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An Update on Long COVID

A clinical perspective

22 November 2023

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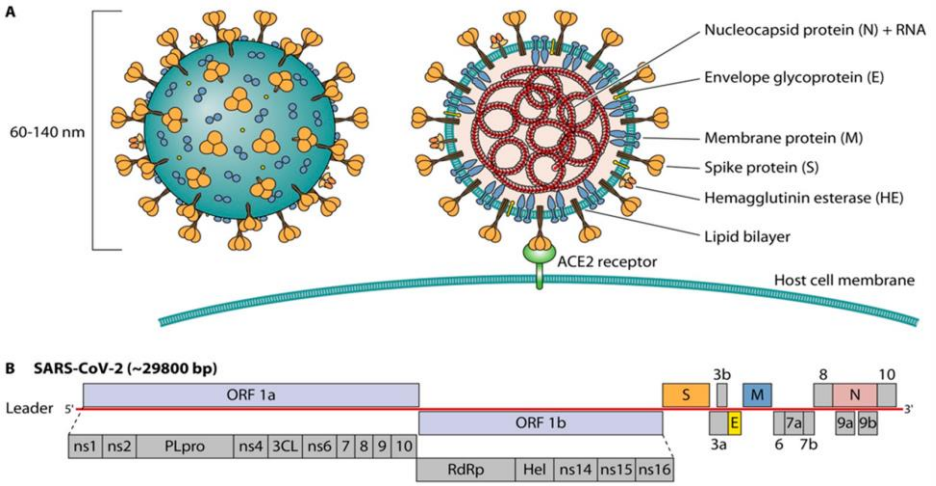
COVID-19



- Caused by SARS-CoV-2 virus
- Causes a disease with a wide spectrum of severity
- Asymptomatic (40-80%) to critical illness (~5%)
- Case fatality rate approximately 2.3%
- Different SARS-CoV-2 variants associated with varying risks of severe disease

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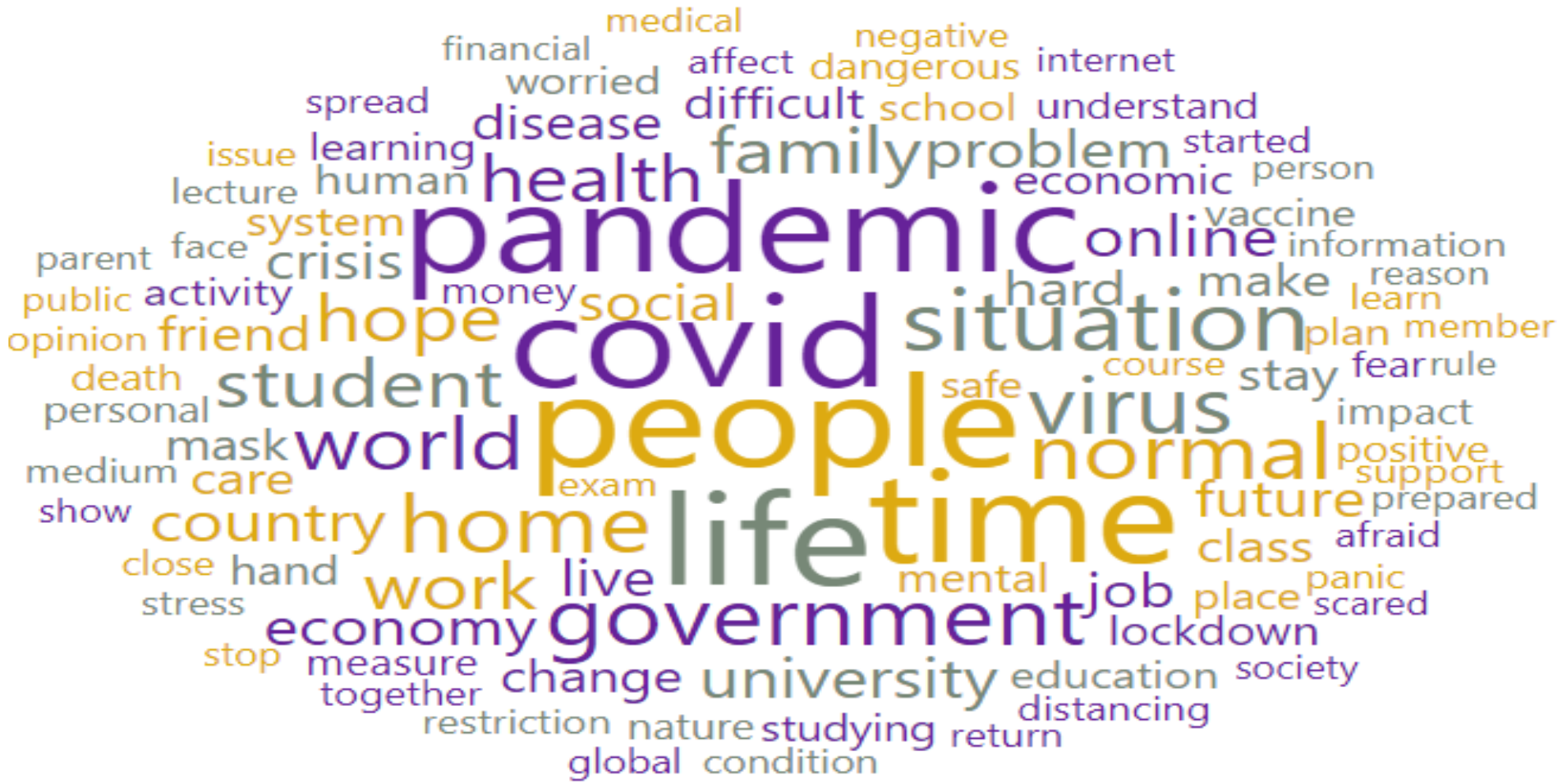
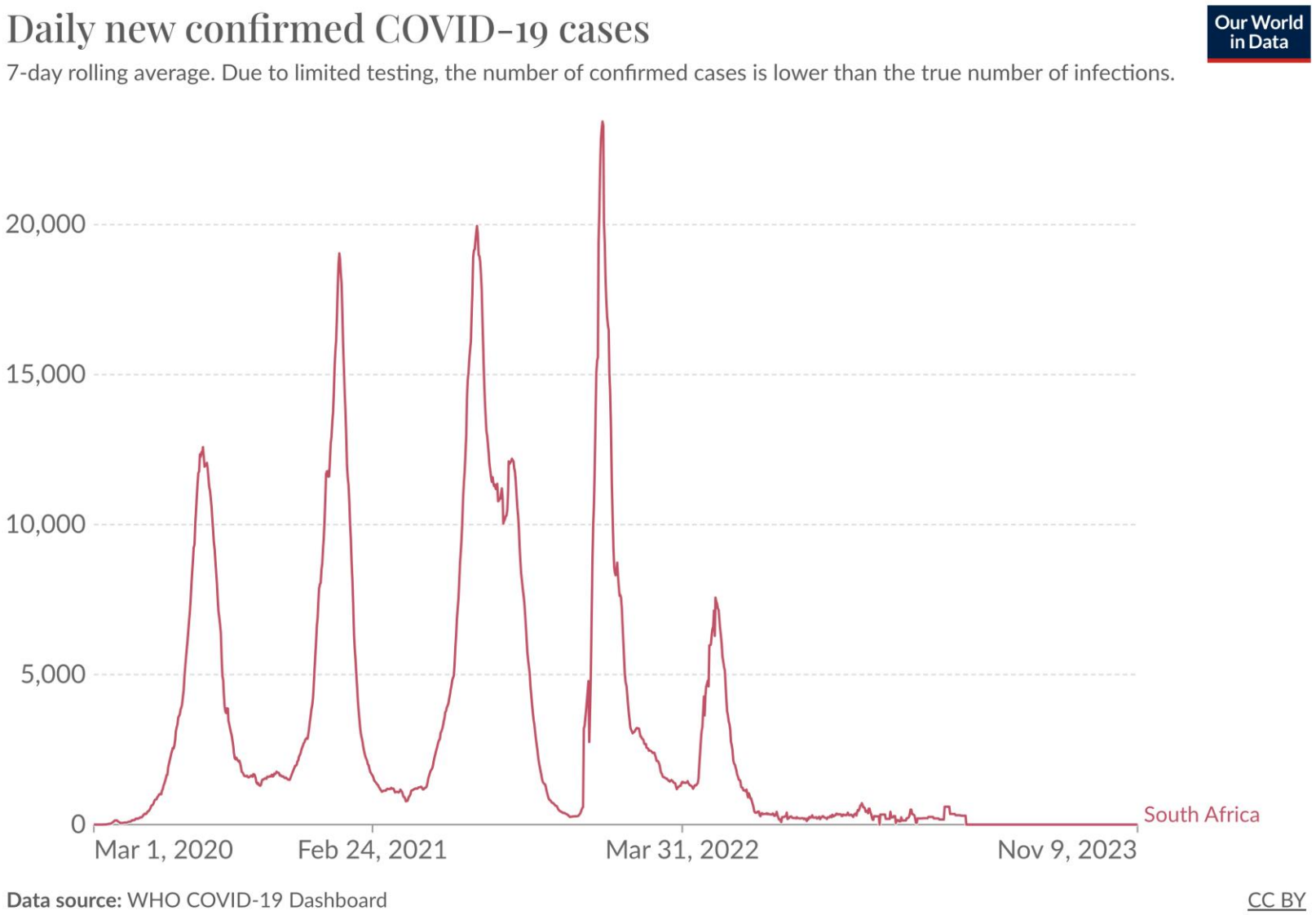
Davis et al., Nat Rev Micro, 2023
Gitman et al., Diagnostics, 2021



