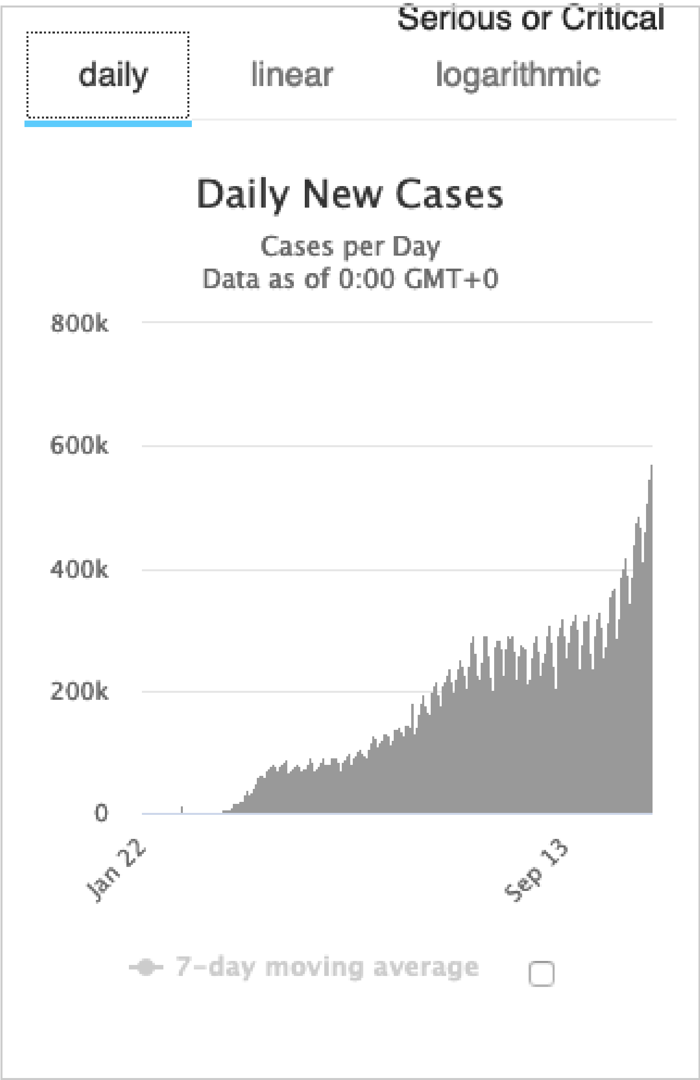
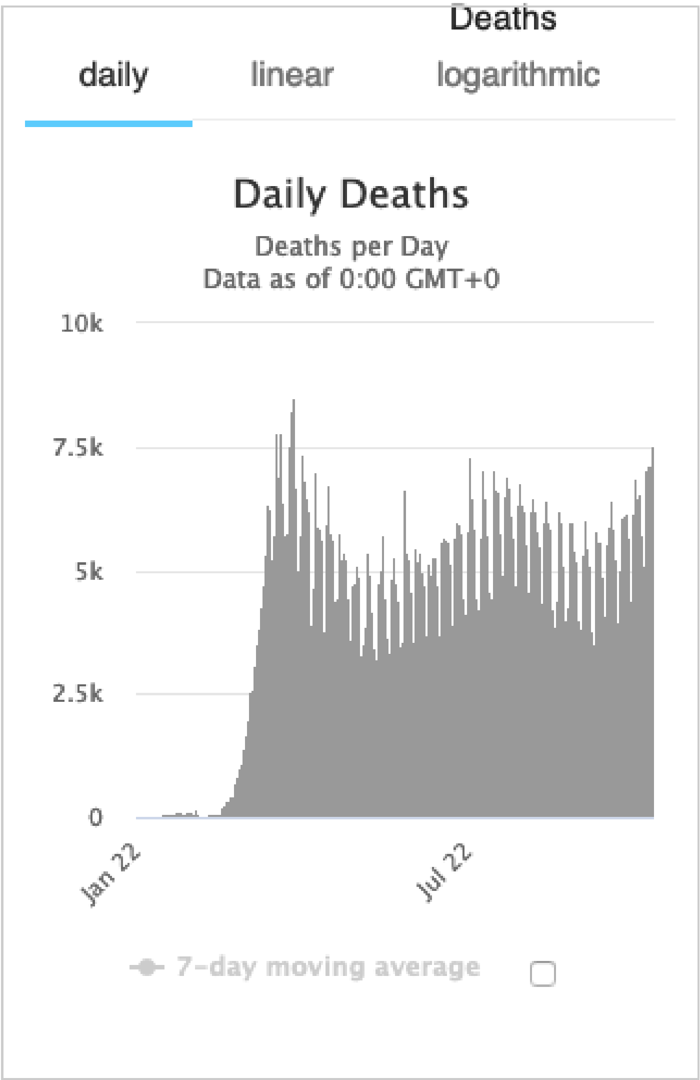
Global new cases and deaths





