MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

OCTOBER 23-24, 2024
MEETING SUMMARY

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

WEDNESDAY: OCTOBER 23, 2024

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Melinda Wharton (ACIP Executive Secretary) called the October 23, 2024, Advisory Committee on Immunization Practices (ACIP) meeting to order. She made opening announcements about the availability of presentation slides on the ACIP website, scheduled oral public sessions, and the written public comment process. She reviewed conflict of interest policies for ACIP members. She welcomed and introduced the new committee members: Dr. Edwin Asturias, Dr. Noel Brewer, Dr. Lin Chen, Dr. Helen Chu, Dr. Mini Kamboj, Dr. George Kuchel, and Ms. Charlotte Moser. She then conducted a roll call, which established a quorum. 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 first day of this meeting. Dr. Bonnie Maldonado disclosed that she previously served as a Data Safety Monitoring Board member for Pfizer's meningococcal vaccine trials and as a site Principal Investigator for Pfizer's pediatric COVID and maternal respiratory syncytial virus vaccine trials as well as AstraZeneca's varicella zoster vaccine trial.

PNEUMOCOCCAL VACCINES

Dr. Jamie Loehr, Chair of the ACIP Pneumococcal Vaccines Work Group, introduced the pneumococcal vaccines session. He pointed out that PCV21 is not PCV20 plus one additional serotype; PCV21 includes serotypes not included in previous pneumococcal vaccines and is missing other serotypes previously included in earlier pneumococcal vaccines. Serotype 4 is not in PCV21 and may be relevant to specific populations. PCV20 included serotypes accounting for 54% of cases of invasive pneumococcal disease (IPD) among adults 65 years of age and older during the period 2018-2022, while PCV21 included serotypes accounting for 85% of cases.

There are several Pneumococcal vaccines in advanced stages of development.

- 24-valent pneumococcal vaccines (Pn-MAPS24v, GSK; VAX-24, Vaxcyte)
- 31-valent pneumococcal vaccine (VAX-31, Vaxcyte)

Adults currently recommended to receive a dose of pneumococcal conjugate vaccine (PCV) include:

- Adults aged ≥65 years who have not received a PCV
- Adults aged 19–64 years with certain underlying conditions or risk factors who have not received a PCV
- Certain adults who have received PCV13 but have not received PCV20

PCV21 was developed to target pneumococcal serotypes that commonly cause disease in adults. The manufacturer currently does not have plans to seek an indication for routine PC21 use in infants. However, they will seek an indication for the use of PCV21 in children 2-18 years old with a risk condition for which there is a Phase 3 trial currently in progress. The work group does not expect PCV21 to offer similar indirect protection from its additional serotypes that were observed from PCV7 or PCV13 use in children.

In June 2024 the work group agreed that available evidence supports PCV21 use for adults currently recommended to receive a PCV but could not reach a consensus on whether the age-based recommendations for PCV21 should be lowered from ≥65 to ≥50 years. Most work group members believed there was insufficient evidence to support lowering the age-based recommendation for other recommended PCVs, specifically PCV15 and PCV20.

At the June ACIP meeting, the committee requested that the work group come back to the committee with a summary of data on whether the recommended age should be lowered to ≥50 years for all PCVs (not just PCV21) at today's meeting, as the committee felt that there was not enough data to decide on PCVs other than PCV21 at that time. Another request was to share data on the possible consideration of discontinuing the recommendation for PPSV23 in the future.

The initial policy options considered by the work group were

1. Lower the age-based recommendations for all PCVs to age ≥50 years
2. Lower the age-based recommendation for all PCVs to age ≥60 years or age ≥55 years
3. Lower the age-based recommendation to age ≥50 years but only for PCV21
4. Shared clinical decision-making for PCV use for adults aged 50–64 years who currently do not have a risk-based vaccine indication
5. Status quo (i.e., age-based at age ≥65 years, risk-based for younger adults)

The final proposal from the work group was to lower the age-based recommendations for all PCVs to age ≥50 years. The majority supported this option after a targeted discussion of the policy question. An additional dose may be needed in the future to avoid increased pneumococcal disease burden in older adults. Several key uncertainties remain: indirect effects from new pediatric pneumococcal vaccines; the duration of protection from adult vaccination; and the impact of new higher-valency vaccines for adults. Key factors in the work group proposal were higher pneumococcal disease rates in Black adults, with an earlier peak; many adults 50-64 years of age already have an indication for risk-based pneumococcal vaccination; an age-based recommendation is more likely to improve uptake than is a risk-based recommendation; it will be easier to implement a uniform recommendation across all PCVs; PCV21 had a more favorable health economic profile than PCV20, although both would be expected to improve health outcomes; and the serotype compositions of PCV20 and PCV21 are quite different.

Dr. Charles Stoecker (Tulane University) discussed PCV use's economic analysis and public health impact for adults aged ≥50 years. The request to the work group was to evaluate the cost-effectiveness of an age-based recommendation for PCV20 or PCV21 in adults younger than 65 years of age. The motivation is to get higher vaccine uptake among adults with underlying risk conditions, by changing from a risk-based to an age-based recommendation. Additionally, this may lead to higher pneumococcal vaccine uptake among the general population. The model evaluated the program's cost and savings and looked at changes in disease, medical, nonmedical, and work productivity costs. The population was a cohort of about 4 million 50-year-olds. Separate categories were created for immunocompromised individuals (IC), individuals with chronic medical conditions (CMC), and others or the general population that are not IC or have CMC.

Moving Strategies and Adding Strategies were used to evaluate the study question. The Moving Strategies will move the age-based recommendation from 65 to 50 years of age. This will shift the disease burden from younger adults to older adults, leaving older adults less protected. The Adding Strategies will add a vaccination at age 50 in addition to age 65. This will maintain protective benefits for older adults from the current age-based recommendation.

The first Moving Strategy the work group evaluated was an intervention of PCV20 at age 50 compared to PCV20 at diagnosis of CMC/IC and PCV20 at age 65 (current recommendation). The second Moving Strategy was an intervention of PCV20 at age 60 compared to PCV20 at diagnosis of CMC/IC and PCV20 at age 65 (current recommendation). The first Adding Strategy evaluated was an intervention of PCV20 at ages 50 and 65 compared to PCV20 at diagnosis of CMC/IC and PCV20 at age 65 (current recommendation). The second Adding Strategy evaluated an intervention of PCV20 at ages 60 and 75 compared to PCV20 at diagnosis of CMC/IC and PCV20 at age 65 (current recommendation). The above comparisons were repeated for PCV21.

The PCV20 and PCV21 vaccines are estimated to cost approximately $300, with an additional $75 for administrative and other costs. Two scenarios will be evaluated for waning. There will be no waning for the first 5 years in either scenario. The first will wane to 0 by 15 years, and the second will wane to 0 by 20 years.

The model also includes the impact of herd effects of PCV20 in children. In year 1, the disease will be reduced by 25%, with 75% of the disease remaining for the serotypes in PV20. In year 6, 85% of adult disease will be gone due to PCV20 in children. In years 7+, there is no further decline and will maintain 15% remaining disease seen in year 6. Limitations include uncertainty around waning and herd effects and pneumococcal disease trends. Sequelae from IPD were not modeled explicitly, and disruption from changing pneumococcal schedules was not modeled.

Moving strategies resulted in increased net cases. While lower cases and deaths were seen in people ages 50-64, increased cases and deaths were seen in adults ≥65 years of age. It does have a lower cost, and these results hold under longer vaccine-waning scenarios and scenarios without herd immunity from the childhood program.

Adding a second age-based vaccination increased the cost per quality-adjusted life year (QALY) compared with current recommendations. The incremental cost-effectiveness ratios (ICERs) ranged from $50k/QALY to $500k/QALY. The ICERs are consistently lower for PCV21 recommendations than that of PCV20. Economic efficiency is improved in PCV20 and PCV21 when no herd effects are included. The changes in $/QALY are more significant in PCV20. However, this change is insufficient to make PCV20 more efficient than PCV21. Assumptions surrounding vaccine waning are minimally impactful on ICERs because the waning is extended in both the intervention and comparison strategies. Vaccination at later ages is more economically efficient.

Dr. Andrew Leidner (CDC/NCIRD) summarized three economic analyses on the use of PCVs among 50-64-year-old adults in the U.S. The main objective of cost-effective analysis (CEA) is to calculate an ICER. The ICER value is the cost per outcome and summarizes the difference in value between the two vaccination strategies. The difference in cost of the two strategies is divided by the difference in outcomes to get the ICER. In this case, the two strategies are PCV vaccination intervention at age 50-64, and the comparator is the current set of PCV recommendations.

Economic models of vaccination can be considered calculations that summarize many aspects of a disease vaccine into a single economic value. The economic model inputs include vaccine efficacy, disease burden, fatality rates, and costs. These factors contribute to the estimated ICER. If the underlying factors are uncertain, the estimated ICER can have a range to reflect that uncertainty.

As a reminder, the policy question being considered by these models is “Should a single dose of PCV be recommended for all PCV- naïve adults aged 50-64 years?”

Among the “Moving” comparisons in the models, the intervention is age-based vaccination at age 50, and the comparator is current recommendations for PCV. In this comparison, the intervention increases PCV coverage among 50-64-year-olds and reduces coverage among adults ≥ 65 years of age. The results from the Tulane-CDC and Pfizer models indicated that this comparison would likely increase the burden of disease overall and shift the burden of disease from adults in their 50s to older adults in their 60s and 70s. There was an increased number of cases, hospitalizations, and deaths. Also note that in this “moving” comparison, the intervention has 0% vaccination coverage for adults ≥65.

Among the “Adding” comparisons in the models, the intervention is age-based vaccination at ages 50 and 65 years, and the comparator is current recommendations for PCV. The “Adding” comparison allows for a more direct estimate of the impacts of expanding coverage to adults aged 50-64. This comparison also presumes that older adults (65 and up) would not be left without disease protection if the age-based recommendation is lowered.

Across the main results of the Tulane-CDC and Merck models, looking at age-based use at age 50 and 65 compared to the current recommendations, the cost per QALY for PCV21 ranged from $130,000 to $430,000. Across the main results of all three models, the cost per QALY for PCV20 ranged from $56,000 to $880,000 per QALY. Across all available models, there’s a broader range for PCV20 than for PCV21; this is partially due to 3 models being assessed PCV20 vs only two models that assessed PCV21; this is also due to the impact of indirect effects, which has a larger impact on PCV20 values than PCV21 values. The Tulane-CDC ICERs tended to be lower than ICERs from the Merck model and were higher than ICERs from the Pfizer model. The Tulane-CDC and the Merck models assessed both vaccines; in those models, PCV21 was less expensive than PCV20.

Scenarios with estimated higher vaccine effectiveness and longer duration of protection (>15 years) had lower costs per QALY. Across the Tulane-CDC and Merck model, for PCV21, the ICERs range from $117,000 to $200,000 per QALY. Across all three models, for PCV20, the ICERs range from $62,000 to $420,000 per QALY. Note that the lowest estimates for PCV20 were from the Pfizer model. Indirect effects are another highly uncertain and impactful input in these models. In these scenarios, when indirect effect assumptions are reduced, there will be a more significant disease burden in the adult population; this greater disease burden leads to better values or lower ICERs across all models.

The work group also considered two other models: the Merck health equity model and the Pittsburgh model. The Merck team submitted a separate health equity modeling analysis that used the Atkinson index to quantify inequality across Black and non-Black populations, with and without 50- to 64-year-old PCV vaccination. Their model concluded that 50- to 64-year-old vaccination would reduce health inequality (or improve health equity). The Pittsburgh model was summarized in the meeting last June. This model also focused on the value of PCV use among Black and non-Black population groups, and this model estimated equity benefits associated with 50- to 64-year-old PCV vaccination.

There is substantial uncertainty and limited data available for several key model inputs, including vaccine effectiveness and duration of protection; indirect effects from pediatric PCV20 use; and the impact on vaccine coverage of the proposed age-based recommendation. Additional limitations include the future epidemiology of serotype 4 and 19F, the impact of supplemental PCV doses, the availability of new higher-valency vaccines in coming years, and implementation challenges possibly associated with changing the schedule, which were not considered in the models.

In summary, using the “adding” approach, age-based vaccination at 50 years would improve health but was not cost-saving. Estimated results had a broader range in value for PCV20 than PCV21 because three models, not just two, assessed PCV20. Finally, in the two models that assessed both vaccines, the estimated costs per QALY were lower for PCV21 than for PCV20.

Dr. Chu inquired why the Pfizer model assumed 36% VE compared to 0% after the waning period and whether there were data to support it.

Dr. Leidner replied that the assumptions made in the models are based on expert opinion. To clarify, the Tulane-CDC models showed that vaccine effectiveness (VE) declined linearly from five years to zero by the fifteenth year. In contrast, the Pfizer model exhibited a parabolic decline, gradually decreasing each year. By year 15, the effectiveness was at 36%, and it dropped to 0% in year 16.

Dr. Talbot asked which studies used to determine the 15-year duration.

Dr. Kobayashi explained that there are insufficient data to determine the appropriate duration for the period in question. The decision is based on methodologies used in other studies where assumptions about duration and protection were necessary. More reliable data will be available in the future.

Dr. Talbot asked whether any modeling was done based on a 20-year protection period to see if the model would change.

Dr. Leidner confirmed that all three models varied the duration of protection. The Tulane-CDC and Merk models included a 20-year waning period. When there is a more extended protection period, the ICERs decrease. This decrease is not as large as seen with the herd effects.

Dr. Kobayashi noted that the group explored data from other conjugate vaccines, including meningococcal vaccines. It is essential to recognize that the severity of the diseases can differ, so we cannot automatically apply findings from one vaccine to another. Additionally, studies indicate that the duration of protection provided by meningococcal conjugate vaccines is not very long, typically waning within ten years. While the dosages given to children differ from those administered to adults, some pediatric studies have shown a gradual decline in protection within approximately seven years. Consequently, we assume that the protection period may not extend significantly beyond this estimate, although we acknowledge the uncertainties.

Dr. Talbot mentioned a group of adults who received the PCV13 vaccine, and it would be interesting to review the serology data on this group since it has been 10 years.

Dr. Kobayashi confirmed that the group would like to explore this group in the future.

Dr. Shaw inquired whether considerations for post-infection care, like the need for long-term care, a skilled nursing facility, or increased disability, were considered in the models.

Dr. Leidner confirmed that the Merck model included a disability state following IPD episodes, and the Pittsburgh model included a disability state following a small percentage of IPD episodes and nonbacteremic pneumonia episodes.

Dr. Miwako Kobayashi (CDC/NCIRD) presented the Evidence to Recommendations (EtR) Framework for the policy question, "Should a single dose of PCV be recommended for all PCV-naïve adults aged 50-64 years?" The seven EtR domains are public health problem, equity, benefits and harms, values, acceptability, resource use and feasibility.

For public health importance, Dr. Kobayashi shared that after PCV13 was recommended for children in 2010, IPD rates decreased in children and older adults through the indirect effects of PCV13 use in children. Subsequently, the incidence of IPD in adults aged 50-64 years has been higher than that in children <5 years of age. It's worth noting that although PCV13 was recommended for all adults aged 65 years and older in late 2014, this intervention had minimal population-level impact, leading to the discontinuation of this age-based recommendation in 2019. The IPD mortality rates in adults aged 50–64 years and 65 years of age and older have been the highest across all age groups. Over time, the IPD mortality rate in adults ≥65 years has become closer to that in adults aged 50–64 years. Nearly 90% of adults ages 50-64 with pneumococcal disease had at least one condition that currently qualifies for a risk-based pneumococcal vaccine indication. Data show that the success of the pediatric pneumococcal vaccine program increased the relative burden of pneumococcal disease in adults aged 50–64 years, especially in those with risk conditions. The work group agreed that pneumococcal disease is of public health importance.

Equity was a key consideration among the work group. About 32 to 54% of adults aged 50-64 years have a self-reported condition with risk-based pneumococcal vaccine indications with a broader range across race and ethnicity groups compared with adults ≥65 years of age. When compared to non-Black adults, Black adults' IPD rates peak at age 55-59 years, with higher rates in all age groups than are seen among non-Black adults, in whom rates steadily increase with increasing age. The IPD rates for Black adults aged ≥50 years exceed the average IPD rate for all adults ≥65 years of age. In a hypothetical scenario that applied the current risk-based vaccine coverage by race for adults 19- to 64 years and age-based vaccine coverage by race for adults 65 years of age and older, the rates of non-PCV13-type IPD in American Indian (AI), Alaska Native (AN), and Black adults remain higher than the population average across all racial groups with either PCV20 or PCV21. Another scenario applied the current vaccine coverage for adults ≥65 years of age by race to adults ≥50 years of age and current risk-based vaccine coverage by race to adults 19- to 49 years of age. IPD incidence in AI, AN, and Black adults decreased more compared with scenario 1 with either PCV20 or PCV21; however, the rate decreased below the population average for Black adults in the PCV21 scenario only. Therefore, racial disparities are expected to remain. The Work Group interpretation was that recommending PCV for all PCV-naïve adults aged 50–64 years of age would probably increase health equity.

