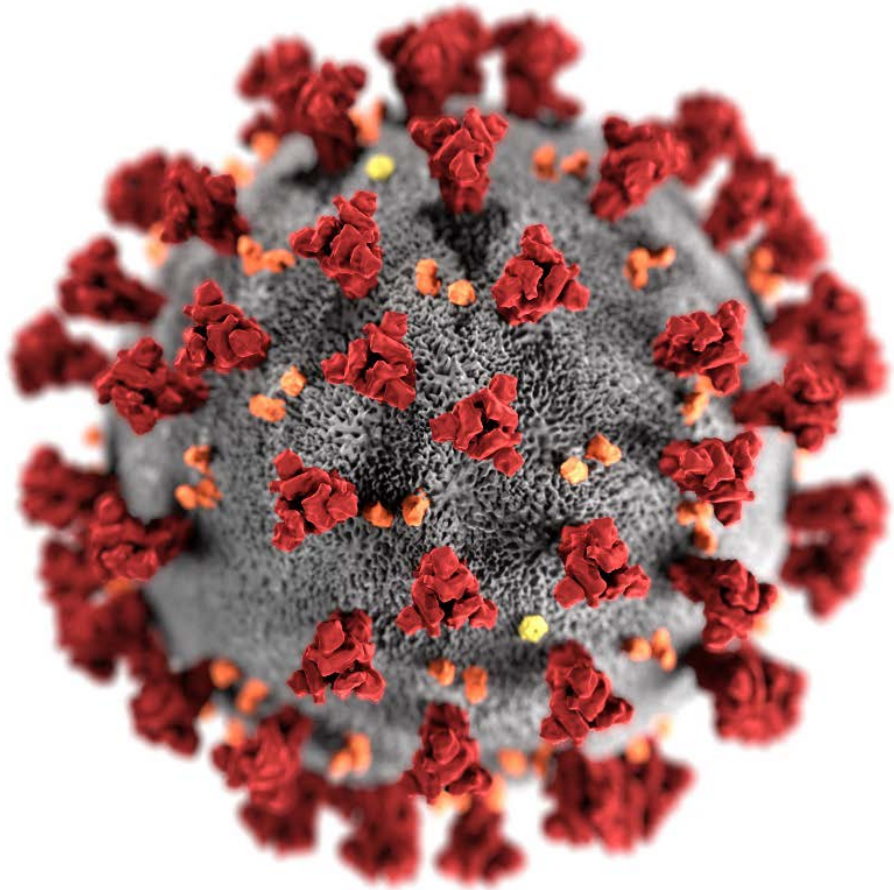
# ACIP COVID-19 Vaccines Work Group



## COVID-19 vaccines: Work Group interpretations

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ACIP Meeting
August 26, 2020

# COVID-19 vaccines in human clinical trials

# COVID-19 vaccines in human clinical trials – United States*

| Candidate | Manufacturer | Type | Phase | Trial characteristics | Trial #s |
|---|---|---|---|---|---|
| mRNA-1273 | Moderna TX, Inc. | mRNA | III | • 2 doses (0, 28d)<br>• IM administration<br>• 18-55, 56+ years | NCT04283461 (II)<br>NCT04405076 (II)<br>NCT04470427 (III) |
| mRNA-BNT162 | Pfizer, Inc./BioNTech | mRNA | I/II/III | • Single or 2 doses<br>• IM administration<br>• 18-85 years | NCT04368728<br>EudraCT 2020-001038-36<br>ChiCTR2000034825 |
| INO-4800 | Inovio Pharmaceuticals, Inc. | DNA plasmid | I/II | • 2 doses (0, 4w)<br>• SC administration/ electroporation<br>• ≥18 years | NCT04336410 (I)<br>NCT04447781 |
| Ad26COVS1 | Janssen Pharmaceutical Companies | Non-Replicating Viral Vector | I/II | • 2 doses (0,56d)<br>• IM administration<br>• 18-55, 65+ | NCT04436276 |

