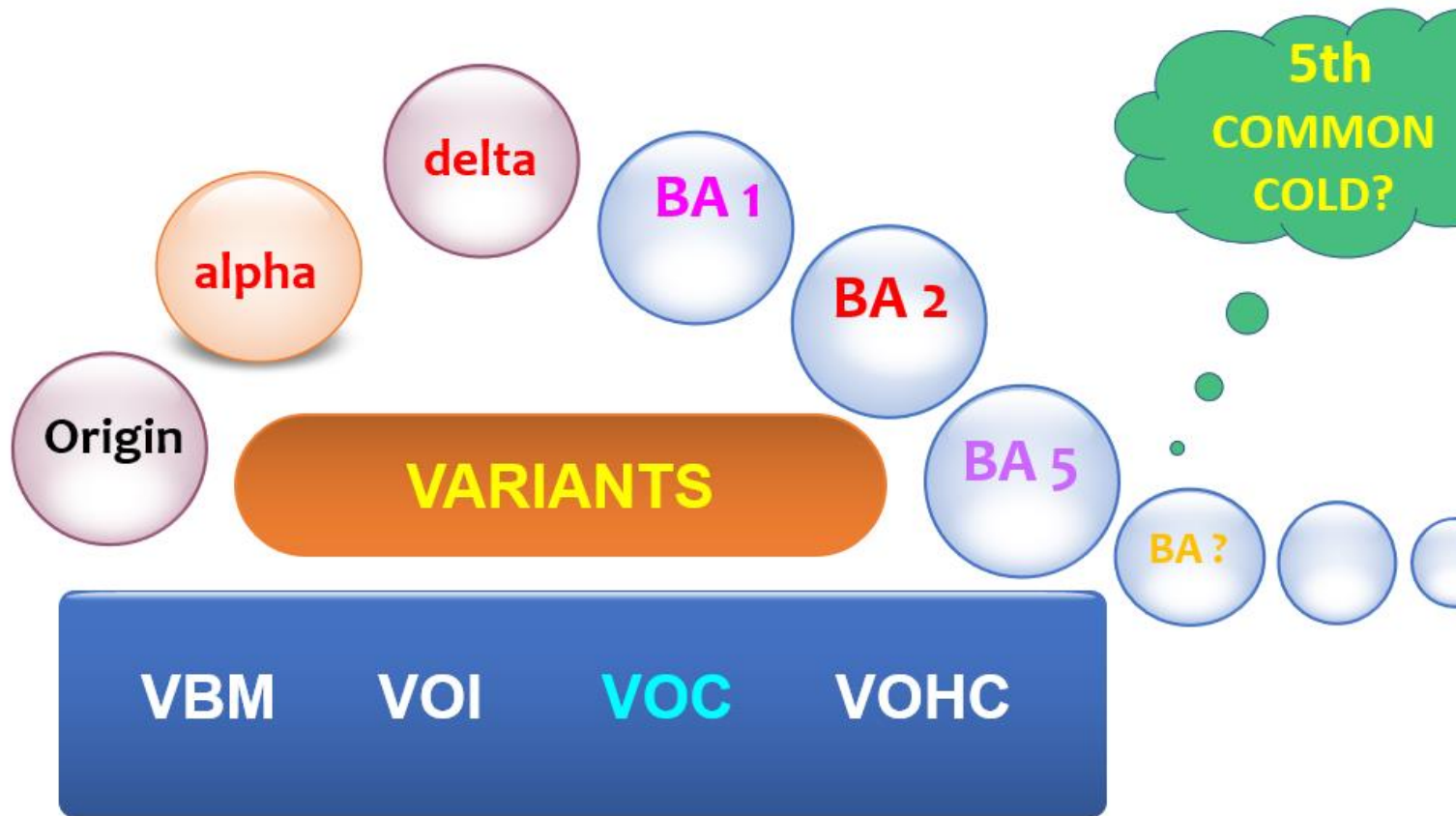
AVOID CROWDS
MAINTAIN 1-2 METRE
DISTANCE
(APPROX 6 FEET)

vancouver.ca/covid19impacts

CORONAVIRUS
PROTECTION



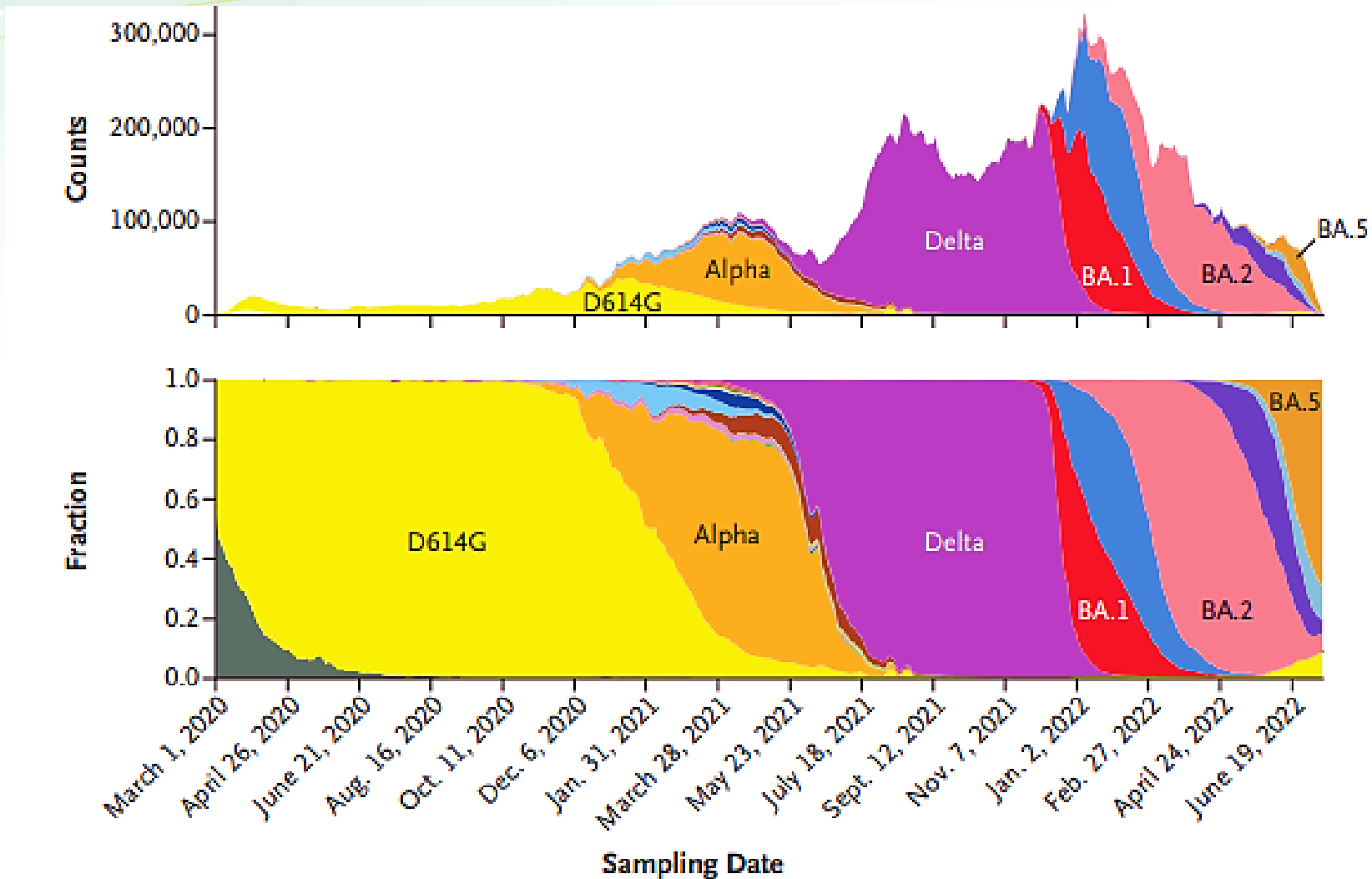
Preventive methods for COVID 19



SARS CoV 2 Variants



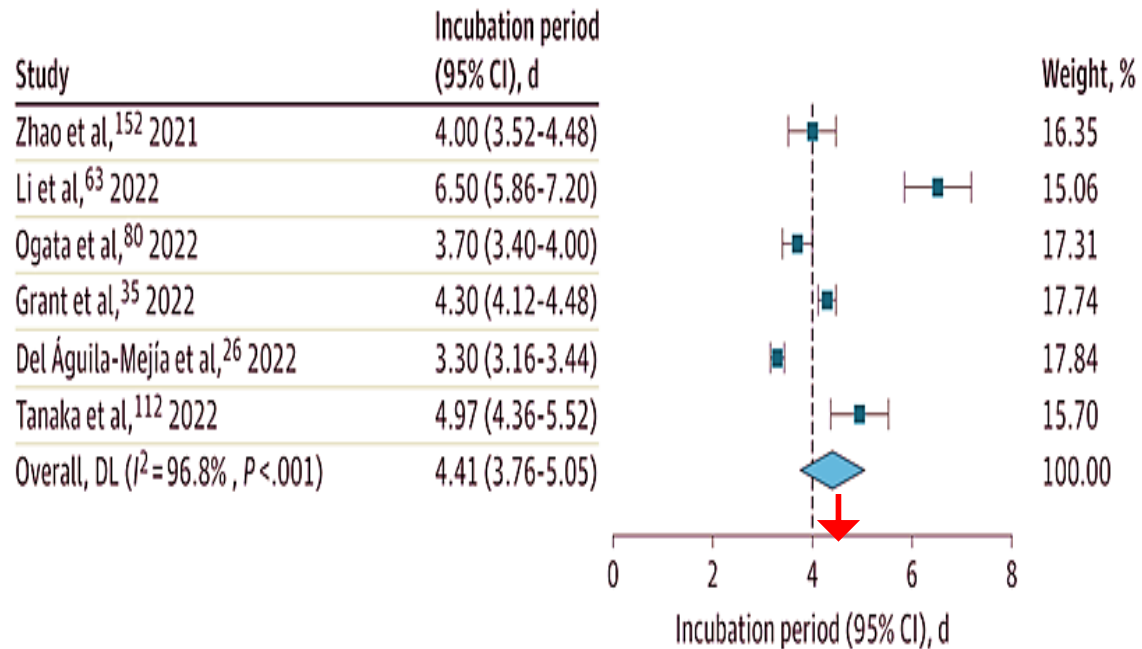
SARS-CoV-2 Variants over Time



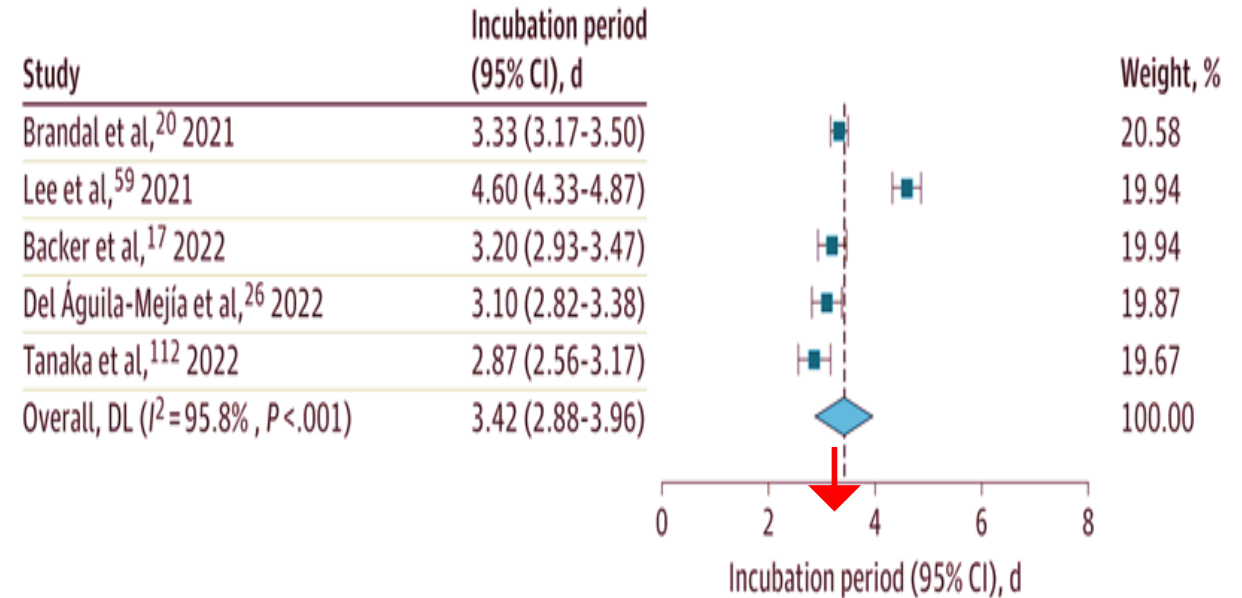


Incubation Period of COVID-19 Caused by Variants

Delta



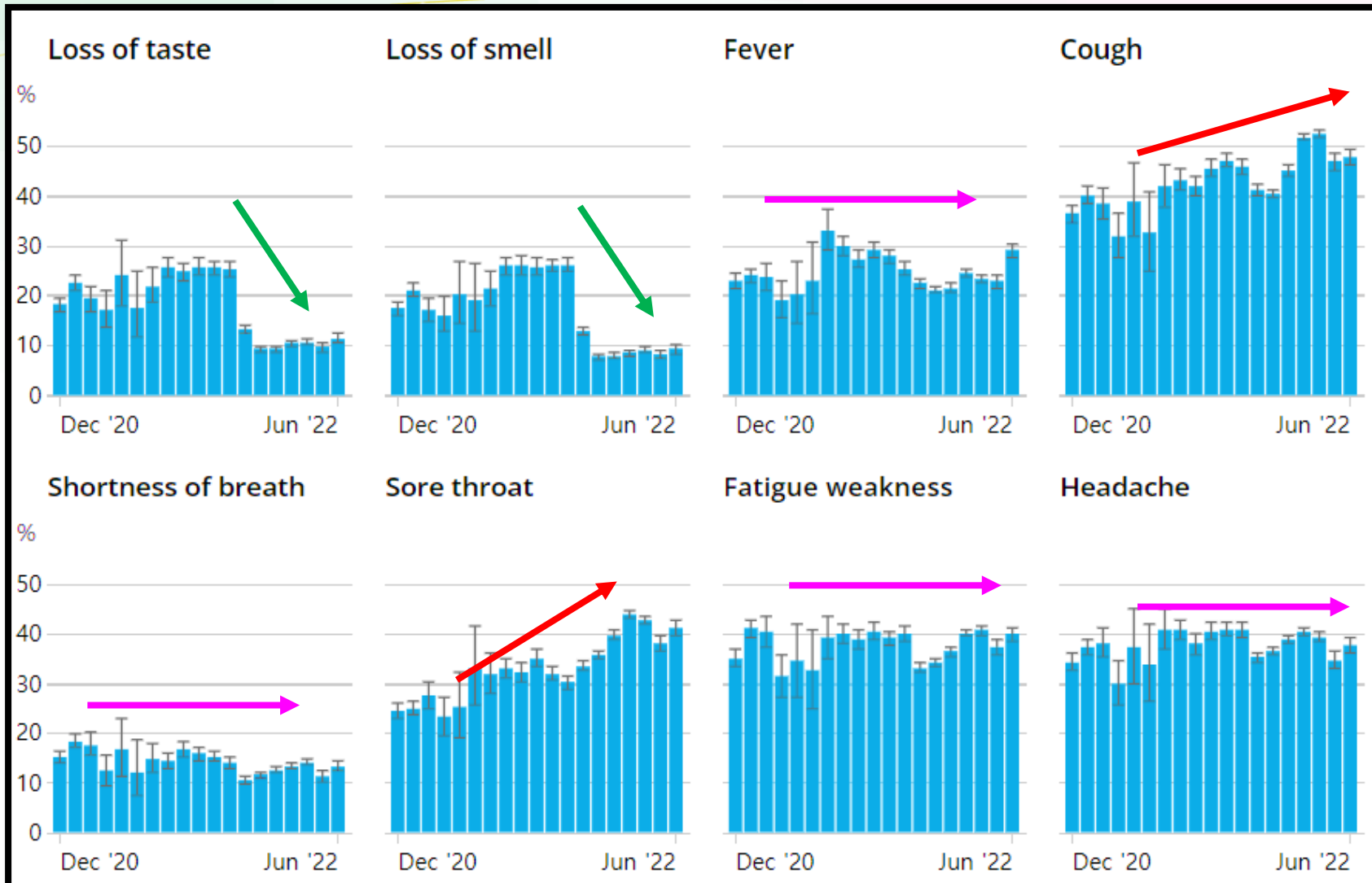
Omicron



The incubation period of omicron variant is about a day shorter than delta.



Percentage of people testing positive who reported symptoms



Source: Office for National Statistics – Coronavirus (COVID-19) Infection Survey

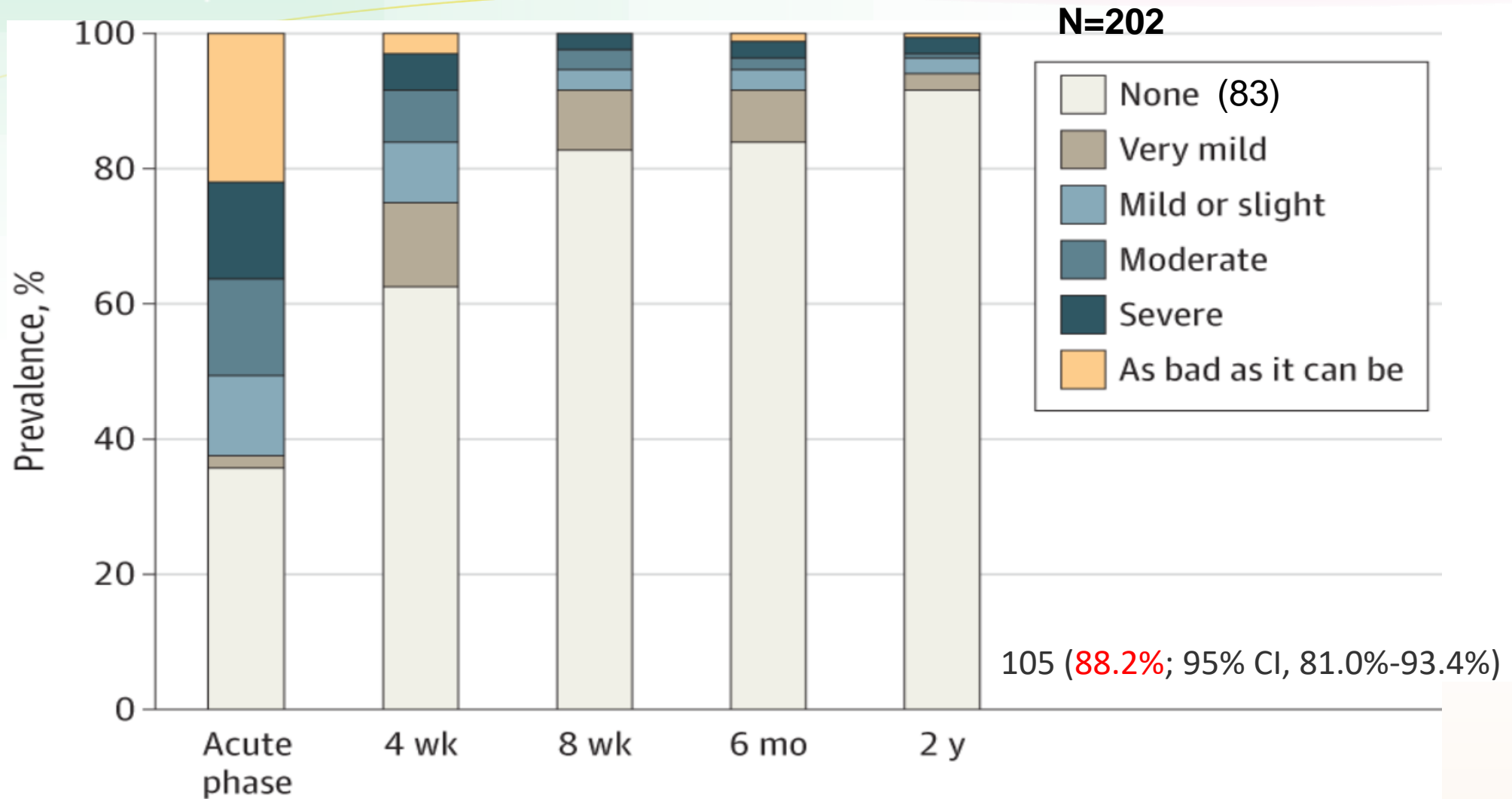


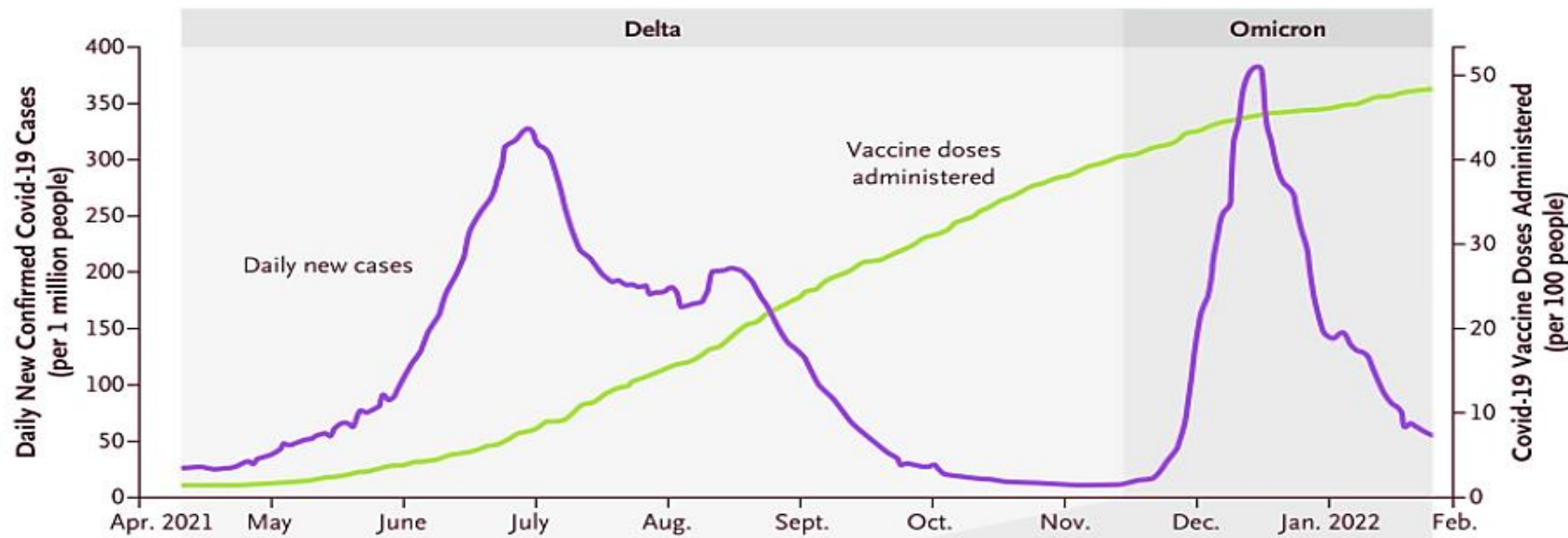
Association Between SARS-CoV-2 Lineage and Self-reported Olfactory Dysfunction

	SARS-CoV-2 lineage			
	Original lineages (n = 4227)	Gamma (n = 768)	Delta (n = 425)	Omicron (n = 633)
Olfactory dysfunction, No. (%) [95% CI]	2223 (52.6) [51.1-54.1]	211 (27.5) [24.3-30.8]	179 (42.1) [37.4-47.0]	37 (5.8) [4.4-8.5]
OR (95% CI)	1 [Reference]	0.34 (0.29-0.40)	0.66 (0.54-0.80)	0.06 (0.04-0.08)
P value		<.001	<.001	<.001
Adjusted OR (95% CI) ^a	1 [Reference]	0.48 (0.39-0.59)	0.90 (0.71-1.15)	0.07 (0.05-0.10)
P value		<.001	.41	<.001

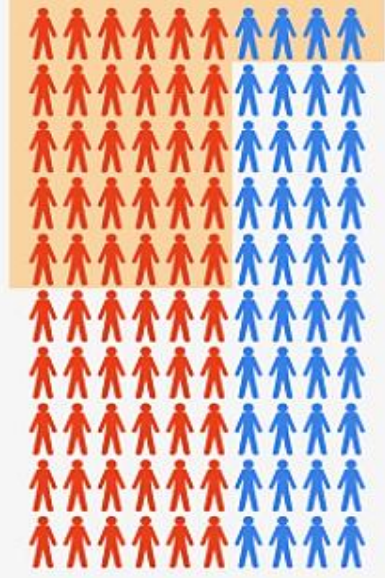


Two-Year Prevalence and Recovery Rate of Altered Sense of Smell or Taste in Patients With Mildly Symptomatic COVID-19

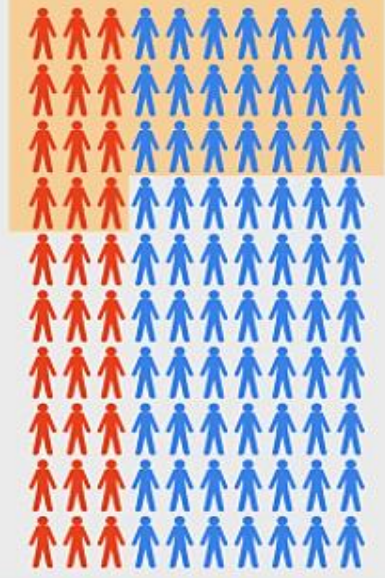




Infected



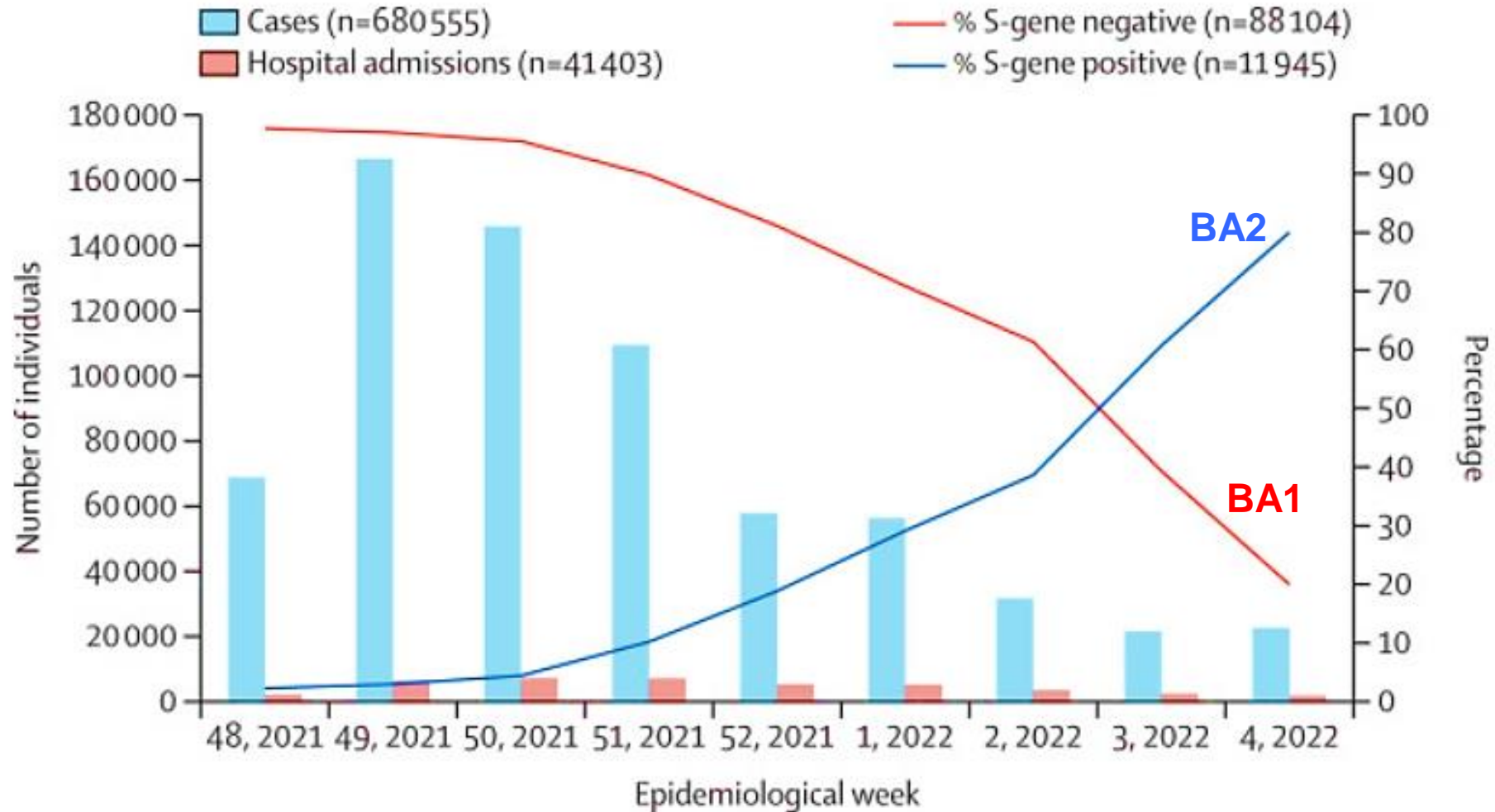
Infected



■ High risk (nonimmune)
 ■ Low risk (vaccinated or previously infected)
 ■ 1% of the population (estimate)



Number of cases, admissions, and percentage of S-gene positive and S-gene target failure (S-gene negative) infections





Clinical severity of omicron lineage BA.2 infection compared with BA.1 infection in South Africa

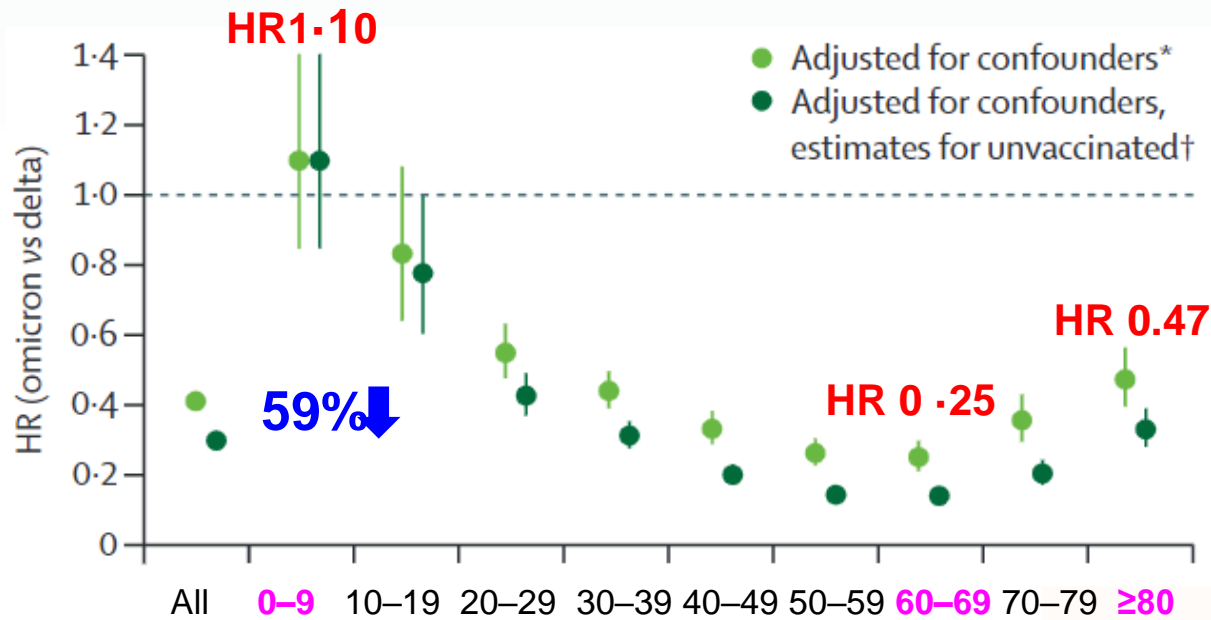
Severity component	Omicron sub-lineage		P-value ^b
	SGTF (BA.1 proxy)	S-gene positive (BA.2 proxy)	
	n (%)	n (%)	
	N=2776	N=282	
ICU admission	252 (9.1)	26 (9.2)	0.937
Oxygen treatment	636 (22.9)	58 (20.6)	0.371
Ventilated	53 (1.9)	4 (1.4)	0.562
Received ECMO	0 (0.0)	0 (0.0)	N/A
ARDS	32 (1.2)	2 (0.7)	0.499
Died	242 (8.7)	20 (7.1)	0.353

SGTF: S-gene target failure, ICU: intensive care unit, ECMO: extracorporeal membrane oxygenation, ARDS:

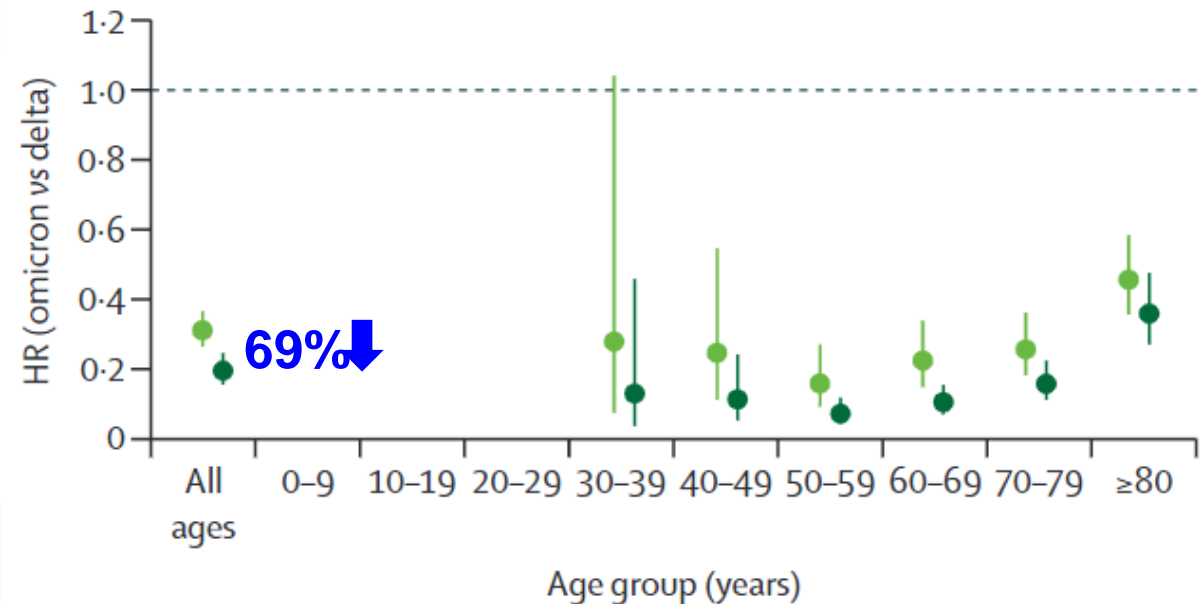


Risk of hospitalisation and mortality for COVID-19 cases with omicron compared with delta, by age group

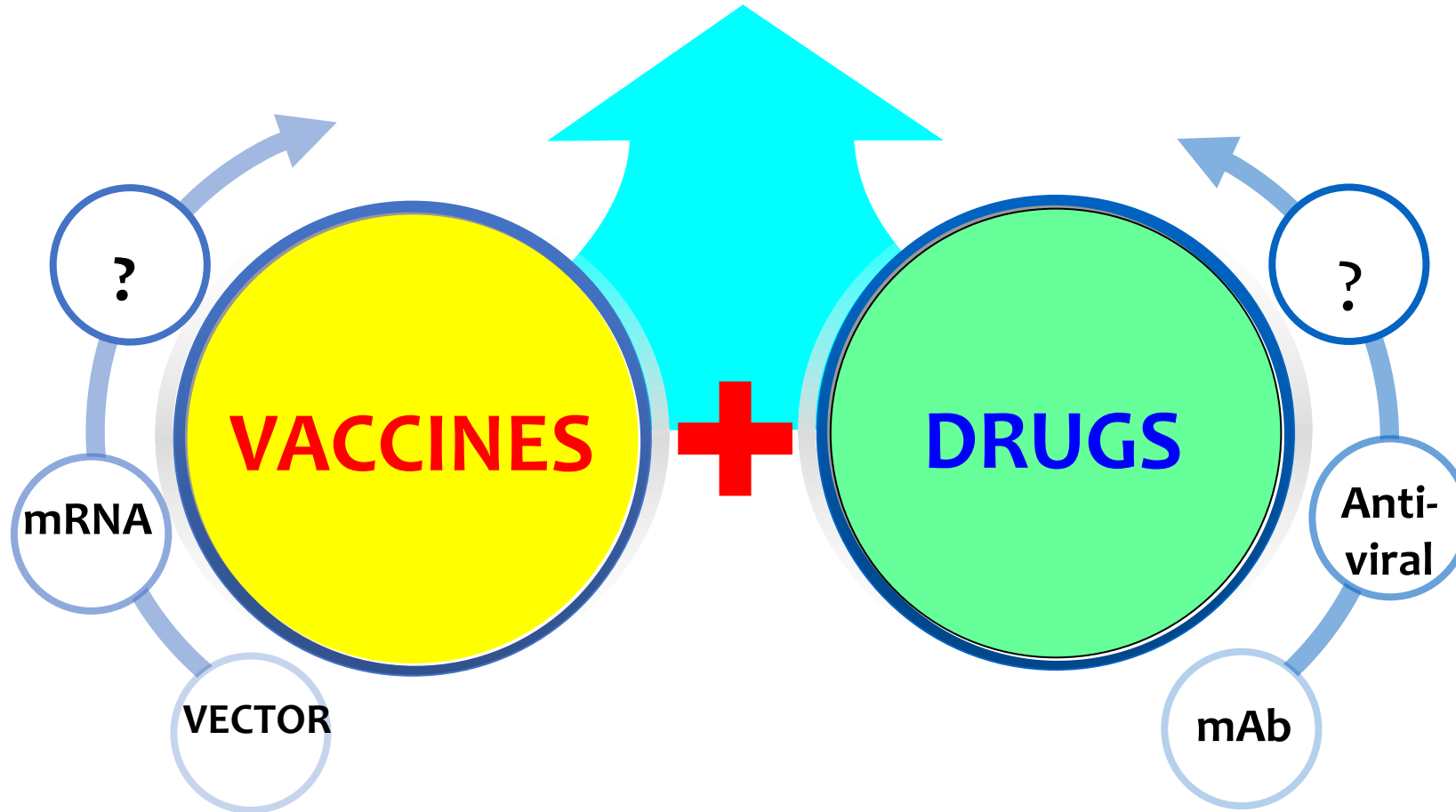
Hospital admission



Deaths

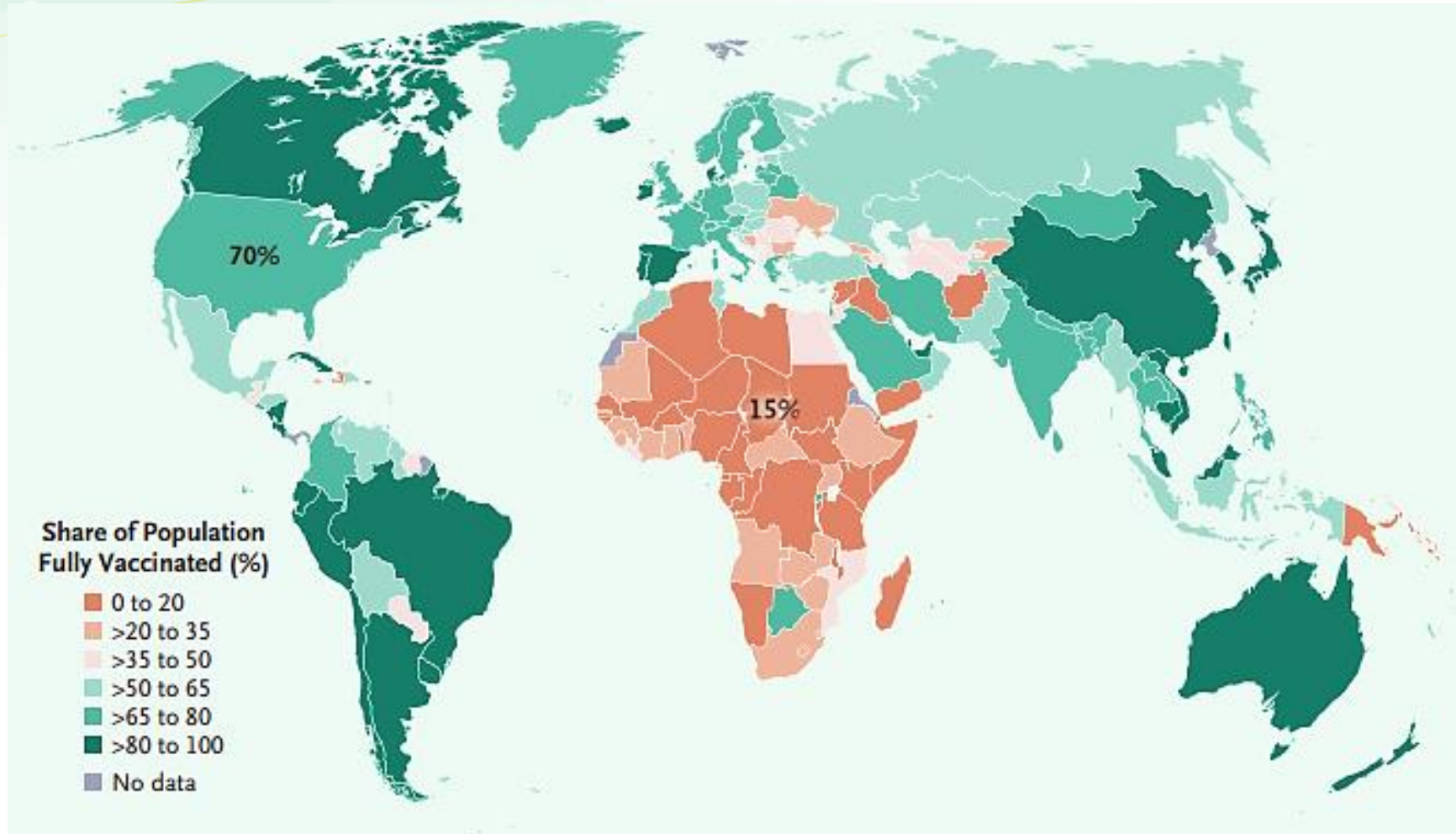


Synergy between vaccines and drugs





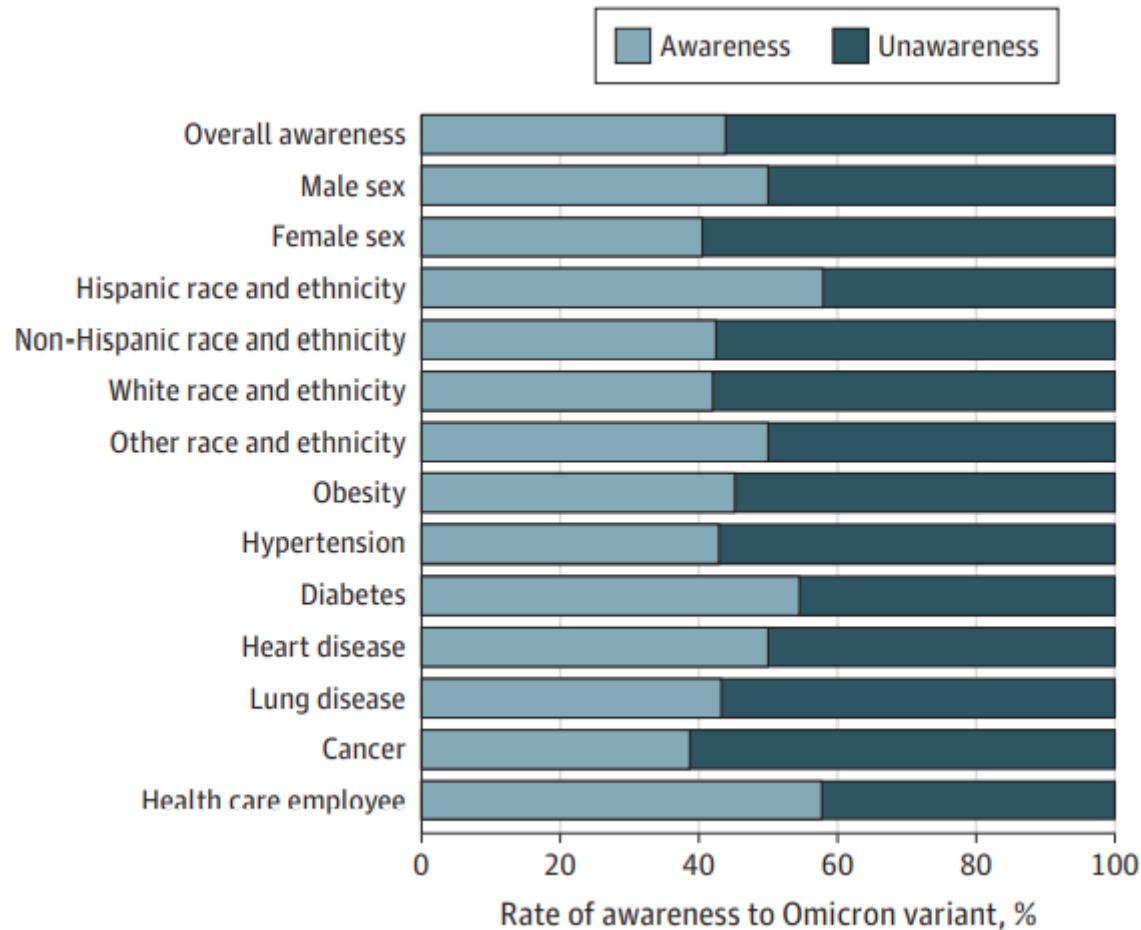
Global Covid-19 Vaccination Rates





Awareness of SARS-CoV-2 Omicron Variant Infection Among Adults With COVID-19 Seropositivity