To inform the benefits and harms domain, the Work Group updated its systematic literature review to include 6 PCV15 trials, 3 PCV20 trials, and 7 PCV21 trials. Immunogenicity data from these trials was used to inform the benefit domain. The overall conclusions on immunogenicity remain unchanged. PCV15 met the noninferiority criteria for all serotypes shared with PCV13

while having statistically significantly greater responses to the additional serotypes 22F and 33F. PCV20 also met the noninferiority criteria for all PCV13 serotypes. Compared to PPSV23, PCV20 met the noninferiority criteria for six out of seven non-PCV13 serotypes, except serotype 8. PCV21 met the noninferiority criteria when compared to PCV20 for all ten shared serotypes and had statistically significantly greater response to ten out of eleven serotypes unique to PCV21; the exception was serotype 15C. The work group believed that the anticipated benefits of the intervention were of moderate magnitude. However, it's important to note that data which directly address the outcomes specified in the PICO question are unavailable for these newer vaccines.

The conclusions from safety data from the PCV clinical trials also remained unchanged. No vaccine-related serious adverse events were reported for PCV15 and PCV20, but two were reported among PCV21 recipients. Post-licensure PCV20 safety data showed a potential Guillain-Barré syndrome (GBS) signal for PCV20 in the Vaccine Adverse Event Reporting System (VAERS). In an updated analysis of Medicare data through May 2024 conducted by the FDA, there was a GBS signal in sequential monitoring for the primary definition but not for the alternate definition or when adjusted for positive predictive value; there is significant uncertainty because of the small number of GBS cases observed. CDC and FDA will continue to monitor post-licensure PCV safety. Given the uncertainties, the work group felt that the undesirable anticipated effects of PCV vaccination were minimal despite the updated PCV20 post-licensure safety data from the FDA. Weighing the desirable and undesirable anticipated effects, the work group believed that supports a recommendation for PCV for all PCV-naïve adults aged 50 –64 years compared with the current risk-based recommendation.

For the values domain, the work group was split between “yes” and “probably yes” regarding the target population's feeling that desirable effects are large relative to undesirable effects. A third of the members responded “don’t know.” Members with experience serving underserved populations with many underinsured or self-pay individuals noted that these groups can be comfortable with pneumococcal vaccines if the benefits are clearly explained. When asked, “Is there important uncertainty about or variability in how much people value the main outcomes?” the work group’s interpretation was “Probably not important uncertainty or variability.”

The work group felt that it is acceptable to recommend PCV for all PCV-naïve adults aged 50–64 years. This is supported by a presentation on the Merck-funded healthcare provider surveys at the June ACIP meeting. These findings showed challenges with risk-based vaccine recommendations and that surveyed providers supported lowering the age-based recommendation to age 50 years.

For resources, the majority of the work group responded either “probably yes” or “yes” that PCV use for PCV-naïve adults aged 50-64 years was a reasonable and efficient allocation of resources. A minority portion of the members said, “probably no.” Those who said “probably no” expressed concerns about the less favorable economic analysis findings for PCV20 than PCV21. Some work group members felt that improved vaccination coverage among those with risk-based pneumococcal vaccine indications could diminish the need for broader age-based vaccination. However, insufficient success of this approach was acknowledged. Some work group members believed the decision varies when considering projections over the next 15 years.

Dr. Kobayashi shared that the work group reached a combined majority of “probably yes” and “yes” regarding the feasibility of implementing PCV for all PCV-naïve adults aged 50-60. Vaccine coverage tends to be lower in younger adults, even with an age-based recommendation. However, with risk-based indications, pneumococcal vaccine coverage was disproportionately lower in adults aged 50–64 years compared with coverage in adults 65 years of age and older. Some Work Group members believed that age-based recommendations are generally easier to implement than risk-based and that the lower vaccine coverage in younger adults is likely due to multiple factors, such as healthcare access, perceived risk of disease, or benefits from vaccination. Work group members agreed that having a different age-based recommendation by vaccine product would be more challenging to implement. At the same time, variability in health insurance coverage might keep PCV20 as the only practical option for some individuals in the short term since PCV21 is new.

Factors supporting lowering the PCV age-based recommendation that the work group recognized were the following:

- The relatively high burden of pneumococcal disease in adults aged 50–64 years, particularly among those with risk conditions
- Potential for improved vaccine uptake through an age-based recommendation
- Potential to reduce pneumococcal disease incidence in demographic groups experiencing the highest burden
- Projected health benefits from economic models despite increased net costs

The work group also identified a number of potential implications for lowering the age-based recommendations for all PCVs. There were significant concerns about the cost of lowering the age recommendation for both PCV20 and PCV21 when considering overall health benefits to society. Variability in health insurance coverage might keep PCV20 as the only practical option for some individuals in the short term, given that PCV21 is a newer vaccine, but the Work Group agreed that it would be challenging to implement different age-based recommendations by vaccine.

The work group highlighted several uncertainties that could impact future policy decisions, including the duration of protection from a dose of PCV in adults; the magnitude of the indirect effects of pediatric PCV15/20 vaccination; and the impact of higher-valency vaccines which are under development.

Despite these uncertainties and concerns, most of the work group believed that recommending a single dose of PCV for all PCV-naïve adults aged 50–64 years would probably result in desirable consequences outweighing undesirable consequences in most settings. The work group members who disagreed with the recommendation had concerns with the higher cost/QALY gained for PCV20 compared to PCV21, the uncertainties regarding the impact of pediatric PCV use, and concerns about the implications of a broad recommendation given that different serotypes are included in PCV20 and PCV21.

The work group agreed to propose the following policy option:

> *ACIP recommends a pneumococcal conjugate vaccine for all PCV-naïve adults aged ≥50 years.*

Dr. Talbot requested clarification on whether, if we move forward with a recommendation for adults older than age 50 years, there would be an evaluation of whether a second dose is required.

Dr. Kobayashi confirmed that there is insufficient evidence to recommend when precisely the second dose should occur. Therefore, today's policy option will not include a second dose.

Dr. Schechter asked what vaccination coverage rates were used in the hypothetical scenarios that were presented and whether they were the same across different race/ethnic groups.

Dr. Kobayashi explained that these analyses used observed vaccine coverage data from the 2021 Behavioral Risk Factor Surveillance System (BRFSS) for age- and risk-based recommendations for each group. For simplicity, they also assumed that all vaccine-type diseases would be prevented. Thus, the reduction in disease predicted is due the observed vaccine coverage by racial group and serotype distribution in each racial group.

Dr. Chu asked for clarification that the recommendation is to move the age recommendation from 65 to 50 years of age. However, in the "moving" strategy, the disease burden rises from the younger population to the older, if a second dose is not recommended at age 65.

Dr. Kobayashi responded that if no future vaccination coverage is offered, that is a potential risk. However, as mentioned during the economic model presentations, it is unlikely that adults will only have an opportunity to get vaccinated at age 50. If the age-based recommendation is lowered, adults will likely be vaccinated at older ages. The work group also does not know what recommendations will made in the future for new vaccines that may come. Because of these uncertainties, the team would like to reevaluate this in the future.

Dr. Chu inquired whether the group had data by race on uninsured 50- to 64-year-olds who would not be able to receive the PCV21.

Dr. Kobayashi estimated that about 10% of adults in the 50- to 64 year old age group do not have insurance coverage, and this value decreases in adults 65 years of age and older. These data are not available for this age group by race.

Dr. Brewer asked whether the vaccine effectiveness remains the same at ages 50 and 65 years and how the work group decided on the vaccination at age 50. He suggested that using an existing vaccination age from the schedule might complicate vaccinating at that age.

Dr. Kobayashi noted evidence suggesting that vaccine effectiveness may be lower in older adults than younger adults. The work group considered age thresholds of 55 and 60 but ultimately selected age 50 because the incidence of IPD is elevated in Black adults beginning at age 50 years with a peak at 55-59 years. The age of 55 was not chosen since it did not align with existing vaccination recommendations, which raised concerns about implementation.

Dr. Shaw asked if guidance would be provided to practitioners treating populations with a higher prevalence of serotype 4 disease since PCV21 does not include this serotype.

Dr. Kobayashi does not have updated data for populations observing a higher prevalence of serotype 4 disease. This guidance is captured in an MMWR published in September 2024. When available, updated data will be shared.

Dr. Asturias asked what proportion of other medical conditions were diagnosed at the time of the pneumococcal infection.

Dr. Kobayashi stated that this information is unavailable, but people may have gotten sick and had undiagnosed risk conditions.

Dr. Brooks asked whether data were available on the vaccination status of those with risk factors who were hospitalized with pneumococcal disease in the age group 50- to 64 years.

Dr. Kobayashi responded that vaccination history is not available in these data sources for individuals with risk conditions but that her team would like to explore this in the future.

Dr. Maldonado commented on the issue of access. Messaging needs improvement for the 50- to 64-year-old group. Referring to COVID-19 vaccination, individuals with underlying conditions had difficulty getting documentation to provide to pharmacies for additional off-label doses of vaccines. She called for action for these groups and studies to see why these individuals are missing vaccinations.

Dr. Loehr clarified that the work group did not intend to penalize individuals over age 65 by recommending the vaccine dose at age 50. If waning immunity is as expected, the work group felt that an additional dose would be needed 15 years after the initial dose. Currently, these data are unavailable, but this issue will be studied over time. He also mentioned that if there is a high prevalence of serotype 4 in a community, clear guidance will be provided recommending PCV20 over PCV21 or a vaccination for serotype 4 if any new options become available. He emphasized that most members of the work group favored lowering the age for all PCVs to age 50 for equity reasons. However, Dr. Loehr stated that as an individual ACIP member he disagrees and believes that only the age recommendation for PCV21 should be reduced to age 50. The work group decided to lower the age for all PCVs to simplify the vaccination schedule for physicians. Dr. Loehr disagrees with this decision due to the differences in cost effectiveness, as PCV20 has a higher cost per QALY than PCV21 when the age is lowered to age 50. He believes that PCV21 is a better vaccine because it covers more serotypes. Despite his personal disagreement, he formally made a motion to recommend that a PCV be administered to all PCV-naïve adults aged 50 years and older.

Dr. Cineas seconded the motion.

Dr. Talbot commented that vaccinating at age 50 and again at age 65 is a win because it means adults have had a healthy life and have not passed away before their grandchildren.

Dr. Brewer stated that the implementation argument has not yet persuaded him and that he cannot support this for PCV20.

Dr. Brooks emphasized that there are seven domains of EtR and questioned whether problems in just one domain should be sufficient to influence a vote on the proposed policy option. He believes the positives in the other domains outweigh the negatives in the areas of concern.

Dr. Shaw reminded the group that even with the proposal to lower the age-based recommendation to age 50 for PCV21, an exception will still need to be made for prevention of serogroup 4 disease in at-risk individuals.

Dr. Loehr confirmed that serogroup 4 will be addressed in clinical considerations. He also emphasized that there is a difference in how different members' values are reflected in the priority they place on different EtR domains. He does, however, respect the work group's decision.

Dr. Jamieson mentioned that, along with cost-effectiveness, another issue is that PCV21 serogroup coverage is better for most adults. It seems that this can be handled in clinical considerations. This may mean a recommendation for 50 and above, but with clinical consideration, PCV21 may be better in some cases based on serogroup coverage.

Dr. Zimmerman commented on behalf of the Association for Prevention Teaching and Research, stating the group was in support of lowering the age of routine vaccination to 50 years due to the benefits on health equity and to better protect individuals with high-risk conditions aged 50- to 64 years because risk-based recommendations result in lower vaccine coverage than age-based recommendations. There is a large burden of pneumococcal disease in persons under 65 years of age with high-risk conditions and the highest rates for pneumococcal disease in Black Americans are seen among those under 65 years of age. A published decision analysis showed that PCV21 at age 50 and again at age 65 will result in a 15% decrease in IPD cases in Black Americans and a 14% decrease in other populations.

Dr. Goldman favored lowering the age recommendation for vaccination because it would improve implementation and benefit the patients. He reiterated that PCV21 is very different from PCV20. He shared that he is concerned with lowering one, not the other, because recommendations would differ for those in this age group with and without underlying medical conditions. It is essential to be concise and clear on who should be vaccinated between 50 and 64, especially among those with other medical conditions.

Dr. Richard Haupt (Merck) expressed strong support for the recommendation and underscored the imperative of this vote for improved adult pneumococcal vaccine utilization and, more importantly, health equity. A vote to expand the age-based recommendation improves access to the benefits of pneumococcal vaccination. It provides opportunities to reduce persistent disparities in pneumococcal disease risk that current recommendations have not addressed. He also noted that Merck has very high payer coverage from both commercial and Medicare Advantage plans for PCV21, licensed in June. The vast majority have already covered PCV21.

Dr. Luis Jodar (Pfizer) stated that despite the different compositions, Pfizer supports the ACIP recommendation to use any currently available PCVs for all adults ages 50 and older. In the case of PCV20, this is supported by the burden of IPD and pneumococcal pneumonia caused by the 20 serotypes which remains a public health concern, which is especially important for serotypes unique to PCV20, including serotype 4, which has been increasing in the U.S. and globally with a focus on disadvantaged populations. Pfizer recommends the coexistence of both PCV21 and PCV15 followed by PCV23 and PCV20 in the population, which will allow a greater choice and less complexity of recommendations and increase equity and improve implementation.

Dr. Kobayashi then provided an overview of proposed clinical considerations for implementation. The proposed language is as follows:

> *A single dose of PCV (PCV15, PCV20, or PCV21) is recommended for all adults aged ≥50 years and for adults aged 19–49 years with certain underlying conditions or risk factors* who have not received a PCV or whose vaccination history is unknown.*

**Alcoholism; chronic heart, liver, or lung disease; chronic renal failure; cigarette smoking; cochlear implant; congenital or acquired asplenia; cerebrospinal fluid leak; diabetes mellitus; generalized malignancy; HIV; Hodgkin disease; immunodeficiency; iatrogenic immunosuppression; leukemia, lymphoma, or multiple myeloma; nephrotic syndrome; solid organ transplant; sickle cell disease; or other hemoglobinopathies.*

For PCV13-experienced adults who completed the recommended vaccine series, the shared clinical decision-making recommendation regarding the use of a supplemental PCV20 or PCV21 dose remains unchanged. The current age threshold is maintained because, under previous recommendations, PCV13-vaccinated adults were only considered to have received all recommended vaccine doses after receiving one final dose of PPSV23 at or after age 65. The proposed language is as follows:

> *Shared clinical decision-making is recommended regarding use of a supplemental PCV20 or PCV21 dose for adults aged ≥65 years who have completed their recommended vaccine series with both PCV13 and PPSV23.*

For PCV13-experienced adults who have not completed the recommended vaccine series, the proposal is to remove the option to complete the vaccine series with PPSV23 and instead to recommend a single dose of either PCV20 or PCV21.

The proposed language is as follows:

> *A single dose of either PCV20 or PCV21 is recommended as an option for adults aged ≥19 years who have started their pneumococcal vaccine series with PCV13 but have not received all recommended pneumococcal vaccine doses.*

The team will work to update guidance for populations experiencing serotype 4 disease.

Vote: Pneumococcal Vaccines
The vote occurred later in the day following public comment but is incorporated here for continuity.

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for pneumococcal vaccines into the record:

> *ACIP recommends a pneumococcal conjugate vaccine (PCV) for all PCV-naïve adults aged ≥50 years*

Motion/Vote: Pneumococcal Vaccines

Dr. Loehr motioned to approve the proposed vote recommendation for pneumococcal vaccines, stating, “ACIP recommends a pneumococcal conjugate vaccine (PCV) for all PCV-naïve adults aged ≥50 years.” Dr. Cineas seconded the motion. No COIs were declared. The motion carried with 14 favoring and 1 opposing. The disposition of the vote was as follows:

14 Favored:	Brooks, Brewer, Maldonado, Kamboj, Cineas, Asturias, Schechter, Jamieson, Chu, Moser, Shaw, Chen, Kuchel, Talbot
1 Opposed:	Loehr
0 Abstained:	

INFLUENZA VACCINES

Dr. Jamie Loehr, Chair of the ACIP Influenza Vaccine Work Group, opened the influenza session by announcing that FluMist® (Live Attenuated Influenza Vaccine) was approved by the FDA for self-administration or administration by a caregiver on September 20, 2024. This change is expected to take effect for the 2025-26 influenza season. Currently, FluMist can only be given by a healthcare provider but in the future it will be available for shipment to private homes.

