Philipps Universität Marburg

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STANDORT MARBURG

Immunologie der COVID-19 Erkrankung

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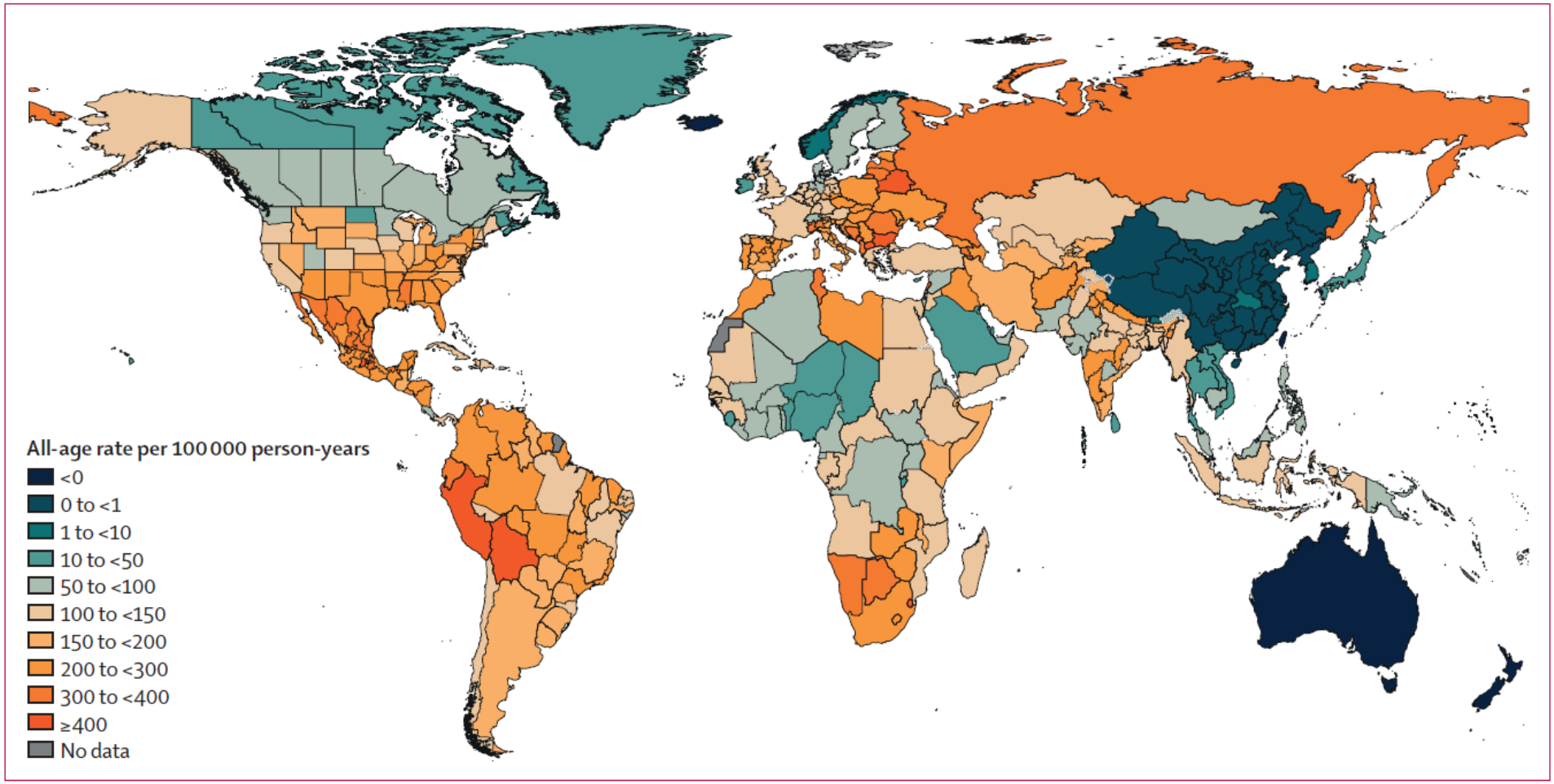
Reported deaths: 5.93 Mio, but estimation of 18.2 Mio deaths



Wang H, The Lancet, 2022

Zu Beginn der Pandemie:

- Keine SARS-CoV2 PCR
- Keine Antigen-(Schnell-)Teste
- Keine Antikörper-Tests
- Kein Impfstoff
- Keine spezifischen Medikamente
- Nicht ausreichend Masken

Clinical manifestation of COVID-19

Lungs

- Pneumonitis
- Pulmonary edema
- Dyspnea
- Hypoxemia
- ARDS

Heart

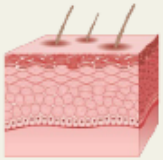
- Hypotension
- Arrhythmias
- Cardiomyopathy
- Ischemia
- Cardiogenic shock

Gastrointestinal system

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Hemorrhage

Skin

- Urticaria
- Rash
- Edema
- Vesicles



Nervous system

- Confusion, delirium
- Dizziness
- Encephalopathy
- Anosmia
- Stroke

Vascular–lymphatic system

- Cytopenia, coagulopathy
- Hyperferritinemia
- Increased CRP, D-dimer, cytokines
- Endothelial damage, hemorrhage

