SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA
68° CONGRESSO NAZIONALE SIGG
Ritorno al futuro
FIRENZE, 13-16 DICEMBRE 2023
PALAZZO DEI CONGRESSI

PROTEGGERE IL PAZIENTE ANZIANO DAL COVID-19: VACCINAZIONE E TRATTAMENTO ANTIVIRALE

Graziano Onder
Università Cattolica del Sacro Cuore
Fondazione Policlinico Gemelli
Roma

Agenda

- COVID-19 oggi
- COVID-19 domani
- Chi è a rischio?
- Vaccinazione
- Trattamento antivirale

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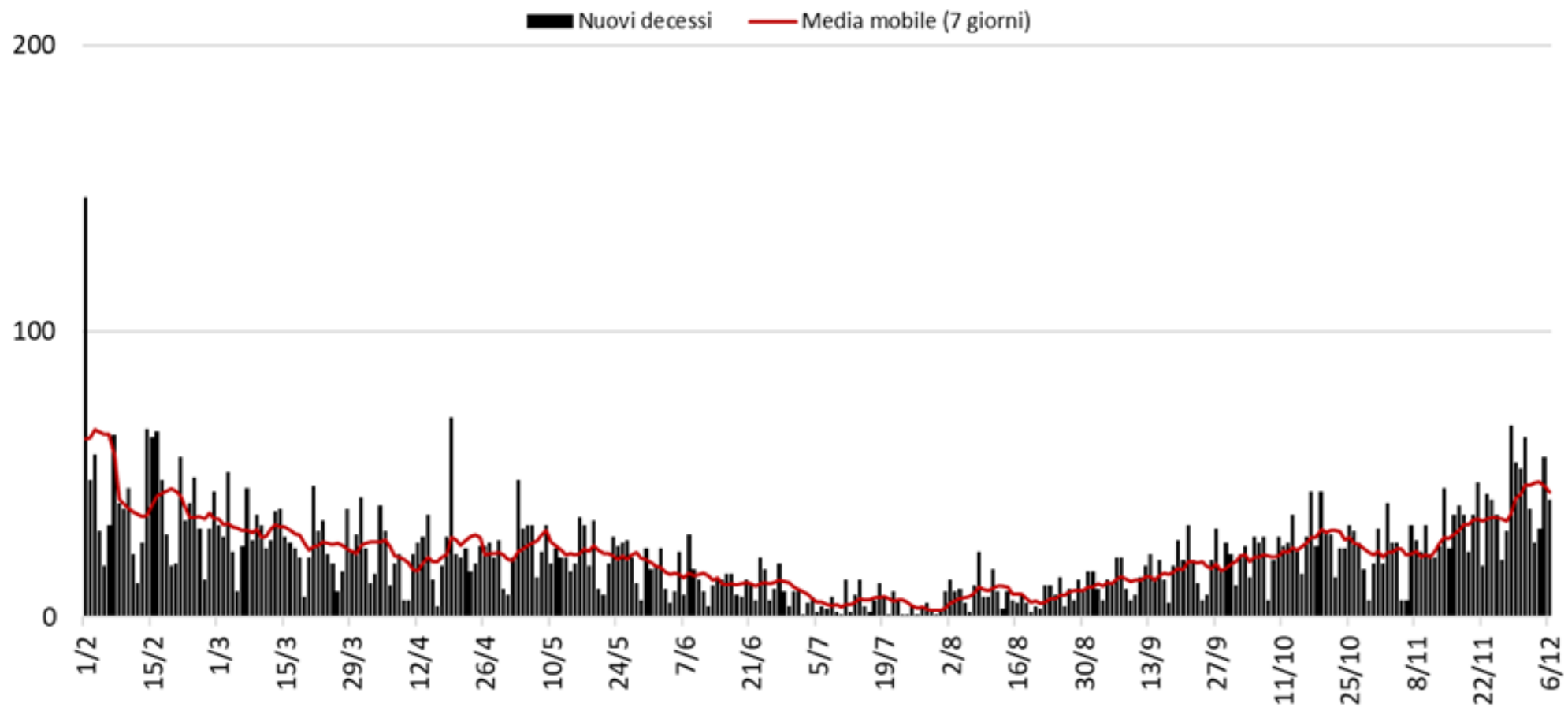
COVID-19 in Italia
Gli ultimi 30 giorni (11 dicembre 2023)

154.496	4.208	59 anni	43% | 57%	587	85.174
Casi negli ultimi 30 giorni***	Casi tra gli operatori sanitari negli ultimi 30 giorni*	Età mediana dei casi negli ultimi 30 giorni	Maschi (%) | Femmine (%) negli ultimi 30 giorni	Deceduti negli ultimi 30 giorni**	Guariti negli ultimi 30 giorni**

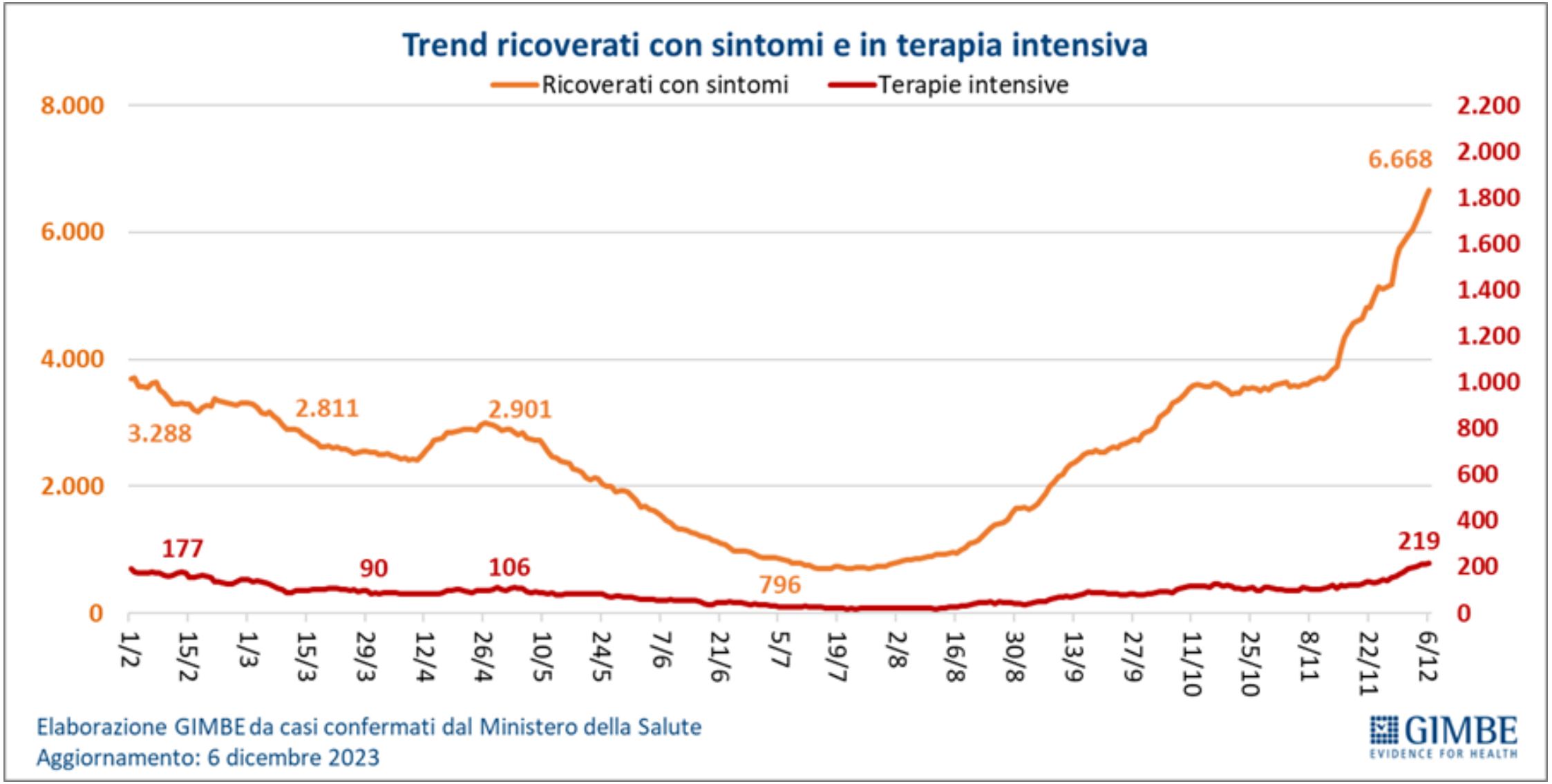
Fonte: ISS

Numero giornaliero dei decessi



Elaborazione GIMBE da casi confermati dal Ministero della Salute
Aggiornamento: 6 dicembre 2023

GIMBE
EVIDENCE FOR HEALTH


Trend ricoverati con sintomi e in terapia intensiva
Ricoverati con sintomi
Terapie intensive
8.000
6.000
4.000
2.000
0
2.200
2.000
1.800
1.600
1.400
1.200
1.000
800
600
400
200
0
3.288
2.811
2.901
796
6.668
177
90
106
219
1/2
15/2
1/3
15/3
29/3
12/4
26/4
10/5
24/5
7/6
21/6
5/7
19/7
2/8
16/8
30/8
13/9
27/9
11/10
25/10
8/11
22/11
6/12
Elaborazione GIMBE da casi confermati dal Ministero della Salute
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GIMBE
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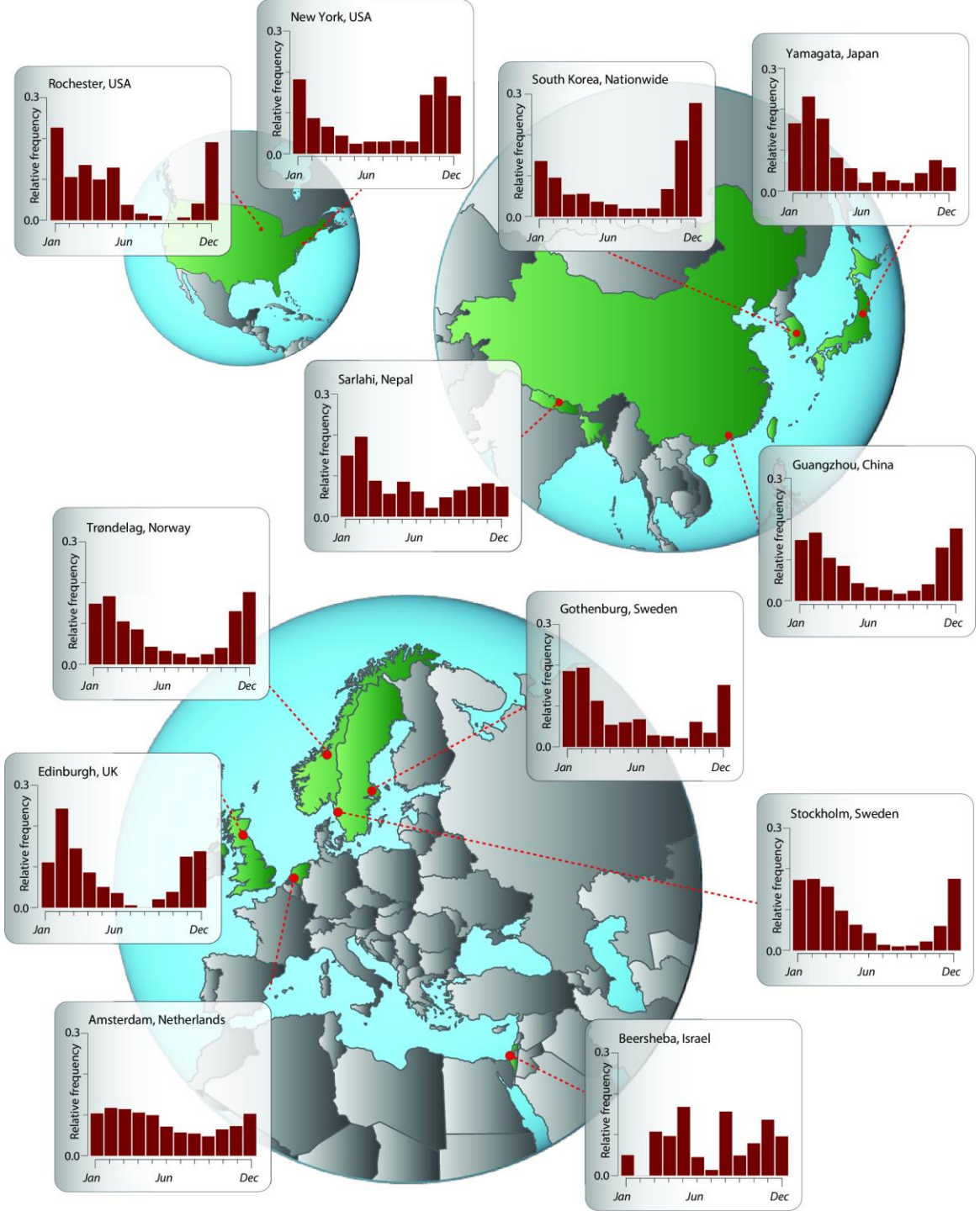
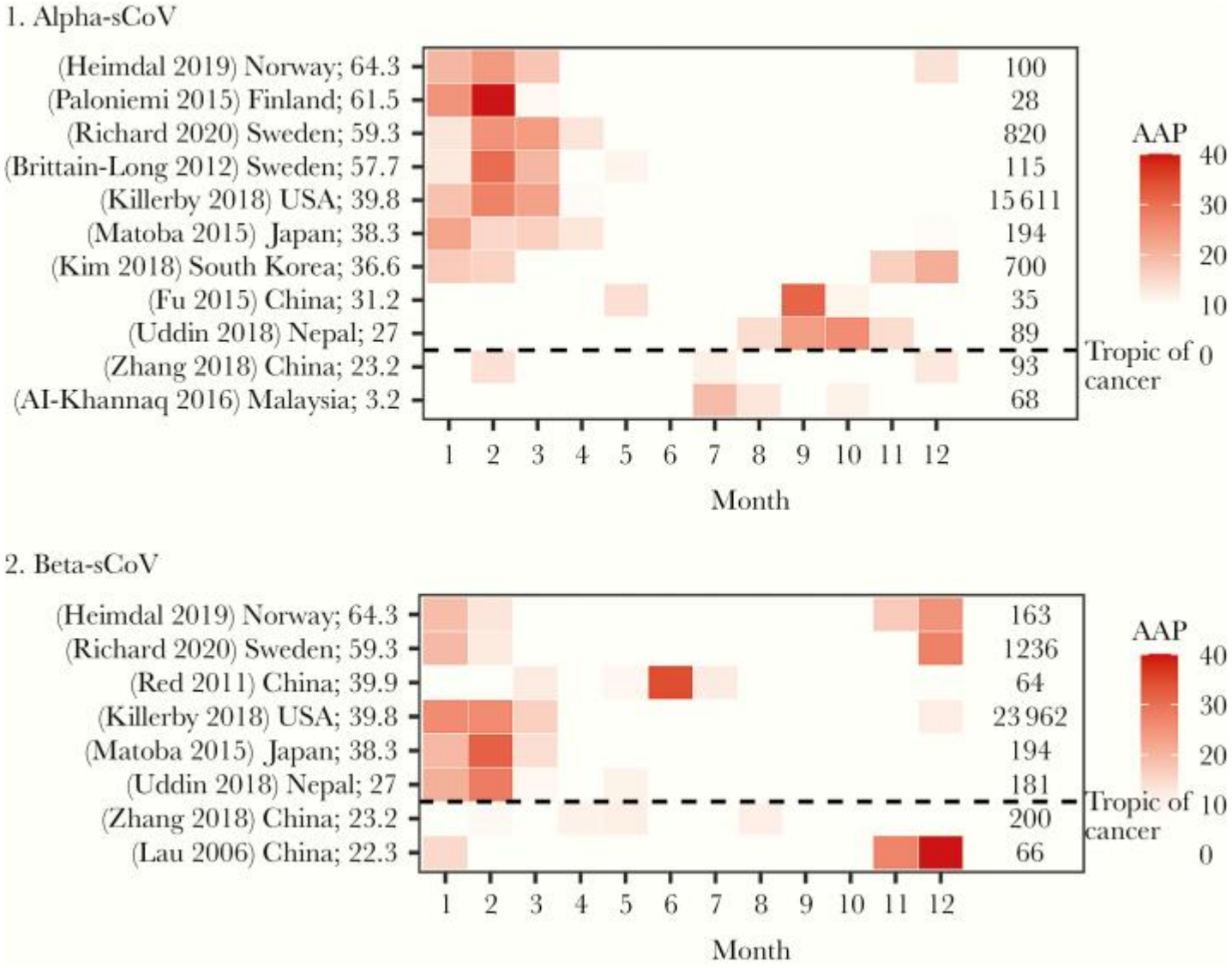


Estimates of the relative monthly incidence of SARS-CoV-2 under endemic conditions

SARS-CoV-2 infections can be expected to transition to a **seasonal pattern of incidence** that is high in late fall and winter months relative to late spring and summer. Our projections also reveal geographic heterogeneity.

