Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases

Overview of September 12, 2023, Meeting of the Advisory Committee on Immunization Practices

National Adult and Influenza Immunization Summit

September 14, 2023

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Background

- **January 26, 2023:** FDA's VRBPAC supports updated monovalent COVID-19 for 2023-2024 and simplification of the schedule
- **February 24, 2023:** CDC's ACIP discussed the proposed simplified schedule and was supportive of the overall direction
- **April 18, 2023:** FDA amended EUAs for Pfizer and Moderna mRNA bivalent vaccines to align with the simplified schedule
- **April 19, 2023:** CDC's ACIP discussed changes; several gaps were identified
- **June 15, 2023:** FDA's VRBPAC supported selection of the XBB lineage for 2023-2024 COVID-19 vaccines
- **June 16, 2023:** FDA advised manufacturers who were updating vaccines to use the XBB.1.5 lineage
- **September 11, 2023:** FDA approved and authorized updated XBB lineage monovalent mRNA vaccines for the 2023-2024 season

Proposed Data Package Needed from Manufacturers for Authorization/Licensure

- Each vaccine manufacturer would prepare a comprehensive data package for regulatory review of their updated COVID-19 vaccine that follows the most recent recommendation of the FDA and its Advisory Committee
- Submitted data would include:
  - Chemistry, manufacturing, and control data for the updated vaccine to ensure product quality and consistency
  - Pre-clinical data to support effectiveness of the updated vaccine
- The need for clinical data prior to authorization/approval would be based on several criteria, including experience of the manufacturer, the genetic and antigenic relatedness of the updated vaccine component to previous vaccines, and the prior demonstration of efficacy with the specific vaccine platform
- Clinical data post-authorization/approval will be crucial for ongoing evaluation of the vaccine composition process

FDA Regulatory Actions -- September 11, 2023

- FDA approved and authorized for emergency use updated mRNA COVID-19 vaccines containing the Omicron variant XBB.1.5.
- Individuals 5 years of age and older regardless of previous vaccination are eligible to receive a single dose of an updated mRNA COVID-19 vaccine at least 2 months since the last dose of any COVID-19 vaccine.
- Individuals 6 months through 4 years of age who have previously been vaccinated against COVID-19 are eligible to receive one or two doses of an updated mRNA COVID-19 vaccine (timing and number of doses to administer depends on the previous COVID-19 vaccine received).
- Unvaccinated individuals 6 months through 4 years of age are eligible to receive three doses of the updated authorized Pfizer-BioNTech COVID-19 Vaccine or two doses of the updated authorized Moderna COVID-19 Vaccine.

FDA Takes Action on Updated mRNA COVID-19 Vaccines to Better Protect Against Currently Circulating Variants | FDA

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CDC Recommends Updated COVID-19 Vaccine for Fall/Winter Virus Season

Press Release

For Immediate Release: Tuesday, September 12, 2023

Contact: Media Relations
(404) 639-3286

Meeting of the Advisory Committee on Immunization Practices

September 12, 2023

Current Landscape of SARS-CoV-2 Lineages

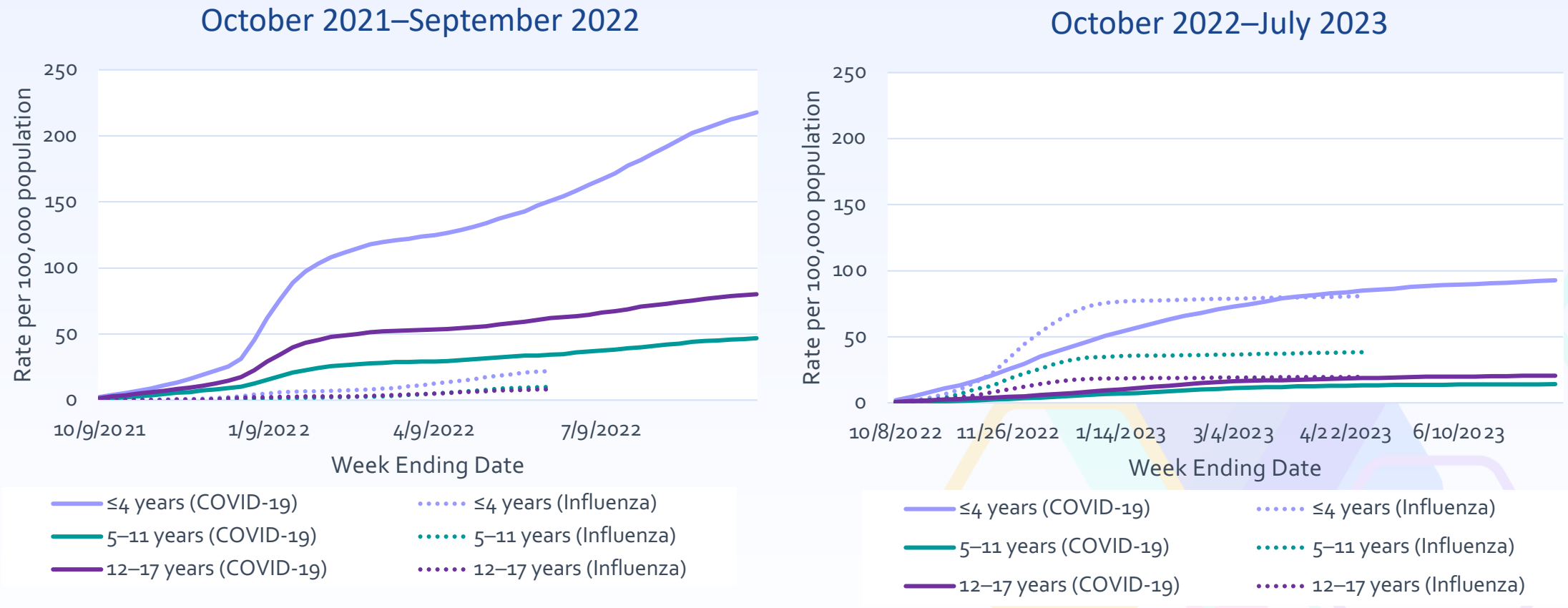
- More than 90% of currently circulating viruses are XBB lineage viruses with 1-2 additional substitutions in RBD in comparison to XBB.1.5

