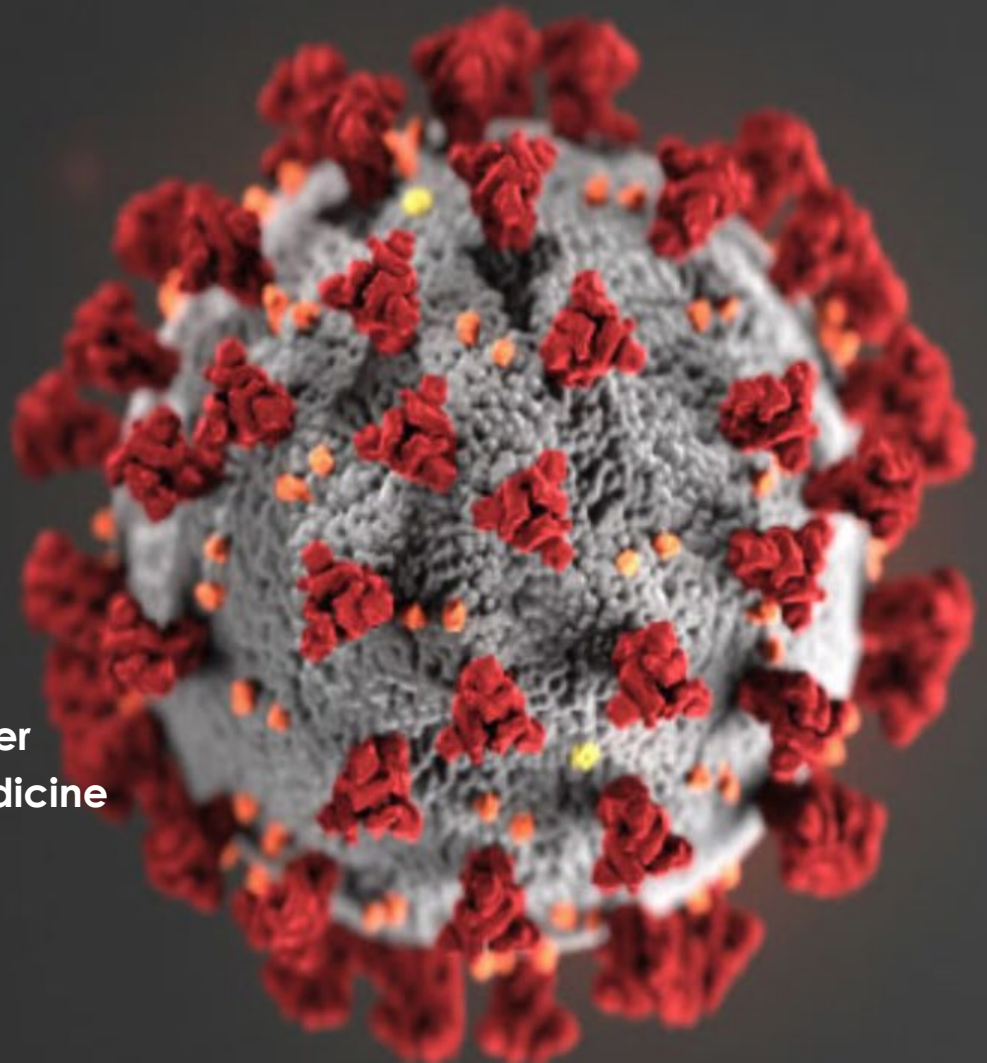
COVID-19 Vaccine Development



Larry Corey, MD
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Conceptual Framework for COVID-19 Vaccine Development

April 2020

We need to develop multiple vaccine platforms.

No single vaccine platform can be manufactured at enough scale to immunize the 4.4 billion adult population on the planet and 3 billion children

- 220 million adults in US alone.

Use known platforms to cover the field scientifically. Manufacturing scalability is a key factor.

Coordinated USG effort to involve global vaccine manufacturing companies.

There must be an unprecedented coordinated approach to test, manufacture the vaccine at scale, and deliver the vaccine into peoples' arms throughout the world.

