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COVID-19 vaccines update

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13th PACER Dialogue, Asia Development Bank

International Vaccine Institute

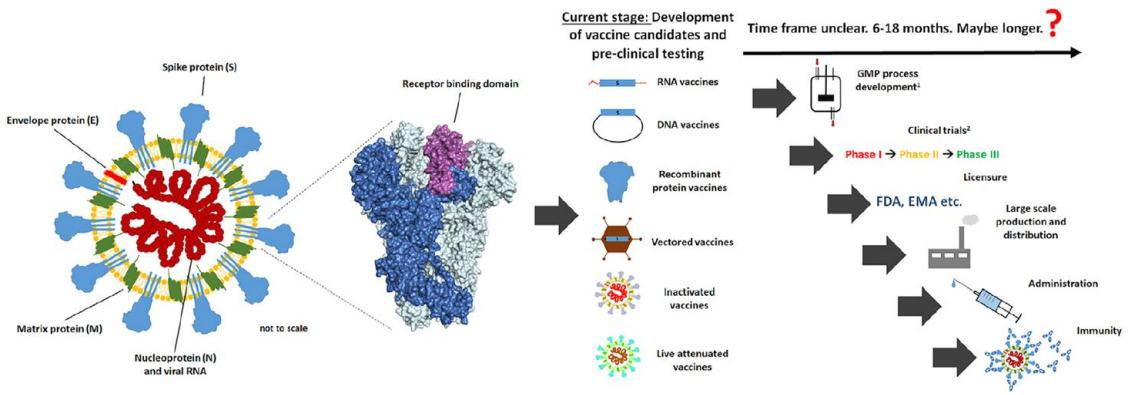
24 February 2021

International Vaccine Institute

Disclosures:

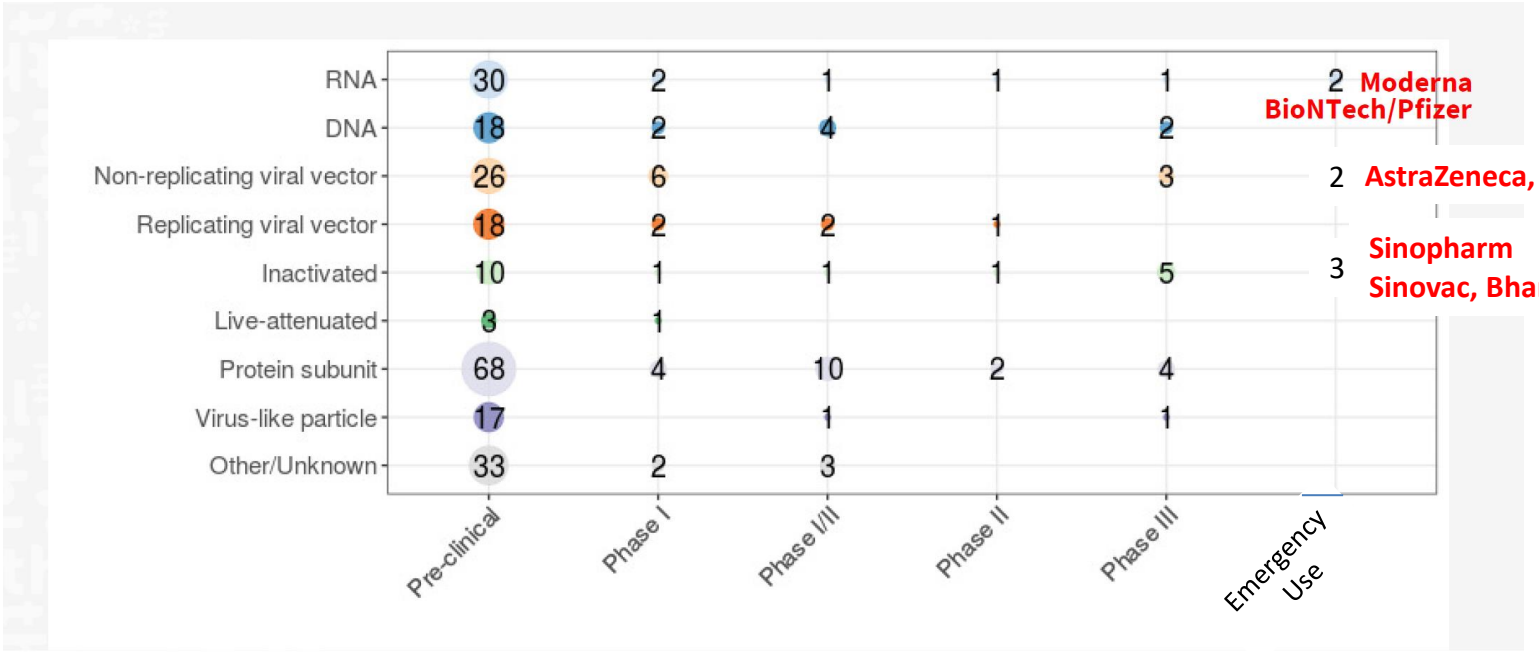
- **Dr. Kim is a consultant for SK biosciences**
- **IVI works on the Inovio, Genexine, Cellid and Clover vaccines in human clinical trials**

From 291 candidates, we have 9 efficacy signals



291 vaccines, 68 in clinical trials, 7 approvals (15 Feb 21)