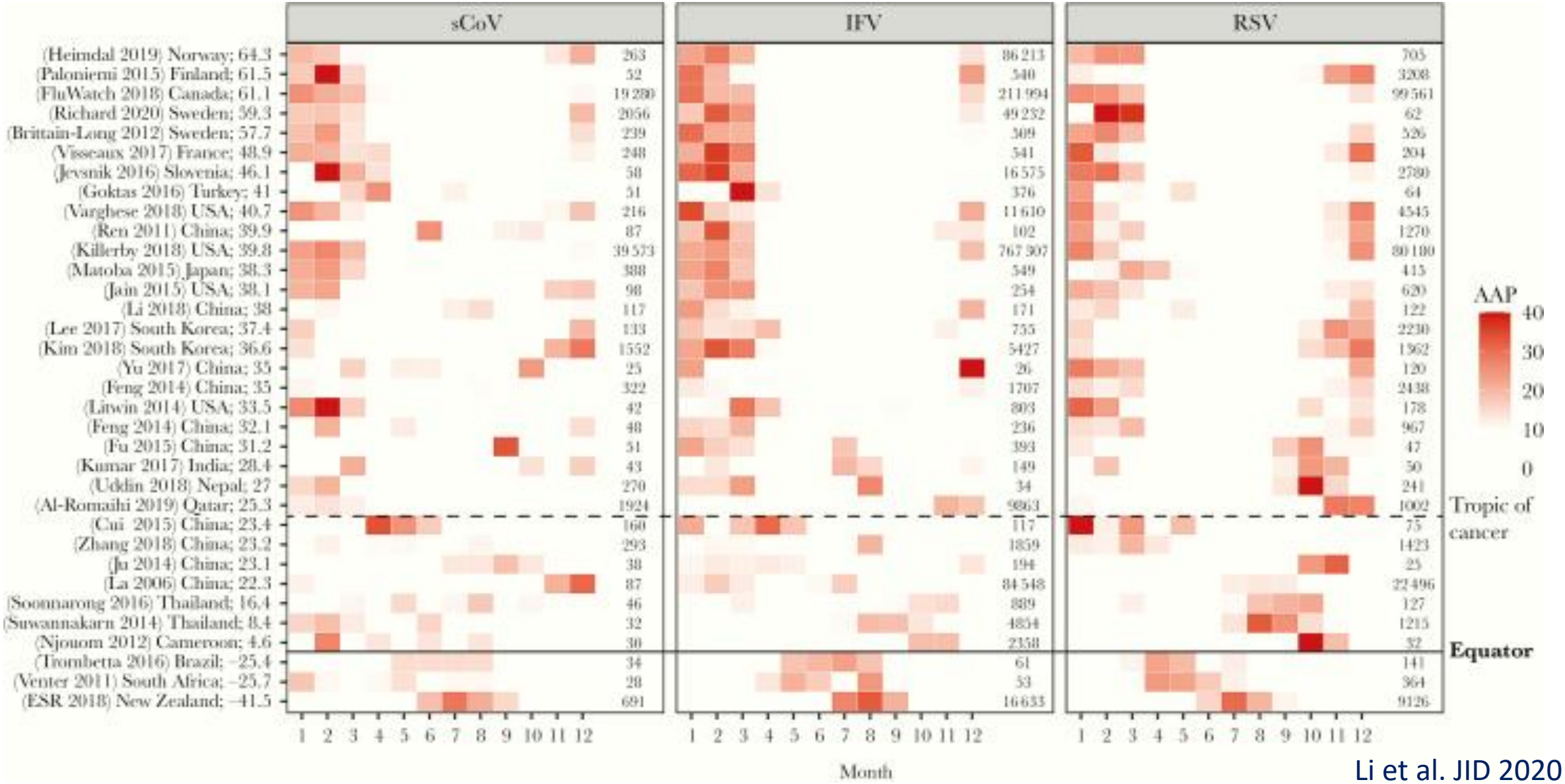
Townsend et al. Mbio 2023

Global monthly activity of alphacoronaviruses and betacoronaviruses



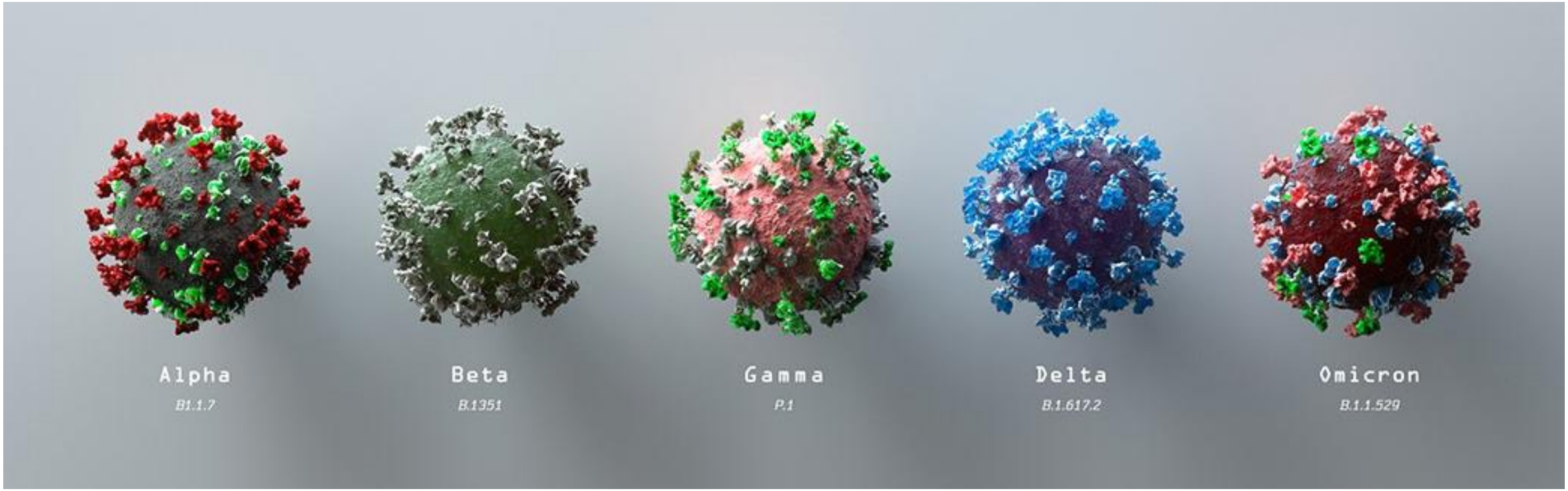
Latitudine

Li et al. JID 2020

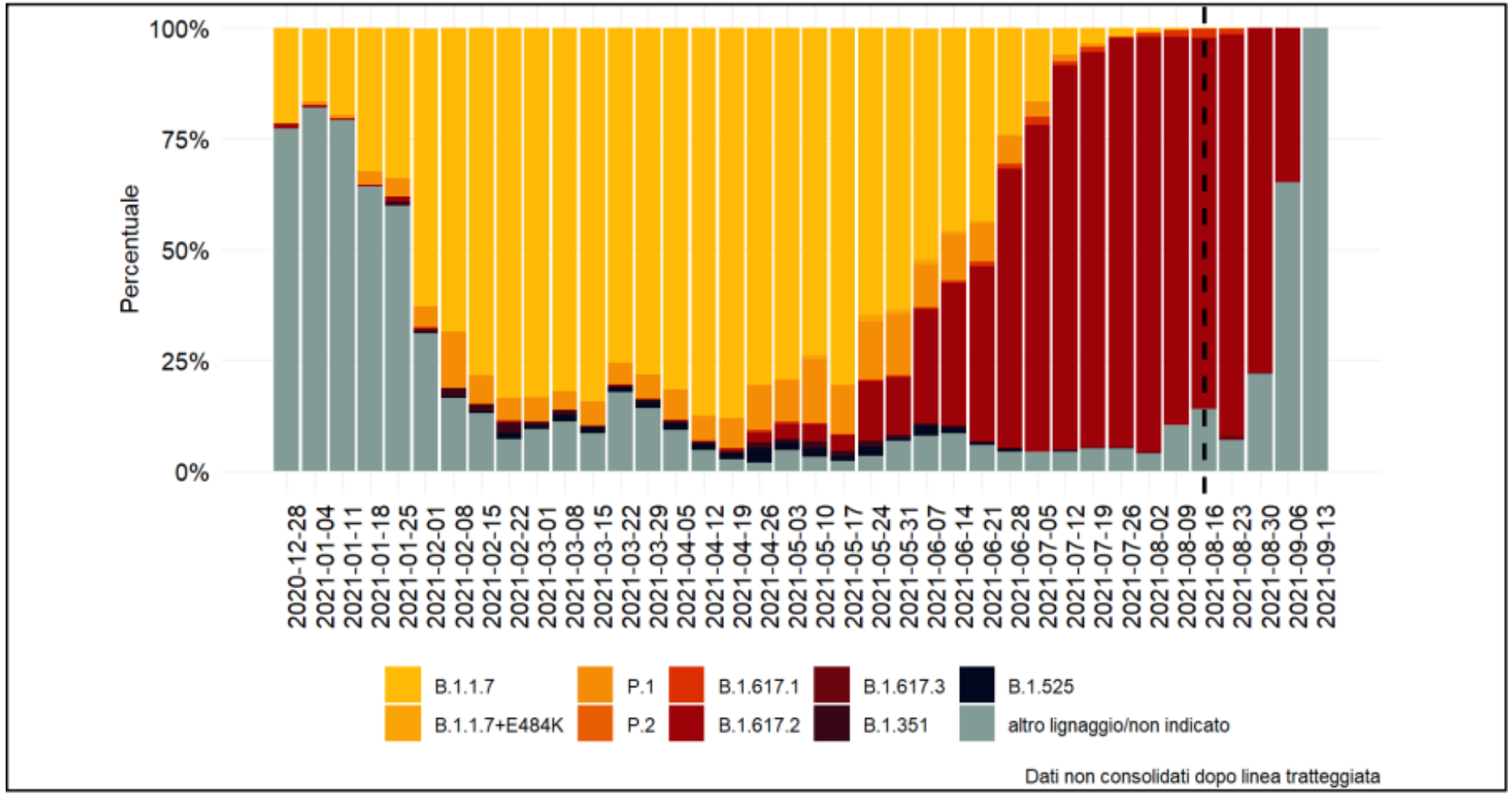


Li et al. JID 2020

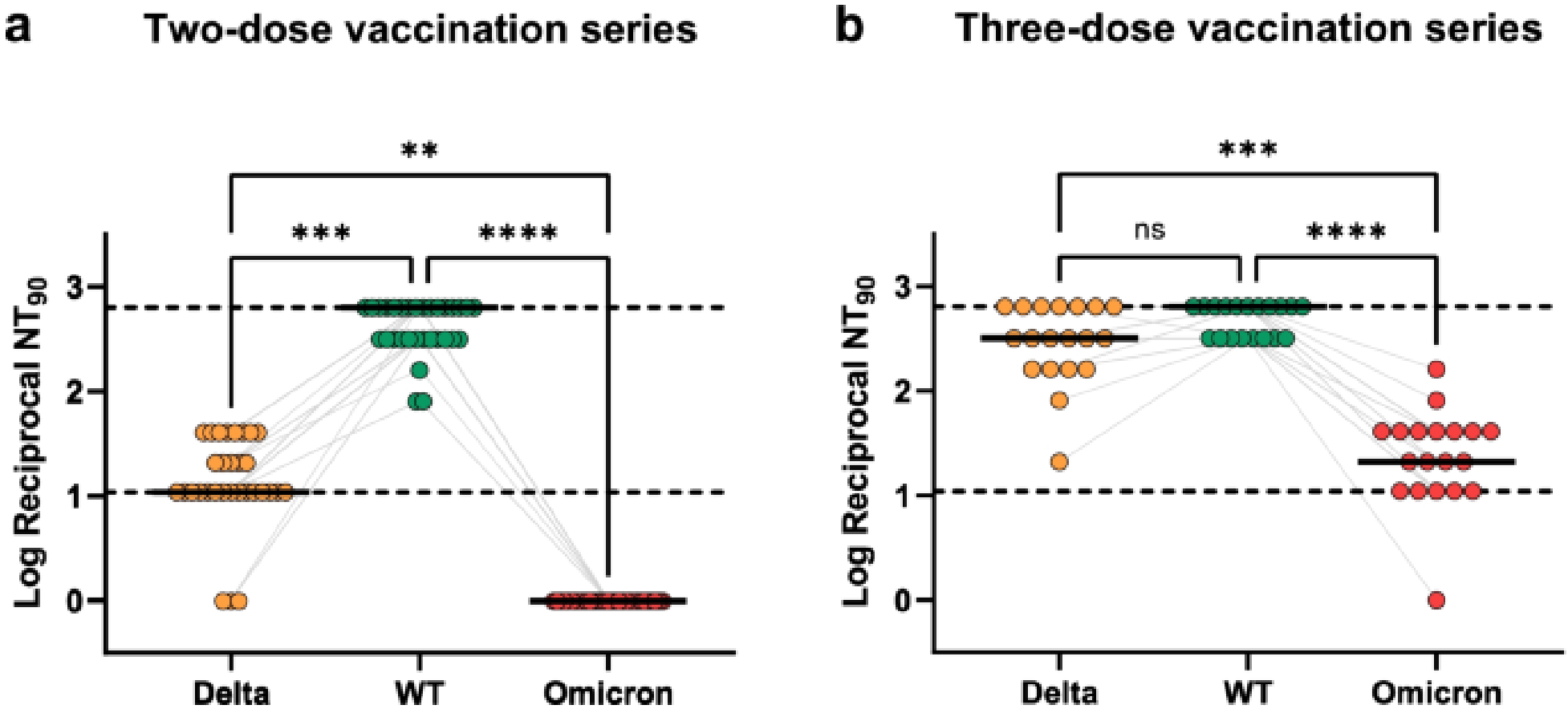
Varianti Sars-CoV-2



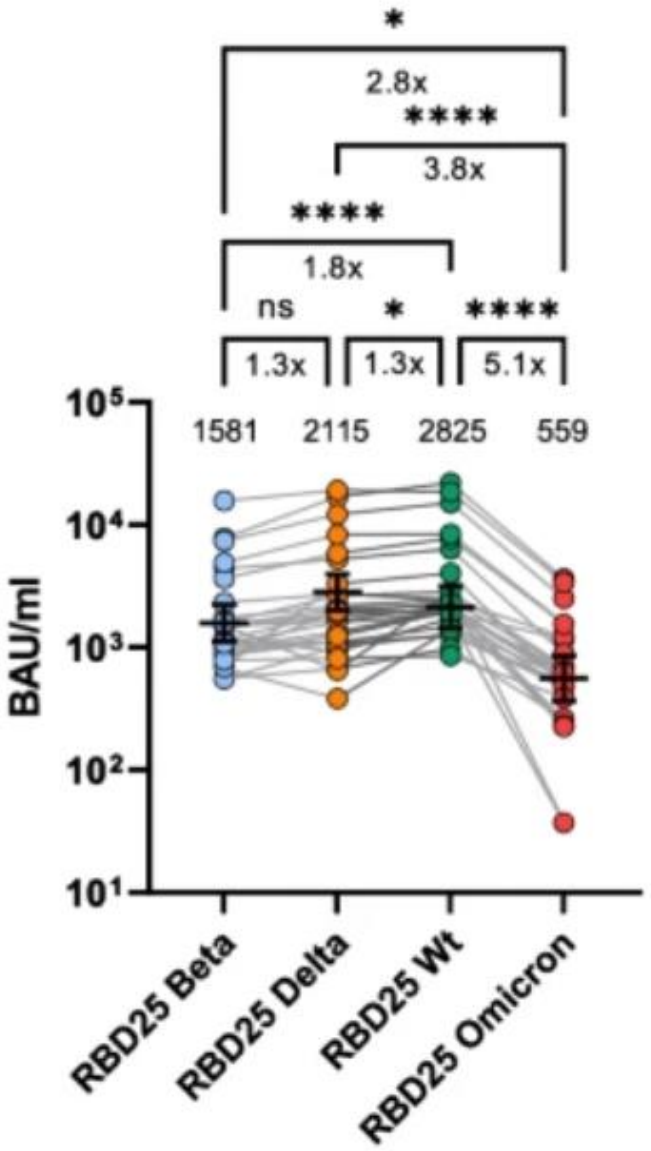
Varianti Sars-CoV-2 – Bollettino ISS 2021



Neutralization of SARS-CoV-2 WT, Delta, and Omicron using sera of BNT162b-vaccinated individuals.



Schubert et al. BMC Med 2022



