MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

FEBRUARY 28-29, 2024
MEETING SUMMARY

Trade names are used for identification purposes only and do not indicate endorsement.

WEDNESDAY: FEBRUARY 28, 2024

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Melinda Wharton (ACIP Executive Secretary & Acting Chair, CDC) called to order and presided over the February 28-29, 2024, Advisory Committee on Immunization Practices (ACIP) meeting. She made opening announcements about the availability of presentation slides on the ACIP website and scheduled oral public sessions as well as the written public comment process and then reviewed conflict of interest policies for ACIP members. She announced that new ACIP members have been approved by the Department of Health and Human Services (HHS). Official letters of invitation will be released soon to these individuals, and the ACIP looks forward to having them join a future ACIP meeting. As allowed under the ACIP charter, the ACIP's six *Ex Officio* members were temporarily designated as voting members. Dr. Wharton noted that during role call and prior to the votes, she would ask that the *Ex Officio* members state any conflicts of interest (COIs). She also announced that because the process for the new ACIP Chair to join the committee had not yet been completed, she would be chairing the meeting. She then conducted a roll call, which established that a quorum was present. A list of Members, *Ex Officios*, and Liaison Representatives is included in the appendixes at the end of this summary document. The following COIs were identified for the first day of this meeting:

- ❑ Dr. Chen is working with MassBiologics on a diarrhea therapeutic product that is funded by the Bill and Melinda Gates Foundation. MassBiologics is a non-profit vaccine manufacturer associated with the University of Massachusetts Chan Medical School and maker of a diphtheria/tetanus (DT) vaccine. Because this meeting will include a vote on the addition of DT to the Vaccines for Children (VFC) program, he indicated that he would recuse himself from the VFC vote for that vaccine.

COVID-19 VACCINES

Dr. Matthew F. Daley introduced this session on behalf of the ACIP COVID-19 Vaccines Work Group. To review current COVID-19 vaccine policy, the ACIP met on September 12, 2023, to review the available evidence for the updated 2023-2024 formula of COVID-19 vaccines. At that time, ACIP recommended an updated COVID-19 vaccine as authorized under Emergency Use Authorization (EUA) or approved by a Biologics License Application (BLA) in persons aged ≥6 months of age. This included Moderna COVID-19 vaccine in persons ≥6 months of age, Pfizer-BioNTech COVID-19 vaccine in persons ≥6months of age, and Novavax COVID-19 vaccine in persons ≥12 years of ager. The recommendation also included a recommendation that everyone ≥5 years of age get an updated dose of the 2023-2024 formula to protect against serious illness from COVID-19 regardless of prior vaccination or infection history. Children 6 months–4 years of age were recommended to receive multiple doses of COVID-19 vaccines to be up to date, including at least 1 dose of updated COVID-19 vaccine. Additional recommendations were made for those who are moderately or severely immunocompromised, who may get additional doses of updated COVID-19 vaccine.

Dr. Christopher Taylor (CDC/NCIRD) reported on data from the COVID-19-Associated Hospitalization Surveillance Network (COVID-NET). COVID-NET collects data from more than 300 acute-care hospitals in 98 counties across 13 states, including about 10% of the United States (US) population. Hospitalizations reported to COVID-NET include all those for which a positive SARS-CoV-2 test result was reported within 14 days prior or during hospitalization. Screening for SARS-CoV-2 is driven by clinical judgment and facility policies.

The majority (67%) of hospitalizations captured in COVID-NET between October 2023–January 2024 were among adults ≥65 years of age. Adults ≥75 years of age comprised 46% of hospitalizations. Among adults ≥75 years of age during October 2022–November 2023, 25% of COVID-19-associated hospitalizations were residents of a long-term care facility (LTCF) at the time of admission. Among all adults hospitalized with COVID-19 for the period October 2022─November 2023, 3.8% died in-hospital. Among those, 1.4% were 18─49 years of age. The highest proportions of in-hospital deaths occurred among adults ≥65 years of age, with 5.5% of adults 65─74 years of age and 4.4% ≥75 years of age dying in-hospital. Among adults ages ≥65 years of age who died in-hospital, 28% were residents of LTCFs. An examination of death certificate data from March 2020–April 2022 found that among all deaths in adults with COVID-19-associated hospitalization, 67% occurred in-hospital and 33% occurred ≤30 days post-discharge. The proportion of deaths occurring post-discharge increased with age.

For the period October 2022─November 2023, 16% of all adults hospitalized with COVID-19 had an immunocompromising condition. These percents varied by age, ranging from 12% or 1 in 8 adults 18─49 years of age to 21% in adults 65─74 years of age with an immunocompromising condition. Looking at the proportion of COVID-19-associated hospitalizations among adults by immunocompromised status overall and by intervention or outcome for the period October 2022─November 2023, 16% of all COVID-19-associated hospitalizations were among persons with an immunocompromising condition. Among those admitted into the ICU, 17% had an immunocompromising condition and 28% of those who died in-hospital had an immunocompromising condition. The most common underlying conditions observed among hospitalized adults varied by age group.

Data pertaining to COVID-19-associated hospitalizations by vaccination status among adult age groups were limited to October─November 2023, given that they were the 2 months of data available for the updated 2023-2024 monovalent dose. Overall, no more than 5% of hospitalized adults in any age category received the updated 2023-2024 monovalent dose. The largest proportion of hospitalized adults who received the updated monovalent dose was adults ≥65 years of age at 5%. It is important to note that these 2 months of data are preliminary data and that continued examination of these data is ongoing.

Dr. Kevin Chatham-Stephens (CDC/NCIRD) presented COVID-19 vaccination coverage data and attitudes and experiences regarding COVID-19 vaccination. According to CDC's National Immunization Survey (NIS), among adults overall, 21.9% reported being up-to-date, with a range from 43.5% among adults ≥75 years of age down to 9.5% among adults 18─29 years of age. Among children overall, 12.2% were reported to be up-to-date, with the range from 15.8% among those 12─17 years of age down to 5.9% among those 6 months─4 years of age.

COVID-19 vaccine coverage among adults varied by jurisdiction, ranging from 9.5% in Puerto Rico and 10.5% in Mississippi to 41.9% in the District of Columbia (DC). In terms of COVID-19 vaccination status and intent among adults ≥18 years of age, the percent of adults who were vaccinated with the 2023-2024 COVID-19 vaccine gradually rose from about 3% percent in late September 2023 to 21.9% as of February 3, 2024. The percent of adults reporting they definitely will get vaccinated decreased from 28.2% to 11.3%. The percent of adults reporting they probably will get vaccinated or are unsure if they will get vaccinated has remained relatively stable between approximately 27% to 32%.The percent reporting they probably or definitely will not get vaccinated has also remained relatively stable between 37% to 42%.

Coverage also varied by race/ethnicity, with coverage highest amongst white non-Hispanic adults at 24.4% and lowest among American Indian/Alaska Native (AI/AN) adults at 11.4%, Native Hawaiians and Other Pacific Islanders (NH/OPI) at 14.1%, and Hispanic adults at 13.3%. Coverage by urbanicity was lower in rural areas at 16.8% than coverage in suburban and urban areas at 21.3% and 29.9%, respectively. Adults with health insurance at 22.7% percent had higher vaccination coverage than adults without health insurance at 6.9%. Coverage also varied by household income, with coverage increasing with increasing income. Those with incomes greater than $75,000 had the highest coverage at 26.1% percent. Coverage did not vary based on disability status.

Data on the percent of pregnant persons 18─49 years of age vaccinated with a 2023-2024 COVID-19 vaccine come from the Vaccine Safety Datalink (VSD), which is a collaborative project between CDC and integrative healthcare organizations and networks across the US that uses electronic health data from participating sites to monitor and assess the safety of vaccines. Overall, 12.5% of pregnant persons received an updated COVID-19 vaccine as of January 27, 2024. Coverage ranged from 4.8% among Black Non-Hispanic persons to 21.3% among Asian persons.

How people think and feel about COVID-19 vaccines has changed since 2022. Comparing results from January 2022 to results from January 2024 from the NIS, most Americans still consider COVID-19 vaccines to be safe and important, but vaccine confidence has declined. Disease risk perception has also changed, as reflected in the percentage of Americans who are moderately or very concerned about getting COVID-19. The percent of US adults who think that a COVID-19 vaccine is very or completely safe has declined from 67.3% to 55.6% percent. The percent of US adults who think that a COVID-19 vaccine is somewhat or very important has declined from 83.9% to 69.6%. The percentage of US adults who are moderately or very concerned about getting COVID-19 has declined from 55% to 32.7%. The percent of adults reporting that their health care provider (HCP) recommends the COVID-19 vaccine decreased from 36.1% in May 2021 to 20.4% in January 2024.

A survey was conducted by CDC, RAND, and the University of Iowa of HCP in February 2023 that involved a panel of HCP comprised of all physician specialties and other health-related professions, such as nurses and pharmacists. Based on results for physicians who spend at least half of their time in outpatient primary care where vaccines are administered in their worksite, most physicians reported that they always recommend bivalent boosters, with the highest percentage being for patients ≥65 years of age at 80.9%. Regarding the reasons HCP (e.g., physicians, nurses, pharmacists) reported for not recommending the COVID-19 bivalent boosters to eligible patients, the most common response was a medical reason. That was followed by patients will refuse booster vaccination, patients are tired of hearing about COVID-19 vaccines, and there is a high level of vaccine resistance in the community.

Potential reasons for primary care providers (PCP) to not stock COVID-19 vaccines included perceived low interest for COVID-19 vaccination in the patient population, cost of the COVID-19 vaccine and other associated vaccination costs, their healthcare system decided to not stock the COVID-19 vaccines, and availability of the COVID-19 vaccines elsewhere in the community (e.g., pharmacies).

Based on data from the Omnibus Surveys between November 30─December 21, 2023 on the acceptability of co-administration of influenza, COVID-19, and RSV vaccines, respondents were asked, "If you were due for them and they were offered, would you get more than one of these vaccines in the same visit: COVID-19, flu, RSV?" Approximately 2/3 of US adults indicated they would be open to co-administration of these vaccines.

Dr. Daley asked CDR Chatham-Stephens about racial and ethnic disparities in uptake of the 2023-2024 COVID-19 vaccine formula in the context of recognizing that low coverage overall is the biggest problem. It seems like some disparities have returned and wondered if there was a sense of why that is.

Referring to the coverage data overall he presented for adults, Dr. Chatham-Stephens confirmed that there were some racial/ethnic disparities. There also have been some racial and ethnic disparities among pregnant people. However, that is not necessarily unique to the COVID-19 vaccine. Unfortunately, similar disparities have been observed with other vaccines. There are likely multiple reasons for this, such as disparities in access to vaccine and access to healthcare, as well as misinformation and disinformation circulating among different populations. Some of the disparities were mitigated to some degree during the height of the federally-distributed COVID-19 vaccine program, but have begun to return. CDC is engaged in a number of activities to address some of these issues.

Dr. Loehr took a moment to speak to the primary care providers of the country, pointing out that COVID vaccine is now just a regular vaccine like vaccines for everything else and he acknowledged that many people do not want it. However, since he has had it in his office, 2 or 3 people a day are pleased to be able to easily get the vaccine there. Anything that can be done to lower the barrier of getting a vaccine in someone's arm is wonderful. Therefore, he treats COVID vaccine like influenza and other vaccines he offers to his patients. Some people do not want it, but a lot of others are glad he has it in his office.

Regarding Dr. Taylor's presentation, Dr. Long said she found it difficult to interpret the slide on hospitalized patients and the percent who had various conditions without knowing the population at large with these conditions in the same age groups.

Dr. Taylor indicated that the work group acknowledges this as a limitation. Early in the pandemic, an analysis was published that paired COVID-NET data from the early months of the pandemic through June 2020 with population-level underlying conditions that were available through the Behavioral Risk Factor Surveillance System (BRFSS), which provides estimates of underlying chronic conditions at a population level. That paper looked at those risks of hospitalization versus the risk in the population. That analysis is being updated and is anticipated to be ready for presentation at the next ACIP meeting.

Dr. Brooks commented that they had received a lot of information with these excellent presentations, but had to figure out the synopsis. Income reduces coverage. Insurance status reduces coverage. Only 5% of Black pregnant women got vaccinated. Why? Lower rates among African-Americans. He asked whether there are any data coverage in urban versus rural areas.

Dr. Chatham-Stephens responded that urban and suburban residents had 21.9% and 21.3% percent coverage respectively compared to rural respondents at 16.8%.

Dr. Kotton stressed how devastating it was to see how many elderly and immunocompromised people are being admitted to hospital, are in the intensive care unit (ICU), and are dying from COVID-19. It was shocking to see that only 30% to 40% of higher-risk elderly and immunocompromised people are getting the updated vaccine. She encouraged that during this meeting, the ACIP provide clarity on the recommendation for an updated vaccine and for immunocompromised individuals. In September 2023, ACIP said that they could get 2 doses of vaccine at least 2 months apart. However, the community needs to be provided with clarity on that because people do not understand what that recommendation means. This is a life-and-death situation for many of the patients she takes care of.

Dr. Ruth Link-Gelles (CDC/NCIRD) shared CDC's current data on the effectiveness of updated 2023–2024 monovalent XBB.1.5 COVID-19 vaccine against symptomatic SARS-CoV-2 from several CDC vaccine effectiveness (VE) platforms.

By July—August 2023 just before the updated vaccines were introduced, individuals in the US had high rates of infection-induced immunity that were above 70% for all age groups and almost 90% for those 16—49 years of age. Infection can provide some protection from future infection. Therefore, 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.

Data from multiple systems demonstrated that updated 2023-2024 COVID-19 vaccination provided increased protection against symptomatic SARS-CoV-2 infection and COVID-19-associated emergency department (ED) and urgent care (UC) visits and hospitalizations compared to no updated vaccine dose. Receipt of an updated dose provided protection against JN.1, the most common circulating variant currently, as well as other circulating variants. These are relatively early estimates from all 3 VE studies, with no substantial waning. However, waning is expected based on past experience with COVID-19 vaccines, and CDC will continue to monitor VE.

Dr. Lisa A. Prosser, University of Michigan, presented the results from an economic analysis of an additional dose of COVID-19 vaccine among adults. The presentation was an extension of an economic model that previously had been presented to the committee. There were 2 updates to the model which were to: 1) revise the probability of hospitalization from October 2022—September 2023 to reflect more recent lower rates; 2) adjust vaccine impact for seasonality; and 3) add a new intervention strategy to include an additional dose of vaccine approximately 6 months following an additional dose, referred to as the 2-dose strategy.

Incremental cost-effectiveness ratios (ICERs) were calculated comparing an updated mRNA booster 1-dose strategy to no booster, using the updated hospitalization and seasonality-adjusted vaccine impact inputs. This analysis also provided ICERs for the base case and uncertainty analyses comparing 1-dose, 2-dose, and no booster vaccination strategies. Updating the model to include revised hospitalization rates and seasonality-adjusted vaccine impact yielded slightly higher ICERs for all age groups compared to the September 2023 analysis. In the updated analysis, the ICER for the 1-dose strategy for adults 18—49 years of age was roughly $163,000 per QALY gained. For adults 50—64 years of age, it was about $80,000 per QALY gained. For individuals ≥65 years of age, 1 dose of an updated vaccine was no longer cost-saving but yielded an ICER of about $12,000 per QALY.

In terms of the 2-dose strategy, the ICER was greater than $1.3 million per QALY for adults 18─49 years of age, greater than $700,000 per QALY for adults 50─64 years of age, and great than $255,000 per QALY for adults ≥65 years of age using base-case assumptions.

Varying the probability of hospitalization had a substantial impact on the results. For probability of hospitalization from 2 to 4 times the base case, the incremental cost-effectiveness ratios dropped to about $120,000 per QALY at 2 times the base case, $65,000 per QALY at 3 times the base case, and $34,000 per QALY at 4 times the base case. These higher rates correspond to underlying condition: chronic obstructive pulmonary disease (COPD), history of stroke, coronary artery, asthma, hypertension, obesity, diabetes, chronic kidney disease (CKD), and severe obesity.

Lower costs of vaccination also were associated with lower ICERs. Varying only the cost of the vaccine dose would move a 1-dose strategy into the cost-saving range for cost per dose of $20 or $60 per dose. The ICER for a 2-dose strategy would fall below $150,000 per QALY for a cost per dose of $60 or less. Varying all vaccination-related costs to lower bounds yielded cost savings for a 1-dose strategy and about $51,000 per QALY for the 2-dose strategy.

Dr. Kotton asked Dr. Prosser whether immunocompromised persons were included in the modeling.

Dr. Prosser indicated that immunocompromised individuals were not explicitly considered in this analysis, so these results should be considered to apply to the immunocompetent population. Some inferences were drawn to the extent possible from the higher hospitalization rates or other higher-risk scenarios that might correspond to immunocompromised population, but those were not explicitly defined in that way.

Referring to Dr. Link-Gelles's presentation, Dr. Daley noted that there may be a perception in the public that vaccines are getting less effective. Comparing the news of November 8, 2020, when they heard that these vaccines were 94% to 95% percent effective, 50% effectiveness is not that compelling. As Dr. Link-Gelles has explained, those are completely different because now the vaccinated have a history of multiple vaccines plus infection and the unvaccinated comparison group has some immunity. He wondered how to convey that 50% VE in this context still prevents negative outcomes, such as hospitalizations and deaths.

Dr. Link-Gelles emphasized the importance of the context. Early in the pandemic, most of the population had yet to be infected and had received zero doses of vaccine collectively. The vaccine had the opportunity to protect almost absolutely, which was reflected in the clinical trials with VE in the 90% range. There was nowhere to go but up in terms of collective immunity from COVID-19. At this point in the pandemic, most people in the population have been infected. Adding the people who have been vaccinated and not infected reaches about 98% who have some type of prior immunity from infection, vaccination, or both. That provides protection against future infection and future severe disease, but it does not protect absolutely. In that context, vaccines are now providing an incremental or extra benefit beyond whatever benefit someone has remaining from their past infection or past vaccination. It is known that protection wanes from past vaccination and past infection. Over time, whether someone has been infected or vaccinated multiple times, their protection will decrease. Vaccines can then provide important extra protection in terms of boosting whatever protection one has. That is important for all people in the US, especially those who are at the highest risk such as pregnant people, people with high-risk conditions, and individuals ≥65 years of age.

Even in the context of prior infection and prior vaccination, people are getting infected, being hospitalized, having critical illness, and dying. The vaccine gives them extra protection, particularly those who have high-risk conditions.

Dr. Long asked whether the 50% of the population with a lowered chance of being hospitalized were used in the cost-effectiveness model.

Dr. Link-Gelles clarified that the estimates from the cost-effectiveness model came from the IVY and VISION Networks. While those data were slightly older data, they were essentially the same and cost-effectiveness of the booster was reasonable.

Dr. Megan Wallace (CDC/NCIRD) presented the Evidence to Recommendations (EtR) Framework for the policy question, "Should persons ages 65 years and older be recommended for an additional dose of 2023-2024 formula COVID-19 vaccine?" The additional dose should be at least 4 months after receipt of the previous updated COVID-19 vaccine dose. As a reminder, the currently authorized and approved 2023-2024 formula COVID-19 vaccines include Moderna, Novavax, and Pfizer-BioNTech vaccine. This policy question would apply to all 3 of these vaccines. ACIP recommended the 2023-2024 formula COVID-19 vaccine in September 2023. This session focused on whether an additional dose should be recommended in older adults this year.

There are already recommendations for additional doses of the 2023-2024 formula COVID-19 vaccine among people who are moderately or severely immunocompromised, who have the option to receive 1 additional dose of updated COVID-19 vaccine at least 2 months following the last recommended updated COVID-19 vaccine dose. Further additional doses may be administered, informed by the clinical judgment of a healthcare provider and personal preference and circumstances. Any further additional doses should be administered at least 2 months after the last updated COVID-19 vaccine dose.

To summarize the public health problem, COVID-19 hospitalizations peaked in late December 2023—early January 2024. However, there are still approximately 20,000 new hospital admissions and 2,000 deaths due to COVID-19 each week. Persons ≥65 year of age have the highest COVID-19 hospitalization rates, and hospitalization rates within this age group increase with increasing age. Persons ≥75 years of age have the highest COVID-19 mortality rates. Immunosenescence and higher prevalence of vaccine-only immunity in older adults compared to younger adults suggest that more frequent doses may be needed to maintain protection in this population. While there are increases in COVID-19 during respiratory virus season, COVID-19 hospitalizations and deaths continue throughout the year due to ongoing circulation of SARS-CoV-2. Inequities in COVID-19 hospitalizations by race and ethnicity continue and should be considered in the context of an age-based recommendation. The work group agreed that COVID-19 disease among persons ≥65 years of age is of public health importance.

For benefits and harms, Dr. Wallace summarized evidence that 2023-2024 formula COVID-19 vaccination provided increased protection against symptomatic SARS-CoV-2 infection and COVID-19-associated ED/UC visits and hospitalizations compared to no updated vaccine dose. COVID-19 VE from previous vaccine formulations has waned over time but appears more durable against critical illness. An additional dose of 2023-2024 formula may restore VE, which is expected to wane, providing additional protection until the next updated vaccine is available. COVID-19 vaccines have a favorable safety profile. Local and systemic symptoms have been reported following receipt of COVID-19 vaccines. However, symptoms are less frequent and severe among older adults compared with adolescents and younger adults.

The available data do not provide clear and consistent evidence of a safety issue for ischemic stroke with bivalent mRNA COVID-19 vaccines, either when given alone or when given simultaneously with influenza vaccines. The work group determined that the desirable anticipated effects were moderate and that the undesirable anticipated effects were small. A minority of work group members were of the opinion that the undesirable anticipated effects were minimal. The work group felt that the desirable effects outweigh the undesirable effects.

For the values domain, adults ≥65 years of age were more concerned about COVID-19 disease and had higher confidence in vaccine safety and vaccine importance than those <65 years of age. Black adults were more concerned about COVID-19 disease than people of other racial and ethnic groups. Confidence in COVID-19 vaccine safety and importance varied by race and ethnicity. Half of adults reported that they planned to take precautions because of COVID-19 during the fall and winter months, with 41% of adults ≥65 years of age and older planning to avoid large gatherings. Larger proportions of Black and Hispanic adults reported that they planned to take precautions against COVID-19 than white adults. The work group's opinion was that older adults feel that the desirable effects are large compared to the undesirable effects. Regarding whether there is important uncertainty about, or variability in, how older adults value the main outcomes, the majority opinion of the work group was that there probably is important uncertainty or variability, and the minority opinion was that there is probably no important uncertainty or variability.

The vaccine coverage data presented provided evidence to support acceptability. As of February 2024, vaccination coverage with the 2023-2024 COVID-19 vaccine was highest among older adults 65—74 years of age and ≥75 years of age compared to younger age groups. Disparities in COVID-19 vaccine coverage have been observed across many demographic factors, including race, ethnicity, insurance status, and rurality. Adults who were vaccinated or definitely plan to get vaccinated were more likely to report that a healthcare provider recommended that they get a COVID-19 vaccine. Adults ≥65 years of age were more likely to report HCP recommendation than younger adults. Among adults ≥65 years of age who had already received a 2023-2024 formula COVID-19 vaccine dose, 68.4% percent reported that they definitely would get an additional dose of 2023-2024 formula COVID-19 vaccine if it is recommended for them. The majority of work group members thought recommending an additional dose of 2023-2024 formula COVID-19 vaccine for older adults probably would be acceptable to key stakeholders.

For feasibility, Dr. Wallace reminded the committee that COVID-19 vaccines are currently on the commercial market and an ACIP recommendation would be needed for insurance coverage of an additional dose. An additional dose recommendation would leverage existing infrastructure and vaccine product. However, it would add complexity to the current recommendations, which could enhance vaccine and system fatigue. Access-related barriers to COVID-19 vaccines and disparities in vaccine uptake remain. Additional dose recommendations may further heighten those inequities, but lack of recommendation limits access to those able to pay for vaccine out of pocket. The work group's opinion was that an additional dose of the 2023-2024 formula of vaccine probably would be feasible to implement among older adults.

In terms of the *resource use* domain, the full economic analysis presented by Dr. Proser showed that an additional dose among adults ≥65 years of age had an ICER of about $250,000 per QALY. However, the ICERs became more favorable in scenarios that approximated the higher risk, which may be seen with underlying medical conditions or advanced age.

An additional dose of COVID-19 vaccine is likely more cost-effective in populations with a higher prevalence of risk factors, such as underlying conditions, which increase their probability of hospitalization due to COVID-19. When asked whether an additional dose of the 2023-2024 formula COVID-19 vaccine in older adults is a reasonable and efficient allocation of resources, the work group response was "probably yes."

To summarize the work group interpretations, the greatest benefit of a vaccine dose would be in those who have not yet received a 2023-2024 formula dose, particularly older adults and those with underlying medical conditions. The data presented during this session emphasize the importance of any dose of updated COVID-19 vaccine in older adults. Risk of severe illness due to COVID-19 continues throughout the year and is highest in those ≥65 years of age. Within adults ≥65 year of age, risk increases with increasing age. Receipt of the 2023-20 24 formula COVID-19 vaccine provides protection against JN.1 and other circulating variants. However, VE is expected to wane. In the past, greater durability has been observed in the protection against critical illness. A "may" recommendation would provide flexibility for older adults to obtain an additional dose if they or their HCP feel they would benefit. The most benefit would likely be in those with underlying medical conditions, advanced age, or circumstances that may increase risk, such as being a nursing home resident. An additional dose in adults ≥65 years of age may restore protection that has waned. However, this will be a smaller incremental benefit on top of the protection that is still being provided by the initial 2023-2024 formula COVID-19 vaccine dose. The cost-effectiveness of an additional dose depends on COVID-19 hospitalization rates in the coming months and the patient risk factors for severe illness due to COVID-19. As COVID-19 epidemiology changes with time, additional dose recommendations may not be needed in the future.

When considering an additional dose recommendation, the work group felt that a "may" recommendation would provide flexibility for those ≥65 years of age to get an additional dose if they or their HCP feel they would benefit. For the overall balance of consequences, the work group was split between judgments that "the balance between desirable and undesirable consequences is *closely balanced or uncertain*" and "desirable consequences *probably outweigh* undesirable consequences in most settings." For type of recommendation, the majority polled to recommend the intervention for individuals based on shared clinical decision-making, which for COVID-19 vaccines has typically been referred to as a "may" recommendation. The proposed ACIP language is as follows:

> *ACIP recommends that persons ≥65 years of age may receive an additional dose of the 2023-2024 formula COVID-19 vaccine.*

The proposed Clinical Considerations language is as follows:

> *People ages 65 years and older may receive 1 additional dose of any updated (2023–2024 Formula) COVID-19 vaccine (i.e., Moderna, Novavax, Pfizer-BioNTech), informed by the clinical judgement of a healthcare provider and personal preference and circumstances. Considerations for the additional dose may include a person's risk for severe COVID-19 due to age and the presence of underlying medical conditions. The additional dose is administered at least 4 months following the previous dose of updated (2023–2024 Formula) COVID-19 vaccine.*

Dr. Loehr asked whether the work group considered recommending this for people ≥75 years of age, given that there seems to be a fairly dramatic change between 65 and 75.

Dr. Wallace indicated that the work group did have considerations of other age groups, including those ≥75 years of age. One of the key drivers that led to dropping it down to ≥65 years of age was the equity concerns that people ≥75 years of age would likely cause inequities for those in minority groups that are still experiencing severe illness in persons 65–74 years of age.

Dr. Long said it seemed like it would be difficult to inform providers on what they ought to do with this recommendation as far as timing, and whether certain people should be given the booster now or wait to see what is occurring with the epidemiology and give it closer to when they might be at more risk.

Dr. Loehr said he was wrestling with “should” versus “may” because he was thinking that there is a fair amount of benefit, and he tends to be more flexible. While “should” was appealing to him at this point, he also could see many reasons why “may” would makes sense, including cost-effectiveness and seasonality. In his personal opinion, he probably would give this again in February or March for those people who are particularly high risk (e.g., those ≥75 years of age, immunocompromised persons, those with high-risk conditions).

Dr. Kotton said she had similar thoughts as Dr. Loehr. From her perspective as an active clinician in the field, many people she has spoken with did not even know that they should have had an updated vaccine since September 2023. “May” seemed too soft to her, especially for the most vulnerable populations. The American public is not aware of the fact that they actually should be getting these vaccines. They should have already had the 2023-2024 updated vaccine, but the majority have not. From a public health perspective, she would be concerned if ACIP did not make a clear-cut recommendation. She would advocate for clarity for “should” get the updated vaccine, which was what ACIP said in September 2023, and people in the highest risk groups “should” get an additional dose. Furthermore, also advocated for clarity and simplicity in terms of the issue of 4 months after the prior dose and 2 months for immunocompromised after the last dose, which is confusing to clinicians.

Dr. Cineas voiced her agreement with Dr. Kotton about harmonizing “should” for both the first and second dose to make it easier for providers in counseling patients and to enhance uptake among those who may be getting their first updated vaccine.

Dr. Brooks noted that the work group discussed "should" versus "may." In terms of the potential cons, beyond the science, it is still necessary to get the population vaccinated. There is now more vaccine hesitancy, vaccine fatigue, and lack of confidence in a single dose. People under 65 years of age will wonder why they do not get the vaccine. Allowing for the flexibility of "may" versus "should" may get more people vaccinated, including those <65 years of age, immunocompromised, and those ≥65 years of age.

Dr. Loehr said that while he appreciated that perspective, most people come in either wanting the vaccine or not. They do have the data for people who have already gotten their 2023-2024 formula, 68% of whom would be happy to get a booster if they knew it was recommended. He was thinking more about making it easier for providers to recommend this for everyone who walks in the door who fits the criteria. While he was not yet sure how he would vote, he did not think a “may” recommendation would get more people vaccinated.

Dr. Daley acknowledged that the work group considered a number of these options, and there was some difference of opinion among work group members. In some ways, a "may" recommendation was a reflection of some difference of opinion on the part of the work group. Everyone recognizes that communication is key and that how strongly a provider endorses this in their practice is really important. It is also important to recognize that vaccination is giving in many settings now, such as pharmacies, where long conversations might not be possible. It might be harder to communicate a "may" recommendation than a "should" recommendation, which might be a shorter conversation of, “You should get your vaccine today.”

Dr. Loehr moved that ACIP accept the language as presented, specifically saying "may" receive an additional dose. Dr. Brooks seconded the motion.

Dr. Kotton made a motion to strengthen the language to read "should" rather than "may." Dr. Long seconded the motion.

Dr. Daskalakis echoed what Dr. Daley said about "may" providing permissiveness for people who are already very connected to and interested in vaccination. He also agreed with Dr. Kotton’s comment that it is important to do better in terms of communicating the importance of the initial dose. More absolute statements around vaccines sometimes will create a chilling effect for the folks who have not been vaccinated. In this scenario, it may be worth thinking about the population of folks who have already been vaccinated, who are suggestible for a vaccine, and who will likely take this recommendation on the value of an additional dose as something that may be right for them.

Dr. Kotton said that as a clinician who provides a tremendous number of vaccines to adults, she has not necessarily found that to be true in her practice. When CDC says "may," some people do not think that means anything and does not mean someone needs to do it. “Should” is quite clear. She would like additional data to back up that in this scenario, the focus should be on those who are already vaccinated.

Dr. Long thought perhaps they were getting too hung up on “should” and asked whether “may” could be deleted so that the statement simply read, “ACIP recommends that persons ≥65 years of age receive an additional dose of the 2023-2024 formula COVID-19 vaccine.” This way, the implication would be “should.”

Dr. Wharton said she thought that would be acceptable language for an ACIP recommendation, although it was not how many other vaccine recommendations have been worded. However, that would be an amendment.

Dr. Kotton requested clarity on the work group interpretation. The work group interpretation on Slide 77 states, “We recommend the intervention for individuals based on shared clinical decision-making.” That was not actually the proposed voting language for the vote. She asked whether they actually would be recommending the somewhat dreaded shared clinical decision-making, which makes vaccine implementation very challenging.

Dr. Wharton clarified that the “may” language as the COVID vaccine recommendations have been made over the last couple of years is a shared clinical decision-making recommendation. For plain language purposes, it has been worded as proposed. From an implementation perspective, this is a shared clinical decision-making recommendation.

Dr. Loehr asked for clarity on whether they would first vote on the amended recommendation using the word “should” and then carry forward the final language to the afternoon voting session.

Dr. Long requested more time to hear other opinions before voting on the amendment to the language.

Dr. Wharton clarified that the “should" recommendation from the fall for everyone to receive a single updated dose still stands and would not be replaced by this vote in anyway. Everyone should still get their updated 2023-2024 vaccine.

Dr. Chen said he was struck by the fact that, even though there is a waxing and waning of the burden of disease, it really did not completely disappear. It is probably lost, even on some clinicians, that there are significant hospitalizations and deaths even in the summer. The burden of disease, risks associated with age, and other underlying conditions also motivated him to see the importance of how the second booster dose could have a significant improvement in the population who receives it. Therefore, he favored the change to "should." Having heard that this vote is applicable to a very small portion of the population, he was now stuck and was thinking that the "may" language would be okay. However, he still wanted to make clear that vaccination is extremely important and whatever they can do to improve language overall to increase clinicians to be motivated to give a very strong recommendation to their patient population in addition to all patients understanding the importance of vaccination would be a goal.

Dr. Wharton clarified that they would be voting first on the amended language that would replace "may" with "should." If that amendment passed, the amended language would be taken forward for a vote in the afternoon following public comment. If the amendment failed, they would return to the original motion that had the "may" language.

Dr. Fryhofer (AMA) said that speaking as a practicing physician and a member of the COVID Vaccine Work Group, she found the day’s discussion very helpful. There is still so much preventable disease, because COVID does not have a defined seasonality like influenza and there are still many hospitalizations and deaths that could be prevented. She appreciated Dr. Daskalakis’ comment about the people who are against vaccines and how a "should" recommendation might affect them. However, a "should" recommendation does support vaccine confidence and the belief that this vaccine will save lives, prevent hospitalizations, and prevent deaths. She worries about shared clinical decision-making, or a "may" recommendation, because many people are getting vaccines in pharmacies. There is still confusion about what pharmacies can and cannot administer, and they do not have the knowledge of a patient's medical conditions and chronic illnesses like their personal physician or provider does. She was very impressed with Dr. Kotton’s and Dr. Long's comments, which changed the way she was thinking about this voting language.