Aristovnik et al., Sustainability, 2020



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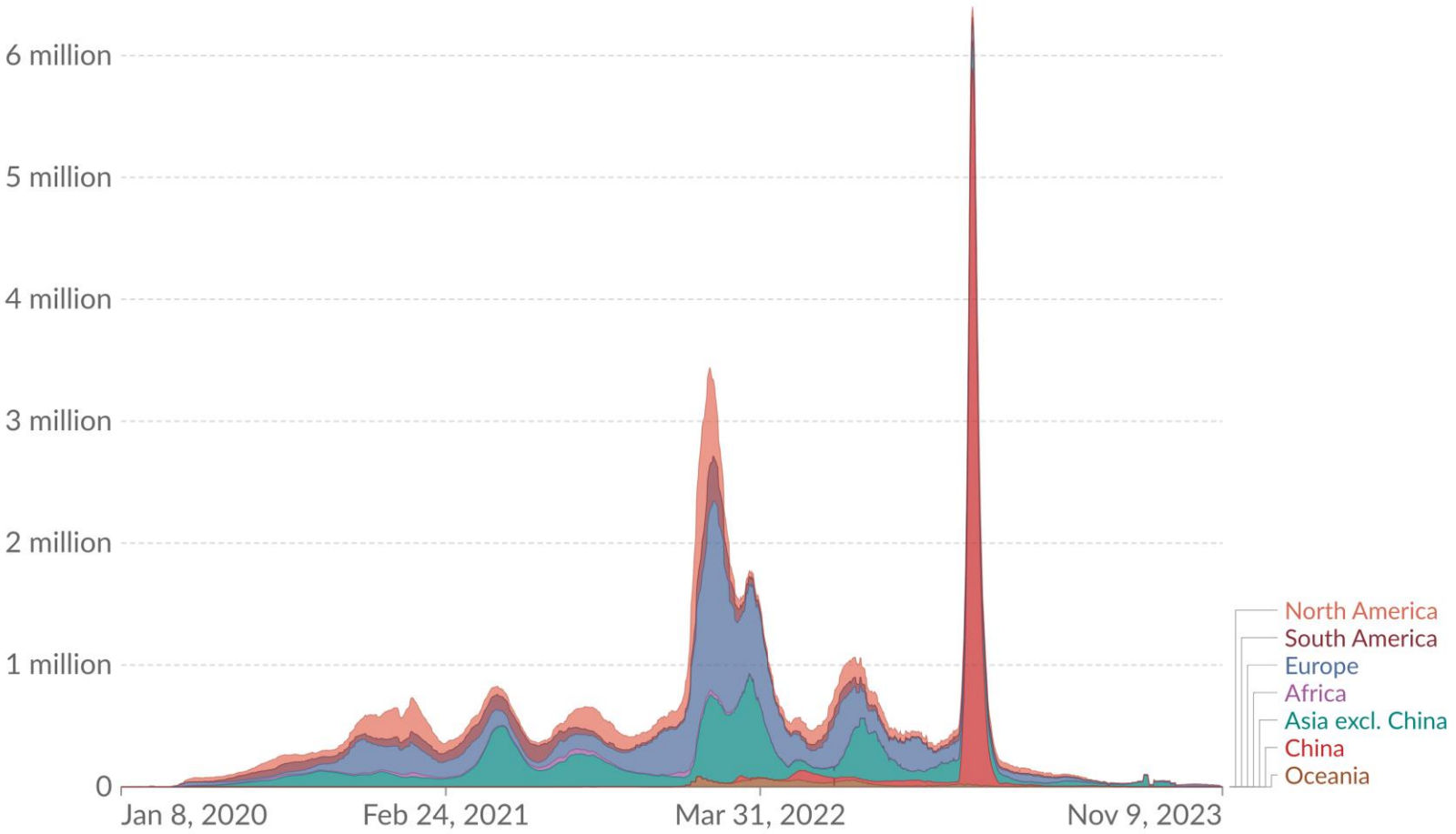
Data source: Our World in Data