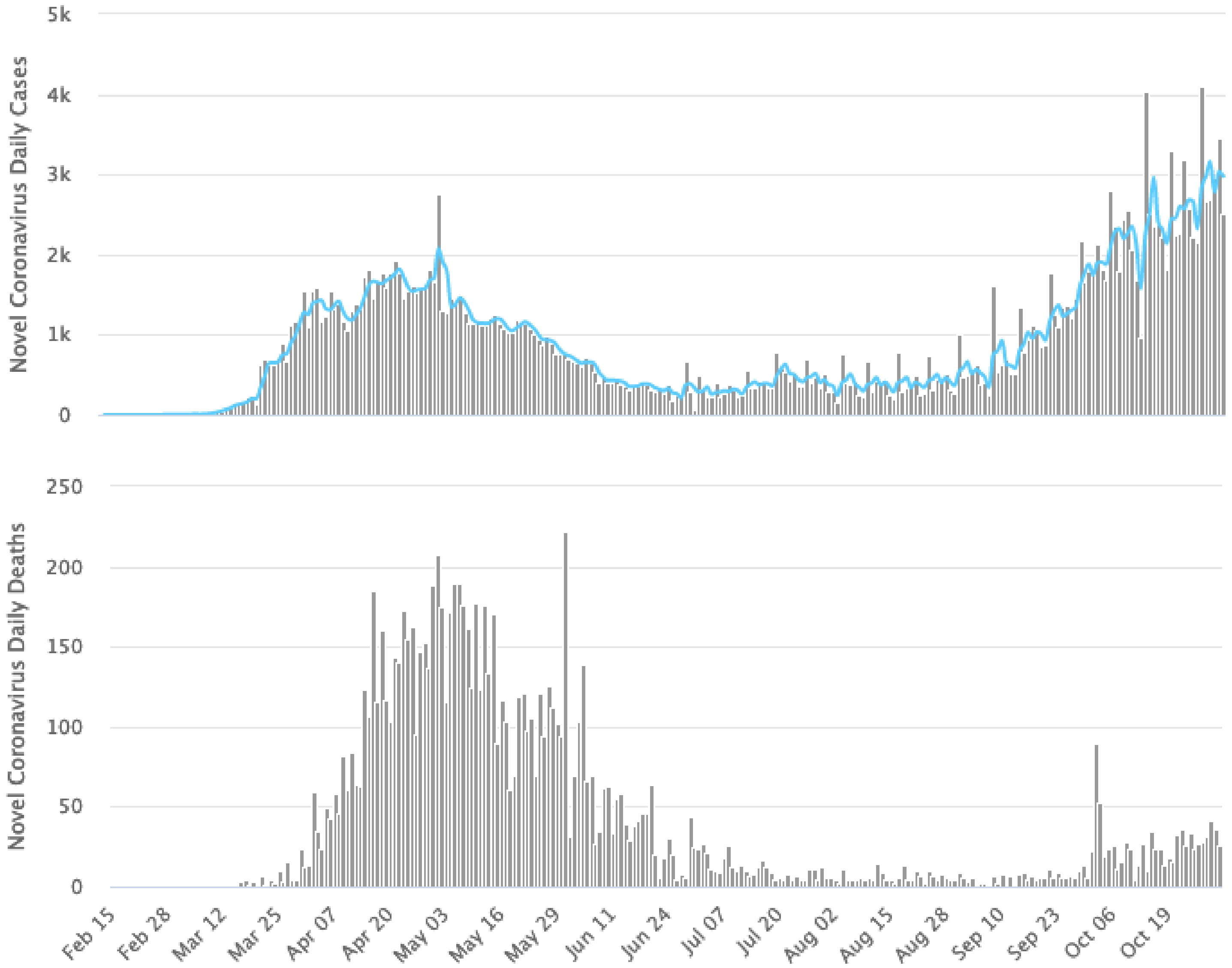
Total cases: 47M

Total deaths: 1.2M

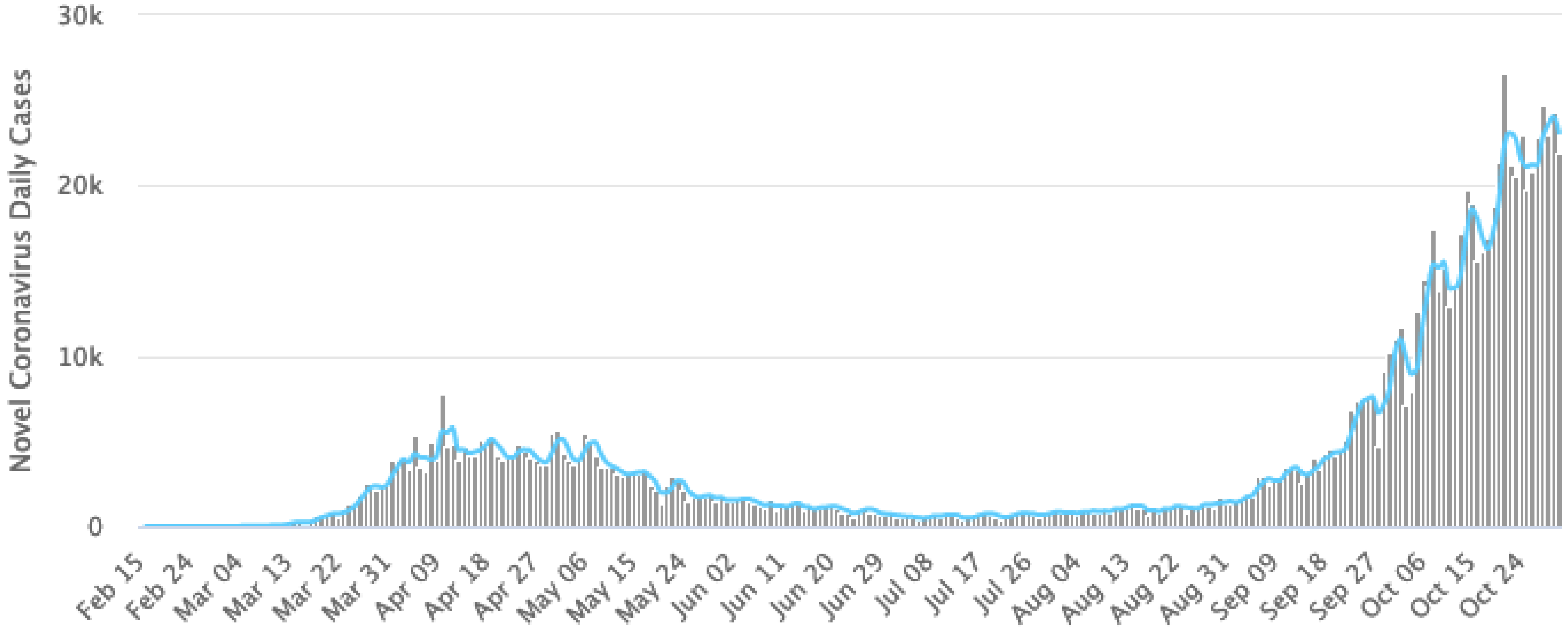
The second wave in Canada

Daily cases

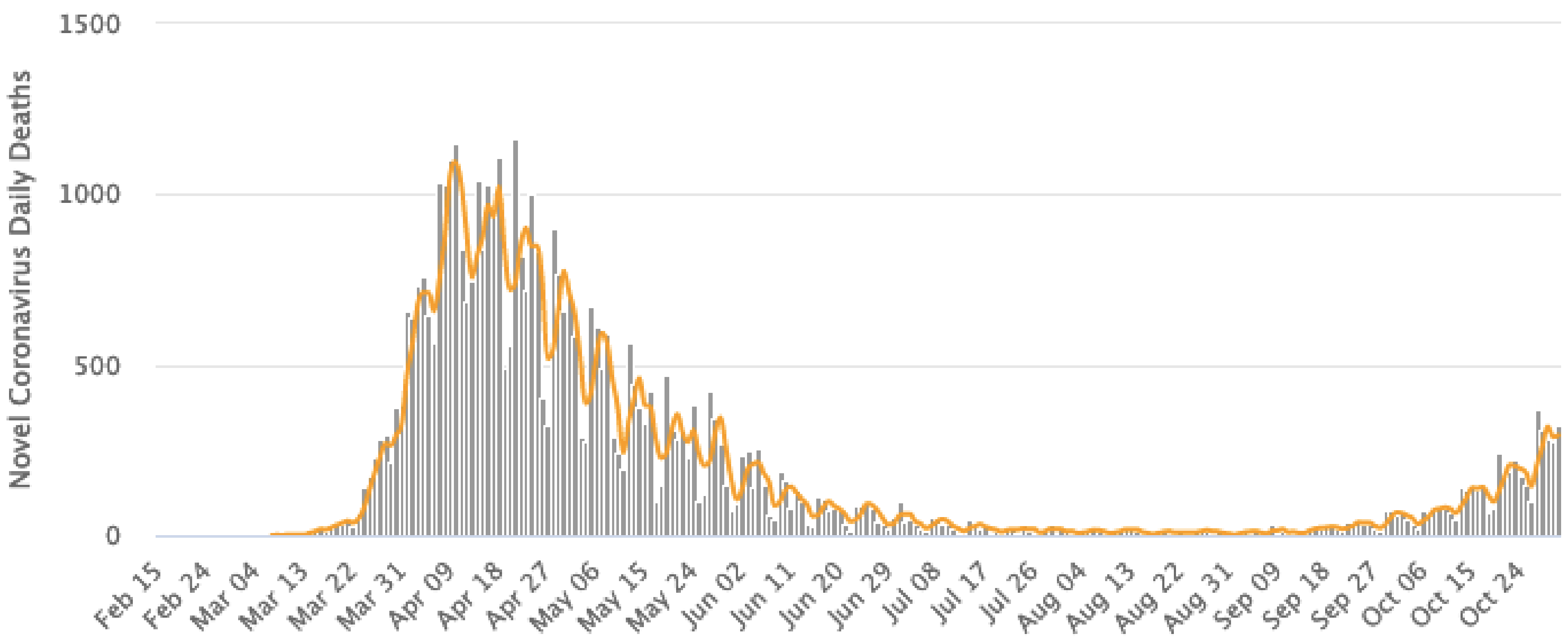
Daily deaths



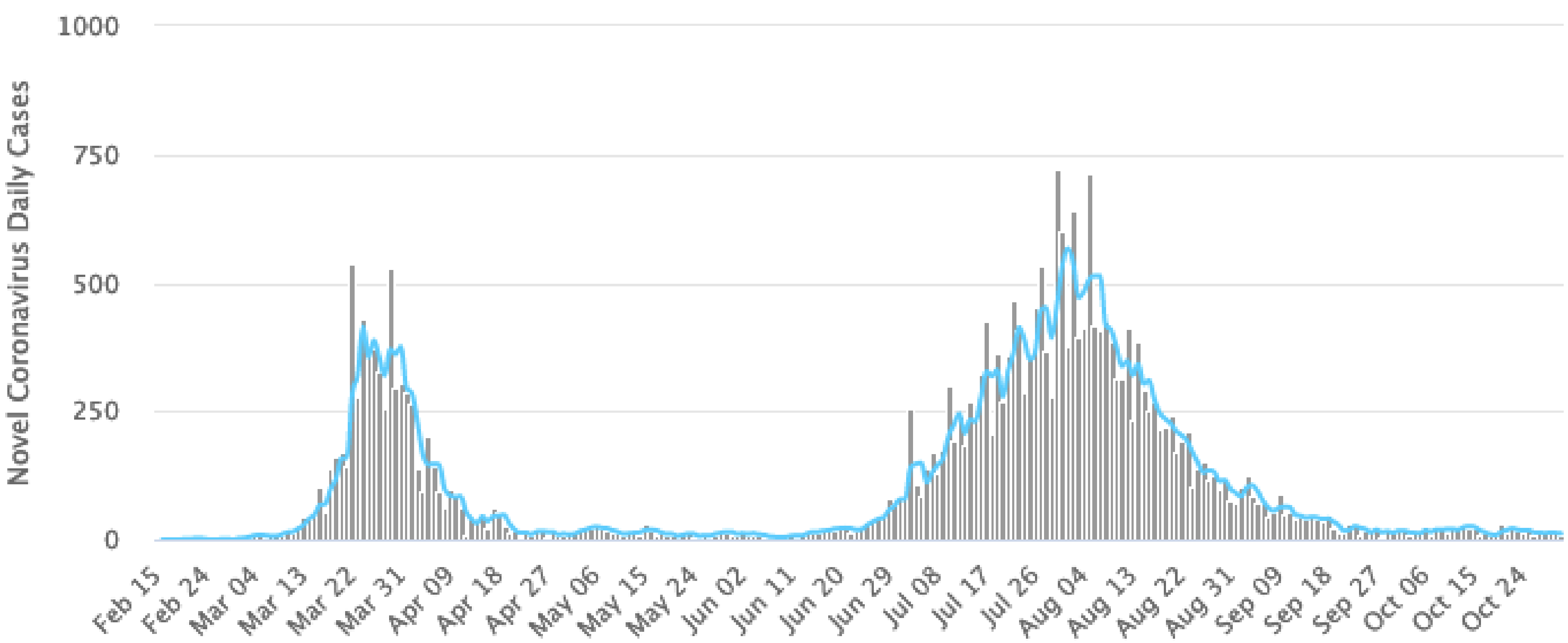
The second wave in the United kingdom (cases)



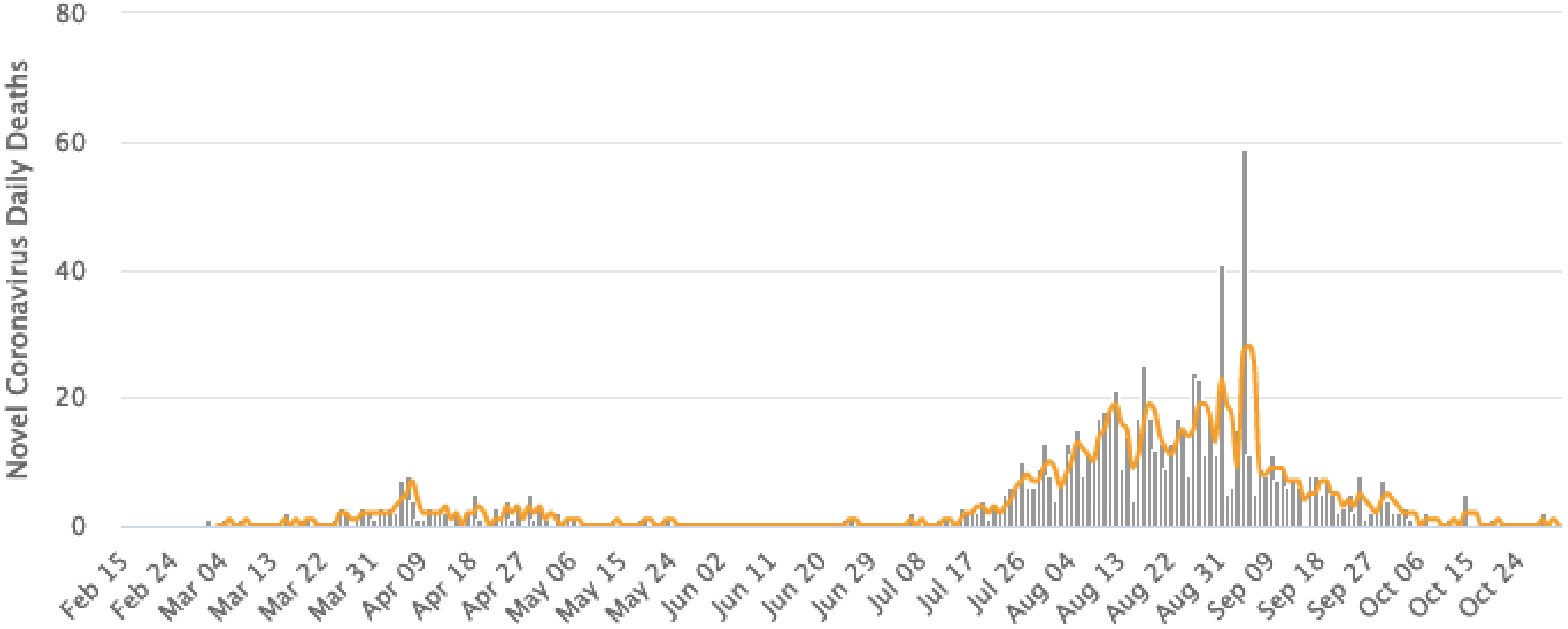
The second wave in the United kingdom (deaths)



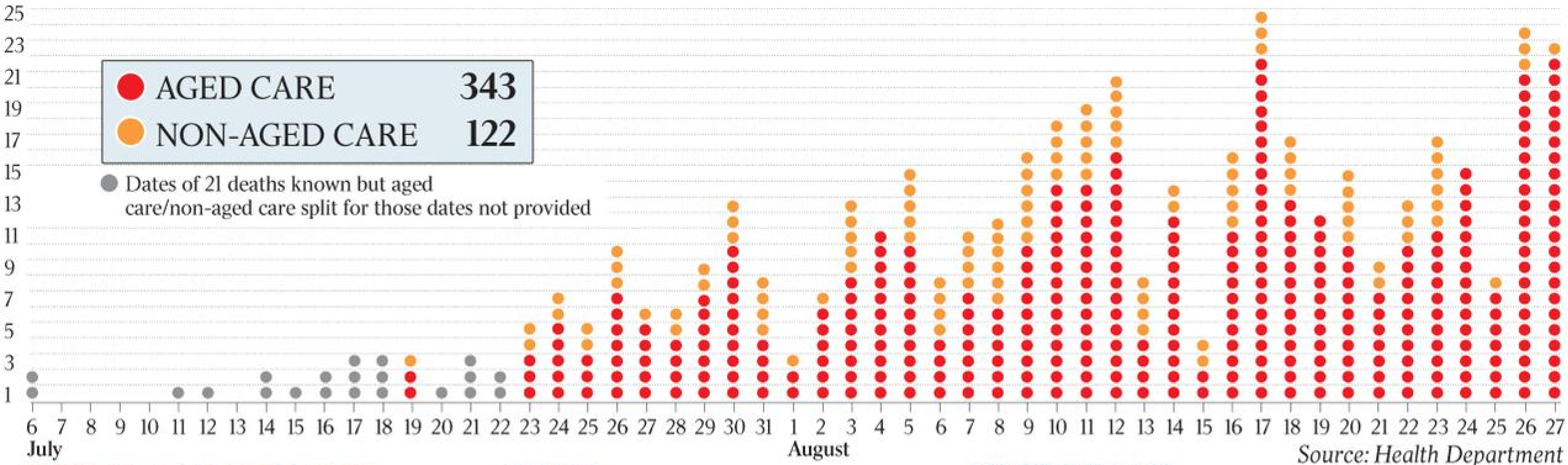
The second wave in Australia
(cases)



The second wave in Australia
(deaths)



SECOND WAVE DEATHS



Source: Health Department

VICTORIAN DEATHS BY AGE AND GENDER

	Female	Male	Total
90+	91	65	156
80-89	112	99	211
70-79	27	56	83
60-69	5	14	19
50-59	3	9	12
40-49	0	1	1
30-39	0	2	2
20-29	0	1	1
Total	**238**	**247**	**485**

GRIM MILESTONES

	Deaths	Last death
Victoria	485	Aug 27
NSW	54	Aug 16
Tas	13	May 1
WA	9	May 3
Qld	4	Apr 5
SA	4	Apr 12
ACT	3	Apr 7

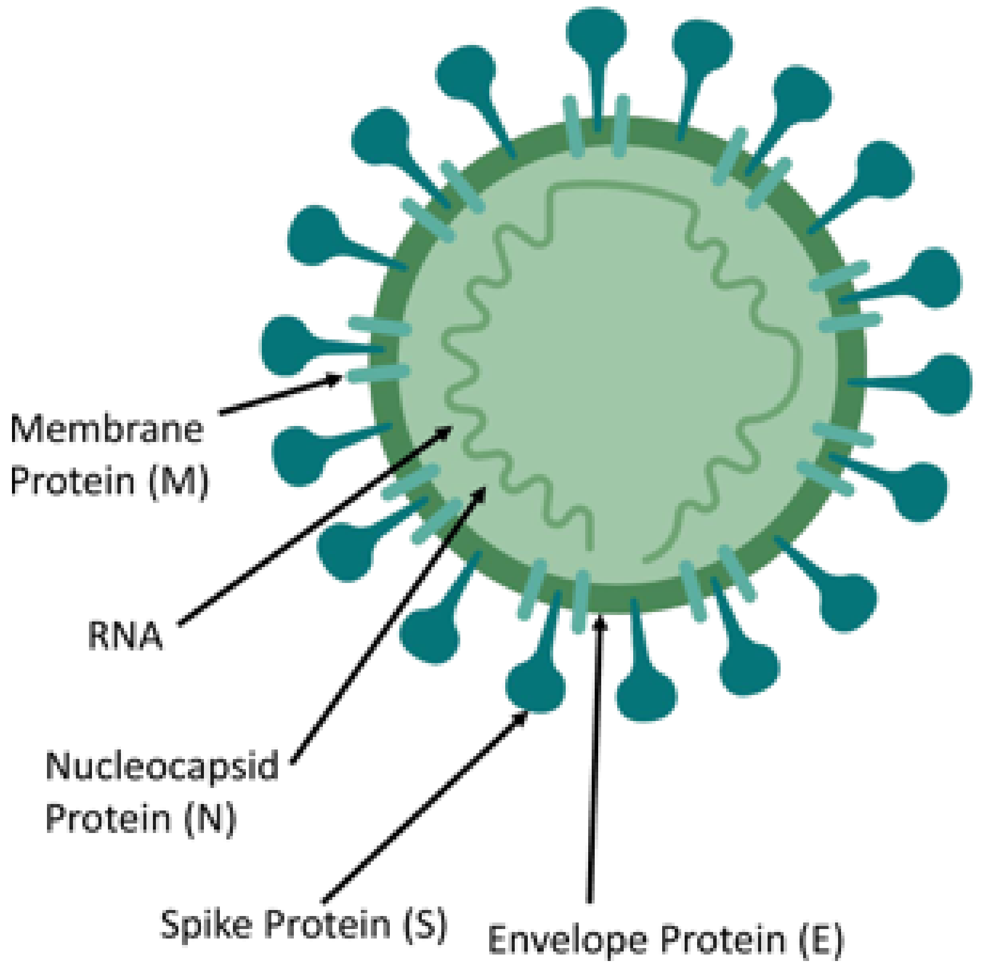
* Two Queenslanders died in NSW

VICTORIA'S SURGE

DEATHS	January to June	July	August	Total
Victoria	20	93	372	**485**
Rest of Aus	84	0	3	**87**

