



# Storage and Handling of the COVID-19 Vaccines

**James Allen, MD**

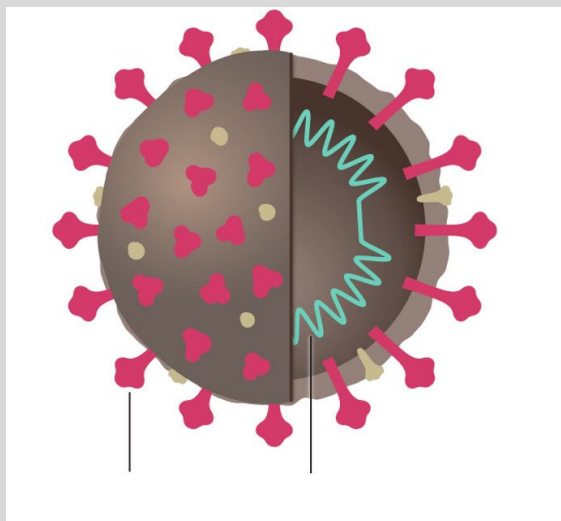
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**MedNet21**  
Center for Continuing Medical Education



**Spike Protein**



**Spike Protein**

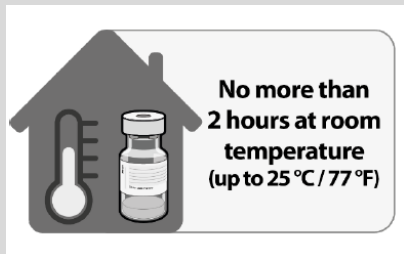
## Pfizer COVID-19 Vaccine

- Storage: -76° to -112° F
  - Temporary storage in dry ice
  - Cannot refreeze thawed vials
- Thawing:
  - In refrigerator: 35° to 46° F for 2-3 hours
    - Can store in refrigerator up to 5 days
    - Must use within 6 hours of dilution
  - Room temperature: 77° F for 30 minutes
    - Must use within 2 hours

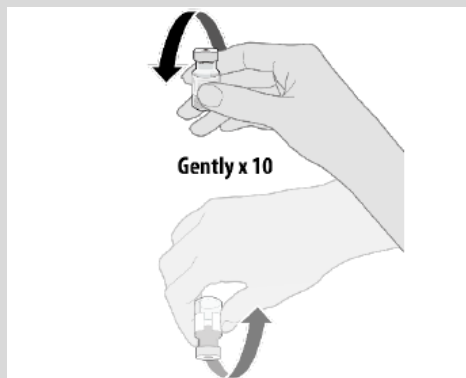
## Pfizer COVID-19 Vaccine

- Dilution:
  - Thaw vial
  - Invert vial *gently* 10 times
  - Add 1.8 ml 0.9% sodium chloride injection USP
    - NOT bacteriostatic sodium chloride injection
- Each vial contains 6 doses, 0.3 ml each
- Administer intramuscularly

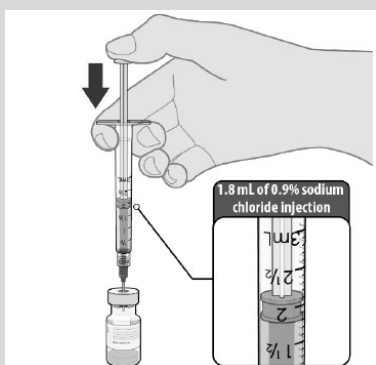
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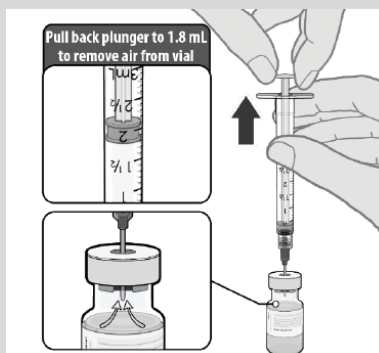
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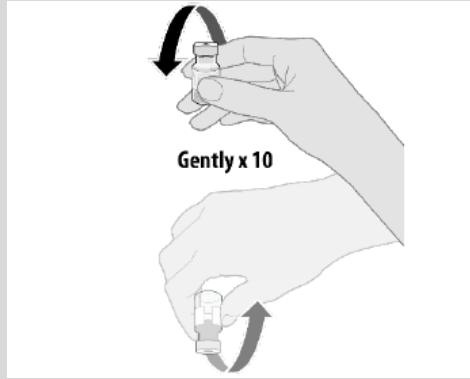
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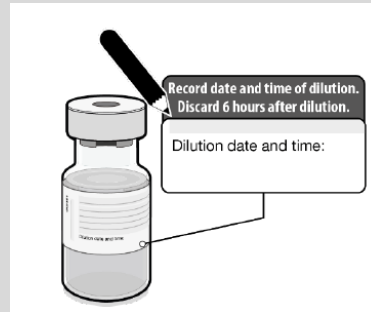
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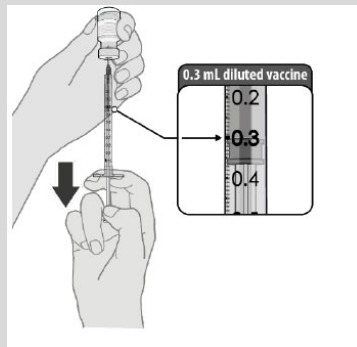


