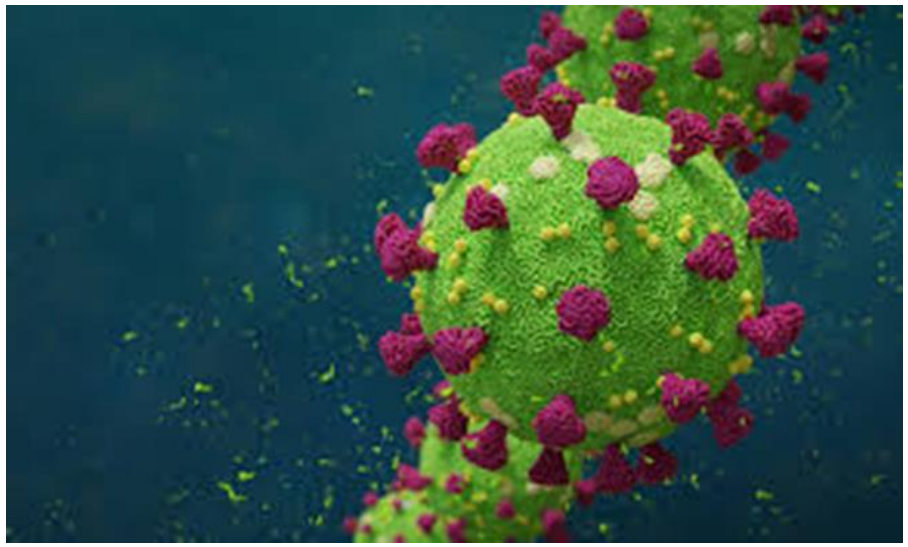
SARS-CoV-2: COVID-19

Update
17 June 2020



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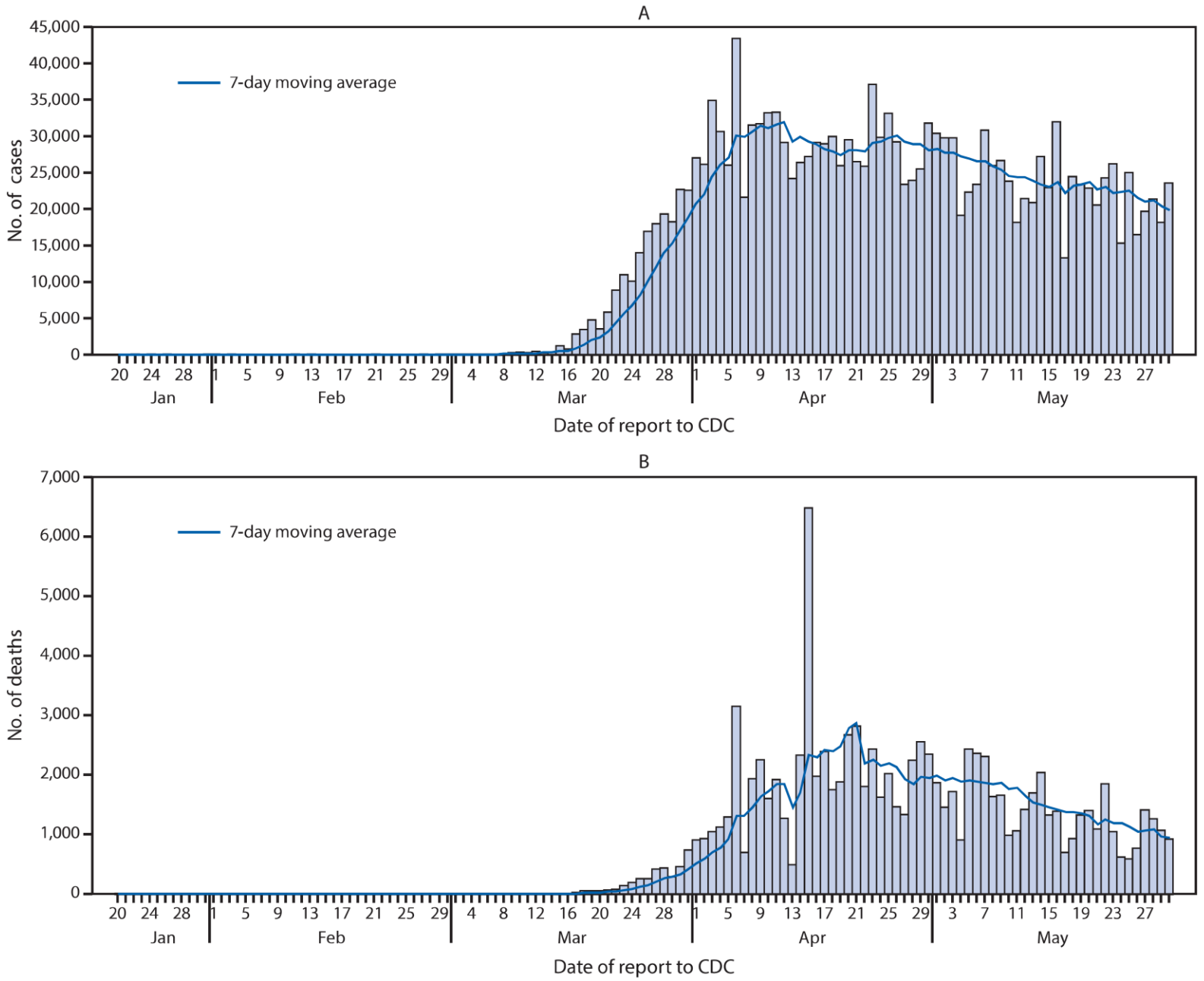
Professor
Department of Pediatrics
Division of Infectious Diseases and Tropical Pediatrics
University of Maryland School of Medicine
Center for Vaccine Development and Global Health

FIGURE. Daily number of COVID-19 cases*,†,§,¶ (A) and COVID-19–associated deaths (B) reported to CDC — United States, January 22–May 30, 2020**