Dr. Sascha Ellington (CDC/NCIRD) presented an update on the 2023-24 end-of-season influenza vaccine effectiveness. This season was a predominant A(H1N1)pdm09 season with lower levels of A(H3N2) and B/Victorian circulation. Peak activity occurred in week 52 of 2023. Vaccines were quadrivalent and included A(H1N1)pdm09, A(H3N2), and B components. The four CDC VE investigating networks are the Investigating Respiratory Viruses in the Acutely Ill (IVY), the New Vaccine Surveillance Network (NVSN), the US Flu Vaccine Effectiveness Network (US Flu VE), and the Virtual SARS-CoV-2, Influenza, and Other Respiratory Viruses Network (VISION). The networks include all ages across inpatient and outpatient settings and are geographically diverse, including patients from 23 states.

Dr. Ellington described the methods for estimation of influenza vaccine effectiveness for the 2023-2024 season. Enrollees were people with acute respiratory illness who presented for medical care. The test-negative design was used to determine VE. Vaccination odds were compared among case patients with influenza confirmed by molecular assay versus control patients testing negative for influenza and SARS-CoV-2. Persons were classified as vaccinated based on receipt of any 2023–24 seasonal flu vaccine according to medical records, immunization registries, claims data, and/or self-report. VE was calculated as 1 minus the adjusted odds ratio times 100%. Estimates were adjusted for geographic region, age, and calendar time of illness. In IVY, US Flu VE, and VISION estimates were also adjusted for sex and race and ethnicity, and the US Flu VE estimates were also adjusted for days between illness onset and enrollment and self-reported general health status.

The final estimates for VE among children 6 months to 17 years of age against any influenza ranged from 56% to 59% in outpatient settings and 59% to 64% in the inpatient setting. These were comparable to the interim estimates that included data through the end of January that were presented at the February 2024 ACIP meeting. The final estimate for VE against influenza A in the pediatric population ranged from 43% to 50% in outpatient settings and 44% to 51% in the inpatient setting, similar to the interim estimates. The final estimate for VE against influenza B in the pediatric population ranged from 64% to 74% in outpatient settings and 78% to 85% in inpatient settings; the interim estimates were similar in the outpatient setting but data were insufficient for an interim estimate for children in the inpatient setting.

For adults aged 18- to 49 years of age, the final estimate for influenza VE against any influenza ranged from 37% to 54% in outpatient settings and 51% to 53% in inpatient settings. The final estimate in this age group for VE against influenza A ranged from 20% to 45% in outpatient settings and 37% to 44% in inpatient settings and for influenza B, 67% to 75% in outpatient settings and 68% to 72% in inpatient settings.

For adults aged 50- to 64 years of age, the final estimate for influenza VE against any influenza ranged from 22% to 44% in outpatient settings and 40% to 48% in inpatient settings. The final estimate in this age group for VE against any influenza A ranged from 11% to 39% in outpatient settings and 38% to 39% in inpatient settings and for influenza B, 81% to 82% in outpatient settings and 61% to 86% in inpatient settings.

For adults ≥65 years of age, the final estimate for influenza VE against any influenza ranged from 37% to 40% in outpatient settings and 31% to 36% in inpatient settings. The final estimate in this age group for VE against any influenza A ranged from 36% to 37% in outpatient settings and 27% to 35% in inpatient settings and for influenza B, 67% to 80% in outpatient settings and 39% to 66% in inpatient settings.

The three active surveillance networks were used to estimate the VE against subtypes of influenza A. For A(H1N1), all estimates were under 50% for adults, with the lowest VE observed in adults <65 years of age. VE was about 50% from NVSN in inpatient and outpatient settings for children. The US Flu network estimated 60% VE for children in outpatient settings.

Because it was a predominantly an A(H1N1) season, less data were available for A(H3N2), resulting in wider confidence intervals. The lowest VE was among adults ≥65 years old. For children, VE was around 40% against hospitalization and 50% against outpatient influenza from NVSN. The US Flu network estimated lower VE for children in outpatient settings.

Dr. Ellington concluded that vaccination with a 2023–2024 influenza vaccine reduced the risk of medically attended influenza outpatient visits and hospitalizations among children, adolescents, adults, and adults over age 65 years. Most results were consistent across all four networks and these end-of-season estimates were similar to interim estimates from February.

Dr. Tom Shimabukuro (CDC/NCIRD) provided an update on Highly Pathogenic Avian Influenza A (H5N1). A substantial number of cases in 2024 were reported in the U.S. and are attributed to outbreaks in dairy cattle. Historically, human infection has resulted from exposure to sick or dead poultry and live poultry markets, as well as to other infected animals; in the case of the U.S. outbreak, these animals were dairy cows. Limited, non-sustained human-to-human transmission has occurred globally in the past but has not been seen in the U.S.

CDC priorities include supporting and engaging public health and agricultural partners, protecting human health and safety, understanding the risk to people from HPAI A(H5N1) viruses, and assessing HPAI A(H5N1) viruses for genetic changes.

As of October 18, 2024, USDA has confirmed HPAI A(H5N1) in U.S. dairy herds in 324 farms across 14 states. A significant decrease in the quality and production of milk was observed in early 2024. USDA reported HPAI A(H5N1) confirmed cases in cows from Texas and Kansas on March 25, 2024.

In 2024, there were 27 reported human cases in the U.S., most of whom had known exposure to dairy cattle or poultry. Additionally, one case in Missouri had an unknown exposure. The individuals exposed to dairy cattle and poultry experienced mild clinical symptoms, such as mild eye irritation, respiratory issues, and systemic effects.

The Missouri case, which had multiple underlying health conditions, was hospitalized with gastrointestinal symptoms, chest pain, and other symptoms not typical of respiratory illness. The illness, however, was not severe, and the patient recovered. The case was discovered through regular surveillance. The case's contacts' serology results are pending.

Sequences maintain primarily avian genetic characteristics and lack changes to make the virus better adapted to infect or spread among humans. There is no impact on the current CDC influenza diagnostic assay's ability to detect A(H5N1) viruses and no known markers of resistance were detected. Hemagglutinins of human influenza viruses remain antigenically related to two available Candidate Vaccine Viruses (CVVs). Assessment of newer California viruses is underway. Dr. Shimabukuro reiterated that seasonal vaccines are not expected to protect against influenza A(H5N1) viruses.

All people with direct or close exposure to animals infected with influenza A(H5N1) should be monitored for illness during exposure and 10 days after their last exposure. Signs and symptoms may include fever, cough, sore throat, runny or stuffy nose, muscle or body aches, headaches, fatigue, eye redness, shortness of breath, or difficulty breathing and less commonly, diarrhea, nausea, vomiting, or seizures. If signs or symptoms develop, these persons should seek medical evaluation for possible influenza testing and antiviral treatment. Symptomatic people should be isolated away from others during this evaluation. State and local health departments can facilitate testing and treatment.

The CDC supports state and local health departments monitoring exposed people during and for 10 days after the last exposure. Over 5,100 people have been monitored, and over 260 have been tested due to targeted surveillance, and 26 cases have been detected. Through enhanced regular surveillance, 54,360 specimens have been tested, with one person testing positive (the Missouri case). There have been no indicators of unusual influenza activity in people, including avian influenza A(H5N1), in regular surveillance.

In June 2024, the Michigan Department of Health collected blood samples from 35 dairy workers. The samples were tested for antibodies against influenza A(H5N1) and a seasonal influenza virus. None of the participants showed neutralizing antibodies specific to the avian influenza A(H5N1) virus although many showed antibodies to seasonal influenza viruses. This suggests that these people were not previously infected with influenza A (H5N1) despite the high risk of exposure.

Ferrets are used to study both the severity and transmissibility of influenza. They exhibit many clinical signs of infection similar to those observed in humans. Dr. Shimabukuro shared that in a study of A(H5N1) viruses, ferrets were inoculated with two A(H5N1) virus strains: Michigan and Texas. The results showed that the Michigan virus caused less severe illness in ferrets than the Texas virus. The Michigan virus resulted in less weight loss and lower mortality rates. However, transmission through respiratory droplets was similarly observed for both viruses. The Michigan virus is considered better to represent the currently circulating strains of the virus.

The CDC Influenza Risk Assessment Tool (IRAT) is an evaluation tool for prioritizing resources for pandemic preparedness. The U.S. government subject matter experts assess viruses based on ten risk factors related to their emergence and public health impact. Emergence is the risk of a novel influenza virus acquiring the ability to spread quickly and efficiently in people. The public health impact is the potential severity of human disease caused by the virus and the burden on society. The IRAT is not intended to predict a pandemic and is not to be used to assess the overall population or individual risk. Based on available data, CDC's current assessment is that the risk to the general public from avian influenza A(H5N1) virus remains low.

In summary, the overall risk to the public for HPAI A(H5N1) remains low. There is a greater risk for people with close, prolonged, or unprotected exposure to infected animals or environments contaminated by infected animals. Exposed individuals should monitored for symptoms after the first exposure and for 10 days after the last exposure.

Dr. Chu asked whether CDC had sequencing data to indicate changes in receptor binding with the Texas and Michigan strains that were used in the ferret studies.

Dr. Shimabukuro responded that he currently does not have the data available. However, he stated that the sequences primarily retain avian genetic characteristics and do not exhibit changes that would enhance the virus's adaptation to infect humans.

Dr. Chu inquired whether there can be speculation about why the two viral strains' lethality is different and whether any household studies are being done to examine transmission in the farm worker communities.

Dr. Shimabukuro said he would have to contact the lab for additional information. He stated that CDC has teams in the field working with partners to do epidemiologic investigations, contact tracing, and studying animal-to-human and human-to-human spread, so there will be more information to come.

Dr. Schechter asked if there is additional seroprevalence data for poultry workers in recent years. He also sought comments on the genetic differences between the Michigan and Texas strains.

Dr. Shimabukuro said he thought that there might be data from outside the U.S. but was unsure of any data within the U.S. He agreed to follow up on the differences between the strains.

Dr. Shaw inquired if H5N1 has been found in wastewater and whether it is possible to identify humans from animal sources. He also asked if there has been specific outreach to dairy and poultry farm workers to encourage them to receive seasonal influenza vaccines.

Dr. Shimabukuro stated that wastewater surveillance is being done in addition to regular surveillance. H5N1 has been detected in wastewater and has been usually in areas associated with animals or animal products but it's difficult to definitively determine source as animal or human. There is a program to support jurisdictions with infected herds, promoting seasonal vaccinations for agricultural workers to protect them from seasonal influenza and potentially help prevent respiratory illnesses.

Dr. Loehr inquired whether a patient who receives the flu vaccine and contracts the flu will experience a less severe case.

Dr. Ellington clarified that none of the VE studies presented today were designed to answer this question, but there are studies with other designs that show less severe illnesses with vaccination. Dr. Grohskopf added that there are other studies that suggest this.

Dr. Chris Hahn addressed an earlier question about wastewater as an epidemiologist serving states affected by H5N1. Although wastewater detection is taking place, it remains unclear where the contamination originates. All impacted states have implemented targeted vaccination efforts, and we are careful in our messaging to clarify that these vaccinations are intended to protect against seasonal influenza.

Dr. Shimabukuro clarified a previous answer on the ferret studies discussed. While he does not have genetic sequencing, he would like to reinforce that the Michigan human virus better represents currently circulating viruses.

Dr. Kamboj asked whether challenge studies with the candidate virus vaccines are being done in ferrets.

Dr. Shimabukuro confirmed that other ferret studies are being conducted.

Dr. Chu asked if the at-home flu test detects H5 and whether there is a plan to scale these types of tests in farmworker communities if they do.

Dr. Shimabukuro clarified that if an over-the-counter test detects influenza A, it should also be able to detect influenza A(H5N1). However, these tests do not do subtyping, which must be done by a laboratory and then confirmed at CDC. There are partnering programs to explore expanding testing capacity if needed; that work is ongoing.

Dr. Maldonado recalled that the transmission from cows to cats involved drinking raw milk. She inquired about additional messaging around this information, such as data on the pasteurization of milk.

Dr. Shimabukuro shared that the CDC recommends that people do not drink raw milk. All the data point to pasteurization resulting in a safe commercial milk supply.

Dr. Daskalakis reinforced that pasteurization is highly effective in addressing H5N1. Both CDC and FDA have issued clear guidance on raw milk.

Dr. Jeanne Santoli (CDC/NCIRD) shared the Vaccine for Children (VCF) resolution update. The purpose of this resolution is to (1) update the Inactivated Influenza Vaccine component of the resolution to add options for vaccination of 18-year-olds who are solid organ transplant recipients and (2) update the links in the contraindications and precautions sections of both components of the resolution.

There were no changes to the inactivated component of the influenza vaccine-eligible groups and the recommended vaccine schedule and dosage intervals. Two vaccine products (Fluzone® High-Dose and FLUAD®) have been added, which are indicated for people ≥65 years and older. A table note was added that states, “Persons aged 18 y should receive an age-appropriate influenza vaccine (i.e., one approved for their age), with the exception that solid organ transplant recipients on immunosuppressive medication regimens may receive high-dose inactivated influenza vaccine (HD-IIV3) or adjuvanted inactivated influenza vaccine (aIIV3) as acceptable options, without a preference over age-appropriate IIV3s.” No changes to dosage, contraindications, or precautions were made. There is, however, an update to the link for this information.

No changes have been made to the live attenuated influenza vaccine-eligible groups or their recommended vaccine schedule and dosage intervals. There are recommendations for the dosage to be consistent with how it is depicted in the resolution of the inactive influenza vaccine component and an update to the link of the contraindications and precautions information.

Dr. Kamboj requested that the Work Group consider a high-dose flu vaccine beyond solid organ transplant, especially for hematopoietic stem cell transplant recipients.

Dr. Brooks questioned whether there was any consideration for younger children.

Dr. Wharton clarified that this resolution aligned VFC with the committee's vote in June. Younger children were not considered.

Dr. Loehr inquired whether there was a recommendation for recombinant RIV in 18-year-olds and, if not, why it was not considered.

Dr. Santoli confirmed that this vaccine was not included in the VFC program because it was not brought forward for inclusion when it was licensed. Managing a vaccine designated to only one age cohort is also challenging.

Dr. Loehr motioned to approve VFC resolution for vaccines to prevent influenza.

Dr. Cineas seconded the motion.

Vote: Influenza Vaccines

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP resolution for Influenza Vaccines for Children (VFC) into the record:

> Approve the Vaccines for Children (VFC) resolution for vaccines to prevent influenza.

Motion/Vote: Influenza Vaccines

Dr. Loehr made a motion to approve the VFC resolution for influenza vaccines. Dr. Cineas seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored: Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schecter, Shaw and Talbot
0 Opposed:
0 Abstained:

CHIKUNGUNYA VACCINES

Dr. Edwin Asturias, chair of the ACIP Chikungunya Vaccines Work Group, introduced the session. The Work Group was formed in May 2022. The currently available vaccine, Valneva's live attenuated vaccine, was licensed in November 2023. A virus-like particle vaccine has been submitted for licensure by Bavarian Nordic. The Work Group is developing policy options for ACIP's consideration for using the chikungunya vaccine among U.S. persons at risk of chikungunya, including travelers, laboratory workers, and residents of U.S. territories and states with risk of transmission.

Dr. Susan Hills (CDC/NCEZID) updated the committee on chikungunya and chikungunya vaccines. Chikungunya is a mosquito-borne disease. Key vectors are *Aedes aegypti* and *Aedes albopictus* mosquitoes. It is typically transmitted in tropical and subtropical regions, with about 120 countries and territories where transmission has ever been documented. A key feature of the virus is that it periodically causes explosive outbreaks, often with high attack rates. Clinical illness is characterized by fever and joint pain, which is typically severe and can be debilitating. The approach to management is supportive; no specific antiviral treatment is available. Rare serious complications include myocarditis, hepatitis, and neurologic illness. Deaths are rare and are primarily seen in older adults, particularly those with comorbidities and young infants. Acute symptoms usually resolve in 7-10 days. Some patients have continuation or relapse of their joint symptoms. Studies have reported variable proportions of patients with persistent symptoms, but ongoing arthralgia of variable severity might be present in up to about half of patients at 3 months after infection and up to about 30% at 12 months. It is a reportable disease in the United States; approximately 100-200 cases are reported annually among U.S. travelers, although 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. Unquestionably, the greatest risk for US travelers to acquire chikungunya is traveling to an area with an outbreak.