**6**



Store at 35° to 77° F  
for up to 6 hours

**7**



Do not pool vaccine  
from multiple vials for  
any single injection

## **Pfizer COVID-19 Vaccine: What's in the vial?**

- Lipids
- Polyethylene glycol
- Cholesterol
- Potassium chloride
- Potassium phosphate
- Sodium chloride
- Sucrose
- 30 mcg mRNA to the spike glycoprotein
- Vial stopper does **NOT** contain natural rubber latex
- Vaccine is preservative-free

## **Moderna COVID-19 Vaccine**

- Storage: -13° to 5° F
  - DO NOT store in dry ice or below -40° F
  - Can store refrigerated 36° to 46° F for 30 days
  - Cannot refreeze thawed vials
- Unpunctured vials 46° to 77° F for 12 hours
- Punctured vials 36° to 77° F for 6 hours

## Moderna COVID-19 Vaccine

- Thaw in refrigerator 2 hours 30 minutes
  - After thawing, let stand 15 minutes at room temperature
- Alternatively thaw at room temperature 1 hour

## Moderna COVID-19 Vaccine

- Swirl gently
  - **DO NOT** shake
- Each dose = 0.5 ml
- Vials contain 10 doses
- Administer intramuscularly
- FDA-approved for 18 years and older

## Moderna COVID-19 Vaccine: What's in the vial?

- Lipids
- Polyethylene glycol
- Cholesterol
- Tromethamine
- Acetic acid
- Sodium acetate
- Sucrose
- 100 mcg mRNA to the spike glycoprotein
- Vial stopper does **NOT** contain natural rubber latex
- Vaccine is preservative-free





# Vaccine Administration Logistics

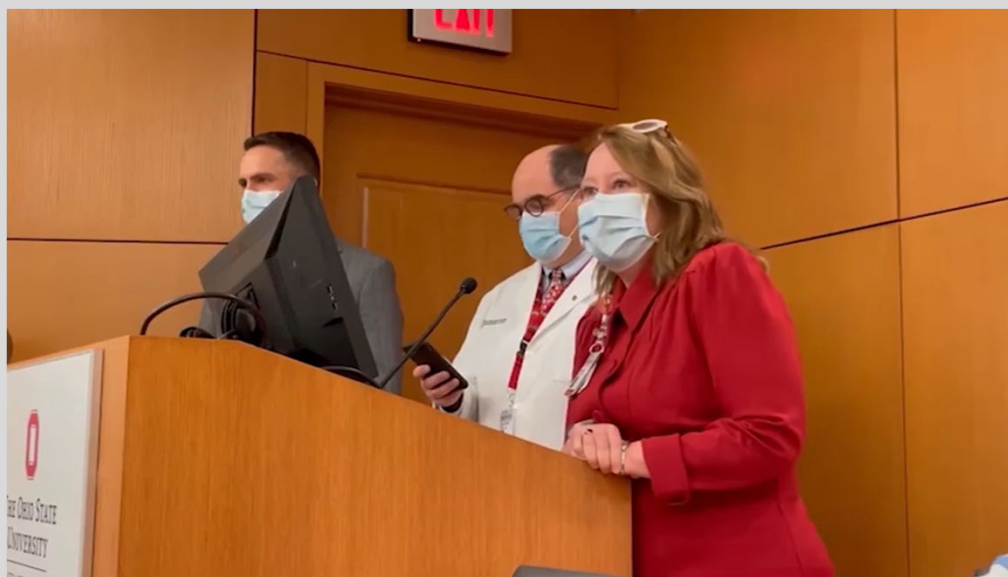
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**MedNet21**  
Center for Continuing Medical Education

**THE OHIO STATE UNIVERSITY**  
WEXNER MEDICAL CENTER

## Our First Doses Administered





## Assembling the Teams

- Vaccine Prioritization: Dr. Nick Kman & Dr. Ryan Nash
  - Goal: Defining and Implementing the Prioritization of Vaccine
  - Met 3x week
- Vaccine Administration: Dr. Crystal Tubbs & Ryan Haley
  - Goals: Managing Supply Chain & Administration Process
  - Met 2x week but had multiple subgroups
- Vaccine Education: Beth Necamp
  - Goals: Developing education for internal and external groups
  - Established later in the process

## Assembling the Workforce

- Vaccine Administration Roles
  - Manager
  - Scheduling (Call Center)
  - Pharmacist Station
  - Check-In / Registration Staff
  - Runner/Navigator
  - Vaccinator
  - Physician
  - Campus Police
- Indirect Support
  - IT
  - Marketing
  - Legal Services
  - Revenue Cycle
  - Volunteer / Staffing Management

## The Vaccine Administration Process

- Before the Visit
  - Invitations / Notifications
  - Scheduling (Online vs Phone) w/screening questions
  - Reminders
- Day of the Visit
  - Arrival / Check-In
  - Review of Screening Questions
  - **Vaccine Administration**
  - Post-vax monitoring (15 min vs 30 min)
  - Full registration
  - Scheduling of 2<sup>nd</sup> visit
- After the Visit
  - Billing for Service
  - Post-vax Nurse Line
  - Vsafe reporting

