ONE HEALTH Knowledge-Café

Webinars | Dicussions | Online courses | Networkings

is supported by DAAD exceed with financial support from

SPEAKERS

Florian Krammer
Icahn School of Medicine at Mount Sinai

Pasquale Pagliano
University of Salerno, baronissi, Italy

Monica Gandhi
University of California, SanFrancisco

Vaccine and Treatments for COVID-19: Progress since 2020

The development of vaccines against SARS-CoV-2 represents one the most impressive global efforts seen so far in terms of resources mobilized, scientists involved and speed and implementation of the results achieved.
In parallel, hundreds of clinical trials have been performed to find effective treatment protocols for infected patients.

In this webinar, we will discuss the progresses made in the field of preventive and therapeutic measures and the expectations for the near future

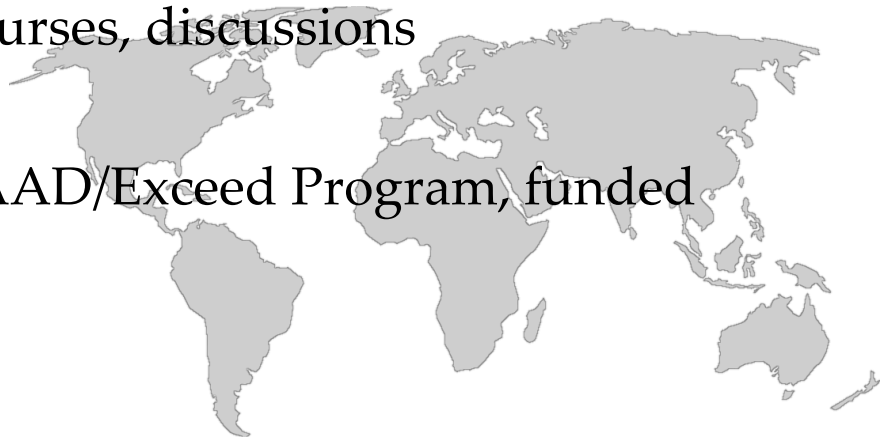
Join with us to learn more about the topic

2:30 PM - 4:00 PM GMT |
8:15 PM NPT | 4:30 PM CET
| 7:30 AM PST |

27th May 2021 |
Thursday

One Health Knowledge Café

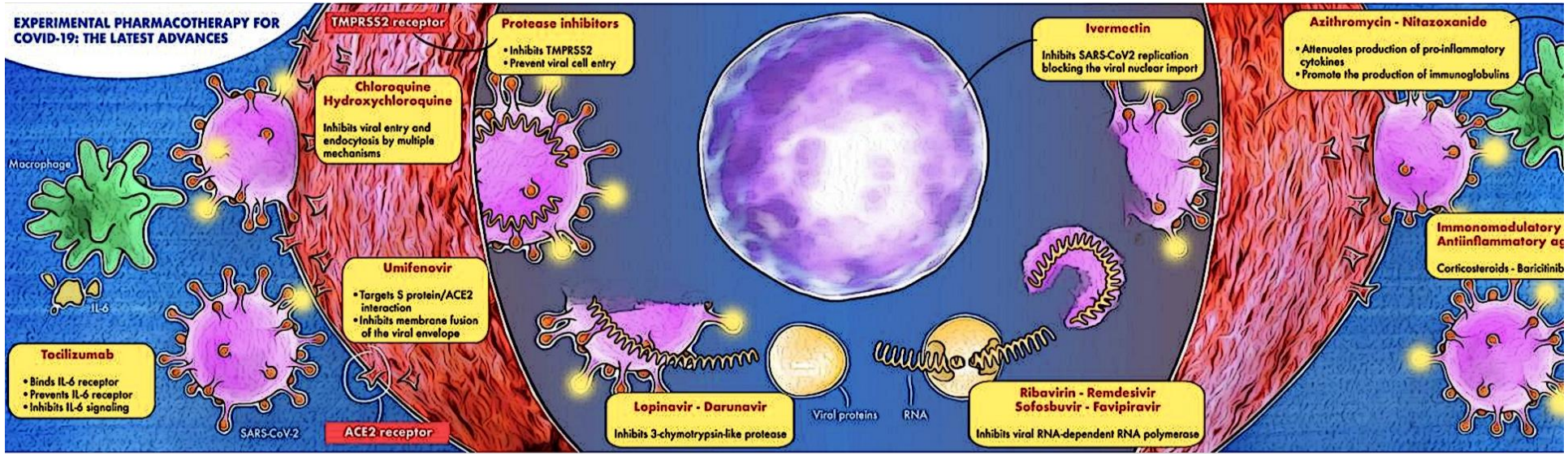
- A collaborative effort of more than 11 individuals representing CIH partners and alumni
- Represents Asia, Africa, Europe, South America and North America
- Brings together the expertise and network of researchers and professionals from various disciplines, countries and expertise to enable cross learning, sharing and network building
- Monthly talks, webinars, online courses, discussions
- Supported by LMU^{CIH} through DAAD/Exceed Program, funded by BMZ



Pharmacotherapy of COVID-19

Prof. Pasquale Pagliano
Department of Medicine, Surgery and Dentistry
“Scuola Medica Salernitana”,
Unit of Infectious Diseases
University of Salerno, Baronissi, Italy

Repurposing therapy for COVID-19



Pagliano P, Scarpati G, Sellitto C, et al. Experimental Pharmacotherapy for COVID-19: The Latest Advances. J Exp Pharmacol. 2021;13:1-13. Published 2021 Jan 7. doi:10.2147/JEP.S255209

- Key question:

  can antiviral drugs be effective
  in reducing COVID-19 mortality?

ANTIVIRAL AGENTS INVESTIGATED AGAINST COVID-19

Cell Research

www.nature.com/cr
www.cell-research.com

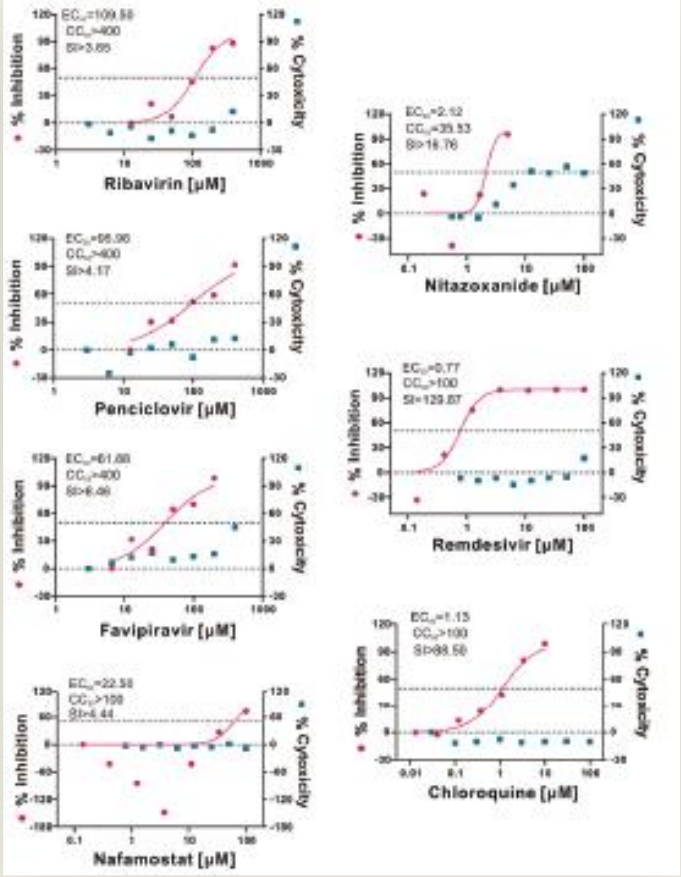
LETTER TO THE EDITOR OPEN

Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro

Cell Research (2020) 30:269–271; https://doi.org/10.1038/s41422-020-0282-0

EC90 value of remdesivir against 2019-nCoV in Vero E6 cells was 1.76 μM, suggesting its working concentration is likely to be achieved in NHP.

EC90 value of chloroquine in Vero E6 cells was 6.90 μM, which can be clinically achievable as demonstrated in the plasma of rheumatoid arthritis patients

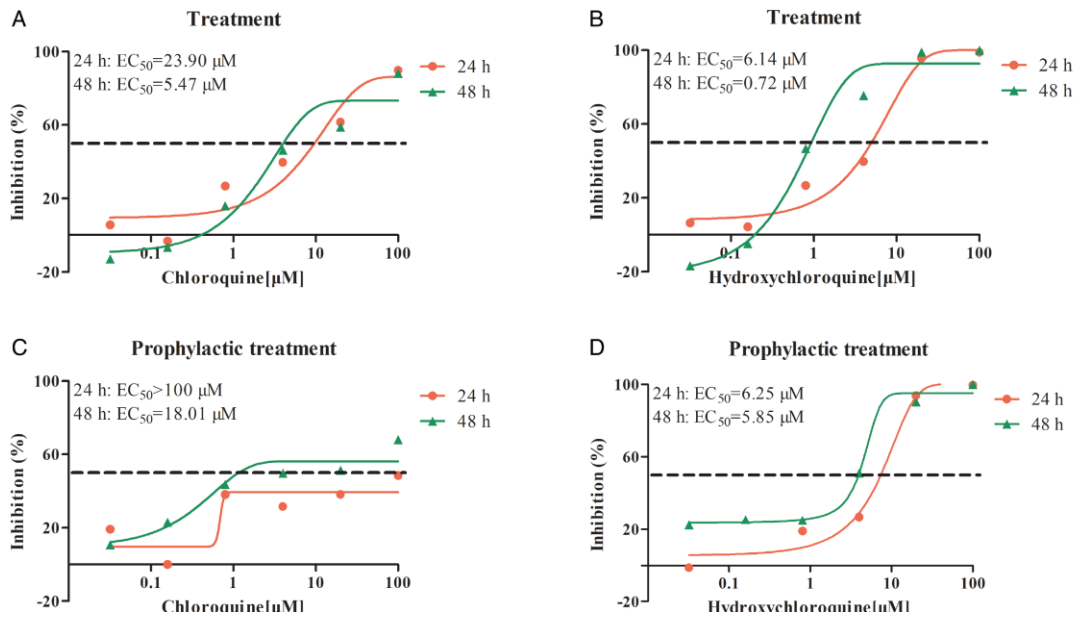


Clinical Infectious Diseases

MAJOR ARTICLE

In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

Xueting Yao,[1,a] Fei Ye,[2,a] Miao Zhang,[1,a] Cheng Cui,[1,a] Baoying Huang,[2,a] Peihua Niu,[2] Xu Liu,[1] Li Zhao,[2] Erdan Dong,[3] Chunli Song,[4] Siyan Zhan,[5] Roujian Lu,[2] Haiyan Li,[1,3,b] Wenjie Tan,[2,b] and Dongyang Liu[1,b]



CQ/HCQ achieve a high concentration within lungs

Clin Infect Dis 2020

HCQ/CQ ACTIVITY AGAINST SARS-CoV-2

- interfere with the early phase of SARS-CoV-2 replication
  - modifying the pH on the surface of the cell membrane
  - inhibiting the fusion of the virus with the host cell, finally
- interfere with important viral functions
  - attachment, assembly, transport of new particles,
  - Accumulation in lysosomes, and release into intracellular space.
- bind to the sialic acids of the respiratory tract cells, interacting with the N-terminal domain of the SARS-CoV-2 spike protein, finally inhibiting cell/virus fusion during the early phase of the infection
- administered to patients with COVID-19 associated pneumonia, lung concentration rises up to 200–700 times than plasma concentration

Yao, Clin Infect Dis 2020

JAMA Network | Open

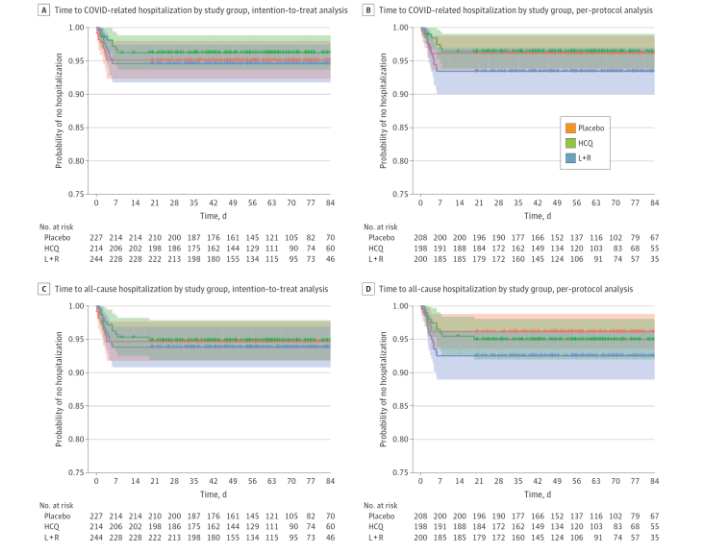
Original Investigation | Infectious Diseases

Effect of Early Treatment With Hydroxychloroquine or Lopinavir and Ritonavir on Risk of Hospitalization Among Patients With COVID-19

The TOGETHER Randomized Clinical Trial

Gilmar Reis, MD; Eduardo Augusto dos Santos Moreira Silva, MD; Daniela Carla Medeiros Silva, MD; Lehana Thabane, PhD; Gurmit Singh, PhD; Jay J. H. Park, MSc; Jamie I. Forrest, MPH; Ofir Harari, PhD; Castilho Vitor Quirino dos Santos; Ana Paula Figueiredo Guimarães de Almeida, MD; Adhemar Dias de Figueiredo Neto, MD; Leonardo Cançado Monteiro Savassi, MD; Aline Cruz Milagres, RN; Mauro Martins Teixeira, MD; Maria Izabel Campos Simplicio, BScPharm; Luciene Barra Ribeiro, RN; Rosemary Oliveira; Edward J. Mills, PhD; for the TOGETHER Investigators

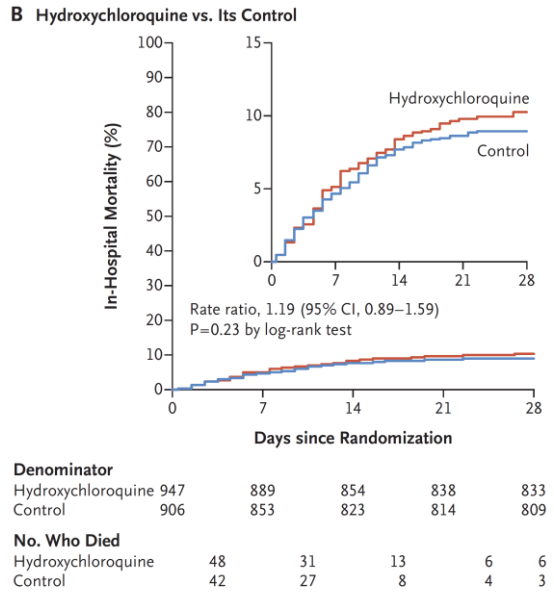
Figure 2. Time to Hospitalization by Study Group



Main Studies Investigating CQ/HCQ and Remdesivir Efficacy Against COVID-19

Drugs	Clinical Trials (N.)*	Main Clinical Trials Published (Reference)	Clinical Efficacy	Enrolled Patients
Chloroquine/hydroxychloroquine	335	7	Yes	491
		8	Yes	31
		10	Yes	36
		11	No	181
		12	Yes	440
		14	Yes	8075
		15	No	821
Remdesivir	49	17	Yes	61
		20	Yes	397
		21	Yes	1063

Solidarity Trial NEJM, 2021



The NEW ENGLAND JOURNAL of MEDICINE

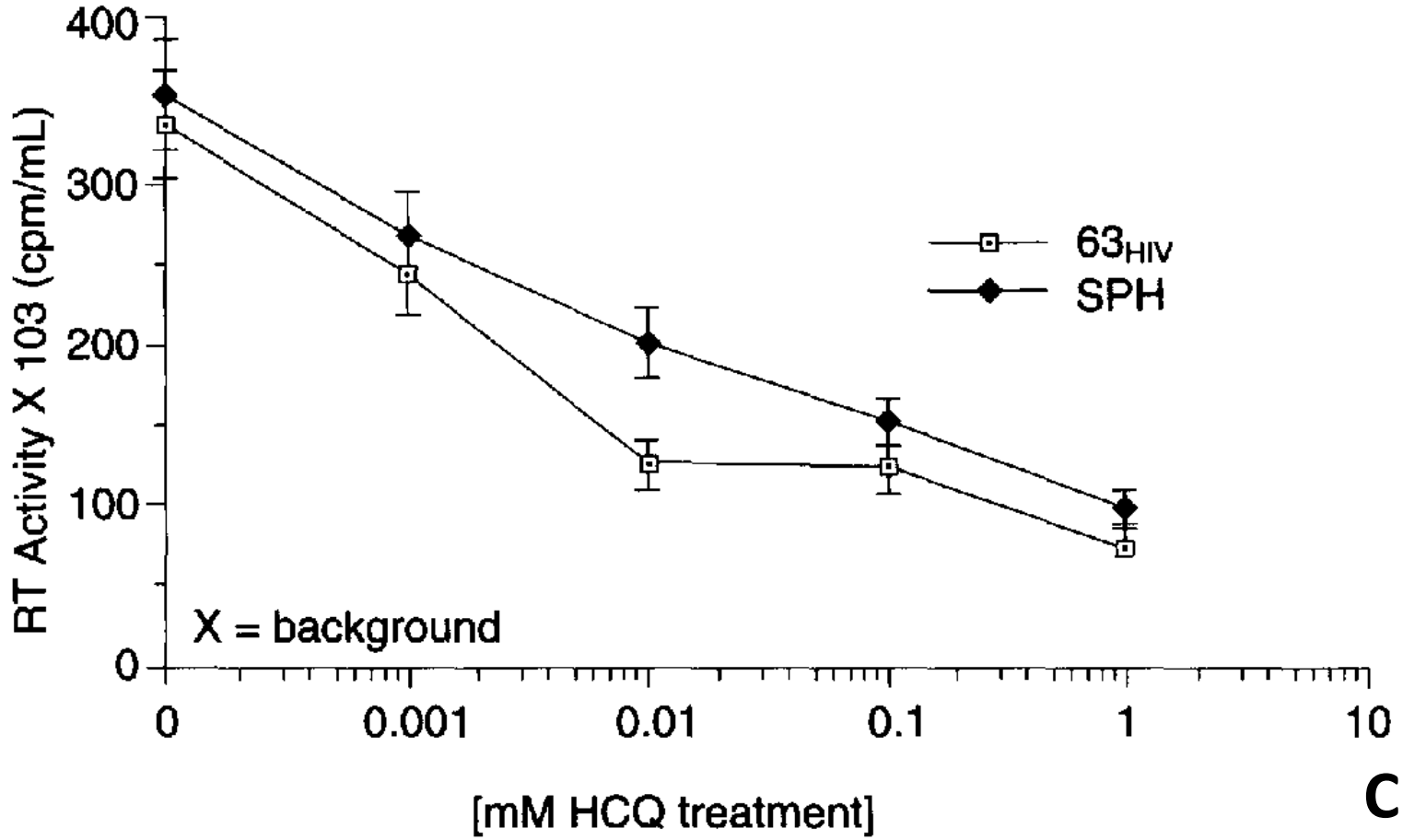
ORIGINAL ARTICLE

Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium*

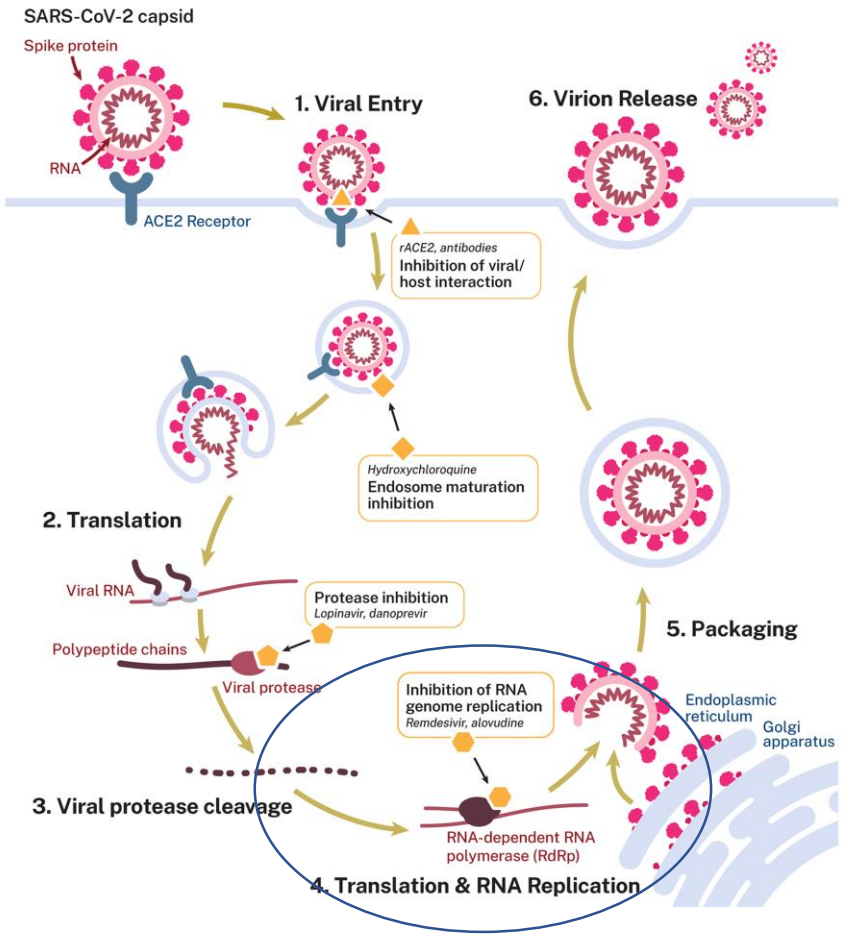
Subgroup	Active Treatment	Control	Log-Rank Statistics for No. of Deaths in Active-Treatment Group O–E	Variance	Rate Ratio for Death (99% CI; 95% CI for total)
	no. of deaths reported/no. of patients (%)				
Hydroxychloroquine					
Age at entry					
<50 yr	19/335 (5.7)	19/317 (5.8)	0.9	9.2	1.10 (0.47–2.57)
50–69 yr	55/410 (12.1)	31/396 (7.1)	10.8	21.2	1.66 (0.95–2.91)
≥70 yr	30/202 (14.0)	34/193 (17.8)	−3.5	15.8	0.80 (0.42–1.53)
Respiratory support at entry					
No mechanical ventilation	69/862 (7.4)	57/824 (6.6)	4.7	31.4	1.16 (0.73–1.84)
Mechanical ventilation	35/85 (39.2)	27/82 (32.3)	3.4	14.8	1.26 (0.65–2.46)
Total	**104/947 (10.2)**	**84/906 (8.9)**	**8.1**	**46.2**	**1.19 (0.89–1.59)**
Heterogeneity around total: χ^2_3=5.0					P=0.23

Inhibition of HIV-1 Replication by Hydroxychloroquine: Mechanism of Action and Comparison with Zidovudine



Chiang, 1996

ANTIVIRAL MECHANISMS AGAINST SARS-CoV-2



Adaptive COVID-19 Treatment Trial (ACTT-1)

Multinational, placebo-controlled, double-blind RCT in hospitalized patients (n = 1,062)

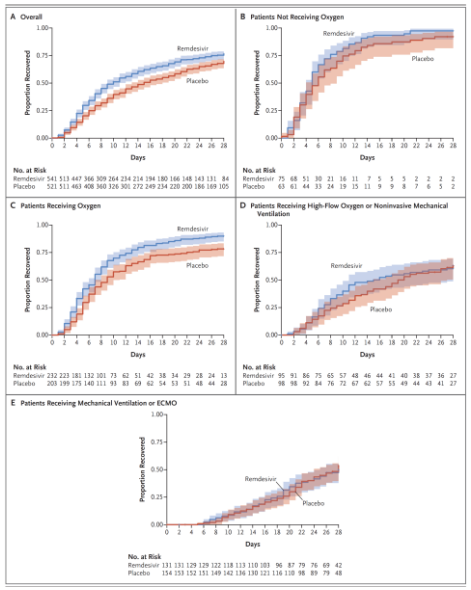
- RDV reduced time to recovery compared to placebo (10 days vs. 15 days; RRR 1.29; 95% CI, 1.12–1.49; P < 0.001).
- Clinical improvement based on ordinal scale was higher at Day 15 in RDV arm (OR 1.5; 95% CI, 1.2–1.9; P < 0.001).
- No statistically significant difference in mortality by Day 29 between RDV and placebo arms (HR 0.73; 95% CI, 0.52–1.03; P = 0.07).
- Benefit of RDV was greatest in patients randomized during the first 10 days after symptom onset.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Remdesivir for the Treatment of Covid-19 — Final Report

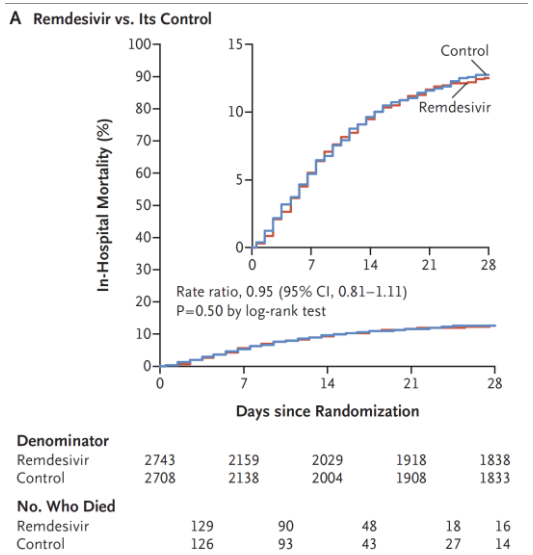
J.H. Beigel, K.M. Tomashek, L.E. Dodd, A.K. Mehta, B.S. Zingman, A.C. Kalil,



Subgroup	No. of Patients	Recovery Rate Ratio (95% CI)
All patients	1062	1.29 (1.12–1.49)
Geographic region		
North America	847	1.30 (1.10–1.53)
Europe	163	1.30 (0.91–1.87)
Asia	52	1.36 (0.74–2.47)
Race		
White	566	1.29 (1.06–1.57)
Black	226	1.25 (0.91–1.72)
Asian	135	1.07 (0.73–1.58)
Other	135	1.68 (1.10–2.58)
Ethnic group		
Hispanic or Latino	250	1.28 (0.94–1.73)
Not Hispanic or Latino	755	1.31 (1.10–1.55)
Age		
18 to <40 yr	119	1.95 (1.28–2.97)
40 to <65 yr	559	1.19 (0.98–1.44)
≥65 yr	384	1.29 (1.00–1.67)
Sex		
Male	684	1.30 (1.09–1.56)
Female	278	1.31 (1.03–1.66)
Symptoms duration		
≤10 days	676	1.37 (1.14–1.64)
>10 days	383	1.20 (0.94–1.52)
Baseline ordinal score		
4 (not receiving oxygen)	138	1.29 (0.91–1.83)
5 (receiving oxygen)	435	1.45 (1.18–1.79)
6 (receiving high-flow oxygen or noninvasive mechanical ventilation)	193	1.09 (0.76–1.57)
7 (receiving mechanical ventilation or ECMO)	285	0.98 (0.70–1.36)

Figure 3. Time to Recovery According to Subgroup.
The widths of the confidence intervals have not been adjusted for multiplicity and therefore cannot be used to infer treatment effects. Race and ethnic group were reported by the patients.