- Pfizer/BioNTech: VE 95%
- Gamaleya: VE 92%
- Moderna: VE 94.5%
- AstraZeneca: 70% overall
  - 90% VE: ½ dose / full dose
  - 62% VE: full dose/ full dose
- Sinopharm: 79%
- Sinovac: 50% 65% 78%? 91%
- Novavax 89%
- Johnson and Johnson 66%
- Cansino 66%



https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

Phase III vaccines, neutralizing antibody, efficacy

MANUFACTURER	Vaccine	Dose	seroconversion	ID_{50}	Efficacy	Regulatory approval	WHO approval
CANSINO	Ad5 spike	1×10^{11} VP	50%	16		China	
		1.5×10^{11} VP	75%	34	**66%**		
SINOVAC	WIV/alum	3 ug x2 (14d)	>90%	28	**50%**	China	
		3 ug x 2 (28d)	97%	44 [1]	**65%**	Brazil	WHO expected
		6 ug x2 (14d)	>90%	34	**78%**	Indonesia	Mar
		6 ug x2 (28d)	>90%	~60	**91%**	Turkey	
GAMALEYA	Ad26 spike - Ad5 spike prime boost	10^{11} VP each	100%	49	**92%**	Russia	Unknown
Bharat	WIV/alum	6 ug x 2 (14d)	83%	62		India	
	WIV/alum+IMDG	3 ug x 2 (14d)	88%	66			
		6 ug x 2 (14d)	92%	48			
Johnson & Johnson	stabilized Spike-Δfurin-S.PP	5×10^{10} VP	92%	214	**66%**		
		1×10^{11} VP	92%	243	**72% (USA)** **57% (RSA)** **85% severe disease**		
SINOPHARM	WIV/alum	4 ug x 2 (0,14)	100%	211	**79%**	China	WHO expected
		8 ug x 2 (0,28)	100%	229			Mar
PFIZER/BNT	prefusion Spike	30 ug x 2	100%	267	**95%**	US, UK, EU	**WHO approved**
AstraZeneca/ JENNER/ Serum Institute / SK bio	chimp ad Spike	5×10^{10} VP	100%	201	**62% full dose**	UK, India, Thailand, EU	WHO expected
		5×10^{10} VP x2	100%	372	**90% split dose**		Jan-Feb
Moderna	prefusion stabilized spike	25 ug x 2	100%	340 $PRNT_{80}$	**94.5%**	US, EU	**WHO approved**
		100 ug x 2	100%	654 $PRNT_{80}$			
NOVAVAX	prefusion stabilized spike/ Matrix M	5 ug x 2	100%	3350 ID_{99+}	**89.3% (UK)** **60.1% (RSA)**		

	< 100
	100-500
	> 1000

ID50 groupings
CAVEAT: assays not standardized

If “vaccines” are the answer, what are the questions?

The BIG questions

- Can you prove it works? YES
- Can you make it? ???
- Can you use it effectively, fairly? ???

COVAX: potential for near concurrent access

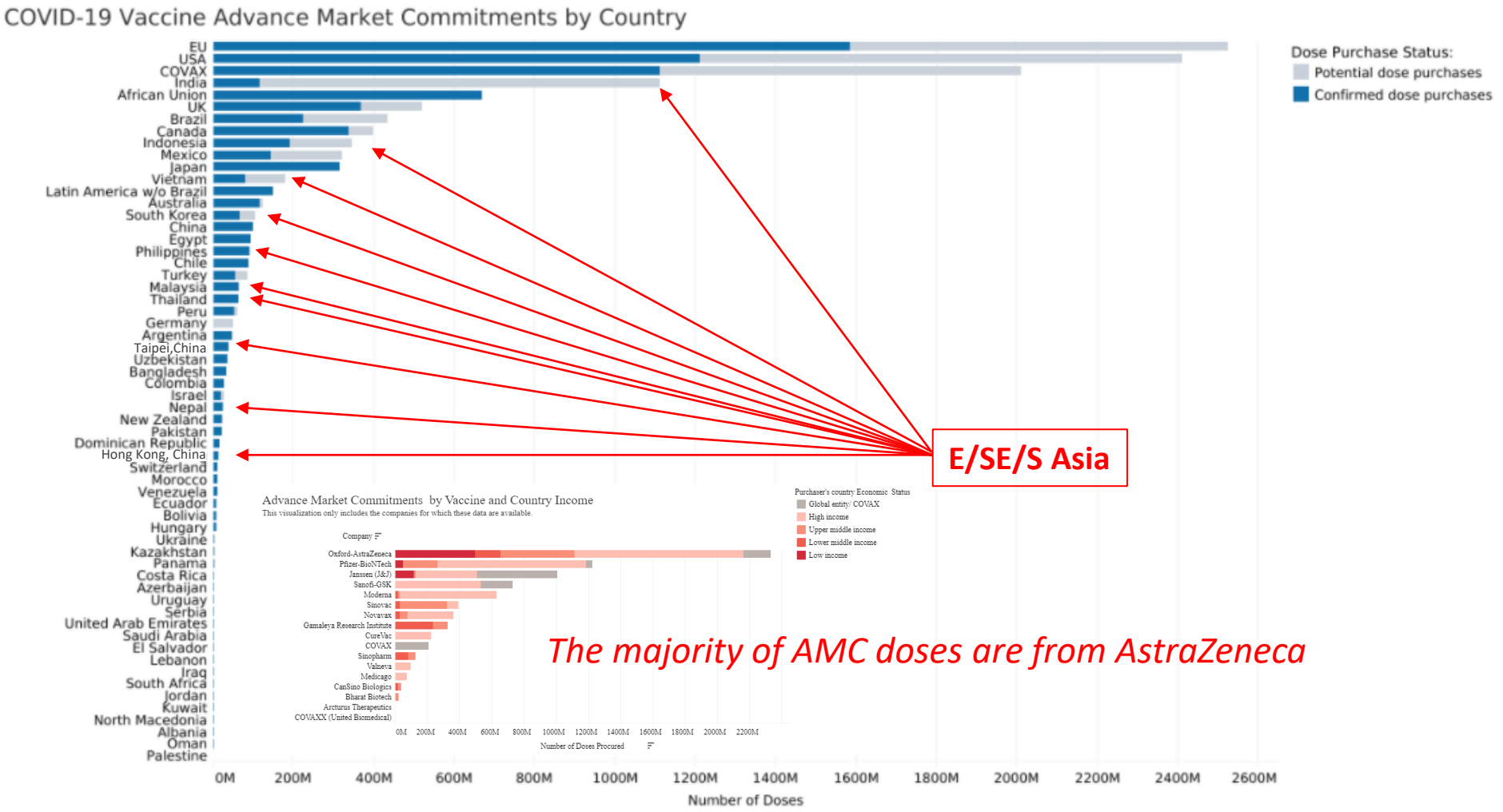
Updated 29 Oct 2020, Duke Global Health Innovation Center. (2020). Launch and Scale Speedometer. Duke University. Retrieved from: https://launchandscalefaster.org/covid-19

189 countries have joined COVAX

- Organized by CEPI, GAVI, WHO
- Coordinated by Gavi under ACT Accelerator activity
- 92 LMIC could be supported by the COVAX AMC
- 2 billion doses of WHO PQ'd vaccines by end of 2021
- Roughly 20% of need

- **But** 8.8 billion doses are reserved, mainly by high income countries
- Modeling suggests that exclusive use of the first 2 billion doses by high income countries without some equity will **double** global deaths
- 49% of the global economic costs of the pandemic in 2021 ($4-5 trillion) are borne by the advanced economies despite universal vaccination in their own countries (NBER, Jan 2021)
- Is COVAX at high risk of failure (Reuters/Gavi) or hitting its vaccine commitment targets (WHO)?