*As of August 22, 2020. Trials listed as actively recruiting on clinicaltrials.gov
Sources: https://milkeninstitute.org/covid-19-tracker; https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines; https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

# COVID-19 vaccines in human clinical trials – outside United States*

## mRNA/DNA vaccines

| Candidate | Manufacturer | Type | Trial Location | Phase | Trial # |
|---|---|---|---|---|---|
| CVnCoV | CureVac | mRNA | Belgium, Germany | I/II | NCT04449276, NCT04515147 |
| -- | People's Liberation Army Acad. Med. Sciences | mRNA | China | I | ChiCTR2000034112 |
| -- | Arcturus/Duke-NUS | mRNA | Singapore | I/II | NCT04480957 |
| LNP-nCoVsaRNA | Imperial College London | saRNA | U.K. | I | ISRCTN17072692 |
| GX-19 | Genexine Consortium | DNA | South Korea | I/II | NCT04445389 |
| -- | Osaka University/AnGes | DNA plasmid+adjuvant | Japan | I/II | NCT04463472 |
| -- | Cadila Healthcare Limited | DNA plasmid | India | I/II | CTRI/2020/07/026352 |

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# COVID-19 vaccines in human clinical trials – outside United States*
# Protein subunit vaccines

| Candidate | Manufacturer | Type | Trial Location | Phase | Trial # |
|---|---|---|---|---|---|
| NVX-CoV2373 | Novavax | Protein subunit | Australia | I/II | NCT04368988 |
| -- | Anhui Zhifei Longcom/ Chinese Academy of Science | Protein subunit | China | II | NCT04445194, NCT04466085 |
| SCB-2019 | Clover/GSK/Dynavax | Protein subunit | Australia | I | NCT04405908 |
| Covax-19 | Vaxine | Protein subunit | Australia | I | NCT04453852 |
| -- | University of Queensland/CSL/Seqirus | Protein subunit | Australia | I | ACTRN12620000674932p |
| -- | Instituto Finlay de Vacunas | Protein subunit | Cuba | I/II | RPCEC00000332 |

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Sources: https://milkeninstitute.org/covid-19-tracker; https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines; https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

# COVID-19 vaccines in human clinical trials – outside United States*
# Viral Vector vaccines

| Candidate | Manufacturer | Type | Trial Location | Phase | Trial # |
|---|---|---|---|---|---|
| -- | Medicago | VLP | Canada | I | NCT04450004 |
| ad5-nCov | CanSino Biologics, Inc. | Viral vector (NR) | China | II* | NCT04313127, NCT04398147, NCT04341389 |
| AZD1222 | University of Oxford/AstraZeneca consortium | Viral vector (NR) | UK, South Africa, Brazil | II/III | NCT04324606, NCT04400838 EudraCT 2020-001072-15, EudraCT 2020-001228-32 |
| aAPC | Shenzhen Geno-Immune Medical Institute | Viral vector | China | I | NCT04299724 |
| LV-SMENP-DC | Shenzhen Geno-Immune Medical Institute | Viral vector | China | I | NCT04276896 |
| Ad26COVS1 | Janssen | Viral Vector (NR) | Belgium | I/II | NCT04436276, NCT04505722 |
| Gam-COVID-Vac | Gamaleya Research Institute | Viral vector (NR) | Russia | I | NCT04437875, NCT04436471 |
| -- | Institut Pasteur/ Themis/ University of Pittsburgh CVR/ Merck Sharp & Dohme | Viral vector | France, Belgium | I | NCT04497298 |

*As of August 22, 2020. Trials listed as actively recruiting on clinicaltrials.gov
Sources: https://milkeninstitute.org/covid-19-tracker; https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines; https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

