COVID-19 & KIDS: UPDATE & VACCINE DEVELOPMENT

TeamPeds NAPNAP TOWN HALL
November 5, 2020

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Infectious Disease PNP
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@InfectiousPS on Twitter

President-Elect, National Foundation for Infectious Disease
Children’s Minnesota
Faculty Disclosure Announcement

- I have no financial disclosures or conflicts of interest

- I am a liaison member of the Center for Disease Control’s (CDC) Advisory Committee on Immunization Practices (ACIP) representing NAPNAP which have included attending special COVID vaccine meetings over the summer

- Thank you to Dr. Aimee Sznewajs at Children’s Minnesota for use of some slides

- ACIP meeting slides/audio available on their website 2 weeks after each meeting
Objectives

- Review the current COVID epidemiology
- Review general understanding of the virus and the immune responses
- Provide clinical updates on pediatric COVID-19
- Describe what is known about COVID-19 transmission in children
- Review current state of SARS- CoV2 vaccine platforms
- Discuss global vaccine distribution including tiered approach to delivery
- Review the importance of ethical principles including transparency in vaccine development
EPIDEMIOLOGICAL TRENDS
Global Cases: 48,005,784

Cases by Country/Region/Sovereignty:
- US: 9,480,195
- India: 8,313,876
- Brazil: 5,590,025
- Russia: 1,680,579
- France: 1,591,152
- Spain: 1,284,408
- Argentina: 1,205,928
- Colombia: 1,108,084
- United Kingdom: 1,102,305
- Mexico: 943,630

Cases by Region:
- North America: 48,005,784
- South America: 0
- Europe: 0
- Asia: 0
- Oceania: 0
- Africa: 0

Pediatric US Data:
- Total No. Children: 513,415
- % TOTAL COVID-19 cases: 9.8%
- Hospitalizations: 4,321 (0.7-3.7%)
- Mortality: 103 (0-0.3%)

Analysis by AAP and CHA, 9/3/2020
Fig 5. Cumulative Child COVID-19 Cases and Percent Increase in Child Cases

A. Cumulative Child COVID-19 Cases, 10/22/20
Nine states with 25,000+ cumulative child cases

B. Percent Increase in Child Cases, 10/8/20-10/22/20
From 10/8-10/22, there were 94,555 new child cases reported

See detail in Appendix. Data from 48 states, NYC, DC, and PR (TX excluded from figures).
All data reported by state/local health departments are preliminary and subject to change. Analysis by American Academy of Pediatrics and Children’s Hospital Association
Demographics: Race & Ethnicity

Race and ethnicity for confirmed and probable cases. Race and ethnicity is reported during case interview. Individuals who report more than one race are categorized into the multiple race category.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Minnesota Population (2018)</th>
<th>% of Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, non-Hispanic</td>
<td>4,438,071</td>
<td>80%</td>
</tr>
<tr>
<td>Black, non-Hispanic</td>
<td>336,505</td>
<td>6%</td>
</tr>
<tr>
<td>Asian, non-Hispanic</td>
<td>260,797</td>
<td>5%</td>
</tr>
<tr>
<td>American Indian/Alaska Native, non-Hispanic</td>
<td>53,168</td>
<td>1%</td>
</tr>
<tr>
<td>Native Hawaiian/Pacific Islander, non-Hispanic</td>
<td>1,799</td>
<td>4%</td>
</tr>
<tr>
<td>Multiple Races, non-Hispanic</td>
<td>137,233</td>
<td>2%</td>
</tr>
<tr>
<td>Other, non-Hispanic</td>
<td>7,021</td>
<td>4%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>292,764</td>
<td>5%</td>
</tr>
</tbody>
</table>

Minnesota Department of Health Weekly COVID-19 Report: Updated 10/29/2020 with data current as of 4 p.m. the previous day.
All Ages Affected but not equally:
Minnesota COVID-19 Data

Demographics: Age

Age groups, median age, and range for confirmed and probable cases.