Human serum binding to SARS-CoV-2 WT, Beta, Delta, and Omicron receptor-binding domain, using sera from hospitalized COVID-19 patients

Schubert et al. BMC Med 2022

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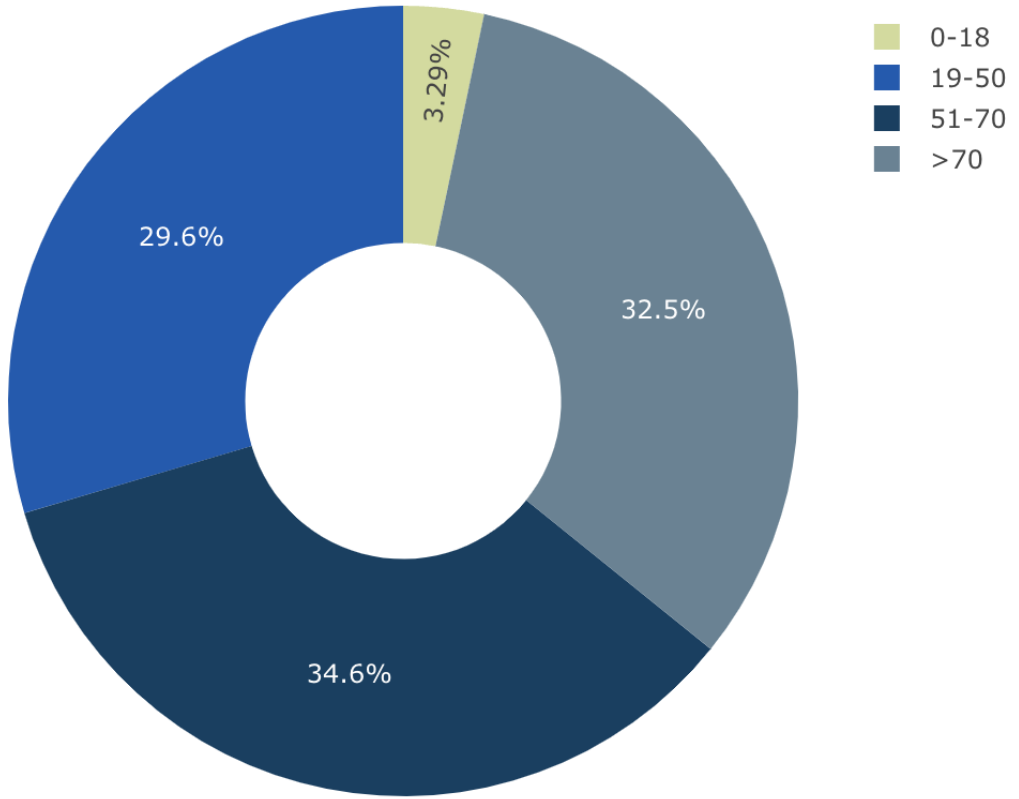
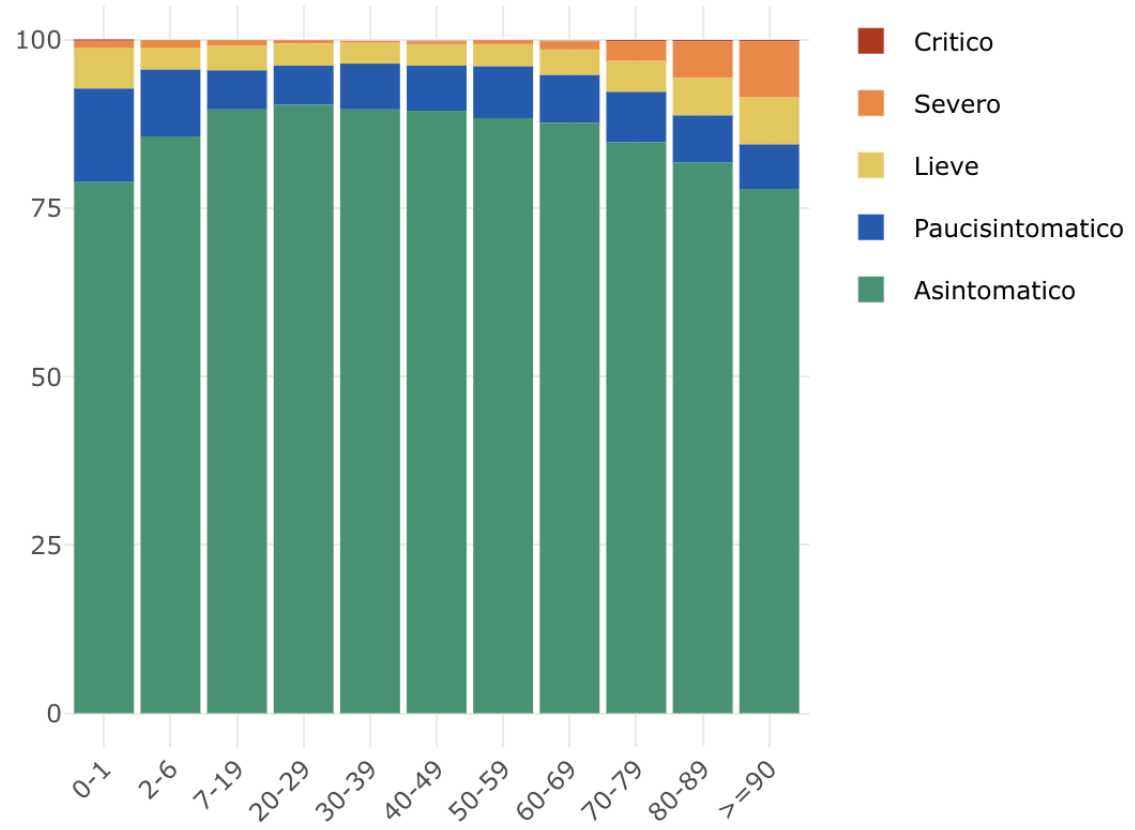
Proporzione (%) di casi di COVID-19 segnalati in Italia negli ultimi 30 giorni per classe di età (dato disponibile per 154.493 casi)

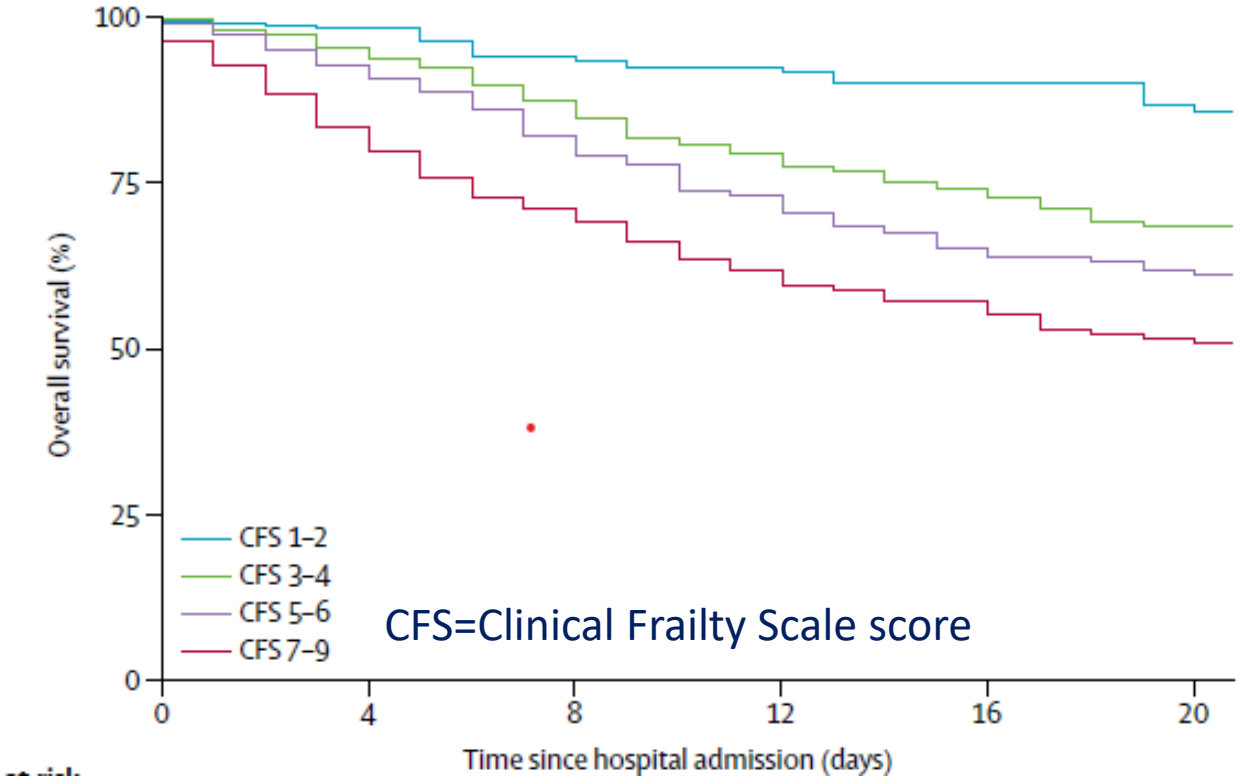


Proporzione (%) di casi di COVID-19 segnalati in Italia negli ultimi 30 giorni per stato clinico e classe di età (dato disponibile per 75.035 casi)