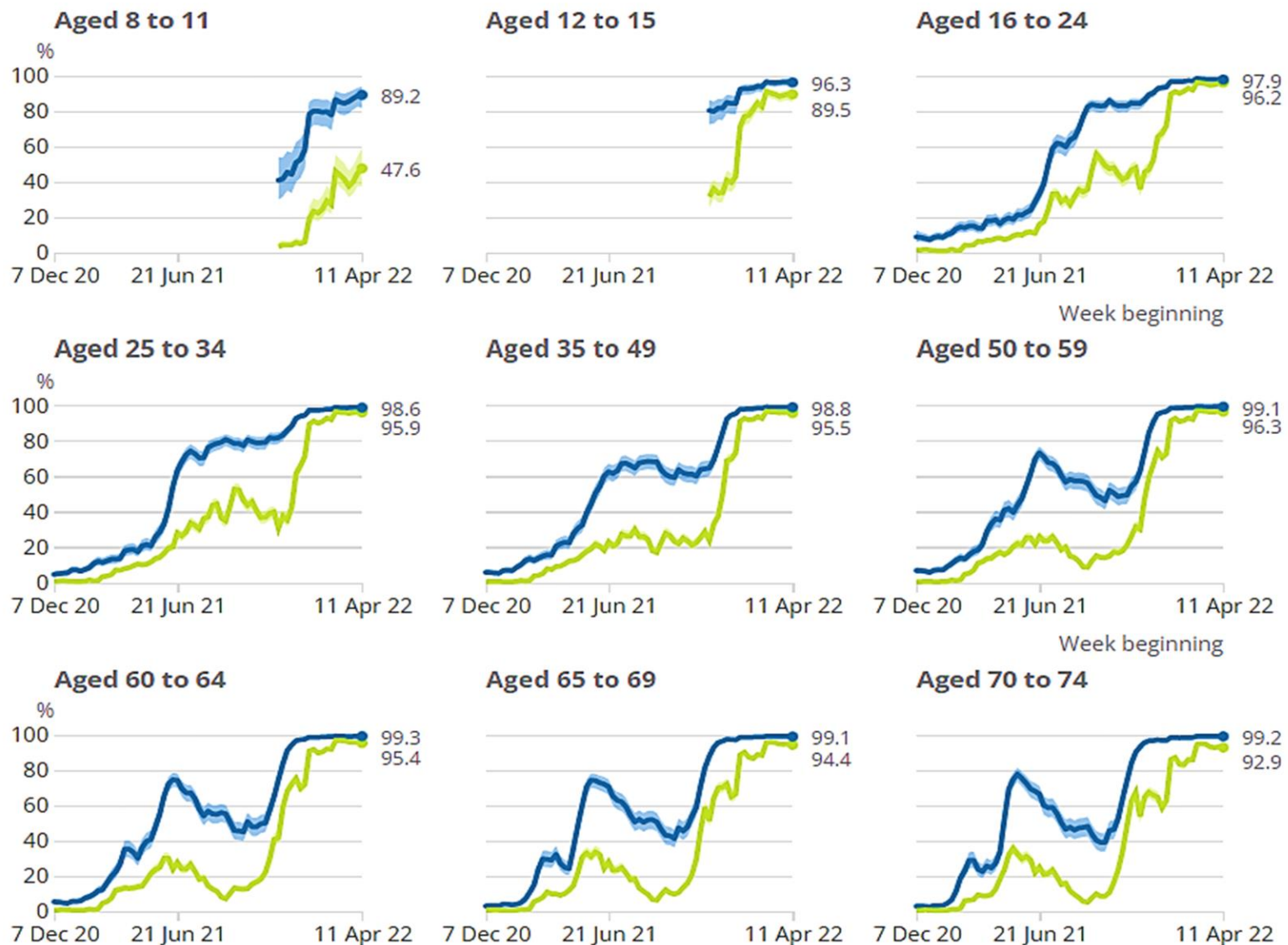
- **44% (92)** demonstrated awareness of Omicron infection and **56% (118)** reported unawareness



Patient characteristic	Multivariable-adjusted OR (95% CI)
Age, per decade	0.78 (0.64-1.00)
Male sex	1.87 (1.01-3.45)
Health care employee	2.46 (1.30-4.65)
Coronary disease or heart failure	2.39 (0.98-5.85)

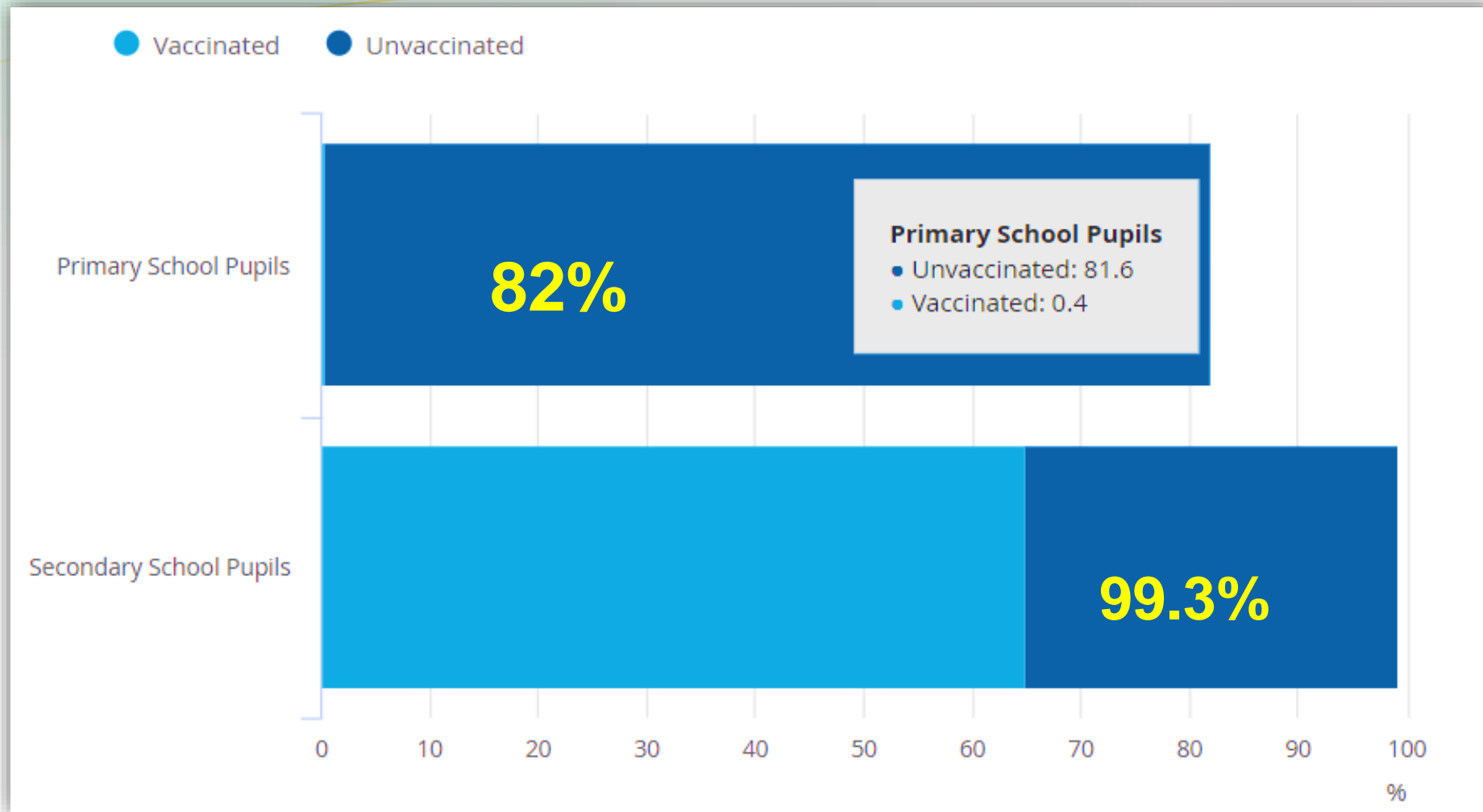


■ Modelled % of the population with antibodies against SARS-CoV-2 at or above the **179ng/ml threshold** and the **800ng/ml threshold** with ■ 95% credible intervals





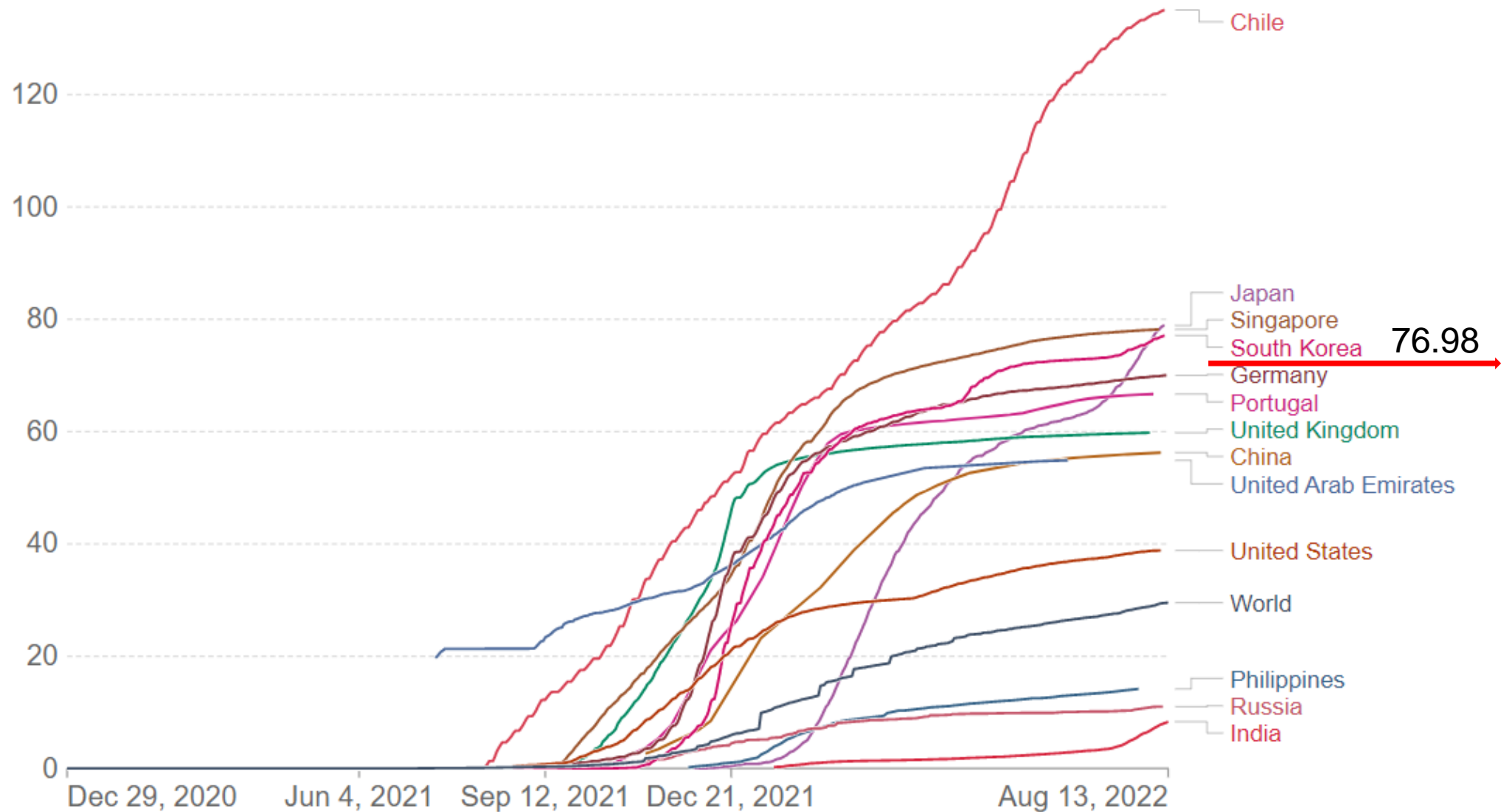
percentage of pupils testing positive for antibodies to COVID-19 by vaccination status, England, March 2022



Source: Office for National Statistics – Coronavirus (COVID-19) Schools Infection Survey

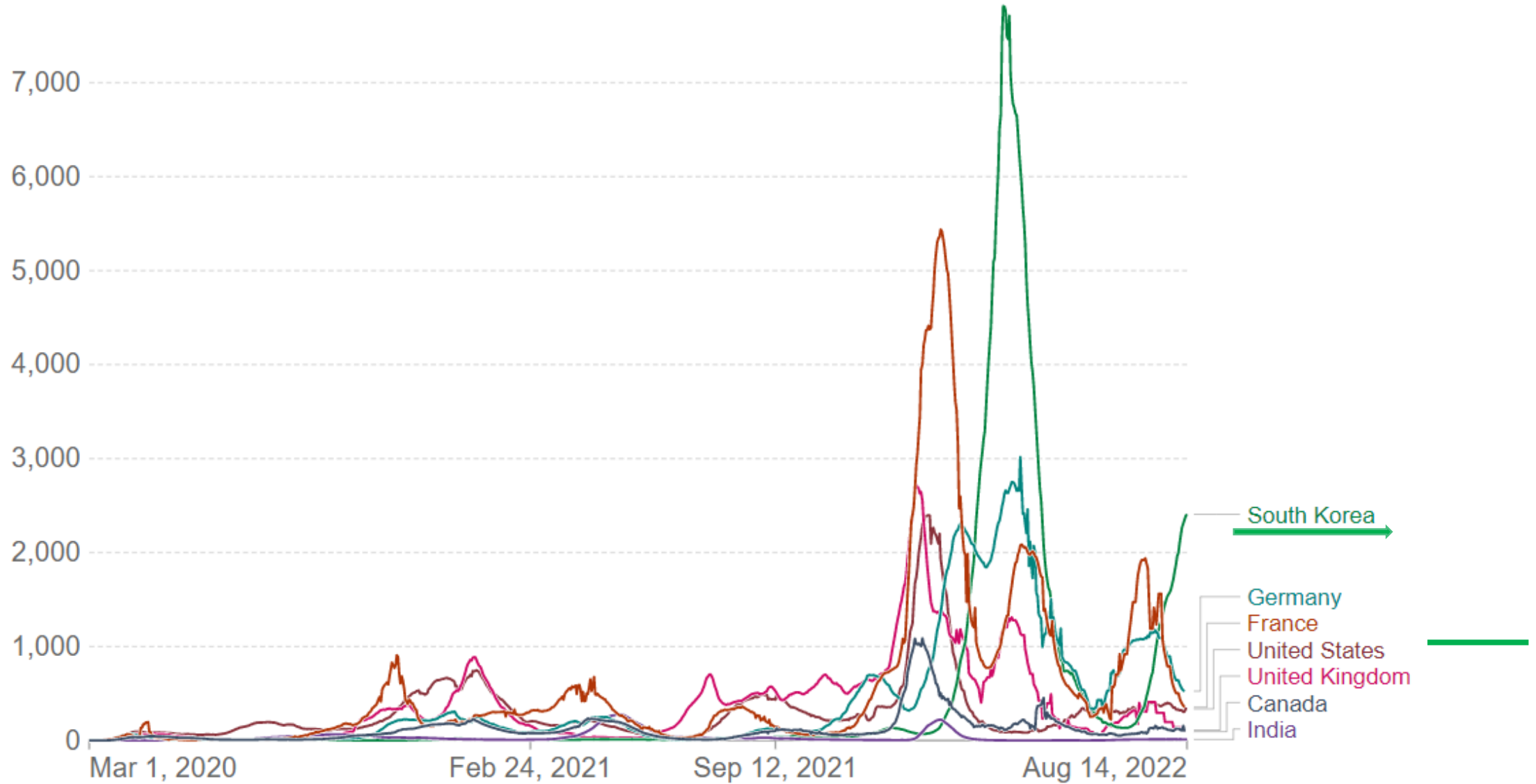
COVID-19 vaccine boosters administered per 100 people

Total number of vaccine booster doses administered, divided by the total population of the country. Booster doses are doses administered beyond those prescribed by the original vaccination protocol.

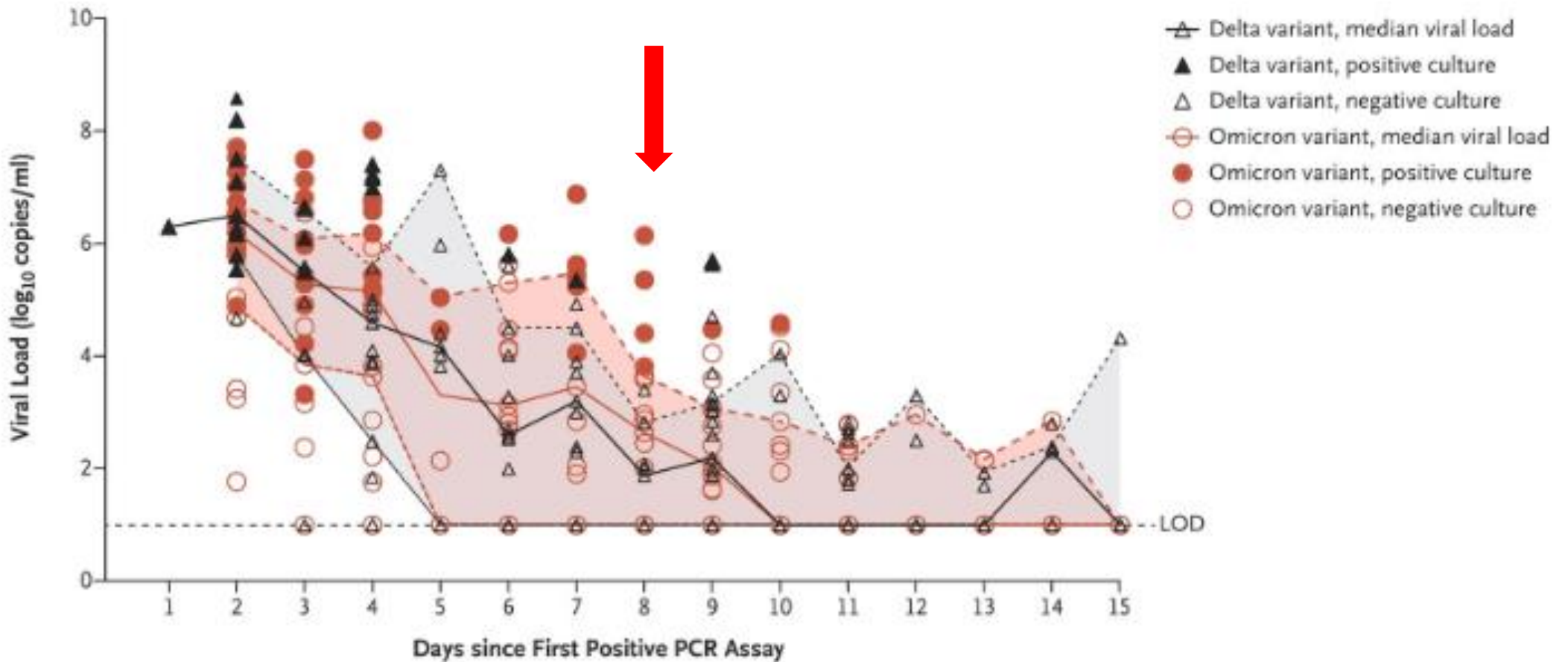


Daily new confirmed COVID-19 cases per million people

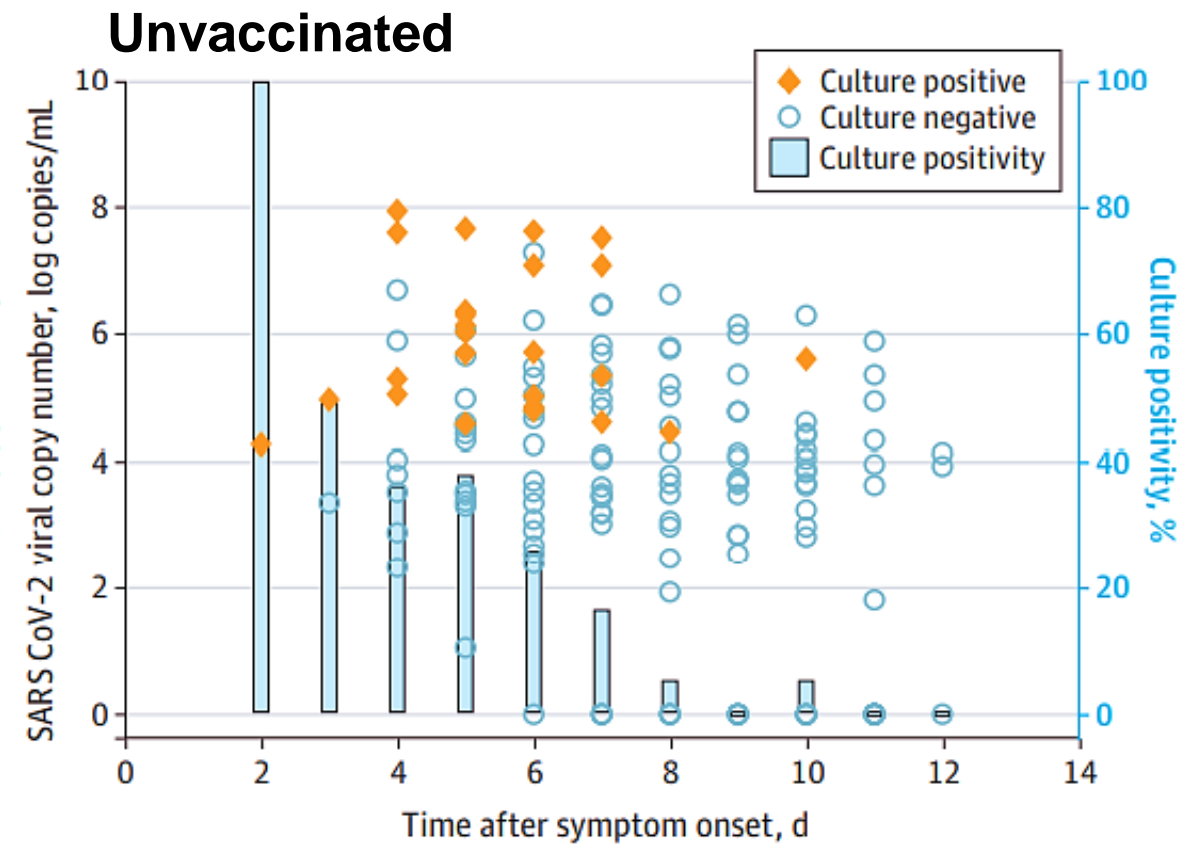
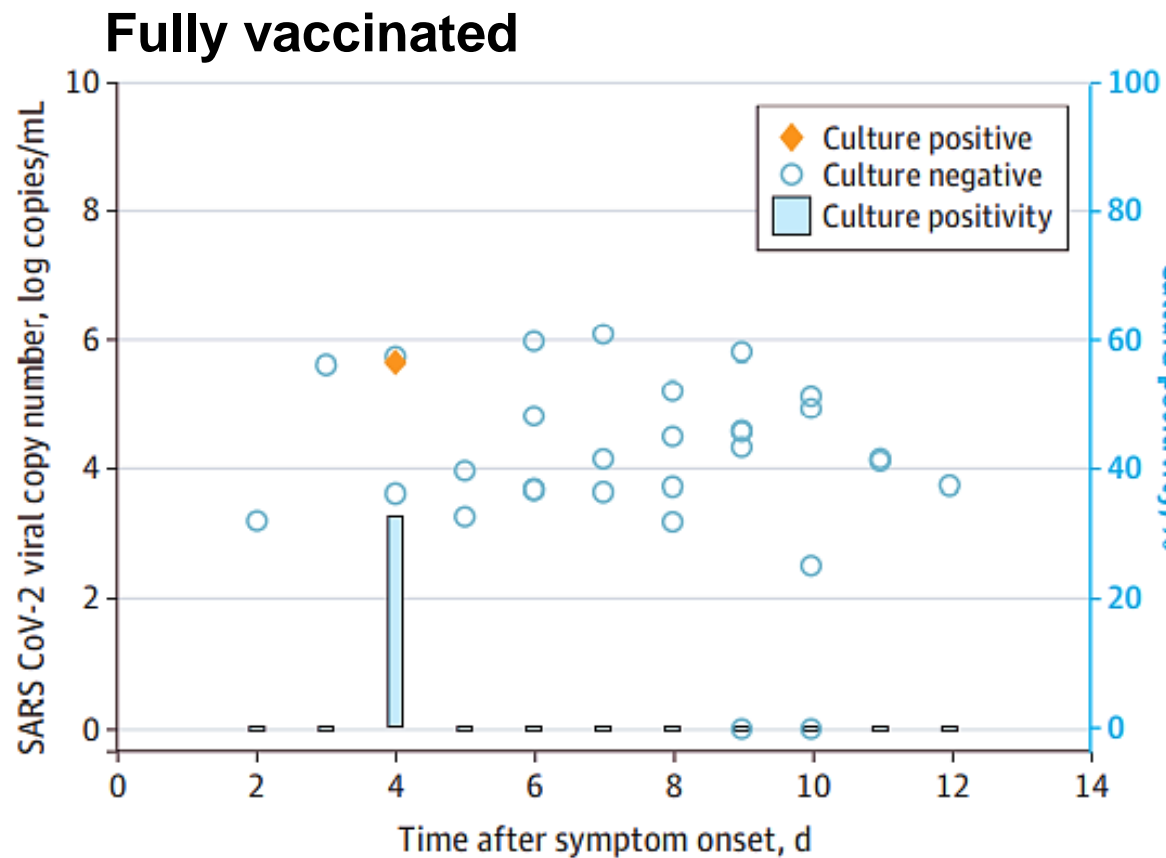
7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.



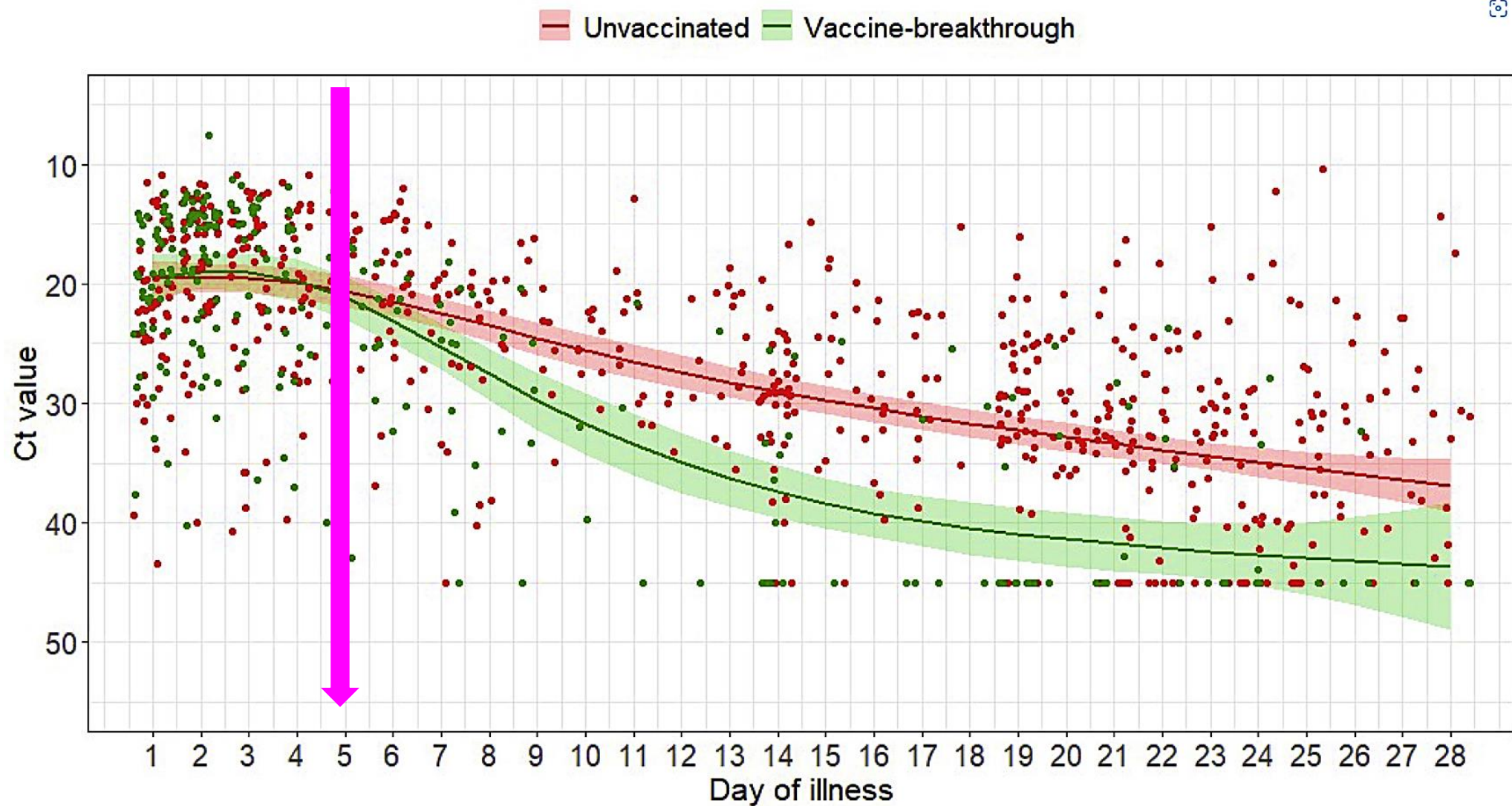
Duration of Shedding of Culturable Virus in SARS-CoV-2 Omicron (BA.1) Infection



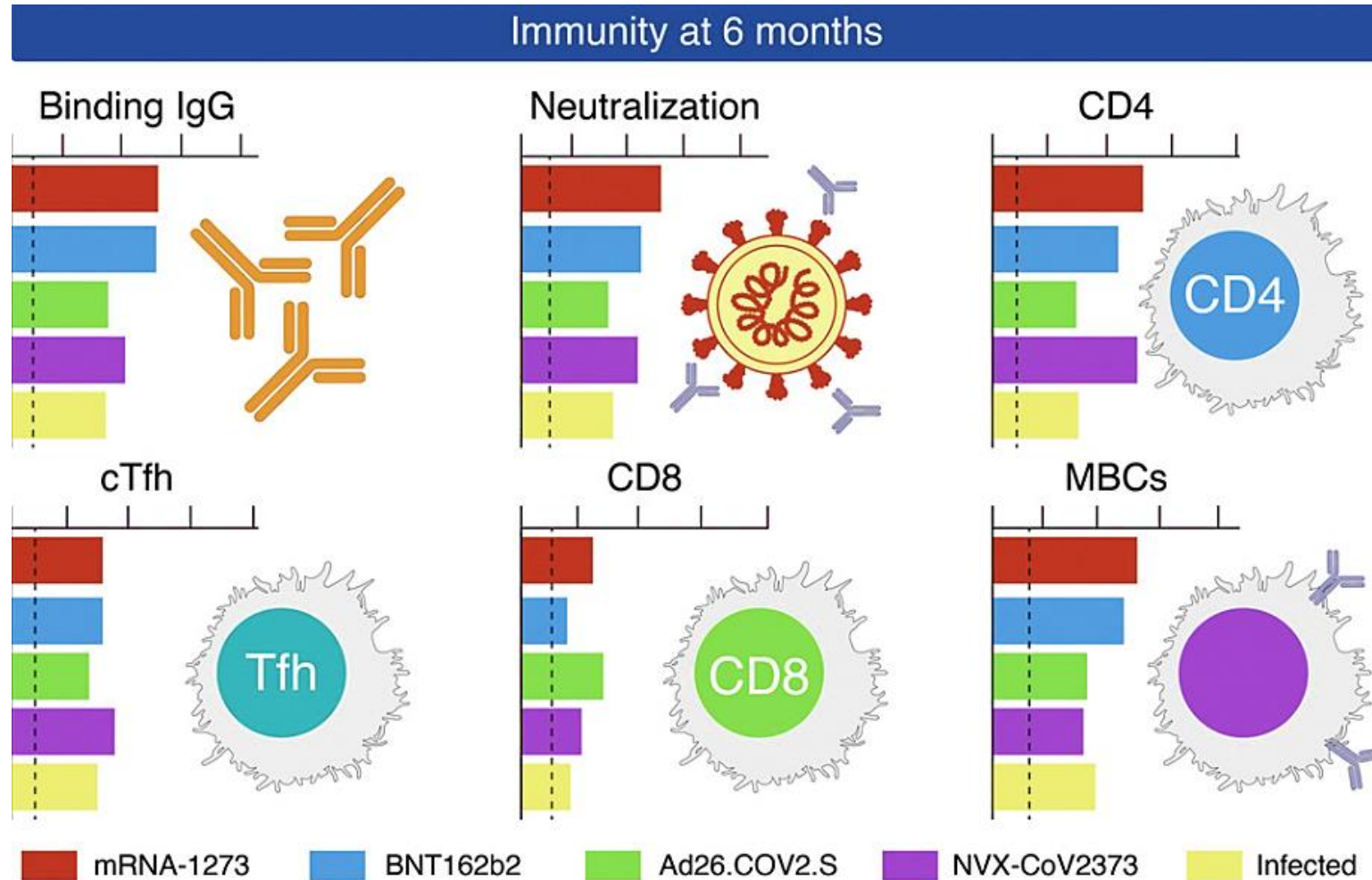
Viral copy number and culture positivity according to the symptom onset date



Ct values of COVID-19 B1.617.2 infected patients between vaccination status and day of illness.



