

IVAC WEBINAR

AVOIDING BARRIERS TO ACCESS FOR A COVID-19 VACCINE

September 16th, 2020

Featuring



Jerome Kim, MD
Director General, International
Vaccine Institute



Naor Bar-Zeev, PhD
Deputy Director, International
Vaccine Access Center



**International
Vaccine
Institute**

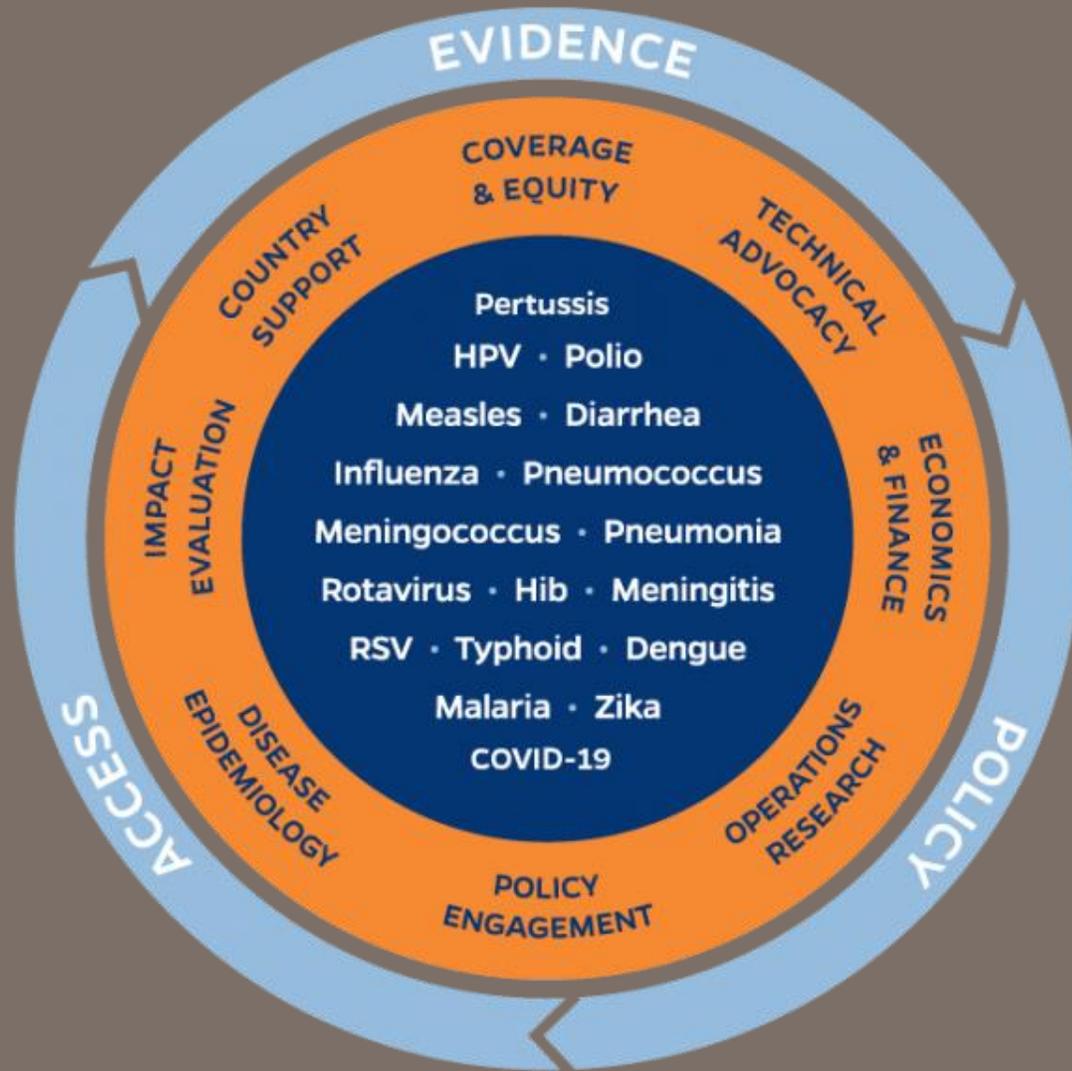


**INTERNATIONAL
VACCINE ACCESS
CENTER**



JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH

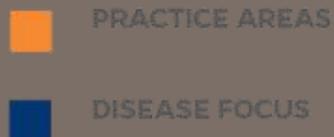
International Vaccine Access Center



8 Practice Areas

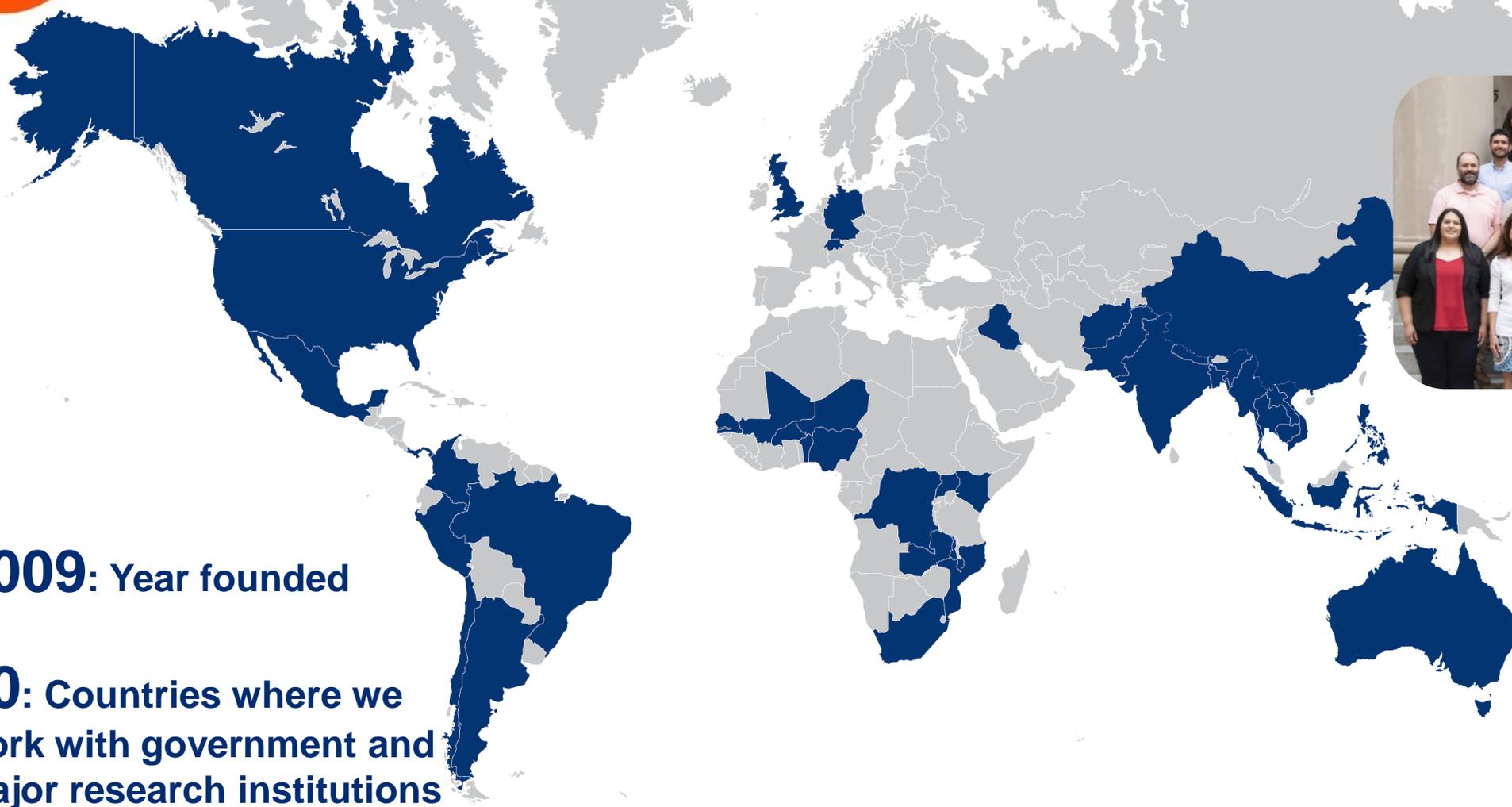
Technical leadership on
15+ disease and syndromes

Rooted in Evidence-Policy-Access
value chain





The IVAC Team & Where We Work



- Physicians
- Professors
- Economists
- Epidemiologists
- Researchers
- Advocates

2009: Year founded

40: Countries where we work with government and major research institutions

50: Faculty and Staff

>227: Johns Hopkins students trained from 24 countries



Vaccines have taken much longer to get to low- and middle-income countries

- Time from first product licensure to first Gavi-supported country introduction was slower for PCV (including PCV 7, 10.8 years) than the median time across all VPDs (5.4 years, n=6), but faster if considering only PCV10/PCV13 (2.0 years).

