Evidence to Recommendations Framework:

2023 – 2024 (Monovalent, XBB Containing) COVID-19 Vaccine

Megan Wallace, DrPH, MPH
ACIP Meeting
September 12, 2023
Evidence to Recommendations Framework
Evidence to Recommendations (EtR) Framework

- Structure to describe information considered in moving from evidence to ACIP vaccine recommendations
- Provide transparency around the impact of additional factors on deliberations when considering a recommendation
### Evidence to Recommendations (EtR) Framework

<table>
<thead>
<tr>
<th>EtR Domain</th>
<th>Question(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public Health Problem</td>
<td>• Is the problem of public health importance?</td>
</tr>
<tr>
<td>Benefits and Harms</td>
<td>• How substantial are the desirable anticipated effects?</td>
</tr>
<tr>
<td></td>
<td>• How substantial are the undesirable anticipated effects?</td>
</tr>
<tr>
<td></td>
<td>• Do the desirable effects outweigh the undesirable effects?</td>
</tr>
<tr>
<td>Values</td>
<td>• Does the target population feel the desirable effects are large relative to the undesirable effects?</td>
</tr>
<tr>
<td></td>
<td>• Is there important variability in how patients value the outcome?</td>
</tr>
<tr>
<td>Acceptability</td>
<td>• Is the intervention acceptable to key stakeholders?</td>
</tr>
<tr>
<td>Feasibility</td>
<td>• Is the intervention feasible to implement?</td>
</tr>
<tr>
<td>Resource Use</td>
<td>• Is the intervention a reasonable and efficient allocation of resources?</td>
</tr>
<tr>
<td>Equity</td>
<td>• What would be the impact of the intervention on health equity?</td>
</tr>
</tbody>
</table>
Evidence to Recommendations (EtR) Framework

<table>
<thead>
<tr>
<th>EtR Domain</th>
<th>Question(s)</th>
<th>Domain Equity Question(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public Health</td>
<td>• Is the problem of public health importance?</td>
<td>• Does the problem impact all populations equally?</td>
</tr>
<tr>
<td>Problem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefits and</td>
<td>• How substantial are the desirable anticipated effects?</td>
<td>• Are the desirable and undesirable anticipated effects demonstrated across all populations equally?</td>
</tr>
<tr>
<td>Harms</td>
<td>• How substantial are the undesirable anticipated effects?</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Do the desirable effects outweigh the undesirable effects?</td>
<td></td>
</tr>
<tr>
<td>Values</td>
<td>• Does the target population feel the desirable effects are large relative to the undesirable effects?</td>
<td>• Is there important variability in how patients or populations value the outcome?</td>
</tr>
<tr>
<td></td>
<td>• Is there important variability in how patients value the outcome?</td>
<td></td>
</tr>
<tr>
<td>Acceptability</td>
<td>• Is the intervention acceptable to key stakeholders?</td>
<td>• Is the intervention equally acceptable across all populations?</td>
</tr>
<tr>
<td>Feasibility</td>
<td>• Is the intervention feasible to implement?</td>
<td>• Is the intervention equally feasible to implement across all populations?</td>
</tr>
<tr>
<td>Resource Use</td>
<td>• Is the intervention a reasonable and efficient allocation of resources?</td>
<td>• Is the intervention a reasonable and efficient allocation of resources across all populations?</td>
</tr>
</tbody>
</table>

The intervention = 2023 – 2024 (monovalent, XBB containing) COVID-19 vaccine
The problem = COVID-19
Evidence to Recommendations (EtR) Framework

Policy Question

- Should 2023 - 2024 (monovalent, XBB containing) COVID-19 vaccines authorized under EUA or approved by BLA be recommended for use in persons ≥6 months of age?

Products and ages currently authorized or approved by FDA include:
- Moderna COVID-19 vaccine for ages 6 months and older
- Pfizer-BioNTech COVID-19 vaccine for ages 6 months and older

Products and ages under review for authorization or approval by FDA include:
- Novavax COVID-19 vaccine for ages 12 years and older

EUA: Emergency Use Authorization; BLA: Biologics License Application
Bivalent COVID-19 vaccine recommendations for mRNA COVID-19 vaccines

**Unvaccinated**

- 2 doses Moderna
- **OR**
- 3 doses Pfizer-BioNTech

**6 months – 4/5 years**

- 1 dose Moderna
- **OR**
- 1 dose Pfizer-BioNTech

**≥5/6 years**

**Previously vaccinated**

- 1 dose Moderna
- **OR**
- 1 dose Pfizer-BioNTech

**≥6 months**

Note: Those ages 6 months – 4 years who have previously received a single dose of Pfizer-BioNTech would need 2 additional doses. Additional doses are recommended for persons with immunocompromising conditions.
Proposed 2023 – 2024 COVID-19 vaccine recommendations for mRNA COVID-19 vaccines

Unvaccinated

- 2 doses Moderna
- OR
- 3 doses Pfizer-BioNTech
- OR
- 1 dose Moderna
- OR
- 1 dose Pfizer-BioNTech

6 months – 4 years

≥ 5 years

Previously vaccinated

- 1 dose Moderna
- OR
- 1 dose Pfizer-BioNTech

≥6 months

Note: Those ages 6 months – 4 years who have previously received a single dose of Pfizer-BioNTech would need 2 additional doses. Additional doses are recommended for persons with immunocompromising conditions.
Current recommendations for Novavax COVID-19 vaccine

- The original Novavax COVID-19 vaccine remains authorized for use as a 2-dose primary series
- The original Novavax COVID-19 vaccine can be given as booster dose in limited situations to
  - People ages 18 years and older who previously completed primary vaccination using any FDA-approved or FDA-authorized COVID-19 vaccine
  - Have not received any previous booster dose(s)
  - Are unable (i.e., mRNA vaccine contraindicated or vaccine not available) or unwilling to receive an mRNA vaccine and would otherwise not receive a booster dose
- Authorizations or approvals for 2023 – 2024 Novavax COVID-19 vaccine will be determined by FDA with CDC recommendations to follow
COVID-19 vaccine nomenclature

- Updated COVID-19 vaccine referred to as the “2023–2024 COVID-19 vaccine” in this presentation
- Following ACIP meeting, both “updated COVID-19 vaccine” and “2023–2024 COVID-19 vaccine” will be used to refer to the monovalent XBB.1.5 containing vaccines
EtR Domain:
Public Health Problem

Gray boxes indicate potential reporting delays. Interpretation of trends should be excluded from these weeks.

Rates highest in ≥75 years, followed by infants <6 months and adults 65–74 years
COVID-19 new hospital admissions, by week, in the United States National Healthcare Safety Network (NHSN), August 2020 – August 2023

Source: COVID-19–associated hospitalization data reported to CDC’s National Healthcare Safety Network (NHSN).
https://covid.cdc.gov/covid-data-tracker/#trends_weeklyhospitaladmissions_select_00
### Other pediatric vaccine preventable diseases: Annual hospitalizations per 100,000 population prior to recommended vaccines compared to COVID-19

<table>
<thead>
<tr>
<th></th>
<th>Hepatitis A¹</th>
<th>Varicella² (Chickenpox)</th>
<th>Vaccine-type Invasive Pneumococcal Disease³</th>
<th>COVID-19⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>5–14 years</td>
<td>0–4 years</td>
<td>0–4 years</td>
<td>6 months–&lt;18 years</td>
</tr>
<tr>
<td><strong>Hospitalization Burden</strong> (Annual rate per 100,000 population)</td>
<td>&lt;1</td>
<td>29-42</td>
<td>40⁵</td>
<td>≤4 years: 92–220 5–11 years: 15–47 12–17 years: 20–80</td>
</tr>
</tbody>
</table>

¹ [https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5603a1.htm](https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5603a1.htm)
⁴ COVID-NET data October 2021 – September 2022 and October 2022 – July 2023. COVID-19 rates have not been adjusted for reason for admission. COVID vaccine first introduced in 12-17 years in May 2021; in 5-11 years in November 2021 and in 6 months – 4 years in June 2022
COVID-19 Scenario Modeling Hub

- A multi-team effort aimed at creating and modeling planning scenarios of the mid- to long-term COVID-19 situation
- Scenarios developed in close collaboration with government agencies and other stakeholders
- Project hospitalizations and deaths

https://covid19scenariomodelinghub.org/
Assumptions of COVID-19 Scenario Modeling Hub Round 17

- **Six** scenarios focusing on three vaccine recommendation scenarios and two different rates of immune escape
  - No vaccine recommendation vs recommendation for 65+ years vs universal recommendation
  - Low immune escape vs high immune escape

- Assumed vaccines reformulated to target strains circulating on June 15\(^{th}\) of each year, made available September 1.

- Reformulated vaccines assumed to have **65% VE against symptomatic infection** with the strain targeted by reformulation.

- Vaccine uptake based on **first booster uptake** (September 2021)

- Teams required to **project a minimum of 2 years** into the future

- Eight teams provided national level projections

---

1. Low immune escape: immune escape occurs at a constant rate of 20% per year; high immune escape: immune escape occurs at a constant rate of 50% per year.
Based on ensemble projections, weekly hospitalizations are likely to increase this winter and stay within last year’s range.