- BA.2.86 is a newly detected lineage with > 30 amino acid substitutions in spike
  - Thus far, the number of viruses detected is still low
  - Sequence numbers are too low to calculate proportion (<0.05%)

- Preliminary pseudovirus neutralization data generated by multiple labs do not indicate a large reduction in neutralizing activity against BA.2.86

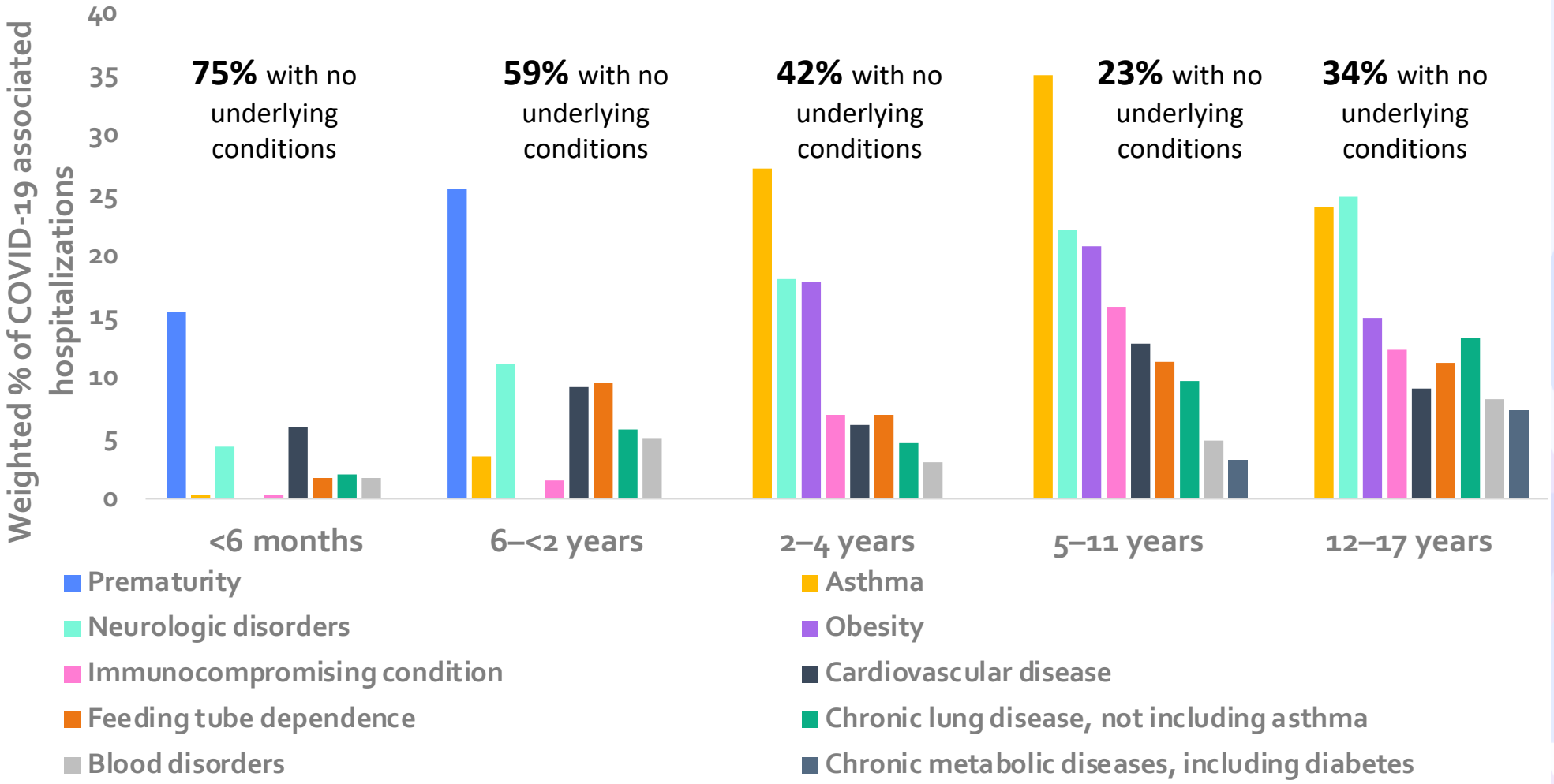
- CDC has generated a BA.2.86 isolate, is currently working on titrations before neutralization and has begun distribution to external laboratories for further examination

Cumulative Weekly Rates of COVID-19- and Influenza-Associated Hospitalizations among Infants, Children, and Adolescents Ages ≤17 Years — COVID-NET and FluSurv-NET*, October 2021—July 2023



* Influenza Hospitalization Surveillance Network. Seasonal FluSurv-NET surveillance was extended into June for the 2021-2022 season. Surveillance ended on April 30, 2023, for the 2022–2023 season. Hospitalization rates are among those with laboratory-confirmed influenza and SARS-CoV-2 and are not adjusted for likely reason for admission.