## Safety

- Universal masking
- Physical distancing both in lines and at the vaccine stations
- Visual indicators to demonstrate whether vaccine station is clean or dirty
- One way traffic flow
- Vaccine screening questions
- Vaccine manufacturer double checks

## Supply Chain / Schedule Management

- Managing the extreme variability of weekly supply (ranging from 975 in a week to 8850)
- Balancing allocated supply with specific number of appointment slots (how much risk do you take?)
- Multiple manufacturers
- 1<sup>st</sup> Dose vs 2<sup>nd</sup> Dose
- Visit Type by Manufacturer
- Goal to get all shipments out within 7 days or less of receipt
- ZERO DOSES WASTED from overdraws

## Communication / education

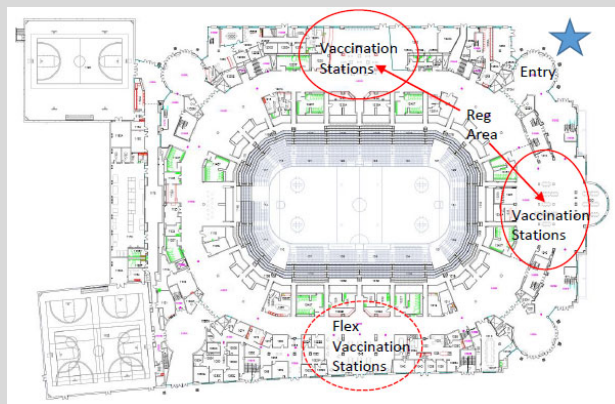
- Town halls
- eLearning
- HealthBeat Hub FAQs
- Daily updates from chancellor
- Vaccine email address

## OSUWMC's Vaccine Hours Locations

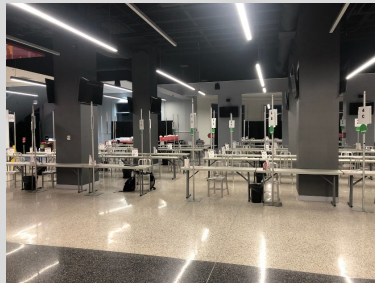
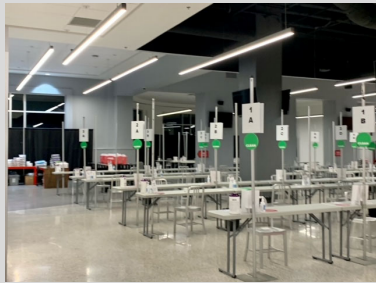
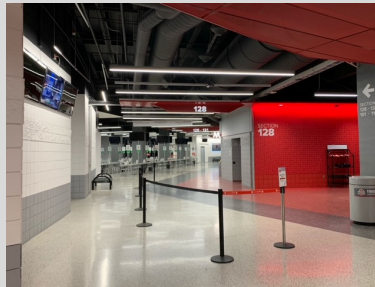
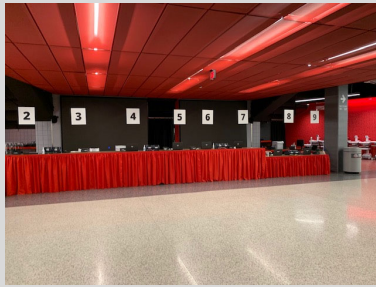
- Initially used 3 different locations on campus
  - Biomedical Research Tower (capacity 900 patients per day)
  - East Hospital Conference Room (capacity 450 patients per day)
  - Ackerman Administrative Building (capacity 1100 patients per day)
- Days and Hours – somewhat dependent upon demand
  - M-F 7a-7p (12 hours, w/10.5 hours of vaccine uptime)
  - Saturdays 7a-3p (8 hours, w/7 hours of vaccine uptime)

## Scaling Up: Shots at the Schott

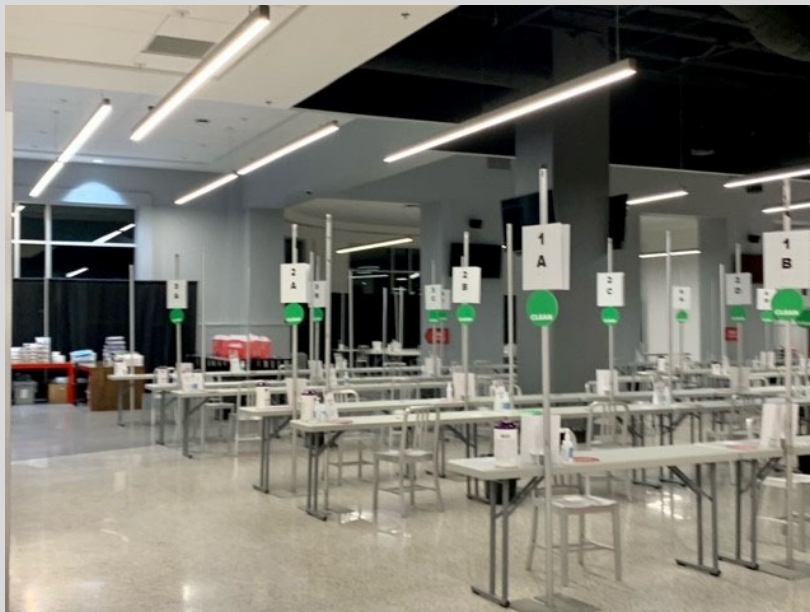
- Schottenstein Center
  - 2 Concourses (~150-160 vaccine stations)
  - Max capacity in 12 hour shift ~ 3K
  - Goal of 2 table turns per hour