Dr. Schmader (AGS) said that from a geriatrics perspective and within a society, talking with patients and geriatricians, there is a wide variety of opinions about this that land toward "should" but at least "may." "May" has to do with uncertainty about disease burden and effectiveness. There is definitely a subset of people with vaccine fatigue and inertia. Some of the individuals in this subset will go out right away and get the vaccine and others will not. A lot of people are thinking that there will be a vaccine in the fall, so they will just wait for that.

Dr. Hopkins (NFID) said he thought this very important discussion would affect many people in the population. While it is important to think about this additional dose, it needs to be coupled with very strong language from ACIP and the liaisons to make sure that those who have not received a first dose of the 2023-2024 vaccine get that. Efforts must be made to better protect those ≥65 years of age, and acknowledging Dr. Kotton's comments, the immunocompromised population needs additional protection.

Dr. Rockwell (AAFP) said that speaking as a clinician and for private practice physicians, she thought the stronger language of "should" was better because it helped take out some of the ambiguity about the "may." In scholarly work and academics, they understand that. It also helps with EHRs when there are best practice alerts.

Dr. Goldman (ACP) said that as a practicing internal medical physician, he thought jurisdictions have different populations that can create some contention around vaccines. The "may" recommendation can be more effective as far as explaining the need for vaccine and the flexibility to practicing physicians in different areas. While he does think this is an effective vaccine and there is still vaccine-preventable disease, with the issues of vaccine fatigue and the contention that this particular vaccine has created over the years, having a "should" vaccination recommendation may actually create other issues with getting the rest of patients vaccinated as necessary for other recommended vaccines on the schedule. He suggested "may" because that could at least give the flexibility for the practicing physician to be able to have the conversation with the patient and separate it from issues of other vaccines they need to get as well.

Ms. Howell (AIM) noted that with long-term care residents being at high risk for severe outcomes due to COVID-19, she wondered whether with a "may" recommendation, there would still be a requirement for LTCFs to offer COVID-19 vaccine to their residents or if it need to be a "should" recommendation for that to happen.

Dr. Wallace said she thought that LTCF could offer the vaccine to their residents under either recommendation, and they certainly would fall into the high-risk category that would be particularly important under a "may" recommendation.

As a reminder, Dr. Kotton made a motion to strengthen the language to read "should" rather than "may." Dr. Long seconded the motion. The motion passed with 12 affirmative votes and 1 abstention to take the following language forward for a vote:

> *ACIP recommends that persons ≥65 years of age should receive an additional dose of the 2023-2024 formula COVID-19 vaccine.*

As a point of clarification, Dr. Kotton asked whether they would be voting on the immunocompromised and the second dose.

Dr. Wharton said that they would not be voting on this but would ask the team how this might be handled in the context of clinical considerations to make guidance clearer.

Dr. Lakshmi Panagiotakopoulos (CDC/NCIRD) presented the next steps for the COVID-19 vaccine program, beginning by discussing the question, “Can we improve the current COVID-19 vaccine policy timeline?” In Fall 2023, the COVID-19 vaccine policy decision occurred as follows. The mRNA updated 2023-2024 formula vaccines were authorized or approved on September 11, 2023. The ACIP met September 12, 2023, to review the available evidence for the updated COVID-19 vaccines.

During that meeting, ACIP recommended the updated COVID-19 vaccines as authorized under EUA or approved by BLA in persons ≥6 months of age. Moderna and Pfizer-BioNTech vaccines were recommended for person ≥6 months of age and the Novavax COVID-19 vaccine, which was authorized for use on October 3, 2023, was recommended in persons ≥12 years of age. Of note, there was a general expectation that vaccines would be widely available immediately following the recommendations.

In fall 2023, there was uncertainty around the recommendations prior to the meeting, which made planning for state and local vaccine programs challenging. Vaccine orders had to be placed prior to knowing the groups for whom the vaccine would be recommended. Stakeholder presentations, provider toolkits, and webpages all had to be updated after the recommendation was made, which limited the available window for communication of the recommendation prior to the respiratory virus season. There were also reports of issues with vaccine access, including among those at highest risk of severe illness.

A revised timeframe for the 2024-2025 COVID-19 vaccine vote and recommendation during the June meeting would allow for more lead time between when a recommendation is made to when vaccines are manufactured and distributed. The proposed plan for 2024 would include a June ACIP meeting to review the evidence for updated COVID-19 vaccine recommendations, which would include World Health Organization (WHO) and Food and Drug Administration (FDA) antigen selections, manufacturer studies, immunogenicity data, cumulative effectiveness and safety data, epidemiology from current and prior years, uptake from current and prior years, and cost-effectiveness analyses. ACIP would then vote on the updated COVID-19 vaccine recommendations in June. The 2024-2025 formula would become available as regulatory actions are taken by the FDA and vaccines are distributed by manufacturers.

One of the biggest benefits of a June COVID-19 vaccine policy decision is that it would enable early planning across the entirety of the healthcare delivery system, including national, state, and local public health departments; large and small practices; and other venues for vaccine delivery, such as pharmacies. Another benefit is that it would allow time for clear communication of recommendations. It also would provide vaccine sites with earlier information on which to base vaccine ordering decisions. Vaccines potentially could become available immediately following FDA authorization or approval.

There are over 4 years of data on COVID-19 and over 3 years of data on COVID-19 vaccines. There is a well-established precedent from the influenza vaccine recommendations. The influenza virus also evolves rapidly and requires updates to vaccine antigens. It is unlikely there will be more data between June and September that would influence the updated COVID-19 vaccine policy decision. The increased lead time would ease implementation challenges for vaccine providers, including earlier information on vaccine recommendations to inform ordering, which would allow providers to recommend the vaccine in anticipation of availability, train staff to counsel patients who are making appointments for influenza vaccine, and make informed decisions. The increase lead time also would allow for clearer messaging in provider and patient educational materials.

This plan was presented to the COVID-19 ACIP Work Group. Work group members were in favor of moving the decision to June and discussed many ways that this could ease implementation challenges, including clearer communication of vaccine policy and increased lead time for clinicians. Work group members emphasized that communication surrounding a recommendation prior to vaccine availability, as done routinely for influenza vaccine, will be important.

Dr. Chen asked whether there is an understanding of how the Bridge Access Program has had an effect on implementation and uptake and if there is an update on the move beyond the Bridge Access Program and Vaccines for Adults. In addition, he asked whether there would be more data on concomitant administration of COVID, influenza, and RSV vaccines. The lack of data has been a barrier in trying to communicate confidence with these vaccines and trying to accomplish administration of all of them in a single visit.

Dr. Chatham-Stephens responded that the Bridge Access Program has been tracking these discussions. As noted, additional lead time would help with any transition to an updated vaccine for the next season. They are aware of this and are incorporating these discussions into their plans.

Dr. Wallace indicated that simultaneous administration is still part of general best practice. There are no concerns with administering COVID vaccines with influenza, RSV, or other vaccines. This is always being monitored and new information is continuously being collected.

Dr. Long thought the June decision sounded appropriate in terms of marrying it to what doctors anticipate now with influenza. However, it was unclear whether the vote in June would be to recommend a universal dose for adults ≥ 65 years of age or for strain selection.

Dr. Wharton clarified that strain selection is done by FDA and the FDA's advisory committee, VRBPAC, will be weighing in on that. That is not a decision that ACIP is asked to weigh in on. The expectation is that in June, the work group will have a proposal for the committee on proposed use of COVID-19 vaccines in the fall. Dr. Kaslow (FDA) confirmed that the strain selection decision would be made by FDA following the VRBPAC meeting, which is scheduled for May 16, 2024.

Dr. Long observed that if the vote later in the afternoon was going to be for everyone ≥65 years of age or ≥70 years of age to get the vaccine now, it has been well over 4 months since September or October when most people got the vaccine. It seems like it would impact the cost-effectiveness if 6 months later ACIP suggested that they all get it again. A window of 4 months did not make sense when circulation is pretty low right now. For example, about 10% of specimens in Philadelphia are positive for COVID-19 at this time. It was not clear why they would make a very short-term recommendation when they would be considering a longer-term recommendation in less than 4 months.

Dr. Wharton said that assuming that there is an updated vaccine for 2024-2025, that vaccine will not be available until fall. That is a number of months away, even though ACIP will be discussing it in June.

Dr. Daley expressed appreciation for Dr. Long's call for clarification and distinction between those. Work group members raised the issue of what happens in June 2024 in terms of who should get the vaccine. Influenza vaccination is thought of as seasonal, with vaccination continuing through March. The strategy for COVID is different. If someone wanted a vaccine in June and had not received a 2023-2024 vaccine, they would still be eligible and the vaccines would not be expired. The likelihood of that happening given that they have had 9 months of opportunity probably continues to decrease but does not go down to zero. The vote planned for later in the day was distinctly different because it would be for now and for a group that is at particularly high risk by virtue of age.

A fresh decision will be made next year with an updated vaccine that is information by what is learned over the past season about safety, effectiveness, barriers, and attitudes. If there is a benefit now for people ≥65 years of age, he did not think ACIP should postpone that decision until June because it is a different decision for a different circumstance and different population. The work group was unanimous that there are many benefits to making a June decision, with the recognition that there are some risks given unknown epidemiology, et cetera. He asked Dr. Kaslow whether, from the FDA perspective, ACIP's plan to make a recommendation for who should receive a 2024-2025 vaccine during the June ACIP meeting made sense.

Dr. Kaslow (FDA) confirmed that this does make sense.

Ms. Coyle (AIRA) acknowledged the role of health information technology systems (e.g., electronic health records, pharmacy systems, immunization information systems). Some of these codes will have to be developed, and being able to get those out and updated in systems takes time. Therefore, it is important to build in as much time as possible for that to ensure that as many systems as possible can make updates before vaccine administration and would be greatly appreciated. That is, lengthening the lead time between licensure, recommendations, and vaccine administration would be helpful.

Vote: COVID-19 Vaccines

Although public comment was presented prior to all of the votes during this meeting, the votes were incorporated in summary with their respective sessions for the purpose of continuity.

Dr. Megan Wallace (CDC/NCIRD) read the following proposed ACIP voting language for COVID-19 vaccines into the record:

> *ACIP recommends that persons ≥65 years of age should receive an additional dose of the 2023-2024 formula COVID-19 vaccine.*

Dr. Kaslow (FDA) made a few pre-vote comments noting that: 1) Only 40% of people over 65 years of age have received the indicated dose in the current package insert for the 2023-2024 formula. The biggest public health impact likely would come from increasing the number of individuals ≥65 years of age getting that indicated dose; 2) There are suggestive data of longer duration, particularly against the outcomes that are most important, severe disease and death, in those who have had multiple exposures to the spike protein by infection or vaccines. In the current context, individuals ≥65 years of age already have had multiple exposures to the spike protein; 3) There is a paucity of evidence for mRNA vaccines and protein-based vaccines given at this time in the ongoing pandemic. The context of receiving an additional dose now is quite different than it was earlier in the pandemic. As presented, pre-existing immunity is quite robust and different than it was early in the pandemic; 4) If an antigen update is recommended this year and is available in September, giving an additional dose of the current 2023-2024 formulation any later than June this year may not be optimal. Based on the current context and the available data, this seems to be truly a "may" recommendation supported by what is basically Level 3 evidence.

Motion/Vote: COVID-19 Vaccines

Dr. Kotton made a motion to approve the proposed recommendation stating, "ACIP recommends that persons ≥65 years of age should receive an additional dose of the 2023-2024 formula COVID-19 vaccine." Dr. Cineas seconded the motion. No COIs were declared. The motion carried with 11 favoring, 1 opposing, and 1 abstaining. The disposition of the vote was as follows:

11 Favored: Brooks, Beigel, Chen, Cineas, Clark, Daley, Grimes, Hance, Kotton, Loehr, Marshall
1 Opposed: Long
1 Abstained: Kaslow

Discussion Points

Members and Ex Officios were invited to make comments following the votes.

Reflecting on the COVID vaccination vote, Dr. Daley indicated that he personally would have felt comfortable with a "should" or "may" recommendation. While the ACIP voted for a "should" recommendation, the points Dr. Kaslow raised do not go away and should be taken back to the work group and discussed. The COVID Work Group had differences of opinion about where they landed. This decision will arise for years to come, including in June. This is a reason to pause and be humble.

CHIKUNGUNYA VACCINE

Dr. Wilbur Chen, Chair of the ACIP Chikungunya Vaccines Work Group, introduced the chikungunya vaccines session. He reminded the committee that the chikungunya vaccine manufactured by Valneva was licensed in the US in November 2023. No other chikungunya vaccine is licensed globally, and there are no existing ACIP chikungunya vaccine recommendations. The Chikungunya Vaccines Work Group is developing policy options for ACIP's consideration for use of chikungunya vaccine among US persons at risk of chikungunya, including travelers, laboratory workers, and residents of US territories and states with risk of transmission.

Dr. Susan Hills (CDC/NCEZID) reported that the FDA licensed the Valneva's live attenuated chikungunya vaccine IXCHIQ® was approved on November 9, 2023. The vaccine was approved for individuals at increased risk of exposure to chikungunya virus as a single dose in individuals ≥18 years of age. The vaccine is contraindicated for immunocompromised individuals and to individuals with a history of a severe allergic reaction to any component of IXCHIQ®. Two "Warnings and Precautions" are listed; first, the vaccine may cause severe or prolonged chikungunya-like adverse reactions, and second, vaccine viremia occurs in the first week following vaccination and there are no data on the risk of vertical transmission.

Dr. Hills told the committee that the vaccine was licensed through the accelerated approval pathway. With accelerated approval, demonstration of effectiveness is based on controlled clinical trials showing the vaccine has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefits. For the chikungunya vaccine, the marker of protection was based on a neutralizing antibody titer estimated from a validated non-human primate (NHP) model. With this approval pathway, there is a post-licensure requirement for controlled trials to confirm the clinical benefits. The FDA has required 2 post-marketing studies. The first is a VE case-control study in adolescents and adults ≥12 years of age. This study will be conducted in Brazil and is planned to start by March 2026 and be completed by March 2028. The second is a pragmatic randomized control trial (RCT) for effectiveness and safety in adults in an endemic area, which is planned for initiation by October 2025 and completion by July 2029.

Dr. Hills (CDC/NCEZID) reminded the committee that chikungunya virus is an alphavirus that is transmitted primarily by *Aedes* species mosquitoes, primarily *Aedes aegypti* and *Aedes albopictus.* Uncommon modes of chikungunya virus transmission include laboratory exposure, intrauterine and intrapartum transmission, and bloodborne transmission through needlestick injury. Chikungunya virus occurs in tropical and subtropical regions and periodically causes large outbreaks throughout most parts of the world. Occasional transmission has occurred in temperate areas. The virus periodically causes large outbreaks, with high attack rates among one-third to three-quarters of the population affected.

Clinical illness is characterized by the acute onset of fever and joint pain, which is often severe and can be debilitating. Other symptoms may include headache, rash, myalgia, and/or anorexia. In the absence of specific antiviral treatment, the approach to management typically involves rest, fluids, and use of analgesics and antipyretics. Deaths are rare and are reported mostly in older adults, particularly those with comorbidities, and young infants infected perinatally or by mosquito bites. Acute symptoms of chikungunya usually resolve in about 7 to 10 days, but some patients have a continuation or relapse of their joint symptoms in the months after acute illness and experience other symptoms, such as fatigue. About 50% of people have ongoing arthralgia of variable severity for up to 3 months after infection, and about 30% may have ongoing arthralgia for up to 12 months after infection.

Chikungunya is a reportable disease in the US, with approximately 100 to 200 cases reported annually; there is likely substantial underdiagnosis and underreporting. Infections are most commonly acquired in Asia and the Americas, with specific locations of acquisition influenced by local transmission patterns which vary from year-to-year. In 2023, there was a large outbreak of chikungunya in Paraguay. Among all US travelers to destinations with risk of chikungunya, fewer than 1% travel to Paraguay. Among all US traveler chikungunya cases reported in 2023, 25% (20 of 80) were among persons who traveled to Paraguay.

Dr. Hills reviewed data on vaccine safety that had been reviewed by the work group. Overall, the work group summary of vaccine safety is that the live attenuated chikungunya vaccine is a reactogenic vaccine. Because safety data have only been gathered in about 3,500 subjects, it will be important to continue to monitor vaccine safety post-licensure as the vaccine is used in larger populations.

The work group's assessment was that chikungunya is a disease that can result in severe arthralgia during the acute illness, rare serious complications, and sometimes long-term arthralgia. The highest risk for severe outcomes is among older adults, particularly those with comorbidities, and neonates and young infants.

There is moderate disease burden among US travelers, with 100-200 cases reported annually. There is substantially higher risk for infection if travel occurs during an outbreak. The vaccine is immunogenic, but it also is reactogenic.

Dr. Hills presented the following draft recommendations for ACIP's consideration:

Chikungunya vaccine is recommended for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak.

In addition, chikungunya vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years:

- ❑ Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure to mosquitoes OR
- ❑ Persons staying for a cumulative period of 6 months or more

An outbreak will be defined as occurring when CDC posts information on an outbreak on the CDC website. A notice will be posted as soon as CDC becomes aware of an outbreak. A similar process is used in relation to cholera and for the cholera vaccine recommendations, with information posted when cholera outbreaks occur.

The second part of the proposed recommendation is a shared clinical decision-making recommendation for certain individuals traveling to an area with documented human cases. There is more uncertainty in the risk-benefit assessment in these cases. However, there are likely to be circumstances in which some individuals might reasonably choose vaccination or some providers might wish to recommend it. In these circumstances, it is appropriate for there to be a conversation between the HCP and patient about the risks and benefits, including the likelihood of exposure based on factors such as activities, time of year, and duration of travel; the disease and its potential severity; the vaccine's efficacy; and the possibility of vaccine-associated adverse events. This approach also allows the traveler's personal perceptions and tolerance of risks to be taken into account.

Key risk factors for severe chikungunya disease include older age and underlying medical conditions (e.g., diabetes, cardiac disease, hypertension) and that key risk factors for chronic arthralgia after chikungunya are older age and pre-existing joint problems. A key risk factor for chikungunya virus infection among travelers is the intensity of transmission. If there is equivalent transmission in different areas, the cumulative duration of exposure becomes important. Moderate exposure could include travelers who might have at least 2 weeks of cumulative exposure to mosquitoes in indoor or outdoor settings. This does not include travelers who might have limited exposure to mosquitoes (e.g., those traveling for business and likely to be mainly in mosquito-protected indoor settings).

Dr. Hills noted that when the work group was developing the recommendation options for ACIP's consideration, they aimed to develop recommendations that balance the desirable and undesirable effects of vaccination based on consideration of all of the disease and vaccine factors. The "recommended" component of the recommendations aims to target the travelers with highest risk, where the benefits of receiving the vaccine almost certainly outweigh the risks. The "may be considered" recommendation aims to include groups with higher risk where the work group did not think a specific recommendation was justified because there is more uncertainty in the risk-benefit assessment, but for which some individuals might reasonably choose vaccination, some providers might reasonably wish to recommend it, and a discussion

and decision-making based on a conversation between the provider and patient would be valuable.

Dr. Kotton asked whether there were any thoughts about an upper age limit by which this vaccine no longer would be given. Her concern regarded safety among non-immunocompromised people in their 70s and 80s.

Dr. Hills shared some data to help provide some context to this. Data for arthralgia by age group do not show that frequency and maximum severity increase with age. While there are few data, frequency of any particular adverse event (AE) is similar or lower in older age groups.

Dr. Daley made a motion to approve the draft recommendation language as presented, which Dr. Long seconded.

Dr. Kotton noted that while it did not necessarily have to be in the vote language, it should be non-immunocompromised persons ≥18 years of age. Dr. Hills indicated that this is clearly indicated in the top right corner of the package insert and will be included in the *MMWR*.

Dr. Cineas asked whether there were any data beyond 1 year in terms of how durable the vaccine is for people who might be traveling multiple times to endemic or areas where there is an outbreak.

Dr. Hills indicated that the work group reviewed data for 2 years and found that seroresponse rates are very high at 2 years. The manufacturer is planning to continue to monitor for at least 5 years.

Dr. Hills indicated that the plan is to create a table to accompany the recommendations that describes the various risk factors for chikungunya and risk of chikungunya virus infection. The work group preferred to leave the proposed recommendation language fairly straightforward, and provide the table to facilitate provider/patient discussions.

Dr. Hills next presented the proposed policy options for chikungunya vaccine use among laboratory workers. At least 44 cases of chikungunya virus infection among laboratory workers have been reported worldwide during the last 50 years. Of these, 43 cases were overt disease, 1 was an asymptomatic infection, and there were no deaths. Among US laboratorians, 4 disease cases have been reported in the 8-year period since chikungunya became a nationally notifiable disease in the US in 2015. Documented routes of transmission of chikungunya virus in the laboratory have been through the aerosol route and the percutaneous routes. Among cases of percutaneous transmission with more detailed information available, 2 researchers experienced a needlestick injury while they were working with and injecting mice. For the third case, a researcher experienced a forceps prick while dissecting mosquitoes infected with chikungunya virus. Although not documented, transmission through accidental mucosal exposure is also possible.

Factors the work group considered regarding recommendations for laboratory workers were that vaccination is required for only limited number of staff who might be exposed to live chikungunya virus. Vaccination is not necessary for workers handling routine clinical samples who should be consistently using standard practices for handling patient samples. Therefore, recommendations are only for laboratorians undertaking research or very specific diagnostic work using live virus (e.g., plaque reduction neutralization tests). The work group surmised that the benefits of vaccination outweigh risks for small group of laboratorians working with live virus, given potential for acquiring chikungunya virus infection which can result in severe polyarthralgia and possibly chronic arthralgia. The work group proposed the following draft recommendation for ACIP consideration:

> Chikungunya vaccination is recommended for laboratory workers with a potential for exposure to chikungunya virus.

The recommendations would be accompanied by clear information for implementation, including noting that a local institutional biosafety committees should undertake a risk assessment of the potential for exposure to chikungunya virus for each laboratory worker working with the virus, considering the type of work to be performed and the biosafety level at which work will be conducted; vaccination is not necessary for workers handling routine clinical samples.

Dr. Loehr made a motion to accept the proposed recommendation as written. Dr. Cineas seconded the motion.

Dr. Hills presented clinical guidance for use of live attenuated chikungunya vaccine in pregnant and breastfeeding individuals. The spectrum of illness of chikungunya in pregnant persons appears to be similar to that among non-pregnant persons. Adverse outcomes such as fetal loss, stillbirth, or preterm birth as a result of vertical transmission have been documented but are rare. However, infection commonly results in adverse neonatal outcomes if pregnant individuals are infected around the time of delivery. In these cases, intrapartum transmission occurs in about 30% to 50% of cases. When infection occurs following intrapartum transmission, severe and sometimes fatal illness can result. Clinical presentation in the newborn is commonly with encephalopathy, sepsis-like illness, cardiac, dermatologic, and hemorrhagic manifestations. In the setting of neonatal infection, neurocognitive outcomes are often poor, particularly if the initial clinical presentation is with encephalopathy. Young infants infected by mosquito-borne transmission are also at risk for severe disease, particularly during the first few months of life. Clinical presentations in young infants are similar to presentations in infected neonates. This issue is important because of its relevance to possible protection of young infants by transplacental transfer of antibodies after maternal vaccination, although this is theoretical.

The data are insufficient to determine whether there are any safety risks in vaccination during pregnancy, given that pregnancy was an exclusion criterion in the clinical trials and only 2 pregnant persons were inadvertently vaccinated. Both of the 2 women were vaccinated during the first trimester. One was a 36-year-old who experienced a spontaneous abortion 59 days after vaccination at a gestational age of about 10 to 14 weeks. The other was a 23-year-old who had anembryonic pregnancy noted 53 days after vaccination and experienced a spontaneous abortion at 55 days at about 8 weeks gestation. It is important to note that anembryonic pregnancies generally result from a chromosomal problem at conception. An estimated 20% to 25% of all pregnancies lead to pregnancy loss, with the highest rates in the first trimester and increasing rates with increasing maternal age.

Vaccine viremia occurs in the first week following administration of chikungunya vaccine, and it is not known if the vaccine virus can be vertically transmitted and cause fetal or neonatal adverse reactions. Under “Use in Specific Populations,” the package insert notes that a decision to administer chikungunya vaccine during pregnancy should take into consideration the individual's risk of wild-type chikungunya virus infection, gestational age, and risks to the fetus or neonate from vertical transmission of wild-type chikungunya virus. It notes that if neonates are born within 14 days of their mother receiving chikungunya vaccine, they should be closely monitored after birth for potential disease due to vaccine virus.

In the future, the work group will be considering recommendations for persons in US territories and states with risk of chikungunya virus transmission. Therefore, the vaccine potentially could be used in a larger population of pregnant individuals in future than is anticipated with its use among travelers and laboratory workers in the near-term. Having considered the issues around risks of chikungunya disease for pregnant individuals and their infants and vaccine use in pregnancy, the objectives of chikungunya vaccination during pregnancy are to protect the pregnant person from chikungunya virus infection and avoid maternal infection around the time of delivery to prevent intrapartum virus transmission and severe disease in the newborn. In addition, transplacental transfer of antibodies might also protect young infants from mosquito-borne transmission and severe disease.

The following is the work group’s proposed clinical guidance language for use of chikungunya vaccine in pregnant individuals:

- ❑ Pregnant individuals should avoid the risk for chikungunya virus infection, if possible (e.g., by avoiding travel to an area with virus transmission, particularly during an outbreak).

- ❑ Pregnancy is a precaution for vaccination with a live attenuated chikungunya vaccine. In general, vaccination should be deferred until after delivery. However, when the risk of infection is high and exposure cannot be avoided, a healthcare provider should discuss with a pregnant person the potential risks of chikungunya virus infection and the potential benefits and risks of vaccination so that vaccination can be considered.

- ❑ If pregnant persons choose to be vaccinated, out of caution vaccination should genuinely be avoided during the 1st trimester (until 14 weeks) gestation and after the 36th week of gestation.
  - Avoiding vaccination during the first trimester is preferred for two reasons. Firstly, pregnancy loss has been reported in two individuals vaccinated during the first trimester, although one was an anembryonic pregnancy. In addition, the vaccine is reactogenic and can cause fever, and fever has been linked to birth defects in the 1st trimester.
  - Avoidance of vaccination after the 36th week of gestation is to limit the risk of vaccine-induced viremia occurring in the intrapartum period, and thus to reduce the theoretical risk for perinatal transmission and potential adverse outcomes.*

*Vaccine viremia is considered to occur in most individuals in the first few days after vaccination and to decrease thereafter; viremia was no longer detectable in any clinical trial subjects at 14 days after vaccination.

- ❑ In line with common practice following vaccination with live vaccines, non-pregnant vaccine recipients should generally wait 4 weeks before becoming pregnant. If a pregnant person is inadvertently vaccinated outside of the preferred period or becomes pregnant within 4

weeks after the chikungunya vaccination, this should not be considered a reason to terminate the pregnancy.

- ❑ This guidance is intended to maximize the benefits of vaccination while minimizing risks associated with vaccination during pregnancy.

Chikungunya viral ribonucleic acid (RNA) has been detected in breast milk of women in endemic areas on very rare occasions. No studies have reported detection of replicating virus. Although the data are limited, chikungunya virus transmission through breastfeeding has not been reported. No human data are available on whether chikungunya vaccine virus or antibodies are present in breast milk after vaccination. It is known in general that neonates and other infants less than 1 year of age are at risk for severe disease, particularly in the first few months of life, if infected with wild-type chikungunya virus. The vaccine virus is attenuated, but there are no data on potential outcomes for an infant if chikungunya vaccine virus was transmitted by breastfeeding.

In the package insert for the vaccine, breastfeeding is neither a contraindication nor precaution for vaccination. The language in the package insert notes that the developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for the vaccine and any potential adverse effects on the breastfed child from the vaccine or from the mother's susceptibility to chikungunya. The package insert also notes that vaccine viremia occurs after vaccination, but that any potential for transmission of the vaccine virus from mother to infant through breast milk is unknown.

The following is the work group's proposed clinical guidance language for use of chikungunya vaccine in breastfeeding individuals:

- ❑ Breastfeeding individuals and their infants should avoid the risk for chikungunya virus infection, if possible (e.g., by avoiding travel to an area with transmission particularly during an outbreak).

- ❑ In the absence of data, breastfeeding is a precaution for vaccination. When the risk of infection is high (e.g., during an outbreak) and exposure cannot be avoided, a health care provider should discuss with a breastfeeding individual the developmental and health benefits of breastfeeding for the infant, the risks of chikungunya virus infection, and the potential benefits and risks of vaccination, and offer the vaccine to the breastfeeding person. At the current time, the data are insufficient to make a recommendation to defer breastfeeding for any period after vaccination.

Dr. Riley, liaison representative from the American College of Obstetricians and Gynecologists (ACOG), expressed ACOG's support for the use of the chikungunya vaccine in pregnancy as a precaution when infection risk is high and exposure cannot be avoided using shared clinical decision-making. When chikungunya infection occurs around the time of delivery, it frequently results in antepartum transmission that in and of itself results in severe outcomes for neonates. Vaccination during pregnancy, particularly around the time of delivery or ≤36 weeks gestation, could protect the mother and the fetus. It is also possible that transplacental transfer of antibodies occurs and could protect young infants from mosquito-borne transmission. With the observed severe outcomes when a pregnant individual gets infected around the time of delivery, any opportunity to protect a pregnant person before the antepartum period is beneficial.

While some live attenuated vaccines are contraindicated during pregnancy, other vaccines such as dengue, Ebola, and yellow fever have been licensed with pregnancy as a precaution. Therefore, in an outbreak situation or other time when infection risk is quite high, ACOG supports the use of this vaccine during pregnancy to prevent the chances of a pregnant person acquiring the infection around the time of delivery.

Dr. Long said she was struck that there are no data on giving this vaccine to pregnant women, but they do not want to disenfranchise them from being immunized. She recalled the two inadvertently administered vaccines in the first trimester, both of which had adverse outcomes.

Dr. Dana Meaney-Delman, CDC, indicated that one was an anembryonic pregnancy that likely was chromosomal in nature and unlikely biologically plausible to be related to the vaccine. While they may never know more about those two pregnancies, the pregnancy losses occurred more than 50 days out from vaccination, which also makes it unlikely.

Although public comment was presented prior to the votes during this meeting, the votes were incorporated in this summary with their respective sessions for the purpose of continuity.

Vote #1: Chikungunya Vaccines for Travelers

Dr. Susan Hills (CDC/NCEZID) read the following proposed ACIP voting language into the record for chikungunya vaccines pertaining to travelers:

> *Chikungunya vaccine is recommended for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak.*
>
> *In addition, chikungunya vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years:*
>
> - *Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure to mosquitoes, OR*
> - *Persons staying for a cumulative period of 6 months or more.*

Motion/Vote #1: Chikungunya Vaccines for Travelers

Dr. Daley made a motion to approve the proposed Vote #1 recommendation for chikungunya vaccines stating, "Chikungunya vaccine is recommended for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak. In addition, chikungunya vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years: Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure to mosquitoes, OR Persons staying for a cumulative period of 6 months or more." Dr. Long seconded the motion. No COIs were declared. The motion carried with 12 favoring, 0 opposing, and 1 abstaining. The disposition of the vote was as follows:

12 Favored: Brooks, Beigel, Chen, Cineas, Clark, Daley, Grimes, Hance, Kotton, Loehr, Long, Marshall
0 Opposed: N/A
1 Abstained: Kaslow

Vote #2: Chikungunya Vaccines for Laboratory Workers

Dr. Hills read the following proposed ACIP voting language into the record for chikungunya vaccines pertaining to laboratory workers:

> *Chikungunya vaccination is recommended for laboratory workers with potential for exposure to chikungunya virus.*

Motion/Vote #2: Chikungunya Vaccines for Travelers

Dr. Loehr made a motion to approve the proposed Vote #2 recommendation for chikungunya vaccines stating, "Chikungunya vaccination is recommended for laboratory workers with potential for exposure to chikungunya virus." Dr. Cineas seconded the motion. No COIs were declared. The motion carried with 13 favoring, 0 opposing, and 0 abstaining. The disposition of the vote was as follows:

13 Favored: Brooks, Beigel, Chen, Cineas, Clark, Daley, Grimes, Hance, Kaslow, Kotton, Loehr, Long, Marshall
0 Opposed: N/A
0 Abstained: N/A

Members and *Ex Officios* were invited to make comments following the votes. Dr. Chen noted that while the chikungunya vaccine was first licensed in the US, the burden of disease is global. He expressed his hope that the discussions they had throughout the day would not negatively affect the consequences of implementation of the vaccine globally. He would like to continue to see additional vaccines for other mosquito-borne agents in the US and around the world.

DIPHTHERIA AND TETANUS TOXOID (DT) VACCINE

Dr. Michele Hughes (CDC/NCIRD) provided an update on CDC's guidance for Td vaccines for young children. As part of the routine vaccination schedule, CDC recommends a primary series of the pediatric diphtheria-, tetanus-, and pertussis-containing vaccines (DTaP) vaccines for children <7 years of age. For children<7 years of age who developed a contraindication to pertussis-containing vaccines, CDC previously recommended the pediatric diphtheria and tetanus toxoid vaccine (DT) instead of DTaP. Recently, the sole DT vaccine manufacturer in the US discontinued DT production. The last available lot expired in April 2023. There is no longer DT vaccine available in the US.

The only contraindication specific to the pertussis component in DTaP is encephalopathy within 7 days of vaccination that is not attributed to another cause. While the exact numbers are not known, the occurrence of this AE is extremely rare. In light of DT no longer being an available option, CDC issued the following updated vaccination guidance for the use of Td in young children with a contraindication to pertussis-containing vaccines:

- ❑ CDC recommends young children receive DTaP as the first dose in the diphtheria, tetanus, and pertussis childhood vaccination series.

- ❑ CDC recommends continued use of DTaP unless a contraindication to pertussis-containing vaccines develops.

- ❑ For young children who develop a contraindication to pertussis-containing vaccines, vaccine providers may administer Td for all recommended remaining doses in place of DTaP.

The impact on diphtheria protection is uncertain. Td is a tetanus- and diphtheria toxoid-only formulation licensed only for ages ≥7 and older. The use of Td in this situation would be an off-label use. Td contains a lower dose of diphtheria toxoid compared to DT and the impact of this lower dose on the protection provided against diphtheria in young children is uncertain. There are no available data evaluating the effectiveness of Td against diphtheria when used as part of the primary series in young children. Children may have less protection against diphtheria and no additional protection against pertussis if they receive Td instead of DTaP. CDC has posted this guidance on its website at www.cdc.gov/vaccines/vpd/dtap-tdap-td/hcp/td-offlabel.html. In order to be covered by VFC for children <7 years of age, a minor update is needed.