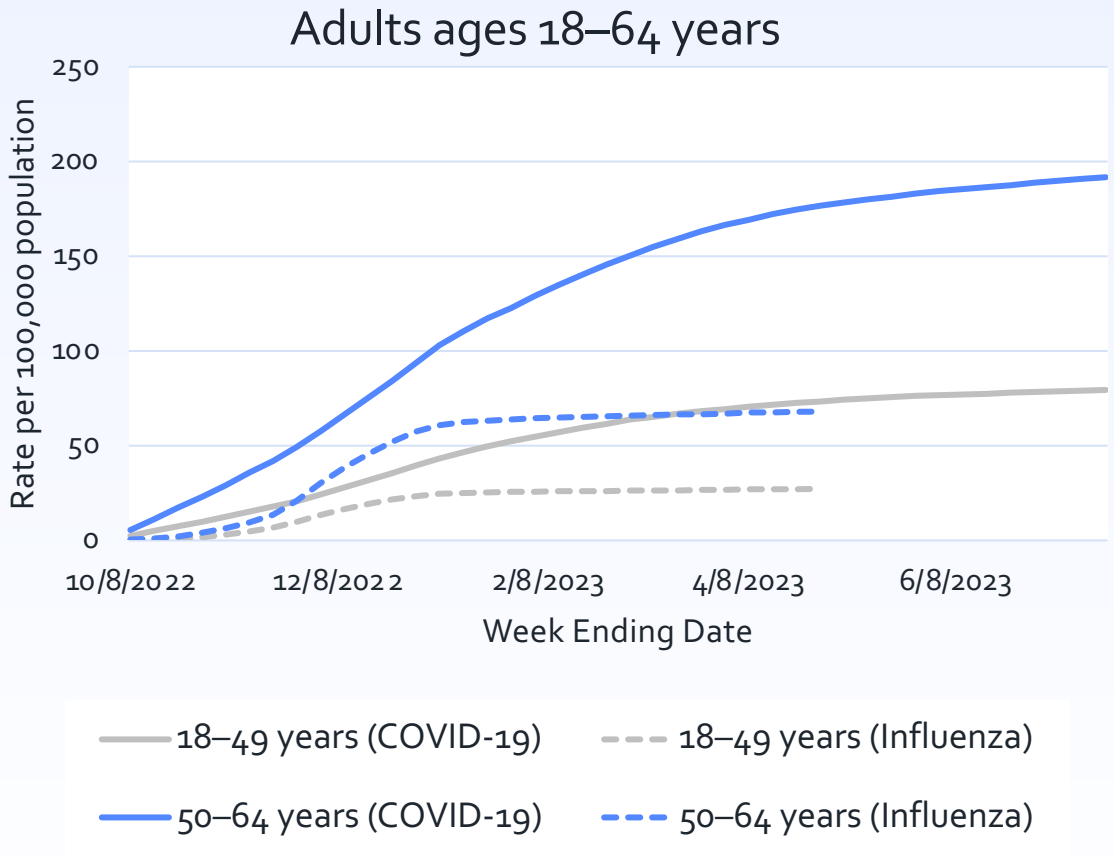
Percent of COVID-19-Associated Hospitalizations with Underlying Medical Conditions among Children and Adolescents Ages 5–17 Years by Age Group — COVID-NET, January–June 2023

