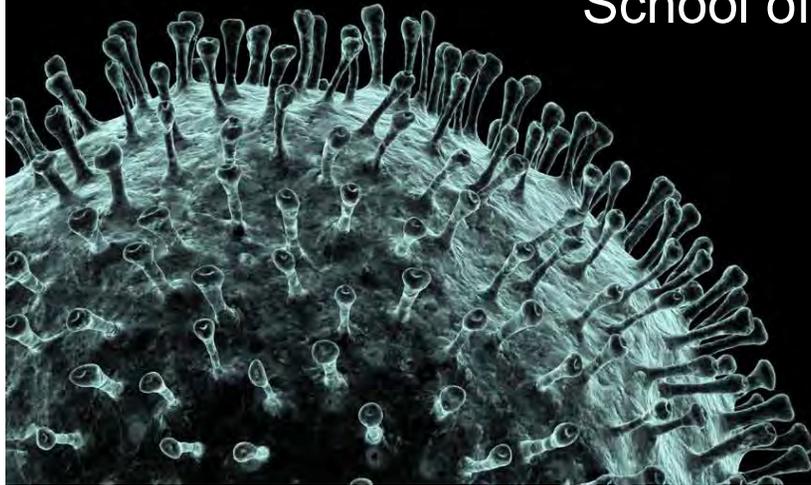


# COVID-19 Conversations



**Kathleen M. Neuzil**

Myron M. Levine, MD Professor in Vaccinology  
Director, Center for Vaccine Development and  
Global Health, University of Maryland  
School of Medicine



[COVID19Conversations.org](https://COVID19Conversations.org)

[#COVID19Conversations](https://twitter.com/COVID19Conversations)