<table>
<thead>
<tr>
<th>Age Group (in years)</th>
<th>Percent of Cases</th>
<th>All Cases (1/2)</th>
<th>Medium Age (Range) in Years</th>
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<tbody>
<tr>
<td>0-4</td>
<td>0</td>
<td>2,778</td>
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<td>5-9</td>
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<td>26,894</td>
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<td>65-69</td>
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<td>28,547</td>
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<tr>
<td>70-74</td>
<td>0</td>
<td>29,494</td>
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<td>75-79</td>
<td>0</td>
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Minnesota Department of Health Weekly COVID-19 Report: Updated 10/29/2020 with data current as of 4 p.m. the previous day.
### COVID-19 Hospitalization and Death by Age

#### Factors That Increase Community Spread and Individual Risk

<table>
<thead>
<tr>
<th>Rate ratios compared to 10-29 year olds</th>
<th>0-4 years</th>
<th>5-17 years</th>
<th>10-29 years</th>
<th>30-39 years</th>
<th>40-49 years</th>
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<th>85+ years</th>
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<tbody>
<tr>
<td>HOSPITALIZATION¹</td>
<td>4x lower</td>
<td>9x lower</td>
<td>Comparison Group</td>
<td>2x higher</td>
<td>3x higher</td>
<td>4x higher</td>
<td>5x higher</td>
<td>8x higher</td>
<td>13x higher</td>
</tr>
<tr>
<td>DEATH²</td>
<td>9x lower</td>
<td>16x lower</td>
<td>Comparison Group</td>
<td>4x higher</td>
<td>10x higher</td>
<td>30x higher</td>
<td>90x higher</td>
<td>220x higher</td>
<td>630x higher</td>
</tr>
</tbody>
</table>

#### Actions to Reduce Risk of COVID-19

- Wearing a mask
- Social distancing (6 ft goal)
- Hand hygiene
- Cleaning and disinfection

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[cdc.gov/coronavirus]
Pediatric COVID-19 Transmission

What Do We Know About Children and Coronavirus Transmission?
As of late July, children under the age of 18 account for:

- 9.8% of COVID-19 cases in the US
- 2% of COVID-19 hospitalizations
- <0.5% of COVID-19 deaths

Reference: Kaiser Family Foundation 2020
Take home messages

- 12 kids in 2 child care centers +
- 12 more infections from them in community
- COVID less severe in kids than adults
- Kids can transmit to parents
- 8 month old transmitted to both parents
- 2 of 3 asymptomatics confirmed spread
- 1 adult hospitalized
- Mask in kids 2 and older
- Daycare worker household ill needs quarantine
Findings from a prospective household study with intensive daily observation for ≥7 consecutive days indicate that transmission of SARS-CoV-2 among 191 household members was frequent from either children or adults.

Household transmission of SARS-CoV-2 from 101 index patients was common and occurs early after illness onset.

Persons should self-isolate immediately at the onset of COVID-like symptoms, at the time of testing as a result of a high risk exposure, or at time of a positive test result, whichever comes first.

Secondary infection rate of 53% (95% confidence interval [CI] = 46%–60%). Among fourteen households in which the index patient was aged <18 years, the secondary infection rate from index patients aged <12 years was 53% (95% CI = 31%–74%) and from index patients aged 12–17 years was 38% (95% CI = 23%–56%).

Approximately 75% of secondary infections were identified within 5 days of the index patient’s illness onset, and substantial transmission occurred whether the index patient was an adult or a child.