Liver

- Hepatomegaly
- Elevated bilirubin
- Liver failure
- Increased AST, ALT, LDH

Kidneys

- Acute kidney injury
- Proteinuria
- Hematuria
- Kidney failure

Constitutional symptoms

- Fever
- Headache
- Fatigue
- Anorexia

Rheumatologic system

- Vasculitis
- Arthritis
- Arthralgia

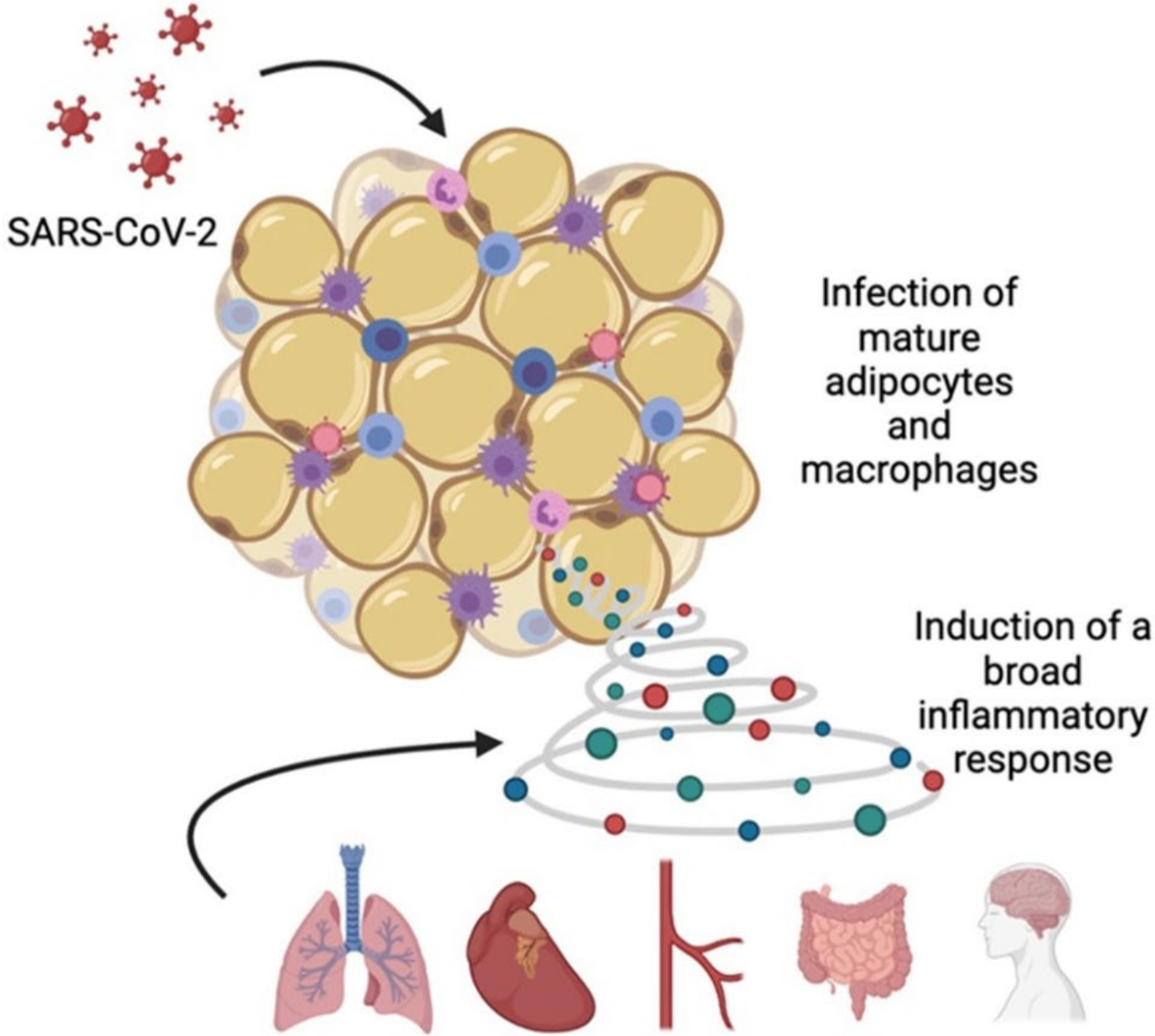
Diamond et al.,
Nature Immunology, 2022

COVID-19 and comorbidities

Characteristic	All patients (n = 548)	Nonsevere (n = 279)	Severe (n = 269)	*P* value
Underlying comorbidity				
Chronic obstructive pulmonary disease	17 of 548 (3.1%)	4 of 279 (1.4%)	13 of 269 (4.8%)	.026
Asthma	5 of 548 (0.9%)	2 of 279 (0.7%)	3 of 269 (1.1%)	.681
Tuberculosis	9 of 548 (1.6%)	5 of 279 (1.8%)	4 of 269 (1.5%)	1.000
Diabetes	83 of 548 (15.1%)	31 of 279 (11.1%)	52 of 269 (19.3%)	.009
Hypertension	166 of 548 (30.3%)	62 of 279 (22.2%)	104 of 269 (38.7%)	.000
Coronary heart disease	34 of 548 (6.2%)	6 of 279 (2.2%)	28 of 269 (10.4%)	.000
Hepatitis B	5 of 548 (0.9%)	3 of 279 (1.1%)	2 of 269 (0.7%)	1.000
Chronic kidney disease	10 of 547 (1.8%)	4 of 278 (1.4%)	6 of 269 (2.2%)	.539
Tumor	24 of 513 (4.7%)	10 of 256 (3.9%)	14 of 257 (5.5%)	.531

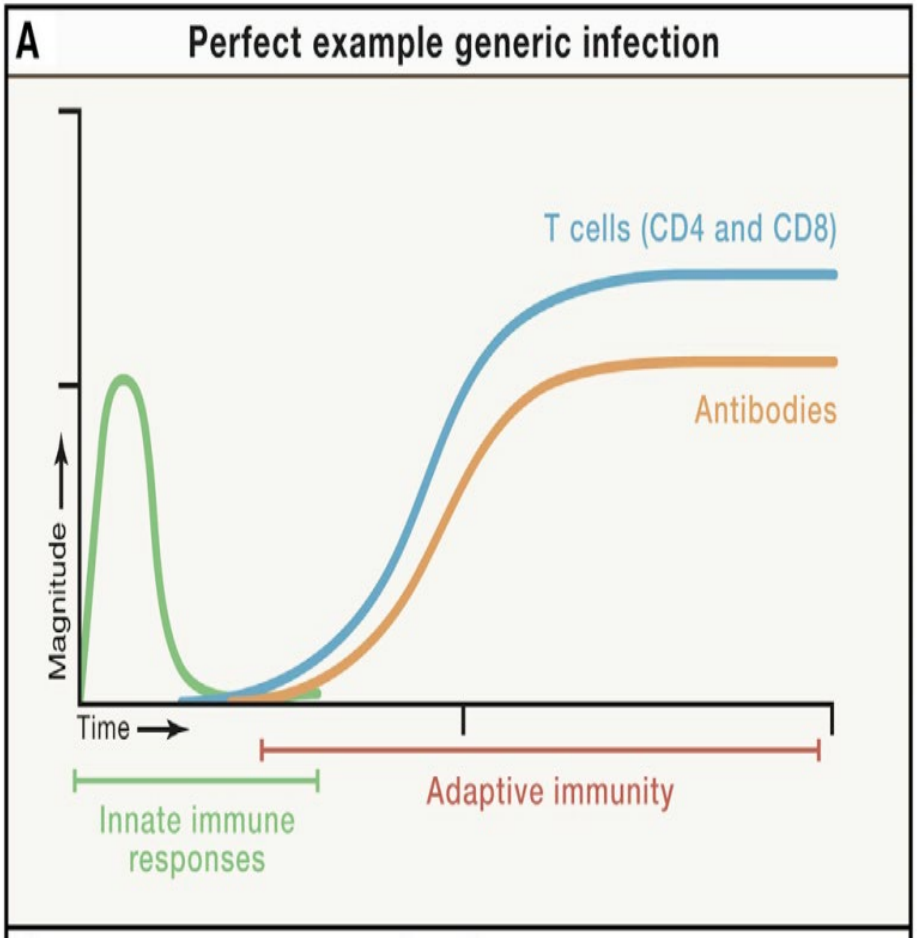
Li et al., JACI 2020

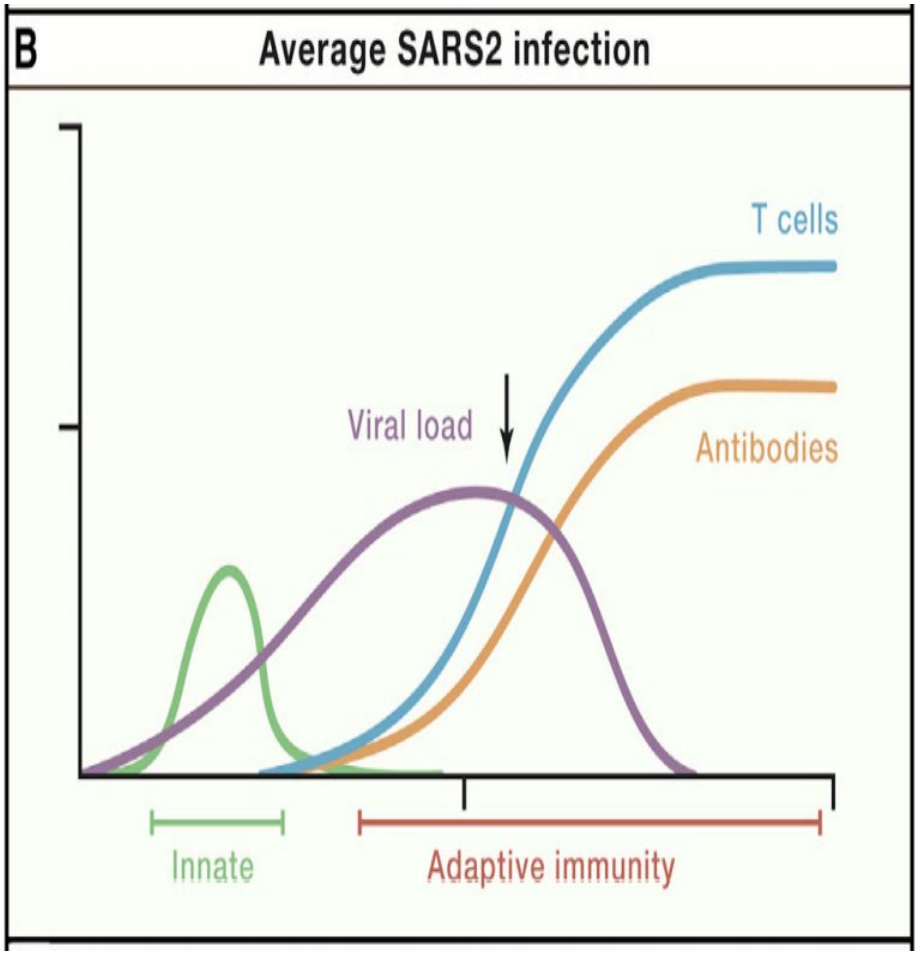
Obesity a risk factor for more severe COVID-19