Daily confirmed COVID-19 cases by world region

Our World in Data

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



Data source: WHO COVID-19 Dashboard

OurWorldInData.org/coronavirus | CC BY

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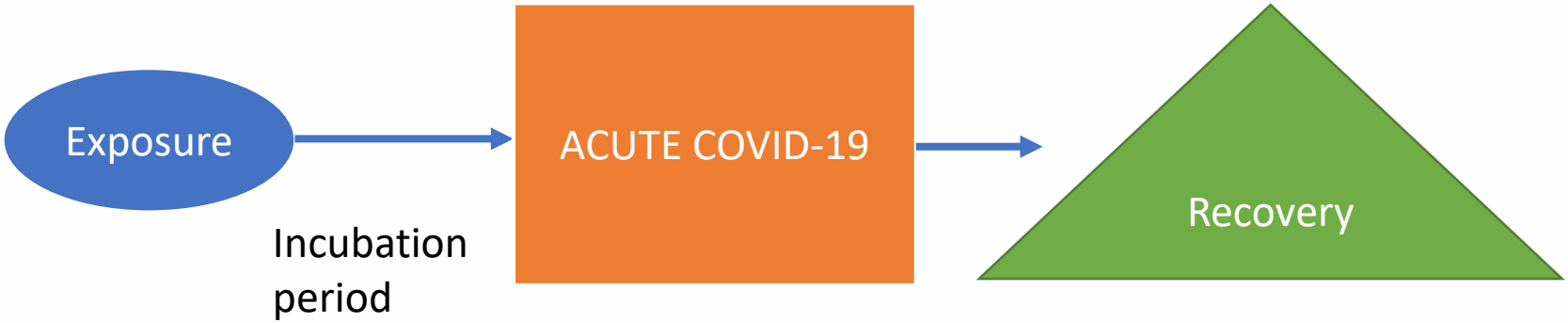
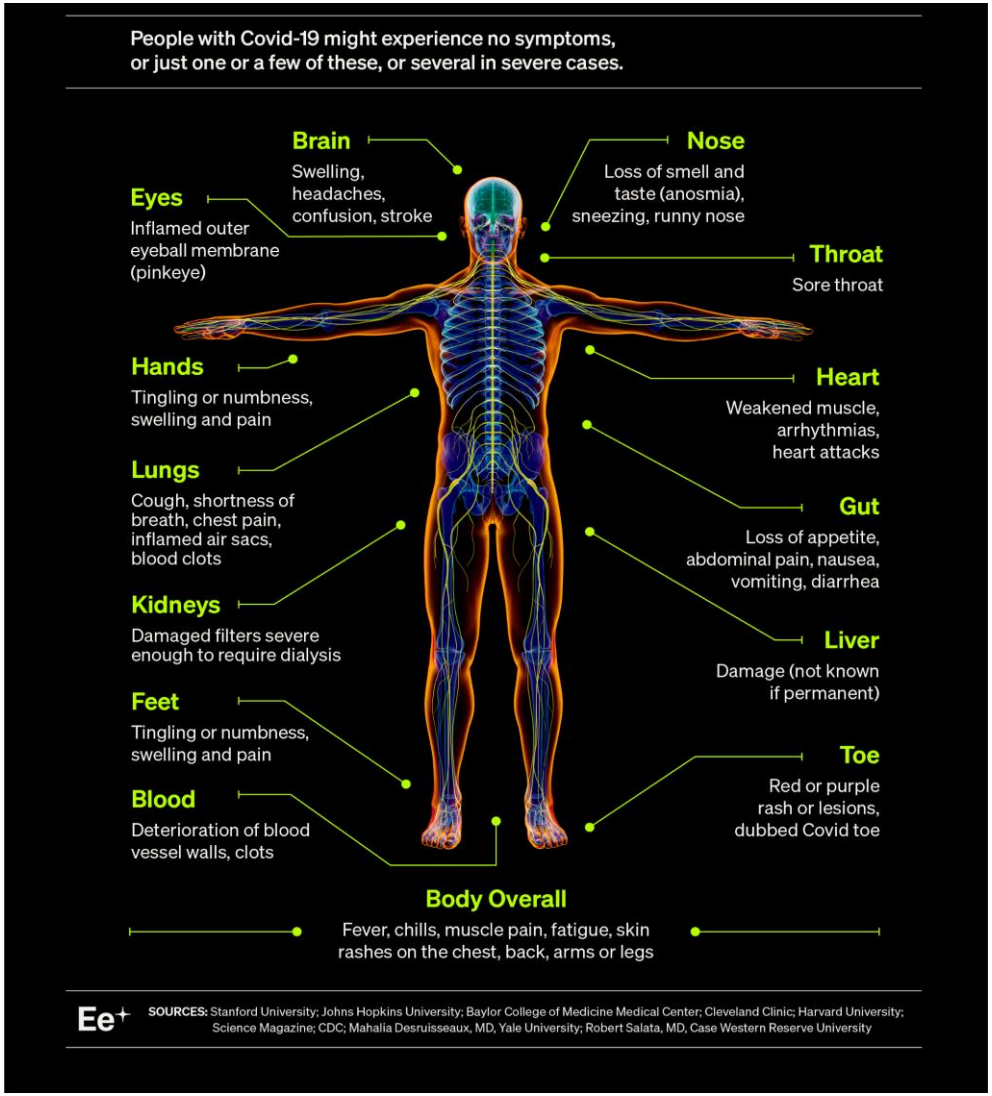
Data source: Our World in Data

Stages of COVID-19 disease and recovery



Stages of COVID-19 disease and recovery

Acute COVID-19



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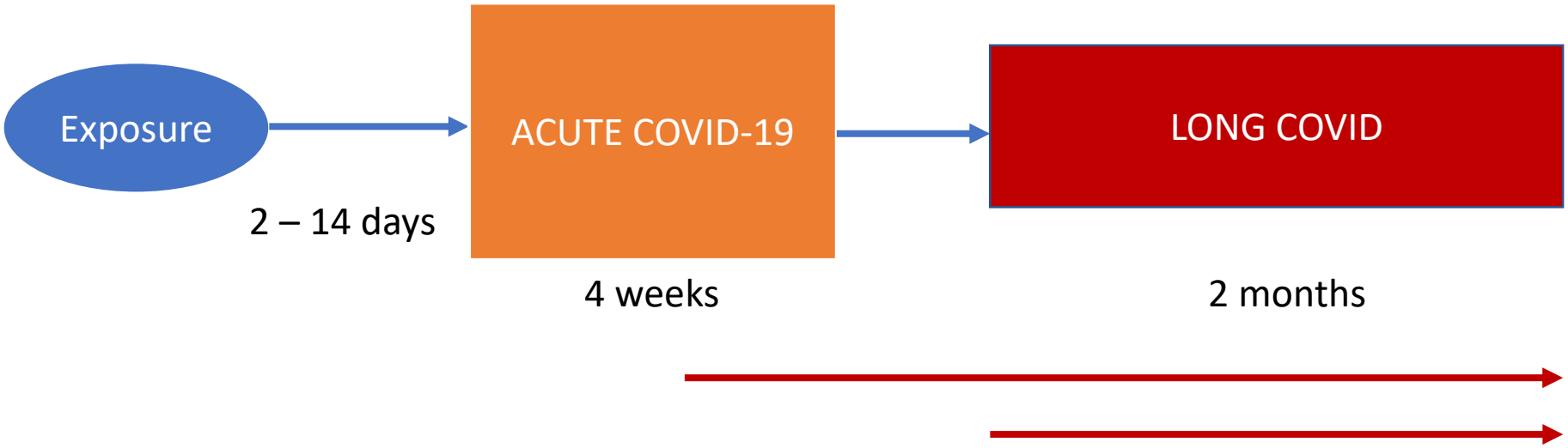
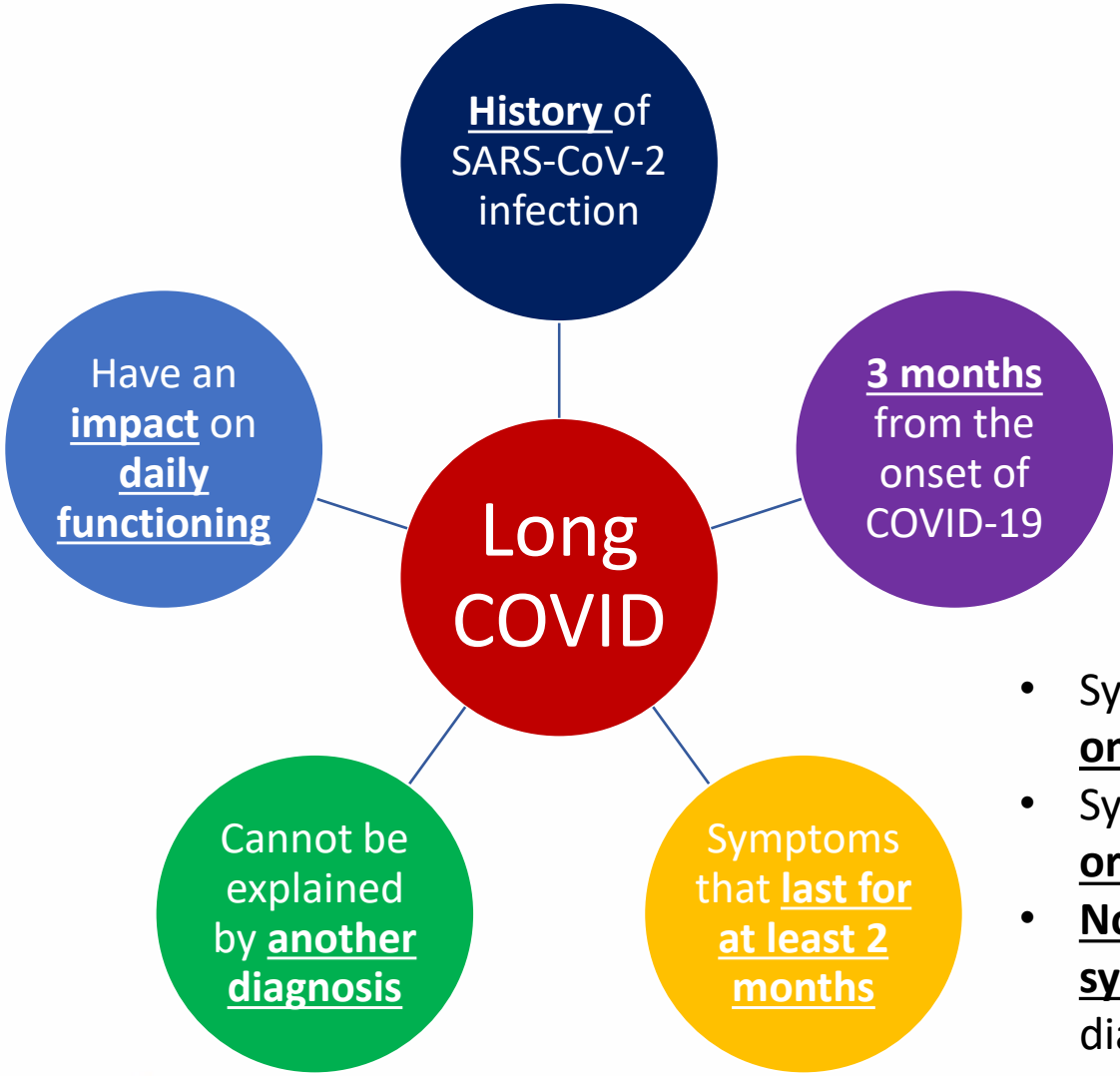
What is Long COVID?