Advanced Market Commitments by Country & Company



The majority of AMC doses are from AstraZeneca

Unicef: vaccine production by companies with WHO PQ experience (purple)

unicef | for every child COVID-19 Vaccine Market Dashboard

Overview | Pipeline | Capacity

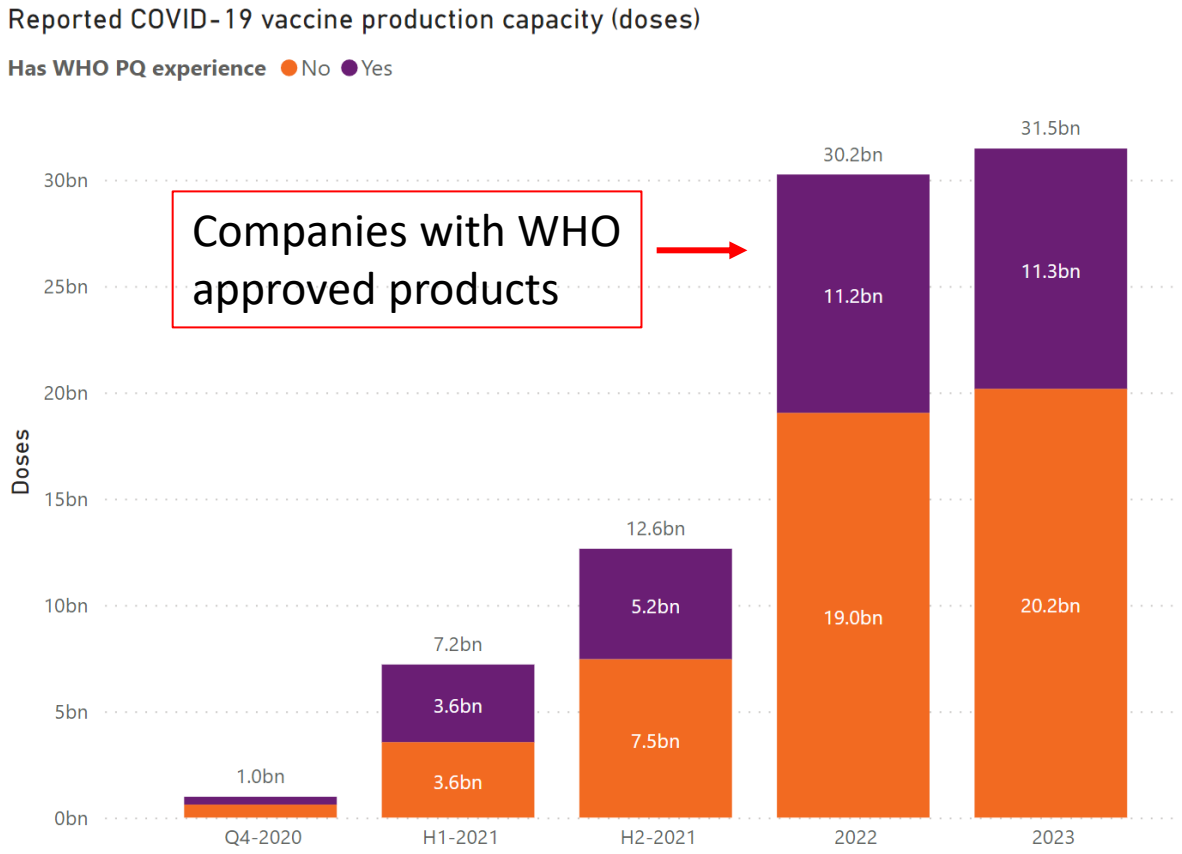
Reported global COVID-19 vaccine production capacity

The capacity information does not account for vaccine probability of success and may project a highly optimistic view of the potential supply