Solidarity Trial NEJM, 2021



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium*

Subgroup	Active Treatment	Control	Log-Rank Statistics for No. of Deaths in Active-Treatment Group O–E	Variance	Rate Ratio for Death (99% CI; 95% CI for total)
	no. of deaths reported/no. of patients (%)				
Remdesivir					
Age at entry					
<50 yr	61/961 (6.9)	59/952 (6.8)	2.3	29.8	1.08 (0.67–1.73)
50–69 yr	154/1282 (13.8)	161/1287 (14.2)	−7.6	77.5	0.91 (0.68–1.21)
≥70 yr	86/500 (20.5)	83/469 (21.6)	−2.9	41.5	0.93 (0.63–1.39)
Respiratory support at entry					
No mechanical ventilation	203/2489 (9.4)	232/2475 (10.6)	−15.8	108.0	0.86 (0.67–1.11)
Mechanical ventilation	98/254 (43.0)	71/233 (37.8)	7.6	40.8	1.20 (0.80–1.80)
Total	**301/2743 (12.5)**	**303/2708 (12.7)**	**−8.3**	**148.8**	**0.95 (0.81–1.11)**
Heterogeneity around total: χ^2_3 = 3.9					P=0.50

Remdesivir

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Search

Medicines | Human regulatory | Veterinary regulatory | Committees | News & events | Partners & networks | About us

Veklury

Share RSS

remdesivir

AUTHORISED
This medicine is authorised for use in the European Union.

Table of contents

Overview

Veklury is an antiviral medicine used to treat coronavirus disease 2019 (COVID-19). It is used in adults and adolescents (from 12 years of age and weighing at least 40 kilograms) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at the start of treatment).

COVID-19, which is caused by SARS-CoV-2 virus, was declared a pandemic by the World Health Organization on 11 March 2020.

Veklury contains the active substance remdesivir.

Favipiravir

Viral RNA-dependent RNA-polymerase inhi bitor approved in Japan for the treatment of influenza

Favipiravir was compared to umifenovir in an RCT enrolling 240 patients with COVID-19 associated pneumonia. The seven-day recovery rate was higher in those receiving favipiravir compared to those treated with umifenovir

Preliminary data from a non-randomized control study have shown that among 340 patients, those who received favipiravir improved respiratory conditions. Favipiravir shortened the duration of fever and increased viral clearance rate

Cai Q, Yang M, Liu D, et al. Experimental treatment with favipir avir for COVID-19: an open-label control study Engineering (Beijing). 2020. doi:10.1016/j.eng.2020.03.00725.
Chen C, Zhang Y, Huang J, et al. Favipiravir versus arbidol for COVID-19: a randomized clinical trial. MedRxiv. 2020. doi:10.1101/2020.03.17.20037432

NON ANTIVIRAL AGENTS

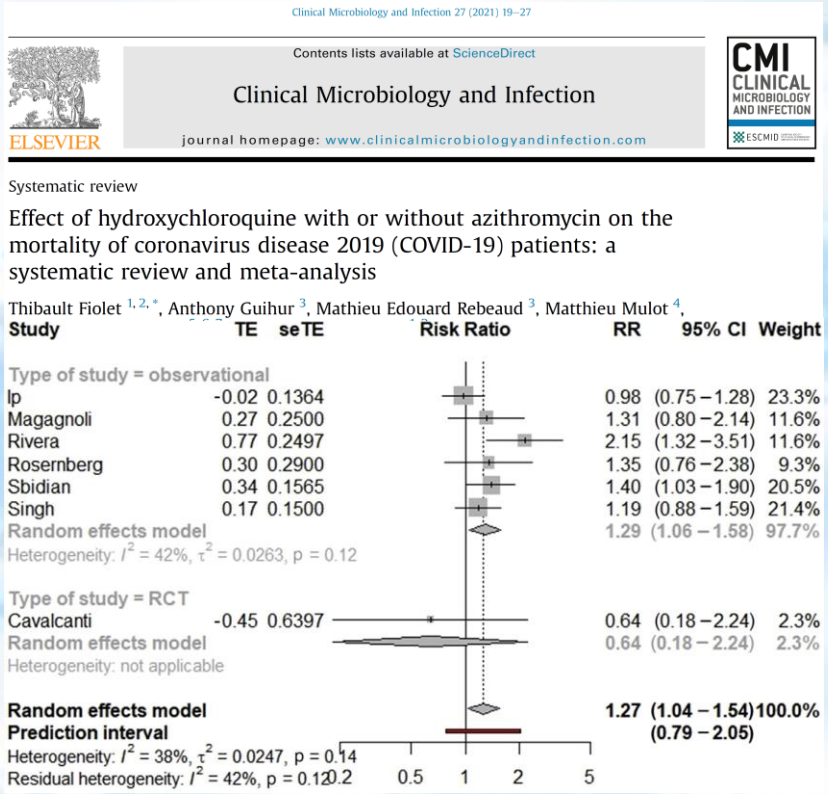
Azithromycin

In addition to their antibacterial effects, macrolides demonstrate immunomodulatory and anti-inflammatory effects

Clinical investigations on small series of COVID-19 patients suggested that adding azithromycin to HCQ led to significant improvement, regardless of the absence of direct effect on viral load

Several doubts arise on HCQ/azithromycin combination due to an excess in terms of mortality and the increased risk of arrhythmias

Efficacy?



Clinical Microbiology and Infection 27 (2021) 19–27

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Effect of hydroxychloroquine with or without azithromycin on the mortality of coronavirus disease 2019 (COVID-19) patients: a systematic review and meta-analysis

Thibault Fiolet [1,2,*], Anthony Guihur [3], Mathieu Edouard Rebeaud [3], Matthieu Mulot [4],

Azhytromicin + HCQ administration is Associated to an increased mortality

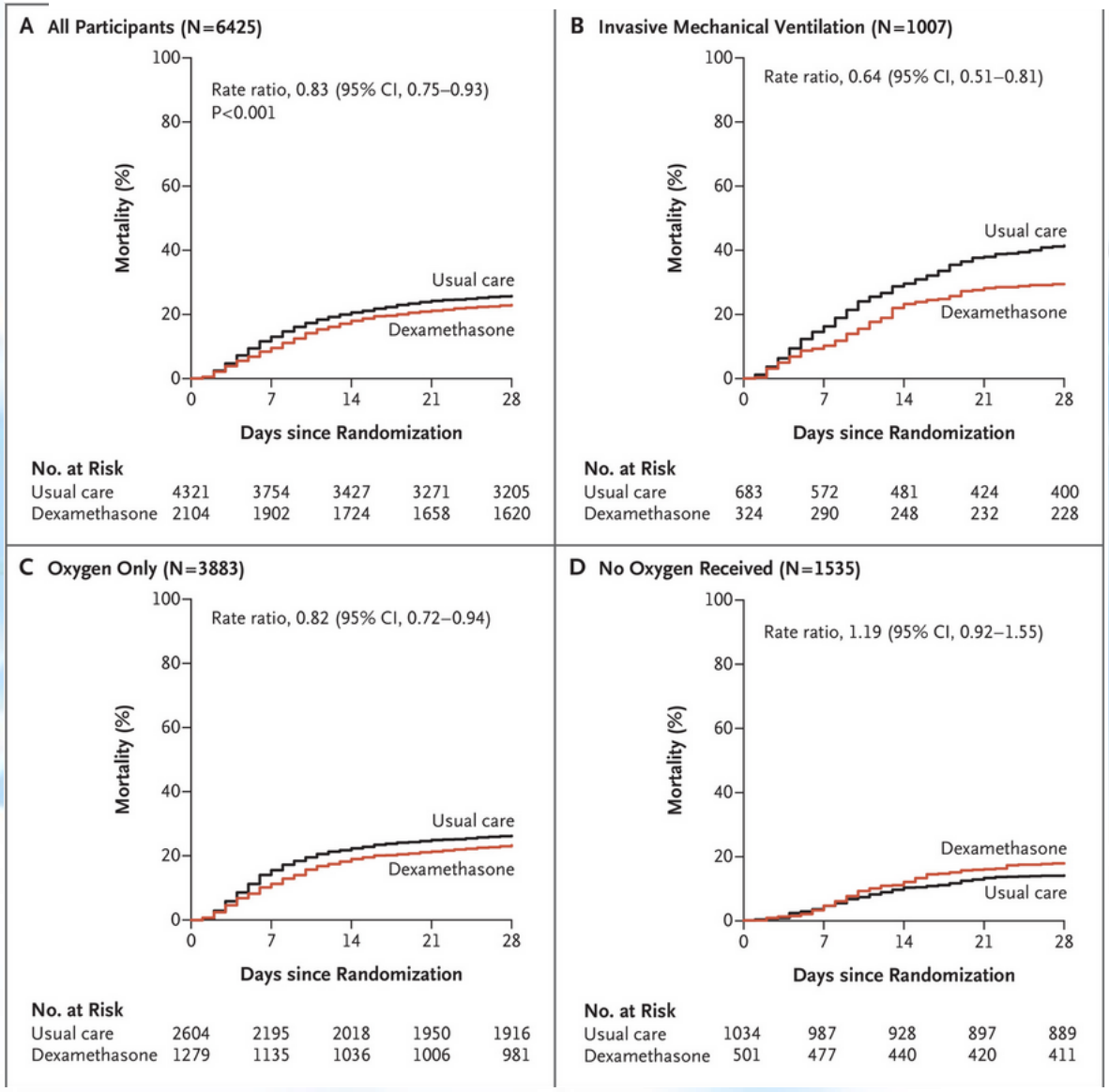
Fiolet T, Guihur A, Rebeaud ME, Mulot M, Peiffer-Smadja N, Mahamat-Saleh Y. Effect of hydroxychloroquine with or without azithromycin on the mortality of coronavirus disease 2019 (COVID-19) patients: a systematic review and meta-analysis. Clin Microbiol Infect. 2020.71

ORIGINAL ARTICLE

Dexamethasone in Hospitalized Patients with Covid-19

The RECOVERY Collaborative Group*

February 25, 2021
N Engl J Med 2021; 384:693-704
DOI: 10.1056/NEJMoa2021436



Recovery trial

Mortality at 28 Days in All Patients and According to Respiratory Support at Randomization

Is there a difference in terms of mortality in respect to the steroid administered?

Prospective meta-analysis that pooled data from 7 randomized clinical trials that evaluated the efficacy of corticosteroids in 1703 critically ill patients with COVID-19.

The trials were conducted in 12 countries from February 26, 2020, to June 9, 2020, and the date of final follow-up was July 6, 2020.

Pooled data were aggregated from the individual trials, overall, and in predefined subgroups

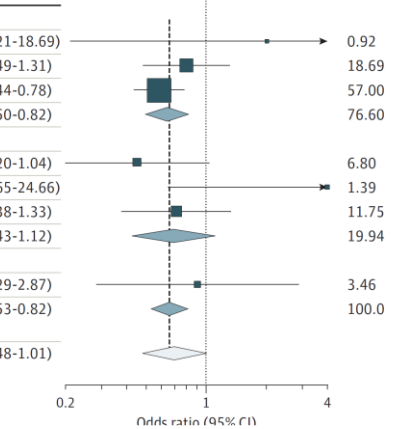
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19
A Meta-analysis

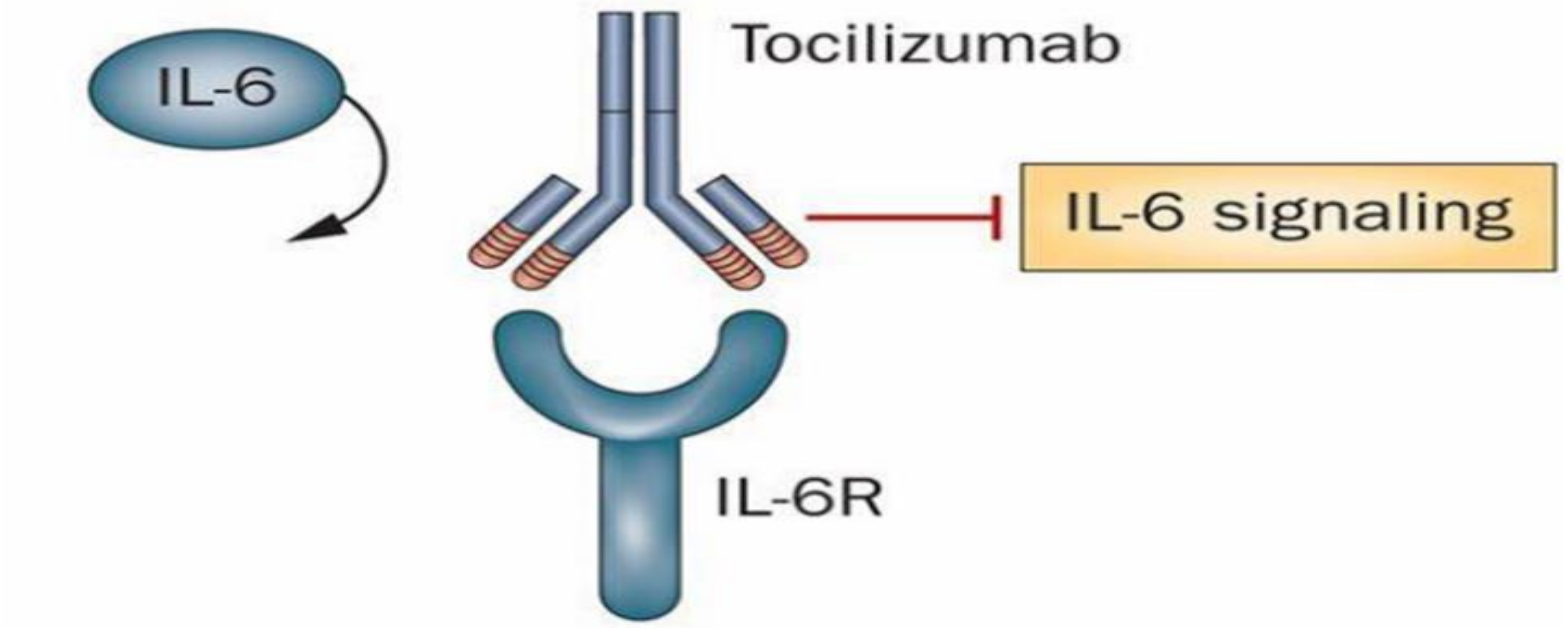
The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group

Figure 2. Association Between Corticosteroids and 28-Day All-Cause Mortality in Each Trial, Overall, and According to Corticosteroid Drug

Drug and trial	ClinicalTrials.gov identifier	Initial dose and administration	No. of deaths/total No. of patients: Steroids	No. of deaths/total No. of patients: No steroids	Odds ratio (95% CI)	Weight, %
Dexamethasone						
DEXA-COVID 19	NCT04325061	High: 20 mg/d intravenously	2/7	2/12	2.00 (0.21-18.69)	0.92
CoDEX	NCT04327401	High: 20 mg/d intravenously	69/128	76/128	0.80 (0.49-1.31)	18.69
RECOVERY	NCT04381936	Low: 6 mg/d orally or intravenously	95/324	283/683	0.59 (0.44-0.78)	57.00
Subgroup fixed effect			166/459	361/823	0.64 (0.50-0.82)	76.60
Hydrocortisone						
CAPE COVID	NCT02517489	Low: 200 mg/d intravenously	11/75	20/73	0.46 (0.20-1.04)	6.80
COVID STEROID	NCT04348305	Low: 200 mg/d intravenously	6/15	2/14	4.00 (0.65-24.66)	1.39
REMAP-CAP	NCT02735707	Low: 50 mg every 6 h intravenously	26/105	29/92	0.71 (0.38-1.33)	11.75
Subgroup fixed effect			43/195	51/179	0.69 (0.43-1.12)	19.94
Methylprednisolone						
Steroids-SARI	NCT04244591	High: 40 mg every 12 h intravenously	13/24	13/23	0.91 (0.29-2.87)	3.46
Overall (fixed effect)			222/678	425/1025	0.66 (0.53-0.82)	100.0
$P = .31$ for heterogeneity; $I^2 = 15.6\%$						
Overall (random effects[a])			222/678	425/1025	0.70 (0.48-1.01)	

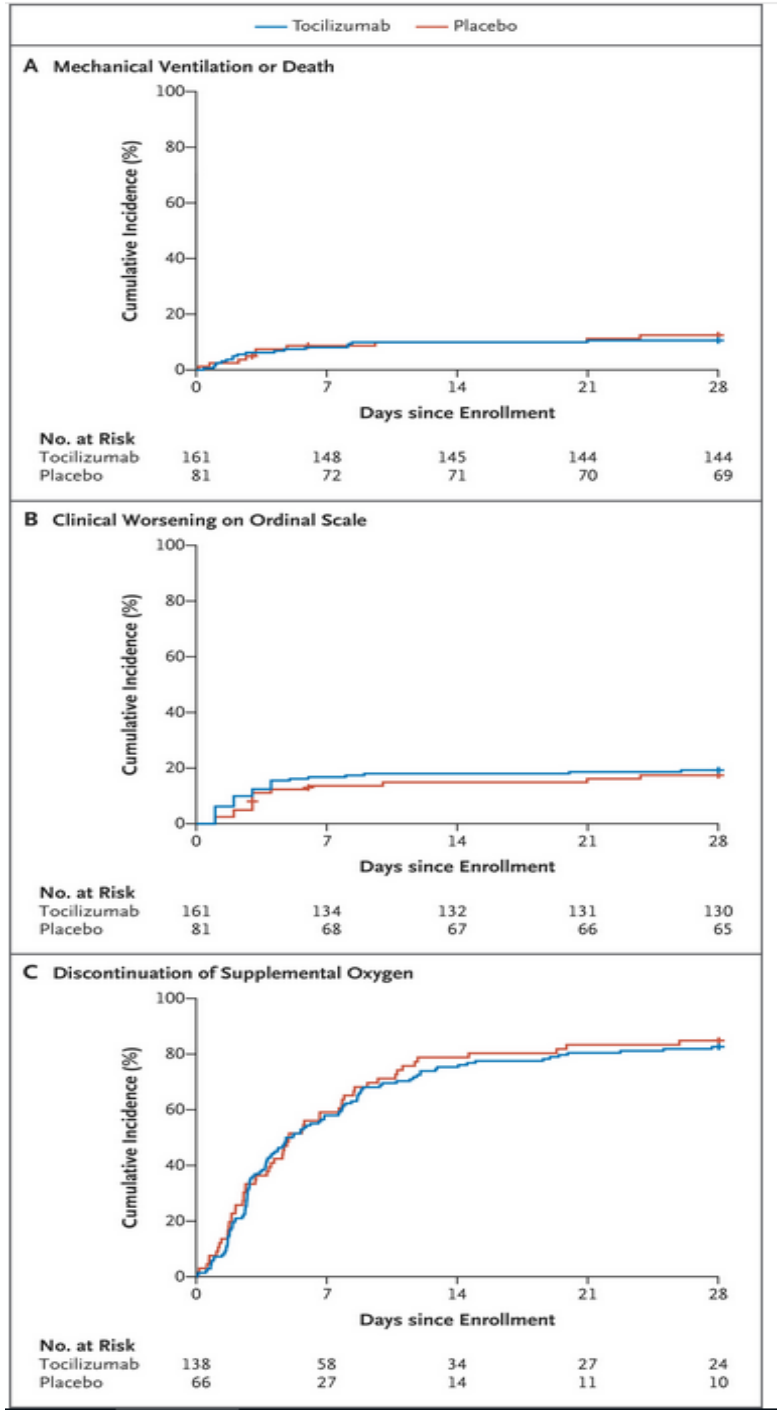


Tocilizumab



Tocilizumab (TCZ) is a humanized anti-interleukin-6 receptor monoclonal antibody able to inhibit interleukin 6 activity which is commonly used in patients with rheumatoid arthritis. Its role in the treatment of COVID-19 was based on the efficacy in decreasing serum values of leukins IL-6, IL-2, IL-7, IL-10, and TNF, which are crucial in determining pulmonary damage after SARS-CoV-2 infection

BACC BAY trial



Kaplan–Meier Analyses of Efficacy Outcomes

EMPACTA trial

Table 2. Primary and Key Secondary Efficacy Outcomes by Day 28 in the Modified Intention-to-Treat Population.*