All household members, including the index case, should wear masks within shared spaces in the household.
Clinical Manifestations of COVID-19

**Neurologic:**
- Eyes: conjunctivitis
- ENT: Hyposmia, dysgeusia, lymphadenopathy

**Lungs:**
- Cough, sob, pneumonia, ARDS

**CV:**
- Myocarditis, cardiomyopathy, vasculitis

**GI:**
- Diarrhea, nausea/vomiting, abdominal pain

**Liver:**
- Transaminitis

**Heme:**
- Thrombosis

**Constitutional:**
- Fever → systemic inflammation

**Skin:**
- Rash

Mild: 90%

Asymptomatic
Moderate
Severe
Critical

Dong et al., Epidemiology of COVID-19 Among Children in China. Pediatrics. 2020; 145 (6)
Clinical Features: COVID vs Influenza

• **Study Design:**
  - Retrospective review
  - 315 children with COVID-19 and 1402 diagnosed with Flu A/B 2019-2020
  - Excluded asymptomatic COVID-19
  - March 25 to May 15, 2020

• **Clinical Characteristics:**
  - Similar rates of hospitalization (~ 20%), admission to ICU, use of mechanical ventilation
  - < 1 year and > 15 years more commonly hospitalized in COVID-19
  - Fever, diarrhea, vomiting, headache, body aches and chest pain found more often in hospitalized children with COVID-19
MIS-C in Children in the US

**Study Design:**
- 38 sites
- Prospective and retrospective surveillance of patients with MIS-C
- Study period: March 15 to May 20, 2020
- Standard case definition of MIS-C

**Clinical Characteristics:**
- Median age 8.3 years
- 27% had an underlying medical condition
- 80% required ICU admission and 1 in 5 needed mechanical ventilation
- 70% fully recovered, 28% still in hospital
- 4 deaths

*Figure 1. Statewide pooled percentages of positivity for SARS-CoV-2 laboratory testing of respiratory specimens from person < 21 years as compared with hospitalization dates for patients with MIS-C included from participating hospitals during study time period.*
Clinical Manifestations of MIS-C

**Constitutional:** Fever, systemic inflammation

**Eyes:** conjunctivitis

**ENT:** lymphadenopathy

**Lungs:** infiltrate, respiratory insufficiency and/or failure

**Heart (80%):** myocarditis, cardiomyopathy, vasculitis, hypotension, depressed function

**GI (91%):** abdominal pain, diarrhea, nausea/vomiting

**Skin (72%):** rash mucocutaneous

**Hematologic (76%):** DVT or pulmonary embolism

**Neurologic or Renal**

**CDC Case Definition:**
- < 21 years old with fever
- Lab evidence of inflammation
- Illness requiring hospitalization
- > 2 organ involvement
- No other reasons for disease
- Positive COVID testing now or recently
Immunity from COVID 19 Disease

Natalie J. Thornburg, PhD  Respiratory virus immunology team lead  ACIP SARS-CoV-2 working group  June 24, 2020

What is known

• Most COVID-19 patients mount IgG and IgM responses to the virus
• Many CoVID-19 patients mount neutralizing antibody responses
• Magnitude of antibody response correlates to disease severity

What is not fully known

• Are COVID-19 patients susceptible to reinfection?
• Are antibodies a correlate of immunity?
• If so, what quality (Isotype, antigenic region, neutralizing)?
• Is there a threshold of protection?
• How long will serum antibodies last?
Genetically what do we know?

• SARS CO-V2 has had a very slow genetic drift to date
• Seems to be a highly stable genome
• Remarkably low genetic diversity makes it well suited for a vaccine
• Difference in glycoproteins is main thing to follow
• Mutation rate is one third of influenza
COVID VACCINE UPDATE
Path from clinical development to recommendation

Clinical Development
- Generates safety, immunogenicity, and efficacy data
- Close coordination within OWS (DHHS [CDC, NIH, ASPR], DoD)
- Manufacturing of vaccine - could save months of time post-approval

FDA
- Licensure
- Emergency Use Authorization (AVA Anthrax for PEP)
- Expanded Access IND (MenB vaccine during college outbreaks)

ACIP
- Review Evidence, utilize Evidence to Recommendation Framework
- Make recommendations regarding the use of vaccines to the CDC Director

CDC Recommendation
Post-approval monitoring
Vaccine Approval & Distribution Plan

Framework for Equitable Allocation of COVID-19 Vaccine
ACIP Meeting Presentation 10.30.20

