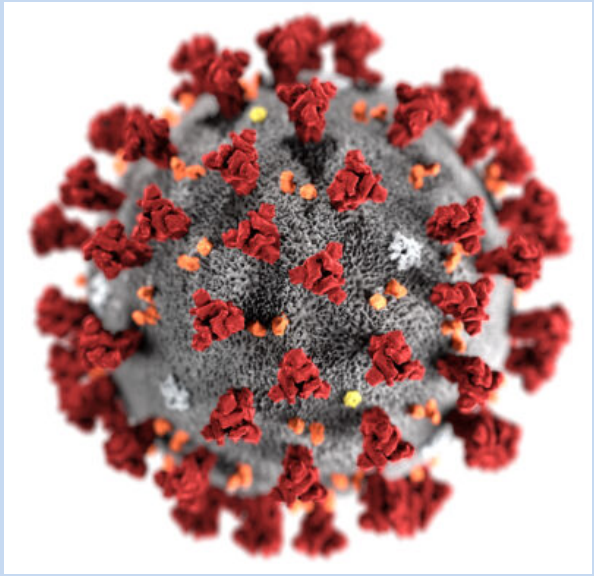
Non-technical update on vaccines against Covid-19



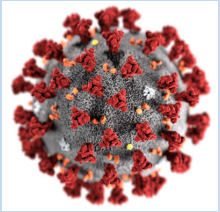
EATG webinar:
16 December 2020

Simon Collins, i-Base.info
Richard Jefferys, TAG

Non technical review

- Effective vaccines essential goal.
- Three main types of vaccines.
- Range of current candidates.
- Results for three leading vaccines.
- Access: plans for fair global distribution.
- Future timeline.

Vaccine basics



Vaccines trick your body to produce strong immune responses to a virus or bacteria. The body stores these so they can be rapidly produced if needed in the future.

Early vaccines often used a weaker dose of the actual virus.

Modern approaches are much safer - for example, only using inactive sections of a virus or getting the body to produce similar viral proteins.

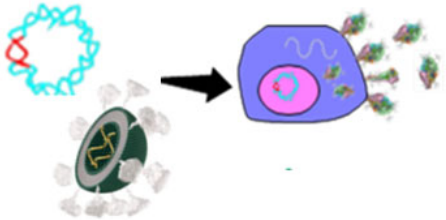
Global COVID-19 Vaccine Landscape

28 Vaccine Candidates in Clinical Evaluation

Nucleic acid

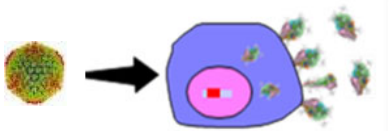
DNA

mRNA

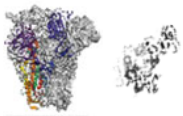


Whole-inactivated virus

Recombinant Adenovirus Vectors

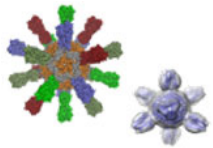


Recombinant proteins or subdomains



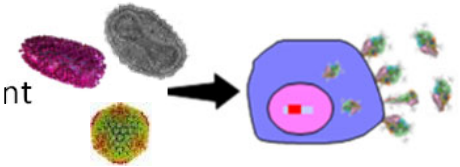
139 Vaccine Candidates in Pre-clinical Evaluation

Nanoparticle display of structurally defined proteins

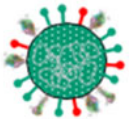


live attenuated virus

Recombinant Vectors



Recombinant or chimeric viruses



Virus-like particles

Peptides

Source: WHO 7 July 2020

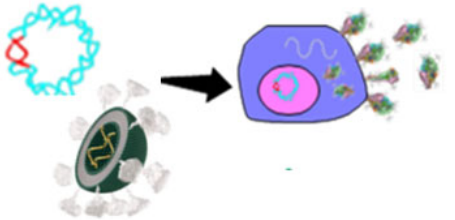
Global COVID-19 Vaccine Landscape

28 Vaccine Candidates in Clinical Evaluation

Nucleic acid

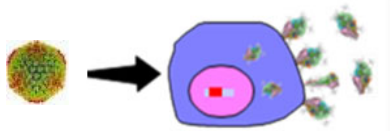
DNA

mRNA

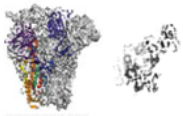


Whole-inactivated virus

Recombinant Adenovirus Vectors



Recombinant proteins or subdomains



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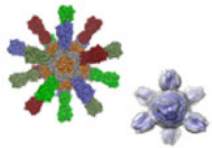
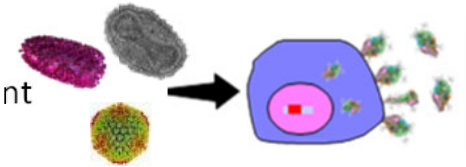
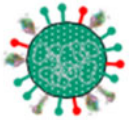


live attenuated virus

Recombinant Vectors



Recombinant or chimeric viruses

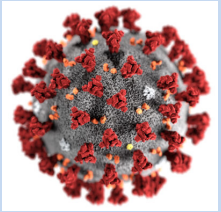


Virus-like particles

Peptides

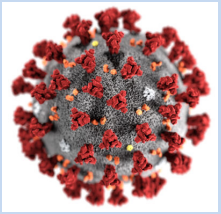
Source: WHO 7 July 2020

mRNA approach



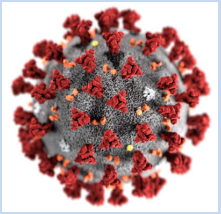
- In research for years but none had been approved.
- Both Pfizer/BioNTech and Moderna/NIH use mRNA.
- mRNA contains instructions for muscle cells to produce spike proteins on the surface of SARS-CoV-2.
- Delivered directly to cells.
- Produces an immune response against these proteins.
- The mRNA is then broken down (transient - like SnapChat).
- Produced in a lab and can easily be scaled up.

viral vectors



- Viral vectors use an inactivated harmless virus to deliver spike proteins (as a Trojan horse) so that when immune cells respond to the transporting virus they also respond to SARS-CoV-2.
- Oxford/AZ, CanSino and Janssen use different adenovirus (Chimp Ad, Ad5, Ad26 etc - common cold).
- Can produce both cellular responses (T cells) and antibody responses (B cells).
- Caution: prior exposure to carrier virus can reduce immune response - so a second booster dose might use different vaccine?
- Non-replicating - only produce antigen.
- Replicating - also produces new carrier virus.