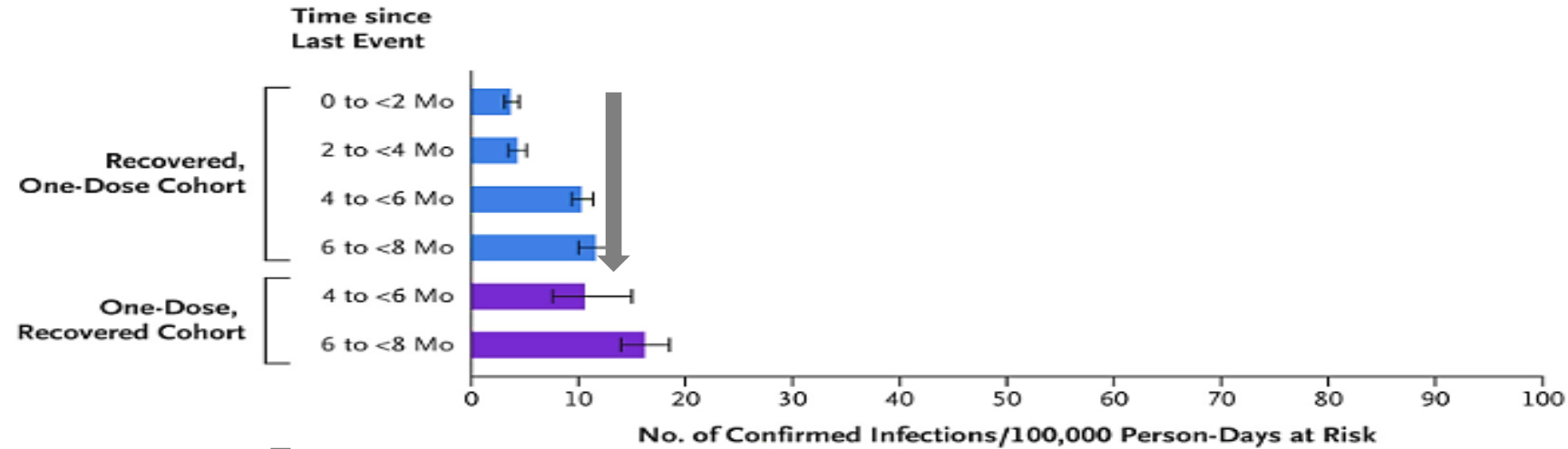
Humoral and cellular immune memory to four COVID-19 vaccines



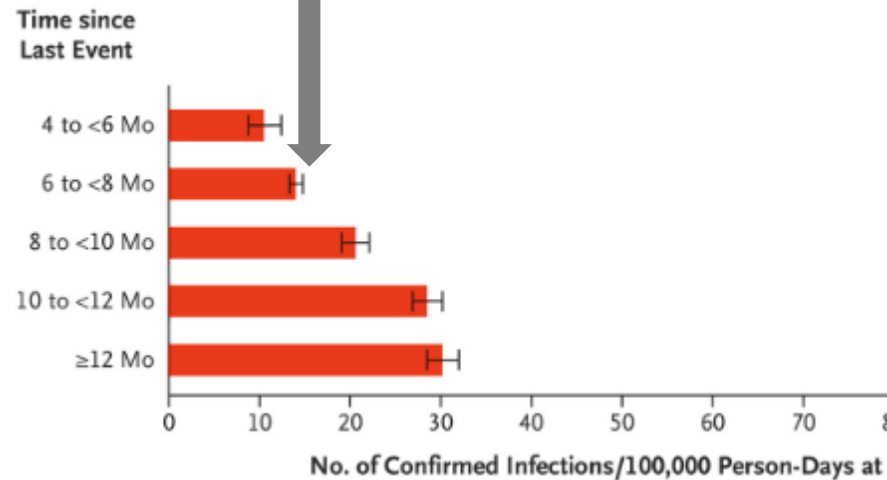
Antibody wanes in response to mRNA vaccines, but memory T and B cells are comparatively stable

Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2

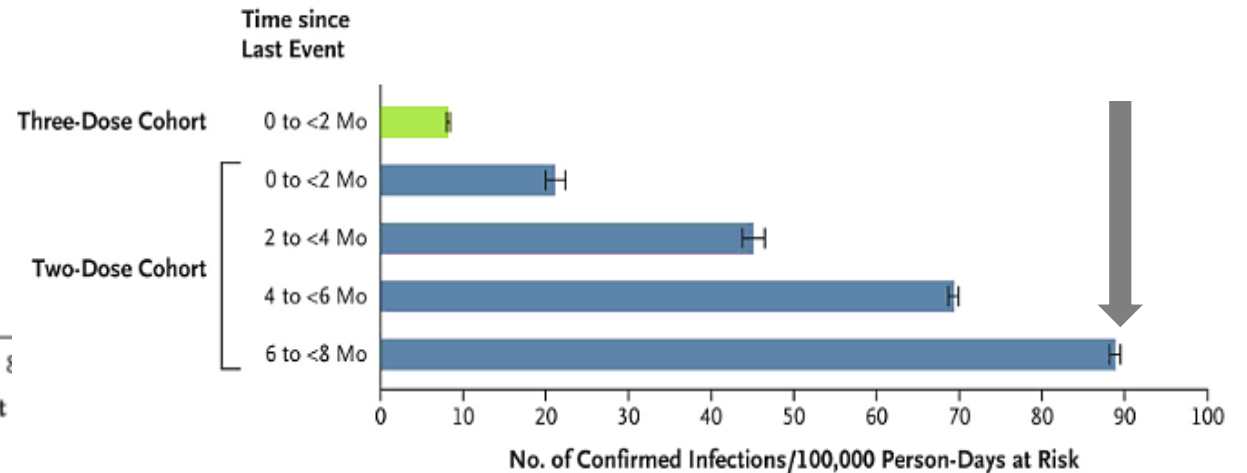
Cohorts with Hybrid Immunity



Recovered, Unvaccinated Cohort

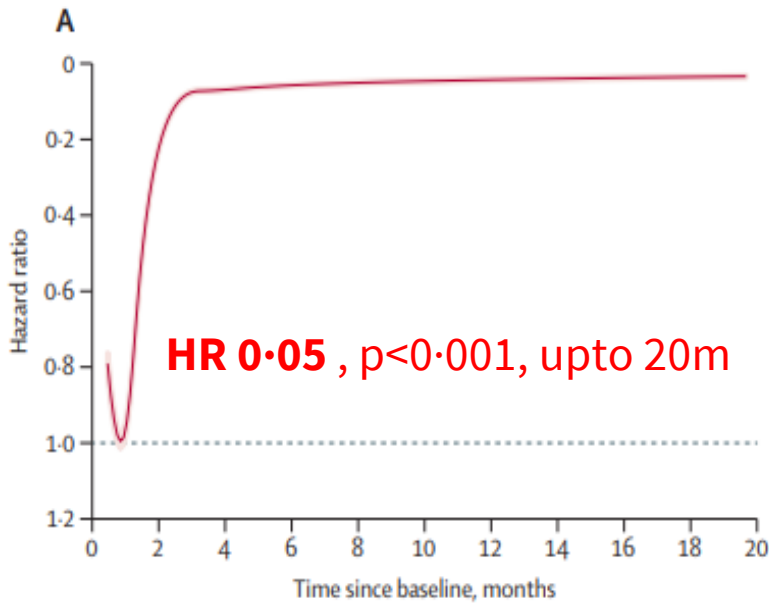


Two-Dose and Three-Dose Cohorts

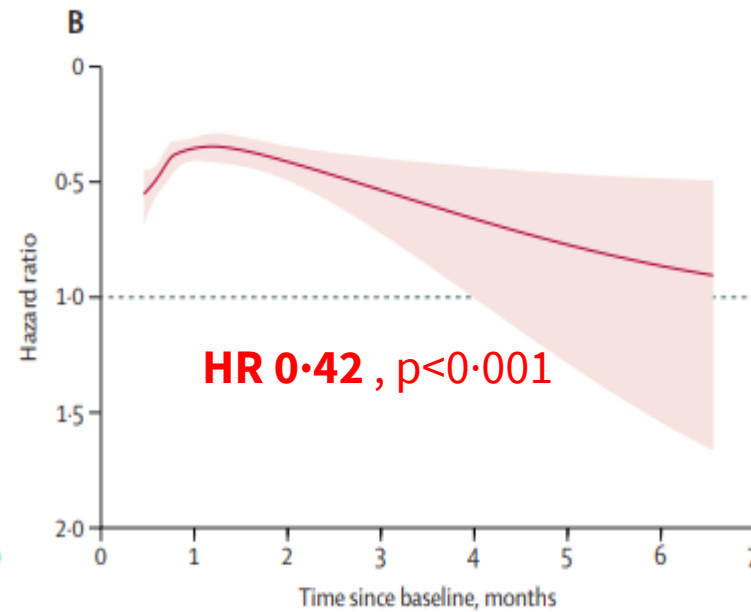


Risk of SARS-CoV-2 reinfection and hospitalisation in individuals with natural and hybrid immunity:

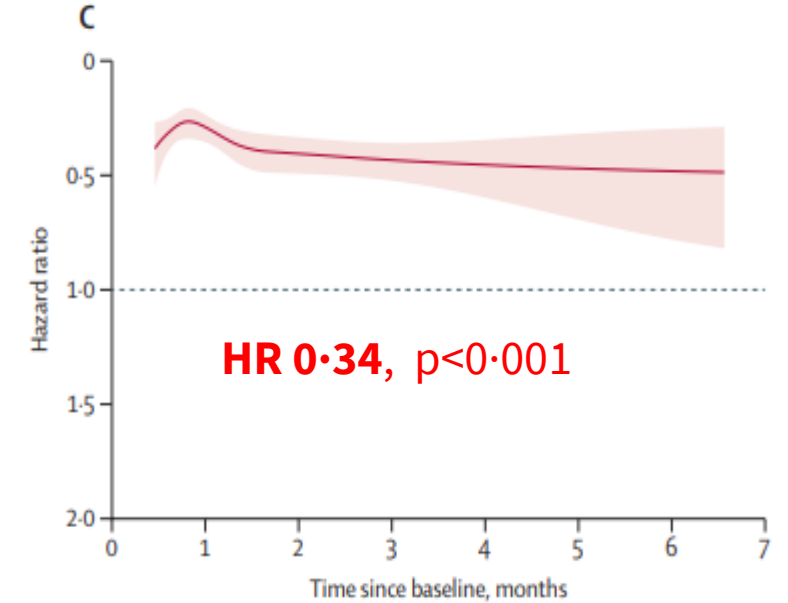
Natural immunity compared with individuals **without immunity**



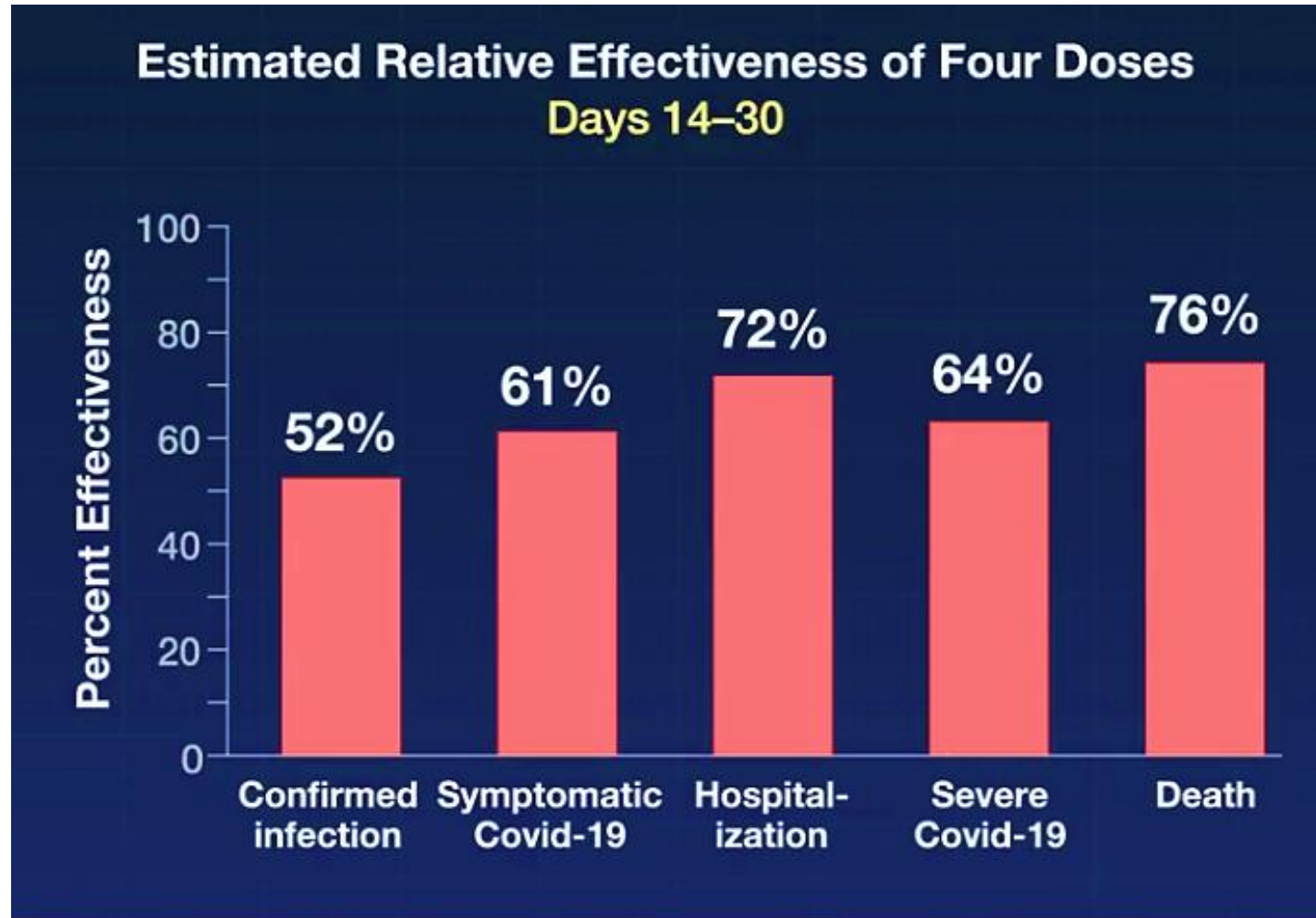
One-dose hybrid immunity compared with **natural immunity**



Two-dose hybrid immunity compared with **natural immunity**



Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting



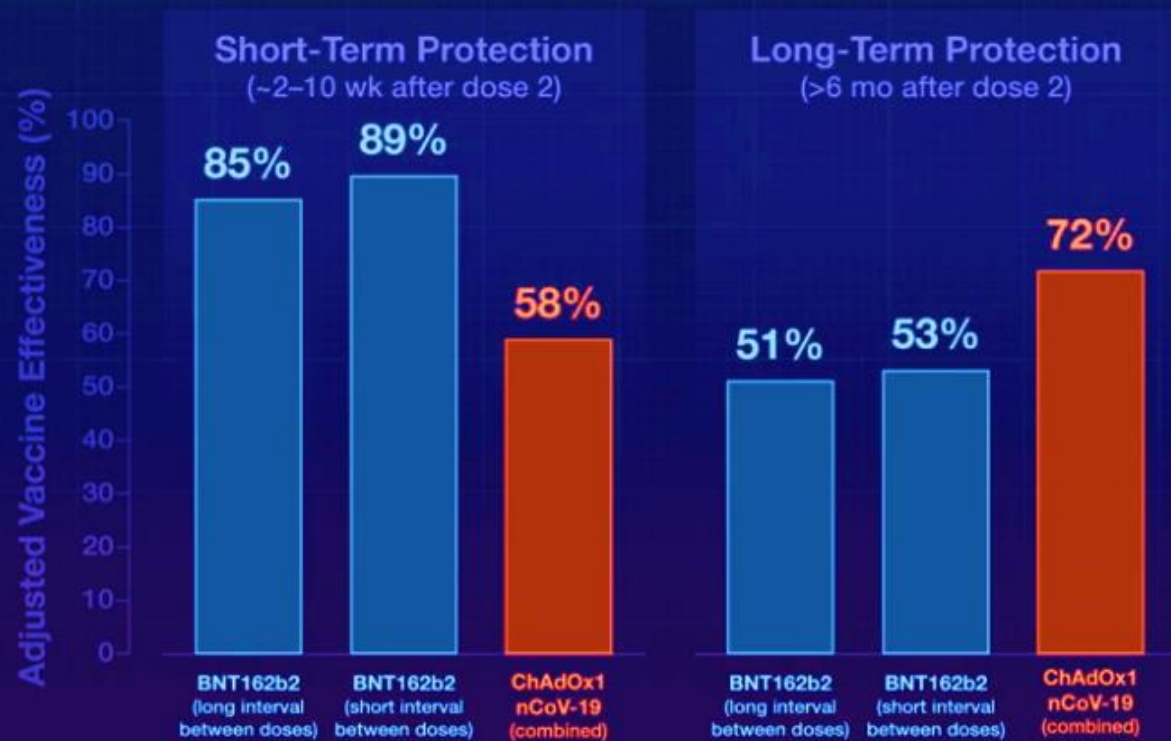
Relative vaccine effectiveness of the fourth dose against mortality in residents of long-term care facilities

	Fourth-dose group		Third-dose group		Relative vaccine effectiveness (95% CI)	
	Deaths	Deaths/100,000 person-days	Deaths	Deaths/100,000 person-days	Adjusted for age and baseline date	Fully adjusted*
7-60 days, total cohort (N = 21,623)	573	79.8	292	105.2	37 (27-45)	39 (29-48) 39%
Men (N = 6996)	206	89.1	97	104.2	30 (11-45)	31 (12-46)
Women (N = 14,627)	367	75.4	195	105.7	40 (28-50)	43 (31-53)
Age >85 years (N = 12,030)	389	97.0	193	135.1	38 (26-48)	39 (27-49)
Age ≤85 years (N = 9593)	184	58.1	99	73.5	34 (16-49)	39 (21-52)
>4 months since vaccination in the third-dose group (N = 16,809)	470	82.2	223	122.0	45 (35-53)	46 (36-55)
≤4 months since vaccination dose in the third-dose group (N = 4814)	107	70.6	69	72.8	15 (-16-38)	20 (-10-43)
>4 months since vaccination in the fourth-dose group (N = 20,927)	549	79.0	287	106.9	38 (29-47)	41 (31-49)
61-126 days, total remaining cohort (N = 13,853)	214	22.0	45	25.5	30 (3-49)	27 (-2-48) 27%

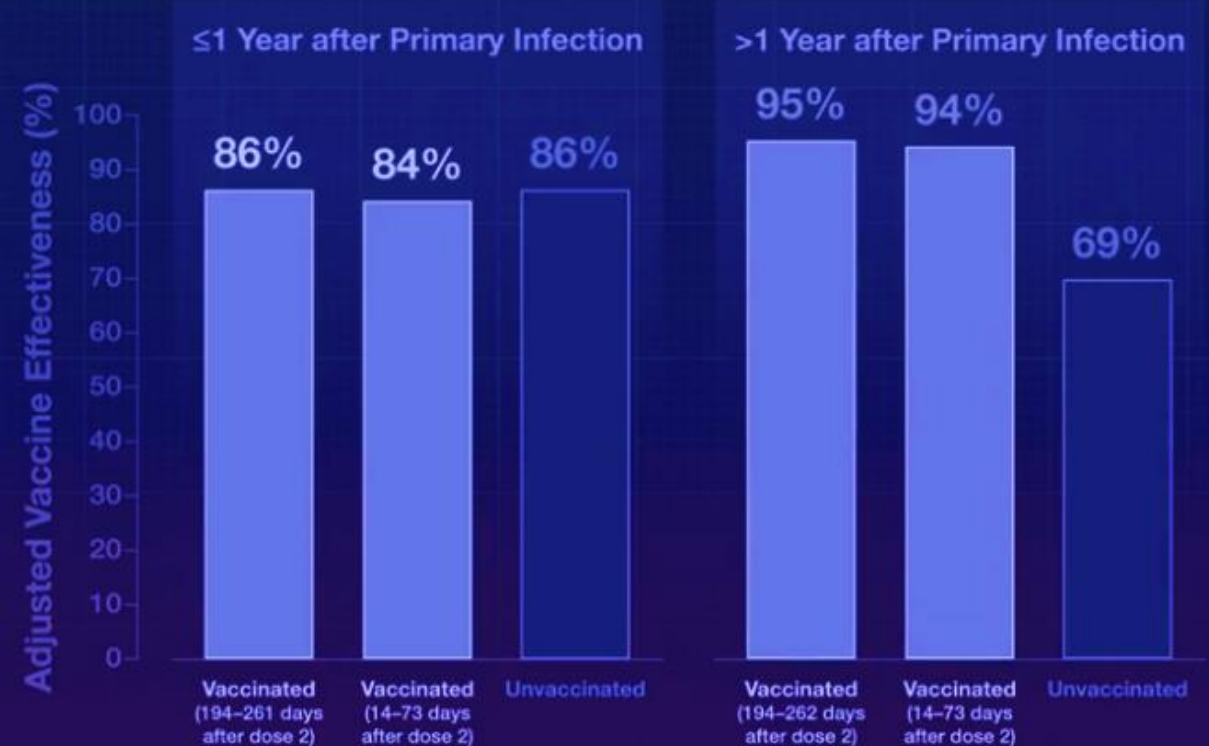


Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection

Vaccine Effectiveness over Time in Previously Uninfected Participants **6m**



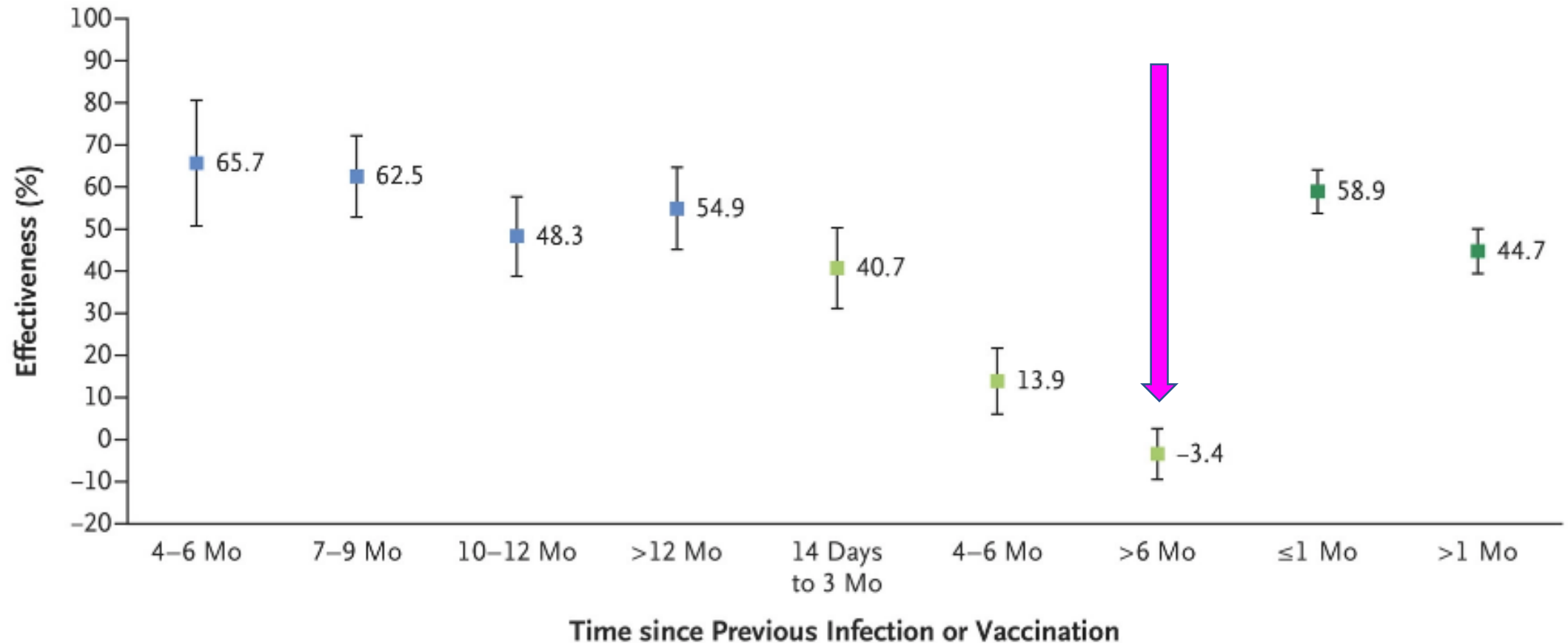
Protection against Reinfection in Previously Infected Participants **1y**



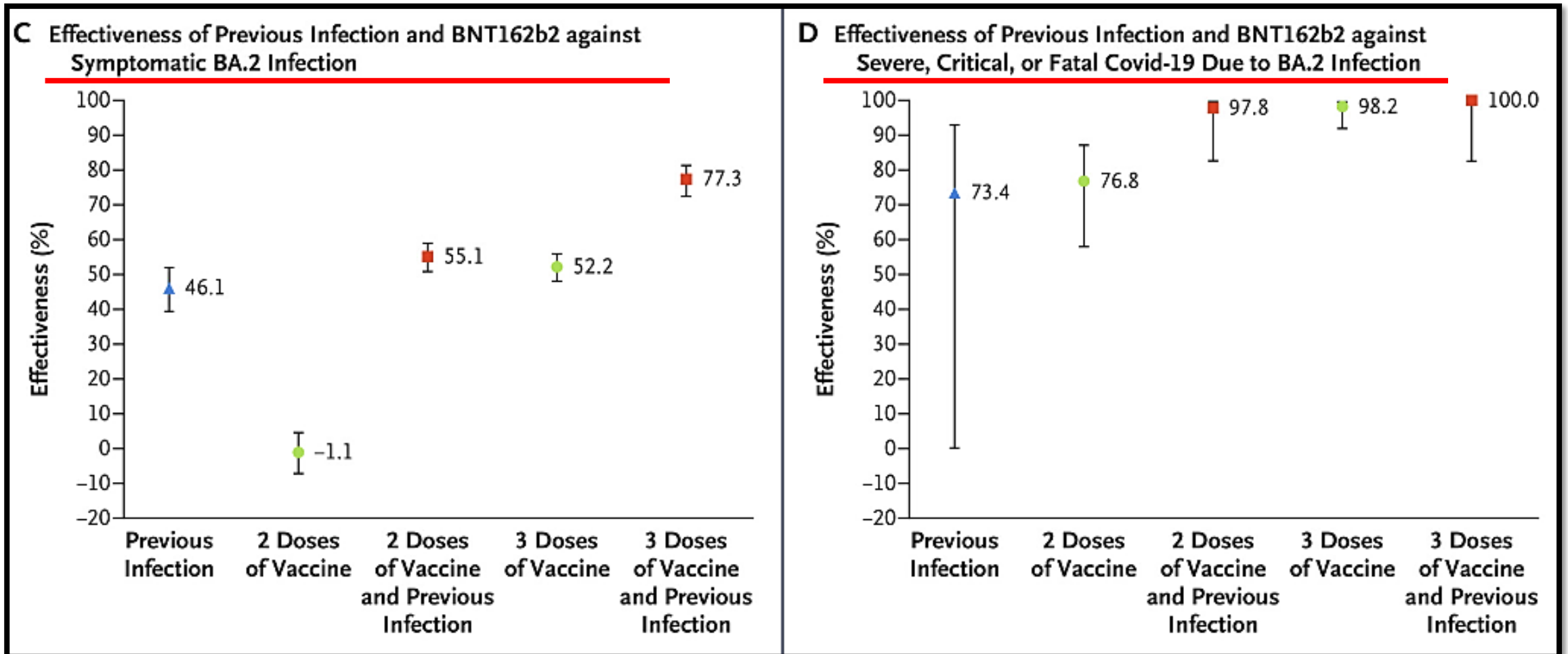
Effects of Previous Infection and Vaccination on Symptomatic Omicron Infections

■ Previous infection ■ 2-Dose vaccination ■ 3-Dose vaccination

A Effectiveness of Previous Infection and BNT162b2 against Any Symptomatic Omicron Infection



Effectiveness of Infection, Vaccination and Hybrid Immunity against Symptomatic BA.2 Infection and Severe, Covid-19

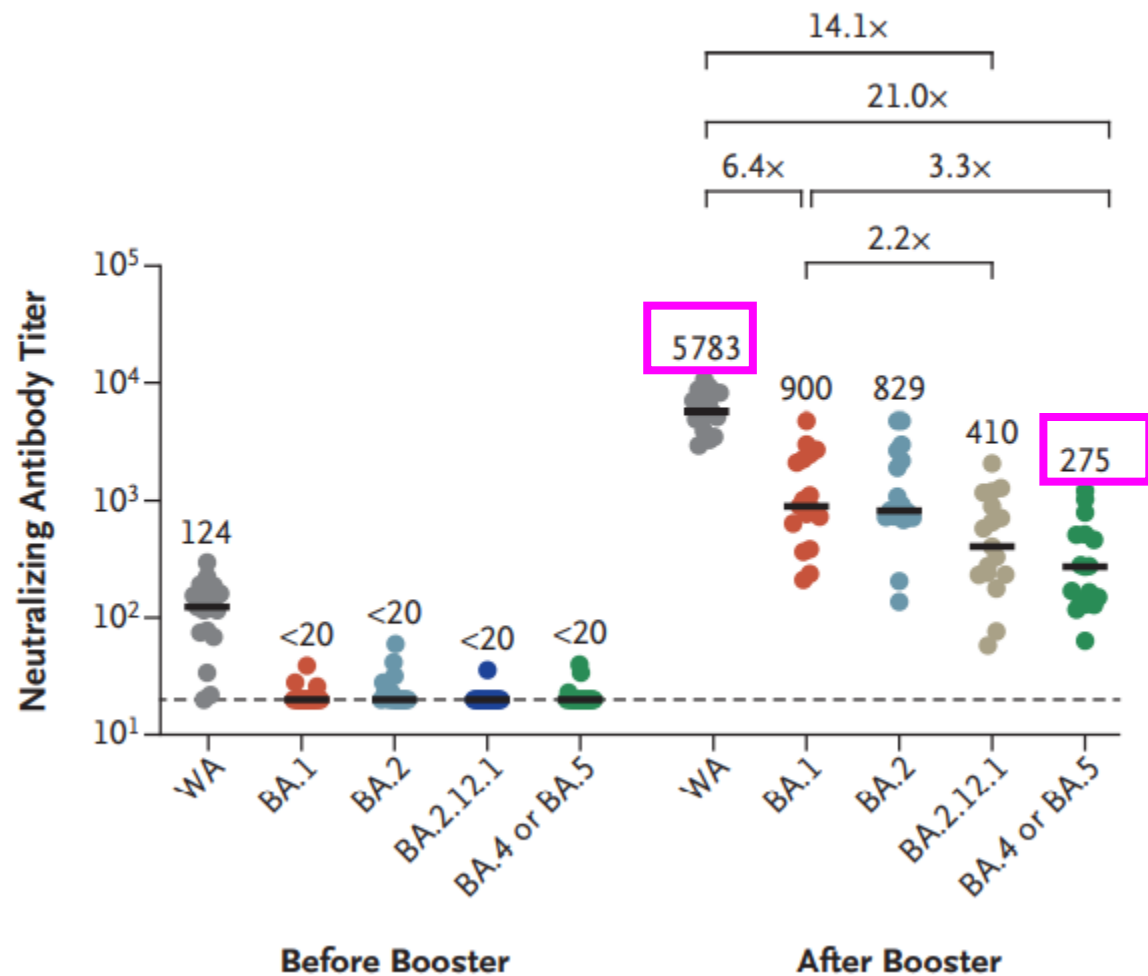


Vaccine effectiveness against SARS-CoV-2 infection of any severity up to 9 months after full vaccination

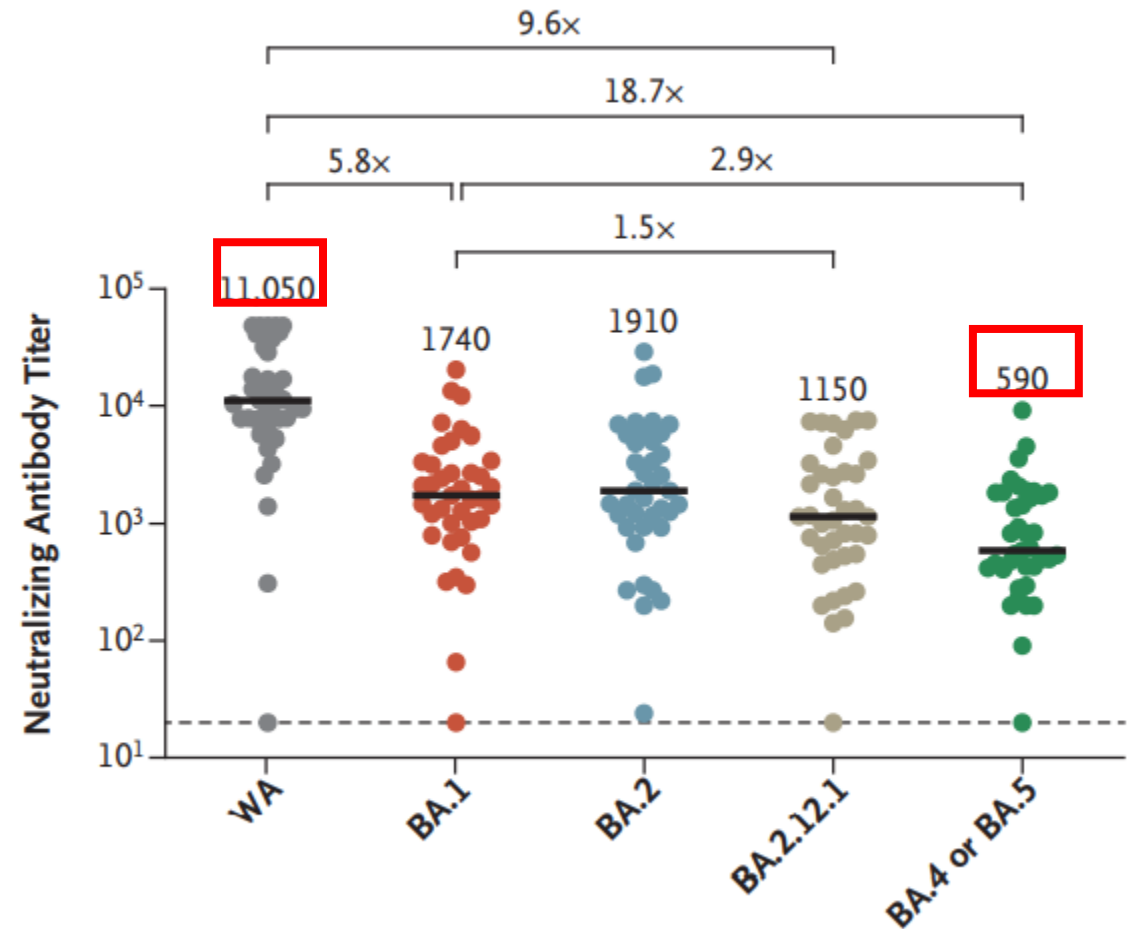
	Number of individuals	Vaccinated		Unvaccinated		Vaccine effectiveness (95% CI)	
		Number of events	Incidence per 100 000 person-days	Number of events	Incidence per 100 000 person-days	Adjusted for age and baseline date	Fully adjusted*
Total study cohort (any vaccine)	1 685 948	6147	4.9	21 771	31.6	84% (83 to 84)	84% (83 to 84)
15–30 days	1 685 948	397	1.6	4 719	19.5	92% (91 to 93)	92% (91 to 93)
31–60 days	1 544 326	1 254	2.5	8 908	22.5	89% (88 to 90)	89% (88 to 89)
61–120 days	1 363 616	2 436	2.6	7 522	14.4	83% (82 to 83)	82% (81 to 83)
121–180 days	635 402	820	1.0	399	1.8	52% (46 to 58)	48% (41 to 54)
181–210 days	327 257	718	1.2	161	2.1	42% (31 to 51)	32% (19 to 43)
>210 days	239 822	522	1.0	62	1.2	23% (0 to 41)	23% (–2 to 41)
BNT162b2 subcohort	1 274 214	5 062	5.1	19 121	36.4	84% (84 to 85)	85% (84 to 85)
15–30 days	1 274 214	333	1.7	4 039	22.1	92% (91 to 93)	92% (92 to 93)
31–60 days	1 166 247	1 095	2.9	7 982	26.7	89% (88 to 90)	89% (88 to 90)
61–120 days	1 032 971	1 796	2.6	6 601	16.6	85% (84 to 85)	84% (84 to 85)
121–180 days	480 153	631	1.0	292	1.7	52% (45 to 58)	47% (39 to 55)
181–210 days	304 298	688	1.2	145	2.1	39% (26 to 49)	29% (15 to 41)
>210 days	231 006	519	1.1	62	1.3	23% (1 to 41)	23% (–2 to 41)

Neutralization Escape by SARS-CoV-2 Omicron Subvariants BA.2.12.1, BA.4, and BA.5

B Vaccinated Participants before and after Booster Dose (2 weeks)

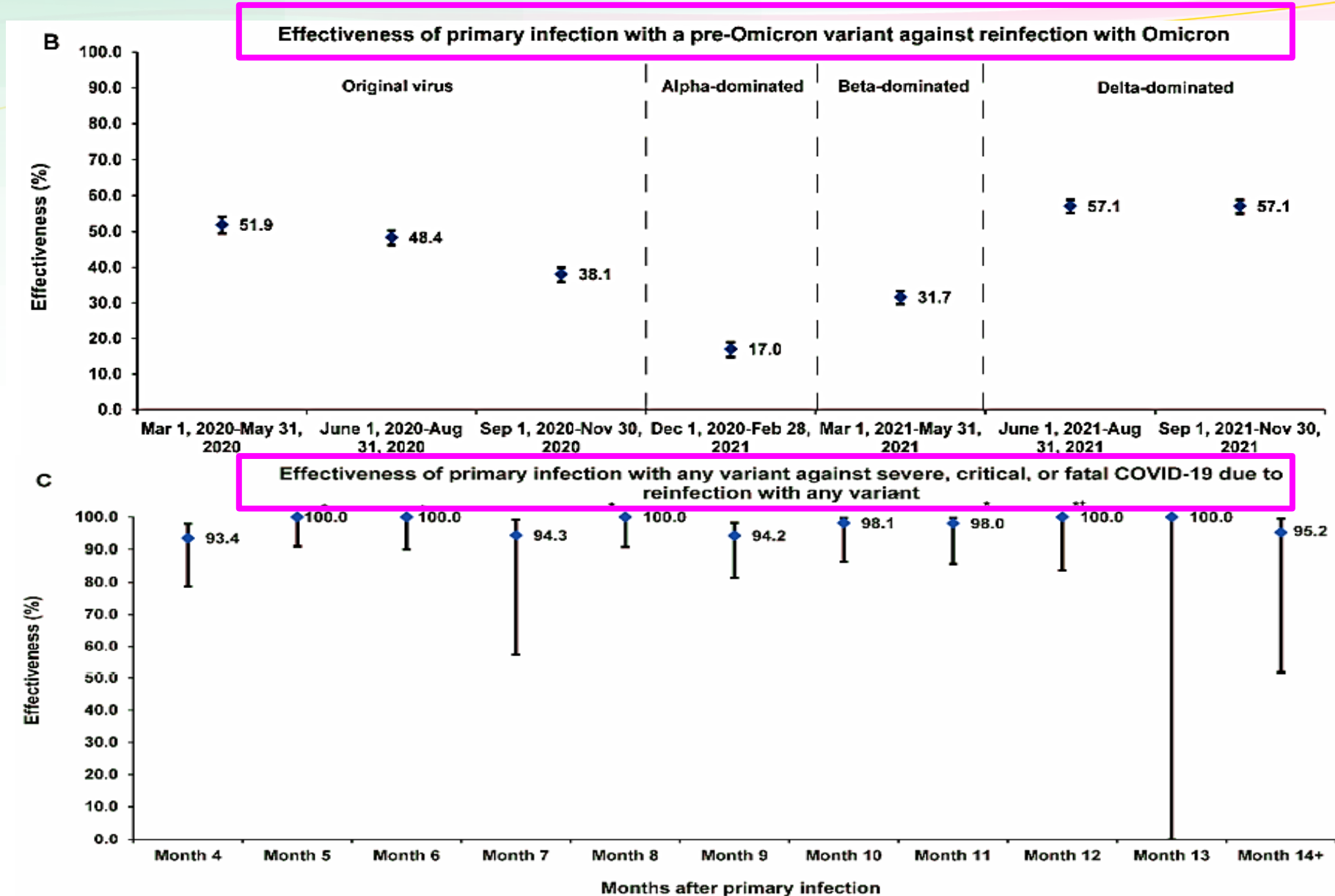


C Infected Participants with BA.1 or BA.2 Subvariant (vaccinated)



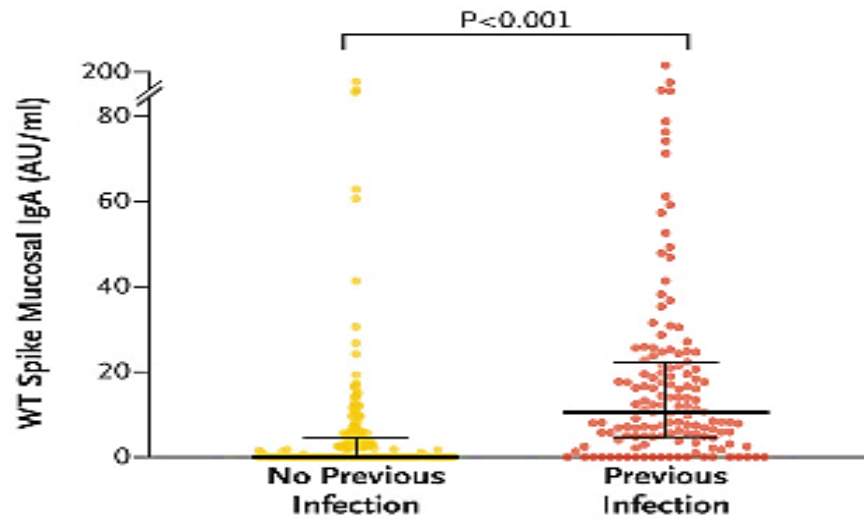


Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar

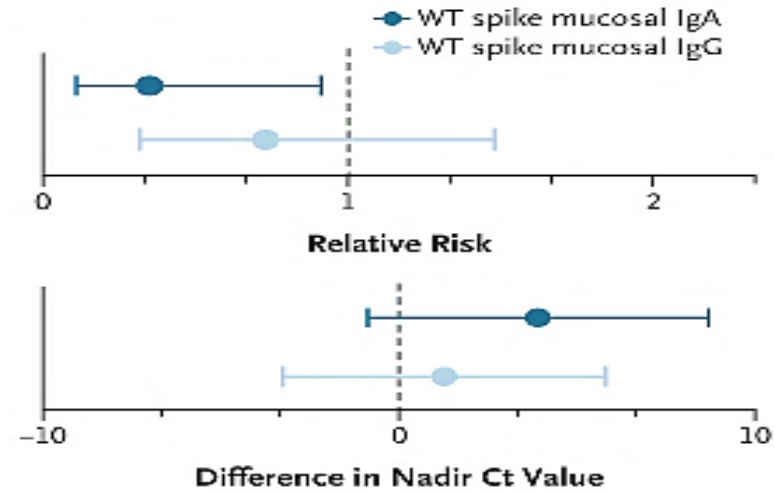


Anti-Spike Mucosal IgA Protection against SARS-CoV-2 Omicron Infection

B WT Spike Mucosal IgA Levels at Baseline

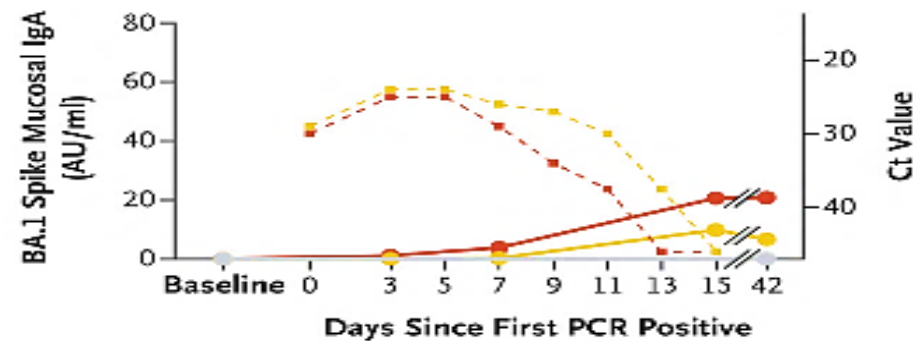


C Risk of Omicron Breakthrough Infection and Effect on Viral Replication



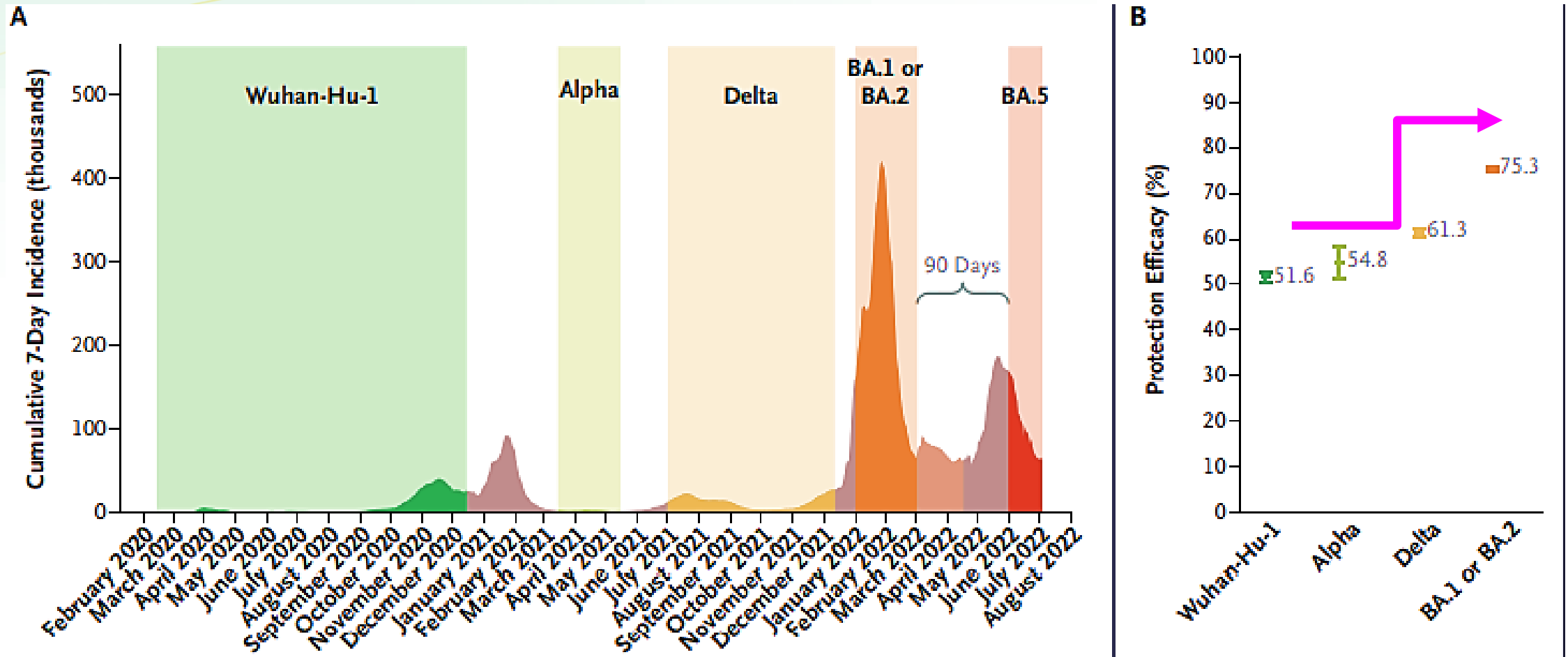
D WT and BA.1 Spike Mucosal IgA Responses after Omicron Breakthrough Infection

- IgA after omicron infection (participants with previous infection)
- IgA after omicron infection (participants without previous infection)
- IgA, no breakthrough infection (participants with previous infection)
- IgA, no breakthrough infection (participants without previous infection)
- Ct value (participants with previous infection)
- Ct value (participants without previous infection)