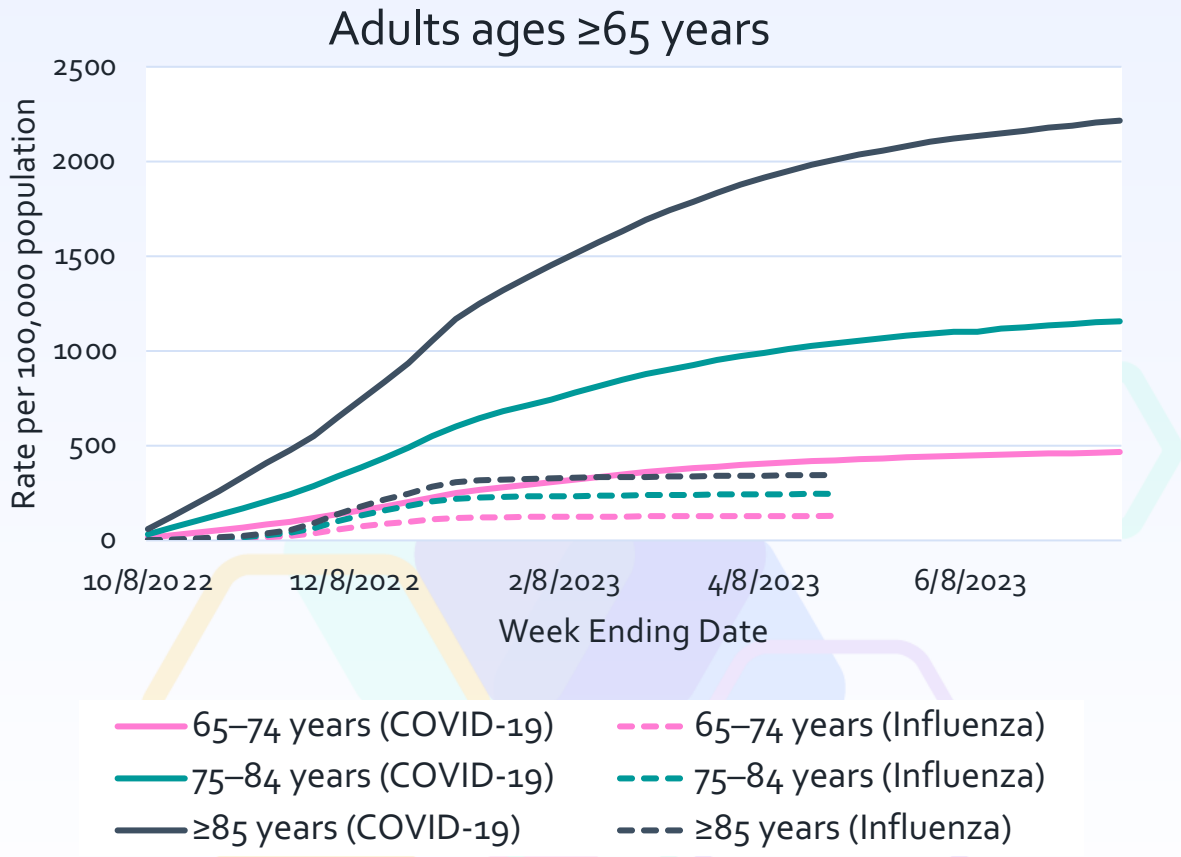


- **54%** of hospitalized infants, children, and adolescents ages ≤17 years have **no underlying medical conditions**.
- Hospitalizations children and adolescents **ages ≥5 years** are **more likely to have underlying medical conditions** relative to children and infants ages ≤4 years.

Data are limited to hospitalizations where COVID-19 is a likely primary reason for admission. Figure displays underlying medical conditions present in ≥5% in ≥1 age group.

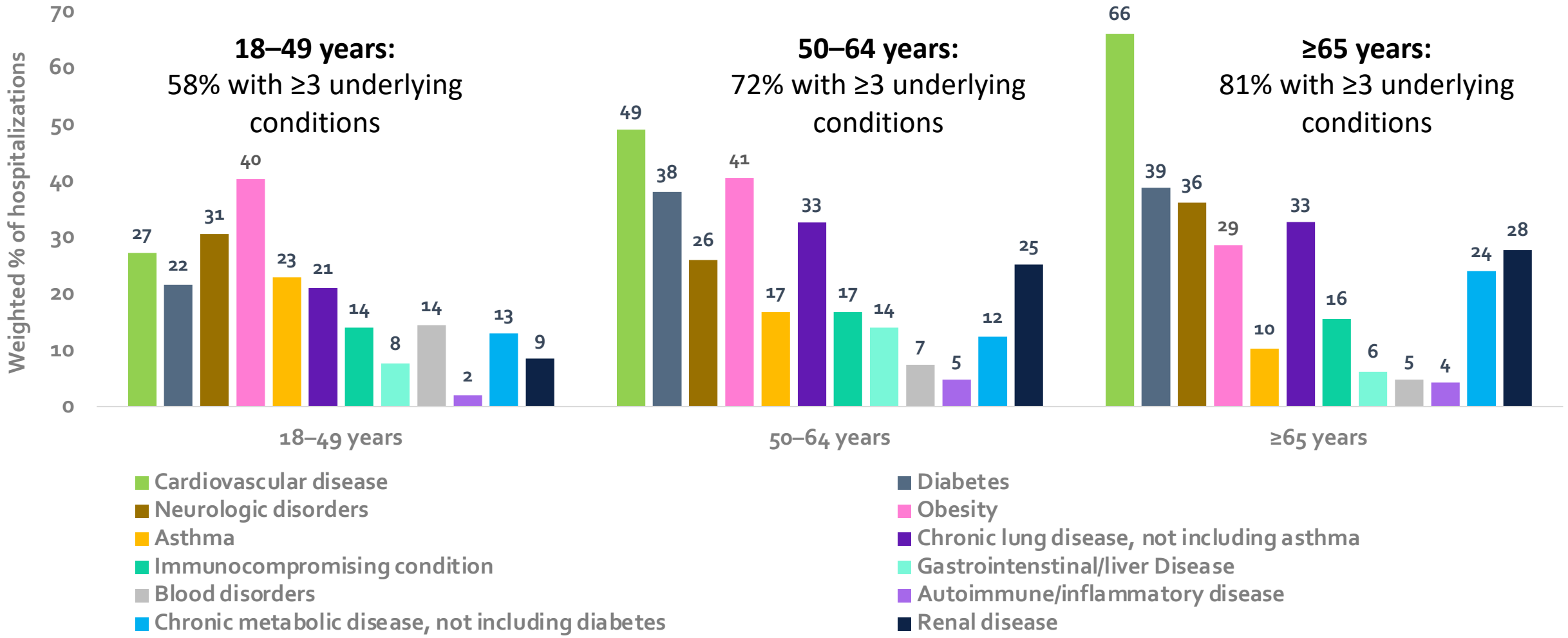
Cumulative Weekly Rates of COVID-19- and Influenza-Associated Hospitalizations among Adults Ages ≥18 Years — COVID-NET and FluSurv-NET*, October 2022–July 2023





* Influenza Hospitalization Surveillance Network. Seasonal FluSurv-NET surveillance ended on April 30, 2023, for the 2022–2023 season.