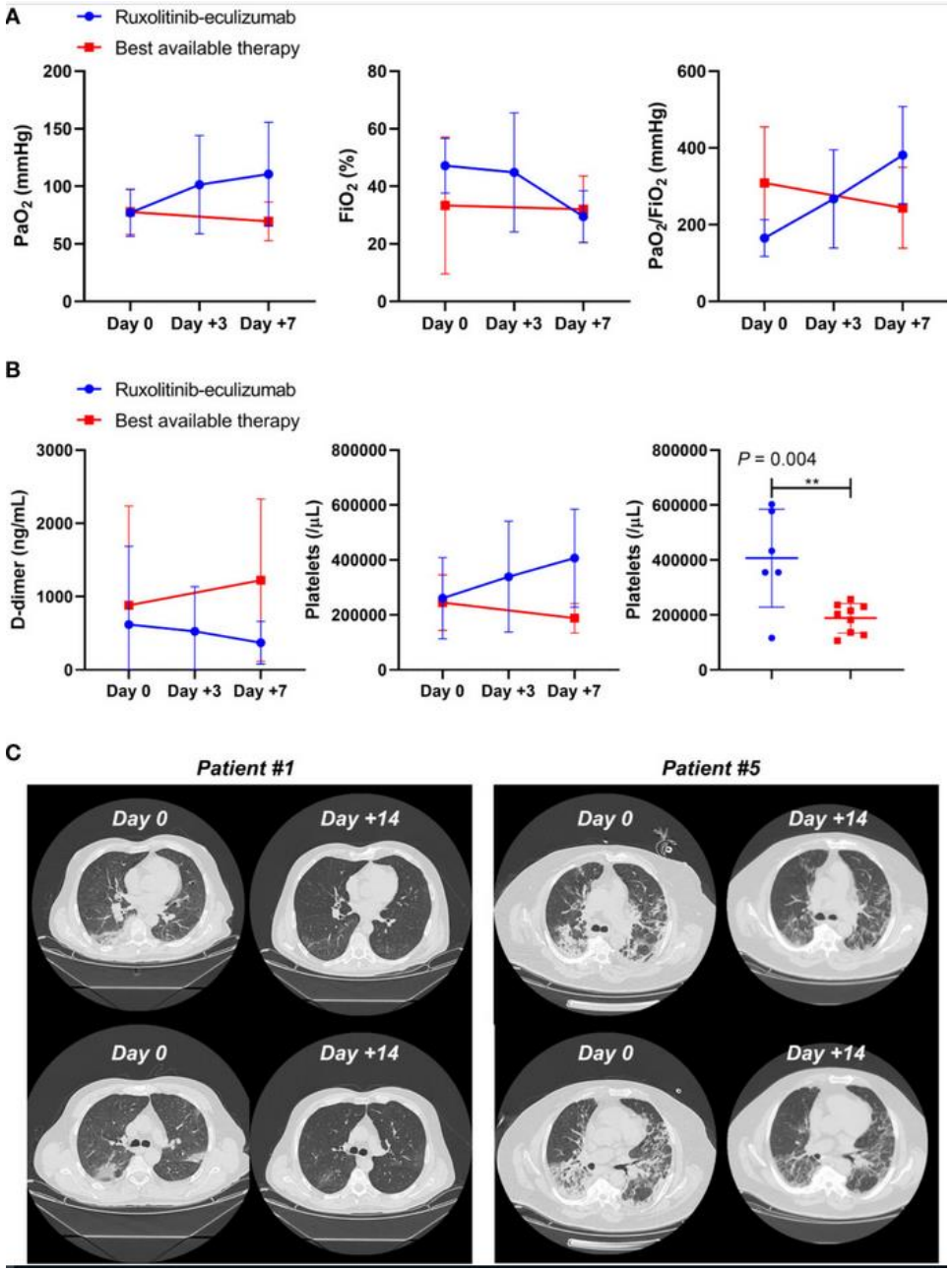
Outcome	Tocilizumab (N=249)	Placebo (N=128)	Hazard Ratio (95% CI)	Weighted Difference (95% CI)	P Value†
Primary outcome: mechanical ventilation or death — % (95% CI)‡	12.0 (8.5 to 16.9)	19.3 (13.3 to 27.4)	0.56 (0.33 to 0.97)	NA	0.04
Secondary outcomes					
Median time to hospital discharge or readiness for discharge (95% CI) — days§	6.0 (6.0 to 7.0)	7.5 (7.0 to 9.0)	1.16 (0.91 to 1.48)	NA	
Median time to improvement in clinical status (95% CI) — days§¶	6.0 (6.0 to 7.0)	7.0 (6.0 to 9.0)	1.15 (0.90 to 1.48)	NA	
Median time to clinical failure (95% CI) — days§	NE	NE	0.55 (0.33 to 0.93)	NA	
Death — no. (% [95% CI])‖	26 (10.4 [7.2 to 14.9])	11 (8.6 [4.9 to 14.7])	NA	2.0 (−5.2 to 7.8)**	

Primary and Key Secondary Efficacy Outcomes by Day 28 in the Modified Intention-to-Treat Population

RECOVERY trial

		Treatment allocation		RR (95% CI)	p value
		Tocilizumab group (n=2022)	Usual care group (n=2094)		
Primary outcome					
28-day mortality		621 (31%)	729 (35%)	0·85 (0·76–0·94)	0·0028
Secondary outcomes					
Median time to being discharged, days		19	>28	..	..
Discharged from hospital within 28 days		1150 (57%)	1044 (50%)	1·22 (1·12–1·33)	<0·0001
Receipt of invasive mechanical ventilation or death*		619/1754 (35%)	754/1800 (42%)	0·84 (0·77–0·92)	<0·0001
	Invasive mechanical ventilation	265/1754 (15%)	343/1800 (19%)	0·79 (0·69–0·92)	0·0019

Effect of allocation to tocilizumab on main study outcomes



Ruxolitinib-eculizumab

Clinical outcomes in ruxolitinib and eculizumab treated COVID-19 patients

Giudice V, Pagliano P, Vatrella A, Masullo A, Poto S, Polverino BM, Gammaldi R, Maglio A, Sellitto C, Vitale C, Serio B, Cuffa B, Borrelli A, Vecchione C, Filippelli A, Selleri C. Combination of Ruxolitinib and Eculizumab for Treatment of Severe SARS-CoV-2-Related Acute Respiratory Distress Syndrome: A Controlled Study. Front Pharmacol. 2020 Jun 5;11:857. doi: 10.3389/fphar.2020.00857. PMID: 32581810; PMCID: PMC7291857.

Thank you for your attention!

State of the art of COVID-19 vaccines and progress made since 2020

Florian Krammer

Mount Sinai Professor in Vaccinology

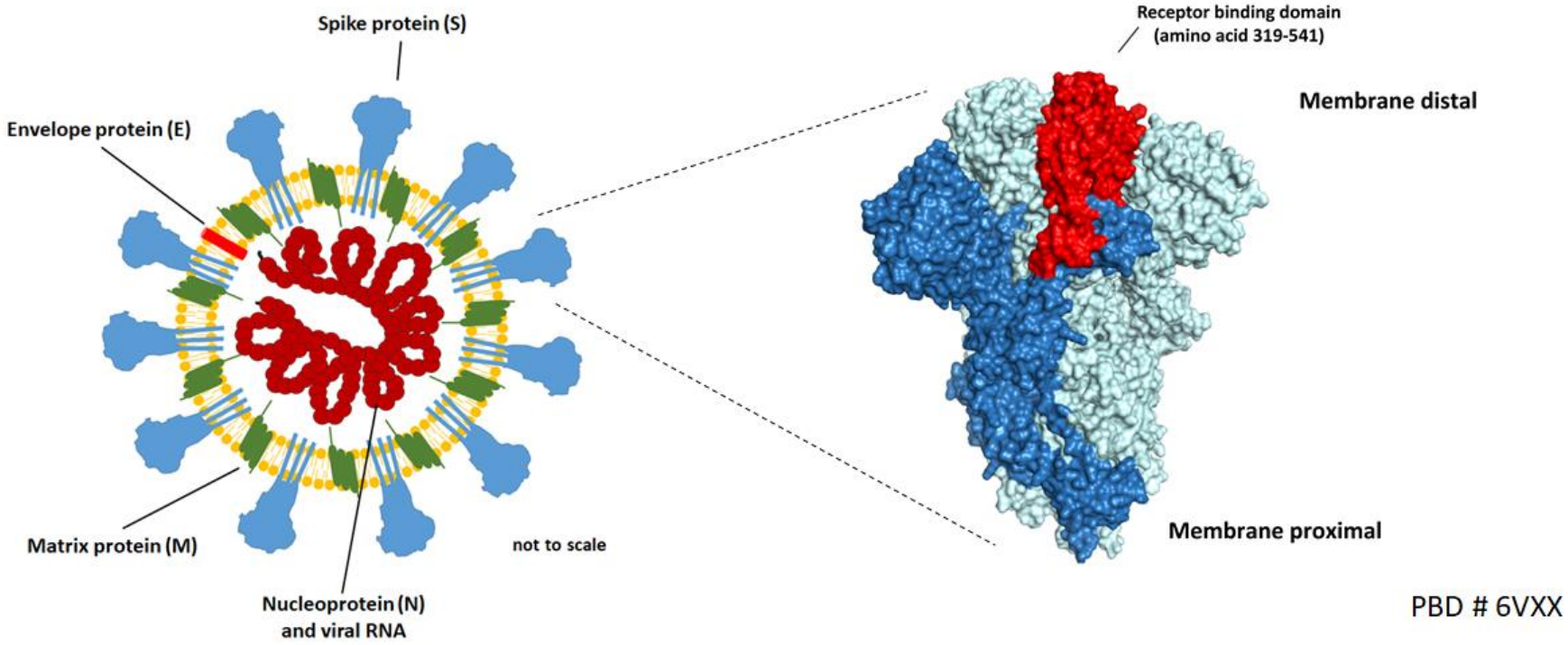
Icahn School of Medicine at Mount Sinai

One Health Knowledge Café

May 27th, 2021

Mount Sinai

Immunity?



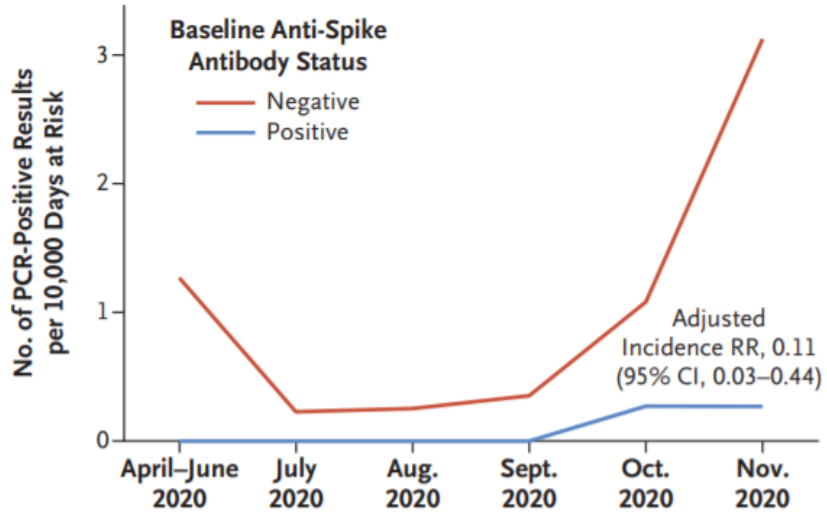
- Antibody responses target the spike protein including the receptor binding domain as well as the nucleoprotein and other targets
  - Anti-spike (and RBD) antibodies are neutralizing and correlate with protection
  - NP antibodies are not neutralizing (we do not know if they are helpful)
- T-cell responses target several proteins, including the spike protein
  - Strong CD4+ response
  - Relatively weak CD8+ response

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers

S.F. Lumley, D. O'Donnell, N.E. Stoesser, P.C. Matthews, A. Howarth, S.B. Hatch, B.D. Marsden, S. Cox, T. James, F. Warren, L.J. Peck, T.G. Ritter, Z. de Toledo, L. Warren, D. Axten, R.J. Cornall, E.Y. Jones, D.I. Stuart, G. Screaton, D. Ebner, S. Hoosdally, M. Chand, D.W. Crook, A.-M. O'Donnell, C.P. Conlon, K.B. Pouwels, A.S. Walker, T.E.A. Peto, S. Hopkins, T.M. Walker, K. Jeffery, and D.W. Eyre, for the Oxford University Hospitals Staff Testing Group*

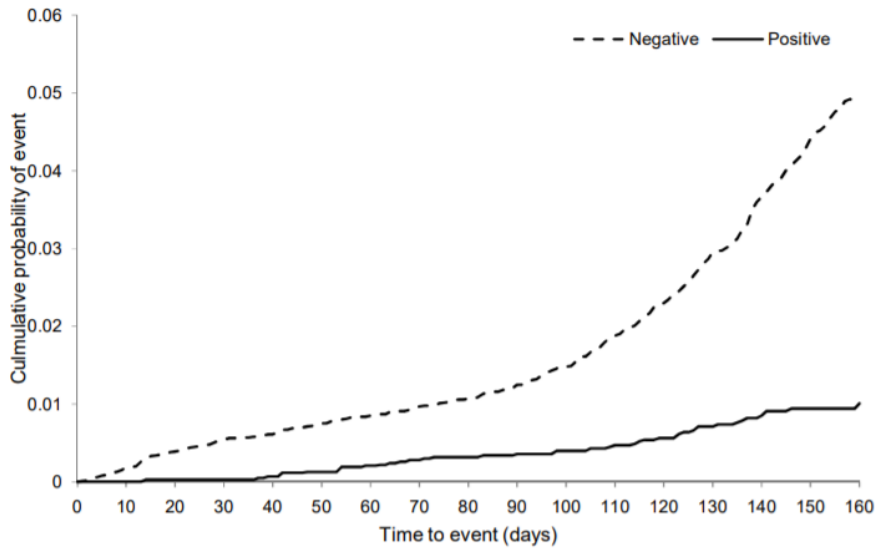


Days at Risk						
Seronegative	456,963	307,508	316,141	312,027	332,704	329,469
Seropositive	316	19,474	31,601	34,011	36,824	37,098

THE LANCET

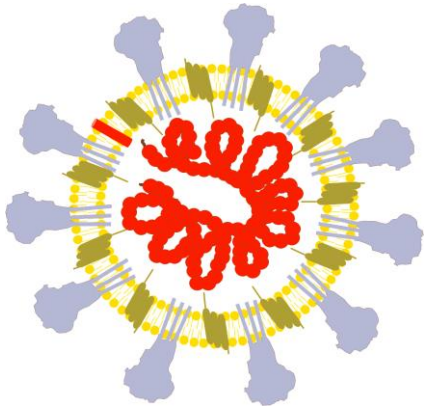
SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN)

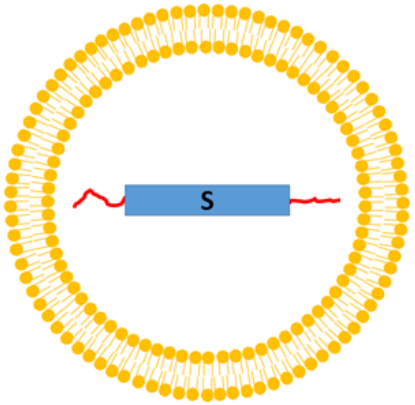
Victoria Jane Hall, Sarah Foulkes*, Andre Charlett, Ana Atti, Edward J M Monk, Ruth Simmons, Edgar Wellington, Michelle J Cole, Ayoub Saei, Blanche Oguti, Katie Munro, Sarah Wallace, Peter D Kirwan, Madhumita Shrotri, Amoolya Vusirikala, Sakib Rokadiya, Meaghan Kall, Maria Zambon, Mary Ramsay, Tim Brooks, Colin S Brown, Meera A Chand, Susan Hopkins, and the SIREN Study Group†*



Which types of COVID-19 vaccines are there and how do they work?

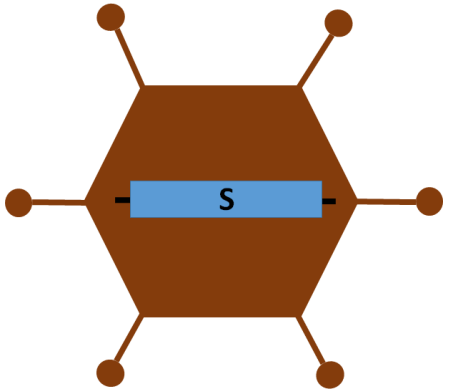
Inactivated virus vaccines





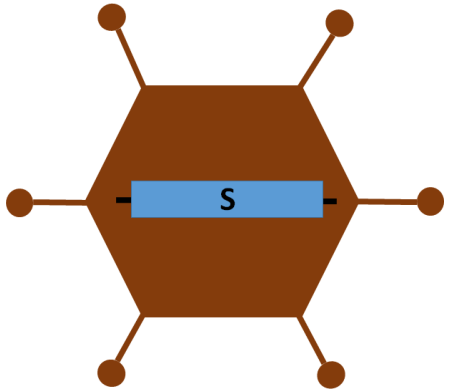
mRNA vaccines

Viral vector vaccines



Recombinant protein vaccines

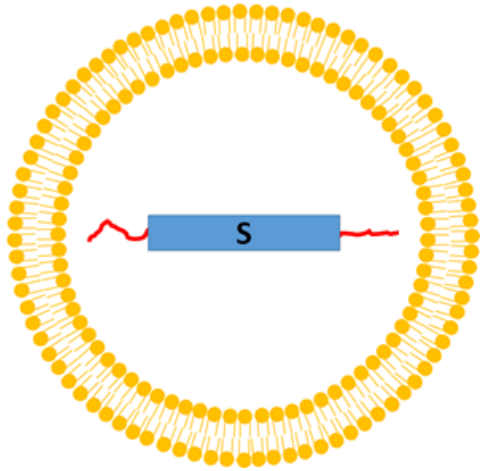
Viral vector vaccines



- Are based on harmless viruses (e.g. adenoviruses that cause colds and GI tract infections)
- Part of their genome is deleted so that they can't amplify themselves anymore
- Then, the information for the SARS-CoV-2 spike protein is added to their genome
- They enter our cells, make the spike protein but can't replicate
- Vaccines based on that concept are currently already authorized (J&J, in the US and Europe, AZ in Europe) or in Phase III (AstraZeneca, in the US)
- Ad26-based Ebola vaccine licensed in the EU and Ad4 and Ad7 vaccines in use in the US military since 1971

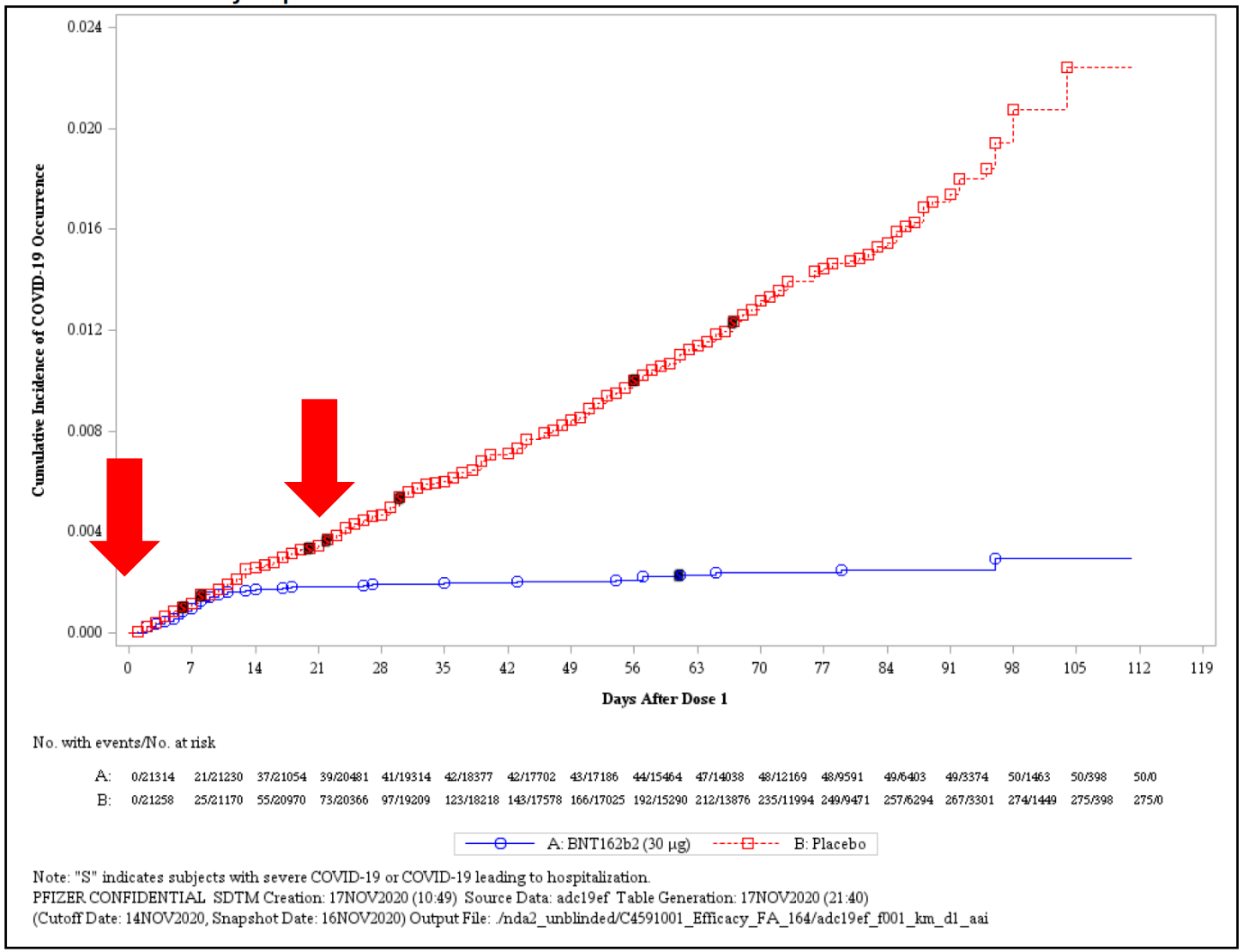
RNA Vaccines (Pfizer, Moderna)

- mRNA that codes for the SARS-CoV-2 surface glycoprotein (spike) is biochemically synthesized and packaged into lipid nanoparticles
- The particles are taken up by cells at the injection site after vaccination
- The cells then produce spike and our body makes an immune response against it
- Two mRNA vaccines now widely used in the US (Moderna, Pfizer/BioNTech), another one is on the way (CureVac)



Pfizer Phase III Trial Data

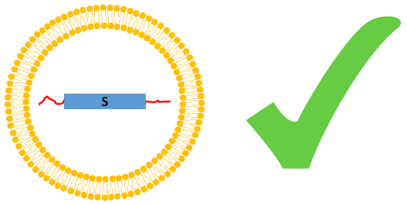
Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1, Dose 1 All-Available Efficacy Population



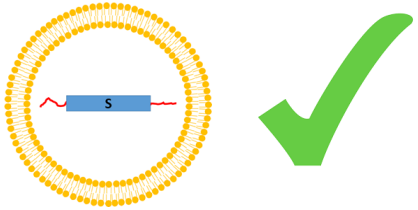
https://www.fda.gov/media/144245/download accessed 8Dec20

Authorized vaccines and vaccines in phase III trials

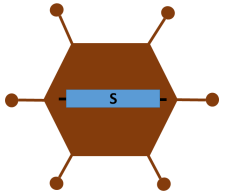
- Moderna (94)%



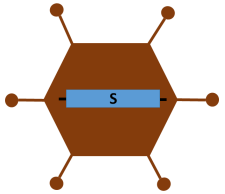
- Pfizer (95%)



- AstraZeneca (60-90%)



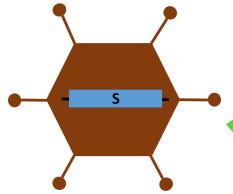
- J&J (72%)



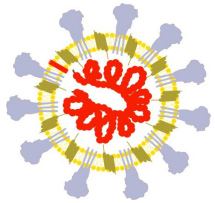
- Novavax (89-96%)

IR

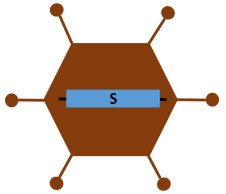
- Gamaleya (91.6%)



- Sinovac/Sinopharm/Bharat (50-90%)

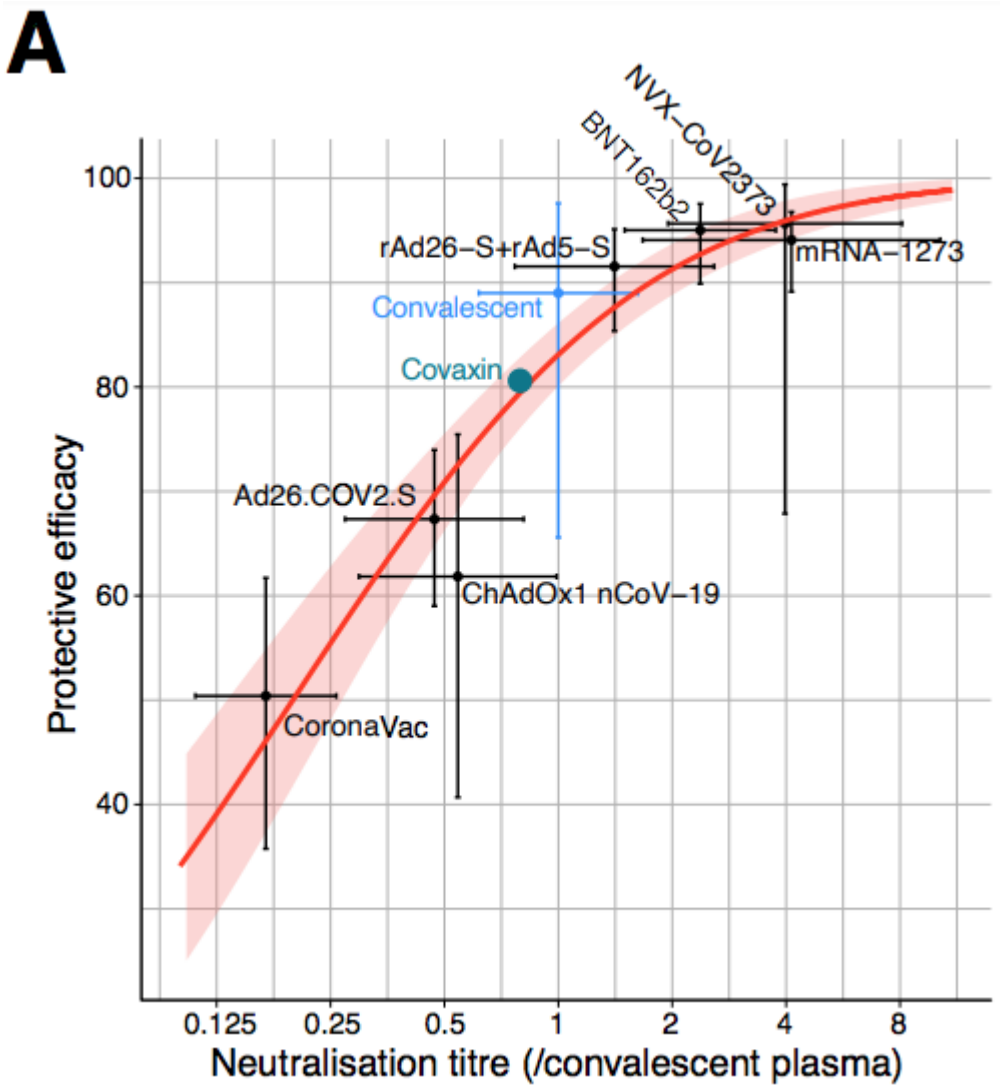


- Cansino



For most of these vaccines two injections are required.