- Postacute COVID-19
- Postacute sequelae of SARS-CoV-2 infection
- Chronic COVID-19
- Post-COVID syndrome
- Post COVID-19 Condition (PCC)

Definitions



Definitions



- Symptoms may be **new onset** or **persist**
- Symptoms **may fluctuate or relapse**
- **No minimum number of symptoms** required for diagnosis

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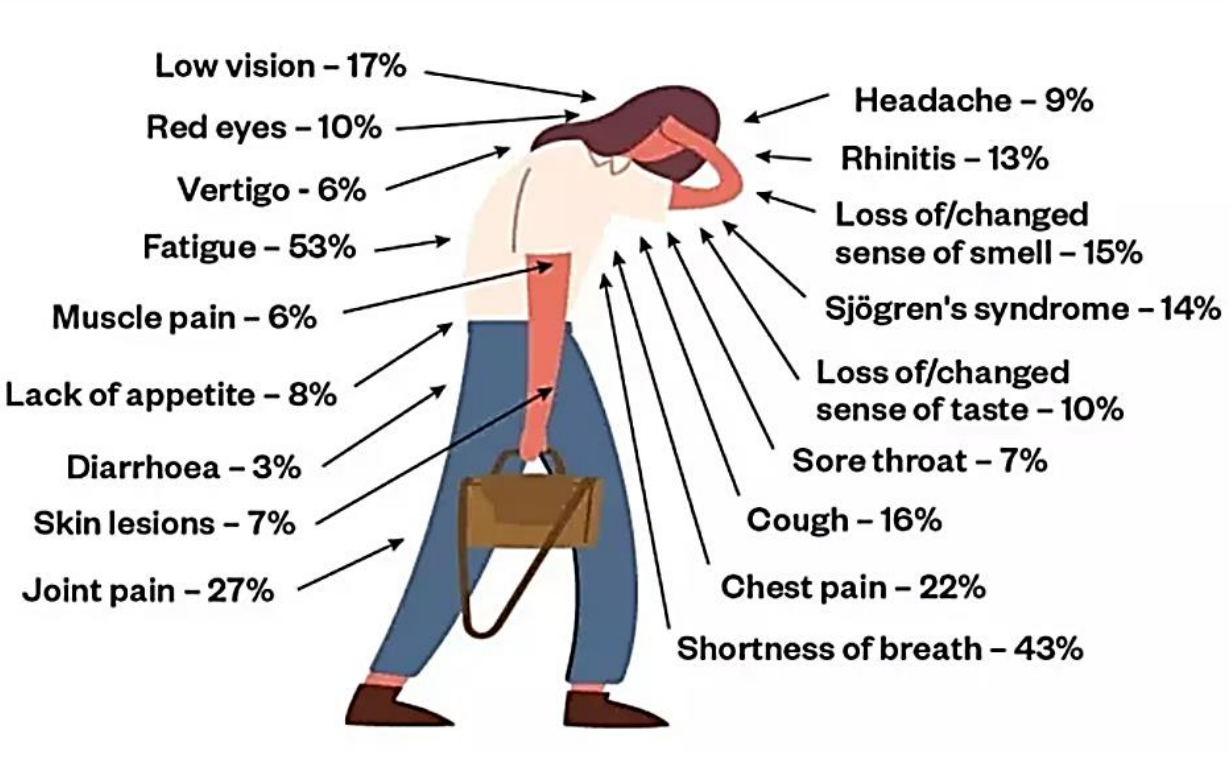
WHO case definition of Post COVID-19 Condition 2021

Manifestations



- Study of a cohort of 3762 people in 56 countries
- Time to recovery in >90% exceeded 8 months
- Most frequent symptoms after 6 months:
  - Fatigue
  - Post-exertional malaise
  - Cognitive dysfunction & memory problems