Underlying Medical Conditions among Adults Ages ≥18 Years Hospitalized for COVID-19, by Age Group — COVID-NET, January–June 2023



Data are limited to hospitalizations where COVID-19 is a likely primary reason for admission.

COVID-19-associated hospitalizations

- Hospitalization rates increased in all age groups since mid-July
- Hospitalization rates highest in older adults and infants <6 months
- Most children <5 years hospitalized with COVID-19 illness have no underlying medical conditions
  - A higher proportion of hospitalized children and adolescents 5-17 years have underlying medical conditions
  - Most hospitalized adults have multiple underlying medical conditions
- COVID-19 continues to cause severe illness; clinical outcomes generally comparable to influenza-associated hospitalizations
- Most children and adults hospitalized for COVID-19 since January 2023 had not received an updated bivalent booster

Post-COVID Conditions

- Post-COVID Conditions are common following SARS-CoV-2 infection, decrease with time since infection, and has decreased since the start of the pandemic
- Symptoms and conditions associated with Post-COVID Conditions are not unique to having had SARS-CoV-2 infection
- Post-COVID Conditions are associated with increased health care utilization and significant activity limitations
- Accumulating evidence that COVID-19 vaccination reduces Post-COVID Conditions among both children and adults

Context for interpreting VE across age groups

- High rates of infection-induced immunity by July–August 2022.*
- VE findings should be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of infection-induced immunity.

Age group	% with infection-induced immunity
6-11 month	66%
12-23 months	74%
2-4 years	83%
5-11 years	88%
12-17 years	86%
16-29 years	83%
30-49 years	78%
50-64 years	68%
≥65 years	48%

* https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-COVID-Jones-508.pdf; data on children aged 6 months – 17 years is from cross-sectional blood specimens collected by commercial laboratories. Data on persons aged ≥16 years is from a longitudinal, national cohort of >70,000 blood donors.

Conclusions: Updates to waning of bivalent vaccine effectiveness

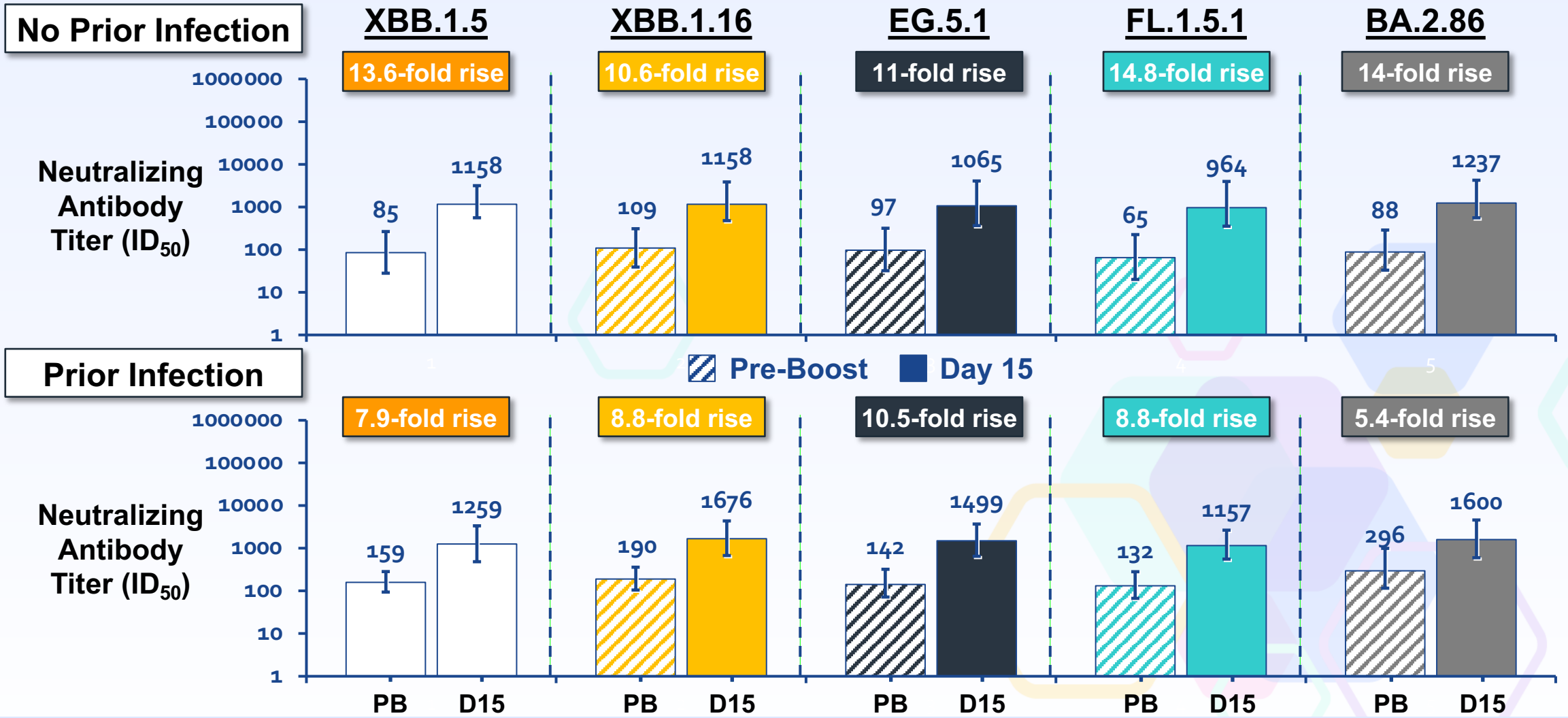
- VE waning against hospitalization and ED/UC; more sustained protection against critical illness
  - Difficult to separate impact of time since vaccination from emergence of new variants
- Patterns are similar across age groups, though low uptake of bivalent doses in younger age groups prevented assessment of waning beyond 4 months from the bivalent dose.
- Persons with immunocompromise may have reduced protection after COVID-19 vaccination, compared with persons without immunocompromise. Historically, COVID-19 VE has been lower and waned more quickly for adults with immunocompromise compared to adults without immunocompromise. Trends in bivalent VE are less clear and additional data are needed.
- VE findings should be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of infection-induced immunity.