Neutralizing antibodies correlate with vaccine efficacy



https://www.medrxiv.org/content/10.1101/2021.03.09.21252641v1.full.pdf

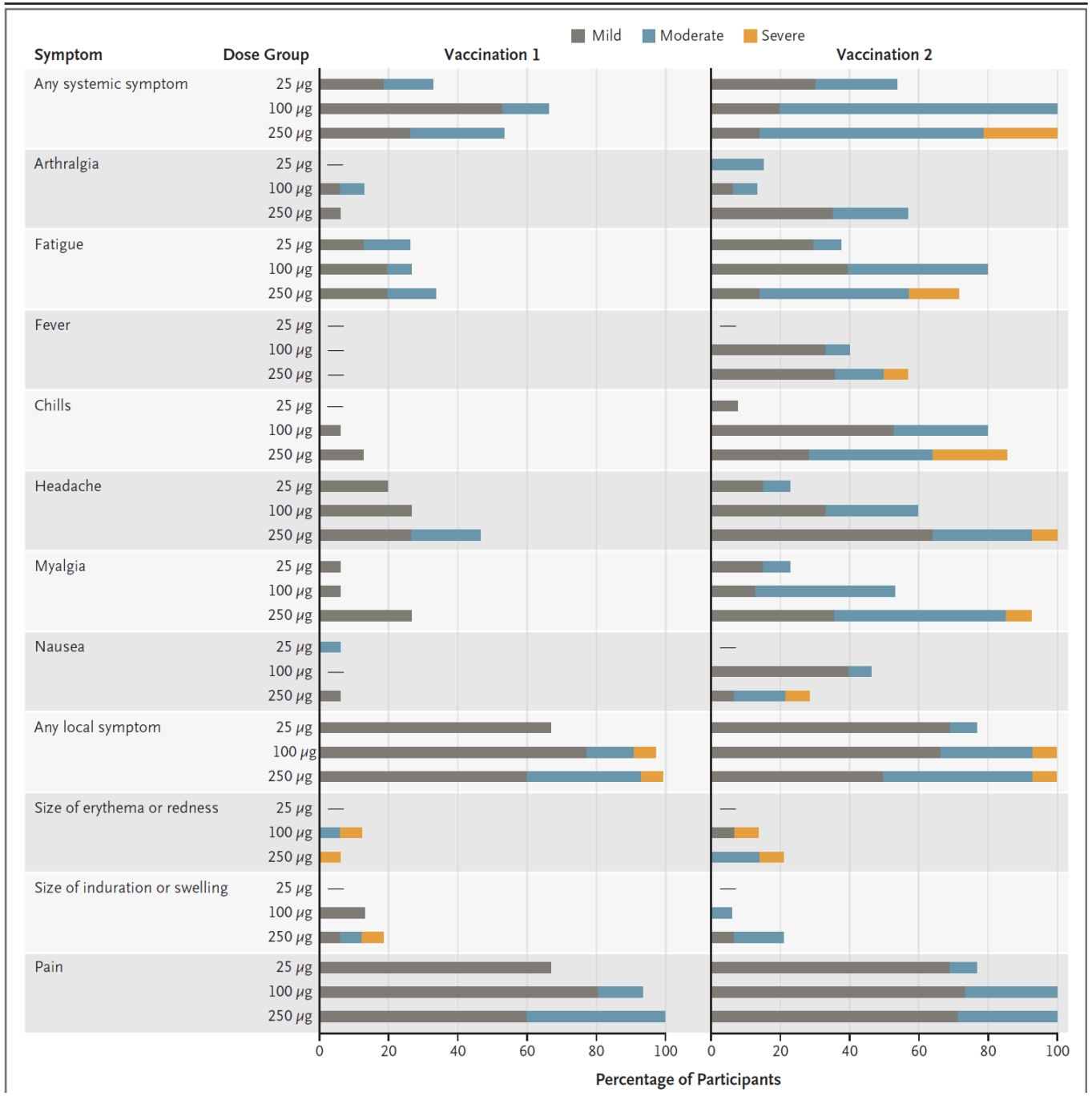
Reactogenicity

- Injection site pain
- Headache
- Fatigue
- Elevated temperature
- Myalgia
- Mild flu-like symptoms

→unpleasant, but not dangerous

AdV=mRNA>recombinant protein>inactivated vaccine

Moderna/VRC mRNA 1273 via LNPs



Rare severe reactions

- Severe allergic reactions: The rate is approximately 11 reactions per 1 million vaccinated individuals for Pfizer and 2.5 per 1 million for Moderna (CDC)
- Cerebral sinus vein thrombosis and splanchnic vein thrombosis associated with AstraZeneca vaccine, mostly in females under 60 years of age (rates: 62 CSVT and 24 SVT per 25 million vaccinated individuals)
  - Also an issue with J&J vaccine
  - Now termed TTS (Thrombosis with Thrombocytopenia Syndrome)
- Myocarditis under investigation for mRNA vaccines

Does the vaccine protect from asymptomatic infection?

- Asymptomatic infections are possible, especially after the first vaccination (60%-80% reduction)
- 90% reduction after 2nd shot with mRNA vaccines
- If a vaccinated person gets infected, she/he is likely less infectious and for a shorter period of time
- This is similar to other vaccines like influenza and pertussis

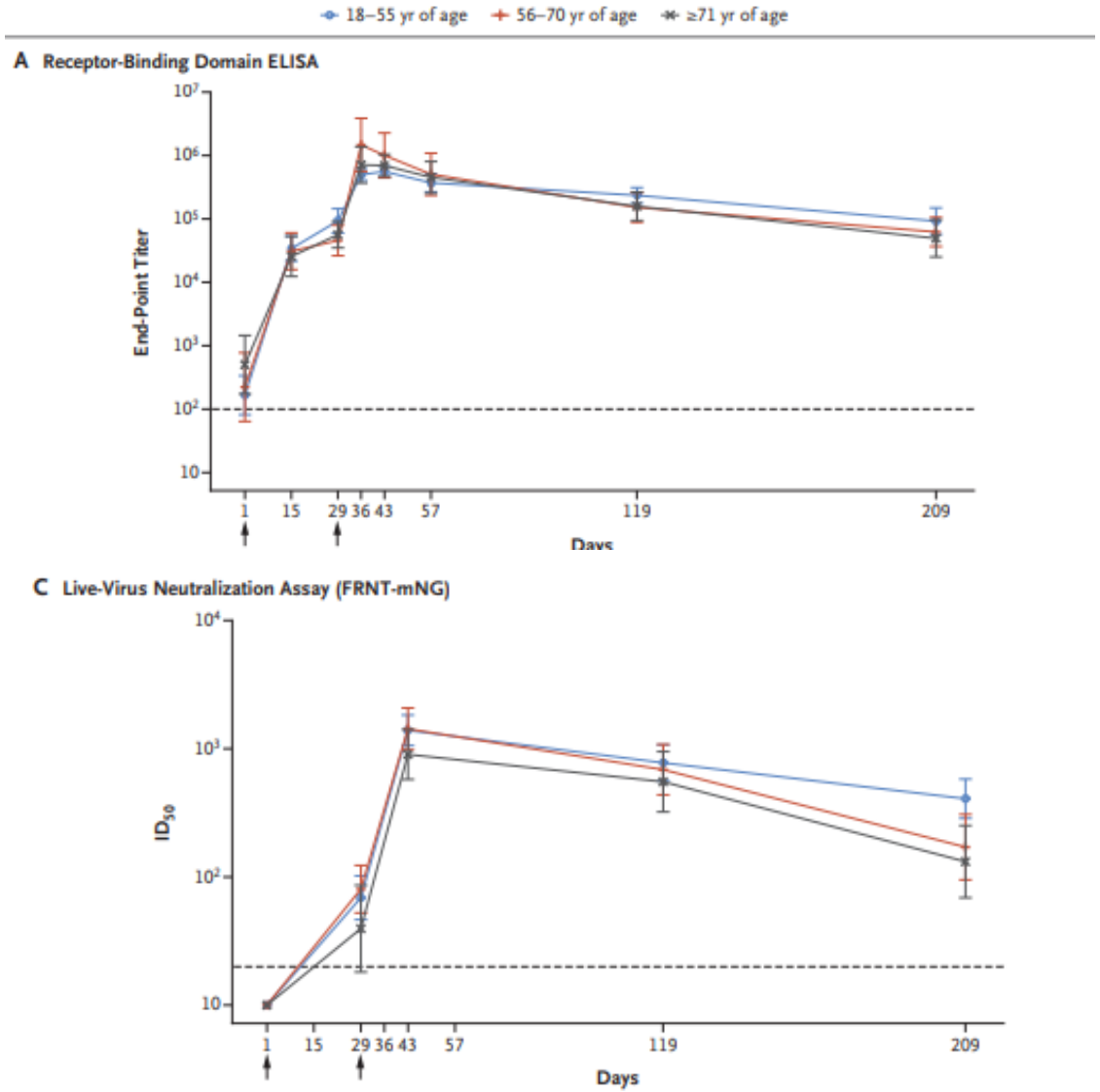
The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

How long does protection last?

- Protection for at least 6 months was shown by Pfizer
- Likely for years, based on what we know about immune responses in general and immune responses to SARS-CoV-2
- It might be that booster doses are needed at some point, but that is similar to other vaccines (e.g. tetanus)

Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19

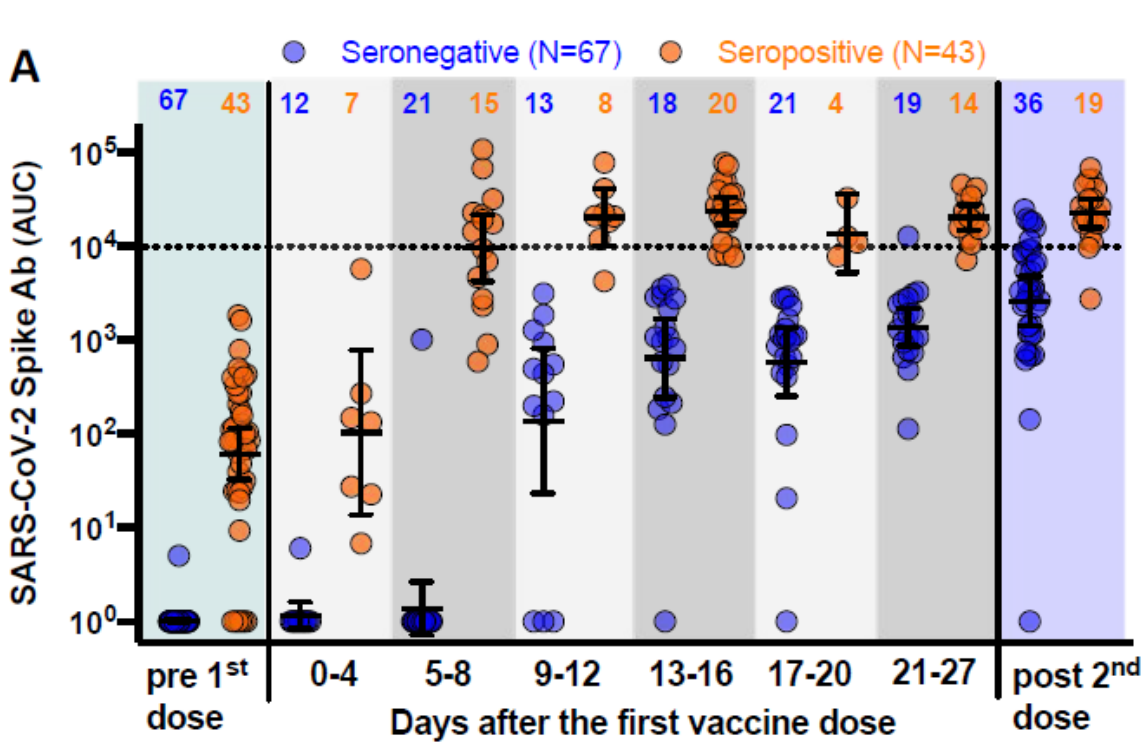


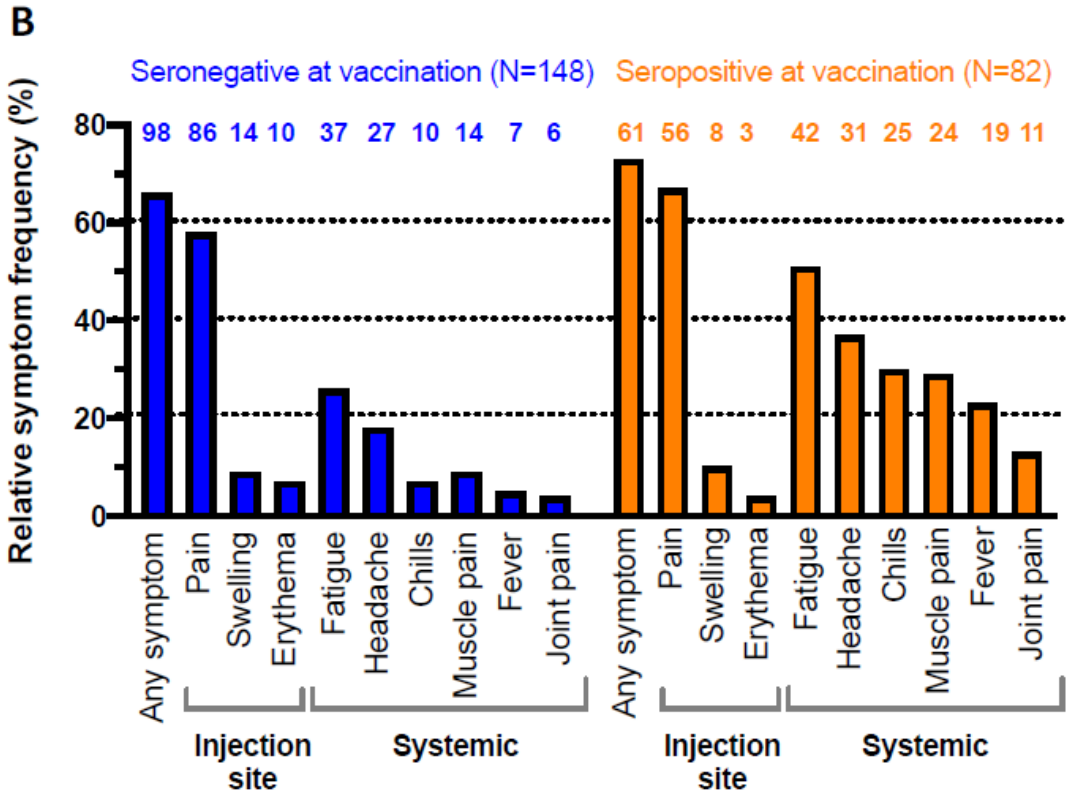
Should individuals who already had a SARS-CoV-2 infection get vaccinated? And if yes, how often?

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine

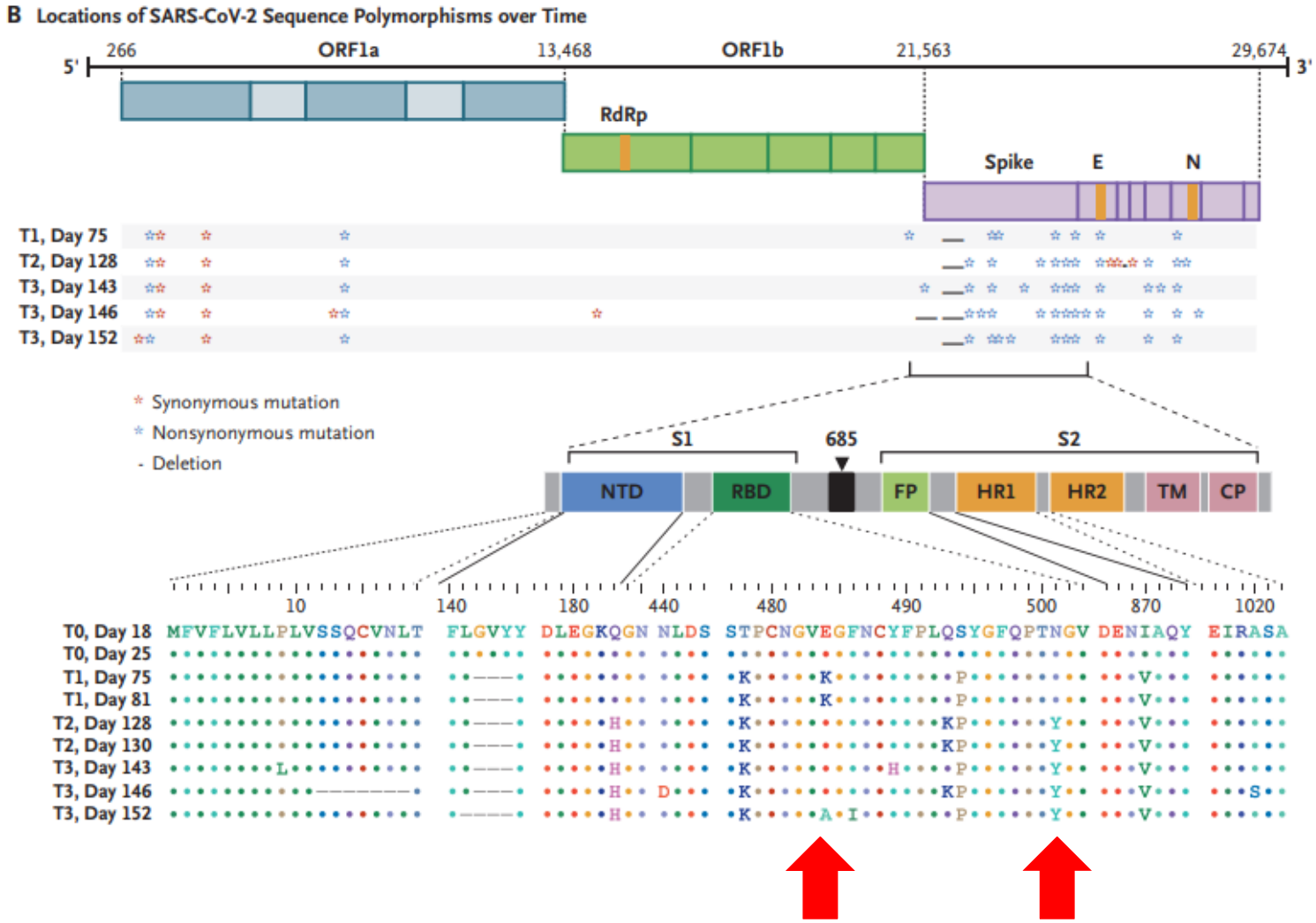




Variants of Concern (VoC)

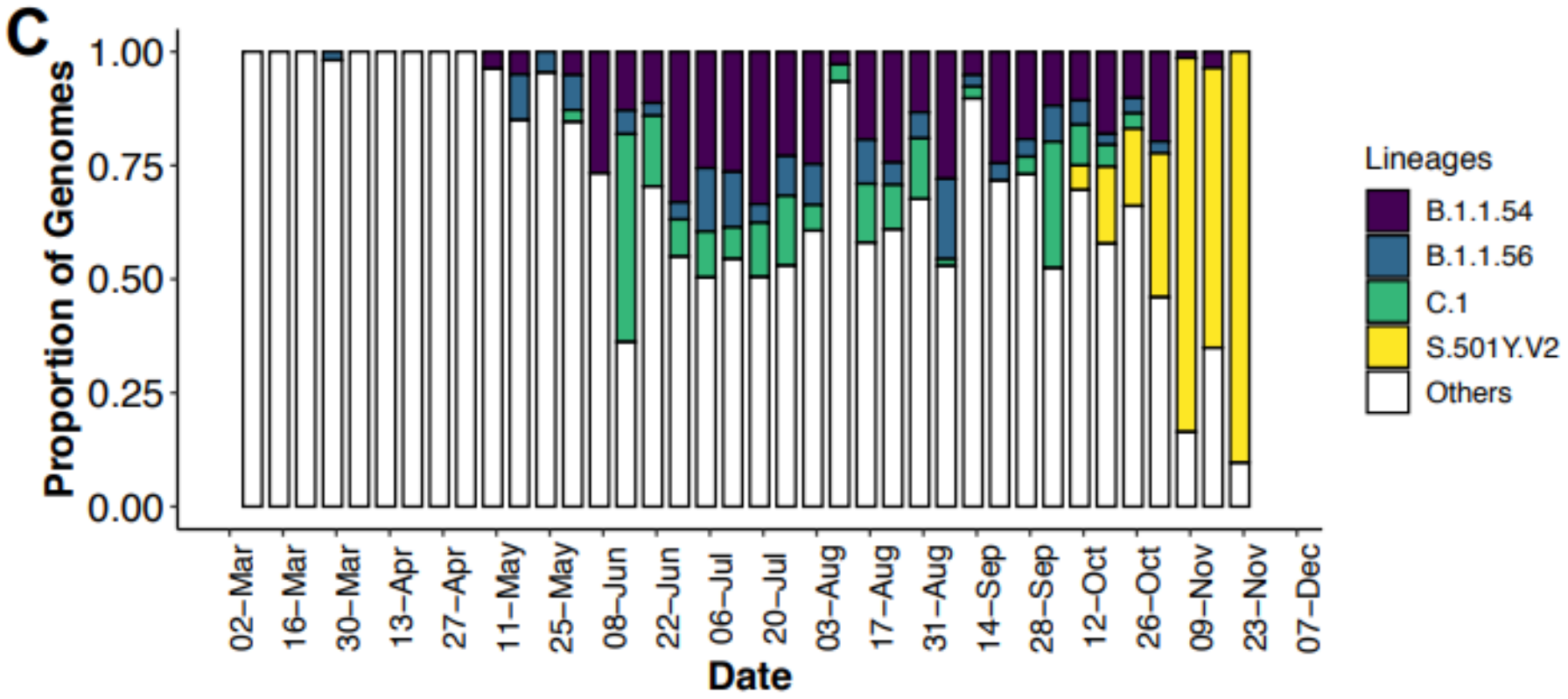
Coronaviruses are exceptional among RNA viruses

- They have proofreading activity
- However, explosive spread (like in a pandemic) drives higher diversity
  - More infections=more replications cycles=more mutations
- ‘Faster’ evolution in immunocompromised hosts