Risk of BA.5 Infection among Persons Exposed to Previous SARS-CoV-2 Variants

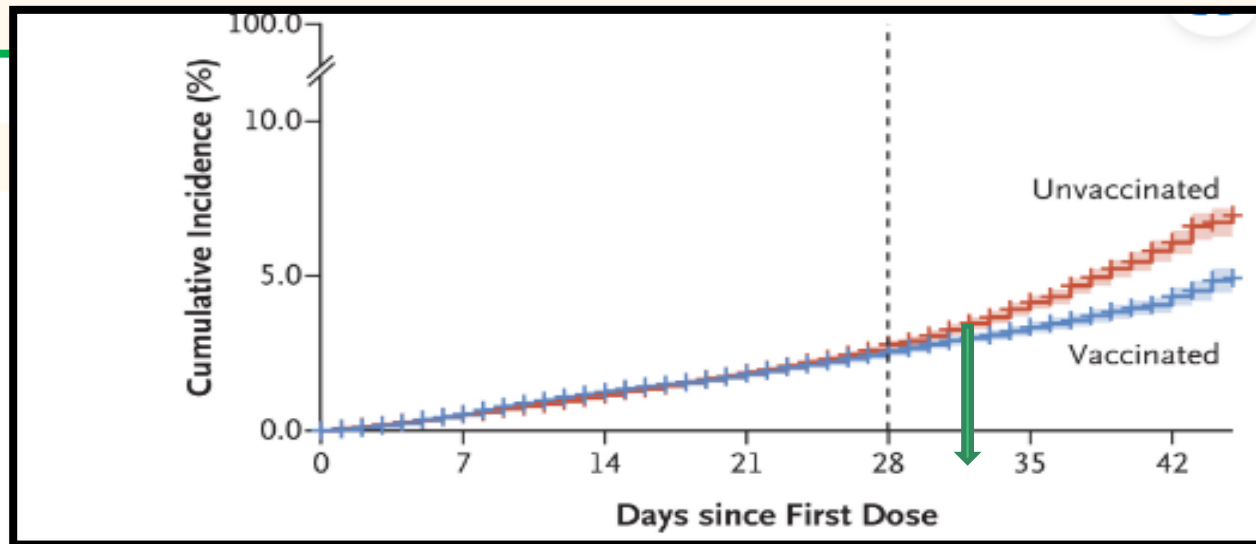




BNT162b2 Vaccine Effectiveness against Omicron in Children 5 to 11 Years of Age

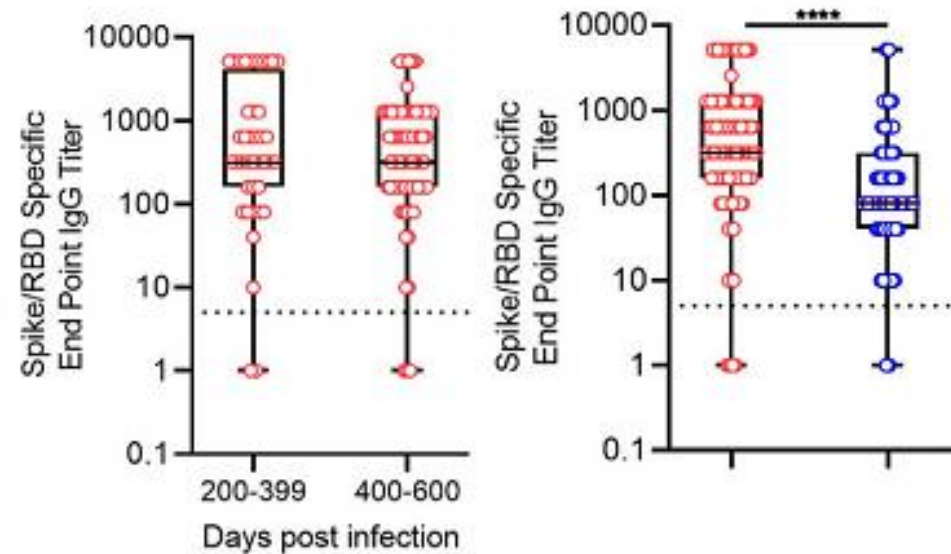
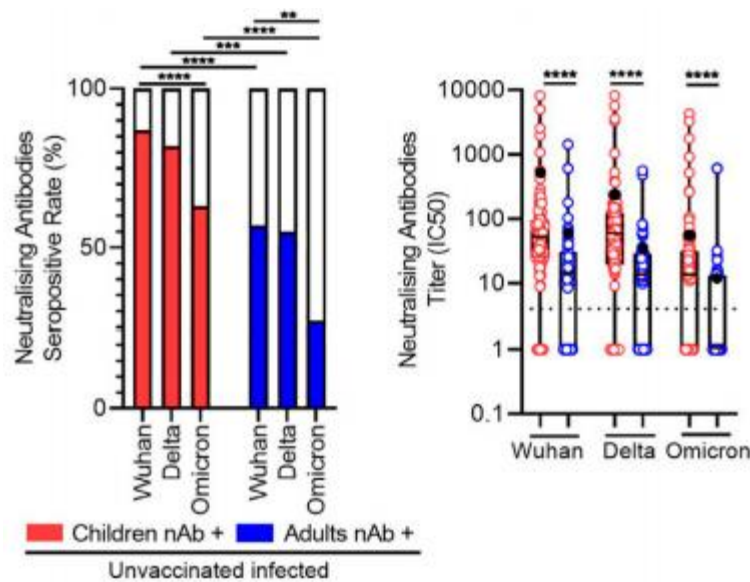
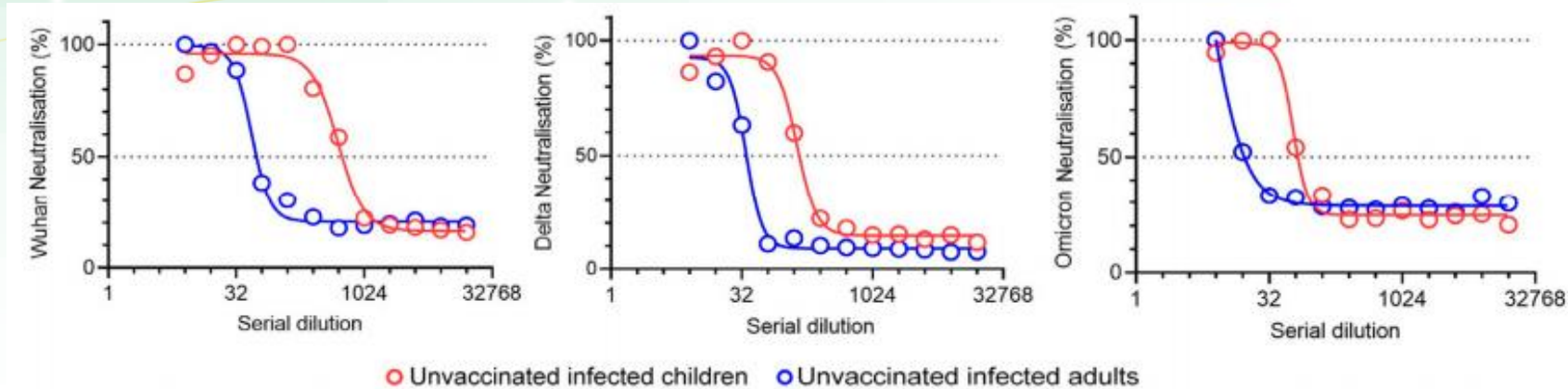
Table 3. Vaccine Effectiveness against Documented SARS-CoV-2 Infection and Symptomatic Covid-19 at 7 to 21 Days after the Second Dose, Stratified According to Age Subgroup.

Outcome	Total Population in Each Study Group*	Events in the Unvaccinated Group	Events in the Vaccinated Group	Risk in the Unvaccinated Group†	Risk in the Vaccinated Group†	Vaccine Effectiveness (95% CI)	Risk Difference (95% CI)
		number		events/100,000	events/100,000	percent	events/100,000
Documented SARS-CoV-2 infection‡							
Age 5 or 6 yr	5418	71	23	2867	922	68 (43 to 84)	1944 (977 to 2915)
Age 7 to 9 yr	9324	177	75	3575	1559	56 (41 to 68)	2016 (1279 to 2764)
Age 10 or 11 yr	7367	175	103	4586	2850	38 (18 to 53)	1736 (703 to 2753)
Symptomatic Covid-19							
Age 5 or 6 yr				67	69 (30 to 91)		822 (224 to 1444)
Age 7 to 9 yr				91	49 (6 to 76)		480 (39 to 919)
Age 10 or 11 yr				29	36 (0 to 61)		585 (-3 to 1195)





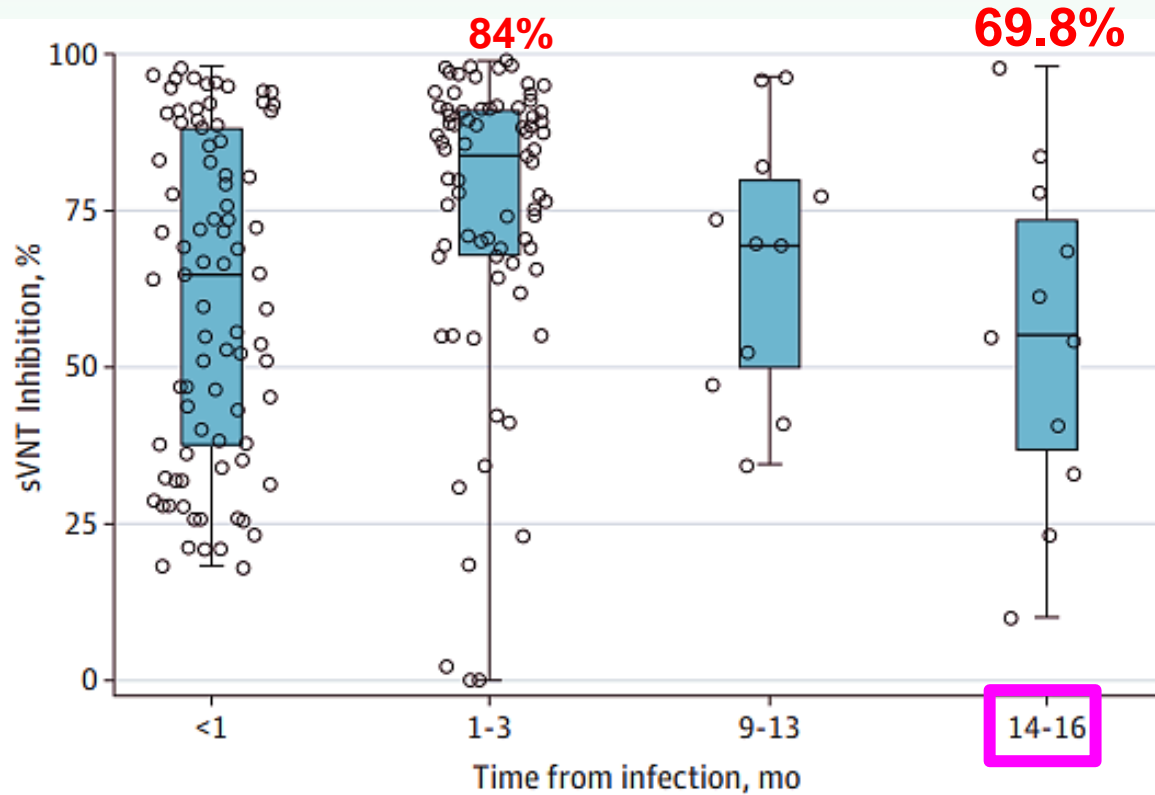
Antibody response against SARS-CoV-2 variants in children infected with pre-Omicron variants



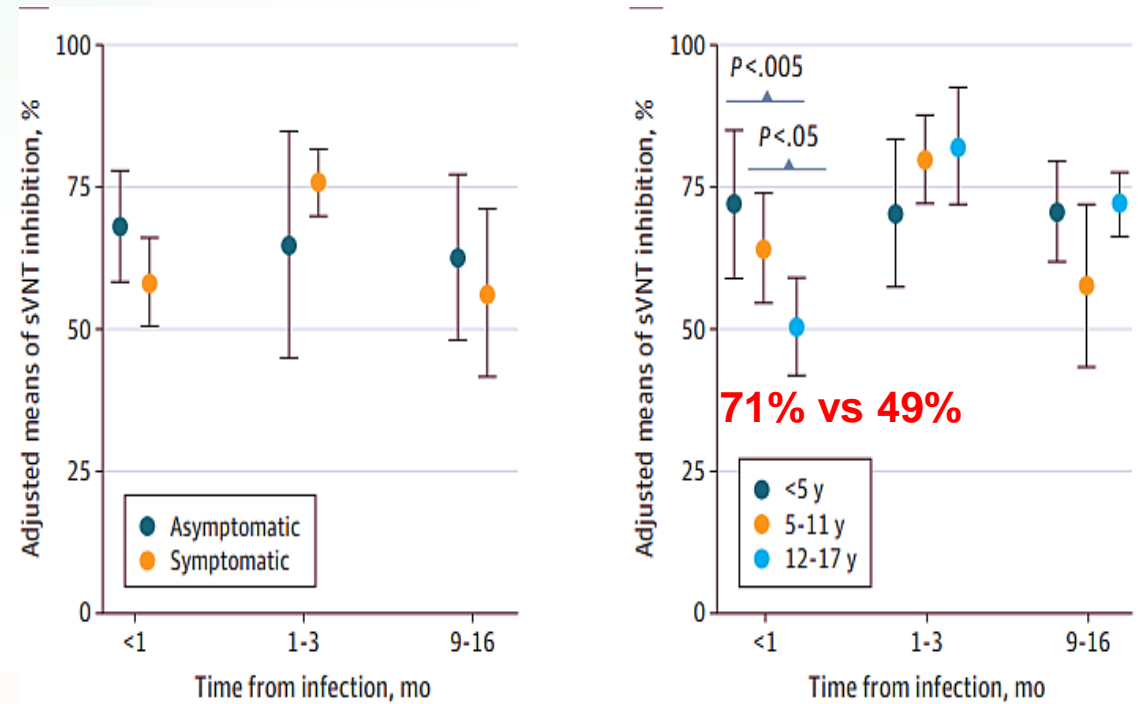


Neutralizing Antibody Levels in Children and Adolescents Up to 16 Months After SARS-CoV-2 Infection

Total Neutralizing Antibody Levels in Children and Time

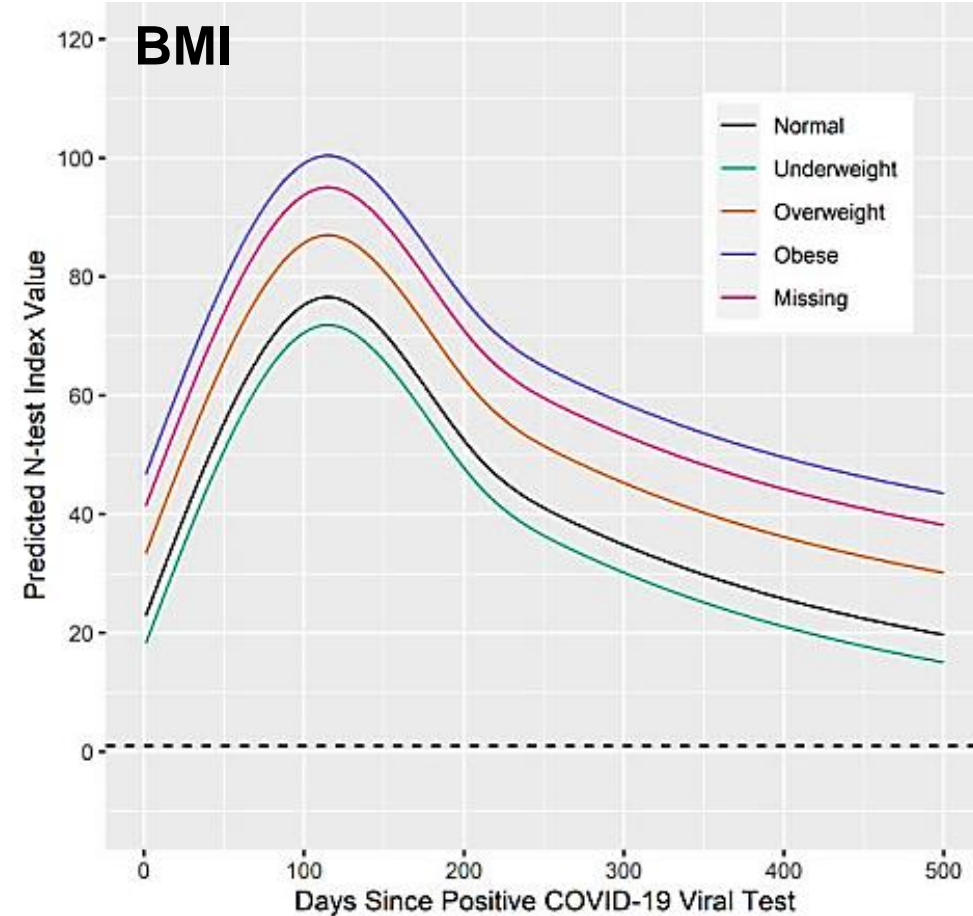
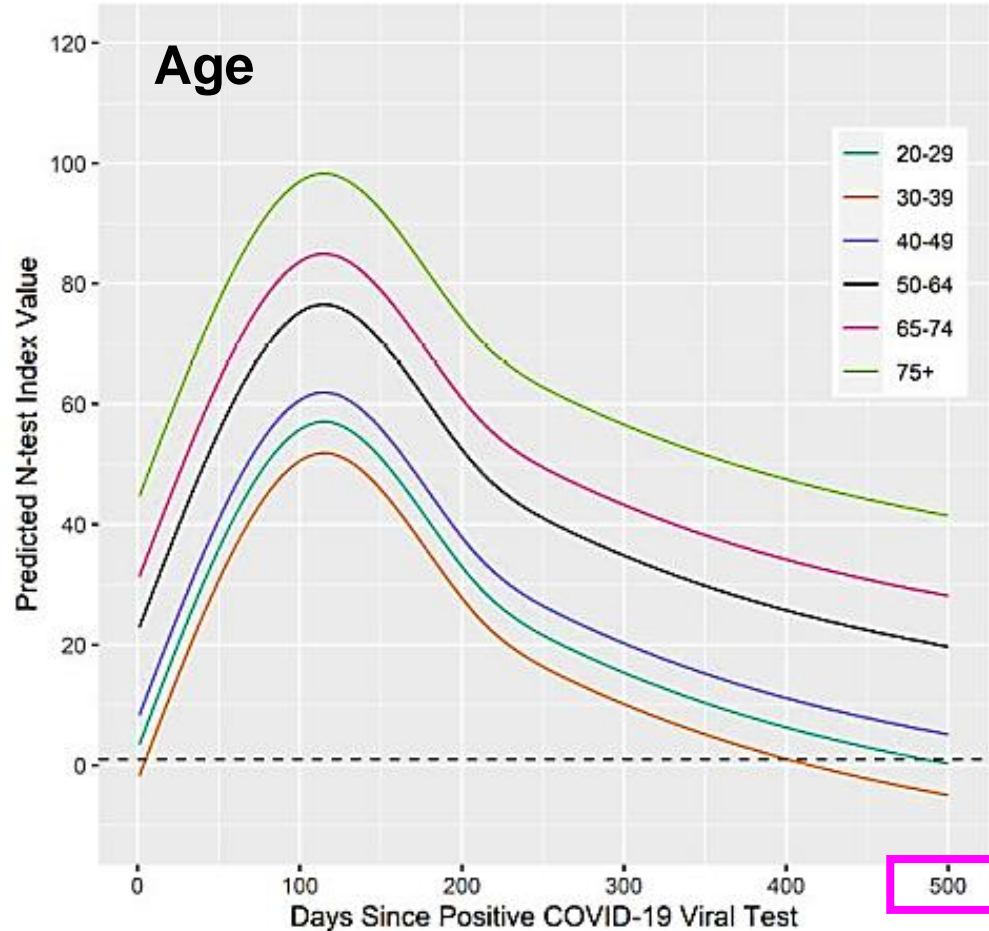


Neutralizing Antibody Level Over Time in Children by symptoms and age



Antibody Duration After Infection From SARS-CoV-2

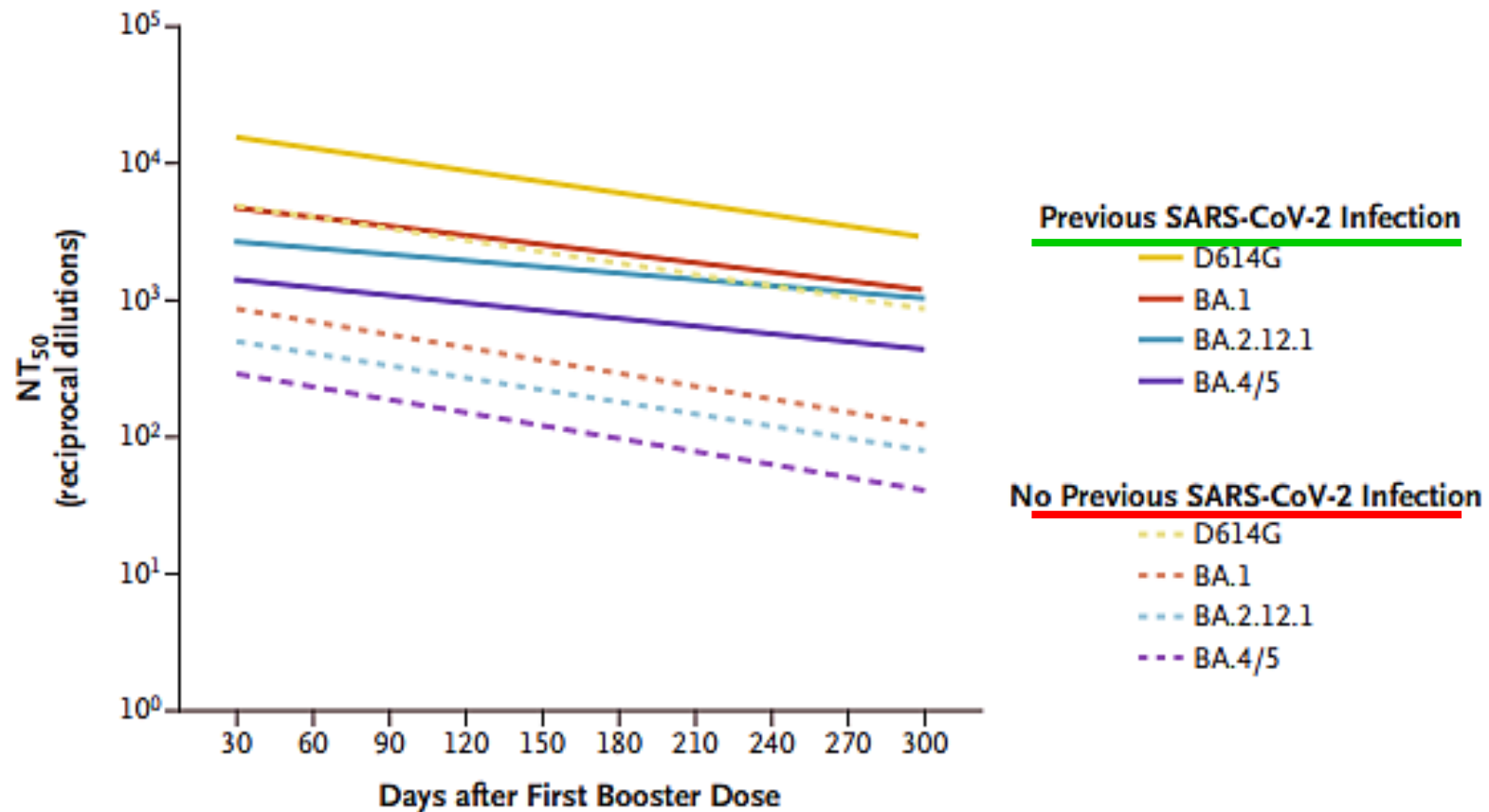
N=4588



Nucleocapsid antibody: 7.4% negative between 401 and 500 days after infection

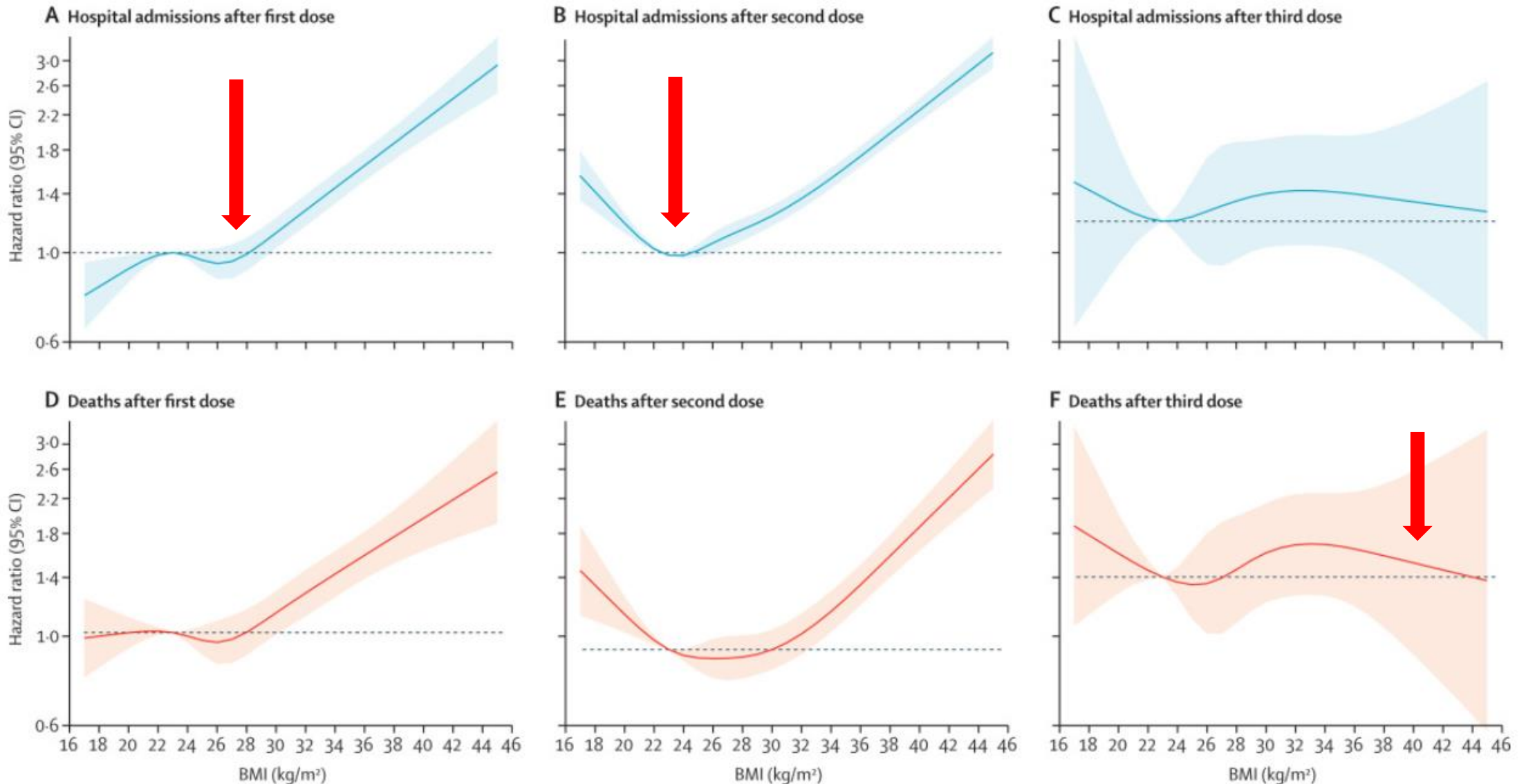
Durability of Booster mRNA Vaccine against SARS-CoV-2 BA.2.12.1, BA.4, and BA.5 Subvariants

Decay Trend in Neutralizing-Antibody Titers According to Previous SARS-CoV-2 Infection Status





Associations of BMI with COVID-19 vaccine effectiveness, and risk of severe COVID-19 outcomes in England





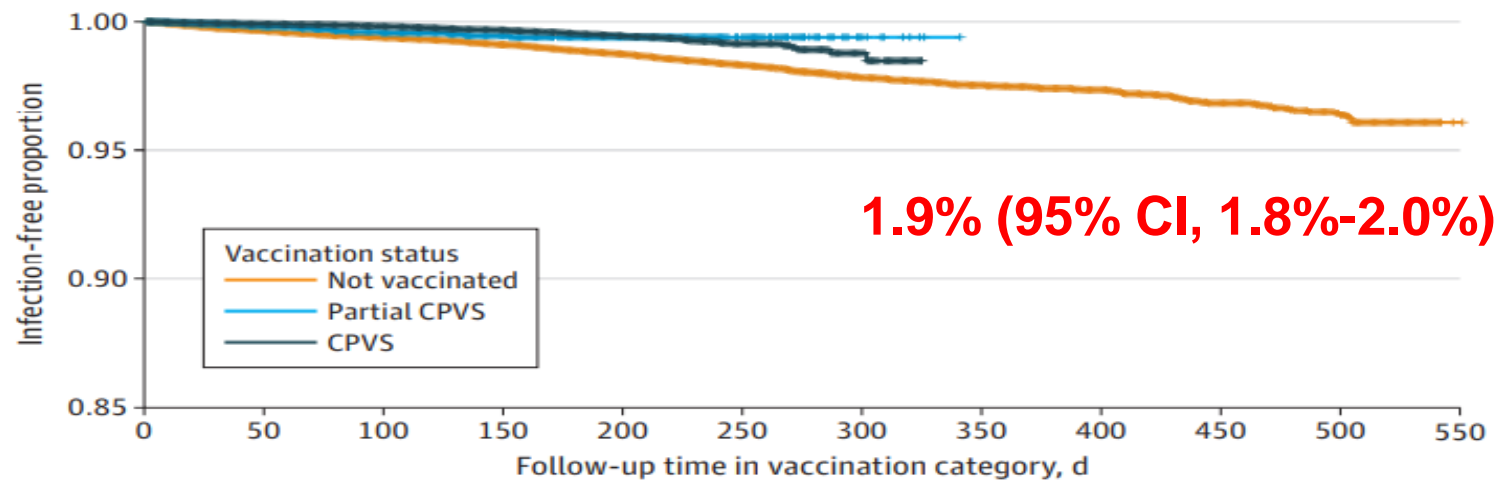
Reinfected With SARS-CoV-2 During the Omicron Wave of Infections in Iceland, December 1, 2021, to February 13, 2022

Variable	Reinfected individuals, No./total No. (%)	OR (95% CI)	
		Unadjusted	Adjusted ^a
Age group, y			
≤17	229/2113 (10.8)	0.68 (0.58-0.81)	0.81 (0.66-0.98)
18-29	475/3136 (15.1)	1 [Reference]	1 [Reference]
30-49	477/3724 (12.8)	0.82 (0.72-0.94)	0.79 (0.66-0.95)
50-74	136/2316 (5.9)	0.35 (0.29-0.43)	0.32 (0.24-0.44)
≥75	10/247 (4.1)	0.24 (0.15-0.45)	0.22 (0.08-0.61)
Sex			
Male	685/5888 (11.6)	1 [Reference]	NA
Female	642/5648 (11.3)	0.97 (0.87-1.09)	NA
Vaccine status			
≤1 Dose	1007/8598 (11.7)	1 [Reference]	1 [Reference]
≥2 Doses	320/2938 (10.9)	0.92 (0.81-1.05)	1.42 (1.13-1.78)
Elapsed time from initial infection, mo			
≤3	338/3671 (9.2)	0.74 (0.65-0.85)	0.88 (0.65-1.20)
4-17	729/6082 (12.0)	1 [Reference]	1 [Reference]
≥18	260/1783 (14.6)	1.25 (1.08-1.46)	1.41 (1.05-1.90)

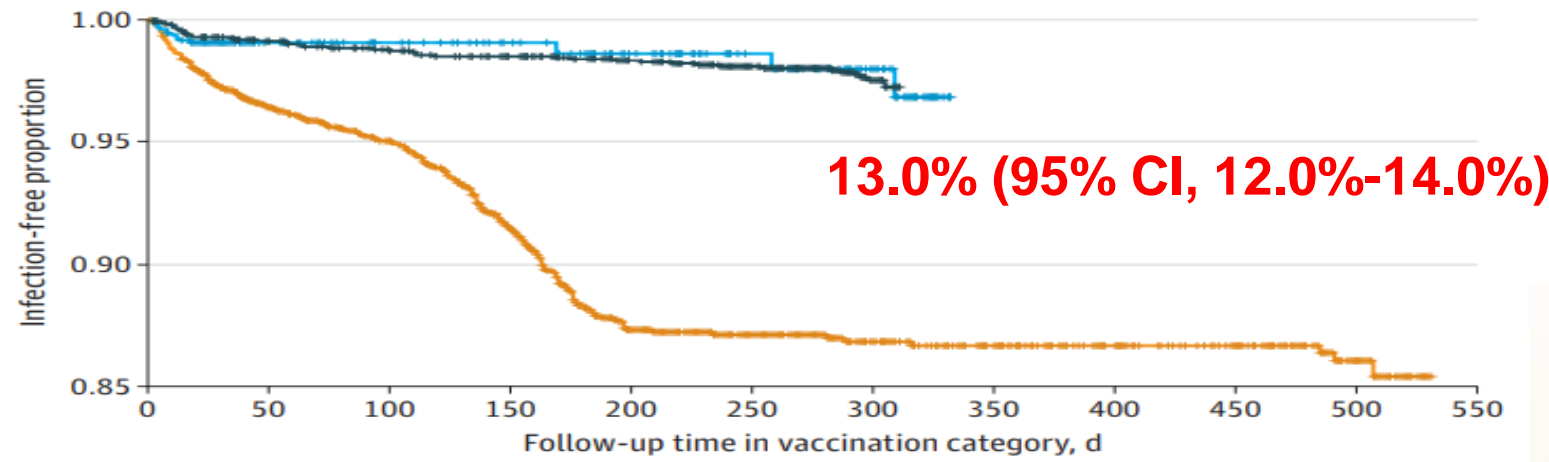


Effectiveness Associated With Vaccination After COVID-19 Recovery in Preventing Reinfection

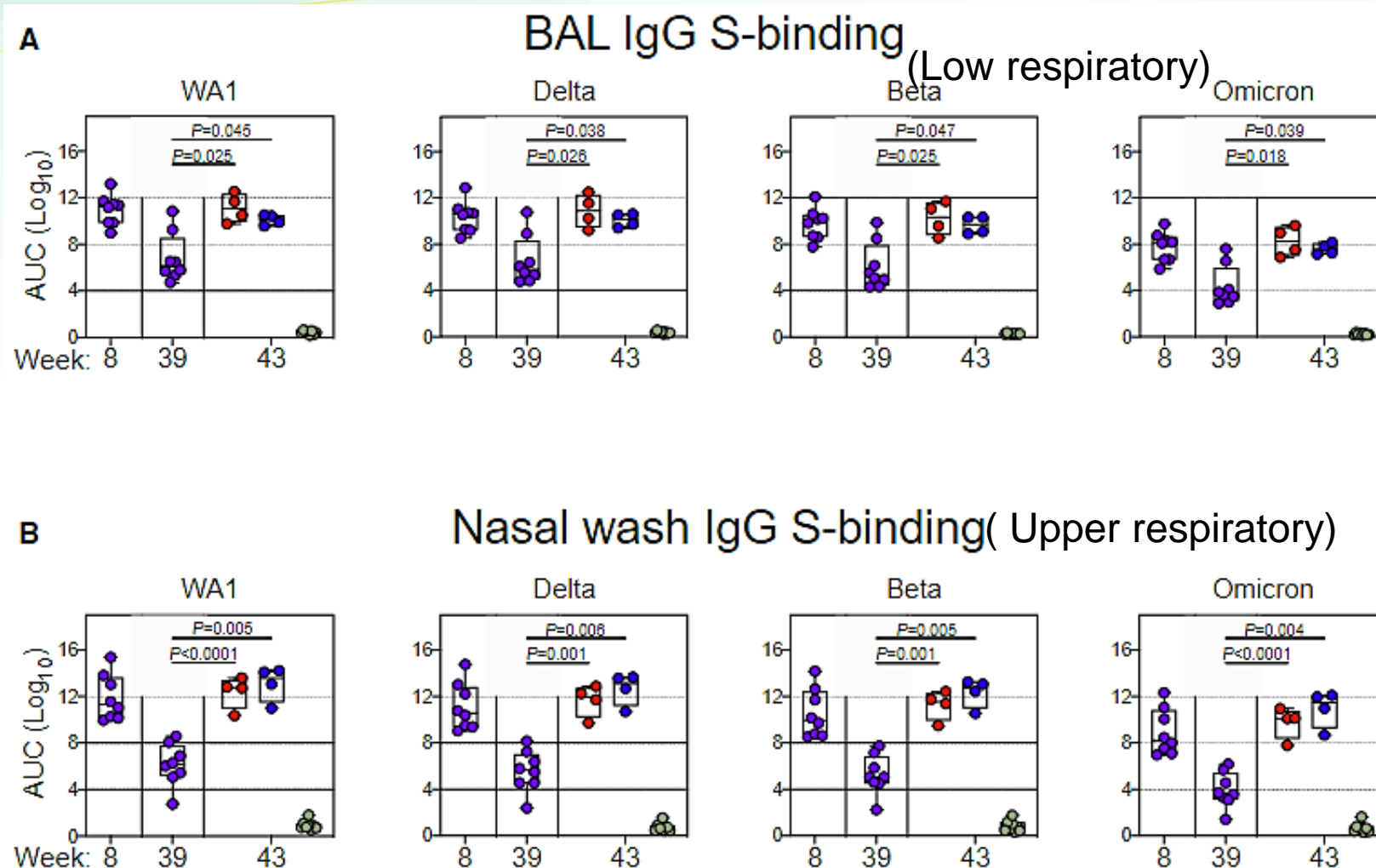
A General population



B LTCC residents

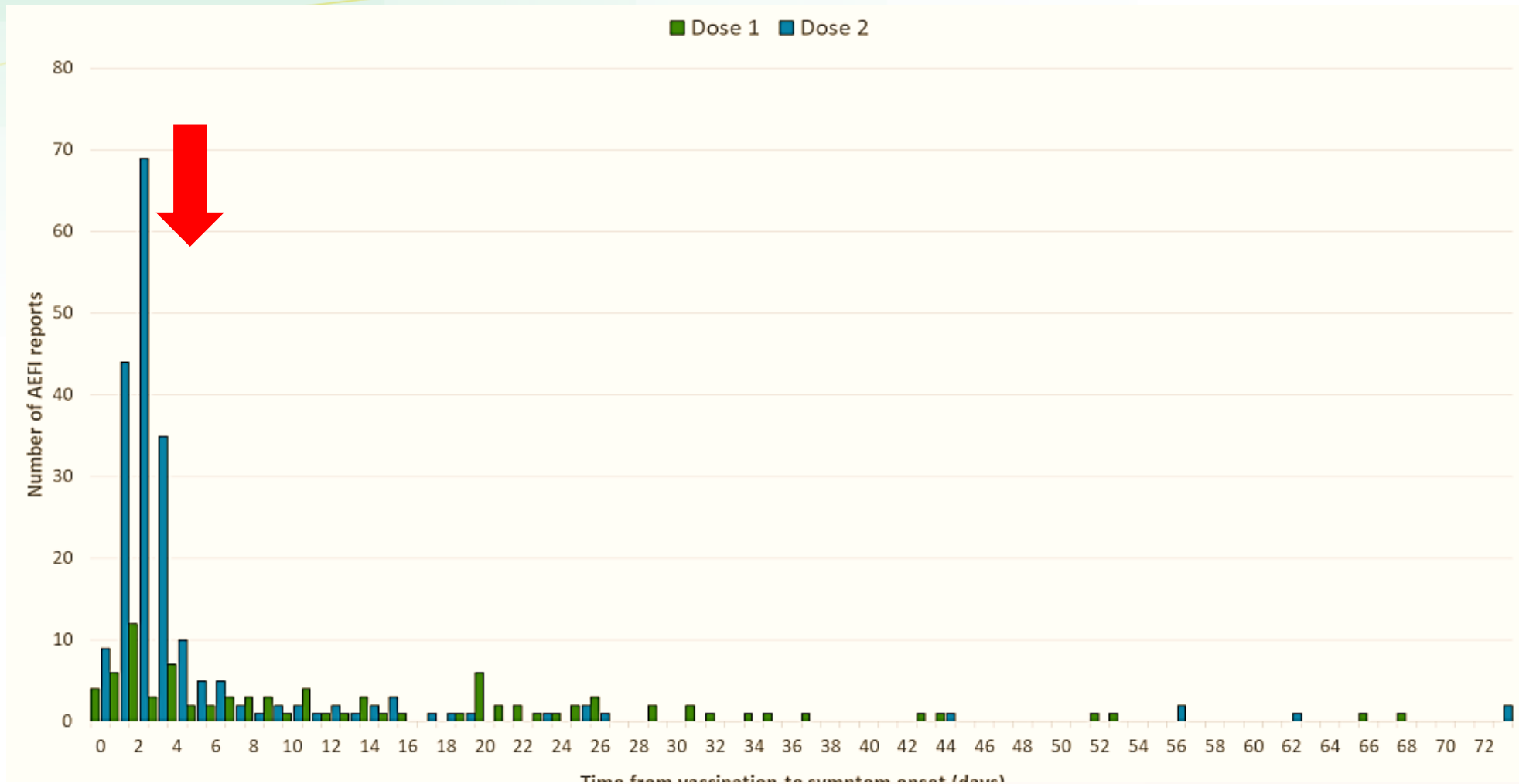


mRNA-1273 or mRNA-Omicron boost in macaques elicits similar B cell expansion, neutralizing responses, and protection from Omicron