Summary
Safety and Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula) *XBB.1.5 Vaccine*

Clinical Study of XBB.1.5 Vaccine	▪ Safety profile of XBB.1.5 vaccine consistent with previously authorized vaccines ▪ Robust neutralizing antibody titers against XBB.1.5, XBB.1.16, EG.5.1, FL.1.5.1, and BA.2.86 measured in sera from recipients of XBB.1.5 vaccine ▪ XBB.1.5 vaccine is anticipated to be effective against current SARS-CoV-2 variants
Moderna's Vaccine Preparedness	▪ Moderna will supply an XBB.1.5 vaccine for Fall 2023 ▪ Moderna will continue its ongoing variant monitoring and risk assessment of emerging variants

Cross Neutralization Results (Day 15) After XBB.1.5 Vaccine in Adults by Baseline SARS-CoV-2 Serostatus - *Moderna Assay*

Study 205J, Subset Analysis (N=20)

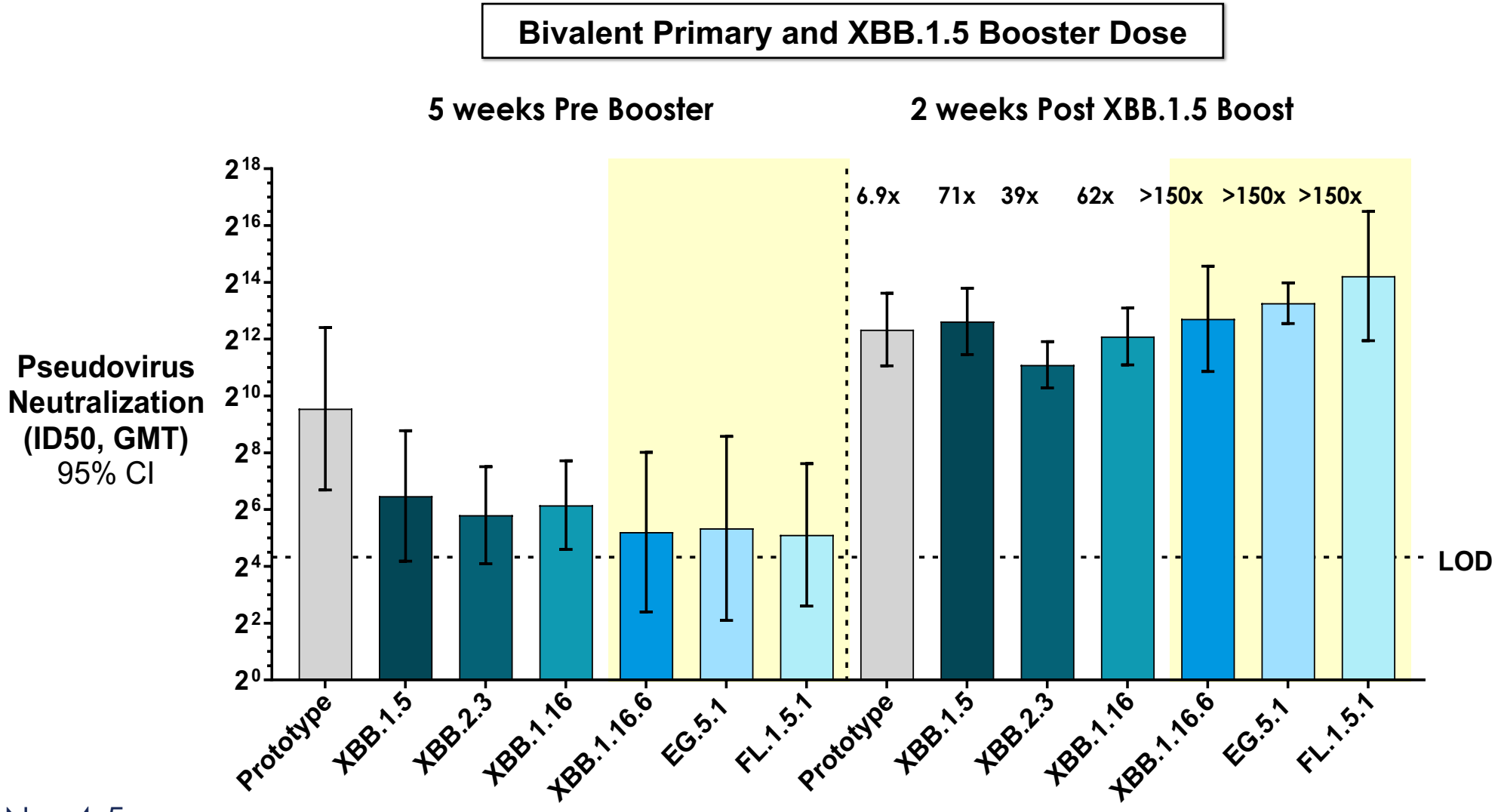