Choi et al., NEJM, 2020

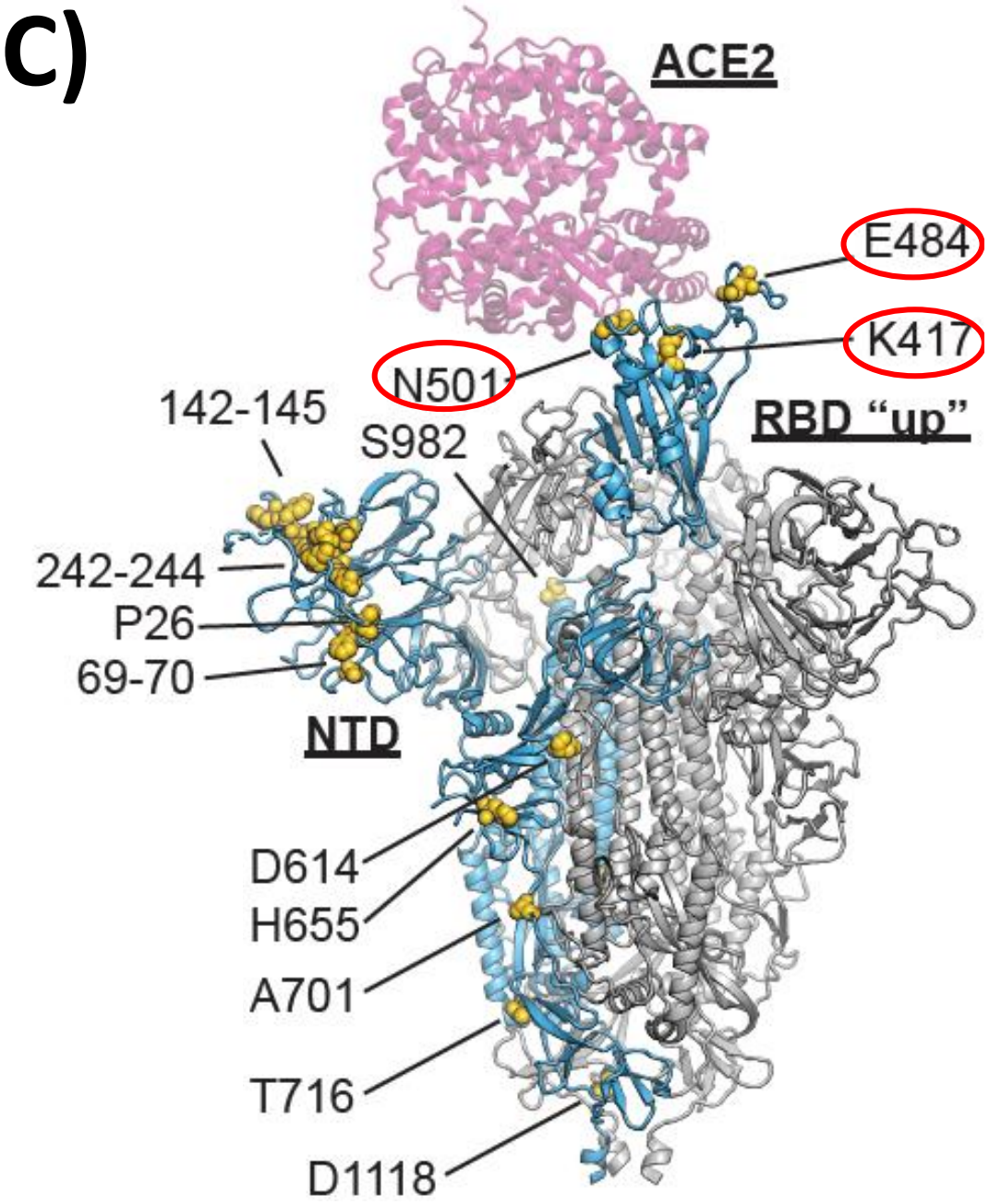
B.1.351 – first detected in South Africa



Tegally *et al.*, medRxiv, 2020
https://www.medrxiv.org/content/10.1101/2020.12.21.20248640v1.full.pdf

Variants of Concern (VoC)

- **B.1.1.7 – first detected in the UK**
  - **RBD changes: N501Y**
  - **A little bit more infectious (approximately 35%)**
  - **No strong evidence that it causes more severe disease**
- **B.1.351 – first detected in South Africa**
  - **RBD changes: K417N, E484K, N501Y**
  - **More infectious**
  - **No strong evidence that it causes more severe disease**
- **P.1 – first detected in Brazil**
  - **RBD changes: K417T, E484K, N501Y**
  - **See B.1.351**



Adapted from Goran Bajic

Efficacy/effectiveness against variants

Variant	J&J (Ad26 vector)	Novavax (recombinant spike)	AstraZeneca	Pfizer/BioNTech	Moderna
Wild type (garden variety) SARS-CoV-2	72%	95.6%	84% (60-90%)	95%	94%
B.1.1.7	*Likely no impact*	85.6%	74.6%	*Likely no impact*	*Likely no impact*
B.1.351	64% (95% B.1.351 lineage in South African part of trial) (100% against hospitalization)	60% (in HIV-individuals, >90% B.1.351 lineage in South African part of trial)	10%?	75%	*In vitro* data only, but likely only moderate impact on efficacy
P.1	ND	ND	ND	ND	ND
B.1.617.2	ND	ND	60%	88%	ND

Important point:
Even if vaccine efficacy against symptomatic disease is reduced, efficacy against severe disease is likely to remain high

With viruses it never gets boring….

- **B.1.1.7 + E484K (e.g. Tyrol, Austria)**
- **P.2 (E484K)**
- **B.1.525 (E484K)**
- **B.1.526 (partial E484K) – NY variant**
- **B.1.427/B.1.429 – California variants (more a ‘scariant’ – going down in frequency)**
- **P.3 (E484K and N501Y) – Philippines**
- **B.1.617 (plus sub-variants) und B.1.618 (India)**
- **B.1.1.1 (Chile)**
- **…….**

- **‘Variants of Concern’ versus ‘Variants of Interest’**
- **Not every variant that shows an increase in frequency in a location is necessarily dangerous**

COVID-19 vaccines work <u>really well</u> in real life (reports from Israel and Scotland)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting

Noa Dagan, M.D., Noam Barda, M.D., Eldad Kepten, Ph.D., Oren Miron, M.A., Shay Perchik, M.A., Mark A. Katz, M.D., Miguel A. Hernán, M.D., Marc Lipsitch, D.Phil., Ben Reis, Ph.D., and Ran D. Balicer, M.D.

Table 2. Estimated Vaccine Effectiveness against Covid-19 Outcomes during Three Time Perio

Period	Documented Infection		Symptomatic Illness	
	1–RR	Risk Difference	1–RR	Risk Difference
	% (95% CI)	no./1000 persons (95% CI)	% (95% CI)	no./1000 persons (95% CI)
14 to 20 days after first dose	46 (40–51)	2.06 (1.70–2.40)	57 (50–63)	1.54 (1.28–1.80)
21 to 27 days after first dose	60 (53–66)	2.31 (1.96–2.69)	66 (57–73)	1.34 (1.09–1.62)
7 days after second dose to end of follow-up	92 (88–95)	8.58 (6.22–11.18)	94 (87–98)	4.61 (3.29–6.53)

THE LANCET

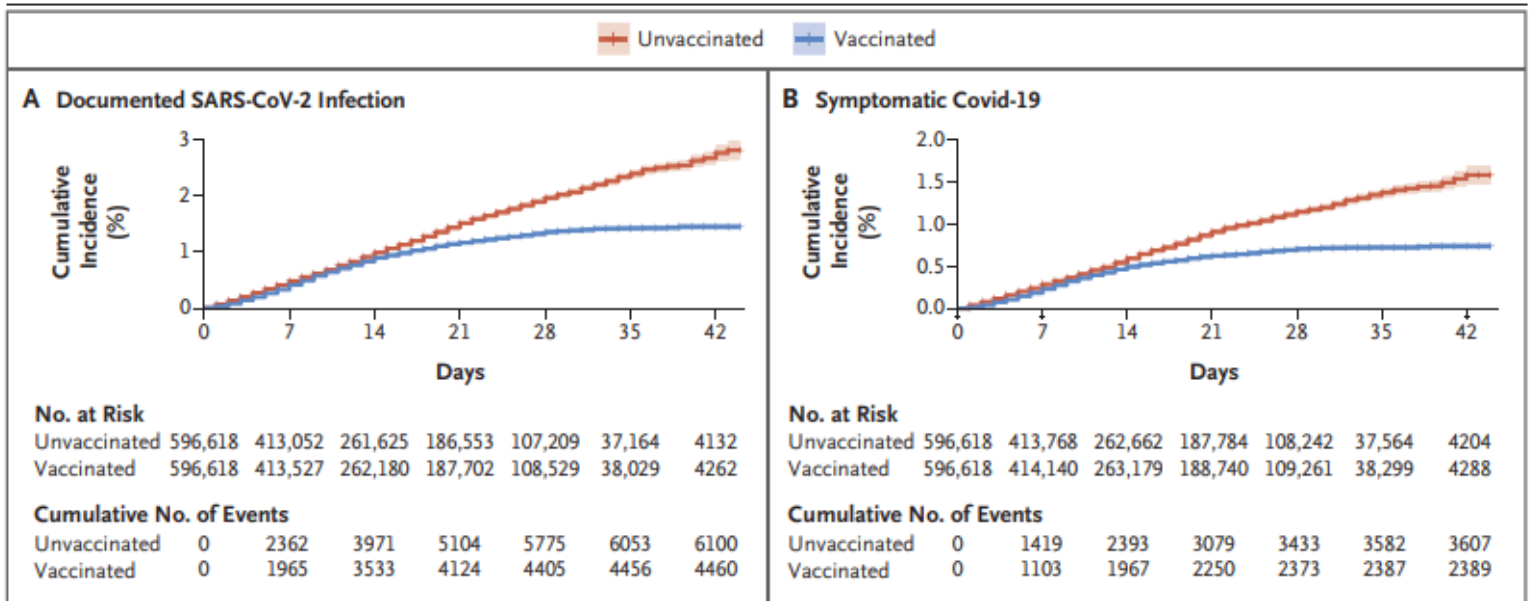
Access provided by Icahn School of Medicine at Mount Sinai

CORRESPONDENCE | ONLINE FIRST

Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients

Sharon Amit • Gili Regev-Yochay • Arnon Afek • Yitshak Kreiss • Eyal Leshem

Published: February 18, 2021 • DOI: https://doi.org/10.1016/S0140-6736(21)00448-7



Effectiveness of First Dose of COVID-19 Vaccines Against Hospital Admissions in Scotland: National Prospective Cohort Study of 5.4 Million People

21 Pages • Posted: 19 Feb 2021

Eleftheria Vasileiou
University of Edinburgh - Asthma UK Centre for Applied Research

Colin R. Simpson
Victoria University of Wellington - School of Health

Preprints with THE LANCET

More...

Summary

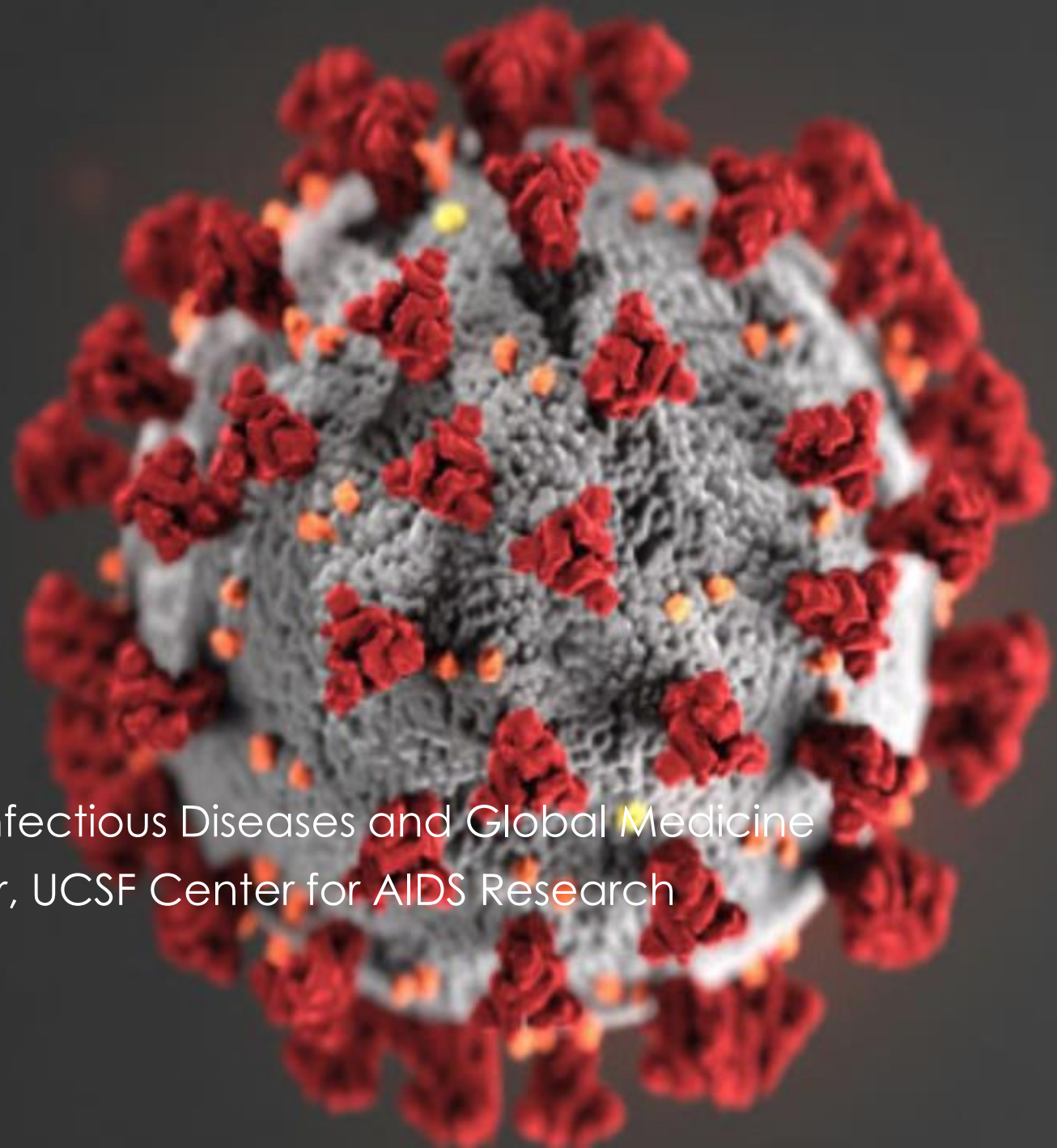
Vaccines against SARS-CoV-2 work and protect well against disease.

Data from ten thousands of people in phase III trials and millions of vaccinated people suggests the vaccines are very safe.

Vaccines will hopefully bring us back to normal life in the next few months.

Get vaccinated!

COVID-19 vaccines

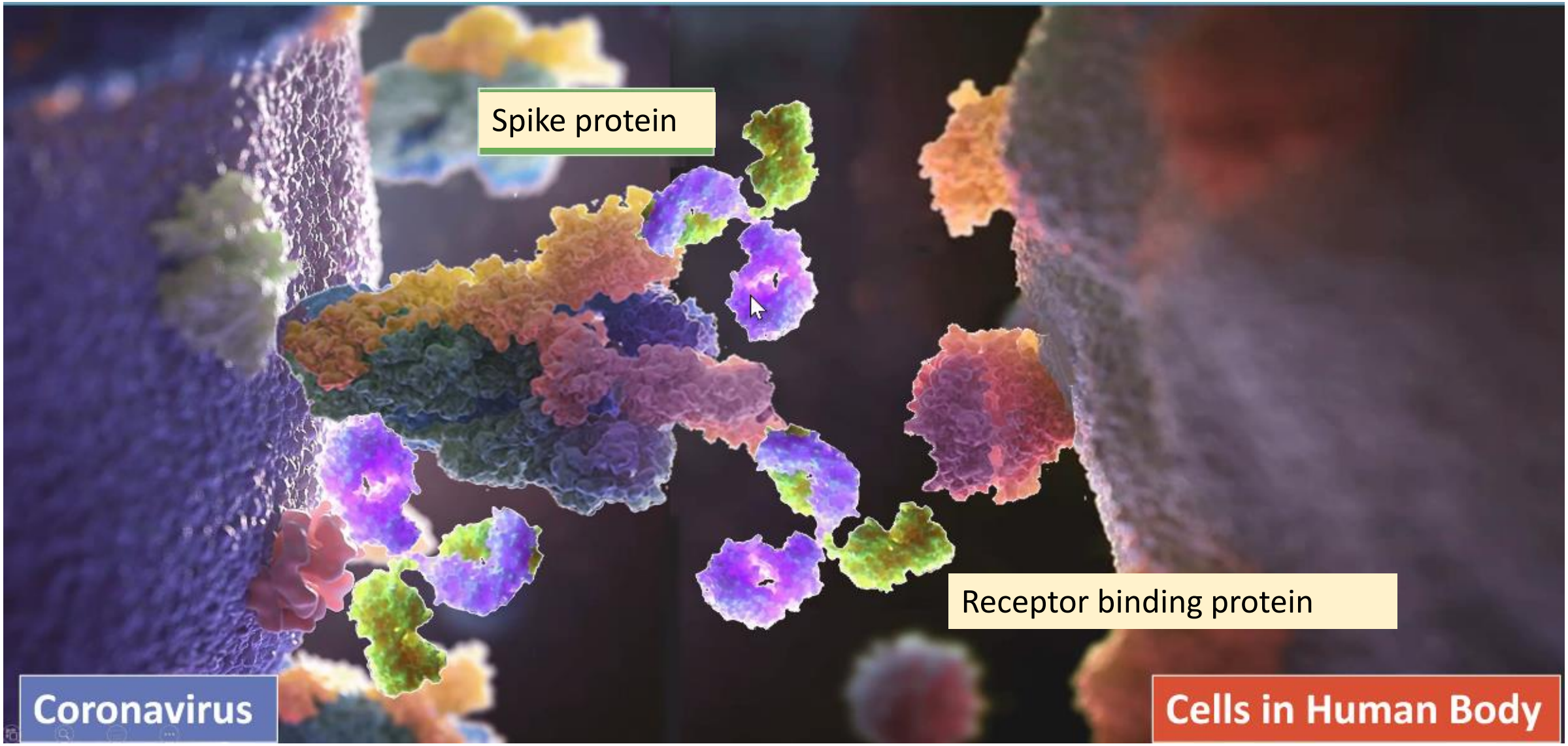


Monica Gandhi MD, MPH
Professor of Medicine, Division of HIV, Infectious Diseases and Global Medicine
Medical Director, Ward 86 and Director, UCSF Center for AIDS Research
May 27, 2021

Company or name	Form of publication for phase 3 data/ type of vaccine	Reference
moderna	Peer reviewed publication/ mRNA	Baden NEJM, Feb 4, 2021
Pfizer	Peer reviewed publication/ mRNA	Polack NEJM, December 31, 2020
Johnson & Johnson	Press release only/ adenovirus + DNA	J&J press release January 29, 2021; FDA document Feb 24
AstraZeneca	Two peer-reviewed publications but ongoing (adenovirus + DNA)	Voysey Lancet December 8, 2020; Preprint Feb 1, 2021
NOVAVAX Creating Tomorrow's Vaccines Today	Press release and abstract only (phase 3 UK; phase 2b S. Africa) (protein + adjuvant)	Novavax press release 1/28 and NYAS abstract 2/2/21
Sputnik V	Peer-reviewed publication (DNA plus adenovirus)	Logunov Lancet, February 2, 2021
sinovac	Press release (whole inactivated)	Sinopharm, January 16, 2021
SINOPHARM	Press release (whole inactivated)	Sinovac, February 5, 2021
BHARAT	Press release (whole inactivated)	Bharat Covaxin, April 21, 2021

There are actually 9 vaccines out there for COVID-19, three authorized in U.S.

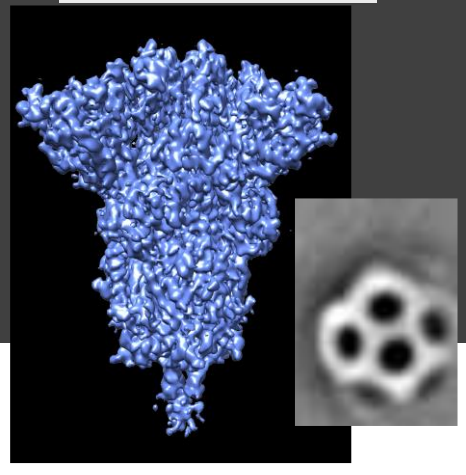
6 vaccine candidates to date involve spike protein and receptor binding domain of SARS-CoV-2 - either mRNA or adenoviral-vector DNA vaccines or protein adjuvant itself; 3 inactivated virus

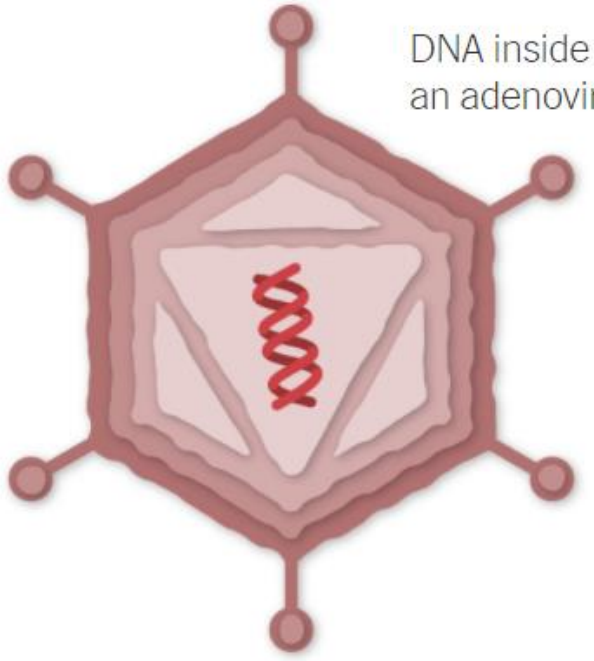


Three types of vaccines involving spike protein

- mRNA vaccines (2)
- Adenoviral vector DNA vaccines (3)
- Spike protein + M-adjuvant vaccine (1)

NOVAVAX
Creating Tomorrow's Vaccines Today

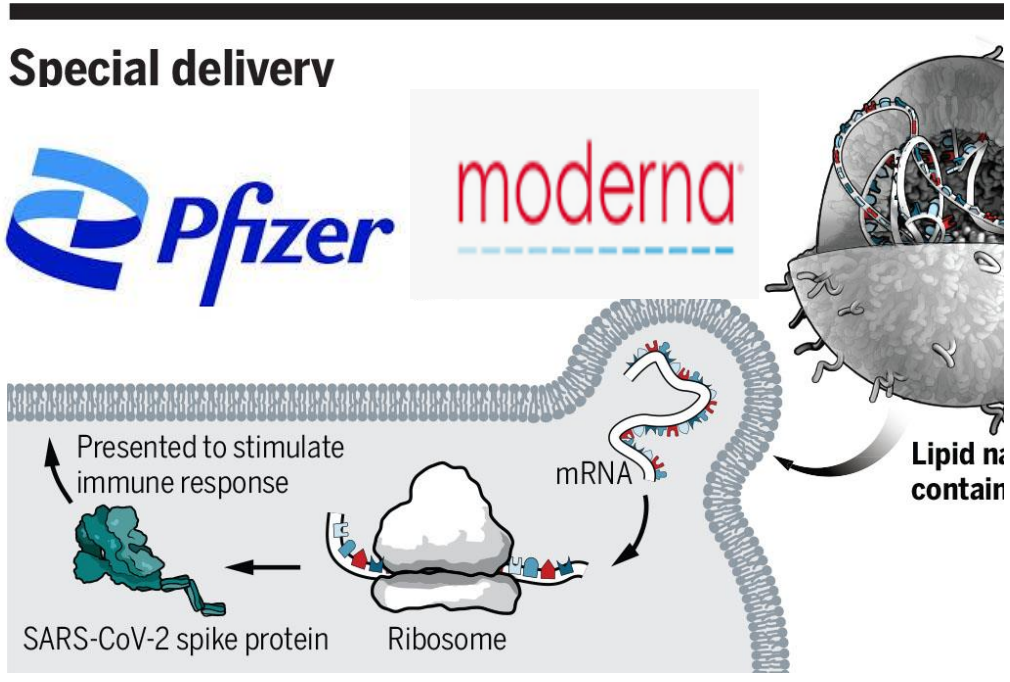




Johnson & Johnson

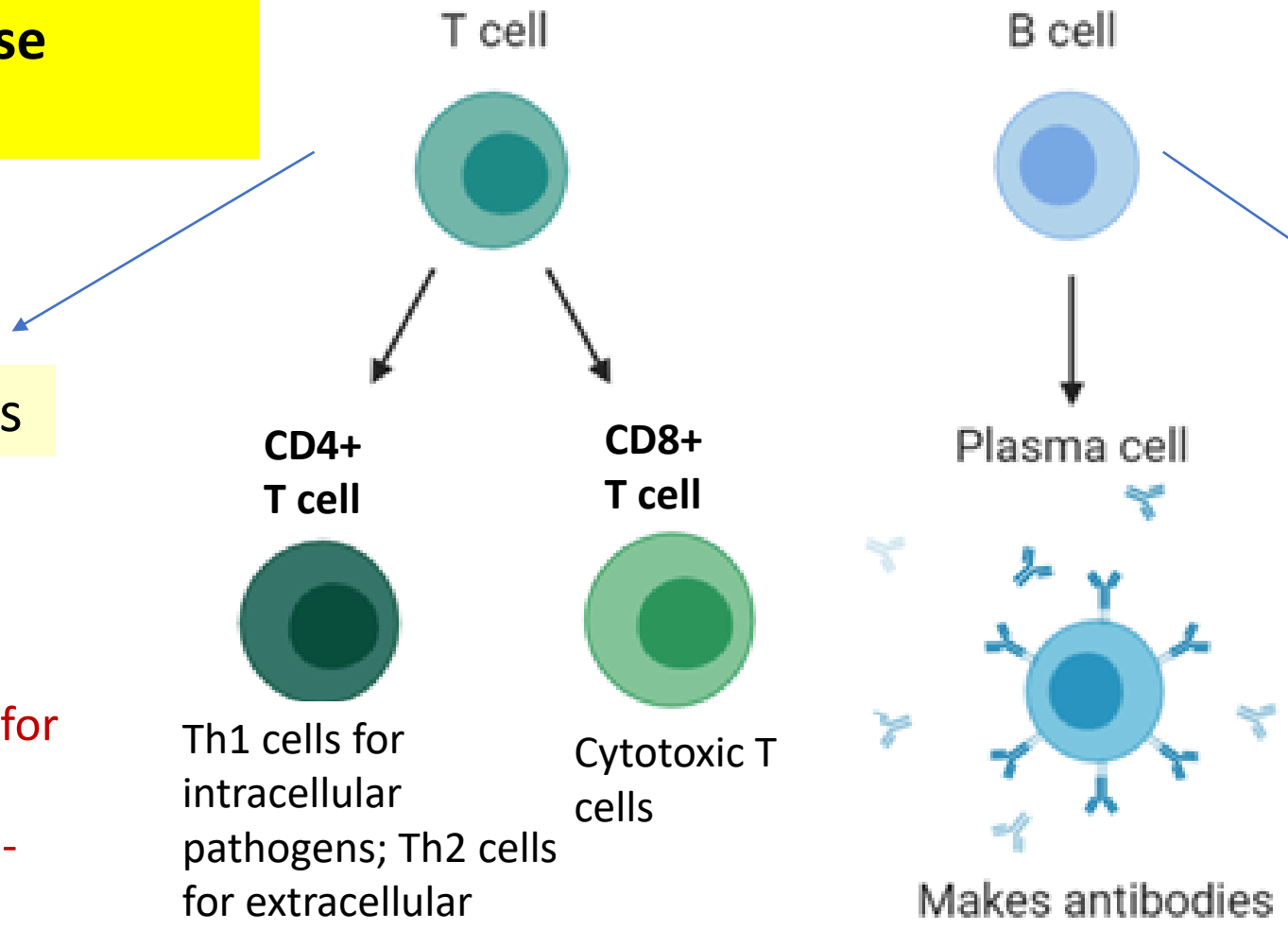
AstraZeneca

Sputnik V



Remember immunity -antibodies and cell-mediated

T cells are the major immune defense against viruses



Of note, want Th1:Th2 ratio >>1 for viruses; Th2 CD4s block antiviral Th1-CD4s and CD8s

