COVID-19 RESEARCH: NEW KNOWLEDGE, NEW APPROACHES
Thursday, November 4, 2021
COVID-19 VACCINE TRIALS IN CHILDREN

Mary T. Caserta, MD
COVID-19 IN US CHILDREN

Fig 2. Cumulative Number of Child COVID-19 Cases: 10/28/21

- 6,396,278 total child COVID-19 cases (cumulative)
- Ten states reported 200,000+ child cases
- One state reported fewer than 10,000 child cases
COVID-19 Weekly Cases per 100,000 Population by Age — United States, March 1, 2020–October 10, 2021

>1.9 million cases among children 5-11 years of age

https://covid.cdc.gov/covid-data-tracker/#demographicsovertime

Jones, Epi Task Force, CDC COVID-19 Public Health Response, 2 Nov 2021
COVID-19-Associated Weekly Hospitalizations per 100,000 — COVID-NET by Age Group, March 21, 2020–October 23, 2021


Jones, Epi Task Force, CDC COVID-19 Public Health Response, 2 Nov 2021
COVID-19 Deaths by Age Group, NCHS

Children 5-11 years:
94 COVID-19 deaths*
(1.7% of all deaths among
U.S. children 5–11 years)

*Lag in reporting of deaths might result in underestimate

Jones, Epi Task Force, CDC COVID-19 Public Health Response, 2 Nov 2021
## Leading Causes of Death in Children 5-11 Years of Age, NCHS, 2019

<table>
<thead>
<tr>
<th>Causes of Death</th>
<th>Death (n)</th>
<th>Crude rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accidents (unintentional injuries)</td>
<td>969</td>
<td>3.4</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td>525</td>
<td>1.8</td>
</tr>
<tr>
<td>Congenital malformations, deformations and chromosomal abnormalities</td>
<td>274</td>
<td>1.0</td>
</tr>
<tr>
<td>Assault (homicide)</td>
<td>207</td>
<td>0.7</td>
</tr>
<tr>
<td>Diseases of the heart</td>
<td>115</td>
<td>0.4</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
<td>107</td>
<td>0.4</td>
</tr>
<tr>
<td>Influenza and pneumonia</td>
<td>84</td>
<td>0.3</td>
</tr>
<tr>
<td>Intentional self-harm (suicide)</td>
<td>66</td>
<td>0.2</td>
</tr>
<tr>
<td>Cerebrovascular diseases</td>
<td>56</td>
<td>0.2</td>
</tr>
<tr>
<td>Septicemia</td>
<td>48</td>
<td>0.2</td>
</tr>
</tbody>
</table>

**66 COVID-19 associated deaths in children 5–11 10/3/20-10/2/2021**

Total population 5-17 years, 2019: 52,715,248
Pfizer-BioNTech PEDIATRIC COVID-19 VACCINE BNT162b2: STUDY OVERVIEW: 5 to <12 YEARS

**Phase 1**

- **48 PARTICIPANTS**
- 5 to <12 yrs
- Identification of preferred dose level(s)
  - 10 µg
  - 20 µg
  - 30 µg

**Phase 2/3**

- 2:1 randomization
- ~1500 BNT162b2
- 750 placebo

- ~Additional 1500 BNT162b2 and 750 placebo recipients most with ≥2 weeks post dose 2 safety data

- Initial enrollment group 2268 participants
- Safety expansion group 2379 participants

- Median follow-up time 2.3 months
- Additional follow-up time to 3.3 months

- Days of follow-up

Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2Nov 2021
Subjects Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose in 5 to <12 Year Olds by Baseline SARS-CoV-2 Status

Redness and swelling severity definition: Mild = >2-5cm; Moderate = >5-10 cm; Severe = >10 cm; Grade 4 = necrosis
Pain at injection site severity definition: Mild = no interference; Moderate =some interference; Severe =prevents daily activity; Grade 4 =ER visit or hospitalization
Dose 1: Positive N=198; Negative N=2062  Dose 2: Positive N=195; Negative N=2047
Subjects Reporting Systemic Events, by Maximum Severity, Within 7 Days After Dose 1 and Dose 2 in 5 to <12 Year Olds by Baseline SARS-CoV-2 Status