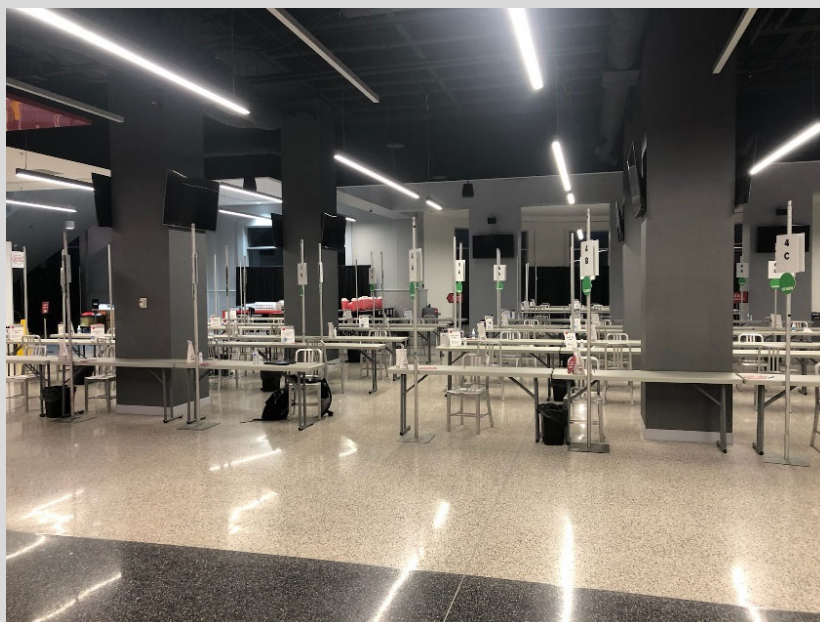
### Schottenstein Center Pictures



### Schottenstein Center Pictures



## Schottenstein Center Pictures



## mRNA COVID-19 Vaccines

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*Medical Director of Clinical Epidemiology, Ross Heart Hospital  
Assistant Professor of Medicine, Department of Internal Medicine  
Division of Infectious Diseases*

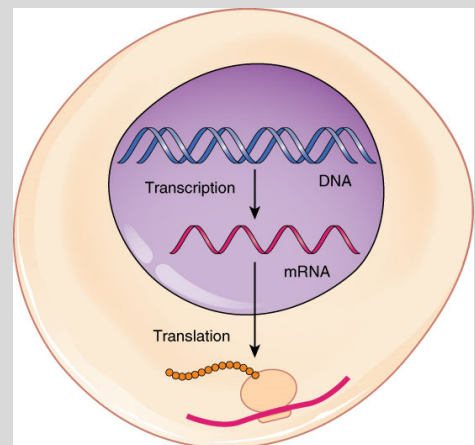
*The Ohio State University Wexner Medical Center*

## Traditional Vaccines

| Type of Vaccine   | Mechanism of Action  | Examples  |
|---|--|---|
| Live-attenuated   | Weakened virus that infects cells and induces immune response.   | Measles, Mumps, Rubella<br>Variola (Smallpox)<br>Varicella (Chickenpox)<br>Yellow Fever<br>Influenza (intranasal) |
| Inactivated   | Virus is inactivated. Not pathogenic to host, but can induce an immune response.                                   | Hepatitis A<br>Rabies<br>Influenza (IM)   |
| Subunit<br>(recombinant,<br>polysaccharide,<br>conjugate) | Antigenic material (sugar, protein, etc) that are components of the organism are used to induce an immune response | <i>Haemophilus influenzae</i> type b<br>Hepatitis B<br>HPV<br>Pneumococcus<br>Meningococcus                       |
| Toxoid  | Toxin produced by the organism is inactivated and used to induce an immune response.                               | Diphtheria<br>Tetanus   |

## Nucleic Acid Vaccines

- Nucleic acid that encodes the desired antigenic protein is inserted into the cell.
- The cell uses its own machinery to transcribe and/or translate the nucleic acid into the protein.
  - DNA Plasmid
    - Examples: Zika, influenza
  - Viral Vector
    - Examples: Zika, HIV, Ebola, SARS-CoV-2
  - mRNA Vaccines



Source: <https://cnx.org/contents/FPtK1zmh@8.25:fEi3C8Ot@10/Preface>

## mRNA Vaccine Research

- 1990 - 1<sup>st</sup> successful use in animal model of mRNA was injected into mice and protein production was detected
- Very promising technology for vaccines against infectious agents, cancer therapies, and protein replacement therapies.

| <u>Early Barriers</u>                             | <u>Advancements</u>   |
|---|---|
| Rapid mRNA degradation                            | Development of cationic lipid/polymer molecules to usher the mRNA in the cell |
| Inefficient <i>in vivo</i> delivery into the cell |   |
| High innate immunogenicity                        | Immunogenicity can be down-regulated  |

Parti et al. Nature Reviews. 2018.