Most vaccine trials measured antibodies and T cell responses

nature Vol 455|25 September 2008|doi:10.1038/nature07231

LETTERS

Neutralizing antibodies derived from the B cells of 1918 influenza pandemic survivors

Xiaocong Yu[1]*, Tshidi Tsibane[2]*, Patricia A. McGraw[1], Frances S. House[1], Christopher J. Keefer[1], Mark D. Hicar[1], Terrence M. Tumpey[3], Claudia Pappas[2,3], Lucy A. Perrone[3], Osvaldo Martinez[2], James Stevens[3,4], Ian A. Wilson[4], Patricia V. Aguilar[2], Eric L. Altschuler[5], Christopher F. Basler[2] & James E. Crowe Jr[1]

nature

Article

SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

nature reviews immunology

Biochemical and Biophysical Research Communications

T cell immunity to SARS-CoV-2 following natural infection and vaccination

JEM Journal of Experimental Medicine

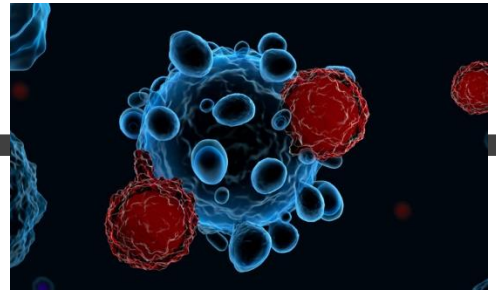
ARTICLE

Highly functional virus-specific cellular immune response in asymptomatic SARS-CoV-2 infection

Nina Le Bert[1], Hannah E. Clapham[2], Anthony T. Tan[1], Wan Ni Chia[1], Christine Y.L. Tham[1], Jane M. Lim[2], Kamini Kunasegaran[1]

nature reviews immunology

T cell responses in patients with COVID-19



CellPress

Trends in Immunology

Opinion

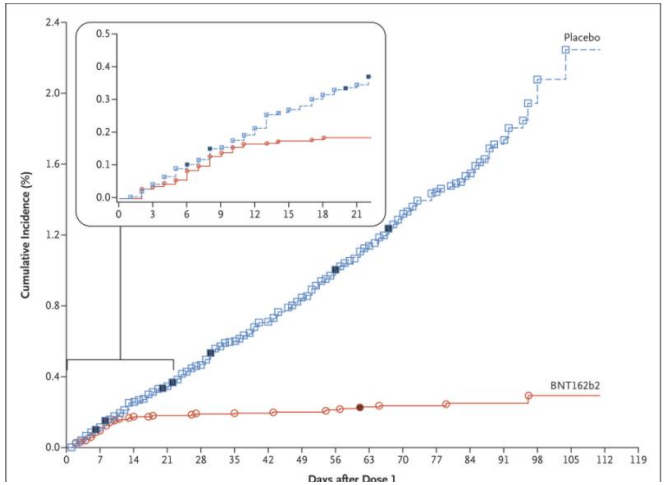
T Cells: Warriors of SARS-CoV-2 Infection

How does functional T-cell response modulate severity of disease?

- T cell responses modulate the severity of disease
- Strong T cell responses in all of these trials seem to have led to prevention of severe disease
- JEM study shows us that those with asymptomatic infection mounted good T cell responses to COVID-19
- If you get re-infected after natural infection or vaccine (rare), should be mild if mounted good T-cell response
- Fun fact: Study from 1918 survivors of influenza pandemic show durable B cell immunity (memory B- Ab) 90 years later!

Company	Platform	Doses	Non-clinical results	# with vaccine (same placebo)	Protection from COVID-19 hospitalization	Protection from COVID severe dz (some at home)	Efficacy against milder COVID
moderna	mRNA-1273 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+ protection from challenge (macaques)	~15,000	90% (1 in vaccine arm after 2nd dose hospitalized)	97% (30 cases in placebo arm; 0 in vaccine reported but 1 severe per FDA)	94.1%
Pfizer	BNT162b2 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+, CD8+; protection from challenge (macaques)	~18,600	100%	100% (9 cases in placebo arm; 0 in vaccine- 1 initially severe but not)	95%
Johnson & Johnson	JNJ-78436725 Non-replicating human adenovirus/DNA	1	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; challenge protection (macaque)	~22,000 US, Latin America, S. Africa	100%	85.4% across 3 sites (7 deaths, 16 hospitalizations, all in placebo arm)	72% US; 61% Latin America; 64% S. Africa (95% B1.351)
AstraZeneca	AZD 1222 Non-replicating Chimp Adenovirus-DNA	2	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; protection from challenge (macaques)	~28,588 (UK, SA, US/Peru/ Chili)	100%	100% (UK, 15 placebo arm hospitalized, 0 in vaccine; US, 8 severe in placebo, 0 vaccine)	76% US (85% in >65 yrs); 70% UK; S. Africa halted for mild
NOVAVAX Creating Tomorrow's Vaccines Today	NVX-CoV2373 Spike protein/RBD + Matrix M adjuvant	2	Neutralizing Abs; Strong Th1 CD4 > Th2; macaque challenge protection	~8833 (Phase 3 UK; 2b SA)	100%	100% (10 severe in placebo in UK/SA; 0 in vaccine)	96.4% UK; 89% B117 UK; 55% SA (94% B1351)
Sputnik V	Ad26 and Ad5 adenovirus/DNA	2	NAbs; IFN-γ secretion PMBCs, cellular response	~14964	100%	100% (20 in placebo; 0 vaccine)	91.6%

Two mRNA vaccines clinical trials



Pfizer

- 2 shots, 3 weeks apart
- Trial participants: half female, 83% White; 9.9% African America; 28% Hispanic/Latino
- 21% >65 years
- Some risk factors for severe illness: obesity (35%), diabetes 8%; pulmonary disease 8%
- 170 symptomatic COVID-19, 162 in placebo arm and 8 in vaccine arm so 95% effective
- 9 cases of severe disease all in placebo

moderna

- 2 shots, 4 weeks apart
- ~half female, 36.5% of participants communities of color
- 25%, ≥65 years of age
- Some risk factors for severe illness, including obesity (mean BMI 29.3)
- 196 symptomatic COVID-19, 185 in placebo arm and 11 in vaccine arm so 94.1% effective
- 30 cases of severe disease in placebo; 1 in vaccine arm

NEJM 2020

Johnson and Johnson 1-dose phase 3 trial

- 43,783 participants, 44% from US, 41% Central and South America, 15% South Africa
- 59% White; 45% Hispanic and/or Latinx; 17.2% AA or African; 9% Native American, 3% Asian
- 41% risk factors for severe illness, e.g. obesity or diabetes
- 486 cases symptomatic COVID-19
- All hospitalizations (16) and deaths (9) from COVID-19 in placebo arm
- High efficacy against variants (95% B.1.351 S. Africa; 69% P1 Brazil) and 85% effective against all severe disease
- Variable against mild disease (72% U.S., 64% in South Africa, 61% Latin America)

Press release: Phase 3 ENSEMBLE trial; FDA document February 24, 2021

Will vaccines work against variants?
Short answer: yes

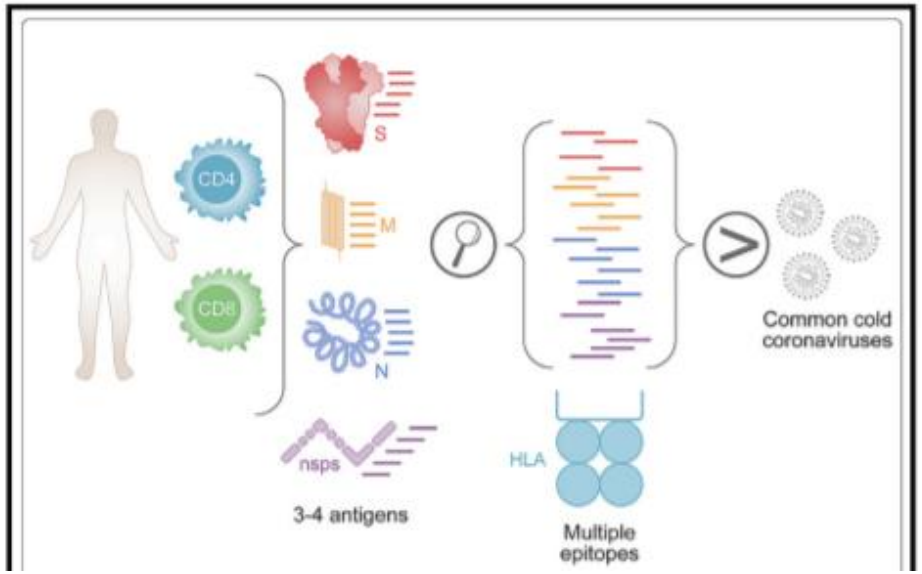
Why T cell response will work against variants? First look at natural infection

Cell Reports
Medicine

Article

Comprehensive analysis of T cell immunodominance and immunoprevalence of SARS-CoV-2 epitopes in COVID-19 cases

Graphical Abstract



Authors

Alison Tarke, John Sidney, Conner K. Kidd, ..., Daniela Weiskopf, Alba Grifoni, Alessandro Sette

Correspondence

agrifoni@lji.org (A.G.), alex@lji.org (A.S.)

In Brief

Tarke et al. show a broad T cell repertoire, suggesting that viral escape of T cell immunity is unlikely. CD4 immunodominant regions correlate with

Broad T cell repertoire (>19 CD4 epitopes; 17 CD8 epitopes) after infection. Means viral escape of T cell-immunity (from both natural infection and vaccination) unlikely, re-infection if happens mild

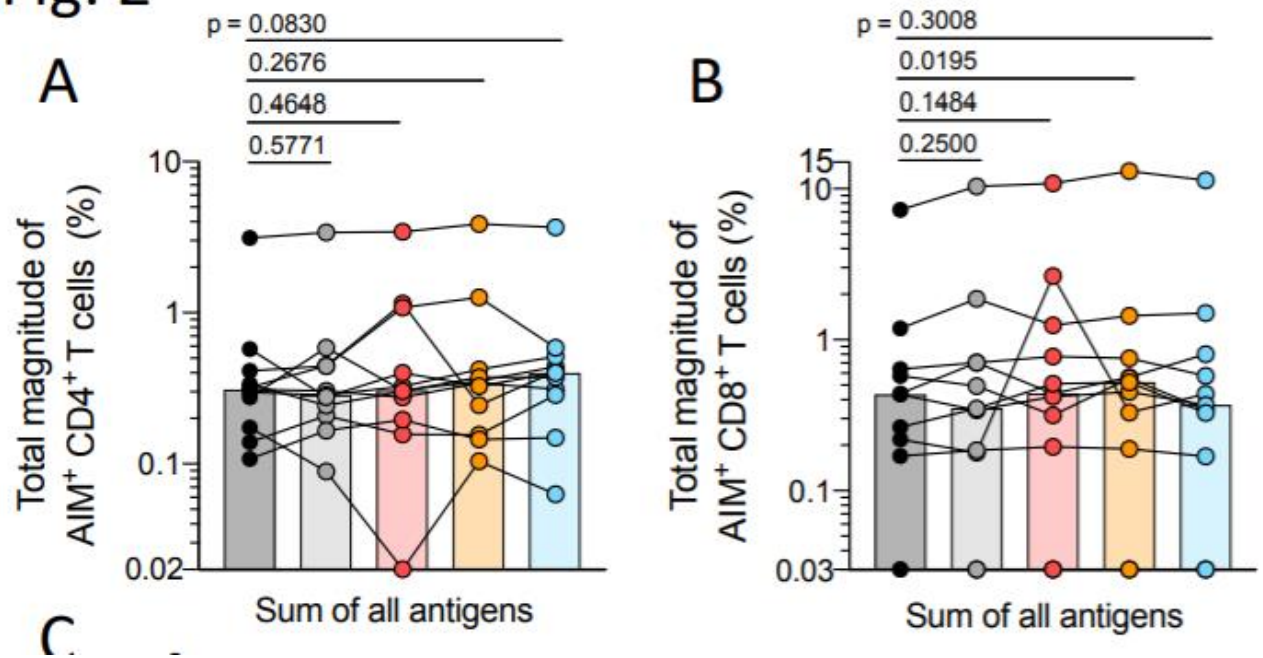
Then look at T-cell response to variants after vaccines- still intact

bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees.

Alison Tarke, John Sidney, Nils Methot, Yun Zhang, Jennifer M Dan, Benjamin Goodwin, Paul Rubiro,

Fig. 2



- Looked at SARS-CoV-2-specific CD4+ & CD8+ T cell responses from those with natural infection with non-variant & examined activity against B.1.1.7, B.1.351, P.1, CAL.20C
- T cell reactivity against those variants remained intact if you had natural infection or mRNA vaccination (Pfizer/Moderna)
- CD4/CD8 responses in South Africa AztraZeneca trial[1] showed 75 out of 87 T cell epitopes in the spike protein remained unaffected by B.1.351 mutations

[1]Madhi. NEJM. March 16, 2021

National Institutes of Health
Turning Discovery Into Health

NEWS RELEASES

ACCEPTED MANUSCRIPT

CD8+ T cell responses in COVID-19 convalescent individuals target conserve epitopes from multiple prominent SARS-CoV-2 circulating variants

Andrew D Redd ✉, Alessandra Nardin, Hassen Kared, Evan M Bloch,

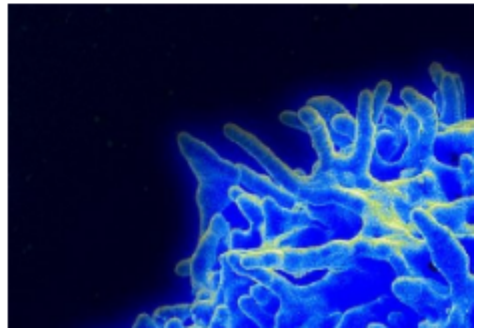
Tuesday, March 30, 2021

T cells recognize recent SARS-CoV-2 variants

52 epitopes for CD8 cells after infection & 51/52 preserved against B.1.351, B.1.1.7, P.1

What

When variants of SARS-CoV-2 (the virus that causes COVID-19) emerged in late 2020, concern arose that they might elude protective immune responses generated by prior infection or vaccination, potentially making



CORRESPONDENCE

May 5, 2021

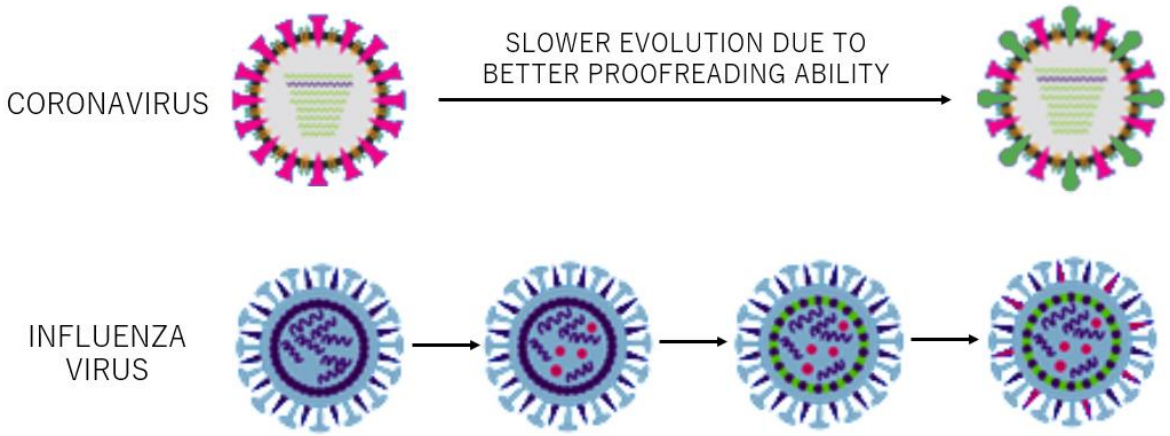
The NEW ENGLAND JOURNAL of MEDICINE

Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants

- Qatar mass vaccination campaign December 21-March 31, 2021
- Nearly all cases in which virus was sequenced after March 7 were caused by either B.1.351 or B.1.1.7
- Vaccine effectiveness against severe, critical (hospitalization) or fatal disease due to infection from COVID-19 in Qatar with these variants was very high, at 97.4%
- Shows the power of T cell immunity (preserved against variants) against severe disease

Why not to worry clinically too much about variants

- This is what RNA viruses do, mutate more readily than DNA viruses
- SARS-CoV-2 doesn't mutate that fast, it is just transmitted a lot
- T cell responses preserved against variants & protect against severe disease
- mRNA vaccines and DNA vaccines can be readily "tweaked" (as they are being) from companies to code for new variant 'boosters' in future if needed (

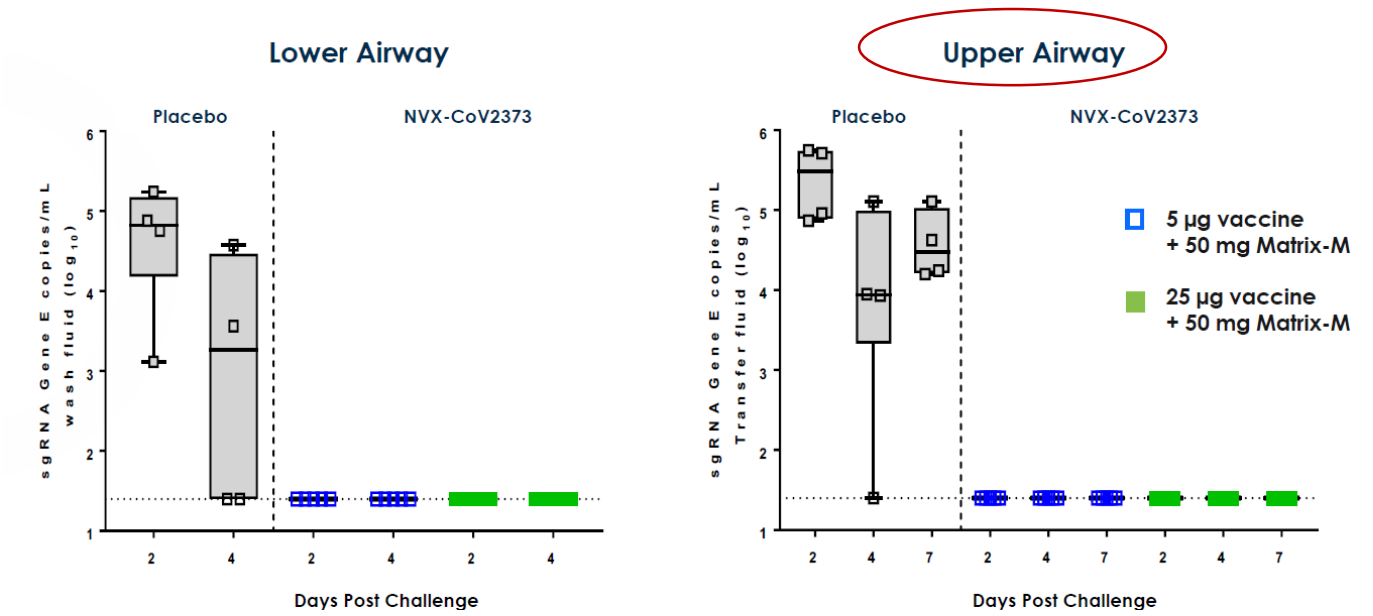


Do vaccines reduce transmission?
Short answer: yes

Will vaccines halt transmission? Biological plausibility (4 main reasons)

NVX-CoV2373 Protected Lower & Upper Airways in Rhesus Macaques

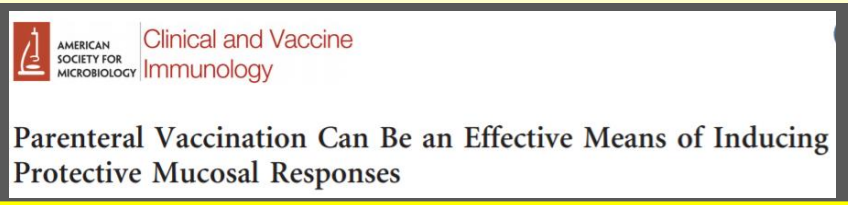
No viral replication observed following Day 38 challenge with WT SARS-CoV-2

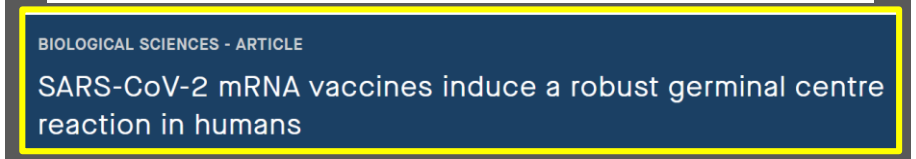


4. Challenge experiments with macaques in pre-clinical trials show blocking of viral replication (or no/low viral RNA) in BAL and nasal swabs (Mercado Nature J&J vax, 2020; Guebre-Xabier Vaccine Novavax 2020)

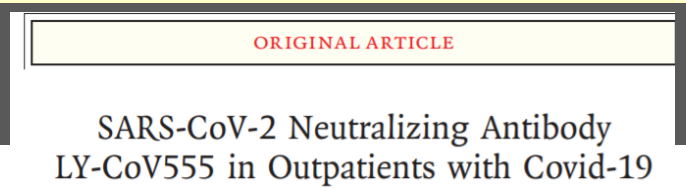
1. IgG antibodies measured in trials found in high levels in nasal mucosa