# COVID-19 vaccines in human clinical trials – outside United States*
# Inactivated vaccines

| Candidate | Manufacturer | Type | Trial Location | Phase | Trial # |
|---|---|---|---|---|---|
| BBIBP-CorV | Beijing Institute of Biological Products/Sinopharm | Inactivated | China | III | ChiCTR2000032459 ChiCTR2000034780 |
| -- | Wuhan Institute of Biological Products/Sinopharm | Inactivated | China, UAE | III | ChiCTR2000031809 ChiCTR2000034780 |
| CoronaVac | Sinovac/Instituto Butantan | Inactivated | China, Brazil | III | NCT04352608, NCT04383574, NCT04456595 |
| -- | Inst. of Med. Biology/Chinese Acad. Med. Sciences | Inactivated | China | II | NCT04412538, NCT04470609 |
| BBV152 | Bharat Biotech | Inactivated | India | I/II | CTRI/2020/07/026300, NCT04471519 |

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Sources: https://milkeninstitute.org/covid-19-tracker; https://www.who.int/who-documents-detail/draft-landscape-of-covid-19-candidate-vaccines; https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

# Work Group Interpretation: Clinical Trial Data

# Information Reviewed by Work Group

- Phase I Immunogenicity data from 2 COVID-19 mRNA vaccines
- Phase I Safety data from 2 COVID-19 mRNA vaccines
- Overview/Plans for Phase II/III studies for 2 COVID-19 mRNA vaccines

# Immunogenicity and Safety Information Reviewed by Work Group

## mRNA1273 (Moderna)  N=130

- **Immunogenicity**
  - Neutralizing antibodies (pseudovirus neutralization assay titers) and binding antibodies (ELISA) measured 7 days post-dose 2
  - Responses similar to or exceeded convalescent sera comparison
  - Th1-biased CD4+ T-cell response
  - **100µg** dose selected for Phase III clinical trials

- **Safety**
  - Local and systemic symptoms followed for 7 days post-vaccination
    - Pain, myalgia, fatigue most common symptoms reported
  - Reactogenicity symptoms higher after second dose
  - No vaccine-related serious adverse events (SAEs) reported

# Immunogenicity and Safety Information Reviewed by Work Group

## BNT162b2 (Pfizer/BioNTech) N=195

- **Immunogenicity**
  - Neutralizing antibodies (50% neutralization titers) measured 7 days post-dose 2
  - Responses similar to or exceeded human convalescent panel
  - CD4+ and CD8+ T cell response demonstrated
  - Th1-biased CD4+ T-cell response
  - **30µg** dose of BNT162b2 selected for Phase III clinical trials

- **Safety**
  - Local and systemic symptoms followed after administration
    - Fatigue, headache and muscle pain most common
  - Reactogenicity symptoms lower in older population (65-85 years)

# Plans for Phase III

- Both vaccine candidates currently enrolling large (~30,000 people) Phase III efficacy trials
- Primary endpoints: symptomatic, virologically confirmed COVID-19 disease
- Attempting to enroll diverse populations:
  - Race and ethnicity
  - Age (<65 years and ≥65 years of age)
  - Underlying medical conditions

# Work Group Interpretation

- Phase I data from both mRNA vaccines show induction of neutralizing antibodies at 7 days post-dose 2 that exceed levels in convalescent sera
- Data from both mRNA vaccines support advancing to large scale Phase III clinical trials to assess safety and efficacy
- Diverse cold-chain or ultra-low temperature requirements can substantially affect implementation efforts

# Work Group Interpretation:
## Current Phase III Clinical Trials

- Emphasized the importance of enrolling **diverse** study participants
- Emphasized the need to allow for sufficient time post-dose 2 to evaluate **safety** signals
- Need to report **maternal** and **fetal** outcomes for women who become pregnant during the clinical trials
- Evaluate vaccine impact on viral **shedding** or **transmission**, among symptomatic and asymptomatic populations