Dr. Jeanne Santoli (CDC/NCIRD) gave an update on the current Td supply and the proposed VFC updates. As noted, MassBiologics has discontinued production of their Td vaccine, TdVax™. Grifols, who is the exclusive distributor for TdVax™, expects to have product available through approximately June 2024. Sanofi, who manufacturers Tenivac®, the only other US-licensed Td vaccine, is taking steps to augment their available supply of Td for the US. However, it is anticipated that the supply of Td vaccine in the US market will be constrained during 2024. Temporary ordering controls have been put into place in the public and private sectors to help manage the gap in supply. Adult formulation tetanus and diphtheria toxoids and acellular pertussis vaccine (Tdap) is available from both US-licensed manufacturers without supply constraints at this time. Based on the rarity of developing a contraindication to pertussis-containing vaccines, the temporarily constrained supply of Td vaccine is not anticipated to prevent providers from utilizing Td vaccine for these children in the VFC program.

Dr. Santoli indicated that the purpose of this resolution was to: 1) add Td vaccine for use in children <7 years of age for whom receipt of the pertussis component is contraindicated; and 2) update the language regarding the Tdap booster to align with ACIP recommendations. Eligible groups include children and adolescents aged 6 weeks through 18 years, which was unchanged.

Because Td is not currently included in the VFC program, the proposed language to add it to the VFC resolution is as follows:

> *Approve the Vaccines for Children (VFC) resolution for diphtheria, tetanus, and pertussis vaccines.*

Dr. Long noted that with anticipation that Td is frequently not stocked in places like emergency departments anymore, there already is language in the Red Book stating that Tdap can be used if there is no Td.

Dr. Santoli indicated that in terms of the VFC Resolution, Tdap is absolutely covered for persons >7 years of age. It is not covered for the persons <7 years of age.

In terms of the recommendation, Dr. Hughes added that ACIP's previous recommendation that Tdap can be used in lieu of Td would remain.

Dr. Long made a motion to accept the proposed wording for a vote, which Dr. Kotton seconded.

Vote: VFC Resolution for Diphtheria, Tetanus, and Pertussis Vaccines
While public comment was presented prior to the votes, the votes were combined in this summary with their respective sessions for the purpose of continuity.

> *Approve the Vaccines for Children (VFC) Resolution for diphtheria, tetanus, and pertussis vaccines.*

Motion/Vote: VFC Resolution for Diphtheria, Tetanus, and Pertussis Vaccines

Dr. Long made a motion to approve the proposed recommendation for the VFC Resolution stating, “Approve the Vaccines for Children (VFC) Resolution for diphtheria, tetanus, and pertussis vaccines.” Dr. Kotton seconded the motion. Dr. Chen declared a COI due to his active collaboration with MassBiologics, the maker of a DT vaccine. The motion carried with 12 favoring, 0 opposing, 0 abstaining, and 1 recusing. The disposition of the vote was as follows:

12 Favored:	Brooks, Beigel, Cineas, Clark, Daley, Grimes, Hance, Kaslow, Kotton, Loehr, Long, Marshall
0 Opposed:	N/A
0 Abstained:	N/A
1 Recused:	Chen

INFLUENZA VACCINES

The influenza session was opened by Dr. Jamie Loehr, ACIP Influenza Vaccine Work Group Chair.

Dr. Aaron Frutos (CDC/NCIRD/ID) presented CDC's interim estimates of 2023/2024 seasonal influenza VE. This year, 4 networks contributed to the interim estimates of VE against laboratory-confirmed influenza for children, adolescents, and adults in the out-patient and in-patient settings.

The methods used by each network to estimate influenza VE are very similar. All enrollees across all networks sought medical care for acute respiratory illness (ARI). Patients are included from fall 2023 to early 2024. Each network uses a test-negative design, which compares the vaccination odds among case patients with influenza confirmed by molecular assay versus control patients testing negative for influenza and SARS-CoV-2. Vaccination status was determined as the receipt of any of the 2023-2024 seasonal influenza vaccines according to medical records, immunization registries, claims data, and/or self-report. VE estimates were calculated for influenza A subtypes A(H1N1)pdm09 and A(H3N2) when possible. VE was not estimated for some age groups and settings when the sample size was small or when models did not converge.

Pediatric VE against any influenza ranged from 59% to 67% in out-patient settings and 52% to 61% in the in-patient setting. VE estimates were consistent across networks. Pediatric VE against influenza A ranged from 46% to 59% in out-patient settings and 46% to 56% in the in-patient setting. Pediatric VE against influenza A(H1N1)pdm09 ranged from 54% to 61% in out-patient settings and was 60% in the in-patient setting. Pediatric VE against influenza A(H3N2) was 55% in out-patient settings and was not estimated in the in-patient setting. Pediatric VE against influenza B ranged from 64% to 89% in out-patient settings and was not estimated in the in-patient setting.

For adults ≥18 years and older, vaccination prevalence ranged from 39% to 52% among test-negative controls across settings. Adult VE against any influenza ranged from 33% to 49% in the out-patient settings and 41% to 44% in the in-patient setting. Adult VE against influenza A ranged from 27% to 46% in out-patient settings and 40% to 42% in the in-patient setting. Adult VE against influenza A(H1N1)pdm09 was 25% in out-patient settings and 50% in the in-patient setting. Adult VE against influenza A(H3N2) was 54% in the out-patient setting and was not estimated in the in-patient setting. Adult VE against influenza B was 78% in out-patient settings in 2 networks and 60% in the in-patient setting. Again, consistent results were observed across networks.

Among adults ≥65 years of age, the prevalence of vaccination among test-negative controls ranged from 48% to 68% across settings. VE against any influenza ranged from 41% to 51% in out-patient settings and was 42% in 2 networks in the in-patient setting. Among adults ≥65 years of age, VE against influenza A ranged from 40% to 52% in out-patient settings and 42% to 47% in the in-patient setting. VE against influenza B for adults ≥65 years of age was 69% in out-patient settings and was not estimated in the in-patient setting.

These estimates showed that vaccination with the 2023-2024 influenza vaccine reduced the risk for medically-attended influenza out-patient visits and hospitalizations among children, adolescents, and adults across 22 US states. Vaccination was effective against both influenza A, mostly subtype A(H1N1)pdm09, and B Victoria viruses that have circulated this season.

Dr. Sophie Zhu (California Department of Public Health and CDC/PHIC/DWD) presented interim influenza VE against laboratory-confirmed influenza in California for October 2023—January 2024. New public health data reporting requirements in California offer an opportunity to calculate VE against laboratory-confirmed influenza, resulting in estimates that are available ahead of traditional platforms. As of January 1, 2023, all influenza vaccination records became reportable to the California Immunization Registry (CAIR). Positive influenza results have been reportable in California since October 2019. Negative influenza results became reportable as of June 15, 2023 to the California Reportable Disease Information Exchange (CalREDIE), the state electronic communicable disease reporting system.

For this analysis, influenza laboratory results were matched to immunization registry data to calculate early VE estimates against laboratory-confirmed influenza in California during the 2023-2024 influenza season. The estimates from this analysis reflect VE against laboratory-confirmed influenza using nucleic acid amplification tests and include persons tested for influenza from diverse care settings and symptom severity levels. VE is calculated using a case-control design in which persons testing positive for influenza are case patients and persons testing negative for influenza are control patients.

Persons included in the analysis were all California residents ≥6 months of age with molecular tests for influenza A or B captured by the state electronic laboratory reporting system. Most influenza testing performed at clinical and commercial laboratories that report influenza A and B test results do not perform subtyping. The dates of this analysis were October 1, 2023, through January 31, 2024. Participants were considered vaccinated if there was at least 1 dose of seasonal influenza vaccine documented in CAIR ≥14 days before testing. Adjusted VE was calculated as VE = (1 – adjusted odds ratio) x 100%. A mixed-effects logistic regression model was used that was adjusted for age, ethnicity, testing week (random effect), and county (random effect).

In California, overall influenza virus positivity the week of February 19, 2024, was 6.5% and had declined from prior weeks. Based on subtyping at public health laboratories in California, this is a predominantly H1 season so far. Of the samples, 82% have been influenza A and 75% have been H1. A total of 678,422 individuals were included in this analysis. This included 77,501 influenza-positive cases, which is about 11% positivity, and 600,921 influenza-negative control patients. The median age was 31 years for case patients and 44 years for control patients. There was a similar breakdown of race and ethnicity for the case and control patients. Overall, 28% of individuals were vaccinated and 18% of case patients were vaccinated overall versus 29% of controls. Vaccination increased month-by-month from 13% during October to 34% during April. A similar lower vaccination rate was seen in case versus control patients throughout all time periods.

Adjusted VE against laboratory-confirmed influenza overall was 45%. VE declined with increasing age and was highest at 56% in children ≤18 years of age, 48% in adults 18–49 years of age, 36% in adults 50–64 years of age, and lowest at 30% in adults ≥65 years of age. VE against influenza A was lower than overall influenza VE, but was still protective at 42%. Over 90% of cases in this analysis were influenza A, which is consistent with both California and national trends.

Age-specific VE declined with increasing age and was lowest for adults ≥65 years of age at 29%. VE for influenza B was high at 76%. Estimates were generally comparable across younger age groups, ranging from 75% to 79% for persons 6 months–49 years of age. Similar to influenza A, estimates were lower among adults ≥50 years of age. Less than 10% of cases were influenza B.

Mandatory public health data can be leveraged to calculate timely in-season influenza VE as an additional estimate supporting existing public health influenza prevention efforts. Earlier estimates can inform public health action and messaging for additional prevention measures prior to the peak of influenza infections and could be especially informative for healthcare settings that may need to reallocate resources to prepare for increased hospital capacity.

C. Buddy Creech, MD, MPH (Vanderbilt University Medical Center) presented on the safety of quadrivalent live attenuated influenza vaccine (LAIV4) in children with asthma. In this study, 151 children and adolescents 5–17 years of age with persistent asthma were randomized to LAIV (n = 79) or quadrivalent inactivated influenza vaccine (IIV4) (n = 72). The primary objective was to compare the proportion of participants who experienced asthma exacerbation during the 6 weeks after LAIV4 versus IIV4. Persistent asthma was defined as provider diagnosis of asthma plus prescription of a long-acting controller medication and an asthma exacerbation was defined as an acute episode of progressively worsening shortness of breath, cough, wheezing, chest tightness, or respiratory distress for which the patient sought medical attention or received a new prescription for systemic corticosteroids.

LAIV4 was not associated with increased asthma symptoms or asthma exacerbations in the 14- or 42-day windows following immunization. Rates of reactogenicity were similar between the 2 groups, although myalgia and sore throat were more common in the IIV4 arm. LAIV4 may be a suitable option for children ≥5 years of age who have asthma, including those with moderate to severe asthma.

Dr. Lisa Grohskopf (CDC/NCIRD/ID) provided an update on influenza B/Yamagata surveillance. Up until the late 1970s, the number of viruses in influenza vaccines varied from year-to-year. There was variability in the formulation from year-to-year, starting around the 1978-1979 season. Consistent seasonal vaccination has been available with trivalent vaccines with an A/H1, A/H3, and 1 B virus. During the 1980s, there was an appreciation that there were 2 lineages of influenza B viruses for which research evidence suggested that there was not optimal cross-immunity. There was only one B lineage in the vaccine, so one of the two had to be selected for inclusion in the vaccine. Quadrivalent influenza vaccines became available in the market in 2013-2014 and contained 2 B viruses, 1 from each lineage. After the 2013-2014 season, there was a gradual phase-in of the quadrivalent influenza vaccines. Some manufacturers went from one season to the next from trivalent to quadrivalent. Some phased them in within their brand over time. The transitioned to quadrivalent influenza vaccines was largely complete before the 2021-2022 season, with only 1 lot of trivalent released that season. There have now been a couple of seasons with only quadrivalent vaccines.

As Dr. Kondor presented during the October 2023 meeting, there have been no confirmed naturally occurring influenza B/Yamagata viruses in global surveillance since March 2020. The LAIV contains B/Yamagata, so it is conceivable that this might be seen in surveillance. However, there have been no wild-type detections of naturally occurring B/Yamagata viruses. During the Fall 2023 discussions for Southern Hemisphere influenza vaccine composition, WHO and FDA concluded that coverage of influenza B/Yamagata was no longer warranted and should be removed from vaccines as soon as feasible.

Since then, WHO met and made recommendations for the Northern Hemisphere for the 2024-2025 season that include a second B virus for those countries that elect to use/market a quadrivalent vaccine. Decisions regarding the composition are made by individual national regulatory authorities. For the US, that is the FDA. The FDA is set to discuss composition of 2024-2025 US influenza vaccines on March 5, 2024.

Ms. Rebecca Coyle (AIRA) pointed out that the codes for trivalent vaccine have been inactivated because they have not been used in the last several seasons. For any upcoming decisions, particularly by manufacturers that will be moving to trivalent influenza vaccine as soon as this year, it will be to be important to have conversations as soon as possible about reactivating the old codes versus trying to create new codes. There is a relatively short period of time between now and the next influenza season, so the time is now to make sure the codes are correct for billing to make this as seamless as possible.

POLIO VACCINE

Dr. Oliver Brooks, chair of the ACIP Polio Vaccine Work Group, introduced the polio vaccine session.

Dr. Sarah Kidd (CDC/NCIRD) reminded the committee that paralytic disease occurs in <1% of poliovirus infections and approximately 75% of infections are asymptomatic. There are 3 poliovirus serotypes with different epidemiological and clinical characteristics and immunity to one serotype does not result in significant immunity to other serotypes. The ratio of paralytic cases to infections varies by serotype, ranging from approximately 1 in 190 infections for Type 1 to approximately 1 in 1,900 infections for Type 2. Poliovirus is considered highly infectious and is spread through the fecal-oral or oral-oral routes. Fecal-oral transmission is considered the most important pathway, particularly in settings with suboptimal hygiene and sanitation. Virus may be present in the stool of infected persons for up to 6 weeks and sometimes longer. Individuals who are asymptomatic can still shed virus and transmit it to others.

Inactivated polio vaccine (IPV) is the only polio vaccine that has been used in the US since 2000. It contains inactivated poliovirus Types 1, 2, and 3. It cannot replicate, infect, or cause disease. It induces effective humoral immunity and prevents paralysis. It also induces some nasopharyngeal mucosal immunity but does not provide substantial intestinal immunity or prevent gastrointestinal shedding.

Oral polio vaccine (OPV) is no longer used in the US. It is a live-attenuated vaccine that can come in different formulations. Trivalent vaccine (tOPV) contains poliovirus Types 1, 2, and 3. Bivalent vaccine (bOPV) contains Types 1 and 3 poliovirus. Monovalent OPV (mOPV) contains just a single serotype. OPV replicates in the gut and is shed in the stool. It induces both humoral and mucosal immunity, so that it prevents paralysis and transmission of poliovirus. For this reason, it has been considered the historical vaccine of choice for countries experiencing polio outbreaks. However, the attenuated vaccine virus can revert to a neurovirulent form that causes paralysis. nOPV2 is a next-generation version of the Sabin Type 2 mOPV that was designed to be more genetically stable and less likely to revert to a neurovirulent form. Between March 2021 and December 2023, almost a billion doses were administered as part of outbreak responses in 35 countries under a WHO Emergency Use Listing (EUL) approval. As of December 2023, it earned WHO prequalification status.

In the US, the incidence of paralytic polio decreased rapidly after the introduction of the Salk IPV in 1955. The Sabin OPV was used for routine childhood immunization for decades, but an enhanced potency IPV was introduced in 1997 as part of a sequential schedule with OPV. In 2000, the US moved to an IPV-only schedule. IPV has been the only polio vaccine recommended in the US since that time. Wild poliovirus type 1 (WPV1) and vaccine-derived polioviruses are still circulating in certain parts of the world. Approximately 450 paralytic polio cases caused by WPV1 and circulating vaccine-derived polioviruses (cVDPV) that have been identified in the last 12 months.

A case of paralytic polio caused by VDPV Type 2 (VDPV2) was confirmed in an unvaccinated young adult from Rockland County, New York on July 21, 2022. Genetic sequencing has indicated a linkage between this case to polioviruses collected in wastewater in Israel, the UK, and Canada. Of note, Rockland County has reported overall low vaccine coverage for over 20 years. When this case was identified in summer 2022, only 60% of children under 2 years of age had received 3 doses of IPV. ZIP Code level coverage in the area was as low as 37% in some areas. Fortunately, no additional paralytic cases were identified.

Poliovirus related to the case was detected in wastewater in several New York State (NYS) counties and in New York City (NYC). Retrospective testing detected poliovirus in the area as early as April 2022, indicating circulation and asymptomatic infections in the area since at least that time. Related virus continued to be consistently detected in wastewater until the beginning of November 2022. The most recent detection was February 22, 2023, in Rockland County. Samples collected in the last year have all been negative.

The primary vaccination response to the 2022 outbreak was focused on identifying under-vaccinated and unvaccinated persons and providing catch-up vaccination with IPV. However, in fall 2022 when there were still wastewater detections of poliovirus, it was unclear whether the strategy was going to be sufficient to interrupt circulation. WHO recommendations for polio outbreaks in countries like the US with exclusive IPV vaccination and high sanitation and hygiene are to conduct a timely outbreak response with IPV only if poliovirus transmission is confined in a well-defined population group or geographic area. However, if transmission persists, WHO recommends considering an OPV response. Therefore, the work group was asked to discuss considerations for the potential use of nOPV2 as an outbreak response measure in the US.

Given that the New York outbreak had already waned at the time of the work group discussions, the question the work group took up was a theoretical one, “Should nOPV2 be used in combination with a catch-up IPV campaign during a future Type 2 poliovirus outbreak in the US?” The population under consideration would be persons living in an area with circulating poliovirus. The intervention would be nOPV2 vaccination for the general population in addition to catch-up IPV vaccination for un- or under-vaccinated persons. That would be compared to the intervention of catch-up IPV vaccination only. The outcomes of interest were prevention of paralytic poliomyelitis; the extent and duration of poliovirus circulation in the community; serious adverse events, including vaccine-associated paralytic polio; and possible introduction of a new VDPV2.

The work group used the ACIP EtR Framework and domains to frame their discussions. Based on the information presented, the work group had previously agreed that polio is a problem of public health importance. For potential benefits and harms, the work group noted that there are high rates of seroconversion following 1 and 2 doses of nOPV2 when administered to infants.

Given that vaccination with IPV is already recommended in this country, the main benefit of nOPV2 would be to confer gastrointestinal immunity.

Sabin OPV2 reduces the odds of fecal shedding following a subsequent oral challenge dose by more than 90% compared to no vaccination. There are no direct data for nOPV2, but it has performed as expected in the field in terms of slowing or stopping outbreaks. A small Phase 1 study among adults showed evidence of gastrointestinal immune response following nOPV2 administration. It is known that nOPV2 is a live virus and it is shed in stool by nOPV2 recipients following vaccination. When measured by PCR, 85% had detectable vaccine virus in stool at 7 days. This decreased to 40% to 57% by 28 days. When measured by culture, which is probably a better measure of infectious virus, 40% were shedding at 7 days. This decreased to 1% to 14% by 28 days.

nOPV2 was developed to be more genetically stable than Sabin OPV2 and less likely to regain neurovirulence in the laboratory. However, there is still a risk of vaccine-associated paralytic polio (VAPP) in recipients. The estimated risk of VAPP for nOPV2 is estimated to be 0.07 cases per million recipients or 1 case per 14.3 million recipients. This is compared to Sabin OPV with an estimated case rate of 0.25 to 4 cases per million recipients or 1 per 0.25 million to 4 million recipients. The risk of VAPP is known to be highest in previously unimmunized children who are receiving their first dose of OPV or in immunocompromised patients. And the risk of VAPP could be mitigated by limiting nOPV2 administration to persons who had previously received at least 1 dose of IPV. It also is known that there is a risk of ongoing transmission of the nOPV2 virus with reversion to a VDPV.

The risk is difficult to quantify, but so far, there have been at least 7 separate emergences of new cVDPV2 linked to nOPV2 (cVPDV2-n) and at least 61 associated paralytic cases worldwide from these emergences. These are the numbers that have been published in the literature so far, but the actual numbers are likely higher as nOPV2 use increases globally. However, nOPV2 is estimated to be 80% less likely than Sabin OPV to seed a new cVDPV2. The risk of a new cVDPV is highest when campaign coverage is low in a population with low immunity against polioviruses.

When thinking about the balances of risks and harms for the individual recipient, most recipients will have already been vaccinated with IPV during childhood immunization and are already protected against paralytic disease. The anticipated benefits of nOPV2 to the individual recipient would be a higher anti-polio Type 2 antibody titer and increased odds of mucosal immunity to poliovirus Type 2. For an under-vaccinated person, this would mean additional protection against paralytic disease. However, for a previously vaccinated person, there is unlikely to be a clinically significant benefit of vaccination. For potential harms, there is an extremely low but non-zero risk of VAPP. There also is a risk of chronic infection if nOPV2 is given to a child with unrecognized immunocompromise.

At the population level, decreased transmission among nOPV2 recipients potentially could result in the outbreak ending earlier and fewer paralytic cases. Given that the vaccine virus can be shed in stool and transmitted to others, there likely would be some degree of passive vaccination of unvaccinated persons, which also would lead to decreased transmission and fewer paralytic cases. Potential harms at the population level include passive vaccination of the unvaccinated and a risk of VAPP among the unvaccinated, possible ongoing transmission of the nOPV2 virus leading to a new cVDPV2 virus, and possible chronic infection in immunocompromised persons.

The magnitude of these benefits and harms will depend on nOPV2 coverage and the extent of mixing between nOPV2 recipients, unvaccinated persons, and immunocompromised persons.

Dr. Kim Thompson and her colleagues at Kid Risk modelled the expected number of paralytic cases under different mixing scenarios for a cVDPV2 outbreak similar to the 2022 New York outbreak. They compared the number of cases expected with an IPV-only response to responses that used a Sabin OPV2 or an nOPV2. In their model, they assumed that the number of vaccine doses administered was the same as the number of IPV doses that were actually administered during the 2022 New York outbreak. They concluded that use of any type of OPV2 likely would have ended transmission slightly earlier than with IPV alone. However, less than 1 additional paralytic case was predicted in all IPV or OPV2 vaccine scenarios. They also ran a similar model for an aVDPV1 outbreak instead of aVDPV2 outbreak. Recall that Type 1 poliovirus infection is associated with a higher rate of paralytic disease than Type 2. The results of this model suggested that use of an OPV1 would likely end VDPV1 transmission faster and result in fewer paralytic cases than use of IPV alone.

When assessing how substantial the desirable anticipated effects of nOPV2 would be on both the individual and population levels, approximately half of the work group felt the desirable effects of using nOPV2 in addition to IPV were small. Some members felt that the desirable effects would be minimal, while some felt they would be moderate. When asked about the undesirable anticipated effects, the work group was evenly divided between minimal, small, and moderate. When asked whether the desirable effects of nOPV2 would outweigh the undesirable effects, half of the work group felt that the desirable effects would not outweigh the undesirable effects, and that the information favored the use of IPV only. However, about 1/3 of the group felt that it varies depending on the situation.

Moving to resource use and feasibility, nOPV2 is not yet approved for use in the US. If the US wanted to use nOPV2, the mechanism for doing so would be the Expanded Access Investigational New Drug Application (EA-IND), formally known as “Compassionate Use.” This requires application to the FDA and FDA authorization. If implemented, the nOPV2 EA-IND program must include signed informed consent by vaccinees and/or their guardians, an enhanced system for monitoring vaccine safety, enhanced surveillance for possible VAPP cases and environmental surveillance for new VDPVs, and a system for tracking and accounting for every dose for containment purposes. This includes every dose given, every dose wasted, and doses returned.

The work group had a variety of opinions on whether this would be a reasonable and efficient use of resources. Half of the work group responded that it was probably not a reasonable use of resources, but about 1/4 responded that it would vary depending on the specifics of the situation. The work group also was divided about whether an nOPV2 campaign would be feasible to implement. Half of the work group responded that it probably would be feasible, but about a third responded that it probably would not be feasible.

For values and acceptability considerations, tOPV was removed from the US vaccination schedule in 2000 and was replaced with IPV because any risk of VAPP was deemed unacceptable at that time. This removal might be a barrier to acceptance of a new OPV vaccine in the future. In addition, the need for a signed informed consent likely will be a deterrent, especially for those who are concerned about vaccine safety and new vaccines. It is unclear whether the general public will accept an OPV vaccine if they are already protected from paralytic infection by IPV. It is unclear whether the general public will accept a vaccine to reduce community transmission and risk to others if they would not benefit from it individually.

Similarly, it is unclear whether the populations most at risk (e.g., those with low childhood vaccination coverage and those with high rates of vaccine skepticism) would accept an OPV vaccine.

The work group noted that perceptions of risk and vaccine acceptance might shift in an outbreak setting, particularly if there is more than 1 paralytic case in a community. A clear majority of the work group agreed that the target population probably does not feel that the desirable effects of nOPV2 are large relative to the undesirable effects. However, they were divided about whether there was important uncertainty or variability in how much people would value the main outcomes. The work group was similarly divided about whether nOPV2 would be acceptable to key stakeholders. Some felt that it probably would not be acceptable to stakeholders, some felt that it probably would be, and some felt that it would vary.

In terms of equity considerations, there is only 1 manufacturer of nOPV2, BioFarma in Indonesia, which is managed via a global stockpile. Supply shortages have occurred in the past. In the US, IPV is readily available and provides protection against paralysis from cVDPV2. In many countries with cVDPV2 outbreaks, there is limited protection against cVDPV2, unless there are nOPV2 or Sabin OPV2 campaigns. In terms of equity within the US, the work group noted that preventing transmission of the outbreak virus does protect unvaccinated, under-vaccinated, immunocompromised persons. Again, there was a spread of opinions among the work group members. The plurality of the work group felt that using nOPV2 probably would not have a significant impact on health equity.

Putting it all together, most of the work group felt that the undesirable consequences of using nOPV2 during an outbreak in the US probably outweigh or are closely balanced with the desirable consequences.

In summary, the work group believes at this time that the undesirable consequences of using nOPV2 probably outweigh or are closely balanced with the desirable consequences. The main considerations for the work group's interpretation was that IPV is readily available in the US and protects against paralytic disease, and that the primary benefit of adding nOPV2 to an outbreak response would be to reduce transmission of outbreak virus and reduce risk of paralytic disease in under-vaccinated and immunocompromised persons. There were differences of opinion regarding the value of reducing asymptomatic transmission or ending asymptomatic transmission earlier during an outbreak. The work group was concerned about the extremely low but non-zero risk of VAPP or new cVDPV2. There was uncertainty about public and stakeholder acceptance of a nOPV2 vaccine. However, the work group did acknowledge that the balance of undesirable consequences compared to desirable consequences might shift in the future depending on size and scope of the outbreak. As modeling showed, the calculus might be different for a Type 1 outbreak where more paralytic cases would be expected, and public perception of risk might be higher.

Dr. Kidd then introduced the topic of fractional doses of IPV. Wild poliovirus Type 2 was eradicated in 2015, prompting a global switch in April 2016 during which all the Sabin Type 2 virus was withdrawn from routine immunization. Countries that were still using OPV as part of routine immunization replaced tOPV with bOPV that contains only Types 1 and 3. At the same time, it was recommended that countries that still used OPV include at least 1 dose of IPV as part of their routine immunization schedule. Subsequently, based on clinical trial data and limited IPV availability in some countries, WHO has supported the use of 2 fractional doses of IPV (1/5 full dose IPV) given intradermally in place of a single full dose.

Clinical trials have shown that 1 fractional dose of IPV (fIPV) is less immunogenic than 1 full dose of IPV; clinical trial data also have suggested that 2 fractional doses are more immunogenic than 1 full dose of IPV.

Currently, 6 countries representing about 20% of the global birth cohort use fIPV in their routine immunization schedules (Bangladesh, Cuba, Ecuador, India, Nepal, Sri Lanka). They all use 2 fractional doses in combination with at least 3 bOPV doses. One example would be India's polio vaccination schedule in which a child would receive 5 doses of bOPV and 2 doses of fIPV. The current US guidance recommends a total of either 3 or 4 doses of IPV, depending on the age of the last vaccination. When assessing vaccine records for vaccines administered outside the US, the guidance is that only tOPV doses or IPV doses are considered valid for the US vaccination schedule. If a child who was vaccinated under the India vaccination schedule immigrated to the US and wanted to attend school in the US, current guidance is that none of their bOPV or fIPV doses would be considered full doses. The child would need either 3 or 4 full IPV doses to be considered fully vaccinated against polio in the US.

Therefore, the question for the work group was, "Should 2 fIPV doses administered outside the US be counted as either 1 or 2 doses toward the US vaccination schedule?" A meta-analysis was conducted to update to the meta-analysis that was previously published in 2021.

Overall, 2 fractional doses were associated with higher rates of seroconversion compared to 1 full dose of IPV. Infants receiving 2 doses of fIPV were 1.5 times as likely to seroconvert compared to infants who received 1 full dose of IPV. Moving to comparisons between 2 fractional doses and 2 full doses, 2 fractional doses were associated with slightly lower rates of seroconversion than 2 full doses of IPV. This especially is the case when administered at younger ages. Peak antibody titers are also lower after 2 fractional doses compared to 2 full doses. Based on this information, the work group group agreed with the following proposed language to be included in CDC Clinical Considerations for persons receiving polio vaccines outside of the US:

- ❑ For persons who received fractional (1/5 full dose) IPV administered intradermally outside of the United States, 2 fractional doses of IPV (fIPV) should be considered valid and counted as 1 full intramuscular dose of IPV toward the US vaccination schedule.
- ❑ If a person received only 1 dose of fIPV, this dose should not be considered valid or counted toward the US vaccination schedule.

Following discussion, several ACIP members expressed that they thought it was reasonable to accept 2 fractionated doses as 1 IPV dose and agreed with the work group's recommendation.

PUBLIC COMMENTS

The floor was opened for public comment on February 28, 2024, at 1:40 PM EST. The comments made during the meeting are summarized in this document. Members of the public also were invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket Number ID CDC-2024-0001. Visit regulations.gov for access to read comments received.

Diana Olson
National Foundation for Infectious Diseases

Diana Olson from the National Foundation for Infectious Diseases thanked the committee for its work. She highlighted the public health and economic benefits of COVID-19 vaccines but pointed out that coverage with an updated 2023-2024 COVID-19 vaccine remains low. Immunization rates for other recommended vaccines also remained below public health goals. Only about half of US children and adults have received an influenza vaccine during the current season and only about 22% of eligible adults aged 60 years and older and about 16% of eligible pregnant women have received an RSV vaccine. Clearly, there is more work to be done to build vaccine confidence, address health disparities, and increase overall immunization rates. NFID supports implementation of a Vaccines For Adults program to build upon the Vaccines for Children and Bridge Access Program and further expand access to these lifesaving tools; continued support for US vaccine safety systems; and strong public health infrastructure to help ensure that ACIP, CDC, and state and local public health agencies have the resources to do their important work.

Mr. Robert Blancato
Executive Director
National Association of Nutrition and Aging Services Programs

Mr. Blancato spoke as Executive Director of the National Association of Nutrition and Aging Service Programs (NANASP) and on behalf of 18 other national aging and patient advocacy associations, calling on ACIP to reverse your June 20 recommendation requiring shared decision-making for the use of the new RSV vaccines for adults 60 and over. CDC has reported that only 21.9% of adults and reported receiving the RSV vaccine; Mr. Blancato stated that this low coverage was a consequence of ACIP's recommendation with shared clinical decision-making, which he stated was difficult for health care providers to implement. He stated that these organizations also oppose shared decision-making due to its negative impact on vulnerable adults who are part of already underserved communities. He stated support for co-administration of these vaccines and that he was encouraged by the morning's discussion on the recommendation for an additional COVID vaccine shot and the resulting amendment in favor of "should" instead of "may." If the goal is preventing serious health outcomes in older Americans from respiratory illness, clear, broad, and easy to communicate guidance should be the standard for adult vaccines.

Martha Nolan, JD
Senior Policy Advisor
HealthyWomen

Martha Nolan, Senior Policy Advisor for HealthyWomen, asked for clarification of recommendations in several areas. She expressed concern around how the seasonal recommendations for maternal RSV vaccine translate to reimbursement and coverage. Specifically, many are confused about whether there is cost-sharing on the part of the patient if they receive the vaccine after January 31, 2024, because the CDC guidance notes that in certain US jurisdictions where RSV seasonality differs, providers may consider RSV vaccination after January 31, but it is not clear if insurance will cover the cost. She asked that ACIP consider ways to ensure there are no coverage barriers for patients, particularly when considering future seasonal recommendations. Lack of coverage for a vaccine is a barrier that often leaves patients to forego that care option. She expressed discouragement over the low uptake of RSV and COVID vaccines in older adults during the '23-'24 respiratory season.

Despite there being many tools to protect ourselves against respiratory illnesses than ever before, there is also increasing confusion about who should receive what vaccine and when. She asked ACIP to evaluate existing guidance and provide necessary changes to ensure clarity around who should receive them and when and ensure coverage for all populations.

Hannah Berk
Unaffiliated Community Member

Hannah Burke asked the committee to support the proposed recommendation on a booster dose of the COVID-19 vaccine in this meeting and to develop action steps to go further after this meeting. She stated that people of all ages and health statuses need updated COVID vaccines covered by insurance and/or public funds at least every 6 months. Twice annual vaccination allows healthy people to safely share space with high-risk family and friends so long as they take precautions, which include vaccinating after immunity wanes significantly after 4 to 6 months and multiple COVID-19 infections compound systemic damage to the body that makes any person more vulnerable to illness and disability, even if they are otherwise healthy. She expressed her hope that the committee will approve the proposal to announce COVID vaccine recommendations on an earlier timeline this year, which can help ensure appropriate time to increase the accessibility of these vaccines. Ms. Burke shared that many of her friends and relatives have asked their doctors about booster availability and have been told they don't need the vaccine, and uninsured friends received their boosters months later than they could have because they hadn't heard about the Bridge Program. She expressed her support for a “should” recommendation on boosters for older adults and for an expedited vaccine decision-making timeline. She urged the committee to make updated vaccines accessible twice annually for people of all ages and at no cost and to recommend continued vaccination in the clearest, strongest terms.