June 1= April 1

> 1000 deaths/day

MMWR Vol 69 June 15, 2020

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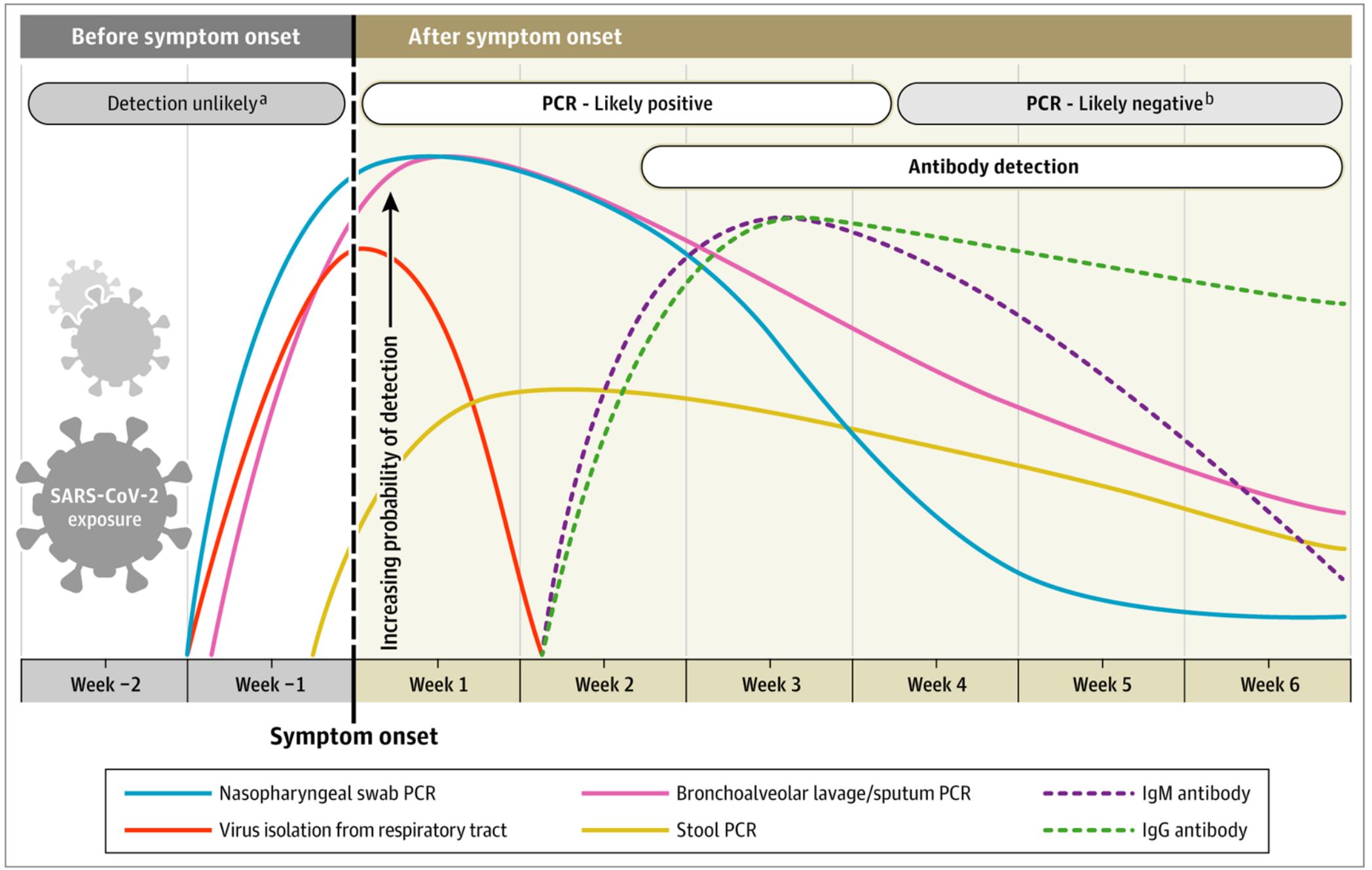
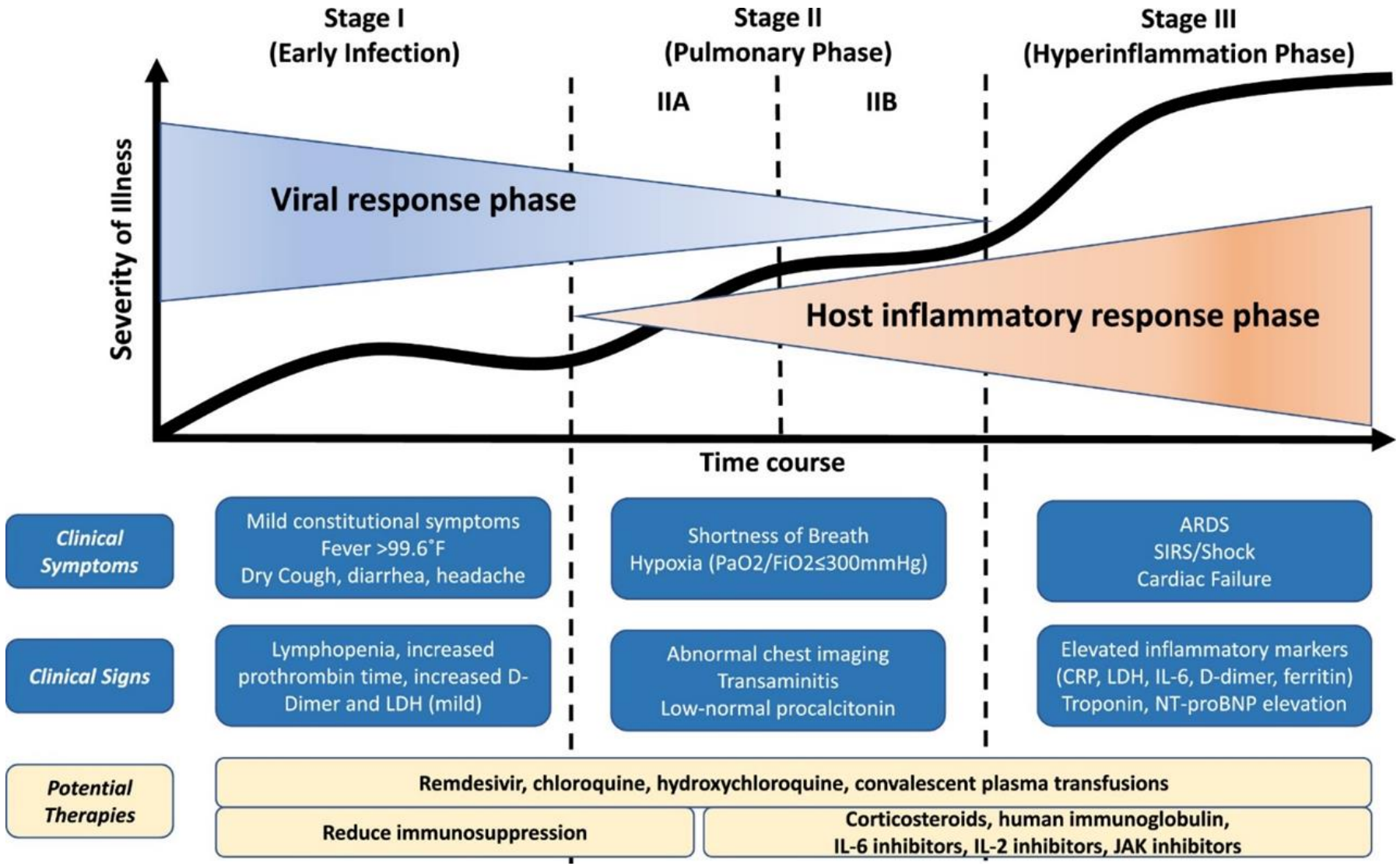
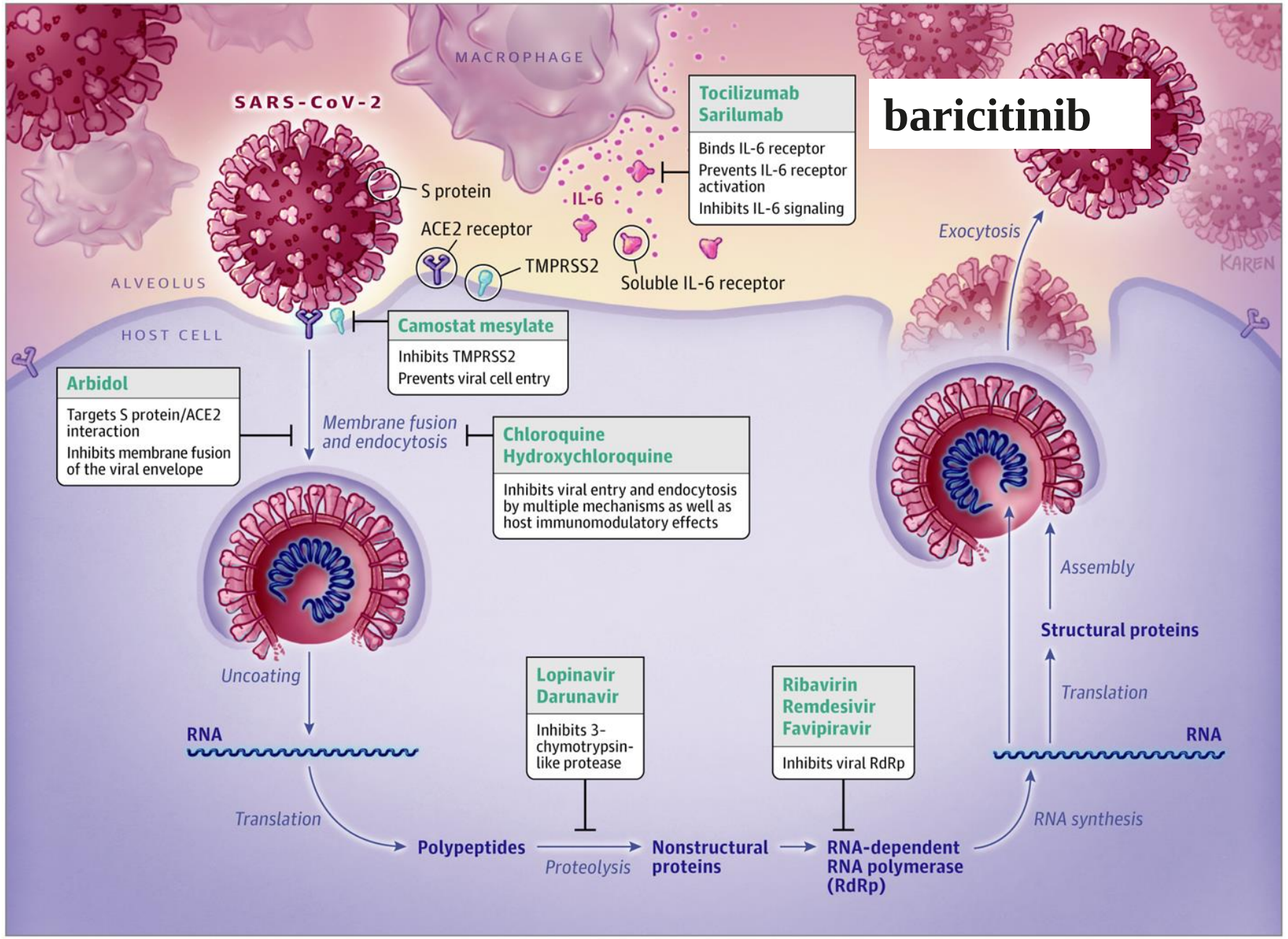