# Work Group Interpretation:
## Current Phase III Clinical Trials

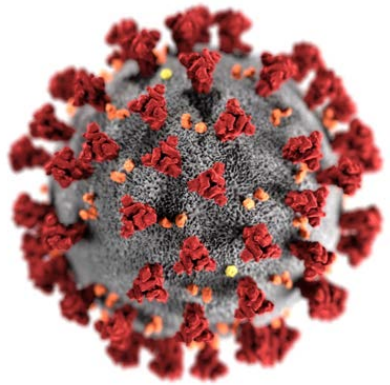
- Emphasized the importance of enrolling **diverse** study participants
- Emphasized the need to allow for sufficient time post-dose 2 to evaluate **safety** signals
- Need to report **maternal** and **fetal** outcomes for women who become pregnant during the clinical trials
- Evaluate vaccine impact on viral **shedding** or **transmission**, among symptomatic and asymptomatic populations
  - **Co-administration** of other vaccines especially influenza vaccine
  - Pregnant women
  - Children

## Work Group Interpretation:
## Future/Additional Studies

# Work Group Interpretation: Epidemiology Data

# Information Reviewed by Work Group

- COVID-19 epidemiology among U.S. population
- Epidemiology among various occupational settings
- Epidemiology among individuals at increased risk of severe COVID-19 disease



# Healthcare Personnel

- **Healthcare Personnel** (HCP) are essential workers defined as **paid** and **unpaid** persons serving in healthcare settings who have the potential for direct or indirect exposure to patients or infectious materials

# Healthcare Personnel within COVID-NET

March 1 to July 11, 2020

- Healthcare Personnel Type: N=512
  - Respiratory Therapist: 3 (<1%)
  - Physician: 23 (5%)
  - Nurse: 125 (24%)
  - Other: 276 (54%)
  - Not specified: 85 (17%)

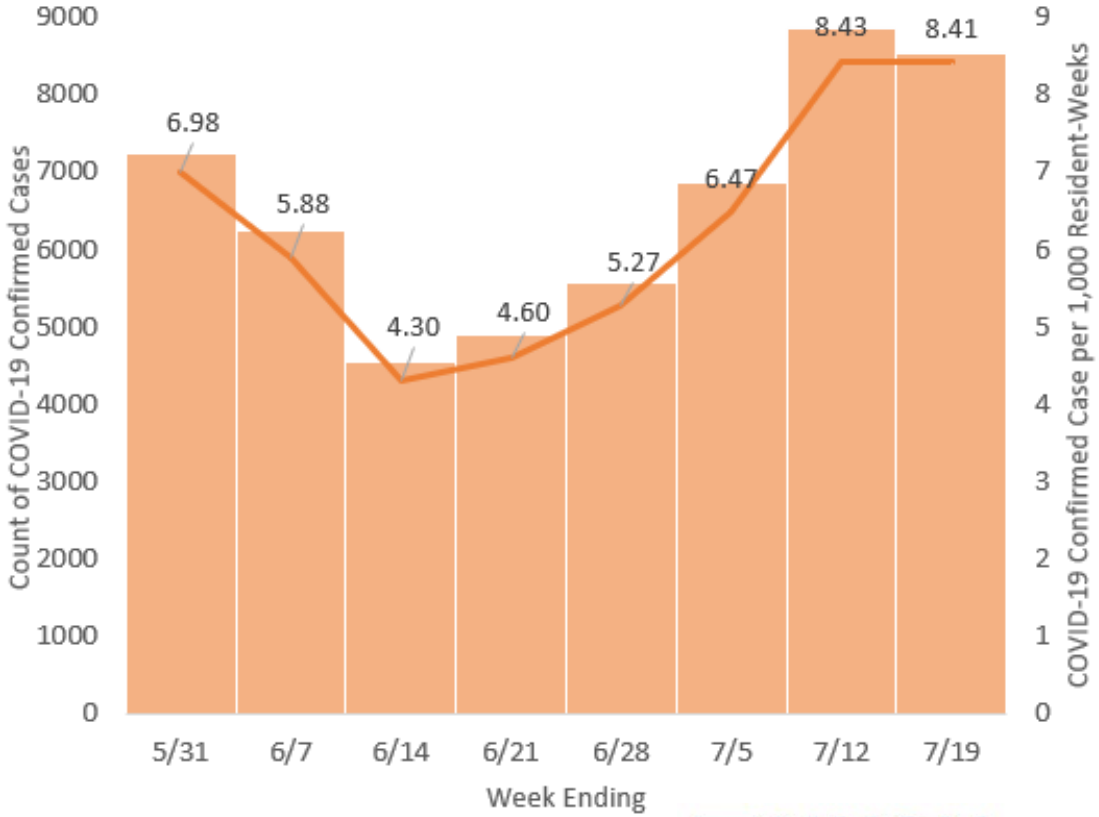
| | |
|---|---|
| Hospital-based patient care support (e.g. nursing assistant) | 73 |
| Other patient care | 21 |
| Housekeeping/Environmental Services | 20 |
| Other nursing home/LTCF staff | 17 |
| Technicians | 15 |
| Management | 12 |
| Home health worker | 12 |
| Emergency medical personnel | 10 |
| Social work/counselor | 10 |
| Pharmacy | 9 |
| Food Services | 8 |
| Dentistry | 6 |
| Laboratory | 6 |
| Other | 57 |