Fatigue, headache, chills, muscle pain, joint pain severity definition: Mild=no interference; Moderate=some interference; Severe=prevents daily activity; Grade 4=ER visit or hospitalization

Vomiting severity definition: Mild=1-2 times in 24h; Moderate=>2 times in 24h; Severe=Requires IV hydration; Grade 4=ER visit or hospitalization

Diarrhea severity definition: Mild=2-3 times in 24h; Moderate=>4-5 times in 24h; Severe=>6 or more times in 24h; Grade 4=ER visit or hospitalization

Dose 1: Positive N=198; Negative N=2052; Dose 2: Positive N=195; Negative N=2047
Geometric Mean Titers (NT50), by Age Subgroup – Subjects 5 to <12 Years – Evaluable Immunogenicity Population
Immunogenicity Subset – Without Evidence of Prior Infection up to 1 Month Post Dose 2

NT50 = 50% neutralizing titers

Gurtman, Pfizer Clin Research and Dev. Presentation to FDA, 2 Nov 2021
High Efficacy was Observed in 5 to <12 Year Olds Descriptive Analysis of First COVID-19 Occurrence From 7 Days After Dose 2

Subjects WITHOUT Evidence of Infection Prior to 7 Days After Dose 2

<table>
<thead>
<tr>
<th>Efficacy Endpoint</th>
<th>BNT162b2 (10 μg) N=1305</th>
<th>Placebo N=663</th>
<th>VE (%)</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>First COVID-19 occurrence ≥7 days after Dose 2</td>
<td>n=3 0.322 (1273)</td>
<td>n=16 0.159 (637)</td>
<td>90.7</td>
<td>(67.7, 98.3)</td>
</tr>
</tbody>
</table>

No severe cases of COVID-19 were reported
No cases of MIS-C were reported
Cumulative Incidence of COVID-19 After Dose 1:
5 to <12 Years of Age
NEW COVID-19 VIRUS STRAINS, BREAKTHROUGH CASES, BOOSTERS

David J. Topham, PhD
In the US, the Delta variant is responsible for nearly 100% of COVID-19 infections.
Breakthrough infections: A vaccine breakthrough infection is defined as the detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person ≥14 days after they have completed all recommended doses of an FDA authorized COVID-19 vaccine. (CDC)

Hospitalized or fatal COVID-19 vaccine breakthrough cases reported to CDC as of October 18, 2021

As of October 18, 2021, more than 189 million people in the United States had been fully vaccinated against COVID-19.

During the same time, CDC received reports from 50 U.S. states and territories of 41,127 patients with COVID-19 vaccine breakthrough infection who were hospitalized or died.

<table>
<thead>
<tr>
<th></th>
<th>Deaths</th>
<th>Hospitalized, non-fatal*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=10,857</td>
<td>N=30,270</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>4,619</td>
<td>(43%)</td>
</tr>
<tr>
<td>People aged ≥65 years</td>
<td>9,172</td>
<td>(85%)</td>
</tr>
<tr>
<td>Asymptomatic or not COVID-related**</td>
<td>2,299</td>
<td>(21%)</td>
</tr>
</tbody>
</table>

*This table separates all reported vaccine breakthrough infections that resulted in hospitalization and/or death into two columns. While most deaths were also among hospitalized individuals, a small number were not.

**Includes cases in which the patient did not have symptoms of COVID-19, or their hospitalization or death was not COVID-related. For example, people may be hospitalized for reasons other than COVID-19, such as an auto accident, and test positive when screened upon hospital admission.

0.02% of 189M vaccinated people in the US
Breakthrough Covid-19 Cases Remain Rare In The U.S.