Cross neutralization demonstrated regardless of prior SARS-CoV-2 infection

Pseudovirus neutralization assay

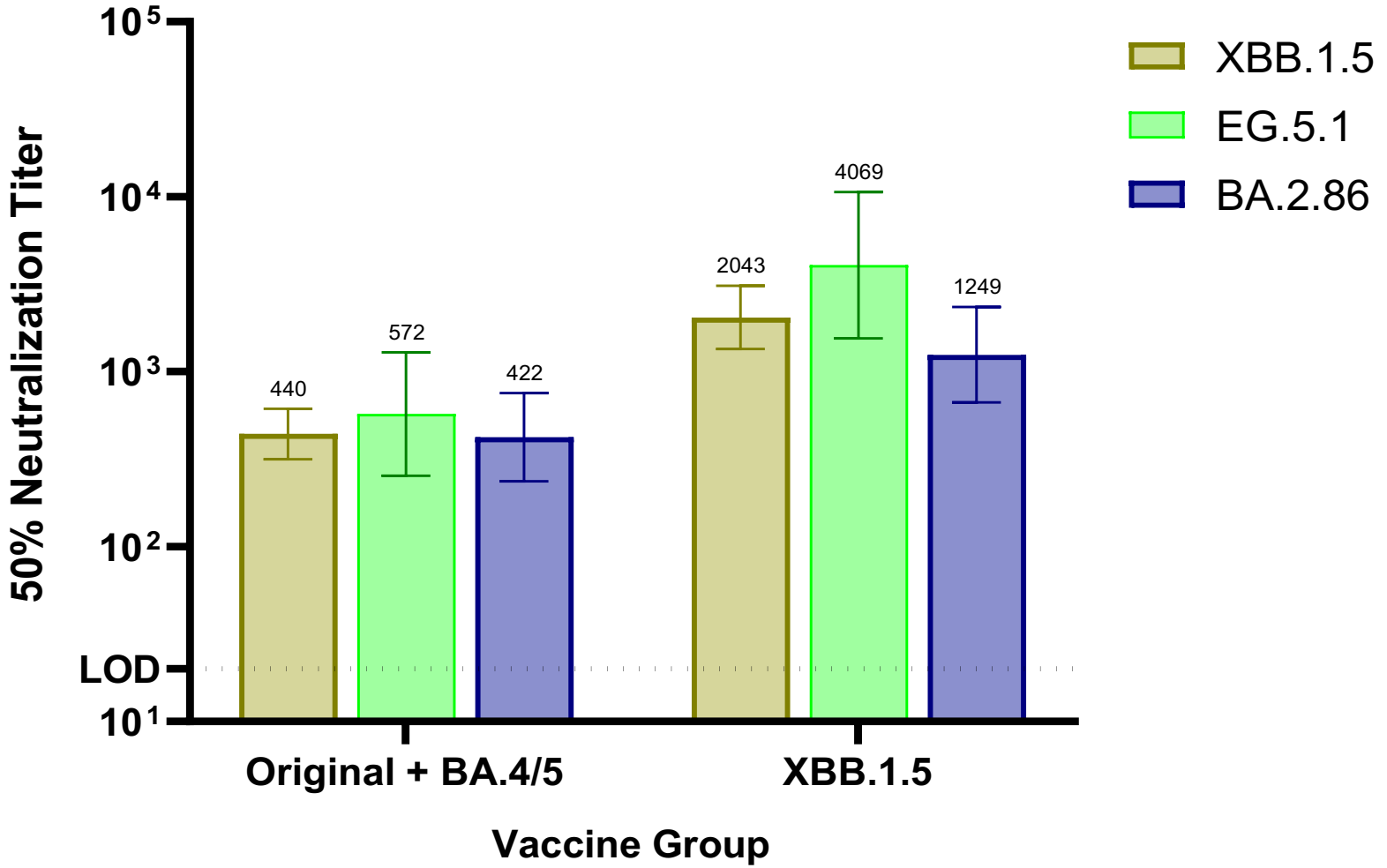
Neutralizing Responses in Macaques: Primary Vaccination Bivalent BA.5 Vaccine and Boost with XBB.1.5

Boosting with XBB.1.5 induces robust neutralizing responses against emerging XBB subvariants



N = 4-5

Monovalent XBB.1.5 BNT162b2 Booster Vaccine Effectively Neutralized Predominant and Emerging Variants



Data were generated by the same pseudovirus neutralization assay and from sera of same mouse study that generated data that were presented at VRBPAC June 15, 2023 Meeting (https://www.fda.gov/media/169541/download).
50% Neutralization Titers are Geometric Mean Titers of 10 mice per vaccine group. LOD, limit of detection; the lowest serum dilution of 1:20.