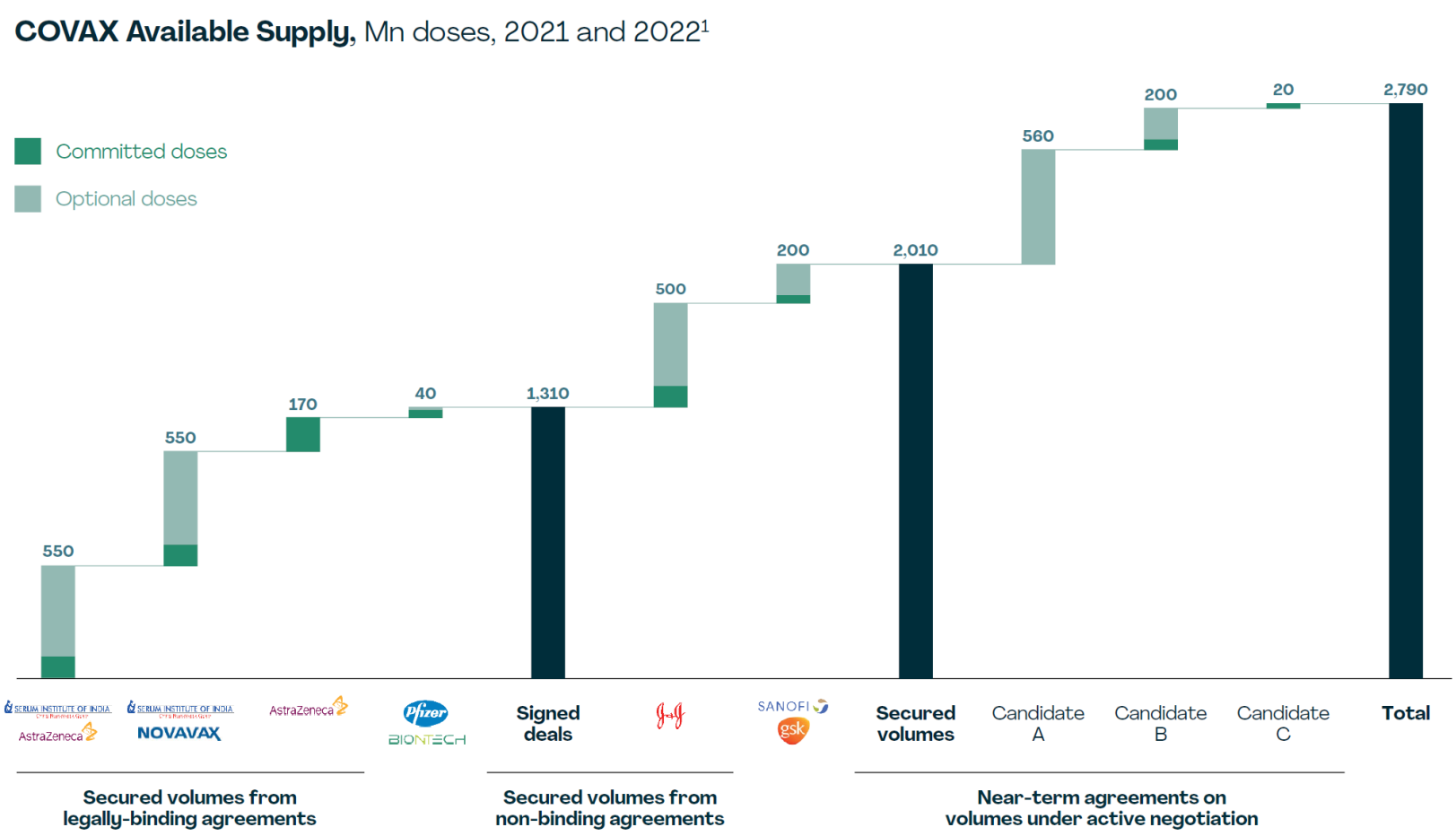
View option

- By vaccine platform
- By development stage
- By licensure experience
- By WHO PQ experience

'WHO PQ Experience' encompasses reported production capacities from developers who have at least one othe in addition to having been licensed, has been prequalified by the World Health Organization



MFR: Expected deliveries to COVAX (2021-22 est)



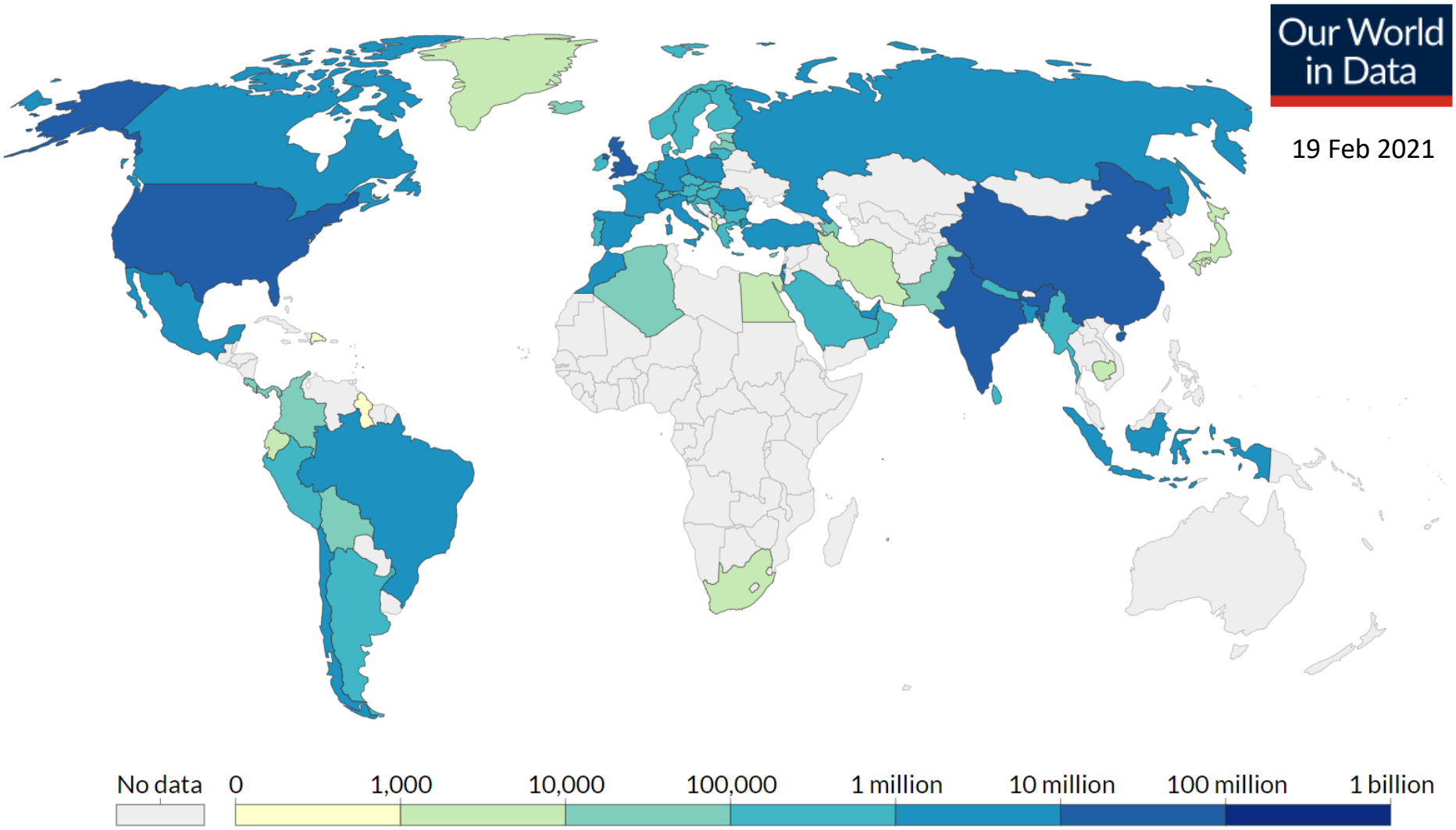
- If each person globally receives 2 doses = 16 billion doses
- To reach global "herd immunity" = 10-14 billion doses?
- Some estimates 2023-2024 before enough vaccine can be manufactured for all countries to have sufficient vaccination levels

Delivery: Vaccines don't save lives, vaccination does

- 16 billion doses
- Going from extended program of immunization to a universal program of immunization?
- Logistics, cold chain >> 8,000 jumbo jets for single dose vaccine, -70°C?
- Multiple vaccine formats, prioritization programs, safety >> record keeping?
- Campaigns, drug stores, schools, work?