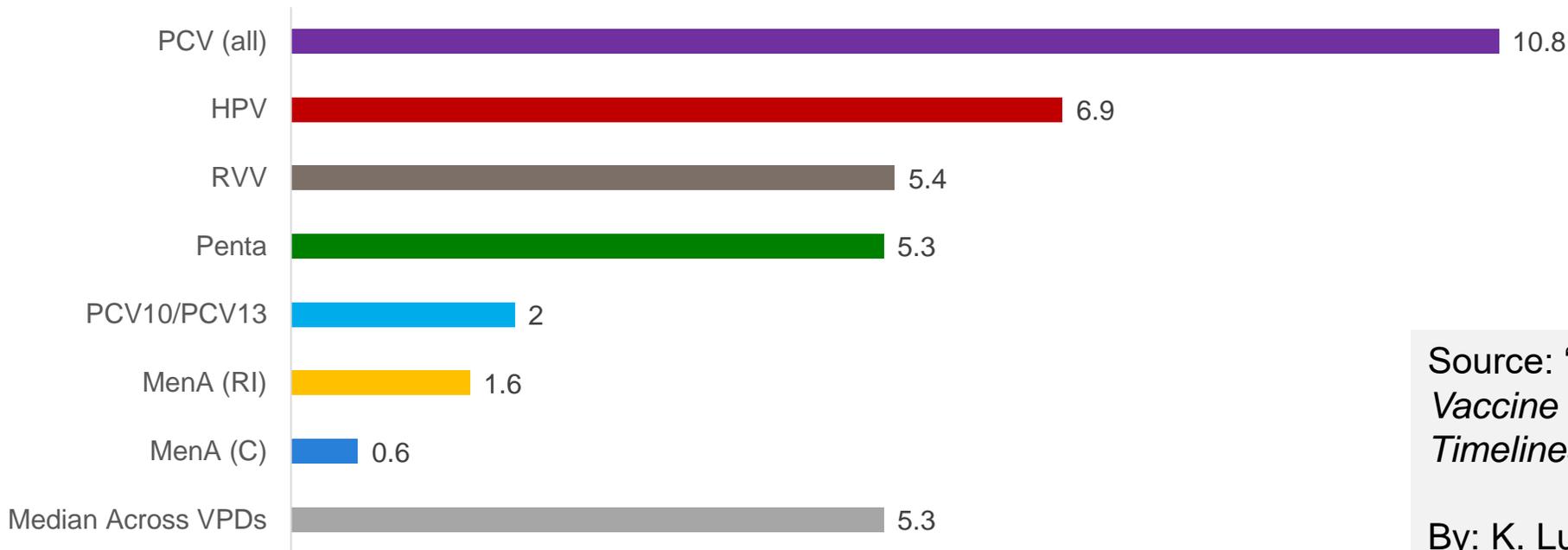


Figure: 1st Licensure to 1st Gavi-Supported Intro.

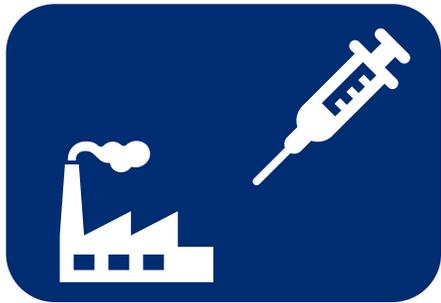
Source: “*Pneumococcal Conjugate Vaccine Introduction And Uptake Timelines For Gavi-supported Countries*”

By: K. Luthra, A. Zimmermann Jin, P. Vasudevan, and L. Privor-Dumm

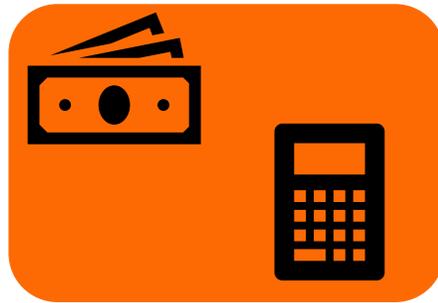


Barriers to vaccine access in LMICs

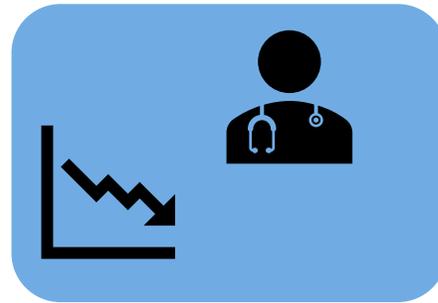
- PCV and RVV vaccines had longest delays in country introduction, likely due to a variety of reasons such as



Supply
Constraints



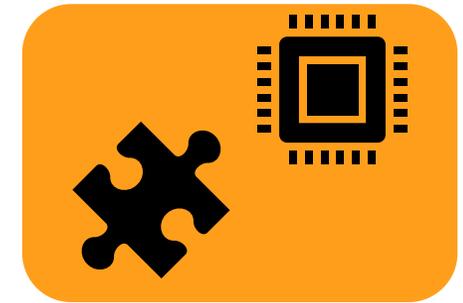
Cost &
Financing



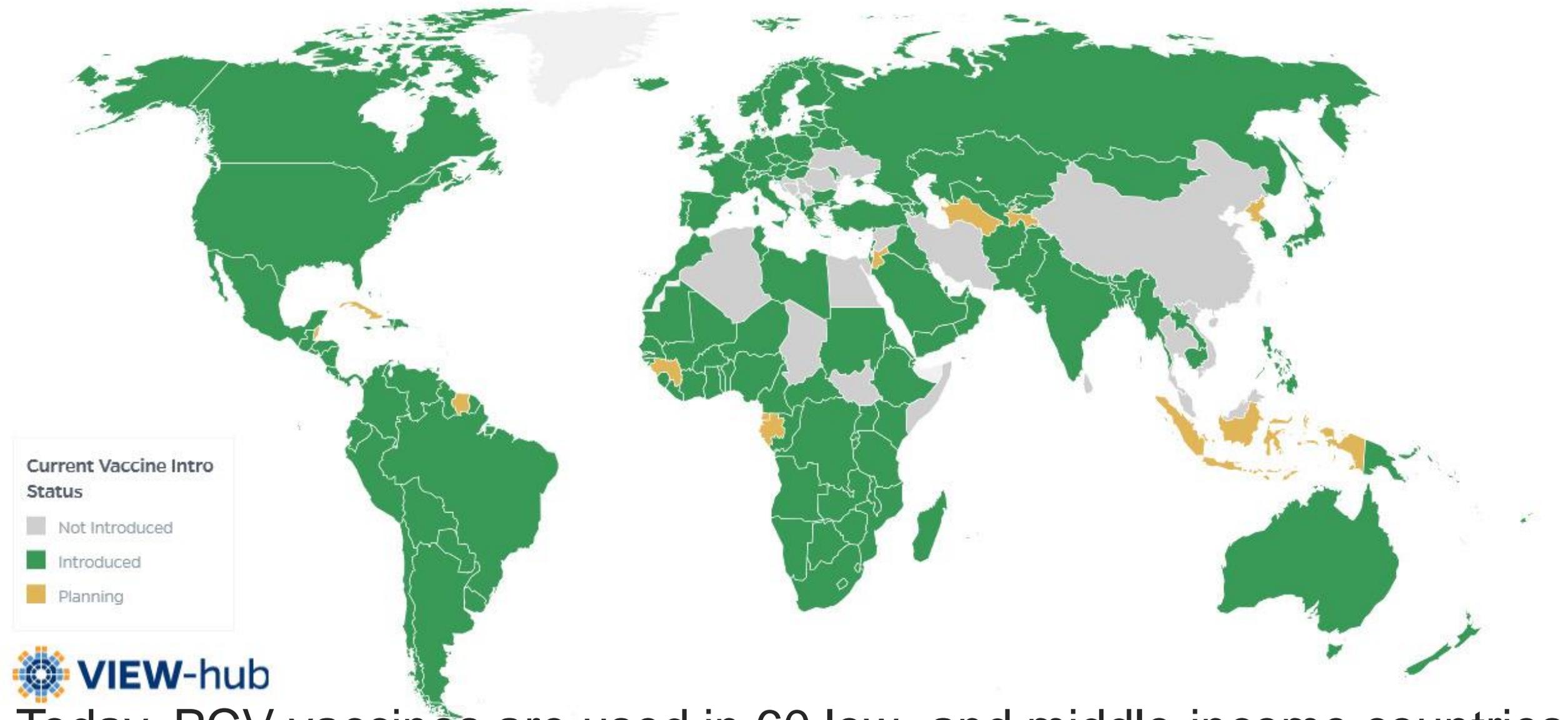
Perceived low
burden



Vaccine safety
concern



Programmatic
challenges



Current Vaccine Intro Status

- Not Introduced
- Introduced
- Planning



Today, PCV vaccines are used in 60 low- and middle-income countries

COVID-19 Vaccine Development: Remembering Vaccine Access and Equity at Warp Speed

Jerome H. Kim, MD
International Vaccine Institute



International
Vaccine
Institute

Does infection provide immunity?