Scenario A: No booster, low immune escape
Scenario B: No booster, high immune escape
Scenario C: 65+ booster, low immune escape
Scenario D: 65+ booster, high immune escape
Scenario E: All booster, low immune escape
Scenario F: All booster, high immune escape

https://covid19scenariomodelinghub.org/
People ages 6 months – 49 years with no underlying conditions are still admitted to the ICU with COVID-19

COVID-NET: Underlying Medical Conditions among Patients Admitted to ICU among Children, Adolescents, and Adults Ages 6 Months – 49 Years, July 2022–June 2023

<table>
<thead>
<tr>
<th>Age category</th>
<th>% with no underlying conditions</th>
<th>Of those with no underlying conditions, what % were admitted to ICU?</th>
<th>% admitted to ICU with no underlying conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>6–23 months</td>
<td>57%</td>
<td>27%</td>
<td>53%</td>
</tr>
<tr>
<td>2–4 years</td>
<td>39%</td>
<td>19%</td>
<td>32%</td>
</tr>
<tr>
<td>5–11 years</td>
<td>24%</td>
<td>23%</td>
<td>24%</td>
</tr>
<tr>
<td>12–17 years</td>
<td>25%</td>
<td>31%</td>
<td>22%</td>
</tr>
<tr>
<td>18–49 years</td>
<td>16%</td>
<td>15%</td>
<td>13%</td>
</tr>
</tbody>
</table>

- Relative standard errors >30%; estimates might be unstable due to small sample size
- Limited to COVID-NET hospitalizations with COVID-19-related illness as likely reason for admission
Provisional COVID-19 deaths, by week, in the United States, reported to CDC

The most recent 3 weeks of mortality counts are shaded grey because NVSS reporting is <95% during this period.
COVID-19-associated deaths in persons ages ≥20 years (by underlying cause of death), by age group and year – National Vital Statistics System

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System, Provisional Mortality on CDC WONDER Online Database. Data are from the final Multiple Cause of Death Files, 2018-2021, and from provisional data for years 2022-2023, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Number of deaths includes COVID-19 code (U07.1) as the underlying cause of death. Accessed at http://wonder.cdc.gov/mcd-icd10-provisional.html on Aug 25, 2023 4:53:59 PM
COVID-19-associated deaths in persons ages ≤19 years (by underlying cause of death), by age group and year – National Vital Statistics System

1 Provisional data
2 Partial data

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System, Provisional Mortality on CDC WONDER Online Database. Data are from the final Multiple Cause of Death Files, 2018-2021, and from provisional data for years 2022-2023, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Number of deaths includes influenza codes (J09-J11) or COVID-19 code (U07.1) as the underlying cause of death. Accessed at [http://wonder.cdc.gov/mcd-icd10-provisional.html](http://wonder.cdc.gov/mcd-icd10-provisional.html) on Aug 25, 2023 4:53:59 PM
Among children ≤17 years who died in-hospital, 50% had no underlying conditions

COVID-NET: Underlying Medical Conditions among Patients with In-Hospital Death among Children and Adolescents Ages ≤17 Years, January 2022–June 2023

<table>
<thead>
<tr>
<th>Age category</th>
<th>% with no underlying conditions</th>
<th>Of those with no underlying conditions, what % died in-hospital?</th>
<th>% of those who died in-hospital with no underlying conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤17 years</td>
<td>51%</td>
<td>1%*</td>
<td>50%</td>
</tr>
</tbody>
</table>

Limited to COVID-NET hospitalizations with COVID-19-related illness as likely reason for admission

* Relative standard error >30; indicates estimate might be unstable due to low sample size (n=24).
## Pediatric vaccine preventable diseases: Deaths per year in the United States prior to recommended vaccines compared to COVID-19

<table>
<thead>
<tr>
<th>Age</th>
<th>Hepatitis A</th>
<th>Meningococcal (ACWY)</th>
<th>Varicella</th>
<th>Rubella</th>
<th>Rotavirus</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>3</td>
<td>8</td>
<td>16</td>
<td>17</td>
<td>20</td>
<td>≤1 year: 156</td>
</tr>
<tr>
<td>11–18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1–4 years: 101</td>
</tr>
<tr>
<td>5–9 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5–19 years: 292</td>
</tr>
<tr>
<td>All ages</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months–&lt;18 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6http://wonder.cdc.gov/mcd-icd10-provisional.html on Aug 1, 2023. COVID vaccine first introduced in 12-17 years in May 2021; in 5-11 years in November 2021 and in 6 months – 4 years in June 2022.
COVID-19 and Influenza-associated deaths in persons ages ≤19 years (by underlying cause of death), by age group and year – National Vital Statistics System

![Bar chart showing COVID-19 and Influenza-associated deaths in persons ages ≤19 years by age group and year]

Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Vital Statistics System, Provisional Mortality on CDC WONDER Online Database. Data are from the final Multiple Cause of Death Files, 2018-2021, and from provisional data for years 2022-2023, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Number of deaths includes influenza codes (J09-J11) or COVID-19 code (U07.1) as the underlying cause of death. Accessed at [http://wonder.cdc.gov/mcd-icd10-provisional.html](http://wonder.cdc.gov/mcd-icd10-provisional.html) on Aug 25, 2023 4:53:59 PM
Domain Equity Question:

Does the problem impact all populations equally?
Age-adjusted COVID-19-associated hospitalization rates by race and ethnicity* — COVID-NET, October 2022 – August 2023

3-week moving average rate
January – August 2023

Cumulative hospitalization rates remain highest in American Indian/Alaska Native and Black persons

Cumulative rates
October 2022 – August 2023

Rates per 100,000 population

1/7/2023 2/7/2023 3/7/2023 4/7/2023 5/7/2023 6/7/2023 7/7/2023 8/7/2023

White Black Asian/Pacific Islander American Indian/Alaskan Native Hispanic

* Black, White, American Indian/Alaska Native and Asian/Pacific Islander people were categorized as non-Hispanic; Hispanic people could be of any race.

Risk ratio of death, invasive mechanical ventilation (IMV), and admission to intensive care unit (ICU), by the number of underlying medical conditions among adults hospitalized with COVID-19, March 2020–March 2021
Prevalence of any condition:

Selected chronic conditions by U.S. county, 2018

Based on Razzaghi H, Wang Y, Lu H, Marshall KE, Dowling NF, Paz-Bailey G, Twentyman ER, Peacock G, Greenlund KJ, Estimated County-Level Prevalence of Selected Underlying Medical Conditions Associated with Increased Risk for Severe COVID-19 Illness - United States, 2018 MMWR Morb Mortal Wkly Rep 2020;69[945-950]. The underlying medical conditions included in these prevalence estimates were selected using a subset of the list of conditions with the strongest and most consistent evidence of association with increased risk for severe COVID-19-associated illness on CDC’s website as of June 25, 2020 and for which questions on the BRFSS are available. https://covid.cdc.gov/covid-data-tracker/#underlying-med-conditions
Number of chronic conditions by age among Asian, Black, Latino/Hispanic, and White adults in the National Health Interview Survey, 1999 to 2018

COVID-19 burden is currently lower than at previous points in the pandemic, however the absolute number of hospitalizations and deaths is still high.

Although hospitalization rates are currently low in some age groups, we have seen rates increase in recent weeks and anticipate further increases as we enter respiratory virus season.

Infants and older adults have the highest COVID-19-associated hospitalization rates.

Children and adults with no underlying medical conditions still experience severe illness due to COVID-19.

Post-COVID Conditions are common following SARS-CoV-2 infection, decrease with time since infection, and have decreased since the start of the pandemic.

People of racial and ethnic minority groups continue to be disproportionately impacted by COVID-19.

High proportions of underlying conditions may put certain groups at increased risk for severe outcomes due to COVID-19.
Is COVID-19 disease among persons ≥ 6 months of public health importance?

- No
- Probably no
- Probably yes
- Yes
- Varies
- Don’t know
EtR Domain:
Benefits and Harms
Summary of available data

- Data from COVID-19 vaccine manufacturers
  - Moderna monovalent XBB.1.5 containing vaccine clinical trial data
  - Novavax monovalent XBB.1.5 containing preclinical data
  - Pfizer-BioNTech monovalent XBB.1.5 containing preclinical data

- GRADE
  - Benefits and harms of an updated COVID-19 vaccine

- Post-authorization safety and effectiveness monitoring
  - Vaccine Safety Datalink and other vaccine safety monitoring systems
  - CDC vaccine effectiveness platforms

- Additional considerations
  - Benefit-risk assessment
  - Modeling data
Available data from COVID-19 vaccine manufacturers

- **Moderna**
  - Clinical trial data
    - Randomized 101 patients to monovalent XBB.1.5 containing dose or bivalent BA.4/5 + XBB.1.5 containing dose
    - Patients that received the monovalent XBB.1.5 containing dose demonstrated an increase in neutralizing antibodies, with similar levels of neutralization across several XBB sub-variants
    - Reported reactogenicity was similar to or lower than that reported from previous doses

- **Novavax**
  - Preclinical data
    - Macaques boosted with XBB.1.5 demonstrated increased neutralizing response across several XBB pseudoviruses

- **Pfizer-BioNTech**
  - Preclinical data
    - Mice boosted with XBB.1.5 demonstrated increased neutralizing response across several XBB pseudoviruses
GRADE

- GRADE approach was applied to assess the type and quality of evidence for the anticipated benefits and harms of an updated COVID-19 vaccine.
- The PICO question and inclusion/exclusion criteria were intentionally narrow to best capture evidence most applicable to what can be anticipated from this year’s vaccine dose in the U.S., including limiting evidence to U.S. studies of an updated vaccine formulation (i.e., bivalent mRNA vaccine).
- Two separate PICO questions were evaluated based on dosing cut-offs.
- These narrow criteria reduced the number of studies available in the body of evidence, however this GRADE assessment builds upon a large body of evidence from the original monovalent vaccines.