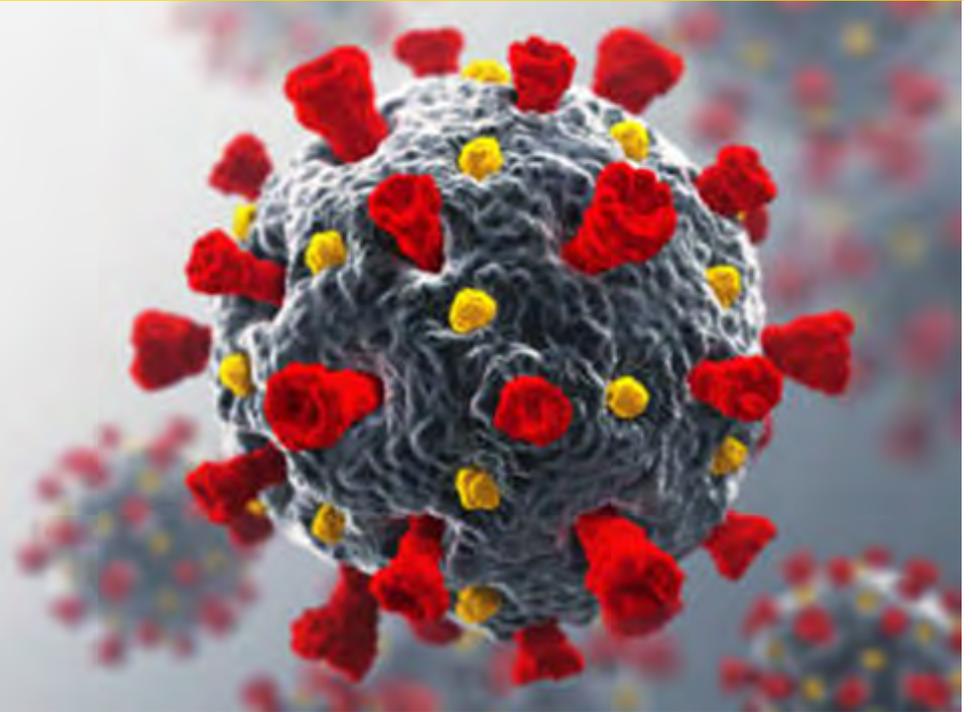
# CVD·GLOBAL HEALTH

CENTER FOR VACCINE DEVELOPMENT AND GLOBAL HEALTH

COVID Vaccine Development: From Discovery to Impact

Kathleen Neuzil, MD, MPH  
10 June 2020

 UNIVERSITY of MARYLAND  
SCHOOL OF MEDICINE  
CENTER FOR VACCINE DEVELOPMENT  
AND GLOBAL HEALTH

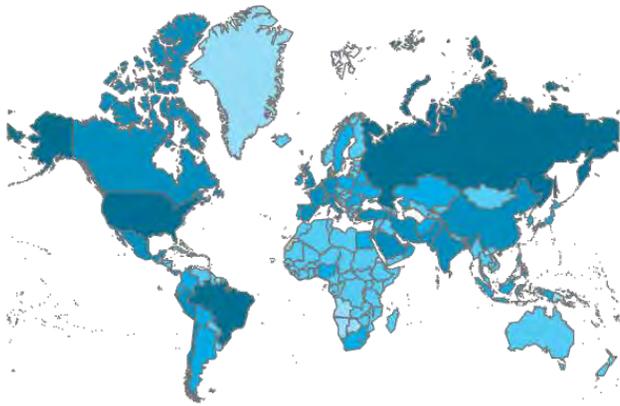


# Vaccine Development: A Continuum from Discovery to Impact

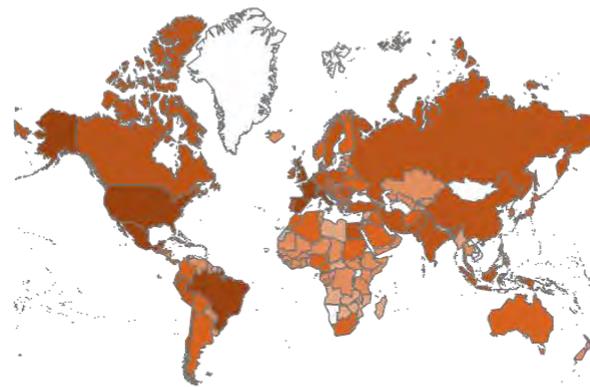


**Vaccines as a tool for healthy equity**

# The Case for a Vaccine: WHO Coronavirus Dashboard



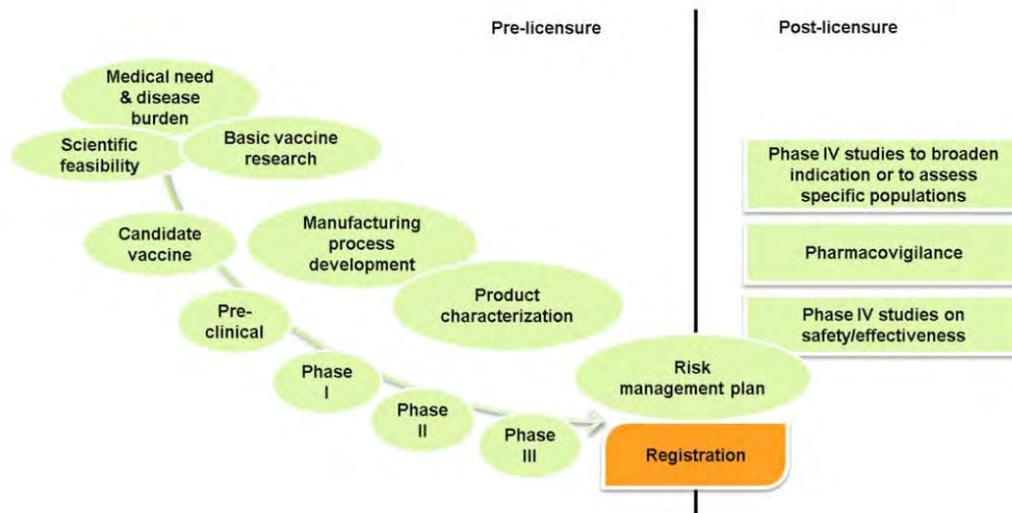
7,258,842 cases



411,694 deaths

<https://covid19.who.int/>

# Clinical Vaccine Development: Where Do We Begin? What is the Goal?

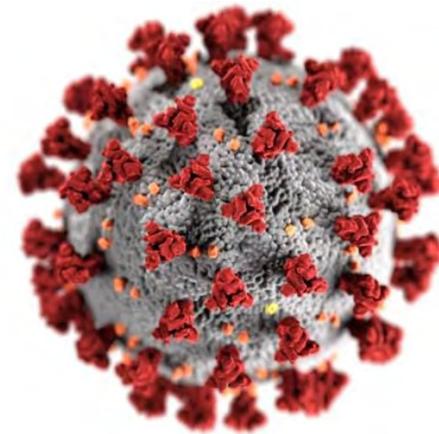


- Indication
- Target population
- Safety, reactogenicity
- Immunogenicity
- Efficacy
- Co-administration
- Duration of protection