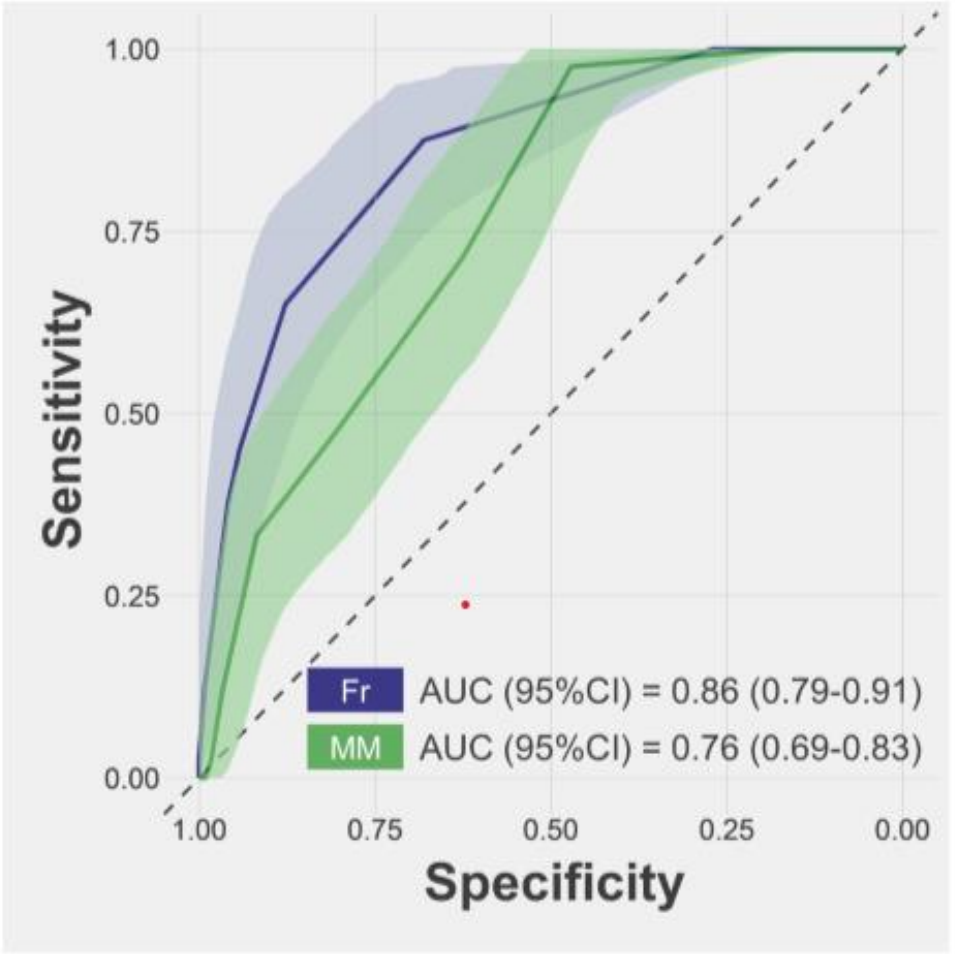
Fonte: ISS

COVID-19, frailty and multimorbidity



Survival by Clinical Frailty Scale score

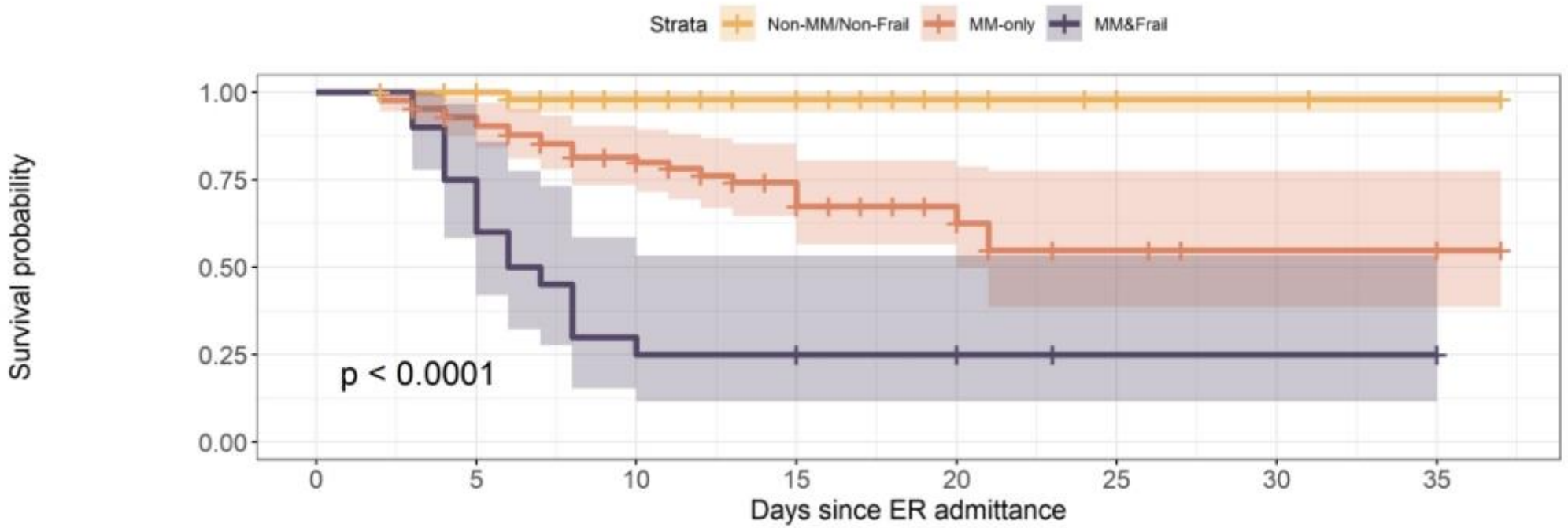
Hewitt J et al. Lancet Public Health 2020



ROC curves for Clinical Frailty Scale (Fr) score and mulimorbidity (MM) in the prediction of mortality.

Marengoni A et al. J Gerontol 2020

COVID-19, frailty and multimorbidity



Beyond chronological age: Frailty and multimorbidity predict in-hospital mortality in patients with COVID-19

Marengoni A et al. J Gerontol 2020

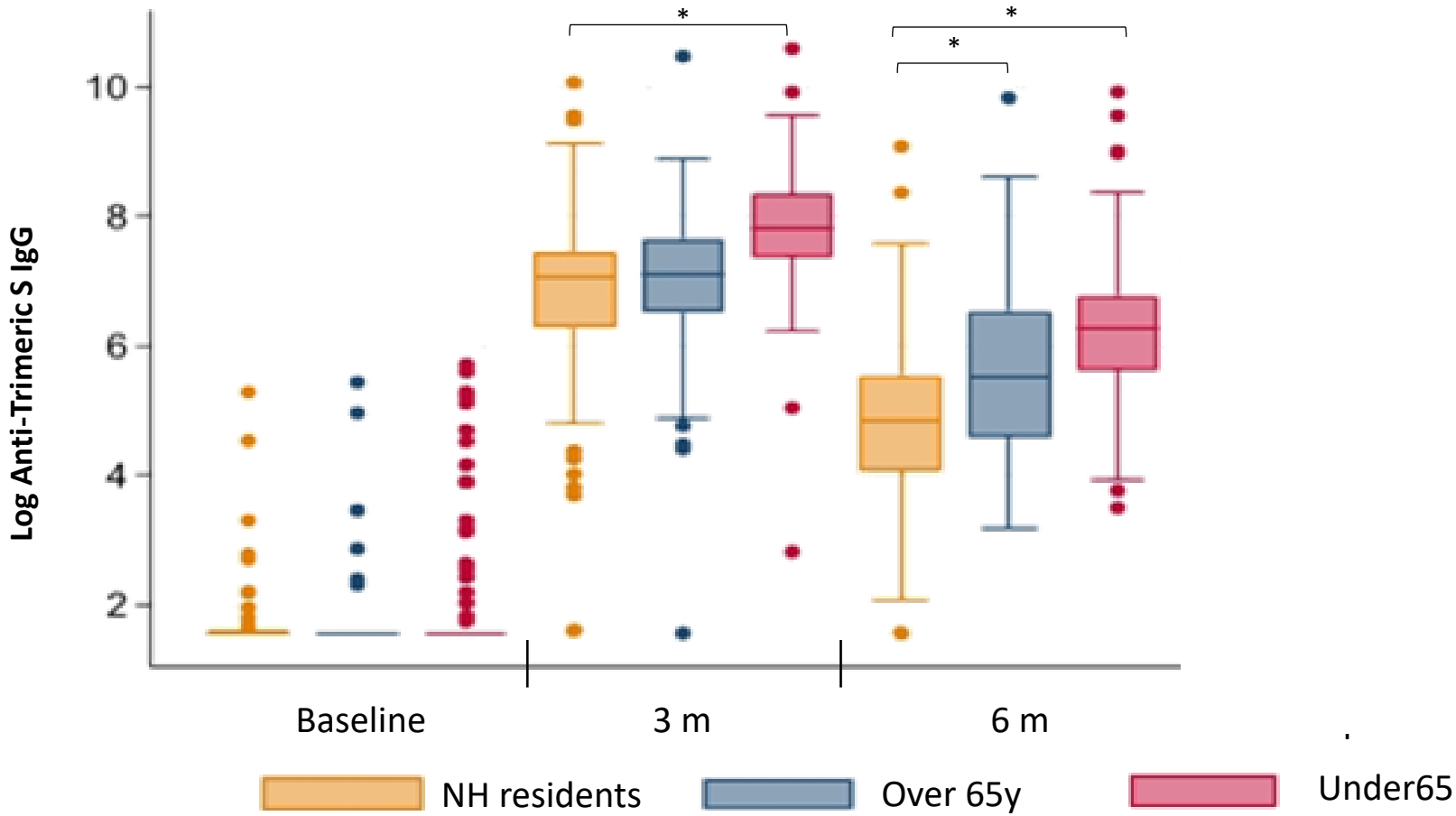
COVID-19 and deaths in Down Syndrome

In Italy **0.5% of COVID-19 related deaths occurred in persons with DS**
Prevalence of DS in the Italian population is about 0.05%
Mortality in DS is **10 times greater** than the general population

Compared with individuals without DS, those with DS deceased with COVID-19 were **younger (52 vs. 78 years)** and presented a higher incidence of **superinfections (31% vs. 13%)**.
Autoimmune diseases (43% vs. 4%), **obesity** (37% vs. 11%) and **dementia** (38% vs. 16%) were more prevalent in individuals with DS.

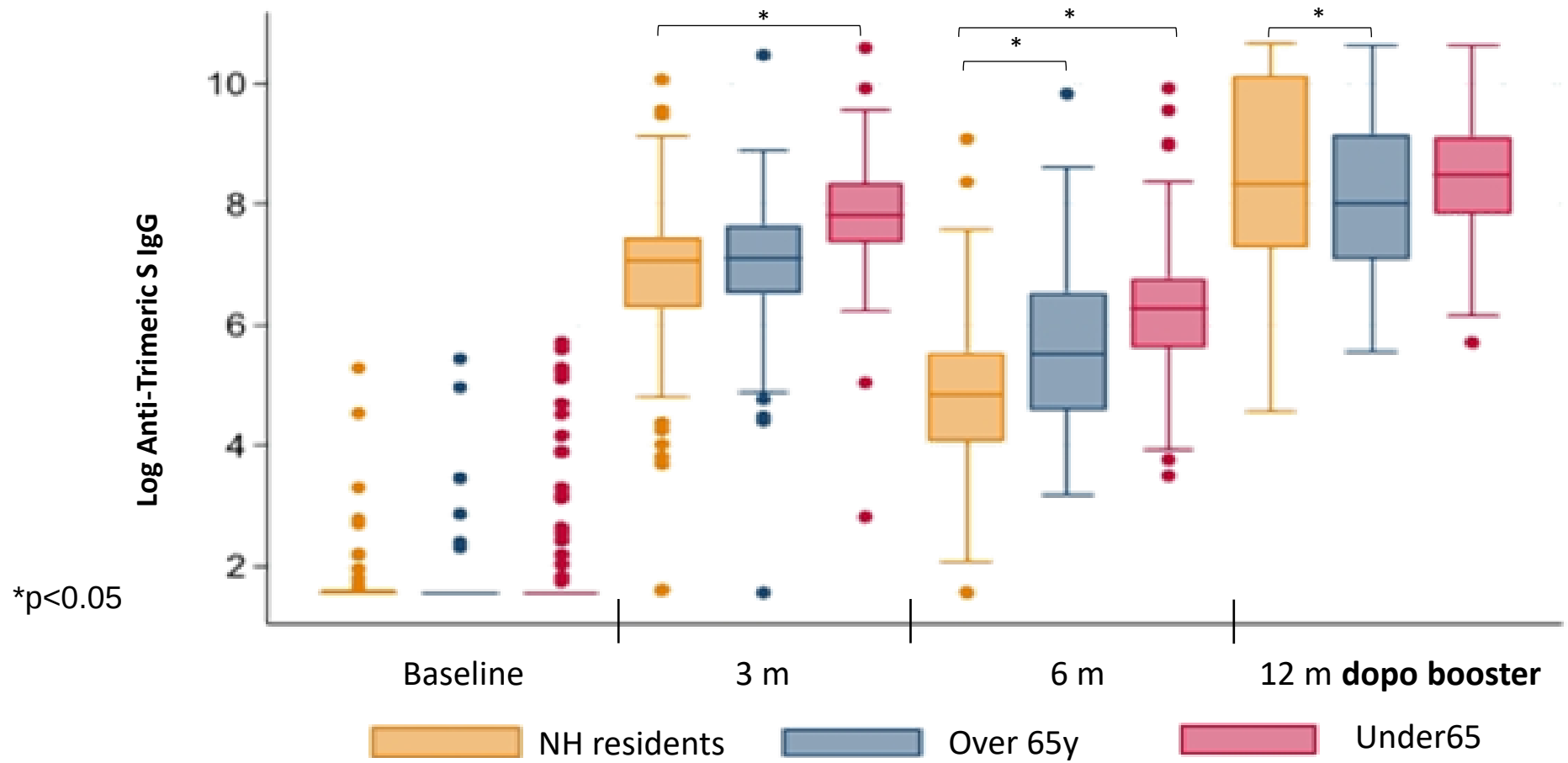
Villani ER et al. Am J Med Genet A 2020

Studio Gerovax – Risposta anticorpale vaccino



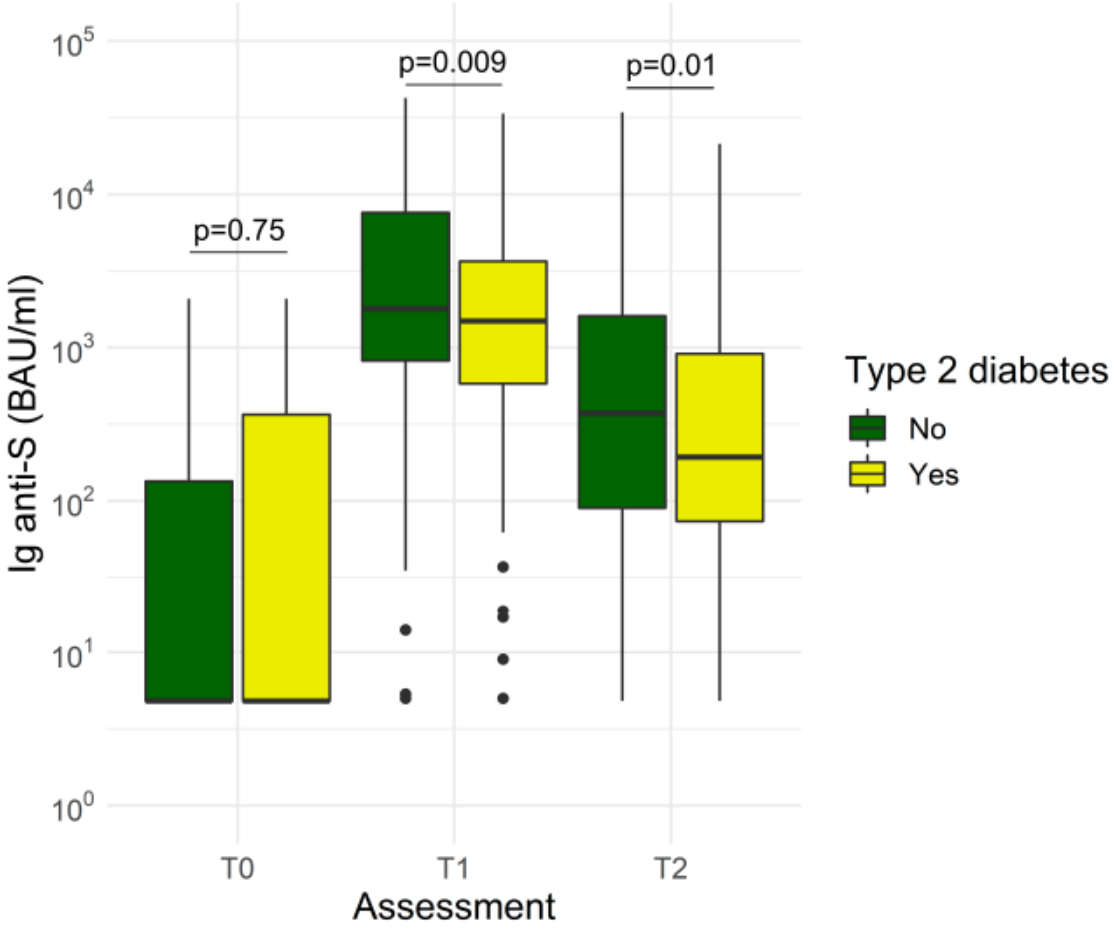
*p<0.05

Studio Gerovax – Risposta anticorpale vaccino



*p<0.05

Diabetes and Antibody Response to SARS-CoV-2 Vaccination in NH Residents: the GeroCovid Vax Study



- **Older residents of LTCFs with diabetes tended to have weaker antibody response to COVID-19 vaccination**.
- **Insulin treatment might buffer this effect** and establish humoral immunity similar to that in individuals without diabetes.