Maria Shreve, RN
Parents, Nurses, Herself

Ms. Shreve is a Registered Nurse and said that her family is so grateful to have access to children's COVID vaccines and now the new RSV vaccine, but it wasn't easy. She asked the committee to make children's vaccines available before school starts this year, which would help decrease transmission and infection. She said that children's uptake would be higher if supply was available and urged support for more accessible locations for kids of all ages, and mass vaccination clinics where parents can take kids of all ages for vaccines together instead of taking one to a pharmacy, one to the pediatrician, and one to the Minute Clinic. She said a better plan is quickly needed for the development and implementation of more RSV and COVID treatments. Unvaccinated children's hospitalization rates last year with COVID were as high as the elderly, which could have been prevented by increased access to vaccines. She also expressed support for options that allow access to vaccines every 6 months instead of yearly.

AGENCY UPDATES

Centers for Disease Control and Prevention

Dr. Demetre Daskalakis highlighted CDC's work during the winter respiratory season. Influenza, COVID-19, and RSV are still elevated in some parts of the country. As of February 10th, 22% of adults ≥18 years of age and 12% of children 6 months to 17 years of age have received COVID-19 vaccination. Pharmacies have administered over 750,000 doses of COVID-19 vaccines and over half a million doses were ordered by public health providers through the Bridge Access Program. In the US, influenza vaccine coverage rates have decreased; about 6.5 million doses of influenza vaccine have not been given this season compared to last.

The ACIP was a very important part of RSV vaccine launches for pregnant people and immunization launches for newborns. Despite an initial supply and demand mismatch with nirsevimab, 30% of infants <8 months of age received nirsevimab and about 16% of eligible pregnant persons received an RSV vaccine between 32 and 36 weeks gestation. In the context of new vaccine products, this is remarkable uptake.

As of February 22, 2024, a total of 35 cases of measles have been reported this year in 15 jurisdictions compared to 58 cases of measles last year in 20 jurisdictions in the US. This is not a good slope of the curve, particularly given that measles is preventable with safe and effective vaccines. As measles continues to increase in other parts of the world, importations continue to happen. When importations occur in places where coverage is low, there is risk for ongoing larger outbreaks.

Centers for Medicare and Medicaid Services

Mary Beth Hance began by announcing the passing earlier in the month of Dr. Jeffrey Kelman following an illness. Dr. Kelman was a Centers for Medicare and Medicaid Services (CMS) colleague who was the Chief Medical Officer for CMS's Center for Medicare. He was involved with the ACIP for many years, representing CMS on many work groups. Dr. Kelman was a pulmonologist by training, which fit perfectly into much of the work he did supporting CMS on the influenza, pneumococcal, COVID, and many other ACIP work groups. He also worked closely with FDA on using data and was absolutely committed to the idea that valuable data within agencies could be used across agencies. Dr. Wharton and other colleagues in attendance mourned the loss of Dr. Kelman and acknowledged his many important contributions.

In terms of updates, on February 12, 2024, CMS issued an updated Medicaid and CHIP vaccine toolkit that reflects the change in commercialization of COVID vaccines and the Inflation Reduction Act provisions that impacted mandatory coverage of vaccines for adults in Medicaid.

Food and Drug Administration

Dr. David Kaslow reported that since the last FDA agency report during the October 2023 ACIP meeting and apropos of discussions earlier in the day on chikungunya, FDA approved IXCHIQ®, a vaccine indicated for the prevention of disease caused by chikungunya virus in individuals ≥18 years of age who are at increased risk of exposure to chikungunya virus (CHIKV). This indication was approved under accelerated approval based on anti-CHIKV neutralizing antibody titers.

Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory studies. The highlights of the US prescribing information include warnings and precautions that IXCHIQ® may cause severe or prolonged chikungunya-like adverse reactions. Other regulatory actions include scores of supplemental Biological License Applications (sBLAs), some pertaining to manufacturing changes and some regarding labeling changes.

Given the ACIP agenda for the next day, Dr. Kaslow highlighted the work FDA continues to do to monitor the safety and effectiveness of vaccines for respiratory illnesses using the Biologics Effectiveness and Safety System (BEST) and the CMS System. Ongoing projects include safety and effectiveness of RSV vaccines, influenza vaccines, and COVID-19 2023-2024 formula vaccines. Although the Vaccines and Related Biological Product Advisory Committee (VRBPAC) has not met since the October 2023 ACIP meeting, FDA anticipates convening VRBPAC twice before the June 2024 ACIP meeting. The VRBPAC is scheduled to meet on March 5, 2024, in open session to discuss and make recommendations on the selection of strains to be included in the influenza vaccine for the 2024-2025 influenza season. As mentioned earlier in the day, VRBPAC is scheduled to meet in open session on May 16, 2024, to discuss and make recommendations on the selection of strains to be included in the 2024-2025 formula for COVID-19 vaccines. Other convenings of VRBPAC may occur as needed. As in the past, Dr. Kaslow took the opportunity to personally thank the review teams, their supervisors, and management at Center for Biologics Evaluation and Research (CBER) who worked and continue diligently to conduct research and review to protect and enhance public health. In addition, he thanked CDC staff for their many contributions and their collegial support of collective efforts to protect and enhance public health for immunization.

Health Resources and Services Administration

CDR Reed Grimes, MD, MPH provided the Health Resources and Services Administration (HRSA) update the National Vaccine Injury Compensation Program (VICP) continues to actively process claims. In Fiscal Year 2024, as of January 1, petitioners have filed 314 VICP claims. Over $41 million was awarded to petitioners and over $13 million was awarded to pay attorney's fees and costs. In addition, the VICP had approximately 600 claims alleging vaccine injury awaiting activation for review. Previously, there was nearly a 12-month wait period between when a petition was found to have adequate medical records to review by a HRSA provider and when a review was completed. As of January 1, 2024, the wait period has been reduced to less than 1 month. More data about the VICP can be found on its website at www.hrsa.gov/vaccine-compensation/data/index.html.

In the decade prior to COVID-19, fewer than 500 claims had been filed with the Countermeasures Injury Compensation Program (CICP). CICP received a direct appropriation for the first time in Fiscal Year 2022, and the program has used those funds to increase its capacity to conduct medical reviews by hiring and training new review staff and contractors as well as to pay compensable claims and improve IT and other communications with requesters. As of January 1, 2024, 12,854 claims alleging injuries or death from COVID-19 countermeasures had been filed with the CICP, including 9,682 claims alleging injuries or death from COVID-19 vaccine. CICP has rendered decisions on 2,214 COVID-19 claims as of January 1, 2024, representing more than 4 times in the prior decade. More information about the CICP can be found at its website at www.hrsa.gov/cicp.

Indian Health Services

Matthew Clark, MD, FAAP, FACP reported that the Indian Health Service (HIS) continues to prioritize vaccination as its principal clinical and public health prevention priority. As part of the IHS National E3 Vaccine Strategy, the IHS seeks to ensure that every patient at every encounter is offered every recommended vaccine when appropriate. Following announcement of this IHS strategic initiative in November 2022, the IHS established the E3 Vaccine Champions Pilot Program in March 2023. Since then, the IHS has designated 28 vaccine champions pilot sites in 9 of the 12 IHS areas, including federal, tribal, and urban programs. IHS has shared clinical and community resources and multidisciplinary best practices to cross-pollinate the IHS system of care and to improve vaccine coverage rates in tribal communities. As part of a proactive strategy of outreach, education, and engagement with its partners in tribal communities, the IHS 2023-2024 Respiratory Viral Vaccine Campaign has worked to ensure timely access to immunizations for COVID, seasonal influenza, and RSV among its vulnerable service population across the age spectrum.

Following reported supply chain constraints in the fall, IHS worked diligently to secure a supplemental supply of the long-acting monoclonal antibody, nirsevimab, to ensure that this life-saving immunization was available in support of ACIP recommendations for administration of nirsevimab to AI/AN infants and children up to 19 months of age. To date, nearly 8,000 supplemental doses of nirsevimab have been distributed and administered to mitigate the risk of serious RSV disease among infants and children in Indian Country. Due to persistently elevated rates of respiratory viral illness in Indian Country, in collaboration with IHS obstetric and pediatric subject matter experts (SMEs), last month the IHS Chief Medical Officer, Dr. Loretta Christensen announced extension of the period for administration of maternal RSV vaccine to eligible pregnant AI/AN persons through the end of February for this season in seeking to mitigate the risks of RSV in IHS's high-risk service population. Preliminary surveillance suggests favorable uptake of novel RSV countermeasures in Indian Country. This is especially true in regions historically most impacted by high rates of RSV-related morbidity and mortality, such as the YK Delta Region in Alaska, where proactive efforts by tribal partners included bush plane flights to over 25 villages to administer nirsevimab to eligible infants and children, many of whom also received other ACIP recommended vaccines. Moving forward in collaboration with its partners in tribal communities, IHS will continue to promote access, quality, value, and equity related to immunizations in Indian Country.

National Institutes of Health

Dr. John Beigel provided several updates from the National Institute of Health (NIH) on vaccine-related research of interest to the ACIP. Regarding NIH leadership, In November 2023, Dr. Monica Bertagnolli started as the 17th Director of the NIH. She is the first surgeon and second woman to hold the position. Nominated by President Biden, she was confirmed on a bipartisan basis in the US Senate and transitioned from her role as Director of the National Cancer Institute (NCI), a position she held since October 2022.

For COVID-19, Dr. Beigel highlighted 2 studies about the value of maternal vaccine. First was a study that demonstrated maternal vaccination may prevent infant COVID-19 in a cohort. Study researchers aimed to quantify protection against infection from maternally-derived vaccine antibodies in the first 6 months of an infant's life. Higher transplacental binding and neutralizing antibodies substantially reduced the COVID-19 infection in the infants. Until infants are age-eligible for vaccination, maternal vaccination provides passive protection against symptomatic infection during early infancy.

These same findings extend to preterm infants. In a separate study, it was shown that preterm infants born to people who are vaccinated for COVID-19 have roughly the same antibody titers as those of term infants. Moreover, in all infants, antibodies to the spike protein were higher among those born to individuals who received 3 or more vaccines before delivery compared to those who only had 2. These findings may help allay concerns that fewer antibodies might pass from preterm infants compared to term infants.

In a study regarding the ancillary benefits of COVID-19 vaccines versus a prospective cohort study of adults, researchers identified SARS-CoV-2 infections and followed them for the presence of post-acute sequelae. COVID vaccination not only prevented disease, but also was associated with lower prevalence and severity of long COVID symptoms. There also was an interesting study about looking at the spike in preterm birth rates that started at the beginning of the pandemic. That analysis showed that by late 2022, widespread COVID-19 vaccination in pregnant people likely halted the spike in preterm infants, and those rates have come down toward normal. This underscores the need for pregnant people to keep current on COVID-19 vaccination.

In October 2023, the Nobel Prize for Physiology or Medicine was awarded to Drew Weissman, MD, PhD and Katalin Karikó, PhD for their work on messenger ribonucleic acid (mRNA) that enabled the development of mRNA vaccines. Dr. Weissman and Dr. Karikó had decades long work on mRNA with incremental steps in the science. Ultimately, those steps and those scientific advancements were critical to enable the unprecedented development of the mRNA vaccines that stemmed the pandemic.

For influenza, Dr. Beigel highlighted a study that evaluated 2 doses of high-dose trivalent influenza vaccine (HD-TIV) compared to standard dose quadrivalent influenza vaccine in a pediatric hematopoietic stem cell transplantation (HSCT) population. The high-dose vaccine resulted in higher antibody responses, especially for influenza A. Because influenza causes substantial morbidity and mortality in that population, optimization of vaccine strategies is critical. The use of high-dose inactivated vaccines may be a practical strategy to overcome the poor immunogenicity in that population.

Office of Infectious Disease and HIV/AIDS Policy

CDR Valerie Marshall reported that the Interagency Vaccine Working Group (IVWG) of the HHS is scheduled to convene in March 2024 to deliberate on an interagency progress report which addresses the achievements and strides made from 2021 to 2023 toward achieving the goals outlined in the Vaccines National Strategic Plan (VNST). This collaborative effort underscores the commitment of multiple federal agencies toward transparent communication and the pursuit of vaccination goals. The National Vaccine Advisory Committee (NVAC) held a meeting on February 22-23, 2024, to discuss critical policy matters related to vaccination. The committee's deliberations included a discussion on the resurgence of measles cases, which underscored the pressing need for proactive public health measures to improve vaccine confidence and counter misinformation about vaccines.

With no additional business posed for the day, the ACIP meeting stood in recess until 8:00 AM on February 29, 2024.

THURSDAY: FEBRUARY 29, 2024

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Melinda Wharton (ACIP Executive Secretary & Acting Chair, CDC) called to order and presided over the February 28-29, 2024 ACIP meeting because the process for the new ACIP Chair to join the committee had not yet been completed. As allowed under the ACIP charter, the ACIP's six *Ex Officio* members were temporarily designated as voting members. She then conducted a roll call, which established that a quorum was present. A list of Members, *Ex Officios*, and Liaison Representatives is included in the appendixes at the end of this summary document. No COIs were identified for the second day of this meeting.

RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES ADULTS

Dr. Camille Kotton, Chair, ACIP Adult RSV Work Group, introduced the RSV session, reminding everyone that in June 2023 ACIP recommended that adults ≥60 years of age may receive RSV vaccination using shared clinical decision-making. There are currently 2 licensed and recommended products for adults ≥60 years of age:

- ❑ GSK RSV vaccine (AREXVY), which is a 1-dose adjuvanted (AS01E) recombinant prefusion F (preF) protein vaccine.
- ❑ Pfizer RSV vaccine (ABRYSVO®), which is a 1-dose recombinant preF vaccine.

In October, GSK presented data to the ACIP demonstrating that the humoral immune response to a single dose of GSK RSV vaccine in adults 50–59 years of age was non-inferior to that in adults >60 years of age. The ACIP Adult RSV Work Group shared their early interpretations of this data and the potential role of RSV vaccination in adults younger than 60 years of age, including subpopulations who would benefit most from vaccine and equity implications. At that time, ACIP members expressed the importance of reviewing safety surveillance data to inform future preferred policy recommendations.

The work group has been simultaneously reviewing additional data to prepare for the upcoming policy decisions, especially focusing on the risk of severe RSV disease in adults 50–59 years of age, especially those with chronic medical conditions; RSV vaccine uptake among different demographic groups; and potential policy options that would transition away from shared clinical decision-making. The work group also has begun reviewing data from Moderna on their investigational RSV vaccine (mRNA-1345) in adults ≥60 years of age.

Dr. Rituparna Das (Moderna) presented clinical data on Moderna's investigational RSV candidate vaccine, mRNA-1345, among adults ≥60 years of age. The data package on adults ≥60 years of age was submitted to the FDA for review in September 2023. The investigational RSV vaccine, mRNA-1345, is a lipid encapsulated mRNA-based vaccine that encodes the RSV fusion (F) glycoprotein stabilized in the prefusion conformation. The prefusion F protein contains epitopes that elicit antibodies that are potently neutralizing and cross-reactive between RSV-A and RSV-B. Following administration of a single 50 microgram (µg) dose, robust immunogenicity was observed in Phase 1 that was persistent through 12 months post-vaccination.

The pivotal Phase 2/3 safety and efficacy trial, Study 301, enrolled adults ≥60 years of age. Participants were randomized 1:1 to receive mRNA-1345 or saline placebo and 24 months of planned follow-up. Randomization was stratified by age (60─74 years and ≥75 years) and presence or absence of congestive heart failure (CHF) or COPD. The study started in November 2021 and weekly surveillance was conducted via electronic diary to look for RSV symptoms. Given the importance of risk factors on morbidity and mortality with RSV in older adults, participants also were included with a number of high-risk medical conditions. Frailty status was assessed of all participants at entry using the Edmonton Frail Scale (EFS). Participants were characterized on a 0- to 17-point scale as being fit (0-3), vulnerable (4-5), or frail (6-17).

A total of 36,550 participants were enrolled as of the April 30, 2023 data cutoff, approximately 50% of whom came from the US. Vaccinations in Study 301 began in late November 2021 and continued through December 2022. The primary analysis was driven by the accumulation of a target number of cases, and study success was declared at that time. The study continued in a blinded fashion. When nearly all study participants reached 6 months of follow-up, an additional analysis was conducted as agreed with the FDA. The median follow-up for this additional analysis was almost 9 months, with a range up to 17.7 months.

The demographics of Study 301 were well-matched between the vaccine and placebo recipients. The median age was 67 years, 30% of the study participants were 70─79 years of age, just under 3,000 participants were ≥80 years of age, 12% were Black or African American, and 33% identified as Hispanic or Latino. Race/ethnicity in the study was representative of the US population. Approximately 2,600 participants had CHF or COPD, almost 1/3 of trial participants had 1 or more of the comorbidities that put them at higher risk for RSV-related morbidity or mortality, 16% percent of the population was considered vulnerable, and 6% were considered to be frail.

The median safety follow-up was 8.6 months and almost all participants had been followed for more than 6 months. In general, mRNA-1345 was well-tolerated. Injection site pain was the most common local reaction, followed by axillary swelling or tenderness. Most events were mild, with onset within 1 to 2 days post-injection and lasting 1 to 2 days. Solicited systemic reactions of fatigue, myalgia, and headache were the most common. Fever was rare and most reactions were mild, with onset within 1 to 2 days post-injection and lasting 1 to 2 days. Severe events also were rare. Unsolicited events were well-balanced overall between vaccine and placebo recipients. The occurrence of SAEs, AEs leading to discontinuation, and AESIs also were balanced between vaccine and placebo recipients. There was 1 event in the vaccine group, which was aspiration following intoxication. There were 6 fatal events in the placebo group.

There were no cases of Guillain-Barré syndrome (GBS) or acute disseminated encephalomyelitis (ADEM). There was no imbalance in neurological disorders such as Bell's palsy or facial paralysis. For cardiac events, there was no imbalance in cardiac arrhythmias, including atrial fibrillation. No myocarditis was identified in vaccine recipients and there were no cases of pericarditis with onset within 6 weeks of vaccination.

Co-primary endpoints were protection against RSV-lower respiratory tract disease (RSV-LRTD) with ≥2 or ≥3 signs and symptoms. Protection against RSV-associated acute respiratory disease (ARD) and RSV-related hospitalizations were key secondary endpoints. RSV-LRTD was defined as new or worsening of ≥2 or ≥3 of signs/symptoms for ≥24 hours and RSV-ARD was defined as new or worsening of ≥1 signs/symptoms for ≥24 hours. Identification of a symptom prompted a visit to the site and a nasopharyngeal swab.

All cases had to be confirmed for RSV by reverse transcription polymerase chain reaction (RT-PCR). Continuous year-round weekly surveillance was conducted throughout the study.

The target number of cases for the first analysis was met in November 2022 which became the primary analysis. Follow-up was a median of 3.7 months, with a range from 0.5 to 12.6 months. The efficacy against RSV-LRTD with ≥2 symptoms was 83.7% (66.0%, 92.2%) and efficacy against RSV-LRTD with ≥3 symptoms was 82.4% (34.8%, 95.3%). Efficacy against RSV-ARD, the secondary objective, was 68.4% (50.9%, 79.7%). The observed RSV cases were subtyped for RSV-A and RSV-B, with efficacy observed for both RSV-A and RSV-B.

Efficacy was maintained in older ages and was similar for those with or without co-morbidities and in those who were considered vulnerable or frail. There were no hospitalizations in the primary analysis. For LRTD with shortness of breath as a marker of severity, efficacy was 86.7%. For RSV cases that were medically attended in the emergency department or urgent care, there were 5 cases in placebo recipients and no cases among vaccine recipients.

An additional analysis of efficacy was conducted at the end of April 2023; the median follow-up was 8.6 months, with the upper bound of the range being 17.7 months. The efficacy of mRNA-1345 against RSV-associated LRTD and ARD remained high, with overlapping confidence intervals to the primary analysis estimates over this longer follow-up time. VE against LRTD with ≥2 symptoms and ≥3 symptoms was 63% (48.7%, 73.7%) and for ARD was 54% (40.5%, 64.3%). Protection was seen for both RSV-A and RSV-B.

Efficacy was consistent for adults 60─69 years of age and 70─79 years of age. Among adults ≥80 and older, there were only 11 cases of LRTD with ≥2 symptoms, precluding the conclusions. The group of adults ≥80 years of age had the lowest incidence of RSV in the placebo recipients compared to adults 60─69 years of age and 70─79 years of age, perhaps as a carryover of pandemic measures in these trial participants. Efficacy in participants with co-morbidities and participants who were vulnerable or frail also were very consistent in this analysis. Assessing the impact of mRNA-1345 on preventing severe RSV as indicated by the shortness of breath measure, efficacy was 74.6% (50.7%, 86.9%). More participants in the placebo groups sought a higher level of care in an ED or UC, with efficacy of 61.8% (-7.35, 86.45). A total of 2 participants were hospitalized, a 73-year-old and an 84-year-old, both of whom had asthma and were from the placebo group. There were no hospitalizations in the vaccine group.

The vaccine was immunogenic, resulting in an 8-fold rise in the RSV-A neutralizing titers and a 5-fold rise in the RSV-B neutralizing titers. Responses were consistent across the age spectrum and there was no evidence of decreasing response as age increased. Cellular immune responses were evaluated for CD4 and CD8 in a separate study of adults 50─75 years of age. The vaccine was found to elicit strong and persistent T-cell responses as well. In the Phase 1 study, antibody remained detectable at 12 months, with GMTs 2- to 3-fold over baseline for both RSV-A and RSV-B. In that study, re-vaccination at 12 months was evaluated. Administration of a second dose of mRNA-1345 increased both RSV-A and RSV-B neutralizing titers 5- to 7-fold. The question of re-vaccination is important since protection from RSV by natural infection is not lifelong, but additional durability data will be needed to determine the timing. Moderna is studying re-vaccination at 1 and 2 years in Phase 3 studies.

Co-administration was explored with standard-dose quadrivalent influenza vacCcine (Afluria) and the Moderna bivalent COVID-19 vaccine in adults ≥50. Concomitant administration of the RSV and influenza vaccines was immunogenic for RSV-A, RSV-B, and all 4 influenza types and was well-tolerated in terms of local and systemic reactions. The same trend was observed with concomitant administration of mRNA-1345 and COVID-19 vaccine.

To summarize, the mRNA-1345 vaccine was well-tolerated in over 19,000 adults ≥60 years of age. No cases of GBS, ADEM, or other safety concerns were identified. The vaccine was shown to be efficacious, met all pre-specified criteria for licensure, and continued to be efficacious through a median of 8.6 months with a range up to 17.7 months. The vaccine prevented severe RSV disease as evaluated by the prevention of shortness of breath and medically-attended AEs. Strong antibody and cellular immune responses were seen through 12 months, and boosting was evident at 1 year. The antibody responses were similar across age groups, including those ≥80 years of age. Pre-specified immunogenic criteria were met, and no new safety signals were seen with concomitant administration.

Dr. Daley observed that VE was lower in the later data than the earlier data and asked Dr. Das to expand on how the results were interpreted for the durability of a single dose.

Dr. Das indicated that durability of a single dose was assessed in several ways. The confidence intervals at both time points overlapped. A detailed time-to-event (TTE) analysis was performed, which was reassuring in that the cases that were occurring in the longer follow-up were not in people who were vaccinated earlier. Efficacy also was consistent in a before 6 months and after 6 months analysis. Perhaps there is some waning, but there also is an effect from underlying force of infection. Immune responses lasting out to 12 months are also reassuring.

Dr. Long said that regarding the immunogenicity of the second dose at 1 year, “boost” is a word that could be used. “Reinforcing might be another word. However, no data were shown to suggest that there was an anamnestic response. Since the GMTs after the second dose did not quite equal the titers after an initial dose in the mRNA vaccines against COVID and influenza, she wondered whether a similar lack of robustness was observed after a second dose or if this specific to RSV and if there were any ideas about why this is different.

Dr. Das responded that for RSV, there is still a highly seropositive population. While a good response was observed in these small studies, both 1 and 2 years are being examined to determine whether there is any benefit to a 2-year gap. In terms of COVID-19 vaccines, the boosts have gone higher than the initial vaccination, but the immunologic experience with COVID at the point that those studies were conducted was quite different and it may not be completely fair to put those vaccines side-by-side. To reiterate, persistent immune responses are observed through 12 months. While boosting is observed with a second dose, it does not recapitulate the original dose, but it is quite close. Again, Moderna will be bringing the larger studies forward for both 1-year and 2-year revaccination later in 2024.

Dr. Beigel (NIH) asked whether Moderna had thought about or started work on correlates of protection to help understand what titers are actually needed.

Dr. Das responded that Moderna is very well-positioned to perform a correlates of protection analysis since samples were collected from every person in this study at baseline and Day 29. Initial analyses have been performed of the correlates, which show that RSV neutralizing titers are very well-correlated with protection. These data are being investigated in more detail to look for whether a threshold can be determined.

Rebecca C. Woodruff, PhD, MPH (CDC/NCCDPHP) presented preliminary results exploring chronic conditions as risk factors for RSV-associated hospitalizations. Using methods developed for a previous study, 3 data sources were leveraged to calculate RSV hospitalization rates during the 2017-2018 RSV season stratified by chronic condition and age group. The data source for the numerator was RSV-NET and the data sources for the denominator were the BRFSS and Census county-level population estimates.

RSV-NET is a population-based hospitalization surveillance platform. Currently, RSV-NET conducts active population-based surveillance of laboratory-confirmed RSV-associated hospitalizations for more than 300 acute care hospitals in 58 counties across 12 states (Oregon, California, Utah, Colorado, New Mexico, Minnesota, Michigan, New York, Connecticut, Maryland, Tennessee, Georgia). This area includes about 8.6% of the US population. In the 2017-2018 surveillance season, the catchment area was slightly smaller. It included about 38 counties across 8 states. Hospitalizations reported to RSV-NET include all of those where a positive RSV test was reported within 14 days prior to or during hospitalization. Testing for RSV is driven by clinical judgment and facility policies.

The BRFSS is an annual CDC-funded telephone-based health survey that operates in 50 US states, DC, and 3 US territories. BRFSS uses both landlines and cell phone numbers for sampling and collects about 400,000 interviews of adults each year. The questionnaire assesses a variety of health-related characteristics, including self-reported history of select chronic conditions. The BRFSS sample is designed to represent the civilian community-dwelling adult population ≥18 years of age in each jurisdiction. Adults who are not community-dwelling, including those living in nursing homes or other LTCFs, are not eligible to participate.

The study evaluated 9 chronic medical conditions as potential risk factors for RSV-associated hospitalization, including asthma; chronic kidney disease (CKD); chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), current smoking, diabetes mellitus, obesity (body mass index 30-39 kg/m^2), severe obesity (body mass index ≥40 kg/m^2), and stroke. This list was determined based on chronic conditions that were abstracted by RSV-NET and included in the BRFSS questionnaire.

RSV hospitalization rates were calculated using RSV-NET data to obtain counts of RSV hospitalizations among community-dwelling adults ≥50 years of age with and without chronic medical conditions of interest. These counts served as the numerator data in the rate calculation. To align with the BRFSS data, RSV-NET cases were excluded among adults living in nursing homes or other LTCFs. Next, a combination of BRFSS and the Census data were used to obtain estimated counts of community-dwelling adults ≥50 years of age with and without chronic medical conditions for the 38-county RSV-NET catchment area, which served as the denominator data for the rates. These data were used to calculate RSV hospitalization rates per 100,000 population among adults with and without each chronic medical condition, which was summarized by 3 age groups: 50─64 years of age, 65─74 years of age, and ≥75 years of age. Finally, rates were multiplied by burden multipliers to account for the under-detection of RSV among hospitalized adults and sensitivity of diagnostic tests. To calculate the rate ratios, the RSV-associated hospitalization rates in adults were divided with versus without chronic medical condition overall and within each age group. Monte Carlo simulation and generalized Poisson models were used to estimate rate ratios and 95% Monte Carlo intervals after adjusting for sex and race or ethnicity group.

For adults 50–64 years of age, the RSV hospitalization rate was about 7.9 times higher for adults with versus without CKD, 5.8 times higher for adults with COPD, about 4 times higher for adults with severe obesity or CAD, and about 2 to 3 times higher for adults with asthma, diabetes, and current smokers. The RSV hospitalization rates were similar for adults regardless of obesity or history of stroke. To put these rates into the context, adults ≥75 years of age have substantially higher hospitalization rates compared with adults 50–60 years of age.

For adults 65–74 years of age, the rates were higher across the board than for adults 50–64 years. There also was a generally similar pattern with RSV hospitalization rates at about 6 times higher for adults with CKD, 4.5 times higher for adults with severe obesity, 4.2 times higher for adults with COPD, and 2 to 3 times higher for adults with asthma, current smokers, CAD, or diabetes. For context, the RSV hospitalization rate was about 6.1 times higher for adults ≥75 years of age with versus without CKD, 4.2 times higher for adults with COPD, and about 2 to 3 times higher for adults with severe obesity, asthma, or CAD.

RSV hospitalization rates were lowest among adults in the youngest age group of 50–64 years of age and were highest among adults in the oldest age group of ≥75 years of age. Although the absolute rates clearly increased with age group, the adjusted rate ratios did not. Among adults ≥50 years of age, RSV hospitalization rates were about 6.5 times higher for adults with CKD, about 4.6 times higher for adults with COPD, around 3 times higher for adults with asthma or severe obesity, and about 2 times higher for adults with CAD, diabetes, and current smokers. The adjusted rate ratio for stroke and obesity were not statistically significant.

Adults with 2 or more chronic conditions had the highest RSV hospitalization rates compared to those with no chronic conditions. The adjusted rate ratios comparing the RSV hospitalization rate among those with 2 or more conditions to those with no conditions ranged from about 6.4 to 12.4 depending on the age group. The adjusted rate ratios comparing RSV hospitalization rate among those with 1 condition to those with no conditions ranged from about 2.6 to 2.9 depending on the age group.

Based on these preliminary results, the conclusion was that select chronic medical conditions were associated with greater rates of RSV-associated hospitalization among community-dwelling adults ≥50 years of age and varied by condition and age group. This information could help identify populations that might benefit most from RSV vaccines available to adults.

Dr. Carla Black (CDC/NCIRD) presented data on implementation of older adult RSV vaccines during the 2023-2024 season. Based on information from immunization information systems (IISs) submitted by jurisdictions to CDC through December 2023, coverage among adults ≥60 years of age who had received ≥1 dose RSV vaccine varied by state and ranged from about 5% to about 18% among the 37 states reporting at that time. Data are not available from all states, so these data are likely incomplete and probably are an underestimation of coverage.

According to the National Immunization Survey, as of February 3, 2024, coverage among adults ≥60 years of age was about 22.4%. Notably, the number who said they probably would get vaccinated or were unsure has remained consistent over time. Looking at coverage by demographics based on monthly data using a Kaplan-Meier estimation procedure using all data collected since September and including coverage as of the end of December 2023, coverage was slightly lower. By age group, coverage was lowest in adults 60–64 years of age and highest in all age groups ≥65 years of age. Coverage was highest among White adults at 22.5%. Asian adults had similar coverage to White adults at 16.7%, but every other racial ethnic group had lower coverage compared to White adults.

For example, Black adults had about 10 percentage points lower coverage at 12.9%. Some groups like NH/OPI had quite low coverage, which was 3.2%.

Adults ≥60 years with 1 or more chronic conditions had significantly higher RSV vaccination coverage of about 25% than those with no chronic conditions at about 18%. Each individual chronic condition was elevated compared to people with no conditions, with the exception of people with neurological conditions who had lower coverage compared to people with no conditions. Coverage decreased as the Social Vulnerability Index (SVI) of the county of residence increased. Coverage was higher among people who received an influenza vaccine for the season or an updated COVID vaccine. Among people who received an influenza vaccine, RSV coverage was about 30.5% and among those who had an updated COVID vaccine, RSV coverage was 38.5%. Coverage also varied by region. Coverage was lower among people residing in rural areas compared to those in urban and suburban areas. Coverage increased with increasing income and with increasing education.

Regarding co-administration among adults ≥60 years of age, among those who received an RSV vaccine, 57.1% received RSV alone, about 20% received RSV and influenza together, about 15% received 3 vaccines together (RSV, Influenza, COVID), and 8.5% received RSV and COVID vaccines together. The most recent data show that 84.4% of people were vaccinated in a pharmacy compared to about 14% who were vaccinated in medical settings (e.g., physician offices, hospitals, health departments, mass vaccination sites, and other medical settings).

IQVIA data are based on medical claims from pharmacies and physicians practicing in medical offices. IQVIA uses a sample of claims from medical offices to project vaccinations given in all medical offices in the US, which is based on a fairly small number of physicians. There is a lag with the medical office data, which do not completely mature until about 2 months. The national retail pharmacy data are a projection based on a much larger percentage of all pharmacies in the US. Claims from pharmacies come in much faster, so there is higher confidence in the completeness of the pharmacy data. None of the IQVIA data include vaccinations given in other medical settings such as public health clinics and hospitals, nor do they include vaccinations given in non-medical settings. Therefore, it is known that this is not a complete assessment of all RSV vaccines given in all settings in the US.

In terms of cumulative projected vaccines given to date in pharmacies and physician offices, a combined total of 9.65 million RSV vaccinations were administered in retail pharmacies (9.36 million) and physician medical offices (291,599) as of February 3, 2024. An additional 164,254 RSV vaccinations were administered in long-term care pharmacies. Each week, the majority of vaccines were the GSK product at about 69% compared to 31% of the Pfizer product. In pharmacies, vaccinations peaked in about late October to early November and have been declining since. Co-administration data from IQVIA showed similar patterns as in the NIS data among all people who received RSV vaccine and other vaccines that were given on the same day. About 52% received RSV only, about 22% received RSV and influenza vaccine, about 12% received RSV and COVID vaccine, and approximately 13.5% received RSV, influenza, and COVID vaccines together.
Using data from both NIS and IQVIA, the estimated range of persons vaccinated was approximately 11–18 million and estimated percent of persons vaccinated was 14%–22%.

Transitioning to RSV vaccination attitudes, data for this analysis were collected through the IPSOS KnowledgePanel and NORC AmeriSpeak Omnibus Surveys, which use probability-based panels to survey a nationally representative sample of US adults ≥18 years of age. CDC fields questions about vaccination status, intent, knowledge, attitudes, beliefs, and behaviors on each survey for 2 waves each month, for a combined sample size of approximately 4,000 respondents. Data were weighted to represent the non-institutionalized US population and mitigate possible non-response bias. All responses were self-reported. Among respondents who reported that they received or definitely would get the vaccine, 84% reported no concerns or issues. The top 3 reasons cited by those who expressed concerns were side effects (4.6%), not having enough knowledge about RSV or the vaccine (2.6%), and not having time (2.5%). Among those who said they probably would get the vaccine or were unsure, about 35% reported no concerns or issues. In this group, the top concerns cited were no HCP recommendation (25.8%), do not know enough about RSV or the vaccine (23%), and the vaccine is too new (11.8%). Of respondents who said they probably or definitely would not get the vaccine, about 26% reported that they had no concerns or issues. The top 3 concerns cited among those who had concerns were not trusting the government or pharma (28.2%), not knowing enough about RSV or the vaccine (23%), and the vaccine is too new (21.2%). The most common concerns reported the previous day for COVID vaccines pertained to safety and side effects, while for RSV vaccine it was more about lack of information and lack of provider recommendation.