- **Does infection provide immunity?**
 - Classic vaccine – disease model (e.g. Hepatitis A, polio)
 - Almost all recover completely (polio, rubella, influenza)
 - Vaccine induced immune response or natural immune response clear virus completely
 - Lifelong immunity from reinfection (or with booster immunization)
 - Or is this like EBV, cytomegalovirus, HIV, or TB?
 - If it does provide immunity how long does it last?



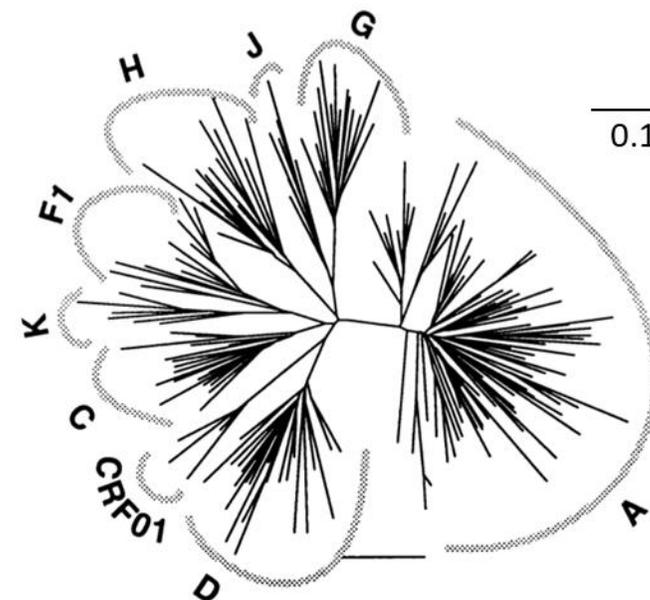
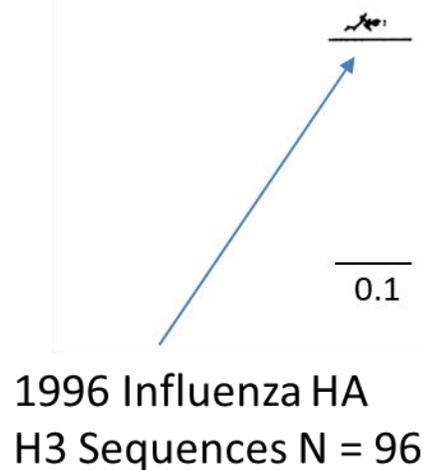
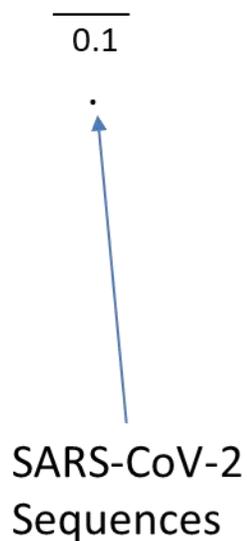
M. Sweerts, The Plague of Athens

SARS-CoV-2: Maybe, probably

- Three monkey challenge studies have shown that infection with SARS-CoV-2 is associated with protection against a SARS-CoV-2 challenge, durability unknown (Chandrashekhar et al, Science 2020; Deng et al, Science 2020; Bao et al, Biorxiv 2020)
- Syrian hamsters that survive SARS-CoV-2 infection are protected against rechallenge (Imai et al, PNAS 2020)
- 12 weeks after vaccination in NHP there is protection against infection and memory immune responses (Pate et al, Biorxiv, 2020)

Will we need seasonal SARS-CoV-2 vaccines?

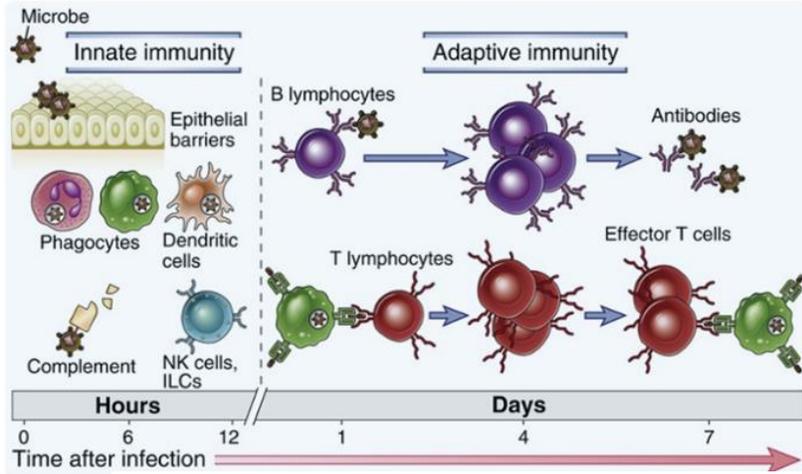
Will COVID-19 be like influenza or like rotavirus with regard to vaccines?



Compared to influenza and HIV there is little sequence variation in SARS-CoV-2

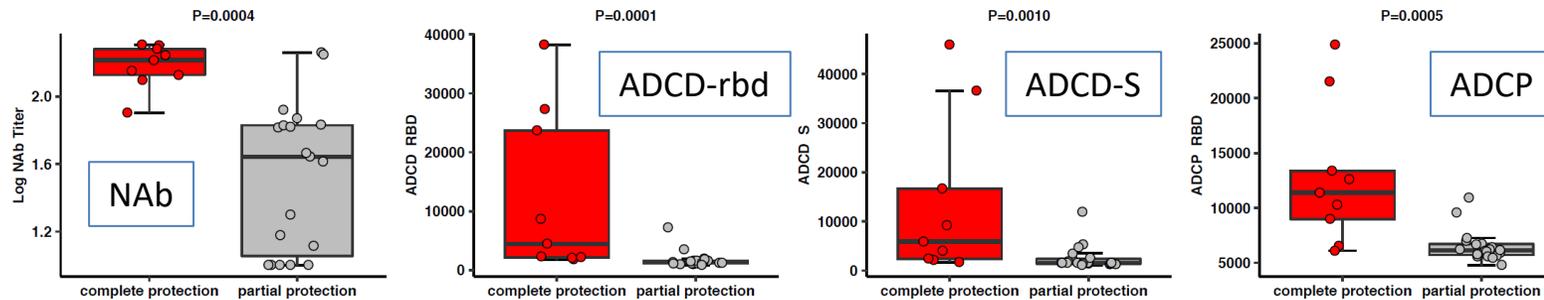
Korber et al, Brit Med Bull 2001

What are the relevant protective immune responses?