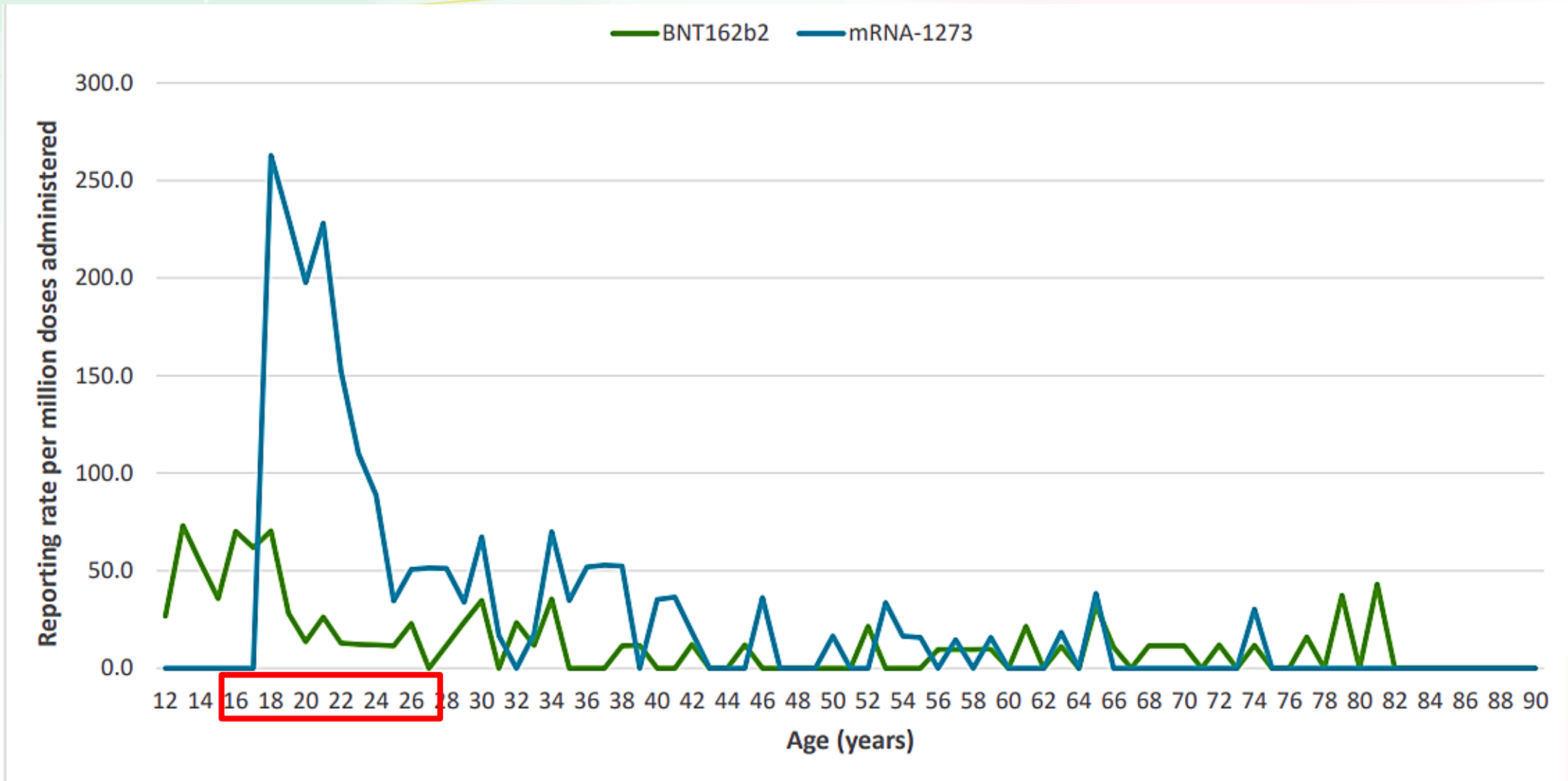


Myocarditis and pericarditis following COVID-19 mRNA vaccines by dose number and time to symptom onset



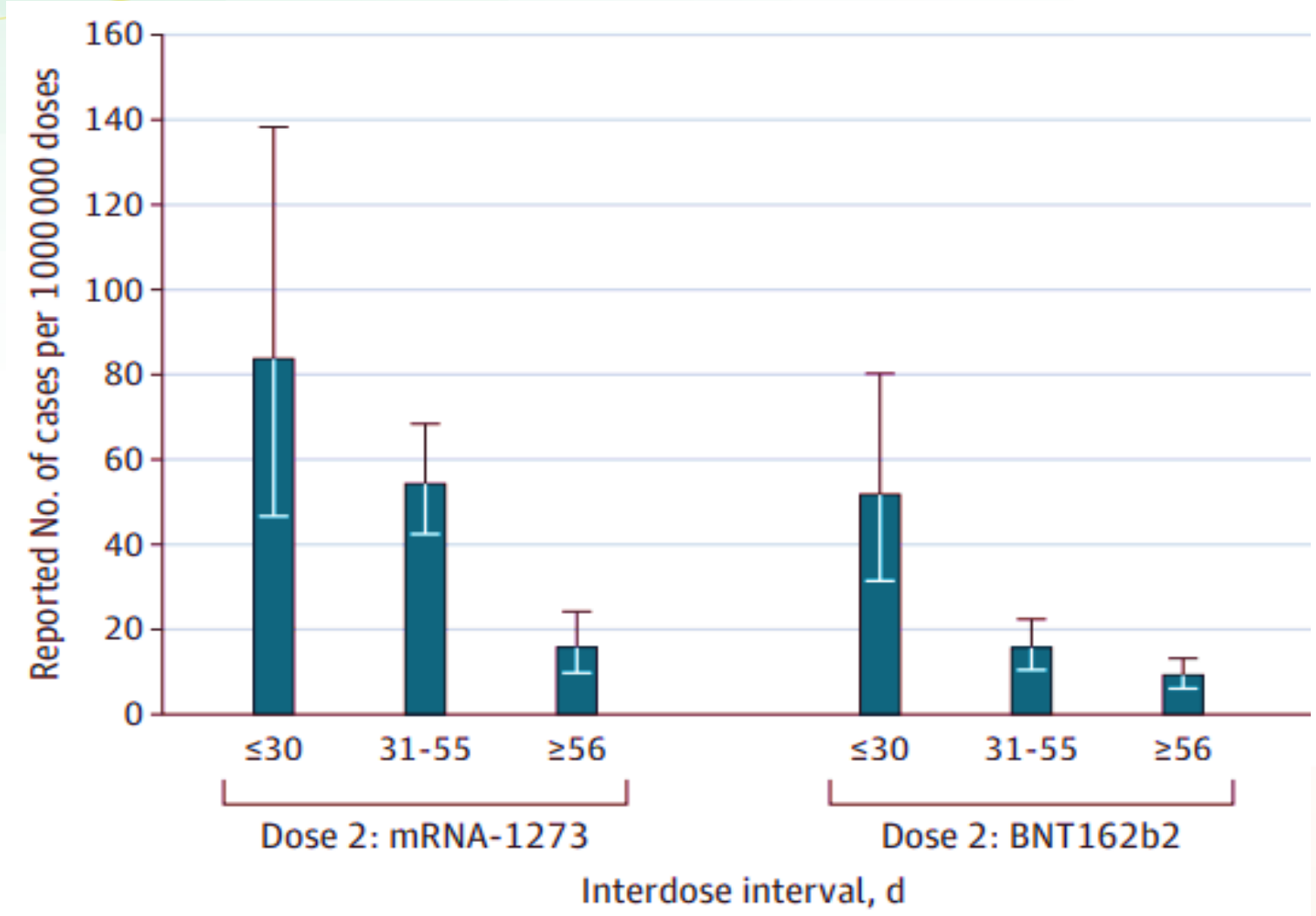


Rate of myocarditis and pericarditis per million doses administered following dose 2 of mRNA vaccine



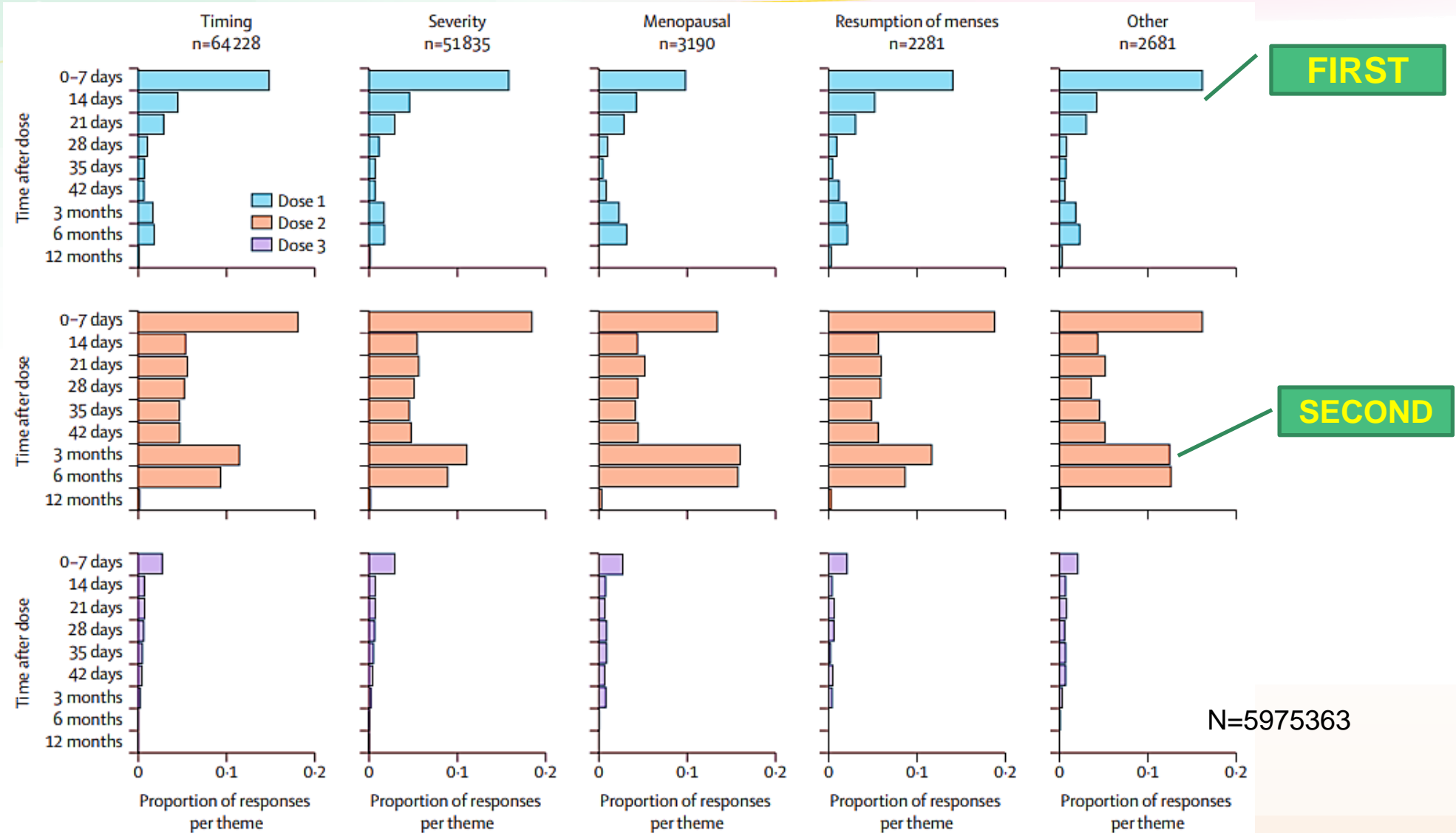


Reported Myocarditis or Pericarditis Among People: rate by interdose intervals





Menstrual irregularities and vaginal bleeding after COVID-19 vaccination reported to v-safe surveillance USA December, 2020–January, 2022





Pharmacologic treatments for COVID 19

Global Covid 19 drugs

Emergency use authorization

Monoclonal antibody

REGEN-COV, Bamlanivimab & etesevimab, Sotrovimab, Evusheld, **Bebtelovimab**

Antiviral agent

Remdesivir, Paxlovid, Molnupiravir, **xocova**, **sabizabulin**

Antiphlogistic drugs

Dexamethasone, Baricitinib, Tocilizumab



BA.2, IM



New Drugs against SARS CoV 2

Anti-S protein antibody

- REGEN-COV(Regeneron)
- Bamlanivimab/Etesevimab(Lily)
- Xevudy(GSK)
- Regkirona(Celltrion)

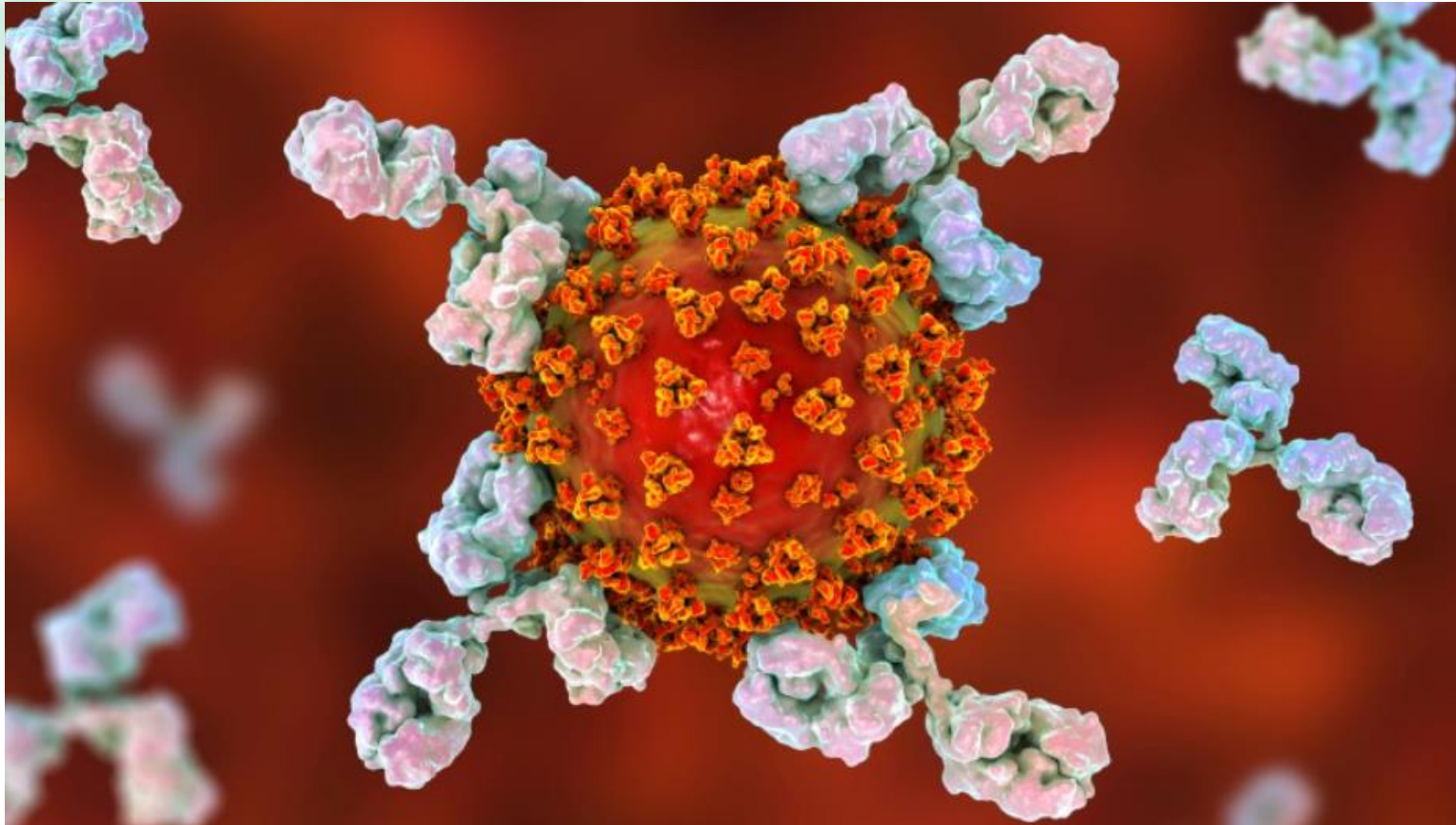
Oral antiviral drug

3CL^{pro} Inhibitor

- Paxlovid(Pfizer)
- Xocova(Shionogi)

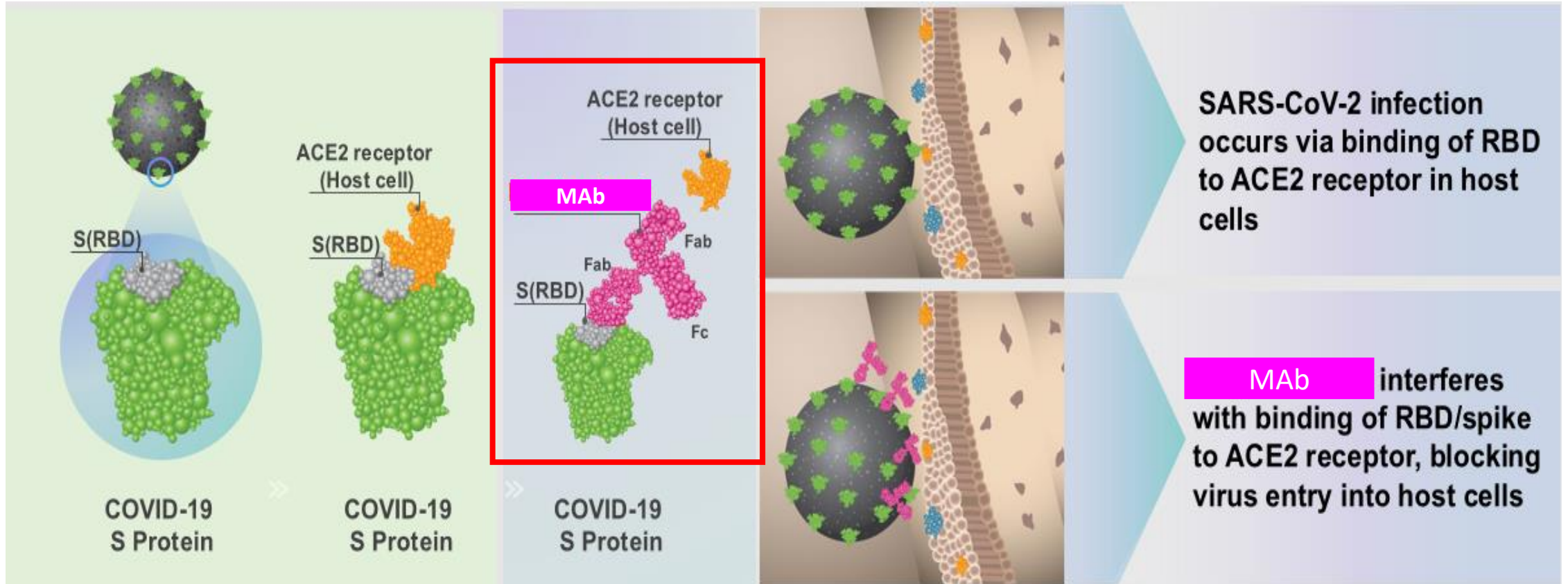
RNA Polymerase Inhibitor

- Lagevrio(Merck)

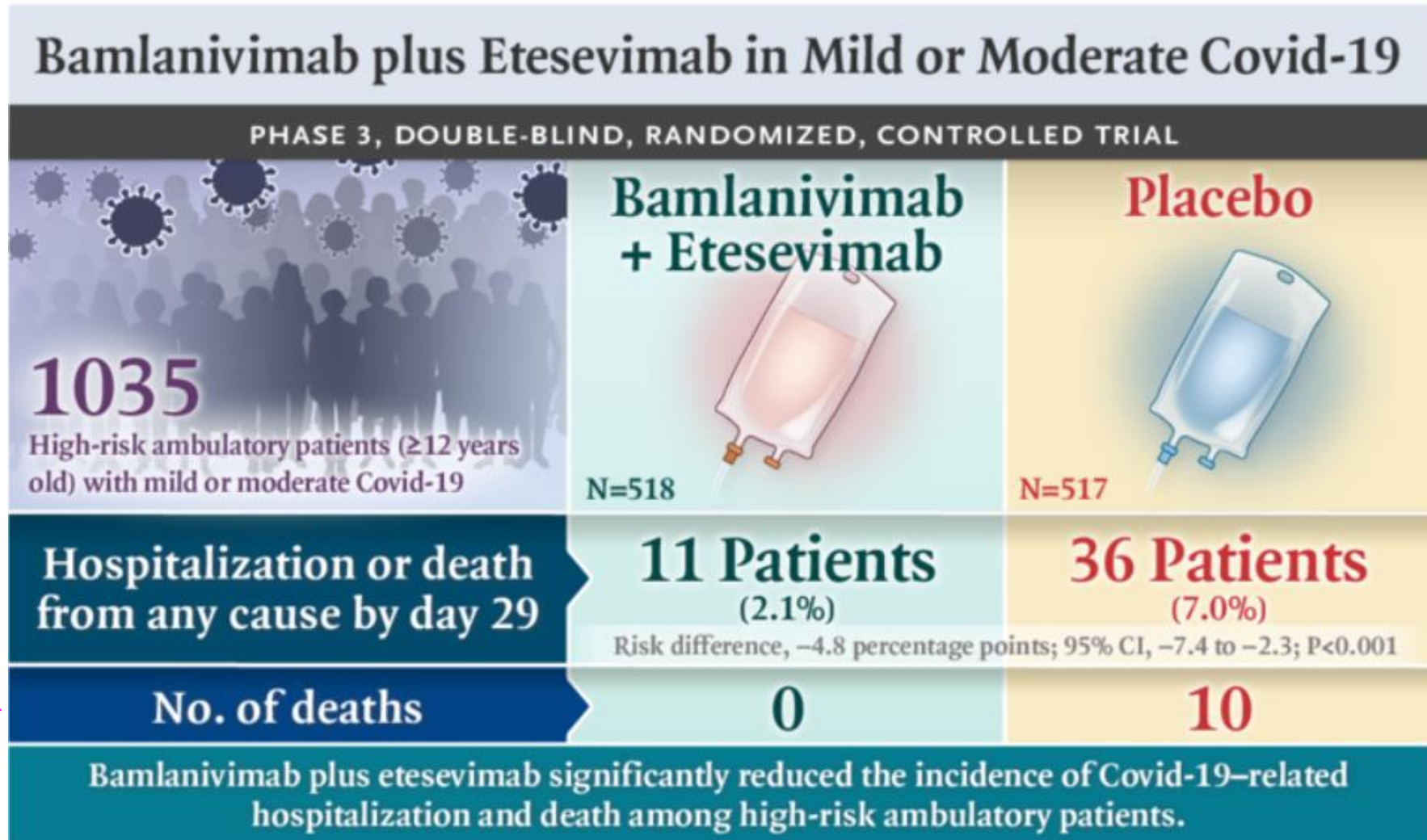


Monoclonal Antibody

Mechanism of monoclonal antibodies



Bamlanivimab plus Etesevimab in mild or moderate covid-19



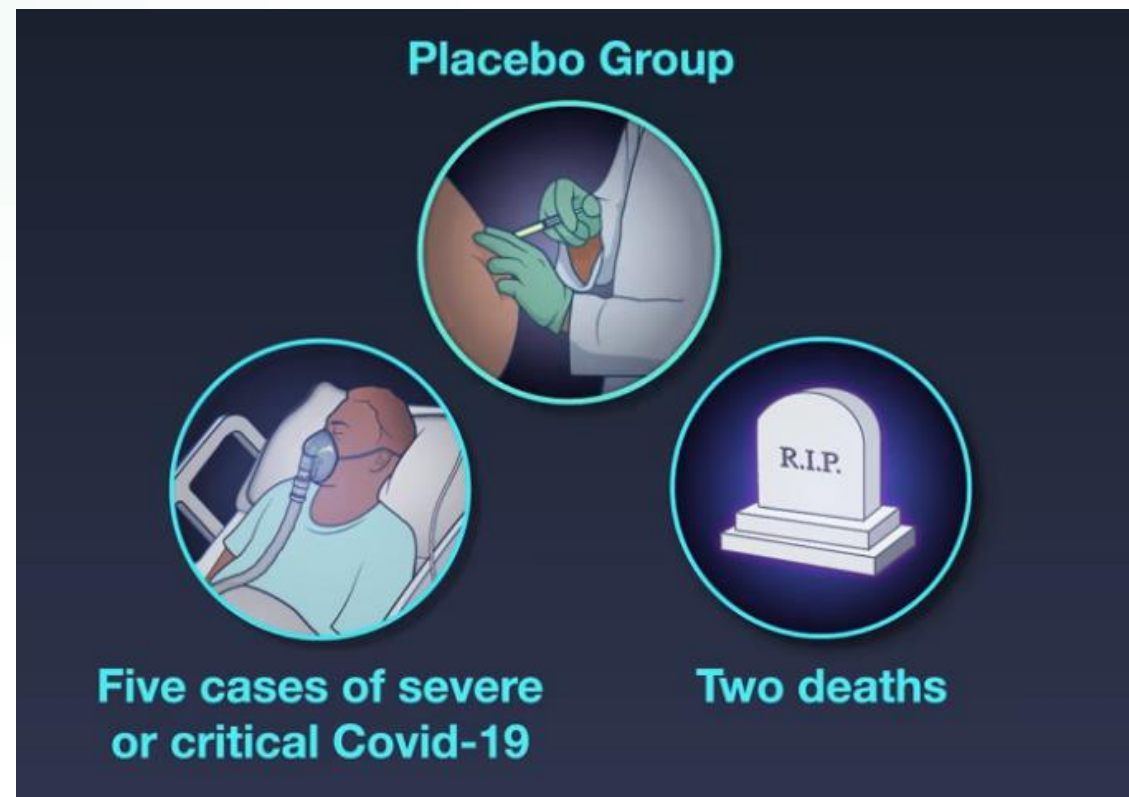
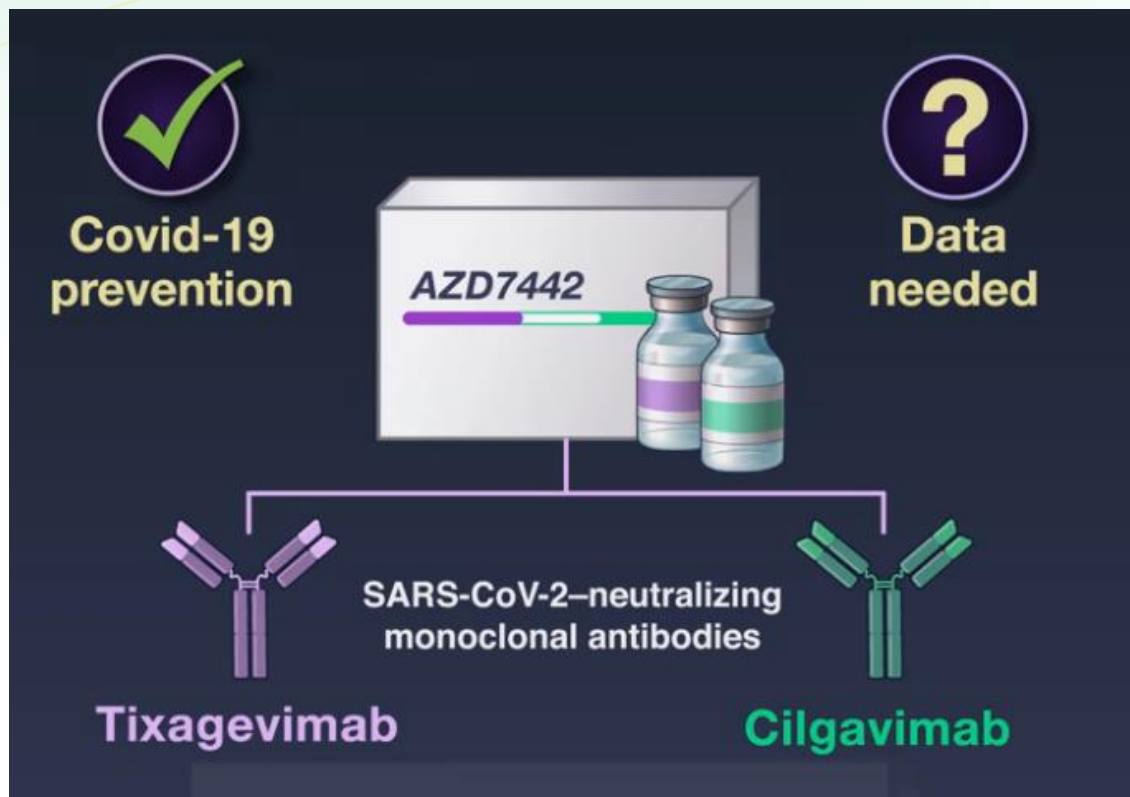


EVUSHELD

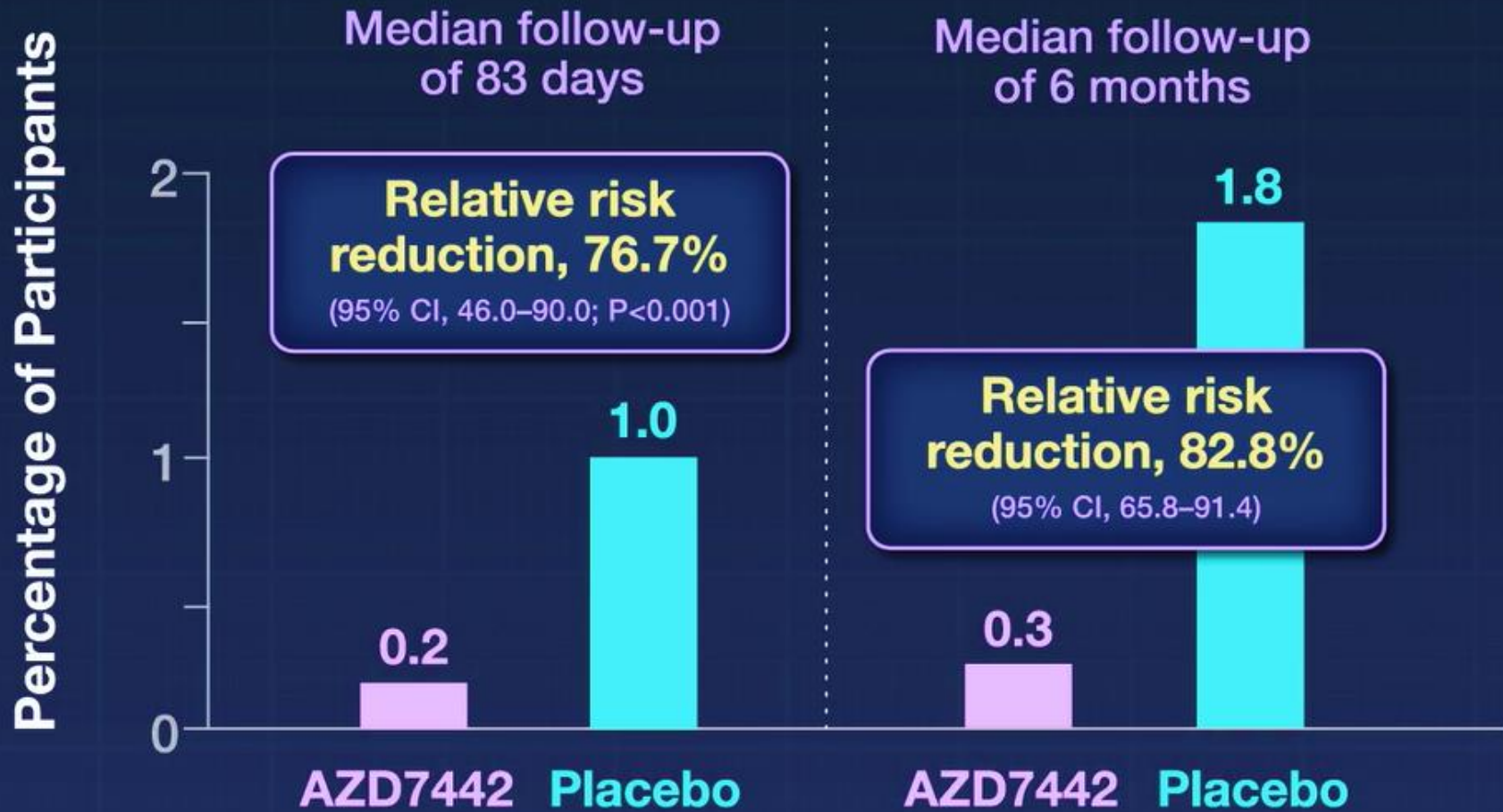
Evusheld

- AstraZeneca's intramuscular *Evusheld* (AZD7442; tixagevimab with cilgavimab), **a long-acting antibody**. EUA for the **pre-exposure prophylaxis** in aged 12 years and older weighing at least 40 kg.
- **Unlikely to mount an immune response** from vaccination or for whom vaccination is not recommended.
- Evusheld should be treated **every 6 months** to maintain protection

Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19



Incidence of Symptomatic Covid-19



Tixagevimab/Cilgavimab for Prevention of COVID-19 during the Omicron

	Matched Controls N=6,354	Tixagevimab/cilgavimab recipients N=1,733	Propensity Score Survival Analysis	Difference in Difference [^] Analysis
	Number of Events (%)	Number of Events (%)	Hazard Ratio (95% CI)	Incidence Rate Ratio (95% CI)
Composite outcome (COVID-19 infection, COVID-19 hospitalization, and all-cause mortality)				
Overall Cohort	206 (3.2%)	17 (1.0%)	0.31 (0.18-0.53)	
Immunocompromised	147 (3.5%)	12 (1.0%)	0.32 (0.18-0.62)	
Severely Immunocompromised	87 (3.7%)	11 (1.4%)	0.44 (0.21-0.93)	
Not Immunocompromised* but at High Risk	59 (2.8%)	(<1%) ^{&}	0.27 (0.13-0.56)	
Individual Outcome (Overall Cohort)				
COVID-19 Infection	69 (1%)	(<0.5%) ^{&}	0.34 (0.13-0.87)	0.32 (0.24-0.44)
COVID-19 related hospitalization	38 (0.5%)	(<0.5%) ^{&}	0.13 (0.02-0.99)	0.10 (0.05-0.22)
All-cause Mortality	99 (2%)	(<0.5%) ^{&}	0.36 (0.18-0.73)	
Falsification: Urinary Tract Infection	127 (2%)	36 (2%)	1.05 (0.68-1.62)	

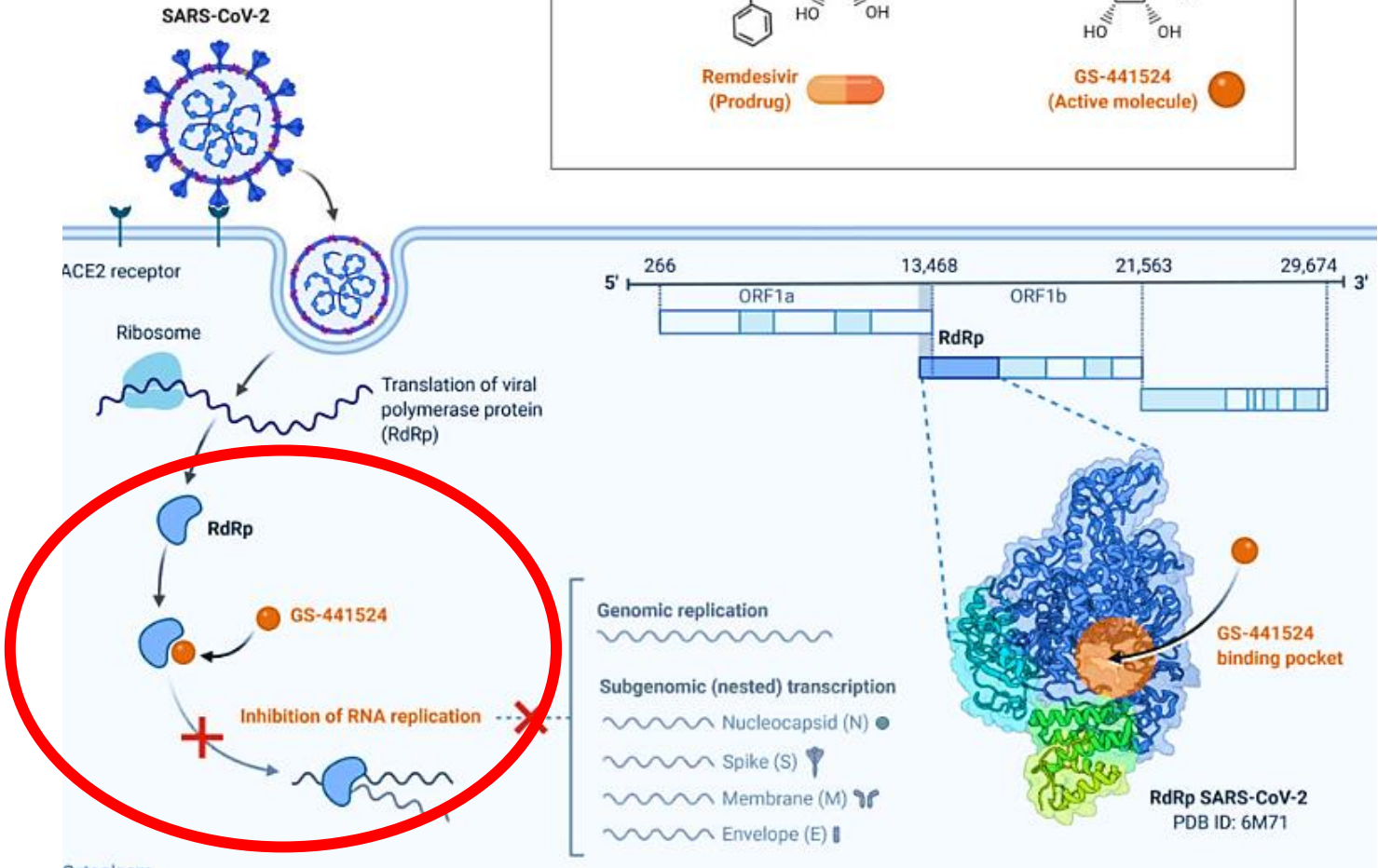
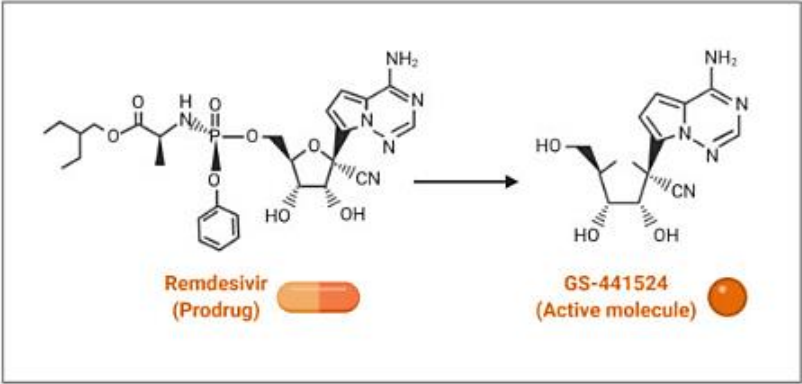


Oral antiviral drug

Remdesivir- Mechanism of Action for COVID-19

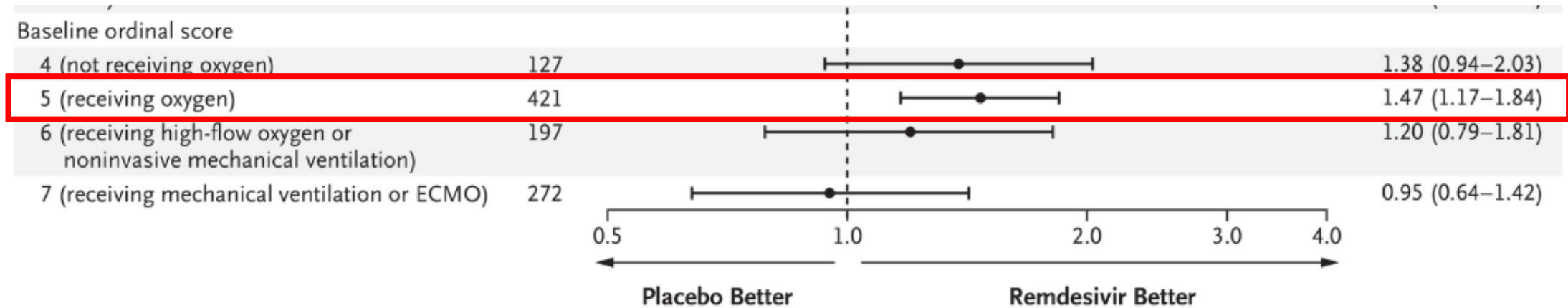
Remdesivir

Potential repurposed drug candidate for COVID-19



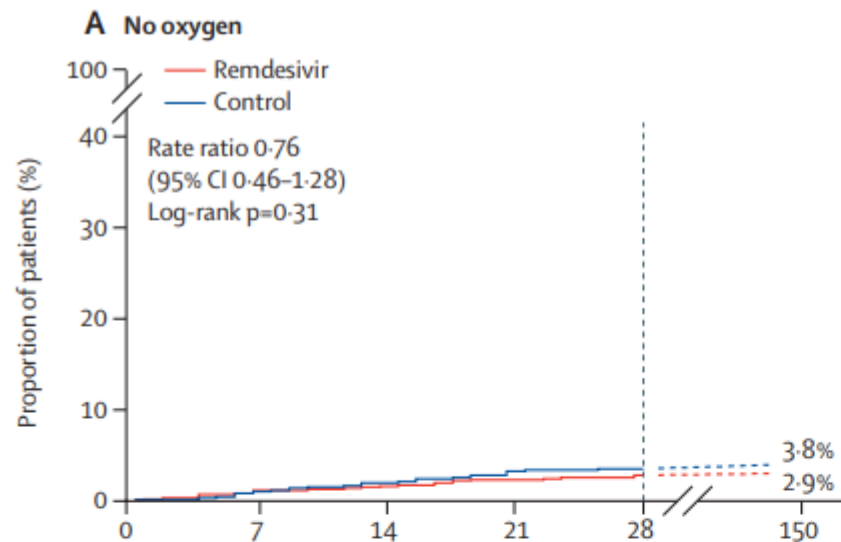
Time to Recovery According to treatment Subgroups

Median recovery time of 11 days (95% [CI], 9 to 12), as compared with 15 days (95% CI, 13 to 19) in placebo (**1.32**; 95% CI, 1.12 to 1.55; P<0.001)