Regarding implementation considerations, there are a number of potential factors contributing to relatively low vaccination coverage among people ≥60 years of age. As with any new vaccine, it takes time to integrate into systems, gain wide access, increase awareness among HCP, and normalize among the population. The 22% coverage seen for RSV vaccine is not out of line with what has been observed with other new vaccines within the first year of introduction. Because RSV is recommended based on shared clinical decision-making and the denominator for all of these calculations was the population ≥60 years of age, not everybody ≥60 years of age is actually expected to be vaccinated because it is not a universal recommendation. There are several other issues with a shared clinical decision-making recommendation. There is feedback from HCP that that having these conversations is not simple in practice, and they are confusing for providers and patients compared with routine universal recommendations. Also, vaccines are often administered by nurses, medical assistants, and pharmacists who are not always comfortable with a shared clinical decision-making conversation or who do not feel like it is within their scope of practice. In addition, these provider types often give vaccines under standing orders, which are difficult with shared clinical decision-making and may not be allowed in some states. People who do not have access to healthcare might not have a primary provider with whom they can have a shared clinical decision-making discussion. RSV vaccine is billed under Medicare Part D unlike influenza and COVID vaccines, which results in billing issues in provider offices. Vaccines are costly, meaning a costly upfront investment to carry the vaccine. However, referral to a pharmacy means that a patient may be less likely to be vaccinated. Residents of long-term care have additional, specific challenges.

Dr. Tom Shimabukuro (CDC/NCIRD) provided an update on CDC vaccine safety monitoring for RSV vaccines in adults ≥60 years of age. In the pre-licensure studies for Pfizer among 20,255 vaccine recipients ≥60 year of age, 2 cases of GBS were observed within 42 days of vaccination. In the pre-licensure studies for GSK among 18,304 recipients ≥60 years of age, 1 case of GBS was observed within 42 days of vaccination.

Due to the small number of GBS cases and the size of the pre-licensure studies, it is not known at this time whether these GBS cases or other neuroinflammatory events occurred due to random chance or whether RSV vaccination might increase the risk of these events. Post-licensure safety monitoring of RSV vaccines is ongoing.

A new version of V-safe is now available that requires previous and new users to create an account. It includes email and text messaging functionality. Including an email address is an additional feature in this version of V-safe. Vaccines currently monitored include RSV vaccines for older adults and pregnant persons and COVID vaccines for persons ≥6 months and older. V-safe sends health surveys after vaccination daily during the first week and then weekly through 6 weeks. The daily surveys solicit local and systemic reactions and health impacts. There are additional questions for persons who reported immunocompromising conditions at vaccination. The weekly surveys solicit new symptoms or conditions after vaccination. Participants reporting medically-attended health impacts are encouraged to complete a VAERS report.

In terms of the demographic characteristics for adults ≥60 years of age who reported RSV vaccination from the early V-safe data, there were 15,745 registrants between October 20, 2023─January 28, 2024. Respondents were predominantly of White race and most participants reported that their current state of health was excellent, very good, or good. Vaccines that were commonly reported as co-administered with RSV vaccines were COVID-19 and influenza. Reactions and health impacts reported for adults ≥60 years of age at least once during Days 0─7 following vaccination by manufacturer, injection site reactions and systemic reactions were fairly commonly reported. They were more commonly reported following the GSK vaccine in the first week following vaccination than the Pfizer vaccine. As a reminder, the GSK vaccine contains an adjuvant. A small number of individuals reported receiving medical care, which was not necessarily tied to a vaccine AE.

VAERS is the nation's early warning system for vaccine safety. It is a spontaneous reporting or passive surveillance system that is co-managed by CDC and FDA. The strengths of VAERS are that it can rapidly detect safety signals and can detect rare AEs. As a spontaneous reporting system, the main limitation of VAERS is that it is not designed to assess causality. VAERS accepts all reports from all reporters without making judgements on causality or judging the clinical seriousness of the event. As a hypothesis-generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems. For all vaccines, signs and symptoms of AEs are coded using the Medical Dictionary for Regulatory Activities (MedDRA) Preferred Terms (PTs). MedDRA PTs are not mutually exclusive, so a single report may be assigned more than 1 MedDRA PT. Reports of SAEs were individually reviewed along with accompanying medical records if available. Brighton Collaboration Case Definitions were applied for neuroinflammatory conditions, GBS, and ADEM. Reporting rate calculations used doses of vaccine administered for each type of RSV vaccine. Empirical Bayesian data mining was conducted by FDA to detect disproportional reporting for the entire post-marketing period for each product.

A number of AESIs that are currently being monitored for RSV vaccination include death, Guillain-Barré syndrome, acute disseminated encephalomyelitis, transverse myelitis, chronic inflammatory demyelinating polyneuropathy, anaphylaxis, atrial fibrillation, other supraventricular tachycardia, optic neuritis, multiple sclerosis, Bell's palsy, encephalitis/encephalomyelitis, meningitis/meningoencephalitis, myelitis, vaccination errors, and adverse events following simultaneous administration with COVID-19, inactivated influenza, or other adult vaccines.

As of February 16, 2024, there were 3,689 total reports to VAERS after RSV vaccines, which was after approximately 9.6 million doses administered. The total number of reports for the 2 products was 2,516 for GSK and 1,045 for Pfizer, which tracks closely with the doses administered. The median age, female proportion, and serious and non-serious proportions were similar between the 2 vaccines and similar to what is seen with other vaccines administered among adults ≥60 years of age. Looking at the most frequently reported MedDRA-preferred terms in adults ≥60 years of age broken down by manufacturer, for both the Pfizer and the GSK vaccines, the most commonly reported symptoms were local and systemic reactions. The safety profile for these most commonly reported symptoms for the 2 vaccines were similar. MedDRA-preferred terms of the reports by non-serious and serious status, non-serious reports dominated and was similar to local and systemic reactions. Some of the serious reports were general conditions like asthenia, fatigue, gait disturbance, muscular weakness, and GBS.

On January 19, 2024, a data mining alert for disproportional reporting was detected in FDA's Empirical Bayesian data mining for the Pfizer vaccine and GBS. No data mining alert for the GSK vaccine and GBS has been detected to date. Empirical Bayesian data mining is product-specific and analyzes product-specific VE event pairings compared to the overall VAERS database. A total of 37 preliminary reports were received as of February 16, 2024. Of these, 6 are currently under review, 7 were excluded based on medical record review, and 1 was verified but was excluded due to onset after 42 days. This left 23 verified GBS reports by medical record review, of which 15 were after the Pfizer vaccine and 8 were after GSK vaccine. The median age in these reports was 71 years, with an interquartile range of 63─75 years of age. There was 1 report in a non-pregnant female in her 50s who received Pfizer. That vaccine was either given off-label or in error.

The median time to onset was 9 days, with a range 1─22 days. There were 14 males and 9 females, none of whom were pregnant. There was 1 death in a male patient in his 70s who received the GSK vaccine. All 23 verified reports met Brighton Collaboration criteria for GBS comprised of 3 Brighton Level 1, 12 Level 2, 8 Level 3. Brighton Level 1 is the highest level of diagnostic certainty. Level 4 or 5 are not considered cases. Commonly administered vaccines were COVID-19 vaccines and influenza vaccines.

The reporting rate in the 21-day risk window was 4.6 reports per million doses administered for the Pfizer vaccine and 1.1 reports per million doses administered for the GSK vaccine. For the 42-day risk window, the reporting rate was the same for Pfizer because all of those cases had onset within 21 days. There was 1 case with a 22-day onset. For the 42-day risk window, there were 4.6 reports per million doses administered for the Pfizer vaccine and 1.2 reports per million doses administered for the GSK vaccine. Putting the observed reporting rates into the context of what would be expected can be challenging with VAERS data passive surveillance. The chart-confirmed rate of GBS after mRNA COVID-19 vaccination in the VSD was used as a proxy for background rate. To be clear upfront, safety monitoring of the mRNA COVID-19 vaccines in VSD did not detect an increased risk of GBS associated with either of the mRNA COVID-19 vaccines. Therefore, the rate of GBS following mRNA COVID-19 vaccination can be used as a proxy for the background rate of GBS in a vaccine-accepting population.

This rate is appropriate because it is a relatively current rate within the past several years. This is primarily monovalent mRNA vaccination. All of these cases were a priori chart-reviewed during the normal process of VSD surveillance for mRNA COVID-19 vaccines. There are some limitations with this method (e.g., different populations, different time periods, different age groups).

The estimated rate of GBS in adults ≥65 years of age following mRNA COVID-19 vaccines primary series in VSD in the 21-day risk interval was 3.4 per 100,000 person years and in the 42-day risk interval was 4.5 per 100,000 person years. Again, because the mRNA COVID-19 vaccines are not associated with an increased risk of GBS, this can be considered the background incidence of GBS in a vaccine-accepting population. When that is converted to per million doses in the 21-day risk interval, the expected cases per 1 million RSV doses administered would be 2 cases per million doses administered with a range from the 95% confidence interval of 0.7—4.2. For the 42-day risk interval, the expected cases per 1 million RSV doses administered would be 5.2 cases per million doses administered with a range from the 95% confidence interval of 2.8—8.9.

Returning to the observed VAERS reporting rates after RSV vaccination among adults ≥60 years of age compared to the expected rate per million doses administered, in the 21-day risk interval for the Pfizer vaccine, the VAERS reporting rate was 4.6 per million doses administered and the expected rate based on VSD data would be 2 per million doses administered with the upper bound of the confidence interval at 4.2. That point estimate for the reporting rate was elevated for the Pfizer vaccine. For the GSK vaccine, reporting rates after RSV vaccination among adults ≥60 years of age compared to the expected rate per million doses administered in the 21-day risk interval for the GSK vaccine was 1.1 per million doses administered compared to the expected rate of 2.0. That falls within the 95% confidence interval. For the 42-day risk window for the Pfizer for 4.6 per million doses administered, the estimated expected rate based on VSD data would be 5.2 with a confidence interval of 2.8—8.9. For the GSK vaccine, it increased to 1.2 per million doses administered because of the extra case at 22 days. The reporting rate was not elevated when compared to the background in VSD. The caveat is that there is known to be underreporting in VAERS, so the observed VAERS reporting rates are likely an underestimate of the true rate.

The VSD is CDC's active surveillance system used for Rapid Cycle Analysis (RCA) and research that was established in 1990. It has about 13.5 million individuals across the sites, including about 2.8 million adults ≥60 years of age. Looking at the observed VSD GBS rates following RSV vaccination in adults ≥60 years of age through December 30, 2023, the VSD identified 4 GBS cases within 1—84 days of receipt of the GSK vaccine. All 4 cases underwent medical record review and were adjudicated. The rates for the GSK vaccine were 9.5 per million doses administered 21-day risk window and 14.3 per million doses administered in the 42-day risk window. Qualitatively, these rates were higher than rates observed for high-dose influenza and Shingrix. The caveat is that these are very early data based on a small number of cases and a small number of doses administered. The 4th case was not included because it was classified as Level 4 and is pending additional review. Currently, no cases of GBS have been observed after the Pfizer vaccination, but only about 10% of all vaccinations in the VSD have been with Pfizer. The VSD will continue to monitor the safety of RSV vaccines in adults ≥60 years of age. Formal sequential safety analyses will begin March 2024 using a vaccinated concurrent comparison group, which is similar to what was done for COVID.

To summarize, local and systemic symptoms were the most commonly reported AEs following either of the RSV vaccines. Monitoring in VAERS indicated a higher-than-expected number of GBS reports following the Pfizer vaccine, but VAERS is subject to the limitations of passive surveillance. GBS cases were observed in the pre-licensure clinical trials for both the Pfizer and the GSK vaccines. GBS is included as an AE in the labels of both vaccines. Early data from VSD suggests a potential for an increased rate for GBS after the GSK vaccine, but additional analyses are needed to further assess this potential risk. Insufficient doses of the Pfizer vaccine have been used in VSD to inform risk.

Monitoring for GBS following RSV vaccines in FDA and CDC population-based active surveillance systems is in progress. CDC and FDA will continue to monitor RSV vaccine safety in VAERS and CDC will continue to monitor in V-safe.

Dr. Patricia Lloyd (FDA) presented results from FDA's preliminary analysis of GBS following RSV vaccination among adults ≥65 years of age. The objective of this analysis was to evaluate preliminary rates of GBS following 1 dose of either GSK RSV vaccine (trade name AREXVY) or Pfizer vaccine (trade name ABRYSVO®) to compare the observed rates of GBS to the historical or expected rates. A retrospective cohort analysis was used with a historical comparator group. The data were from CMS administrative claims data and enrollment information derived from CMS Medicare Shared Systems Data (SSD) for Medicare Parts A, B, and D. The study population included all CMS Medicare beneficiaries ≥65 years of age enrolled in Fee-for-Service (FFS) and Part D on the day of their first observed RSV vaccination. The study period was the date of vaccine approval, which was May 31, 2023 for ABRYSVO® and May 3, 2023 for AREXVY. The exposure included 1 dose of either ABRYSVO® or AREXVY that occurred following RSV vaccine approval and prior to the data through December 2, 2023. For the outcome of GBS, the risk window was 1-42 days and an inpatient care setting with primary physician only was used.

This was an observed versus expected analysis. The expected number of outcomes was standardized by age and sex using the 2022 GBS background rates from CMS. The analyses were adjusted for observational delay based on estimates from historical data. Incidence rate ratios (IRRs) were calculated by dividing observed rates by expected rates, with corresponding 95% confidence intervals provided. The estimated GBS positive predictive value (PPV)-adjusted rates were based on multiple imputed datasets and the previous PPV estimate of 71% was used for GBS.

In terms of the number of RSV vaccinations in CMS service data by vaccine brand during the study period with data through December 2, 2023, administration of RSV doses was observed beginning in July 2023. The majority of administrations occurred in October and early November 2023, with more administrations of AREXVY compared to ABRYSVO®. Findings from the analyses following RSV vaccination stratified by age and sex, approximately 2 million RSV vaccine doses were administered. Approximately 680,000 doses were ABRYSVO® and 1.4 million doses were AREXVY. GBS was observed for both vaccines post-RSV vaccination. There were 13 cases following vaccination with the ABRYSVO® and less than 11 cases following AREXVY. An elevated IRR was observed for GBS following vaccination for ABRYSVO® of 6.4 and for AREXVY of 2.76. Elevated risk was observed by age groups and sex, but the number of cases were small by subgroups at <5.

Applying the PPV adjustment based on multiple imputations, an elevated IRR was observed for GBS following vaccination with ABRYSVO® of 6.9 and a non-statistically significant elevated IRR for GBS following AREXVY vaccination of 2.8. The GBS rates following 1 million doses, assuming a 42-day risk window, was 25.1 following ABRYSVO® and 10.0 following AREXVY. Notably, multiple imputation was not successful in estimating the IRR for age and sex subgroups due to the small number of cases. Medical charts for the observed cases have been requested and will be reviewed.

These data are preliminary and there are several limitations to take into consideration. First, the observed versus expected analysis used aggregate historical rates rather than individual historical individuals or persons as comparators. This increases the potential for confounding and bias. Second, health outcomes were identified using ICD-10 diagnosis codes in administrative claims databases. Therefore, they are subject to outcome misclassification. Third, GBS is a rare outcome and the number of cases observed was small, so the uncertainty is high. Therefore, this poses a challenge for verification of a potential signal.

In conclusion, an elevated risk of GBS was observed following both RSV vaccines. This included 13 cases following ABRYSVO® and less than 11 cases following AREXVY. The elevated risk of GBS did not remain statistically significant following vaccination with AREXVY when adjusted for the PPV. Safety monitoring following RSV vaccination using a self-controlled case series (SCCS) design is planned and will provide more conclusive evidence of the potential risks following RSV vaccination.

Dr. Kotton asked when the date of capture might be moved closer to the present and thus included more robust data.

Dr. Lloyd indicated that data are continuing to accrue. As mentioned, a SCCS analysis is planned with more recent data that will provide more conclusive evidence. Power calculations have been done to determine the estimated risk ratios or rate ratios.

Dr. Daley said he was trying to integrate across platforms to put into context the current status. He called on Dr. Shimabukuro from the standpoint of the ISO and his experience with vaccines like this in the past to help the committee integrate the results in terms of the timing of different products, recognizing that there would be a different study design and chart-validated cases from the CMS data for example.

Dr. Shimabukuro summarized that the early post-licensure safety data presented during this session from CDC and their FDA colleague came from several monitoring systems administered by CDC and FDA. Taking these data together suggests a potential increased risk for GBS after RSV vaccination among adults ≥60 years of age. A potential risk was previously identified in the pre-licensure clinical trials in older adults for both Pfizer's ABRYSVO® vaccine and GSK's AREXVY vaccine. Due to the uncertainties and limitations at this point, these early data cannot establish whether there is an increased risk for GBS after vaccination in this age group. More robust active surveillance and population-based systems are ongoing. Analysis from these systems will be better able to determine whether an increased risk for GBS after RSV vaccination is present and if so, the magnitude of the risk. He assured the committee that CDC and FDA will remain vigilant in their monitoring of RSV vaccines as they do for all vaccines, and that timely and transparent communication is a priority. Additional findings on RSV vaccine safety will be presented as the data become available.

Michael Melgar, MD (CDC/NCIRD) presented the results of an analysis on the estimated benefits and risks of older adult RSV vaccination on behalf of the ACIP Adult RSV Work Group. The analysis compared the estimated benefits stratified by age and potential risk of GBS from RSV vaccination in this age group, with results stratified by the 2 products, GSK's AREXVY vaccine and Pfizer's ABRYSVO® vaccine. He noted that he would be referring to the vaccines by their trade names for ease of reference.

To estimate the benefits, the numbers of preventable RSV illnesses were estimated over 2 consecutive RSV seasons per 1 million vaccine doses administered to adults ≥60 years of age. That included outpatient illnesses, hospitalizations, ICU admissions, and in-hospital deaths. The assumption regarding the underlying burden of RSV disease was derived from published and unpublished RSV incidence data, and application of VE estimates from clinical trials. In short, it was assumed that everyone in a cohort of 1 million older adults were vaccinated with a single dose of vaccine. Preventable illnesses was tallied over the subsequent 2 RSV seasons after vaccination. Revaccination was not considered in this analysis. Potential risk of GBS was informed by the observed rate of GBS per 1 million doses administered to adults ≥60 years of age in FDA's analysis that Dr. Lloyd presented earlier using CMS data.

As mentioned, the potential benefits of RSV vaccination were stratified by adult age because RSV disease disproportionately impacts the oldest adults. A comparison of the estimated age distribution of national RSV-associated hospitalizations, ICU admissions, and in-hospital deaths was derived by applying CDC RSV-NET rates from the 2022–2023 surveillance season to Census population estimates. Adults ≥65 years of age, and especially adults ≥75 years of age, are vastly overrepresented among adults with severe RSV illness. Looking closer at RSV-NET hospitalization rates per 100,000 adults of RSV-associated hospitalization stratified by age over 7 recent seasons, even among adults ≥60 years of age, RSV hospitalization rates increased with each progressive age group, with an inflection point at age 75 years during most of the surveillance seasons.

In the absence of observational VE data post-licensure, it was assumed that clinical trial VE would apply in the real-world. Efficacy against medically-attended acute respiratory illness (ARI) was assumed to represent effectiveness against outpatient illness. Efficacy against medically-attended lower respiratory tract disease (LRTD) was assumed to represent effectiveness against hospitalization, ICU admission, and in-hospital death. Due to differing case definitions of clinical trial outcomes and differing durations of follow-up, efficacy estimates cannot be directly compared across trials.

Clinical trials of both vaccines were underpowered to estimate efficacy among adults ≥75 years of age due to low enrollment of this age group. Aging results in lowered immune responsiveness to infection and vaccination, so adults in the oldest age group might experience reduced efficacy or effectiveness. To address this, a sensitivity analysis was conducted in which VE was assumed to be reduced by half among adults ≥75 years of age compared with the other age groups.

Transitioning to the estimated benefits of RSV vaccination over 2 consecutive seasons for every 1 million vaccinations among adults ≥60 years of age, RSV vaccinations may prevent 23,000 to 26,000 outpatient visits; 2,400 to 2,700 hospitalizations; 450 to 520 ICU admissions; and 120 to 140 in-hospital deaths. These values are similar for each of the 2 vaccine products. The uncertainty intervals reflect the uncertainty in estimates of RSV disease burden. Stratifying by age, the number of preventable outcomes per 1 million doses was highest in the oldest age groups in which there is the most existing RSV burden to prevent.

The results for GSK's AREXVY vaccine focusing on the more severe outcomes (e.g., hospitalization, ICU admission, and in-hospital death), assumed that all adults ≥60 years of age experience the same VE. If instead, VE is assumed to be reduced by half among adults ≥75 years of age, the amount of preventable disease is reduced in this age group accordingly.

In spite of that, the estimated benefits per 1 million vaccinations are still greatest among adults ≥80 years of age compared with any other age group, and the estimated benefits among adults 75–79 years of age still exceed those among adults in their 60s. This indicates how the benefits of vaccination are driven in large part by the pre-existing burden of RSV disease. The results were similar for Pfizer's vaccine, ABRYSVO®. The estimated benefits per 1 million doses increase with an increasing age. Next slide. In the sensitivity analysis in which VE was assumed to be reduced by half in adults ≥75 of age, the estimated benefits per 1 million doses were still greatest among adults ≥80 years of age. The estimated benefits among adults 75–79 years of age still exceed those among adults in their 60s.

Moving to the potential risk of GBS per 1 million vaccine doses administered, to recap the results presented by Dr. Lloyd of the of the FDA analysis in partnership with CMS among Medicare beneficiaries ≥65 years of age during a 42-day risk interval after vaccination, after adjustment for claims delay, approximately 10 GBS cases were observed per 1 million doses of GSK's AREXVY administered. For Pfizer's ABRYSVO®, 25 GBS cases were observed for 1 million doses. By comparison over a 42-day period, the historical background rate from 2022 of GBS among Medicare beneficiaries would be expected to result in 5 GBS cases per 1 million persons. The historical background rate among all adults ≥65 years of age may not be applicable to adults electing to receive RSV vaccination under shared clinical decision-making. For this reason, GBS observation rates have not been adjusted for a background rate. Recipients of each of the 2 vaccine products might differ on average in degree of baseline risk of GBS. More robust analyses are needed to confirm and to quantify risk of GBS after RSV vaccination.

In terms of the estimated benefits and potential risks over 2 consecutive RSV seasons per 1 million doses administered of each vaccine, along with the GBS observation rate from this FDA-CMS partnership, from a population perspective among adults ≥60 years of age, the estimated numbers of outpatient visits, hospitalizations, ICU admissions and in-hospital deaths exceeded the range of estimated GBS observation rates. This was true for both vaccine products. Iin terms of the age-stratified results for GSK's AREXVY vaccine, the preventable illnesses per 1 million vaccinations were lowest in adults 60–64 years of age who are at the lowest baseline risk of severe RSV disease. For those adults and across all age groups, the number of preventable outcomes exceeded the range of GBS observation rate for this vaccine. The observation rate was not adjusted for background GBS rate, so not all observed GBS cases can be assumed to be associated with vaccination. Regarding the age-stratified results for Pfizer's ABRYSVO® vaccine, the estimated number of preventable outcomes in each age group exceeded the observation rate of GBS, including in the youngest age group of adults 60–64 years of age.

In summary, from a population perspective, the benefits of RSV vaccination are estimated to outweigh the potential risk of GBS in adults ≥60 years of age. However, estimated benefits of RSV vaccination vary by age group and RSV incidence. Estimated benefits likely also vary by individual level risk of severe RSV disease and by the timing of vaccination relative to the RSV season. There is substantial uncertainty in the estimates of both benefit and risk. This analysis will be updated as additional data become available that might include additional vaccine safety data, additional efficacy data from clinical trials, observational VE data, and additional epidemiological data enabling more detailed subgroup analysis.

Leonard Friedland, MD
Vice President
Director Scientific Affairs and Public Health
Vaccine Research Physician
GSK Vaccines North America

Dr. Friedland expressed concern in the representation of VE for the 2 licensed RSV vaccines in today's ACIP presentation on RSV vaccination in older adult benefit-risk discussion. Although some slides state the VE estimates are not directly comparable for both vaccines, it is not clearly stated on all representative slides that there are no head-to-head studies of the 2 licensed vaccines, nor is it stated on all representative slides that the follow-up time in the second season after the initial vaccination differs significantly for the 2 vaccines. He noted that the VE data for GSK's vaccine represented in one of the slides is over a complete second RSV season with 6 months median follow-up in that season, while the VE for the Pfizer vaccine represents a mid-second RSV season with much shorter follow-up in that season. VE may be expected to decline the longer the time from the initial vaccination. Data from GSK's pivotal RSV adult VE trial showed VE against lower respiratory tract disease for AREXVY is 81% through mid-second season, with a median follow-up of 14 months from vaccination and 75% through a complete second season with a median follow-up of 18 months from vaccination. Use of similar time of follow-up VE for both vaccines in the benefit-risk slides will show a more accurate representation of a substantial clinical impact of AREXVY.

Pfizer

Reema (Jain) Mehta, PharmD, MPH
Vice President
Head, Risk Assessment and Management for Worldwide Safety
Pfizer

Dr. Reema Mehta, Vice President and Head of risk assessment and management for Worldwide Safety at Pfizer, expressed Pfizer's commitment to achieving the safe use of their products in collaboration with their stakeholders and partners for the betterment of patients and public health globally. Dr. Mehta noted that given the multiple sources of uncertainty for GBS, some of which include the background rates of GBS among adults who received the vaccine, co-administration with other vaccines, seasonality of GBS, and underlying conditions at the time of vaccination such as concurrent infection, age at the time of administration, comorbid conditions, and even the differences in the distribution of the vaccine in the various health settings and finally, the system and methodology limitations with respect to being able to attribute causality, there was agreement with the CDC and FDA that the assessments of post-vaccine GBS is complex. The findings are preliminary, and these important considerations can have meaningful impact on the analyses. Dr. Mehta expressed Pfizer's commitment to the continuous monitoring and evaluation of the safety of ABRYSVO®. In addition to routine pharmacovigilance monitoring activities, the company is conducting 4 different post-approval safety studies to ensure robust and continuous monitoring of GBS. With over 3 million administrations in the older adult population to date, Pfizer believes ABRYSVO® is safe and effective and provides protection against RSV and its complications. Dr. Mehta stated support for ACIP's recommendations and the common goal for more robust data to inform decision-making, with the ultimate goal to reduce the public health burden of RSV amongst older patients.

Dr. Amadea Britton (CDC/NCIRD) presented the work group's interpretation and discussion of RSV vaccination in older adults. The work group believes that contextualization and understanding of current safety data are paramount in determining the future-preferred policy options for the adult RSV vaccination program. The objectives of the presentation were to summarize the work group's interpretations of current RSV vaccine safety surveillance data and the balance of estimated benefits versus potential risks associated with use of RSV vaccines in adults ≥60 years of age; share new work group considerations for incorporating timing of RSV vaccine administration in shared clinical decision-making; and an update on expected future policy considerations.

The initial RSV vaccine recommendation for adults ≥60 years of age was made in the setting of a small number of cases of inflammatory neurologic events, particularly GBS, observed in the clinical trials for both GSK's and Pfizer's RSV vaccines for older adults. It was unclear whether the small number of cases observed in the trials represented a genuine association between RSV vaccination and risk of GBS or whether the cases were observed due to chance alone. The potential for increased risk of GBS was discussed extensively during deliberations for the older adult recommendation. The Adult RSV Work Group and ACIP expressed that they would have preferred additional data on safety and efficacy from manufacturers to support their recommendation but concluded that the estimated benefits of RSV vaccination outweighed potential risks. CDC, FDA, and ACIP all highlighted a commitment to immediate post-licensure safety monitoring. However, partially in response to this uncertainty, ACIP recommended that RSV vaccines be given using shared clinical decision-making with a HCP. The shared clinical decision-making recommendation was intended to facilitate individualized risk-benefit discussions, acknowledging that the balance of risks and benefits may depend upon the characteristics of the individual vaccine recipient. The subsequent clinical guidance shared by CDC advised that a patient's risk for severe RSV-associated disease should be the core of shared clinical decision-making, with vaccination targeted to those who are at highest risk for severe RSV disease and therefore most likely to benefit from vaccination.

CDC first became aware of GBS cases in VAERS in the Fall of 2023. Some GBS reports are expected in VAERS after a new vaccine is recommended because GBS occurs in the population for reasons unrelated to vaccination at some rate, which is referred to as a background rate. In the Fall, the number of cases observed in VAERS raised the possibility that cases observed might be above the expected background. However, as Dr. Shimabukuro highlighted, VAERS has multiple limitations and cannot establish an association between vaccination and an AE. CDC convened calls with clinical experts in neurology through its CISA Project to further review the cases in VEARS. Meanwhile, safety surveillance teams at CDC and FDA were simultaneously reviewing all available data in more robust active surveillance systems.

Earlier in the session, CDC's ISO and FDA shared preliminary data from VEARS, VSD, and the FDA-CMS partnership. As a reminder, the data from VSD and the FDA-CMS partnership are near real-time summaries of what is available. Taken together, the available data to date support a potential increased risk for GBS after RSV vaccination among adults ≥60 years of age. However, as reviewed across earlier presentations in this session, there remains considerable uncertainty in the estimates of risk that can be generated using data from these systems and, therefore, in how to interpret them. While the concern of a genuine association between GBS and RSV vaccination may be increasing, there is insufficient evidence currently to confirm this association or to estimate the magnitude of increase. Assessing the risk for GBS in more robust analyses and active vaccine safety surveillance systems will be crucial and is underway.

The work group endorsed that any increase in the potential risk of GBS should be placed in the context of the benefits of RSV vaccination using the best understanding of the data available now. From a population perspective, the estimated benefits of RSV vaccination outweigh the estimated risk for adults ≥60 years of age. Benefits of RSV vaccination vary by age group and RSV incidence. Benefits also likely vary by individual-level risk and by timing of vaccination relative to the RSV season. Adults with certain chronic conditions are at increased risk of severe RSV disease, even at younger ages.

The work group reviewed examples from other licensed and recommended vaccines. The first of these was seasonal influenza vaccination. The data on the association between GBS and seasonal influenza vaccination are variable and inconsistent across influenza seasons. If there is an increased risk of GBS following influenza vaccination, it is small, on the order of 1 to 2 additional cases per million doses of influenza vaccine administered. Studies also suggest that it is more likely that a person will get GBS after getting influenza disease than after influenza vaccination. This means that influenza vaccination itself is likely able to avert some GBS cases.

Comparing what is known about RSV and influenza estimated disease-associated hospitalizations, estimated vaccine-avertable hospitalizations, and potential vaccine-associated GBS risk, there are an estimated 1,700 to 2,800 disease-associated hospitalizations per 1 million population ≥65 years of age. RSV vaccination is estimated to avert 1,800 to 4,200 RSV-associated hospitalizations over 2 seasons. Influenza is estimated to cause 3,200 to 9,200 disease-associated hospitalizations per 1 million population ≥65 years of age, with seasonal influenza vaccination estimated to avert 300 to 5,500 hospitalizations over 1 influenza season. For RSV, the FDA-CMS estimates of GBS cases observed per 1 million doses in adults ≥65 years of age were used. However, these are not adjusted for background rate and therefore do not represent additional cases over background. As noted for influenza vaccine, the risk of GBS is variable and inconsistent. If present, it is on the order of 1 to 2 additional cases per million. In this case, the additional means the background rate is accounted for.

The work group continues to believe that the estimated benefits of RSV vaccination outweigh potential risks when vaccination is implemented using the current recommendation. A majority of work group members expressed that the balance of estimated benefits outweighed potential risk for all adults ≥60 years of age. However, the work group expressed that estimated benefits most clearly outweigh potential risks among adults ≥60 years of age who are at increased risk of severe RSV disease. This includes adults who are ≥60 years of age with chronic medical conditions such as CLD, heart failure, immunocompromised, those of advanced age, and those living in LTCFs.

The work group also stressed that discussion of benefits versus risks should remain the core of shared clinical decision-making. Providers will need support in appropriately framing shared clinical decision-making discussions and may need additional communications materials clarifying which of their patients are at increased risk of severe RSV disease and would benefit most from vaccination, and more materials to support discussing current safety data.

Safety surveillance is ongoing and new data will be shared as soon as they become available. In the interim, the work group wishes to affirm the importance of the RSV vaccination program. RSV is a disease that causes significant morbidity and mortality among persons across the age spectrum. Based on preliminary data, the work group is cognizant that premature changes in the RSV vaccination program have the potential to limit access to RSV vaccine. CDC and the work group are committed to incorporating what they are learning from post-licensure data in a transparent way that ensures safety for the public and clarity for providers.

The current recommendation for RSV vaccines in adults ≥60 years of age is for year-round administration. The work group concluded that it is now advisable for providers and patients to consider timing of RSV vaccination as part of shared clinical decision-making discussions. This is a result of the return to predictable RSV seasonality and as a way to maximize the benefits of RSV vaccination as ongoing safety monitoring continues. For most older adults, benefits will be highest when RSV vaccination is given in the late summer or early fall just before the onset of RSV season so that vaccine recipients experience highest protection during the times of peak RSV transmission over the fall and winter. In addition, because clinical trial data suggest that protection will wane over time, vaccinating just before a season starts also maximizes protection for subsequent seasons for which the vaccine offers protection. This means that for adults ≥60 years of age who remain unvaccinated and who decide with their HCP to get an RSV vaccine, the best time for vaccination will be just before the start of the next RSV season. In most of the US, RSV vaccination will have the most benefit if given in the late summer or early fall.

RSV seasonality does have regional differences. Therefore, the exact timing of season onset peak varies by region. Looking at the mean of the curves for 4 seasons from the National Respiratory and Enteric Virus Surveillance System (NREVSS) by US region, it is first important to note that these data exclude Florida, Hawaii, and Alaska where seasonality of RSV may be different. Increasing circulation begins and peaks the earliest in the South and the latest in the West. However, in general in the continental US, RSV season onset is between September and November. This means that the ideal time to get vaccinated to ensure protection by the start of the RSV season will be August to October in most of the continental US.