BLA: Biologics License Application; EUA: Emergency Use Authorization
## PICO Question – Adolescents and Adults

<table>
<thead>
<tr>
<th><strong>Population</strong></th>
<th>Persons ages 12 years and older</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intervention</strong></td>
<td>Updated mRNA COVID-19 vaccine</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>No updated vaccine</td>
</tr>
</tbody>
</table>
| **Outcomes** | Medically-attended COVID-19 (ED/UC visits)  
Hospitalization due to COVID-19  
Death due to COVID-19  
Post-COVID Conditions  
Specified Serious Adverse Events  
Reactogenicity |

**PICO**: Population, intervention, comparison, outcomes  
**ED**: emergency department; **UC**: urgent care
**PICO Question - Infants and Children**

<table>
<thead>
<tr>
<th>Population</th>
<th>Persons ages 6 months – 11 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Updated COVID-19 mRNA vaccine</td>
</tr>
<tr>
<td>Comparison</td>
<td>No updated vaccine</td>
</tr>
</tbody>
</table>
| Outcomes            | Medically-attended COVID-19 (ED/UC visits)  
                       Hospitalization due to COVID-19  
                       Death due to COVID-19  
                       MIS-C  
                       Post-COVID Conditions  
                       Specified Serious Adverse Events  
                       Reactogenicity |

**PICO**: Population, intervention, comparison, outcomes  
**ED**: emergency department; **UC**: urgent care  
**MIS-C**: Multisystem inflammatory syndrome in children
# Outcomes, Importance, and Data Sources

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importancea</th>
<th>Data sources</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Benefits</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medically-attended COVID-19 (ED/UC visits)</td>
<td>Critical</td>
<td>Observational studies of vaccine effectiveness</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>Observational studies of vaccine effectiveness</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>Observational studies of vaccine effectiveness</td>
</tr>
<tr>
<td>MIS-C – <em>pediatrics only</em></td>
<td>Important</td>
<td>Observational studies of vaccine effectiveness</td>
</tr>
<tr>
<td>Post-COVID Conditions</td>
<td>Important</td>
<td>Observational studies of vaccine effectiveness</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specified serious adverse events (SAEs)</td>
<td>Critical</td>
<td>Safety surveillance for specified SAEs</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>Important</td>
<td>RCTs for monovalent doses</td>
</tr>
</tbody>
</table>

a Three options: Critical; Important but not critical; Not important for decision making

ED: emergency department; UC: urgent care MIS-C: Multisystem inflammatory syndrome in children
Evidence Retrieval

- **Observational Studies for Benefits (Vaccine Effectiveness)**
  - *Published or preprint* articles from International Vaccine Access Center (IVAC) systematic review\(^a\)
  - Restricted to PICO defined population, intervention, comparison, and outcome

- **Safety Surveillance for Serious Adverse Events**
  - Data on safety signals identified by vaccine safety surveillance systems
  - Based on input from CDC Immunization Safety Office (ISO)

- **Randomized Controlled Trials (RCTs) for Reactogenicity**
  - Data on reactogenicity identified by relevant phase 1, 2, or 3 RCTs from clinicaltrials.gov
  - Unpublished data from vaccine manufacturers

\(^a\) Articles were eligible for inclusion if *published or uploaded to a preprint* server before 6/29/2023;
Observational Data (n = 6)

- 6 records identified (one or more PICO outcomes)
- Assessed risk of bias using Newcastle-Ottawa Scale (9-point scale)
  - For cohort studies: Selection of cohorts, Comparability of cohorts, Assessment of outcome
  - For case-control or test-negative design studies: Selection of cases and controls, Comparability of cases and controls, Ascertainment of exposure
- Two reviewers assessed each study for each outcome
- Serious limitations identified by score <7
Pooling of Vaccine Effectiveness (VE) Estimates

- For each outcome, assessed body of evidence for suitability for pooling
  - Most representative study selected if multiple studies in same population
- Meta-analyses conducted
- Estimates evaluated for heterogeneity
- Resulting pooled estimates summarize real-world data available at time of GRADE analysis
Medically-Attended COVID-19 (ED/UC Visits), Adults and Adolescents (n=2)

Pooled VE = 53.1% (95% CI: 49.7% to 56.3%)*

*Pooled RR based on a fixed effects meta-analysis, using adjusted vaccine effectiveness estimates on a log scale. Fixed effects model was used for this analysis due to imprecise estimates of the between-studies variance.

ED: emergency department; UC: urgent care
GRADE: Medically-Attended COVID-19 (ED/UC Visits), Adults and Adolescents (n=2)

- **Observational Studies (n=2)**
  - Pooled RR 0.47 (95% CI: 0.44 to 0.50)
  - No serious concerns in certainty assessment.
  - Evidence type: Low certainty

CI: Confidence interval; RR: Risk ratio; ED: emergency department; UC: urgent care
Hospitalization due to COVID-19, Adults and Adolescents (n=4)

*Pooled RR based on a random effects meta-analysis, using adjusted vaccine effectiveness estimates on a log scale.
Note: 6 studies were identified in the systematic review, however 2 studies had overlapping populations and were excluded from the pooled analysis.
GRADE: Hospitalization due to COVID-19, Adults and Adolescents (n=4)

- Observational Studies (n=4)
  - Pooled RR 0.52 (95% CI: 0.39–0.70)
  - No serious concerns in certainty assessment.
  - Evidence type: Low certainty
Death due to COVID-19, Adults and Adolescents (n=2)

Lin, ≥14 days post bivalent dose, ≥2 monovalent doses comparator

Tseng, ≥14 days post bivalent dose, ≥2 monovalent doses comparator

Pooled Estimate

Pooled VE = 60.5% (95%CI: 40.7% to 73.7%)*

*Pooled RR based on a fixed effects meta-analysis, using adjusted vaccine effectiveness estimates on a log scale. Fixed effects model was used for this analysis due to imprecise estimates of the between-studies variance.
Observational Studies (n=2)

- Pooled RR 0.39 (95% CI: 0.26 to 0.59)
- Serious concern for inconsistency was present. The magnitude of effect and 95% confidence intervals from the two studies in the body evidence varied widely, possibly reflecting differences in study methods.
- Evidence type: Very low
Post-COVID-Conditions, Adults and Adolescents

- No published or preprint captured in systematic review
- Common reasons for exclusion
  - Review article
  - Self-reported vaccination status
  - Combines vaccine platforms
  - Not a VE study
  - Vaccination as a therapeutic (after infection)
- Data not captured in the systematic review indicate that COVID-19 vaccine provides some protection against post-COVID conditions
# Specified Serious Adverse Events (Myocarditis/Pericarditis)

Incidence Rate of Verified Myocarditis/Pericarditis in the 0 to 7 Days After mRNA COVID-19 Vaccination among Persons Aged 12 – 39 Years by Product, Age Group, Sex.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Cases/Doses Administered</th>
<th>Incidence Rate/Million Doses (95% CI)</th>
<th>Cases/Doses Administered</th>
<th>Incidence Rate/Million Doses (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monovalent Booster Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17 y</td>
<td>-</td>
<td>-</td>
<td>0/55649</td>
<td>0.0 (0.0 – 53.8)</td>
</tr>
<tr>
<td>12-15 y</td>
<td>5/81613</td>
<td>61.3 (19.9 – 143.0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>16-17 y</td>
<td>9/47874</td>
<td>188.0 (86.0 – 356.9)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>18-29 y</td>
<td>7/166973</td>
<td>41.9 (16.9 – 86.4)</td>
<td>1/60338</td>
<td>16.6 (0.4 – 92.3)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>3/197554</td>
<td>15.2 (3.1 – 44.4)</td>
<td>0/97171</td>
<td>0.0 (0.0 – 30.8)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-17 y</td>
<td>-</td>
<td>-</td>
<td>0/57776</td>
<td>0.0 (0.0 – 51.9)</td>
</tr>
<tr>
<td>12-15 y</td>
<td>0/84114</td>
<td>0.0 (0.0 – 35.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>16-17 y</td>
<td>2/55004</td>
<td>36.4 (4.4 – 131.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>18-29 y</td>
<td>1/240226</td>
<td>4.2 (0.1 – 23.2)</td>
<td>0/95162</td>
<td>0.0 (0.0 – 31.5)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>1/268412</td>
<td>3.7 (0.1 – 20.8)</td>
<td>0/133305</td>
<td>0.0 (0.0 – 22.5)</td>
</tr>
<tr>
<td><strong>Bivalent Booster Dose</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderna</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29 y</td>
<td>7/109337</td>
<td>64.0 (25.7 – 131.9)</td>
<td>0/22247</td>
<td>0.0 (0.0 – 134.7)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>1/149468</td>
<td>6.7 (0.2 – 37.3)</td>
<td>1/41820</td>
<td>23.9 (0.6 – 133.2)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-29 y</td>
<td>1/156707</td>
<td>6.4 (0.2 – 35.6)</td>
<td>0/35393</td>
<td>0.0 (0.0 – 84.6)</td>
</tr>
<tr>
<td>30-39 y</td>
<td>2/191765</td>
<td>10.4 (1.3 – 37.7)</td>
<td>0/55816</td>
<td>0.0 (0.0 – 53.7)</td>
</tr>
</tbody>
</table>

Specified Serious Adverse Events (Anaphylaxis), Adults and Adolescents

- Among persons 12 and older, based on events occurring in a 0-1 day risk interval after vaccination, the estimated incidence of confirmed anaphylaxis among adolescents and adults was:
  - 4.8 (95% CI 3.2-6.9) per million doses of Pfizer-BioNTech original monovalent vaccines
  - 5.1 (95% CI: 3.3-7.4) per million doses of Moderna original monovalent vaccines
  - There were fewer cases of anaphylaxis post dose 2 compared with dose 1

GRADE: Specified Serious Adverse Events, Adults and Adolescents

- Observational Studies (n=2)
  - Two specific, rare SAEs have been associated with vaccination through safety surveillance
  - No serious concerns in certainty assessment.
  - Evidence type: Low certainty

CI: Confidence interval; RR: Risk ratio; SAE: serious adverse events
Reactogenicity*, Severe (Grade ≥3), Adults and Adolescents (n=4)

<table>
<thead>
<tr>
<th>Study</th>
<th>Experimental Events</th>
<th>Total Events</th>
<th>Control Events</th>
<th>Total Weight</th>
<th>Risk Ratio MH, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer BLA, 16+</td>
<td>531</td>
<td>4948</td>
<td>111</td>
<td>4921</td>
<td>12.4% 4.76 [3.89; 5.82]</td>
</tr>
<tr>
<td>Pfizer BLA, 12-15</td>
<td>121</td>
<td>1131</td>
<td>22</td>
<td>1129</td>
<td>2.4% 5.49 [3.51; 8.58]</td>
</tr>
<tr>
<td>Moderna BLA, 18+</td>
<td>3275</td>
<td>15379</td>
<td>685</td>
<td>15359</td>
<td>76.3% 4.77 [4.41; 5.17]</td>
</tr>
<tr>
<td>Moderna BLA, 12-17</td>
<td>629</td>
<td>2485</td>
<td>60</td>
<td>1240</td>
<td>8.9% 5.23 [4.05; 6.76]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>23943</td>
<td>22649</td>
<td>100.0%</td>
<td></td>
<td>4.83 [4.50; 5.18]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0; Chi² = 0.79, df = 3 (P = 0.85); I² = 0%

*Reactogenicity data are from the original monovalent Moderna and Pfizer randomized controlled trials

BLA: Biologics License Application
GRADE: Reactogenicity, Severe (Grade ≥3), Adults and Adolescents