Goldman B., Stanford Medicine, Photo by biorender.com, 2022

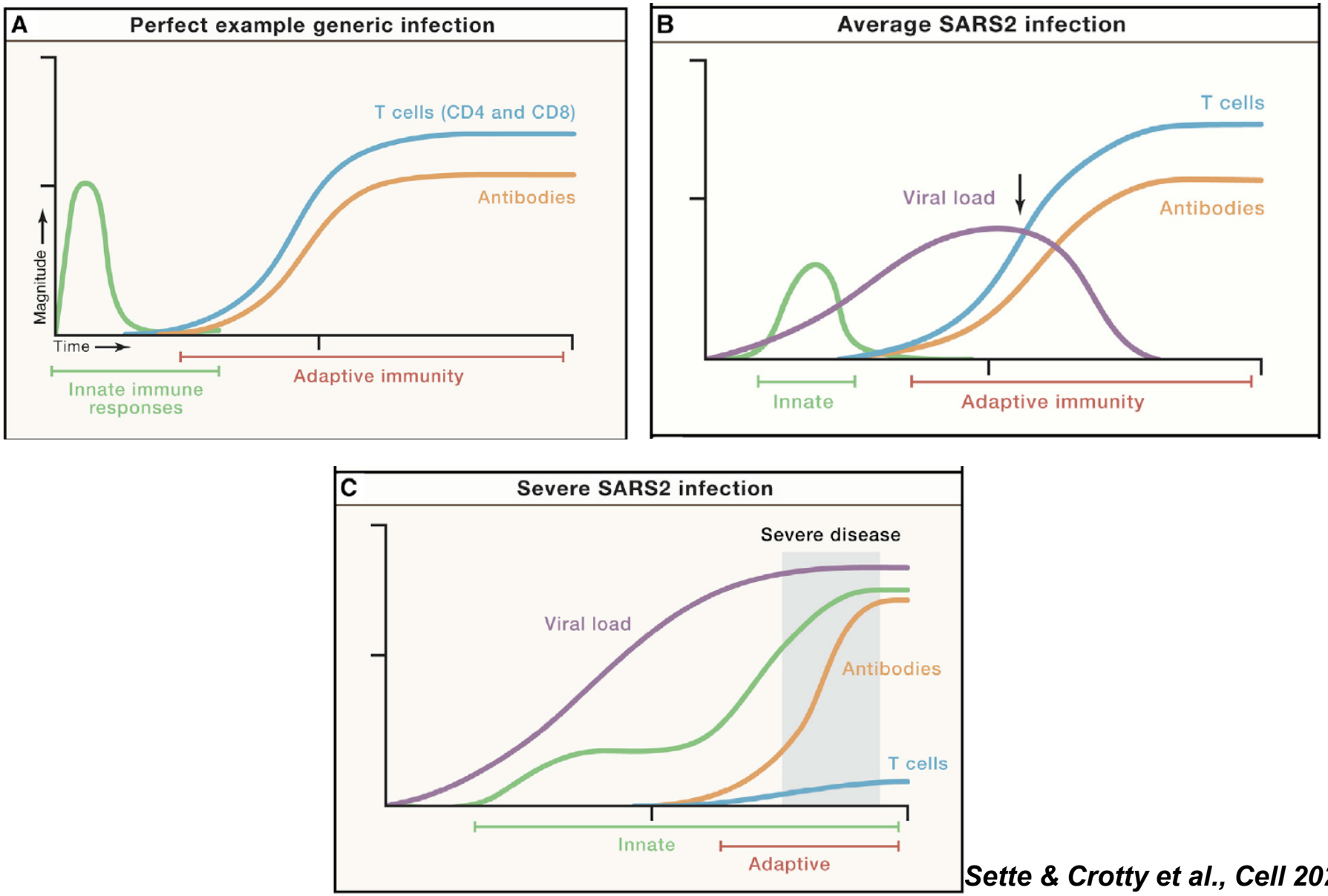
An integrated working model of COVID-19 immunology and disease severity (I)





Sette & Crotty et al., Cell 2021

An integrated working model of COVID-19 immunology and disease severity (II)



Sette & Crotty et al., Cell 2021

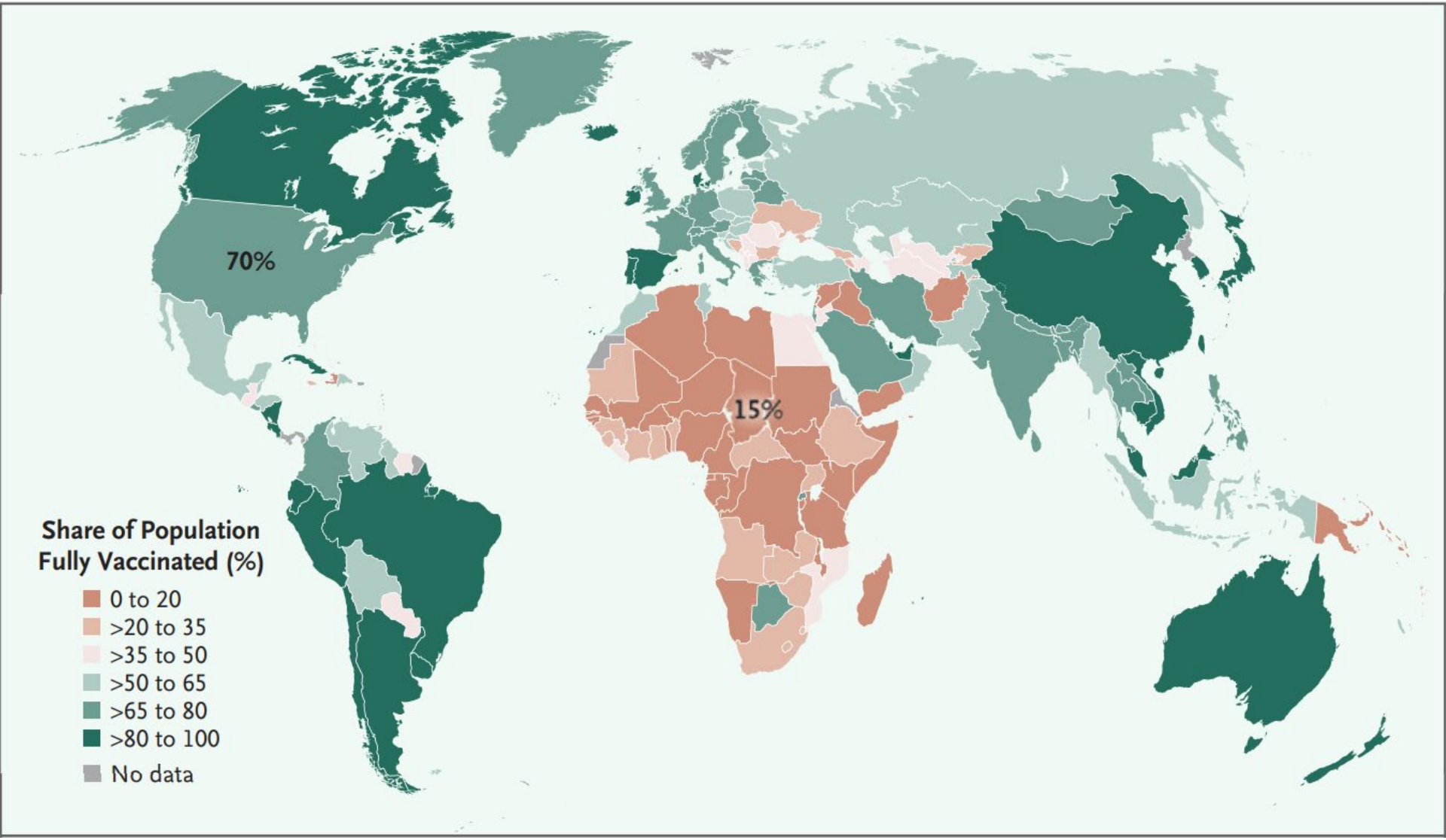
Immune responses for protection against COVID-19