Sethuraman N, Jeremiah SS, Ryo A. **Interpreting Diagnostic Tests for SARS-CoV-2.** *JAMA*. Published online May 06, 2020. doi:10.1001/jama.2020.8259

Pathophysiology and Timing of Interventions



Siddiqi and Mehra, J Heart Lung Transplant, DOI: (10.1016/j.healun.2020.03.012)



Sanders JM, Monogue ML, Jodlowski TZ, Cuttrell JB. Pharmacologic Treatments for Coronavirus Disease 2019 (COVID-19): A Review. JAMA. Published online April 13, 2020. doi:10.1001/jama.2020.6019.

Adaptive COVID-19 Treatment Trial (ACTT)

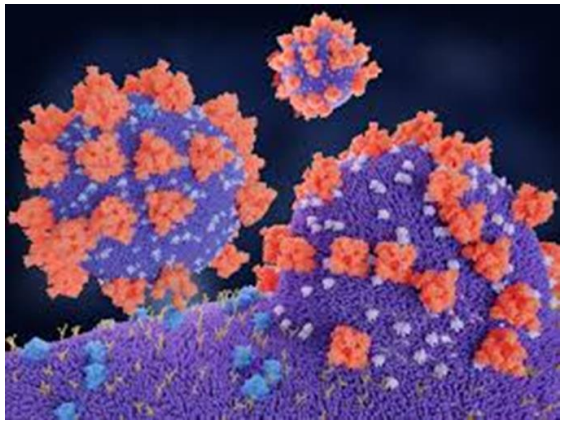
Adaptive COVID-19 Treatment Trial (ACTT)

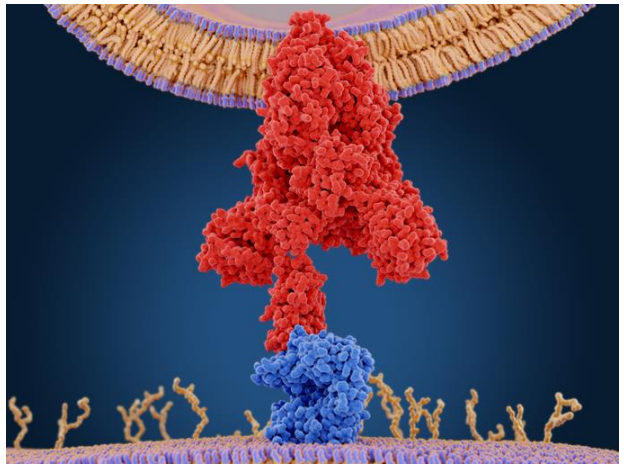
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Preliminary Report

J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman
E. Hohmann, H.Y. Chu, A. Luetkemeyer, S. Kline, D. Lopez de
R.W. Finberg, K. Dierberg, V. Tapson, L. Hsieh, T.F. Patterson, R.
D.A. Sweeney, W.R. Short, G. Touloumi, D.C. Lye, N. Ohmagari
G.M. Ruiz-Palacios, T. Benfield, G. Fätkenheuer, M.G. Kortepeter,
C.B. Creech, J. Lundgren, A.G. Babiker, S. Pett, J.D. Neaton, T.H.
T. Bonnett, M. Green, M. Makowski, A. Osinusi, S. Nayak, and H

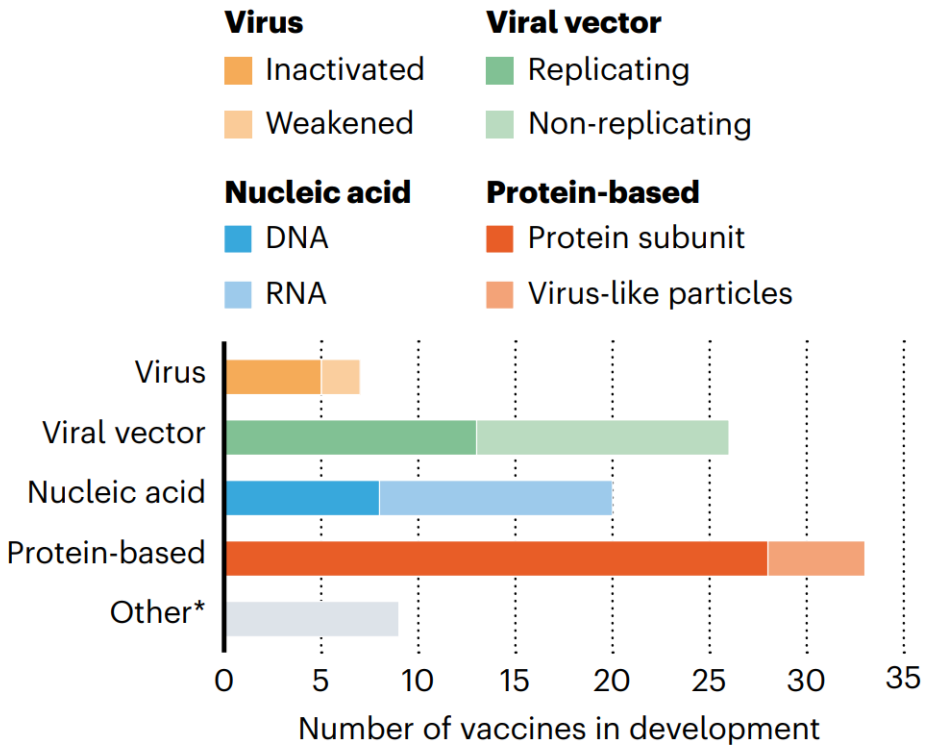




	Remdesivir (N=538)	Placebo (N=521)
Recovery		
No. of recoveries	334	273
Median time to recovery (95% CI) — days	11 (9–12)	15 (13–19)
Rate ratio (95% CI)†	1.32 (1.12–1.55 [P<0.001])	
Mortality		
Hazard ratio (95% CI)	0.70 (0.47–1.04)	
No. of deaths by day 14	32	54