CASES				
Victoria	2159	8418	8137	**18,714**
Rest of Aus	5675	643	269	**6587**

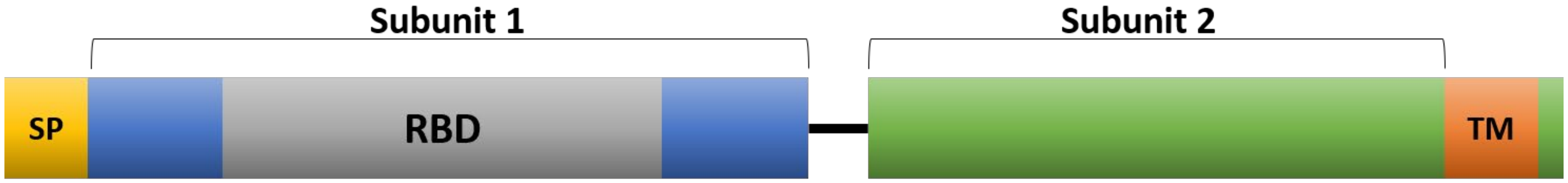
Coronavirus structure



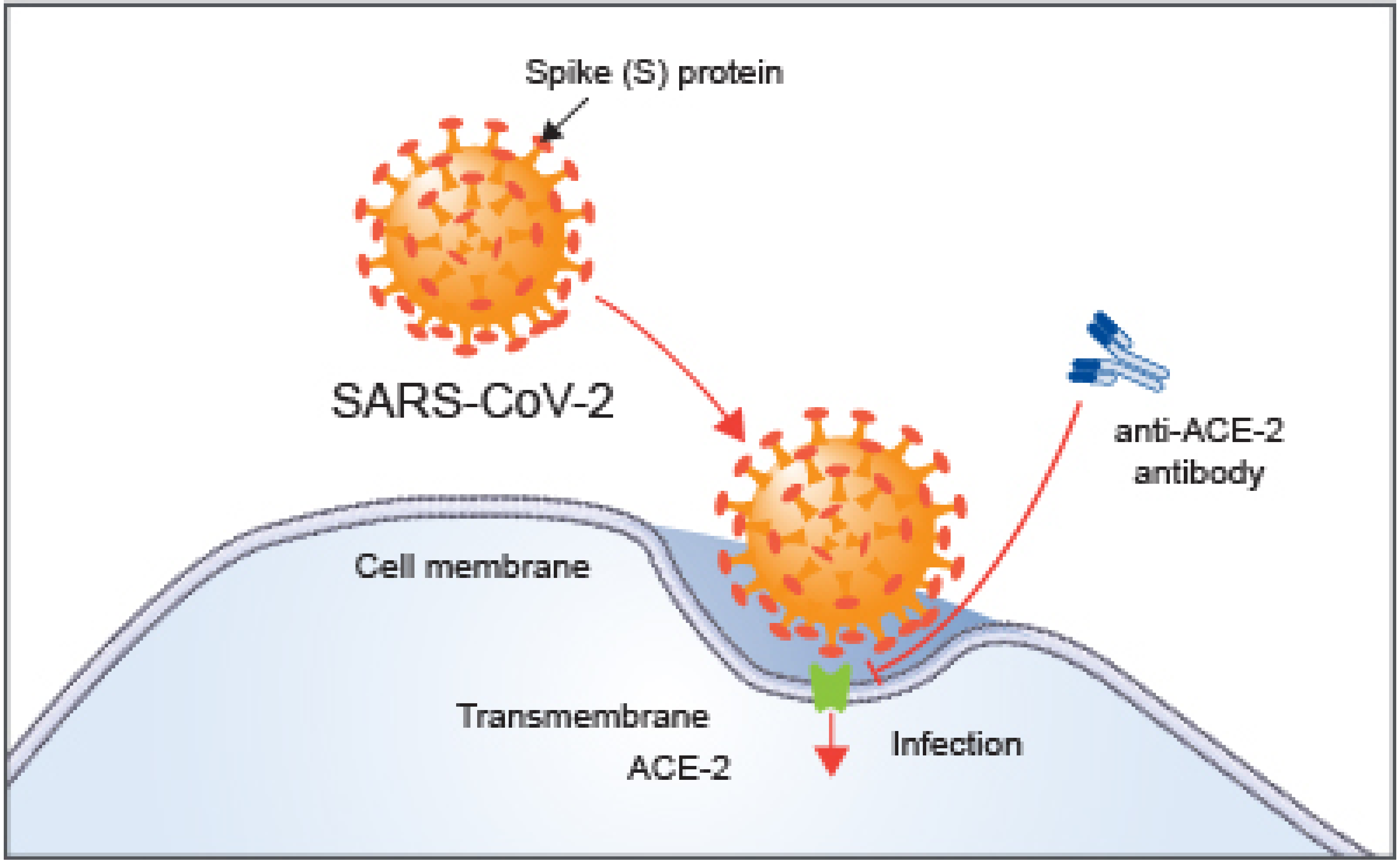
Structural Protein	Function of Protein
Nucleocapsid Protein (N)	• Bound to RNA genome to make up nucleocapsid
Spike Protein (S)	• Critical for binding of host cell receptors to facilitate entry of host cell
Envelope Protein (E)	• Interacts with M to form viral envelope
Membrane Protein (M)	• Central organiser of CoV assembly • Determines shape of viral envelope

- It has been noted that some CoVs do not need to have the full ensemble of structural proteins to make virions, highlighting that certain proteins may be dispensable or compensated by the function of non-structural proteins.

Spike protein



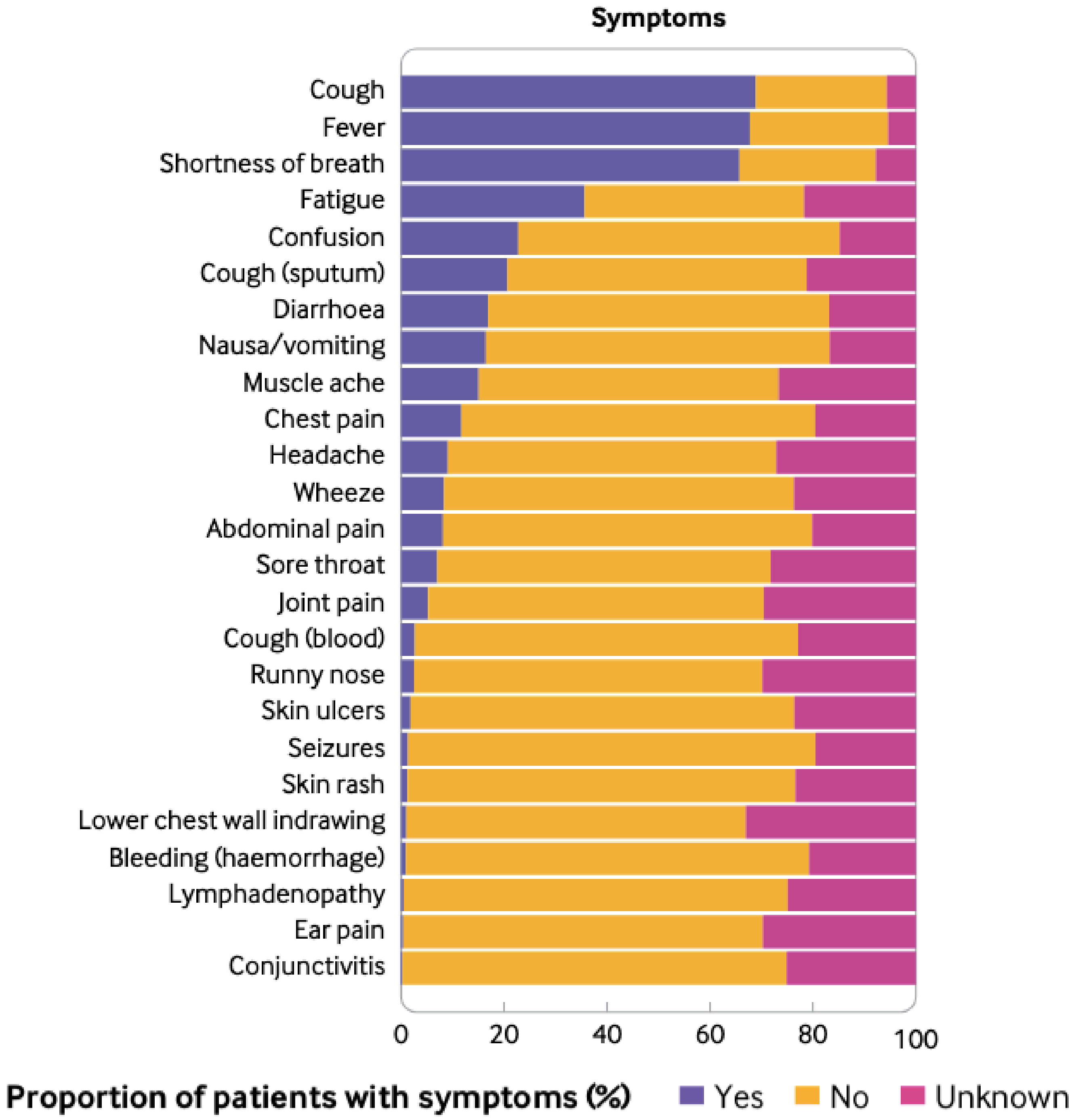
Human angiotensin converting enzyme-2 (ACE-2)is the principal receptor for the SARS-CoV-2's Spike protein



Coronaviruses that infect people

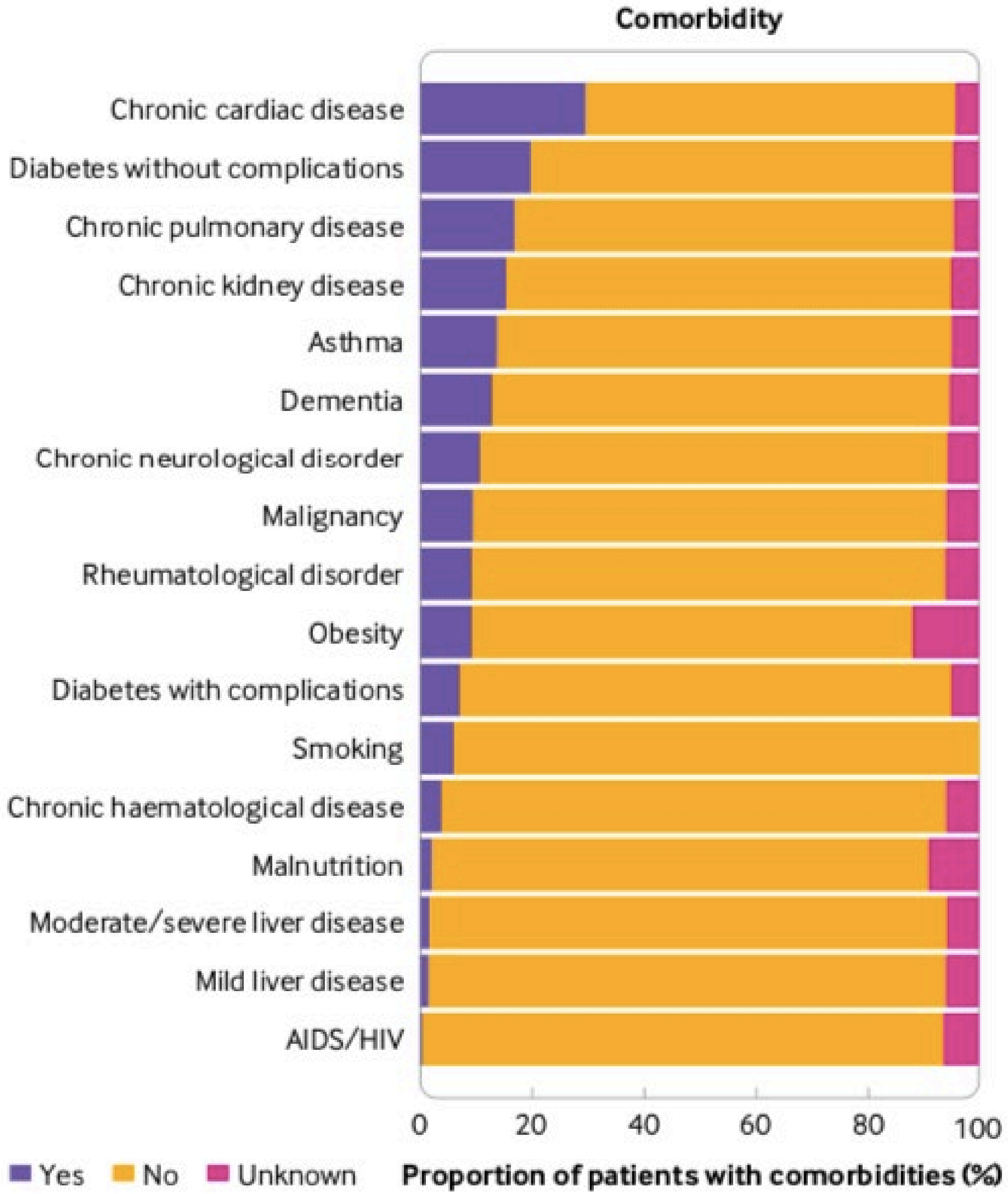
1. 229E (alpha coronavirus)
2. NL63 (alpha coronavirus)
3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)
5. MERS-CoV (beta coronavirus), identified 2012
6. SARS-CoV (beta coronavirus), identified 2002
7. SARS-CoV-2 (beta coronavirus), identified 2019