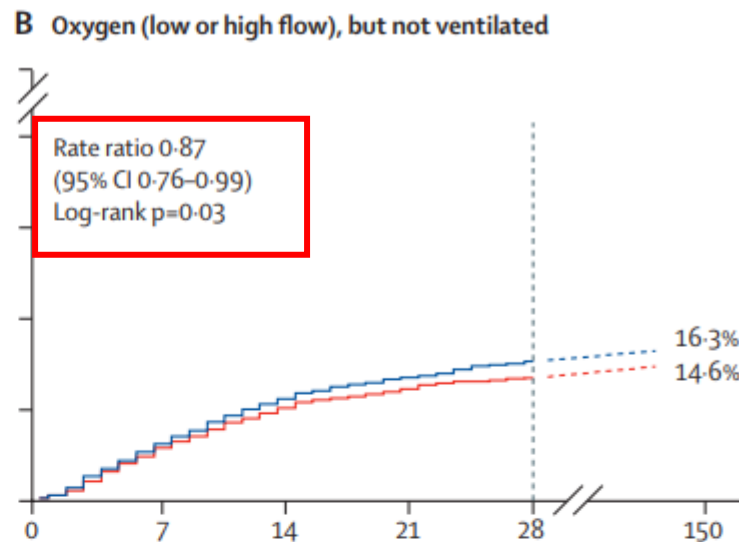
N=14220

WHO
Solidarity Trial Consortium*

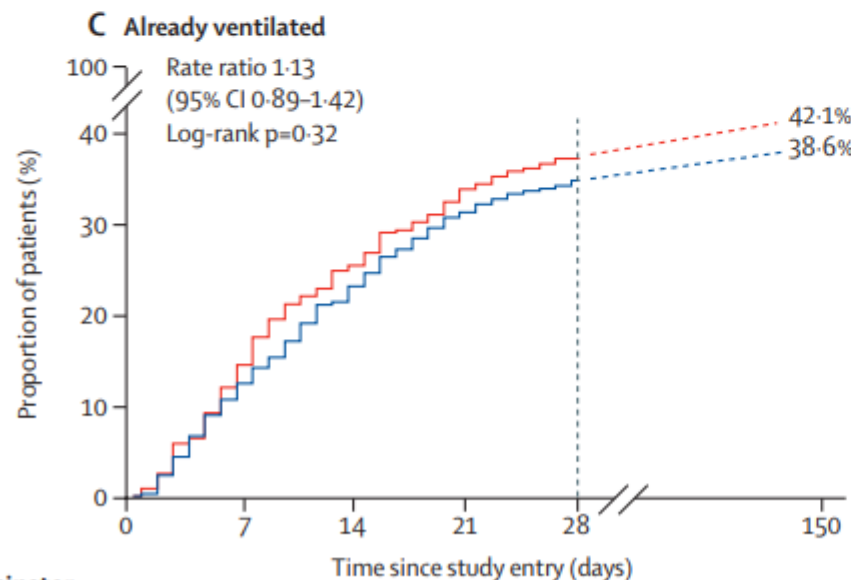


Denominator
(number of deaths)

Remdesivir	869 (9)	847 (4)	842 (6)	836 (4)	831 (2)
Control	861 (8)	842 (8)	834 (11)	823 (2)	821 (4)

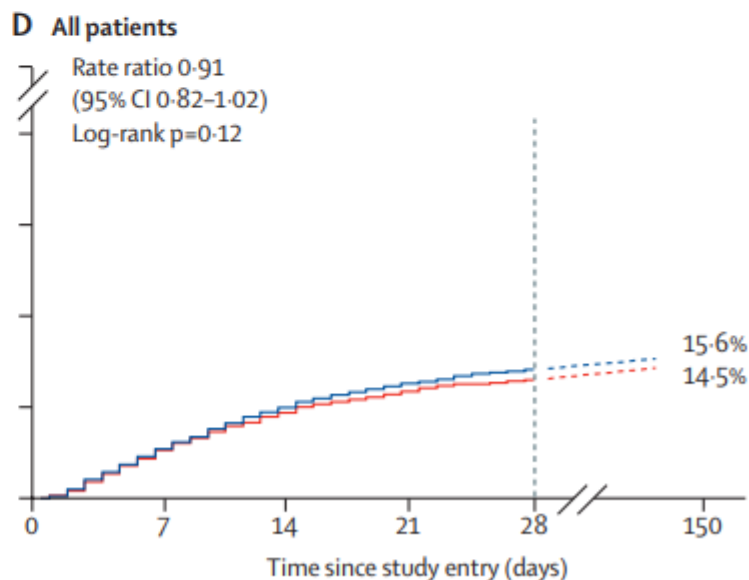


Remdesivir	2918 (161)	2726 (128)	2597 (60)	2536 (35)	2501 (42)
Control	2921 (174)	2718 (144)	2568 (69)	2499 (51)	2447 (38)



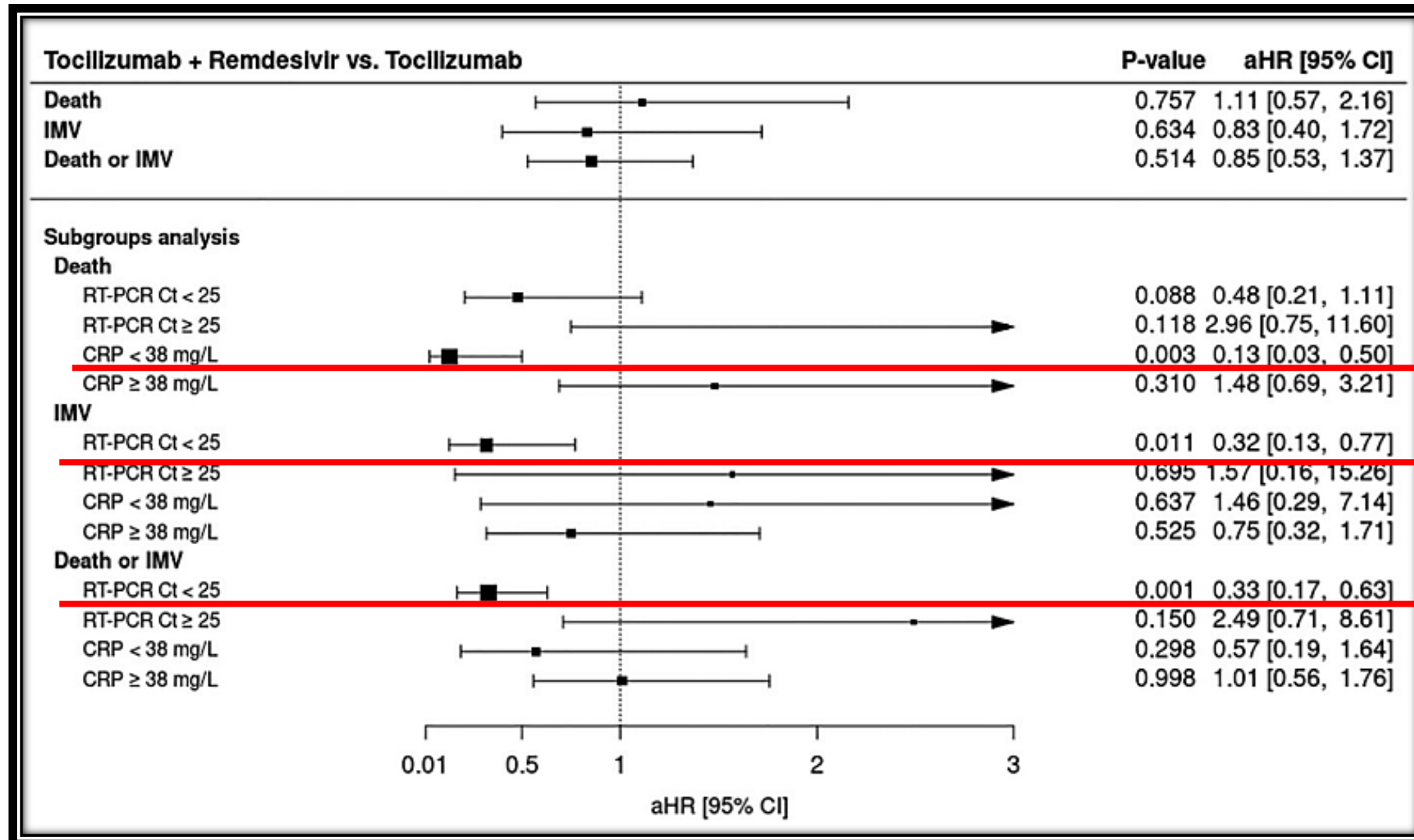
Denominator
(number of deaths)

Remdesivir	359 (52)	305 (39)	264 (30)	234 (12)	222 (18)
Control	347 (43)	301 (37)	263 (28)	235 (12)	222 (14)



Remdesivir	4146 (222)	3878 (171)	3703 (96)	3606 (51)	3554 (62)
Control	4129 (225)	3861 (189)	3665 (108)	3557 (65)	3490 (56)


Benefit of remdesivir in hospitalized COVID-19 patients with high viral loads and low-grade systemic inflammation



87%

Early Remdesivir to Prevent Progression to Severe Covid-19

DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL



562
Outpatients with Covid-19,
<7 days from symptom onset and with
≥1 risk factor for disease progression

**Covid-related hospitalization
or death from any cause
by day 28**

N=279


**Intravenous
Remdesivir, 3 days**



0.7%
(2 patients)

N=283

Placebo



5.3%
(15 patients)

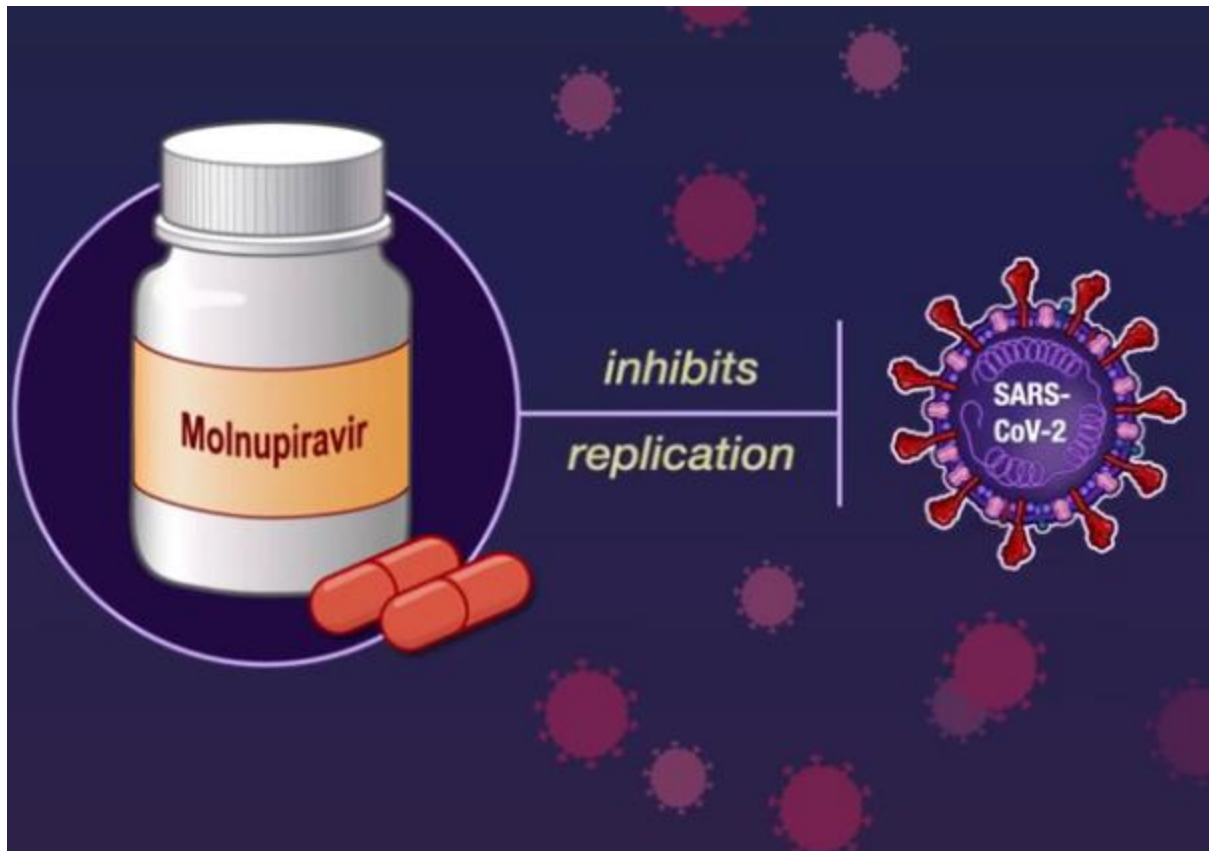
HR, 0.13; 95% CI, 0.03–0.59 (P=0.008)

**Remdesivir resulted in an 87% lower risk of Covid-related hospitalizations
or death than placebo and had an acceptable safety profile.**

2. Molnupiravir —first oral therapies for Covid-19


- **Strive for therapy** to begin within **72** hours in all patients
- **Animal studies** may affect bone and cartilage growth.
- **Contraception** is recommended during treatment and for 4 days after the last dose in women of childbearing potential, and for at least 3 months after the last dose in men
- **Active against the variants** and showed a modest antiviral effect.

Molnupiravir for Covid-19 in Nonhospitalized Patients: study design

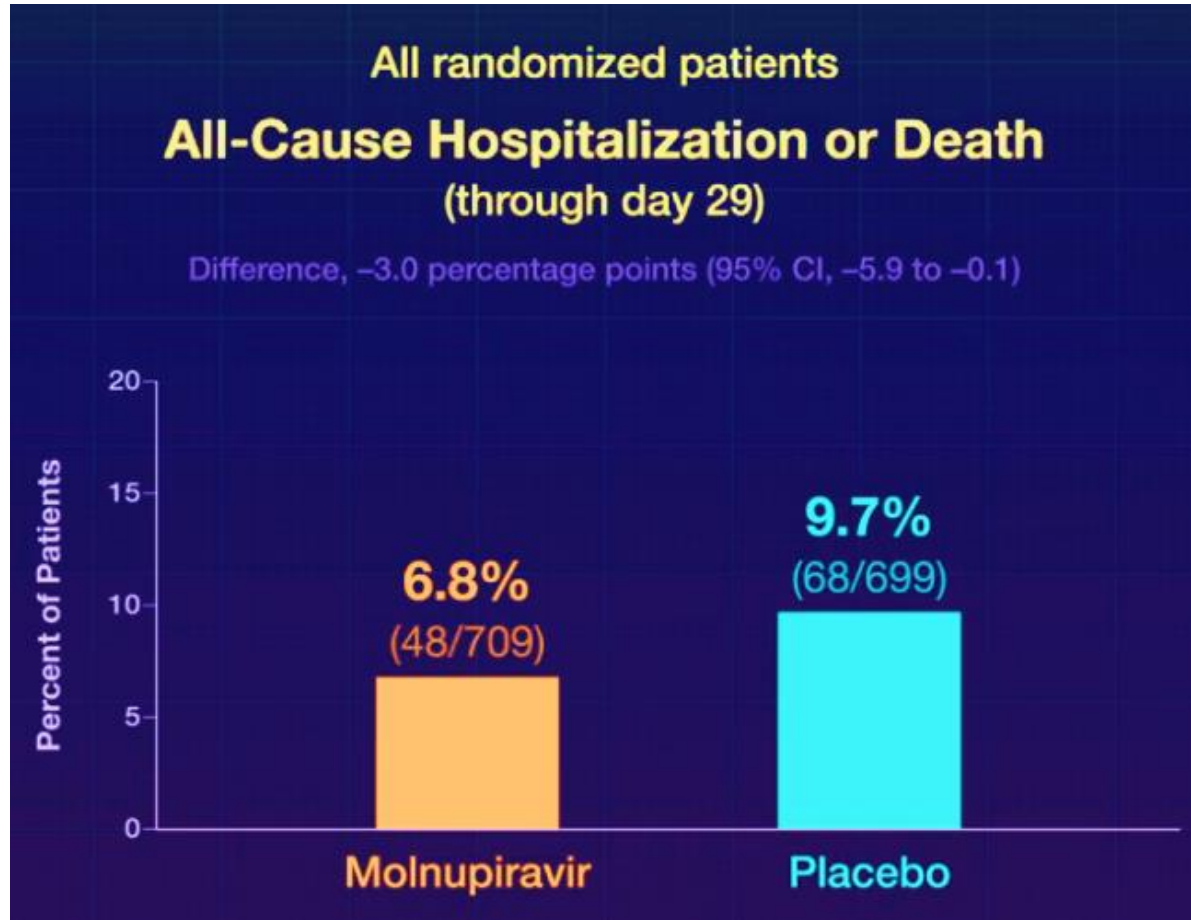


1433 outpatients
with mild or moderate Covid-19

- Symptoms for 5 days or less
- At least one risk factor for severe illness
- Unvaccinated



Molnupiravir for Covid-19 in Nonhospitalized Patients



Subgroups
All-Cause Hospitalization or Death
(through day 29)

- Evidence of previous SARS-CoV-2 infection
- Low baseline viral load
- Diabetes mellitus

The illustration shows a purple SARS-CoV-2 virus particle with red spikes, labeled 'SARS-CoV-2'. Below it is a white glucose meter with a green display showing the number '152'.

No benefit observed with Molnupiravir

Oral Paxlovid for High-Risk, Nonhospitalized Adults with Covid-19

EPIC-HR TRIAL

2246 patients

- Symptomatic
- Unvaccinated
- Nonhospitalized
- High-risk
- Confirmed SARS-CoV-2 infection

Nirmatrelvir Group N = 1120



Placebo Group N = 1126



- Every 12 hours for 5 days
- Beginning ≤ 5 days after symptom onset



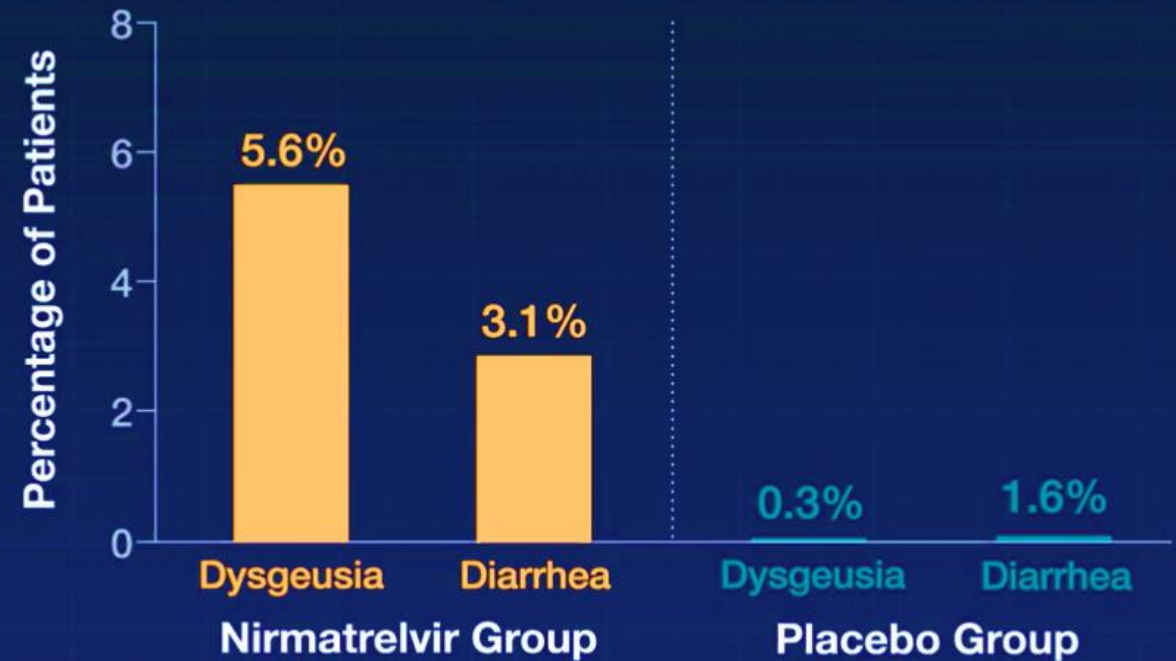
Efficacy and adverse effects of Nirmatrelvir plus Ritonavir in Preventing Covid-19–Related Hospitalization or Death

Covid-19–Related Hospitalization or All-Cause Death through day 28, ≤ 5 days after symptom onset

Difference from placebo percentage points (95% CI): -5.62 (-7.21 to -4.03); $P < 0.001$



Dysgeusia and Diarrhea



Hospitalization and Emergency Department Encounters for COVID-19 After Paxlovid Treatment

- 5,287 persons aged ≥ 12 years received a prescription.
- **Six (0.11%)** hospitalizations and **39 (0.74%)** ED encounters among persons with symptoms consistent with COVID-19.
- Twenty-one (46.7%) of these 45 patients were aged ≥ 65 years and 35 (77.8%) had at least one underlying medical condition.

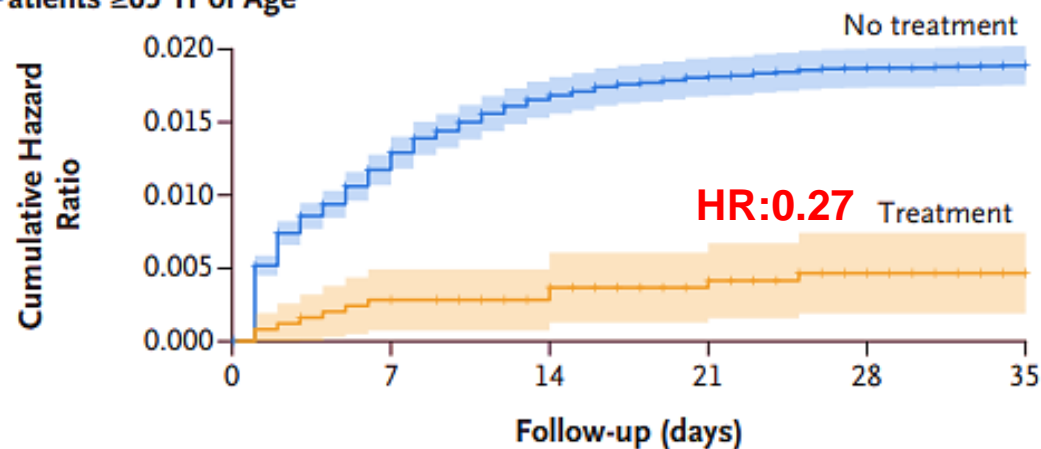


Nirmatrelvir Use and Severe Covid-19 Outcomes during the Omicron Surge

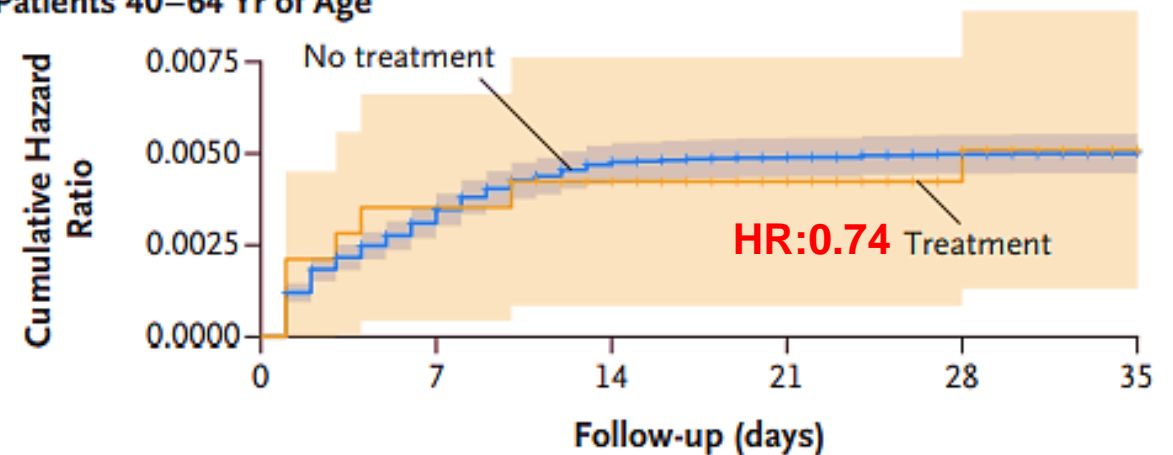
Table 3. Hazard Ratios for Hospitalization Due to Covid-19, According to Immunity Status and Age Group.

Variable	All Patients		Patients without Previous Immunity		Patients with Previous Immunity	
	40–64 yr (N = 66,433)	≥65 yr (N = 42,821)	40–64 yr (N = 20,555)	≥65 yr (N = 3318)	40–64 yr (N = 45,878)	≥65 yr (N = 39,503)
Hazard ratio for hospitalization (95% CI)	0.74 (0.35 to 1.58)	0.27 (0.15 to 0.49)	0.23 (0.03 to 1.67)	0.15 (0.04 to 0.60)	1.13 (0.50 to 2.58)	0.32 (0.17 to 0.63)

A Patients ≥65 Yr of Age



B Patients 40–64 Yr of Age

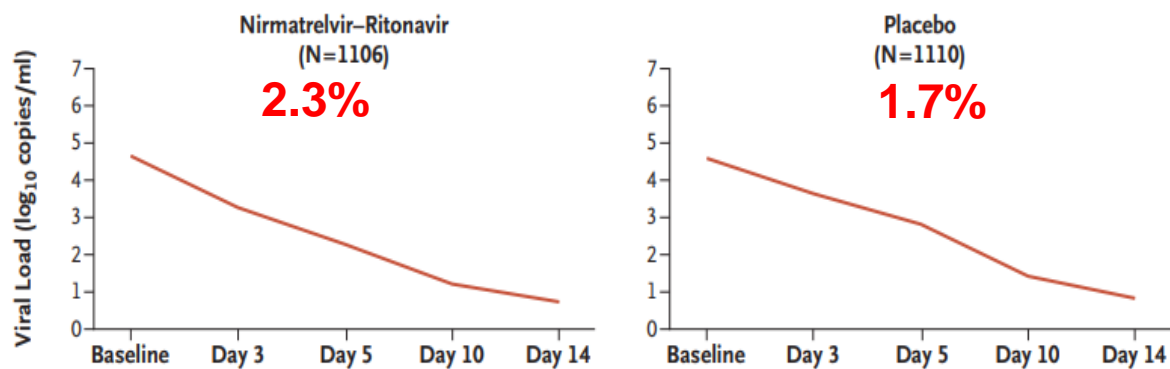




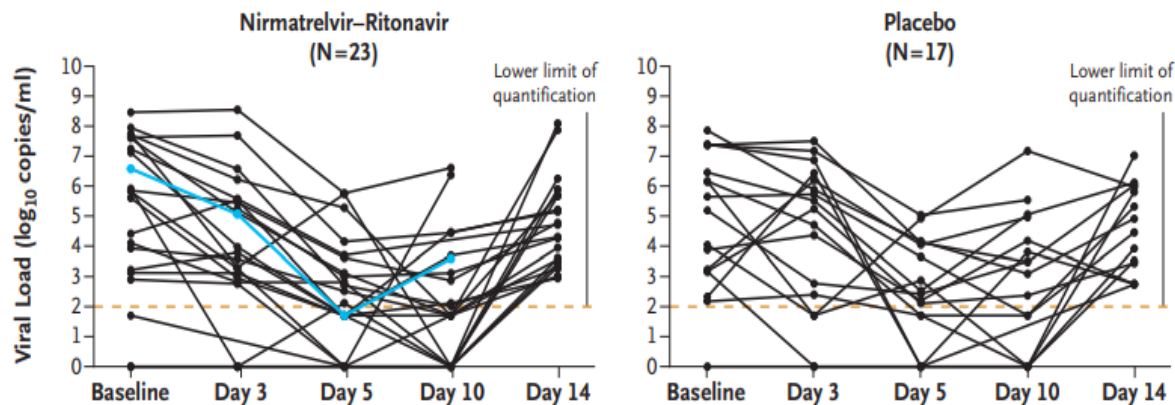
Nirmatrelvir–Ritonavir and Viral Load Rebound in Covid-19

Delta

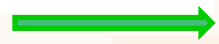
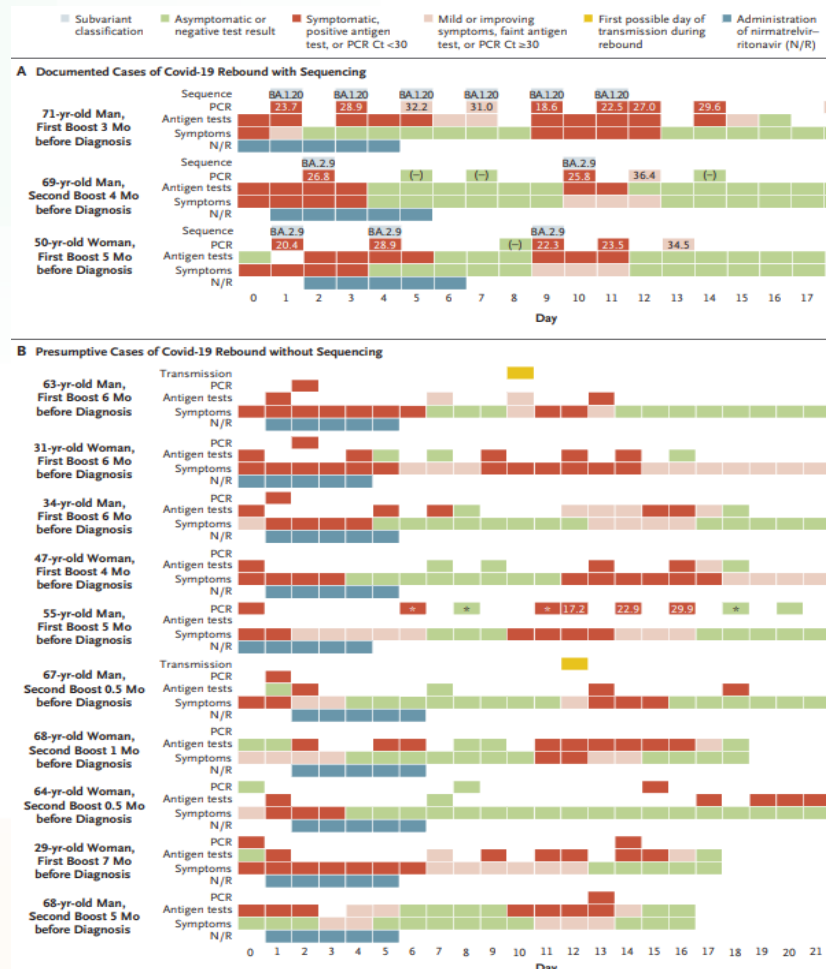
A Viral Load after Receipt of Nirmatrelvir–Ritonavir or Placebo within 5 Days after Symptom Onset



B Present Viral Load Rebound, Persistent Viral Load Rebound, or Both



Omicron



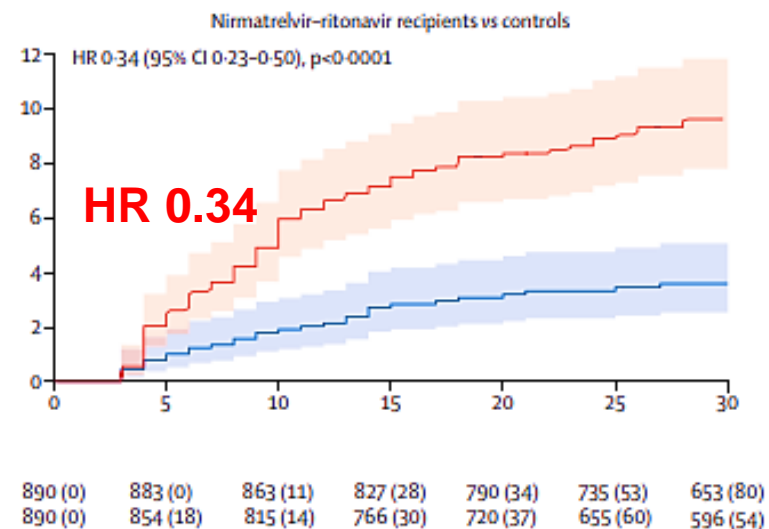
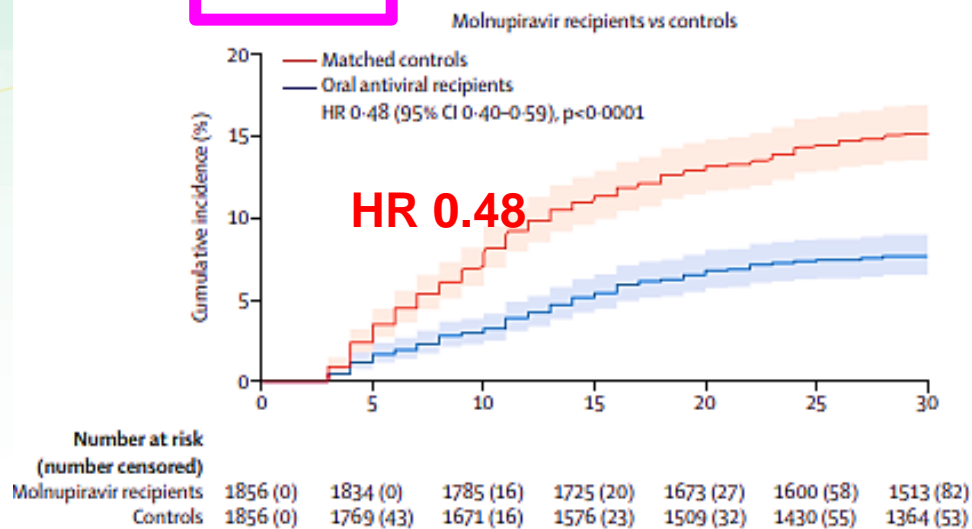
The future of paxlovid for Covid 19

- **Relapse symptoms** after finishing the courses:
FDA : Paxlovid is “not authorized for use longer than five days.
- **The effect of post-exposure prophylaxis**
does not reduce symptomatic infection with SARS-CoV-2.
- Not enough evidence to support antiviral therapy for **long COVID**

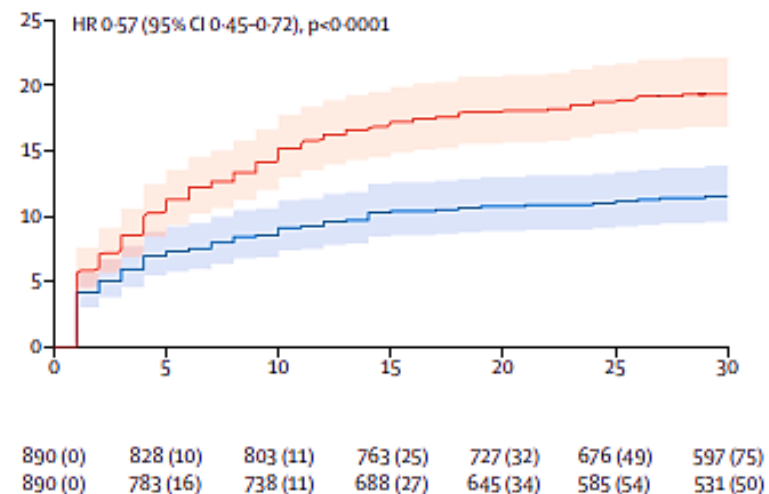
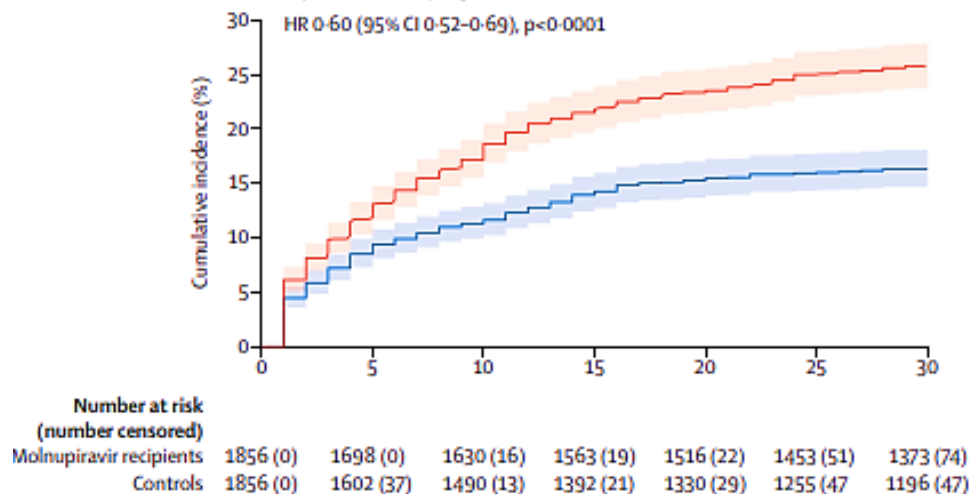


Real-world effectiveness of molnupiravir or nirmatrelvir– ritonavir in hospitalised patients with COVID-19 without oxygen during omicron BA.2

A All-cause death

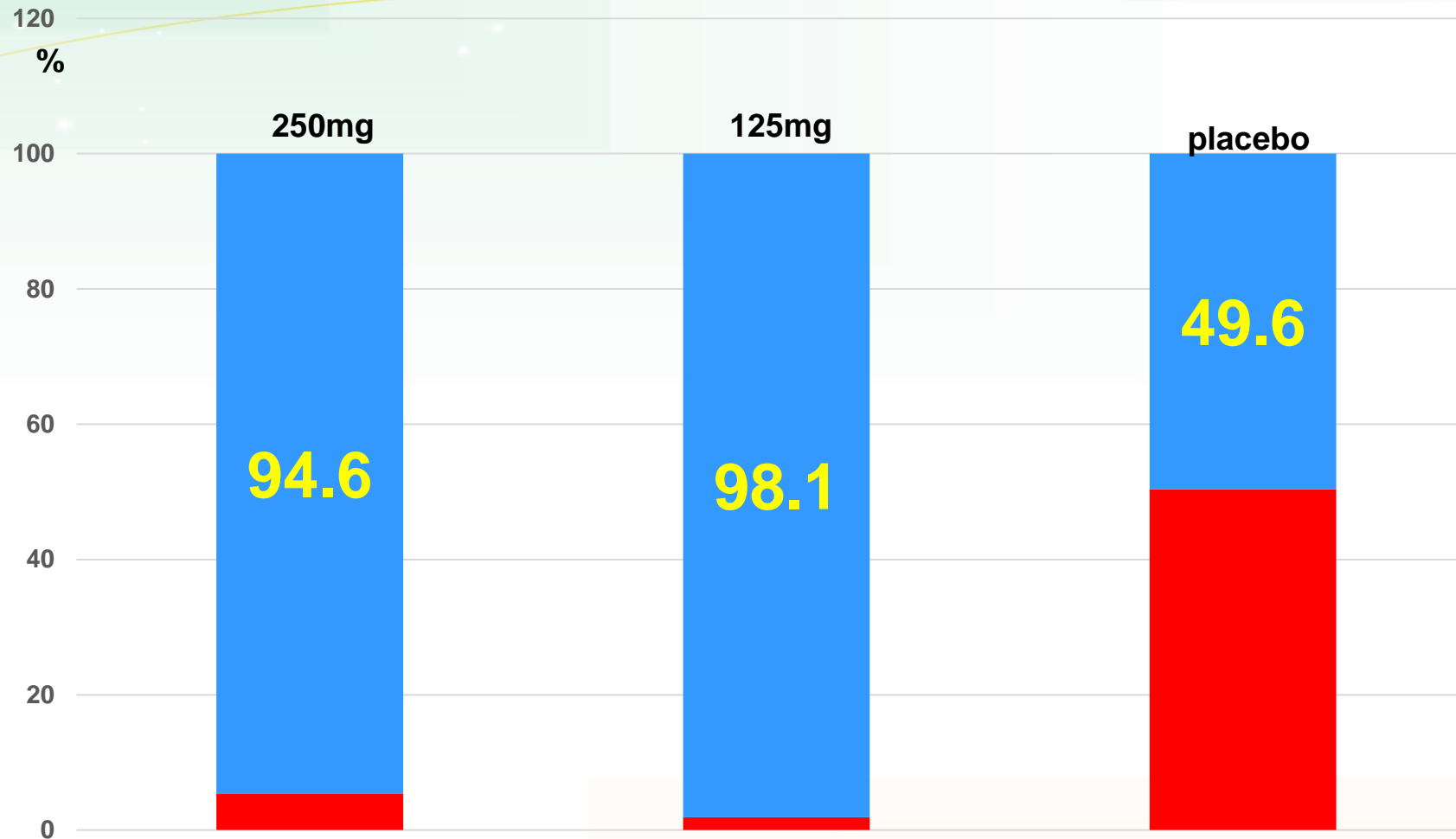


B Composite disease progression outcome



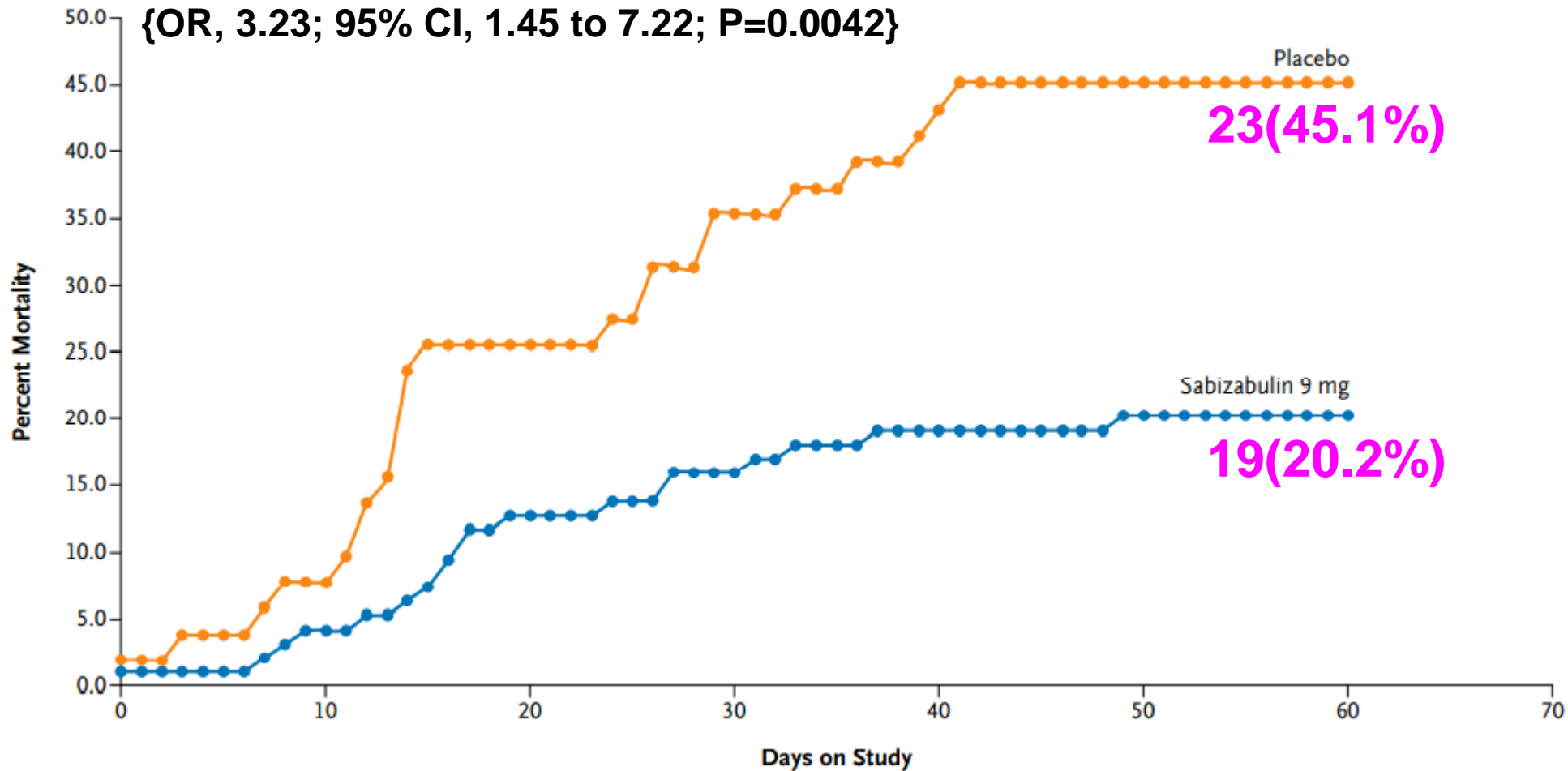


XOCOVA(Ensitrelvir) S-217622 Oral ECL Protease Inhibitor Positivity on day 4





Oral Sabizabulin for High-Risk, Hospitalized Adults with Covid-19:



Available drugs for Children and Pregnant People

- **Monoclonal antibodies** are generally considered safe during pregnancy.
- **Paxlovid** is authorized for children 12 years and older, 40 kg or more.
- **Molnupiravir** is not recommended during pregnancy.
- **Remdesivir** has been used during pregnancy and no safety concerns.