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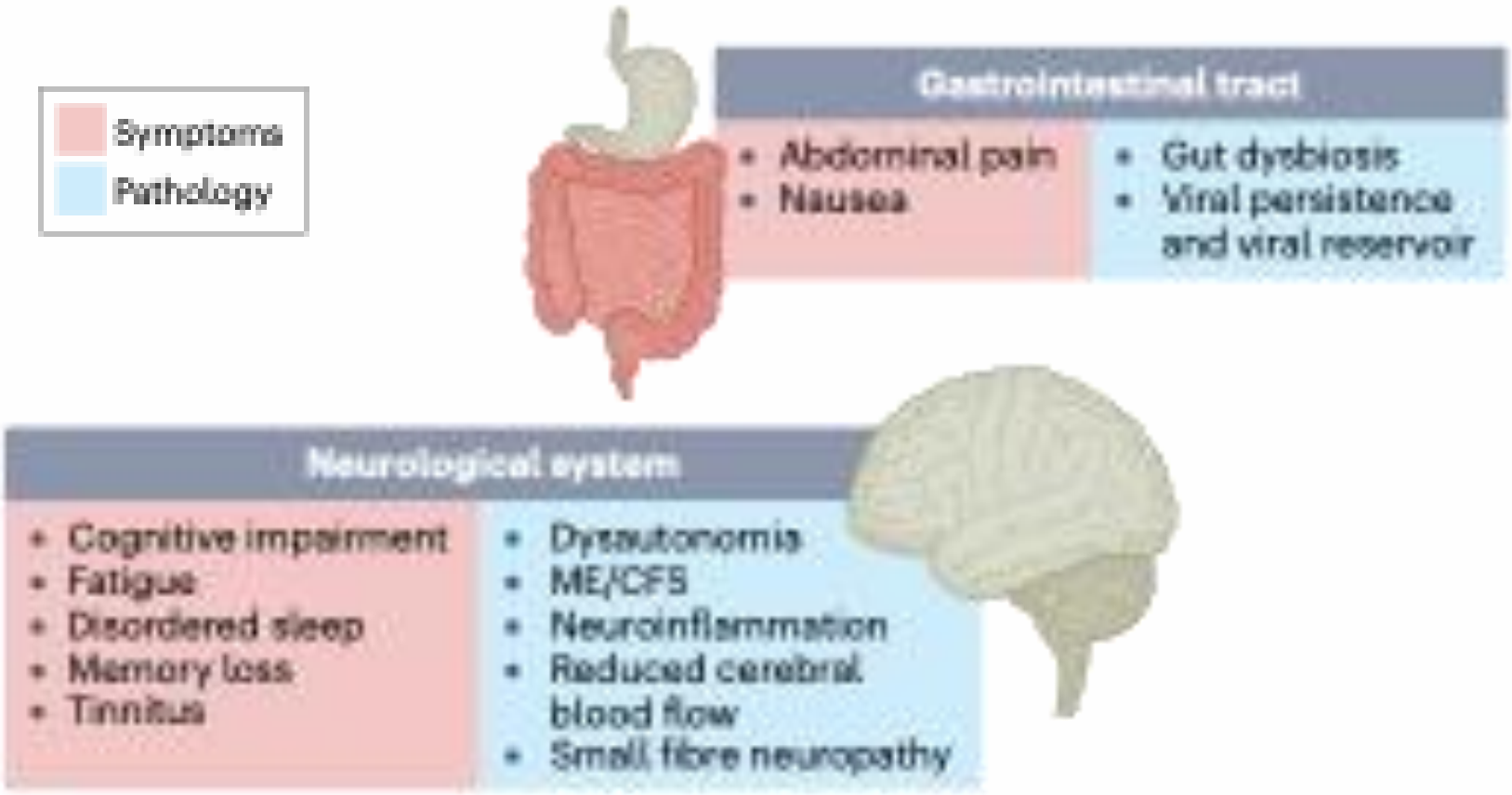
Davis et al., eClinicalMedicine, 2021

Manifestations



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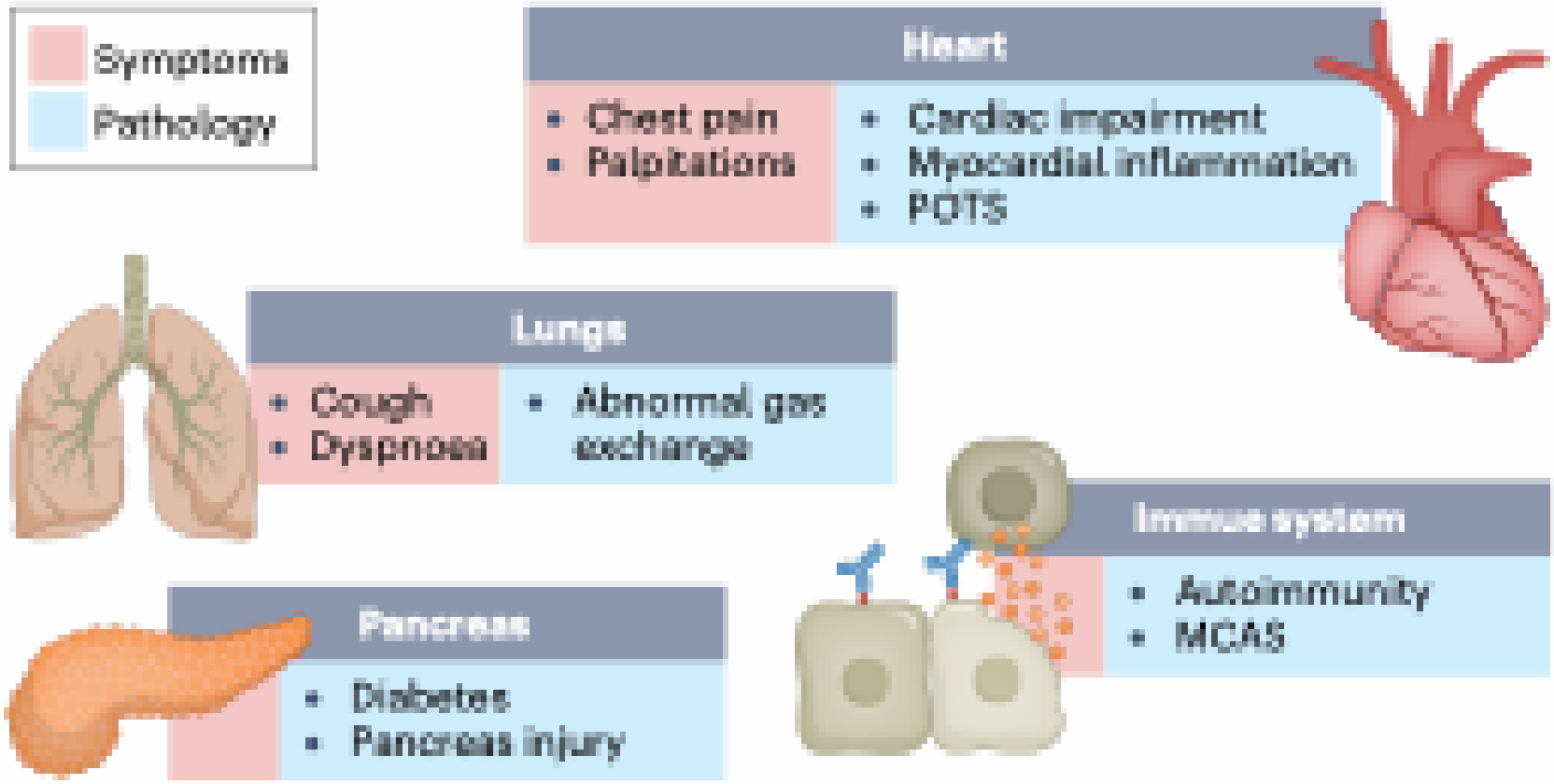
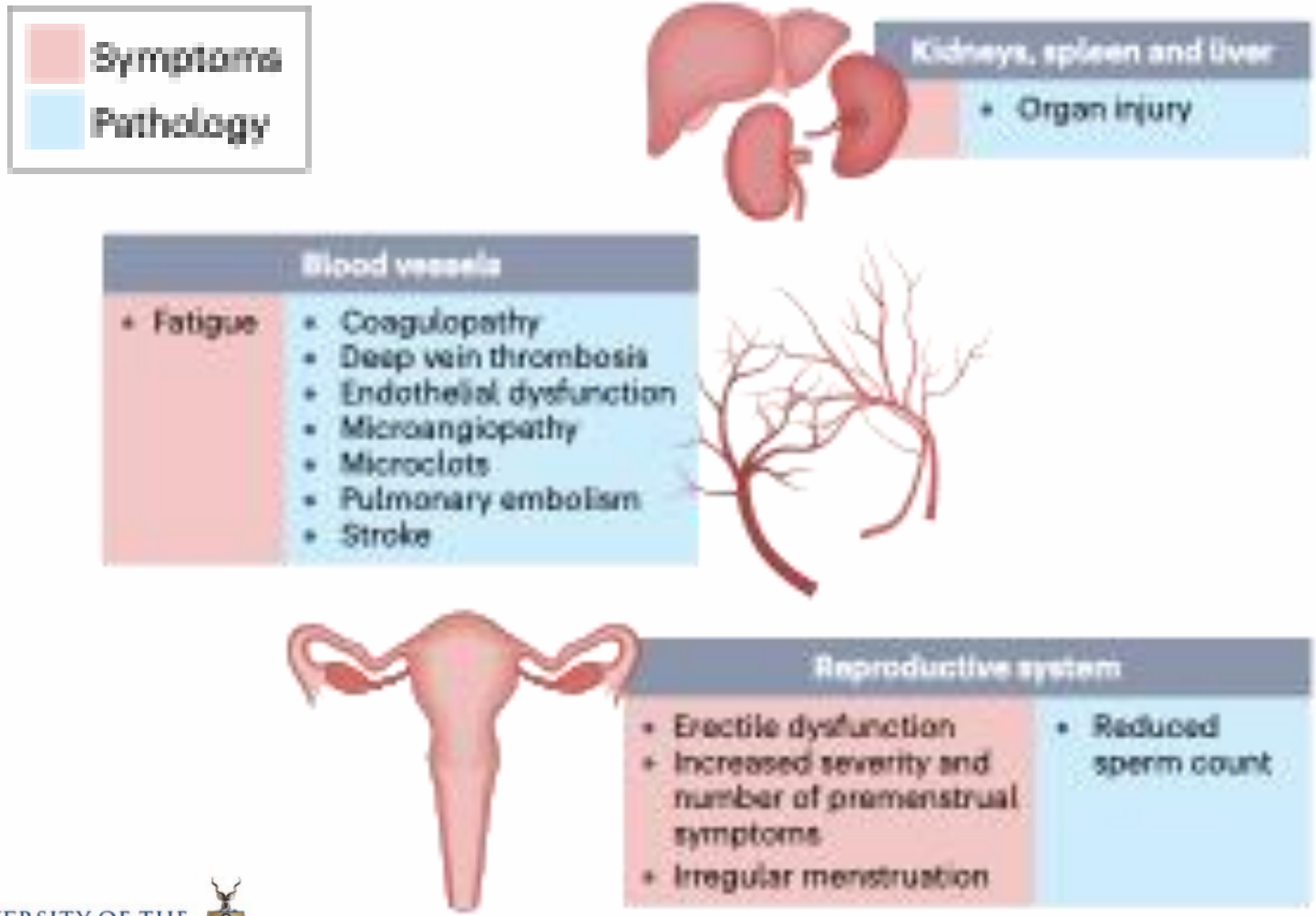
Davis et al., Nat Rev Micro, 2023