protein based



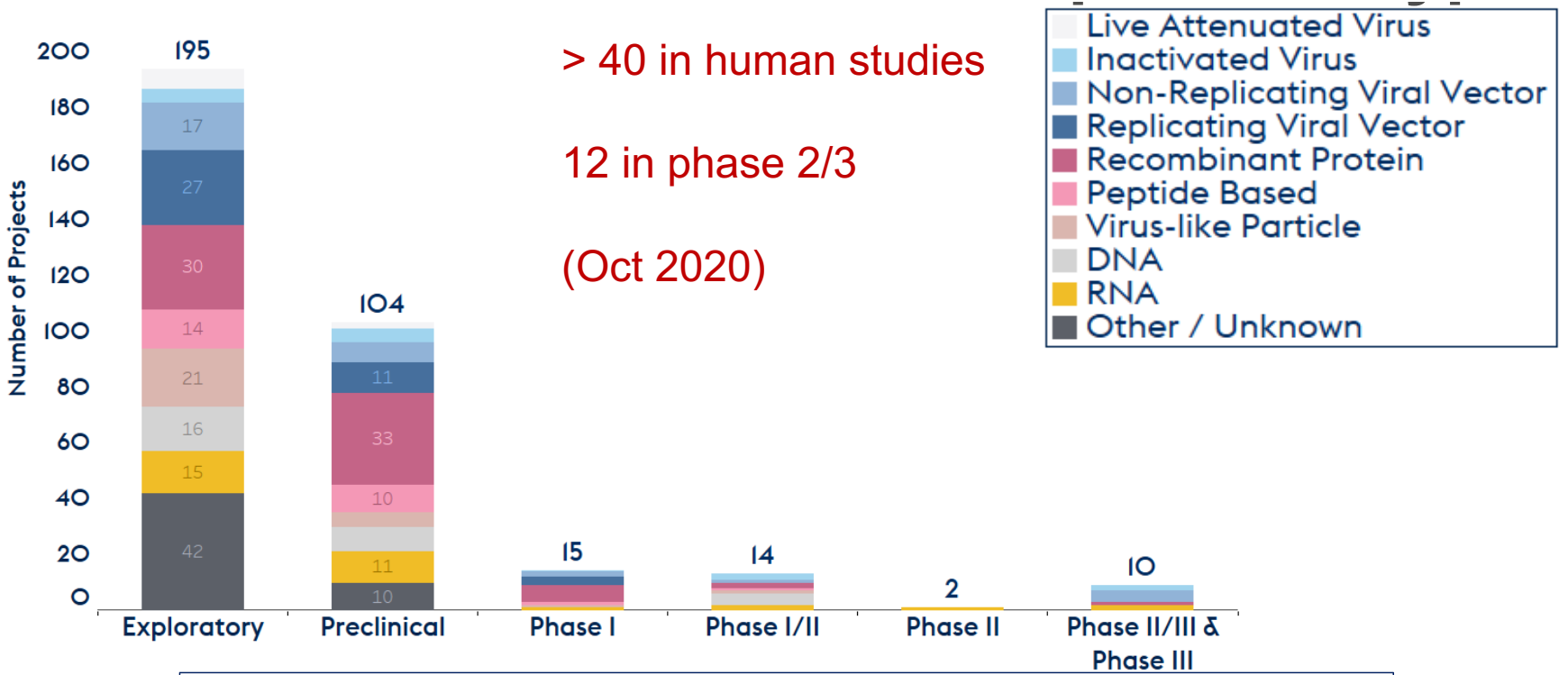
- Protein- based vaccines also get the body to respond to recombinant versions of a viral protein - for example the ‘spike’ for SARS-CoV-2.
- Novavax uses protein-based approach (also Sanofi/GSK).
- They also rely on a second component - an adjuvant - to prime the immune system to respond to the protein.
- Slower to develop but they can generate strong immune responses and have good safety record.

COVID candidates

- Many groups started early in January 2020 - some switched ongoing work on Ebola, SARS or MERS to SARS-CoV-2.
- Pipeline includes hundreds of potential candidates and >40 now in human studies.
- High short-term efficacy - ***against COVID-19 - no transmission endpoints***.
- Universal global access now essential.
- Economic outcomes unclear.

Slide: COVAX Oct 2020

>330 candidate compounds



> 40 in human studies

12 in phase 2/3

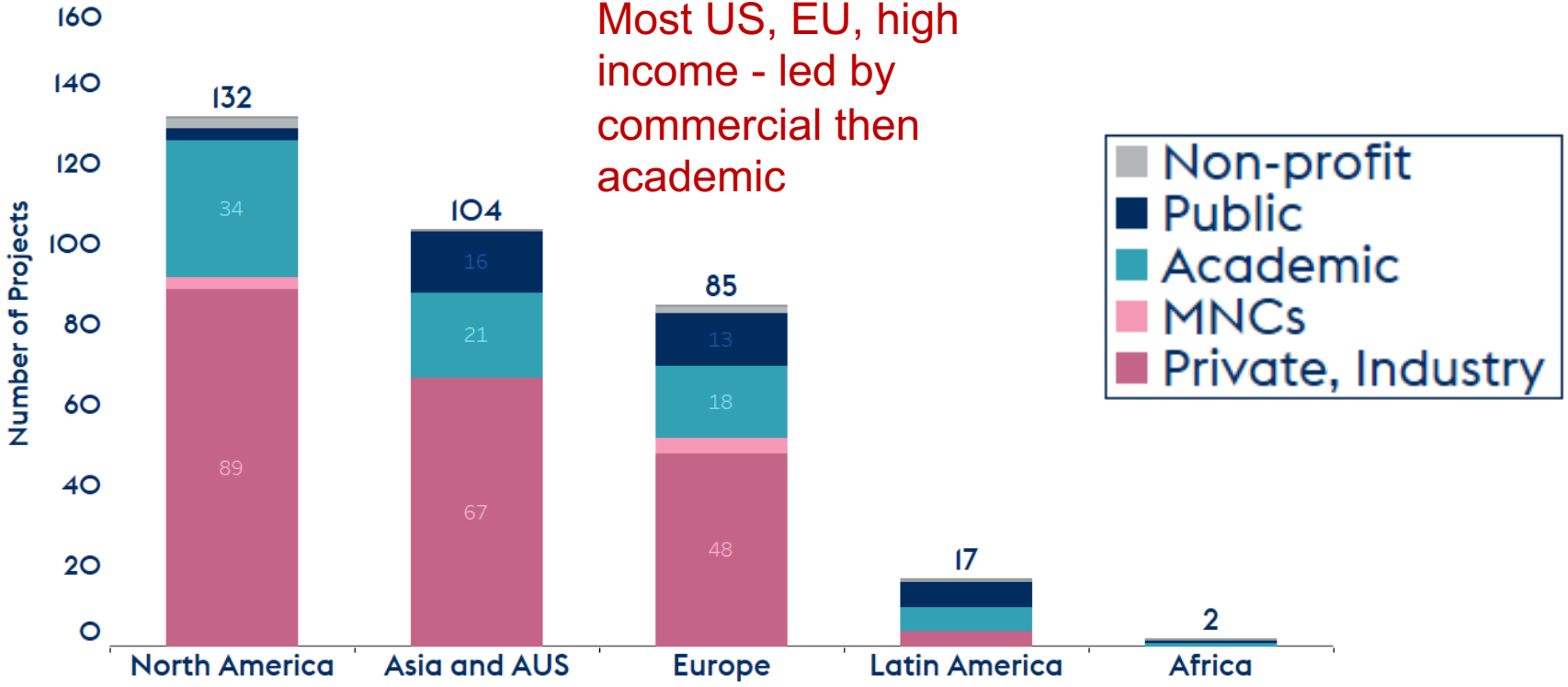
(Oct 2020)