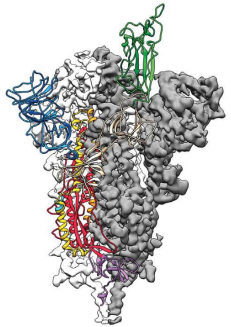
Goal of OWS Program: To Assess Major Vaccine Platforms to COVID-19

Platform Vaccine Technologies

- Protein vaccines

  - **soluble prefusion trimer (Sanofi/GSK)**

  - **transmembrane bound spike nanoparticle (Novavax)**

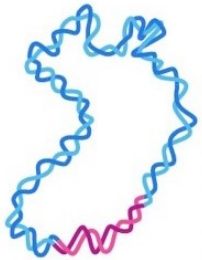


- Viral vector vaccines

  - Ad26 vector

  - ChimpAdOx1

- RNA and DNA technology



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Prevention Network

Published online May 11, 2020

Science

A Strategic Approach to COVID-19 Vaccine R&D

L Corey, JR Mascola, AS Fauci & FS Collins

The full development pathway for an effective vaccine for SARS-CoV2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. . . .We further discuss a collaborative platform for conducting harmonized, randomized controlled vaccine efficacy trials. This mechanism aims to generate essential safety and efficacy data for several candidate vaccines in parallel, so as to accelerate the licensure and distribution of multiple vaccine platforms and vaccines to protect against COVID-19

Organizational Structure of OWS Clinical Trials Program

Harmonized Efficacy Trials

RNA Platform 1	ChAdOx1 Platform 2	Ad26 Platform 3	Nanoparticle Platform 4	Pre-fusion Spike Recombinant Protein Platform 5

Collaborating clinical trial networks (CoVPN)

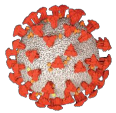
Harmonized endpoint data collection

Common Labs

1. Defining infection from disease
2. Quantitative immune responses to spike and spike epitopes
3. T-cell responses

Corelates of protection analyses within and cross protocols

Common DSMB



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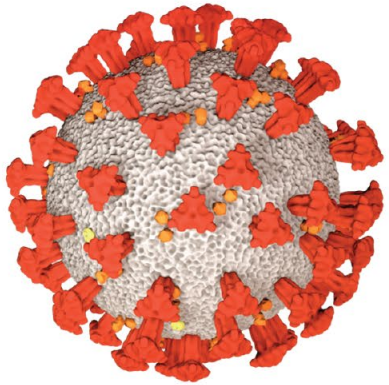
HIV VACCINE TRIALS NETWORK

IDCRC
Infectious Diseases Clinical Research Consortium

HPTN
HIV Prevention Trials Network



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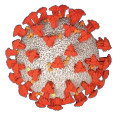
www.preventcovid.org

COVID-19 PREVENTION NETWORK PHASE 3 EFFICACY TRIAL TIMELINE

July	August	September	October	November
Moderna July 27 Pfizer July 28	AstraZeneca August 29 Paused Sept 9	Johnson & Johnson September 22	Novavax Early December	Sanofi Late December

Safe to Proceed

- To initiate the Phase 3 trial, the safety and immune response data from the Phase 1 and the Phase 2 trials needed to be completed and reviewed by the FDA and the DSMB.
- The non-human primate model experiments needed to show no enhanced disease.
- The protocol and all its consents and materials needed to be approved by FDA and all the Ethics Committees.
- Community consultations were completed.



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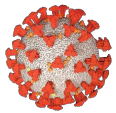
Balancing Harmonized Clinical Trial Design with Regulatory Realities

Main Goal: To evaluate each candidate vaccine with high veracity for safety and potential efficacy in reducing COVID-19 Disease.

- Each trial 30,000 persons; 150 disease endpoints
- Critical to enroll Black, LatinX and Tribal Communities into each trial
- Essential to evaluate vaccines in the epidemiological setting of persons at greatest risk of its complications; including comorbidities, age and race