Symptoms of 20,133 patients admitted to hospital in the UK



AB Docherty *et al, BMJ* 2020

Co-morbidities of 20,133 patients admitted to hospital in the UK



AB Docherty *et al, BMJ* 2020

Independent risk factors for death from COVID of patients admitted to hospital

		Hazard ratio (95% CI)	P value
Age on admission (years)	<50		
	50-59	2.63 (2.06 to 3.35)	<0.001
	60-69	4.99 (3.99 to 6.25)	<0.001
	70-79	8.51 (6.85 to 10.57)	<0.001
	≥80	11.09 (8.93 to 13.77)	<0.001
Sex at birth	Female	0.81 (0.75 to 0.86)	<0.001
Chronic cardiac disease	Yes	1.16 (1.08 to 1.24)	<0.001
Chronic pulmonary disease	Yes	1.17 (1.09 to 1.27)	<0.001
Chronic kidney disease	Yes	1.28 (1.18 to 1.39)	<0.001
Diabetes	Yes	1.06 (0.99 to 1.14)	0.087
Obesity	Yes	1.33 (1.19 to 1.49)	<0.001
Chronic neurological disorder	Yes	1.17 (1.06 to 1.29)	0.001
Dementia	Yes	1.40 (1.28 to 1.52)	<0.001
Malignancy	Yes	1.13 (1.02 to 1.24)	0.017
Moderate/severe liver disease	Yes	1.51 (1.21 to 1.88)	<0.001

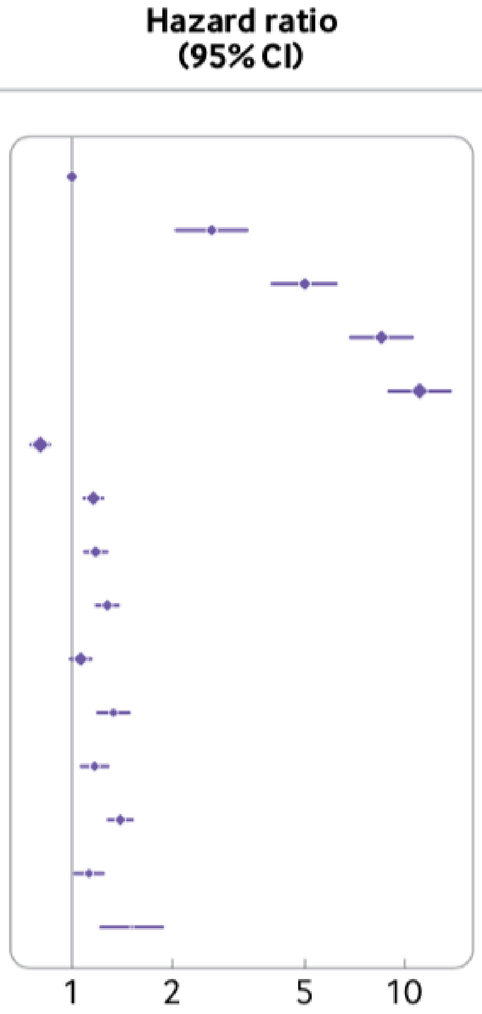


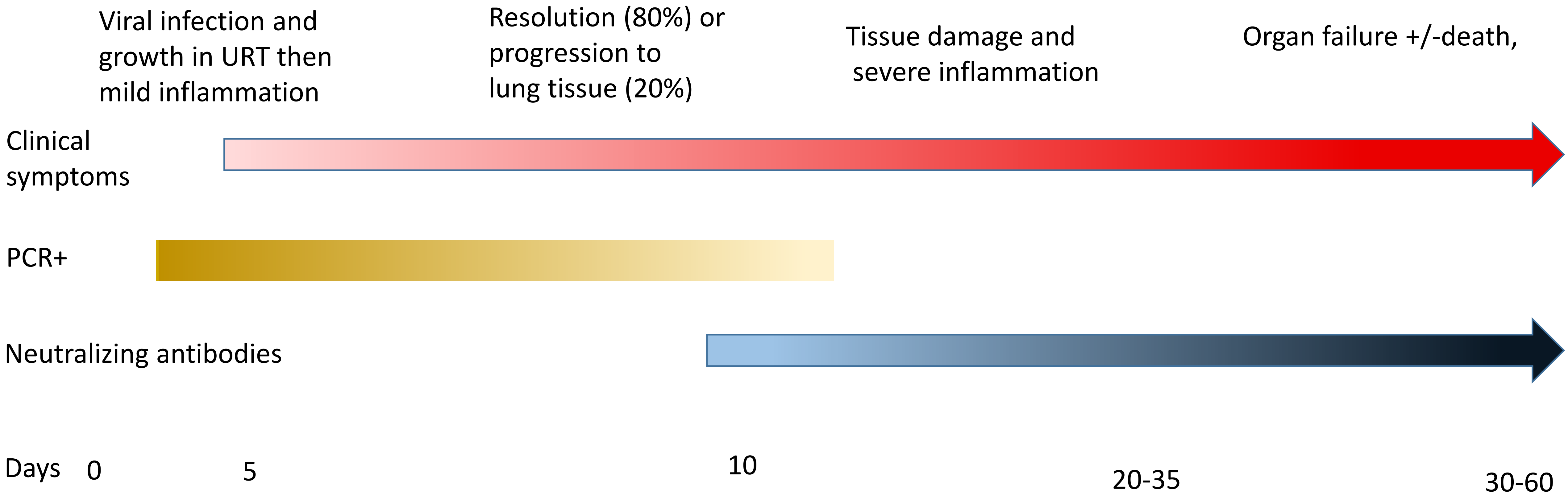
Fig 5 | Multivariable Cox proportional hazards model (age, sex, and major comorbidities), where hazard is death. Patients who were discharged were kept in the risk set (n=15 194; No of events=3911)

Infection fatality rates and sero-prevalence in Geneva, May 2020

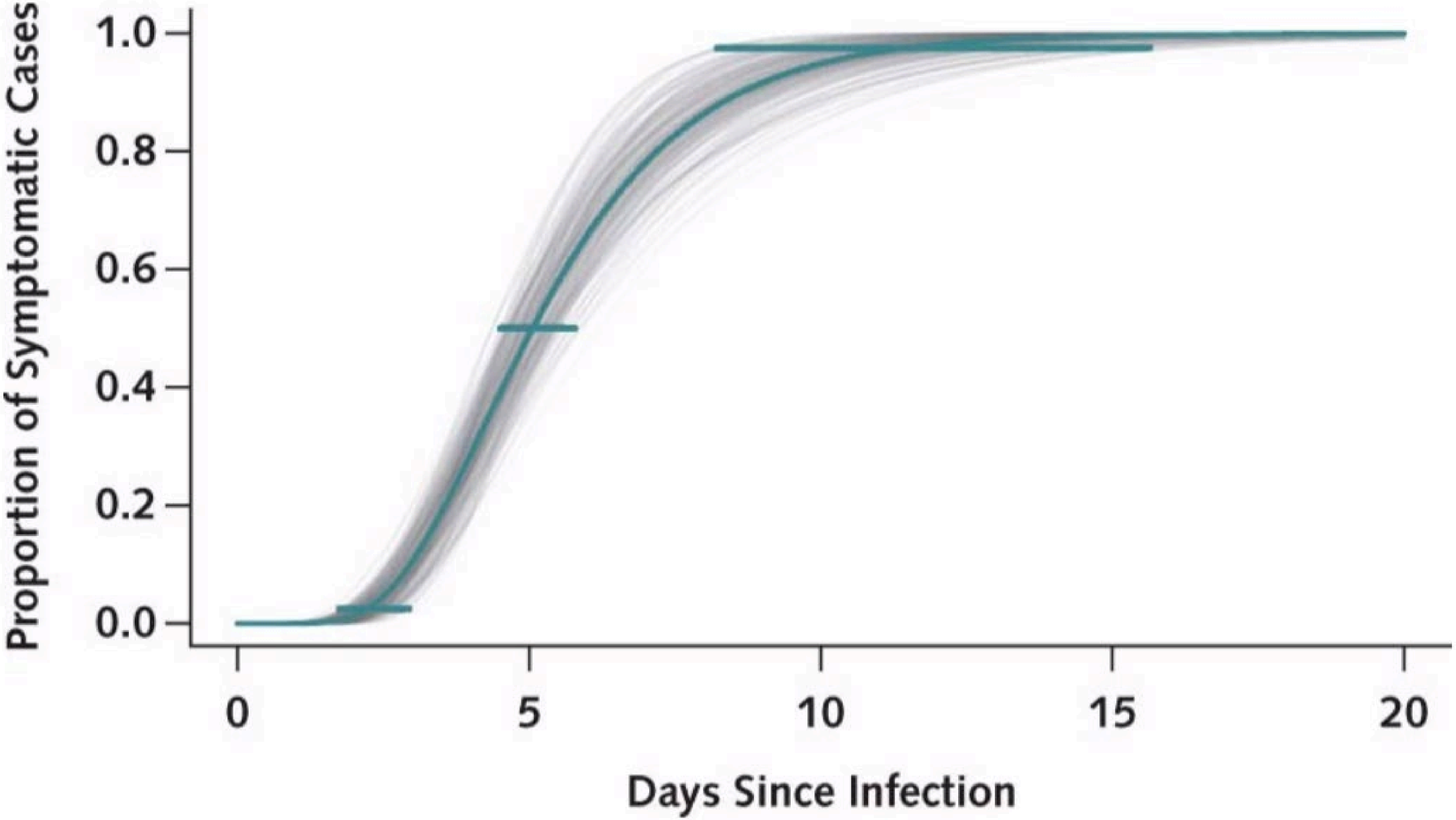
Age range (years)	Seroprevalence (%)	Infection fatality rate
5-9	4.5	1/62,000
10-19	11.4	1/312,500
20-49	13.2	1/10,800
50-64	10.4	1/714
$\geqq$ 65	6.8	1/18
All	10.8	1/156

J. Perez-Saez, *Lancet Infect. Dis*. 2020

Progression of COVID in a patient



Distribution of Time to Development of Symptoms



Pre-symptomatic *versus* Asymptomatic

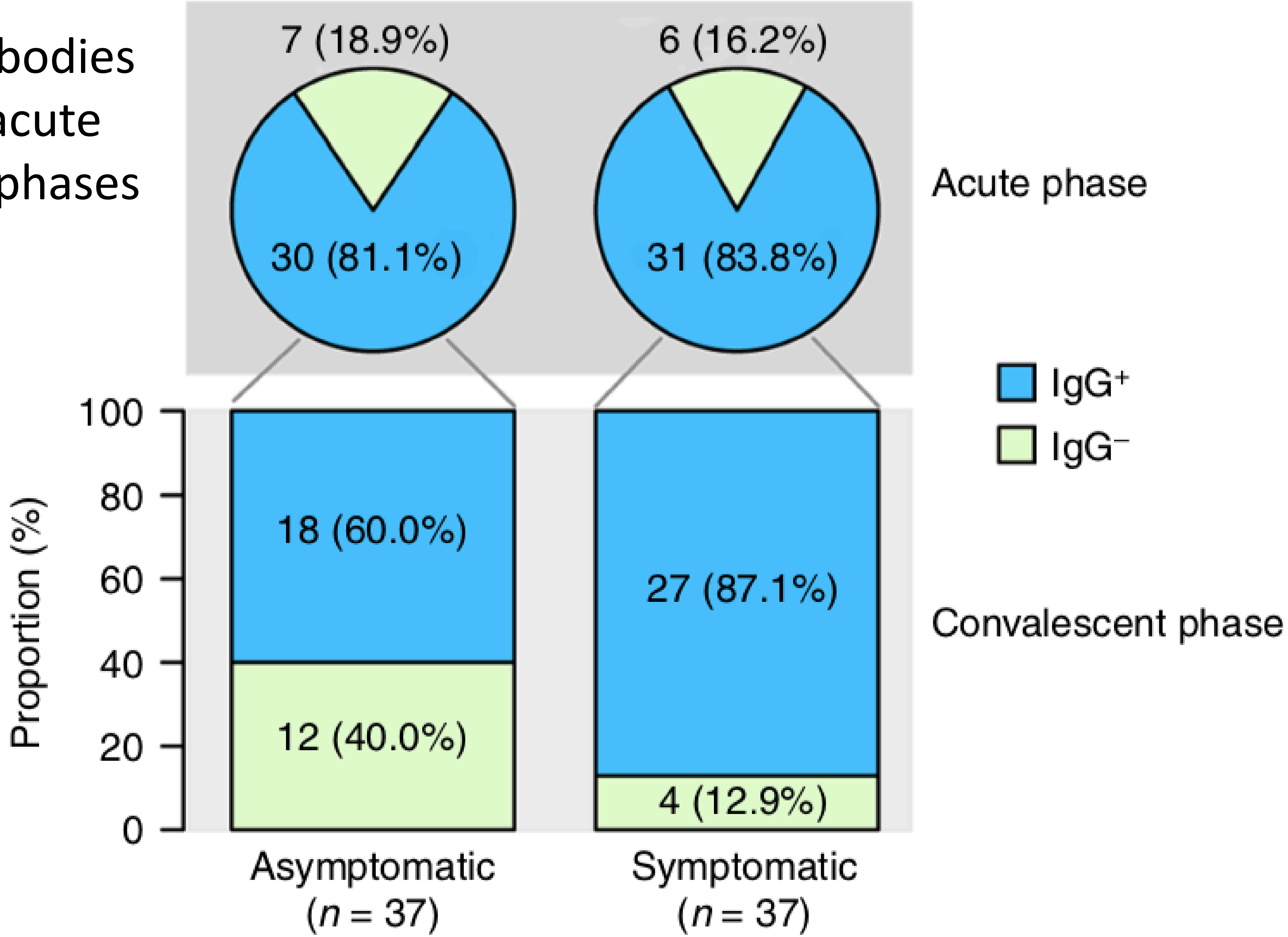
Results: We screened 998 articles and included nine low risk-of-bias studies from six countries that tested 21,035 at-risk people, of which 559 were positive and 83 were asymptomatic. Diagnosis in all studies was confirmed using a RT-qPCR test. The proportion of asymptomatic cases ranged from 4% to 41%. Meta-analysis (fixed effect) found that the proportion of asymptomatic cases was 15% (95% CI: 12% - 18%) overall; higher in non-aged care 16% (13% - 19%), and lower in long-term aged care 8% (3% - 18%). Four studies provided direct evidence of forward transmission of the infection by asymptomatic cases but suggested considerably lower rates than symptomatic cases.