## Types of mRNA Vaccines

|                           | Delivery Method                                       | Pathogens Studied  |
|---------------------------|---|--|
| <b>1. Self-Amplifying</b> | Complex to lipid nanoparticle and injected into host  | RSV, influenza, CMV, HCV, rabies, HIV, Ebola, Zika<br><i>Toxoplasma gondii</i><br>Group A Strep, Group B Strep |
| <b>2. Non-replicating</b> | <i>Ex vivo</i> loading of DC, then infusion into host | HIV, CMV   |
|                           | Complex to lipid nanoparticle and injected into host  | <b><i>Influenza</i></b> , rabies, HIV, <b><i>Zika</i></b>  |

Parti et al. Nature Reviews. 2018.

Feldman et al. Vaccine. 2019 May 31;37(25):3326-3334.



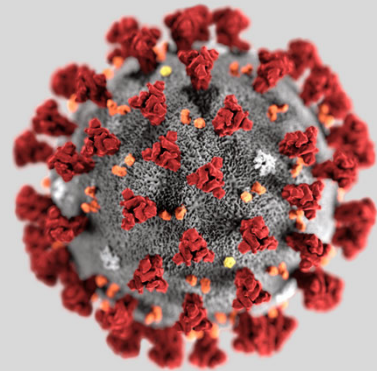
## mRNA - promising alternative to traditional vaccine methodologies

- **Safety**
  - No potential risk of infection
  - Non-integrating platform
  - Degraded by normal cellular processes
  - High innate immunogenicity can be down-regulated
- **Efficacy**
  - mRNA can be modified to be more stable and highly translatable
  - Carrier/delivery molecules have been developed to efficiently deliver the mRNA into the cytoplasm before degradation can occur
- **Production**
  - Able to implement rapid, inexpensive, scalable manufacturing

Parti et al. Nature Reviews. 2018.

## SARS-CoV-2 Vaccine Candidates in Phase 3 Trials

| Type of Vaccine     | Sponsor   |
|---------------------|---|
| mRNA                | Pfizer<br>Moderna                                 |
| Viral Vector        | Astra Zeneca/Oxford<br>Janssen (J&J)<br>CanSino   |
| Recombinant Protein | Novavax   |
| Inactivated         | Sinovac<br>Wuhan Institute of Biological Products |



This media comes from the Centers for Disease Control and Prevention's Public Health Image Library (PHIL), with identification number #23312.  
<https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines/>

## Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine

- Published in NEJM December 2020
- Multinational, placebo-controlled, observer-blinded efficacy trial
- 16 and older
- 1:1 randomization of placebo vs BNT162b2 vaccine candidate
  - Lipid nanoparticle-formulated, nucleoside-modified RNA vaccine that encodes the SARS-CoV-2 full-length spike protein

Polack et al. NEJM 2020;383:2603-15.

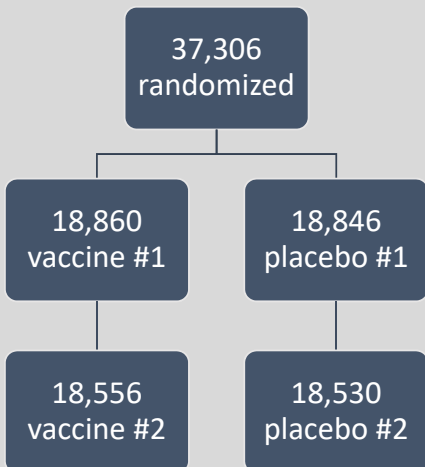
## Primary Endpoints

- Efficacy
  - Confirmed COVID-19 at least 7 days after 2<sup>nd</sup> dose in subjects with no history of infection
  - Confirmed COVID-19 in all subjects regardless of past infection
- Safety
  - Solicited adverse events and use of antipyretics within 7 days of injection
  - Unsolicited adverse events through 1 month after 2<sup>nd</sup> dose and serious adverse events through 6 months after 2<sup>nd</sup> dose

**Confirmed COVID-19** = at least 1 symptom + positive NAAT test

Polack et al. NEJM 2020;383:2603-15.

