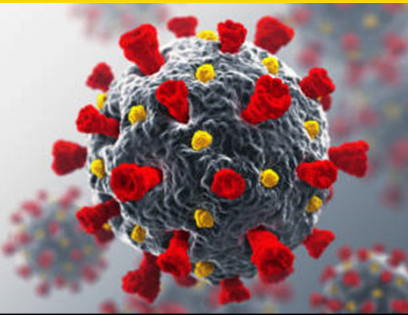


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COVID-19 Vaccines Update

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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).

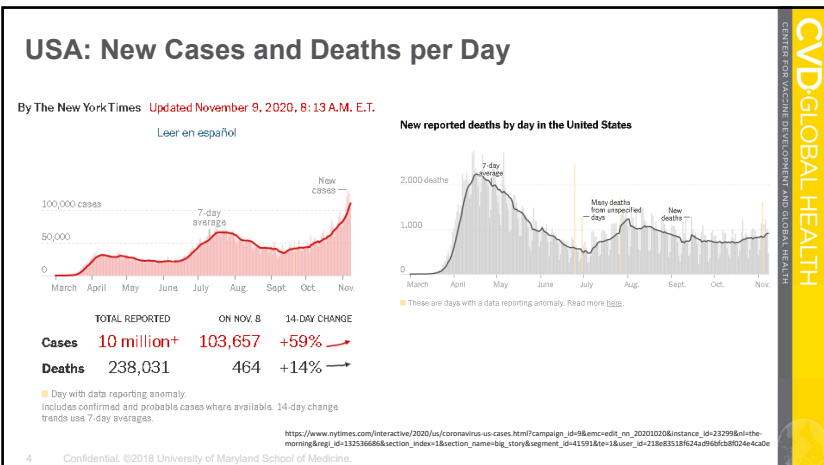
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SARS-CoV-2 and COVID-19

- 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



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Racial and Ethnic Disparities in COVID-19

COVID-19 Hospitalization and Death by Race/Ethnicity

Updated Aug. 18, 2020

[Print](#)



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

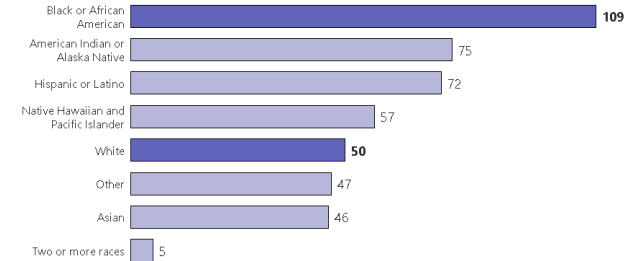
Rate ratios compared to White, Non-Hispanic Persons	American Indian or Alaska Native, Non-Hispanic persons	Asian, Non-Hispanic persons	Black or African American, Non-Hispanic persons	Hispanic or Latino persons
Cases¹	2.8x higher	1.1x higher	2.6x higher	2.8x higher
Hospitalization²	5.3x higher	1.3x higher	4.7x higher	4.6x higher
Death³	1.4x higher	No increase	2.1x higher	1.1x higher

<https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html>

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Racial and Ethnic Disparities in COVID-19