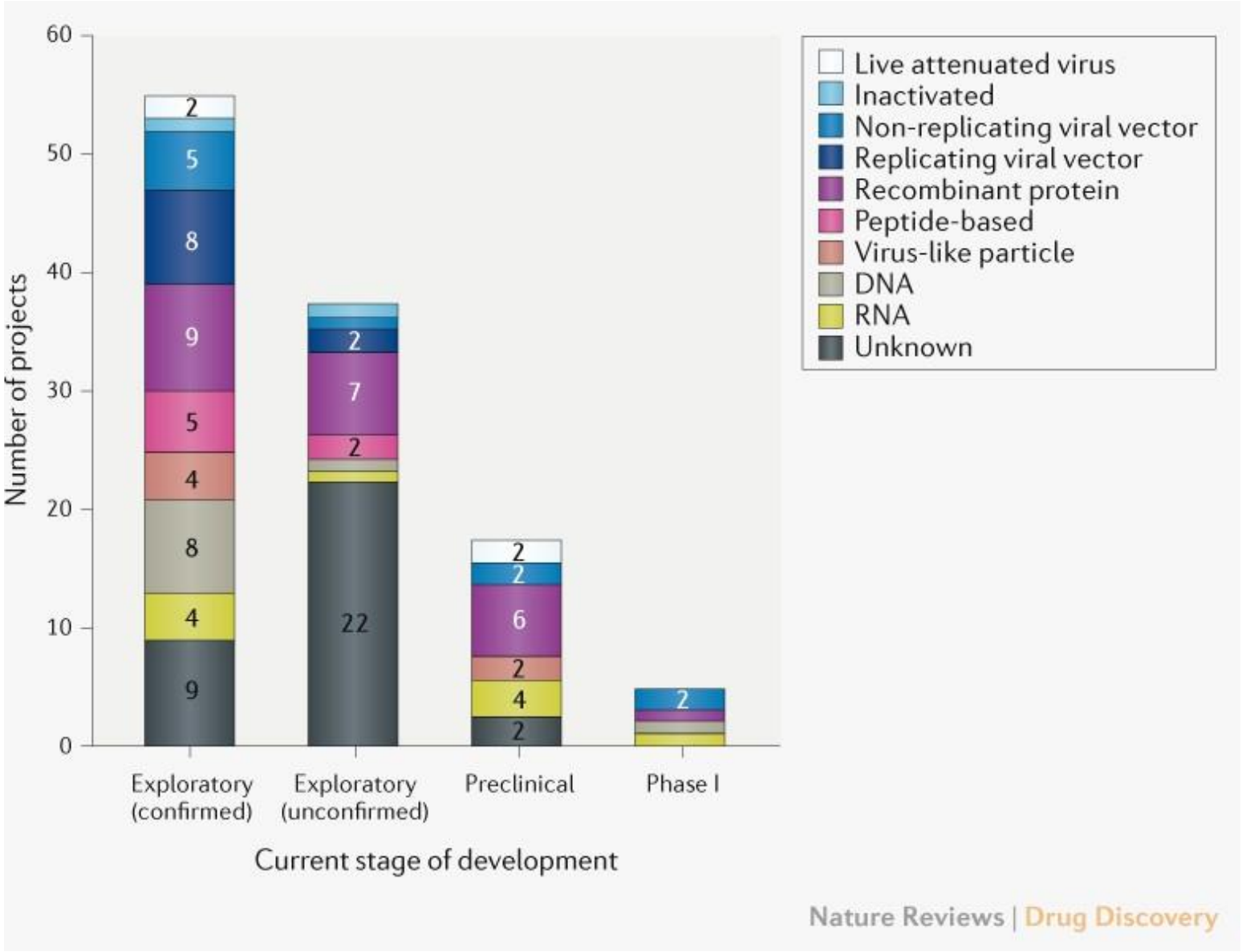
AN ARRAY OF VACCINES

All vaccines aim to expose the body to an antigen that won't cause disease, but will provoke an immune response that can block or kill the virus if a person becomes infected. There are at least eight types being tried against the coronavirus, and they rely on different viruses or viral parts.



* Other efforts include testing whether existing vaccines against poliovirus or tuberculosis could help to fight SARS-CoV-2 by eliciting a general immune response (rather than specific adaptive immunity), or whether certain immune cells could be genetically modified to target the virus.