Symptomatic *versus* persistent asymptomatic

	Symptomatic	Asymptomtic	
Viral load (PCR) at enrolment	Ct – 31.7	Ct – 32.8	n.s.
Duration of viral Shedding (by PCR)	14 days (IQR:9-22)	19 days (IQR: 15-26)	P= 0.028
Pro-inflammatory cytokines	High	Low	
IgG Levels	84% pos	81% pos (lower titers)	

Q X Long et al, *Nat. Med.* 2020

Prevalence of antibodies to SARS-CoV-2 in acute and convalescent phases



Q X Long et al, *Nat. Med.* 2020

Inflammatory and pro-Inflammatory cytokines elevated in symptomatic patients

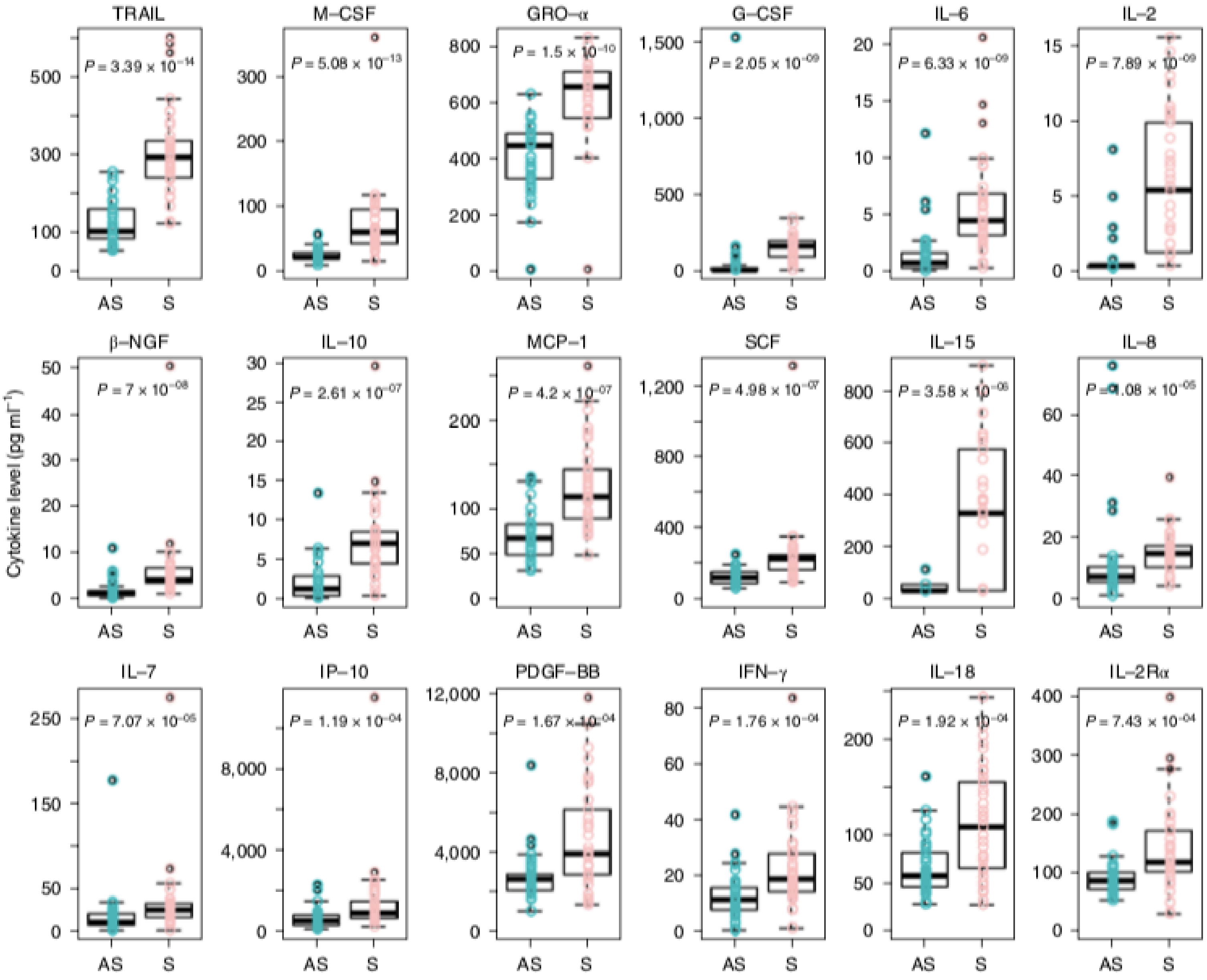


Fig. 4 | Comparison of serum cytokine/chemokine concentrations between the asymptomatic and symptomatic groups. Samples from asymptomatic (n = 37) and symptomatic (n = 37) patients with COVID-19 were collected in the acute phase during hospitalization, and assays were performed to measure the concentrations of 48 cytokines and chemokines. The box plots show the medians (middle line) and first and third quartiles (boxes), and th whiskers show 1.5× the IQR above and below the box. Unpaired, two-sided Mann–Whitney U test P values are depicted in the plots, and the significant P value cutoff was set at 0.001.

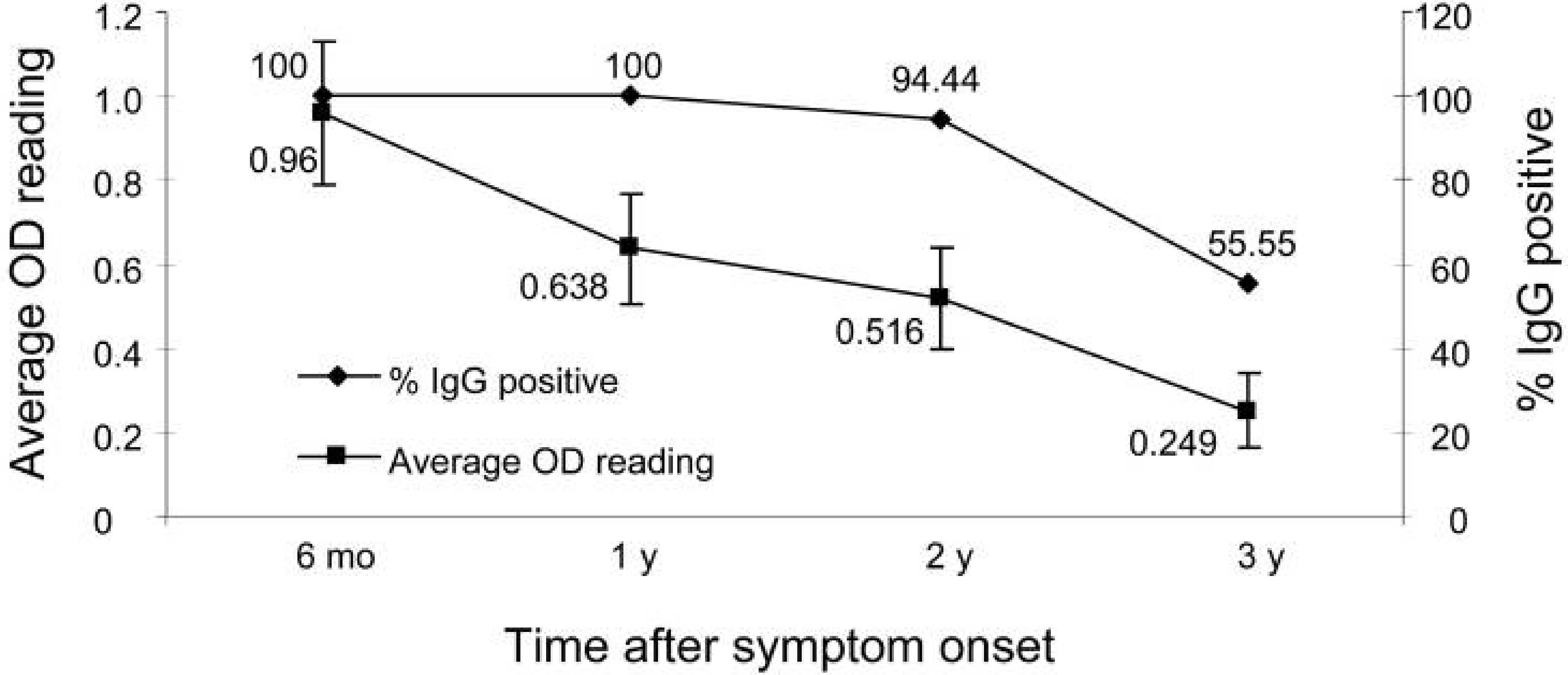
QX Long *et al*, *Nat. Med*, 2020

Immunity to coronaviruses

Immunity to common cold coronaviruses is very short-lived

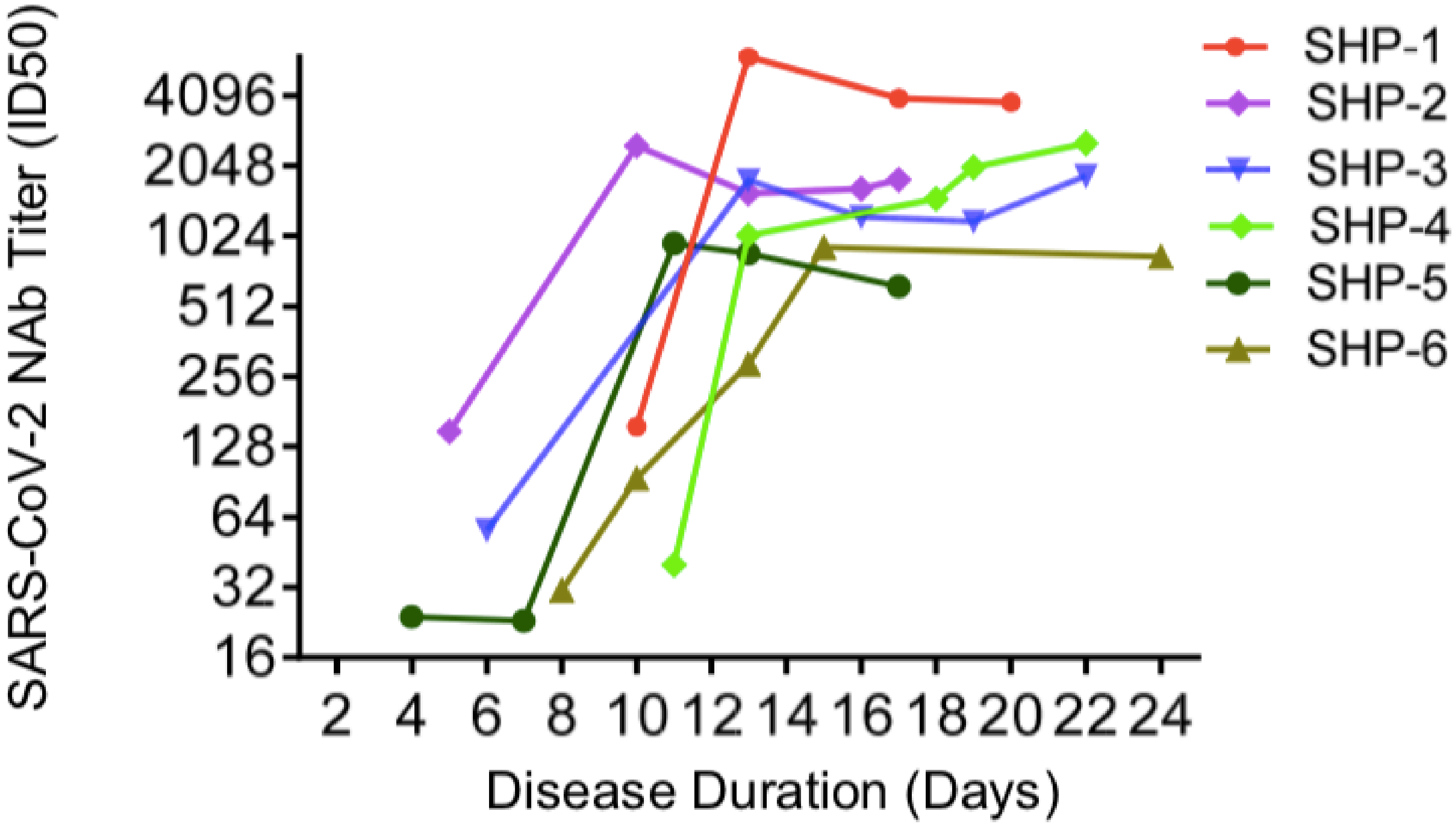
Antibody levels drop quickly and people lose immunity within 1 year