<http://www.mdpi.com/2076-393X/1/3/204/htm>

# What Do We Know About Immunity in Humans?

- Immune response post-infection to spike protein
  - Neutralizing responses
- Level of antibody needed to prevent re-infection?
- Duration of protection from natural immunity?
- Importance of T cell immunity?
- Phase 1 human trials in SARS, MERS
  - Broadly neutralizing antibodies



Cite as: B. S. Graham *et al.*, *Science* 10.1126/science.abb8923 (2020).

## Rapid COVID-19 vaccine development

By **Barney S. Graham**

Vaccine Research Center, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA. Email: bgraham@mail.nih.gov

Finding the fastest pathway to vaccine availability includes the avoidance of safety pitfalls

### Potential risks associated with vaccine development for COVID-19

Antibodies that bind virus without neutralizing infectivity can cause disease through increased viral replication or formation of immune complexes that deposit in tissue and activate complement pathways associated with inflammation. T helper 2 cell (T<sub>H</sub>2)-biased responses have also been associated with ineffective vaccines that lead to enhanced disease after subsequent infection. Antibody-dependent enhancement (ADE) of viral replication has occurred in viruses with innate macrophage tropism. Virus-antibody immune complexes and T<sub>H</sub>2-biased responses can both occur in vaccine-associated enhanced respiratory disease (VAERD).

	Antibody-mediated		T cell-mediated
	ADE	VAERD	VAERD
<b>Mechanism</b>	Fc-mediated increase in viral entry	Immune complex formation and complement deposition	T <sub>H</sub> 2-biased immune response
<b>Effectors</b>	Macrophage activation and inflammatory cytokines	Complement activation and inflammatory cytokines	Allergic inflammation and T <sub>H</sub> 2 cytokines
<b>Mitigation</b>	Conformationally correct antigens and high-quality neutralizing antibody		T <sub>H</sub> 1-biasing immunization and CD8 <sup>+</sup> T cells

# Is There a Role for Controlled Human Infection Models?

## ● PANDEMIC VACCINE DEVELOPMENT MODEL – Overlapping Phases

*Shorten Development Time*

Define target product profile,  
pre-clinical, assay development

Large-scale production

Clinical Development

Licensure

Phase I

Phase 2/3

Regulatory  
pathway

## ● HYBRID MODEL – Adding New Controlled Human Infection Model (CHIM)

*Provides supporting data; does not accelerate initial timeline*

Manufacture SARS-CoV-2  
challenge strain, engage  
communities/ethicists

Develop SARS-CoV-2  
CHIM when disease  
characteristics better  
known and rescue  
drug available

Begin testing  
of vaccines  
in model

# Vaccine Development: A Continuum from Discovery to Impact



**Vaccines as a tool for healthy equity**

# ACCESS TO COVID-19 TOOLS (ACT) ACCELERATOR

24 April 2020

A Global Collaboration to Accelerate the Development, Production and Equitable Access to New COVID-19 diagnostics, therapeutics and vaccines

## COMMITMENT and CALL TO ACTION

### Our Vision and Mission

Grounded in a vision of a planet protected from human suffering and the devastating social and economic consequences of COVID-19, we, an initial group of global health actors (BMGF, CEPI, Gavi, Global Fund, UNITAID, Wellcome Trust, WHO) and private sector partners and other stakeholders, are launching a landmark, global and time-limited collaboration to accelerate the development, production and equitable global access to new COVID-19 essential health technologies.

Our Mission is not only accelerated development and availability of new COVID-19 tools – it is to accelerate equitable global access to safe, quality, effective, and affordable COVID-19 diagnostics, therapeutics and vaccines, and thus to ensure that in the fight against COVID-19, no one is left behind.