Virgilio E, Trevisan C et al. Diabetes Care 2022

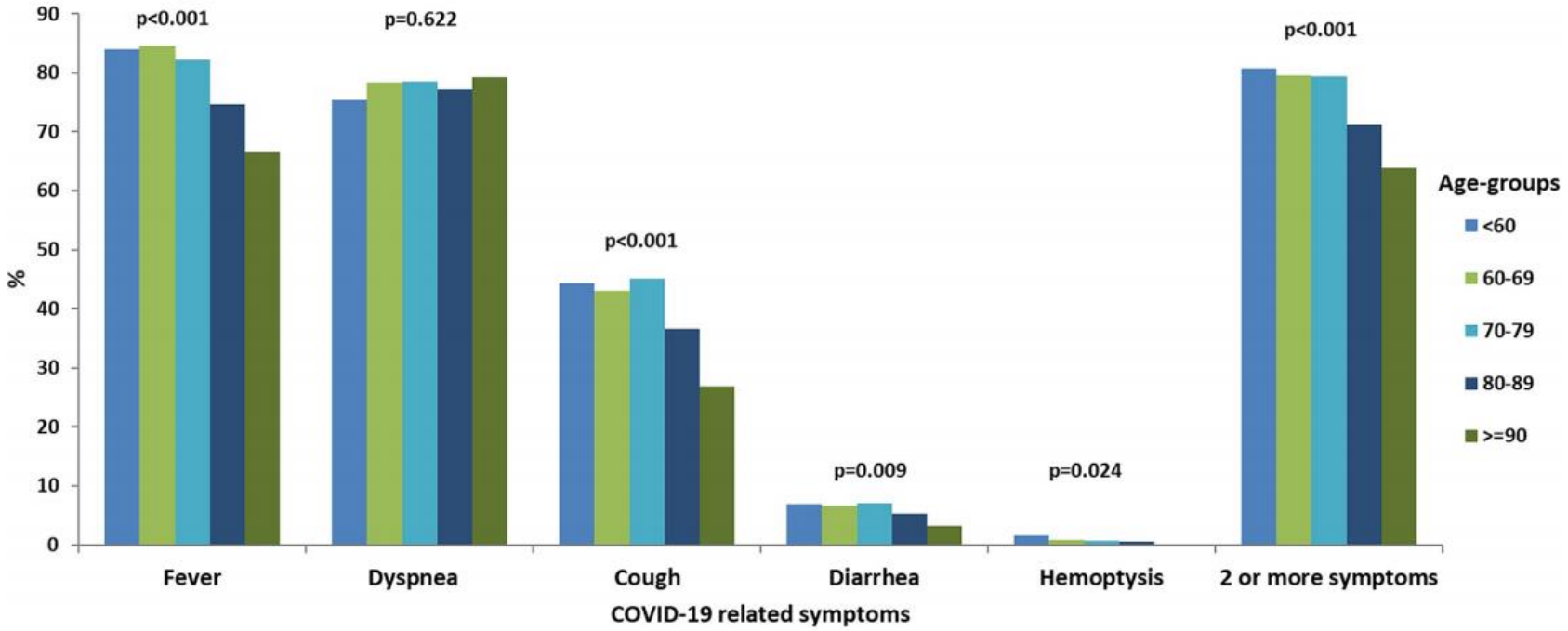
Polypharmacy and Antibody Response to SARS-CoV-2 Vaccination in NH Residents: The GeroCovid Vax Study

Results: … hyperpolypharmacy was associated with a steeper antibody decline after 6 m from the first vaccine dose (β = – 0.29, 95% CI: – 0.54, – 0.03, p = 0.03) than no polypharmacy, while no significant differences were observed at 12 m.

Conclusions: The humoral immune response to vaccination seemed less durable among older residents with hyperpolypharmacy, the booster dose administration equalized such a difference

Trevisan C et al. Drug & Ageing 2023

Symptoms at hospital admission by age group



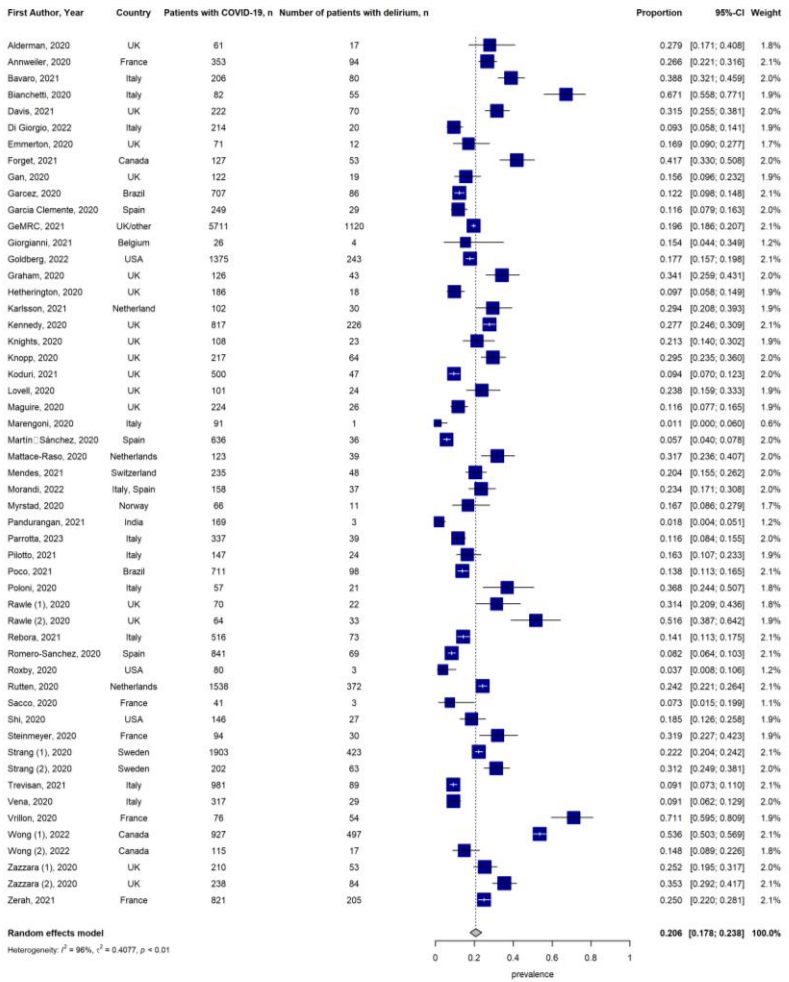
Sintomi atipici dell'anziano:

- Delirium
- Cadute
- Apatia
- Confusione
- Disorientamento
- Sonnolenza

Unim B et al. Aging Clin Exp Res 2021

Delirium and COVID-19

Zazzara MB et al. EGM in press

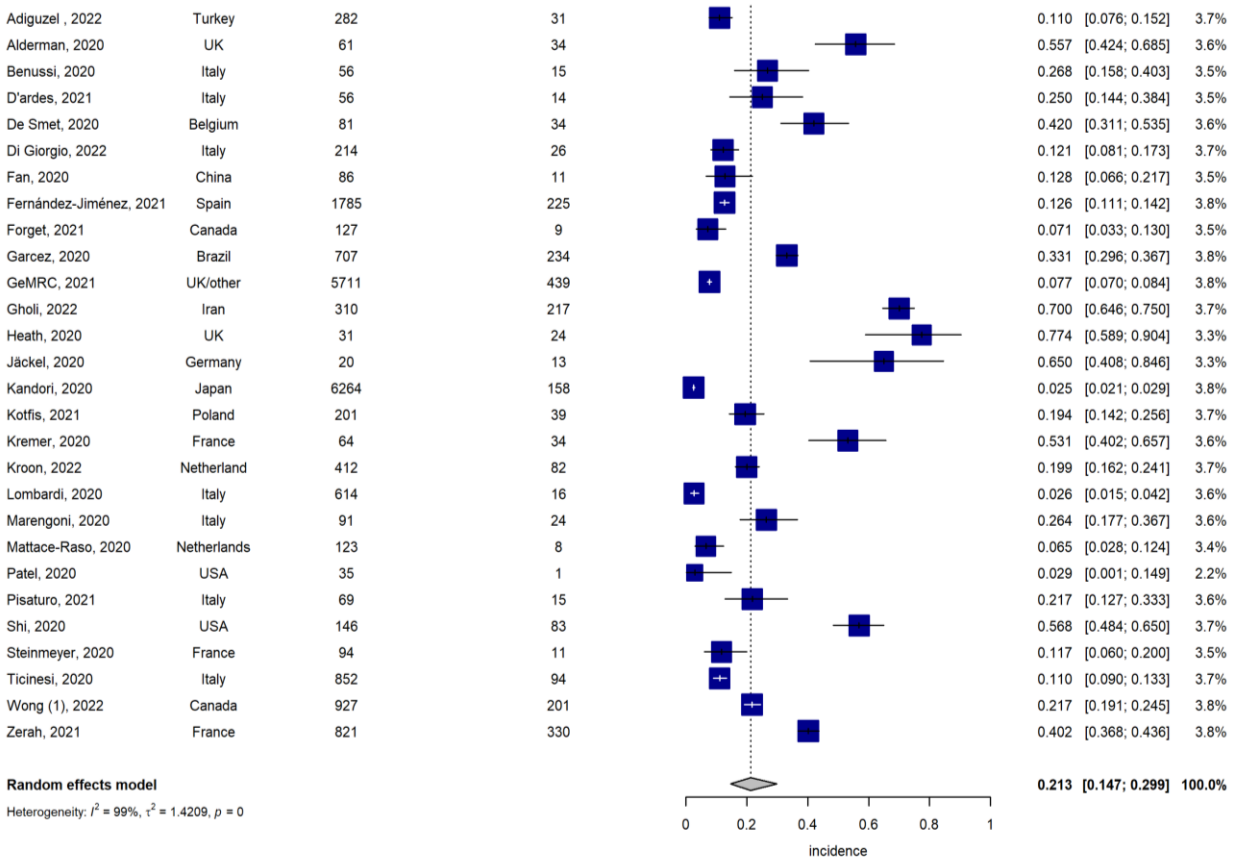


First Author, Year	Country	Patients with COVID-19, n	Number of patients with delirium, n	Proportion	95%-CI	Weight
Alderman, 2020	UK	61	17	0.279	[0.171; 0.408]	1.8%
Annweiler, 2020	France	353	94	0.266	[0.221; 0.316]	2.1%
Bavaro, 2021	Italy	206	80	0.388	[0.321; 0.459]	2.0%
Bianchetti, 2020	Italy	82	55	0.671	[0.558; 0.771]	1.9%
Davis, 2021	UK	222	70	0.315	[0.255; 0.381]	2.0%
Di Giorgio, 2022	Italy	214	20	0.093	[0.058; 0.141]	1.9%
Emmerton, 2020	UK	71	12	0.169	[0.090; 0.277]	1.7%
Forget, 2021	Canada	127	53	0.417	[0.330; 0.508]	2.0%
Gan, 2020	UK	122	19	0.156	[0.096; 0.232]	1.9%
Garcez, 2020	Brazil	707	86	0.122	[0.098; 0.148]	2.1%
Garcia Clemente, 2020	Spain	249	29	0.116	[0.079; 0.163]	2.0%
GeMRC, 2021	UK/other	5711	1120	0.196	[0.186; 0.207]	2.1%
Giorgianni, 2021	Belgium	26	4	0.154	[0.044; 0.349]	1.2%
Goldberg, 2022	USA	1375	243	0.177	[0.157; 0.198]	2.1%
Graham, 2020	UK	126	43	0.341	[0.259; 0.431]	2.0%
Hetherington, 2020	UK	186	18	0.097	[0.058; 0.149]	1.9%
Karlsson, 2021	Netherland	102	30	0.294	[0.208; 0.393]	1.9%
Kennedy, 2020	UK	817	226	0.277	[0.246; 0.309]	2.1%
Knights, 2020	UK	108	23	0.213	[0.140; 0.302]	1.9%
Knopp, 2020	UK	217	64	0.295	[0.235; 0.360]	2.0%
Koduri, 2021	UK	500	47	0.094	[0.070; 0.123]	2.0%
Lovell, 2020	UK	101	24	0.238	[0.159; 0.333]	1.9%
Maguire, 2020	UK	224	26	0.116	[0.077; 0.165]	1.9%
Marengoni, 2020	Italy	91	1	0.011	[0.000; 0.060]	0.6%
Martín□Sánchez, 2020	Spain	636	36	0.057	[0.040; 0.078]	2.0%
Mattace-Raso, 2020	Netherlands	123	39	0.317	[0.236; 0.407]	2.0%
Mendes, 2021	Switzerland	235	48	0.204	[0.155; 0.262]	2.0%
Morandi, 2022	Italy, Spain	158	37	0.234	[0.171; 0.308]	2.0%
Myrstad, 2020	Norway	66	11	0.167	[0.086; 0.279]	1.7%
Pandurangan, 2021	India	169	3	0.018	[0.004; 0.051]	1.2%
Parrotta, 2023	Italy	337	39	0.116	[0.084; 0.155]	2.0%
Pilotto, 2021	Italy	147	24	0.163	[0.107; 0.233]	1.9%
Poco, 2021	Brazil	711	98	0.138	[0.113; 0.165]	2.1%
Poloni, 2020	Italy	57	21	0.368	[0.244; 0.507]	1.8%
Rawle (1), 2020	UK	70	22	0.314	[0.209; 0.436]	1.8%
Rawle (2), 2020	UK	64	33	0.516	[0.387; 0.642]	1.9%
Rebora, 2021	Italy	516	73	0.141	[0.113; 0.175]	2.1%
Romero-Sanchez, 2020	Spain	841	69	0.082	[0.064; 0.103]	2.1%
Roxby, 2020	USA	80	3	0.037	[0.008; 0.106]	1.2%
Rutten, 2020	Netherlands	1538	372	0.242	[0.221; 0.264]	2.1%
Sacco, 2020	France	41	3	0.073	[0.015; 0.199]	1.1%
Shi, 2020	USA	146	27	0.185	[0.126; 0.258]	1.9%
Steinmeyer, 2020	France	94	30	0.319	[0.227; 0.423]	1.9%
Strang (1), 2020	Sweden	1903	423	0.222	[0.204; 0.242]	2.1%
Strang (2), 2020	Sweden	202	63	0.312	[0.249; 0.381]	2.0%
Trevisan, 2021	Italy	981	89	0.091	[0.073; 0.110]	2.1%
Vena, 2020	Italy	317	29	0.091	[0.062; 0.129]	2.0%
Vrillon, 2020	France	76	54	0.711	[0.595; 0.809]	1.9%
Wong (1), 2022	Canada	927	497	0.536	[0.503; 0.569]	2.1%
Wong (2), 2022	Canada	115	17	0.148	[0.089; 0.226]	1.8%
Zazzara (1), 2020	UK	210	53	0.252	[0.195; 0.317]	2.0%
Zazzara (2), 2020	UK	238	84	0.353	[0.292; 0.417]	2.1%
Zerah, 2021	France	821	205	0.250	[0.220; 0.281]	2.1%
Random effects model				**0.206**	**[0.178; 0.238]**	**100.0%**