Duration of antibody response to SARS-CoV



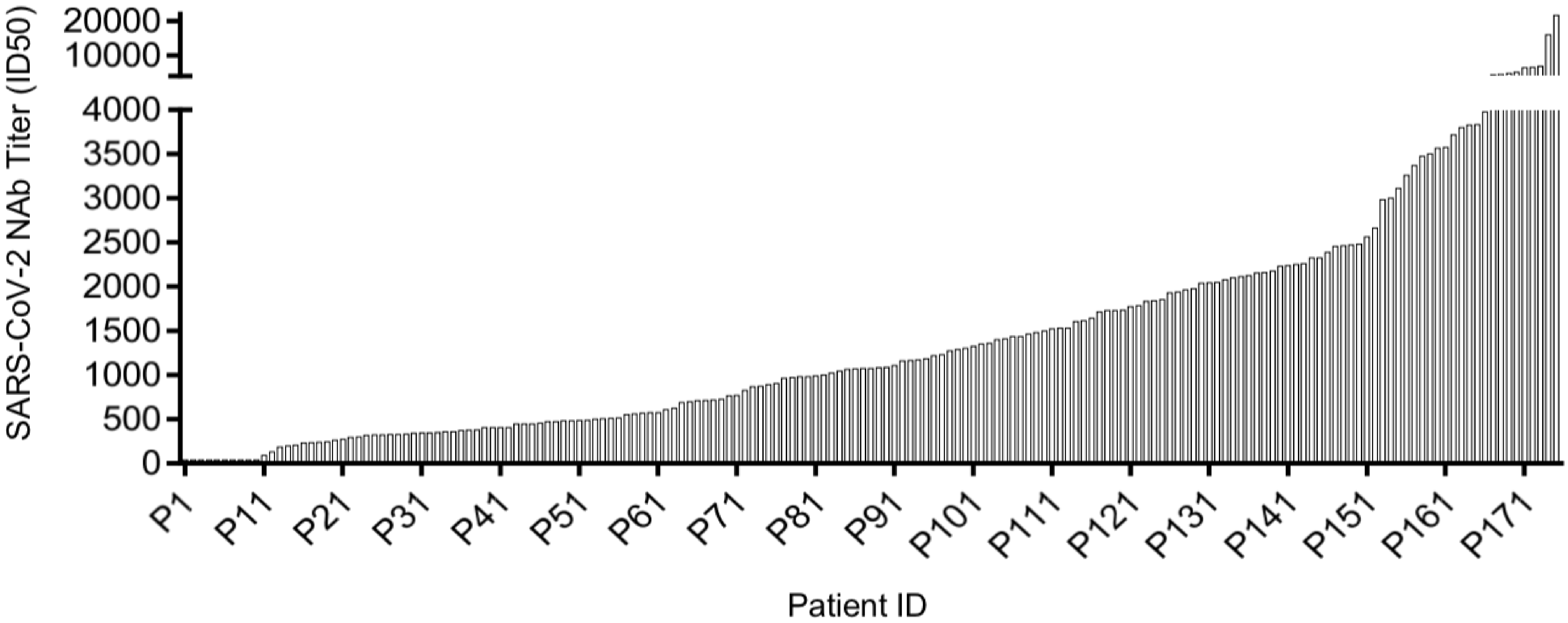
LP Wu *et al, EID* 2007

Induction of NAbs to SARS-CoV2 from day of onset of symptoms



F. Wu *et al, MedRxiv* 2020

Range of Nab titers in 175 patients at discharge



F. Wu *et al, MedRxiv* 2020

Science RESEARCH ARTICLES

Cite as: A. Chandrashekar *et al.*, *Science*
10.1126/science.abc4776 (2020).

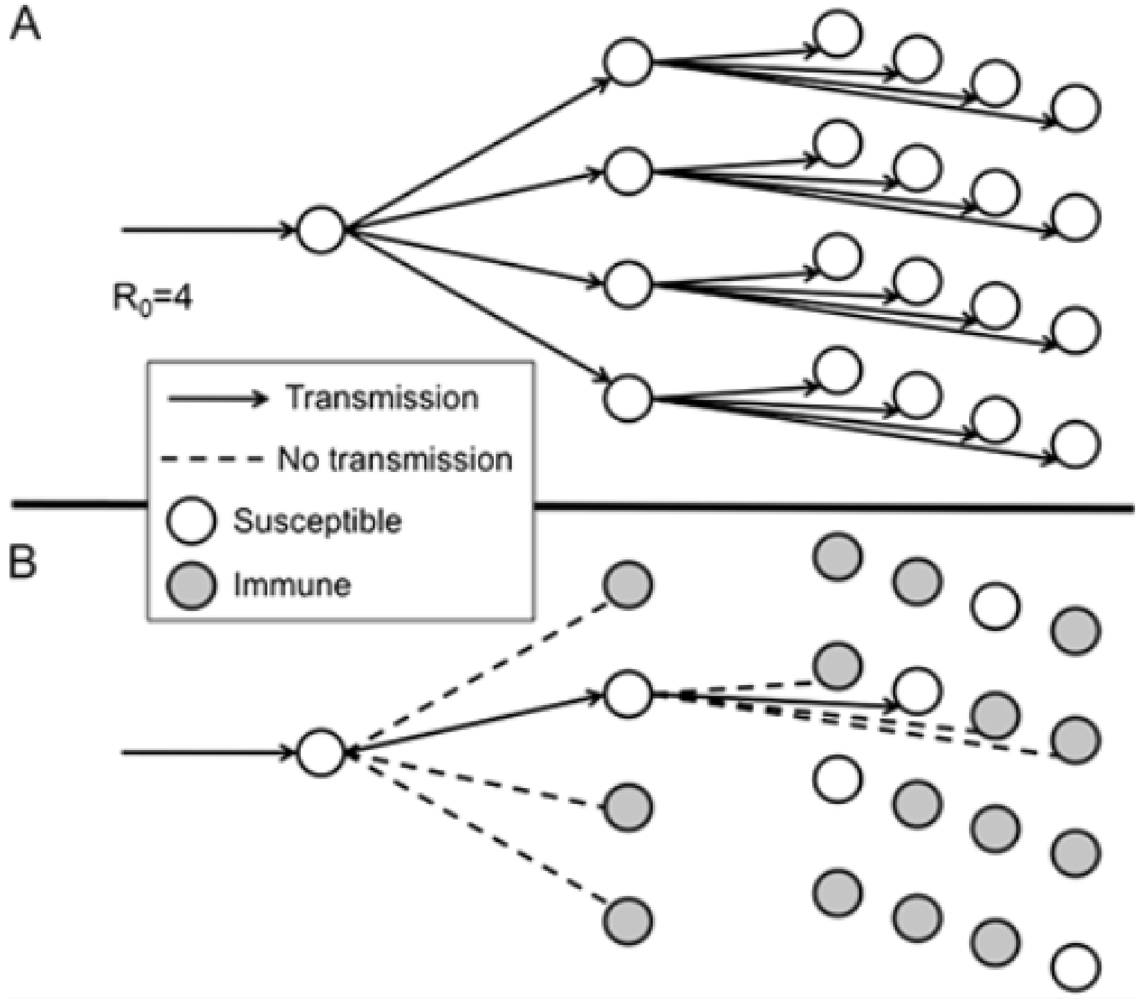
SARS-CoV-2 infection protects against rechallenge in rhesus macaques

Abishek Chandrashekar[1*], Jinyan Liu[1*], Amanda J. Martinot[1,2*], Katherine McMahan[1*], Noe B. Mercado[1*], Lauren Peter[1*], Lisa H. Tostanoski[1*], Jingyou Yu[1*], Zoltan Maliga[3], Michael Nekorchuk[4], Kathleen Busman-Sahay[4], Margaret Terry[4], Linda M. Wrijil[2], Sarah Ducat[2], David R. Martinez[5], Caroline Atyeo[3,6], Stephanie Fischinger[6], John S. Burke[6], Matthew D. Slein[6], Laurent Pessaint[7], Alex Van Ry[7], Jack Greenhouse[7], Tammy Taylor[7], Kelvin Blade[7], Anthony Cook[7], Brad Finneyfrock[7], Renita Brown[7], Elyse Teow[7], Jason Velasco[7], Roland Zahn[8], Frank Wegmann[8], Peter Abbink[1], Esther A. Bondzie[1], Gabriel Dagotto[1,3], Makda S. Gebre[1,3], Xuan He[1], Catherine Jacob-Dolan[1,3], Nicole Kordana[1], Zhenfeng Li[1], Michelle A. Lifton[1], Shant H. Mahrokhian[1], Lori F. Maxfield[1], Ramya Nityanandam[1], Joseph P. Nkolola[1], Aaron G. Schmidt[6,9], Andrew D. Miller[10], Ralph S. Baric[5], Galit Alter[6,9], Peter K. Sorger[3], Jacob D. Estes[4], Hanne Andersen[7], Mark G. Lewis[7], Dan H. Barouch[1,6,9†]

Herd immunity

Term	Symbolic Expression	Definition
Basic reproduction number	R_0	Number of secondary cases generated by a typical infectious individual when the rest of the population is susceptible (ie, at the start of a novel outbreak)
Critical vaccination level	V_c	Proportion of the population that must be vaccinated to achieve herd immunity threshold, assuming that vaccination takes place at random

Herd immunity



Vc = 1 – 1/Ro = ‘herd immunity threshold’

Some Ro values

Seasonal influenza A	~2
Hepatitis C	2
Ebola	2
1918/19 pandemic flu.	~3
HIV	4
SARS	4
Mumps	10
Measles	18

> Emerg Infect Dis. 2020 Apr 7;26(7). doi: 10.3201/eid2607.200282. Online ahead of print.

High Contagiousness and Rapid Spread of Severe Acute Respiratory Syndrome Coronavirus 2

Steven Sanche, Yen Ting Lin, Chonggang Xu, Ethan Romero-Severson, Nick Hengartner, Ruian Ke

PMID: 32255761 DOI: 10.3201/eid2607.200282

Free article

Abstract

Severe acute respiratory syndrome coronavirus 2 is the causative agent of the 2019 novel coronavirus disease pandemic. Initial estimates of the early dynamics of the outbreak in Wuhan, China, suggested a doubling time of the number of infected persons of 6-7 days and a basic reproductive number (R_0) of 2.2-2.7. We collected extensive individual case reports across China and estimated key epidemiologic parameters, including the incubation period. We then designed 2 mathematical modeling approaches to infer the outbreak dynamics in Wuhan by using high-resolution domestic travel and infection data. Results show that the doubling time early in the epidemic in Wuhan was 2.3-3.3 days. Assuming a serial interval of 6-9 days, we calculated a median R_0 value of 5.7 (95% CI 3.8-8.9). We further show that active surveillance, contact tracing, quarantine, and early strong social distancing efforts are needed to stop transmission of the virus.

Keywords: 2019 novel coronavirus disease; COVID-19; China; SARS-CoV-2; Wuhan; modeling; respiratory infections; severe acute respiratory syndrome coronavirus 2; transmission potential; viruses; zoonoses.

Ro directly affects the required vaccine coverage for elimination

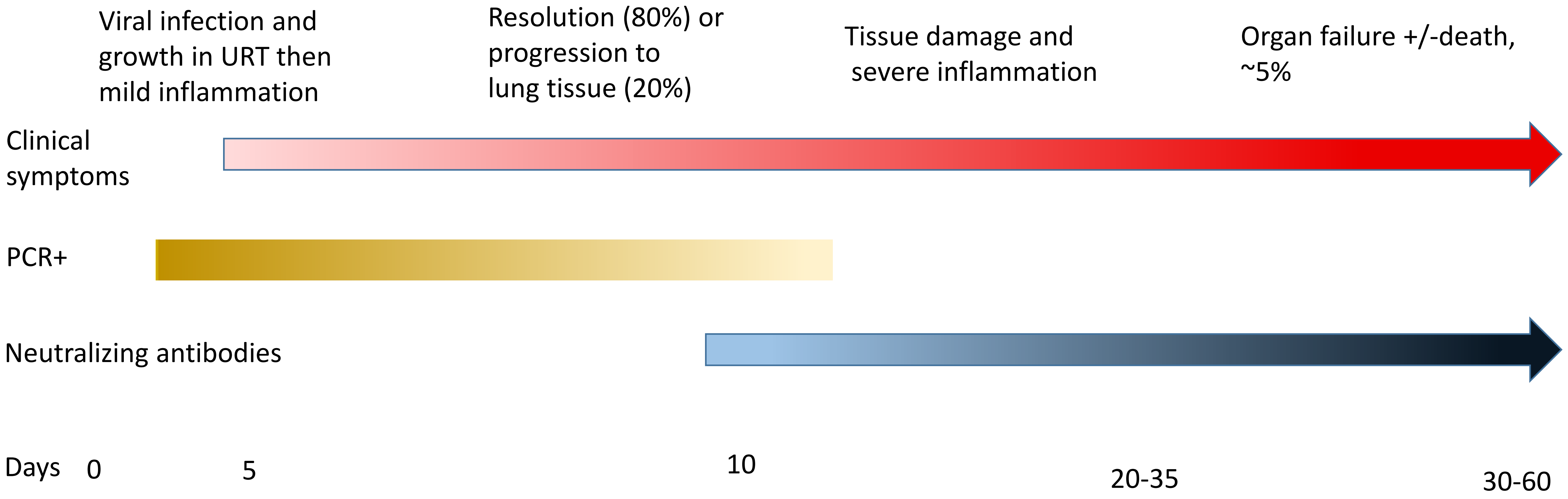
Ro	Vc
2.5	60%
5.7	82%

Critical vaccination level of $1 - 1/R_0$ changes if vaccine efficacy (E) is <100%