Pediatric vaccine preventable diseases: Deaths per year in the United States prior to recommended vaccines compared to COVID-19

	Hepatitis A[1]	Meningococcal (ACWY)[2]	Varicella[3]	Rubella[4]	Rotavirus[5]	COVID-19[6]
Age	<20 years	11–18 years	5–9 years	All ages	<5 years	6 months–<18 years
Time period	1990–1995	2000–2004	1990–1994	1966–1968	1985–1991	2022
Average deaths per year	3	8	16	17	20	≤1 year: 156 1–4 years: 101 5–19 years:292

[1]Vogt TM , Wise ME, Bell BP, Finelli L. Declining hepatitis A mortality in the United States during the era of hepatitis A vaccination. J Infect Dis2008; 197:1282–8.
[2]National Notifiable Diseases Surveillance System with additional serogroup and outcome data from Enhanced Meningococcal Disease Surveillance for 2015-2019.
[3]Meyer PA, Seward JF, Jumaan AO, Wharton M. Varicella mortality: trends before vaccine licensure in the United States, 1970-1994. J Infect Dis. 2000;182(2):383-390. doi:10.1086/315714
[4]Roush SW , Murphy TV; Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. JAMA 2007; 298:2155–63.
[5] Glass RI, Kilgore PE, Holman RC, et al. The epidemiology of rotavirus diarrhea in the United States: surveillance and estimates of disease burden. J Infect Dis. 1996 Sep;174 Suppl 1:S5-11
[6] http://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

Summary

Public Health Problem

- 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

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

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

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]

1. Fall 2022 DocStyles, unpublished data

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

Summary

- 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

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

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**

Proposed ACIP Voting Language

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

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

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

Commercialization of COVID-19 Vaccines

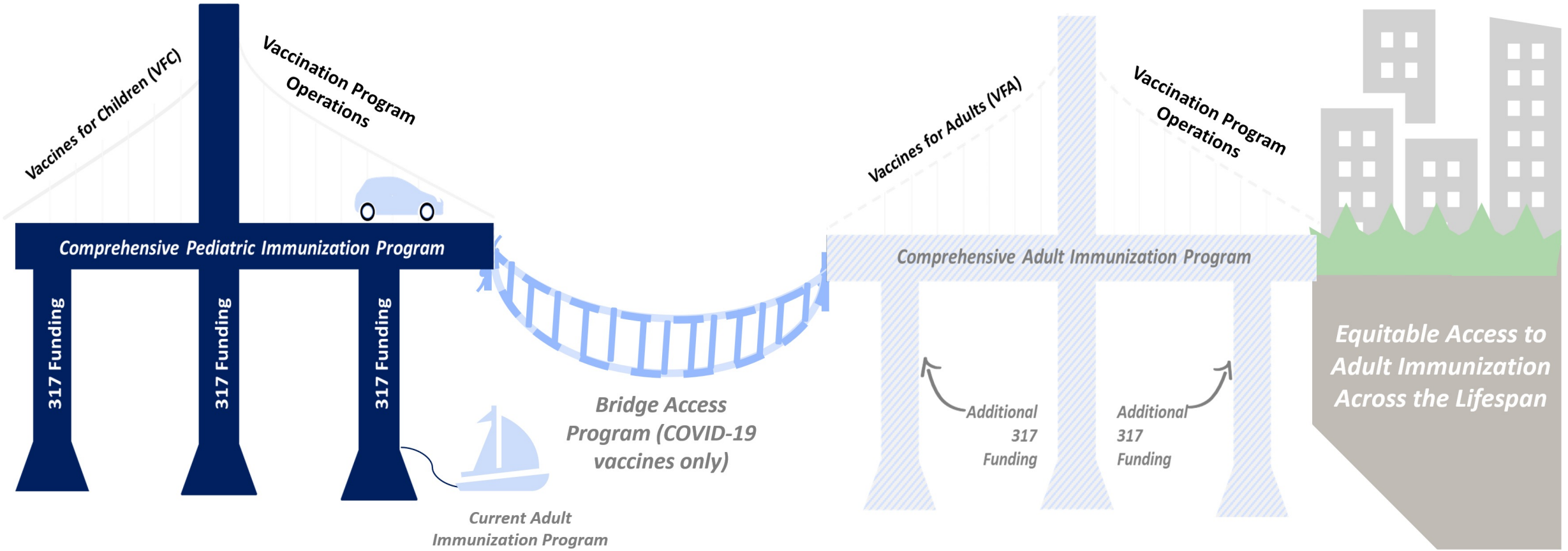
What will change

- Transition of federal procurement and distribution of all COVID-19 vaccines to more traditional public/private model
- End of CDC COVID-19 Provider Agreement
- Vaccine data reporting transitions to routine reporting processes for jurisdictions that have signed data use agreement (DUA) with CDC

What will not change

- Evidence-based vaccination program to develop recommendations, monitor safety and effectiveness, and strengthen vaccine confidence
- CDC's commitment to ensuring access to COVID-19 vaccines at no cost

The Bridge Access Program is a temporary "bridge" to a permanent Vaccines for Adults (VFA) Program



The Bridge Access Program serves as a temporary solution for access to COVID-19 vaccines for adults. VFA and additional 317 funding are needed to **bridge the gap in equitable access to immunization across the lifespan.**

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

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.