Abbas AK, et al (eds), *Cellular and Molecular Immunology*, 8e, 2015

Yu et al, *Science* 2020: DNA vaccines against S, S1, RBD protect NHP against infection. Correlates of protection: NAb, ADCD, ADCP



- Neutralizing antibody and functional antibody
 - Titers may be low and decrease post -- infection, do these protect?
- Cellular immunity present and may be important for a vaccine may be important in immune memory

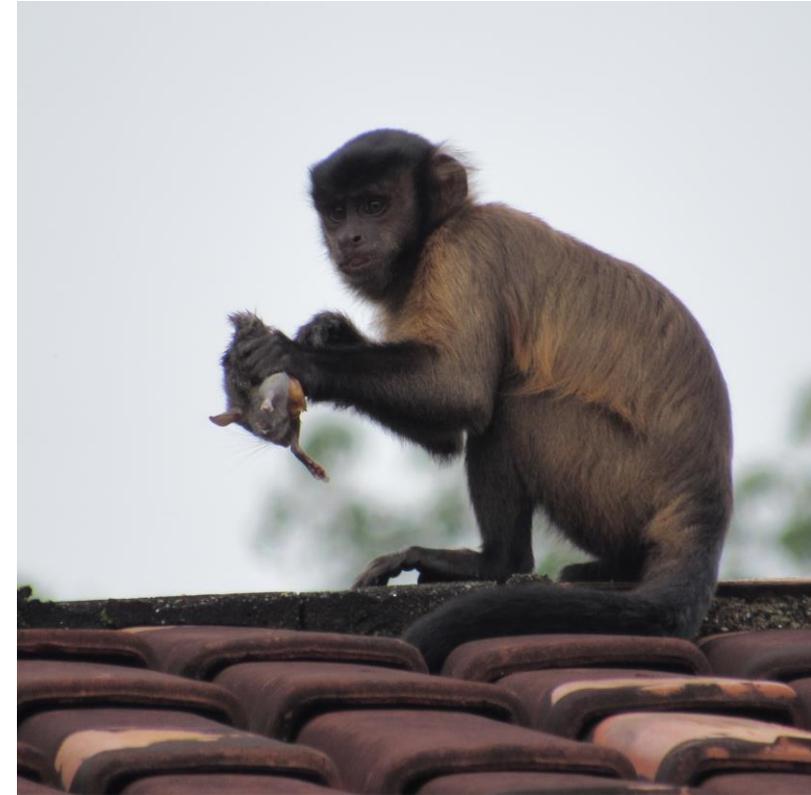
NAb = neutralizing antibody; **ADCD** = antibody dependent C' deposition; **ADCP** = antibody dependent monocyte cellular phagocytosis

Is there a reliable animal model?

- Prof. David Weiner: mice lie, monkeys exaggerate, only humans tell the truth
- You can infect monkeys, ferrets, hamsters and ACE2 mice with SARS-CoV-2 and can adapt SARS-CoV-2 to infect regular mice
- Animal models should be validated against efficacy testing in humans

Many studies show vaccine protection of NHP

- Whole inactivated virus w/alum – Sinovac
- Chimp adenovirus S, Oxford AstraZeneca
- RNA S-2p (stabilized), Moderna
- Ad26 – S, Johnson and Johnson
- WIV w/alum, Sinopharm/Wuhan & Beijing
- DNA S – Inovio
- DNA (multiple) – Yu et al, not commercial



Are there safety issues?



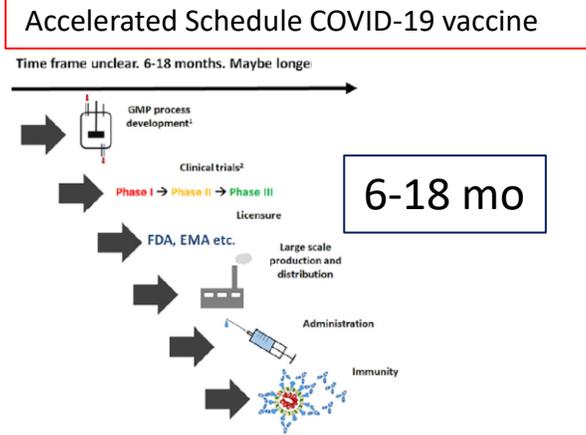
There are two potential safety questions that have come from work on SARS-CoV-(1) and MERS

- ADE
- SARS-1 > MERS eosinophilic infiltrates after challenge /vaccine associated enhanced respiratory disease (VAERD, ERD) seen in mice > ferrets > NHP
- Associated with alum? Whole inactivated viruses? Th1-Th2 imbalance

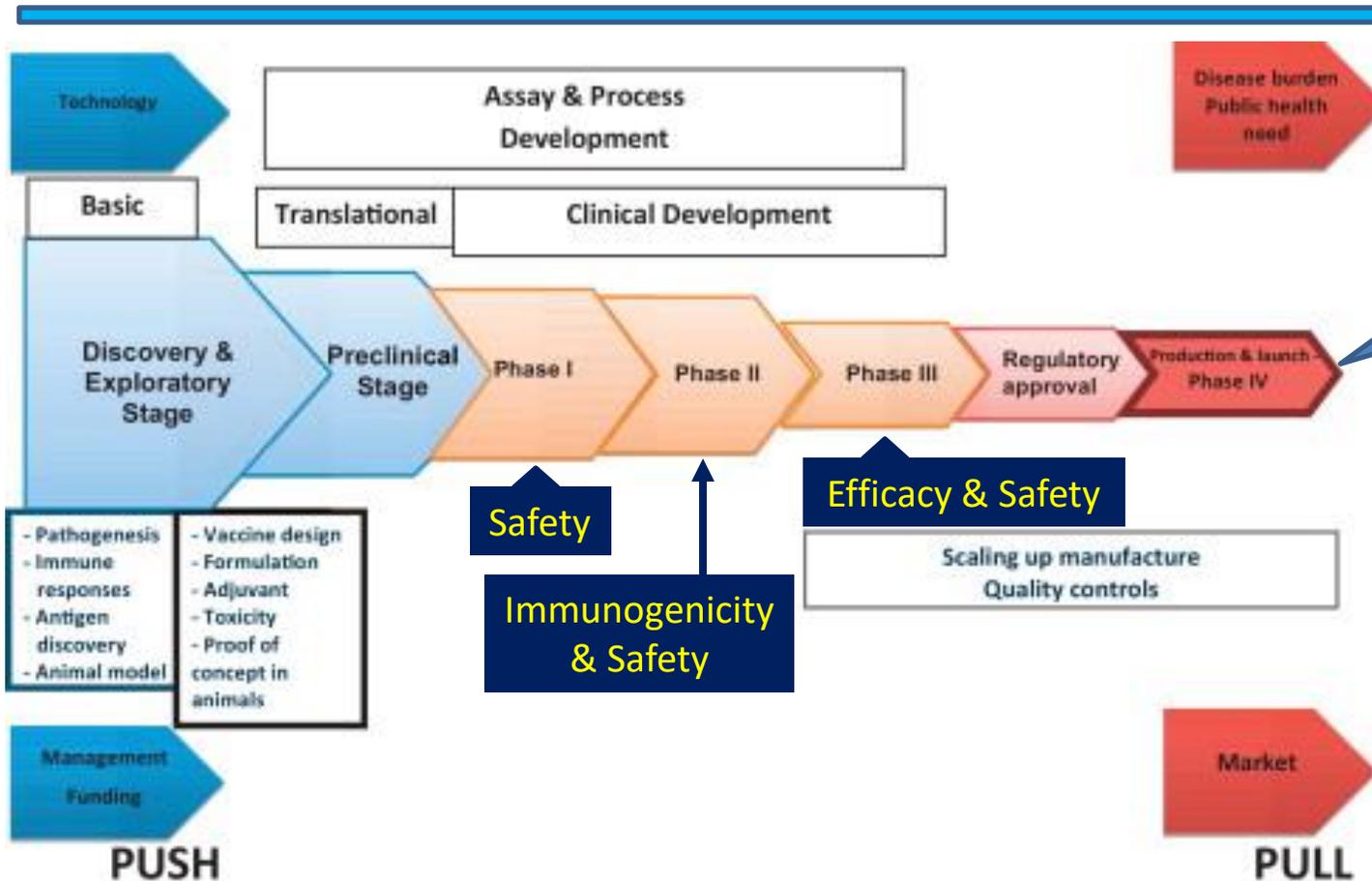
To date, ADE and ERD have not been seen in any of the 7 vaccine – challenge studies in NHP for SARS-CoV-2 with different vaccines