- **Exploratory:** project has not started with in-vivo testing
- **Preclinical:** project started to test in-vivo / manufacture CTM but not yet started with testing on human
- Start of **clinical phases** is defined as first subject dosed

Slide: COVAX Oct 2020

By region and funding

Most US, EU, high income - led by commercial then academic



Summary of human studies

Approach	ph 1, 2	ph 2, 3	
Viral vectors	11	4	Gamaleya, Oxford/AZ, CanSino, Janssen
RNA	4	2	Moderna, Pfizer **
DNA	4	0	
Protein-based	12	1	Novavax
Inactivated	4	3	CNBG (2), Sinovac

*** Pfizer now approved. Plus others globally - ie Sputnik in Russia*

Slide: AVAC/Barney Graham: Nov 2020

By county, phase & platform

COVAX-funded

	Phase I	Phase I/II	Phase II	Phase II/III and Phase III
Viral vectors	Shenzhen GIMI - aAPC Merck TMV-083 Wantai / U.HK LAIV DelNS1[1] ReiThera Srl - GRAd-COV2 Vaxart VXA-CoV2-1 IDT MVA	Shenzhen GIMI - LV		Gamaleya rAd5, rAd26 [3] AstraZeneca AZD1222[5] Cansino Ad5 [2] Janssen Ad26.COV2-S[6]
RNA	Walvax Biotech mRNA	Imperial saRNA Arcturus ARCT-021	CureVac CVnCoV	Moderna mRNA-1273 Pfizer BNT162[5]
DNA		Genexine GX-19 Inovio INO-4800 Osaka / AnGes - AG0301 Cadila ZyCoV-D		
Protein-based	VLP Medicago Sichuan RBD Vaxine Covax-19 Medigen MVC-CO Covaxx UB-612 U.Q SClamp Clover SCB-2019	FBRI SRC EpiVacCorona[3] SpyBio / SII VLP-Spycatcher Finlay Soberana 01 Sanofi / GSK Recombinant	Anhui Zhifei Recombinant	Novavax NVX-CoV2373
Inactivated	Shenzhen Kangtai	Bharat BBV 152 IMB CAMS RIBSP QazCovid-in		CNBG, WIBP [4] Sinovac Biotech CNBG, BIBP [4]

[1] U.HK programme distinct from CEPI-funded programme
[2] Cansino has been approved for military use in China
[3] Gamaleya (rAd5, rAd26) and FBRI SRC (EpiVacCorona) has been conditionally registered in Russia
[4] Emergency use approval in China and UAE
[5] Under regulatory rolling review
[6] Under study pause

Results: Pfizer/BioNTech

- mid-Nov: top-line interim phase 3 results using BNT 162b2 vs placebo in ~43,500 adults (>16 years, 44% > 55 years) in 152 sites globally (130 in the US). Data from 36,000 pts.
- Dec10: Full results in NEJM & FDA documents.
- 95% efficacy: 162 vs 8 cases
- Severe COVID: 9 vs 1 case.
- Conditional approval: UK (2 Dec), US (12 Dec).
- No US funding. Requires ultra cold chain (UCC, minus 80° to transport etc). 96% to high income countries.

Results: Moderna/NIH

- mid-Nov: top-line interim phase 3 results using mRNA-1273 vs placebo in ~30,000 adults in 100 US sites.
- 94% efficacy: 90 vs 5 cases (FDA report: now 185 vs 11 cases): but 86% in >65 yo.
- Severe COVID: 30 vs 0 cases.
- FDA hearing: 17 Dec 2020 - documents online.
- Did have US funding. Requires cold chain (minus 20˚ to transport etc). 100% pledged to high-income countries.

Results: Oxford/Astra-Zeneca

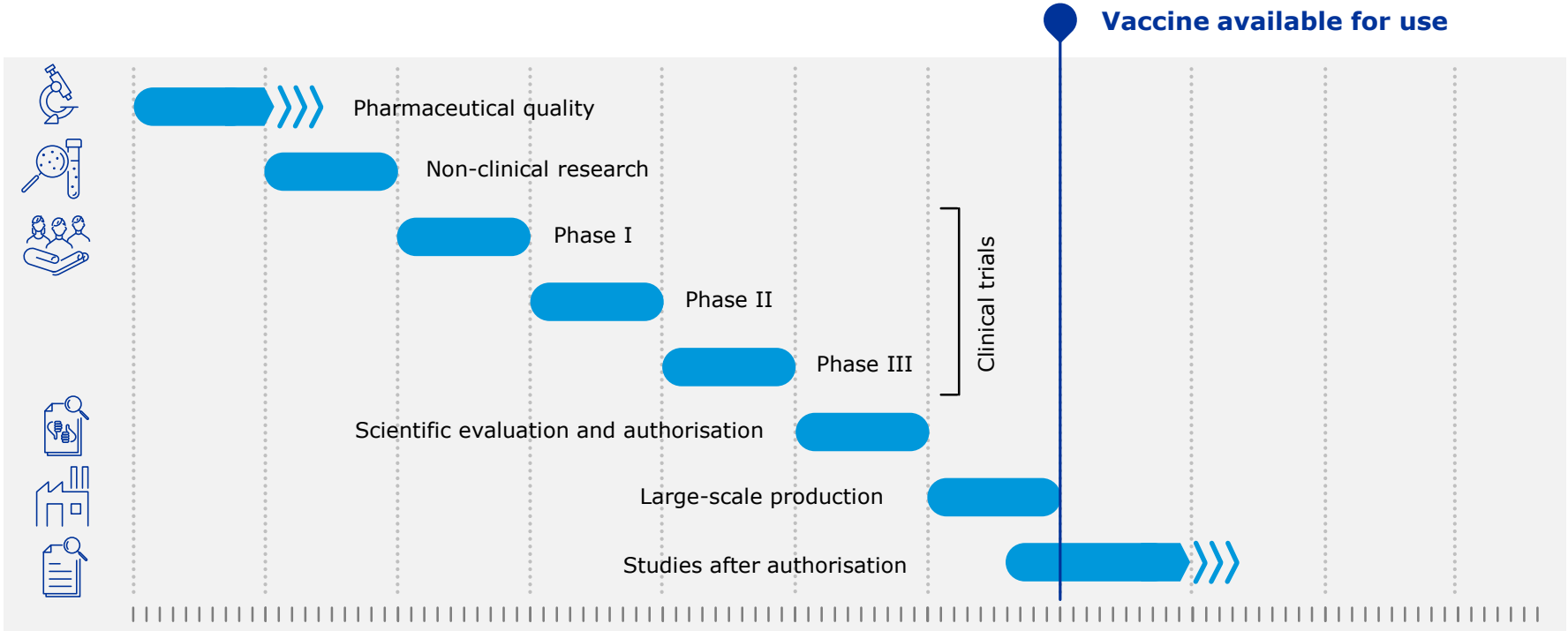
- 18 Nov: top-line interim phase 3 results using ChAdOx1 vs placebo in ~11,500 adults in UK and Brazil (+ some data from South Africa).
- 70% overall efficacy: but 90% in 2741 UK participants who used half-dose/full dose (error) vs 62% in those using two full doses. Includes transmission as an endpoint.
- >50% doses also separated by 12 weeks.
- Some US funding. No cold chain (+ 2-8˚ to transport etc). Lowest price ~ $4 a shot : 64% pledged to low income countries (mainly India).