# Long Term Care Facility Workforce

- Disproportionately lower-wage workers
- **39%** of workers are 50 years of age or older
- **82%** of workers are female, **26%** non-Hispanic Black persons
- Staff can be shared among multiple facilities
- In many instances, COVID-19 activity increases among LTCF **staff** first, and then residents

**Cases among Staff at Skilled Nursing Facilities**

Count and Incidence per 1,000 Resident Weeks




Data from NHSN LTCF module:
https://data.cms.gov/stories/s/COVID-19-Nursing-Home-Data/bkwz-xpvg/

NHSN NATIONAL HEALTHCARE SAFETY NETWORK

# Workers in Food Processing and Agriculture

- Among 14 states reporting total number of workers in affected **meat and poultry processing plants** from April–May 2020, COVID-19 diagnosed in **9.1**% of workers
  - Among cases with race and ethnicity reported, **87**% occurred among racial or ethnic minorities

- Outbreaks have been reported in many **food production/agriculture** sectors
  - Multiple factors that increase workers' risk for exposure to SARS-CoV-2:
    - Prolonged **close workplace contact** with coworkers
    - Shared transportation and/or congregate housing
    - Lack of paid sick leave

# Workers in Correction and Detention Facilities

- **Correction and detention** staff members can introduce the virus through their daily movements between the facility and the community

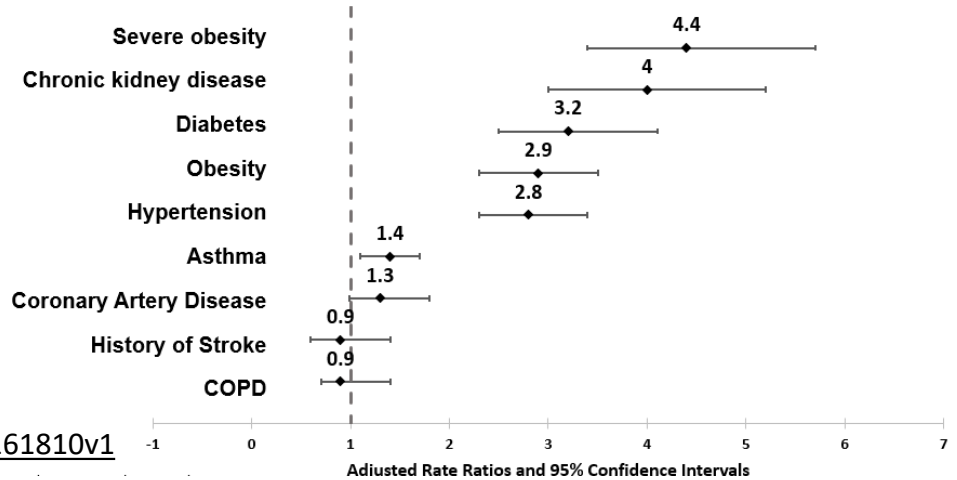
- In an analysis of 16 U.S. prisons and jails, more than half of the facilities identified their first case of COVID-19 among **staff** members[1]