Under normal circumstances it takes 5-10 years to make a vaccine

- **COST: USD 500M – 1.5B**
- **FAILURE RATE: 93% (to Market Authorization)**

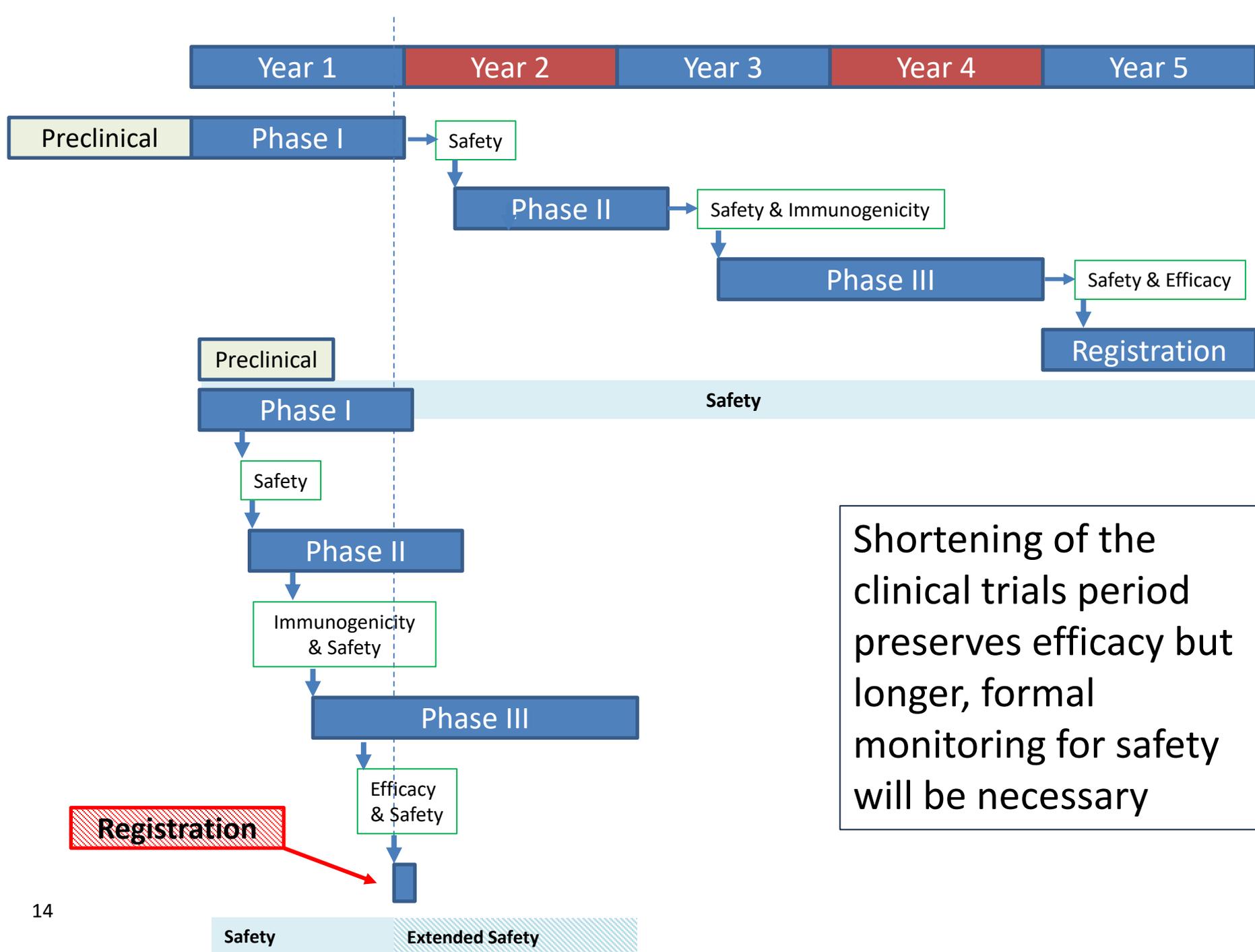


5-10 years



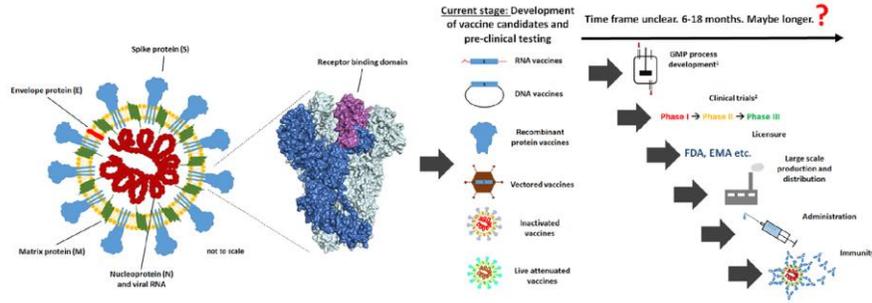
Only 1 in 10 vaccines make it here





For COVID-19 there are 180+ possible candidates, and 35 currently in human clinical testing

HUMAN CLINICAL TRIALS



COVID-19: Vaccine technology platforms, September 2020^[2]

Molecular platform	Total number of candidates	Number of candidates in human trials
Non-replicating viral vector	24	5 ^[1]
RNA-based	24	3 ^[1]
Inactivated virus	8	3 ^[1]
Protein subunit	62	2 ^[1]
DNA-based	14	3
Replicating viral vector	18	0
Virus-like particle	12	0
Live attenuated virus	4	0

i. ^ a b c d One or more candidates in Phase II or Phase II–III trials

Wikipedia: COVID-19 Vaccines
10 Sept 2020

COVID-19 Vaccine developer/manufacture	Vaccine platform
University of Oxford/AstraZeneca	Non-Replicating Viral Vector
CanSino Biological Inc./Beijing Institute of Biotechnology	Non-Replicating Viral Vector
Gamaleya Research Institute	Non-Replicating Viral Vector
Janssen Pharmaceutical Companies	Non-Replicating Viral Vector
Sinovac	Inactivated
Wuhan Institute of Biological Products/Sinopharm	Inactivated
Beijing Institute of Biological Products/Sinopharm	Inactivated
Moderna/NIAID	RNA

Clover Biopharmaceuticals Inc./GSK/Dynavax	Protein Subunit
Vaxine Pty Ltd/Medytox	Protein Subunit
University of Queensland/CSL/Seqirus	Protein Subunit
Medigen Vaccine Biologics Corporation/NIAID/Dynavax	Protein Subunit
Instituto Finlay de Vacunas, Cuba	Protein Subunit
FBRI SRC VB VECTOR, Rospotrebnadzor, Koltsovo	Protein Subunit
West China Hospital, Sichuan University	Protein Subunit
Institute Pasteur/Themis/Univ. of Pittsburgh CVR/Merck Sharp & Dohme	Replicating Viral Vector
Beijing Wantai Biological Pharmacy/Xiamen University	Replicating Viral Vector
Imperial College London	RNA
People's Liberation Army (PLA) Academy of Military Sciences/Walvax Biotech.	RNA
Medicago Inc.	VLP

BioNTech/Fosun Pharma/Pfizer	RNA
Novavax	Protein Subunit
Anhui Zhifei Longcom Biopharmaceutical/Institute of Microbiology, Chinese Academy of Sciences	Protein Subunit
Curevac	RNA
Institute of Medical Biology, Chinese Academy of Medical Sciences	Inactivated
Research Institute for Biological Safety Problems, Rep of Kazakhstan	Inactivated
Inovio Pharmaceuticals/ International Vaccine Institute	DNA
Osaka University/ AnGes/ Takara Bio	DNA
Cadila Healthcare Limited	DNA
Genexine Consortium	DNA
Bharat Biotech	Inactivated
Kentucky Bioprocessing, Inc	Protein Subunit
Sanofi Pasteur/GSK	Protein Subunit
Arcturus/Duke-NUS	RNA
ReiThera/LEUKOCARE/Univercells	Non-Replicating Viral Vector

WHO 10 Sept 2020

Key candidates – with production timelines



BioPharma Dive, 1 Sept 2020



US Government funding for COVID-19 vaccines

COMPANY	VACCINE TYPE	USD (x10 ⁶)	doses (x10 ⁶)	optional doses (x10 ⁶)
AstraZeneca	chimpanzee adenovirus	1,200	300	
Johnson & Johnson	adenovirus type26	1,000	100	200
Moderna	RNA	1,530	100	400
Novavax	nanoparticle-bac	1,600	100	
Merck	VSV	38		
Sanofi + GSK	protein	2,100	100	500
Inovio	DNA	71		
Vaxart	oral Ad5	?		
Pfizer	RNA	1,950	100	500
Emergent/ology/SiO2 Materials Science	contract manufacturing	782		
Total		10,271		

**CEPI
funding for
COVID-19:
\$1.4 billion!**

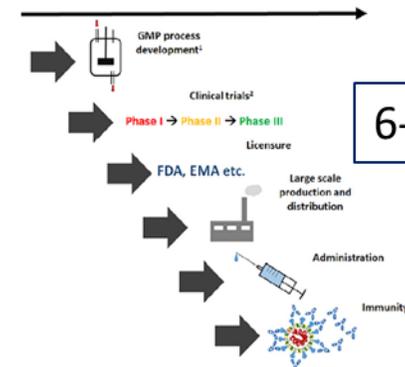
- **TIME: 5-10 years**
- **Cost: USD 500M – 1.5B**
- **FAILURE RATE: 93% (lab-to-licensure)**