Manifestations



Davis et al., Nat Rev Micro, 2023

Manifestations



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Davis et al., Nat Rev Micro, 2023

How common is Long COVID?

- 10% of infected people
  - ~ 70 million people
- 10-20% of non-hospitalized cases
- 50-70% of hospitalized cases
- Most Long COVID cases occur in non-hospitalized cases with mild acute COVID-19

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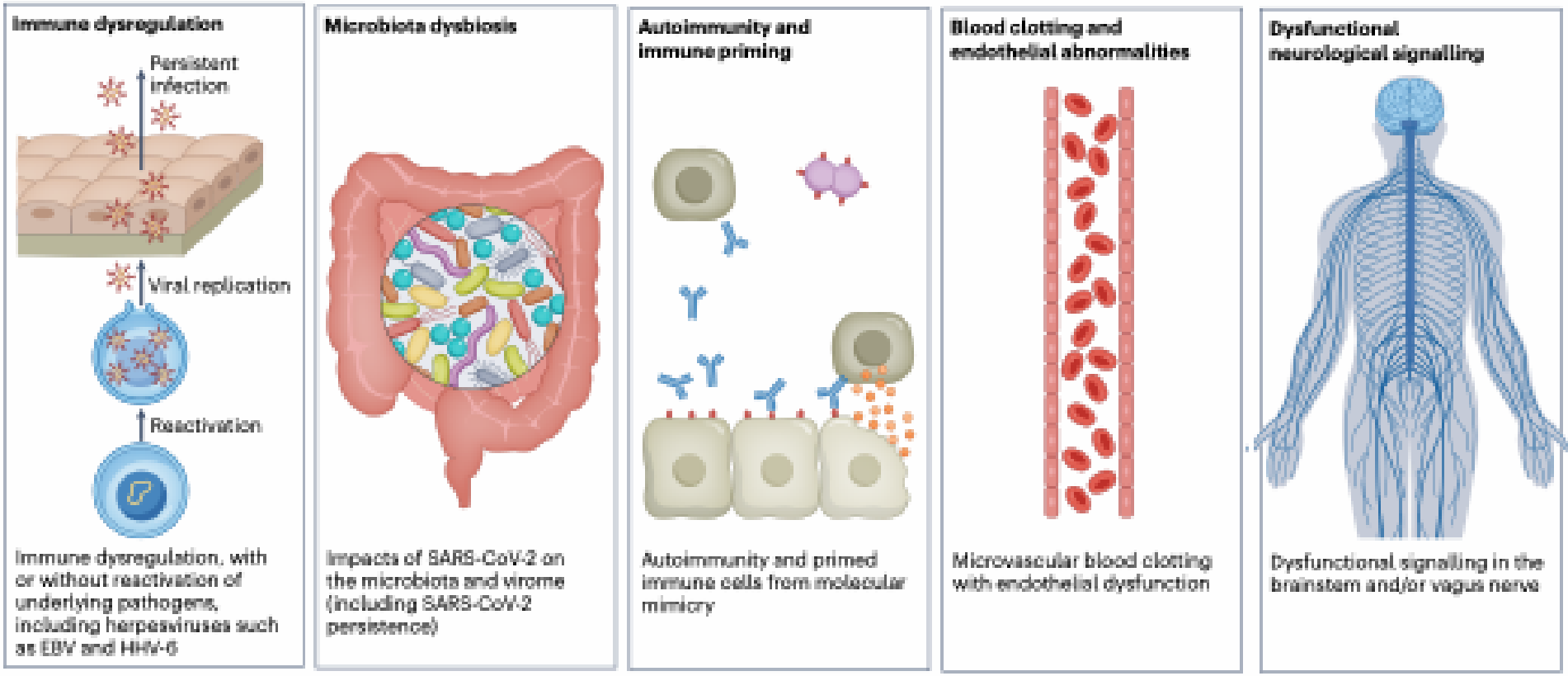
WHO COVID Dashboard 2023
Bull-Otterson et al., MMWR, 2021
Ceban et al., Bran Behav. Immun., 2022

What causes Long COVID?