### Our Commitment

1. We commit to the shared aim of equitable global access to innovative tools for COVID-19 for all.

BILL & MELINDA  
GATES foundation

**dcvmn**  
Developing Countries Vaccine  
Manufacturers Network

 **The Global Fund**

  
INTERNATIONAL GENERIC AND  
BIOSIMILAR MEDICINES ASSOCIATION

  
wellcome

**CEPI**

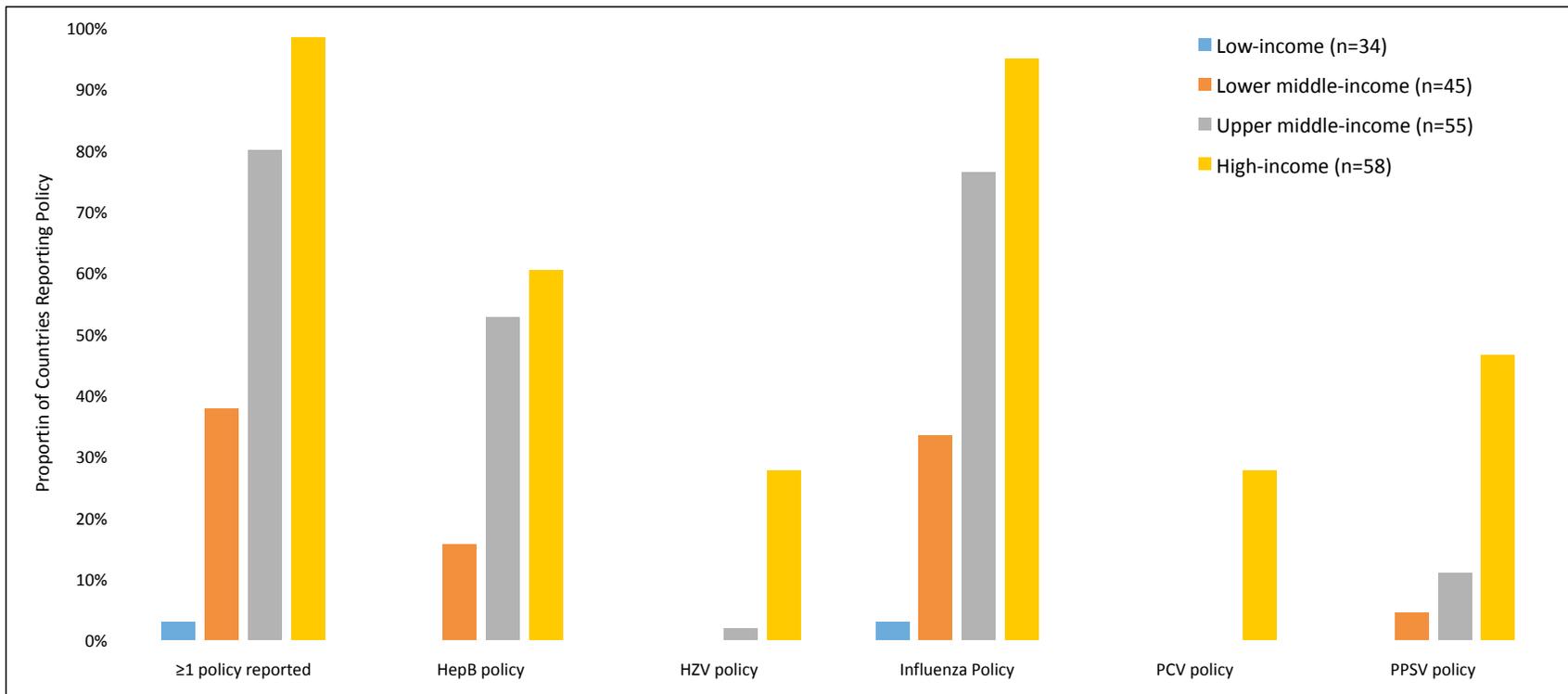
  
Gavi  
The Vaccine Alliance

  
International Federation  
of Pharmaceutical  
Manufacturers & Associations

 **Unitaid**  
Innovation in Global Health

 **World Health Organization**

## Reported Adult Immunization Programs by World Bank Income Category in 2018



# Summary

- Safe and effective vaccines are needed for COVID-19; must be accessible, affordable and globally available
- Vaccine development is a staged, deliberate and careful process
  - Many challenges – New disease, poorly understood immunity, uncertain trajectory of outbreak
  - Vaccine safety will be meticulously assessed
  - If enhanced disease occurs it will be carefully assessed and immune mechanisms investigated