**Acknowledge &
Mitigate Risk**



Accelerated Schedule COVID-19 vaccine

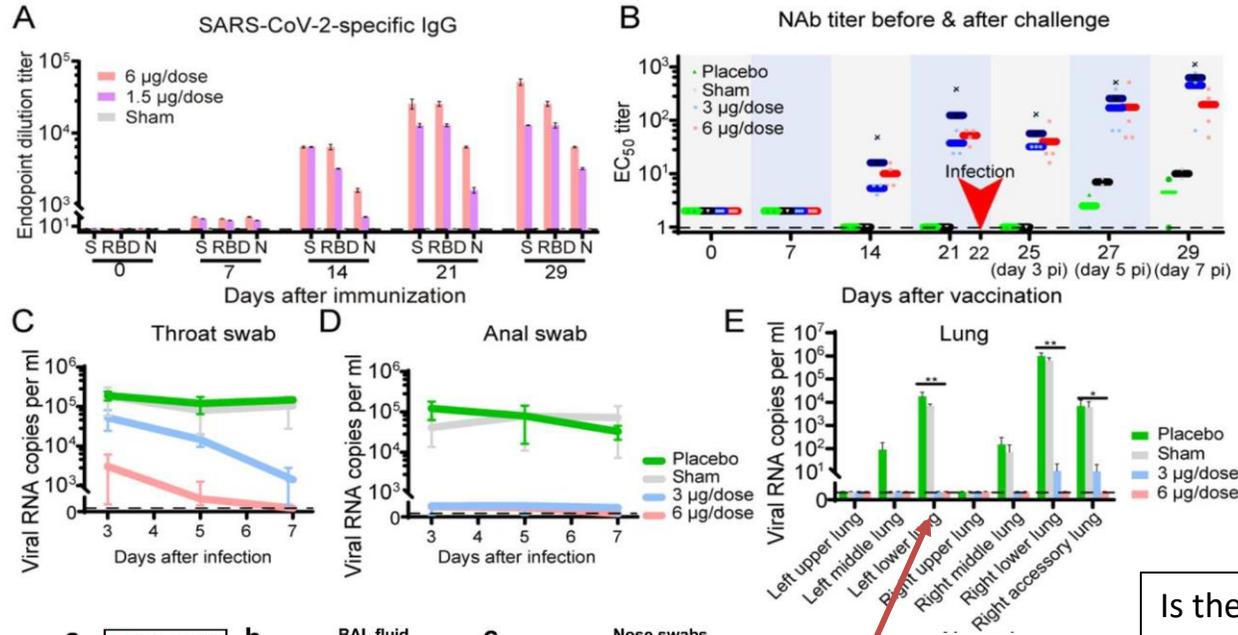
Time frame unclear. 6-18 months. Maybe longer



6-18 mo

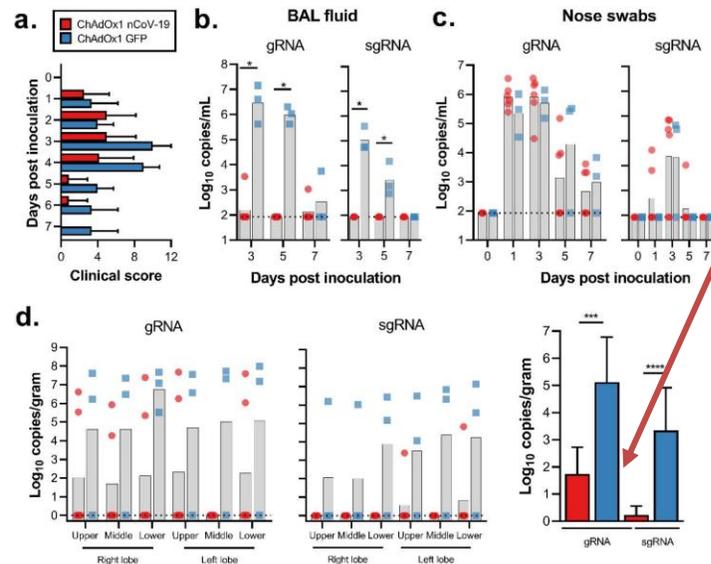
To accelerate, de-risk!

SARS-CoV-2 vaccine protect monkeys against infection



Sinovac WIV/alum prevents infection in NHP

Gao et al, Science 2020

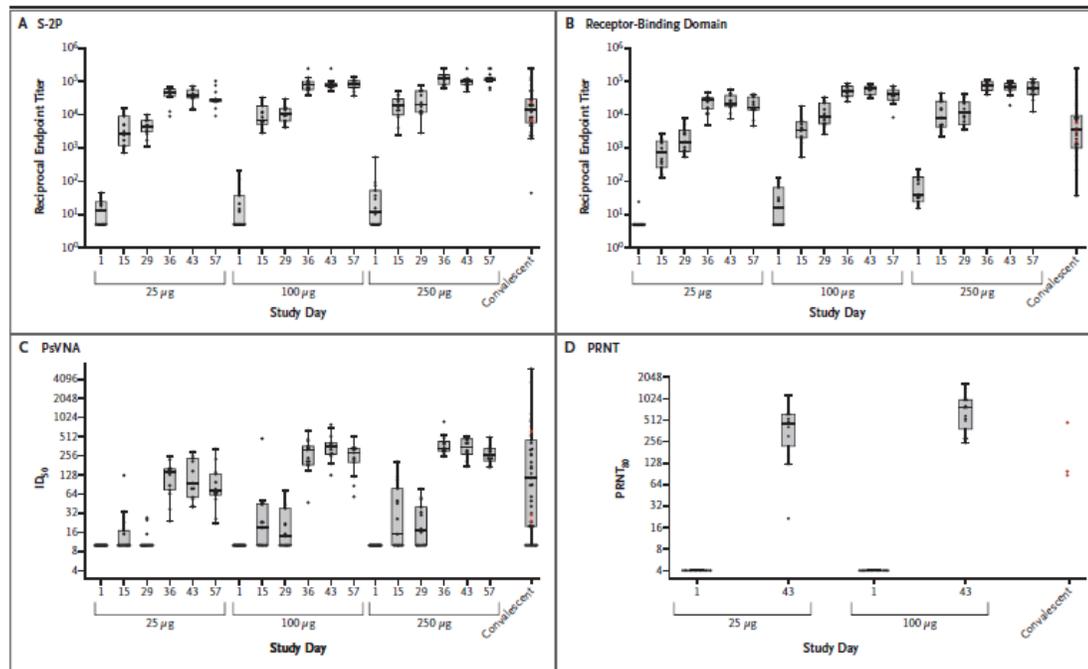


Is there viral replication post challenge in ChAdOx vs WIV vaccinated monkeys and what does this mean?

Oxford/AstraZeneca ChAdOx1 SARS CoV 2 vaccine decreases lung viral load and symptoms post infection

Van Doremalen et al, Nature 2020

Testing of COVID-19 vaccines in humans



Moderna RNA S vaccine induces binding and neutralizing antibody in humans. 100% had systemic symptoms (mild-moderate) at 100 ug dose these were more severe after the 250 ug dose which was dropped from consideration.

Jackson et al, NEJM, 2020

	Day 14				Day 28			
	Low dose group (n=36)	Middle dose group (n=36)	High dose group (n=36)	p value	Low dose group (n=36)	Middle dose group (n=36)	High dose group (n=36)	p value
ELISA antibodies to the receptor binding domain								
GMT	76.5 (44.3-132.0)	91.2 (55.9-148.7)	132.6 (80.7-218.0)	0.29	615.8 (405.4-935.5)	806.0 (528.2-1229.9)	1445.8 (935.5-2234.5)	0.016
≥4-fold increase	16 (44%)	18 (50%)	22 (61%)	0.35	35 (97%)	34 (94%)	36 (100%)	0.77
Neutralising antibodies to live SARS-CoV-2								
GMT	8.2 (5.8-11.5)	9.6 (6.6-14.1)	12.7 (8.5-19.0)	0.24	14.5 (9.6-21.8)	16.2 (10.4-25.7)	34.0 (22.6-50.1)	0.0082
≥4-fold increase	10 (28%)	11 (31%)	15 (42%)	0.42	18 (50%)	18 (50%)	27 (75%)	0.046

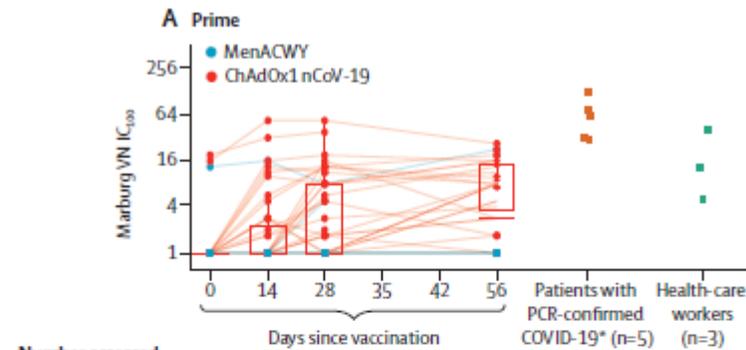
Data are mean (95% CI) or n (%). The p-values are the result of comparison across the three dose groups. If the difference was significant across the three groups, the differences between groups were estimated with 95% CIs. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. GMT=geometric mean titre.