Turning now to upcoming policy considerations being discussed by the Adult RSV Work Group, the work group may address the potential FDA approval of Moderna mRNA-1345 vaccine for use in adults ≥60 years of age, the potential FDA approval of GSK RSV vaccine for use in adults 50─59 years of age at increased risk for RSV disease, and consideration of whether shared clinical decision-making remains the preferred policy option during the 2024 ACIP meeting.

In regard to the potential licensure of Moderna's mRNA-1345 RSV vaccine for use in adults ≥60 years of age, the work group highlighted several points. Interim efficacy with median 9 months follow-up showing VE against RSV LRTD was 63.3% for 2 or more symptoms and 63% for 3 or more symptoms. In total, there were only 2 recorded RSV-associated hospitalizations, both in the placebo arm. Efficacy against hospitalization was unable to be estimated. There were no recorded RSV-associated deaths, including in the placebo arm. The work group noted no reported cases of GBS, ADEM, or other inflammatory and neurological events. Therefore, if licensed by FDA for use in adults ≥60 years of age, the work group plans to present full GRADE and EtR Framework to support ACIP deliberations around adding Moderna as a vaccine option for adults ≥60 years of age to protect against LRTD.

Regarding the work group's interpretations of GSK RSV vaccine for use in adults 50─59 years of age at increased risk. In October 2023, GSK presented data to ACIP demonstrating that the humoral immune response to a single dose in adults 50─59 years of age is non-inferior to that in adults ≥60 years of age. The work group noted that if FDA licensure is granted for use of GSK's RSV vaccine in adults 50─59 years of age at increased risk of RSV disease, the ACIP likely will need to make a policy recommendation on whether RSV vaccination should be recommended in this age group and, if so, how CDC will define populations at increased risk. Earlier in the day, data were presented demonstrating the relative risk of severe RSV disease across a range of chronic medical conditions by age group.

The work group members broadly agree that use of RSV vaccine among adults 50–59 years of age with certain chronic medical conditions is likely to have public health benefit. However, upcoming data on safety and effectiveness will be pivotal to determine the preferred policy option at that time.

The work group has begun analyzing the experience with shared clinical decision-making this season; there has been feedback from many partners that shared clinical decision-making has been challenging to implement. The work group continues to endorse shared clinical decision-making as more is learned about the estimated benefits and potential risks associated with the currently available RSV vaccines. However, the work group has begun reviewing evidence to deliberate on changing the current recommendation for adults ≥60 years of age from shared clinical decision-making to a universal recommendation among adults older than a specific age cutoff such as 75 years of age, and a risk-based recommendation in adults ≥50 years of age up to the determined age cutoff.

In summary, the first ever respiratory virus season in which vaccines were available to protect older adults against RSV disease is coming to a close. Over the coming months, CDC and the work group will be analyzing these data to inform discussion of future RSV vaccine policy for older adults. Data from pre-licensure clinical trials and early findings from post-licensure vaccine safety surveillance suggest the potential for increased risk of GBS after RSV vaccination in older adults. However, these early data are insufficient to confirm if there is an increased risk. Assessing the risk for GBS following receipt of the RSV vaccine among older adults and more robust analyses in active vaccine safety surveillance systems will be crucial and are underway. Currently, the work group continues to endorse the benefits of RSV vaccination for adults ≥60 years of age, especially those at increased risk of severe RSV disease using shared clinical decision-making. Benefits can be maximized by administering RSV vaccine just before the start of RSV season. The work group recommends that timing of RSV vaccination should be a part of the shared clinical decision-making discussion. CDC and the Adult RSV Work Group will continue to transparently share new information with ACIP and the public and incorporate it into future policy recommendations to ensure the greatest benefit and least risk in the RSV program for older adults.

ACIP was asked to discuss their interpretation of the currently available RSV vaccine safety surveillance data; whether or not they are supportive of adding timing of RSV vaccination as a consideration in shared clinical decision-making, with an emphasis on uptake in late summer and early fall; and what additional data would ACIP like to review in preparation for June 2023 policy considerations, including a potential risk-based recommendation with or without a universal recommendation and expansion to adults 50–59 years of age.

In closing, Dr. Britton shared condolences to the family and friends of Dr. Jeffrey Kelman, who was a wonderful contributor to the work group and will be greatly missed.

Dr. Daley highlighted the potential challenges for pharmacists in implementing a recommendation with shared clinical decision-making. He stated that he is comfortable with including timing in shared clinical decision-making, given that it is reasonable based on continued uncertainty. He expressed appreciation for how the work group considered and laid out the issue and did not come to any overarching conclusions, particularly given that ACIP may have to make some difficult decisions during the June 2024 meeting.

Dr. Loehr agreed that this was an incredibly thoughtful safety review. He also expressed gratitude to the work group, CDC, and FDA for gathering all of this information, sharing it with the full ACIP, and contextualizing it. It gave him a lot of reassurance and he hoped it would give the public a lot of reassurance that these organizations care about and are transparent about safety and are taking this very seriously. He noted that he is one of the minority of people who like shared clinical decision-making and thinks it is very important in this context. The way he phrases this to his patients is that he is 61 years old and is generally healthy, so he did not get the vaccine this year. His mom is 89 years old and very frail, so she did get the vaccine this year. There is a significant difference between the 2 groups, so he thinks shared clinical decision-making is actually perfect for this. He also appreciated the information he could take back to his office to use immediately. The concept of using the timing difference and perhaps not recommending it now and holding off is very important for practitioners.

Dr. Long said she was surprised by the amount of vaccine that was given in pharmacies and was surprised when she got hers at the local pharmacy that she did not need a doctor's prescription. The ability for pharmacies to engage in shared clinical decision-making questions is unclear. There really was not shared clinical decision-making this year with RSV, and she is relieved that there was relatively low uptake until the safety question is satisfied. She asked what the rules would be going forward about pharmacies administering vaccines and who would make them.

Dr. Wharton indicated that those are state decisions based on state scope of practice laws and regulations, so it varies by locality and can vary by vaccine and age group. At least pre-COVID, the scope of practice rules allowed pharmacists almost everywhere to give influenza vaccine to adults, and that was generally without a prescription. While she thought there had been expansions post-COVID, she was not able to comment on that but called upon Kelly Goode with the American Pharmacist Association (APhA) to respond.

Dr. Goode confirmed that scopes of practices are state-based for pharmacists and for immunizations. While many times that is under a protocol, sometimes it is based on pharmacist decisions. She reminded the ACIP that pharmacists are one of the healthcare professionals who are able to apply shared clinical decision-making to vaccine recommendations. While someone may not have been able to see the pharmacist to ask questions, a patient's medication list reflects medical conditions and provides insight for the pharmacist. Pharmacists are well-prepared and trained to complete a medical history if needed. Pharmacists receive over 20 hours of continuing education in immunizations through home study and a live program. This is taught throughout the curriculums across the country. In pharmacy schools, it is now a required part of the curriculum to receive potentially more education than many other healthcare professionals dedicated to just vaccines and vaccine science. Pharmacists are very well-equipped to interpret and implement recommendations to protect patients against vaccine-preventable diseases.

Dr. Brooks underscored what Dr. Loehr said about it giving him confidence to know that there is this much scrutiny about this signal. Slide 20 had data from the V-safe, VAERS, and VSD surveillance systems, as well as information about how to interpret that. Based on what he heard, he would continue to recommend the vaccine and look forward to more information. Dr. Melgar's presentation ultimately brought everything together and he expressed his hope that the public understands active surveillance and how seriously CDC and ACIP take this.

Dr. Kotton said that in terms of the list of discussion points, she wanted to highlight that regarding expansion to adults 50─59 years of age, she is especially concerned about what has been learned about people of color having a higher risk of severe RSV in their late 50s compared to White and Asian people who have a higher risk of severe RSV in their early 70s. Thinking about immunologic equity, she would like to have additional data on the more vulnerable populations within that age group. She also would include a focus on immunocompromise in that population. She is concerned about the signals they heard about during this session, so she wants to ensure that there is a targeted risk base for adults 50─59 years of age who would benefit from vaccine.

Dr. Britton reiterated that the work group has begun reviewing evidence and is considering a shift away from shared clinical decision-making for adults ≥60 years of age to a universal recommendation among adults older than a specific age cut-off, as well as a risk-based recommendation for adults ≥50 years of age up to that age cut-off. This potentially would avoid younger and healthier adults who have very low risk of severe RSV disease. In addition, explicitly outlining risk conditions may be easier for providers to implement because as the NIS data showed, one of the issues is that there is not necessarily a healthcare provider recommendation.

Dr. Long said that before deciding on younger age groups, she would like to know more about the cost-effectiveness depending on the underlying condition and the potential for boostability. She would not want to give it to people with increased risk at 50─65 years of age who are still much lower than 75─80 years of age. The vaccine is known to wane to almost nothing by 2 years, which is the nature of vaccines for mucosal diseases. What if people are not protected when they get to the major risk age and have underlying conditions? While she did not know where this information might come from, perhaps they should obtain input from some immunologists.

MENINGOCOCCAL VACCINES

Dr. Jamie Loehr, chair of the ACIP Meningococcal Vaccines Work Group, introduced the meningococcal vaccines session. During previous ACIP meetings, members asked for review of the current adolescent schedule for the meningitis vaccines. The work group has had a very robust discussion about the options. With over 10 options at one point, they finally narrowed it down to about 4. He asked ACIP members to think about whether they concurred with the 4 options the work group selected for further assessment, and what additional information would help the ACIP determine the preferred option as they listened to the presentations. As a reminder, ACIP approved the Pfizer pentavalent vaccine in October 2023. That was approved as an option when both MenACWY and MenB are recommended at the same time. The work group is using that same framework for the GSK pentavalent vaccine and would provide information during this session about the planned considerations. Therefore, the presentations and discussions during this session focused on the adolescent change and GSK's MenABCWY vaccine.

The plan for the June 2024 meeting is to review the epidemiology of meningitis disease in terms of the disease burden stratified by race and ethnicity in adolescents; cases and deaths averted by a MenACWY dose at 11-12 years of age; risk factors for serogroup B disease among college students; and breakthrough disease in vaccinated individuals. During the October 2024 ACIP meeting, the work group will present a GRADE and the EtR analysis and a cost-effectiveness analysis, with a plan for a vote in February 2025.

Evidence to be considered by the work group in the development of future recommendations includes but is not limited to the epidemiology of meningococcal disease, expected public health impact, immunogenicity and safety of the GSK pentavalent vaccine only, GRADE and EtR, and cost-effectiveness.

Dr. Sarah Schillie (CDC/NCIRD) presented on revising the adolescent meningococcal vaccine schedule and considerations with respect to meningococcal vaccine recommendations and coverage data, the epidemiology of meningococcal disease, duration of vaccine-induced protection, and options for changing the immunization schedule.

MenACWY vaccine is routinely recommended for adolescents, with Dose 1 administered at 11─12 years of age and Dose 2 at 16 years of age. MenB vaccine is recommended for adolescents based on shared clinical decision-making and is typically a 2-dose series. The recommended age range is 16─23 years of age, with a preferred range of 16─18 years of age. The doses in the MenB series need to be from the same manufacturer. The pentavalent MenABCWY vaccine is recommended as an option when both MenACWY and MenB are indicated at the same visit.

The 2022 coverage for ≥1 dose of MenACWY at 13 years of age was 84.5%, ≥1 dose at 16 years of age was 89.8%, and ≥2 doses at 17 years of age was 60.8%. As expected, coverage was much lower for MenB vaccine, as those recommendations are based on shared clinical decision-making. The coverage for ≥1 dose at 17 years of age was 29.4% and for ≥2 doses at 17 years of age was 11.9%.

Looking at the incidence of meningococcal disease in the US from 1996 through 2022, incidence started to decline before the introduction of MenACWY vaccine in 2005. There was an uptick in disease incidence in recent years. The proportion of disease caused by serogroup varies with age. In terms of the proportion of disease by serogroup from 2012─2021, predominantly pre-pandemic data, serogroup B accounted for more than half of cases among adolescents. Preliminary data revealed 416 cases of invasive meningococcal disease in 2023, which is the highest number of cases since 2014. The rates of disease were greatest in children <1 year of age, with a second peak in adolescence. When considering the 2021 cases for which the most recent data are available, 19 of the 210 cases (9%) were among persons 11─23 years of age.

Because the decline in meningococcal disease incidence began prior to the introduction of vaccine, measuring the association between vaccination and disease incidence is challenging, but has been modeled using surveillance data. Among adolescents 11─15 years of age, incidence decreased 16.3% during the pre-vaccine period and 27.8% during the post-primary dose period. Among adolescents 16─22 years of age, incidence decreased 10.6% during the post-primary dose period and 35.6% during the post-booster dose period. An estimated 222 cases of serogroup C,W, or Y disease were averted through vaccination of adolescents from 2006─2017.

In terms of the incidence of disease following MenACWY vaccine implementation, ACWY MenACWY disease increased around 15─16 years of age. Following MenACWY vaccine implementation disease decreased dramatically, However, there was still a peak at 12 years of age, which could increase if the dose at 11─12 years of age was eliminated. B disease became the dominant cause of meningococcal disease in adolescents over time, although incidence has increased slightly since the pre-vaccine era.

Serogroup B disease is higher among college students, who have a 3.5-fold greater risk of serogroup B disease than non-college students. Incidence peaks at 19 years of age and declines after age 20.

Higher risk is associated with students at 4-year colleges who had a 5.2-fold higher risk of serogroup B disease than non-undergraduates 18-24 years of age. Risk among 2-year college students was comparable to non-undergraduates as opposed to 2-year colleges. First-year students were at 3.8-fold higher risk of serogroup B disease than non-first-year students. On-campus residents were at 2.9-fold higher risk of serogroup B disease than off-campus residents. Students participating in Greek life were at 9.8-fold higher risk of serogroup B disease than other students during outbreaks.

Duration of vaccine-induced protection wanes over time following meningitis vaccination. For MenACWY vaccines, protection wanes between 3 to 8 years post-vaccination. Within 1 year of vaccination, vaccine effectiveness is 79%. Between 1 to 3 years post-vaccination, vaccine effectiveness is 69%. Between 3- and 8-years post-vaccination, vaccine effectiveness is 61%. For MenB vaccines, protection wanes 1 to 2 years following primary vaccination.

BEXSERO is recommended for the prevention of serogroup B meningococcal disease. Deliberations regarding the adolescent meningococcal vaccine schedule will primarily consider meningococcal disease prevention. BEXSERO also appears to provide some protection against gonorrhea. *Neisseria meningitidis* and *Neisseria* gonorrhoeae are genetically closely related, sharing about 80% to 90% sequence homology. As such, it is plausible for outer membrane vesicle (OMV)-containing MenB vaccines such as BEXSERO to provide cross-protection against gonorrhea.

Revisions to the adolescent meningococcal vaccine schedule should optimize protection against meningitis. Considerations to optimize meningitis protection include ages at higher risk for meningitis, recent epidemiology, and duration of vaccine-induced protection. Maintaining harmonization with the existing adolescent platform is an additional consideration, as is the use of pentavalent vaccines that provide the opportunity to reduce the number of injections.

There are several options under consideration for revising the adolescent schedule. For MenACWY, an option is to eliminate the dose for adolescents 11—12 years of age or to change the recommended ages for vaccination given the low incidence of disease in young adolescents. For MenB, an option is to change the recommended age for vaccination to increase protection upon college entry, given the limited duration of protection. Another option for MenB is to change the shared clinical decision-making recommendation to either a routine or risk-based recommendation. If there is a change to a risk-based recommendation, the work group expressed a preference to include permissive language for vaccinations of persons requesting protection but who may lack risk factors. For example, college attendance would not be a requirement to receive protection for MenB vaccination. The intent of this preference would be to address equity considerations.

Option 1 maintains the current MenACWY recommendations and changes MenB recommendations to routine recommendations, with Dose 1 administered at 16 years of age and Dose 2 administered at 17—18 years of age. Option 2 is similar to Option 1, except that the recommendations for MenB for Option 2 are risk-based as opposed to routine recommendations. Option 3 is similar to Option 2, except that Option 3 eliminates the dose of MenACWY at 11—12 years of age.

Option 4 is for Dose 1 of MenACWY at 15 years of age and Dose 2 of MenACWY at 17—18 years of age and for Doses 1 and 2 of MenB at 17—18 years of age, with a routine recommendation. The work group preferred Option 1 or 3. There are instances when doses of MenACWY are recommended at the same age as doses of MenB, representing instances for which the pentavalent vaccine may be an option.

To summarize the work group's comments, there was variability in the desire to keep versus eliminating the dose of MenACWY at 11—12 years of age. Those in favor of keeping it noted that it has taken years to engrain the 11—12 years of age platform, and that dose may have reduced carriage and has worked. Those in favor eliminating that dose pointed to the epidemiology, which seems to support starting the series at 16 years of age. Other comments were to consider administering MenB starting at 15 years of age, which is not among the 4 options for consideration, and to try to achieve acceptable efficacy for duration of disease incidence peak in young adulthood. Work group members opposed shared clinical decision-making recommendations, citing poor uptake, missed vaccination opportunities, implementation challenges, prevention of institutions from implementing policies due to lack of a strong recommendation, and not being understandable to clinicians. As such, the work group had interest in changing MenB recommendations to either risk-based or routine. Members noted that harmonization of MenACWY and MenB schedules could reduce the number of injections if using the pentavalent vaccine, but also pointed out that if the use of the pentavalent resulted in extra antigen administration, extra antigen administration has not been a concern in the past with other vaccines. Members also noted that a change in the schedule may impact school requirements.

In closing this presentation, Dr. Schillie asked if ACIP concurred with the four schedule options for further assessment' and what additional information will help ACIP determine the preferred option.

Dr. Loehr noted that the work group considered that harmonization with other organizations is very important. With that mind, he called on pediatric and family practice liaisons to provide comments or organization opinions.

Dr. Middleman (SAHM) expressed appreciation for this thorough presentation that highlighted the majority of issues that SAHM has been discussing. They had a talk during which the attendees, who were adolescent medicine providers, were asked to provide input. Among the 25 respondents, there was a clear concern about potentially eliminating the dose at 11—12 years of age for multiple reasons. The health and safety of adolescents is obviously paramount, but integration of that into the platform is important. Immunization platforms are intended to remind people that it is time to think about vaccines and specific vaccines. The reason childhood platforms are so successful is they have not been changed in a long time. Change to the platform would take significantly more data than are available to indicate that it would be of benefit to the health of teens. There also was a strong sense that the use of the pentavalent vaccine, especially if there are associated cost-savings, would be far preferable in terms of the ability to decrease the number of products that are required for vaccination. Making an age-based recommendation for MenB would make administration of all of these vaccines more streamlined, efficient, and easier to follow. About 80% of those responding to a group survey after the talk also felt that the pentavalent vaccine given at 16 years of age with a second dose at 16—18 years of age would be ideal.

Dr. Rockwell (AAFP) agreed with Dr. Middleman's comments. Speaking as a family physician and not on behalf of AAFP, she favored Option 1 not to eliminate the tried-and-true 11─12 years of age vaccine recommendation. She also was somewhat swayed by the argument that perhaps getting this vaccine over so many years has lowered the community carriage of this disease. In addition, she favored making this a definitive routine recommendation rather than shared clinical decision-making for the reasons Dr. Middleman outlined. This is a cleaner and easier approach. Speaking for clinicians in practice, she feels like it makes for better discussions with patients who might be hesitant. Otherwise, they just receive their vaccine as recommended. Regarding the pentavalent vaccine, she did not know personally about the financial cost-savings of holding that in clinics versus 2 products, but it is always desirable to reduce the number of vaccine vials in clinic refrigerators.

Dr. O'Leary (AAP) indicated that they are not as far along in their deliberations as SAHM and AAFP, but he thought there were a few data points that would be helpful. He did not know that the cost effectiveness-analyses would be as helpful in these distributions as in some others, given the current epidemiology. However, he would appreciate modeling that looks at cases and deaths averted based on the various scenarios. Options 3 or 4 seemed to align with the current epidemiology, but he understands the concerns about the potential impact that vaccination at 11─12 years of age has had in terms of disease averted or carriage. The other data he thinks would be helpful is adolescent visits. One of the reasons to vaccinate at the younger ages is that adolescents tend to present to the office more. However, those visits have changed over the years in terms of how often people seek well childcare, sports physicals, and so forth. Better understanding visits among adolescents and the older age groups would help inform decision-making.

Dr. Long emphasized that these are very difficult decisions. While ACIP is reluctant to take away vaccine recommendation, the epidemiology of meningococcal disease has done nothing but decrease since any of these recommendations were made. She does not think it is as clear as it may seem and perhaps there are new data that suggest the vaccine program has not had anything to do with the epidemiology. The epidemiology of this disease is more behavior-associated and may be related to smoking and the epidemiology of decreasing cases due to smoking cessation in public places in this country. Smoking also irritates mucous membranes. There was a wonderful article from Atlanta about bar patronage and meningococcal disease in terms of smoke and alcohol and not protecting oneself while under the influence of alcohol. While she did not know any of these things for sure, she is concerned that the idea that college is ideal may not address the problem as it is not limited to college students. She worries about the data pertaining to who non-college students are (e.g., inner city, overcrowded, smoking, alcohol-using youth), and would be surprised if they have a lower risk of meningococcal disease. While she is somewhat against the risk-based recommendation, she also does not think the epidemiology of the disease suggests that a dose should continue to be given to adolescents 11─12 years of age. ACIP has not seen cost-effectiveness models, but does not think it should be just about ICERs over what is currently done. The very short protection from meningococcal B vaccine is potentially not worth the effort and cost. Meningococcal disease cannot really be treated when it occurs. She cannot tell parents that their child who presents with meningococcemia is going to be alive in 12 hours because of the cytokine response and that it is one of the few diseases for which there are no treatments that greatly alter mortality once the disease is fully expressed. That is very difficult because the disease is so terrible, but it does not follow the usual rules of vaccination programs and protection of the public because it is such an uncommon disease now.

Dr. Brooks observed that in terms of looking at the data for ACWY, the incidence at ages 11─12 is very low. Incidence per 100,000 is 0.02 and there are perhaps 50 deaths a year, which is extremely low. Therefore, he would be comfortable with removing the dose at 11─12 years of age altogether. It is simply changing the schedule and removing a vaccine. Looking at the graph, serogroup B is basically the same. While there is a higher rate among college students, that may be behavioral-related as opposed to college-related as Dr. Long pointed out. Perhaps there should be another option that includes no dose at 11─12 years of age, harmonizes 16 years of age, and includes a MenB dose at 16 years of age and 17─18 years of age, with no risk-based recommendation at all.

Dr. Kotton said she thought she would favor Option 1. While it was hard to tell whether the low numbers at 11─12 years of age are due to the vaccination program that already is in place, she would favor moving a second dose of MenB closer to college age since it only lasts for about 1 to 2 years. While she thought it could be left as risk-based, that is hard in terms of equity. Those planning to go to college could change, and behavior is also a factor in that age group.

CDR Grimes (HRSA) said he also would favor Option 1, especially in the setting of the highest number of cases since 2014. Understandably, it is in a very young age group. Nonetheless, he did not think now would be the time to reduce vaccination for severe disease in a population that overall has done well with vaccination. He noted that a criterion for coverage under the Vaccine Injury Compensation Program (VICP) is a routine administration recommendation. Currently, the excise tax language says, “any meningococcal vaccine.” Therefore, the MenB vaccines would continue to be covered.

Dr. Loehr indicated that his personal opinion, which he emphasized was separate from his work group Chair opinion, was that he will never vote for routine recommendation for MenB because the cost-effectiveness is too high and the duration is too short. He is very comfortable removing the dose at 11─12 years of age.

Dr. Schillie next discussed the TOR for the GSK pentavalent MenABCWY vaccine. There are 2 new MenABCWY vaccines, 1 manufactured by Pfizer and 1 manufactured by GSK. The Pfizer vaccine, PENBRAYA™, is licensed and ACIP voted on its use during the October 2023 meeting. The GSK vaccine is currently in clinical trials. Each vaccine is a combination of an existing MenACWY vaccine and an existing MenB vaccine. The work group has previously assessed the Pfizer vaccine and will assess the GSK vaccine separately in the coming months. Notably, there is a lack of data directly comparing these 2 vaccines.

For the Pfizer vaccine, the ACWY component is Nimenrix and the B component is TRUMEMBA®. For the GSK vaccine, the ACWY component is MENVEO and the B component is BEXSARO. Both vaccines are intended to be administered as 2 doses separated by 6 months, and are indicated or anticipated to be indicated for persons 10─25 years of age. The clinical trial participants included both MenACWY primed naïve subjects, and MenB naïve subjects. Longer interval studies are planned for both vaccines. Note that the Pfizer pentavalent vaccine does not provide protection against gonorrhea, while the GSK pentavalent vaccine provides some protection against gonorrhea.

The policy questions for GSK's pentavalent vaccine mirror those previously used for the Pfizer vaccine, and are as follows:

- ❑ Should the pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines at the same visit? For example, 16-year-olds.

- ❑ Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only? For example, 11–12-year-olds.

- ❑ Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only? For example, during a serogroup B outbreak.

PNEUMOCOCCAL VACCINES

Dr. Jamie Loehr, Chair of the ACIP Pneumococcal Vaccines Work Group, introduced the pneumococcal vaccines session. The incidence of invasive pneumococcal disease (IPD) decreased in the early 2020s, reaching a fairly low level around 2015. While IPD incidence decreased to a historically low level during the COVID-19 pandemic, it recently started returning to a pre-COVID level. As a reminder of what has been done over the last few years, ACIP has recommended PCV15 and PCV20 vaccines for adults and later for children. In between, the committee approved PCV20 vaccine with an expanded indication for adults who previously received PCV13. There are 2 24-valent vaccines in clinical development that include an additional 4 serotypes, GSK's Pn-MAPS24 and Vaxcyte's VAX-24 vaccine. The focus of this session was on Merck's 21-valent V116 vaccine (PCV21). There was a significant change in the serotypes in V116. There are approximately 10 serotypes in PCV20 that are not in PCV21, and 9 serotypes in PCV21 that are not in PCV20. V116 includes a completely different set of serotypes versus the addition of serotypes to an already established vaccine. There are 2 additional pneumococcal vaccines under development, Iventprise's IVT PCV-25 and Vaxcyte's VAX-31. IVT PCV-25 is a 25-valent pneumococcal vaccine candidate that has completed a Phase 2 dose ranging study in young adults. VAX-31 is a 31-valent vaccine that has completed enrollment of Phase 1/2 study in adults ≥50 years of age.

As a reminder, the following groups are currently recommended by the ACIP to receive a dose of PCV:

- ❑ Adults ≥65 years of age who have not received a PCV1 vaccine
- ❑ Adults 19–64 years of age with certain underlying conditions or risk factors who have not received a PCV1
- ❑ Certain adults who have received PCV13 but have not received PCV20

A key factor in the decision-making for the work group is that adults who have a risk-based vaccine recommendation have lower vaccine coverage compared to those with an age-based recommendation. Coverage of ≥1 dose of any pneumococcal vaccine among adults 19–64 years of age with a risk-based indication is 22.2% and among adults ≥65 years of age is 65.8%.

The 3 policy questions currently being considered by the work group are:

1. Should PCV21 be recommended for US adults aged ≥19 years who currently have a recommendation to receive a PCV? This question includes the following:
   - Adults ≥65 years of age who have never received a PCV
   - US adults 19–64 years of age with a risk condition who have never received a PCV
   - US adults ≥19 years of age who have received a PCV (i.e., PCV7, PCV13, or PCV15), but have not completed the recommended series

2. Should PCV21 be recommended for US adults aged 50–64 years who currently do not have a risk-based pneumococcal vaccine indication?

3. Should PCV21 be recommended for U.S. adults aged 19–49 years who currently do not have a risk-based pneumococcal vaccine indication?

The committee was asked to provide feedback on the policy questions being considered by the work group and advise the work group of additional data that would be helpful to inform the discussions on PCV21 use in adults.

Mr. Ryan Gierke (CDC/NCIRD) discussed the current epidemiology of pneumococcal disease among adults in the US. Pneumococcus is transmitted through airborne droplets from person-to-person. It can colonize the nasopharynx and can then spread locally to cause otitis media or sinusitis. It also can be aspirated and cause pneumonia in the lungs. Pneumococcus also can invade the bloodstream and cause septicemia. These different infections can be characterized into noninvasive disease and invasive disease. IPD is the less frequent but more severe form of this illness, and is defined as isolation of pneumococcus from a normally sterile site.

Based on PCV15 and PCV20 coverage among Medicare Part A/B beneficiaries ≥65 years of age between October 1, 2021 and December 31, 2023, PCV20 coverage was 12% among adults ≥65 years of age, with a range of 9% among adults ≥85 years of age to 25% among adults ≥65 years of age. Only 0.2% of adults ≥65 years of age received PCV15, with less than 1% coverage across all ages. Looking at National Health Interview Survey (NHIS) data of the estimated proportion of adults who ever received any pneumococcal vaccination from 2021, 65% of adults ≥65 years of age have received a pneumococcal vaccine. Only 22% of adults 19–64 years of age with a risk-based indication have received a pneumococcal vaccine. Broken down by race among adults 19–64 years of age, Hispanics (19%) and Asians (16.9%) had significantly lower coverage compared to whites (23.3%) who had the highest rates of vaccination. Among adults, pneumococcal pneumonia is the most common form of pneumococcal disease. As mentioned, IPD is less frequent but more severe. In 2018 and 2019, the case fatality ratio (CFR) of IPD among adults ≥65 years of age was 14%.

Data on invasive pneumococcal disease are obtained from the Active Bacterial Core Surveillance System (ABCs), which provides population-based surveillance in 10 sites across the US. Cases are defined as pneumococcus isolated from a normally sterile site in residents of the 10 surveillance areas. Isolates are serotyped at reference laboratories using whole-genome sequencing (WGS), Quellung, or polymerase chain reaction (PCR). US Census Bureau estimates were used as denominators to calculate the incidence rates for both overall and serotype-specific IPD, and are presented as cases per 100,000 population.

During the period 2007—2022, adults ≥65 years of age had the highest rates of disease, followed by adults 50—64 years of age, then children <5 years of age. Adults 19—49 years of age had the lowest rates of disease among the age groups in this analysis. After the introduction of PCV13 in children in 2010, rates of IPD in children <5 years of age declined sharply. Rates of IPD also declined in all adult age groups due to the indirect effects of vaccinating children. These declines plateaued around 2014 and remained relatively stable through 2019. No additional declines in IPD were observed after PCV13 was recommended for adults ≥65 years of age in late 2024. Although during the 2022 COVID-19 pandemic rates of IPD declined sharply in all age groups to historic lows, they rebounded in 2021 and 2022. Among children <5 years of age and adults 19—49 years of age, rates had returned to pre-pandemic levels by the end of 2022. Additionally, PCV15 and PCV20 were recommended for adults in late 2021 and PCV15 was recommended for children in 2022. Among adult IPD cases, 82% to 87% had at least 1 risk-based indication for pneumococcal vaccination. The proportion of persons with risk-based indications increased slightly with age.

PCV20 contains 10 serotypes that are not included in PCV21 (1, 4, 5, 6B, 9V, 14, 18C, 19F, 23F, 15B). These are referred to as “PCV20 non-PCV21.” PCV20 contains 10 serotypes that are also included in PCV21 (3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, +6C). These are referred to as “PCV20 and PCV21.” This also includes 6C due to cross-protection from the 6A antigen included in the vaccines. PCV21 contains 11 serotypes not included in PCV20 (9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, 35B), which are referred to as “PCV21 non-PCV20.”

In terms of incidence rates of IPD among adults 19—64 years of age by vaccine type from 2011—2022, rates of IPD caused by PCV20, PCV21, PCV20, non-PCV20 serotypes all remained relatively stable in adults 19-49 years of age and 50-64 years of age during the years preceding the pandemic (2014—2019). Although the rates in these vaccine types declined during the pandemic, they began returning to pre-pandemic rates in both age groups in 2022. Notably, the rates of IPD caused by PCV20 non-PCV21 serotypes were relatively small. However, they have been creeping up in the years following the pandemic. In 2022, the rates were higher in adults 19-49 years of age and 50-64 years of age than they were in their pre-pandemic levels. Serotypes 4 and 19F made up a large proportion of this serotype grouping. These trends will continue to be monitored.

Looking at IPD incidence rates among adults ≥65 years of age by vaccine type from the same 2011—2022 data, similar trends were observed to trends among younger adults, with stable rates from 2014—2019. However, an increase was not seen in rates of PCV20 non-PCV21 serotypes in older adults. Regarding the proportion of IPD by each vaccine type among adults with a pneumococcal vaccine indication from 2018—2022, adults 19—64 years of age with a risk-based indication and ≥65 years of age, PCV20 non-PCV21 accounted for 7% to 13% of IPD. PCV20 and PCV21 accounted for 45% to 47%, while PCV21 non-PCV20 accounted for 36% to 38%. Non-vaccine types (NVT) accounted for 6% to 8% of IPD. PCV20 provided 54% to 58% serotype coverage among adults with a vaccination indication, while PCV21 provided 81% to 85% serotype coverage.

In conclusion, rates of IPD declined during the pandemic but are now returning to pre-pandemic levels. Over 80% of adult IPD cases have a risk-based indication for vaccination. PCV21 has greater coverage of the serotypes causing IPD in adults compared with PCV20. PCV20 covers 54% to 58% of IPD in adults with a vaccine indication, while PCV21 covers 81% to 84%.

Dr. Wesley H. Self (Vanderbilt University Medical Center) presented interim results from the PNEUMO study sponsored by Merck. PNEUMO study is an epidemiologic study that has been ongoing since 2018 that is enrolling adults at 3 hospitals across Tennessee and Georgia who have community-acquired pneumonia (CAP). The design in the US is to enroll patients prospectively who present to the hospital with radiographically-confirmed pneumonia. The goals are to estimate pneumococcal pneumonia incidence and serotype prevalence using Merck PCV15 and a V116 serotype-specific urinary antigen detection (SSUAD) assay, with longitudinal evaluation of functional status, QALY, and cost. This presentation focused on the prevalence of serotypes in the study's hospitalized CAP population.

The enrollment period started in September 2018 and is ongoing. This presentation focused on results through 2022 from the enrolling sites at Vanderbilt in Nashville, Tennessee and 2 hospitals affiliated with the Emory University system in Atlanta, Georgia.