- Randomized Controlled Trials (n=4)
  - Pooled RR 4.83 (95% CI: 4.50–5.18)
  - Very serious concern for indirectness, as the body of evidence did not include anyone who received an updated dose, were from a prior period of the pandemic, and excluded persons with prior COVID-19 infection, pregnant or breastfeeding women, and persons who were immunocompromised.
- Evidence type: Low certainty

CI: Confidence interval; RR: Risk ratio
## Summary of GRADE – Adults and Adolescents

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically-attended COVID-19 (ED/UC visit)</td>
<td>Critical</td>
<td>OBS (2)</td>
<td>Updated COVID-19 vaccine is effective in preventing medically attended COVID-19 ED/UC visits.</td>
<td>Low</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>OBS (4)</td>
<td>Updated COVID-19 vaccine prevents hospitalization due to COVID-19</td>
<td>Low</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>OBS (2)</td>
<td>Updated COVID-19 vaccine prevents death due to COVID-19</td>
<td>Very low</td>
</tr>
<tr>
<td>Post-COVID Conditions</td>
<td>Important</td>
<td>OBS (0)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### Benefits

**Post-COVID Conditions**

- *Importance*: Important
- *Design*: OBS (0)
- *Findings*: -
- *Evidence type*: -

### Harms

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious adverse events</td>
<td>Critical</td>
<td>OBS (2)</td>
<td>In post-authorization safety monitoring, myocarditis and anaphylaxis were rare but more common following vaccination</td>
<td>Low</td>
</tr>
<tr>
<td>Reactogenicity</td>
<td>Important</td>
<td>RCT (4)</td>
<td>Severe reactions within 7 days were more common in vaccinated</td>
<td>Low</td>
</tr>
</tbody>
</table>

**ED**: emergency department; **UC**: urgent care; **OBS**: observational; **RCT**: randomized controlled trial
Infants and Children Benefits GRADE: Adolescent and adult benefits downgraded for indirectness

- Systematic review for benefits of vaccination did not capture a sufficient amount of data for evidence synthesis in pediatrics, however data in adults provide indirect evidence of benefits

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Design (# of studies)</th>
<th>Pooled VE (95% CI)</th>
<th>Evidence type</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically-attended COVID-19 (ED/UC visit)</td>
<td>OBS (2)</td>
<td>53.1 (49.7-56.3)</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>OBS (4)</td>
<td>47.8 (29.6-61.4)</td>
<td>Low</td>
<td>Very low</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>OBS (2)</td>
<td>60.5 (40.7-73.7)</td>
<td>Very low</td>
<td>Very low</td>
</tr>
</tbody>
</table>

ED: emergency department; UC: urgent care; OBS: observational
Specified Serious Adverse Events (Myocarditis/Pericarditis), Infants and Children

A single observational study from the Vaccine Safety Datalink (VSD) evaluated chart-reviewed cases of myocarditis occurring among children aged 5-11 years following a monovalent booster based on events occurring in a 7-day risk interval after vaccination vs. a comparison interval in vaccinated individuals.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Cases/Monovalent Booster Doses Administered</th>
<th>Incidence Rate/Million Doses (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pfizer</strong> Male&lt;br&gt;5-11 y</td>
<td>0/50415</td>
<td>0.0 (0.0-59.4)</td>
</tr>
<tr>
<td>Female&lt;br&gt;5-11 y</td>
<td>0/49261</td>
<td>0.0 (0.0-60.8)</td>
</tr>
</tbody>
</table>

Specified Serious Adverse Events (Anaphylaxis), Infants and Children

- Risk of anaphylaxis in children can be indirectly inferred from the known risk in persons ages 12 and older
  - 4.8 (95% CI 3.2-6.9) per million doses of Pfizer-BioNTech original monovalent
  - 5.1 (95% CI: 3.3-7.4) per million doses of original Moderna monovalent
  - There were fewer cases of anaphylaxis post dose 2 compared with dose 1

Observational Studies (n=2)

- Two specific, rare SAEs have been associated with vaccination through safety surveillance.
- Serious concern for indirectness, as the body of evidence for myocarditis was only among children aged 5-11 receiving a monovalent booster and the body of evidence for anaphylaxis was among adults and adolescents aged 12 years and older receiving a primary series.
- Evidence type: **Very low certainty**
Reactogenicity*, Severe (Grade ≥3) (n=2), Infants and Children

*Reactogenicity data are from the original monovalent Moderna and Pfizer randomized controlled trials.
GRADE: Reactogenicity, Severe (Grade ≥3) (n=2)

- RCTs (n=2)
  - Pooled RR 4.69 (95% CI: 3.43–6.41)
  - Very serious concern for indirectness was present. The available body of evidence did not include anyone who received an updated dose and excluded children were immunocompromised. While children with a history of COVID-19 infection were included in the safety sets, the RCTs were conducted at a time of low seroprevalence.
  - Evidence type: **Low certainty**
## Summary of GRADE – Infants and Children

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Importance</th>
<th>Design (# of studies)</th>
<th>Findings</th>
<th>Evidence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medically-attended COVID-19 (ED/UC visit)</td>
<td>Critical</td>
<td>OBS (2)</td>
<td>Updated COVID-19 vaccine is effective in preventing medically attended COVID-19 ED/UC visits, although the body of evidence is limited to indirect data from adolescents and adults</td>
<td>Very low</td>
</tr>
<tr>
<td>Hospitalization due to COVID-19</td>
<td>Critical</td>
<td>OBS (4)</td>
<td>Updated COVID-19 vaccine prevents hospitalization due to COVID-19, although the body of evidence is limited to indirect data from adolescents and adults</td>
<td>Very low</td>
</tr>
<tr>
<td>Death due to COVID-19</td>
<td>Important</td>
<td>OBS (2)</td>
<td>Updated COVID-19 vaccine prevents death due to COVID-19, although the body of evidence is limited to indirect data from adolescents and adults</td>
<td>Very low</td>
</tr>
<tr>
<td>Post-COVID Conditions</td>
<td>Important</td>
<td>OBS (0)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MIS-C</td>
<td>Important</td>
<td>OBS (0)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

### Benefits

| Serious adverse events                      | Critical   | OBS (2)               | In post-authorization safety monitoring, two specific adverse events have been associated with vaccination                                           | Very Low      |
| Reactogenicity                              | Important  | RCT (2)               | Severe reactions within 7 days were more common in vaccinated                                                                                                                                       | Low           |

ED: emergency department; UC: urgent care; OBS: observational; RCT: randomized controlled trial
Novavax vaccine effectiveness and safety

- Due to lower uptake of Novavax COVID-19 vaccine, no post-authorization vaccine effectiveness estimates from prior COVID-19 vaccine formulation are available.
- Post-authorization safety data are also limited by the low number of doses administered \(^1\)
  - Available data from the Vaccine Adverse Event Reporting System (VAERS) are consistent with those from preauthorization clinical trials.
  - Most VAERS reports were classified as nonserious.
    - The most commonly reported AEs included dizziness, fatigue, and headache.
  - No new safety concerns were identified.

\(^1\) [https://www.cdc.gov/mmwr/volumes/72/wr/mm7231a4.htm](https://www.cdc.gov/mmwr/volumes/72/wr/mm7231a4.htm)
Estimated COVID-19 hospitalizations prevented over 6 months for every million mRNA COVID-19 doses, among those age <50 years, by age group

Based on hospitalization rates from Spring 2023 (low), December 2022 (high winter), Summer 2022 (high past year)
Calculating Risk: Myocarditis and COVID-19 vaccines

- Limited data to inform myocarditis risk after bivalent COVID-19 vaccine booster dose
  - Myocarditis rates following booster doses in adolescent and young adult males are lower than rates following primary series, but estimates are limited by fewer numbers of doses for both the bivalent boosters and the previous monovalent boosters administered in VSD

- Myocarditis risk lower with longer time between doses
  - Rates of myocarditis lower with extended interval between dose 1 and dose 2 for primary series
  - Longer interval between updated doses may also impact myocarditis rates

- Most individuals with myocarditis/pericarditis have fully recovered at follow-up

- The risk of adverse cardiac outcomes were 1.8 – 5.6 times higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination among males ages 12-17 years

4 https://www.cdc.gov/mmwr/volumes/71/wr/mm7114e1.htm?s_cid=mm7114e1_w
Estimated COVID-19 hospitalizations prevented vs. potential myocarditis cases for every million mRNA COVID-19 vaccine doses: 12 – 17-year-olds

Per million doses in 12 – 17-year-olds over 6 months

- 19 – 95 hospitalizations prevented
- 5 – 19 ICU admissions prevented
- 0 – 1 death prevented

0 myocarditis cases in 55,649 males with a bivalent dose
0 myocarditis cases in 57,776 females with a bivalent dose

1 Results were adjusted to account for potential incidental findings of SARS-CoV-2 infection by multiplying the estimated hospitalizations, ICU admissions, and deaths prevented by the estimated percent of COVID-NET hospitalizations that are likely due to COVID-19 among 12 – 17-year-olds during Omicron BA.5 predominant period (55%)  
2 Ranges presented for benefits are based on the high and low incidence scenarios presented on slides 7 and 8  
3 Based on preliminary Pfizer-BioNTech bivalent booster safety data from VSD (incident rate/million doses): 0 (95% CI: 0-54) in males and 0 (95% CI: 0-52) in females
Universal vaccine recommendations projected to prevent about 400,000 hospitalizations and 40,000 deaths over the next 2 years compared with no recommendation, regardless of level of immune escape.

https://covid19scenariomodelinghub.org/
Compared with only vaccinating those 65+ years, universal vaccine recommendations projected to prevent about 200,000 more hospitalizations and 15,000 more deaths over the next 2 years.

https://covid19scenariomodelinghub.org/
Domain Equity Question:
Are the desirable and undesirable anticipated effects demonstrated across all populations equally?
Are the desirable and undesirable anticipated effects demonstrated across all populations equally?