Covid-19 Disease Severity →

	Asymptomatic Infection	Symptomatic Infection	Severe Disease, Hospitalization	Death
Antibodies	++++	+++	++	++
T Cells	+	++	++++	++++

Barouch, Dan H., N Engl J Med, 2022

Global COVID-19 vaccination rates (8 July 2022)



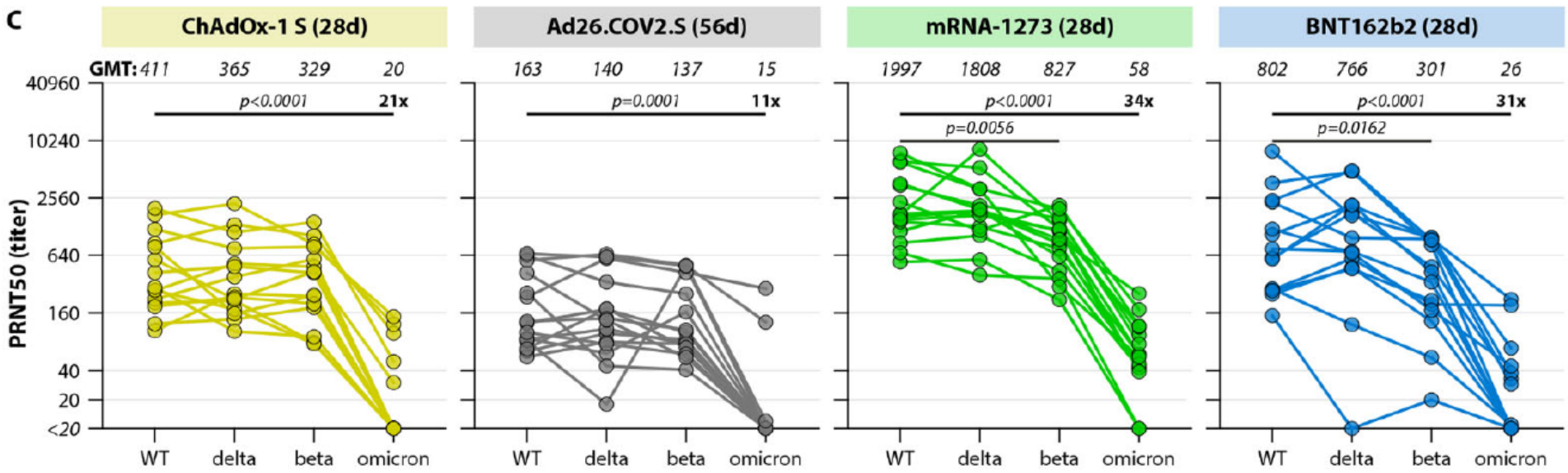
Barouch, Dan H., N Engl J Med, 2022

Protective efficacy of COVID 2019 vaccines

Vaccine (Dose)	Efficacy against Symptomatic Disease	Efficacy against Hospitalization	Efficacy against ICU Admission
	United States, Ancestral Strain*	South Africa, Omicron Variant†	
	percent	*percent*	
Pfizer BNT162b2 (two shots)	95	70	70
Moderna mRNA-1273 (two shots)	94	ND	ND
Janssen Ad26.COV2.S (two shots)	94	72	82
Janssen Ad26.COV2.S (one shot)	72	ND	ND

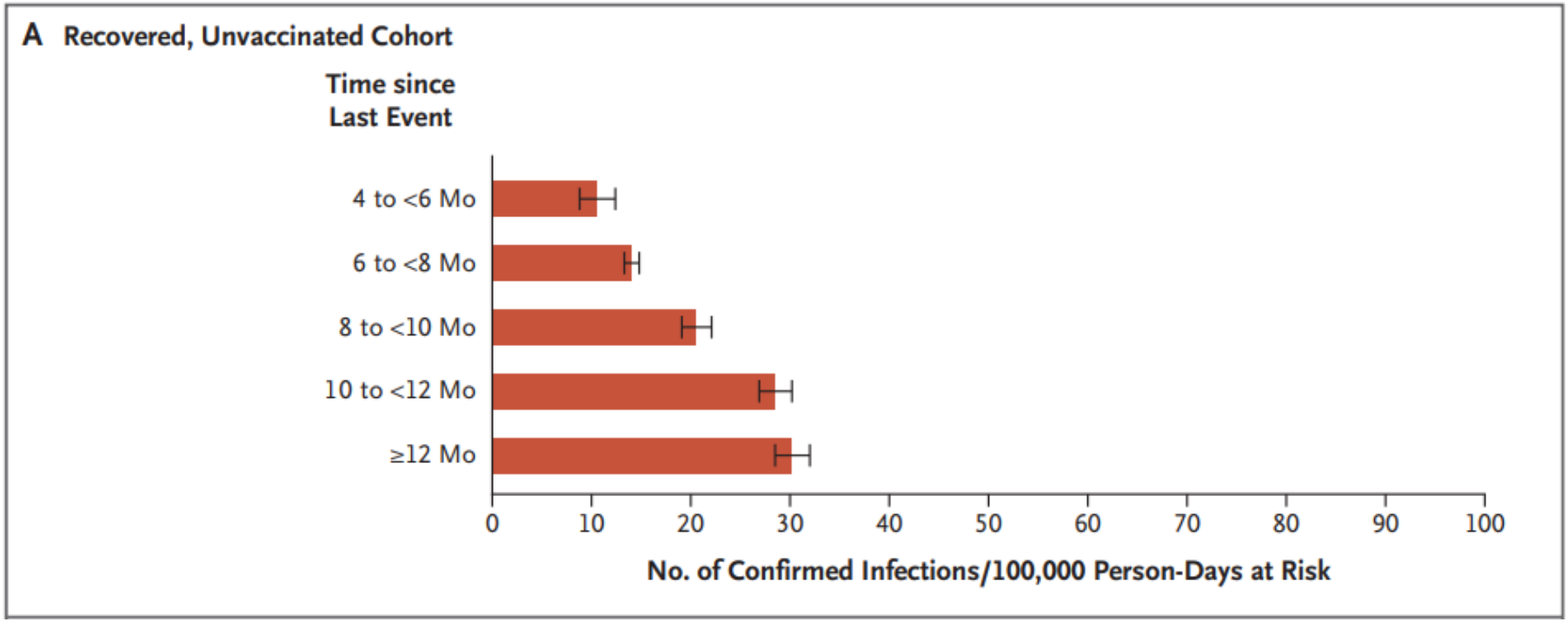
Barouch, Dan H., N Engl J Med, 2022

SARS-CoV-2 variant-specific neutralizing antibody responses in convalescent donors after 6 months and early after completion of the vaccination regimen