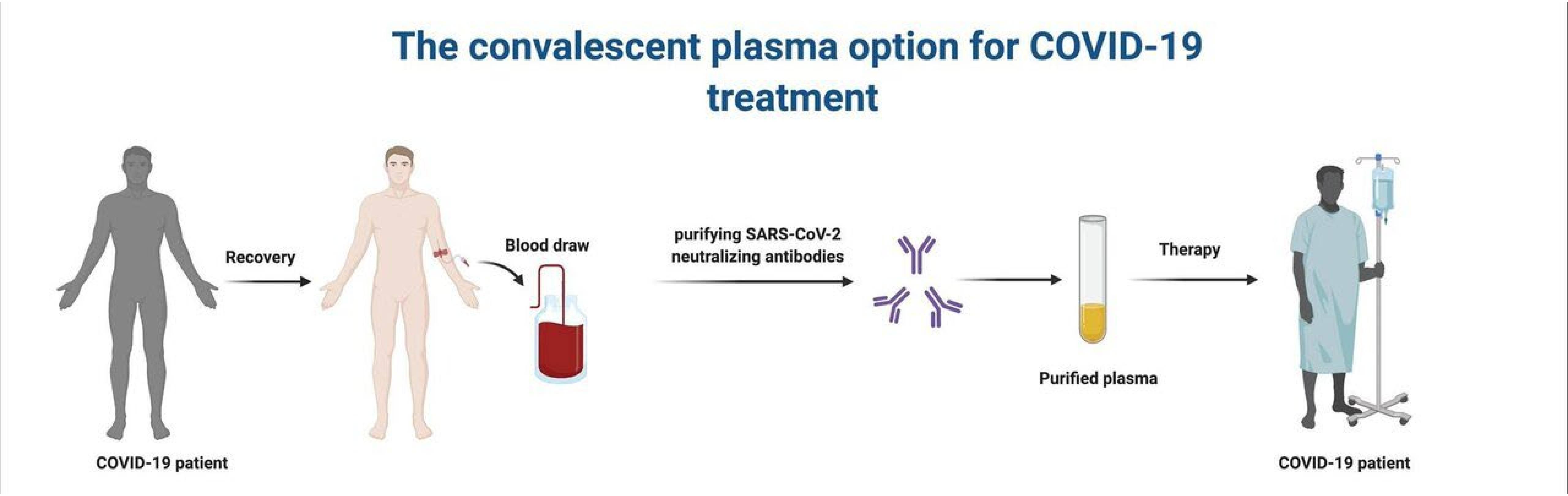
Treatment options

- Passive immunity, anti-viral drugs (Remdesevir) EARLY
- Dexamethasone LATE

Progression of COVID in a patient



Passive vaccination

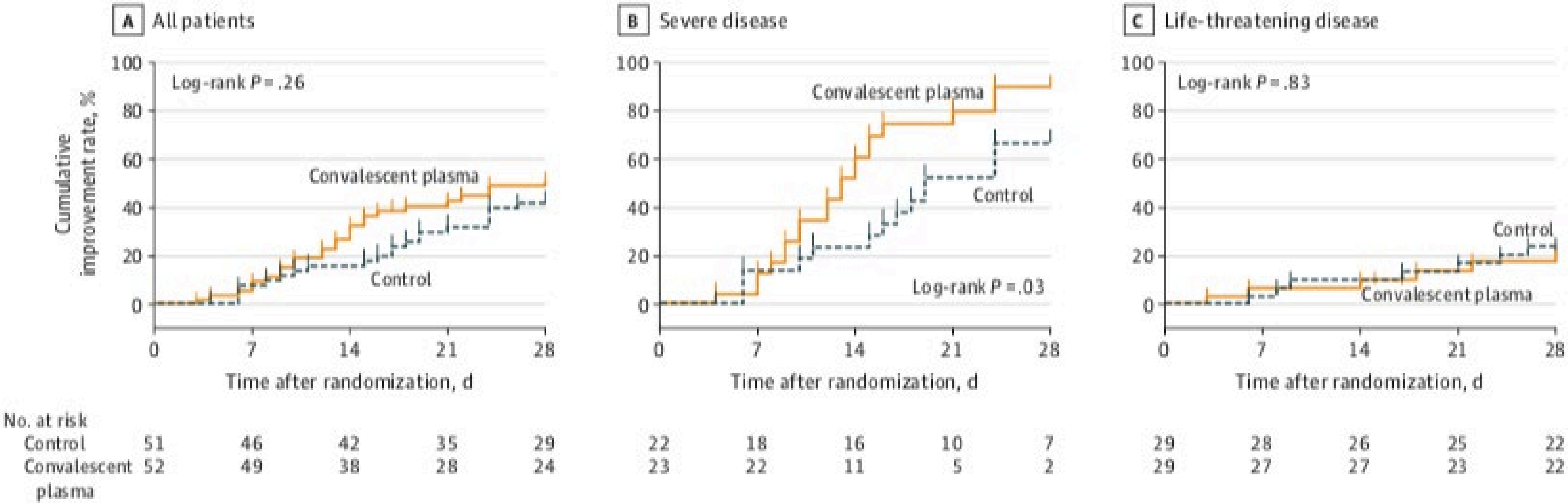


JAMA | Original Investigation

Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19
A Randomized Clinical Trial

Ling Li, MD, PhD; Wei Zhang, MD; Yu Hu, MD, PhD; Xunliang Tong, MD, PhD; Shangen Zheng, MD; Juntao Yang, PhD; Yujie Kong, MD;
Lili Ren, PhD; Qing Wei, MD; Heng Mei, MD, PhD; Caiying Hu, MD; Cuihua Tao, MD; Ru Yang, MD; Jue Wang, MD; Yongpei Yu, PhD;
Yong Guo, PhD; Xiaoxiong Wu, MD; Zhihua Xu, MD; Li Zeng, MD; Nian Xiong, MD; Lifeng Chen, MD; Juan Wang, MD; Ning Man, MD;
Yu Liu, PhD; Haixia Xu, MD; E. Deng, MS; Xuejun Zhang, MS; Chenyue Li, MD; Conghui Wang, PhD; Shisheng Su, PhD; Linqi Zhang, PhD;
Jianwei Wang, PhD; Yanyun Wu, MD, PhD; Zhong Liu, MD, PhD

Figure 2. Time to Clinical Improvement in Patients With COVID-19



Passive Vaccination
(Monoclonal antibody)

A randomized, double-blind, placebo-controlled, study evaluating the efficacy and safety of otilimab IV in patients with severe pulmonary COVID-19 related disease	GSK3196165 (Otilimab), monoclonal antibody	GlaxoSmith Kline

Also, Eli Lilly and Regeneron are developing MAbs for clinical trial.

Vaccines

47 in clinical trial

8 Phase III trials

- mRNA (Moderna)
- mRNA (Biontech/Pfizer/FosunPharma
- Adenovirus 5 (‘Ad5’), vectored (CanSinoBio)
- Chimp Adenovirus vectored (ChAdOx1) (AstraZeneca, University of Oxford)
- Whole virus inactivated (Sinopharm) – 2 separate trials
- Whole virus inactivated (Sinovac)
- BCG (Murdoch Children’s Research Institute)

Potential vaccine problems

1. Lack of functional antibodies
2. Non-persisting antibody responses
3. Lack of immunological memory
4. Antibody-dependent enhancement

Antibody Dependent Enhancement (ADE) of coronavirus infections

Non-neutralizing antibodies are produced and enhance viral entry into target cells via Fcγ receptors, seen in:

- dengue virus,
- human immunodeficiency virus,
- influenza virus,
- other alpha and flaviviruses,
- SARS-CoV,
- Ebola virus

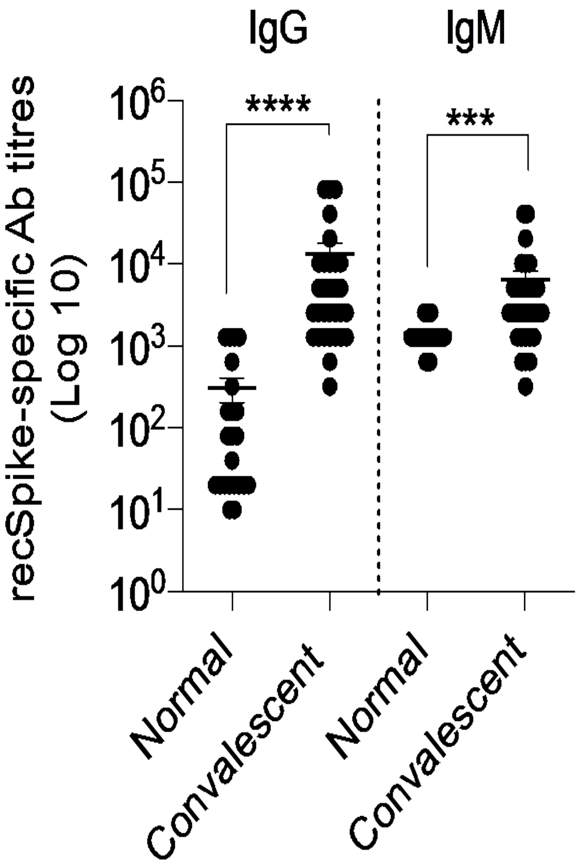
*Can be prevented by masking non-neutralizing epitopes, or immunofocusing

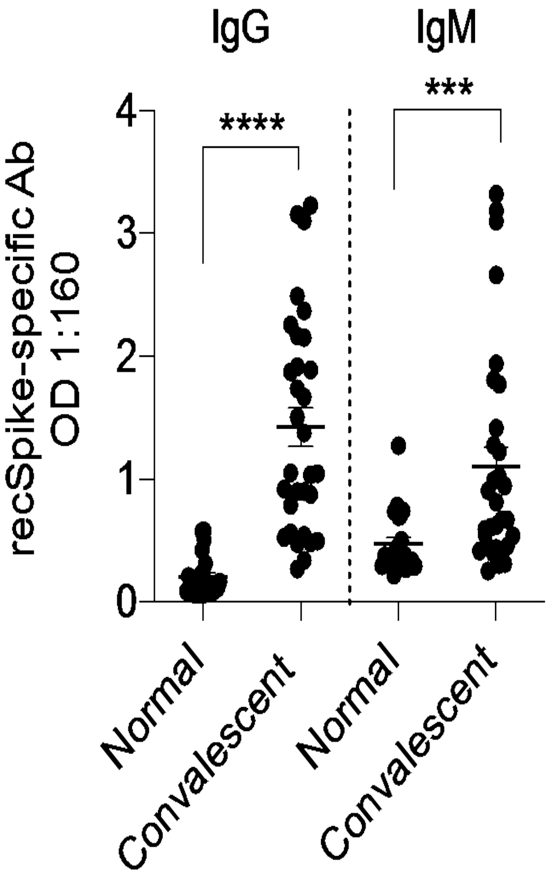
Designing a vaccine focused on neutralizing epitopes

Convalescent Plasma patient details

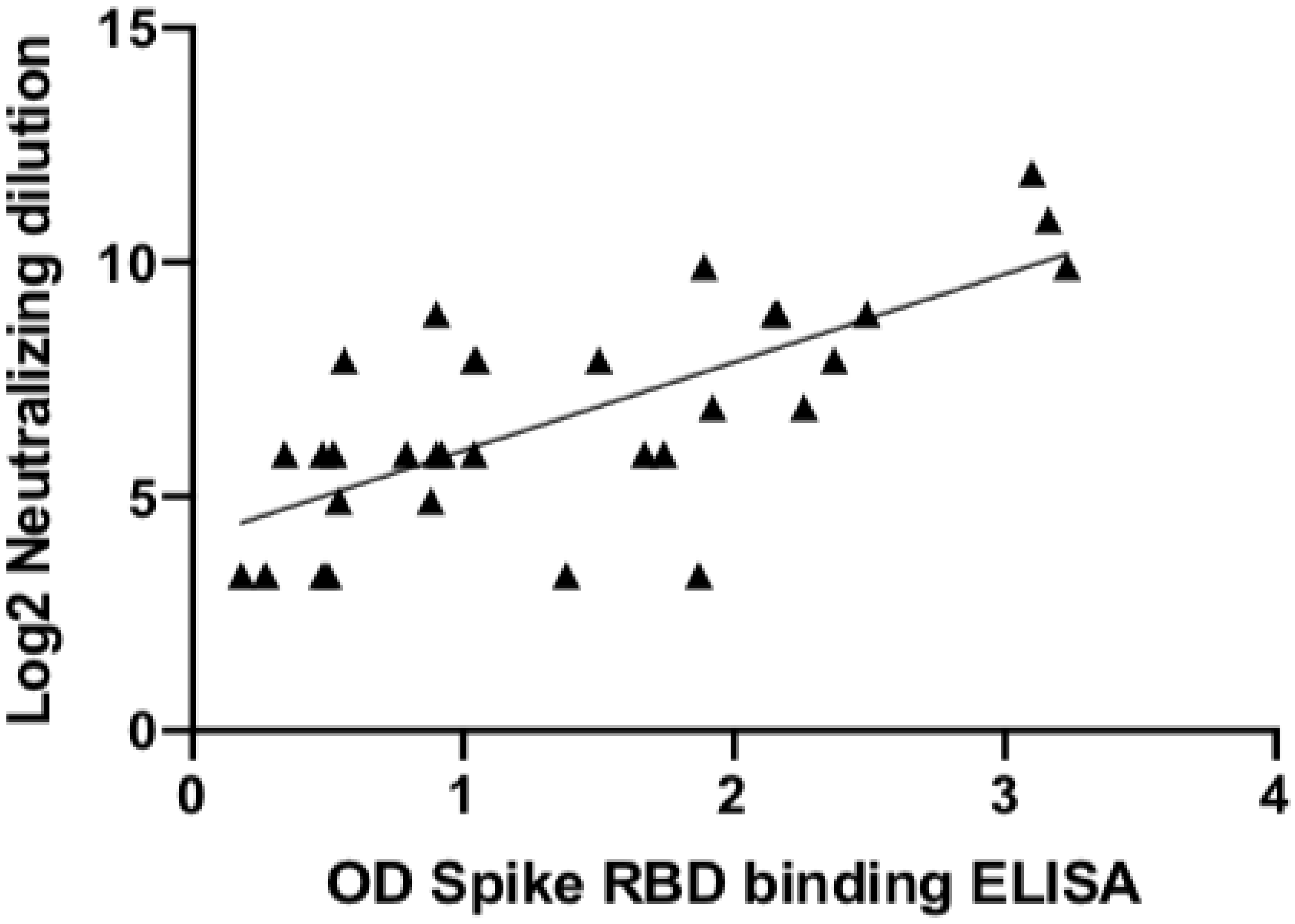
- 34 samples, collected in April and May 2020
- Age range: 21-78 years
- 55% male
- ~1/4 hospitalized
- All symptomatic
- None treated with anti-virals, one treated with HCQ
- Samples taken 22-44 days post recovery