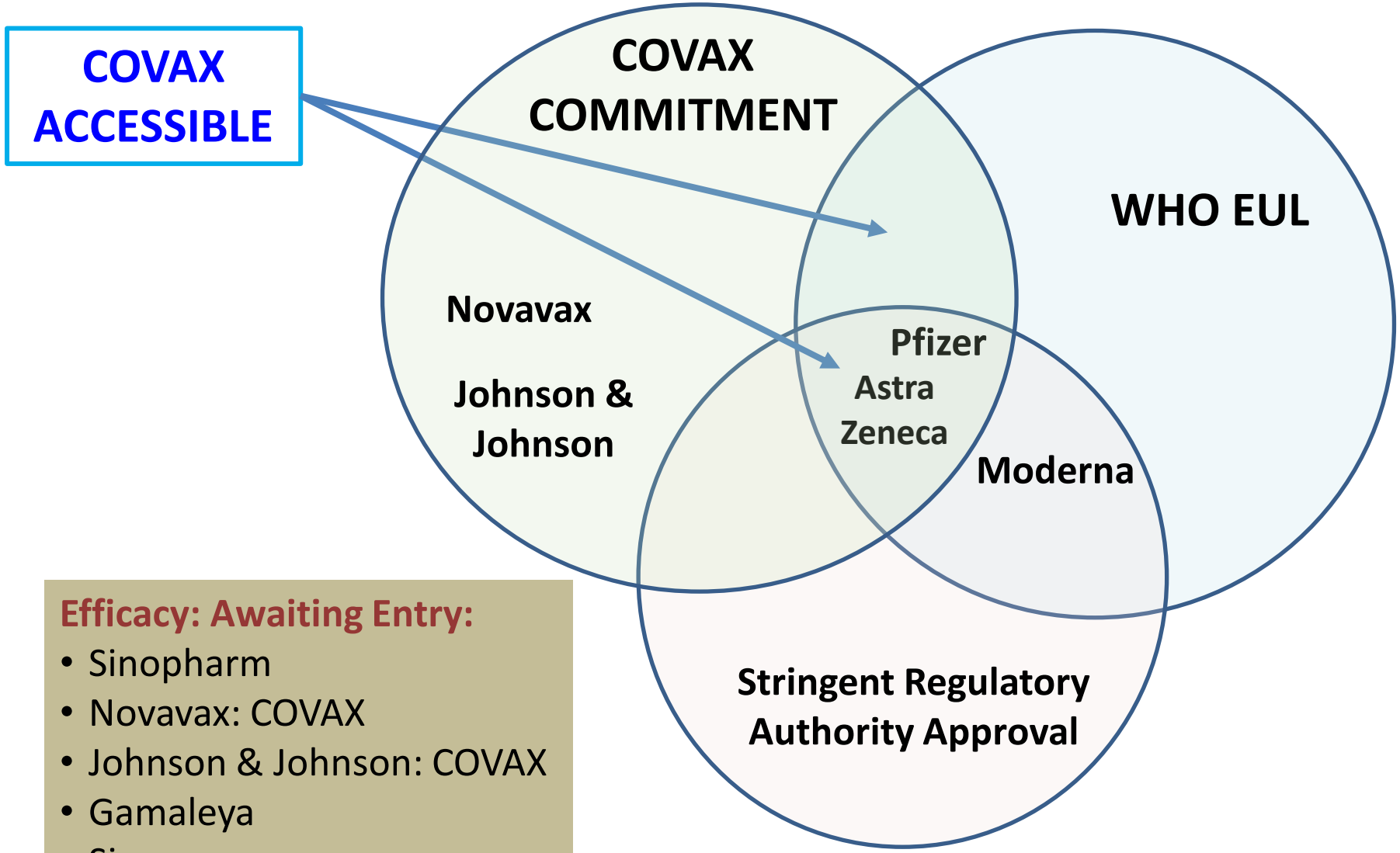
The vaccine is only a weapon in the fight against COVID, and it needs a comprehensive strategy of prevention, good logistics, an army of vaccinators, and a receptive public.

COVID-19 vaccination: total doses administered



Our World in Data, 2021

Entry into COVAX



Efficacy: Awaiting Entry:

- Sinopharm
- Novavax: COVAX
- Johnson & Johnson: COVAX
- Gamaleya
- Sinovac
- Cansino

Additional questions

- We have 9 vaccines showing short term efficacy & safety: what's next for vaccines?

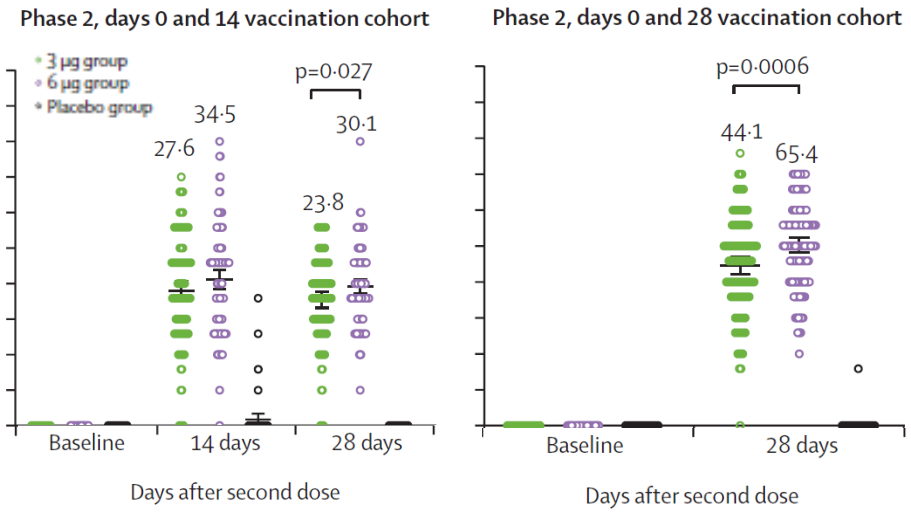
- The other big questions:
  - Optimization of dose, schedule, boosts
  - Correlates of protection
  - Effectiveness – Herd immunity?
  - Surveillance for mutations or new emerging coronaviruses
  - Longer term safety follow-up / post-licensure safety monitoring
  - Opposition to vaccination