Dr. Hills reminded the committee that there is currently one licensed vaccine in the U.S. and one vaccine submitted to the FDA for licensure. The licensed vaccine is a live attenuated vaccine manufactured by Valneva as IXCHIQ®. It was licensed in November 2023 and is currently approved for use in adults aged 18 years and older. This vaccine has a single-dose schedule.

ACIP approved recommendations for use of this vaccine in adult travelers in February 2024. The recommendations note that ACIP recommends the live attenuated chikungunya vaccine for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak. In addition, the vaccine may be considered for certain persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years. The groups include 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. ACIP also recommends live attenuated chikungunya vaccine for laboratory workers who are potentially exposed to the chikungunya virus. Updates on this vaccine include that for adolescents aged 12-17 years, Valneva plans a submission to the FDA this year, which, if ultimately approved, will allow use in this age group. A clinical trial began in December 2023 and is in progress for children aged 1-11 years. Finally, monitoring of the vaccinated cohort from the pivotal clinical trial in adults aged ≥18 years is continuing to investigate the persistence of seroresponse following the single dose of the vaccine. At two years, a high seroresponse rate of 97% was maintained. Monitoring will continue for 10 years to determine if a booster dose will be needed in the future.

Bavarian Nordic manufactures the second vaccine, and licensure is possible in February 2025. The virus-like particle vaccine's intended age group is adolescents and adults aged ≥12 years. The vaccine has a single-dose primary schedule. Like the live attenuated vaccine, the virus-like particle vaccine will be licensed through the accelerated approval pathway. Traditional approval would have been challenging, and clinical development would likely have been delayed if this approach had been required. FDA can grant accelerated approval for products that are for serious conditions and that fill an unmet medical need. In this pathway, the demonstration of effectiveness is based on controlled clinical trials showing the vaccine affects a surrogate endpoint that is reasonably likely to predict clinical benefit. For the virus-like particle vaccine, the marker of protection was based on a neutralizing antibody titer estimated from a validated non-human primate model. This pathway has a post-licensure requirement for controlled trials to confirm clinical benefit.

The ACIP Chikungunya Vaccines Work Group has four groups for whom vaccine recommendations are being considered. These include travelers, laboratory workers, residents of U.S. territories at risk of chikungunya virus transmission, and residents of U.S. states at risk of transmission. For the live attenuated chikungunya vaccine, ACIP has made recommendations for use among travelers aged 18 years and older and among laboratory workers; the Work Group is currently considering policy options to present to ACIP for use of the vaccine among residents of US territories and states with risk of transmission. Regarding the virus-like particle chikungunya vaccine, policy options for the use of the vaccine among all four groups are under consideration and will be presented for ACIP’s consideration at future meetings.

Dr. Victoria Jenkins (Bavarian Nordic) discussed the virus-like particle chikungunya vaccine (CHIKV VLP). CHIKV VLP consists of 3 recombinant proteins that mimic the virus but cannot replicate in the host. It is adjuvanted with aluminum hydroxide in a single 40µg VLP dose administered intramuscularly. The PDUFA target action date is February 14, 2025. The proposed indication is to prevent CHIKV infection in individuals ≥ 12 years of age. The proposed contraindications are hypersensitivity, including severe allergic reactions, to any component of the vaccine.

A defined threshold of serum-neutralizing antibodies was used as a surrogate efficacy endpoint in Phase 3 clinical trials. The CHIKV luciferase assay used in the study was based on the CHIK181/25 live-attenuated virus (Asian lineage) engineered to express luciferase transgene. The neutralization assay was based on an 80% reduction of luciferase activity, resulting in an NT_{80} value. The assay measures cross-neutralization as the vaccine is heterologous to the assay strain (West African vs. Asian).

The submitted vaccine clinical program included three Phase 2 studies and two Phase 3 studies conducted in the U.S. The Phase 2 dose and schedule studies were conducted in healthy participants aged 18-45 years. The single 40 µg CHIKV VLP adjuvanted dose was chosen for further development because it had superior immunogenicity after the first vaccination, showed a rapid and durable response, and was well-tolerated. The study also looked at the need for a booster dose, but the need for a booster is still unknown.

The Phase 3 studies were completed in parallel, placebo-controlled, and conducted in the U.S. One was done in participants 12 to 64 years of age and the other in adults ≥65 years of age. Both studies had coprimary end points of superiority of GMT at day 22 vs. the placebo, difference in the seroresponse rate vs. placebo at day 22, and safety. In addition, in the study of adolescents and adults, lot-to-lot consistency of anti-CHIKV SNA GMT at Day 22 was evaluated in a subgroup of participants 18-45 years of age. The demographic profile of participants in both studies were balanced between vaccine and placebo groups. All co-primary and secondary endpoints were met in both studies. CHIKV VLP vaccine was well-tolerated in individuals 12 to 64 years of age. The incidence of adverse events of special interest (AESI) and medically-attended adverse events (MAAE) did not differ between the CHIKV VLP vaccine group and the placebo group in individuals 12 to 64 years. CHIKV VLP vaccine was well-tolerated in individuals ≥65 years of age. Incidence of AESI and MAAE did not differ between the CHIKV VLP vaccine group and the placebo group in individuals ≥65 years of age.

Dr. Jenkins summarized that the Phase 3 trials demonstrated a rapid and robust immune response in individuals ≥12 years of age. A durable and boostable immune response was also observed in a subpopulation of the Phase 2 trial. The vaccine was well tolerated, and there were no treatment-related SAEs, as determined by the sponsor. Most solicited and unsolicited adverse events were mild or moderate in intensity.

Dr. Cineas inquired whether the studies included immunocompromised patients and those with chronic medical conditions.

Dr. Jenkins responded that the Phase 3 study only included healthy participants. However, persons with stable immunocompromising conditions will not be excluded from a Phase 3B confirmatory efficacy study.

Dr. Susan Hills (CDC/NCEZID) concluded with a review of the work group's interpretation of data for the virus-like particle chikungunya vaccine following their preliminary review of the data. Regarding VE, results are based on immunogenicity data since no VE data is available. Short-term immunogenicity data reflecting seroresponse rates at 3 weeks after vaccination are available from 2,750 vaccinated subjects in two Phase 3 studies, most of whom were adults aged 18-64 years, with smaller numbers of adolescents and older adults with data, with about 200 subjects with data in each of these age groups. The work group noted there was a robust response to vaccination, with seroresponse rates 21 days after vaccination of 98% in adolescents and younger adults and 87% in older adults, and seroresponse rates at 6 months after vaccination of 86% and 76% in the younger and older age groups respectively.

Data after 6 months are not yet available from Phase 3 studies, so the need for a booster dose is unknown.

Safety data are available from about 3,000 vaccinated subjects in two Phase 3 studies, most of whom were adults aged 18-64 years. Data from smaller numbers of adolescents aged 12-17 years and adults aged ≥65 years are also available, with about 210 subjects with data in each age group. Based on the overall data, the work group concluded that the overall safety profile of the vaccine was acceptable. Solicited adverse events were reported within 8 days of vaccination. The following data reflect results among adolescents and adults aged 12-64 years. Local events were reported by 24%, with 0.2% graded as severe. Solicited systemic events were reported by 32%, with severe events in fewer than 2% of subjects. The most frequent events were fatigue, headache, and myalgia, all reported by 18 to 20% of vaccinated persons. There was no concerning signal with arthralgia after vaccination. One serious adverse event – a retinal detachment -- was assessed as related by the study investigator but unrelated by the safety monitoring committee chair. For adults ≥65 years, all adverse event rates were lower than those seen in 12-64-year-olds.

The work group summary for the chikungunya VLP vaccine:

- Will provide an option, in addition to the licensed live attenuated vaccine, for vaccination of adults aged ≥18 years
- Will provide a new option for adolescents aged 12–17 years
- Immunogenic vaccine but no vaccine effectiveness data, which will be gathered post-licensure, and the need for a booster dose is currently unknown
- There are no apparent safety concerns, but safety data only from ~3,000 people, so data are insufficient to detect rare events, and post-marketing surveillance will be important
- Work group to conduct comprehensive data review and present GRADE assessment as part of the Evidence to Recommendations framework at a future meeting

During 2025, the work group anticipates presenting recommendations for ACIP's consideration and asking for votes on vaccine recommendations in various groups, including the use of live attenuated vaccine among travelers aged 12-17 years, use of the virus-like particle vaccine in travelers aged ≥12 years, use of the virus-like particle vaccine among laboratory workers, use of both vaccines among residents of U.S. territories with transmission risk, and use of both vaccines among residents of U.S. states with transmission risk.

Dr. Schechter inquired about short- and long-term plans for using the VLP vaccine in pregnant individuals.

Dr. Hills confirmed that the work group is discussing the topic and will be able to provide additional details at a future ACIP meeting. The use of the live attenuated vaccine has previously been considered. One of the main recommendations is that pregnant women avoid traveling to areas with CHIKV if possible, particularly during an outbreak, due to the concern of infection and subsequent transmission during the intrapartum period. If travel is unavoidable, the licensed vaccine should be considered a precaution for use, with avoidance during the first trimester and after 36 weeks of gestation.

Dr. Chu asked whether there were any Development and Reproductive Toxicity (DART) studies for the VLP vaccine candidate.

Dr. Hills clarified that she was referring to animal data and redirected the question to Dr. Jenkins.

Dr. Jenkins confirmed that DART data are available and referred to a colleague, Dr Vang.

Dr Vang confirmed that DART studies were conducted in rabbits and rats. The results showed that the vaccine was safe and there were no observations of concern.

Dr. Maldonado questioned whether the work group was considering making preferential recommendations or whether there might be blanket recommendations for both vaccines and asked whether the work group would continue to monitor strains circulating in the Western Hemisphere.

Dr. Hills confirmed that the vaccines would be considered independently due to the differences between the vaccines and the way immunogenicity and safety were assessed. For example, with immunogenicity, a different assay was used with a different marker for protection for each vaccine, so those comparisons are difficult. For safety, data are only available for about 4,000 subjects for each vaccine, and with such little data, it's hard to make definitive comparisons. The data suggest that the vaccines will protect against the various chikungunya strains, but as usage increases, CDC will be looking for any evidence of vaccine failure.

Dr. Asturias reiterated that the work group should consider the vaccines independently because the surrogates of protection differ. However, given the increasing burden in the Americas, having the option of two vaccines is encouraging.

COVID-19 VACCINES

Dr. Robert Schechter (ACIP, Work Group Chair) introduced this session on behalf of the ACIP COVID-19 Vaccines Work Group. As a reminder, ACIP recommended 2024–2025 COVID-19 vaccines as authorized or approved by the FDA in persons ≥6 months. Everyone ≥5 years should get one dose of a 2024–2025 vaccine. Children aged 6 months-4 years need multiple doses of COVID-19 vaccine to be up to date, including at least one dose of the 2024–2025 vaccine. Moderate or severely immunocompromised people may receive additional 2024–2025 vaccine doses. There are no recommendations for additional 2024–2025 doses for older adults. Today's session will focus on additional doses for adults ages 65 years and older and moderate or severely immunocompromised people.

Dr. Georgina Peacock (CDC/NCIRD) presented the implementation considerations for additional COVID-19 vaccine doses. For children, coverage of 2024–2025 vaccine to date is 3.7% vs. 3.1% of 2023–2024 vaccine at this time last year. For adults ≥18 years of age, coverage of 2024–2025 vaccine is 11.7% vs. 6.8% 2023–2024 vaccine at this time last year, and for ages ≥75 years, coverage is 30.6% vs. 17.7% last year.

Among adults ≥65 years of age, vaccination coverage for ≥1 2023–2024 COVID-19 vaccine dose through June 2024 was about 40% and 8.9% for ≥2 doses of 2023–2024 COVID-19 vaccine, based on the National Immunization Survey-Adult COVID Module. Within the group receiving ≥2 doses, higher coverage is seen in urban than in rural areas. Minimal differences in ≥2 dose coverage are seen by low, moderate, or high Social Vulnerability Index. Higher coverage is seen in people with underlying health conditions and those with a healthcare provider's recommendation.

36.8% of ≥65-year-olds surveyed from April-June 2024 had received ≥1 2023–2024 COVID-19 vaccine dose. Of that 36.8% who received ≥1 dose, 20% were vaccinated with ≥2 doses, 44.3% "definitely will get another dose," 30.9% "probably will get another dose," and 4.7% "probably or definitely will not get another dose." There was greater intention to get a second dose in people ≥80 years of age and people living in urban areas. From April to June 2024, there was a modest increase in the intent of adults ≥65 years of age to receive another dose.

Among immunocompromised adults aged ≥18 years, 5.4% received ≥2 doses of 2023–2024 COVID-19 vaccine through June 2024. Within this group, higher coverage is seen among immunocompromised adults ≥65 years old, those living in suburban areas, those who had received a healthcare provider recommendation, and those with insurance.

The Omnibus Survey of adults ≥18 years of age with health conditions and adults aged ≥65 years, conducted in August 2024, asked respondents whether they intended to receive a second dose for the current season if it were recommended. Overall, one-third of those surveyed intended to receive a second dose. Intentions were higher among adults over 65 years old. There was lower intent in rural areas and among those who are uninsured.

The proposed recommendations for additional doses would not be overly burdensome to implement because the additional dose would be the same formula as the current vaccine, there is administration infrastructure and product can be used, and the recommendations can be integrated into existing systems and structures. Minor challenges include the need for additional education and a possible increase in existing vaccine fatigue as well as availability at practices after the fall supply has been exhausted.

The new proposed recommendations include "should" rather than "may" (or shared clinical decision-making) recommendations for overall ease of implementation. The recommended and minimal interval for vaccination is consistent with language for other vaccines. It is also standardized across adults aged ≥65 years and immunocompromised populations, which eases implementation. Furthermore, a minimum interval of 2 months allows for flexibility in vaccine administration when accounting for individual risks and circumstances.

Of adults aged ≥18 years who have received a 2024–2025 COVID-19 vaccine, the majority (81.9%) received their vaccination at a pharmacy or drug store. Similarly, of adults aged ≥65 years who received a 2024–2025 COVID-19 vaccine, the majority (82.8%) have received their vaccination at a pharmacy or a drug store. Within pharmacy settings, "may" (or shared clinical decision-making) recommendations can be challenging. CDC has dedicated healthcare provider engagement to assist with the denial of vaccination that may take place due to changes in guidance. Differences in vaccine access can create disparities in uptake, and these may be exacerbated by due to issues with insurance, disability, and vaccination settings (e.g., long-term care).

Dr. Swamy made a statement representing the American College of Obstetricians and Gynecologists. The group is supportive of the COVID-19 vaccine in pregnancy. Data show that the vaccine is safe and efficacious and decreases the risk of severe disease and hospitalization rates in infants when administered in pregnancy. Maternal vaccination can help reduce the risk of transmission to newborns during pregnancy, delivery, and breastfeeding. Due to the decreased rate of vaccination within this population, the group feels COVID-19 vaccine should be prioritized and recommended.

Dr. Christopher Taylor (CDC/NCIRD) presented updates on COVID-19-associated hospitalizations. COVID-NET data captures 10% of the U.S. population, and data presented today will be limited to hospitalizations identified in 90 counties across 12 states. Hospitals reported all positive SARS-CoV-2 test results within 14 days before or during hospitalizations. Clinical data are collected from an age- and site-stratified random sample.

Adults ≥65 comprise 70% of all COVID–19–associated hospitalizations among adults ≥18 years of age from October 2023 to September 2024. Rates of COVID-19 hospitalizations are highest among adults ≥75 years of age. COVID–19–associated hospitalizations increased with age from October 2023 to September 2024. Rates among those ≥75 years of age are three times as high as adults aged 65-74 years, nearly nine times as high as adults aged 50-64 years, and 24 times as high as adults 18-49 years of age.