Efficacy of Antiviral Agents against the Omicron Subvariant BA.2.75

WHO Label (Pango Lineage): Virus Strain

Neutralization Activity of Monoclonal Antibody†

Viral Susceptibility to Drug‡

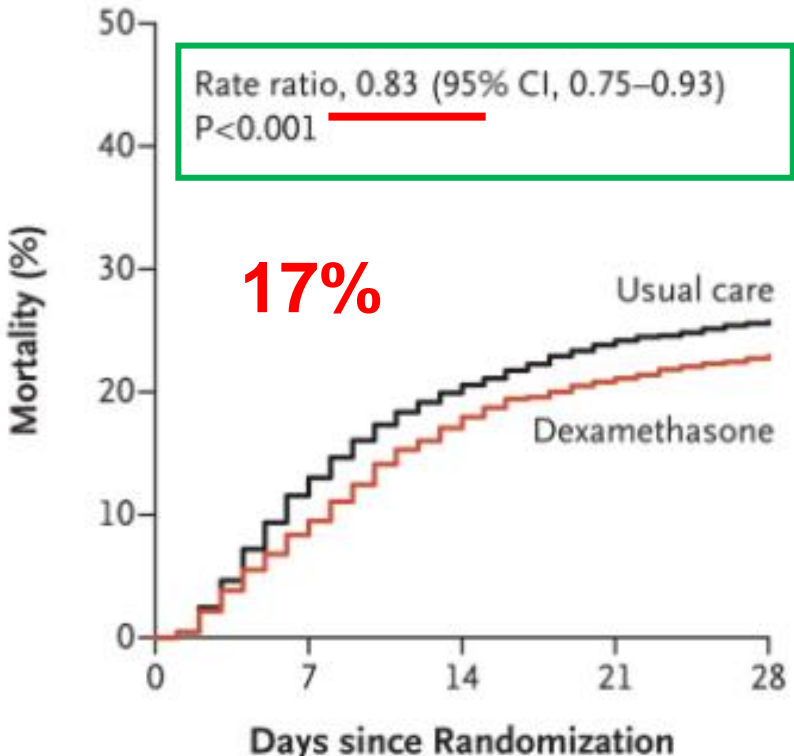
WHO Label (Pango Lineage): Virus Strain	REGN10987, Imdevimab	REGN10933, Casirivimab	COV2-2196, Tixagevimab	COV2-130, Cilgavimab	S309, Sotrovimab Precursor	LY-CoV1404, Bebtelovimab	REGN10987 plus REGN10933	COV2-2196 plus COV2-2130	GS-441524, Remdesivir§	EIDD-1931, Molnupiravir¶	PF-07321332, Nirmatrelvir
	nanograms per milliliter						micromoles				
Ancestral strain (A): SARS-CoV-2/UT-NC002-1T/Human/2020/Tokyo	4.36 ±0.96	2.42 ±0.93	1.91 ±0.95	5.36 ±1.21	32.80 ±11.22	1.40 ±0.79	2.23 ±0.42	6.47 ±2.31	0.98 ±0.30	0.59 ±0.11	1.71 ±0.29
Omicron (BA.2): hCoV-19/Japan/UT-NCD1288-2N/2022	958.28 ±363.87	>50,000	4374.21 ±1483.72	21.59 ±8.57	>50,000	6.09 ±0.67	968.50 ±58.35	43.22 ±8.16	1.32 ±0.21	0.25 ±0.08	1.69 ±0.66
Omicron (BA.5): hCoV-19/Japan/TY41-702/2022	174.37 ±52.55	>50,000	>50,000	54.02 ±20.29	6240.39 ±1883.65	2.43 ±1.26	192.91 ±82.50	123.65 ±55.81	0.45 ±0.09	0.23 ±0.07	1.50 ±0.34
Omicron (BA.2.75): hCoV-19/Japan/TY41-716/2022	>50,000	1153.19 ±104.61	122.31 ±67.08	101.71 ±53.24	28,536.48 ±6444.42	6.21 ±2.80	1811.78 ±600.23	34.19 ±7.60	1.52 ±0.42	0.90 ±0.18	1.78 ±0.35



Antiphlogistic drugs

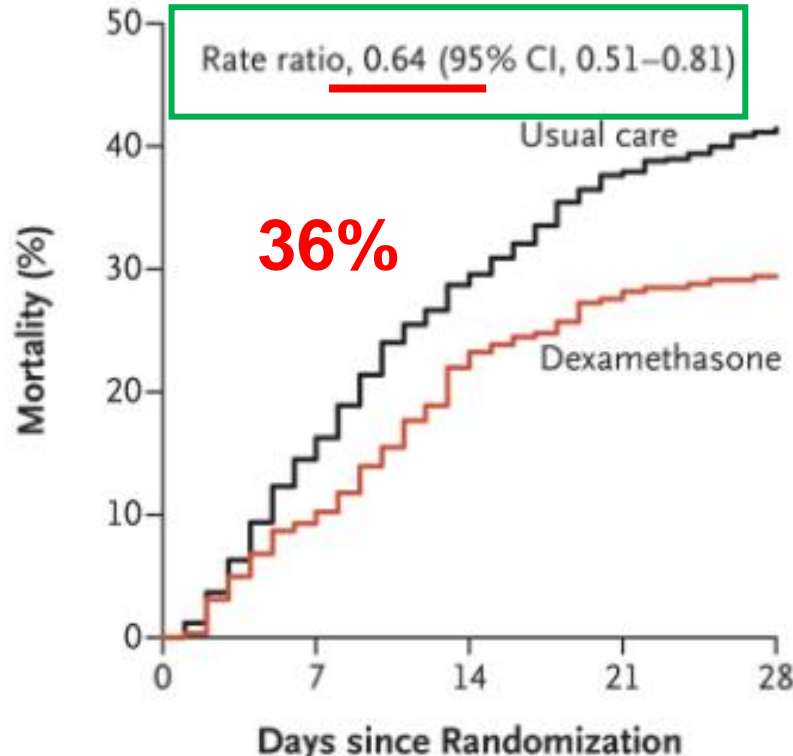
Dexamethasone in Hospitalized Patients with Covid-19

A All Participants (N=6425)



No. at Risk		0	7	14	21	28
Usual care		4321	3754	3427	3271	3205
Dexamethasone		2104	1903	1725	1659	1621

B Invasive Mechanical Ventilation (N=1007)

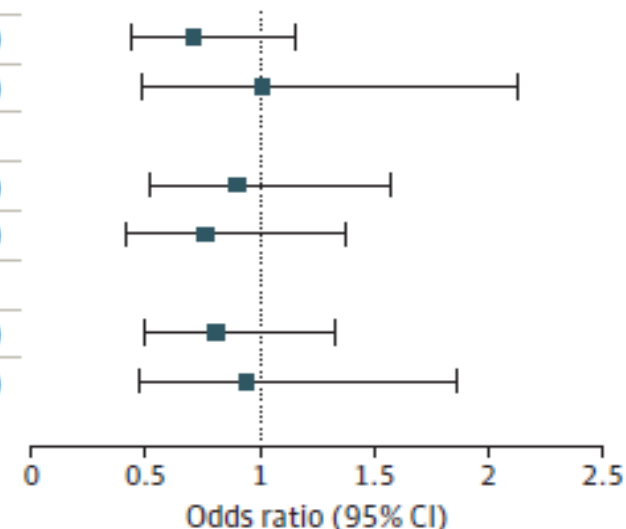


No. at Risk		0	7	14	21	28
Usual care		683	572	481	424	400
Dexamethasone		324	290	248	232	228

Association Between Dexamethasone Treatment After Hospital Discharge for Patients With COVID-19

Characteristic	No. of patients	Adjusted odds ratio (95% CI) ^a
Main analysis		
Continued dexamethasone at discharge	692	0.87 (0.58-1.30)
Discontinued dexamethasone at discharge	472	1 [Reference]
Sensitivity analysis		
Received exactly 10 d of dexamethasone	350	0.89 (0.55-1.43)
Discontinued dexamethasone at discharge	472	1 [Reference]

Subgroup	No. of patients	Odds ratio (95% CI) ^a
Inpatient dexamethasone treatment		
1-3 d	479	0.71 (0.43-1.16)
4-9 d	685	1.01 (0.48-2.12)
Oxygen requirement at discharge		
Room air	606	0.91 (0.53-1.59)
Supplemental oxygen	558	0.76 (0.42-1.37)
Symptom duration at discharge		
≤10 d	396	0.81 (0.49-1.33)
>10 d	768	0.94 (0.48-1.86)

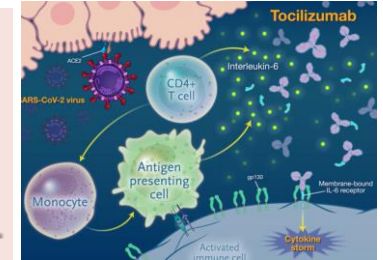


Tocilizumab in patients admitted to hospital with

COVID-19 (RECOVERY): a randomised, controlled, open-label,

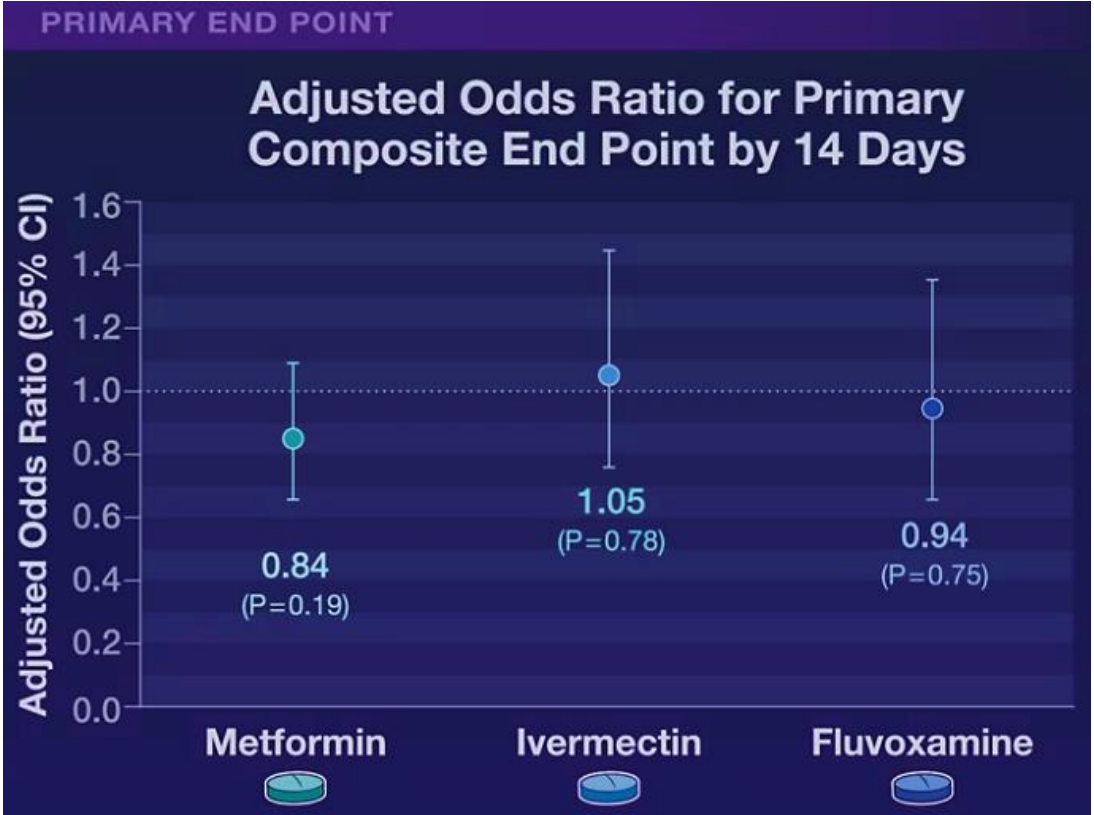
Recombinant monoclonal antibody directed against membrane-bound forms of IL-6R

	Treatment allocation		RR (95% CI)	p value
	Tocilizumab group (n=2022)	Usual care group (n=2094)		
Primary outcome				
28-day mortality	621 (31%)	729 (35%)	0.85 (0.76–0.94)	0.0028
Secondary outcomes				
Median time to being discharged, days	19	>28
Discharged from hospital within 28 days	1150 (57%)	1044 (50%)	1.22 (1.12–1.33)	<0.0001
Receipt of invasive mechanical ventilation or death*	619/1754 (35%)	754/1800 (42%)	0.84 (0.77–0.92)	<0.0001
Invasive mechanical ventilation	265/1754 (15%)	343/1800 (19%)	0.79 (0.69–0.92)	0.0019
Death	490/1754 (28%)	580/1800 (32%)	0.87 (0.78–0.96)	0.0055








Randomized Trial of Metformin, Ivermectin, and Fluvoxamine for Covid-19


Time to Stop Using Ineffective Covid-19 Drugs



Metformin, Ivermectin, Fluvoxamine

 Did not improve a composite of:

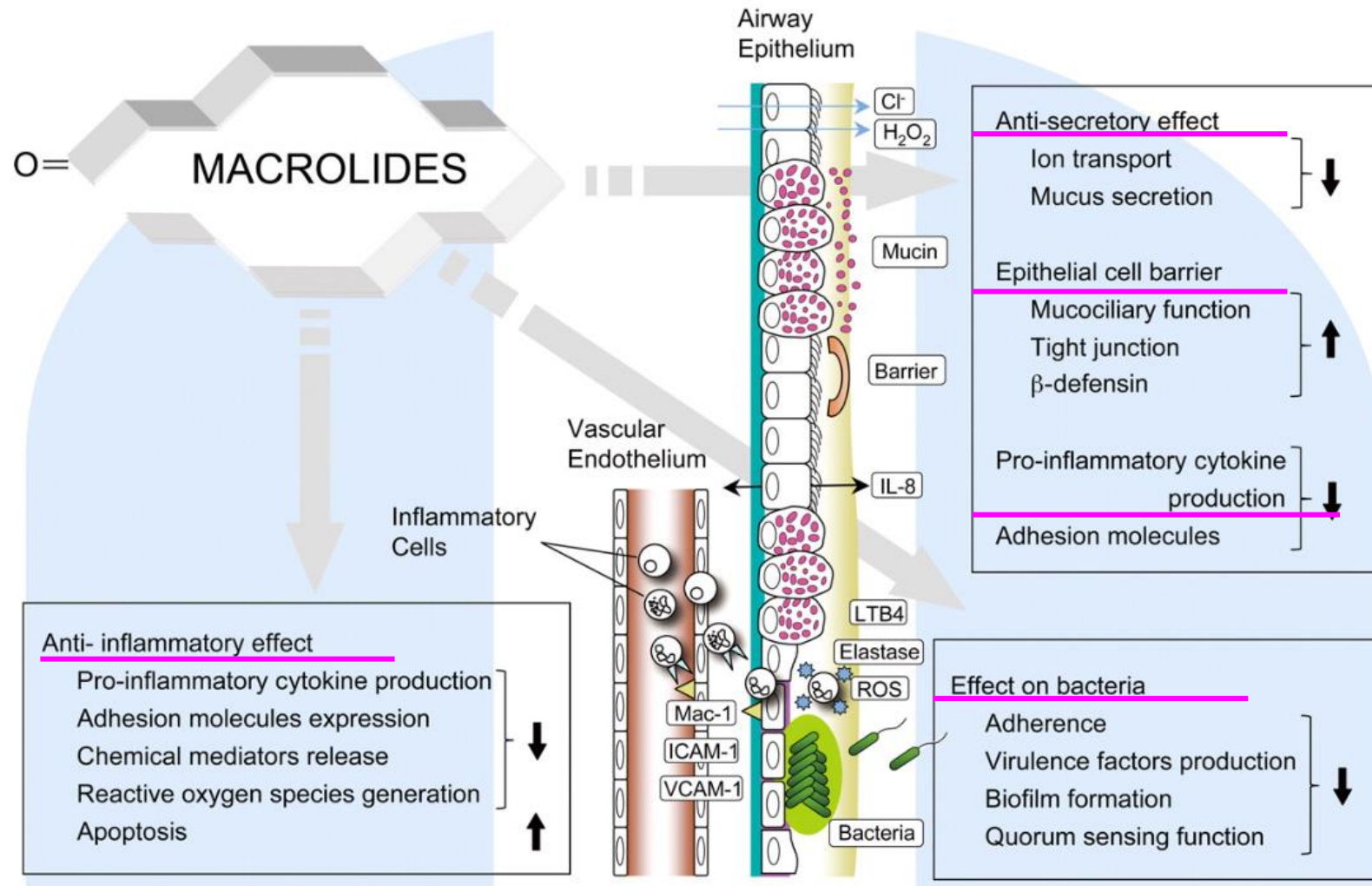
-  Nonhospitalized patients
-  SARS-CoV-2 infection
-  Overweight or obesity
- 





Drugs Alleviating symptoms

Mechanisms of Action of Macrolides as Immunomodulatory Medications



Azithromycin for community treatment of suspected COVID-19 in people at increased risk in the UK (PRINCIPLE)

	Azithromycin plus usual care	Usual care alone	Estimated treatment effect (95% Bayesian credible interval)	Probability of meaningful effect	Probability of superiority
Primary outcomes (primary analysis population)					
First reported recovery	402/500 (80%)	631/823 (77%)
Time to first reported recovery (days)	7 (3 to 17)	8 (2 to 23)	1.08 (0.95 to 1.23)*	0.23*	0.89*
Hospitalisation or death at 28 days	16/500 (3%)	28/823 (3%)	0.3% (-1.7 to 2.2)†	0.042†	0.64†
Primary outcomes (SARS-CoV-2-positive analysis population)					
First reported recovery	136/186 (73%)	163/236 (69%)
Time to first reported recovery (days)	9 (4 to not reached)	13 (5 to not reached)	1.12 (0.91-1.38)*	0.47*	0.86*
Hospitalisation or death at 28 days	11/186 (6%)	17/236 (7%)	1.6% (-3.1 to 6.2)†	0.43†	0.76†

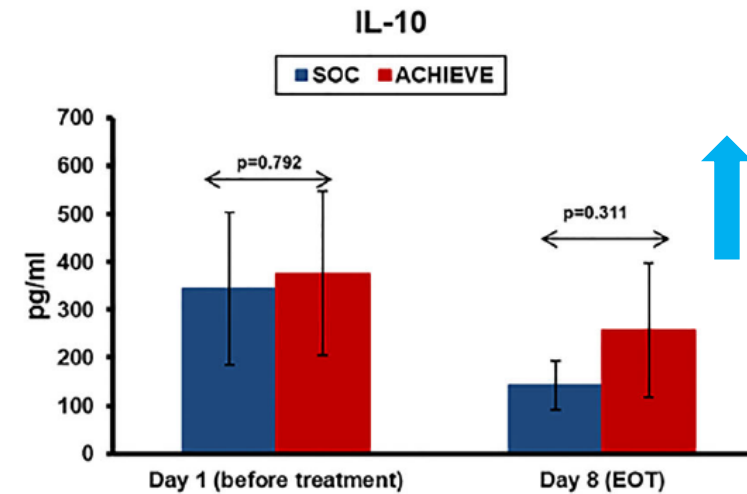
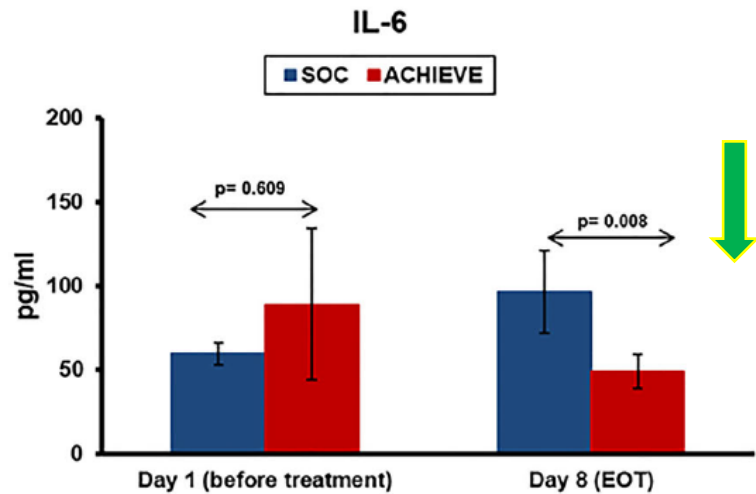
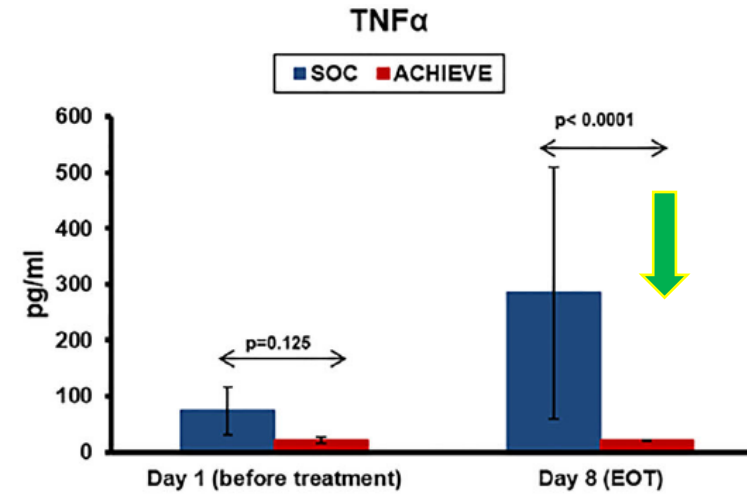
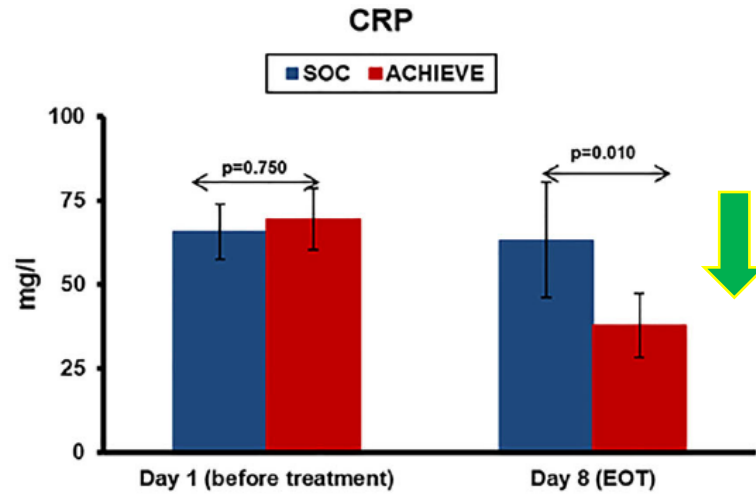
Eligible if they were aged 65 years and older, or 50 years and older with comorbidities
azithromycin 500 mg daily for three days

Therapeutic efficacy of macrolides in management of patients with mild COVID-19

Variables	Azithromycin Group N= 107	Clarithromycin Group N= 99	Control Group N= 99	P1 value (1,2)	P2 value (1,3)	P3 value (2,3)	P value ANOVA
Time to PCR -ve (Mean ± SD, days)	(8.7 ± 2.8)	(8.3 ± 2.6)	(13.2 ± 4.2)	0.351	<0.0001	<0.0001	<0.0001
Fever days (Mean ± SD)	(5.2 ± 2.3)	(4.9 ± 1.5)	(12.9 ± 2.2)	0.353	<0.0001	<0.0001	<0.000
Cough days (Mean ± SD)	(5.4 ± 2.7)	(5.1 ± 2)	(12.9 ± 2.2)	0.481	<0.0001	<0.0001	<0.0001
Dyspnea days (Mean ± SD)	(4.6 ± 3.3)	(4.7 ± 2.9)	(9.3 ± 2.7)	0.726	<0.0001	<0.0001	<0.0001
Anosmia days (Mean ± SD)	(0.48 ± 0.9)	(1.2 ± 3)	(0.9 ± 2.3)	0.024	0.208	0.323	0.076
GIT symptoms days (Mean ± SD)	(0.9 ± 1.7)	(1.5 ± 2.4)	(1.2 ± 2)	0.046	0.406	0.250	0.134
CT chest follow-up							
Improved	70 (65%)	76 (77%)	53 (54%)				0.0001

The anti-inflammatory potential of macrolides to reduce the production of MMPs, (TNF-), (IL)-6, and IL-8 has been reported in critical cases. **500mg for 7 days**

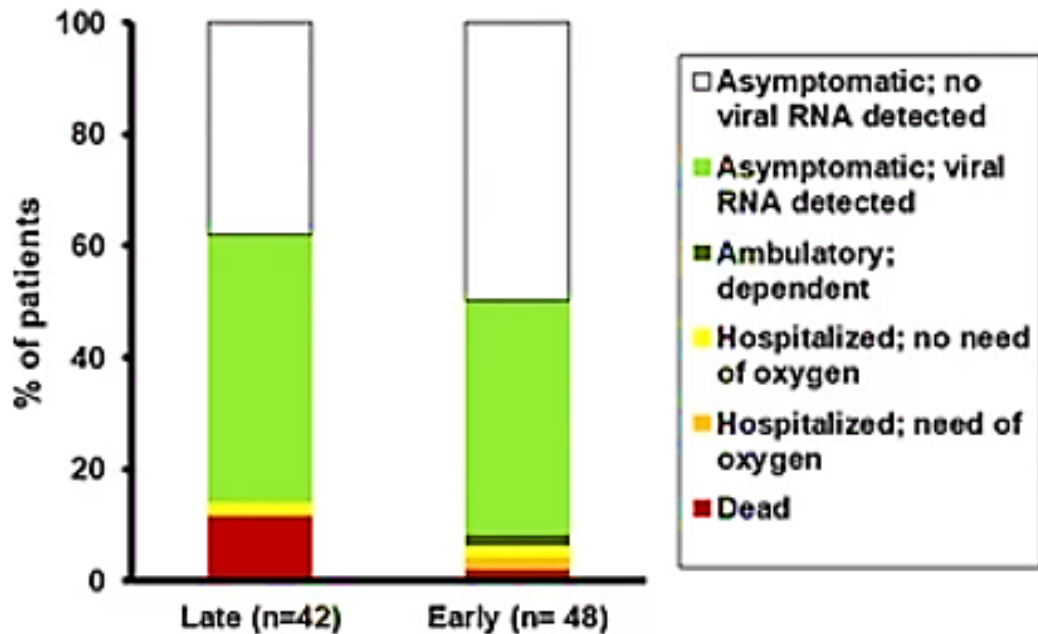
Attenuation of pro-inflammatory responses in COVID-19 following treatment with clarithromycin.



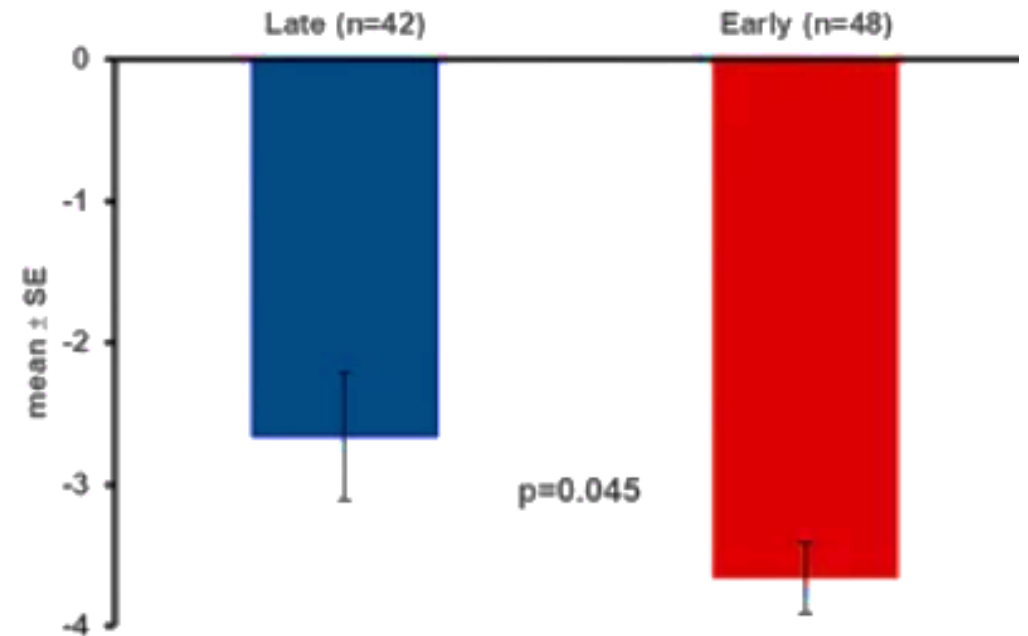
Early Start of Oral Clarithromycin Is Associated with Better Outcome in COVID-19 of Moderate Severity:

The ACHIEVE Open-Label Single-Arm Trial

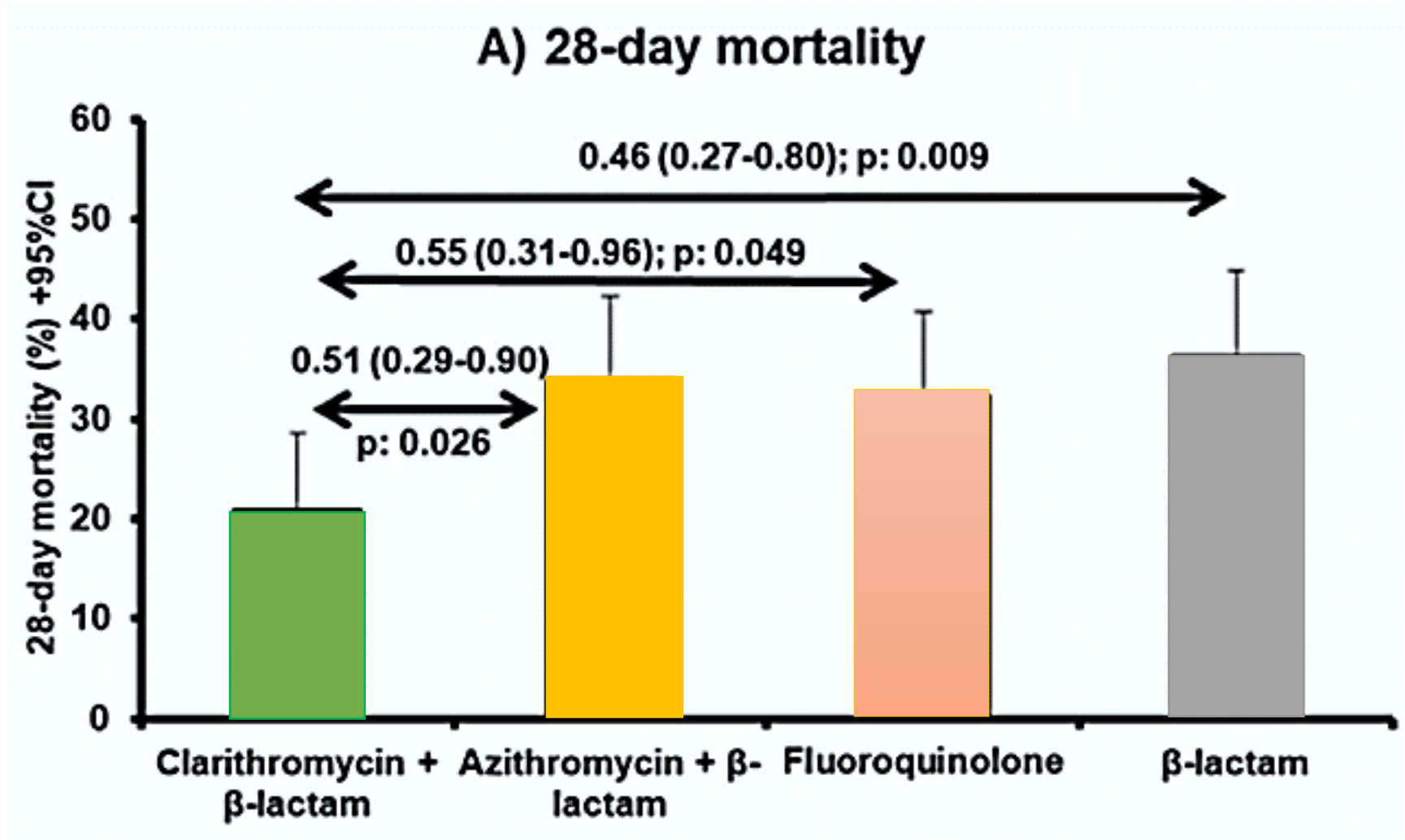
Allocation of patients at the WHO-CPS scale after 28 d



Comparative change of points of the WHOC-CPS scale on day 28d

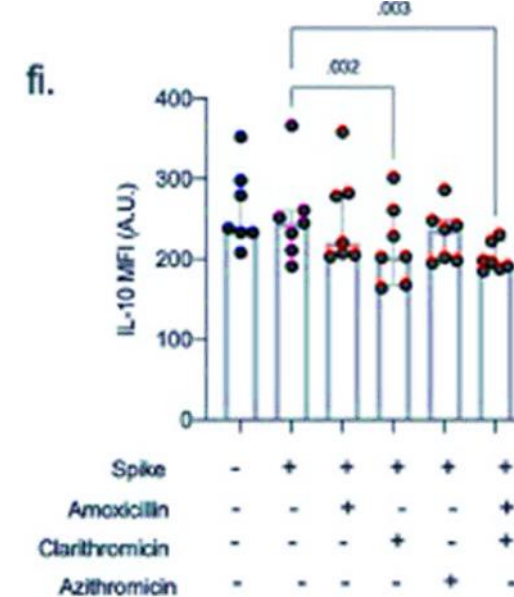
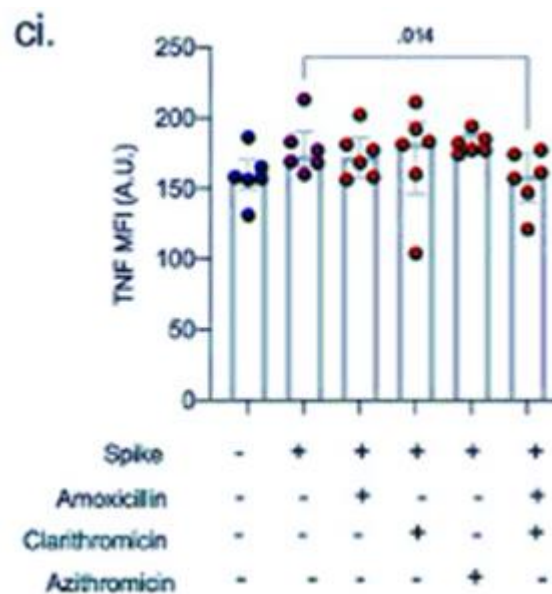
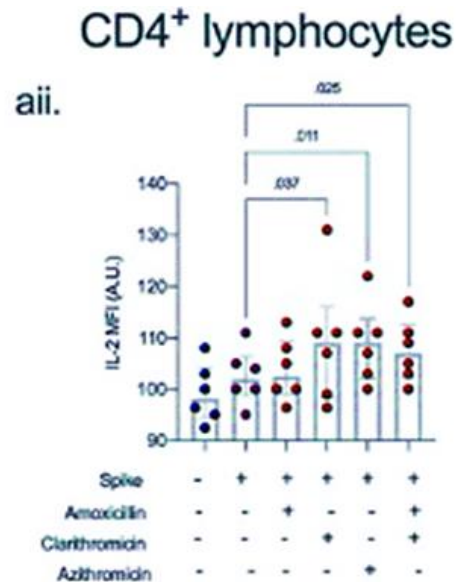
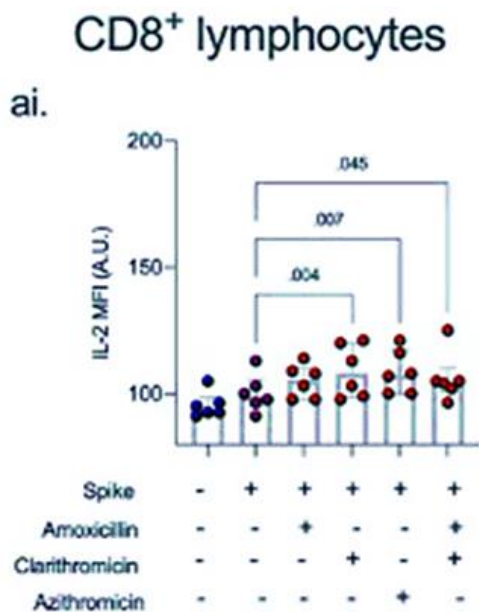


28-day mortality of patients treated with the combination of clarithromycin and one β -lactam vs the other groups in severe community-acquired pneumonia

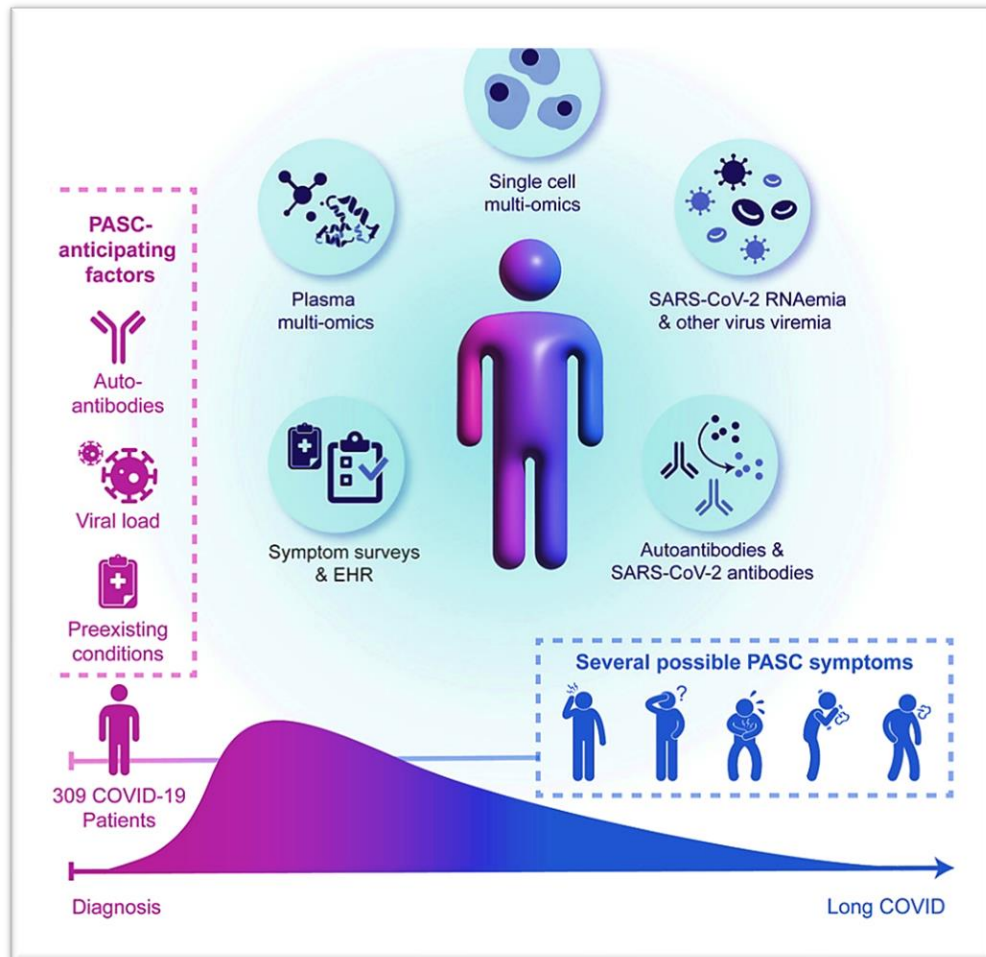


Beneficial *ex vivo* immunomodulatory and clinical effects of clarithromycin in COVID-19

Amoxicillin in addition to clarithromycin is associated with synergistic *ex vivo* immunomodulatory properties

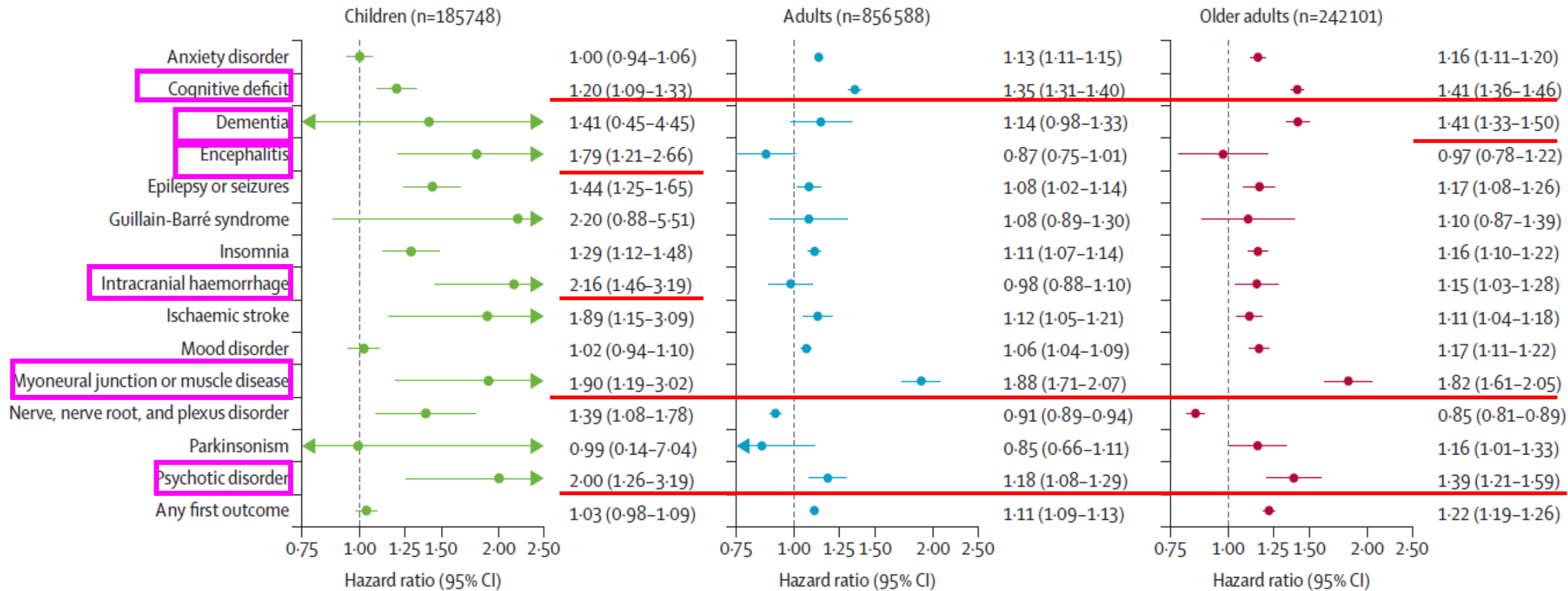


Multiple early factors anticipate post acute COVID 19 sequale



1. Type 2 diabetes,
2. SARS-CoV-2 RNAemia
3. Epstein-Barr virus viremia
4. Specific auto-antibodies

Neurological and psychiatric risk after SARS-CoV-2 infection: 2-year retrospective cohort studies(1 284 437)



Association Between BNT162b2 Vaccination and Long COVID Not Requiring Hospitalization in Health Care Workers (>4 WEEKS)

	OR (95% CI)	P value
Male sex	0.65 (0.44-0.98)	.04
Age ^b	1.23 (1.01-1.49)	.04
BMI ^b	1.10 (0.92-1.31)	.30
Allergies	1.50 (1.06-2.11)	.02
No. of comorbidities ^c	1.32 (1.04-1.68)	.03
COVID-19 wave		
2	0.72 (0.48-1.08)	.11
3	1.34 (0.26-7.01)	.73
Vaccine dose ^d		
1	0.86 (0.21-3.49)	.83
2	0.25 (0.07-0.87)	.03
3	0.16 (0.03-0.84)	.03

The benefits by Vitamin D associated with COVID 19

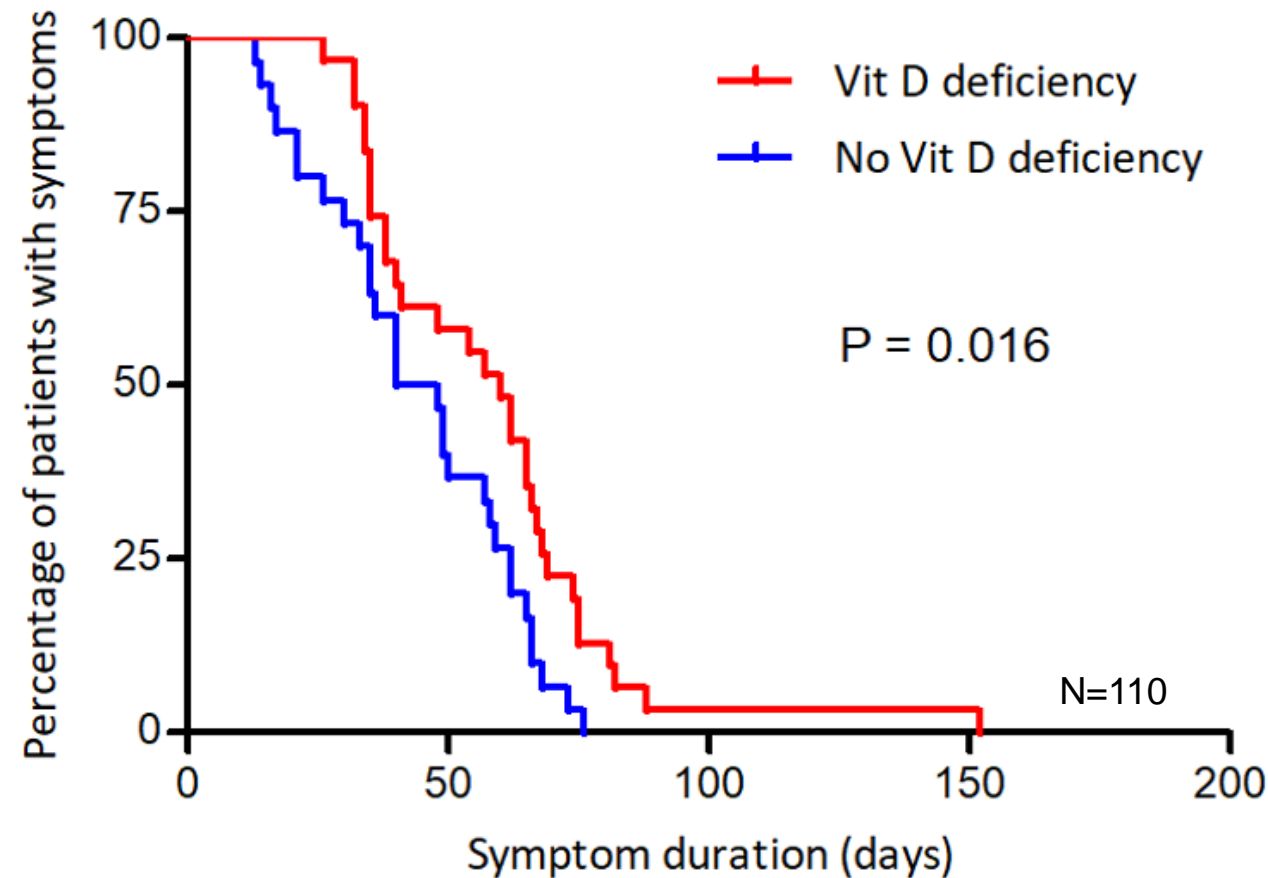
Low vitamin D levels have been associated with an **increase in inflammatory cytokines** and **an increase in thrombotic episodes**.