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Davis et al., Nat Rev Micro, 2023

Risk factors for Long COVID

JAMA Internal Medicine | Original Investigation

Risk Factors Associated With Post–COVID-19 Condition

A Systematic Review and Meta-analysis

Vasiliki Tsampasian, MD, MSc; Hussein Elghazaly, MBBS; Rahul Chattopadhyay, MBBS, MSc; Maciej Debski, MD, PhD; Thin Kyi Phyu Naing, MBBS; Pankaj Garg, PhD; Allan Clark, PhD; Eleana Ntatsaki, MD(Res), MA; Vassilios S. Vassiliou, MBBS, PhD

Risk factors associated with increased risk of Long COVID	
Female sex	Comorbidities
Increased age	Previous hospitalisation
High BMI	ICU admission
Smoking	*COVID-19 severity*

Comorbidities:

- Diabetes, anxiety/depression, asthma, COPD, CKD, immunosuppression and ischaemic heart disease

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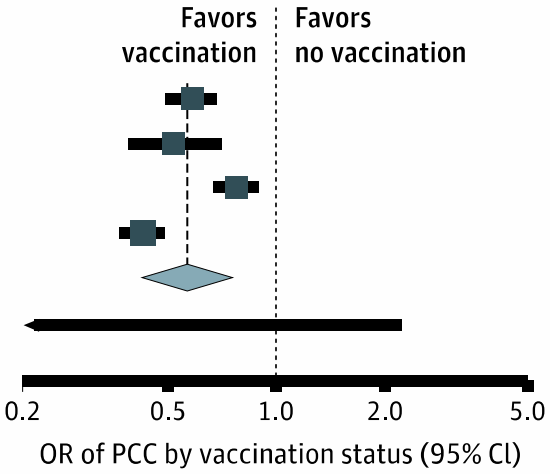
Vaccination and PCC

Figure 4. Association of Vaccination Status With Post–COVID-19 Condition (PCC), 2021 to 2022

Source	OR (95% CI)
Ayoubkhani et al[18]	0.59 (0.50-0.69)
Emecen et al[26]	0.53 (0.40-0.71)
Ioannou et al[34]	0.78 (0.68-0.90)
Zisis et al[12]	0.43 (0.37-0.49)
Total (random effects)	0.57 (0.43-0.76)
Prediction interval	(0.15-2.22)

Heterogeneity: $\chi^2_3 = 35.00$ ($P < .001$); $I^2 = 91\%$



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Tsampasian et al., JAMA Int Med, 2023

SARS-CoV-2 variants and Long COVID

- Different SARS-CoV-2 variants may impact the development of Long COVID

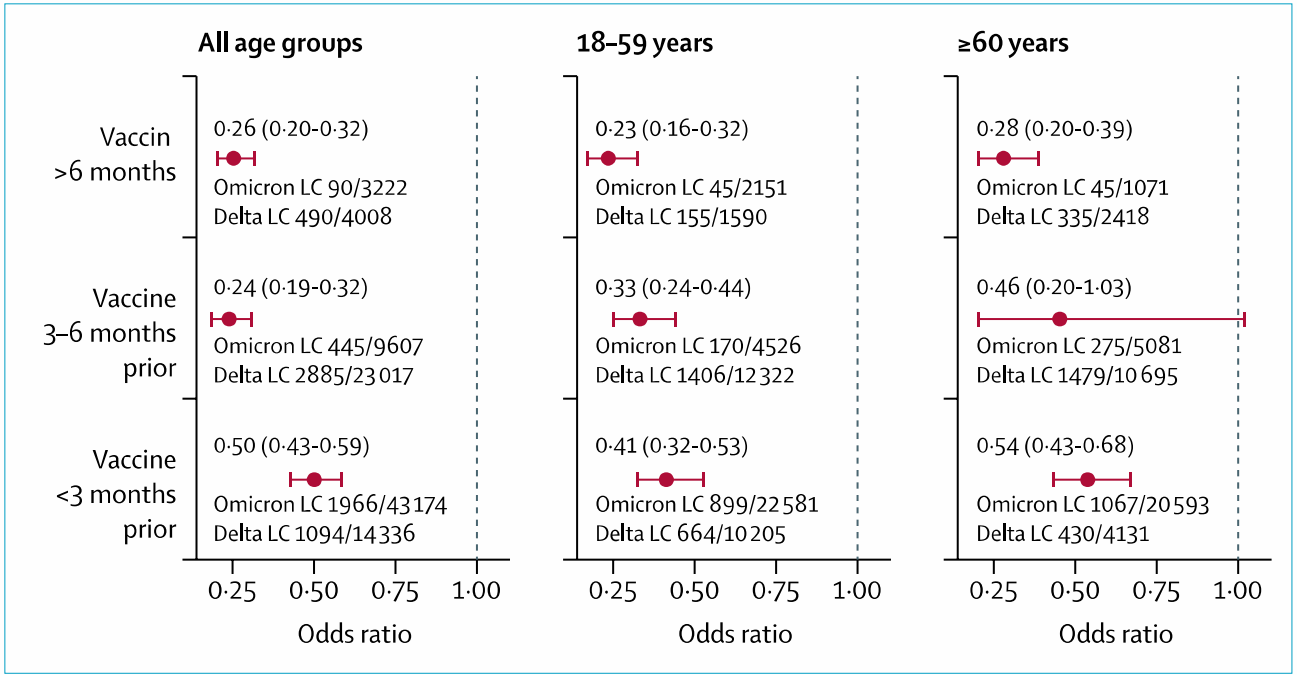

***Figure*: Odds ratio of long COVID (LC) adjusted by age, sex, body-mass index, Index of Multiple Deprivation, presence of comorbidities, and vaccination status**

Omicron long COVID and delta long COVID indicate, for each stratum, the number of users with long COVID over the total number of users of that stratum.

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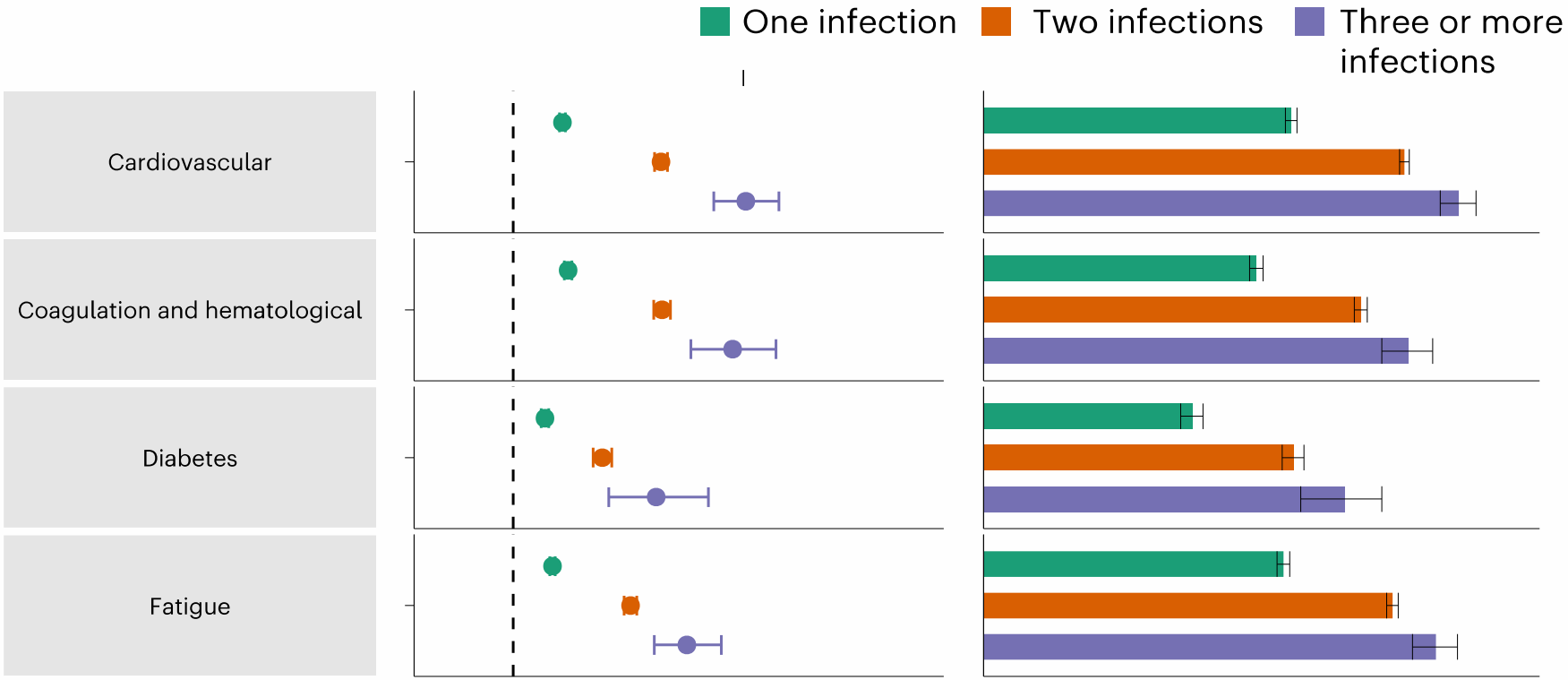
Antonelli et al., Lancet , 2022