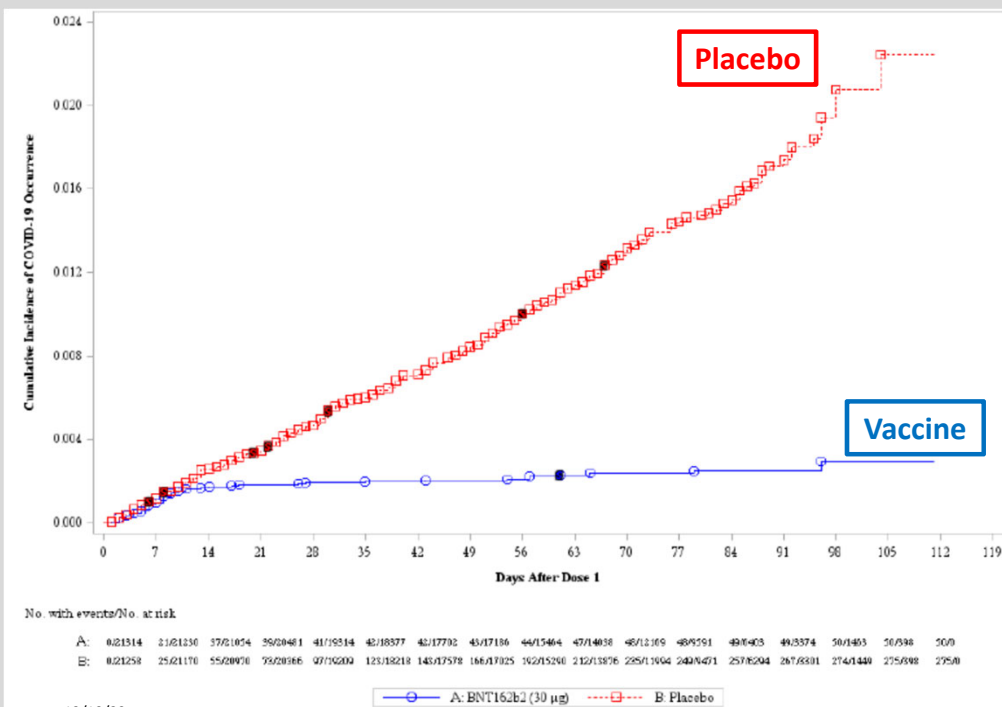
# Interim Analysis 10/9/20



|                 |                    |
|-----------------|--------------------|
| Male            | 50.6%              |
| White           | 82.9%              |
| Black           | 9.3%               |
| Asian           | 4.3%               |
| Hispanic        | 28.0%              |
| Median Age      | 52.0 years (16-91) |
| 16-55 years     | 57.8%              |
| >55 years       | 42.2%              |
| BMI >30         | 35.1%              |
| ≥1 Co-morbidity | 21%                |
| Argentina       | 15.3%              |
| Brazil          | 6.1%               |
| South Africa    | 2.0%               |
| US              | 76.7%              |

Polack et al. NEJM 2020;383:2603-15.

## Pfizer-BioNTech COVID-19 Vaccine



Pfizer & BioNTech. FDA Briefing Document. 12/10/20.

## Primary and Secondary Endpoints

|   | # cases<br>BNT162b<br>2 | # cases<br>Placebo | Vaccine Efficacy, %<br>(95% credible<br>interval) |
|---|-------------------------|--------------------|---|
| COVID-19 at least 7 days after 2 <sup>nd</sup> dose<br>in subjects without evidence of past<br>infection<br>(n = 36,523)          | 8                       | 162                | 95.0%<br>(90.3-97.6)                              |
| COVID-19 at least 7 days after 2 <sup>nd</sup> dose<br>in subjects with and without evidence<br>of past infection<br>(n = 40,137) | 9                       | 169                | 94.6%<br>(89.9-97.3)                              |
| Severe COVID-19 (n=10)  | 1                       | 9                  |   |

Polack et al. NEJM 2020;383:2603-15.

## Vaccine Efficacy by Subgroup

|              | # cases<br>BNT162b2 | # cases<br>Placebo | Vaccine<br>Efficacy, % |
|--------------|---------------------|--------------------|------------------------|
| 16-55 years  | 5                   | 114                | 95.6%                  |
| >55 years    | 3                   | 48                 | 93.7%                  |
| ≥65 years    | 1                   | 19                 | 94.7%                  |
| ≥75 years    | 0                   | 5                  | 100.0%                 |
| Male         | 3                   | 81                 | 96.4%                  |
| Female       | 5                   | 81                 | 93.7%                  |
| White        | 7                   | 146                | 95.2%                  |
| Black        | 0                   | 7                  | 100.0%                 |
| All others   | 1                   | 9                  | 89.3%                  |
| Hispanic     | 3                   | 53                 | 94.4%                  |
| Non-Hispanic | 5                   | 109                | 95.4%                  |

**Between Dose #1-#2 = 52%**

**1<sup>st</sup> 7 days after Dose #2 = 91%**

## mRNA-1272 – Moderna Vaccine

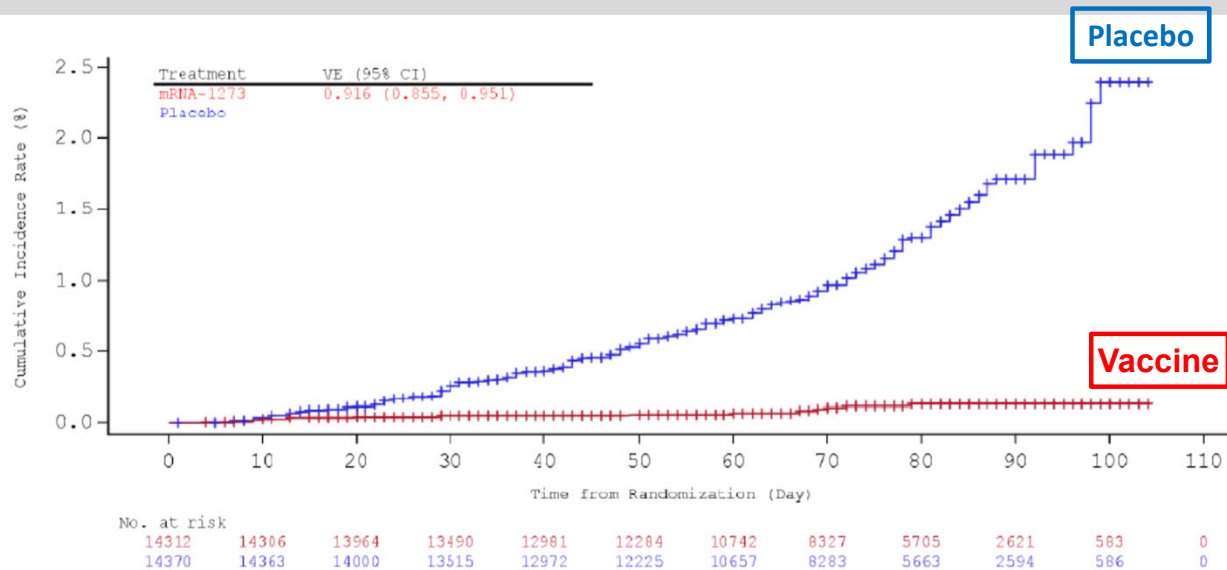
- 27,817 participants
- 82% of subjects considered at occupational risk for exposure
  - 25.4% were HCW
- 22.3% with at least 1 risk factor for severe disease