After adults hospitalized with CAP are enrolled in the study, they undergo systematic testing for *Streptococcus pneumoniae*. Urine is collected within 72 hours of hospital admission and undergoes 2 sets of tests. The first is the BinaxNOW™ commercially available pneumococcal antigen test, which is run locally by the research team immediately after enrollment. The second is a series of SSUAD assays run on aliquots sent to Merck Laboratories to test for 30 serotypes (1, 3, 4, 5, 6A*, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15C#, 16F, 17F, 18C, 19A, 19F, 20A, 22F, 23A, 23B, 23F, 24F, 31, 33F, 35B). Notably, this contains all of the serotypes in PCV15, PCV20, and V116 with the exception of serotype 15B that is in PCV20. Additionally, the results are recorded of all of the bacterial cultures that are obtained in the hospital from these patients. These are split into sterile site cultures (blood, pleural fluid, BAL fluid, CSF, synovial fluid) and non-sterile site cultures (high-quality respiratory samples >25 WBC <10 epi, sputum, endotracheal aspirate).

During the period 2018–2022, about half of the enrollment period occurred before COVID-19 onset in the US and about half occurred during the COVID-19 pandemic. The 3 sites screened about 5,300 patients and enrolled about 3,200 patients who met the eligibility criteria. The analytical population was 2,917 pneumonia patients in the hospital from whom a urine sample was collected. In terms of pneumococcal detection, 12.1% of all of the hospitalized CAP patients had pneumococcus detected. Therefore, a prevalence of 12.1% is reported for pneumococcal disease among all-cause hospitalized CAP adults. Among patients with pneumococcal pneumonia, 51% had invasive disease and 301 had non-invasive disease. Thus, about 85% of pneumococcal pneumonia in this cohort was non-invasive.

To highlight some of the patient characteristics for this cohort, the age range for the pneumococcal and non-pneumococcal groups were about the same, with a median age of 60 years. A higher proportion of pneumococcal pneumonia patients were Black at 41%. A higher proportion in the pneumococcal groups smoked, drank alcohol, and interacted with a young child regularly. There was a higher prevalence of COPD and a lower prevalence of obesity in the pneumococcal group compared to the non-pneumococcal group. About half of the cohort was enrolled before onset of COVID-19 and about two-thirds of the pneumococcal cases were enrolled before onset of COVID-19, which is consistent with the declines seen in pneumococcal incidence and prevalence during the pandemic.

In terms of testing for pneumococcus, there were 352 patients with ≥1 positive pneumococcal tests. Of these, 283 patients who were positive for pneumococcus were detected with the SSUAD assay. The SSUAD was the only positive test in 57% of those with pneumococcus detected. BinaxNOW™ detected 125 positive patients and cultures detected 56 positive patients. In terms of what was found about pneumococcal serotype distribution, 316 serotypes were detected by SSUAD (denominator) among 283 unique patients. Serotype 3 was the most prevalent and was detected in 14.6% of all serotypes. A serotype included in V116 was found in 9.3% of patients and 4.1% had a serotype unique to V116 that is not in the 2 currently licensed pneumococcal vaccines. The most common detected serotypes that were unique to V116 were 35B, 9N, 23A, and 23B. Testing was notT done for serotype 15B, which has been fairly uncommon in prior studies. Types included in PCV20 (excluding 15B, which was not tested for) were found in 6.7% of patients and in PCV15 in 5.8%.

Dr. Daley requested additional information about the SSUAD test characteristics in terms of whether they differ by serotype, which would be more influential than if they do not. He was still trying to interpret what is known about whether this was pneumococcal disease and what the serotype was based on the results of the urine test.

Dr. Self explained that these are individual antigen tests looking for polysaccharide in the urine, similar to the set of urine antigen tests developed by Pfizer to accompany PCV13. These are developed and validated using urine from healthy adults, as well as adults with known positive blood cultures for specific serotypes of pneumococcus. The threshold to determine a positive antigen test is serotype-specific. That is calibrated against known positives and negatives. Historically, the BinaxNOW™ urinary antigen tests greatly increased pneumococcal yield compared to blood culture. The SSUAD assays developed previously by Pfizer and now by Merck appear to detect more cases of pneumococcal disease than both BinaxNOW™ and culture. When a test appears to have increased analytical sensitivity compared to historical criterion standards, understanding whether these are false positives or true positives is critically important. The distribution of serotypes by both of the previously developed Pfizer tests and the more recently developed Merck tests are quite similar in the literature, which gives him more confidence that the positives being identified are true positives.

Dr. Thorsten Verch, Senior Director of Vaccine Immunogenicity at Merck, added that the SSUAD detects serotype-specific polysaccharides or the fragments thereof, whereas BinaxNOW™ detects the common polysaccharides across all pneumococci. The polysaccharides in urine are very different from the ones that are on the bacterial surface. For those reasons, there is not total overlap that might be expected theoretically. As Dr. Self pointed out, this type of Venn diagram distribution is very similar to other SSUAD tests versus BinaxNOW™ in the literature.

Dr. Kotton noted that the urinary antigen for Legionella can be positive for many months after infection and she wondered whether that is true in this setting.

Dr. Verch confirmed that the urine antigen assay does remain positive for a while longer, though how much longer is not known. It is a matter of how long polysaccharides are present in the body.

Dr. Self added that these particular patients were ill with pneumonia, but the point is well-taken that positive tests could linger after the acute illness.

Dr. Chen asked whether the serotypes had been examined for the invasive cases and, if so, whether they seemed to align with the epidemiological data that Mr. Gierke presented for the surveillance data that have been seen nationally. He also noted that the diagram of enrolled patients in Dr. Self's presentation showed 51 invasive cases, while the Venn diagram indicated that 56 patients had positive cultures, and requested clarity regarding whether there were 56 or 51 invasive cases.

Dr. Self confirmed that Dr. Chen's assumptions were correct. There were 56 positives with any positive culture, which included some respiratory cultures that met quality criteria (e.g., sputum cultures that meet more than 25 white cells per low-powered film). There were 51 *S. pneumoniae* culture positive from normally sterile sites (e.g., positive blood cultures, synovial, or CSF). In terms of the question regarding analysis of the subset with invasive disease, 41 patients had a serotype identified via blood culture that was positive for *Streptococcus pneumoniae.* Of the 41 that had a serotype tested for in the 30-serotype set of SSUAD, 31 had the corresponding serotype in the urine that was found by blood culture. The distribution of serotypes in the invasive disease in the PNEUMO study match the CDC data quite well.

Dr. Heather Platt (Merck) presented key results from the Phase 3 Clinical Development Program for V116. The direct impact of pneumococcal vaccination of children is substantial, though more modest decreases are observed in adults due to indirect impact. The burden of disease in adults is now higher than it is in children, with approximately 24 cases per 100,000 in adults compared to 7 cases in children. Even with the indirect impact from childhood vaccination, there remains an unmet medical need in adults. V116 is an adult-specific vaccine proposed to meet this need and is intended to complement pediatric immunization programs. V116 contains 21 pneumococcal serotypes conjugated to CRM197, formulated without an adjuvant, and supplied as a single-dose 0.5 mL pre-filled syringe. In the US in 2019, the serotypes in V116 accounted for approximately 85% of IPD, with the 8 unique serotypes accounting for approximately 30% of IPD in adults ≥65 years of age. V116 is currently under priority review by the FDA for the prevention of IPD and pneumonia in adults ≥18 years of age, with a target action date of June 17, 2024. The serotypes in V116 are responsible for the majority of residual IPD in adults, accounting for approximately 83% and 85% of IPD cases in adults 50─64 years of age and ≥65 years of age, respectively.

The Phase 3 Clinical Development Program is comprised of 7 studies, 6 in adults and 1 in pediatrics, and is focused on enrolling participants at risk for pneumococcal disease. The pediatric study is evaluating children 2─18 years of age with increased risk conditions who have already completed a primary pneumococcal vaccine regimen. The 4 studies in the V116 BLA submission represent a broad and diverse patient population. The studies enrolled participants from 21 countries representing 5 continents. A third of the participants are ≥65 years of age and had one or more chronic risk condition, and 18% had previously received a pneumococcal vaccine. Functional OPA responses supported the primary immunogenicity objectives. Additional OPA and IgG endpoints supported the secondary objectives. The primary safety objective is the same for all of the Phase 3 studies and includes the evaluation of solicited injection site and systemic events and vaccine-related SAEs.

V116-003, Protocol 3, is a Phase 3 randomized, double-blind study designed to evaluate the safety, tolerability, and immunogenicity of V116 in pneumococcal vaccine-naïve adults. Over 2,600 participants were enrolled in parallel cohorts. In Cohort 1, participants ≥50 years of age were stratified by age and randomized 1:1 to receive either V116 or PCV20. In Cohort 2, participants 18─49 years of age were randomized 2:1 to receive V116 or PCV20. Immunogenicity samples were drawn at baseline and 30 days post-vaccination, and an electronic vaccine report card was used to record solicited events through day 5 post-vaccination. SAEs were reported through the duration of the study. The primary immunogenicity objectives were evaluated by cohort, with statistical testing for non-inferiority and superiority in Cohort 1. In Cohort 2, immunobridging was evaluated in adults 18─years of age and adults 50─64 years. As mentioned, the primary safety objective is the same for all of the Phase 3 studies. In each cohort, baseline characteristics were balanced between the treatment groups. In Cohort 1, approximately 50% of the participants were ≥65 years of age. Specifically in the US, there was focused enrollment on groups historically underrepresented in clinical studies. In Cohort 1 in the US, approximately 18% of participants were Black or African American.

In terms of the immunogenicity results, in adults ≥50 years of age, V116 was non-inferior to PCV20 for all 10 of the common serotypes based on the lower bound of the 95% confidence interval of the OPA GMT ratio being greater than 0.5. In adults ≥50 years of age, V116 was superior to PCV20 for 10 of 11 serotypes unique to V116. This was based on the lower bound of the 95% confidence interval of the OPA GMT ratio being greater than 2.0. For serotype 15C, the lower bound was 1.77 and did not meet the pre-specified criteria, likely based on cross-reactive immune responses to serotype 15B in the comparator. In adults ≥50 years of age in Cohort 1, V116 was superior to PCV20 for 10 of 11 serotypes. This was based on the percentage of participants with a 4-fold rise or greater in OPA responses, where the lower bound of the 95% confidence interval of the difference between the groups had to be greater than 10 percentage points. Again, for serotype 15C, 83.4% of participants in the V116 group had a 4-fold rise in OPA responses. This is the second highest 4-fold rise of the unique serotypes. V116 elicits robust antibody responses to serotype 15B. These responses are cross-reactive to serotype 15C, which is included in the vaccine. In Cohort 2, immune responses in V116 in participants 18─49 years of age immunobridged to participants 50─64 years of age. Based on the GMT ratio, where the lower bound of the confidence interval was greater than 0.5 for all serotypes in the vaccine. Overall, in V116-003, IgG immune responses were consistent with the OPA responses across the endpoints assessed.

V116-006, Protocol 6, evaluated the safety, tolerability, and immunogenicity in pneumococcal vaccine-experienced adults ≥50 years of age. Approximately 700 participants were enrolled into 1 of 3 cohorts based on the pneumococcal vaccine they received at least 1 year prior to enrollment. In Cohort 1, participants who were previously vaccinated with PPSV23 were randomized in a 2:1 ratio to receive either V116 or PCV15. In Cohort 2, participants who were previously vaccinated with PCV13 were randomized in a 2:1 ratio to receive either V116 or PPSV23. In Cohort 3, participants were previously vaccinated with another pneumococcal vaccine or vaccines, and were allocated to receive open-label V116. The primary immunogenicity objective was to evaluate the serotype-specific OPA responses 30 days after vaccination. Safety was consistent across the Phase 3 studies. Enrollment was balanced in each cohort and reflected the pneumococcal vaccination history, with a higher percentage of participants with a longer time since last vaccination in Cohort 1, likely reflecting the longer time that PPSV23 has been in the recommendations.

In Cohort 1, immune responses were generally comparable between participants who received V116 and PCV15 for common serotypes and higher for serotypes unique to V116. In Cohort 2, immune responses were generally comparable between participants who received V116 and PPSV23 and higher for serotypes unique to V116. V116 was immunogenic in individuals who previously received another pneumococcal vaccine or vaccines. The immune responses to serotype 3 were robust across the 3 cohorts.

To review a summary of an integrated analysis of safety, V116 is well-tolerated in adults ≥18 years of age with a safety profile comparable to currently licensed pneumococcal vaccines. The integrated summary of safety includes participants from 4 Phase 3 studies of participants who received V116 and the control group, which includes participants who received an active comparator of either PCV15, PCV20, or PPSV23. Frequencies of AEs were comparable across the categories of AEs, vaccine-related AEs, and SAEs. There were 2 vaccine-related SAEs across the 4 studies. No deaths were assessed to be vaccine-related. The frequencies of solicited AEs were comparable in the V116 and comparator groups. The majority of solicited events were mild or moderate in intensity and ≤3 days in duration.

In adults ≥18 years of age living with HIV, V116 elicited comparable immune responses to PCV15 plus PPSV23 and higher immune responses for unique serotypes. In participants ≥50 years of age, including both vaccine-naïve and vaccine-experienced adults, V116 elicited robust immune responses when administered concomitantly with influenza vaccine. This met non-inferiority for the concomitant group and the sequential group for 20 of 21 serotypes based on the lower bound of the OPA-GMT ratio being >0.5. In V116-005, QIV administered concomitantly was non-inferior to QIV administered sequentially for 3 of the 4 strains. This was based on the lower bound of the confidence interval of the HAI titers being greater than 0.67. In the lot consistency study, V116-004, immune responses were equivalent across 3 manufacturing lots.

In conclusion, in adults ≥18 years of age who are pneumococcal vaccine-naïve and vaccine-experienced with and without risk conditions, V116 elicits robust immune responses to all 21 serotypes contained in the vaccine. V116 is non-inferior to PCV20 for all common serotypes and superior to PCV20 for 10 of the 11 serotypes unique to V116. V116 is immunogenic in pneumococcal vaccine-experienced adults regardless of the prior vaccine received and is immunogenic when administered concomitantly with inactivated influenza vaccine. V116 is well-tolerated and has a safety profile generally comparable to currently licensed pneumococcal vaccines. V116 is the first adult-specific PCV with the potential for broad public health impact through the prevention of invasive disease and pneumonia due to *streptococcus pneumoniae*.

Dr. Brooks asked which of the influenza strains did not achieve the desired titers.

Dr. Platt replied that H3N2 did not meet the lower bound of the 95% confidence interval, which was exactly 0.67.

Dr. Pedro L. Moro (CDC/NCEZID) described the post-licensure safety surveillance of 20-valent PCV vaccine among US adults in VAERS. In pre-licensure clinical trials, PCV20 was found to be very safe. The serious AEs were balanced among vaccinees and the placebo. No cases of GBS were observed. In June 2021, PCV20 was approved by the FDA. In October 2021, ACIP recommended this vaccine for use in adults ≥65 years of age and adults 19─64 years of age.

For this presentation, the VAERS database was searched for reports of adverse events following PCV20 during the period October 21, 2021 through December 31, 2023 for adults ≥19 years of age. The Brighton Collaboration criteria definition was used for classification of cases of Guillain-Barré syndrome (GBS). Reporting rates were calculated using doses distributed of PCV20. FDA conducted Empirical Bayesian datamining to detect disproportional reporting.

In terms of the characteristics of the reports received after PCV20, a total 2,393 were received in VAERS. Most of these were in adults ≥19 years of age (N=1,976). About 6% of the reports were serious. Regarding the most common signs and symptoms in reports to VAERS following PCV20 in adults 19─64 years of age, the most common AE non-serious reports were injection site or systemic reactions. The most common SAEs were systemic reactions. The most common signs and symptoms in reports to VAERS following PCV20 in persons ≥60 years of age for non-serious reports were local or systemic reactions. The most common SAEs were systemic reactions, with GBS being the 4th most common condition being reported. Empirical Bayesian data mining as of January 26, 2024 found disproportionate reporting for the preferred term Guillain Barré Syndrome" among the serious reports.

Reports to VAERS of GBS after PCV20 vaccination among adults aged ≥19 years as of December 31, 2023 were reviewed. There were 20 reports of GBS after PCV20. Of these, 5 were excluded based upon chart review, 4 are still under review awaiting medical records, and 11 were verified reports of GBS. The median age was 66 years (range 46-79 years), the median time to onset was 14 days (range 0-23 days). There were 4 males and 7 females. Other vaccines were given during the same visit to 5 of the 11, including 2 RZV (Shingrix); 1 Fluad quadrivalent; 1 bivalent mRNA COVID-19 (Pfizer), HD-IIV4, RSV (AREXVY); and 1 Tdap (Boostrix). The reporting rate for GBS after PCV20 was 0.5 cases per million doses distributed, or 0.9 cases per 100,000 person-years. This is below the background rate of 1.72 cases per 100,000 person-years. It is important to keep in mind that this should not be taken as doses administered, because it is unknown how many of the doses distributed were actually administered to persons or the age groups.

In summary, VAERS received 1,976 reports after PCV20 in adults during the study period. Most (~94%) of the reports were non-serious. The most commonly reported AEs were injection site and systemic reactions, which is consistent with findings from pre-licensure studies. Disproportionate reporting for GBS was identified in VAERS after PCV20 vaccine, with 11 verified cases in adults. Potential safety signals detected in VAERS need to be evaluated in more robust population-based active systems, such as the VSD or CMS. Separate studies are currently in progress in the VSD and in the CMS to assess PCV20 vaccine safety. CDC and FDA will continue to monitor the safety of PCV20.

Dr. Richard Forshee (FDA/CBER) described an FDA CBER safety assessment of PCV20 that was funded by the FDA and conducted with FDA's colleagues at CMS and their contractor, Acumen, LLC. For sequential monitoring active surveillance for the PCV20 vaccine, a number of outcomes were evaluated: acute myocardial infarction; myocarditis/pericarditis; anaphylaxis; atrial fibrillation; Bell's palsy; cardiomyopathy; heart failure; cellulitis and infection; cholecystitis or cholelithiasis; Guillain-Barré syndrome; immune thrombocytopenia; thrombocytopenia; and transient ischemic attack.

Dr. Forshee presented the concurrent comparator cohort design that is being used for near real-time sequential analysis. The data source is Medicare SSD data. The population is Medicare FFS beneficiaries ≥65 years of age or older receiving 1 dose of PCV15 or PCV20 on or after the licensing date for the product. The 12 pre-specified health outcomes were identified by claims algorithms and monitored within the follow-up window for each vaccinated beneficiary. For the statistical analyses, a Bayesian approach was used to estimate the association between exposure to PCV20 and the outcomes listed. Bayesian Poisson Regression was used to estimate the posterior distribution of the IRR between pre-specified post-vaccination risk and comparison windows for each outcome. The assumption was made that very little is known about the association between the exposure to PCV20 and the outcomes. The safety signal was assessed by establishing 2 thresholds to evaluate whether the 95% Credible Interval exceeded 1 (Weak Signal) or the 98% Credible Interval exceeded 1 (Strong Signal).

As mentioned earlier, there has been more uptake of PCV20 than PCV15. As of the November 30, 2023 data cut for this study, there were than 2.8 million doses of PCV20 in the database. However, only about 53,000 were PCV15 doses. Therefore, a sequential analysis was done only for PCV20. Dr. Foshee showed tables provided the descriptive statistics for the PCV20 vaccinees and the outcome counts, incidence rates for the PCV20 vaccinated population, and the IRR between risk and comparison windows. In some cases, the cell size had to be suppressed because of small numbers in order to protect any possible personal information from being inadvertently disclosed. For some of the outcomes, a relatively small number of outcomes have been observed. For GBS, only 29 outcomes had been observed at this time of this analysis. While that is good news for public health, it means that estimates are not particularly precise at this point. As of November 30, 2023, no statistically significant elevated risks had been identified. For GBS, the IRR was 2.19 with relatively large confidence intervals.

There are some limitations for this type of sequential monitoring. Statistically significant results may appear and disappear from month-to-month due to the use of Bayesian methods. Events were not chart-confirmed and the PPV for some outcomes is likely low. For instance, the PPV for Bell's Palsy was 12.66% and the PPV for ITP was 4.00% in a recent study. Residual confounding may still exist given the limited number of variables being adjusted in the regression model. There is large uncertainty of IRRs for certain outcomes due to the small number of events and wide credible intervals.

Active monitoring and sequential monitoring will continue monthly. An end of surveillance analysis may be performed using the self-controlled case series (SCCS) method for each outcome where there is sufficient sample size for a powered analysis.

In summary, there was no GBS signal in the clinical trials. As Dr. Moro described, there has not been a GBS signal for PCV20 in VAERS. There also has not been a GBS signal in Medicare sequential monitoring, but that is ongoing. There is still significant uncertainty because of the small number of cases observed, and there are limitations in both the VAERS and Medicare studies.

Dr. Miwako Kobayashi (CDC/NCIRD) presented preliminary work group interpretations of EtR and next steps.

Beginning with the *public health problem* regarding whether pneumococcal disease is of public health importance, prior to the COVID-19 pandemic, there were more than 100,000 non-invasive pneumococcal pneumonia hospitalizations and more than 30,000 IPD cases with 3,000 IPD deaths every year among adults of all age groups. Risk of disease and severe outcomes is higher among older adults and adults with certain risk conditions. In a study of adults aged 65 years and older hospitalized with community-acquired pneumonia, which was not limited to pneumococcal pneumonia, over one-third of adults died within 1 year. More than 80% of IPD cases occurred among adults who currently have risk-based vaccine indications. IPD incidence reached a historically low level early in the COVID-19 pandemic, but is increasing toward pre-COVID levels. Around the same time, the new PCV15 and PCV20 vaccines were recommended for both adults and children. Disease caused by additional pneumococcal serotypes contained in these new vaccines is expected to decrease due to both direct effects from vaccinating adults and indirect effects from vaccinating children. However, 30 to 40% of adult IPD cases are caused by serotypes that are not contained in currently available pneumococcal vaccines. The additional serotypes contained in PCV21 cover most of them.

For adults who are currently recommended to receive a PCV, the work group interpretation was that “yes” pneumococcal disease is of public health importance. Some members chose “probably yes” due to the decrease in pneumococcal disease burden compared to the past. Despite the increase in disease incidence in recent years, the trend is expected to stabilize at pre-pandemic levels. For adults 50─64 years of age who currently do not have a risk-based indication, the work group interpretation was “probably yes” since pneumococcal disease incidence in this age group overall is lower compared with adults ≥65 years of age. For adults 19─49 years of age who currently do not have a risk-based vaccine indication, Group 3, the work group members’ opinions were split. The most common responses were “no,” “probably no,” and “don't know.” “No and “probably no” combined were selected by half of the members. The primary reason expressed by the work group members is because of the even lower disease incidence in this age group compared with adults 50─64 years of age.

In terms of how substantial the desirable anticipated effects of PCV21 vaccination are for adults currently recommended to receive PCV, the work group interpretation was split between moderate and large. For adults aged 50–64 years with no risk-based indication, the work group interpretation was split between small and moderate. For adults aged 19–49 years with no risk-based indication, the work group interpretation was split between minimal and small.

To summarize the work group discussions, members who are in favor of PCV21 use pointed out that based on available data, there are no concerns about the risks outweighing the benefits of PCV21 vaccination. For adults who are currently recommended to receive a PCV, PCV21 provides broader serotype coverage than any of the currently recommended vaccines. Some saw the benefits of PCV21 administration by lowering the age-based recommendation to 50 years of age, because a more robust immune response can be expected by administrating PCV21 before 65 years of age and before a portion of that population develops an immunocompromising condition. Some expressed concerns or uncertainties about lowering the age-based recommendation, especially to 19 years of age. The degree of benefits for adults who currently do not have vaccine recommendations is uncertain. The epidemiology does not support expanding the vaccine indications to younger adults without a risk-based indication. Younger adults in their early 20s would have received a PCV as a child, so the benefits of PCV administration to this group are uncertain. The opportunity could be missed to provide protection against disease later in life if the age-based recommendation is lowered. There are limited data on duration of protection or protection against disease from multiple PCV doses in adults. Some members expressed the need to review cost-effectiveness analysis data.

Transitioning to the *equity* domain and the question pertaining to what the impact would be of recommending PCV21 use for adults on health equity, racial disparities in IPD incidence have existed. However, white non-Hispanic adults who generally have lower disease incidence have higher vaccine coverage compared with other race or ethnicity groups. After PCV13 use in children, disparities in IPD incidence in adults caused by serotypes contained in PCV13 decreased. Most of the remaining disparities are due to non-PCV13-type disease. However, increase in serotype 4, a serotype included in currently available pneumococcal vaccines but not in PCV21, has been reported in certain groups. An increase has been reported in serotype 4 IPD cases, especially in the Western US. The incidence was 100 to 300 times higher in people experiencing homelessness compared to those who are not. In Alaska, IPD incidence due to serotype 4 increased 88-fold in 2019─2020 compared with 2011─2018. The increase was notable, especially among the Alaska Native population.

Regarding what the impact would be of recommending PCV21 use for adults on health equity, for adults currently recommended to receive a PCV, the work group interpretation was "probably increased" equity. Additional serotype coverage by PCV21 is expected to reduce racial disparities in remaining pneumococcal disease burden. However, for adults who have already received a PCV, recommending a second PCV dose to complete the recommended vaccine series might magnify the underlying disparities in vaccine coverage. The work group interpretation also was "probably increased" for the other groups. The work group interpretation considered the possible implications of lowering the age-based vaccine recommendation. Some work group members believed that lowering the age threshold for the age-based recommendation is expected to improve vaccine coverage in adults who currently have risk-based vaccine indications in these groups and would be more equitable.

The next steps for the work group are to: 1) review findings from published and unpublished cost-effectiveness analyses on PCV21 use among adults; 2) review evidence and discuss interpretations of the remaining EtR domains (Values, Acceptability, Resource Use, and Feasibility); and 3) draft policy options for PCV21 use in US adults for consideration by the committee and for a potential vote during the June 2024 ACIP meeting. This will include considerations for expanding the current risk-based vaccine indications to include adults with chronic kidney disease who are not on maintenance dialysis.

Considering that additional pneumococcal vaccines for adults who are currently under investigation and may be approved in the near future, and that dynamic changes in pneumococcal disease incidence are anticipated post-COVID-19 and with increased uptake in PCV15 or PCV20 in children and adults, the work group requested feedback from ACIP on the policy questions being considered by the work group; what additional data would be helpful to inform the discussions on PCV21 use in adults; and what additional data would be needed to help inform the discussions on expanding the risk-based indications to include adults with chronic kidney disease.

Dr. Cineas asked whether there are additional data on adults experiencing homelessness in the Western US and adults in Alaska. She worries about creating a disparity by having a recommendation that might put them at higher risk and is concerned about 88-fold increase in IPD in that population.

Dr. Kobayashi responded that there have been clusters of serotype 4 IPD among people experiencing homelessness. While it is not known why exactly there is serotype 4, there are some hypotheses. There may be some low-level circulation in the community and these populations seem to be susceptible, or there might be introduction of a new strain of serotype 4 into certain pockets that impact people experiencing homelessness disproportionately. While there are still uncertainties, there are reports that are not limited to the US about clusters of serotype 4 IPD among people experiencing homelessness. Alaska Native populations tend to have higher pneumococcal disease incidence in general and tend to have some unique characteristics in serotype distribution. Similar hypotheses apply in that other serotypes have been observed to cause clusters in these populations. While there is not an exact answer as to why specifically, serotype 4 is observed to affect these populations disproportionately.

Dr. Kotton recognized that the work group was split, but she would hold off on vaccination adults 19–49 years of age until there are more robust data and a clear need. There is a lot of vaccine fatigue, so she suggested focusing on the higher yield populations. While the data shown are impressive in general, they should not overwhelm people. Perhaps the focus should be on the vaccines they really need and are not getting.

Dr. Daley said he thought this was a good approach that made sense in terms of the policy questions. He had a similar reaction to adults 19–49 years of age. Based on what he had seen so far, he would be reluctant to extend to that unless there is a strong case made. In terms of adults 50–64 years of age, he was trying to get a sense of the burden, disparities, cases averted and the trade off with the durability of the immune response in terms of whether ACIP feels like persons vaccinated in that age range are going to have a durable response or will need revaccination when they are older. He also has concerns about the complexity, which could create barriers that result in lower coverage.

Dr. Long said that while it was not the question they were addressing during this session, there are a few risks with PCV21. It covers more serotypes and is better matched to adults, it gives up multiple serotypes, one of which is serotype 4. What is occurring in Alaska with serotype 4 is striking and perhaps suggests that Alaska would have to be carved out. She recalled that non-inferiority and superiority aside, the GMT for PCV 20 what somewhat lower than PCV13 and seemed higher for PCV15. Now there is PCV21 that is not non-inferior, but is a little lower than PCV20.

Dr. Kobayashi said it does vary by serotype. For example, a trend was observed when looking more recently at PCV20 versus PCV13 in children of numerically lower immune responses overall in the shared serotypes between PCV13 and PCV20. That was not observed when PCV20 was compared to PCV21.

Dr. Platt added that Merck looked at the common serotypes that are in both PCV20 and PCV21 and used the accepted non-inferiority pre-specified criterion of the lower bound being greater than 0.5, acknowledging that there is a concern of looking at the immunogenicity as serotypes are added to conjugate vaccines. They observed that the non-inferiority criteria were met of the lower bound being greater than 0.5. However, the lower bound of the 95% confidence interval for the ratio was greater than 0.67 for all of the common serotypes. This should provide confidence in overall vaccine performance. In terms of the endpoints, the OPA and IgG responses also were consistent. They also acknowledge the need for effectiveness or efficacy data and plan to evaluate the effectiveness of V116 in a real-world study and will share more details with the work group and the larger committee shortly.

Dr. Loehr commented that it helped him to have the meningitis and the pneumococcal work groups back-to-back. The incidence is dramatically different. Meningitis is literally a one-in-a-million disease. Pneumococcal, even for the lowest group, was maybe 50-in-a-million and for adults ≥65 years of age was 170-in-a-million. That reminded him that sometimes when focusing so much on individual vaccines, they should consider the bigger picture and compare one vaccine versus another in terms of incidence and importance.

COMBINED DIPHTHERIA AND TETANUS TOXOIDS AND ACELLULAR PERTUSSIS, INACTIVATED POLIOVIRUS, HAEMOPHILUS INFLUENZAE TYPE B CONJUGATE, AND HEPATITIS B VACCINE (VAXELIS®)

Dr. Jamie Loehr, Chair of the ACIP Meningococcal Vaccines Work Group, introduced the session on the Combined Diphtheria and Tetanus Toxoids and Acellular Pertussis, Inactivated Poliovirus, *Haemophilus influenzae* Type B Conjugate, and Hepatitis B vaccine (e.g., VAXELIS®) among AI/AN populations.

He reminded the committee that PRP-OMP (PedvaxHIB®) is preferentially recommended for AI/AN infants. It provides a protective antibody response after the first dose. Historically, Hib meningitis peaked at an earlier age among AI/AN infants. VAXELIS® (DTaP-IPV-Hib-HepB) does not currently have a preferential recommendation for AI/AN infants because it contains PRP-OMP in a lower amount than PedvaxHIB® and post-dose 1 immunogenicity data were not previously available.

The policy question is, “Should VAXELIS® (DTaP-IPV-Hib-HepB) be included with PedvaxHIB® in the preferential recommendation for American Indian and Alaska Native (AI/AN) infants?” With that in mind, the work group reviewed the epidemiology of invasive HIB disease in AI/AN populations; reviewed the clinical trial data on a post-dose 1 immunogenicity of VAXELIS® versus PedvaxHIB®; and has been working on drafting a recommended policy based on GRADE and EtR, which will be coming up in the near future.

Dr. Jennifer Collins (CDC/NCIRD) provided background on invasive HIB disease and vaccination among AI/AN populations. *Haemophilus influenzae* are gram-negative bacilli. Often abbreviated as *H. flu* or just *Hi*, infections can range from mild to severe invasive disease. *Haemophilus influenzae* are classified as encapsulated or unencapsulated. Encapsulated or typable *Hi* have a polysaccharide capsule with 6 serotypes lettered A through F based on the particular polysaccharide antigens expressed. Unencapsulated *Hi* do not have a capsule. They cannot be serotyped, and therefore are also referred to as non-typable. *Haemophilus influenzae* serotype B, or HIB, is the most virulent and is the only type preventable through vaccination.

Before the introduction of effective vaccines, HIB was the leading cause of bacterial meningitis and other invasive bacterial disease in the US, primarily among children <5 years of age. Risk factors for invasive HIB disease in the pre-vaccine era include demographic factors such as male sex; AI/AN and Black races; social factors such as household crowding and large household size; and immunocompromising conditions (HIV infection, asplenia/sickle cell disease, IgG deficiency, early component complement deficiency, hematopoietic stem cell transplantation, chemotherapy). The most common clinical syndromes of invasive HIB disease in the post-vaccine era are bacteremic pneumonia, bacteremia without a focus, and meningitis. Epiglottitis was also one of the most common syndromes in the pre-vaccine era.

From 1980–2012, the estimated incidence of invasive HIB disease in children <5 years of age decreased dramatically after introduction of HIB vaccines. HIB polysaccharide conjugate vaccines remain the primary prevention strategy for HIB. These vaccines consist of capsular polysaccharide (PRP) conjugated to carrier proteins, either tetanus toxoid (PRP-T) or outer membrane protein of meningococcal serogroup B (PRP-OMP). They are highly immunogenic via activation of T-cell-dependent immunity. 95% of infants develop protective antibody levels after a primary series. However, they offer no cross-protection against non-B serotypes or non-typable *Hi*. The estimated clinical efficacy against HIB is 95% to 100%. Invasive HIB disease is uncommon in children who are fully vaccinated.

Current HIB vaccines licensed and available in the US are shown here and include 3 monovalent vaccines (PRP-OMP, PedvaxHIB®; PRP-T, ActHIB®; and PRP-T, Hiberix®) and 2 combination vaccines (DTaP-IPV/Hib, Pentace®l; and DTaP-IPV-Hib-HepB, VAXELIS®). The monovalent vaccine PRP-OMP, trade name PedvaxHIB®, is preferentially recommended for AI/AN children. This preferential recommendation relates to the fact that invasive HIB disease disproportionately affects AI/AN populations, especially young children. From 1980–2012, the incidence of HIB disease among US children declined more than 99% following introduction of HIB vaccines into the childhood immunization schedule. However, the incidence of invasive HIB disease among AI/AN children <5 years of age in the pre-vaccine era was up to 280 cases per 100,000 and more than 10 times higher than the incidence among US children <5 years of age. Fortunately, the incidence of HIB disease among AI/AN children <5 years of age declined more than 98% with HIB vaccination. Yet, among children <5 years of age, the incidence of invasive *H. flu* disease remains substantially higher among AI/AN children compared with non-Native children.