GeurtsvanKessel et al., Science Immunology, 2022

Protection and waning of natural and hybrid immunity to SARS-CoV-2



Goldberg et al., NEJM, 2022

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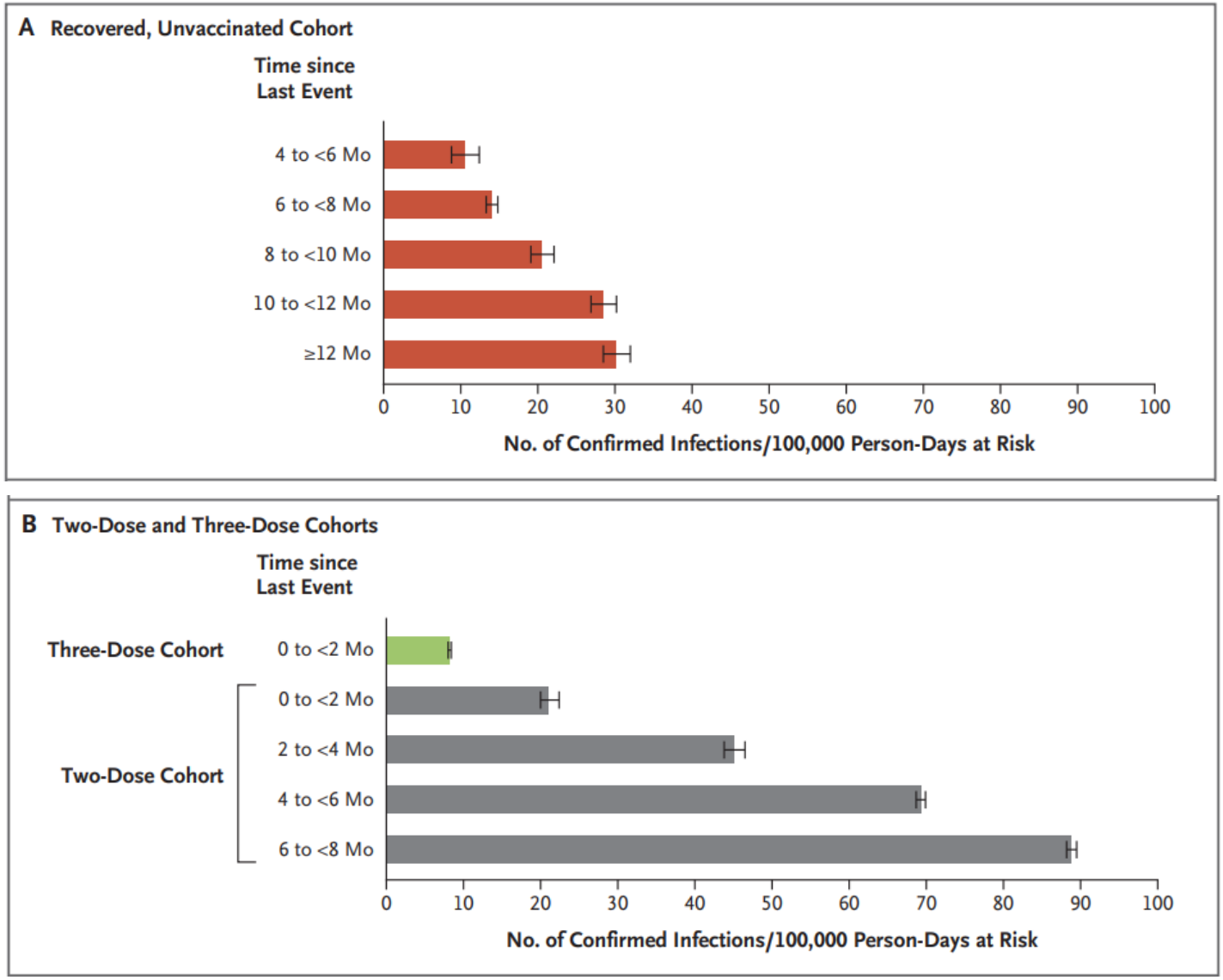

Goldberg et al., NEJM, 2022

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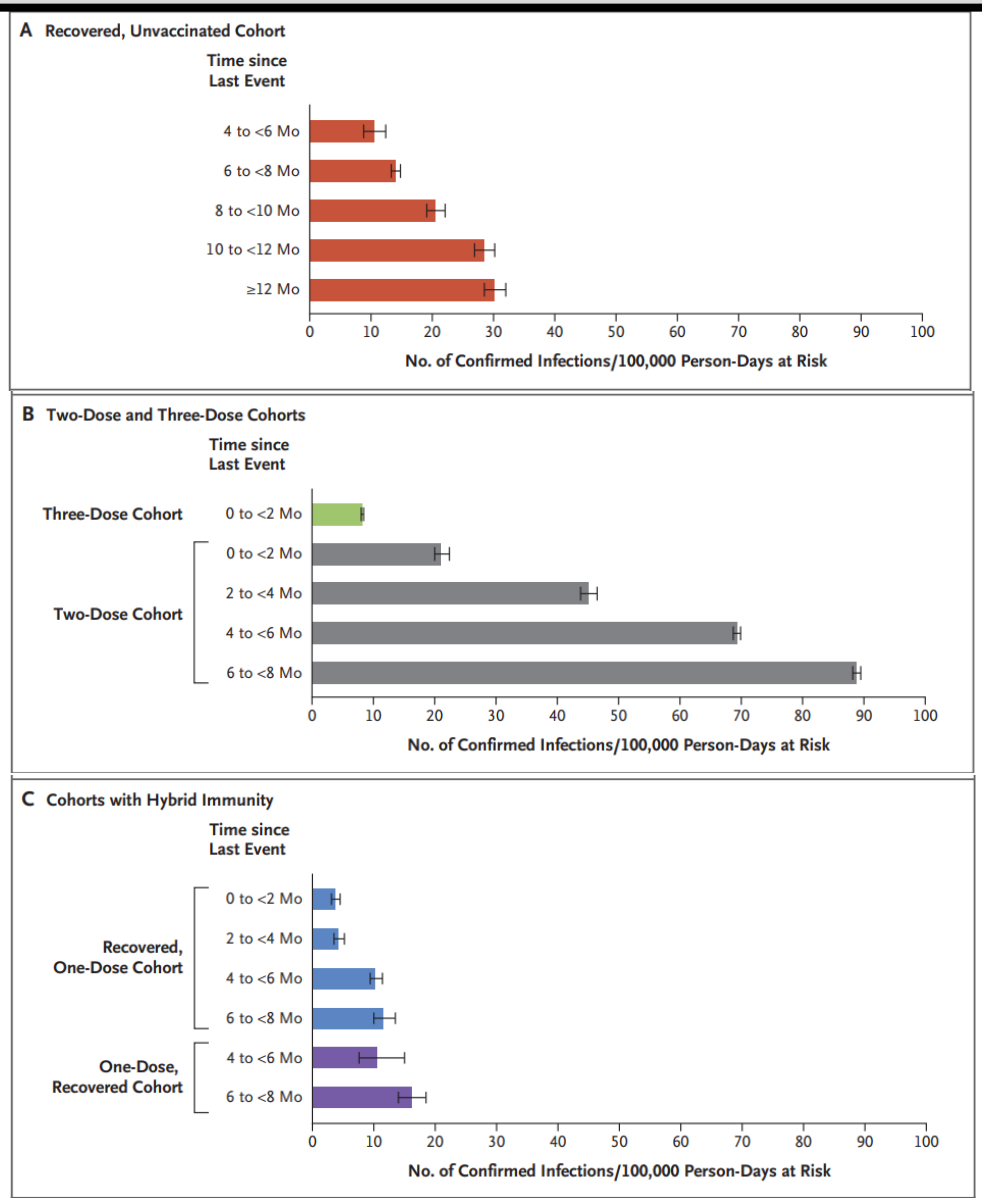
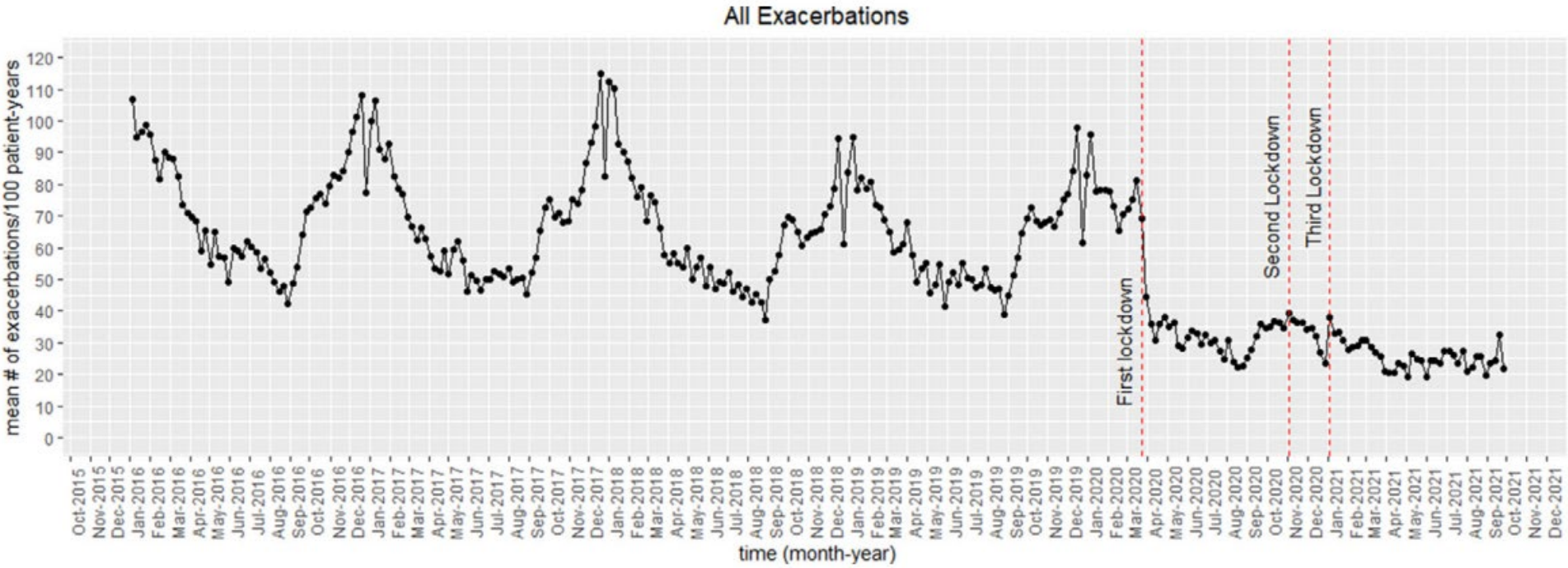


