COVID-19 Vaccines Update
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Disclosures

• This activity will include the discussion of investigational vaccines that are not yet approved for use by the FDA. Any discussion of vaccine candidate products does not imply endorsement.

• I am currently an investigator for the Phase 3 trials of COVID-19 vaccines manufactured by Moderna (mRNA-1273) and Novavax (NVX-CoV2373).

SARS-CoV-2 and COVID-19

• Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
  • Novel coronavirus identified in December 2019 in Wuhan China
  • Global pandemic (>50 million cases and 1.25 million deaths worldwide)
  • Genetically related to SARS-CoV
  • Binds to the human ACE2 receptor
  • Highly transmissible from person-to-person

• Coronavirus disease 2019 (COVID-19)
  • Caused by infection with SARS-CoV-2
  • Multiple manifestations
  • Variable mortality
  • High demands on health-care systems

USA: New Cases and Deaths per Day

By The New York Times
Updated November 8, 2020, 8:10 A.M. ET

New reported deaths by day in the United States

Cases 10 million+ 100,657 +50%
Deaths 238,031 464 +14%

https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html?campaign_id=9&emc=edit_nn_20201020&instance_id=23299&nl=the-morning&regi_id=132536686&section_index=1&section_name=big_story&segment_id=41591&te=1&user_id=218e83518f624ad96bfcb8f024e4ca0e
Racial and Ethnic Disparities in COVID-19

COVID-19 Hospitalization and Death by Race/Ethnicity

Race and ethnicity are risk markers for other underlying conditions that impact health—including socioeconomic status, access to healthcare, and increased exposure to the virus due to occupation (e.g., frontline, essential, and critical infrastructure workers).

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Cases†</th>
<th>Hospitalization</th>
<th>Death‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian or Alaska Native, Non-Hispanic persons</td>
<td>2.8x greater</td>
<td>1.3x greater</td>
<td>1.4x greater</td>
</tr>
<tr>
<td>Asian, Non-Hispanic persons</td>
<td>1.1x greater</td>
<td>1.3x greater</td>
<td>2.1x greater</td>
</tr>
<tr>
<td>Black or African American, Non-Hispanic persons</td>
<td>2.6x greater</td>
<td>4.7x greater</td>
<td>2.3x greater</td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>2.0x greater</td>
<td>4.6x greater</td>
<td>1.3x greater</td>
</tr>
<tr>
<td>Native Hawaiian and Other Pacific Islander</td>
<td>5.7x greater</td>
<td>3.0x greater</td>
<td>5.0x greater</td>
</tr>
<tr>
<td>White</td>
<td>2.6x greater</td>
<td>2.4x greater</td>
<td>1.5x greater</td>
</tr>
<tr>
<td>Other</td>
<td>1.1x greater</td>
<td>1.3x greater</td>
<td>1.5x greater</td>
</tr>
<tr>
<td>Asian</td>
<td>1.4x greater</td>
<td>2.5x greater</td>
<td>3.1x greater</td>
</tr>
<tr>
<td>Two or more races</td>
<td>1.1x greater</td>
<td>1.0x greater</td>
<td>2.5x greater</td>
</tr>
</tbody>
</table>


Vaccine Development

Support Framework for COVID Vaccine Development in US

- Vaccine Development and Manufacture: Moderna, Sanofi-Pasteur, Janssen, AstraZeneca, Novavax
- Clinical and Preclinical Trials: COVID-19 Prevention Network
- Operation Warp Speed: US DoD
- Commercial Research Organizations: EUA, Licensure and Public Use

https://covidtracking.com/race
How are vaccines developed

Lab & animal studies

Phase 1:
- Safety
- Immune responses
- Small numbers
- Healthy adults

Pre-clinical

Phase 2:
- Safety
- Immune responses
- Larger numbers
- Target population

Clinical

Phase 3:
- Safety
- Prevent disease
- Lessen severity

Approaches to vaccine development

RNA for spike protein

mRNA vaccines (Moderna, Pfizer)

Spike protein

Viral vector vaccines (AstraZeneca, Janssen)

Spike protein

rProtein vaccines (Novavax, Sanofi)

Status of vaccine candidates supported by Operation Warp Speed

- mRNA platform
  - Moderna (in Phase III)
  - Pfizer (in Phase III); >90% efficacy after first 94 cases analyzed

- Viral vectored vaccines
  - AstraZeneca (in Phase III)
  - Janssen (Phase III)

- Recombinant proteins (require adjuvants)
  - Novavax (Phase I/II), Phase III slated to start November 2020
  - Sanofi (Phase I/II)
Vaccine safety

What data is available?
• Phase I/II results for safety
  - Moderna (mRNA1273)
  - Pfizer (BNT162b1)
  - Novavax (rS with Matrix M1)
  - AstraZeneca (ChAdOx1 nCoV-19)
  - Janssen (Ad26.COV2.S)

Reactogenicity profiles
• Differ slightly by vaccine candidate
• Most with mild-moderate reactogenicity (some severe)
• Frequently increased with 2nd vaccination (mRNA vaccines)
• For Novavax and Sanofi- increased with adjuvant
• Mostly short-lived
• For ChAdOx1 nCoV-19, reduced with paracetamol

AstraZeneca Covid-19 vaccine study put on hold due to suspected adverse reaction in participant in the U.K.

As AstraZeneca's Covid-19 vaccine trial remains on hold in U.S., participants waiting on a second dose are in limbo
What does a clinical hold mean?

• A clinical hold is an order issued by FDA to the sponsor of an IND application to delay a proposed clinical investigation or to suspend an ongoing investigation.
• All or some of the investigations conducted under an IND application may be placed on clinical hold.
• The reason for a clinical hold is concern for the safety of clinical trial participants.
• An independent review is required to determine whether the event is the result of a vaccine candidate or just a random unrelated illness.

What does a clinical pause mean?

• A clinical pause is a standard component of a clinical trial protocol in which recruitment or dosing is paused by the study sponsor.
• The reason for a clinical pause is concern for the safety of clinical trial participants.
• An independent review is required to determine whether the event is the result of a vaccine candidate or just a random unrelated illness.
Immune responses against SARS-CoV-2

- hACE2 blocking Ab
  - Block the interaction between the virus and its receptor hACE2
- Neutralizing Ab
  - Bind to the virus and prevent the virus from infecting cells
- Total Spike-specific IgG
  - Ab that bind to the surface protein of the virus
- CD4+ and CD8+ T cell responses
  - Th1 responses (IFN-γ, TNF-α, IL-2)
  - Direction of Ab responses
  - Direct killing of infected cells

Immunogenicity of vaccine candidates

- Different assays used
  - Most use a neutralizing Ab assay
  - Demonstrate nAb titers equivalent to convalescent sera/plasma
- T cell responses
  - Not reported in all studies
  - Demonstrate Th1 responses

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CVD Clinical Trials: sign up at www.cvdtrials.org
https://is.gd/Covid_Studies_Screening
Phone: 410-706-6156

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