Focusing on HIB, AI/AN children still have a 31-fold higher incidence of invasive HIB disease than non-Native children. In the pre-vaccine era, the incidence of HIB meningitis peaked at a younger age among AI/AN populations than among the general US population. From 1971–1977, among Alaska Native and Navajo Nation children, the peak was not only higher but also occurred earlier at 4–5 months of age. Among children in the general US population, the peak was lower and occurred later at 6–9 months of age.

Looking at the characteristics of invasive HIB disease cases among American Indian children <5 years of age reported to CDC's ABCs Surveillance System from 2003–2023, the median age was 12 months and 31% of cases occurred among unvaccinated children. The most common syndromes were meningitis in 45% of cases followed by pneumonia in 41% of cases.

PedvaxHIB® (PRP-OMP) is preferentially recommended for AI/AN infants. The ACIP recommendations predate the licensure of VAXELIS® and vaccination with a 2-dose primary series of a HIB vaccine that contains PRP-OMP is preferred for AI/AN infants to provide earlier protection because this vaccine produces a protective antibody response after the first dose. A booster dose, Dose 3 in this case, of HIB vaccine is then recommended at age 12–15 months of age. For the booster dose, there is no preferred vaccine formulation. As noted, PRP-OMP provides earlier protection. PRP-OMP produces a protective antibody response after the first dose based on the correlate of short-term protection of 0.15 µg/mL. Thus, the preferential recommendation for PedvaxHIB® aims to address the earlier peak in meningitis among AI/AN infants from the pre-vaccine era. However, final antibody titers are higher with PRP-T. The current primary series of PRP-OMP is only 2 doses.

Notably, the incidence of invasive HIB disease in Alaska Native populations increased in the late 1990s amid vaccine policy changes. The incidence of invasive HIB disease was declining before universal HIB vaccination began in 1991. Universal HIB vaccination began first with the HIB oligosaccharide CRM197 vaccine (HbOC) in January 1991. This was changed to PRP-OMP in July 1991. In January 1996, a combination vaccine with diphtheria, tetanus, pertussis, and HbOC replaced PRP-OMP in order to decrease the number of injections at each visit. In October 1997, following an increase in cases of invasive HIB disease, an official change was made to PRP-OMP for Dose 1, followed by HbOC for Doses 2─4, though some tribal facilities had made this change as early as July 1996. This change was supported by studies demonstrating that the highest antibody concentrations were obtained by initiating the HIB primary series with 1 dose of PRP-OMP and concluding with 2 doses of either PRP-T or HbOC. In 2001, a change was made back to PRP-OMP for all HIB doses.

During 1996─2000 when vaccine policy changes had been made to include HbOC, a greater proportion of cases occurred among Alaska Native children and partially immunized children and were considered true vaccine failures. Vaccine administration errors may have contributed to some cases when both PRP-OMP and HbOC were used. From October 1997─December 2000, 14 cases occurred in Alaska Native children aged <5 years of age. Of those children, 3 (21%) had inadvertently received HbOC for their first and only dose of HIB vaccine. Increases in HIB disease in Alaska during 1996─2000 were ultimately attributed to the use of HbOC, which did not achieve short-term protective antibody concentrations until the third dose, and low rates of on-time immunization. Recent vaccine coverage data from the NIS-Child estimated vaccination coverage with a HIB full series by age 24 months among AI/AN ranged from 67.5% to 77% for birth cohorts born during 2016─2020. In 2019─2020, AI/AN children were less likely than White children to have received the HIB full series by age 24 months. An estimated 68.7% of AI/AN children had received the HIB full series, which was significantly lower than the estimated 80.8% for White children.

VAXELIS® (DTaP-IPV-Hib-HepB) is a newer hexavalent combination vaccine in the US that protects against diphtheria, tetanus, pertussis, polio, HIB, and hepatitis B. It was licensed in December 2018, and ACIP voted to include it in the VFC program in June 2019. Per the manufacturer, more than 6.2 million doses have been distributed in the US as of Quarter 4 of 2023. VAXELIS® does not currently have a preferential recommendation for AI/AN infants because post-dose 1 immunogenicity data were not previously available. It is not equivalent to PedvaxHIB® because it contains a lower dose of PRP-OMP. PedvaxHIB® has 7.5 micrograms of PRP versus 3 micrograms in VAXELIS®, and PedvaxHIB® has 125 micrograms of OMP versus 50 micrograms in VAXELIS®. In Phase 3 clinical trials, HIB antibody responses after the 3-dose primary series were non-inferior to licensed comparator vaccines in 2 studies. Regarding safety of VAXELIS®, in pre-licensure clinical trials, the safety profile was consistent with that of licensed comparator vaccines except for a higher rate of fever than with DTaP-IPV/HIB. However, rates of fever-related medical AEs were similar between groups. A post-licensure analysis of data from VAERS from June 2019─June 2023 did not identify new or unexpected safety issues.

VAXELIS® protects against 6 infections with fewer injections. There are 3 options for how either VAXELIS® or PedvaxHIB® can be used with other vaccines to complete the routine childhood immunization series for the 6 infections covered by VAXELIS®. (Note that this is not all immunizations in the childhood series.) Option 1 uses VAXELIS® for a total of 5 injections. Option 2 uses PedvaxHIB® and the combination vaccine PEDIARIX for a total of 7 injections. Option 3 uses the individual component vaccines for a total of 12 injections.

The proposed policy question is, “Should VAXELIS® be included with PedvaxHIB® in the preferential recommendation for AI/AN infants?”

Dr. Chen asked what is leading to the lower uptake among AI/AN to be fully vaccinated against HIB at 68.7% versus 80% for white non-Hispanics, and if it perhaps the perception of multiple vaccines at that visit was perhaps leading to this. He wondered whether the multivalent VAXELIS® vaccine perhaps would improve that perception and maybe increase the uptake. Ultimately, the end goal is to increase uptake.

Dr. Collins said that the reason for lower HIB vaccine coverage is unknown and it is rather new in the past several years. Historically, the rates of immunization have been similar between those two groups.

Dr. Brooks asked whether HbOC is the capsular vaccine.

Dr. Collins indicated that it was an oligosaccharide conjugated vaccine, but it was one of the earlier conjugate vaccines.

Dr. Laura Hammitt (Johns Hopkins Bloomberg School of Public Health, Center for Indigenous Health) presented the results of the HibVax study that assessed the immunogenicity of HIB vaccines in AI/AN infants. This study was supported by a research grant from the Investigator-Initiated Studies Program of Merck Sharp & Dohme, LLC acting on behalf of a joint venture with Sanofi known as MSP Vaccine Company. After the ACIP vote to recommend VAXELIS® several years ago for use in US infants but to withhold a preferential recommendation for use in AI/AN infants, knowing the benefits of combination vaccines, Johns Hopkins submitted a proposal through the Merck Investigator-Initiated Studies Program.

Prior to the availability of HIB vaccine, disease incidence was 4-fold higher in Navajo Nation. Widespread use of the PRP-OMP HIB vaccine fortunately led to rapid and sustained reductions in disease, and the average number of invasive HIB cases in children <5 years of age in the Navajo Nation declined from roughly 19 per year to fewer than 2 per year. Fortunately, Navajo Nation has not experienced a case of invasive HIB in a child <5 years of age since 2016.

In terms of the epidemiological characteristics of the 25 invasive HIB cases that have occurred in the past 2 decades in Navajo Nation and White Mountain Apache Tribal lands in the Southwest US, the median age of cases has increased. It is now 14 months with a range of 2 to 52 months. Meningitis was diagnosed in 28% of cases and pneumonia in 40% of cases. Other cases were bacteremia, sepsis, and osteomyelitis. Only 4 cases occurred in unvaccinated infants who ranged in age from 2 to 11 months. There were 7 cases in infants or children who were up to date for age on their HIB vaccine, and they ranged in age from 4 months to 12 months. Most of the cases, 14 in total, were in fully vaccinated children, meaning they had completed the primary series and a booster dose. This highlights a potential vulnerability between the time that the primary series is completed at 4 months of age until the receipt of a booster dose at 12 to 15 months of age, and also suggests that protection does wane some after the booster dose.

In this context, Johns Hopkins sought to assess the potential for use of VAXELIS® in AI/AN infants. In terms of the characteristics of the 2 vaccines, PedvaxHIB® (PRP-OMP Hib vaccine) and VAXELIS®® (DTaP-IPV-Hib-HepB), VAXELIS® is not preferentially recommended for AI/AN infants. It is a PRP-OMP conjugate.

Both of the vaccines use the HIB capsular antigen, the polyribosylribitol phosphate (PRP) conjugated to OMP, the outer membrane protein of *Neisseria meningitidis*. But PedvaxHIB® contains 7.5 µg of the PRP antigen compared to 3 µg in VAXELIS®. PedvaxHIB® uses a 2-dose primary series compared to a 3-dose primary series for VAXELIS®. PedvaxHIB® has been shown to elicit protective antibody concentrations post-Dose 1, but the post-Dose 1 immunogenicity of VAXELIS® is unknown. The advantages of combination vaccines include fewer shots, fewer missed doses, and a lower administrative burden. This led to the effort to identify data that could inform a policy decision and potentially optimize HIB protection for AI/AN children.

The primary objective of the HibVax Study was to answer the question, “Do antibody levels in AI/AN infants meet non-inferiority criteria 30 days after Dose 1 of VAXELIS® compared to PedvaxHIB®?” It was pre-specified that VAXELIS® would be considered non-inferior if the ratio of the GMCs in the VAXELIS® group relative to the PedvaxHIB® group was greater than 0.67. The HibVax study is a Phase 4 prospective open-label randomized controlled trial (RCT). Study visits were aligned with routine well-child checks. Study Day 1 was at approximately 2 months of age. Following informed consent, children underwent a physical exam, parents completed a questionnaire, and a baseline blood sample was collected. Children were then randomized to either the PedvaxHIB® group or the VAXELIS® group and received their first dose of study vaccine along with their other routine infant immunizations.

The study compared 2 licensed vaccines with well-characterized safety profiles. Reactogenicity data were not collected, but SAEs were monitor for from the time of enrollment through the final study visit. Blood samples were collected at 4 time points: Baseline, 30 days post-Dose 1, which was the primary outcome, at the 6-month well-child check 60 days post-Dose 2, and at the final study visit 30 days post-Dose 3 of VAXELIS®, and approximately 90 days after the completion of the PedvaxHIB® primary series for infants in that arm.

Anti-HIB IgG antibody levels were measured by a commercially available enzyme-linked immunosorbent assay (ELISA) by the team at the CDC Arctic Investigations Program (AIP) in Anchorage. GMCs were assessed using constrained longitudinal data analysis (cLDA), which assumes that groups have an equal anti-HIB GMC at baseline based on the randomized study design. This analysis also allows participants who are not able to contribute data at all the time points to contribute data where data are available. Results are presented for all evaluable participants complying with the procedures and intervals between primary doses, as defined in the protocol.

Enrollment began in January 2022 at 5 sites, including 1 site in Anchorage, Alaska and 4 sites in the Navajo Nation. The Navajo Nation sites were Chinle, Arizona; Fort Defiance, Arizona; Gallup, New Mexico; and Shiprock, New Mexico. All study visits were completed by October 2023. There was a target sample size of 330 participants based on the pre-specified non-inferiority objective, and final enrollment was 333 participants. Overall, the study had nearly 90% retention through the final visit. In terms of participant characteristics by vaccine group, the groups were comparable in terms of age at Dose 1, with a median age of 56 days in the PedvaxHIB® group and 60 days in the VAXELIS® group. The proportion of participants who were male was 45% in the PedvaxHIB® group and 50% in the VAXELIS® group. Randomization between groups was balanced within a site and across the sites. Enrollment was lowest in Anchorage and highest in Fort Defiance.

Over the course of the study, 25 SAEs were reported in 21 participants. Three of the PedvaxHIB® recipients had 2 SAEs and 1 VAXELIS® recipient had 2 SAEs. None of the SAEs were considered related to study vaccination. The most common SAE in 21 of the cases was hospitalization for ARI. Last winter saw extensive circulation of numerous respiratory viruses, and the occurrence of ARI hospitalizations in clinical trial participants for this study is consistent with published rates in the population.

In terms of the primary outcome, HIB antibody concentrations at 30 days post-Dose 1 were extremely similar. Observed GMCs were 0.39 in the PedvaxHIB® group and 0.41 in the VAXELIS® group. The results from the cLDA were nearly identical. These results indicate that both vaccines are producing similarly strong immune responses after the first dose. The ratio of the VAXELIS® to PedvaxHIB® GMCs was 1.03, with a confidence interval of 0.75 to 1.41. The pre-specified non-inferiority criterion was therefore met based on the lower bound of the 95% confidence interval around the ratio being greater than 0.67. Data from both groups were pooled at Day 1. At Day 31, 1 month post-Dose 1, antibody GMCs in the PedvaxHIB® group and the VAXELIS® group were nearly identical.

Looking at the anti-Hib IgG GMC on Days 1, 31, 121, and 151, both groups were well above the putative long-term correlate of protection at these time points. At day 121, the GMCs in the PedvaxHIB® and VAXELIS® groups were similar, with overlapping confidence intervals. At Day 151, the GMCs were higher in the VAXELIS® recipients. This makes sense, given that those infants received a 3-dose primary series, whereas the PedvaxHIB® recipients had a 2-dose primary series and therefore likely had peak antibody levels around 5 months of age, which would have corresponded to study Day 90. The proportion of participants with anti-HIB antibody concentrations at or above the short-term correlative protection, ≥0.15 µg/mL, was similar between groups at all time points. Over 90% of infants in both groups were above this threshold at Day 121 and day 151. The proportion of participants with antibody at or above the putative correlative long-term protection, ≥1.0 µg/mL, was similar between groups at the first 3 time points. At Day 151, which was the final study visit, 84% of VAXELIS® recipients were above this threshold compared to 72% of PedvaxHIB® recipients, which was a statistically significant difference. The proportion of participants with a 4-fold rise in anti-HIB antibody concentration was similar between groups, comparing both groups between baseline and each of the subsequent time points.

This study only followed participants through 7 months of age, so it was not possible to evaluate longer-term antibody persistence. Encouragingly, at that final visit at approximately 7 months of age, over 90% of participants had antibody levels above the putative correlate for short-term protection. It is notable that the proportion of participants with antibody levels above the putative correlate of long-term protection, as well as the antibody GMCs, were higher in the VAXELIS® group at the final study visit, which may be a potential advantage of a 3-dose primary series. This could be advantageous, given that the median age of HIB disease in AI/AN children is higher now and durable protection is needed. It is expected, based on where the antibody levels were at 7 months, that protection should be in place through the time of the booster dose. The current strategy for a booster dose is at 12 to 15 months of age. At IHS and tribal health facilities in the Southwest, this is generally slated for the 12-month well-child check.

Data from previous studies suggest that booster doses following a primary series of VAXELIS® are immunogenic. Notably, a heterologous booster, meaning a PRP conjugated to a carrier protein other than OMP, such as PRP conjugated to tetanus toxoid, may provide stronger and more durable protection than a homologous booster.

Data from a prelicensure study of VAXELIS® that included a cohort of American Indian infants showed that children who received a primary series of VAXELIS® followed by a booster with PRP-TT had significantly higher post-booster GMCs of 55.4 compared to 20.9 of children who received a primary series of PRP-TT followed by a booster with the same conjugate. The data are reassuring that booster doses following a primary series of VAXELIS® are immunogenic in American Indian children and also suggest that there may be opportunities to further optimize protection against HIB with consideration of heterologous booster doses.

In conclusion, post-Dose 1 anti-HIB GMCs following VAXELIS® met the pre-specified criteria for non-inferiority. Including VAXELIS® among the vaccines with a preferential recommendation for AI/AN children would expand the available options for this population. A formal qualitative assessment was not done of acceptability, but anecdotally, parents of study participants were strongly supportive of combination vaccines to reduce the number of shots that infants receive. Some parents wanted to be in the trial if they could be guaranteed that the child would be in the VAXELIS® group, which could not be done. The research team also heard regularly from providers who would like to be able to offer this vaccine to their AI/AN patients.

Dr. Loehr expressed gratitude for this study. There was a data gap and this study answered a clinical question and likely will inform decision-making that will probably help patients with care and comfort.

Dr. Clark (IHS) expressed his gratitude to Dr. Collins and Dr. Hammett for the information that they presented, which obviously has a profound impact on the AI/AN population. For context, Dr. Clark is a practicing pediatrician and the Chief Medical Officer for the Alaska Native Health Service. In speaking with his colleagues in Alaska and in the Lower 48 on this topic, he wanted to put forth a few considerations from the IHS perspective. As immunogenicity study in this high-risk population, there are some limitations. The study is small in size and duration. That notwithstanding, the demonstrated non-inferiority in comparison with HIB is encouraging. There is always a question about the generalizability of these types of small studies, particularly with a small number of tribal communities. They have a saying in Indian Country, “If you know 1 tribal community, you know 1 tribal community.” This holds true for clinical research as well. That having been said, there oftentimes is not an advantage to fully generalizable studies in this context. Reflecting on Dr. Chen's earlier comments, while there are multiple variables that impact vaccine access and vaccine acceptance in Indian Country, collectively there is agreement in IHS among the provider community working with tribal partners that having a multivalent vaccine option compared to monovalent vaccines is likely to increase vaccine coverage rates. That is an important consideration. In this situation, the question has to be balanced with regard to post-first dose vaccine immunogenicity. This study addresses that to some extent. That has to be balanced against the potential durability of protection post-Dose 3, as Dr. Hammett very eloquently pointed out. This is an important consideration given that a substantial number of invasive HIB disease cases in Indian Country are occurring in the older age group, even among fully vaccinated children. That having been said, based on the available evidence, IHS supports ACIP’s consideration of a preferential recommendation for VAXELIS® in AI/AN infants and would certainly expect there to continue to be active surveillance for invasive HIB disease post-implementation if the ACIP chooses to take that approach.

Dr. Long asked whether it was the case that some of the children had their boosters and still got invasive disease.

Dr. Collins indicated that they need to explore further to determine precisely what vaccines children in ABCs received to sort that out. It is top of mind and the plan is to look at this for the EtR framework. PedvaxHIB® is a 2-dose series. Historical studies demonstrated that vaccine titers rose quickly after the first dose, but also waned rather quickly compared to other Hib vaccines. A main hypothesis is that waning immunity from only a 2-dose primary series is known to wane before the booster dose is given.

Dr. Long said that could be it. Having taken care of many children with *Haemophilus* disease, 60 cases of meningitis a year at St. Christopher's in North Philadelphia in the early 1980s was unbelievable. There was not that much pneumonia. It occurred, and there were effusions, et cetera. She wondered if this 14-month-old group, the fully vaccinated older than a year, were predominantly pneumonia, and if maybe vaccine does not prevent pneumonia as extremely well as it does meningitis.

Dr. Collins said she has not stratified the syndromes by age group yet. Another point and probably a likely contributor to the residual burden of disease are ongoing disparities in SDOH and things like indoor air quality that could predispose one to pneumonia. In a comparison of American Indian children to other children, 43% of American Indian children had pneumonia compared to 18% of children who were not American Indian.

Dr. Daley asked Dr. Hammitt to remind them what other vaccines those children received at the same time and whether their pneumococcal titers were evaluated.

Dr. Hammitt indicated that they received their routine pediatric immunization. Most of the clinics are using Pediarix, rotavirus orally, and PCV. The study was happening over the transition period from PCV13 to PCV15. They did not evaluate titers. Co-administration had been evaluated previously in the pre-licensure VAXELIS® studies, so that was not done as part of this study.

Dr. Collins presented the work group considerations, reminding everyone that the policy question is, “Should VAXELIS® be included with PedvaxHIB® in the preferential recommendation for AI/AN infants?” Regarding initial work group considerations, it is important to note that 574 federally recognized tribes exist in the US and each is a sovereign nation with their own norms, values, and culture. work group members noted that listening to tribal communities is very important to understand the values and priorities of the communities that will be affected by any policy recommendation and to honor their tribal sovereignty. CDC's Office of Tribal Affairs and Strategic Alliances (OTASA) is helping facilitate the connection with tribal communities. Work group members also noted that ACIP preferential recommendations must be evidence-based. With the help of OTASA, CDC/NCIRD held a listening session with tribal communities in January 2024. The session had 80 attendees, including 9 from tribes or tribal-serving organizations and 46 from IHS. Key questions and concerns raised by participants included whether VAXELIS® will offer the same protection as PedvaxHIB®, the need to monitor for possible breakthrough cases with any change in vaccine policy, and safety and side effects.

To summarize key work group considerations regarding post-Dose 1 immunogenicity of VAXELIS® among AI/AN populations related to Dr. Hammitt's presentation, work group members emphasized several key aspects of the clinical trial. First, they noted that study enrollment included Navajo Nation and Alaska Native infants in Anchorage, but not broader American Indian or Alaska Native populations. Second, they noted that the anti-HIB GMCs 30 days after Dose 1 were non-inferior after VAXELIS® versus PedvaxHIB®. The point estimate for the ratio of GMCs was 1.03, and the lower bound of the 95% confidence interval was above the pre-specified non-inferiority criterion. Work group members noted that GMC differences on Day 151 post-Dose 1 likely reflect the third primary series dose of VAXELIS® versus only 2 primary series doses of PedvaxHIB®. Work group members also noted that GMC titers were not available beyond Day 151 to assess longer-term protection in this population.

Additional work group considerations were that having a second preferred HIB vaccine option that is a combination vaccine may improve equity and the reliability of the vaccine supply for this population. Work group members also noted that the immunologic data are reassuring. However, there was some concern about generalizing to broader AI/AN populations, though there is precedent for this with the preferential recommendation for PedvaxHIB®. Work group members also noted the lack of direct vaccine effectiveness data and that the study did not collect titers beyond infancy regarding whether VAXELIS® might better prevent residual cases occurring before the booster dose. Finally, work group members had some uncertainty as to why AI/AN populations are particularly affected by changes in vaccination type, and they wondered if potentially more than just antibody response contributes to this.

In summary, work group members noted that including VAXELIS® as a second preferred option for AI/AN infants may improve equity, as well as the reliability of vaccine supply. They noted that post-Dose 1 GMCs of VAXELIS® appear non-inferior to that of PedvaxHIB® among Navajo Nation and Alaska Native populations. There are data gaps, including studies in broader AI/AN populations, short-term efficacy, and longer-term immunogenicity and efficacy. The work group would appreciate input from ACIP members regarding these considerations. As a reminder, the work group 's next steps are for the GRADE assessment and EtR Framework to be presented in June 2024, with plans for a vote in June as well.

With no additional business posed for the February 2024 ACIP meeting, the meeting was officially adjourned.

ACIP MEMBERSHIP ROSTER

CHAIR
Vacant

EXECUTIVE SECRETARY
WHARTON, Melinda, MD, MPH
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Atlanta, GA

MEMBERS
BROOKS, Oliver, MD, FAAP
Chief Medical Officer
Watts HealthCare Corporation
Los Angeles, CA
Past President, National Medical Association
Term: 7/26/2021 – 6/30/2025

CHEN, Wilbur H, MD, MS, FACP, FIDSA
Professor of Medicine
Center for Vaccine Development and Global Health
University of Maryland School of Medicine
Baltimore, MD
Term: 12/23/2020 – 6/30/2024

CINEAS, Sybil, MD, FAAP, FACP
Associate Professor of Medicine, Pediatrics, and Medical Science (Clinical)
The Warren Alpert Medical School of Brown University
Associate Program Director
Brown Combined Residency in Internal Medicine and Pediatrics
Providence, RI
Term: 9/28/2021 – 6/30/2025

DALEY, Matthew F, MD
Senior Investigator
Institute for Health Research, Kaiser Permanente Colorado
Associate Professor of Pediatrics
University of Colorado School of Medicine
Aurora, CO
Term: 1/4/2021 – 6/30/2024

KOTTON, Camille Nelson, MD, FIDSA, FAST
Clinical Director, Transplant and Immunocompromised Host Infectious Diseases
Infectious Diseases Division, Massachusetts General Hospital
Associate Professor of Medicine, Harvard Medical School
Boston, MA
Term: 12/23/2020 – 6/30/2024

LOEHR, Jamie, MD, FAAFP
Owner, Cayuga Family Medicine
Ithaca, New York
Term: 7/26/2021 – 6/30/2025

LONG, Sarah S, MD
Professor of Pediatrics
Drexel University College of Medicine
Section of Infectious Diseases
St. Christopher's Hospital for Children
Philadelphia, Pennsylvania
Term: 12/24/2020 – 6/30/2024

EX OFFICIO MEMBERS

Centers for Medicare and Medicaid Services (CMS)
HANCE, Mary Beth
Senior Policy Advisor
Division of Quality, Evaluations and Health Outcomes
Children and Adults Health Programs Group
Center for Medicaid, CHIP and Survey & Certification Centers
for Medicare and Medicaid Services
Baltimore, MD

Food and Drug Administration (FDA)
KASLOW, David C, MD
Director, Office of Vaccines Research and Review
Center for Biologics Evaluation and Research (CBER)
Silver Spring, MD

Health Resources and Services Administration (HRSA)
GRIMES, Reed, MD, MPH
CDR, USPHS
Director, Division of Injury Compensation Programs
Health Systems Bureau
Health Resources and Services Administration
Rockville, MD

Indian Health Service (IHS)
CLARK, Matthew, MD, FAAP, FACP
Physician
Chair, IHS National Pharmacy & Therapeutics Committee
Durango, CO

Office of Infectious Disease and HIV/AIDS Policy (OIDP)
MARSHALL, Valerie, MPH, PMP
CDR, USPHS
Deputy Director
Office of the Assistant Secretary for Health
Department of Health and Human Services
Washington, DC

National Institutes of Health (NIH)
BEIGEL, John, MD
Associate Director for Clinical Research
Division of Microbiology and Infectious Diseases
National Institute of Allergy and Infectious Diseases (NIAID)
Bethesda, MD

LIAISON REPRESENTATIVES

American Academy of Family Physicians (AAFP)
ROCKWELL, Pamela G, DO
Associate Professor, Department of Family Medicine, University of Michigan Medical School
Medical Director, Dominos Farms Family Medicine
Ann Arbor, MI

American Academy of Pediatrics (AAP)
O'LEARY, Sean, MD, MPH
Professor of Pediatrics
Pediatric Infectious Diseases
General Academic Pediatrics
Children's Hospital Colorado/University of Colorado School of Medicine

American Academy of Pediatrics (AAP)
Red Book Editor
KIMBERLIN, David, MD
Professor of Pediatrics
Division of Pediatric Infectious Diseases
The University of Alabama at Birmingham School of Medicine
Birmingham, AL

American Academy of Physician Assistants (AAPA)
LÉGER, Marie-Michèle, MPH, PA-C
Senior Director, Clinical and Health Affairs
American Academy of Physician Assistants
Alexandria, VA

American College Health Association (ACHA)
LEE, Sara, MD
Assistant Vice President of University Health and Counseling Services
Chief Health Officer
Case Western Reserve University
Cleveland, OH

American College Health Association (ACHA) (alternate)
HALBRITTER, Ashlee, MPH
Executive Director, Public Health and Wellbeing
University of Pennsylvania
Philadelphia, PA

American College of Nurse Midwives (ACNM)
HAYES, Carol E., CNM, MN, MPH
Lead Clinician
Clinical Quality Compliance and Management
Planned Parenthood Southeast Atlanta, GA

American College of Nurse Midwives (ACNM) (alternate)
MEHARRY, Pamela M., PHD, CNM
Midwifery Educator, Human Resources for Health
In partnership with University of Rwanda and University of Illinois, Chicago

American College of Obstetricians and Gynecologists (ACOG)
ECKERT, Linda O, MD, FACOG
Professor, Department of Obstetrics & Gynecology
Adjunct Professor, Department of Global Health
University of Washington
Seattle, WA

American College of Physicians (ACP)
GOLDMAN, Jason M, MD, FACP
Affiliate Assistant Professor of Clinical Biomedical Science
Florida Atlantic University, Boca Raton, Florida
Private Practice, Coral Springs, FL

American Geriatrics Society (AGS)
SCHMADER, Kenneth, MD
Professor of Medicine-Geriatrics Geriatrics
Division Chief
Duke University and Durham VA Medical Centers
Durham, NC

America's Health Insurance Plans (AHIP)
GRUBB, Jessica, MD
Medical Director, Infectious Diseases
Elevance Health Companies/Carelon
Charleston, SC

American Immunization Registry Association (AIRA)
COYLE, Rebecca, MSEd
Executive Director, AIRA
Washington, DC

American Immunization Registry Association (AIRA) (alternate)
LONDO, Courtnay, MA
Senior Program Manager
Washington, DC

American Medical Association (AMA)
FRYHOFER, Sandra Adamson, MD
Adjunct Associate Professor of Medicine Emory
University School of Medicine
Atlanta, GA

American Nurses Association (ANA)
RESNICK, Barbara, PhD, RN, CRNP, FAAN, FAANP
Professor, Organizations Systems and Adult Health
University of Maryland, Baltimore
Baltimore, MD

American Osteopathic Association (AOA)
MAHMOUDI, Massoud, DO, PhD, MS
President, American Osteopathic College of Allergy and Immunology
Clinical Professor, Department of Medicine, Division of General Internal Medicine
University of California San Francisco
San Francisco, CA

American Pharmacists Association (APhA)
GOODE, Jean-Venable "Kelly" R., PharmD, BCPS, FAPhA, FCCP
Professor and Director, PGY1 Community-Based Pharmacy Residency Program
School of Pharmacy, Virginia Commonwealth University
Richmond, VA

Association of Immunization Managers (AIM)
HOWELL, Molly, MPH
Immunization Program Manager
North Dakota Department of Health
Bismarck, ND

Association for Prevention Teaching and Research (APTR)
ZIMMERMAN, Richard, MD, MPH
Professor
University of Pittsburgh School of Medicine
Department of Family Medicine and Clinical Epidemiology
Pittsburgh, PA

Association of State and Territorial Health Officials (ASTHO)
JUTHANI, Manisha, MD
Commissioner
Connecticut Department of Public Health
Hartford, CT

Biotechnology Industry Organization (BIO)
ARTHUR, Phyllis A, MBA
Senior Director, Vaccines, Immunotherapeutics and Diagnostics Policy
Washington, DC

Council of State and Territorial Epidemiologists (CSTE)
HAHN, Christine, MD
State Epidemiologist
Office of Epidemiology, Food Protection and Immunization Idaho
Department of Health and Welfare
Boise, Idaho

Canadian National Advisory Committee on Immunization (NACI)
DEEKS, Shelley, MD, MHSc, FRCPC, FAFPHM
Deputy Chief Medical Officer of Health, Department of Health and Wellness, Nova Scotia
Associate Professor, Dalla Lana School of Public Health, University of Toronto
Chair, National Advisory Committee on Immunization
Halifax, Nova Scotia

Infectious Diseases Society of America (IDSA)
DUCHIN, Jeffrey, MD
Health Officer, Public Health - Seattle and King County
Professor in Medicine, Division of Allergy and Infectious Diseases
University of Washington School of Medicine and School of Public Health
Seattle, WA

Infectious Diseases Society of America (IDSA) (alternate)
MCAULEY, James B., DTM&H, MD, MPH
Clinical Director
Whiteriver Indian Hospital
Whiteriver, AZ

International Society for Travel Medicine (ISTM)
BARNETT, Elizabeth D, MD Professor of
Pediatrics
Boston University School of Medicine
Boston, MA

National Association of County and City Health Officials (NACCHO)
ZAHN, Matthew, MD
Medical Director, Epidemiology
Orange County Health Care Agency
Santa Ana, CA

National Association of County and City Health Officials (NACCHO) (alternate)
DUCHIN, Jeffrey, MD
Health Officer and Chief, Communicable Disease
Epidemiology and Immunization Section
Public Health - Seattle and King County
Professor in Medicine
Division of Allergy and Infectious Diseases
University of Washington School of Medicine and School of Public Health
Seattle, WA

National Association of Pediatric Nurse Practitioners (NAPNAP)
DESHON, Dana, DNP, APRN, CPNP-PC
Order of Saint Francis Medical Group
Morton Pediatrics
Morton, IL

National Foundation for Infectious Diseases (NFID)
SCHAFFNER, William, MD
Chair, Department of Preventive Medicine
Vanderbilt University School of Medicine
Nashville, TN

National Foundation for Infectious Diseases (NFID) (alternate)
DALTON, Marla, PE, CAE
Executive Director & CEO
National Foundation for Infectious Diseases (NFID)
Bethesda, MD

National Medical Association (NMA)
WHITLEY-WILLIAMS, Patricia, MD Professor and Chair
University of Medicine and Dentistry of New Jersey Robert Wood
Johnson Medical School
New Brunswick, NJ

Pediatric Infectious Diseases Society (PIDS)
PAULSEN, Grant, MD
Associate Professor of Pediatrics
Pediatric Infectious Diseases
Cincinnati Children’s Hospital Medical Center
Cincinnati, OH

Pediatric Infectious Diseases Society (PIDS) (alternate)
ROSS, Shannon A, MD, MSPH
Professor of Pediatrics
Birmingham School of Medicine
University of Alabama
Birmingham, AL

Pharmaceutical Research and Manufacturers of America (PhRMA)
ROBERTSON, Corey, MD, MPH
Senior Director, US Medical, Sanofi Pasteur
Swiftwater, PA

Society for Adolescent Health and Medicine (SAHM)
MIDDLEMAN, Amy B, MD, MSEd, MPH
Professor of Pediatrics
Chief, Section of Adolescent Medicine
University of Oklahoma Health Sciences Center
Oklahoma City, OK

Society for Healthcare Epidemiology of America (SHEA)
MEHROTRA, Preeti, MD, MPH
Senior Medical Director
Infection Control/Hospital Epidemiology
Beth Israel Deaconess Medical Center
Adult and Pediatric Infectious Diseases
Harvard Medical School
Boston, MA

Society for Healthcare Epidemiology of America (SHEA) (alternate)
DREES, Marci, MD, MS
Chief Infection Prevention Officer & Hospital Epidemiologist
ChristianaCare
Wilmington, DE
Associate Professor of Medicine
Sidney Kimmel Medical College at Thomas Jefferson University Philadelphia, PA