- There is no evidence to suggest that COVID-19 vaccine effectiveness varies substantially by race/ethnicity\(^1,2\)
  - Differences in vaccine hesitancy/uptake, crowding, access to care, and prior infection could impact vaccine effectiveness and these factors may also differ by race/ethnicity

- There is no evidence to suggest that COVID-19 vaccine safety profiles vary by race/ethnicity, however risk has been shown to differ by age and sex
  - Risk for myocarditis is highest in adolescent and young adult males

- Benefits and harms for the U.S. population are best assessed when clinical trial and study populations are optimally representative of the U.S. population

1. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9619452/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9619452/)
2. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9763212/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9763212/)
Summary

Benefits and Harms

- Monovalent XBB containing COVID-19 vaccines **increase the immune response** against the currently circulating variants
- Last year’s updated vaccine was **effective** at preventing medically attended COVID-19, hospitalization due to COVID-19, and death due to COVID-19
- Accumulating evidence that COVID-19 vaccination reduces Post-COVID Conditions among both children and adults
- COVID-19 vaccines have a **high degree** of safety
  - Rare events of myocarditis and anaphylaxis have been seen in post-authorization studies
  - Unlikely that updating the formulation would increase adverse event rates
- **Benefits** are anticipated in all age groups; benefits of COVID-19 vaccines vary by age and incidence of COVID-19 hospitalizations
- **Benefits outweigh risks** in age groups for which risk of myocarditis is highest
- Modeling projects **more hospitalizations and deaths averted** when updated doses are **universally recommended** compared to no recommendation or recommended only for persons ≥65 years
Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial are the anticipated effects for each main outcome for which there is a desirable effect?

<table>
<thead>
<tr>
<th>Minimal</th>
<th>Small</th>
<th>Moderate</th>
<th>Large</th>
<th>Varies</th>
<th>Don’t know</th>
</tr>
</thead>
</table>

**Majority opinion**

**Minority opinion**
Benefits and Harms

How substantial are the undesirable anticipated effects?

• How substantial are the anticipated effects for each main outcome for which there is an undesirable effect?

○ Minimal  ○ Small  ○ Moderate  ○ Large  ○ Varies  ○ Don’t know
Benefits and Harms

Do the desirable effects outweigh the undesirable effects?

• What is the balance between the desirable effects relative to the undesirable effects?

  □ Favors intervention (2023 – 2024 COVID-19 vaccine)
  □ Favors comparison (no vaccine)
  □ Favors both
  □ Favors neither
  □ Unclear
EtR Domain:

Values
Americans’ assessment of COVID-19 in the U.S., February 2023

What’s your impression of the coronavirus situation in the U.S. today?

- % Getting better
- % Staying about the same
- % Getting worse

A nationally representative survey of U.S. adults conducted February 21-28 by web using the Gallup Panel

30% of U.S. adults report they are very or moderately concerned about getting COVID-19, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Concern about serious COVID-19 illness in family, March 2023

Monmouth University. Life Mostly Back to Pre-Covid Normal. Life Mostly Back to Pre-Covid Normal | Monmouth University Polling Institute | Monmouth University Accessed August 29, 2023
Domain Equity Question:
Is there important variability in how patients or populations value the outcome?
Concern about getting COVID-19 by race and ethnicity, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Concern about getting COVID-19 by urbanicity, U.S., August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Concern about getting COVID-19 by income, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Summary

Values

- As of February 2023, the majority of Americans felt COVID-19 was getting better
- 30% of U.S. adults report they are very or moderately concerned about getting COVID-19
- Half of U.S. adults continue to have concern about a family member becoming seriously ill from COVID-19
- Racial and ethnic minority groups, those living in urban areas, and those with lower incomes are more concerned about getting COVID-19
Values

Criteria 1:

Does the target population feel that the desirable effects are large relative to undesirable effects?

- How does the target population view the balance of desirable versus undesirable effects?
- Would patients/caregivers feel that the benefits outweigh the harms and burden?
- Does the population appreciate and value the 2023 – 2024 COVID-19 vaccine?

- Minimal
- Small
- Moderate
- Large
- Varies
- Don’t know

Majority opinion

Minority opinion
Values

Criteria 2:
Is there important uncertainty about, or variability in, how much people value the main outcomes?

- How much do individuals value each outcome in relation to the other outcomes?
- Is there evidence to support those value judgements?
- Is there evidence that the variability is large enough to lead to different decisions?

- Important uncertainty or variability
- Probably important uncertainty or variability
- Probably not important uncertainty or variability
- No important uncertainty or variability
- No known undesirable outcomes

[Options for majority and minority opinion]
EtR Domain:

Acceptability
Intent to get new, updated COVID-19 vaccine, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Bivalent COVID-19 vaccine receipt and intent among adults 18 years and older, June 2023

A nationally representative sample of U.S. adults aged 18 years and older
IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data

### Among 1+ vaccinated (N=3,248)
- **Received bivalent COVID-19 vaccine**: 44.7%
- **Definitely will get vaccine**: 3.4%
- **Probabaly will get vaccine or unsure**: 23.8%
- **Probably/definitely will not get vaccine**: 28.1%

### Among unvaccinated (N=783)
- **Received bivalent COVID-19 vaccine**: 10.5%
- **Definitely will get vaccine**: 88%
- **Probabaly will get vaccine or unsure**: 0%
- **Probably/definitely will not get vaccine**: 0%
# Top concerns or issues regarding bivalent COVID-19 vaccine, June 2023

<table>
<thead>
<tr>
<th>Definitely will</th>
<th>Received 1+ doses of COVID-19 vaccine but not the bivalent vaccine</th>
<th>Unvaccinated with any COVID-19 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Too busy or kept forgetting (36.3%)</td>
<td>Omitted (N&lt;30)</td>
</tr>
<tr>
<td><strong>Probably will or unsure</strong></td>
<td>• Had enough vaccines (27%)</td>
<td>• Unknown serious side effects (37.1%)</td>
</tr>
<tr>
<td></td>
<td>• Too busy or kept forgetting (22.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• No provider recommendation (19.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Unknown serious side effects (12.8%)</td>
<td></td>
</tr>
<tr>
<td><strong>Probably or definitely will NOT</strong></td>
<td>• Unknown serious side effects (43.1%)</td>
<td>• Unknown serious side effects (56.5%)</td>
</tr>
<tr>
<td></td>
<td>• Had enough vaccines (42.4%)</td>
<td>• Do not trust gov’t/pharma (50.5%)</td>
</tr>
<tr>
<td></td>
<td>• Not enough studies (33.8%)</td>
<td>• Not enough studies (47.1%)</td>
</tr>
<tr>
<td></td>
<td>• Do not trust gov’t/pharma (30%)</td>
<td>• Heart-related issues (39.6%)</td>
</tr>
<tr>
<td></td>
<td>• Effectiveness (29.8%)</td>
<td>• Effectiveness (36.1%)</td>
</tr>
<tr>
<td></td>
<td>• Heart-related issues (28.6%)</td>
<td></td>
</tr>
</tbody>
</table>

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data
Confidence in vaccine safety is higher for influenza and other routine adult vaccines than for COVID-19 vaccine, June 2023

Analysis limited to those who responded to all three survey questions (N=4,164). Omitted category of respondents who answered “not sure” is <1%.

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data
Vaccine recommendation by healthcare provider (among those eligible to receive the vaccine), June 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data
Vaccine receipt by healthcare provider recommendation (among those eligible to receive the vaccine), June 2023

A nationally representative sample of U.S. adults aged 18 years and older

[Bar chart showing provider recommendation vs. no provider recommendation for COVID-19, Flu, Pneumonia, Tetanus, and Shingles vaccine receipt]

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data
Data from the Fall 2022 DocStyles survey were analyzed to examine the prevalence of COVID-19 vaccination attitudes and practices among health care providers (HCPs) caring for women of reproductive age, and to assess whether providers recommended and offered or administered the COVID-19 vaccines to their pregnant patients.

Overall, 82.9% of providers reported recommending COVID-19 vaccination to women of reproductive age, and 54.7% offered or administered the vaccine in their practice.

Among HCPs who cared for pregnant patients, obstetrician-gynecologists were more likely to recommend COVID-19 vaccination to pregnant patients (94.2%) than were family practitioners/internists (82.1%).

HCPs were more likely to offer or administer COVID-19 vaccination onsite to pregnant patients if they also offered or administered influenza and Tdap vaccines.
Domain Equity Question:
Is the intervention equally acceptable across all populations?
COVID-19 vaccine safety confidence by race and ethnicity, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Vaccine is completely safe</th>
<th>Very safe</th>
<th>Somewhat safe</th>
<th>Not at all safe</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, non-Hispanic (N=2,830)</td>
<td>23.2</td>
<td>24.9</td>
<td>28.6</td>
<td>23.3</td>
</tr>
<tr>
<td>Black, non-Hispanic (N=476)</td>
<td>18.9</td>
<td>24.6</td>
<td>36.3</td>
<td>20.2</td>
</tr>
<tr>
<td>Hispanic (N=626)</td>
<td>22.3</td>
<td>26.3</td>
<td>30.5</td>
<td>20.9</td>
</tr>
<tr>
<td>Other, non-Hispanic (N=347)</td>
<td>20.6</td>
<td>32.2</td>
<td>32.7</td>
<td>14.5</td>
</tr>
</tbody>
</table>
COVID-19 vaccine safety confidence by income, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data

<table>
<thead>
<tr>
<th>Income Category</th>
<th>Vaccine is completely safe</th>
<th>Very safe</th>
<th>Somewhat safe</th>
<th>Not at all safe</th>
</tr>
</thead>
<tbody>
<tr>
<td>$24,999 or less (N=619)</td>
<td>14.7%</td>
<td>20.5%</td>
<td>35.7%</td>
<td>29.1%</td>
</tr>
<tr>
<td>$25,000-$49,999 (N=797)</td>
<td>18.1%</td>
<td>20.1%</td>
<td>37.1%</td>
<td>24.7%</td>
</tr>
<tr>
<td>$50,000-$74,999 (N=788)</td>
<td>21.2%</td>
<td>26.0%</td>
<td>30.6%</td>
<td>22.2%</td>
</tr>
<tr>
<td>$75,000+ (N=2,075)</td>
<td>26.9%</td>
<td>29.7%</td>
<td>25.5%</td>
<td>17.8%</td>
</tr>
</tbody>
</table>

Weighted %
COVID-19 vaccine safety confidence by urbanicity, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
Intent to get new, updated COVID-19 vaccine by age, August 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data
### Percent of people receiving COVID-19 vaccine by age

**December 14, 2020 – May 10, 2023***

<table>
<thead>
<tr>
<th>Age Group</th>
<th>At Least One Dose</th>
<th>Completed Primary Series</th>
<th>Updated (Bivalent) Booster Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 yrs</td>
<td>8.9%</td>
<td>4.7%</td>
<td>0.6%</td>
</tr>
<tr>
<td>2-4 yrs</td>
<td>10.9%</td>
<td>6.1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>5-11 yrs</td>
<td>40.0%</td>
<td>32.9%</td>
<td>4.8%</td>
</tr>
<tr>
<td>12-17 yrs</td>
<td>72.2%</td>
<td>61.8%</td>
<td>7.8%</td>
</tr>
<tr>
<td>18-24 yrs</td>
<td>82.3%</td>
<td>66.8%</td>
<td>7.4%</td>
</tr>
<tr>
<td>25-49 yrs</td>
<td>85.5%</td>
<td>72.2%</td>
<td>12.1%</td>
</tr>
<tr>
<td>50-64 yrs</td>
<td>95.0%</td>
<td>83.8%</td>
<td>21.7%</td>
</tr>
<tr>
<td>+65 yrs</td>
<td>95.0%</td>
<td>94.4%</td>
<td>43.3%</td>
</tr>
</tbody>
</table>

*Data cutoff on May 10, 2023 is due to the end of the Public Health Emergency (PHE) on May 11, 2023.