Number of breakthrough Covid-19 cases reported in the U.S. as of April 30, 2021*

- Total breakthrough cases: 10,262
- Asymptomatic infections: 2,725
- Hospitalizations: 995
- Deaths: 160

* Vaccinated Americans who were infected with Covid-19.
Source: Centers for Disease Control and Prevention
Colin Powell, first Black US secretary of state, dies of Covid-19 complications amid cancer battle

By Devan Cole, CNN
Updated 5:29 AM ET, Tue October 19, 2021
CURRENT RECOMMENDATIONS FOR RECEIVING A BOOSTER DOSE IF YOU INITIALLY RECEIVED AN mRNA VACCINE:

**PFIZER-BIONTECH**

- Received last dose > 6months ago
- Anyone 65 and older.
- All adults aged 18 to 64 who have cancer, dementia, diabetes, heart disease, HIV and other medical conditions that increase their likelihood of Covid complications.
- Anyone 18 or older who live or work in a long-term care facility, homeless shelter and prison or other congregate setting.
- Front-line personnel 18 or older who are at a higher risk of Covid exposure due to their job, including first responders, teachers, supermarket staff and mass transit employees.

**MODERNA**

- Received last dose > 6months ago
- Anyone 65 and older.
- All adults aged 18 to 64 who have cancer, dementia, diabetes, heart disease, HIV and other medical conditions that increase their likelihood of Covid complications.
- Anyone 18 or older who live or work in a long-term care facility, homeless shelter and prison or other congregate setting.
- Front-line personnel 18 or older who are at a higher risk of Covid exposure due to their job, including first responders, teachers, supermarket staff and mass transit employees.

Recommendations are the same for both Pfizer and Moderna.
CURRENT RECOMMENDATIONS FOR RECEIVING A BOOSTER DOSE IF YOU INITIALLY RECEIVED THE J&J VACCINE:

JOHNSON & JOHNSON

The CDC adopted a slightly different criteria for J&J’s one-shot Covid vaccine, making almost 13 million recipients eligible.

That includes
• All adults who were vaccinated with J&J’s Covid vaccine at least two months ago, instead of six months with Pfizer and Moderna.
• All adult J&J recipients are eligible for a booster even if they don’t have underlying medical conditions or work in a profession or live where there’s a higher risk of Covid.

FDA/CDC also recommend getting any one of the three approved vaccines as a boost

BENEFITS OF BOOSTER (FOR ANY VACCINE TYPE)

• Rise in protective serum antibodies
• Antibodies more cross-reactive against variants
• Increased frequencies of Memory B cells and Memory T cells
  • Can prevent serious illness, hospitalization, and death
THE CHANGING LANDSCAPE OF COVID-19 VACCINES

Angela Branche, MD
Heterologous SARS-CoV-2 Booster Vaccinations—Preliminary Report

- Phase 1/2 open-label clinical trial conducted at ten U.S. sites, adults who received one of three EUA Covid-19 vaccines at least 12 weeks prior received a booster injection with one of three vaccines (Moderna mRNA-1273 100-μg, Janssen Ad26.COV2.S 5×10¹⁰ virus particles, or Pfizer-BioNTech BNT162b2 30-μg).

- The primary outcomes were safety, reactogenicity, and humoral immunogenicity on study days 15 and 29.

<table>
<thead>
<tr>
<th>Group</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary EUA Immunization Vaccine</td>
<td>Janssen</td>
<td>Moderna</td>
<td>Pfizer/BioNTech</td>
<td>Janssen</td>
<td>Moderna</td>
<td>Pfizer/BioNTech</td>
<td>Janssen</td>
<td>Moderna</td>
<td>Pfizer/BioNTech</td>
</tr>
<tr>
<td></td>
<td>Ad26.COV2-S</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
<td>Ad26.COV2-S</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
<td>Ad26.COV2-S</td>
<td>mRNA-1273</td>
<td>BNT162b2</td>
</tr>
<tr>
<td></td>
<td>5×10¹⁰vp</td>
<td>100-mcg</td>
<td>30-mcg</td>
<td>5×10¹⁰vp</td>
<td>100-mcg</td>
<td>30-mcg</td>
<td>5×10¹⁰vp</td>
<td>100-mcg</td>
<td>30-mcg</td>
</tr>
<tr>
<td>Booster</td>
<td>Moderna mRNA-1273 100-mcg</td>
<td>Janssen Ad26.COV2-S 5×10¹⁰vp</td>
<td>Pfizer/BioNTech BNT162b2 30-mcg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Number</td>
<td>53</td>
<td>51</td>
<td>50</td>
<td>50</td>
<td>49</td>
<td>51</td>
<td>53</td>
<td>51</td>
<td>50</td>
</tr>
</tbody>
</table>
HETEROLOGOUS SARS-COV-2 BOOSTER VACCINATIONS – PRELIMINARY REPORT
(MIX AND MATCH)

Figure 2 | Binding Antibody and Neutralizing Antibody Titers
VACCINATION AND PREGNANCY

**Design:** From December 14, 2020, to February 28, 2021, we used data from the “v-safe after vaccination, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.