Data gaps

- Duration of protection? Need for boosters?
- Long-term safety? Head-to-head studies?
- Sub-groups by age? HIV risk from Ad5 (STEP)
- Impact of cormorbidities? HIV? Inflammatory conditions, allergies etc.
- Pregnancy, breastfeeding, children…
- Impact with previous SARS-CoV-2/COVID-19?
- Manufacturing capacity/timeline, stability, shelf-life, price…

STANDARD VACCINES COMPARED WITH COVID-19 VACCINES

Indicative timeline



STANDARD VACCINES COMPARED WITH COVID-19 VACCINES

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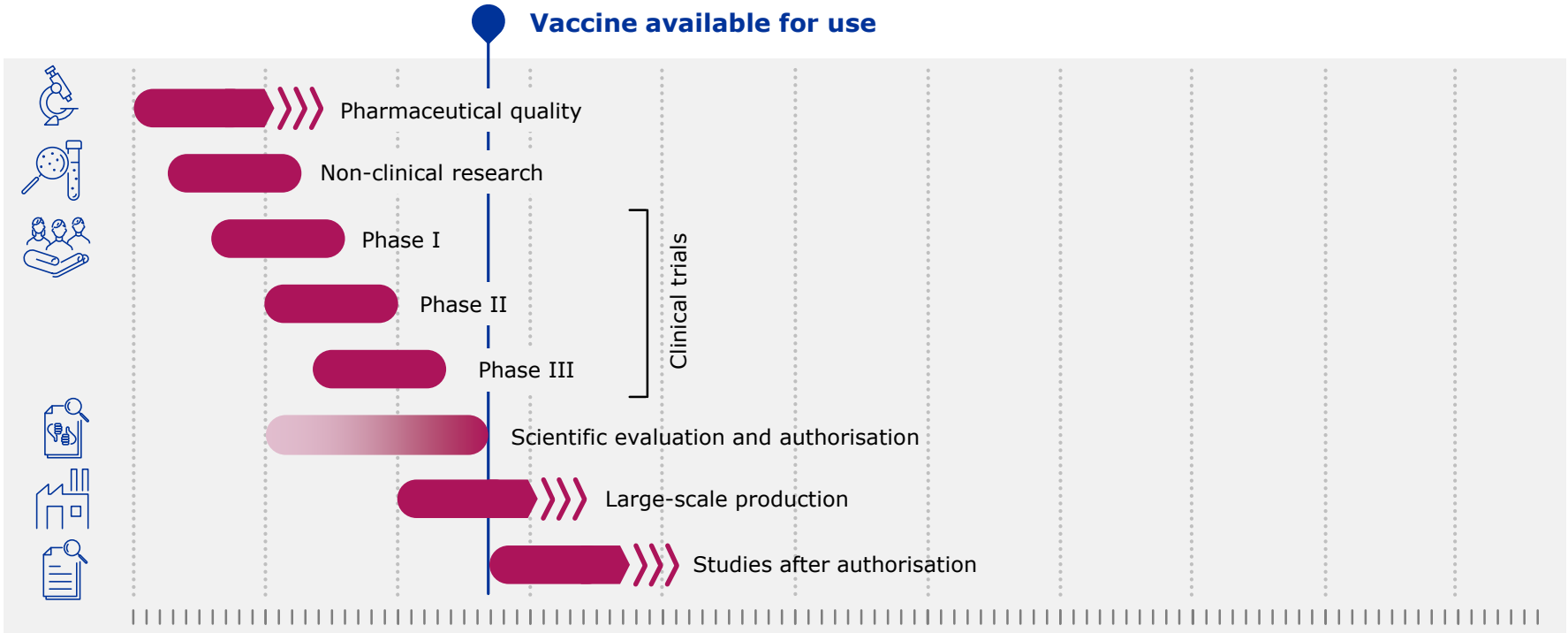


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Covid-19 vaccine trial protocols released

BMJ 2020;371:m4058 (21 October 2020)

Moderna TX. Protocol mRNA-1273-P301, Amendment 3. 2020.
https://www.modernatx.com/sites/default/files/mRNA-1273-P301-Protocol.pdf

Pfizer. PF-07302048 (BNT162 RNA-Based COVID-19 Vaccines) Protocol C4591001. 2020. https://pfe-pfizercom-d8-prod.s3.amazonaws.com/2020-09/C4591001_Clinical_Protocol.pdf

Oxford/AstraZeneca. Clinical Study Protocol - Amend 2 AZD1222- D8110C00001. 2020.
https://s3.amazonaws.com/ctr-med-7111/D8110C00001/52bec400-80f6-4c1b-8791-0483923d0867/c8070a4e-6a9d-46f9-8c32-cece903592b9/D8110C00001_CSP-v2.pdf

Janssen Vaccines & Prevention BV. VAC31518 (JNJ-78436735) clinical protocol VAC31518COV3001 amendment 1. 2020.
https://www.jnj.com/coronavirus/covid-19-phase-3-study-clinical-protocol