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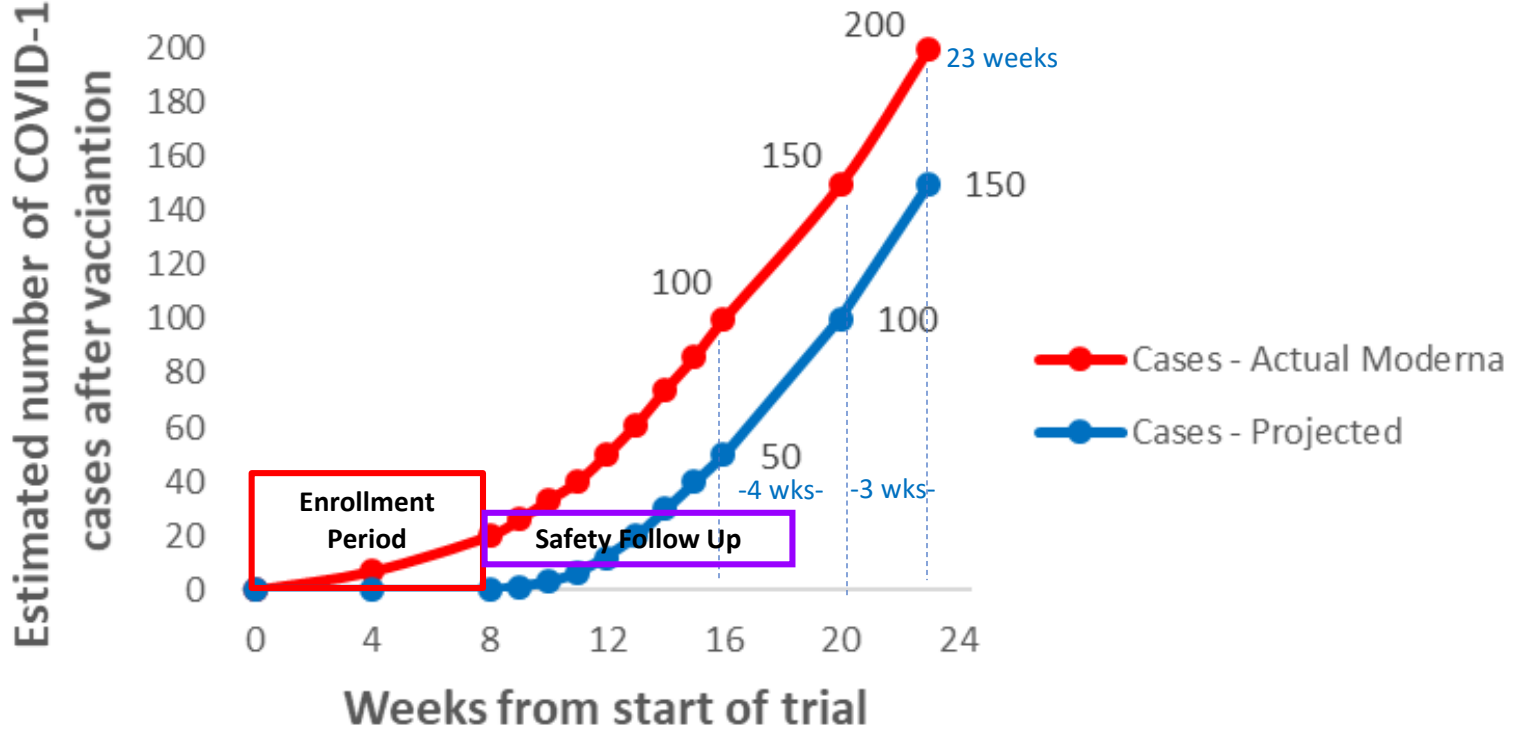
of COVID-19 cases in 30,000-person 2 dose SARS-CoV-2 Vaccine Trial
This is how it is working out



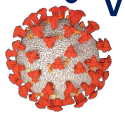
mRNA Vaccines

Pfizer Vaccine

- Prefusion spike transcript
- 2 doses 21 days apart
- VE = 95%
- 162 cases of symptomatic disease in placebo; 8 in vaccine group
- 10 cases of severe disease; 9 in placebo, 1 in vaccine group
- VE 94% in those >65

Moderna Vaccine

- Prefusion spike transcript
- 2 doses 28 days apart
- VE = 94.5% efficacy
- 90 cases of symptomatic disease in placebo; 5 in vaccine group
- 11 cases of severe disease - all 11 in placebo group
- No difference in VE by age and ethnicity (20% endpoints in these groups)



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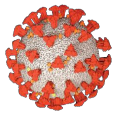
Astonishing

- To have 2 large scale efficacy trials enrolled and completed independently, with such similar results, is remarkable.
- The spike part of the RNA transcript is essentially identical; allowing one to feel quite comfortable about the veracity of the efficacy data.
- The safety data from the trials needs to be made public, so one can evaluate it. Available data suggest the vaccines are well tolerated; more side effects with the second dose and somewhat lower severity of systemic side effects in older persons.
- The similarity of the data means either vaccine can do the job and should simplify that part of the distribution process.



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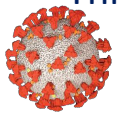
Marvelous - but we are not done!