Goldberg et al., NEJM, 2022

Viral infections and Asthma / COPD exacerbation

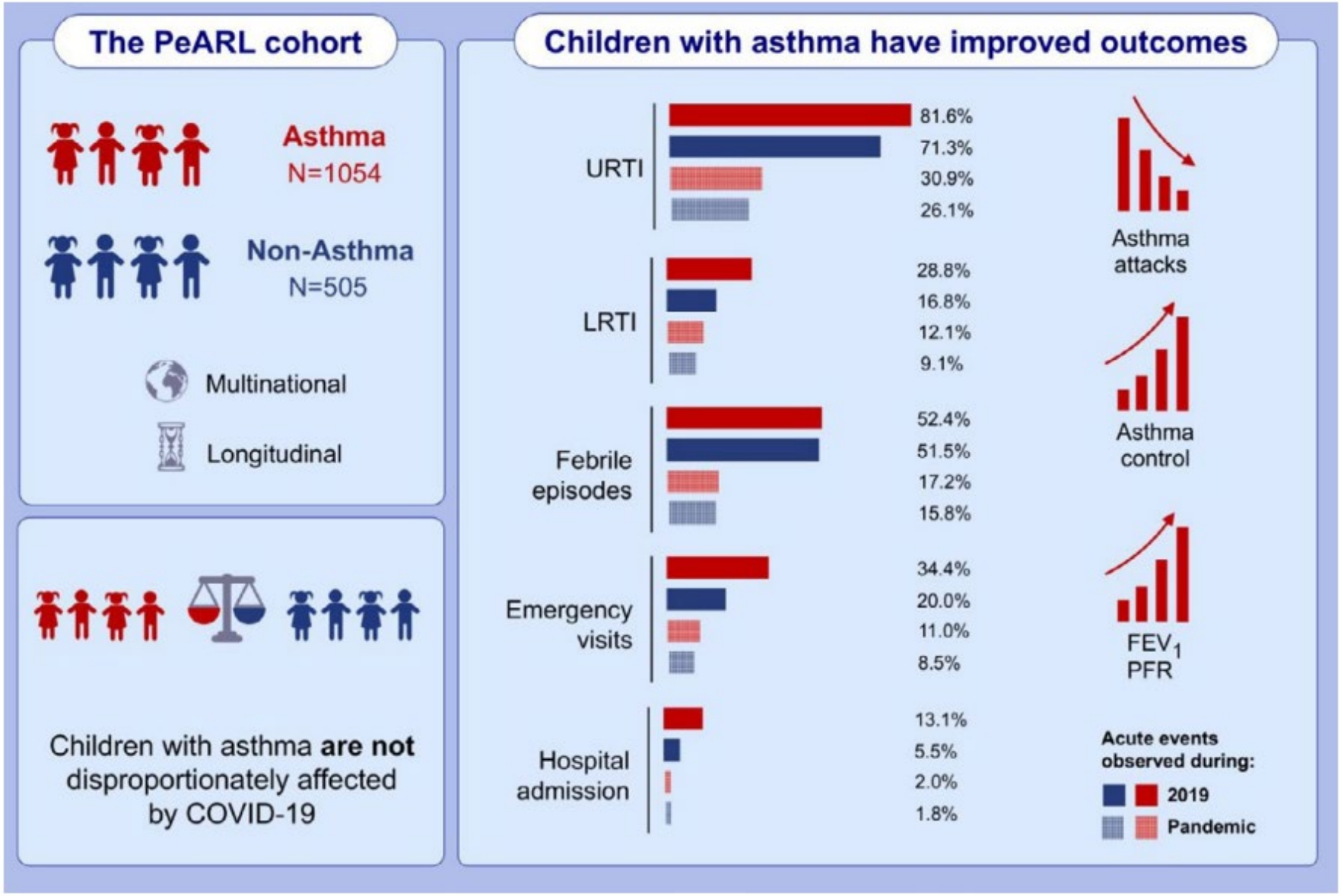
	Asthma exacerbation	COPD exacerbation
Rhino-virus (HRV)	↑↑↑	↑↑↑
Influenza A, B	↑↑	↑↑
RSV	↑	↑
SARS-CoV2	?/↓	?

Reduction in asthma exacerbations across England over the first 18 months after the first lockdown