Vaccine Update Summary

- 248 COVID-19 vaccines currently under development
  - 91 candidates are in human trials worldwide
    - 10 vaccines in human trials within the United States
      - 5 candidates are actively recruiting in the United States
    - 84 candidates are in human trials outside the US
      - 2 candidates have completed trials in Russia
      - 51 candidates outside of the US are recruiting participants
        - 16 candidates recruiting are in Phase III
          - 4 candidates are approved for emergency use in Brazil, China, Indonesia, and UAE

Expect 50% efficacy vs placebo with CI lower bound >30%
At least half of subjects followed up for at least 2 months
Safety data in well over 3K recipients:
  - reactogenicity,
  - adverse events,
  - at least some severe disease prevention
# COVID-19 vaccines in human clinical trials – United States*

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Manufacturer</th>
<th>Type</th>
<th>Phase</th>
<th>Trial characteristics</th>
<th>Trial #</th>
<th>Recruiting</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1273</td>
<td>Moderna TX, Inc.</td>
<td>mRNA</td>
<td>III</td>
<td>2 doses (0, 28d)</td>
<td>NCT04470427</td>
<td>Enrollment complete</td>
</tr>
<tr>
<td>mRNA-BNT162</td>
<td>Pfizer, Inc./BioNTech</td>
<td>mRNA</td>
<td>II/III</td>
<td>Single or 2 doses</td>
<td>NCT04368728</td>
<td>✓</td>
</tr>
<tr>
<td>AZD1222</td>
<td>University of Oxford/AstraZeneca consortium**</td>
<td>Viral vector (NR)</td>
<td>III</td>
<td>2 doses (0, 28d)</td>
<td>NCT04516746</td>
<td>✓</td>
</tr>
<tr>
<td>Ad26COV51</td>
<td>Janssen Pharmaceutical Companies</td>
<td>Viral vector (NR)</td>
<td>III</td>
<td>1 or 2 doses (0, 56d)</td>
<td>NCT04436276</td>
<td>✓</td>
</tr>
<tr>
<td>--</td>
<td>Sanofi/GSK</td>
<td>Protein Subunit</td>
<td>I/II</td>
<td>Single or 2 doses</td>
<td>NCT04537208</td>
<td>✓</td>
</tr>
<tr>
<td>NVX-CoV2373</td>
<td>Novavax</td>
<td>Protein Subunit</td>
<td>I/II</td>
<td>2 doses (0, 21d)</td>
<td>NCT04368988</td>
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<tr>
<td>V591</td>
<td>Merck</td>
<td>Viral Vector</td>
<td>I/II</td>
<td>2 doses (1, 57d)</td>
<td>NCT04498247</td>
<td>✓</td>
</tr>
</tbody>
</table>

*As of October 27, 2020
**Currently on hold in US

Understanding the virus for vaccine development

Basic Structure of *Coronavirinae*

- Single-stranded RNA viruses
- Genomes range from 25 to 32 kilobases
- The coronaviral genome encodes **four major structural proteins**
  (all are required to produce a structurally complete viral particle)
  - Spike (S) protein: binding
  - Nucleocapsid (N) protein: RNA synthesis
  - Membrane (M) protein: organization/assembly
  - Envelope (E) protein: organization/assembly

Image by Belouzard, et al - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3397359/, CC BY 3.0,
https://commons.wikimedia.org/w/index.php?curid=2644769
Here is a look at how different vaccine technologies being developed around the world would ideally elicit an immune response to prevent SARS-CoV-2 in humans. Each vaccine may vary somewhat in how it works, but each would generally follow these steps.
Phase I/II: Determining safety & dose
Published on September 2, 2020, at NEJM.org. DOI: 10.1056/NEJMoa2026920 Accessed 11.5.2020