## Intent to get new, updated COVID-19 vaccine by race and ethnicity, August 2023

A nationally representative sample of U.S. adults aged 18 years and older.

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from August 2023 (N=4,299), unpublished data.

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Definitely will get vaccine</th>
<th>Probably will</th>
<th>Unsure</th>
<th>Probably will not</th>
<th>Definitely will not</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, non-Hispanic (N=2,832)</td>
<td>25.5</td>
<td>16.3</td>
<td>16.2</td>
<td>13.6</td>
<td>28.5</td>
</tr>
<tr>
<td>Black, non-Hispanic (N=478)</td>
<td>27.9</td>
<td>17</td>
<td>19.4</td>
<td>14</td>
<td>21.7</td>
</tr>
<tr>
<td>Hispanic (N=626)</td>
<td>22.2</td>
<td>21.7</td>
<td>22.1</td>
<td>11.6</td>
<td>22.4</td>
</tr>
<tr>
<td>Other, non-Hispanic (N=347)</td>
<td>21.8</td>
<td>19.5</td>
<td>22.7</td>
<td>17.1</td>
<td>18.9</td>
</tr>
</tbody>
</table>

Weighted %
Estimated percent of people ≥ 18 years reporting COVID-19 vaccination by race/ethnicity

National Immunization Survey Adult COVID Module, April 22, 2021 – March 25, 2023

<table>
<thead>
<tr>
<th></th>
<th>AI/AN, NH</th>
<th>Asian, NH</th>
<th>Black, NH</th>
<th>Hispanic/Latino</th>
<th>NHOPI, NH</th>
<th>White, NH</th>
</tr>
</thead>
<tbody>
<tr>
<td>At Least One Dose</td>
<td>81.0%</td>
<td>98.2%</td>
<td>89.2%</td>
<td>89.1%</td>
<td>83.5%</td>
<td>87.0%</td>
</tr>
<tr>
<td>Completed Primary Series</td>
<td>75.8%</td>
<td>97.2%</td>
<td>85.1%</td>
<td>84.0%</td>
<td>82.6%</td>
<td>84.3%</td>
</tr>
<tr>
<td>Updated (Bivalent) Booster Dose Among Adults with a Completed Primary Series</td>
<td>28.5%</td>
<td>36.3%</td>
<td>29.3%</td>
<td>25.6%</td>
<td>18.6%</td>
<td>37.5%</td>
</tr>
</tbody>
</table>

COVID-19 vaccine receipt by healthcare provider recommendation by race and ethnicity, June 2023

A nationally representative sample of U.S. adults aged 18 years and older

IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, results from June 2023 (N=4,214), unpublished data
Percent of pregnant people ages 18-49 years who are up to date* with COVID-19 vaccines overall and by race and ethnicity – Vaccine Safety Datalink, September 1, 2022 – July 29, 2023

*Up to date is defined as the percent of pregnant people who received an updated bivalent dose before or during pregnancy, with the denominator including those pregnant at least 1 day during the specified month ending date, and the numerator including those who received an updated bivalent dose. CDC recommended bivalent boosters to persons age ≥12 years starting September 1, 2022. Data on bivalent boosters among pregnant persons was available starting September 4, 2022, and includes doses received starting September 1, 2022.

CDC. COVID-19 vaccination among pregnant people aged 18-49 years overall, by race and ethnicity, and date reported to CDC – Vaccine Safety Datalink,* United States. https://covid.cdc.gov/covid-data-tracker/#vaccinations-pregnant-women Accessed August 9, 2023
Summary

Acceptability

- Vaccine receipt varies by age and race/ethnicity
- Fall vaccination intent increases with increasing age; those ages 65+ have the highest percentage reporting they “definitely” or “probably” will get the vaccine compared to other age groups
- Confidence in COVID-19 vaccine safety differs across the population
- Compared to other vaccines, COVID-19 vaccines were recommended the least by health care providers
- Those who received a provider recommendation overall and by race and ethnicity were more likely to receive the recommended vaccine
- Encouraging health care providers to recommend, offer, and administer COVID-19 vaccines, could help reinforce vaccine confidence and increase coverage

1. Fall 2022 DocStyles, unpublished data
Acceptability

Is the 2023 – 2024 COVID-19 vaccine acceptable to key stakeholders?

• Are there key stakeholders that would not accept the distribution of benefits and harms?
• Are there key stakeholders that would not accept the undesirable effects in the short term for the desirable effects (benefits) in the future?

○ No  ○ Probably no  ○ Probably yes  ○ Yes  ○ Varies  ○ Don’t know

Majority opinion  Minority opinion
EtR Domain:
Feasibility
Vaccines with a monovalent XBB.1.5 composition will be the first COVID-19 vaccines to be available directly from the manufacturers as part of the commercial market, rather than through the United States Government (USG).

The public will continue to be directed to Vaccines.gov to find providers offering COVID-19 vaccine.

While providers will no longer be required to report inventory to Vaccines.gov after vaccines transition to being available on the commercial market, they will continue to be encouraged to report voluntarily.

– Providers are also strongly encouraged to report the minimum age (in months and years) for whom a location can administer vaccine.

CDC will continue its efforts to make sure that all people have access to COVID-19 medical countermeasures and know where to find product now and in the future.

Feasibility of vaccine implementation

- Inclusion of COVID-19 vaccines in Vaccines for Children (VFC) will likely result in more pediatricians stocking the vaccine.

- There will be single dose vial presentations and smaller minimum order quantities.
  - Directly addresses concerns from health care providers (HCPs), likely to reduce wastage, eases logistics and helps with storage capacity limitations.
  - Moderna, 12+ years: single dose vial (10-pack) and manufacturer-prefilled syringes (10-pack).
  - Moderna, 6 months – 11 years: single dose vial (10-pack).
  - Novavax, 12+ years: 5-dose multi-dose vial (2 vials per carton).
  - Pfizer, 12+ years: single dose vial (10-pack), limited quantity of manufacturer-prefilled syringes (10-pack).
  - Pfizer, 5 – 11 years: single dose vial (10-pack).
  - Pfizer, 6 months – 4 years: 3-dose multi-dose vial (10-pack).

- Preparation is the same or simpler than it was before.
  - Moderna preparation is the same (no dilution).
  - Novavax preparation is the same (no dilution).
  - Pfizer preparation is simplified (currently 2 presentations require dilution; for 2023 – 2024 COVID-19 vaccine, ONLY little peds formulation require dilution).
Storage and handling will be the SAME as it is now
- Moderna: Frozen until expiration; 30 days at refrigerator storage
- Novavax: Stable at 2-8°C (refrigerator storage); 9-month shelf life; use within 12 hours of first puncture
- Pfizer: Ultra-cold storage until expiration; 10 weeks at refrigerator storage
  • Ultra-cold storage continues to be a challenge; most provider offices do not have a unit

Dose volume for Pfizer is simplified (all doses are 0.3mL)
Modernna now only has two presentations, reducing the chance for errors
Barriers to implementation

- There are now THREE seasonal vaccines and preventative products\(^1\) for respiratory diseases to manage
  - More seasonal vaccines to manage
  - Limited storage space and more vaccines
  - More opportunities for vaccine administration errors

- Providers have to adapt to new cap/label colors
  - Moderna: 6 months – 11 years is **blue** cap/**green** label; 12+ years is **blue** cap/**blue** label
  - Novavax: 12+ is **blue**
  - Pfizer: 6 months – 4 years is **yellow**; 5 – 11 years is **blue**; 12+ years is **gray**

- Moderna, Novavax and Pfizer all have products with blue caps, introducing opportunity for error

---

\(^1\) COVID-19 vaccine, Influenza vaccine, RSV vaccine, and nirsevimab, a long-acting monoclonal antibody for RSV prevention in infants

Immunization Services Division, internal planning documents
Domain Equity Question:
Is the intervention equally feasible to implement across all populations?
There are disparities in uninsured status that could impact who gets a COVID-19 vaccine.