Table 3: Specific antibody responses to the receptor binding domain, and neutralising antibodies to live SARS-CoV-2

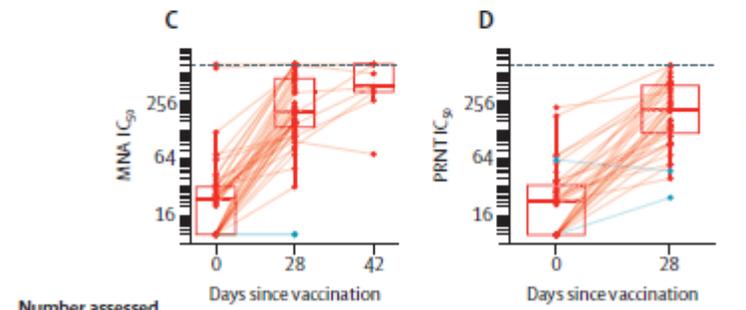
Cansino Ad5 vectored RBD has only 75% of recipients with a 4x rise in titer at the highest dose; 50% at the medium dose, with 42% of persons having fever and 14% with grade III fever at the highest dose.

Zhu et al, Lancet 2020

Testing of COVID-19 vaccines in humans [2]

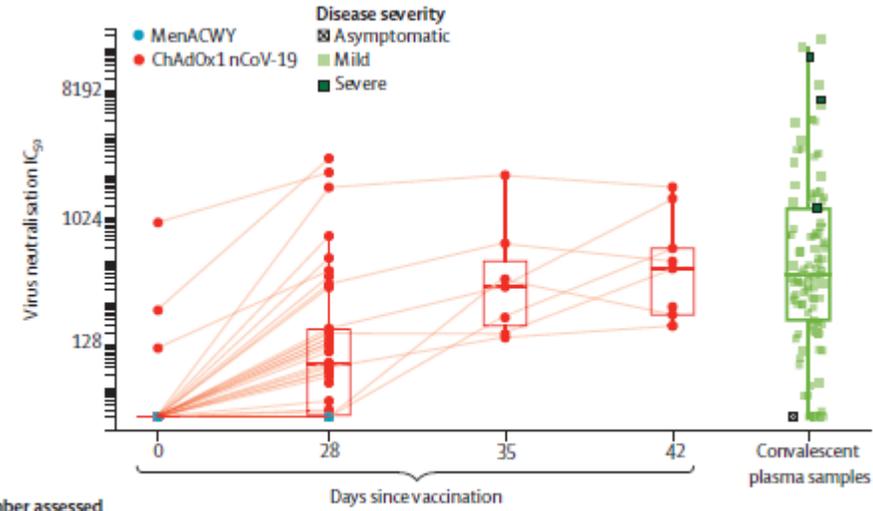


Number assessed	Days since vaccination					Patients with PCR-confirmed COVID-19* (n=5)	Health-care workers (n=3)
	0	14	28	35	42		
ChAdOx1 nCoV-19	44	44	44	0	0	37	-
MenACWY	44	44	43	0	0	25	-



Number assessed	Days since vaccination		
	0	28	42
ChAdOx1 nCoV-19	45	45	9
MenACWY	2	2	0

NAb by plaque reduction



Number assessed	Days since vaccination			
	0	28	35	42
ChAdOx1 nCoV-19	39	38	10	9
MenACWY	30	30	0	0

Pseudovirus NAb

Oxford University - AstraZeneca Chimpanzee adenovirus S vaccine induces binding and neutralizing antibody in 100% of volunteers after 1 dose. 16-18% of volunteers had fever of 38°C or less, 2% had fever of 39°C. Systemic adverse reactions were common but transient and mild-moderate in intensity



Publication by press release...

Sinovac's Vaccine Trial Data Suggest Potential in Virus Defense

Bloomberg News
June 14, 2020, 10:49 AM GMT+9

China-based Sinovac Biotech has reported positive preliminary data from the Phase I/II clinical trials of its Covid-19 vaccine candidate, CoronaVac.

Results from the randomised, double-blind and placebo-controlled trials showed favourable immunogenicity and safety profiles. Of the total 743 healthy participants aged 18 to 59 years, 143 are in Phase I and the remaining 600 in Phase II.

Investigators did not report any severe adverse event in Phase I or Phase II trials. In the Phase II trial, the vaccine triggered neutralising antibodies 14 days following the vaccination with a 0,14 day schedule.

The neutralising antibody seroconversion rate was observed to be more than 90%, which is said to indicate that the vaccine can stimulate positive immune response.

Clinical Trials Arena, June 15 2020

Pfizer Reports Encouraging, Very Early Vaccine Test Results NYT, 1 July 2020

By The Associated Press

July 1, 2020



HEALTH AND SCIENCE

Covid-19 vaccine from Pfizer and BioNTech shows positive results

PUBLISHED WED, JUL 1 2020-8:59 AM EDT | UPDATED WED, JUL 1 2020-9:37 AM EDT

STAT | Matthew Herper



CNBC 1 July 2020

- 10 ug, 30 ug, 100 ug
- N = 45 (12/group; 9 placebo)
- 2 doses, 1 mo apart
- 10 ug dose, 1.8x Nab vs convalescent
- 30 ug dose, 2.8x Nab vs convalescent
- 30 ug dose, 75% of recipients of 2d dose had fever
- b/o 50% reacto no second dose given in 100 ug group
- 20 ug dose being explored
- Single dose 100 ug lower Nab than 2 dose regimens

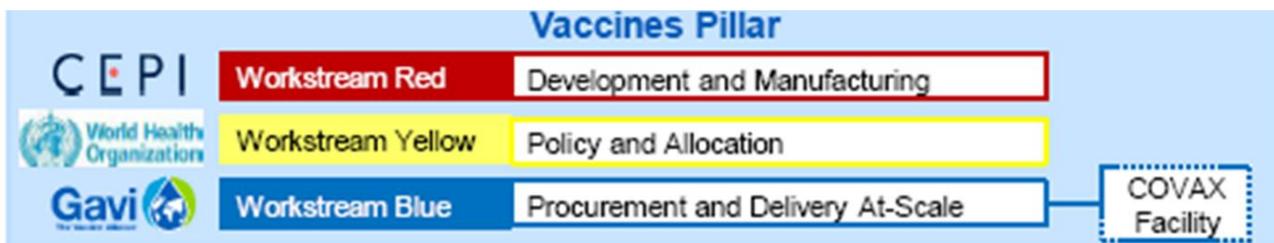
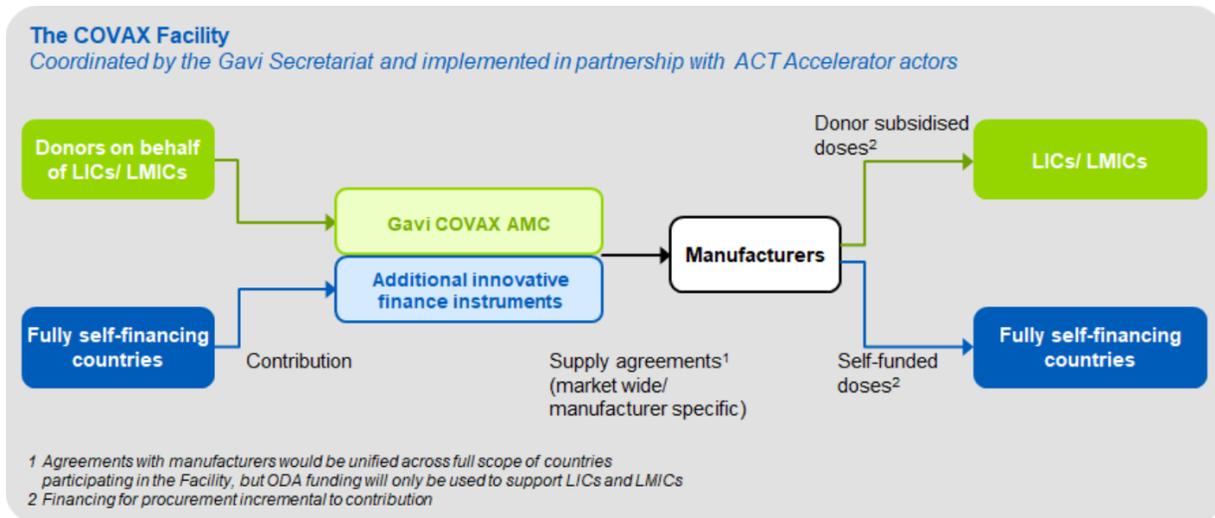