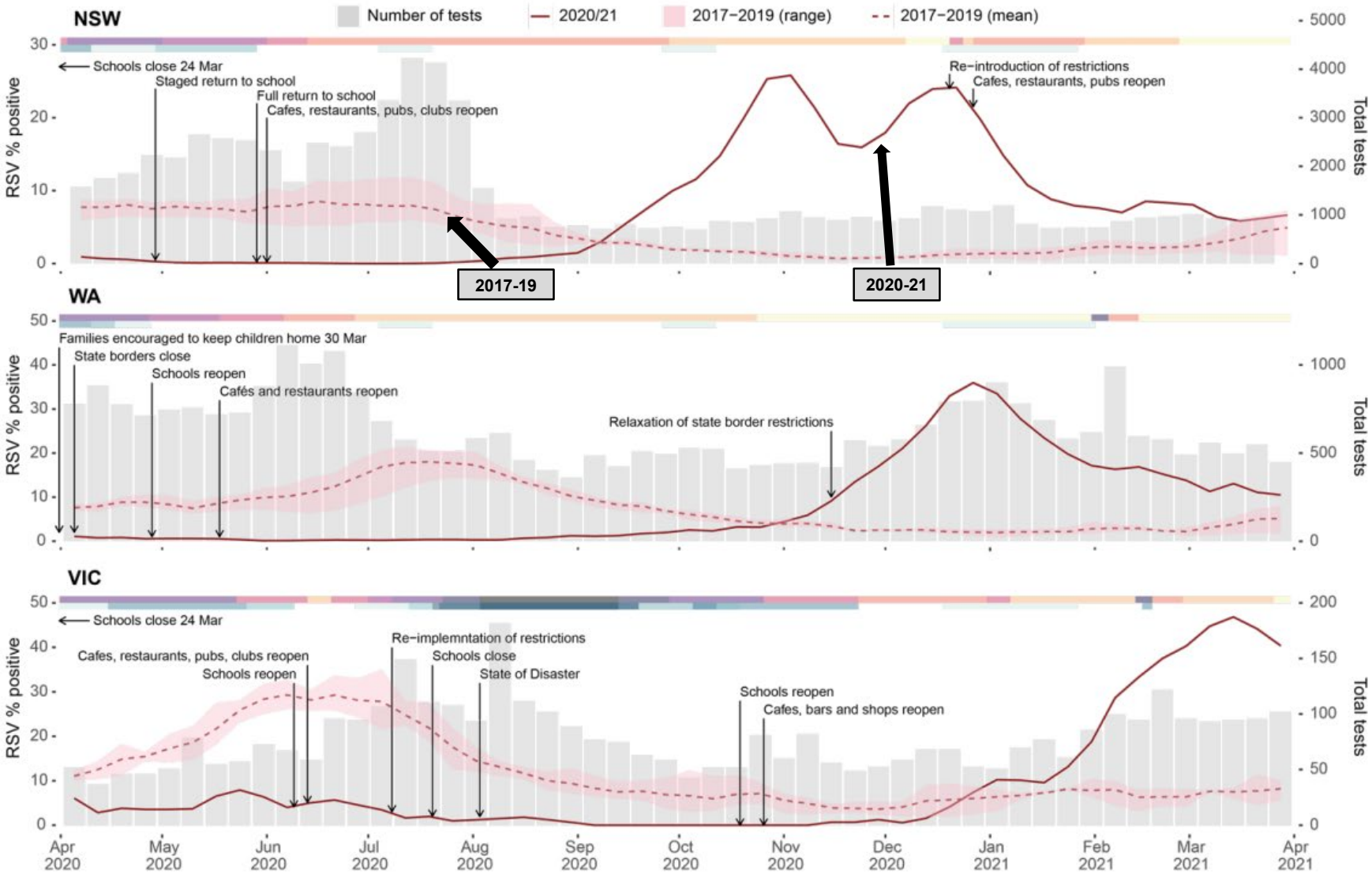
Shah et al., The Lancet Regional Health - Europe, 2022

Childhood asthma outcomes were improved during the first wave of the COVID-19 pandemic