- Vaccines don't save lines; vaccinating people saves lives!
- USG contracts for mRNA is 100 million doses from each company.
- Timeline uncertain, but supposedly we will get these cumulative 200 million by April/May 2021.
  - 25 million doses Pfizer and 15 million Moderna in December
  - 30 million doses Pfizer and 20 million Moderna in January
  - 35 million Pfizer and 25 million Moderna in February and March
  - This is enough for first responders, medical personnel, elderly and staff in nursing homes, and getting close to the complete NAM 1B group
- We need the other vaccines for the rest of the adult populations, as well as kids and pregnant women, where experience is much greater with Ad26 vector and the recombinant protein vaccines with adjuvants.
- Keeping the ongoing trials, as well as creating way to test the Recombinant Protein Platforms post EUA is critical for overall vaccine strategy and getting everyone back to school and work.
- This means keeping the AZ and Janssen trials intact until end of February/mid-March.



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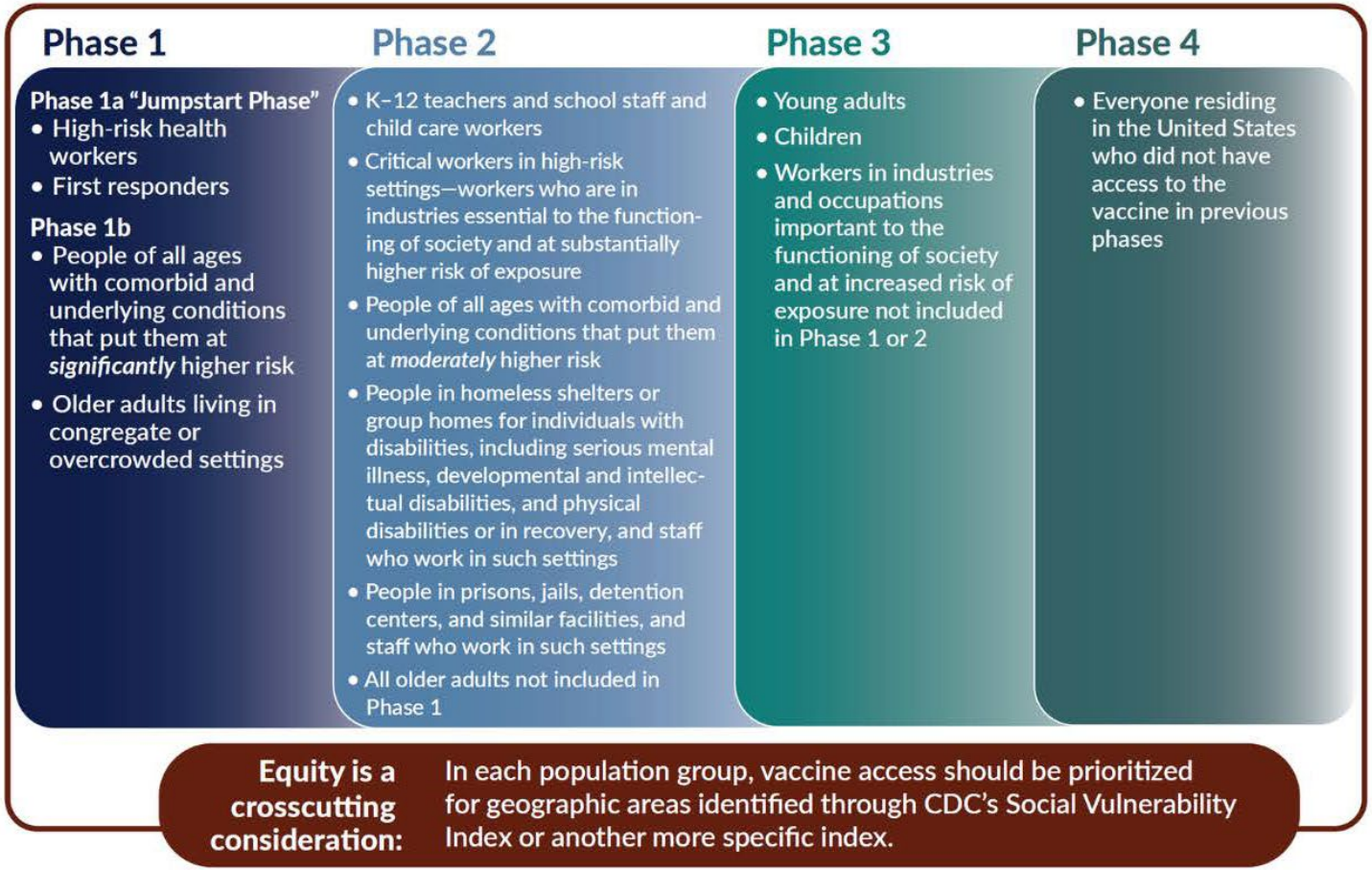