Prove it, make it, use it: COVID-19 Vaccine Manufacturing

- **CEPI** has identified 10 billion doses of vaccine manufacturing capacity
- **COVAX** hopes to have 2 billion doses of a safe and effective vaccine by end 2021
- **Operation Warp Speed (US)** is manufacturing hundreds of millions of doses “at risk”, making vaccine before it is proven to be safe and effective
- **Licensing/Contracting:** Vaccine manufacturers are licensing vaccines to other manufacturers: Serum Institute (ChAdOx), Butantan (Sinovac), SK bioscience (ChAdOx), Lonza (Moderna)



Using vaccines with access and equity: COVAX discussions



More than 150 countries have joined COVAX

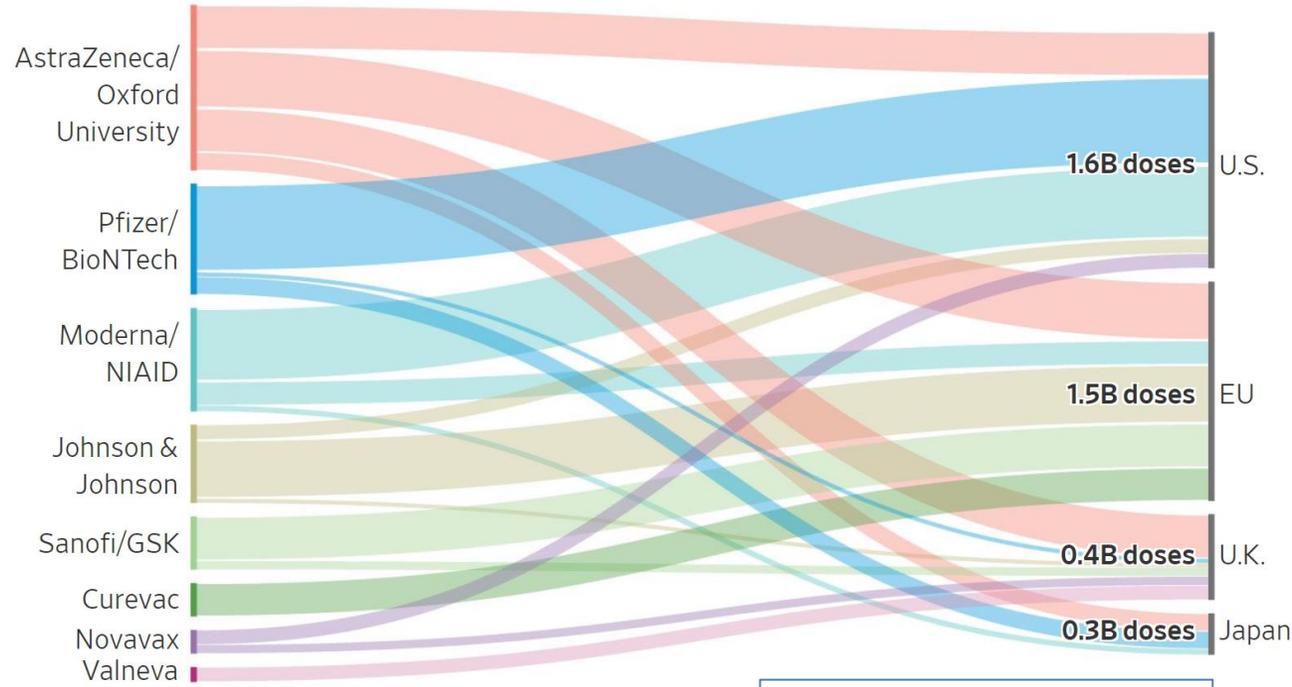
- 75 letters of interest
- 90 LMIC could be supported by the COVAX AMC
- 2 billion doses of WHO PQ'd vaccines by end of 2021
- Roughly 20% of need

OPERATING PRINCIPLES OF COVAX AIM TO ACCELERATE EQUITABLE ACCESS

- **Global access:** open to all countries. Manufacturers commit to amount and minimal returns during the short-term, tiered pricing for longer term sustainability
- **Impact-oriented and transparent:** coordinated strategy for vaccination is needed to reduce the spread of the virus and its impact on lives, health systems and economies
- **Solidarity and collective ownership:** benefit to all participants through clear political and financial commitments

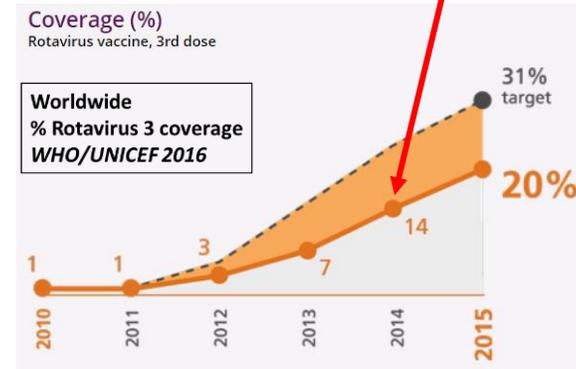
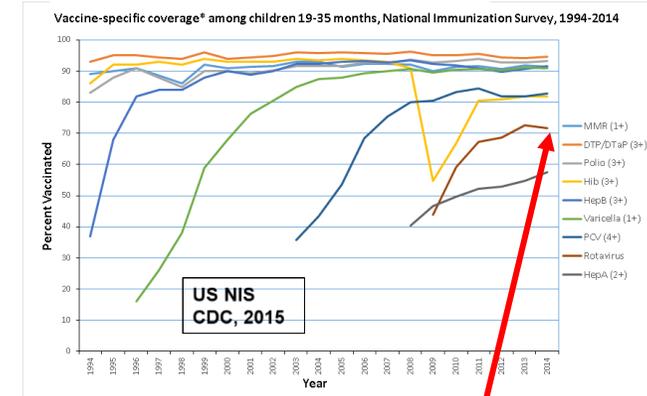
Equity and access – a work in progress

Rich countries have preordered the production of drug makers.



Wall Street Journal, 2 Sept 2020

The rotavirus vaccine story



13 years after rotavirus vaccine was approved by the US FDA and 11 years after WHO recommendation, less than 40% of children receive 3 doses

Vaccines don't save lives, vaccination does

- **Vaccinate 8 billion people?**
 - Prioritization
 - Logistics
 - Delivery
 - Unknowns
 - 1 vs 2 doses
 - Booster needed?
- **Vaccine nationalism**
- **Vaccine hesitancy**
- **Vaccine safety:** Vaccine adverse events reporting system (VAERS)
- **Minding the gap** (in coverage): avoid a situation like rotavirus, US FDA approved RV in 2007 and US coverage since 2009 >70% -- WHO approved vaccine in 2009 and coverage <40% worldwide (2019)



Thoughts on the Future?



IT'S TOUGH TO MAKE
PREDICTIONS,
ESPECIALLY ABOUT
THE FUTURE
Yogi Berra or Niels Bohr



1. Can we prove a vaccine works and is safe?

Answer: Yes

Can we prove that a vaccine works and is safe in 12-18 months?

Answer: Yes, if everything works as planned

2. Can we make a vaccine in sufficient quantity with high quality and at an affordable cost?

Answer: Maybe, CEPI has identified global manufacturing ~10B doses

3. Can we use a vaccine with respect for Access and Equity?

Answer: Hopefully, CEPI has Global Access Agreements and Gavi, CEPI and WHO have initiated COVAX to ensure access and equity in allocation of vaccine resources



**International
Vaccine
Institute**

20 Years Advancing Global Health

Thank You!



IVI website

www.ivi.int



Like us

<https://www.facebook.com/InternationalVaccineInstitute>



Follow us

<https://twitter.com/IVIHeadquarters>

THANK YOU!

Q&A



International
Vaccine
Institute



INTERNATIONAL
VACCINE ACCESS
CENTER



JOHNS HOPKINS
BLOOMBERG SCHOOL
of PUBLIC HEALTH