**Results:** 35,691 v-safe participants 16 to 54 years of age identified as pregnant.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pfizer–BioNTech Vaccine</th>
<th>Moderna Vaccine</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number (percent)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2136 (54.0)</td>
<td>1822 (46.0)</td>
<td>3958 (100)</td>
</tr>
<tr>
<td>Timing of first eligible dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periconception: within 30 days before last menstrual period</td>
<td>55 (2.6)</td>
<td>37 (2.0)</td>
<td>92 (2.3)</td>
</tr>
<tr>
<td>First trimester: &lt;14 wk</td>
<td>615 (28.8)</td>
<td>517 (28.4)</td>
<td>1132 (28.6)</td>
</tr>
<tr>
<td>Second trimester: ≥14 and &lt;28 wk</td>
<td>932 (43.6)</td>
<td>782 (42.9)</td>
<td>1714 (43.3)</td>
</tr>
<tr>
<td>Third trimester: ≥28 wk</td>
<td>533 (25.0)</td>
<td>486 (26.7)</td>
<td>1019 (25.7)</td>
</tr>
<tr>
<td>Missing data</td>
<td>1 (&lt;0.1)</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
</tr>
</tbody>
</table>
Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

<table>
<thead>
<tr>
<th>Participant-Reported Outcome</th>
<th>Published Incidence</th>
<th>V-safe Pregnancy Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pregnancy loss among participants with a completed pregnancy</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous abortion: &lt;20 wk(15^{-17})</td>
<td>Not applicable</td>
<td>104</td>
</tr>
<tr>
<td>Stillbirth: (\geq 20) wk(18^{-20})</td>
<td>&lt;1</td>
<td>1/725 (0.1)†</td>
</tr>
<tr>
<td><em>Neonatal outcome among live-born infants</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preterm birth: &lt;37 wk(21^{-22})</td>
<td>8–15</td>
<td>60/636 (9.4)¶</td>
</tr>
<tr>
<td>Small size for gestational age(23^{-24})</td>
<td>3.5</td>
<td>23/724 (3.2)</td>
</tr>
<tr>
<td>Congenital anomalies(25^{**})</td>
<td>3</td>
<td>16/724 (2.2)</td>
</tr>
<tr>
<td>Neonatal death(26^{††})</td>
<td>&lt;1</td>
<td>0/724</td>
</tr>
</tbody>
</table>

MomiVax

Observational, Prospective Cohort Study of the Immunogenicity and Safety of SARS-CoV-2 Vaccines Administered during Pregnancy or Postpartum and Evaluation of Antibody Transfer and Durability in Infants.

APPROXIMATELY 2,000 STUDY PARTICIPANTS IN 3 GROUPS:

• **GROUP 1**: Individuals who receive a COVID19 vaccine during pregnancy and their Infants.

• **GROUP 2**: Individuals who receive a COVID19 vaccine postpartum and their infants.

• **GROUP 3**: Individuals who receive a COVID19 booster during pregnancy and their infants.
NEW VACCINE PLATFORMS—CAN WE DO BETTER THAN MRNA?

- A Phase 1 open label dose ranging trial to evaluate safety, and immunogenicity of CVXGA1.

- A live recombinant parainfluenza virus 5 (PIV5) expressing SARS-CoV 2 spike (S) protein administered as:
  - Single Dose
  - Intranasally
NEW HORIZONS...

• Are there benefits to mixing vaccine types?

• Will new variants emerge against which current vaccines have little or no neutralizing activities?

• How many doses will be required before durable immunity is achieved?

• Can COVID vaccines be combined with other seasonal vaccines?