The NEW ENGLAND JOURNAL OF MEDICINE

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

Phase III: Check efficacy in diverse subjects

Race and ethnicity

Interim data snapshot - October 21, 2020 - subject to change

- White: 63%
- Hispanic/Latinx: 20%
- Black/AA: 10%
- Asian: 4%
- All others: 3%

© Moderna 2020
Representative Subjects important

Risk factors for severe COVID-19 disease

Interim data snapshot - October 21, 2020 - subject to change

Risk stratification in Cove Study

- >=65 years: 58%
- >=18 and <65 years and at risk of severe disease: 25%
- >=18 and <65 years and not at risk of severe disease: 17%

Comorbidities of at risk participants in Cove Study

- Diabetes: 36%
- Severe Obesity: 19%
- Significant Cardiac Disease: 18%
- Chronic Lung Disease: 25%
- Liver Disease: 2%
Enrollment transparency

A vaccine for everyone...find yourself in the Cove study

- Hispanic
  6,000+ participants
- Educators and Students
  9% of participants
- African American
  3,000+ participants
- Over 65 years of age
  25% of participants
- Male
  53% of participants
- Ages 25-44
  29% of participants
- Healthcare Workers
  22% of participants
- Living with chronic diseases
  Over 8,000 participants
- Female
  Over 14,000 participants
- Ages 45-64
  39% of participants
- Retail, Restaurant, & Hospitality workers
  Almost 2,000 participants
What about kids?

Current enrollment status

- BNT/Pfizer Phase III expanded to 16 & 17 year olds in September
- Sinovac Phase I/II in China registered to enroll 522 kids age 3-17 years
- Sinovac Phase III in Brazil registered to enroll children, pregnant women and older adults >60 years
# VACCINE PLATFORMS

## Virus
- **Inactivated** (polio & flu vaccine)
  - Humoral immune response
  - Antibody titers diminish with time
  - Requires repeat doses
- **Live, attenuated, weakened** (MMR)
  - Mimics human immune response
  - Both humoral and cellular
  - Few doses required for lasting protection

## Viral Vector
- **Replicating** (weakened, Measles)
- **Non-replicating** (Adenovirus) new technology, non-licensed
  - Viral Vector example (Ebola)
  - Stimulates humoral and cellular immune response
  - Single dose highly protective

## Protein Based
- **Protein Based**
- **Protein sub-unit** (flu, pertussis, Hep B)
- **Virus-like particles** (HPV)

## Nucleic Acid
- **DNA spike gene**
- **mRNA encased lipid coat**
  - Unlicensed, new technology
  - Stimulates T and B cell immune response
  - Multiple doses required
  - Stability requires extreme cold
  - Makes genetic material, not virus.
  - Safe but unproven
Weakened or Inactivated Vaccines

Weakened and inactivated virus vaccines, developed by...

<table>
<thead>
<tr>
<th>Vaccine Provider</th>
<th>PC</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>A</th>
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<td>Beijing Institute of Biological Products; Sinopharm</td>
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<td>Sinopharm</td>
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<tr>
<td>Sinovac</td>
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Viral Vectored Vaccines

Viral-vectored vaccines, developed by...

AstraZeneca; University of Oxford

CanSino Biologics; Beijing Institute of Biotechnology; Canada’s National Research Council; Petrovax

Gamaleya Research Institute*
Vaccines using nucleic acid (DNA or RNA)

DNA vaccine
- Spike gene on DNA
- mRNA in lipid shell

RNA vaccine

An electric pulse allows DNA into the cell's nucleus where it forms mRNA, then creates spike proteins.

Antigen-presenting cells (APCs) consume the viral proteins and pass viral peptides to T-helper cells.

Cytotoxic T cells may eliminate virus-infected cells.

A lipid shell delivers mRNA into the cell, where it is used to produce proteins.

Antibodies from B-cells may block the virus.

Nucleic acid vaccines, developed by...