Heterogeneity: I^2 = 96%, τ^2 = 0.4077, p < 0.01

0 0.2 0.4 0.6 0.8 1

prevalence



First Author, Year	Country	Patients with COVID-19, n	Number of patients with delirium, n	Proportion	95%-CI	Weight
Adiguzel , 2022	Turkey	282	31	0.110	[0.076; 0.152]	3.7%
Alderman, 2020	UK	61	34	0.557	[0.424; 0.685]	3.6%
Benussi, 2020	Italy	56	15	0.268	[0.158; 0.403]	3.5%
D'ardes, 2021	Italy	56	14	0.250	[0.144; 0.384]	3.5%
De Smet, 2020	Belgium	81	34	0.420	[0.311; 0.535]	3.6%
Di Giorgio, 2022	Italy	214	26	0.121	[0.081; 0.173]	3.7%
Fan, 2020	China	86	11	0.128	[0.066; 0.217]	3.5%
Fernández-Jiménez, 2021	Spain	1785	225	0.126	[0.111; 0.142]	3.8%
Forget, 2021	Canada	127	9	0.071	[0.033; 0.130]	3.5%
Garcez, 2020	Brazil	707	234	0.331	[0.296; 0.367]	3.8%
GeMRC, 2021	UK/other	5711	439	0.077	[0.070; 0.084]	3.8%
Gholi, 2022	Iran	310	217	0.700	[0.646; 0.750]	3.7%
Heath, 2020	UK	31	24	0.774	[0.589; 0.904]	3.3%
Jäckel, 2020	Germany	20	13	0.650	[0.408; 0.846]	3.3%
Kandori, 2020	Japan	6264	158	0.025	[0.021; 0.029]	3.8%
Kotfis, 2021	Poland	201	39	0.194	[0.142; 0.256]	3.7%
Kremer, 2020	France	64	34	0.531	[0.402; 0.657]	3.6%
Kroon, 2022	Netherland	412	82	0.199	[0.162; 0.241]	3.7%
Lombardi, 2020	Italy	614	16	0.026	[0.015; 0.042]	3.6%
Marengoni, 2020	Italy	91	24	0.264	[0.177; 0.367]	3.6%
Mattace-Raso, 2020	Netherlands	123	8	0.065	[0.028; 0.124]	3.4%
Patel, 2020	USA	35	1	0.029	[0.001; 0.149]	2.2%
Pisaturo, 2021	Italy	69	15	0.217	[0.127; 0.333]	3.6%
Shi, 2020	USA	146	83	0.568	[0.484; 0.650]	3.7%
Steinmeyer, 2020	France	94	11	0.117	[0.060; 0.200]	3.5%
Ticinesi, 2020	Italy	852	94	0.110	[0.090; 0.133]	3.7%
Wong (1), 2022	Canada	927	201	0.217	[0.191; 0.245]	3.8%
Zerah, 2021	France	821	330	0.402	[0.368; 0.436]	3.8%
Random effects model				**0.213**	**[0.147; 0.299]**	**100.0%**

Heterogeneity: I^2 = 99%, τ^2 = 1.4209, p = 0

0 0.2 0.4 0.6 0.8 1

incidence

PREVALENCE 20.6% [95% CI: 17.8-23.8%]

49 studies

INCIDENCE 21.3% [95% CI: 14.7-30%]

28 studies

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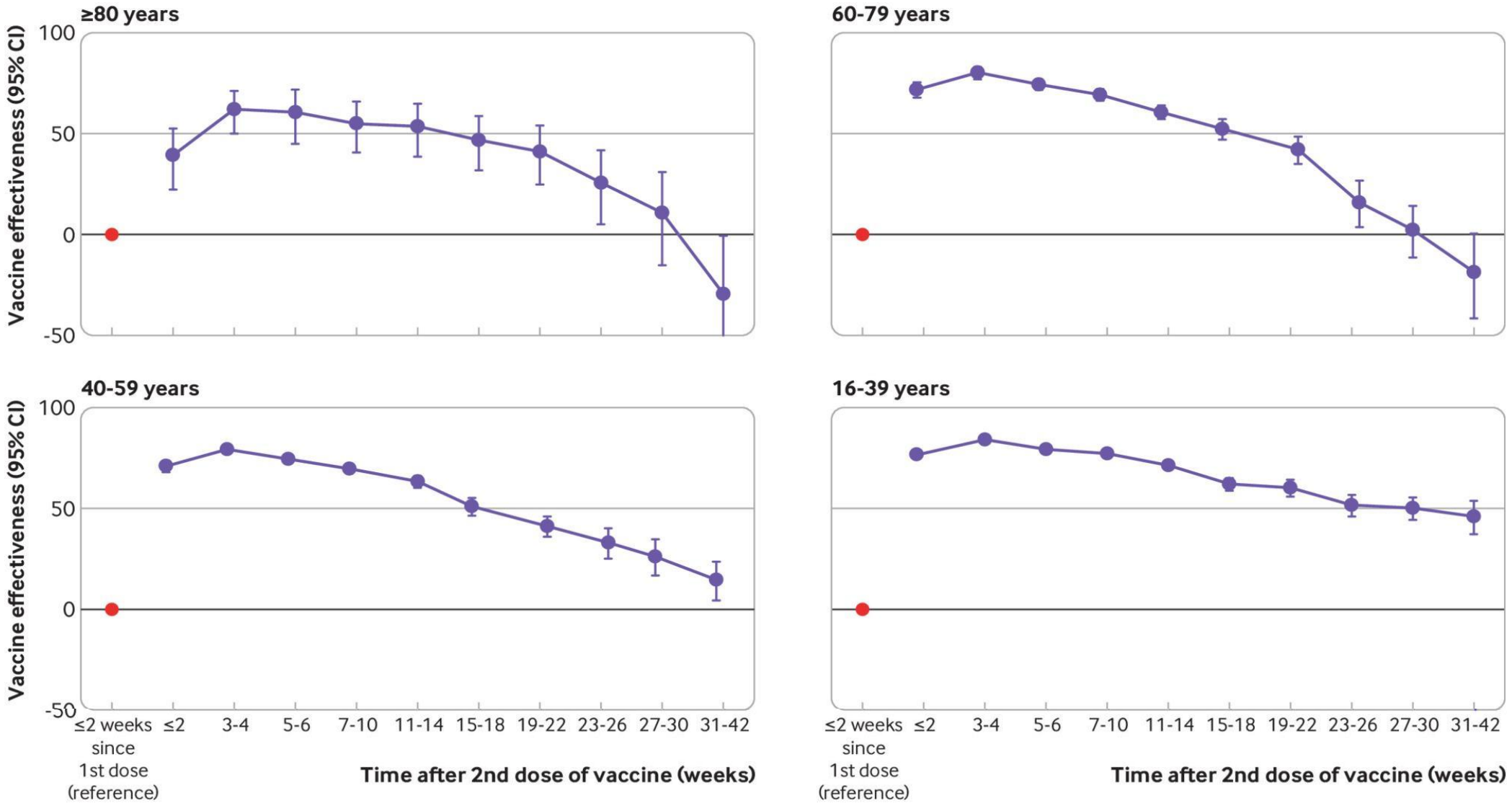
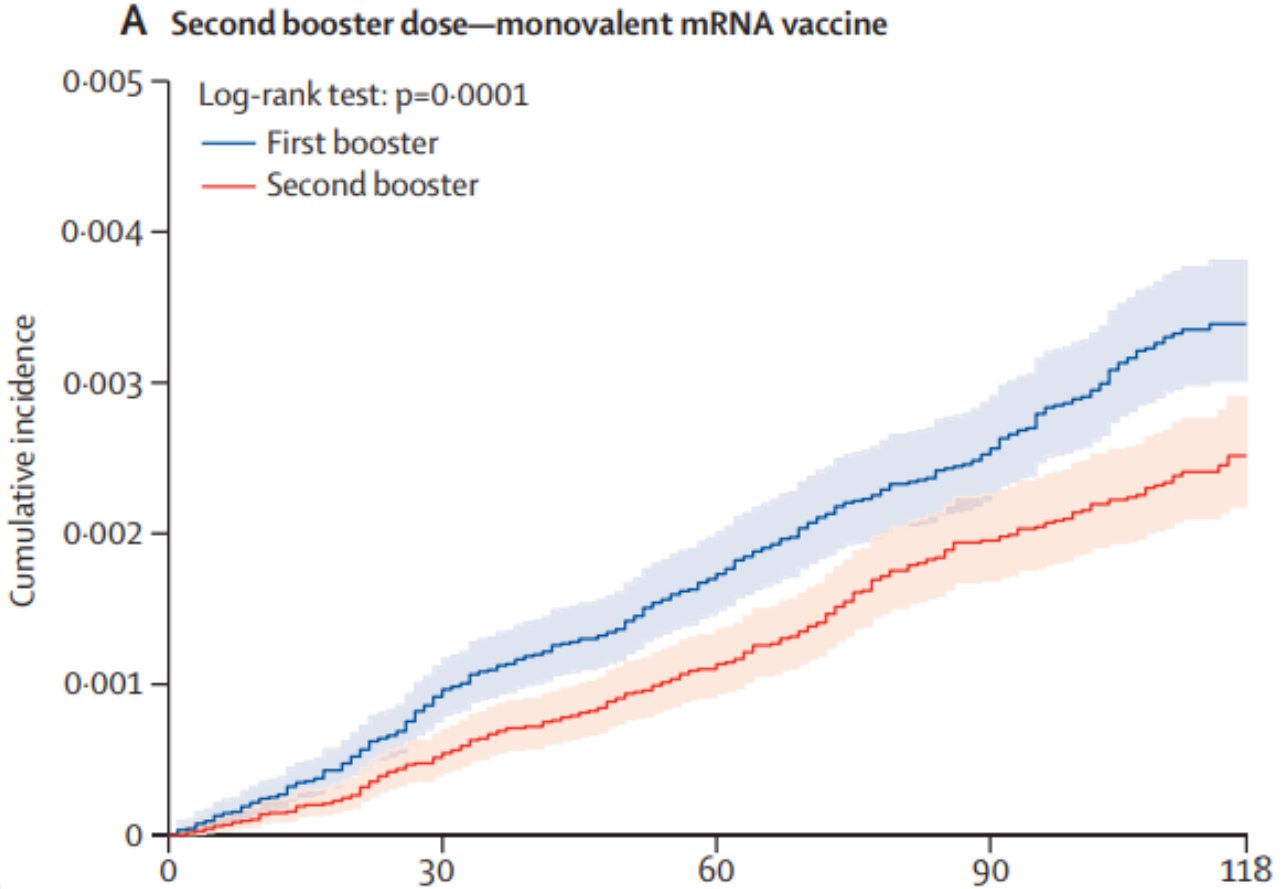
Effectiveness of mRNA vaccines against severe covid-19 during the delta phase



Fabiani et al BMJ 2022

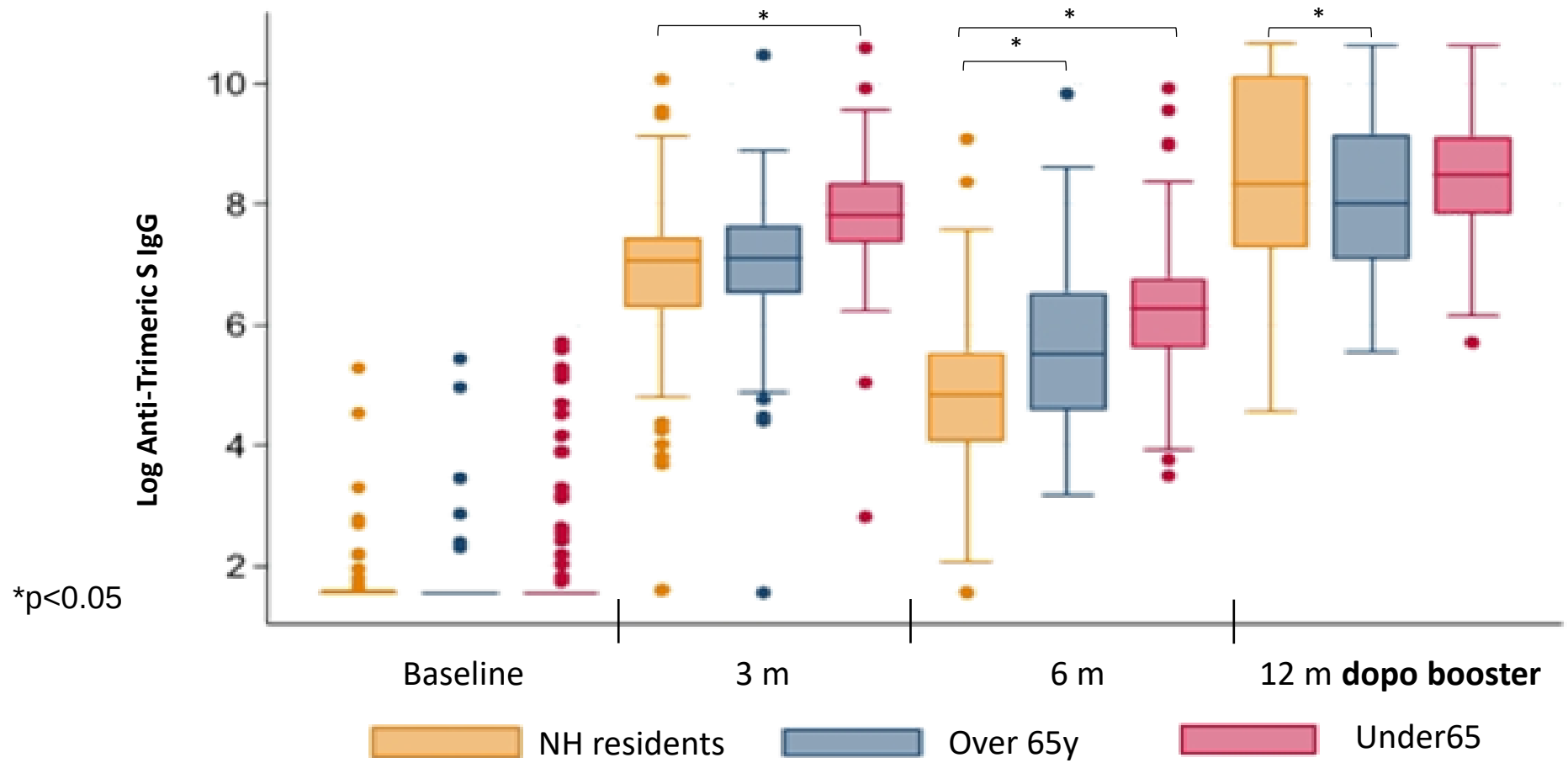


Number at risk (number of severe COVID-19 cases)					
First booster	116 822 (101)	102 748 (74)	87 537 (68)	74 836 (56)	4156
Second booster	116 822 (57)	104 179 (57)	89 850 (72)	77 569 (32)	4336

Cumulative incidence of severe COVID-19 by booster group in persons aged 60 or older

Mateo-Urdiales et al. Lancet Infective Dis 2023

Studio Gerovax – Risposta anticorpale vaccino



*p<0.05

Effectiveness against severe COVID-19 of a second booster dose of mRNA vaccine relative to a first booster dose

	First booster			Second booster			rVE (95% CI)
	Number of events	Person-days	Rate per 100 000 person-days	Number of events	Person-days	Rate per 100 000 person-days	
60–79 years of age (n=907 326 matched pairs)							
Overall (14–118 days)*	644	36 686 991	1·76	302	37 020 456	0·82	53·6% (46·8 to 59·5)
14–30 days	217	13 307 762	1·63	72	13 341 810	0·54	66·9% (56·8 to 74·7)
30–60 days	313	16 704 779	1·87	156	16 768 159	0·93	50·4% (39·8 to 59·0)
60–118 days	112	6 410 754	1·75	67	6 419 257	1·04	40·3% (19·2 to 55·9)
≥80 years of age (n=283 430 matched pairs)							
Overall (14–118 days)*	829	11 166 711	7·42	432	11 250 241	3·84	48·3% (41·9 to 54·0)
14–30 days	311	4 129 319	7·53	136	4 138 064	3·29	56·3% (46·6 to 64·3)
30–60 days	396	5 124 504	7·73	210	5 141 728	4·08	47·2% (37·5 to 55·3)
60–118 days	116	1 811 577	6·40	82	1 812 303	4·52	29·4% (6·3 to 46·8)

rVE=relative vaccine effectiveness. *The analysis by time interval includes only matched pairs still at risk at the start of each of them.