## mRNA-1272 – Moderna Vaccine

|   | # cases<br>nRNA-<br>1272 | # cases<br>Placebo | Vaccine Efficacy,<br>% (95% credible<br>interval) |
|---|--------------------------|--------------------|---|
| COVID-19 at least 14 days after 2 <sup>nd</sup><br>dose in subjects without evidence<br>of past infection<br>(n = 27,817) | 5                        | 90                 | 94.5%<br>(86.5-97.8)                              |
| 18-64 years (n = 20,791)  | 5                        | 75                 | 93.4% (83.7-                                      |
| ≥65 years (n = 7026)  | 0                        | 15                 | 97.3%)<br>100%                                    |
|   |                          |                    |   |
| Severe COVID-19 (n= 11)   | 0                        | 11                 |   |

**After Dose #1 = 80.2%**

## Moderna COVID-19 Vaccine



### Take home points:

- mRNA vaccines have been researched for years with significant recent advancements.
- 2 currently available vaccines with excellent and nearly identical efficacy and safety profiles.

### Remaining questions:

- What is the efficacy for asymptomatic transmission?
- How long dose immunity last?
- When will children be vaccinated?



## COVID-19 Vaccine Safety

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## Adverse drug reactions in the news

### ***2 Alaska Health Workers Got Emergency Treatment After Receiving Pfizer's Vaccine***

One of the workers, who did not have a history of allergies, remained in the hospital on Wednesday night. Some reactions to the vaccine were also reported last week in Britain.

### **Four People Given the New COVID Vaccine in Clinical Trials Developed Bell's Palsy —Should You Be Worried?**

Here's what to know about the condition, which causes temporary facial paralysis, and if a link has been established to the new vaccine.

### **Doctors encourage COVID vaccination despite reports of cosmetic facial filler swelling**

*About 2.7 million Americans get filler injections each year.*

### **VERIFY: Will the COVID-19 vaccine cause infertility in women?**

A Facebook post claims a head researcher for vaccine manufacturer Pfizer has issued a warning that the company's new COVID-19 vaccine would cause sterilization.

## Adverse drug reactions in clinical trials

| Adverse Event   | Moderna (n=15,185) | Pfizer (n=21,621) |
|---|--------------------|-------------------|
| All   | 1242 (8.2%)        | 4484 (20.7%)      |
| Serious   | 6 (<0.1%)          | 4 (<0.1%)         |
| Fatal   | 0                  | 0                 |
| Medically-attended  | 140 (0.9%)         | Not assessed      |
| Leading to study discontinuation after 1 <sup>st</sup> dose | 18 (0.1%)          | Not assessed      |
| Leading to study withdrawal after either dose               | 0                  | 37 (0.2%)         |
| Severe  | 71 (0.5%)          | 240 (1.1%)        |

Baden LR. *N Engl J Med.* Forthcoming 2021. doi 10.1056/NEJMoa2035389  
 Polack FP. *N Engl J Med.* 2020;383:2603-15.

## Adverse drug reactions in clinical trials

- Minor local (e.g., injection site pain) and systemic (e.g., fatigue, headache) side effects were common
  - Onset usually within first 24-48 hours
  - Mean duration 2-3 days

Baden LR. *N Engl J Med.* Forthcoming 2021. doi 10.1056/NEJMoa2035389  
 Polack FP. *N Engl J Med.* 2020;383:2603-15.  
 Castells MC. *N Engl J Med.* Forthcoming 2021. DOI 10.1056/NEJMra2035343.



## Serious reactions in trials: Moderna

- Occurred in 1.5% of Moderna vaccine recipients vs 1.1% placebo
  - Injection site rash, injection site urticaria
  - 1 anaphylactic reaction in each group
  - Facial swelling in 2 patients with history of dermatological fillers (onset 1 and 2 days after vaccination)
- 3 reports of Bell's palsy in Moderna vaccine group
  - Onset: 22, 28, and 32 days after vaccination
  - Insufficient information to determine causal relationship with the vaccine

Baden LR. *N Engl J Med*. Forthcoming 2021. doi 10.1056/NEJMoa2035389

## Serious reactions in trials: Pfizer

- 4 serious reactions related to Pfizer vaccine reported:
  - Shoulder injury related to vaccine administration
  - Right axillary lymphadenopathy
  - Paroxysmal ventricular arrhythmia
  - Right leg paresthesia

Polack FP. *N Engl J Med*. 2020;383:2603-15.