- Moderna; National Institutes of Health
- Pfizer; BioNTech; Fosun Pharma
- AnGes; Osaka University; Takara Bio
- Arcturus Therapeutics; Duke-NUS
Subunit Protein Particle Vaccines

**The Washington Post**

*Democracy Dies in Darkness*

**Subunit vaccines, developed by...**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>PC</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novavax</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anhui Zhifei Longcom; Chinese Academy of Sciences</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Federal Budgetary Research Institution (FBRI) State Research Center of Virology and Biotechnology &quot;VECTOR&quot;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instituto Finlay de Vacunas</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Work Group considerations: Further tiering of target groups may be necessary based on vaccine supply and program planning.
Vaccine Implementation Plan

MULTIPLE CRITICAL COMPONENTS TO VACCINE IMPLEMENTATION

Communication and Stakeholder Guidance
(state, tribal, local, special populations, private sector partners, public)

Prioritizing population → Allocation of Vaccine → Distribution (MFR - Dist - State) → Administration → Safety, Effectiveness, Uptake, Second dose → Vaccine Recovery

- Supply - Monitor, Track, Report
- Vaccine Uptake, Use, and Coverage
- ADE and Vaccine Effectiveness Monitoring and Reporting

Data

Regulatory Considerations

Public health impact relies on rapid, efficient, and high uptake of complete vaccine series, with focus on high-risk groups
The COVID-19 Vaccination Program will require a phased approach

Phase 1: Potentially Limited Doses Available
- Projected short period of time for when doses may be limited
- Key factors:
  - Supply may be constrained
  - Tightly focus vaccine administration
  - Administer vaccine in closed settings best suited for reaching initial critical populations (workplaces, other vaccination sites) specific to Phase 1-A populations

Phase 2: Large Number of Doses Available
- Likely sufficient supply to meet demand
- Expand beyond initial populations
- Use a broad provider network and settings, including:
  - Healthcare settings (doctor’s offices, clinics)
  - Commercial sector settings (retail pharmacies)
  - Public health venues (public health clinics, mobile clinics, FDAs, community settings)

Phase 3: Continued Vaccination, Shift to Routine Strategy
- Likely sufficient supply
- Open access to vaccination
- Administer through additional/private partner sites
- Maintain public health sites where required

**Populations of Focus**

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1-A:</td>
<td>Remainder of Phase 1 populations</td>
<td>Remainder of Phase 1 populations</td>
</tr>
<tr>
<td>- Paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to patients or infectious material and are unable to work from home.</td>
<td>- Critical populations**</td>
<td>- Critical populations**</td>
</tr>
<tr>
<td>Phase 1-B:</td>
<td>General population</td>
<td>General population</td>
</tr>
<tr>
<td>- Other essential workers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- People at higher risk of severe COVID-19 illness, including people 65 years of age and older.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Planning should consider that there may be initial age restrictions for vaccine products.

** See Section 4: Critical Populations for information on Phase 1 subset and other critical population groups.

Phase 1
- **Phase 1a “Jumpstart Phase”**
  - High-risk health workers
  - First responders
- **Phase 1b**
  - People of all ages with comorbid and underlying conditions that put them at significantly higher risk
  - Older adults living in congregate or overcrowded settings

Phase 2
- K–12 teachers and school staff and child care workers
- Critical workers in high-risk settings—workers who are in industries essential to the functioning of society and at substantially higher risk of exposure
- People of all ages with comorbid and underlying conditions that put them at moderately higher risk
- People in homeless shelters or group homes for individuals with disabilities, including serious mental illness, developmental and intellectual disabilities, and physical disabilities or in recovery, and staff who work in such settings
- People in prisons, jails, detention centers, and similar facilities, and staff who work in such settings
- All older adults not included in Phase 1

Phase 3
- Young adults
- Children
- Workers in industries and occupations important to the functioning of society and at increased risk of exposure not included in Phase 1 or 2

Phase 4
- Everyone residing in the United States who did not have access to the vaccine in previous phases

**Equity is a crosscutting consideration:** In each population group, vaccine access should be prioritized for geographic areas identified through CDC’s Social Vulnerability Index or another more specific index.
Scenario 3: FDA has authorized vaccines A and B for EUA in 2020