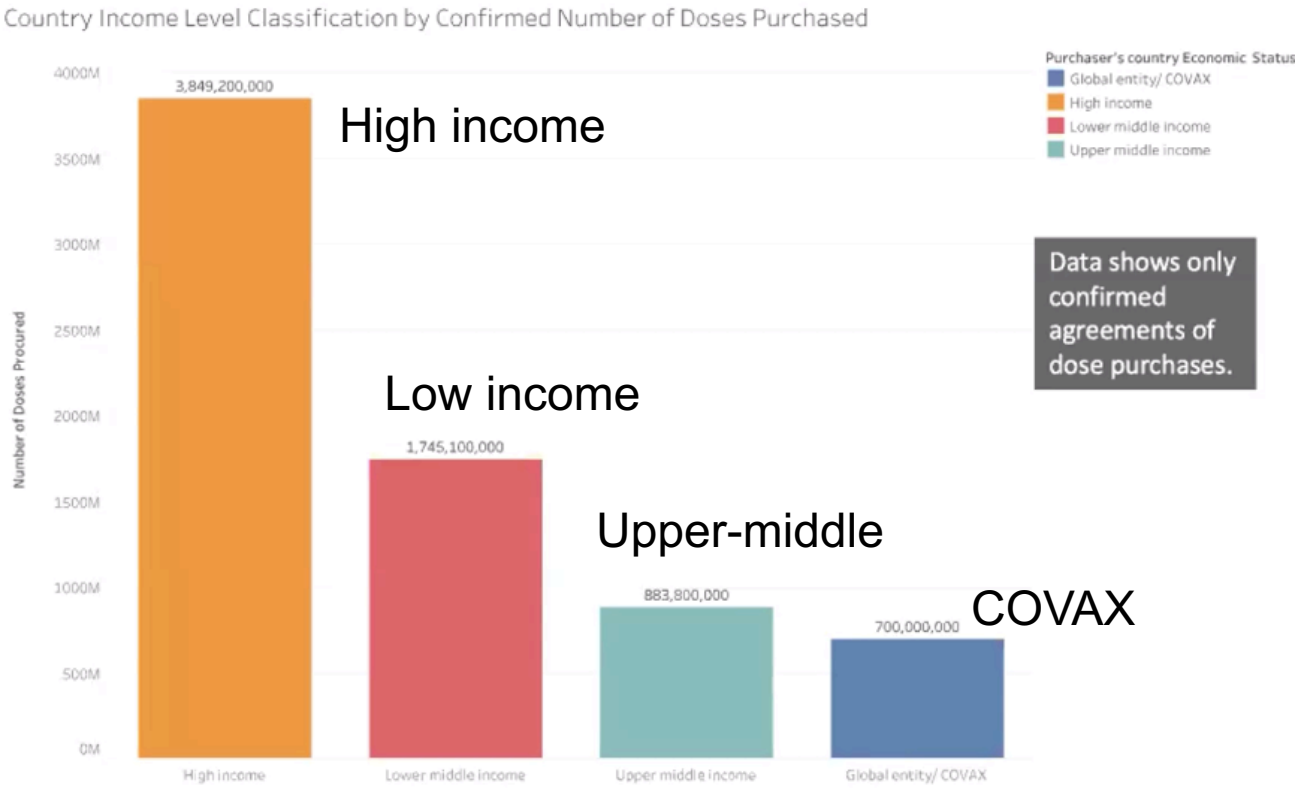
Vaccine access

- Need universal global access.
- “Vaccine nationalism” - high income countries buying first stock plus next options.
- Many countries already have more stock and options (from different vaccines) to treat their population several times.
- Global access to low/middle income countries (LMIC) much lower (3-20% COVAX options are too low for herd immunity).

Vaccine Advance Purchases by Income Category

Over 7.1 billion vaccine doses purchased to date

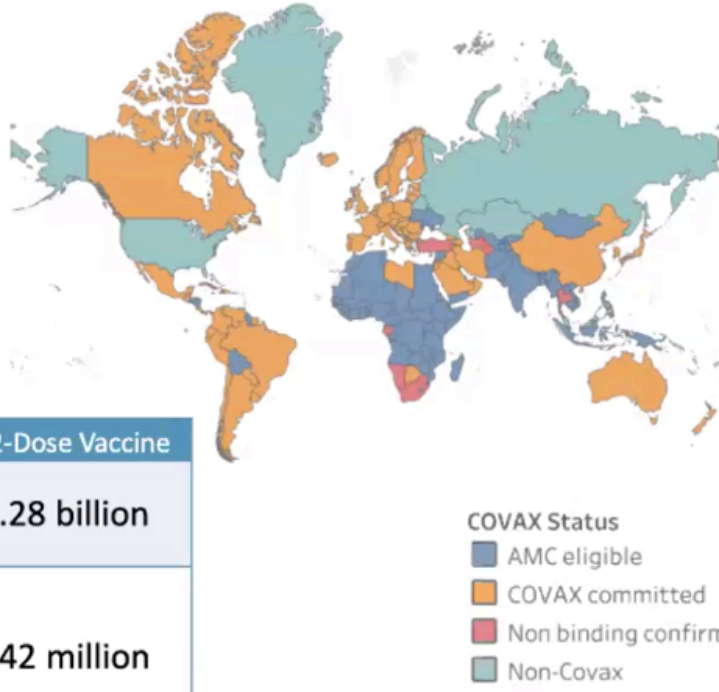
- Over 3.8 billion doses by high-income countries
- Over 1.7 billion doses by lower middle-income countries
- Over 880 million doses by upper middle-income countries
- 700 million by COVAX



LAUNCH & SCALE SPEEDOMETER

The State of COVAX

- COVAX: Vaccines pillar of Access to Covid-19 Tools Accelerator (co-convened by WHO, Gavi, CEPI)
- 186 countries/jurisdictions signed up or AMC eligible
- 2021 goal: procurement of 2 billion doses
- Funding: $2 billion raised in 2020; need additional $5 billion in 2021
- No purchase agreements for Pfizer/BioNTech or Moderna vaccines



	1-Dose Vaccine	2-Dose Vaccine
Needed for 20% of COVAX Country Populations	1.14 billion	2.28 billion
Needed for 3% of COVAX Country Healthcare Workers (COVAX Initial Priority)	171 million	342 million
Vaccine Doses Purchased by COVAX		700 million