Nature. vol 580, 30 April 2020

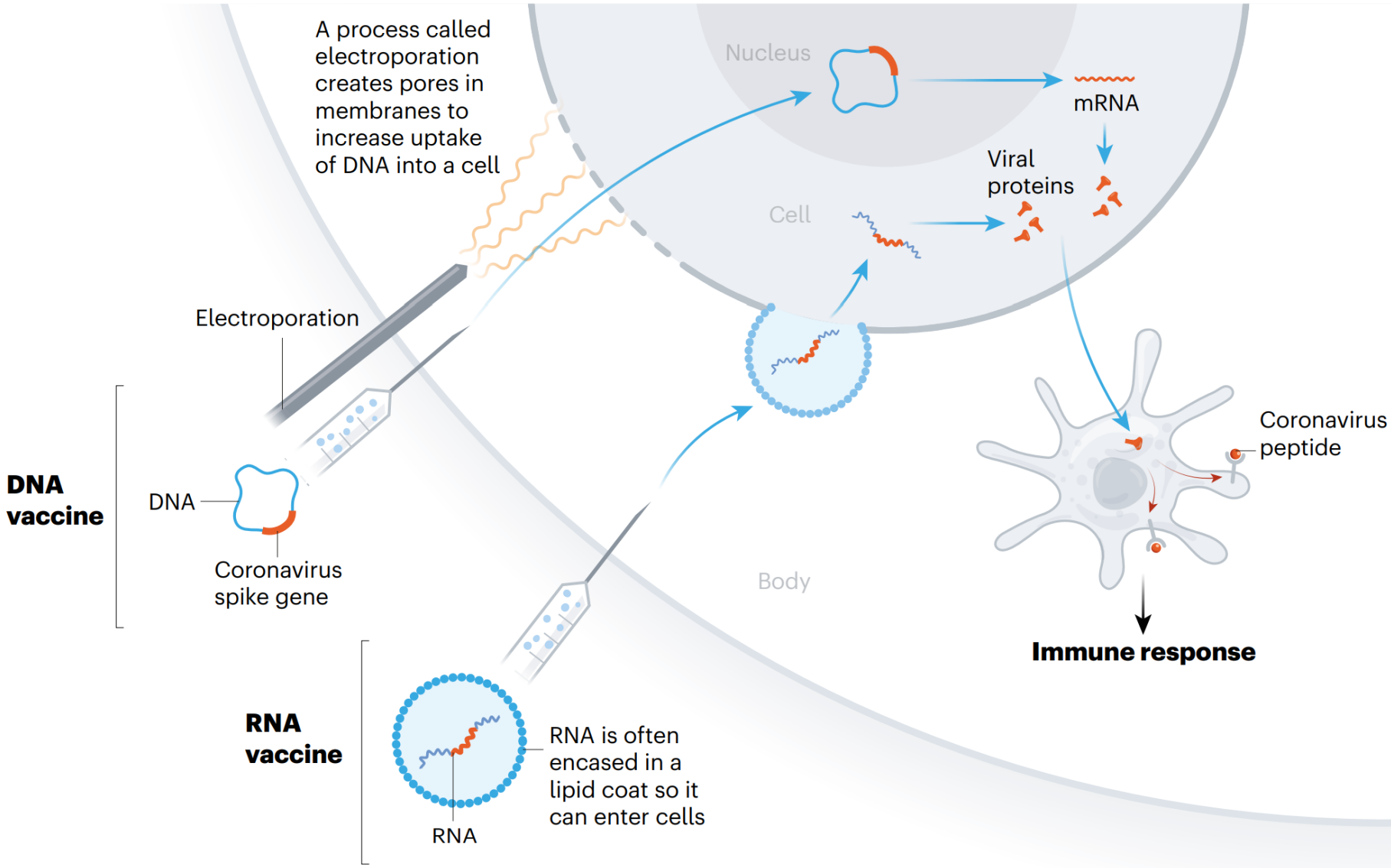


Le TT, et al. *Nature Reviews Drug Discovery*. 09 April 2020

NUCLEIC-ACID VACCINES

At least 20 teams are aiming to use genetic instructions (in the form of DNA or RNA) for a coronavirus protein that prompts an immune response. The nucleic acid is inserted into human cells, which then churn out copies of the virus protein; most of these vaccines encode the virus's spike protein.

RNA- and DNA-based vaccines are safe and easy to develop: to produce them involves making genetic material only, not the virus. But they are unproven: no licensed vaccines use this technology.



Nature. vol 580, 30 April 2020

VIRAL-VECTOR VACCINES

Around 25 groups say they are working on viral-vector vaccines. A virus such as measles or adenovirus is genetically engineered so that it can produce coronavirus proteins in the body. These viruses are weakened so they cannot cause disease. There are two types: those that can still replicate within cells and those that cannot because key genes have been disabled.

Replicating viral vector (such as weakened measles)

The newly approved Ebola vaccine is an example of a viral-vector vaccine that replicates within cells. Such vaccines tend to be safe and provoke a strong immune response. Existing immunity to the vector could blunt the vaccine's effectiveness, however.

Non-replicating viral vector (such as adenovirus)

No licensed vaccines use this method, but they have a long history in gene therapy. Booster shots can be needed to induce long-lasting immunity. US-based drug giant Johnson & Johnson is working on this approach.

PROTEIN-BASED VACCINES

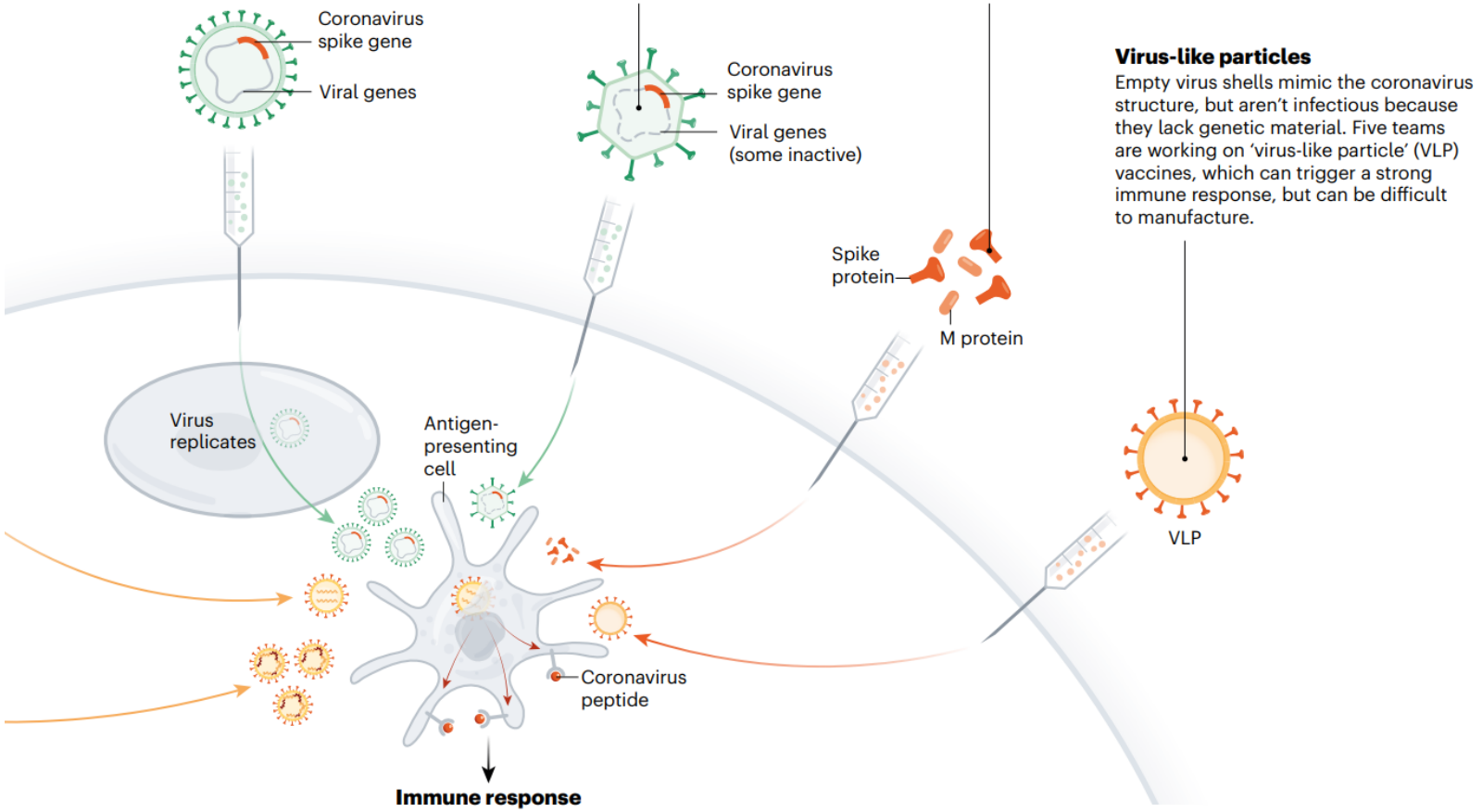
Many researchers want to inject coronavirus proteins directly into the body. Fragments of proteins or protein shells that mimic the coronavirus's outer coat can also be used.

Protein subunits

Twenty-eight teams are working on vaccines with viral protein subunits — most of them are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.