### Availability Assumptions

<table>
<thead>
<tr>
<th>Vaccine availability under EUA by</th>
<th>End of Oct 2020</th>
<th>End of Nov 2020</th>
<th>End of Dec 2020</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine A</td>
<td>~2M doses</td>
<td>10M–20M doses</td>
<td>20M–30M doses</td>
<td>Ultra-cold (-70 °C), for large sites only</td>
</tr>
<tr>
<td>Vaccine B</td>
<td>~1M doses</td>
<td>~10M doses</td>
<td>~15M doses</td>
<td>Central distribution capacity required (-20 °C)</td>
</tr>
<tr>
<td>Total</td>
<td>~3M doses</td>
<td>20M–30M doses</td>
<td>35M–45M doses</td>
<td></td>
</tr>
</tbody>
</table>

### Distribution, Storage, Handling, and Administration Assumptions

#### Vaccine A

**SHIPMENT**

3 separately acquired components (mixed on site)

1. Vaccine
   - Direct to site from manufacturer (on dry ice)
   - Multidose vials (5 doses/vial)
2. Diluent
   - Direct to site from USG (at room temperature)
3. Ancillary supply kits
   - Direct to site from USG (at room temperature)

**ON-SITE VACCINE STORAGE**

Frozen (-70 °C ± 10 °C)

- Must be used/recharged within 10 days
- Storage in shipping container OK (replenish dry ice within 24 hours of receiving shipment and again 5 days later)

Thawed but NOT reconstituted (2–8 °C)

- Must use within 5 days (discard unused doses after 5 days)

Reconstituted (room temperature)

- Must use within 6 hours (discard any unused, reconstituted vaccine after 6 hours)
ACIP Ethical Principles: Emergency COVID vaccine meeting 10.30.2020 CDC ACIP Meeting Minutes

• Maximize benefits and minimize harms

• Promote justice (fairness folded in)

• Mitigate health inequities

• Promote transparency
How is this going so fast?
Vaccine Safety  ACIP Meeting 9.22.2020

- *Safety is not the absence of risk it is the balance of risk.*  Dr. Grace Lee
- Safety and efficacy are primary goals with full commitment for no short cuts
- Expect safety signals like the transverse myelitis—explore, background incidence, etc

- **V-SAFE program** Vaccine Safety Assessment for Essential Workers
- Smart Phone app active surveillance daily sx check in
- Numerator for incidences of site pain, adverse events
- VAERS will be active, electronic surveillance as usual

- Hospitals will track weekly doses to NHSN for denominator
V-Safe CDC program

Vaccine safety assessment for essential workers (V-SAFE)

1. Text messages or email from CDC with follow-up – daily 1st week post-vaccination and weekly thereafter out to 6 weeks

2. Any clinically important event(s) reported by vaccinated person

3. Follow-up on clinically important event, complete a VAERS report if appropriate

Healthcare workers, essential workers, etc.
Vaccinate with Confidence CDC plan


Vaccinate with Confidence

CDC’s strategic framework for strengthening vaccine confidence and preventing outbreaks of vaccine preventable diseases.

Protect communities
- Leverage immunization data to find and respond to communities at risk
- Work with trusted local partners to reach at-risk communities before outbreaks
- Ensure vaccines are available, affordable, and easy-to-get in every community

Empower families
- Expand resources for health care professionals to help them have effective vaccine conversations with parents
- Work with partners to start conversations before the first vaccine appointment
- Help providers foster a culture of immunization in their practices

Stop myths
- Work with local partners and trusted messengers to improve confidence in vaccines among key, at-risk groups
- Establish partnerships to contain the spread of misinformation
- Educate key new stakeholders (e.g., state policy makers) about vaccines
Phase 4: Ongoing Safety Marketing as always