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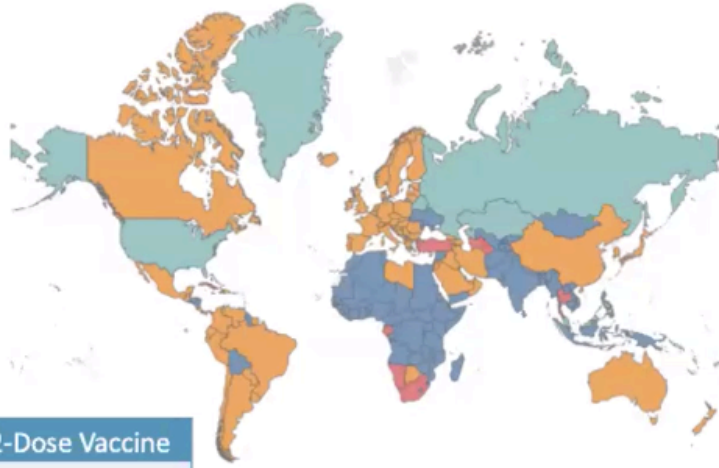

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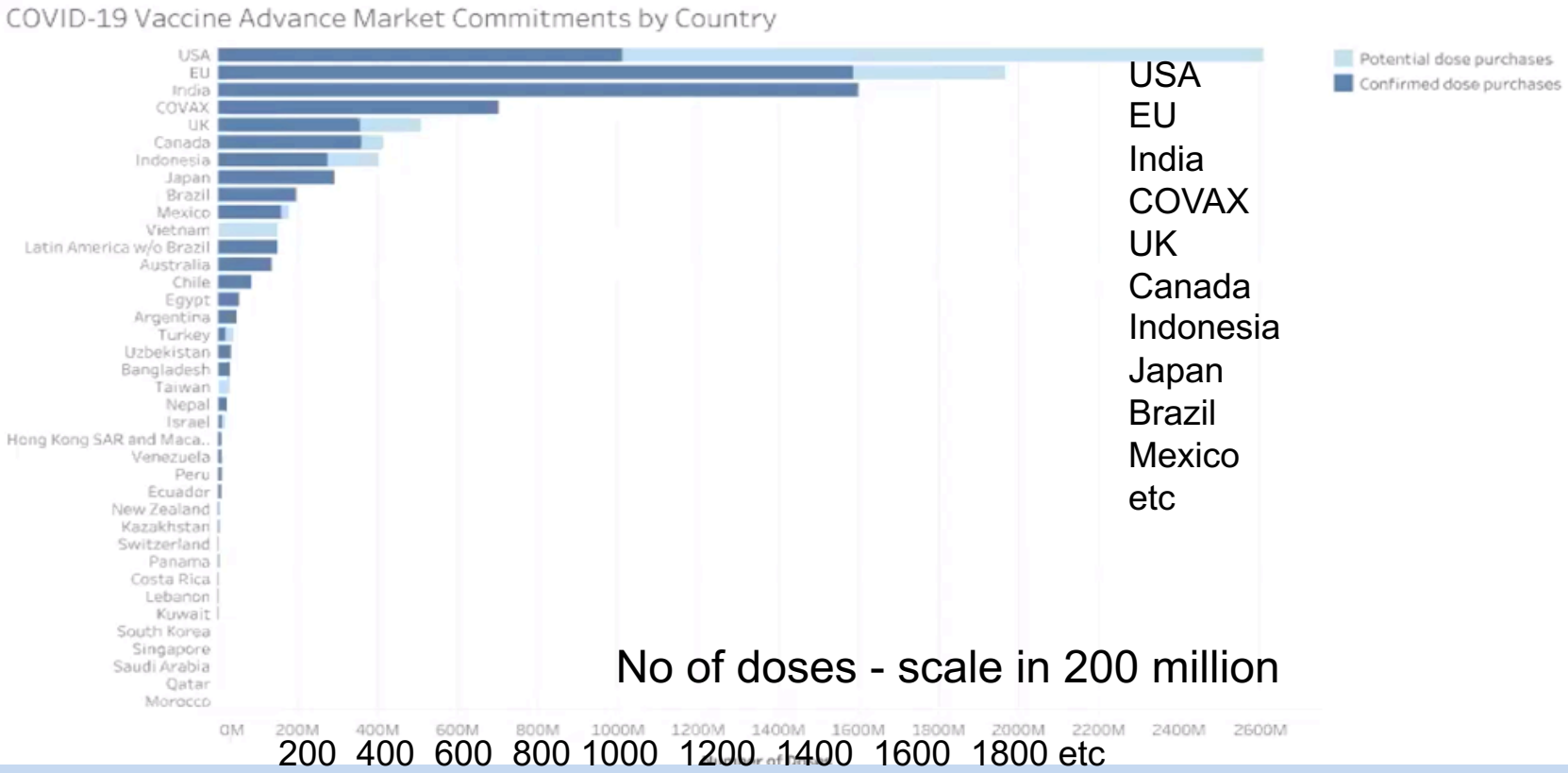
LAUNCH & SCALE SPEEDOMETER