NATIONAL ACADEMY of MEDICINE

FIGURE: A Phased Approach to Vaccine Allocation for COVID-19

The National Academies of SCIENCES ENGINEERING MEDICINE

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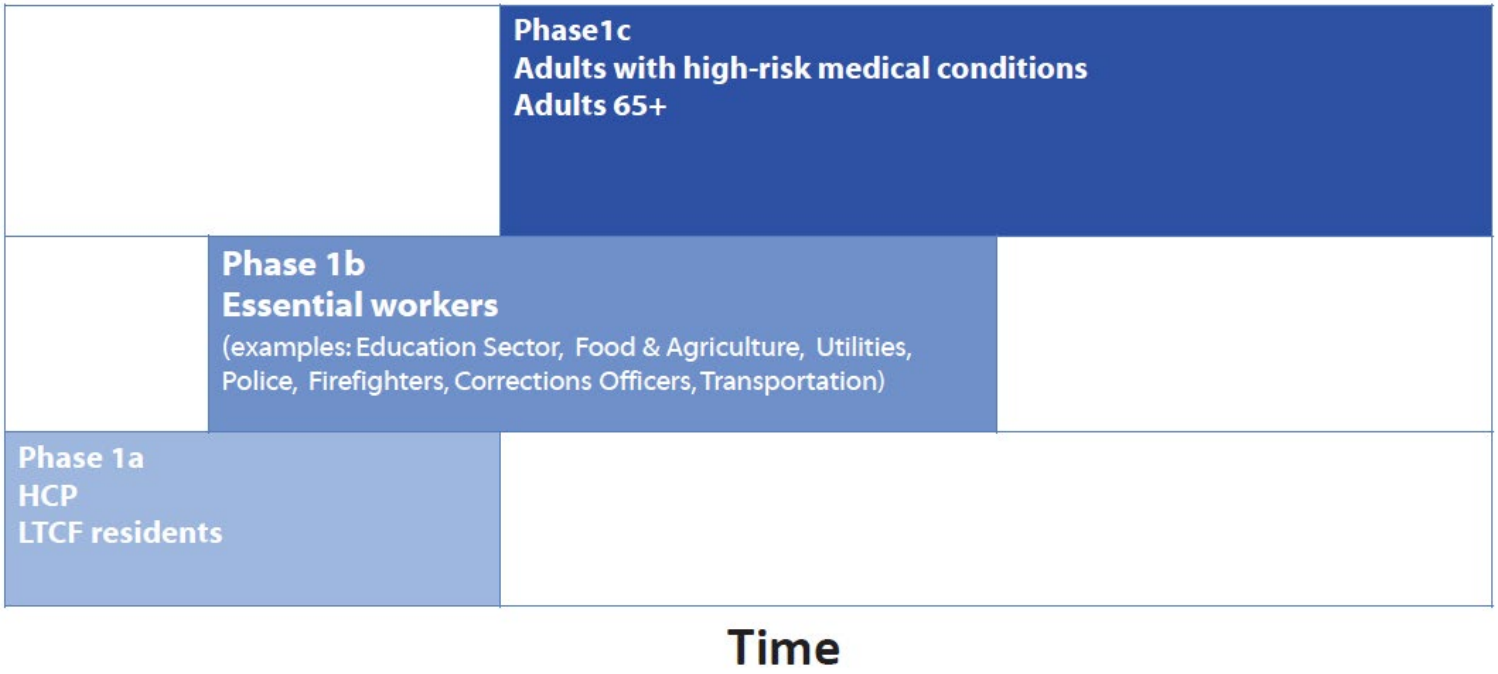
Proposed Interim Phase 1 Sequence



Thank You

Network Collaboration

- HVTN Executive Management Team:
  - Glenda Gray, Scott Hammer, Georgia Tomaras, Dan Barouch, Julie McElrath, Peter Gilbert, Susan Buchbinder, Jim Kublin, Troy Martin
- Mike Cohen / HPTN
- IDCRC
- David Montefiori

DAIDS

- Emily Erbelding
- Carl Dieffenbach

VRC

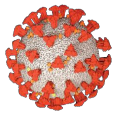
- John Mascola
- Barney Graham
- Julie Ledgerwood

NIH

- Tony Fauci
- Francis Collins
- Hilary Marston
- Hugh Auchincloss

OWS

- Moncef Slaoui
- Mary Marovich
- Merlin Robb
- Tina Tong
- Julie Ake



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