Mateo-Urdiales et al. Lancet Infective Dis 2023

Frequency of adverse events after vaccination in NH

	First dose	Second dose	Third dose
Fever (%)	2.9	2.7	2.4
Muscle weakness (%)	2.0	1.2	0.9
Muscle joints pain (%)	3.9	3.0	1.9
Pain swelling at the injection site (%)	9.9	7.7	3.1
Headache (%)	0.8	1.2	0.8
Swollen lymph nodes (%)	0.3	0.0	0.3
Chills (%)	0.5	0.6	0.1
Difficulty breathing (%)	0.7	0.3	0.3
Insomnia (%)	1.5	1.3	0.5
Sneezing (%)	0.1	0.0	0.2
Fast Heartbeat (%)	0.1	0.3	0.1
Cough (%)	0.6	0.4	0.6
Anorexia (%)	1.0	1.1	0.5
Raynaud's effect (%)	0.0	0.0	0
Nausea or vomiting (%)	0.8	1.2	0.6
Delirium (%)	1.6	0.7	1.2
Diarrhea (%)	1.8	1.1	1.3
Increased blood pressure (%)	0.4	0.2	0.3
Weakness (%)	2.8	2.8	1.9
Cutaneous rash (%)	0.2	0.1	0.2
Confusion (%)	1.4	0.8	0.4
Acute peripheral Bell palsy (%)	0.0	0.0	0
Dizziness (%)	0.3	0.4	0.1
Myelitis transversa (%)	0.0	0.0	0
Guillain Barrè syndrome (%)	0.0	0.0	0
Anaphylaxis (%)	0.0	0.0	0

Malara et al. Front Public Health 2023

Frequency of adverse events after vaccination in NH

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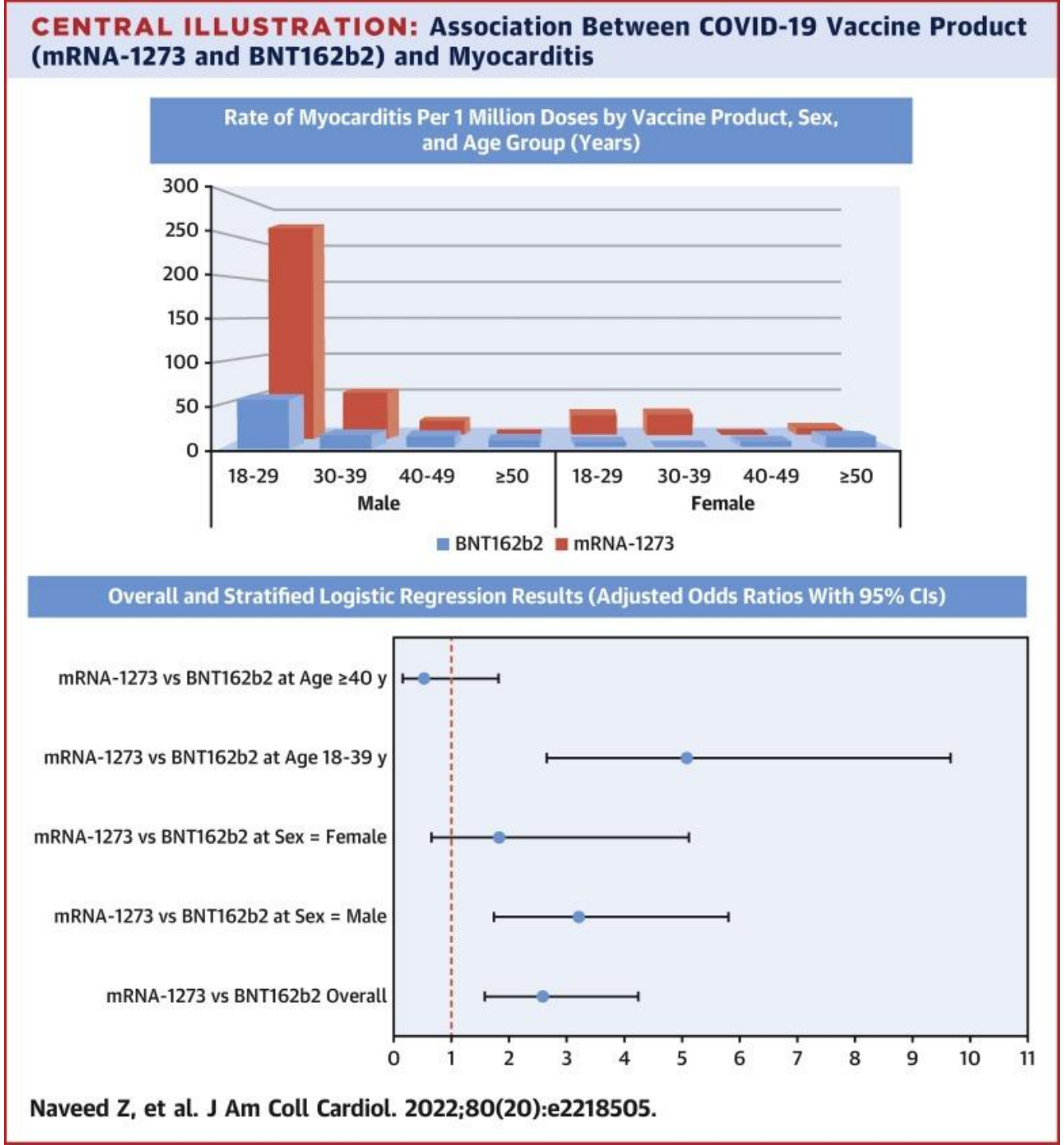
Guillain Barrè syndrome (%)	**0.0**	**0.0**	0
Anaphylaxis (%)	**0.0**	**0.0**	0

Malara et al. Front Public Health 2023



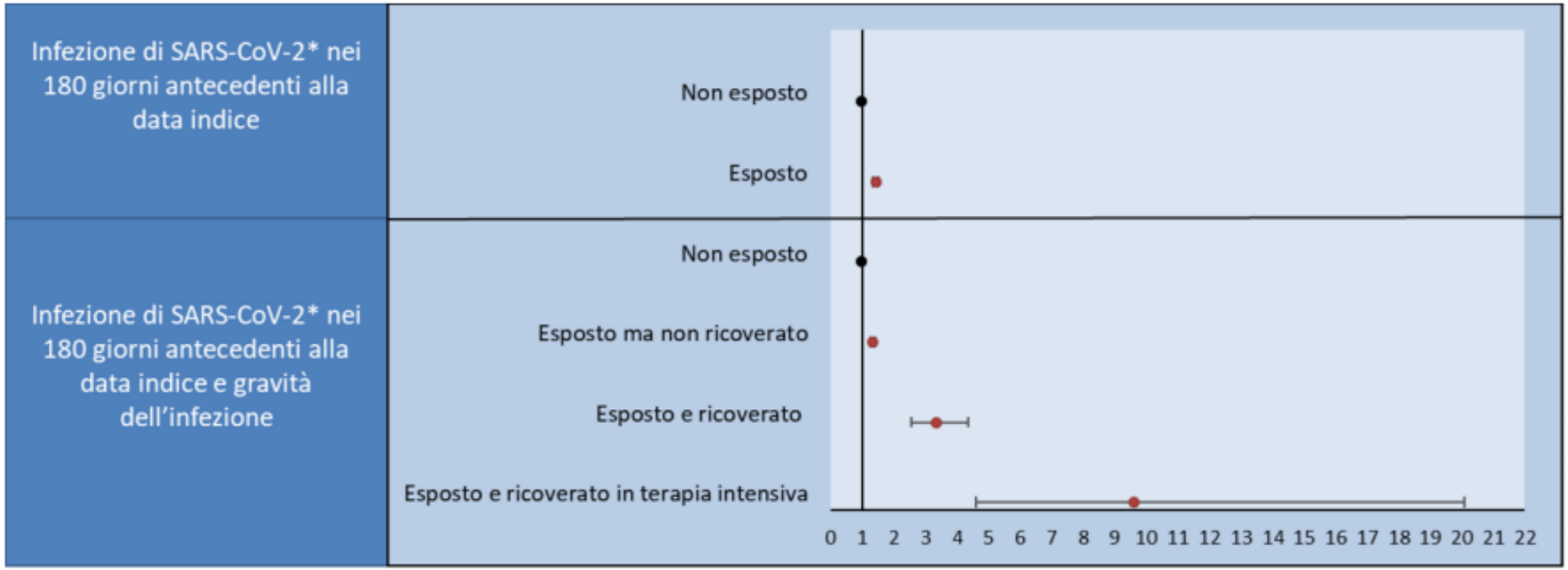
The risk of hospital admission or death from myocarditis is greater after SARS- CoV2 infection than COVID-19 vaccination …, the risk of myocarditis after vaccination is higher in younger men, particularly after a second dose of the mRNA-1273 vaccine

Patone et al. Circulation 2022

RISULTATI - Long COVID e UTILIZZO DI FARMACI ANTIDEPRESSIVI in FRIULI VENEZIA GIULIA

Odds ratios (OR) e intervalli di confidenza del 95% (IC 95%) delle regressioni logistiche condizionate multiple che studiano l'associazione tra la prima prescrizione di antidepressivo e una precedente esposizione all'infezione di SARS-CoV-2 nei 180 giorni antecedenti la data indice. L'esposizione viene valutata come (1) esposto/non esposto e (2) livello di gravità dell'infezione.

I modelli sono aggiustati per provincia di residenza, Multisource Comorbidity Score e residenza in una struttura per anziani alla data indice.



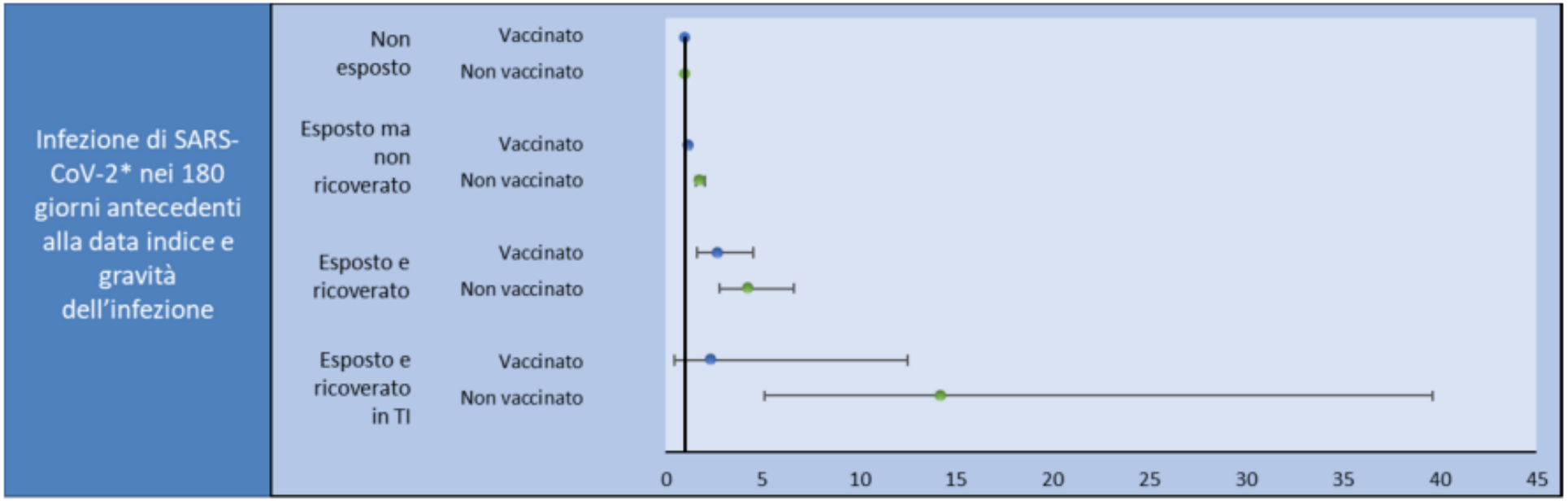
Variabile	Categorie	OR	IC 95%
Infezione di SARS-CoV-2 nei 180 giorni precedenti la data indice:	Non esposto	1.00	
	Esposto	1.42	(1.34-1.50)
Infezione di SARS-CoV-2 nei 180 giorni precedenti e gravità dell'infezione:	Non esposto	1.00	
	Esposto ma non ricoverato	1.32	(1.25-1.40)
	Esposto e ricoverato in area medica	3.34	(2.55-4.36)
	Esposto e ricoverato in terapia intensiva	9.60	(4.59-20.08)

Castriotta L, Onder G et al. In preparation

RISULTATI - Long COVID e UTILIZZO DI FARMACI ANTIDEPRESSIVI in FRIULI VENEZIA GIULIA

Odds ratios (OR) e intervalli di confidenza del 95% (IC 95%) delle regressioni logistiche condizionate multiple che studiano l'associazione tra la prima assunzione di antidepressivo ed una precedente esposizione all'infezione di SARS-CoV-2 nei 180 giorni antecedenti la data indice, tenendo conto anche del livello di gravità. Le analisi sono stratificate per stato vaccinale.

I modelli sono aggiustati per provincia di residenza, Multisource Comorbidity Score e residenza in una struttura per anziani alla data indice.



VACCINATI

Variabile	Categorie	OR	IC 95%
Infezione di SARS-CoV-2 nei 180 giorni precedenti e gravità dell'infezione:	Non esposto	1	
	Esposto ma non ricoverato	1.16	(1.07-1.26)
	Esposto e ricoverato in area medica	2.69	(1.60-4.54)
	Esposto e ricoverato in TI	2.34	(0.44-12.49)

NON VACCINATI

Variabile	Categorie	OR	IC 95%
Infezione di SARS-CoV-2 nei 180 giorni precedenti e gravità dell'infezione:	Non esposto	1	
	Esposto ma non ricoverato	1.75	(1.54-2.00)
	Esposto e ricoverato in area medica	4.29	(2.78-6.62)
	Esposto e ricoverato in TI	14.21	(5.10-39.60)

TI - Terapia Intensiva

Castriotta L, Onder G et al. In preparation

Who should be vaccinated

The high-priority group are:

Health workers are also considered a priority group due to their frequent interaction with patients…

They include **oldest and older adults** with multiple significant comorbidities; younger adults with significant comorbidities (e.g., diabetes and heart disease)…

The high-priority group should be prioritized for the primary series vaccines as well as first and additional booster doses.

World Health Organization

Agenda

- COVID-19 oggi
- COVID-19 domani
- Chi è a rischio?
- Vaccinazione
- Trattamento antivirale

Treating COVID-19

Most people with COVID-19 have mild illness and can recover at home. You can treat symptoms with over-the-counter medicines, such as acetaminophen or ibuprofen, to help feel better.

If you have COVID-19 and are more likely to get very sick from COVID-19, treatments are available that can reduce your chances of being hospitalized or dying from the disease. Medications to treat COVID-19 must be prescribed by a healthcare provider or pharmacist and started within 5–7 days after symptoms appear. Contact a healthcare provider right away to determine if you are eligible for treatment, even if your symptoms are currently mild.