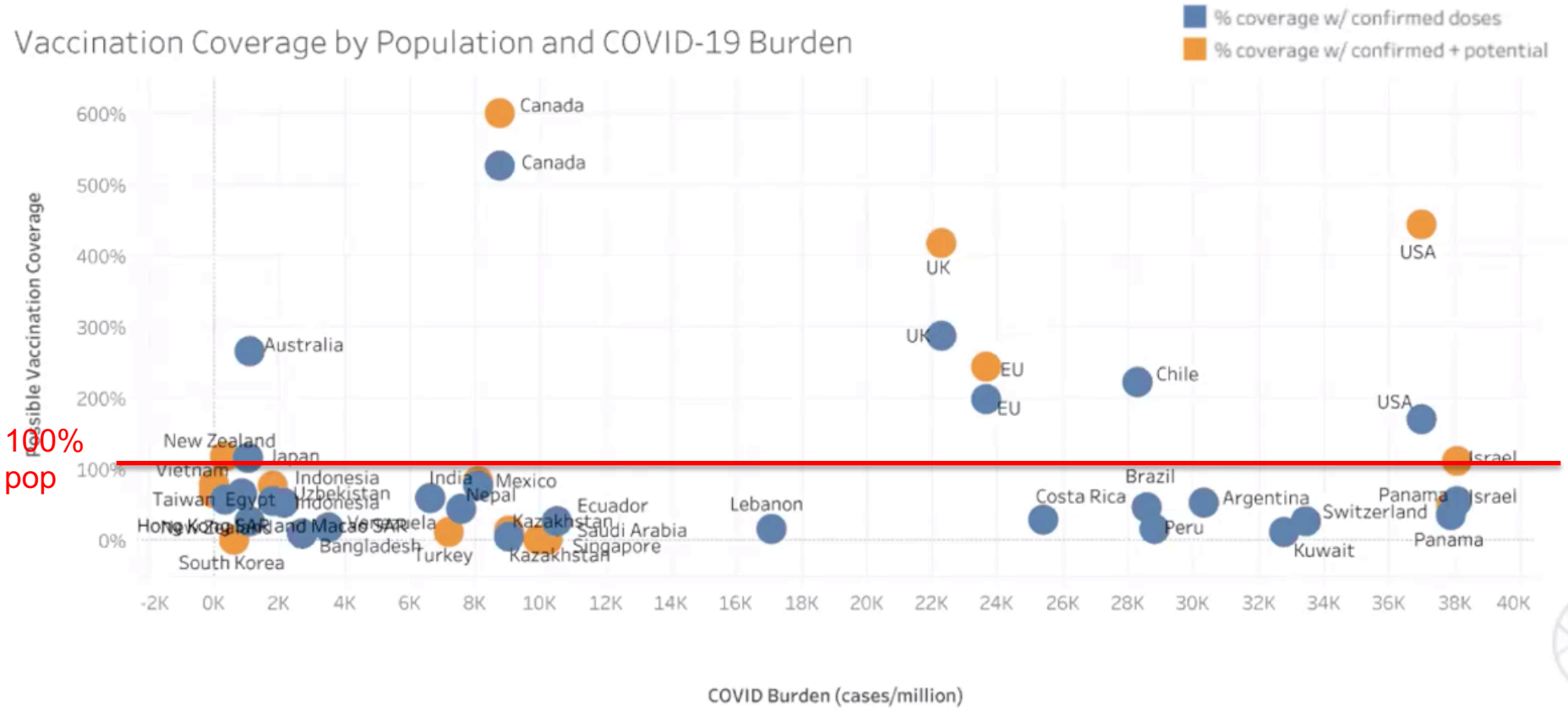
Vaccine Advance Purchases by Country



USA
EU
India
COVAX
UK
Canada
Indonesia
Japan
Brazil
Mexico
etc

No of doses - scale in 200 million

Vaccine Advance Purchases Relative to Population Coverage and Covid Burden



Funding Snapshot as of 16 November 2020

Available funds against the US$ 38 billion ACT Accelerator budget include:

- US$ 5 billion in donor funding commitments (download the document for details)
- US$ 4.8 billion in COVAX Self-Financing Participant down-payments to support facility manufacturing and procurement for all COVAX participants.

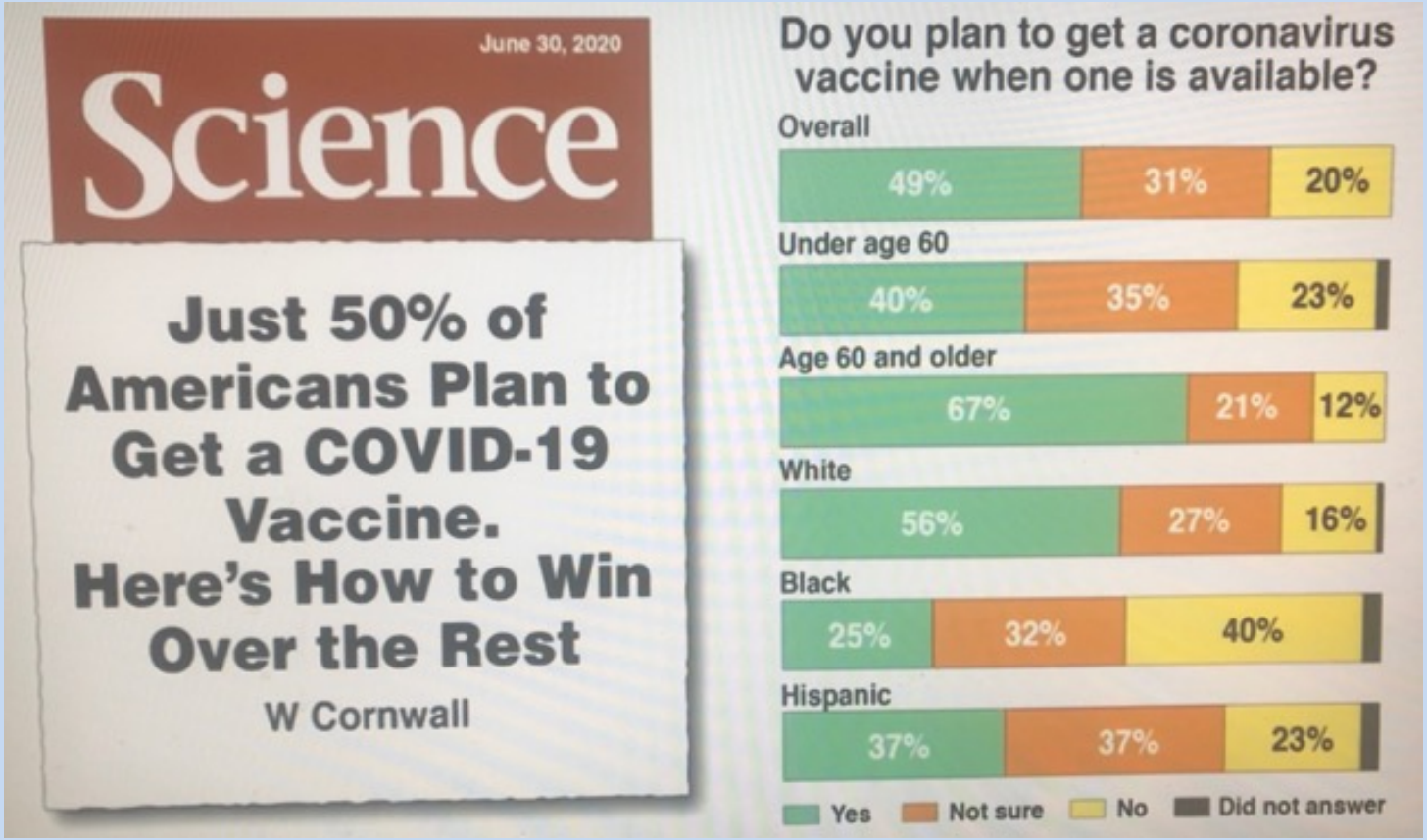
The ACT Accelerator faces a:

- US$ 4.3 billion immediate funding gap
- An additional US $23.9 billion is required for the balance of 2021.

Key access links

- Coalition for Epidemic Preparedness Innovations (CEPI) - 2017
- WHO - Access to COVID-19 Tools (ACT) Accelerator - initiative to coordinate international response.
- COVAX - Vaccine arm of ACT
- GAVI - (co-sponsor COVAX)
- People's Vaccine Alliance (coalition of organisations: Oxfam, UNAIDS)

“vaccine hesitancy”



Communicating for vaccine acceptance

Context matters for vaccine rollout

1. Vaccine Denialism
2. Vaccine Hesitancy
3. Anti-Vaxxer Movement

It is not a given that more information will counter vaccine hesitancy or increase vaccine acceptance

We assume that the drivers for hesitancy and denialism are:

- a lack of knowledge & that more knowledge can solve the problem and that humans calculate risk rationally.
- we have scientists and doctors who are active anti-vaxxers who consciously spread misinformation.
- sometimes knowing more about the detail of the subject increases the individuals concern.