Re-infection and Long COVID



Cohort: 1 SARS-CoV-2 infection(n=443,588), two or more infections (n=40,947) and non-infected controls (5,334,729)

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Bowe et al., Nature Med, 2022

Treatment of Long COVID

- Although there are currently no broadly effective therapies, specific symptoms can be effectively treated
- Evidence is largely lacking or borrowed from other similar conditions

Table 1 | Summary of candidate treatments and supporting evidence

Symptoms and/or biological mechanism	Treatments	Supporting evidence	Comments
Postexertional malaise	Pacing	ME/CFS literature	Exercise, cognitive behavioural therapy and graded exercise therapy are contraindicated
POTS	Pharmacological: β-blockers, pyridostigmine, fludrocortisone, midodrine	POTS and ME/CFS literature	Options can be prioritized on the basis of a specific constellation of symptoms
	Non-pharmacological: increase salt and fluid intake, intravenously administered salt, compression stockings	POTS and ME/CFS literature	–
Immune dysfunction	Intravenous immunoglobulin	ME/CFS literature	Consider consulting an immunologist on implementation
Cognitive dysfunction	Cognitive pacing	ME/CFS literature	Consider implementation alongside pacing physical exertion
Cognitive dysfunction	Postconcussion syndrome protocols	ME/CFS and postconcussion syndrome literature	–
Fatigue	Coenzyme Q_{10}, D-ribose	ME/CFS literature	–
Pain, fatigue, neurological symptoms	Low-dose naltrexone	ME/CFS and other literature	Substantial anecdotal reports of success within the patient community
Fatigue, unrefreshing sleep, brain fog	Low-dose aripiprazole	ME/CFS literature	–

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Davis et al., Nat Rev Micro, 2023

Treatment of Long COVID

PCC-related dyspnea

Table ES3. List of RCTs of interventions for PCC-related dyspnea with primary outcome measures and certainty (n = 6)

Intervention		Overall number of studies including the intervention, n=6	HRQL improvement (n of studies)	Dyspnea improvement (n of studies)	Functional capacity improvement (n of studies)	Pulmonary function improvement (n of studies)	Radiological response (n of studies)	Adverse events (n of studies)	Severe adverse events (n of studies)
Respiratory training	NEW	2	2	2		1			
ADAPT_232 (adaptogens)	NEW	1		1					
Endurance training	NEW	1	1	1					
High dose steroids	NEW	1		1			1	1	1
Treamid	NEW	1		1	1	1		1	

	GRADE High- Moderate certainty	GRADE Low certainty
Beneficial effect		
No significant effect		
Harmful effect		
Uncertain effect		
No evidence or no estimable effect		

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Treatment of Long COVID

- A thorough evaluation is extremely important to identify specific symptoms for management

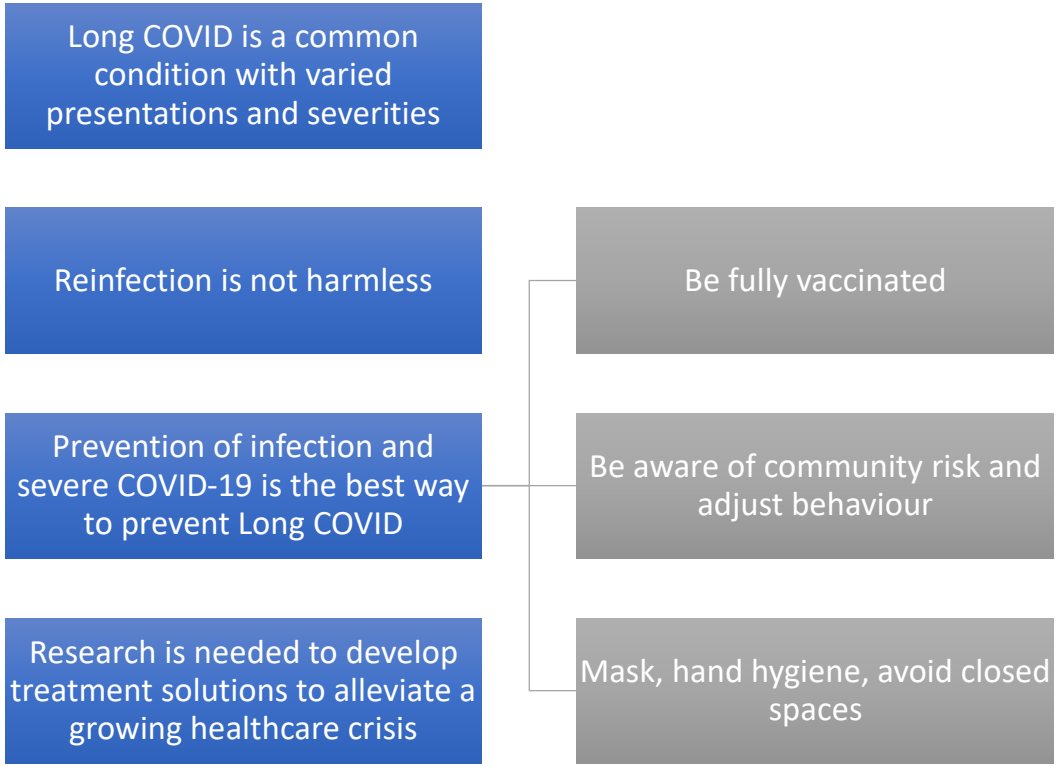
Society of Critical Care Medicine recommended screening tools to detect long-term cognition, mental health, and physical function after critical illness

Domain	Screening test	Comments	Recommendation
Cognition	Montreal Cognitive Assessment (MoCA)[1-4]	Mild cognitive impairment defined as a score of 18 to 25, moderate as 10 to 17, and severe as less than 10	Strong
Anxiety	HADS[2,5]	A score of 8 or greater on the anxiety or depression sub-scale is used to identify symptoms of clinically significant anxiety or depression	Strong
Depression	HADS[2,5]		Strong
Post-traumatic stress disorder	IES-R[6] or the abbreviated IES-6[7,8]	The optimal screening threshold has been established as 1.6 (IES-R)[2] or 1.75 (IES-6)[7]	Weak
Physical function	6-min walk[9-11] and/or EuroOol-5D-5L[12]	Can be evaluated as a percent predicted against available normative data	Weak
		Includes assessments of mobility, self-care, and usual activities, in addition to pain and anxiety/depression	Weak

HADS: Hospital Anxiety and Depression Scale; IES-6: Impact of Event Scale-6; IES-R: Impact of Events Scale-Revised.

www.UpToDate.com

Summary – Long COVID



Thank you for listening