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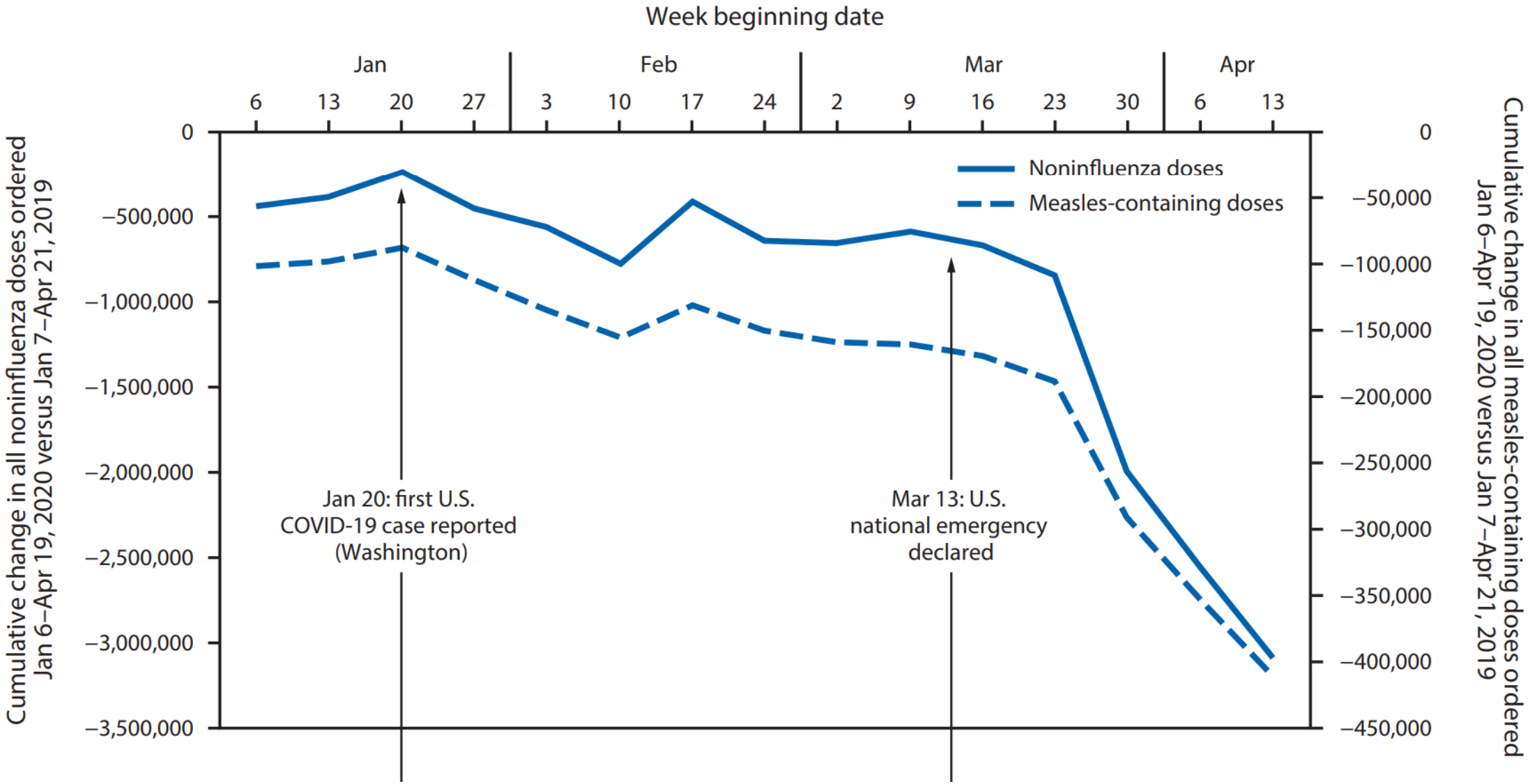
Vaccines that may first reach Phase 3

Vaccine	Characteristic	Trial size	No. doses	Start
Moderna (NIH)	mRNA	30,000	2	July 15
AstraZeneca (Oxford)	Chimp Adeno	30,000	1	Early Aug
J & J	Adeno 26	Unknown	Unknown	Mid Sept
Sanofi	rSpike + ASO3	Unknown	Unknown	Oct-Nov
Merck	VSV Measles vaccine	Unknown	Unknown	Unknown

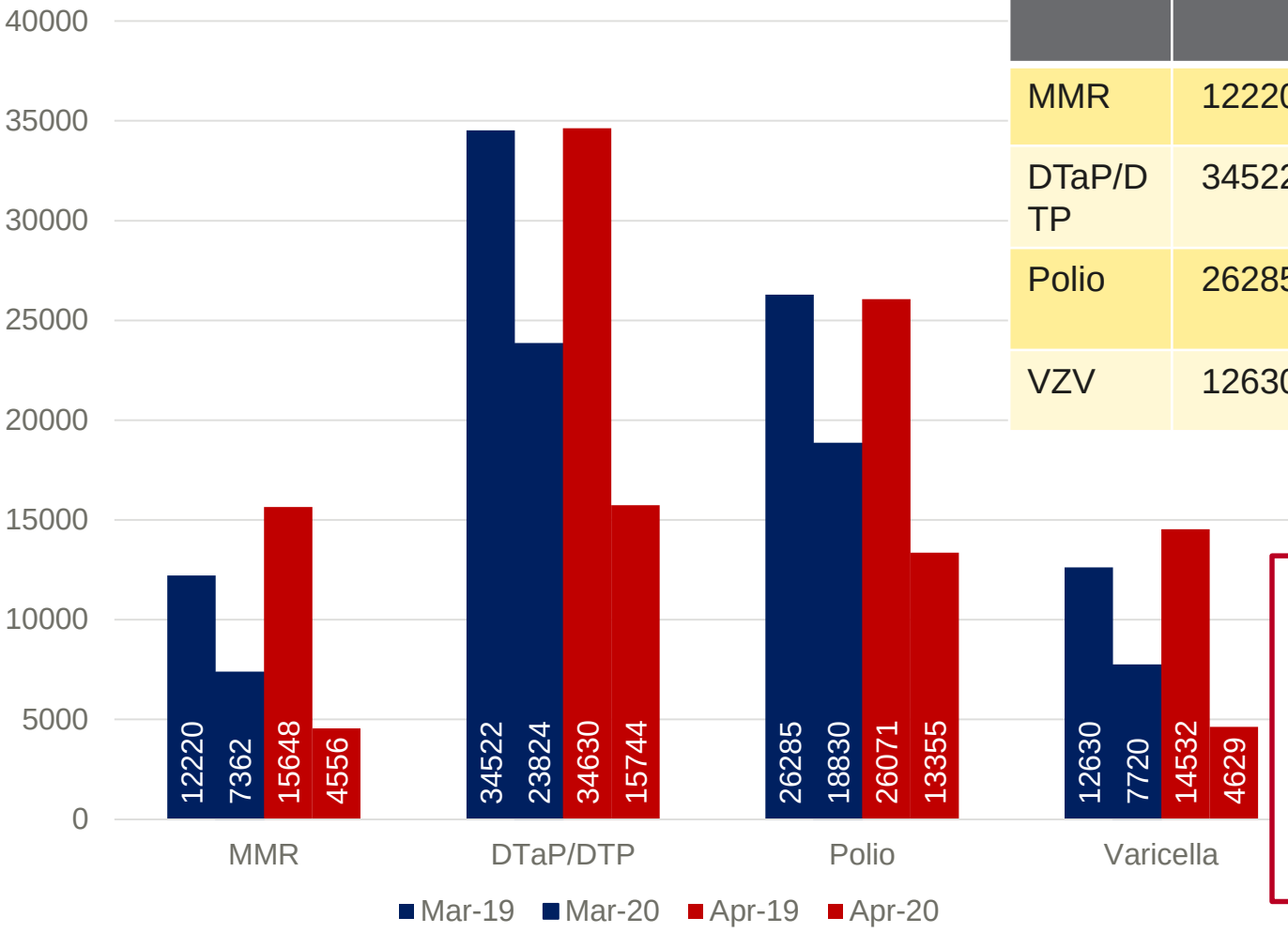
Decline in Immunization Rates - National