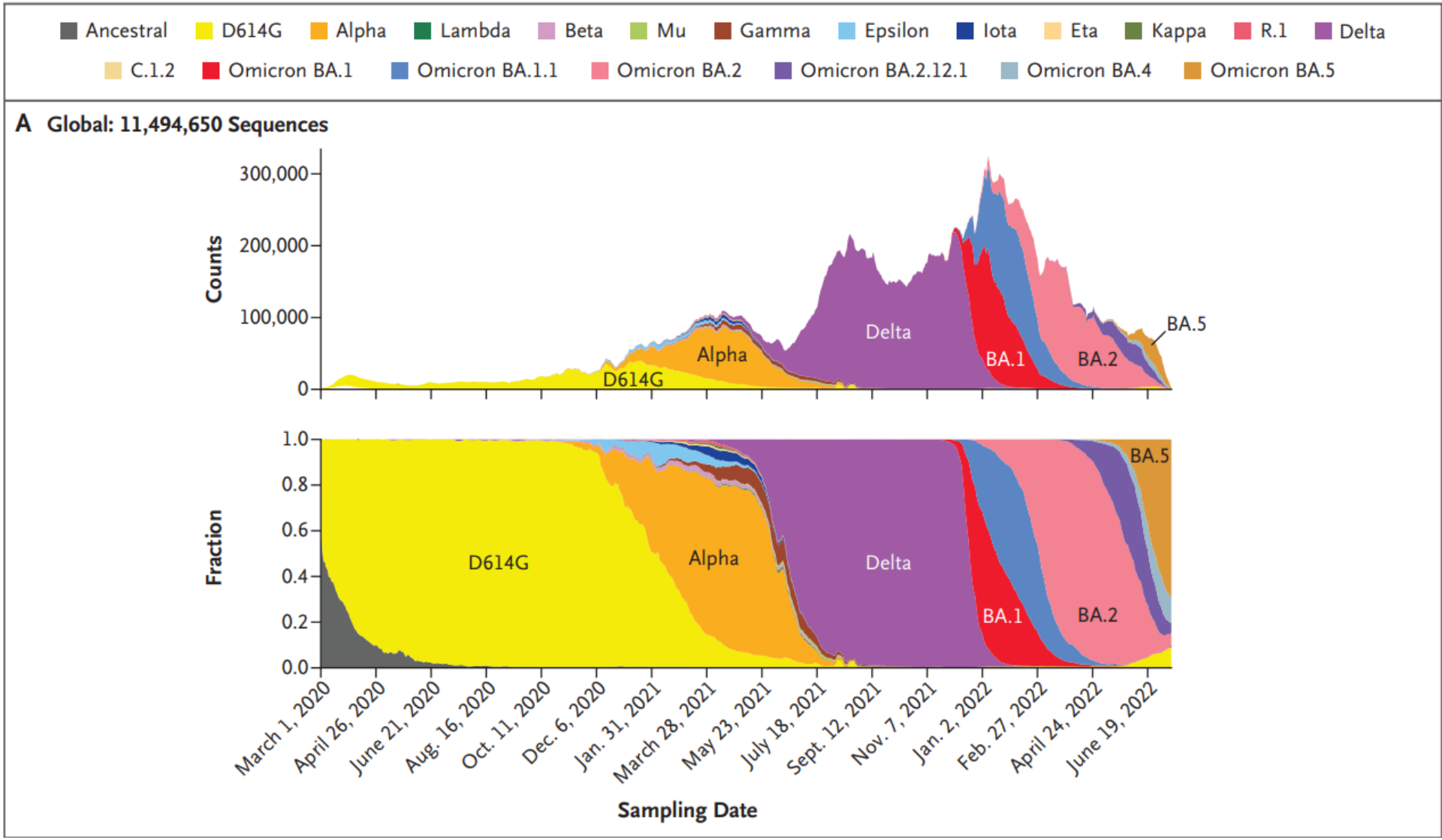
Papadopoulos et al., Allergy, 2021

The epidemiology of RSV detections in three Australian states



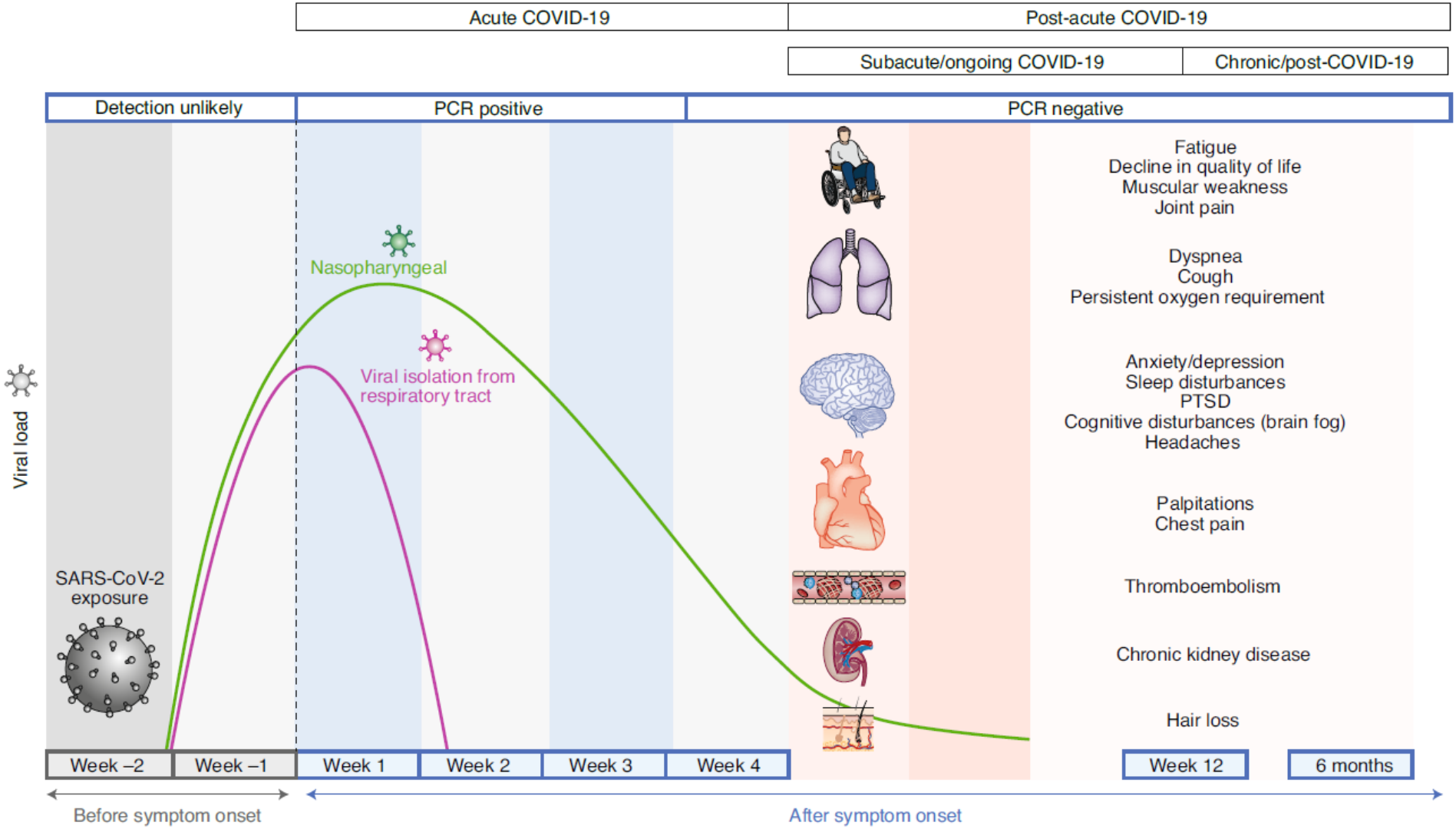
Eden et al., Nature Communications, 2022

SARS-CoV-2 variants over time



Barouch, Dan H., N Engl J Med, 2022

Timeline of post-acute COVID-19



Nalbandian et al., Nature Med 2021

FormName: Ü10 Long-Covid
Formular:
Variante: 4spaltig
Fach: Allgemeinmedizin
Autor: Hr. Prof. Dr. Kramer

Vorschlag von:
Harald Renz
LADR

muss noch angelegt werden
Verfahren bei uns eingestellt

	A 1 MOLIS ↓	Spalte EINS (2-8,5) max. 35 Zeichen		Ziff (8,5-9) max. 5 Zeichen	J 10 MOLIS ↓	Spalte ZWEI (11-17,5) max. 35 Zeichen		Ziff (17,5-18) max. 5 Zeichen	S 19 MOLIS ↓	Spalte DREI (20-26,5) max. 35 Zeichen		Ziff (26,5-27) max. 5 Zeichen
1		**Herzbeteiligung**				**Nierenbeteiligung**				**Chron. Inflammation/**		
2	TNT	Troponin T/I	S	32416	HST	Harnstoff	S	32065		**Re-Akivierung/ Rheumatologie**		
3	BNP	NT-pro-BNP	S	32097	CRE	Creatinin (eGFR)	S	32066	CRPUS	CRP high-sensitive	S	32460
4	MYO	Myoglobin	S	32450	USTA	Urin-Status	U	32033	TNFAST	TNFα	ST	32416
5	HERZ	Herzmuskel-Ak	S	32498	SEDB	Urin-Sediment	U	32031	IL1	IL-1β	SEG	?
6					ANCA	ANCA	S	2x32496	IL2R	löslicher IL2-Rezeptor	S	32381
7									ANF	ANA-Screening	S	32490
8		**Neurologische Beteiligung**				**Gerinnungsstörungen**			DSDNS	ds-DNS-AK	S	32491
9	ACRA	anti-Acetylcholin-Rez. AK	S	32509	Q	Quick (TPZ) + INR	CB	32113	CCP	CCP-Ak	S	32489
10	GABAB	anti-GABA AK	S	32505	PTT	PTT	CB	32112	ZIIM	Zirk. Immunkomplexe		6x32455
11	NMDAAK	anti-NMDA AK	S	32505	DDIM	D-Dimere	CB	32212	LUPU	Lupus-Antikoagulans		(2x32112
12	CASPR2	anti-CASPR2 AK	S	32505		anti-Annexin AK	S					3x32207)
13	MOGGI	anti-MOG AK	S	32505	CARD	anti-Cardiolipin AK	S	3x32503	CK	CK²	S	32074
14	MYELI	anti-Myelin AK	S	32505	B2GLY	ß2- Glykoprotein AK	S	2x32505	RF	RF	S	32461
15	GAD65I	anti-GAD AK	S	32505					BSGE	BSG	EB	32042
16									EBV	EBV	S	(32605/6
17		**Lungenbeteiligung**								(VCA, EA, EBNA-AK)²		32607/8)
18	LDH	LDH	S	32075		**Anämie/Vitamine**				T-Cellspot© EBV* ✈	3xLH	**123,35 €**
19					KBB	Kleines Blutbild	EB	32120	EBVDNS	EBV-Epstein Barr-Virus (PCR)	EB	32844
20					FERR	Ferritin	S	32325	CMV	CMV (Cytomegalie)-Ak²	S	32602/3
21					FE	Eisen	S	32085	NCOVSC	SARS-CoV-2-Antikörper⁴	S	32641
22					TRAF	Transferrin	S	32106	BORR	Borrelien-AK²	S	2x32586
23		**Leber-/Pankreasbeteiligung**			K	Kalium	S	32081		spez. Panel (Stöcker)	???	
24	GPT	GPT/ ALAT	S	32070	MG	Magnesium	S	32248				
25	GOT	GOT/ ASAT	S	32069	VIT25	Vitamin D 25-OH	S	32413				
26	AMY	Amylase	S	32072								
27	LIP	Lipase	S	32073		**Diabetes**						
28	BILI	Bilirubin, gesamt	S	32058	INSEL	Inselzell-Ak	S	32500				
29	BIDI	Bilirubin, direkt	S	32059	GADA	anti-GAD AK	S	32500				
30	AP	Alkal. Phosphatase	S	32068	IA2	anti-Tyrosinphosph. AK (IA2)	S	32505				
31	GGT	γ-GT	S	32071	HBA1C	HbA1c	EB	32094				
32					GLU	Glucose	CF	32057				
33												
34												
35										EBV heterophile Ak		

Symbole & Abkürzungen:

- CB Citrat-Blut
- CF Citrat-Fluorid
- EB EDTA-Blut
- LH Lithium-Heparin
- SEG Serum, gefroren
- S Serum
- ST Stuhl
- U Urin

⁴ = Erfasst Z.n. Impfung / Infektion, z. Zt. Keine Aussagen zur Immunität möglich. Eine Testung ohne direkten Bezug zu einer klinischen Covid-19-Symptomatik ist gemäß EBM keine vertragsärztliche Leistung. ✈ Eiliger Versand, nicht vor dem WE

* = IGeL-Leistung, Abrechnung nach GOÄ, ² = ggf. Bestätigung / Erweiterung / Immunoblot

Long COVID

- More common following *severe* acute COVID-19
- More common with increasing age
- Further risk factors are diabetes T2, EBV infection
- Vaccination protects partly
- Persistant inflammation
- Caused by persisting hidden virus?
- Autoimmunity (anti-U1-suRNP; anti-SS-B/La)

DE GRUYTER

Harald Renz (Hrsg.)

DER CORONA ATLAS

DE G