Antibodies in COVID-19 Convalescent Plasma recognize RBD





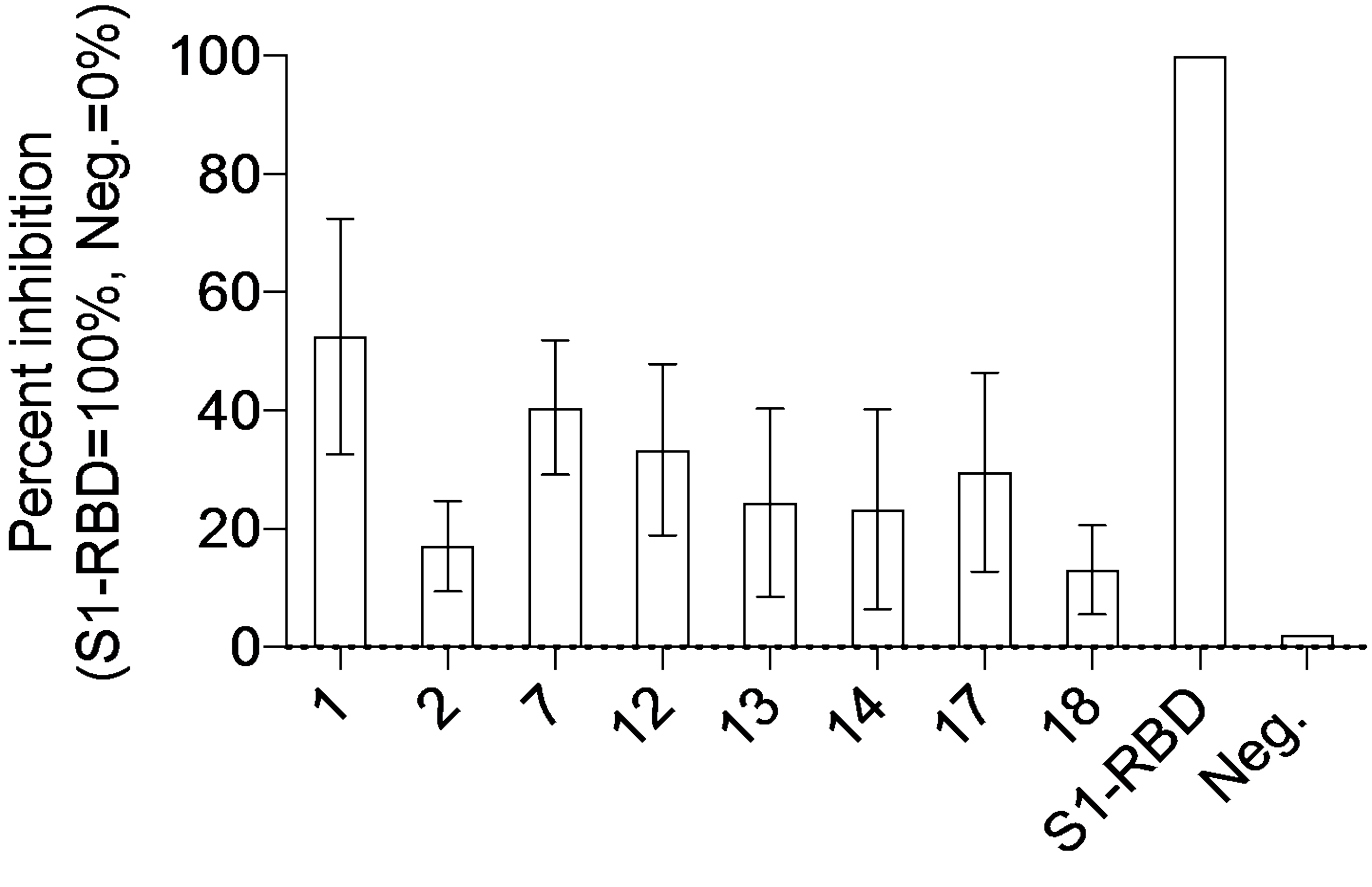
Correlation between neutralization titre and Spike protein RBD



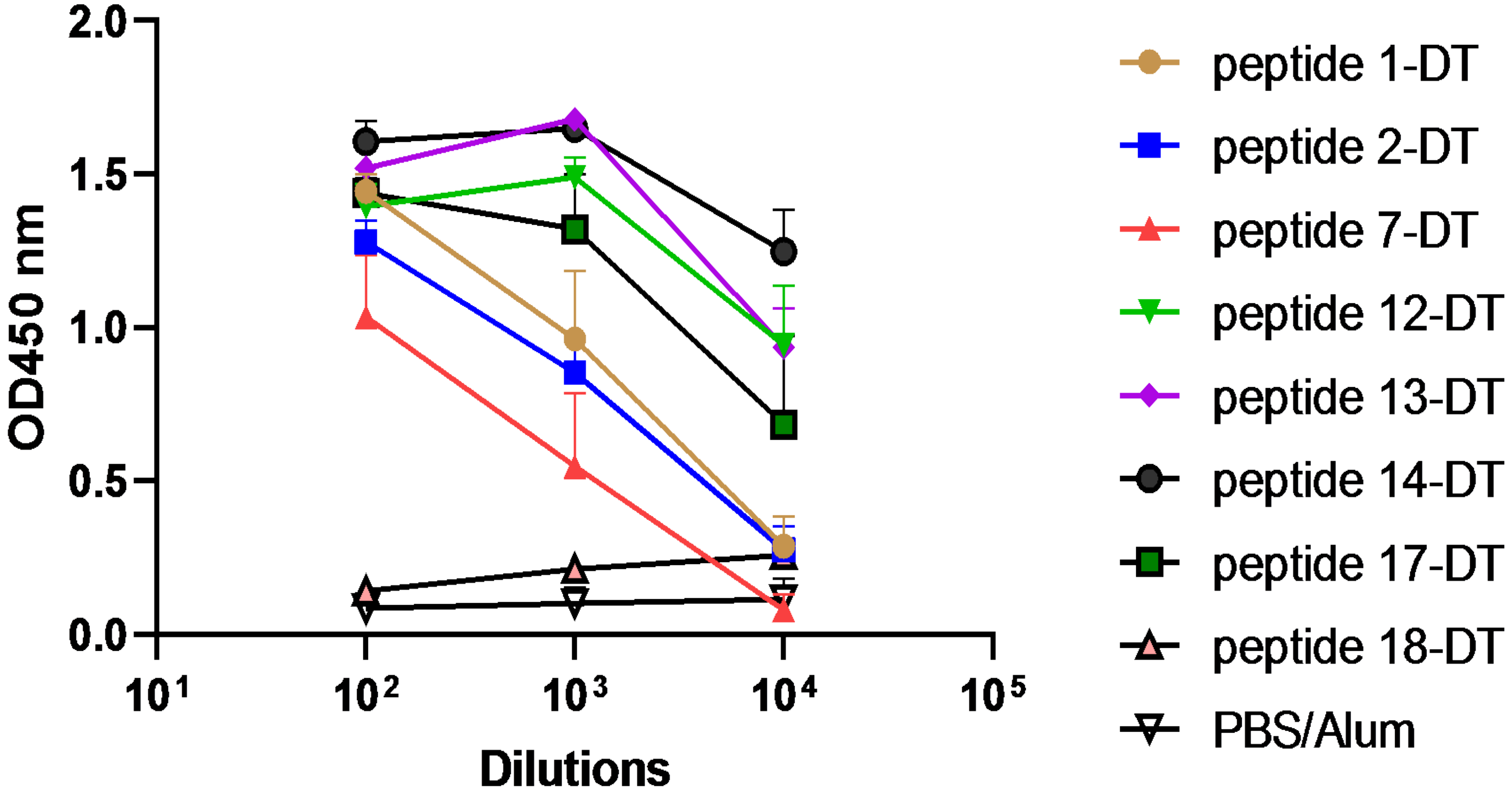
Sequence of Receptor Binding Domain (RBD) of SARS-CoV-2 Spike protein

```
NITNLCPFGE VFNATRFASV YAWNRKRISN CVADYSVLYN SASFSTFKCY GVSPTKLNDL
CFTNVYADSF VIRGDEVRQI APGQTGKIAD YNYKLPDDFT GCVIAWNSNN LDSKVGGNYN
YLYRLFRKSN LKPFERDIST EIYQAGSTPC NGVEGFNCYF PLQSYGFQPT NGVGYQPYRV
VVLSFELLHA PATV
```

Inhibition of convalescent plasma antibodies binding to RBD by specific peptides

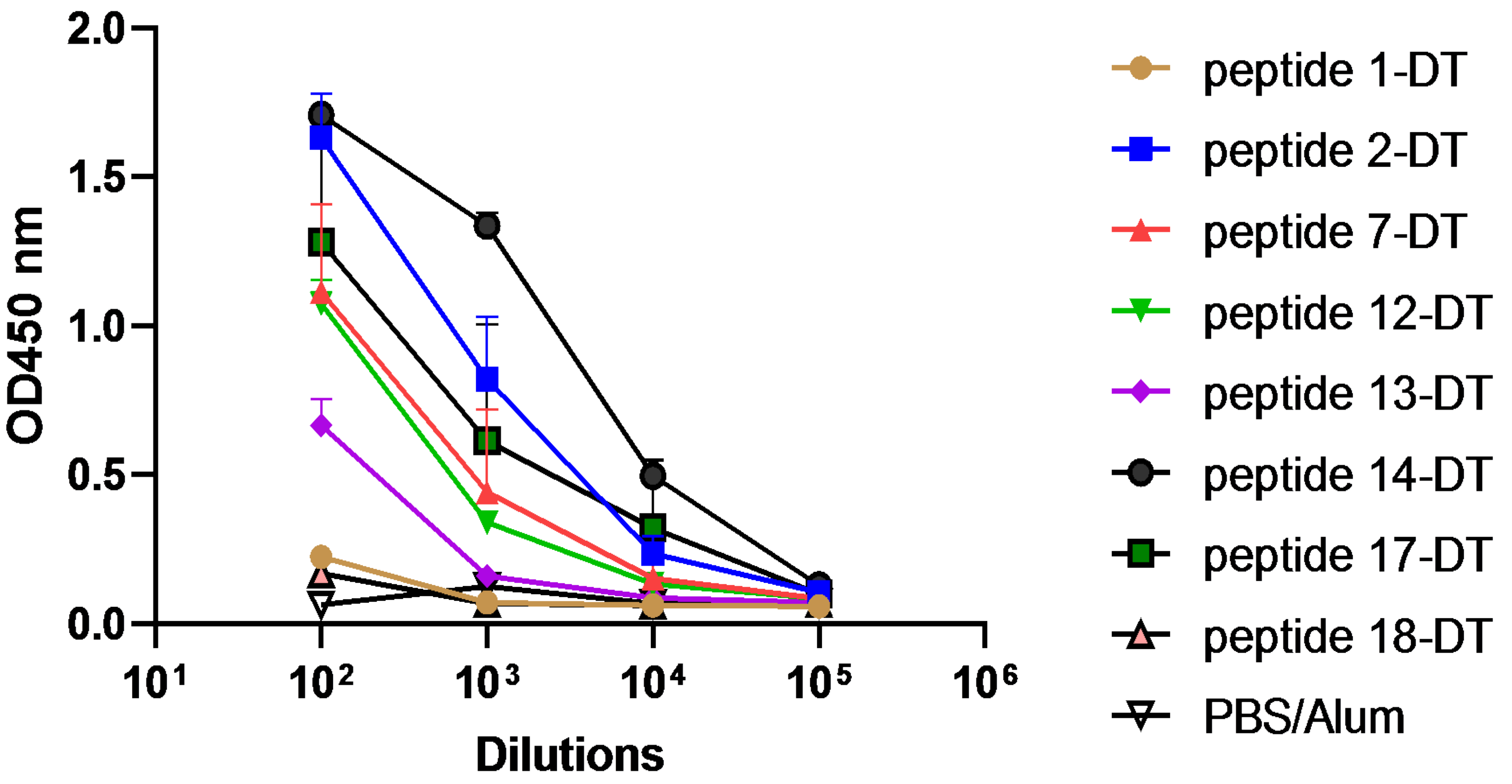


Peptide-specific serum IgG after second boost*



** Biotinylated peptides were immobilized on streptavidin-coated ELISA plates*

Recognition of recRBD by peptide-DT conjugates*



**Sera were taken 7 days after the third immunization*

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Chris Day

Gold Coast University Hospital

John Gerrard
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Mike Joyce
Stephanie Yanow

University of Queensland

Ahmed Shalash
Mariusz Skwarczynski
Istvan Toth

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