2. Systemic vaccines induce IgA (mucosal immunoglobulin) and recent study shows mRNA COVID-19 vaccines induce IgA





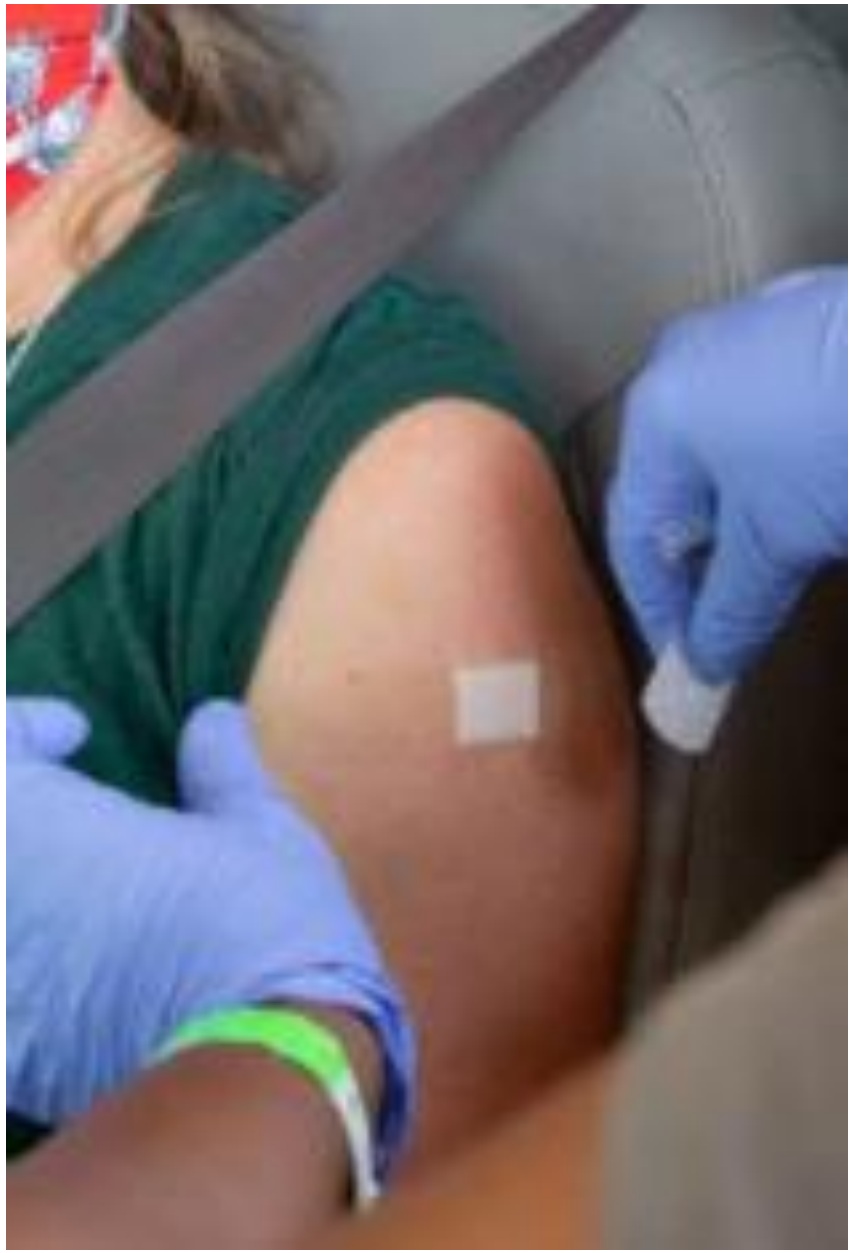
3. Monoclonal antibodies hasten viral clearance from airways



Studies to date that showed COVID-19 vaccines reduce asymptomatic infection (transmission)

Setting	% reduction in asymptomatic infection or transmission	Reference
Healthcare workers in England	**85%**	Hall Lancet, April 23, 2021
Healthcare workers in Israel	**75% and 86%**	Amit, Lancet, March 6; Angel JAMA May 6
Patients in Mayo Clinic health system	**88.7%**	Pawlowski medRxiv, February 27, 2021
Israel Ministry of Health (nationwide) Israel general population (Pfizer)	**94% (largest study)** **90%**	Pfizer press release, March 11, 2021 (and Goldberg Medrxiv, April 24, 2021) Dagan NEJM, February 24, 2021
Pre-surgical patients in Mayo Clinic system swabbed asymptomatically	**80%**	Tande Clin Inf Dis, March 10, 2021
Healthcare workers in Cambridge University Hospitals	**75%**	Weekes Authorea, February 24, 2021
First-line responders and HCWs in US	**90%**	Thompson A. MMWR, March 30, 2021
Israel population (>16) with children unvaccinated	**For every 20-point increase in adult vaccination, rates of kids testing positive halves**	Milman O. Medrxiv. March 31, 2021
Long-term care facility, Spain	**90%**	Salazar P. Medrxiv. April 13, 2021
Nursing homes, U.S. (two studies)	**100%**	Cavanaugh MMWR, April 21 and Terran MMWR, April 30

Nasal viral load values most important determinant of transmissibility (Lancet study, Spain); Viral loads from post-vaccination exposures are low and likely noninfectious per CT values (use rapid antigen tests after vaccination if test symptomatic or incorporate CT)



Pfizer 12-15 trial

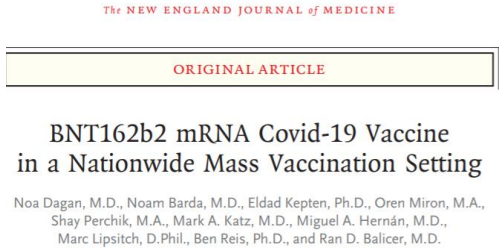
- Trial enrolled 2,260 participants aged 12 to 15 years in the U.S (same 30 microgram dose)
- 1,131 participants got the vaccine and 1,129 participants got placebo
- 18 COVID-19 symptomatic cases, all among placebo recipients so 100% efficacy
- Vaccine induced robust antibody responses, exceeding those aged 16 to 25 years (CD4/CD8 responses not mentioned)
- Adverse effects: pain at the injection site, fatigue, headache, muscle pain, chills, joint pain, and fever all lasting 24 hours
- EUA in US – rare causes of myocarditis
- CDC “mandated” vaccines: MMR, DP

What do real world studies show us?
Vaccine effectiveness even better than efficacy

March 11, 2021- a year after WHO pandemic declared

- Real-world roll-out data from Ministry of Health Israel, Pfizer vaccine
- 94% of asymptomatic infection prevented
- 97% effective against symptomatic COVID-19 cases, hospitalizations, severe and critical hospitalizations, and deaths
- Unvaccinated individuals 44 times more likely to develop symptomatic COVID-19 and 29 times more likely to die from COVID-19
- 80% of circulating virus during roll-out was B117 variant

REAL-WORLD EVIDENCE CONFIRMS HIGH EFFECTIVENESS OF PFIZER-BIONTECH COVID-19 VACCINE AND PROFOUND PUBLIC HEALTH IMPACT OF VACCINATION ONE YEAR AFTER PANDEMIC DECLARED


The NEW ENGLAND JOURNAL of MEDICINE

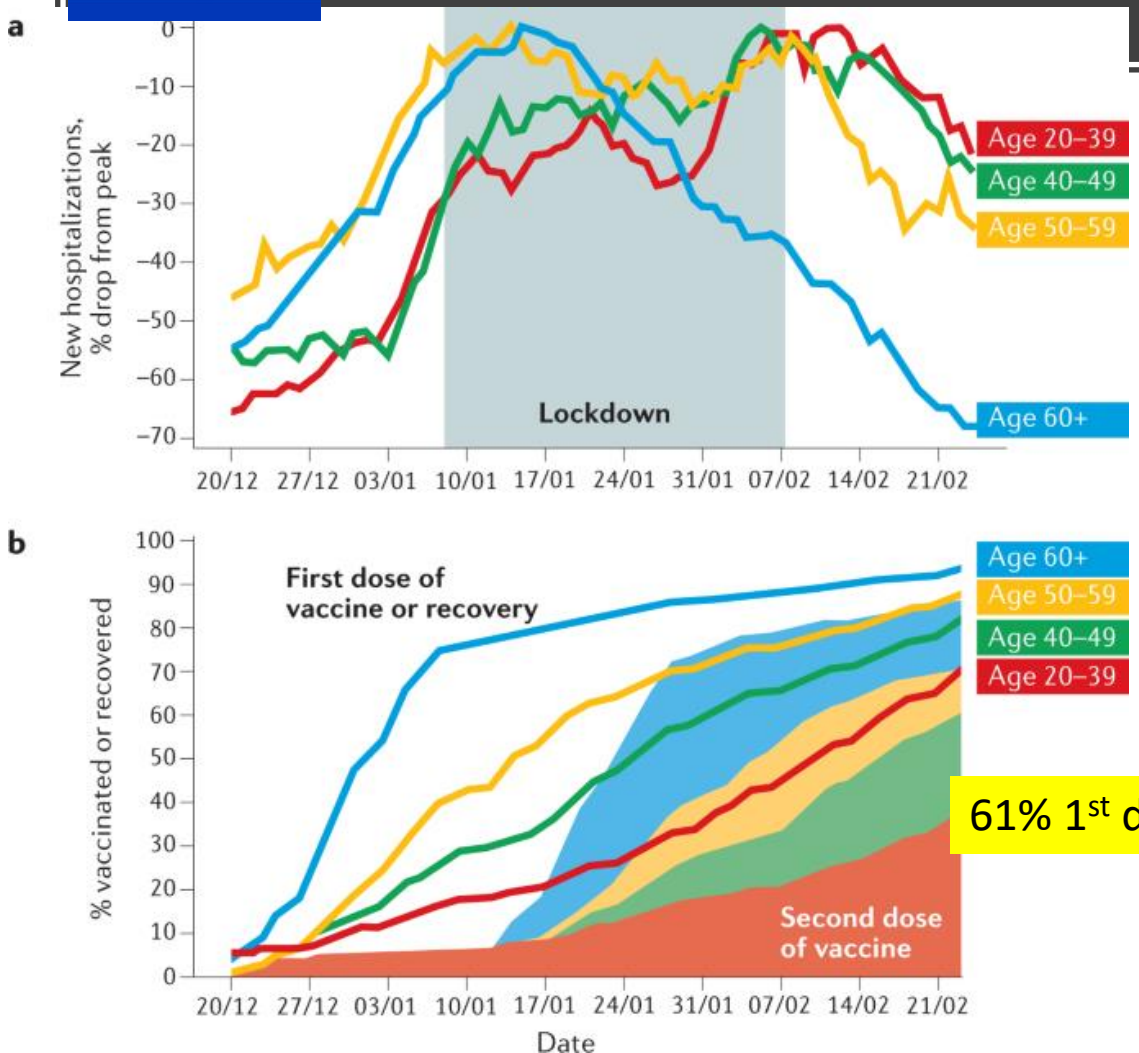
ORIGINAL ARTICLE

BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting

Noa Dagan, M.D., Noam Barda, M.D., Eldad Kepten, Ph.D., Oren Miron, M.A., Shay Perchik, M.A., Mark A. Katz, M.D., Miguel A. Hernán, M.D., Marc Lipsitch, D.Phil., Ben Reis, Ph.D., and Ran D. Balicer, M.D.

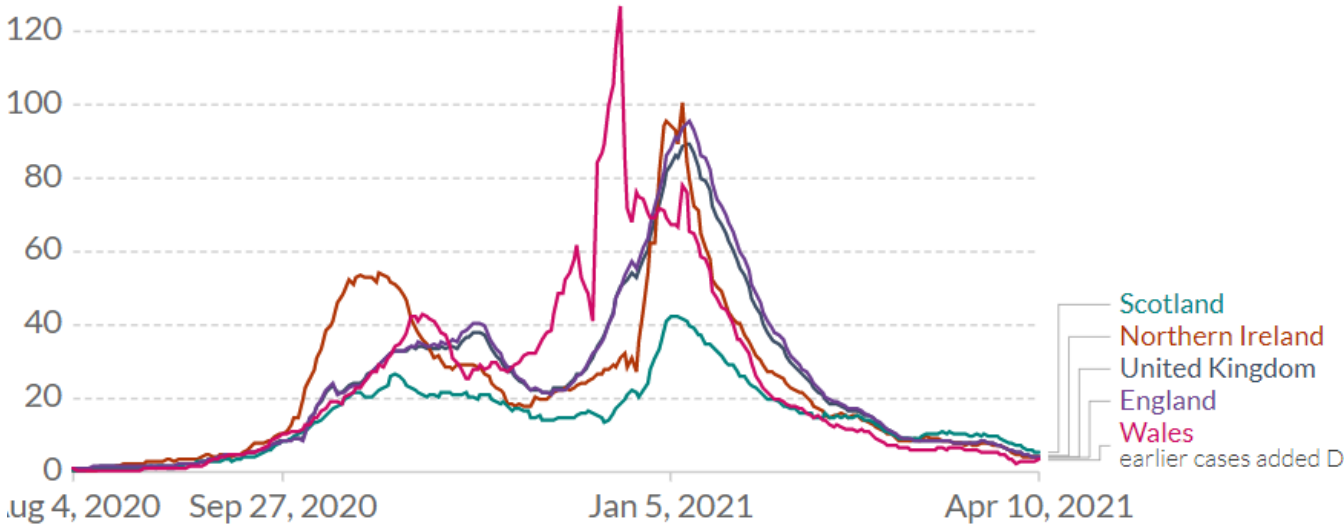
Real-world data amazing (UK, Israel fastest vaccinators)

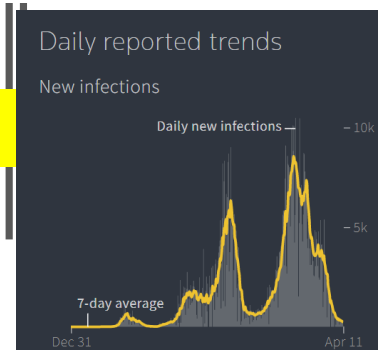
Shiloh Nature Immunology Review



61% 1st dose

52% 1st dose

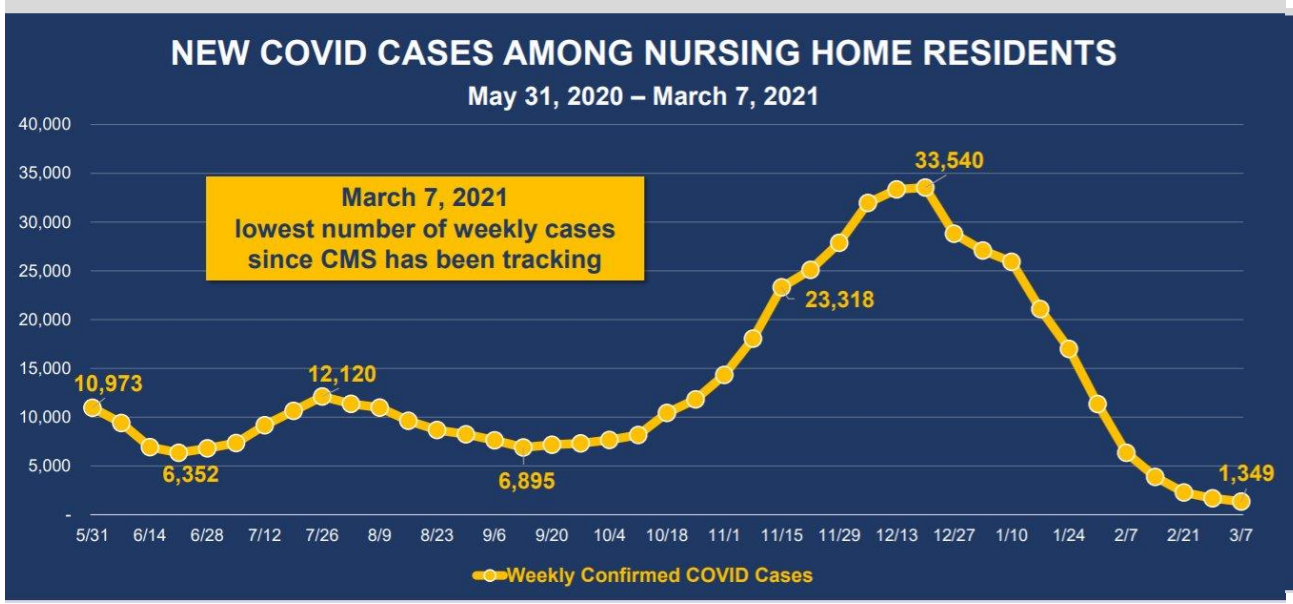


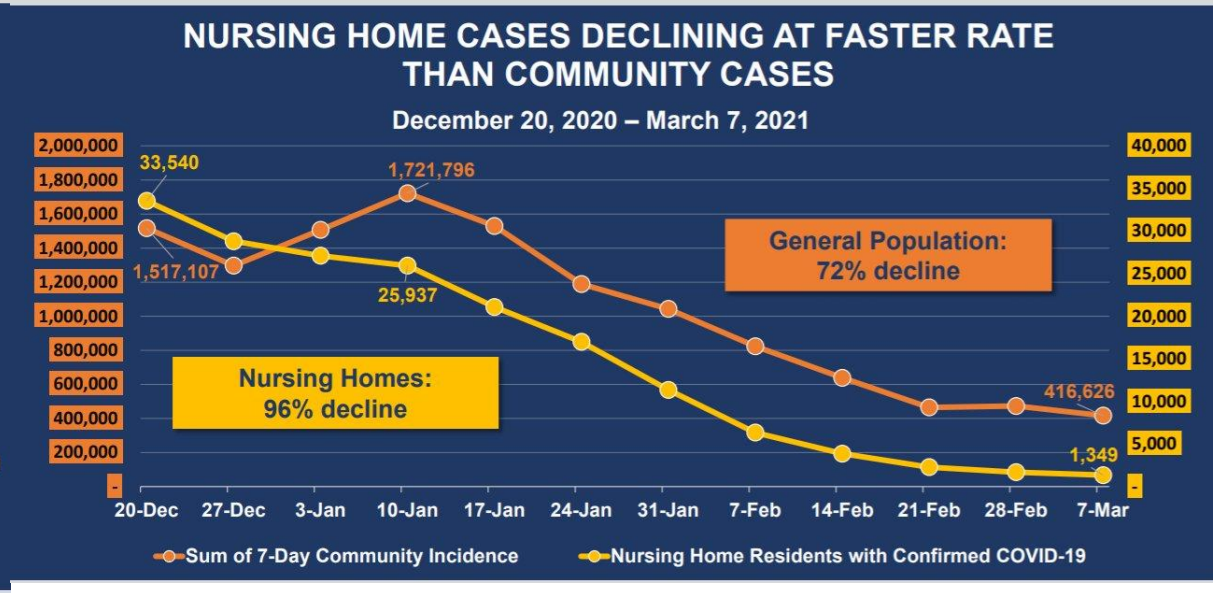


Israel has 0.8 (!) cases per 100K population; UK has 2 per 100K (actually so does CA)

This is what mass vaccinated settings look like in the U.S.

Nursing homes





March 30, CMA data

The NEW ENGLAND JOURNAL of MEDICINE

March 23, 2021

CORRESPONDENCE

SARS-CoV-2 Infection after Vaccination in Health Care Workers in California

UCSD and UCLA began vaccinating HCWs December 16, 2020
Weekly asymptomatic testing at UCSD
Optional asymptomatic testing program at UCLA

379 Vaccinated HCWs tested positive between Dec 16 – Feb 9

- 71% tested positive within the first 2 weeks after 1st dose
- 7 out of 14,990 HCWs who were > 2 weeks after 2nd dose tested positive (0.05%)

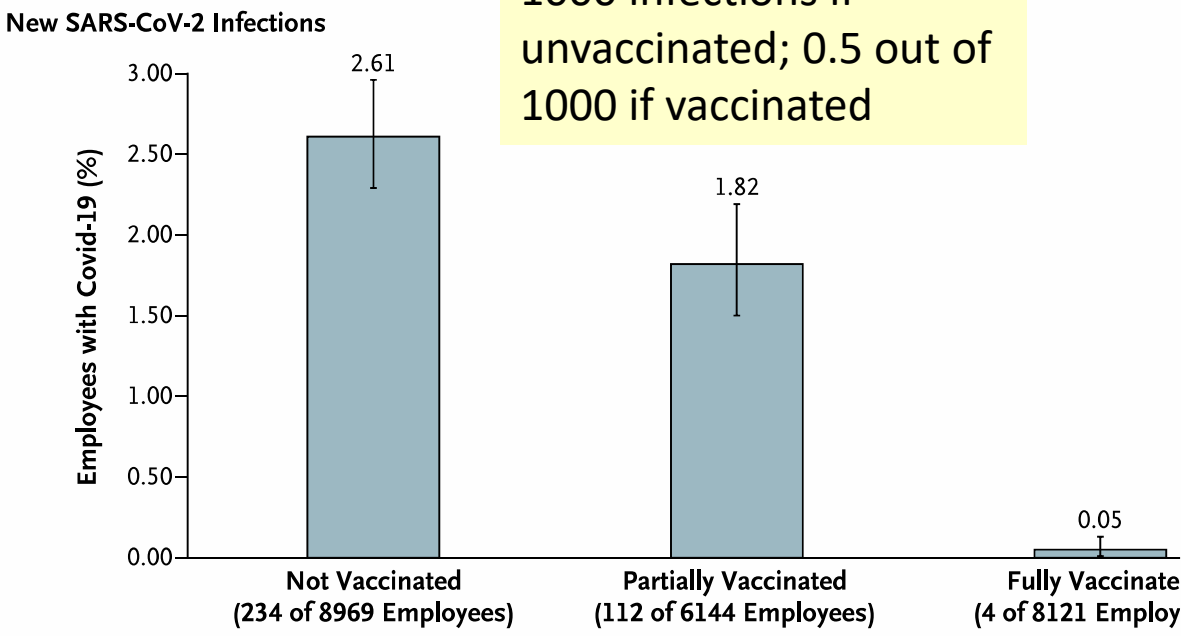
CORRESPONDENCE

Early Evidence of the Effect of SARS-CoV-2 Vaccine at One Medical Center

Evaluation of SARS-CoV-2 infections at UT Southwestern December 15 – January 28 by vaccination status

- 4/8121 fully vaccinated employees (0.05%)

To put simply, 26 out of 1000 infections if unvaccinated; 0.5 out of 1000 if vaccinated



Keehner et al, *NEJM* 2021; Daniel et al, *NEJM* 2021

Morbidity and Mortality Weekly Report (*MMWR*)

CDC

Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021

Early Release / March 29, 2021 / 70

To put simply, 161 COVID infections out of 1000 unvaccinated; 1 out of 1000 if vaccinated

April 1 press release, 100% effectiveness in real-world against severe disease even against B.1.351

Pfizer and BioNTech Confirm High Efficacy and No Serious Safety Concerns Through Up to Six Months Following Second Dose in Updated Topline Analysis of Landmark COVID-19 Vaccine Study

- *Analysis of 927 confirmed symptomatic cases of COVID-19 demonstrates BNT162b2 is highly effective with 91.3% vaccine efficacy observed against COVID-19, measured seven days through up to six months after the second dose*
- *Vaccine was 100% effective in preventing severe disease as defined by the U.S. Centers for Disease Control and Prevention and 95.3% effective in preventing severe disease as defined by the U.S. Food and Drug Administration*
- *Vaccine was 100% effective in preventing COVID-19 cases in South Africa, where the B.1.351 lineage is prevalent*
- *Vaccine safety now evaluated in more than 44,000 participants 16 years of age and older, with more than 12,000 vaccinated participants having at least six months follow-up after their second dose*

Mayo Clinic HCWs Florida, Minnesota, AZ

ACCEPTED MANUSCRIPT

Effectiveness of mRNA COVID-19 vaccines against SARS-CoV-2 infection in a cohort of healthcare personnel

Melanie D Swift ✉, Laura E Breeher, Aaron J Tande, Christopher P Tommas
Caitlin M Hainy, Haitao Chu, PhD, MD, M Hassan Murad, Elie F Berbari,
Abinash Virk

Clinical Infectious Diseases, ciab361, https://doi.org/10.1093/cid/ciab361
Published: 26 April 2021 **Article history** ▾