African Alliance

VACCINE ADVOCACY RESOURCE GROUP

saMRC advancinglife

science & innovation
Department:
Science and Innovation
REPUBLIC OF SOUTH AFRICA

UK access for HIV+

- UK access includes nine priority groups.
- Higher risk - by age, care home residency and front line health workers.
- Severe health conditions is group 4 and other complications (inc. HIV) group 6.
- Supported by BHIVA guidance for people living with HIV (www.bhiva.org)

Community Q's.1 (UK-CAB)

UK-CAB members had many questions when asked about this for upcoming workshop:

Why should I get a vaccine?
How do they know the vaccine is safe? How do I know the vaccine is safe?
What is in the vaccine that they are going to offer me?
Can I get COVID-19 from the vaccine?
What would be the probable symptoms/side effects from the vaccine?
Am I going to get sick with the COVID-19 vaccine like the flu jab?
Can I develop an allergic reaction to the vaccine?
Should I wait to see how my peers react?
Why should I get it if the person administering the vaccines doesn't have it yet?
Who is going to administer my vaccine? My GP or my HIV clinic? Can I choose?
Will the vaccine stop me catching COVID-19 or from getting critically ill? or both?
Could the vaccine interact with my HIV meds? Will my VL blip?
Could the vaccine interact with my estrogen/testorene treatment?

Community Q's.2 (UK-CAB)

Is the vaccine safe if I live with HIV and other comorbidities?

Can I get the vaccine if I have or have had Hepatitis C?

Is it safe fif I use 'chems' like Crystal Meth, GLB or mephedrone?

Is the vaccine going to impact me differently because I'm black/brown?

Are black and brown people more at risk of getting bad symptoms/side effects from the vaccine?

Have vaccine trials included black and brown men and women living with HIV? Or do the findings just relate to the experiences of white gay men?

Who approved these vaccines? Were the interests of my community are represented?

How do I know I'm being treated equally than my white peers in the process? How do I know this isn't another chapter of medical experimentation in Black people?

If the government didn't even try to address my vulnerabilities to the virus, why I'm expected to trust them with a preventative option?

I've experienced racism in the healthcare system and receiving my HIV care, how can you ensure me this won't be another one of those experiences?

Why did we get a COVID-19 vaccine so quickly, but there is still no vaccine for HIV?

If the vaccine is lifesaving, why is not available to everyone in the world?

Conclusion

- Unparalleled crisis and scientific response.
- High-income countries might soon return to low risk of COVID-19 (after terrible cost to life).
- Global access plan at least another year to reach 2 billion in low income countries.
- Huge volume of research and data - on vaccines, treatment, access etc.
- Long-term data still needed.
- Roll of community for education and support.

Thanks

Non-original slides compiled from various webinars (for community use) – thanks to WHO, COVAX, EMEA, PATH, Anthony Fauci, AVAC/Barney Graham, ICAP, African CDC and others.

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www.i-base.info

Additional slides

Clinical studies – efficacy and safety

- **Large number** of **adults** expected (above 30,000)
- Ideally **one quarter** of all participants **above 65 years** of age
- **Some people** with **underlying diseases** at risk of severe COVID-19
- Some studies include **adolescents above 16** years of age
  - Younger children to be studied after analysing data in adults and adolescents
- Some **minorities** represented
- Follow-up data for **at least** the **6 weeks** after last dose of vaccine
  - Most side effects occur within 4-6 weeks of having a dose
- Trials to last **for at least 1 year:** longer-term protection & side effects

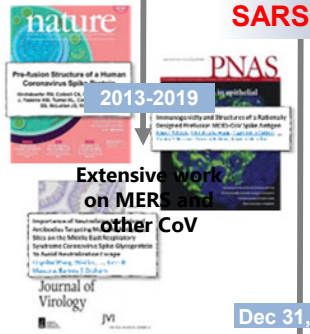
COVID-19	DNA / mRNA			Viral vector			Protein		
	Inovio	**Moderna**	**CureVac**	**Merck / Themis**	**AstraZeneca / Univ. Oxford**	**University of Hong Kong**	**Novavax**	**Clover BioPharma**	**University of Queensland / CSL**
Location	USA	USA	Germany	USA / Austria	UK	China	USA	China	Australia
Platform	DNA	mRNA	mRNA	Viral Vector	Viral Vector	Viral Vector	Protein	Protein	Protein
Antigen / Adjuvant	Full-length S protein	Full-length S protein	Full-length S protein	Full-length S protein	Full-length S protein	Receptor Binding Domain / AS03	Full-length S protein / saponin-based Matrix-M	Full-length S protein/AS03 or CPG1018	Full-length S protein / MF59
Current phase	Phase I/II	Phase III	Phase II	Phase I	Phase III	Preclinical	Phase III	Phase I	Phase I

COVID-19 Vaccine Development

2013-2019

2020

SARS-CoV-2 Outbreak



2013-2019: Extensive work on MERS and other CoV

Dec 31, 2019: 1st report of respiratory virus outbreak in Wuhan, China

Jan 6, 2020: Wuhan outbreak may be CoV

Jan 10, 2020: 2019-nCoV sequences published

Jan 11, 2020: 2019-nCoV constructs ordered

Jan 13, 2020: VRC decides on vaccine sequence with Moderna

Jan 14, 2020: Moderna receives sequence for GMP production

Jan 23, 2020: DMID initiates clinical and regulatory process

Jan 31, 2020: VRC makes nCoV spike protein

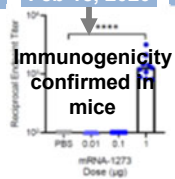
Feb 1, 2020: First nCoV spike ELISA for cross-reactivity

Feb 3, 2020: sol[illegible]e

Feb 4 2020: VRC vaccinates mice

Feb 4, 2020: Moderna vials vaccine

Feb 18, 2020: Immunogenicity confirmed in mice



Feb 19, 2020: Spike structure published in Science

Feb 20, 2020: DMID submits IND

Feb 21, 2020: Moderna ships vaccine to DMID

Mar 2, 2020: FDA safe-to-proceed

Mar 16, 2020: Phase 1 Clinical trial Starts

May 29, 2020: Phase 2 clinical trial starts

Jul 27, 2020: Phase 3 Clinical trial Starts

3 days

38 days

24 days

Clinical: Phase 1 → Phase 2 → Phase 3

Non-clinical: immunogenicity → protection → safety