## Anaphylactic reactions in practice

- 3 cases of anaphylaxis reported within first 24 hours after mass vaccination began in UK and US (Pfizer)
  - 2 females in UK with known food/drug allergies
  - 1 female in US with no known allergies
- Several more cases associated with Pfizer vaccine reported in US
  - Incidence ~1 in 100,000
  - Known stable incidence of anaphylaxis with other vaccines: ~1 in 1,000,000
- Too soon to identify similar potential signal with Moderna vaccine
  - Cases have been reported

Castells MC. *N Engl J Med*. Forthcoming 2021. DOI 10.1056/NEJMra2035343.

## Facial Fillers

- 3 patients with history of cosmetic filler injections reported facial swelling after receiving Moderna vaccine
  - Fillers injected 2 weeks, 6 months, and unknown period of time prior to COVID-19 vaccine
  - Onset 1-2 days after vaccination
  - All resolved

<https://emergency.cdc.gov/coca/ppt/2020/dec-30-coca-call.pdf>

# Safe Vaccine Administration: CDC Recommendations

## CDC Recommendations



Appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of an mRNA COVID-19 vaccine.

- Vaccinated persons should be monitored
  - 30 minutes: history of immediate allergic reaction of any severity to a vaccine or injectable therapy OR anaphylaxis due to any cause
  - 15 minutes: all others

<https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html>

## Vaccination in Special Populations

| System                    | Signs/Symptoms   |
|---------------------------|--|
| Immuno-compromised        | may administer if not otherwise contraindicated, but counsel about lack of data and potential for reduced immune response.   |
| Autoimmune conditions     | administer if not otherwise contraindicated.   |
| History of Guillain-Barré | administer if not otherwise contraindicated.   |
| History of Bell's palsy   | Cases observed in mRNA vaccine clinical trials, but no causality; frequency similar to that expected in general population. Administer if not otherwise contraindicated. |
| Pregnancy                 | No safety concerns in animal models but lack of human data; may administer vaccine if patient wishes (risk/benefit discussion recommended).                              |
| Lactation                 | No data available; may administer vaccine if patient wishes.   |

<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>

## Prevention: Triaging of mRNA Vaccine

| MAY PROCEED WITH VACCINATION  | PRECAUTION TO VACCINATION  | CONTRAINDICATION TO VACCINATION  |
|---|--|--|
| <p><b>ALLERGIES</b><br/>History of allergies that are unrelated to components of an mRNA COVID-19 vaccine<sup>†</sup>, other vaccines, or injectable therapies, such as:</p> <ul style="list-style-type: none"> <li>Allergy to oral medications (including the oral equivalent of an injectable medication)</li> <li>History of food, pet, insect, venom, environmental, latex, etc., allergies</li> <li>Family history of allergies</li> </ul> <p><b>ACTIONS</b></p> <ul style="list-style-type: none"> <li>30 minute observation period: Persons with a history of anaphylaxis (due to any cause)</li> <li>15 minute observation period: All other persons</li> </ul> | <p><b>ALLERGIES</b></p> <ul style="list-style-type: none"> <li>History of any immediate allergic reaction<sup>‡</sup> to vaccines or injectable therapies (except those related to component of mRNA COVID-19 vaccines<sup>†</sup> or polysorbate, as these are contraindicated)</li> </ul> <p><b>ACTIONS:</b></p> <ul style="list-style-type: none"> <li>Risk assessment</li> <li>Consider deferral of vaccination and/or referral to allergist-immunologist</li> <li>30 minute observation period if vaccinated</li> </ul> | <p><b>ALLERGIES</b><br/>History of the following are contraindications to receiving either of the mRNA COVID-19 vaccines<sup>‡</sup>:</p> <ul style="list-style-type: none"> <li>Severe allergic reaction (e.g., anaphylaxis) after a previous dose of an mRNA COVID-19 vaccine or any of its components</li> <li>Immediate allergic reaction<sup>‡</sup> of any severity to a previous dose of an mRNA COVID-19 vaccine or any of its components<sup>‡</sup> (including polyethylene glycol)<sup>#</sup></li> <li>Immediate allergic reaction of any severity to polysorbate<sup>#</sup></li> </ul> <p><b>ACTIONS</b></p> <ul style="list-style-type: none"> <li>Do not vaccinate<sup>#</sup></li> <li>Consider referral to allergist-immunologist</li> </ul> |

<https://emergency.cdc.gov/coca/ppt/2020/dec-30-coca-call.pdf>

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## **Mandatory Reporting to Vaccine Adverse Event Reporting System (VAERS)**

- Vaccine administration errors
- Serious (irrespective of attribution to vaccination)
  - Death
  - Life-threatening adverse drug event
  - Inpatient hospitalization or prolongation of existing hospitalization
  - Persistent or significant incapacity or substantial disruption of ability to conduct normal life functions
  - Congenital anomaly/birth defect
- Cases of COVID-19 that result in hospitalization or death

<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>