Don't delay: Treatment must be started within 5–7 days of when you first develop symptoms.

People who are more likely to get very sick include

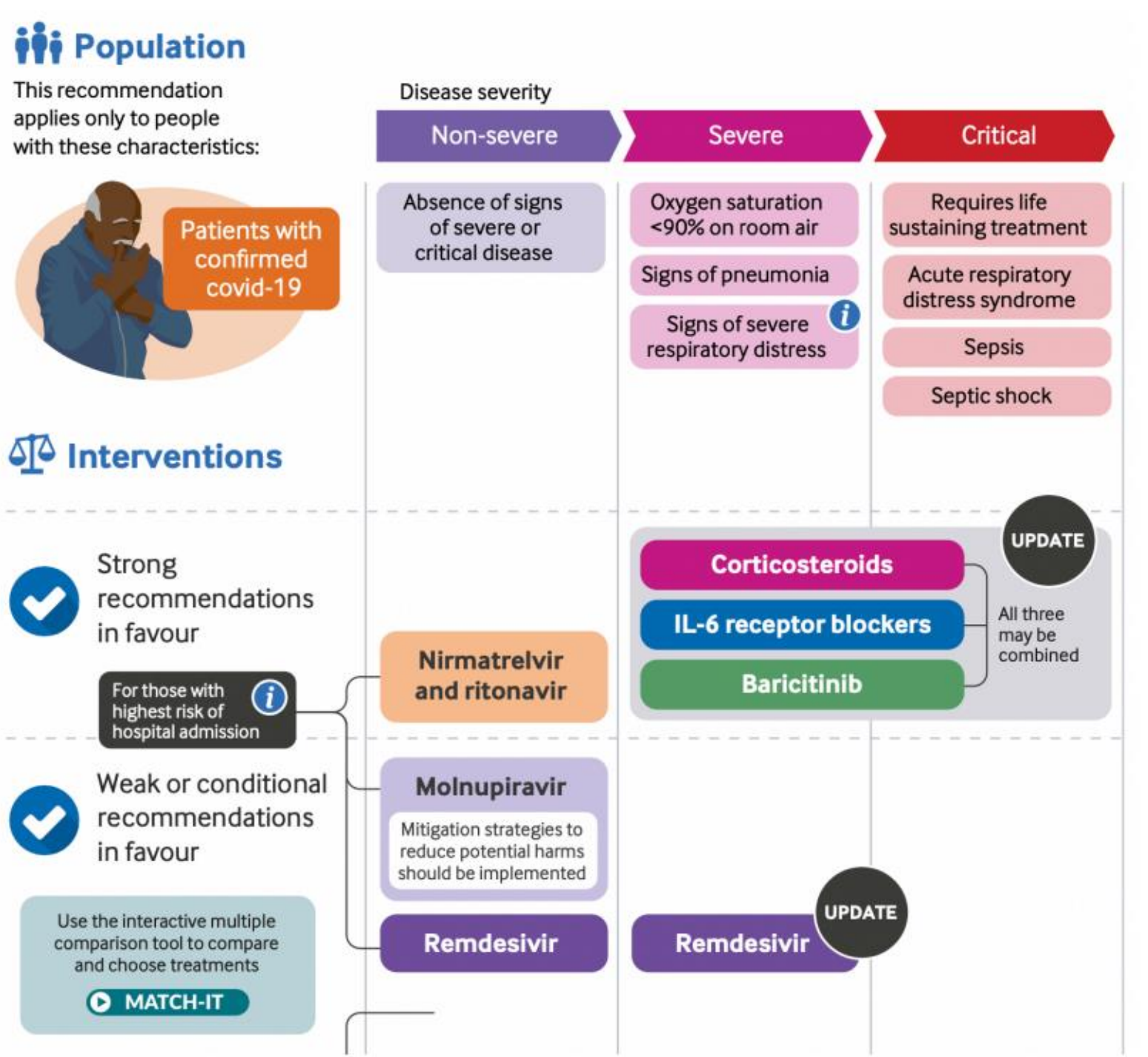
- older adults (ages 50 years or older, with risk increasing with age),
- people who are unvaccinated or are not up to date on their COVID-19 vaccinations,
- and people with certain medical conditions, such as chronic lung disease, heart disease, or a weakened immune system.

CDC –cdc.gov

Therapeutics and COVID-19

LIVING GUIDELINE

World Health Organization



Treatment	Who (Among persons who are at high risk of getting sick)	When	How
Nirmatrelvir with Ritonavir (Paxlovid) *Antiviral*	Adults; children ages 12 years and older	Start as soon as possible; must begin within 5 days of when symptoms start	Taken at home by mouth (orally)
Remdesivir (Veklury) *Antiviral*	Adults and children	Start as soon as possible; must begin within 7 days of when symptoms start	Intravenous (IV) infusions at a healthcare facility for 3 consecutive days
Molnupiravir (Lagevrio) *Antiviral*	Adults	Start as soon as possible; must begin within 5 days of when symptoms start	Taken at home by mouth (orally)

CDC –cdc.gov

AIFA – gestione domiciliare COVID-19 **Antivirali**

https://www.aifa.gov.it/documents/20142/1616529/IT_Raccomandazioni_AIFA_gestione_domiciliare_COVID-19_Vers10_10.03.2023.pdf

FARMACI DA UTILIZZARE SOLO IN SPECIFICHE FASI DELLA MALATTIA	
Antivirali	Sono attualmente autorizzati da EMA due antivirali (remdesivir, nirmatrelvir/ritonavir) per il trattamento di soggetti adulti con COVID-19 che non necessitano di ossigenoterapia supplementare e che sono a maggior rischio di progressione verso forme severe di COVID-19. Il paziente **non deve essere ospedalizzato** a causa di COVID-19, deve presentare una forma di **grado lieve-moderato** e almeno uno fra i seguenti fattori di rischio associati all'evoluzione in malattia severa: • Patologia oncologica/oncoematologica in fase attiva • Insufficienza renale cronica • Broncopneuomopatia cronica ostruttiva e/o altra malattia respiratoria cronica (ad es. soggetti affetti da asma, fibrosi polmonare o che necessitano di ossigenoterapia per ragioni differenti da SARS-CoV-2) • Immunodeficienza primaria o acquisita • Obesità (BMI ≥30) • Malattia cardio-cerebrovascolare (scompenso cardiaco, malattia coronarica, cardiomiopatia, ipertensione con concomitante danno d'organo, ictus) • Diabete mellito non compensato (HbA1c>9.0% 75 mmol/mol) o con complicanze croniche • Età >65 anni • Epatopatia cronica • Emoglobinopatie • Patologie del neurosviluppo e patologie neurodegenerative
Remdesivir – Veklury ® informazioni per gli operatori sanitari https://www.aifa.gov.it/aggiornamento-sui-farmaci-utilizzabili-per-il-trattamento-della-malattia-covid19	
Nirmatrelvir/ritonavir – Paxlovid ® Informazioni per gli operatori sanitari https://www.ema.europa.eu/en/medicines/human/summaries-opinion/paxlovid	

Remdesivir

- Primo farmaco ad azione antivirale ad aver ricevuto autorizzazione, per il "trattamento COVID-19, in pazienti adulti ed adolescenti **con polmonite che richiede ossigenoterapia supplementare**".
- Dal 30 dicembre 2021, è indicato anche per il trattamento di COVID-19 **negli adulti non ospedalizzati per COVID-19 e non in ossigeno-terapia con insorgenza di sintomi da non oltre 7 giorni e in presenza di condizioni cliniche predisponenti** che rappresentino dei fattori di rischio per lo sviluppo di COVID-19 grave.

Fonte: AIFA

Remdesivir

Il trattamento deve essere entro 7 giorni dalla comparsa dei sintomi.
Il dosaggio raccomandato di remdesivir negli adulti è:
- giorno 1: singola dose di carico di remdesivir 200 mg somministrata tramite infusione endovenosa
- dal giorno 2 in poi: 100 mg somministrati una volta al giorno tramite infusione endovenosa.

La durata totale del trattamento deve essere di 3 giorni.

Fonte: AIFA

Nirmatrelvir/Ritonavir

Paxlovid® deve essere somministrato non oltre 5 giorni dall'insorgenza dei sintomi.
Il trattamento consiste nell'assunzione di due compresse di nirmatrelvir e una compressa di ritonavir, due volte al giorno, per 5 giorni.
Duplice modalità di prescrizione:
- da parte dello specialista del centro COVID mediante registro web AIFA e distribuzione diretta da parte delle Aziende Sanitarie
- da parte del MMG

Fonte: AIFA

AIFA
AGENZIA ITALIANA DEL FARMACO

Domande e risposte su Paxlovid per gli operatori sanitari

In quali casi è indicato?

È indicato per il trattamento di pazienti adulti (età ⩾18 anni) con infezione confermata da SARS-CoV-2 che:

a) **non necessitano di ossigenoterapia;**

b) **sono a elevato rischio di progressione a COVID-19 severa** (ad esempio i pazienti affetti da patologie oncologiche, malattie cardiocerebrovascolari, diabete mellito non compensato, broncopneumopatia cronica e obesità grave).

Lagevrio (molnupiravir)

Sospeso dall'AIFA a seguito del parere negativo formulato da EMA in data 24/02/2023 per la mancata dimostrazione di un beneficio clinico in termini di riduzione della mortalità e dei ricoveri ospedalieri.

Fonte: AIFA

MATCH-IT

Non-severe covid-19 at highest risk of hospitalisation

Among a 1000 people

	Standard care	Nirmatrelvir	Remdesivir	Molnupiravir
Mortality 90 days	6 per 1000	6 fewer	2 fewer	6 fewer
	certainty →	⊕⊕◯◯	⊕⊕◯◯	⊕⊕◯◯
Mechanical ventilation 90 days	8 per 1000	No data	5 fewer	No difference
	certainty →		⊕◯◯◯	⊕◯◯◯
Admission to hospital 28 days	100 per 1000	84 fewer	73 fewer	43 fewer
	certainty →	⊕⊕⊕◯	⊕⊕⊕◯	⊕⊕⊕◯
Time to symptom resolution	9 days	No data	1.8 fewer	3.4 fewer
	certainty →		⊕◯◯◯	⊕⊕⊕◯
Adverse effects leading to drug discontinuation 28 days	0 per 1000	No difference	9 more	No difference
	certainty →	⊕⊕⊕⊕	⊕⊕⊕◯	⊕⊕⊕⊕
Practical issues	N/A	Oral twice daily for 5 days, administered early from symptom onset. Numerous potential drug interactions.	IV infusion daily for 3 days, administered early from symptom onset with monitoring (feasibility challenges).	Oral twice daily for 5 days, administered early from symptom onset. Risk mitigation strategies warranted.

Remdesivir

- Remdesivir can cause gastrointestinal symptoms (e.g., nausea), elevated transaminase levels, an increase in prothrombin time
- Before starting patients on remdesivir, perform **liver function** and prothrombin time tests as clinically appropriate and repeating these tests during treatment as clinically indicated.
- It should be discontinued if increases in ALT levels and signs or symptoms of liver inflammation are observed.

Ritonavir- Nirmatrelvir (Paxlovid)

- The most common adverse effects are dysgeusia, diarrhea, hypertension, and myalgia.
- Limited clinical experience with the use of ritonavir-boosted nirmatrelvir in patients with eGFR of <30 mL/min. Based on limited data, some groups have proposed dosing adjustments for ritonavir-boosted nirmatrelvir in these patients.
- Not recommended for patients with known or suspected severe hepatic impairment (i.e., Child-Pugh Class C).

Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications

Prescribe Alternative COVID-19 Therapy

For these medications, management strategies are not possible or feasible, or the risks outweigh the potential benefits.

Anticonvulsants

- Carbamazepine
- Phenobarbital
- Phenytoin
- Primidone

Anti-Infectives

- Glecaprevir/pibrentasvir
- Rifampin
- Rifapentine

Immunosuppressants

- Voclosporin

Cardiovascular

- Amiodarone
- Clopidogrel[a,b]
- Disopyramide
- Dofetilide
- Dronedarone
- Eplerenone
- Flecainide
- Ivabradine
- Propafenone
- Quinidine

Neuropsychiatric

- Clozapine
- Lurasidone
- Midazolam (PO)
- Pimozide

Pulmonary Hypertension[c]

- Sildenafil
- Tadalafil
- Vardenafil

Miscellaneous

- Bosentan
- Certain chemotherapeutic agents[d]
- Ergot derivatives
- Lumacaftor/ivacaftor
- St. John's wort
- Tolvaptan

NIH | COVID-19 Treatment Guidelines

Ritonavir, a strong cytochrome P450 (CYP) 3A4 inhibitor and a P-glycoprotein (P-gp) inhibitor. Ritonavir may also increase blood concentrations of certain concomitant medications.

Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications

Temporarily Withhold Concomitant Medication, if Clinically Appropriate

Withhold these medications during ritonavir-boosted nirmatrelvir treatment and for at least 2–3 days after treatment completion. They may need to be withheld for longer if the patient is an adult of advanced age or if the interacting medication has a long half-life. If withholding is not clinically appropriate, use an alternative concomitant medication or COVID-19 therapy.

Anticoagulants

- Rivaroxaban[e]

Anti-Infectives

- Erythromycin

BPH

- Alfuzosin
- Silodosin

Cardiovascular

- Aliskiren
- Ranolazine
- Ticagrelor[b]
- Vorapaxar

Immunosuppressants[f]

- Everolimus
- Sirolimus
- Tacrolimus

Lipid-modifiers

- Atorvastatin[g]
- Lomitapide
- Lovastatin[g]
- Rosuvastatin[g]
- Simvastatin[g]

Migraine

- Eletriptan
- Rimegepant
- Ubrogepant

Neuropsychiatric

- Daridorexant
- Lemborexant
- Suvorexant
- Triazolam[h]

Erectile Dysfunction

- Avanafil

Respiratory

- Salmeterol

Miscellaneous

- Certain chemotherapeutic agents[d]
- Colchicine[i]

NIH | COVID-19 Treatment Guidelines

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Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications

Adjust Concomitant Medication Dose and Monitor for Adverse Effects

Reduce the dose and/or extend the dosing interval of the concomitant medication. Consult the Liverpool COVID-19 Drug Interactions website or the University of Waterloo/University of Toronto drug interaction guide for specific dosing recommendations.[j] If the dose of the concomitant medication cannot be adjusted, withhold the medication (if clinically appropriate) or use an alternative concomitant medication or COVID-19 therapy.

Anticoagulants

- Apixaban
- Dabigatran
- Edoxaban

Pain

- Fentanyl
- Hydrocodone
- Oxycodone

Cardiovascular

- Amlodipine
- Cilostazol
- Digoxin
- Diltiazem
- Felodipine
- Nifedipine
- Verapamil

Neuropsychiatric

- Alprazolam[h]
- Aripiprazole
- Quetiapine
- Trazodone

NIH | COVID-19 Treatment Guidelines

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COVID-19 Drug Interactions

UNIVERSITY OF LIVERPOOL

About Us | Interaction Checkers | Prescribing Resources | Site News | Contact Us

Presentations from the 2023 Liverpool Masterclass in Antiviral Pharmacology are now available. Click here to view.

Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

Conclusioni

- COVID-19 malattia ancora importante e continuerà ad esserlo in futuro
- Anziani più a rischio
- Vaccino previene malattia efficacemente
- Antivirali per trattamento malattia negli anziani