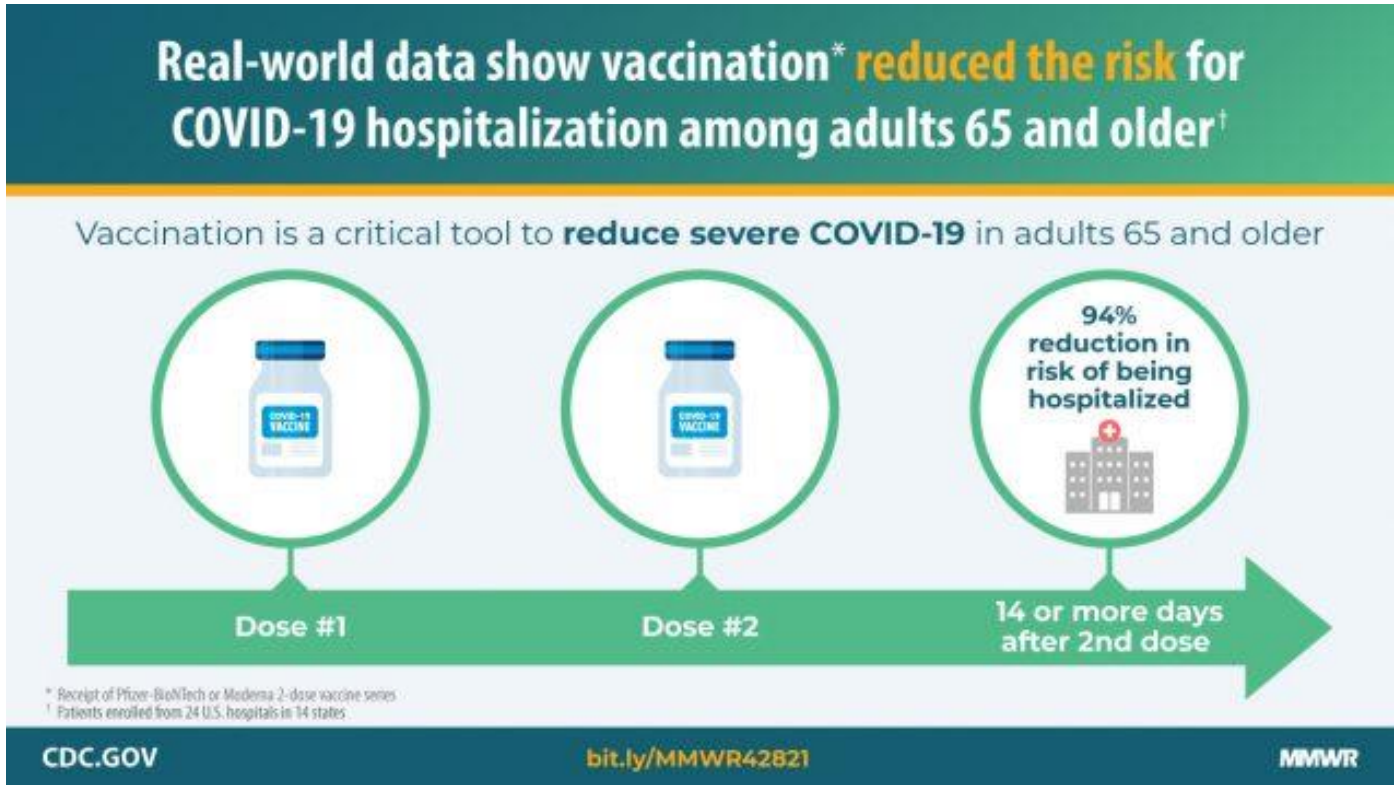
Unvaccinated cohort 23,931
2-dose vax cohort 44,011
(Moderna/Pfizer)

- 96.8% effectiveness for Pfizer vaccine; 98.6% effectiveness for Moderna in real-world cohort (for both disease & asymptomatic infection)

To put simply, 36 symptomatic COVID infections out of 1000 unvaccinated; 0.4 out of 1000 if vaccinated (42 symptomatic+ symptomatic out of 1000 unvaccinated; 0.7 all infections out of 1000 if vaccinated)

Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Among Hospitalized Adults Aged ≥65 Years — United States, January–March 2021

Early Release / April 28, 2021 / 70



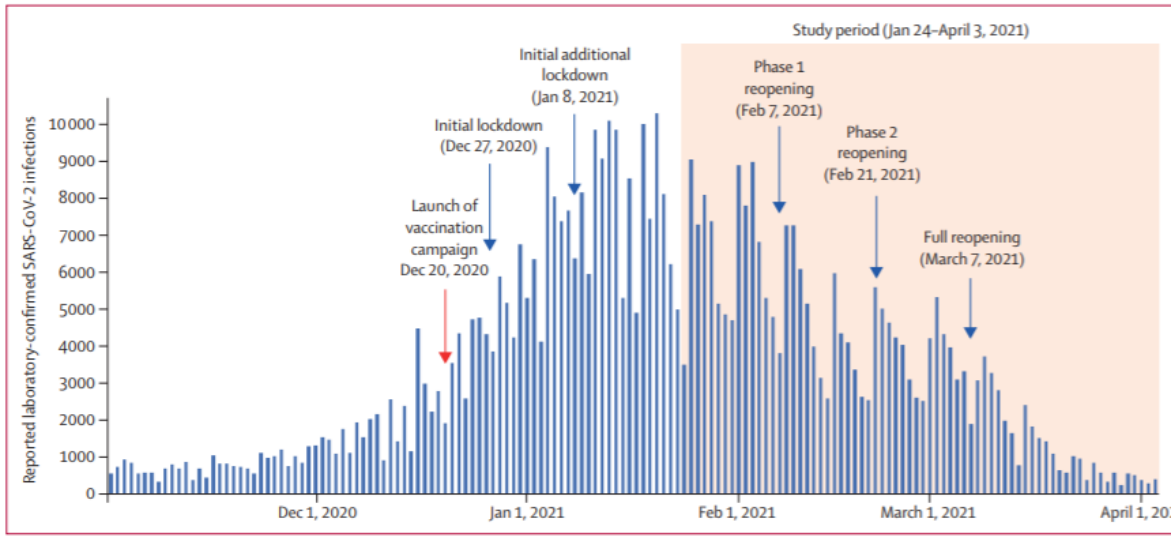
- Examined respiratory illness admissions among adults >65 from January 1, 2021–March 26, 2021 in 24 hospitals across 14 states as vaccines rolled out in this population
- Knew vaccine status and admissions for COVID-19 dropped by 64% after 1st dose and 94% after 2nd dose within this vulnerable group of older patients
- Defanging the virus in the population most at risk of severe illness in real-time during times of high circulating virus in the US (January-March 2021)

Cases continue to decline in Israel with mass vax despite opening

Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data

THE LANCET

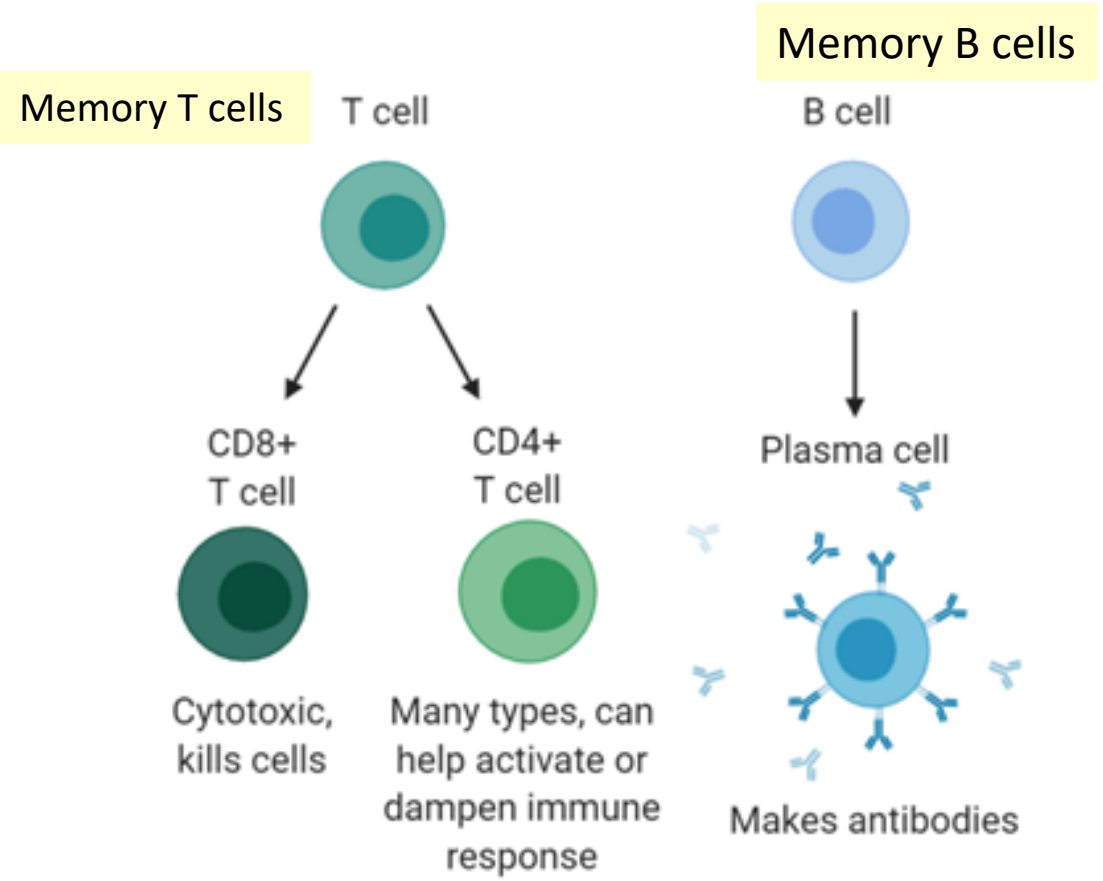
- More data on the real-world effectiveness of the vaccine despite B117 being 95% of SARS-CoV-2 infections during Israel roll-out Jan 24-April 3, 2021
- Pfizer vaccine 95% effective overall against symptomatic COVID-19
- 92% effective in preventing asymptomatic infection
- 98% effective against hospitalizations, 97% effective against death across all age groups even >=85 yrs
- Despite full opening March 2, 2021, cases continue to decline with fastest mass vaccination campaign on planet (and only >16 years vaccinated)



CDC breakthrough data

- CDC keeping track of breakthrough infections in U.S
- Out of >105 million Americans who are fully vaccinated against COVID-19
  - Rare symptomatic breakthroughs (0.007%)
  - Only 0.0006% hospitalizations for COVID-19
  - Deaths 0.0001% for COVID-19
- Not a single breakthrough infection has been reported to have transmitted

7 reasons don't think we will need boosters soon



In the bank!

- 1. Memory B cells can be triggered to produce neutralizing antibodies against an infection 90 years later!
- 2. Memory B cells generated by the COVID-19 mRNA vaccines (study did lymph node biopsies) and natural infection (study did
- 3. Memory T cells generated by natural infections
- 4. T cell immunity long-lasting (measles vaccine 34 years & counting)
- 5. T cells work against variants
- 6. SARS-CoV (first SARS) – T cell immunity 17 years later (pandemic 2003)
- 7. Coronaviruses don't mutate that fast (unlike HIV, influenza), strong proofreading mechanism, only when transmission high

Gandhi M. LeapsMag May 24, 2021

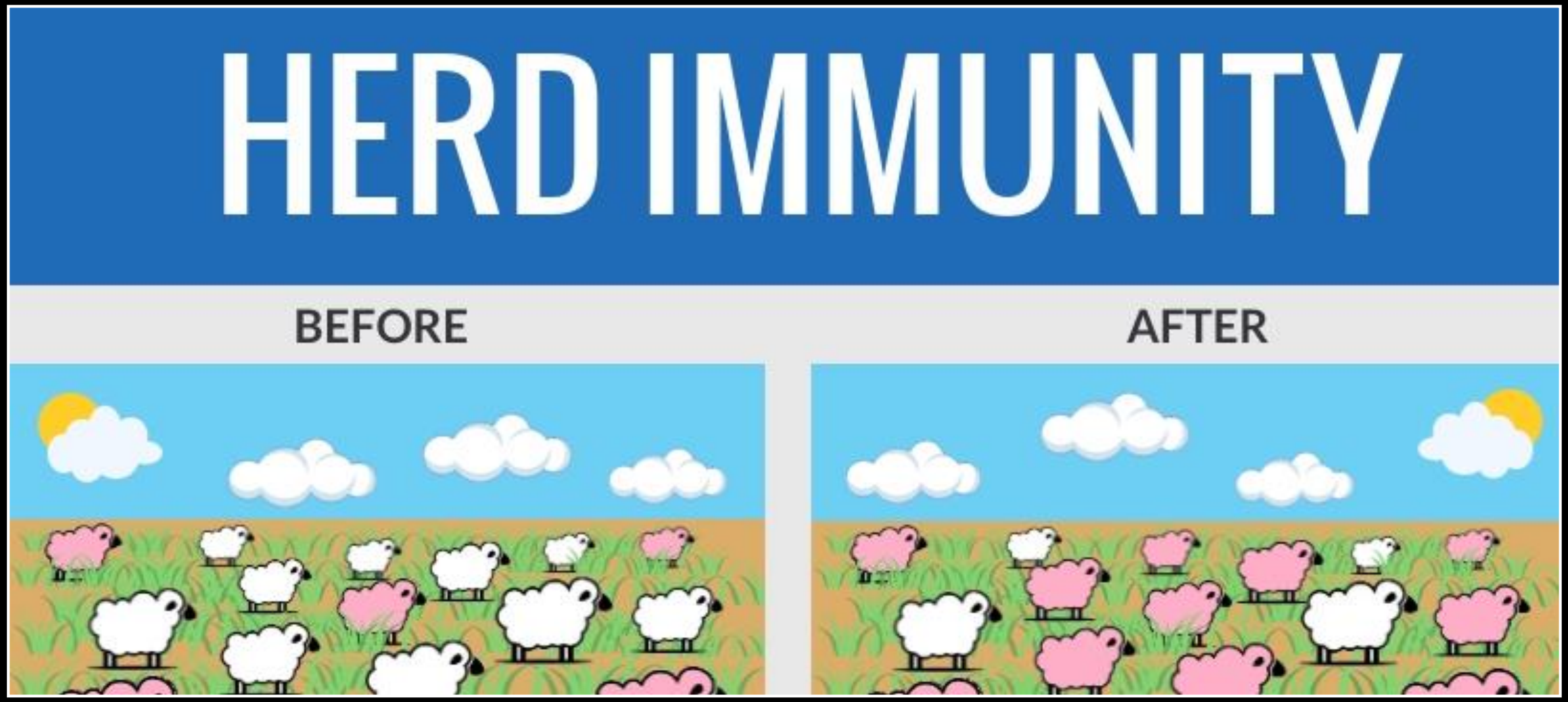
IDEAS

Vaccinated People Are Going to Hug Each Other

The vaccines are phenomenal. Belaboring their imperfections—and telling people who receive them never to let down their guard—carries its own risks.

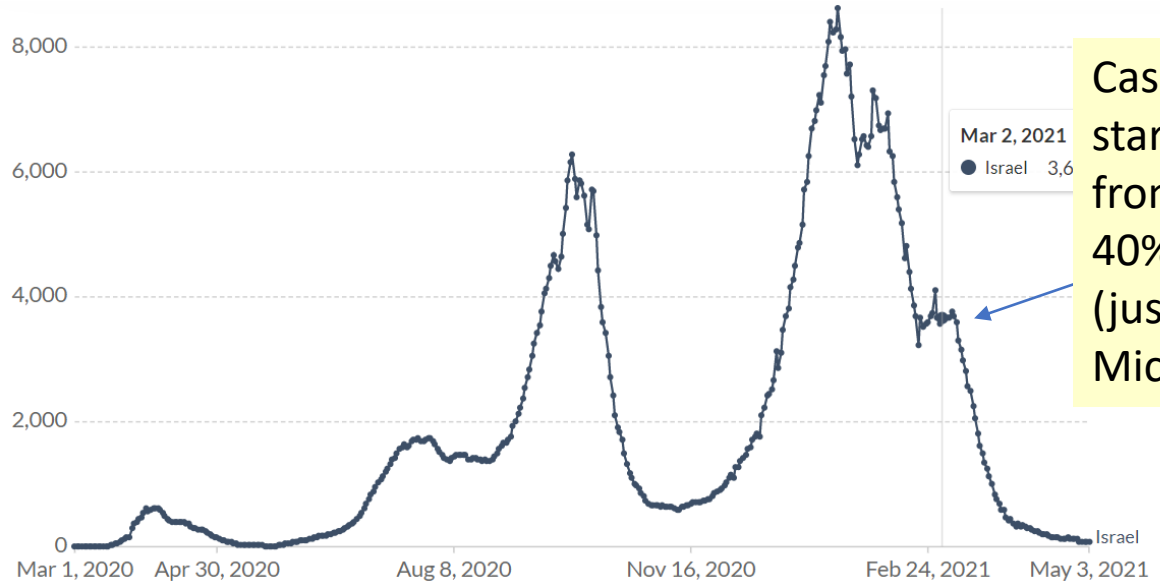
JANUARY 27, 2021

Julia Marcus
Epidemiologist and professor at Harvard Medical School



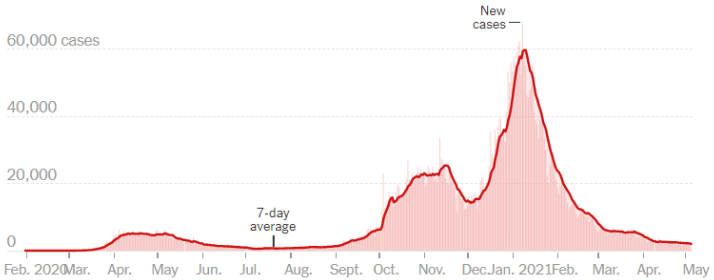
Herd immunity: Form of indirect protection from an infection that occurs when a significant % of population has become immune (through vaccine or previous infection), so children, unvaccinated protected (does not mean eradication)

What is inflection point of keeping cases low and of herd immunity?

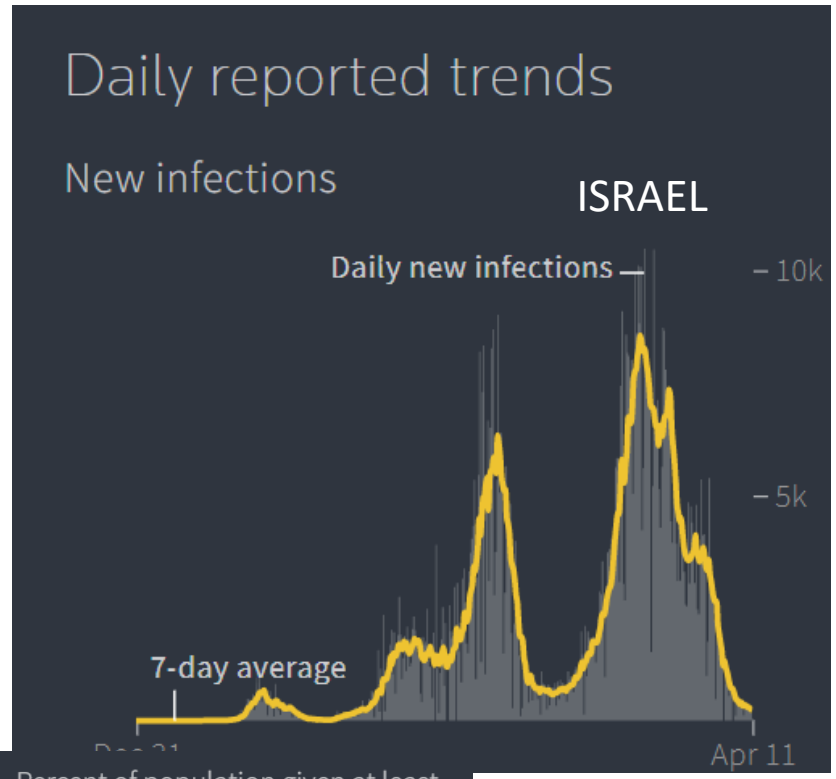


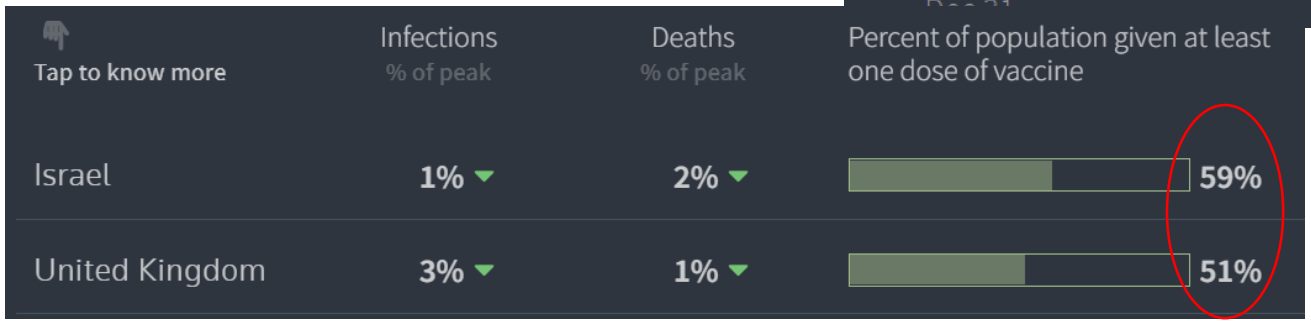
Cases in Israel started falling from high rate at 40% 1st dose (just like in US, Michigan)

May 3: 0.8 cases in 100K in Israel

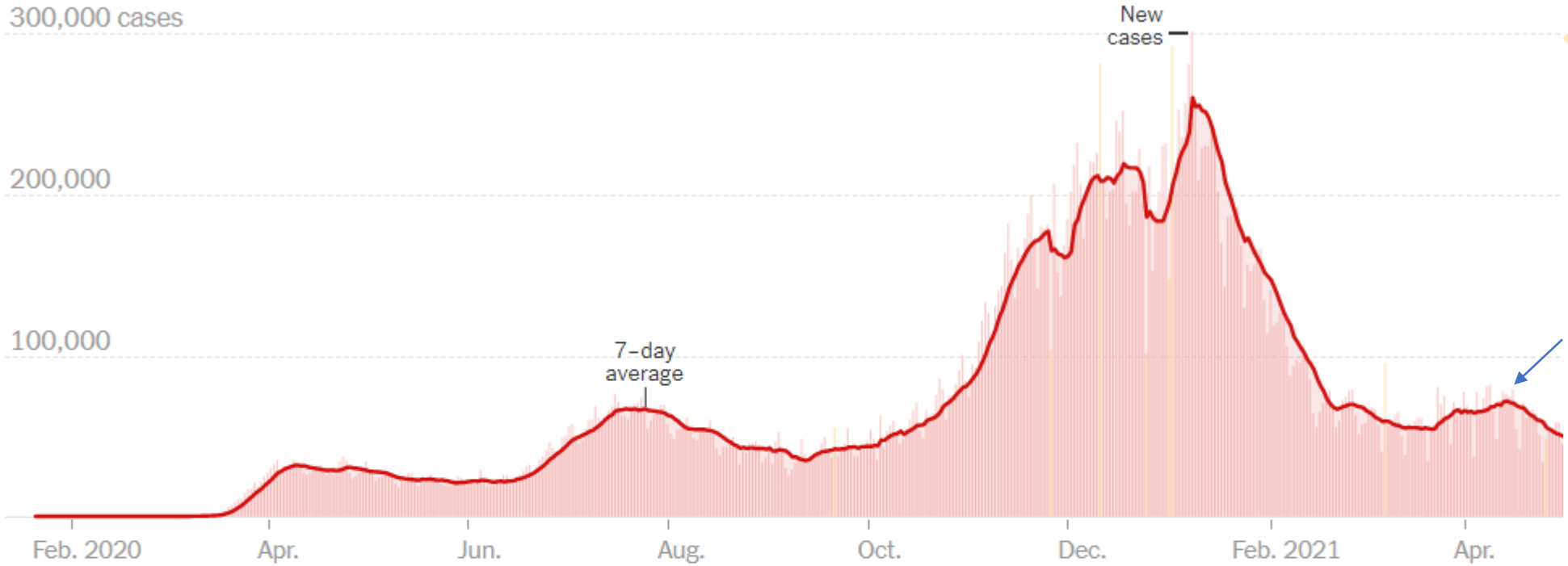


	TOTAL REPORTED	ON MAY 4	14-DAY CHANGE
Cases	4.4 million+	1,946	-19%
Deaths	127,543	4	-50%

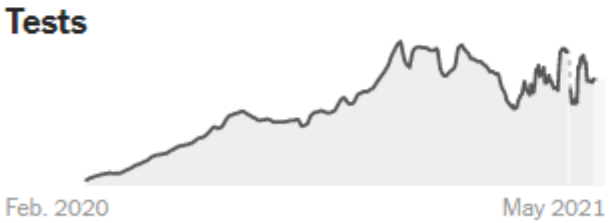


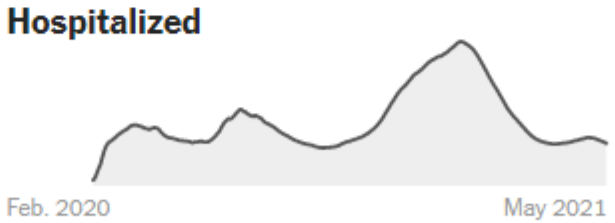


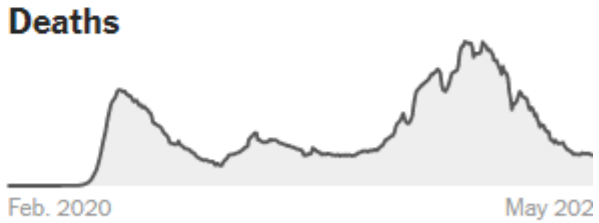
UK has 2.9 per 100K (same as CA)



Our cases started falling around 40% 1st dose too







	AVG. ON MAY 4	14-DAY CHANGE	TOTAL REPORTED
Cases	48,003	-26%	32,577,379


Thank You!