Downregulate the production of inflammatory cytokines, such as TNF-alpha and IL6, while increasing inhibitory cytokines

- ① **Prevention of SARS-CoV2 Infections.**
- ② **Alleviating the Symptoms of SARS-CoV-2 Infections.**
- ③ **Enhancing the remyelination of damaged neuron**

Post acute COVID 19 :Respiratory Symptom duration according to Vitamin D deficiency(< 20ng/ml)

Figure 1. Kaplan-Meier curves for symptom duration according to Vitamin D deficiency.



Median symptom duration: 60 (35 - 69) vs. 44 (30 - 62)

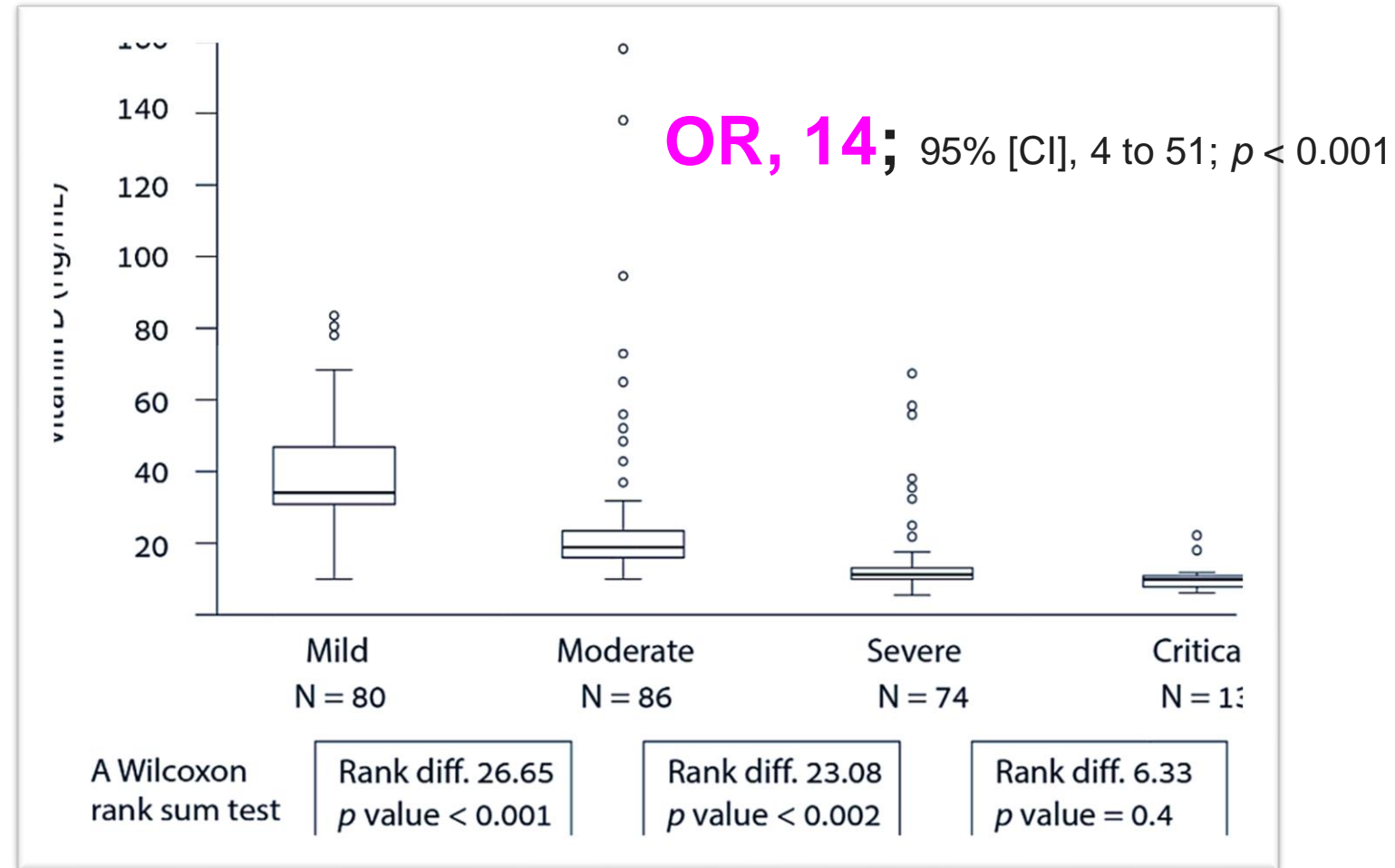
Short term, high-dose vitamin D supplementation for COVID-19 :RCT (SHADE study)

62.5% participants in the intervention group achieved SARS-CoV-2 negativity compared to **20.8%** participants (p=0.018) in the control arm.

Fibrinogen	Intervention group (N=16)	Control group (N=24)	p-value
D0 (ng/ml)	3.82 (2.95 to 4.75)	3.67(3.05 to 4.32)	0.668
D7 (ng/ml)	3.21(2.92 to 4.33)	3.63(2.6 to 4.43)	0.956
DL (ng/ml)	3.04 (2.42 to 4.16)	3.42(2.53 to 4.20)	0.648
Δ Fibrinogen(ng/ml)	-0.64(-1.41 to 0.11)	0.06 (0.01 to 0.51)	0.007*

daily 60 000 IU of cholecalciferol

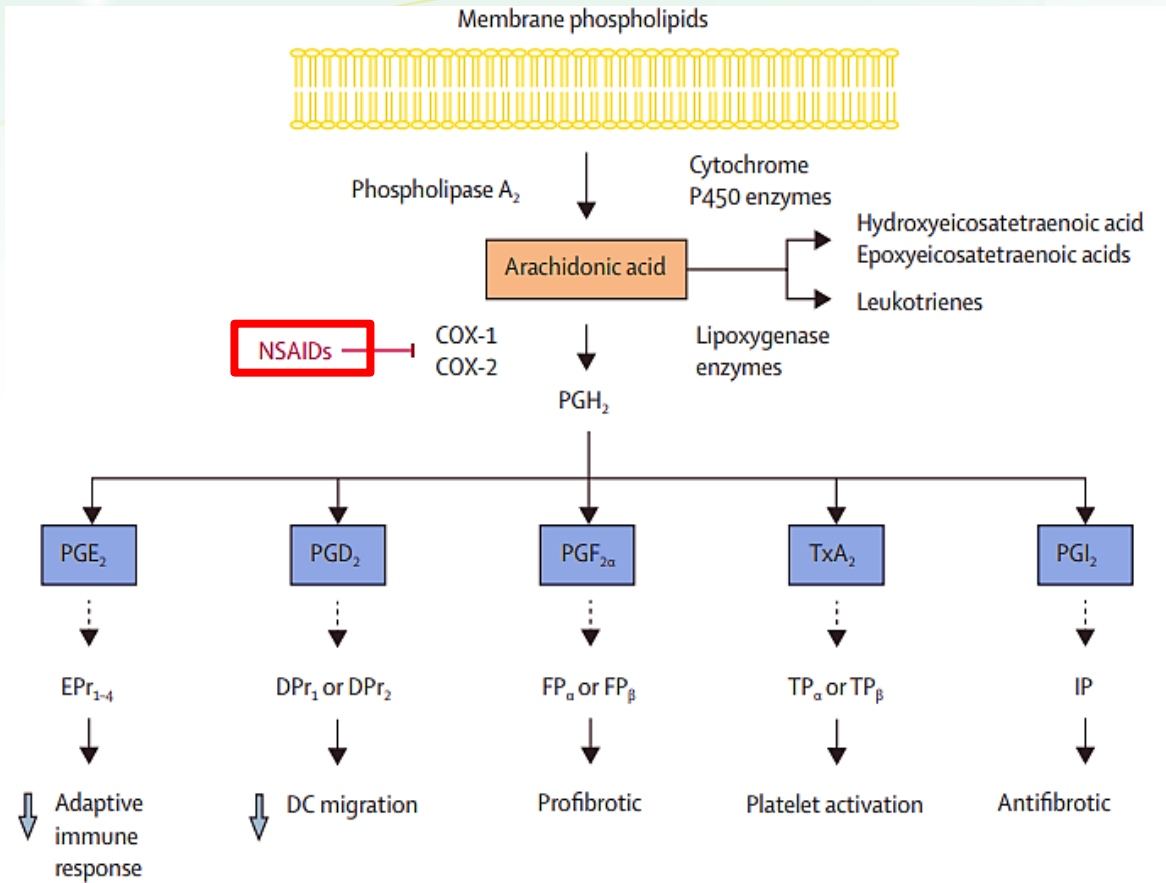
Pre-infection 25-hydroxyvitamin D3 levels and association with severity of COVID-19 illness



Patients with vitamin D deficiency (<20 ng/mL) were 14 times more likely to have severe or critical disease than patients with 25(OH)D \geq 40 ng/mL



At home managements for early outpatients of COVID-19: anti-inflammatory agents



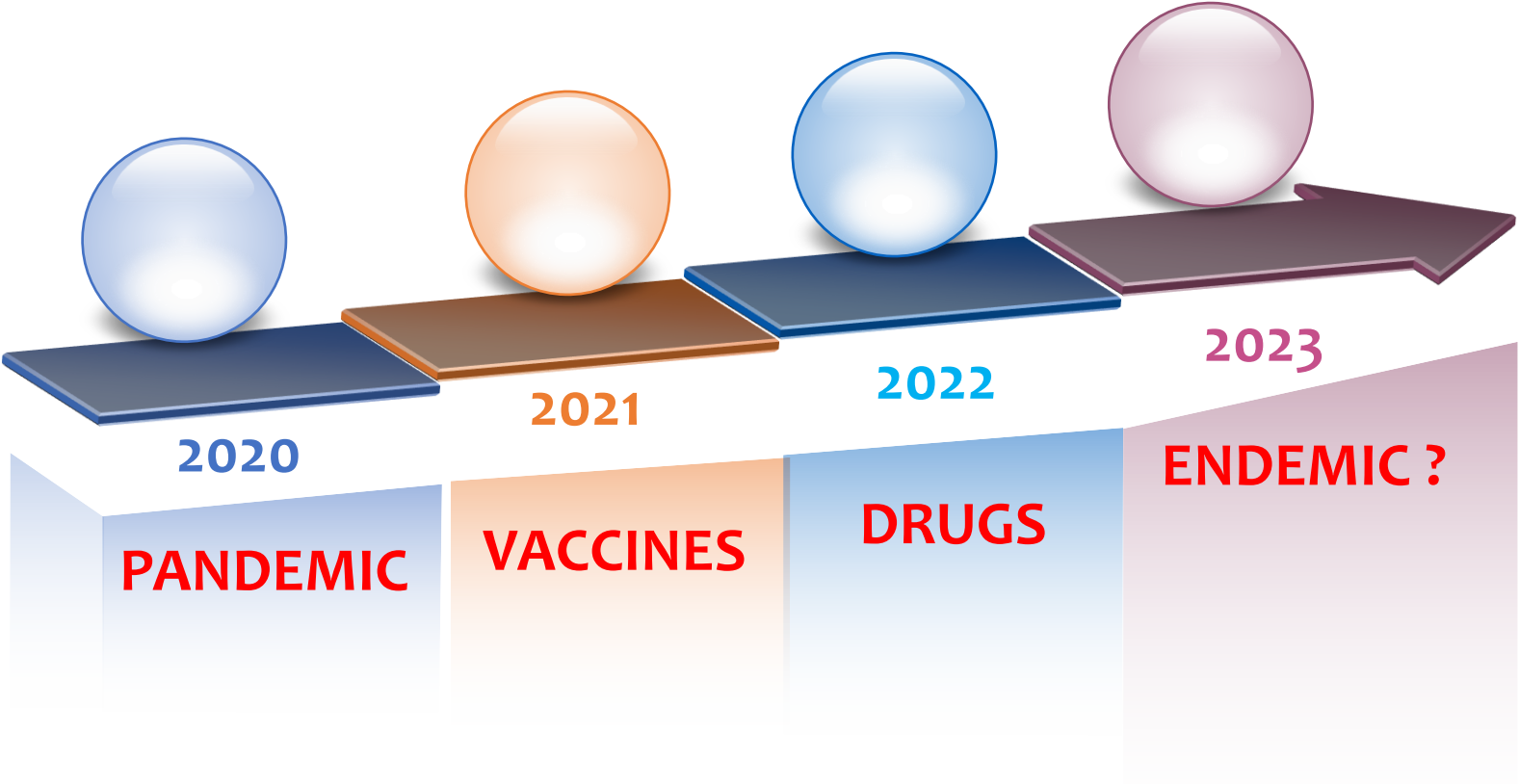
	When to use	Dosage	Time of exposure
NSAIDs			
Relatively selective COX-2 inhibitors			
Nimesulide	At the onset of symptoms (fever, cough, sore throat, headache)	100 mg orally twice a day	For 3–4 days, if symptoms persist, continue for a maximum of 12 days
Celecoxib	At the onset of symptoms (fever, cough, sore throat, headache)	Initial oral dose of 400 mg followed by a second dose of 200 mg on the first day; in the following days, 200 mg/day up to a maximum of 400 mg/day	For 3–4 days, if symptoms persist, continue for a maximum of 12 days
Other NSAIDs			
Ibuprofen	At the onset of symptoms (fever, cough, sore throat, headache)	400 mg orally twice a day	For 3–4 days
Aspirin	At the onset of symptoms (fever) or with laboratory signs of hepatotoxicity associated with nimesulide or contraindications to celecoxib	500 mg orally twice a day	For 3–4 days, if symptoms persist, continue for a maximum of 8 days
Corticosteroids*			
Dexamethasone	Should fever persist after 8–10 days of NSAID treatment, or when oxygen saturation <94–92% occurs	8 mg orally for 3 days, then tapered to 4 mg for a further 3 days, and then to 2 mg for 3 days	Duration of treatment depends on the clinical evolution of the disease



COVID-19 in 2022

**The Beginning of the End or
the End of the Beginning?**

SARS-COV2 from pandemic to endemic





Last Updated at (M/D/YYYY)
2022. 9. 17. 오전 10:23

Total Cases
611,370,593

Total Deaths
6,524,994

Total Vaccine Doses Administered
12,226,931,606

Cases | Deaths by
Country/Region/Sovereignty

28-Day Cases
16,740,456

28-Day Deaths
55,570

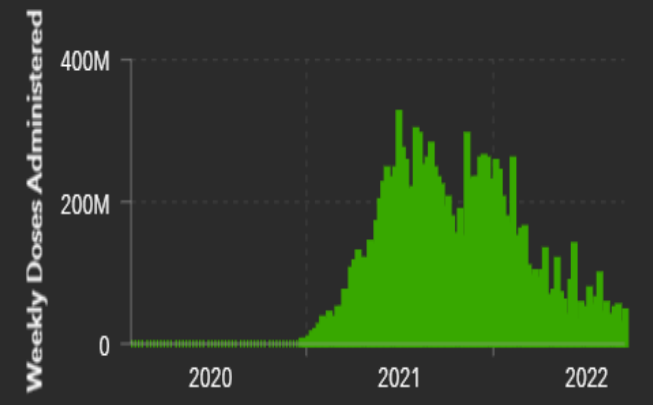
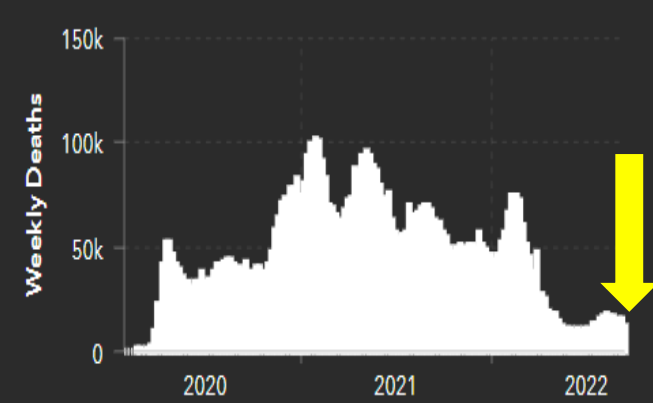
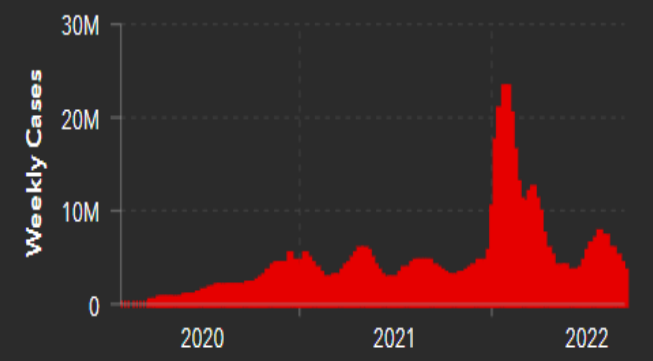
28-Day Vaccine Doses Administered
149,313,517

- Japan**
28-Day: **4,034,713** | 7,093
Totals: **20,558,655** | 43,555
- Korea, South**
28-Day: **2,316,265** | 1,829
Totals: **24,359,702** | 27,782
- US**
28-Day: **2,134,139** | 12,879
Totals: **95,645,792** | 1,053,389
- Russia**
28-Day: **1,247,096** | 2,327
Totals: **20,029,220** | 378,029
- Taiwan***
28-Day: **873,778** | 883
Totals: **5,891,355** | 10,469
- Germany**
28-Day: **871,858** | 2,462
Totals: **20,640,740** | 140,045



Esri, FAO, NOAA, USGS

Powered by Esri



Admin0

28-Day

Weekly

28-Day



Daily new confirmed COVID-19 cases

7-day rolling average. Due to limited testing, the number of confirmed cases is lower than the true number of infections.

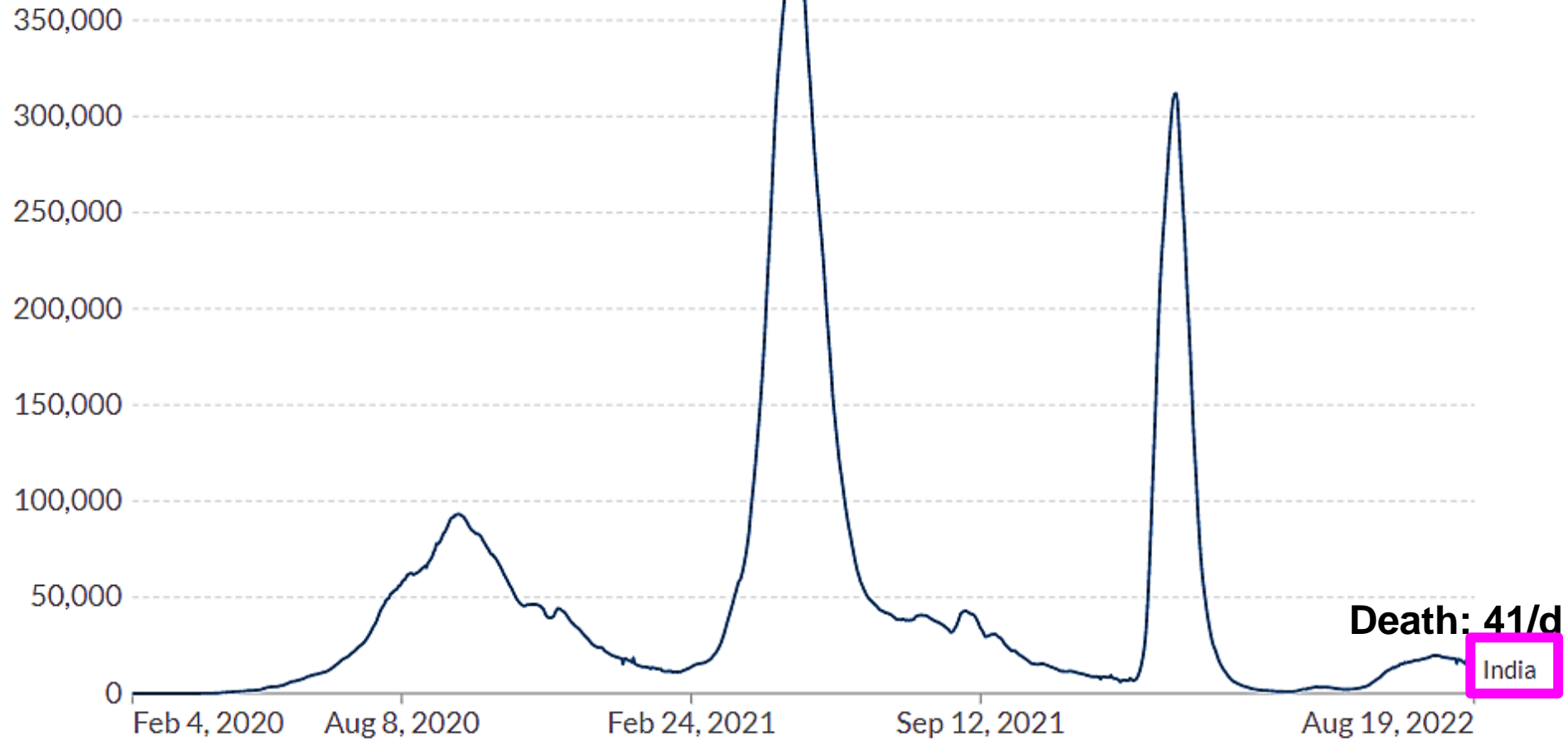
Our World
in Data

LINEAR

LOG

+ Add country

Cumulative covid 19 cases:
44.33 million/1.4billion



Source: Johns Hopkins University CSSE COVID-19 Data

CC BY

▶ Feb 4, 2020

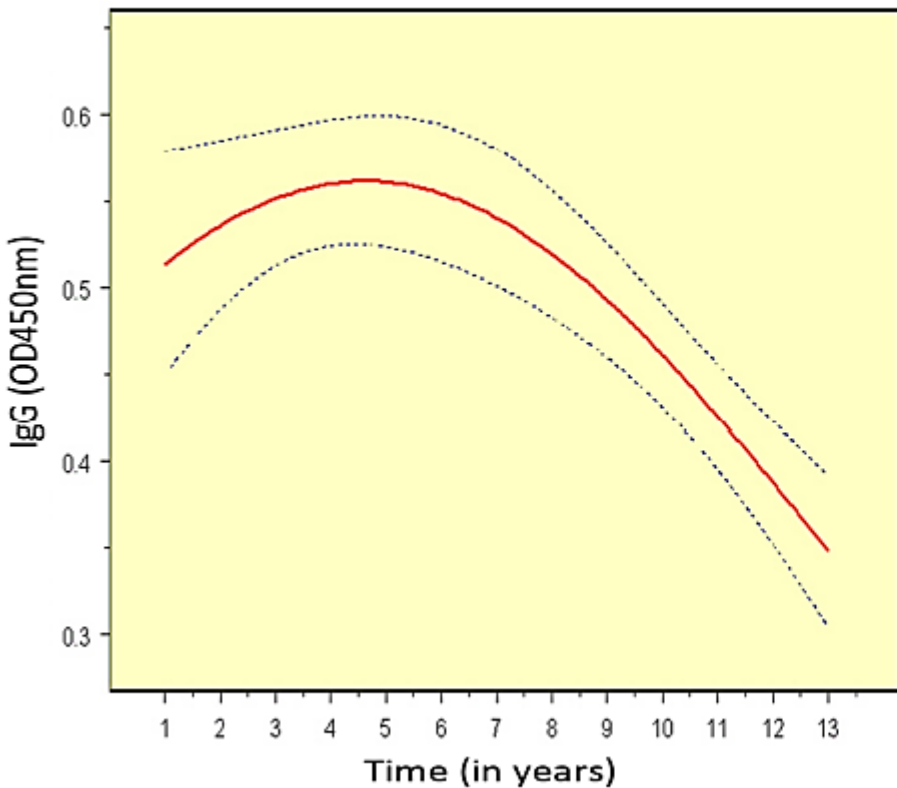


Aug 19, 2022

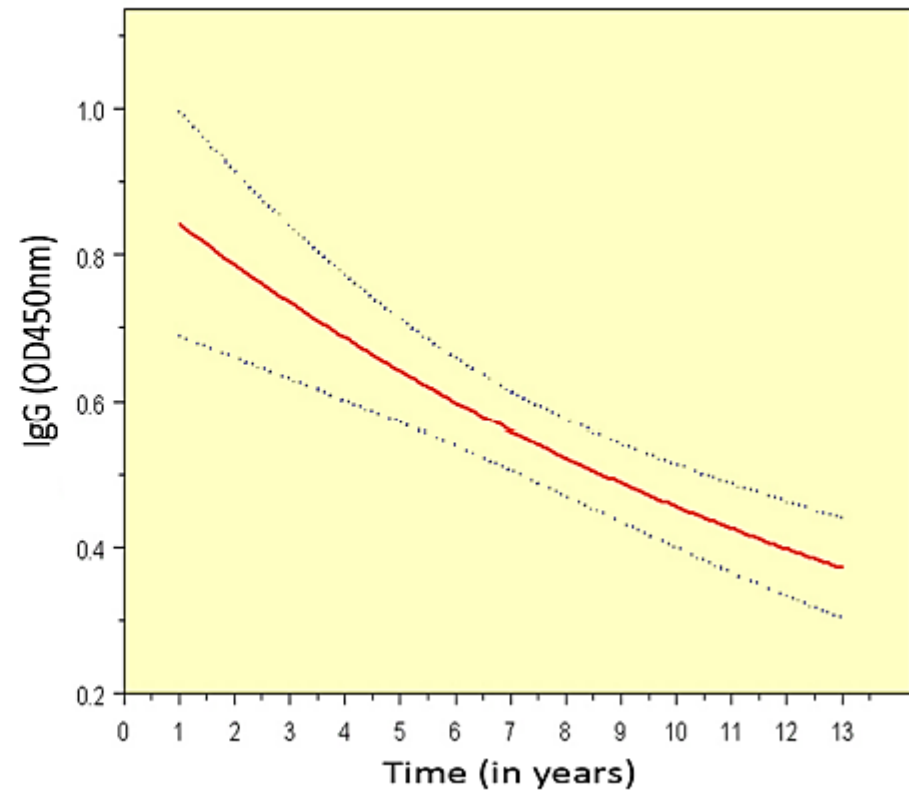


Long-Term Persistence of IgG Antibodies in SARS-CoV CoV Infected 2 Healthcare Workers

A Exponential decay curve for IgG against whole virus



B Exponential decay curve for IgG against N199



Population profiles of IgG against SARS-CoV whole virus and N199 from 2003 to 2015

Accuracy of 2 Rapid Antigen Tests During 3 Phases of SARS-CoV-2 Variants



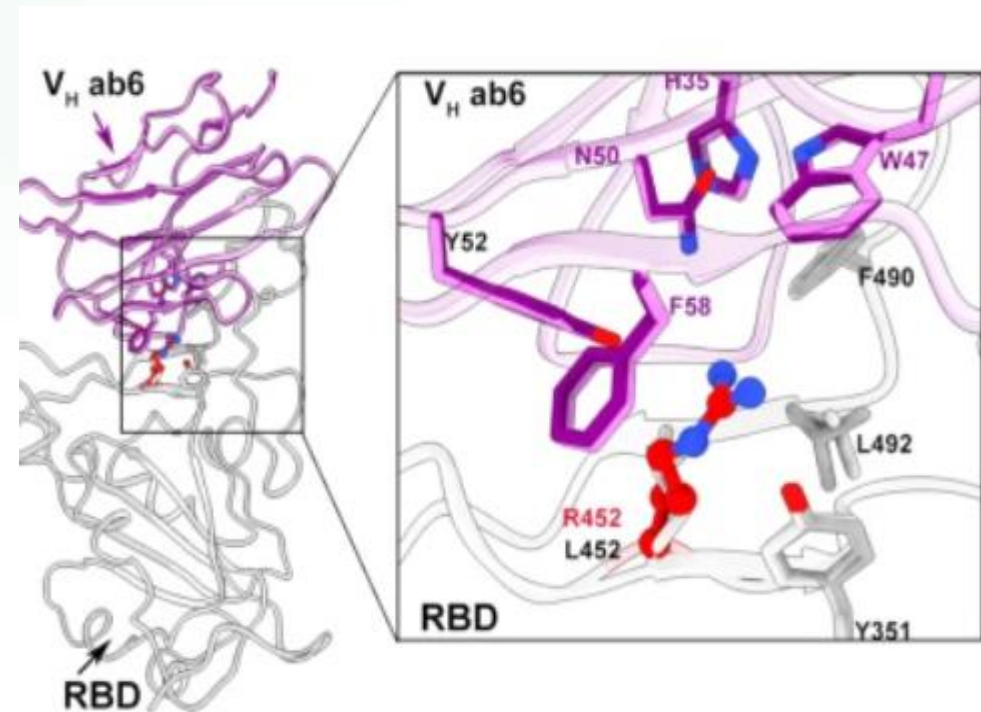
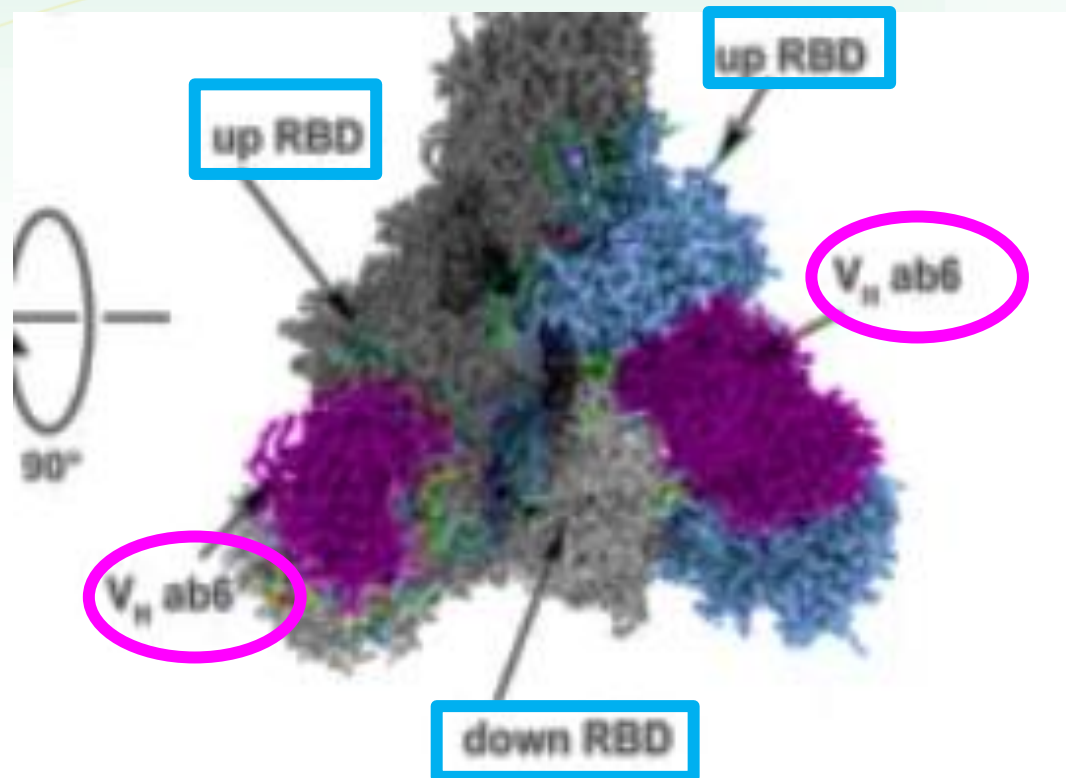
	Pre-Delta ^b	Delta	Omicron	Total ^c
Participants positive for COVID-19/participants with valid RT-PCR results, No. (%) ^d	64/296 (21.6)	43/289 (14.9)	73/212 (34.4)	180/797 (22.6)
Time since symptom onset, mean (SD), d	2.2 (0.2)	2.3 (1.2)	2.5 (1.3)	2.3 (1.2)
Cycle threshold values among specimens positive for SARS-CoV-2 by RT-PCR, mean (SD)	23.9 (5.2)	27.6 (4.6)	28.0 (4.8)	26.5 (5.3)
Agreement for rapid antigen test, % (95% CI) ^e				
Positive	81.2 (69.5-89.9)	90.7 (77.9-97.4)	83.6 (73.0-91.2)	84.4 (78.3-89.4)
Negative	100 (98.4-100)	99.6 (97.8-100)	100 (97.4-100)	99.8 (99.1-100)
Analytical limit of detection for rapid antigen test, TCID ₅₀ per swab	62.5	62.5	62.5	62.5



FDA Authorizes First COVID-19 Test Available without a Prescription That Also Detects Flu and RSV

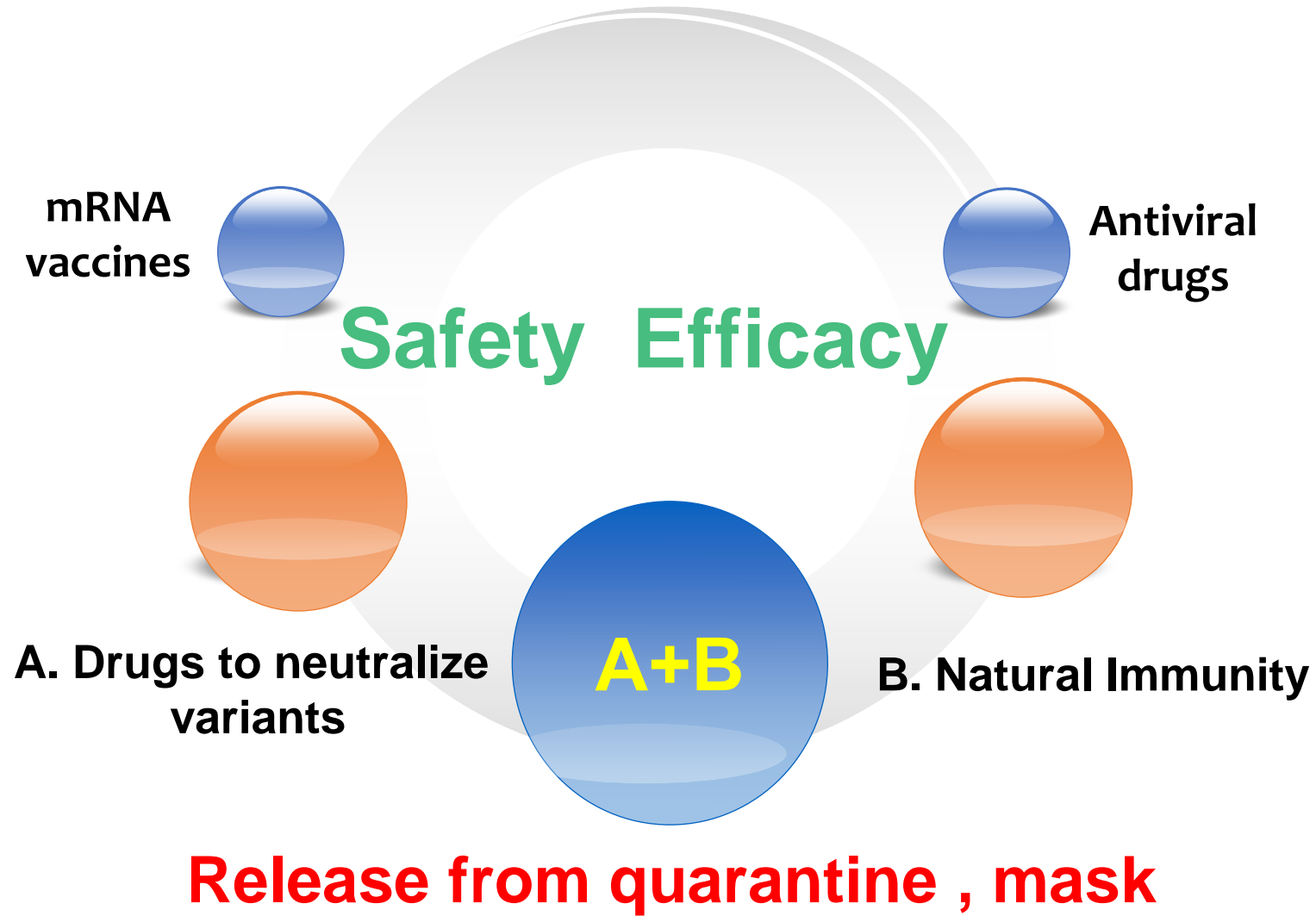
- The first direct-to-consumer (non-prescription) multi-analyte COVID-19 test authorized by FDA and allows an individual to self-collect a nasal swab sample at home and then send to Labcorp.
- Ability to collect your sample at home for flu and RSV without a prescription, brings us one step closer to tests for these viruses that could be performed entirely at home.”

SARS-CoV-2 variants of concern: spike protein mutational analysis and epitope for broad neutralization



Antibody fragment (V_H ab6) that neutralizes all major variants

What are the most effective strategies for COVID 19





Ecosystem restoration: a public health intervention

- The new COVID booster could be the last you'll need for a year.
- Ontario scraps mandatory **five-day isolation** rules for people.
- New York State ends COVID-19 **mask mandates on trains**, transit.
- Malaysia Scraps **Indoor Mask Rule** as Covid-19 Wave Eases.
- Mask mandate ends on **international flights** as COVID-19 rules.
- First **nasal vaccine** for COVID-19 approved in India for emergency use.



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