JAMA Published online October 16, 2020

Postapproval Vaccine Safety Surveillance for COVID-19
Vaccines in the US

Since January 2020, more than 7.8 million cases of coronavirus disease 2019 (COVID-19) and 215,000 deaths have occurred in the US. In response to the pandemic, vaccine development has been moving at record speed through strong public or private partnerships, with nearly 200 vaccine candidates in development or in trials. In the US, 8 vaccine candidates have received federal support under Operation Warp Speed, and 4—from Moderna, Pfizer/BioNTech, Oxford/AstraZeneca, and Janssen—have entered phase 3 trials. Vaccines will be critical for the prevention and control of COVID-19 in the US and worldwide, yet these efforts cannot succeed without public confidence in a vaccination program. Demonstrating vaccine efficacy and safety during clinical trials and implementing a robust postlicensure vaccine safety monitoring system as the vaccine is deployed in larger, more diverse populations is central to public confidence and enabling timely and accurate policy decisions for population-level use.

VoST is reviewing the capabilities and protocols of existing and novel vaccine safety surveillance systems that will be engaged in COVID-19 vaccine safety. A brief overview of key considerations for postauthorization/postlicensure safety surveillance is outlined below, as a starting point for public discussions about plans for COVID-19 vaccine safety monitoring.

In addition to phase 4 studies to monitor safety and effectiveness, passive and active surveillance systems serve critical functions in ensuring vaccine safety and maintaining vaccine confidence (see Table in the Supplement). The Vaccine Adverse Event Reporting System (VAERS) is a passive surveillance system that relies on reporting by patients or family members, healthcare professionals, or manufacturers to capture temporally associated, potential adverse events after vaccination.5 VAERS is comanaged by the FDA and CDC and serves as an early warning system for potential safety signals that may be temporally related to vaccines. The rapid iden-

• VAERS
• CISA
• Vaccine Safety Datalink
• Manufacturer Post-license monitoring
Resources

✓ Clinicaltrials.gov for vaccine research update
✓ cdc.gov/acip for latest slides, audio, upcoming agendas
✓ Coronaviruspreventionnetwork.org for trials enrollment

https://www.childrensmn.org/for-health-professionals/talking-pediatrics-podcast/
  • Clinical practice guidelines
  • COVID-19 updates
  • Health equity
  • AND MORE
Questions?
THANK YOU
## Five Phase III vaccine trial summary

<table>
<thead>
<tr>
<th></th>
<th>Pfizer/BioNTech mRNA</th>
<th>Moderna mRNA</th>
<th>Astra-Zeneca Adeno V</th>
<th>J&amp;J Adeno V</th>
<th>Novavax</th>
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<tbody>
<tr>
<td><strong>Sample Size</strong></td>
<td>30,000</td>
<td>30,000</td>
<td>30,000</td>
<td>60,000</td>
<td></td>
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<tr>
<td><strong>Vaccine Arm</strong></td>
<td>15,000</td>
<td>15,000</td>
<td>15,000</td>
<td>20,000</td>
<td>30,000</td>
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<tr>
<td><strong>Severity Primary</strong></td>
<td>+</td>
<td>++</td>
<td>++</td>
<td>++1/2</td>
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<tr>
<td><strong>endpoint</strong></td>
<td>All include mild infxn, diff criteria</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Efficacy target</strong></td>
<td>60%</td>
<td>60%</td>
<td>50%</td>
<td>60%</td>
<td></td>
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<tr>
<td><strong># of doses</strong></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
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<tr>
<td><strong>Freezing Required?</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td><strong>Lower 95% CI efficacy</strong></td>
<td>30%</td>
<td>30%</td>
<td>30%</td>
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<tr>
<td><strong>Events at Completion</strong></td>
<td>N = 164</td>
<td>151</td>
<td>150</td>
<td>154</td>
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<tr>
<td><strong>Interim Analyses N =</strong></td>
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<td>2</td>
<td>1</td>
<td>NA</td>
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<tr>
<td><strong>Events at 1st Interim Analysis N =</strong></td>
<td>37</td>
<td>53</td>
<td>75</td>
<td>NA</td>
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