Since March 2020, rates of COVID–19–associated hospitalizations among adults aged ≥65 years have decreased, but hospitalizations among adults aged ≥75 years remain the highest across all age groups. Most adults aged ≥65 years hospitalized with COVID-19 have underlying medical conditions. Adults aged ≥65 years remain at risk for severe outcomes during COVID–19–associated hospitalization. Between October 2023 and May 2024, 80% of all adults hospitalized with COVID-19 who died in-hospital were aged ≥65 years. Data suggests that deaths following hospital discharge are more common among older adults within 30 days of release. Fewer than half of adults aged ≥65 years hospitalized with COVID-19 have received any COVID-19 vaccine since September 2022.

Some conditions defined as immunocompromising according to COVID-NET are time-bound relative to admission for COVID-19-associated hospitalization. Immunosuppressive therapy is only considered if treatment was received 12 months before admission. Cancer is only considered if treatment or diagnosis occurred in the 12 months before admission. Inhaled, intranasal, intramuscular, or intraarticular steroids are also not included. Between July 2023 and May 2024, about 15.6% of people hospitalized with COVID-19 had an immunocompromising condition. Three percent of children aged ≤4 years and 15-22% of hospitalized adults had an immunocompromising condition.

The most common immunocompromising conditions were immunosuppressive therapy (46%), solid organ malignancy (34%), steroid therapy (26%), and metastatic cancer (22%). Few persons with an immunocompromising condition hospitalized with COVID-19 had received any COVID-19 vaccine since September 2022.

The time since receipt of the most recent COVID-19 vaccine varied little by the status of the immunocompromising condition. The risk for severe outcomes during COVID–19–associated hospitalization among children and adolescents varied little by immunocompromising condition status; in contrast, the risk for severe outcomes during COVID–19–associated hospitalization among adults did vary by immunocompromising condition status.

Dr. Ruth Link-Gelles (CDC/NCIRD) presented the effectiveness of COVID-19 vaccines to inform ACIP deliberations for two questions: the need for additional doses among those with immunocompromise and the need for additional doses in those aged ≥65 years. Critical issues in COVID-19 vaccine effectiveness (VE) include the impact of time since dose on protection, the impact of changing SARS-CoV-2 variants over time and variant/vaccine mismatch, and the effect of surges in disease, seroprevalence, and time since the last SARS-CoV-2 infection. As context for interpretation of VE, there were high rates of SARS-CoV-2 infection-induced immunity by July-August 2023 among all age groups.

VE findings should, therefore, be interpreted as the added benefit of COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity.

Absolute VE is a measure comparing the frequency of health outcomes in vaccinated vs. unvaccinated people. Relative VE compares the frequency of health outcomes in people who received one type of vaccine to people who received a different type. For 2023-2024 COVID-19 VE, VE was measured by comparing people who received a 2023-2024 dose to those who did not, regardless of past vaccination. This is similar to how influenza VE is measured annually. VE findings should be interpreted as the added benefit of COVID-19 vaccination in a population with a high prevalence of vaccine- and infection-induced immunity at the start of the 2023-2024 respiratory virus season.

Dr. Link-Gelles presented results from three VE platforms. VISION is a multi-site network of >300 emergency departments and urgent cares and >200 hospitals, utilizing a test-negative design and vaccination status from electronic health records and city and state immunization registries. The IVY Network is a multi-site VE platform that uses a test-negative design with vaccination status from electronic medical records, city and state registries, and plausible self-report. Medicare studies used a retrospective cohort design from Medicare-fee-for-service claims data.

Study results presented by Dr. Link-Gelles showed that COVID-19 vaccines protected both persons with and without immunocompromise. Patterns of COVID-19 VE in immunocompromised people differed from season to season, with generally lower VE compared to non-immunocompromised people but inconsistent waning patterns. During 2023-2024, VE against hospitalization in immunocompromised people waned to 0 by ~4-6 months.

In adults aged ≥65 years, 2023-2024 COVID-19 vaccination provided increased protection against COVID-19-associated emergency department and urgent care (ED/UC) visits and hospitalizations compared to no 2023-2024 vaccine dose. Protection waned to 0 against COVID-19-associated ED/UC visits and hospitalization by ~4-6 months. Waning patterns of 2023-2024 COVID-19 vaccines appeared similar to previous COVID-19 vaccine formulations; the most durable protection appeared to be for critical illness. VE against critical illness remained above 40% at 5 months after vaccination among adults aged ≥65 years. As with previous COVID-19 vaccine formulations, effectiveness was similar across age groups. Data from prior seasons show that an additional dose of the same formula appeared to provide additional protection.

Dr. Chu inquired whether messaging was targeted at providers of patients in long-term facilities to increase low vaccine rates in these groups. She also asked whether CDC could measure the vaccine's impact on long-term COVID-19.

Dr. Peacock stated that efforts have been made to increase vaccine rates within this group, but they have had limited success. Dr. Link-Gelles said that research on long-term COVID is challenging because its symptoms can resemble those of many other illnesses. Studies have been conducted on this and generally have found some level of protection by vaccination, but results vary across studies. This is an ongoing area of research both by CDC and by other groups.

Dr. Schechter expressed concern for lower vaccination rates among populations ≥65 years of age and older and pregnant women. COVID-NET shows that only 15% of adults ≥65 years of age received the 2023-24 COVID vaccine last year, and that of pregnant women whose infants 6 months of age and younger were hospitalized, fewer than 5% were vaccinated.

Dr. Asturias requested clarity on the difference in rates of COVID-19 outcomes among immunocompromised children on slide 17 of Dr. Taylor's presentation. The Colorado data show that the rate of hospitalization of healthy children under 1 year of age is relatively high and comparable to adults over 60 years of age. The children with immunocompromising conditions are probably somewhat older.

Dr. Taylor confirmed that infants under six months are comparable to adults older than 65-74 years of age. There are some differences between the populations, but the immunocompromise group's sample size is small, and because of that, it was presented as a broader age group.

Ms. Moser thanked the people who submitted comments on this portion of the agenda. She understands why we are studying the VE and comparing it to last year, but it would be helpful to better understand the "no recent vaccine" comparison group. It is essential to help people understand their protection level moving forward.

Dr. Loehr commented that the incidence rate of hospitalization increased with age. It is stunning that 1 in 70 adults will be admitted to the hospital for COVID. He also stated he is torn on the recommendation for 6 months between the first and second doses. Patients want to get the vaccine in July or August because of a trip and are unsure whether they can receive the next dose in September. I usually say 4 months, but that does not necessarily meet the 6-month time frame.

Dr. Brewer stated that the audience would better follow the presentation if there were language to frame VE data on slides 25 and 26 for the final row of 18-64-year-olds. He also asked for clarification on how this data should be interpreted.

Dr. Link-Gelles clarified that the "7-299 days earlier" is just an average breakdown for the four categories below.

Dr. Brooks stated that the risk for ED/UC visits is increased by about 20% in each category on the same slide. He asked how one interprets the slides and whether the data on this slide reflect relative VE.

Dr. Link-Gelles clarified there is no biological plausibility for a vaccine increasing your risk of disease, so that is not what we think has been happening in the longest time since vaccination. VE, at its root, essentially measures the risk of disease in a vaccinated population compared to an unvaccinated population. The unvaccinated or less vaccinated group can significantly impact the estimated VE. In this case, unvaccinated people get infected in the 6 months while vaccinated people are protected by their vaccine. That raises the infection-induced immunity level in unvaccinated people, which may make the VE look very low when the vaccine has waned, such that vaccinated people are now susceptible. This is a combination of relative and absolute VE.

Dr. Kuchel commented that chronological age is a good research measure for most adult populations. However, as someone practicing geriatric medicine, chronological age is an imperfect measure within older populations. He requested that some VE data be stratified by sex in addition to age because men and women do not age similarly.

Dr. Brewer requested an estimate of how much of the waning immunity in the control group is due to natural infection.

Dr. Link-Gelles described that the earlier phenomenon of the population getting infected, which results in lower than expected VE, probably impacts VE more the further away you get from vaccination. Measured VE can change quite a bit based on background rates of disease. For example, lower VE will be measured if there is a disease surge the month before a vaccine is introduced and the population has a very high rate of infection-induced immunity. The exact amount is difficult to quantify, especially since serology is unavailable in most of our studies.

Dr. Lisa Prosser (University of Michigan) presented the economic analysis of an additional dose of the 2024–2025 COVID-19 vaccine. Updates to the current version of the model include a 2-dose strategy (an additional mid-year dose), 2023-2024 hospitalization rates (COVID-NET data), CDC-negotiated 2024-2025 prices for vaccine costs, and adjustment of all cost inputs to 2024 dollars.

Weekly rates of COVID-19-associated hospitalizations by season for all ages have been declining in recent years. For the 2023-2024 season, the probability of hospitalization due to COVID-19 illness has dropped for all age groups, ranging from 14% lower in the 65 and older age group to 33% lower in the 18-49 year age group compared to the 2022-2023 season.

The analysis plan included a base case and uncertainty analyses. The outcomes were stratified by intervention strategy and by age subgroups. Vaccination for the 2-dose strategy economic analysis shows that the ICERs for age groups <65 years old were less favorable than those ≥65 years old across plausible parameter ranges. For ≥65-year-old age group, ICERs were most sensitive to seasonality-adjusted vaccine impact, probability of hospitalization, and vaccination costs. ICERs are more favorable in scenarios with a higher risk of hospitalization and lower vaccination costs.

Dr. Shaw questioned whether models accounted for the costs of potential post-infection care, e.g., transient or permanent residence in a skilled nursing facility, and the cost of a family member who may need to leave work to care for an elderly adult.

Dr. Prosser responded that the costs associated with hospitalizations and complications are from MarketScan data, which includes episode cost and some costs paid for by the health plan. It is highly likely that some of those costs would not be incorporated there if they're covered at the family level. This would include a conservative estimate of those costs. The cost of informal caregiver time, primarily associated with hospitalization, has been included in the model.

Dr. Loehr commented that he buys his vaccines as a small family practice owner. The current prices at which he purchases the vaccines are about 30% less than what is listed on the private market price slide.

Dr. Prosser agreed that this was an important point to share. Looking at an approximate $100 per dose, for the additional dose strategy, the corresponding incremental cost-effect ratios remain above $600,000 per QALY for age groups under 65 years; perhaps we can get closer to $200,000 per QALY for those 65 and older using a lower vaccine cost.

Dr. Schechter reflected on the previous summer's surge, which had higher hospitalizations in California than the 2023 surge. He asked whether this was reflected in national hospitalization statistics, and about the impact of hospitalization rates on these estimates.

Dr. Taylor responded that COVID-NET is comprised of multiple sites, and each site was different. Some sites that had a mild winter had a larger summer surge. Sites with very high rates during the winter peak in December and January saw a more moderate summer surge.

Dr. Brewer requested that Dr. Prosser speak about how equity would be cost-effective and how the model addresses the cost of time loss (e.g., post-vaccine side effects, time off work to receive the vaccine, etc.).

Dr. Prosser stated that there had been no formal incorporation of health equity considerations into the model. Vaccination would be more cost-effective if a population or sub-population had higher rates of illness, hospitalization, or death. This could be a way to think about equity within this presentation. This is not a current goal in this analysis but can be considered in a future study. Regarding time loss, some costs are incorporated into the time required to receive vaccination.

Ms. Lauren Roper (CDC/NCIRD) reviewed the Evidence to Recommendations (EtR) framework for additional doses of the 2024–2025 COVID-19 vaccine in older adults and people with moderate or severe immunocompromise. On June 27, 2024, ACIP voted to recommend 2024–2025 COVID-19 vaccines for everyone ages ≥6 months. On August 22, 2024, the FDA approved and authorized 2024–2025 Pfizer-BioNTech and Moderna COVID-19 vaccines for people ages ≥6 months. On August 30, 2024, the FDA authorized the 2024–2025 Novavax COVID-19 vaccine for people ages ≥12 years of age.

The EtR framework policy questions are, in addition to previously recommended 2024-2025 vaccination:

- Should a second dose of 2024–2025 COVID-19 vaccine be recommended for adults ages 65 years and older?
- Should a second dose of 2024–2025 COVID-19 vaccine be recommended for people ages 6 months and older who are moderately or severely immunocompromised?
- Should additional doses (i.e., 3 or more) of 2024–2025 COVID-19 vaccine be recommended for people ages 6 months and older who are moderately or severely immunocompromised under shared clinical decision-making?

Currently, the ACIP recommends that people aged ≥5 years receive one dose of the 2024–2025 COVID-19 vaccine at least 2 months after receiving their last dose. People who are previously unvaccinated for COVID-19 and receive Novavax should complete a 2-dose initial series. Current recommendations for people aged ≥6 months who are moderately or severely immunocompromised include a homologous initial COVID-19 vaccine series with at least 1 2024–2025 COVID-19 vaccine dose, and they may receive one additional 2024–2025 COVID-19 vaccine dose with an option for further additional doses of 2024–2025 COVID-19 vaccine informed by the clinical judgment of a healthcare provider and personal preference and circumstances.

Regarding the public health problem, Ms. Roper shared that SARS-CoV-2 continues to circulate year-round, with peaks occurring in the winter and late summer, compared to influenza and RSV, which have clearer increases during the typical respiratory virus months, with periods of low activity during the summer. Adults ≥65 years of age have the highest rates of hospitalizations due to COVID-19. Older adults also have the highest rates of death due to COVID-19. Adults ≥65 years of age have higher vaccination-only seroprevalence rates than younger age groups. Hospitalizations are highest among American Indian/Alaska Native non-Hispanic persons, followed by Black non-Hispanic persons, and are lowest among Asian and Pacific Islander non-Hispanic persons. The number of chronic conditions a person has increases with increasing age and is higher among Black non-Hispanic persons than among other racial and ethnic groups. About 1 in 6 people hospitalized with COVID-19 have an immunocompromising condition. Risk for severe outcomes during COVID–19–associated hospitalization among adults varies by immunocompromising condition status. After reviewing this domain, the work group felt COVID-19 disease among adults ≥65 years of age and among people with moderate or severe immunocompromise is of public health importance.

For benefits and harms, adults ≥65 years of age who received a 2023–2024 COVID-19 vaccination had increased protection against COVID-19-associated ED/UC visits and hospitalizations compared to people who had not received a 2023–2024 vaccine dose. Protection waned to 0 against COVID-19-associated ED/UC visits and hospitalization by ~4-6 months. Waning patterns of 2023–2024 COVID-19 vaccines appeared similar to previous COVID-19 vaccine formulations; most durable protections appeared for critical illness. VE against critical illness remained above 40% at 5 months after vaccination among those ≥65 years of age. VE was similar across age groups. Data from prior seasons shows that an additional vaccine dose appeared to provide some extra protection. Updated COVID-19 vaccination helped protect COVID-19–related thromboembolic events. Based on modeling data, annual and semiannual COVID-19 vaccine doses are likely to have the largest benefit in adults ≥65 years of age and people who are immunocompromised.

COVID-19 vaccines protected persons both with and without immunocompromise. Patterns of COVID-19 VE in immunocompromised persons differed from season to season, with generally lower VE than non-immunocompromised person s but with inconsistent waning patterns. During 2023–2024, VE against hospitalization in people with immunocompromising conditions waned to 0 by ~4-6 months. The inconsistency in waning patterns is likely multifactorial, including heterogeneity among those classified as immunocompromised, variation in underlying immunity and response to prior infection, and differing health behaviors over time and by immunocompromised status.

Safety surveillance demonstrated that serious adverse events after COVID-19 vaccination have been rare. Anaphylactic reactions have been rarely reported following receipt of COVID-19 vaccines. There is a rare risk of myocarditis and pericarditis; however, this is predominately in males ages 12-39 years. No increased risk has been observed in adults aged ≥65 years. Whether the risk might be different in immunocompromised people is unknown. COVID-19 vaccine doses continue to be reactogenic. The rate of local and systemic reactions reported to V-safe was lower with additional doses than after the initial series. Most vaccine recipients have mild reactions, but during 2023–2024, at least 10% reported health impact events during the 7 days post-vaccination, such as being unable to complete daily activities. Symptoms are less frequent and severe among older adults than adolescents and younger adults.