We need to optimize schedule, dose, boosting

Voysey et al. Lancet 2020

	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (CI*)
		n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	
All LD/SD and SD/SD recipients	131	30/5807 (0·5%)	44·1 (248 299)	101/5829 (1·7%)	149·2 (247 228)	70·4% (54·8 to 80·6)†
COV002 (UK)	86	18/3744 (0·5%)	38·6 (170 369)	68/3804 (1·8%)	145·7 (170 448)	73·5% (55·5 to 84·2)
LD/SD recipients	33	3/1367 (0·2%)	14·9 (73 313)	30/1374 (2·2%)	150·2 (72 949)	90·0% (67·4 to 97·0)‡§
SD/SD recipients	53	15/2377 (0·6%)	56·4 (97 056)	38/2430 (1·6%)	142·4 (97 499)	60·3% (28·0 to 78·2)
COV003 (Brazil; all SD/SD)	45	12/2063 (0·6%)	56·2 (77 930)	33/2025 (1·6%)	157·0 (76 780)	64·2% (30·7 to 81·5)‡
All SD/SD recipients	98	27/4440 (0·6%)	56·4 (174 986)	71/4455 (1·6%)	148·8 (174 279)	62·1% (41·0 to 75·7)

Low dose / Standard dose efficacy was 90% vs 62% fo Standard Dose / Standard Dose



Four week interval between doses had a higher neutralizing antibody level than a two week interval– what about 6 month interval?

Zhang et al. Lancet Infect Dis 2020

Efficacy, effectiveness, herd immunity

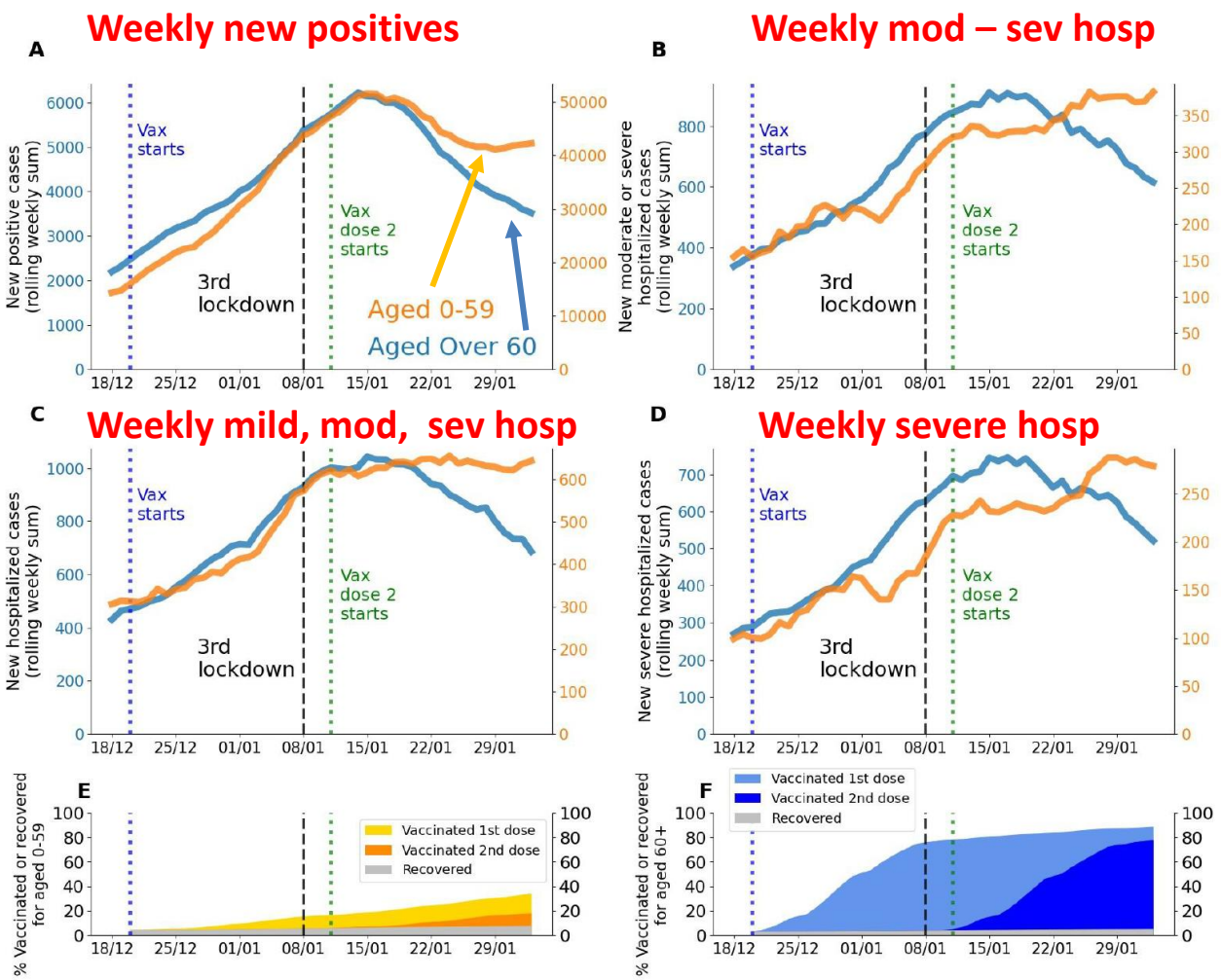
Approximate Basic Reproduction Numbers (in Developed Countries) and Implied Crude Herd Immunity Thresholds (*H*, Calculated as *1-1*/R_0), VE, E for Selected Diseases