Percent of US adults without health insurance:

- White: 5%
- Black: 10%
- American Indian and Alaska Native: 15%
- Asian: 20%
- Native Hawaiian and Other Pacific Islander: 25%
- Hispanic or Latino: 25%

CDC vaccine programs for people who are uninsured

- CDC will provide access to COVID-19 vaccines for uninsured individuals once COVID-19 vaccines become commercially available

- Uninsured children will be able to receive COVID-19 vaccines through the existing Vaccines for Children (VFC) program
  - The VFC program offers vaccines at no low or no cost to eligible children through a national network of participating health care providers

- Adults who are uninsured or underinsured will be able to receive no-cost COVID-19 vaccines through the temporary Bridge Access Program for COVID-19 Vaccines. This program consists of two components:
  - Public health infrastructure: through state immunization programs, State and local health departments and HRSA-supported health centers will provide no-cost COVID-19 vaccines to adults who are uninsured or underinsured
  - Participating retail pharmacies: CVS, Walgreens, and eTrueNorth will continue to provide no-cost COVID-19 vaccines to adults who are uninsured or underinsured

Availability of vaccines in underserved communities

- CDC's Bridge Access Program for COVID-19 Vaccines and COVID-19 vaccine implementation plans are intentionally designed to overcome barriers to access and availability
  - This includes design for maximized proximity to no-cost COVID-19 vaccines among populations of people who are uninsured or underinsured
- CDC and HHS continue to invest in health systems and programs that support vaccine access and outreach in underserved communities – such as HRSA-Supported Health Centers, Rural Health Clinics, and State and local health departments
  - These networks can be leveraged for access to COVID-19 vaccines as well as other needed medicines

Summary

Feasibility

- Implementation of the 2023 – 2024 COVID-19 vaccine will likely reduce wastage, ease logistics, help with storage capacity limitations and reduce the chance of errors.
- Nevertheless, there will be now be three seasonal vaccines for respiratory diseases, in which there will be more seasonal vaccines to manage, limited storage space due to additional vaccines and more opportunities for vaccine administration errors.
- Vaccines will continue to be accessible after commercialization, with readily available resources for those who are uninsured, underinsured, or who reside in underserved communities.
Feasibility

Is the 2023 – 2024 COVID-19 vaccine feasible to implement among populations currently recommended for a dose?
- Is the 2023 – 2024 COVID-19 vaccine program sustainable?
- Are there barriers that are likely to limit the feasibility of implementing the 2023 – 2024 COVID-19 vaccine or require considerations when implementing it?
- Is access to the 2023 – 2024 COVID-19 vaccine an important concern?

- No
- Probably no
- Probably yes
- Yes
- Varies
- Don’t know
EtR Domain:
Resource Use
COVID-19 vaccination is a cost–effective intervention, particularly in persons ages ≥65 years in which the vaccine is cost saving.

Cost-effectiveness estimates in those ages ≥50 years were robust to input changes across plausible ranges.

Cost-effectiveness estimates in those 18-49 years were sensitive to changes in inputs. If vaccine effectiveness or hospitalization rates are higher than anticipated, the cost-effectiveness estimates would be more favorable.

Cost-effectiveness estimates are not yet available for pediatric population.
Domain Equity Question:
Is the intervention a reasonable and efficient allocation of resources across all populations?
Is the intervention a reasonable and efficient allocation of resources across all populations?

- COVID-19 vaccination is **most cost-effective** in older adults in which disease burden is highest compared to younger adults.
- COVID-19 vaccination is **likely more cost-effective** in populations with risk factors, such as underlying conditions, which increase their probability of hospitalization due to COVID-19.
- Additional work is ongoing to evaluate cost-effectiveness in the pediatric populations.
Is the 2023 – 2024 COVID-19 vaccine a reasonable and efficient allocation of resources?

- What is the cost-effectiveness of the 2023 – 2024 COVID-19 vaccine?
- How does the cost-effectiveness of the 2023 – 2024 COVID-19 vaccine change in response to changes in context, assumptions, etc.?

Majority opinion: Yes

Minority opinion: Probably yes
Summary and Work Group Interpretations
The burden of COVID-19 varies by age and underlying condition status with those ages ≥65 years and those with multiple underlying conditions having the highest risk of severe outcomes due to COVID-19.

COVID-19 burden is currently lower than at previous points in the pandemic, however there are still thousands of hospitalizations and hundreds of deaths each week.

Children and adults ages 5 – 49 years had the lowest hospitalization rates overall – Severe outcomes occur in this age group, including in people with no underlying medical conditions.

Although hospitalization rates are currently low, we have seen rates increase in recent weeks and anticipate further increases as we enter respiratory virus season.

Majority of U.S. population has some level of immunity due to infection, vaccination, or both – Vaccine and infection-induced immunity wane and new variants have emerged, suggesting that susceptibility remains and may increase over time.

Racial and ethnic minority groups have been disproportionately affected by COVID-19.
Summary and Work Group Interpretation: Benefits and Risks

- Monovalent XBB containing COVID-19 vaccines **increase the immune response** against the currently circulating variants.
- Last year’s updated vaccine was **effective** at preventing medically attended COVID-19, hospitalization due to COVID-19, and death due to COVID-19.
- COVID-19 vaccines have a **high degree** of safety – unlikely that updating the formulation would increase adverse event rates.
- **Benefits** are anticipated in all age groups; benefits of COVID-19 vaccines vary by **age**, and incidence of COVID-19 hospitalizations.
- **Benefits outweigh risks** in age groups for which there is a risk of myocarditis.
- Modeling projects **more hospitalization and deaths averted** when updated doses are **universally recommended** compared to no recommendation or recommended only for persons ≥65 years.
Summary and Work Group Interpretation: Considerations Regarding a Universal vs. Non-universal Policy

- Work Group considered non-universal policy options, with considerable discussion around the magnitude of benefits in the young, healthy population.
- As part of these deliberations, Work Group requested additional data on severe illness due to COVID-19 in those with and without underlying conditions:
  - No group that clearly had no risk of severe illness.
  - The vast majority of the US population has an underlying condition that would qualify under a risk-based recommendation.
    - Prevalence of overweight and obesity alone is >70% of adults\(^1\).
  - Risk-based recommendation would not allow access to COVID-19 vaccines for all that wanted them.
- Shared clinical decision making could create barriers to vaccination and may not effectively target those at highest risk.
- COVID-19 epidemiology remains uncertain and non-universal recommendations would need to be quickly revisited if there was an increase in burden.
- Still substantial COVID-19 disease burden and simple, stable recommendations may increase vaccine coverage over time.
- Work Group emphasized that COVID-19 recommendations should be reviewed on an ongoing basis as more is learned about COVID-19 seasonality and disease burden in the future.

\(^1\)National Health Statistics Reports; [https://stacks.cdc.gov/view/cdc/106273](https://stacks.cdc.gov/view/cdc/106273)
Summary and Work Group Interpretation:
COVID-19 vaccine recommendations for children

- Burden of severe illness due to COVID-19 is lowest among children ages 5 – 17 years
- Despite lower burden relative to other age groups, hundreds of deaths due to COVID-19 occurred in this age group in 2021 and 2022
  - Half of pediatric COVID-19 deaths were in individuals with no underlying conditions
- Number of COVID-19 hospitalizations and deaths in this age group are comparable to the burden seen in other vaccine preventable diseases for which there are universal recommendations
- Potential additional benefits of vaccination, such as prevention of post-COVID conditions and potential for reduced school absenteeism
- Risk of myocarditis appears lower than the risk observed following primary series doses
  - Potentially lower due to increased interval between doses
  - Certainty is limited by relatively lower sample size of booster recipients in VSD
- Future COVID-19 epidemiology remains uncertain and the low disease burden we are currently seeing may not last
- After a robust discussion, Work Group was supportive of a universal recommendation at this time
<table>
<thead>
<tr>
<th>EtR Domain</th>
<th>Question</th>
<th>Work Group Judgments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Public Health</td>
<td>Is COVID-19 of public health importance?</td>
<td>Yes</td>
</tr>
<tr>
<td>Problem</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benefits and Harms</td>
<td>How substantial are the desirable anticipated effects?</td>
<td>Large</td>
</tr>
<tr>
<td></td>
<td>How substantial are the undesirable anticipated effects?</td>
<td>Small</td>
</tr>
<tr>
<td></td>
<td>Do the desirable effects outweigh the undesirable effects?</td>
<td>Favors intervention</td>
</tr>
<tr>
<td>Values</td>
<td>Does the target population feel the desirable effects are large relative to the undesirable effects?</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Is there important variability in how patients value the outcomes?</td>
<td>Probably important uncertainty or variability</td>
</tr>
<tr>
<td>Acceptability</td>
<td>Is the 2023-2024 COVID-19 vaccine acceptable to key stakeholders?</td>
<td>Yes / Probably yes / Varies</td>
</tr>
<tr>
<td>Feasibility</td>
<td>Is the 2023-2024 COVID-19 vaccine feasible to implement?</td>
<td>Yes</td>
</tr>
<tr>
<td>Resource Use</td>
<td>Is the 2023-2024 COVID-19 vaccine a reasonable and efficient allocation of resources?</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Evidence to Recommendations Framework
### Summary: Work Group Interpretations

<table>
<thead>
<tr>
<th>Balance of consequences</th>
<th>Undesirable consequences clearly outweigh desirable consequences in most settings</th>
<th>Undesirable consequences probably outweigh desirable consequences in most settings</th>
<th>The balance between desirable and undesirable consequences is closely balanced or uncertain</th>
<th>Desirable consequences probably outweigh undesirable consequences in most settings</th>
<th>Desirable consequences clearly outweigh undesirable consequences in most settings</th>
<th>There is insufficient evidence to determine the balance of consequences</th>
</tr>
</thead>
</table>

**Majority opinion**

**Minority opinion**
### Evidence to Recommendations Framework

**Summary: Work Group Interpretations**

<table>
<thead>
<tr>
<th>Type of recommendation</th>
<th>We do not recommend the intervention</th>
<th>We recommend the intervention for individuals based on shared clinical decision-making</th>
<th>We recommend the intervention</th>
</tr>
</thead>
</table>
ACIP recommends 2023–2024 (monovalent, XBB containing) COVID-19 vaccines as authorized under Emergency Use Authorization (EUA) or approved by Biologics License Application (BLA) in persons ≥6 months of age.
Clinical Considerations
Proposed 2023 – 2024 mRNA COVID-19 vaccine recommendations:

- Everyone ages 5 years and older is recommended to receive 1 dose of a 2023–2024 mRNA COVID-19 vaccine.

- Children ages 6 months–4 years should complete a multi-dose initial series (2 doses of Moderna or 3 doses of Pfizer-BioNTech mRNA COVID-19 vaccine) with at least one dose of the 2023–2024 COVID-19 vaccine.\(^1\)

- People who are moderately or severely immunocompromised should complete a 3-dose initial series with at least one dose of the 2023–2024 COVID-19 vaccine and may receive 1 or more additional 2023–2024 COVID-19 vaccine doses.\(^2\)

- Bivalent mRNA COVID-19 vaccines are no longer recommended in the United States.