After reviewing this domain, the work group felt that the desirable anticipated effects of a second dose of 2024–2025 COVID-19 vaccine in adults ages ≥65 years were moderate to large. The work group majority felt that the undesirable anticipated effects of a second dose of a 2024–2025 COVID-19 vaccine in adults ages ≥65 were small, with a minority choosing minimal. The work group felt that the balance of benefits and harms favored the intervention of a second dose in this group. The work group felt that the desirable anticipated effects of a second dose of 2024–2025 COVID-19 vaccine in people with moderate or severe immunocompromise was moderate. The work group majority thought that the undesirable anticipated effects of a second dose of 2024–2025 COVID-19 vaccine in people with moderate or severe immunocompromise were small, with a minority polling minimal. The work group felt that the balance of benefits and harms favored the intervention of a second dose in this group. The work group felt that the desirable anticipated effects of a third dose of 2024–2025 COVID-19 vaccine in people with moderate or severe immunocompromise was moderate. The work group majority thought that the undesirable anticipated effects of a third dose of 2024–2025 COVID-19 vaccine in people with moderate or severe immunocompromise were minimal to small. The work group was split between the balance of benefits and harms, favoring the intervention and being unclear.

For the values domain, adults ≥65 years of age surveyed were more concerned about COVID-19 disease and had higher confidence in vaccine safety and vaccine importance. The work group felt “moderately” that adults ≥65 years of age feel the desirable effects are large relative to undesirable effects. The work group opinion was split between “probably important uncertainty or variability” and “probably not important uncertainty or variability” in how adults ≥65 years of age value the main outcome. Limited data exists on the concern about COVID-19 disease, specifically in people with moderate or severe immunocompromise. The work group opinion was moderate to large that people with moderate or severe immunocompromise feel the desirable effects are large relative to undesirable effects. The work group opinion was split between “probably important uncertainty or variability” and “probably not important uncertainty or variability” in that people with moderate or severe immunocompromise value the main outcome.

For the acceptability domain, the percent vaccinated with 2023–2024 COVID-19 vaccine coverage was higher for adults ≥65 years of age compared to younger age groups. 39.3% of adults aged ≥65 years and 5.4% of immunocompromised adults received at least two 2023–2024 vaccine doses. A healthcare provider recommendation for the COVID-19 vaccine was highest among adults ≥65 years of age. In an October 2024 survey of healthcare providers, 70% of respondents reported recommending a second COVID-19 vaccination to eligible patients ≥65 years of age “most of the time“ or “always” and 68% reported recommending a second COVID-19 vaccination to eligible patients who were immunocompromised “most of the time” or “always.” Feedback through the work group professional organization liaisons indicated they prefer age-based recommendations over risk-based or shared clinical decision-making, frequent changes in vaccine recommendations create confusion, most preferred one to two total doses a year, and need to reiterate that self-attestation of being moderately or severely immunocompromised is permissible.

2023–2024 COVID-19 vaccine coverage of ≥2 doses among adults aged ≥65 years of age varied by race, ethnicity, and urbanicity. Coverage was higher in Black, non-Hispanic adults compared to white, non-Hispanic adults. Coverage was also higher in urban settings compared to rural. 2023–2024 COVID-19 vaccine coverage of ≥2 doses among immunocompromised adults ≥18 years varied by urbanicity, race and ethnicity, healthcare provider recommendation, and insurance status. Coverage was lower in Asian adults compared to white, non-Hispanic adults. It was also higher in suburban areas compared to rural areas.

Coverage was higher among people with health insurance and among those with a healthcare provider recommendation.

When asked if recommending a second dose of the 2024–2025 COVID-19 vaccine for adults ages ≥65 years of age would be acceptable to key stakeholders, the work group's opinion was "probably yes" and "yes." When asked if recommending a second dose of the 2024–2025 COVID-19 vaccine for people ages ≥6 months with moderate or severe immunocompromise would be acceptable to key stakeholders, the work group's opinion was "probably yes" and "yes." When asked if recommending additional doses (i.e., three or more) of the 2024 – 2025 COVID-19 vaccine for people ages ≥6 months with moderate or severe immunocompromise would be acceptable to key stakeholders, the work group's opinion was "probably yes" and "yes."

For the feasibility domain, based on survey data, physicians think shared clinical decision-making (SCDM) increases time and confusion. When asked if a second dose of 2024–2025 COVID-19 vaccine was feasible to implement among adults ≥65 years of age, the work group's opinion was "yes," with a minority saying, "probably yes." When asked if a second dose of 2024–2025 COVID-19 vaccine is feasible among persons with moderate or severe immunocompromise, the work group's opinion was split between "probably yes" and "yes." When asked if additional doses (i.e., three or more) of 2024–2025 COVID-19 vaccine were feasible to implement among persons with moderate or severe immunocompromise, the work group's opinion was split between "yes" and "probably yes".

In the resource use domain, administering a second dose of the COVID-19 vaccine is most cost-effective for older adults, who experience the highest disease burden. An additional dose is likely more cost-effective in populations with a higher prevalence of risk factors. There was no information specific to the cost-effectiveness of additional doses in people with moderate or severe immunocompromise. When asked if a second dose of the 2024–2025 COVID-19 vaccine in adults ≥65 years old is a reasonable and efficient allocation of resources, the work group answered "yes" and "probably yes." When asked if a second dose of the 2024–2025 COVID-19 vaccine in persons ≥6 months of age with moderate or severe immunocompromise was a reasonable and efficient allocation of resources, the work group answered "yes" and "probably yes." When asked whether additional doses (i.e., three or more) of the 2024–2025 COVID-19 vaccine in persons ≥6 months of age with moderate or severe immunocompromise would be a reasonable and efficient allocation of resources, the work group's opinion was split between "probably no," "probably yes," "varies" and "don't know."

The work group felt that a harmonized recommendation for older adults and immunocompromised people would ease implementation. Still, some work group members did not favor a harmonized recommendation but supported differing recommendations in the two populations under consideration. Limited data for immunocompromised people makes making recommendations challenging. Despite hesitations about a shared clinical decision-making recommendation, many work group members acknowledged the benefit for people with moderate or severe immunocompromise. Allowing flexibility in additional doses may allow these patients to time around travel, life events, chemotherapy, etc.

There was a low uptake of more than one dose of the 2023–2024 vaccine. The complexity of the existing schedule has led to reduced adherence by clinicians. Provider recommendations directly impact uptake, and as part of this recommendation, provider education and ensuring providers are on board is critical to improving adherence. More straightforward vaccine recommendations may increase vaccine uptake.

Focusing on the number of doses of 2024–2025 vaccine rather than additional doses in recommendations could help reduce complexity and improve uptake.

The proposed voting language is as follows:

> *In addition to previously recommended 2024–2025 vaccination: ACIP recommends a second dose* of 2024–2025 COVID-19 vaccine for adults ≥65 years. ACIP recommends a second dose** of 2024–2025 COVID-19 vaccine for people ages 6 months–64 years who are moderately or severely immunocompromised. ACIP recommends additional doses (i.e., 3 or more doses) of 2024–2025 COVID-19 vaccine for people ages 6 months and older who are moderately or severely immunocompromised under shared clinical decision-making*

*If previously unvaccinated and receiving Novavax, 2 doses are recommended as initial vaccination series followed by a third dose of any age-appropriate 2024–2025 COVID-19 vaccine 6 months (minimum interval 2 months) after second dose.
**If previously unvaccinated or receiving initial vaccination series, at least 2 doses of 2024–2025 vaccine are recommended, and depending on vaccination history more may be needed. This additional 2024–2025 vaccine dose is recommended 6 months (minimum interval 2 months) after completion of initial vaccination series.

Dr. Lakshmi Panagiotakopoulos (CDC/NCIRD) shared the clinical considerations.

The routine schedule is the schedule for people without moderate or severe immune compromise. The proposed recommendations for adults ages 65 years and older are for two doses of 2024–2025 COVID-19 vaccine at a recommended interval of 6 months (and a minimum interval of 2 months). Having a recommended and minimum interval is standard for all vaccines and additionally allows for some flexibility in the timing of doses. For those adults 65 and older who have never received a COVID-19 vaccine and are receiving their first dose of Novavax vaccine, two doses are recommended as their initial vaccination series, followed by a third dose of any age-appropriate COVID-19 vaccine 6 months after their second dose, with the same 2-month minimum interval.

People with moderate or severe immune compromise ages 6 months and older are recommended to get an initial COVID-19 vaccine series – this consists of 3 homologous mRNA COVID-19 vaccine doses or 2 Novavax COVID-19 vaccine doses. The proposed recommendation for 2024–2025 COVID-19 vaccine doses is for at least two doses with a recommended interval of 6 months and a minimum interval of 2 months. One of these two doses may be a part of the initial vaccination series, and at least 1 of the 2 doses should be received 6 months after completion of the initial series. Beyond that, the additional doses for 2024–2025 COVID-19 vaccine would remain under shared clinical decision-making 2 months after the last dose of 2024–2025 COVID-19 vaccine.

When transitioning from a younger to an older age group, the CDC recommends that people receive the age-appropriate vaccine product and dosage based on their age on the day of vaccination, which is consistent with CDC's General Best Practices for Immunization. Specifically, if a person moves up to an older age group between vaccine doses, they should receive the vaccine product and dosage for the older age group. The previous option to administer a lower dosage is no longer authorized for children who transition from age 4 to 5 and for children moderately or severely immunocompromised who transition from 11 to 12.

The main interchangeability language remains the same – in which COVID-19 vaccine doses from the same manufacturer should be administered whenever recommended. However, there are circumstances in which vaccines from different manufacturers may be administered, including the same vaccine not being available at the time of the clinic visit, the previous dose unknown, a person who would not otherwise receive a vaccine dose, and a contraindication to previously received COVID-19 vaccine. Of note, a VAERS report is not indicated in these circumstances, meaning these are not considered errors. People ages 12 years and older who initiate vaccination with Novavax and receive the first dose of Novavax should complete a 2 dose initial series with Novavax vaccine. However, if more than 8 weeks have elapsed since receipt of the first dose, any 2024–2025 COVID-19 vaccine may be administered. As a reminder, COVID-19 vaccine is recommended for everyone ages 6 months and older, regardless of prior symptomatic or asymptomatic SARS-CoV-2 infection, including people with long COVID. People who recently had SARS CoV-2 infection may consider delaying a COVID-19 vaccine dose by 3 months from symptom onset or positive test if the infection was asymptomatic. Individual factors, such as risk of severe COVID-19 and current indicators of community transmission, should be considered when determining whether to delay getting a COVID-19 vaccination after infection.

The interim Clinical Considerations for Use of COVID-19 Vaccines in the United States webpage continues to be rapidly updated to reflect the most recent COVID-19 vaccine guidance. COVID-19 vaccine recommendations have moved towards simplicity and the standard language used for the ACIP routine immunization schedule and General Best Practices. Recommendations for additional doses in older adults and people with moderate or severe immunocompromise will be updated following the October 2024 ACIP meeting votes.

Dr. Loehr thanked the public for the emails and comments on this topic. There has been a strong push to offer the vaccine to anyone who wants it, not just to individuals ≥65 years of age and immunocompromised. Individuals who care for ill family members are requesting additional vaccine doses. I am not comfortable with that. If an individual is willing to pay for an extra dose out of pocket for off-label use of a vaccine, I do not see a reason why they should not be able to do so.

Dr. Panagiotakopoulos responded that this did come up in the work group discussion. The two considerations were that this is not done for other vaccines and the cost from a societal perspective. It would be unusual to have this done for the COVID-19 vaccines when it is not done for other vaccinations.

Dr. Wharton clarified that paying out-of-pocket for off-label use of vaccines is generally allowed as part of medical practice.

Dr. Asturias questioned whether language should include anything about the ideal time before surges or whether this should be left to others' discretion.

Dr. Panagiotakopoulos replied that considerations for the 6-month recommendation included waning, cost-effectiveness, feasibility, values, and attitudes; some providers who take care of immunocompromised patients expressed that annual vaccination would be sufficient because of the difficulty of vaccinating more than once a year. The two-month minimum interval provides flexibility, allowing local and personal factors to be considered.

Dr. Cineas requested clarification on the interim clinical considerations, whether the guidance on the interchangeability slide refers to children 6 months to 4 years old, and whether this should be added for clarity.

Dr. Panagiotakopoulos stated that in addition to 6 months to 4 years, this also applies to immunocompromised people, people who are recommended to get a homologous series, and people receiving Novavax and who were previously unvaccinated.

Ms. Moser added that some people who were caregivers of high-risk people commented on the public forum and stated that they could not get the vaccine when they were willing to pay out of pocket. If this is allowed, we should ensure the providers and pharmacists know they can provide them. There were also educators and parents of young children concerned that the families would get the vaccine in the fall and would have to wait a whole year to get it again. When people are infected, they can defer for three months, but now we are saying vaccination after six months.

Dr. Fleming-Dutra clarified that while off-label vaccinations are allowed under the practice of medicine, some complexities make it difficult, and this will be discussed in a later session. In certain jurisdictions, there are places where vaccines cannot be given if they are not ACIP-recommended. Although physicians may be able to prescribe it off-label, patients may have difficulty accessing said vaccine. Specific to COVID-19, vaccines must be used in alignment with HHS guidance.

Dr. Shaw requested clarification on which group the statement: "Individual factors such as the risk of severe COVID-19 and current indicators of community transmission should be considered when determining whether to delay getting a COVID-19 vaccination after infection." The vaccine may be ineffective if vaccinated too soon.

Dr. Panagiotakopoulos explained that the statement is not aimed at any specific group. Much of the data is based on low reinfection rates during the first three months following an infection. While some may contemplate delaying the vaccine, receiving it sooner than three months after your infection is possible.

Dr. Chu concurred with Dr. Shaw that the two months in one slide and three months in the other are confusing. Should we instead change the three-month recommendation to “should receive two doses of the age-appropriate vaccine spaced six months apart as close as three months after the last” to align the language?

Dr. Fleming-Dutra clarified that the FDA determines this two-month minimum interval. Dr. Kaslow said they would take this point of two- and three-month intervals between vaccination and infection causing confusion under advisement.

Dr. Loehr motioned that ACIP recommends a second dose of 2024–2025 COVID-19 vaccine for adults 65 years of age and older.

Dr. Jamieson seconded the motion.

Dr. Loehr motioned that ACIP recommends a second dose of 2024–2025 COVID-19 vaccine for moderately or severely immunocompromised people ages 6 months to 64 years.

Dr. Jamieson seconded the motion.

Dr. Loehr motioned that ACIP recommends additional doses (i.e., three or more doses) of 2024–2025 COVID-19 vaccine for people ages 6 months and older who are moderately or severely immunocompromised under shared clinical decision-making.

Dr. Jamieson seconded the motion.

Ms. Hayes inquired whether the current vaccine is not 100% aligned with circulating strains of the virus and whether data was available to speak to this.

Dr. Silk stated he does not have specific data from the lab but is told they are expected to provide good protection given that they are subsets and the sublineages of the JN.1 strain.

Speaking on behalf of the American Geriatrics Society, Dr. Schmader expressed support for the recommendation for an additional dose for those ≥65 years. The AGS also notes that an important population likely to benefit from additional doses that is not included in these recommendations is nursing home residents younger than 65 years of age. This is something to consider.

Dr. Hopkins commented that vaccines are the best defense against respiratory diseases, yet our vaccination rate remains below our goals. Less than 1 in 5 adults are concerned about Flu, COVID-19, or RSV. Only 38% shared they would get a Flu vaccine, and 26% would "definitely get" an updated COVID vaccine. The concerns included side effects and distrust of vaccines in general. To address this problem, it's necessary to directly address the concerns of side effects and safety.

Vote: COVID-19 Vaccines-Vote #1

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for COVID-19 vaccines into the record:

> In addition to previously recommended 2024-2025 vaccination:
> *ACIP recommends a second dose of 2024-2025 COVID-19 vaccine for adults ages 65 years and older*

Motion/Vote: COVID-19 Vaccines

Dr. Loehr motioned to approve the proposed vote recommendation for COVID-19 vaccines vote #1, stating," ACIP recommends a second dose of 2024-2025 COVID-19 vaccine for adults ages 65 years and older." Dr. Jamieson seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored:	Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw and Talbot
0 Opposed:	
0 Abstained:	

Vote: COVID-19 Vaccines-Vote #2

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for COVID-19 vaccines into the record:

> In addition to previously recommended 2024-2025 vaccination:
> *ACIP recommends a second dose of 2024-2025 COVID-19 vaccine for people ages 6 months-64 years who are moderately or severely immunocompromised*

Motion/Vote: COVID-19 Vaccines

Dr. Loehr made a motion to approve the proposed vote recommendation for COVID-19 vaccines vote #2, "ACIP recommends a second dose of 2024–2025 COVID-19 vaccine for people ages 6 months-64 years who are moderately or severely immunocompromised." Dr. Jamieson seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored: Shaw, Schechter, Moser, Maldonado, Loehr, Kuchel, Kamboj, Jamieson, Cineas, Chu, Chen, Brooks, Brewer, Asturias, Talbot
0 Opposed:
0 Abstained:

Vote: COVID-19 Vaccines-Vote #3

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for COVID-19 vaccines into the record:

> In addition to previously recommended 2024-2025 vaccination:
> *ACIP recommends additional doses (i.e., 3 or more doses) of 2024–2025 COVID-19 vaccine for people ages 6 months and older who are moderately or severely immunocompromised under shared clinical decision-making*

Motion/Vote: COVID-19 Vaccines

Dr. Loehr made a motion to approve the proposed vote recommendation for COVID-19 vaccines vote #3, "ACIP recommends additional doses (i.e., 3 or more doses) of 2024–2025 COVID-19 vaccine for people ages 6 months and older who are moderately or severely immunocompromised under shared clinical decision-making." Dr. Jamieson seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored: Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw and Talbot
0 Opposed:
0 Abstained:

PUBLIC COMMENTS

The floor was opened for public comment on October 23, 2024, at 3:45 PM EST. The comments made during the meeting are summarized in this document. Members of the public were also invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket Number ID CDC-2024-0072. Visit regulations.gov for access to read the comments received.