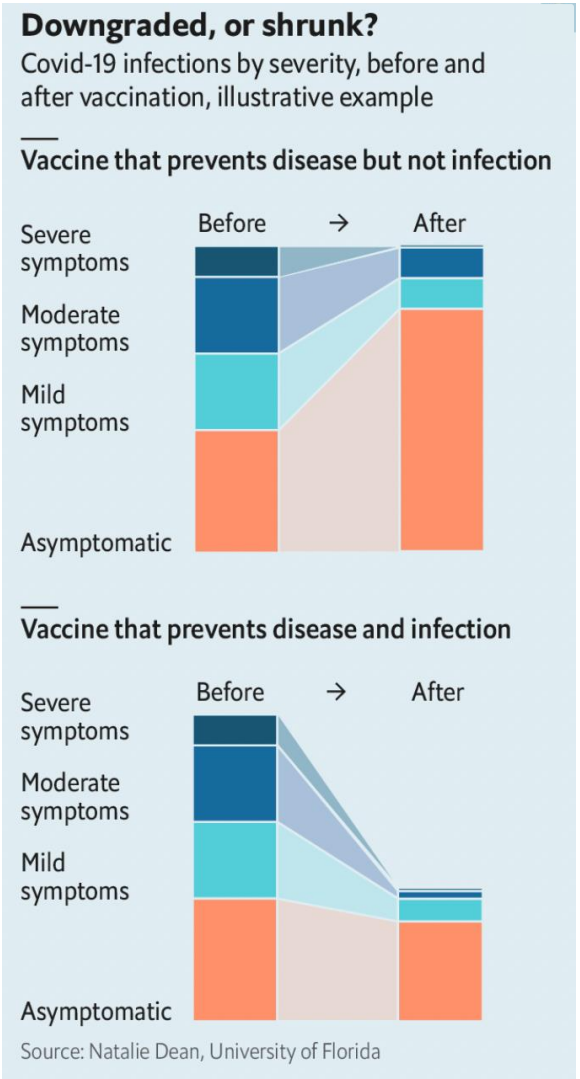
Infection	Basic Reproduction Number (R_0)	Herd Immunity Threshold (%)	Vaccine Efficacy (%)	Effectiveness	References
Diphtheria	6-7	85	97	>95	70,71
Measles	12-18	55-94	94	90-95	71
Mumps	4-7	75-86	95	78	71
Pertussis	12-17	92-94	70-90	75-85	71
Polio	12-15	50-93	80-90	>90	71
Rubella	6-7	83-85	94-95	>95	71
Smallpox	5-7	80-85	90-97	?	71
Ebola	1.5-2.5	33-60	95-100	70	65
Varicella	8-10	87-90	90-98	>95	71
Spanish flu 1918	2-3	50-67	NA	NA	72
Cholera	1-2	50%	42-66%	86%	73-75
SARS-CoV-2	2.5 – 5.8	60-83	60-95%	?	72,76

The vaccines have been shown to prevent disease, not infection or transmission. Herd immunity is about protection from transmission.

[1]Petersen et al, Lancet, 2020 & Ke et al, MedRxiv, 2020
[2]Plotkin SE, et al. Vaccines, 6th ed
[3]US CDC Pink Book, but no formal controlled trials