---

1. Children ages 6 months – 4 years that previously received a single dose of Pfizer-BioNTech vaccine should receive 2 doses of Pfizer-BioNTech vaccine.
2. Additional details in the interim clinical considerations
# Key changes from bivalent mRNA recommendations

<table>
<thead>
<tr>
<th>Bivalent recommendations</th>
<th>Proposed 2023 – 2024 vaccine recommendations</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Everyone ages 6 years and older recommended for a single bivalent dose</td>
<td>Everyone ages 5 years and older recommended for a single 2023 – 2024 dose</td>
<td>Eliminates complex recommendations for 5-year-olds</td>
</tr>
<tr>
<td>Two Moderna dosages authorized for 6 months – 5 years, depending on vaccination history and immune status</td>
<td>All Moderna doses in ages 6 months – 11 years are now 25 µcg</td>
<td>Reduces the number of COVID-19 vaccine products in use</td>
</tr>
<tr>
<td>Optional 2\textsuperscript{nd} bivalent dose for those ages 65 years and older</td>
<td>No additional dose recommendation \textbf{at this time}</td>
<td>Will monitor epidemiology and vaccine effectiveness to determine if additional doses are needed</td>
</tr>
</tbody>
</table>
Acknowledgements

- Monica Godfrey
- Danielle Moulia
- Hannah Rosenblum
- Katherine Fleming-Dutra
- Ruth Link-Gelles
- Sarah Meyer
- Elisha Hall
- Joanna Regan
- Susan Goldstein
- Mary Chamberland
- JoEllen Wolicki
- Josephine Mak
- Morgan Najdowski
- Lauren Roper
- Karen Broder
- Melisa Shah

- Mehreen Meghani
- Romeo Galang
- Sascha Ellington
- Sierra Scarbrough
- Amadea Britton
- Jefferson Jones
- Aron Hall
- Barbara Mahon
- COVID-NET
- COVID-19 Scenario Modeling Hub
- University of Michigan COVID-19 Vaccination Modeling Team
- Immunization Safety Office
- Immunization Services Division
- Coronavirus and other Respiratory Viruses Division
- National Center for Immunization and Respiratory Diseases
Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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.

Photographs and images included in this presentation are licensed solely for CDC/NCIRD online and presentation use. No rights are implied or extended for use in printing or any use by other CDC CIOs or any external audiences.
Additional Clinical Considerations
Proposed recommendations for children aged 6 months–4 years who are not moderately or severely immunocompromised
Proposed recommendations for children aged 6 months – 4 years without immunocompromise

Doses recommended:

- Initial series of 2 Moderna vaccine doses OR 3 Pfizer-BioNTech vaccine doses
- At least 1 dose of 2023–2024 COVID-19 vaccine

- All doses should be homologous (i.e., from the same manufacturer)
- All Moderna doses in ages 6 months – 11 years are now 25 µcg
Proposed recommended 2023–2024 COVID-19 mRNA vaccines for people who are NOT immunocompromised, aged 6 months–4 years*

COVID-19 vaccination status as of September 2023

Unvaccinated

Vaccinated

Previously received COVID-19 vaccine(s)

Unvaccinated

Vaccinated

Recommendations for 2023–2024 vaccine, by manufacturer

*For information about administration intervals and people who transition from age 4 years to age 5 years during an mRNA vaccination series, see Table 1 in the Interim Clinical Considerations for Use of COVID-19 vaccines.
Proposed recommendations for people aged 5 years and older who are not moderately or severely immunocompromised
Proposed recommendations for people aged 5 years and older without immunocompromise

Doses recommended:

• 1 dose of 2023–2024 COVID-19 vaccine, regardless of prior vaccination history

- New harmonized age cutoff for recommendations for young children for Moderna and Pfizer-BioNTech COVID-19 vaccines
- Resulting in simplified recommendations for 5-year-olds
- All Moderna doses in ages 6 months – 11 years are now 25 µcg
- 2023–2024 COVID-19 vaccine dose is recommended at least 2 months after receipt of the last COVID-19 vaccine dose
Proposed recommended 2023–2024 COVID-19 mRNA vaccines for people who are NOT immunocompromised, aged 5–11 years*

COVID-19 vaccination status as of September 2023
- Unvaccinated
- Vaccinated

Previously received COVID-19 vaccine(s)

1 or more doses any mRNA

Recommendations for 2023–2024 vaccine, by manufacturer

- Moderna
  - 2023–2024
  - 1 dose
  - 0.25 mL/25 µg

- Pfizer-BioNTech
  - 2023–2024
  - 1 dose
  - 0.3 mL/10 µg

OR

COVID-19 vaccination status as of September 2023

*For information about administration intervals and people who transition from age 4 years to age 5 years during an mRNA vaccination series, see Table 1 in the Interim Clinical Considerations for Use of COVID-19 vaccines.
Proposed recommended 2023–2024 COVID-19 mRNA vaccines for people who are NOT immunocompromised, aged ≥12 years*

COVID-19 vaccination status as of September 2023

Unvaccinated

Vaccinated

1 or more doses any mRNA

1 or more doses Novavax or Janssen, including in combination with any mRNA vaccine dose(s)

Previously received COVID-19 vaccine(s)

Unvaccinated

1 dose 2023–2024 Moderna

0.5 mL/50 µg

OR

1 dose 2023–2024 Pfizer-BioNTech

0.3 mL/30 µg

Vaccinated

1 or more doses Novavax or Janssen, including in combination with any mRNA vaccine dose(s)

Recommendations for 2023–2024 vaccine, by manufacturer

*For information about administration intervals, see Table 1 in the Interim Clinical Considerations for Use of COVID-19 vaccines.
Proposed recommendations for people who are moderately or severely immunocompromised
Proposed recommendations for people aged ≥6 months who are moderately or severely immunocompromised

Doses recommended:

- Initial COVID-19 vaccine series*
- At least 1 2023–2024 COVID-19 vaccine dose
- May receive 1 or more additional 2023-2024 mRNA COVID-19 vaccine doses**

*Series of 3 homologous mRNA COVID-19 vaccine doses at time of initial vaccination. This could also include a history of receipt of 1 or more doses of Novavax or Janssen, including in combination with mRNA vaccine dose(s).

**Further additional dose(s) may be administered, informed by the clinical judgement of a healthcare provider and personal preference and circumstances. Further additional doses should be administered at least 2 months after the last 2023-2024 COVID-19 vaccine dose.
Proposed recommended 2023–2024 COVID-19 vaccines for people who ARE moderately or severely immunocompromised, aged 6 months–4 years*

<table>
<thead>
<tr>
<th>COVID-19 vaccination status as of September 2023</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previously received COVID-19 vaccine(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recommendations for 2023–2024 vaccine, by manufacturer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*For information about administration intervals, people who transition from age 4 years to age 5 years during an mRNA vaccination series, and administration of additional dose(s), see Table 2 in Interim Clinical Considerations for Use of COVID-19 Vaccines.

*OR*
Proposed recommended 2023–2024 COVID-19 vaccines for people who ARE moderately or severely immunocompromised, aged 5–11 years*

COVID-19 vaccination status as of September 2023

Unvaccinated

Previously received COVID-19 vaccine(s)

Unvaccinated

Vaccinated

Recommendations for 2023–2024 vaccine, by manufacturer

Unvaccinated

Vaccinated

Unvaccinated

Previously received COVID-19 vaccine(s)

Previously received COVID-19 vaccine(s)

Unvaccinated

Vaccinated

Previously received COVID-19 vaccine(s)

*For information about administration intervals, people who transition from age 4 years to age 5 years or age 11 years to age 12 years during an mRNA vaccination series, and administration of additional dose(s), see Table 2 in Interim Clinical Considerations for Use of COVID-19 Vaccines.
Proposed recommended 2023–2024 COVID-19 vaccines for people who ARE moderately or severely immunocompromised, aged ≥12 years*

COVID-19 vaccination status as of September 2023

Unvaccinated

Vaccinated

Previously received COVID-19 vaccine(s)

Unvaccinated

1 dose any Moderna

2 doses any Moderna

1 dose any Pfizer-BioNTech

2 doses any Pfizer-BioNTech

3 or more doses any mRNA vaccine

1 or more doses of Novavax or Janssen, including in combination with any mRNA vaccine dose(s)

Recommended for 2023–2024 vaccine, by manufacturer

Unvaccinated

Vaccinated

Unvaccinated

1 dose any Moderna

2 doses any Moderna

1 dose any Pfizer-BioNTech

2 doses any Pfizer-BioNTech

3 or more doses any mRNA vaccine

1 or more doses of Novavax or Janssen, including in combination with any mRNA vaccine dose(s)

*For information about administration intervals, people who transition from age 11 years to age 12 years during an mRNA vaccination series, and administration of additional dose(s), see Table 2 in Interim Clinical Considerations for Use of COVID-19 Vaccines.
Proposed 2023 – 2024 COVID-19 Vaccine Up to Date Definition

- Everyone aged 5 years and older are recommended to get one 2023–2024 COVID-19 vaccine to be up to date.

- Children aged 6 months–4 years and people who are moderately or severely immunocompromised need multiple doses, including at least one 2023–2024 COVID-19 vaccine dose to be up to date.

- People who are moderately to severely immunocompromised may get additional doses of the 2023–2024 COVID-19 vaccine.
Simultaneous administration of COVID-19 and other vaccines
Simultaneous administration of COVID-19 and other vaccines

In accordance with General Best Practice Guidelines for Immunization, routine administration of all age-appropriate doses of vaccines simultaneously (i.e., administering more than one vaccine on the same clinic day or “coadministration”) is recommended for children, adolescents, and adults if there are no contraindications at the time of the healthcare visit.

– Providers may simultaneously administer COVID-19, influenza, and respiratory syncytial virus (RSV) vaccines to eligible patients; the Health Alert Network (HAN) published on September 5, 2023 may be consulted for additional information about simultaneous administration of these vaccines.

– Simultaneous administration of COVID-19 vaccine and nirsevimab (a long-acting monoclonal antibody for certain infants and young children for prevention of RSV) is recommended.

– Coadministration of COVID-19 and RSV vaccine for older adults is acceptable.

– There are additional considerations if administering an orthopoxvirus vaccine and COVID-19 vaccine.

Interim Clinical Considerations for Use of COVID-19 Vaccines | CDC
Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023 | MMWR (cdc.gov)
Healthcare Providers: RSV Vaccination for Adults 60 Years of Age and Over | CDC
Interim Clinical Considerations for Use of JYNNEOS and ACAM2000 Vaccines during the 2022 U.S. Mpox Outbreak | Mpox | Poxvirus | CDC