Noah Louis-Ferdinand
Voices for Vaccines

Noah Louis-Ferdinand, communications coordinator for Voices for Vaccines, commented on adding the high-dose flu vaccine to the VFC program for transplant recipients. He emphasized the importance of protecting vulnerable populations, noting low vaccination rates among young, healthy individuals. Many of his peers in their 20s are not enthusiastic about getting vaccinated, making additional options beneficial. He also expressed interest in the expanded pneumococcal vaccination recommendations, questioning how likely adults are to receive multiple vaccines in a year. He highlighted the importance of understanding the need for multiple vaccinations and the potential barriers, such as time off for appointments and the possibility of feeling unwell afterward. These public health considerations are crucial for effective implementation, even though the safety and efficacy of these vaccines are established.

Andrew Wang, PhD
Private Citizen

Andrew Wang thanked Dr. Talbot, the committee members, and the public for the opportunity to share his comments. He highlighted ongoing concerns regarding the COVID-19 pandemic, which still affects millions of Americans. He stressed the need for access to vaccines at least twice a year for all individuals, regardless of health status, and urged the committee to revise their policy questions accordingly. A restrictive approach to vaccination creates confusion and discourages high-risk populations, including those under 65, from seeking necessary boosters. He pointed out that public vaccine hesitancy will persist if the committee complicates vaccination criteria. Moreover, the vaccination schedule should address waning efficacy and new variants, aligning with the FDA's approach. Ensuring biannual vaccine access will enhance protection against severe outcomes and align with CDC recommendations. He also emphasized the need for equitable and affordable access to vaccines, especially after the end of the CDC's Bridge Access program in August 2024, which left many uninsured with limited access. He urged the committee to support no-cost access to COVID-19 vaccines to eliminate barriers and improve public health.

Paul Hennessy
Unaffiliated Community Member

Paul Hennessy said that the CDC must allow everyone to receive a second COVID-19 shot two months after the first rather than limiting it to immunocompromised individuals. He requested changes to voting language to broaden eligibility, as restricting access creates barriers and limits protection. Additional shots have been proven effective and safe, and the CDC should make sure this is covered by insurance while restoring the Bridge Access Program. Given the immune damage caused by COVID-19 in the population, all individuals need access to extra doses.

The CDC has noted spikes in cases during summer and winter, suggesting that low transmission periods are not as low anymore—a more frequent vaccination strategy with updated vaccine every six months is needed, rather than just in the fall. Waning vaccine efficacy should also be investigated. The ACIP should accelerate funding for intranasal COVID-19 vaccines and ensure H5N1 vaccines are available to all, especially farmers. Annual H5N1 vaccinations alone will not suffice; preventative vaccines are essential for public health.

Edward Nirenberg
Unaffiliated Community Member

Edward Nirenberg thanked ACIP for the opportunity to speak. Despite advancements in other areas, he expressed concern over the stagnation of influenza vaccine innovation. He noted that most available vaccines are ineffective against the H3N2 virus, partly due to egg-based production methods. He urged increased support at the clinical trial, regulatory, and manufacturing level to modernize influenza vaccines and highlighted the increasing public discomfort with injections. He suggested that combining vaccine and mucosal-administered options might be more acceptable. He supported the FDA's decision to allow caregiver and self-administration of FluMist. He also discussed the durability of antibodies from current vaccines, including mRNA options, and advocated for making additional vaccine doses available. He emphasized the need for clear communication regarding the risks and benefits for those considering extra COVID-19 vaccines. He also noted that immunocompromised individuals want additional doses but need help finding suitable vaccination environments, feeling uncomfortable in crowded, poorly ventilated pharmacies.

Timothy Cestaro
Unaffiliated Community Member

Timothy Cestaro thanked the group for the opportunity to share his concerns. As a father of four boys, he reported that his first three children were vaccinated without issues. Still, his youngest son suffered severe complications due to his pediatrician’s failure to follow safety protocols. He worried about the lack of communication regarding vaccination safety for children with existing health issues. His son experienced severe allergic reactions and was diagnosed with eczema, which the pediatrician suggested was safe for vaccination. Despite being immunodeficient by CDC standards, the child received live vaccines at an early age and later had a febrile seizure after vaccination. He expressed concern that MMRV should not be given due to the risk of febrile seizures. He also criticized the FDA for approving two vaccines that offer similar immunity when one has proven more dangerous, emphasizing that these decisions should not rest solely with parents.

Daniel Bessonov
Masks for All

Daniel Bessonov thanked the group for the opportunity to share his views. He strongly encourages the CDC to recommend COVID-19 vaccines for all ages and health statuses, advocating for at least two vaccinations annually. Full access to spring vaccinations is essential, as the virus persists year-round and often surges. Immunity from vaccines wanes significantly within 4 to 6 months, increasing the risk of infection and complications. Restricting vaccines based on age and health status leaves many unprotected, raising the chances of transmission. Regular updates to the vaccine are necessary to maintain effectiveness. He has faced vaccination barriers due to his health, placing him at higher risk.

The low vaccination rates compared to influenza are concerning. Continuous widespread vaccination is crucial, as relying on infection immunity is risky. Frequent vaccination is vital to prevent serious long-term health issues related to long COVID. The current vaccination restrictions are confusing and may discourage people from getting needed boosters.

Corey Greenblatt, MPH
Global Healthy Living Foundation

Corey Greenblatt, representing the Global Healthy Living Foundation, expressed support for vaccine access and public trust in their safety but raised concerns about specific RSV and PCV vaccine guidelines proposed by the committee. He hopes for revisions before finalization. The foundation advocates for individuals with chronic diseases, especially the most vulnerable, for whom vaccine access is essential. The recommended RSV vaccine for those aged 60 to 74 poses significant implementation challenges, particularly in community settings. The requirement to confirm immunocompromised status may be hindered by inaccessible medical records. While the ACIP suggests patient attestation for risk factors, this can complicate the healthcare providers' decision-making process. Providers should not have to set aside their clinical judgment. Aligning recommendations with FDA guidelines could help ensure informed decision-making while maintaining patient safety. Additionally, the foundation urges routine PCV recommendations for all adults over 50 to address alarmingly low pneumococcal vaccination rates.

RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES- MATERNAL/PEDIATRIC

Dr. Helen Chu (ACIP, Work Group Chair) introduced the Respiratory Syncytial Virus (RSV) section. As of last year, there are now two forms of protection for infants against RSV. They are maternal vaccine (ABRYSVO®, Pfizer) and nirsevimab (Beyfortus®, Sanofi & AstraZeneca). The maternal vaccine is administered at 32- to 36 weeks gestation. Nirsevimab is administered to all infants ≤8 months whose mother did not receive maternal vaccine. Only one of these products is needed in most instances. Nirsevimab and maternal vaccines have different seasonal administration windows to provide optimal protection to the infant. The maternal vaccine is typically administered from September through January. For infants born shortly before October or during October through March who are not protected by the maternal RSV vaccine, immunize within one week of birth, ideally during the birth hospitalization.

Dr. Anushua Sinha (Merck) presented on clesrovimab (MK-1654). Clesrovimab binds with high affinity to RSV F protein site 4 with a highly conserved binding epitope. It has a low rate of mutations detected within its binding site sequences. It has a high potency in vitro against various RSV clinical isolates and is equipotent against RSV-A and RSV-B. Three engineered substitutions termed YTE result in an extended half-life. It achieves high nasal tissue distribution and concentrations at sites of RSV infection.

The proposed indication is the prevention of RSV lower respiratory tract disease in neonates and infants who are born during or entering their first RSV season with a proposed dose of 105 mg administered as a single intramuscular (IM) injection at the same dose to all infants regardless of weight.

Protocol 004 was a Phase 2b/3 double-blinded, randomized, placebo-controlled study in healthy preterm and full-term infants. The study's endpoints were the vaccine's safety, tolerability, and efficacy against medically-attended lower respiratory tract infection due to RSV.

Clesrovimab, administered as a single dose for infants of all weights, provides robust protection against mild, moderate, and severe RSV disease for all healthy infants, including term and preterm. Clinical data demonstrates over 90% efficacy in preventing RSV-associated lower respiratory tract (LRI) hospitalizations through 6 months. Clesrovimab efficacy is durable across all efficacy endpoints through 6 months. No shifting of RSV disease burden was seen in the second RSV season. Clesrovimab is well tolerated in healthy preterm and full-term infants born during or entering their first RSV season, and it has a safety profile that is generally comparable to that of a placebo.

Protocol 007 is a Phase 3 multicenter, randomized, partially blinded palivizumab-controlled trial conducted with active surveillance over 2 RSV seasons. The participants were infants at an increased risk for severe RSV disease. This is an ongoing study. The endpoints are safety, tolerability, and efficacy.

The safety profile of clesrovimab in infants at increased risk of severe RSV disease is generally comparable to palivizumab and consistent with the safety profile in healthy infants. Efficacy in the Protocol 007 population was inferred from efficacy established in Protocol 004 among healthy infants based on comparable clesrovimab pharmacokinetic data. In infants at increased risk for severe RSV disease, a single dose of clesrovimab protects against RSV disease, including RSV hospitalization, through 6 months.

In conclusion, clesrovimab, administered as a single dose for infants of any weight, provides robust protection against mild, moderate, and severe RSV disease for all infants, including term, preterm, and those with risk factors. Clesrovimab is highly efficacious in healthy infants against a broad spectrum of RSV disease endpoints, with no shifting of RSV disease burden in the second RSV season (Protocol 004)—over 90% efficacy in preventing RSV LRI hospitalizations through 6 months. Clesrovimab also protects infants at increased risk for severe RSV disease, comparably to palivizumab (Protocol 007).

Clesrovimab is well-tolerated in infants, with a safety profile generally comparable to controls and consistent across infant populations. It is well tolerated in healthy preterm and full-term infants born during or entering their first RSV season, and its safety profile is generally comparable to that of placebo. The safety profile of clesrovimab in infants at increased risk for severe RSV disease is usually comparable to palivizumab and consistent with the safety profile in healthy infants.

Dr. Jamieson inquired whether it was possible to stratify efficacy by infant weight since the conclusion was robust protection across all infant weights.

Dr. Sinha responded that the group conducted subgroup analyses, including one stratified by weight. What was observed was that the stratified efficacy results were comparable and consistent with the overall efficacy results. This can be shared with ACIP committee members.

Dr. Brooks requested the receipt of the data stratified by race and ethnicity.

Dr. Sinha confirmed this is available and will share it with the ACIP committee members.

Dr. Brewer stated for clarity that the primary outcome is medically-attended lower respiratory tract infection (MALRI) with one or more indicators of LRI severity, while elsewhere, this is listed as a secondary outcome. He also requested clarity on why the LRI hospitalization data looked

similar. When looking at the all-cause data, there is a significant falloff in efficacy for the primary outcome but none for hospitalization data.

Dr. Sinha confirmed that Dr. Brewer's statement was correct. The primary efficacy endpoint was MALRI, which required at least one indicator of LRI/Severity with follow-up through five months. One of the secondary endpoints was the same efficacy endpoint but with follow-up through six months. She also confirmed that efficacy against LRI hospitalization due to any cause is 49%, reflecting the severity of this endpoint; this includes not just RSV determined by the pre-specified endpoint but LRI hospitalization due to any cause. The MALRI endpoint is broad and encompasses many diseases in clinics and hospitals.

Dr. Chu followed up on Dr. Jamieson's request. She would like to see the efficacy stratified by gestational age and weight. She also requested to see the pharmacokinetic (PK) data six months out and whether there will be a faster or slower fall-off with different gestational ages or birth weights.

Dr. Sinha confirmed that these data will be shared with the work group.

Dr. Schechter asked whether PK or other data indicated the expected durability of protection after the first season and whether primary and secondary event counts tended to occur later or sooner after immunization. He also requested data on the durability of protection compared to the timing of the injection and finally inquired whether there was a correlation of protection.

Dr. Sinha clarified that all efficacy points were collected through six months. These data are available. A Kaplan-Meier curve may be helpful to see that the efficacy is durable through the entire six months. Cases were occurring across the entire 180-day period of follow up. There is no formal correlate of protection.

Dr. Brewer was surprised by the outcomes and wanted to know whether additional outcomes could have been reported within the presentation.

Dr. Sinha confirmed that all primary, secondary, and tertiary endpoints were reported in the presentation.

Dr. Brewer shared a concern about data stability for post hoc analysis. It may be helpful to focus on either a primary or a primary and secondary outcome. He is concerned about the intensiveness of inspecting data across too many outcomes.

Dr. Malini B. DeSilva (Health Partners Institute) presented preliminary data about the RSVpreF vaccine, preterm birth, and small for gestational age at birth preliminary results from the Vaccine Safety Datalink (VSD). VSD is a collaborative project between CDC and 13 integrated healthcare organizations. It monitors the safety of vaccines used in the U.S., primarily through observational multisite studies of rare and severe events following vaccination. VSD includes data on ~15.5 million individuals across all sites annually, about 3.4% of the U.S. population. VSD reported an annual birth cohort of about 115,000 live births.

ACIP recommended Pfizer’s maternal RSV vaccine with seasonal administration (September to January) for all pregnant women 32-36 weeks gestation in September 2023. In clinical trials, Pfizer’s maternal RSVpreF clinical trials identified an imbalance in preterm births in the vaccinated group compared to the placebo group. Most were late preterm (34–<37 weeks), occurred >30 days after vaccination, and occurred in a single country.

ACIP judged the benefits of the maternal RSV vaccine (ABRYSVO) at 32–36 weeks' gestation to outweigh the potential risks for preterm birth and the hypertensive disorders of pregnancy.

The group evaluated preterm birth (<37 weeks gestation) and small for gestational age (SGA) at birth following maternal RSV vaccination. Most VSD sites started vaccinating in late October or November 2023. SGA was defined as birthweight below the 10th percentile for gestational age and sex. In this controlled VSD study, Pfizer's maternal RSVpreF vaccine was not found to be associated with an increased risk for preterm birth or SGA at birth. Work is in progress on analyzing acute safety outcomes, stillbirth, and hypertensive disorders of pregnancy [preeclampsia, eclampsia, and HELLP (Hemolysis, Elevated Liver enzymes and Low Platelets)].

Dr. Schechter asked whether the study was limited to a single season or whether there were plans for continued surveillance.

Dr. DeSilva confirmed there are plans to continue the study for this season. However, the data presented is only for the first season.

Dr. Brewer requested an explanation of how to interpret preterm birth risk by gestation age at vaccination from 32 to 36 weeks.

Dr. DeSilva commented that the team does not interpret this to mean that vaccination is protective for preterm birth. The trend is similar in both of the groups.

Dr. Joseph was reassured that maternal immunization is a safe strategy for protecting infants against RSV. However, the analysis does highlight two points. Overall, the maternal vaccination rate was low, and the licensure data included patients vaccinated earlier than 32 weeks gestation. This is different from the approved dosing window. Given the implementation challenges, she inquired whether the work group plans to look at data from other surveillance systems like the United Kingdom to help inform the risk of preterm birth.

Ms. Moulia stated that she thought that the UK started maternal RSV vaccination in September 2024 and that the work group could review data from the UK when available.

Dr. Asturias requested clarification on the RSV groups, including whether there were any exclusions and whether the vaccinated and unvaccinated groups were similar.