Impact of Pfizer mRNA vaccine: real world evidence

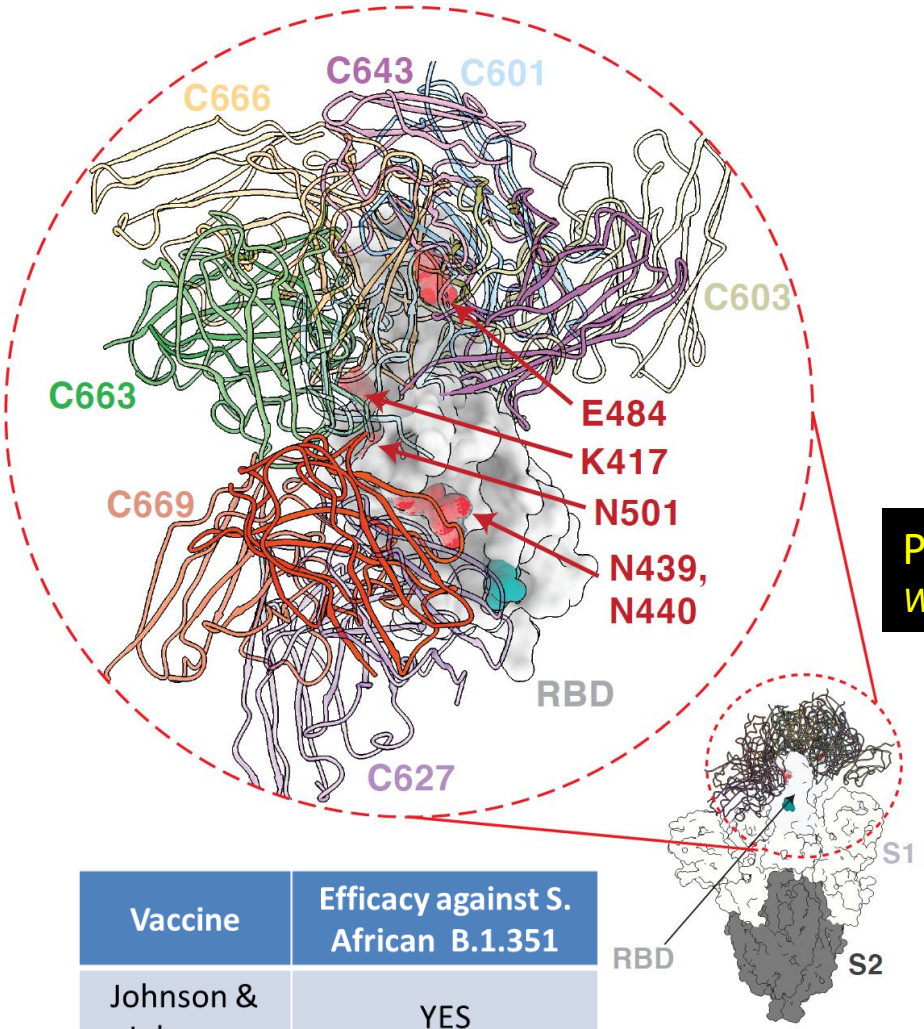




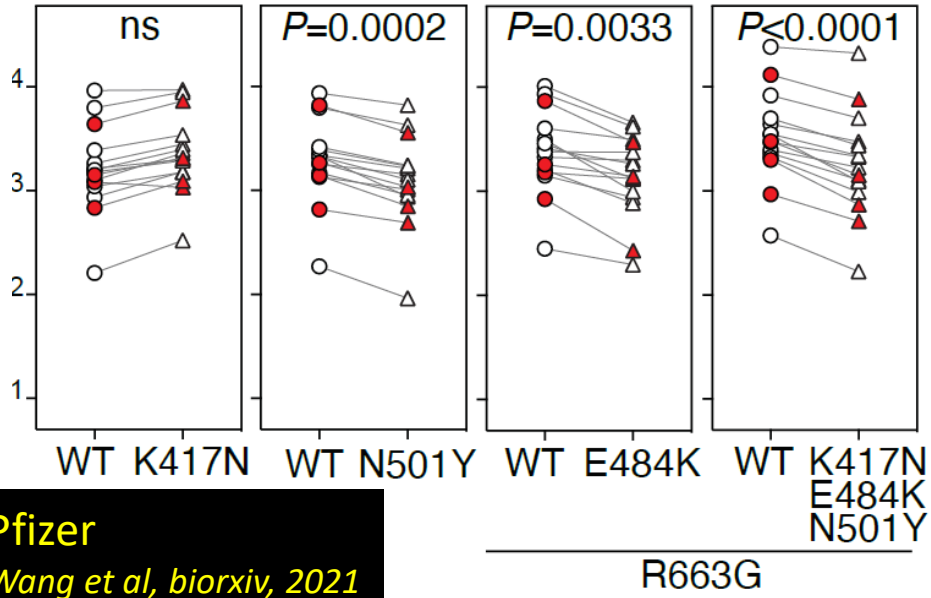
Important questions for COVID-19 vaccines:

- Do COVID-19 vaccines decrease hospitalization and death?
- Do COVID-19 vaccines prevent disease, infection or both?

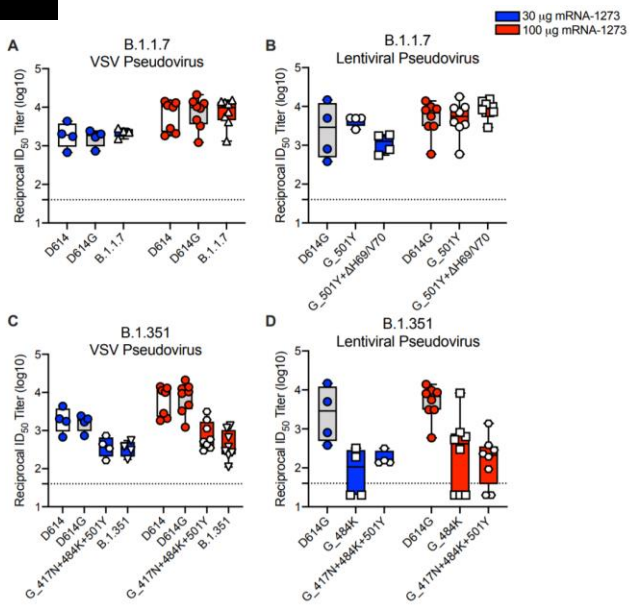
Vaccines and mutant SARS-CoV-2



Vaccine	Efficacy against S. African B.1.351
Johnson & Johnson	YES
Novavax	YES
AstraZeneca	NO



Pfizer
Wang et al, biorxiv, 2021



Moderna
Wu et al, biorxiv, 2021

Update on 5 initial questions for COVID-19 vaccines (2020)

- **Does natural COVID infection prevent re-infection?**
  - With “classical” germ-vaccine pairs infection prevents re-infection and those vaccines may be easier to develop
  - With COVID the strong hypothesis is that infection does provide immunity against reinfection
  - ➢ CAVEAT (2021): For some period of time, and not necessarily against mutants
- **Will we need seasonal COVID vaccines?**
  - The amount of sequence variation in COVID is 8-10x lower than influenza and much, much lower than HIV
  - Current data provides some evidence that COVID-19 infected patients and some vaccines provide protection against the current “new strains”
  - ➢ Uncontrolled spread generates new mutants, and recombination
- **What are the protective immune (defensive) responses?**
  - Probably neutralizing antibody, possibly other functional antibody
  - Killer and helper T cells may be important
- **Are animal models predictive?**
  - ➢ So far, the vaccines that protect mice, ferrets, hamsters, and monkeys also protect humans
- **Are there safety concerns?**
  - Possibly, from other coronaviruses, antibody dependent enhancement and enhanced respiratory disease
  - ➢ Human studies have not shown safety issues (through about 3-4 months)

And new questions for 2021

- **Nine vaccines, how do we know which to use?**
  - Is there anything in the pipeline that looks better
- **Will we need a bivalent vaccine that covers B.1.351 (S. African variant)?**
  - Do we wait for it?
- **Will COVAX deliver on the 20% of vaccine need promised in 2021?**
  - Where does the other 80% come from and *WHEN*?
  - Will vaccine nationalism undermine COVAX?
  - Will vaccine geopolitics undermine COVAX?
- **Vaccine security, patents and know how**
  - Does every country need its own vaccine manufacturing capability?

IVI is an International Organization dedicated to Global Health

Global Vaccine Research Institute

- **HQ and labs at Seoul National University**
- **Field programs in 28 countries: Asia, Africa, Latin America**
- **19 nationalities in workforce of 169**

OECD-recognized International Organization (not for profit)

- **UNDP initiative**
- **First international organization in Korea (1997)**
- **36 countries and WHO as state parties (now 38 – Madagascar & Argentina pending final submission to UN)**

Pending submission of paperwork to UN SG office

Thank you for your attention!