[1]Hagan et al. MMWR – August 21, 2020 https://www.cdc.gov/mmwr/volumes/69/wr/mm6933a3.htm?s_cid=mm6933a3_w

# Adults with increased risk for severe COVID-19 disease

- Accounting for presence of individual underlying medical conditions, higher hospitalization rates were observed among **adults ≥65 years**

- Higher hospitalization rates observed for adults with **underlying medical conditions**, after accounting for age, race and ethnicity, and sex
  - Obesity
  - Chronic kidney disease
  - Diabetes
  - Hypertension




https://medrxiv.org/cgi/content/short/2020.07.27.20161810v1

# Work Group Interpretation-- Modeling

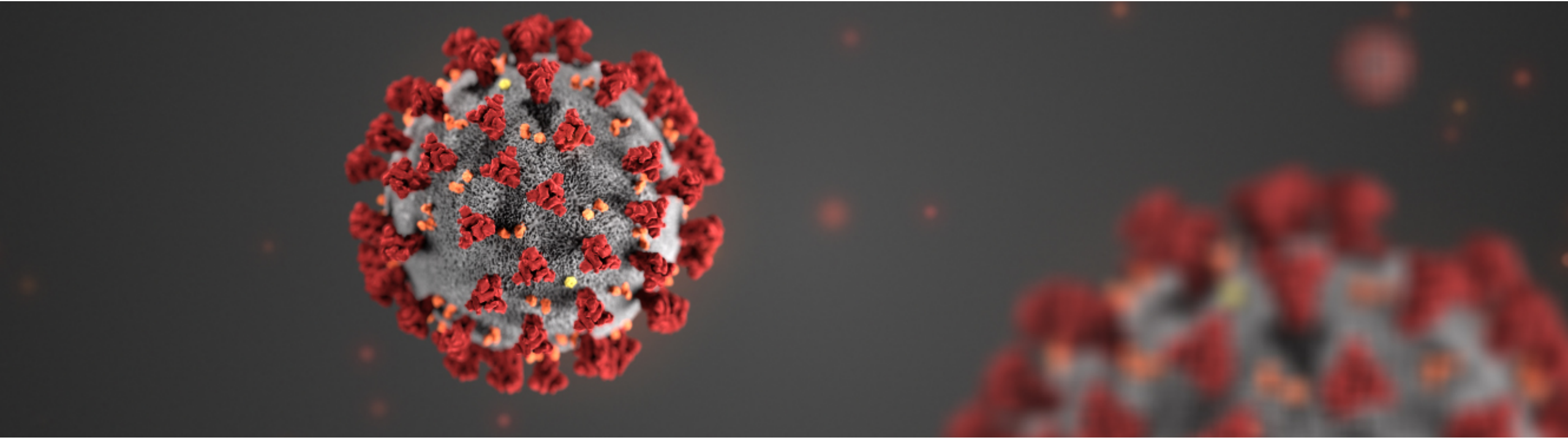
- **Population** model
  - Similar number of infections prevented by vaccinating HCP, essential workers and adults with underlying medical conditions
  - Vaccinating older adults resulted in more modest declines in infections and larger declines in deaths compared to other groups
  - Differences in impact between vaccinating different groups was small

- **Nursing Home** model
  - More infections and deaths prevented by vaccinating HCP compared to vaccinating NH residents

The more infection we prevent now, the more impact the vaccine will have

# Work Group Interpretation

- Many occupations (e.g. “essential workers”) at increased risk of COVID-19 disease
  - Important to consider individuals unable to socially distance or work from home
- **Older adults** and adults with **underlying medical conditions** also at increased risk of COVID-19 disease
  - Many essential workers also older or have an underlying medical conditions
- In many instances, cases increase first among **staff** in congregate settings (e.g. LTCF or correctional facilities)
  - Possible that some protection could be provided to these vulnerable populations by immunity among staff/workers



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

# Thank you

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.