MMWR. May 8, 2020.

Decline in Immunization Rates - Maryland

	March 2019	March 2020	Change March (%)	April 2019	April 2020	Change April (%)
MMR	12220	7362	-40	15648	4556	-71
DTaP/DTP	34522	23824	-31	34630	15744	-55
Polio	26285	18830	-28	26071	13355	-49
VZV	12630	7720	-39	14532	4629	-68



Measles vaccination rates are down 71%!

Source: Maryland ImmuNet (data as of 4/29/2020)

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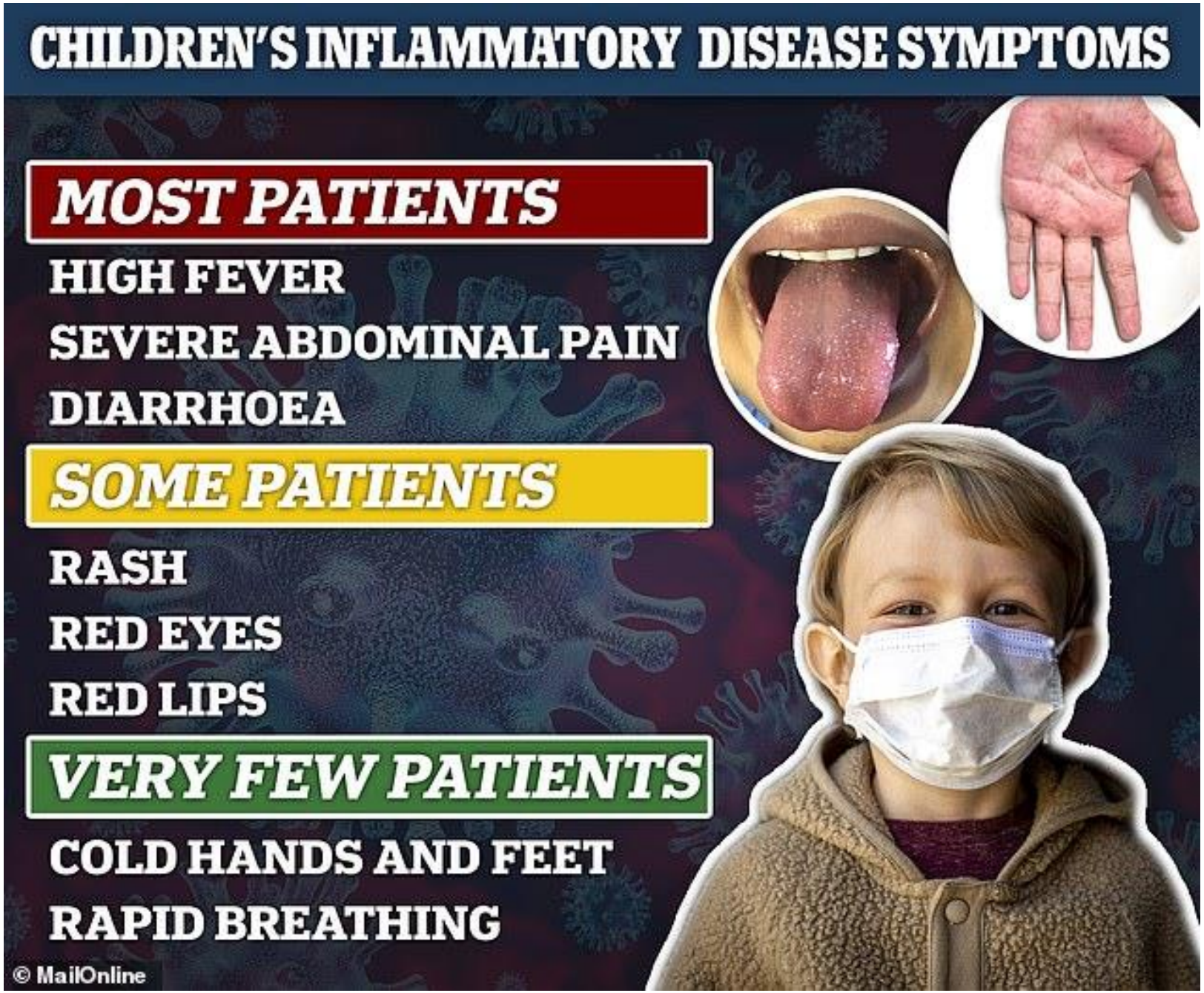
MIS-C

Multisystem Inflammatory Syndrome of Children



Thank You

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