Deaths per 100,000 people by race or ethnicity



<https://covidtracking.com/race>

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Vaccine Development



7

Support Framework for COVID Vaccine Development in US

Vaccine Development and Manufacture



Moderna
Sanofi
Janssen

Novavax
Pfizer
AstraZeneca

Operation Warp Speed

US Government Body:
Strategic approach and resource allocation

Trial design and execution



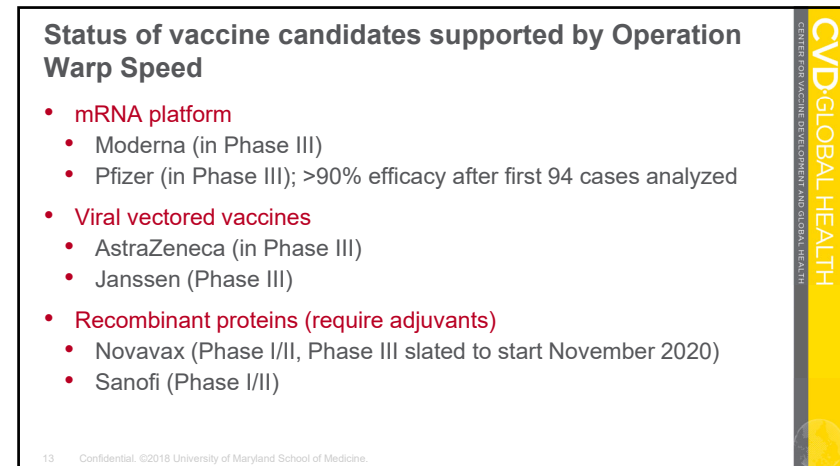
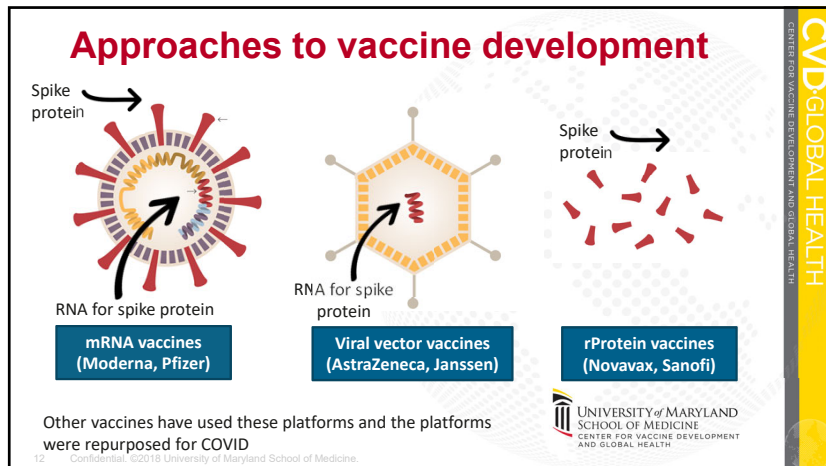
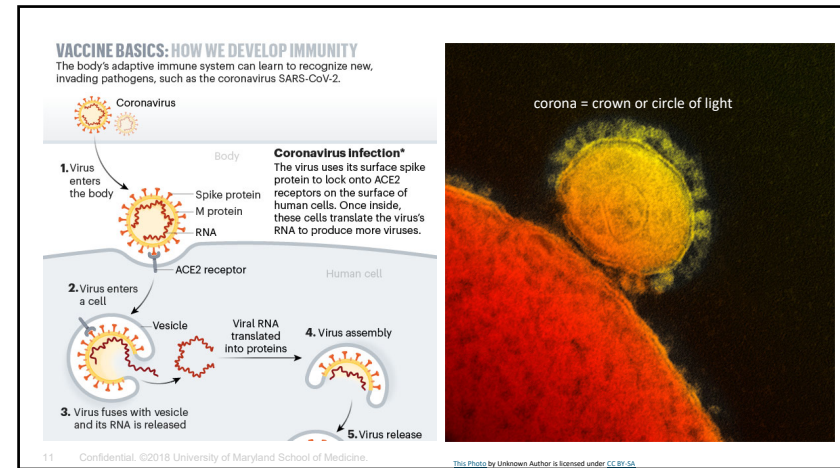
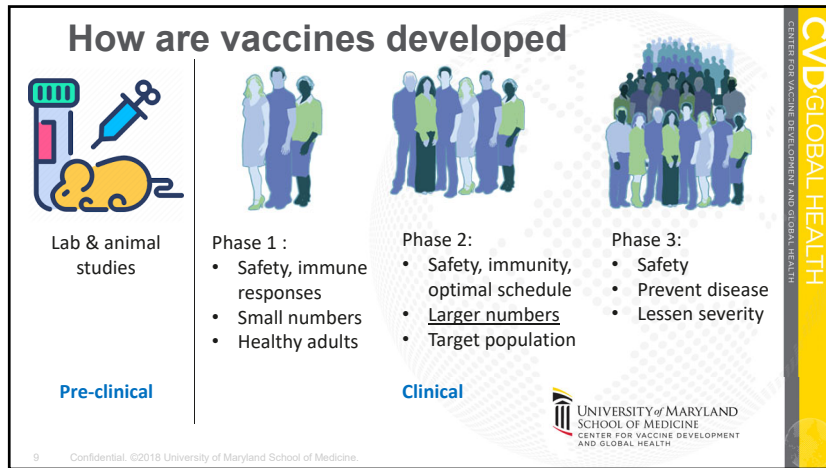
Commercial Research Organizations



US DoD

EUA, Licensure and Public Use

8



Vaccine safety



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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)



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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



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

By REBECCA ROBBINS @rebeccarobbins, ADAM FEUERSTEIN @adamfeuerstein, and HELEN BRANSWELL @helenbranswell / SEPTEMBER 8, 2020



A 19-YEAR-OLD STUDENT IN THE U.K. https://www.statnews.com/2020/09/08/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

By REBECCA ROBBINS @rebeccarobbins / OCTOBER 6, 2020



A participant in AstraZeneca and Oxford's Covid-19 vaccine trial in Brazil receives a shot. While other trials globally have been halted, the U.S. trial remains halted.

https://www.statnews.com/2020/10/06/astrazeneca-covid19-second-dose-trial-vaccine/

17

Johnson & Johnson's Janssen Vaccine Candidate

<https://www.cbsnews.com/news/covid-vaccine-trial-johnson-johnson-pause-sick-participant/>



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Johnson & Johnson pauses COVID-19 vaccine trial over sick participant

UPDATED ON: OCTOBER 13, 2020 / 7:42 PM / APP





Johnson & Johnson COVID-19 vaccine study paused due to unexplained illness in participant

By MATTHEW HERPER [@matherper](#) / OCTOBER 12, 2020



<https://www.statnews.com/2020/10/12/johnson-johnson-covid-19-vaccine-study-paused-due-to-unexplained-illness-in-participant/>



Photo: swissinfo.ch

What does a clinical hold mean?

AstraZeneca's Trial Is on Hold. It's a Sign that the Science Is Working.

COMMENTARY Norman Baylor Sept. 21, 2020 5:00 pm ET

- 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.

<https://www.barrons.com/articles/astrazenecas-trial-on-hold-sign-science-is-working-fda-51600721992>

What does a clinical pause mean?



Photo: wfy.org

Johnson & Johnson Prepares to Resume Phase 3 ENSEMBLE Trial of its Janssen COVID-19 Vaccine Candidate in the U.S.

Updated Statement October 23, 2020

- 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.

<https://www.barrons.com/articles/astrazeneca-trial-on-hold-sign-science-is-working-fda-51600721992>

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Immunogenicity

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Immune responses against SARS-CoV-2

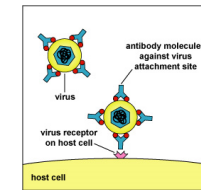
- hACE2 blocking Ab
 - Block the interaction between the virus and its receptor hACE2
- Neutralizing Ab
 - Bind to the virus and prevent the virus from infecting cells
- Total Spike-specific IgG
 - Ab that bind to the surface protein of the virus
- CD4+ and CD8+ T cell responses
 - Th1 responses (IFN-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

22

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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

24

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