Dr. DeSilva shared that vaccinated and unvaccinated people have similar characteristics. However, there are some imbalances including for race, ethnicity, and age.

Ms. Danielle Moulia (CDC/NCIRD) reviewed the maternal and pediatric RSV work group's interpretations and next steps. The policy question being considered is whether clesrovimab should be recommended for all infants <8 months of age entering their first RSV season or born during the RSV season. Initial efficacy and safety data look promising; however, the work group has requested additional pharmacokinetic, efficacy, and safety data from the manufacturer. The work group also highlighted that clesrovimab had demonstrated a shorter half-life than nirsevimab (42 vs. 71 days), the COVID-19 pandemic disrupted the trial enrollment period, and clesrovimab and nirsevimab trial outcomes had different definitions. Overall, the work group felt that the initial data merited moving forward with the evidence review for the policy question.

Future evidence to be reviewed by the work group includes additional data on Phase 2b/3 and Phase 3 studies, GRADE of evidence, cost-effectiveness analysis, and the EtR framework. It is projected to be presented at the February 2025 meeting, with an ACIP vote possibly as early as the June 2025 meeting, depending on FDA licensure.

Data were summarized on the preliminary findings from the first season of maternal RSV vaccine administration in an SD study that found that maternal RSV vaccine during 32–36 weeks' gestation was not associated with an increased risk of preterm birth or small for gestational age. The work group felt that messaging about potential risks for hypertensive disorder of pregnancy should be separated from preterm birth. Some work group members felt that when counseling on maternal RSV vaccination at 32–36 weeks, messaging on potential risks of preterm birth could be softened, or counseling no longer needed to include discussion regarding a possible risk of preterm birth. CDC and FDA will continue to monitor safety data for maternal RSV vaccine, including further VSD analyses for hypertensive disorders of pregnancy.

Dr. Shaw asked whether the preterm birth rates reported in this study were low or within the expected range and if any more was known about the preterm birth signal seen in GSK's clinical trial.

Dr. DeSilva responded that preterm birth rates in the population and the SGA at birth were in the expected range for the VSD.

Dr. Jones addressed the second question and said there was not a clear biologic explanation.

Dr. Schechter encouraged committee consideration for language encouraging the speedy implementation of nirsevimab in birth hospitals.

Ms. Moulia noted that the current guidance is that infants born shortly before or during the RSV season should be immunized within one week of birth, ideally during the birth hospitalization. CDC is organizing learning collaboratives to share promising practices for nirsevimab administration in birthing hospitals.

Dr. Chatham-Stephens followed up with additional information. CDC is working closely with the immunization programs to enroll more birthing hospitals into the Vaccines for Children Program and offering specialized technical assistance to awardees. Some jurisdictions received site visits, focus groups, and key informant interviews. In early August, the CDC held a perinatal and maternal reverse site visit, during which many immunization program managers from across the country also came to discuss these issues.

Ms. Hayes expressed her appreciation for the review of data on vaccinating pregnant women, which shows that vaccination in this group is safe.

Dr. Brooks moved the meeting to recess and reconvening on October 24, 2024, at 8:00 am.

With no additional business posed for the day, the ACIP meeting stood in recess until 8:00 AM on October 24, 2024.

THURSDAY: OCTOBER 24, 2024

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Keipp Talbot (ACIP Chair) called to order and presided over the October 24, 2024, Advisory Committee on Immunization Practices (ACIP) 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. No COIs were identified for the second day of this meeting.

AGENCY UPDATES

Centers for Medicare and Medicaid Services (CMS)

Ms. Mary Beth Hance shared that they have worked hard to amplify CDC and HHS messaging around the importance of seasonal and routine immunization. They have talked to state Medicaid agencies and interested parties at many touchpoints throughout state connections and community involvement. They have appreciated the efforts of representatives from the CDC speaking with state Medicaid agencies to emphasize the importance of immunization and continue to return to the higher pediatric immunization rates seen in previous years. She also highlighted that on September 12, 2024, her colleagues issued a Medicare learning network bulletin that included COVID codes and pricing for this year's COVID-19 vaccine codes and pricing for this year's vaccine.

Centers for Disease Control and Prevention (CDC)

Dr. Demetre Daskalakis thanked colleagues at the FDA, industry, and ACIP for an expeditious rollout of COVID-19 vaccines. COVID-19, Influenza, and RSV are all available and in the field. There have been interesting changes seen by launching earlier in the year. We have seen a higher uptake of the COVID-19 vaccine during this time of year compared to last year's same date. This is a testament to the close collaborations across the various components of government and industry. The number of respiratory illnesses in the U.S. continues to be low. COVID-19 activity continues to decline in all areas. As expected, there is minimal seasonal flu and RSV activity in the southeastern part of the U.S. It tends to start in this area and then sweep across the country.

He flagged the number of measles cases seen. As of October 10, 2024, 32 jurisdictions reported 267 measles cases. There have been 14 outbreaks reported in 2024, and 70% of cases are outbreak-associated. For comparison, four outbreaks were reported during 2023, and 49% of cases were outbreak-associated. Jurisdictions at the highest risk for measles outbreaks continue to be those with communities with persistently low MMR vaccination coverage and importations from international locations with measles outbreaks.

He also highlighted that respiratory infections caused by *Mycoplasma pneumoniae* have increased in the United States since last spring among all age groups, particularly young children. Healthcare providers should consider *M. pneumoniae* as a cause of pneumonia and test when indicated. Macrolides are the first-line treatment for this infection; some first-line antibiotics used to treat pneumonia, like penicillin, will not treat *M. pneumoniae*.

He shed light on the Vaccines for Children Program for its 30th anniversary. With the intervention, 508 million illnesses and 1.29 million deaths in children will be prevented, saving 2.7 trillion in societal costs.

Food and Drug Administration (FDA)

Dr. David Kaslow shared that since the last FDA Agency report at the June 2024 ACIP meeting, our Vaccines and Related Biological Products Advisory Committee (VRBPAC) convened twice and plans to meet again before yearend. The Office of Vaccines Research and Review took several noteworthy supplemental regulatory actions.

In September, VRBPAC met in an open session to discuss considerations related to using pertussis Controlled Human Infection Models (CHIMs) to demonstrate the efficacy of pertussis vaccine candidates for licensure. Two endpoints were discussed: mild disease such as cough, and colonization. Considerations on using these models included their relevance to pediatric populations, their limitations with real-world pertussis infection and disease, and the ability to assess the long-term effectiveness of pertussis vaccine candidates.

In October, VRBPAC also convened in an open session to make recommendations on influenza vaccine strains for the 2025 influenza season in the Southern Hemisphere and discuss pandemic preparedness for highly pathogenic avian influenza virus, including considerations for vaccine composition for (H5) vaccines. The FDA proposed an Inter-Pandemic Period Strain Change Process to use the inter-pandemic period to accrue additional safety and immunogenicity evidence with updated prototype vaccines and potentially save critical pandemic response time to have updated vaccines when needed.

FDA also anticipates a VRBPAC meeting on December 12th to discuss considerations for RSV vaccine safety in pediatric populations.

On 19 August, the meningococcal B vaccine, BEXSERO, with a dosing schedule in individuals 10- to 25 years of age of two doses administered at 0 and ≥1 month under accelerated approval was revised to two doses administered at 0 and 6 months, and to include a three-dose schedule of BEXSERO administered at 0, 1-2, and 6 months for the same age group, now under traditional approval.

On 29 August, Smallpox and Mpox (Vaccinia) Vaccine, Live, ACAM2000®, was approved to include mpox disease prevention in individuals at high risk for mpox infection. It was approved with an updated medication guide.

Finally, on Tuesday this week, the RSV vaccine ABRYSVO was approved to prevent lower respiratory tract disease caused by RSV in individuals 18-59 years of age who are at increased risk for lower respiratory tract disease caused by RSV.

Health Resources and Services Administration (HRSA)

CDR Paul McClung shared that the Division of Injury Compensation Programs (DICP) continues to support the Nation's public health through the administration of the National Vaccine Injury Compensation Program (VICP) and the Countermeasures Injury Compensation Program (CICP). As a part of this support, HRSA, in partnership with the Centers for Disease Control and Prevention (CDC), sponsored a study from the National Academy of Sciences, Engineering, and Medicine (NASEM) to review the evidence from 19 potential harms of COVID-19 vaccines and nine (9) potential shoulder injuries from intramuscular administration of vaccines more broadly. The NASEM committee drew 65 conclusions where it could not find evidence to establish, accept, or reject a causal relationship and drew 20 conclusions with sufficient evidence, with the final release of the report in August 2024. The important conclusions drawn by the committee will support decision-making for VICP and CICP when adjudicating compensation claims.

In support of VICP, the Advisory Commission on Childhood Vaccines (ACCV) was briefed on the NASEM report on July 11, 2024. ACCV made motions to establish a workgroup to amend the Vaccine Injury Table's Qualifications and Aids to Interpretation (QAI) to address conclusions and information provided by NASEM on shoulder injuries. They also added an agenda item to the next ACCV meeting, with input from HRSA/HHS, about potential research areas of interest regarding shoulder injuries.

ACCV currently has several vacancies and is seeking nominations. Additional information is available on the ACCV website. If you have questions or want to submit a nomination, please visit our website or email ACCV@hrsa.gov.

VICP is a no-fault alternative to the traditional legal system for resolving vaccine injury petitions. It was created in the 1980s after lawsuits against vaccine companies and healthcare providers threatened to cause vaccine shortages and reduce U.S. vaccination rates. VICP continues to serve as a keystone program in the Nation's ability to stabilize vaccine supply and protect the Nation's public health by expeditiously processing claims.

Over the past two fiscal years, VICP has made substantial strides in reducing the backlog of claims awaiting review by an HRSA provider. From October 2022 to October 1, 2024, VICP has reduced the number of claims activated by the U.S. Court of Federal Claims from 1,107 to 166. Over this same period, the waiting times for a HRSA medical review have decreased from more than 12 months to 49 days. In FY2024, VICP received 1,161 petitions, adjudicating 1,374 claims and awarding over $149 million to petitioners and over $53 million for attorney's fees and costs.

CICP is also a no-fault compensation program. CICP adjudicates requests for benefits alleging an injury from covered medical countermeasures deployed in response to a pandemic, epidemic, or security threat covered under a Public Readiness and Emergency Preparedness Act declaration by the Secretary of Health and Human Services. As of October 1, 2024, 13,468 claims alleging injuries/deaths from COVID-19 countermeasures had been filed with the CICP. CICP continues to make substantial progress in processing claims and has now rendered decisions on 3,318 COVID-19 claims.

In August 2024, the Bureau of Primary Health Care (BPHC) released its Uniform Data System (UDS) data. The UDS captures the immunization rates for children two years of age and under based on the CDC10 series. BPHC is actively collaborating with CDC to promote immunization efforts across the spectrum by promoting various tools and resources that CDC has developed through different communication channels.

HRSA's HIV/AIDS Bureau also continues its important work through the Ryan White HIV/AIDS Program, which continues to support access to mpox vaccination.

Indian Health Services (IHS)

Dr. Matthew Clark shared that the Indian Health Service remains committed to immunization as our leading clinical and public health prevention priority. As part of our ongoing national E3 vaccine strategy, IHS offers every ACIP-recommended vaccine when appropriate to every patient at every encounter. HIS has designated 32 E3 pilot sites in 9 IHS Areas, including federal, tribal, and urban Indian organization teams.

The IHS E3 Vaccine Strategy continues to bear fruit as pilot sites innovate at the local level and share best practices regarding effective immunization strategies in tribal communities to cross-pollinate our system of care. This year, five IHS E3 Champions have been designated in the Alaska, Bemidji, Great Plains, Nashville, and Oklahoma City Areas. Each has demonstrated excellence by exceeding established thresholds to improve vaccine coverage rates for AI/AN people.

Over the last several months, we have been developing E3 training materials for an academic detailing activity. This week, six healthcare professionals representing federal, tribal, and urban Indian organization programs are undertaking intensive training to become E3 ambassadors in their respective areas. Following completion of training, they will undertake outreach to educate and support immunization staff working in tribal communities in implementing the IHS E3 Vaccine Strategy.

Following ACIP action in June of this year related to a preferential recommendation for the hexavalent vaccine VAXELIS® in AI/AN infants, through a variety of platforms including written guidance and both in-person and virtual events, IHS has been working diligently to communicate this option to vaccination teams serving tribal communities. We plan to monitor the impact of this recommendation on vaccine coverage rates and potentially disease outcomes.

Finally, IHS is actively engaged in its annual seasonal vaccination campaign to reduce the risks of vaccine-preventable respiratory viral diseases in Indian Country, including influenza, COVID, and RSV. This includes aggressive efforts to promote access to and uptake of both maternal RSV vaccine and nirsevimab among AI/AN infants and young children. Like last year, in addition to collaboration with the Vaccines for Children program, IHS procured and distributed a supplemental supply of nirsevimab to support programs, especially those in remote locations, with planned early-season vaccination activities. This year, IHS has also worked closely with federal partners at the CDC and the Administration for Children and Families (ACF) to develop materials and provide education to support home-based outreach to Indigenous families about the importance of recommended RSV immunizations.

Working in collaboration with our federal, Tribal, and Urban Indian organization partners, the Indian Health Service will continue our efforts to mitigate the risk of vaccine-preventable illness in Indian Country.

Office of Infectious Disease and HIV/AIDs Policy (OIDP)

Dr. Chinedu Okeke shared that the National Vaccine Advisory Committee (NVAC) met on September 12-13, 2024. At this meeting, the committee showcased work that can help to strengthen the U.S. vaccine and immunization system and inform vaccine policy. The meeting began with a panel presentation on implementing the ACIP universal vaccine recommendation for adults aged 19- to 59 years of age and adults aged 60 years of age and older with known risk factors for hepatitis B. The committee also heard presentations on provider payment and RSV immunization across lifespan.

Much of the discussion at this meeting also focused on innovation to provide additional context for the report the committee is currently working on. NVAC hosted speakers on tuberculosis vaccine innovation and some challenges of advancing the tuberculosis vaccine pipeline. It also hosted a panel on new research to inform future HIV vaccine development.

On the first day of the meeting, we learned more about a new HHS campaign called *Risk Less. Do More.* NVAC also hosted two panels focused on immunization equity. The first panel showcased two innovative projects, and the second panel explored lessons and evaluation approaches.

To fulfill the charge of providing input to advance the development of the *Vaccine National Strategy*, the committee participated in two working sessions to discuss potential recommendations for new goals, indicators, and objectives.

In collaboration with the HHS Interagency Vaccine Work Group, OIDP has started planning, data gathering, and engagement efforts for the next iteration of the National Vaccine Strategic Plan for 2026-2030. OIDP has posted the Request for Information for the public on the Federal Register, and the 60-day countdown has begun. Everyone is encouraged to provide feedback on all the strategies. We encourage ACIP members to actively submit feedback and recommendations during this process.

OIDP is putting together several virtual and in-person sessions. The first listening session will occur on October 29 from 2 to 3:30 PM ET. The second opportunity is a vaccine strategy-focused listening session on October 31 from 1 to 2:30 ET. In November, OIDP will host two general sessions for all the National Strategic Plans on November 13 and November 14 (Spanish language) from 2 to 3:30 ET.

OIDP continues to lead the "Summer of Pride" Mpox Equity Initiative, a nationwide effort to increase access to mpox vaccines for communities most at risk. This initiative leverages Pride festivals and other events to reach these communities effectively.

On September 4th, OIDP and the HHS Office of Intergovernmental Affairs organized a virtual stakeholder call for community partners. This call served as a continuation of OIDP's previous discussions this year with community partners and health department staff involved in the mpox response. The stakeholder call, led by Assistant Secretary for Health ADM Rachel Levine and CDC Director of the National Center for Immunization and Respiratory Diseases Demetre Daskalakis, provided an update on the Clade 1 mpox virus and the U.S. preparedness and response. OIDP is currently planning another stakeholder call for November.

National Institute of Health (NIH)

Dr. John Beigel shared that NIAID is sponsoring a Phase 1 trial testing the safety of an experimental nasal vaccine for SARS-CoV-2. The vaccine utilizes a new virus vector, murine pneumonia virus, related to human RSV. Scientists at the NIH/NIAID Laboratory of Infectious Diseases designed and tested it in pre-clinical studies. This is part of Project NextGen, a program in both BARDA and NIAID that aims to accelerate the development of next generation COVID-19 vaccines**.**

For mpox, NIAID sponsored a clinical trial of the MVA-BN mpox vaccine in adolescents, demonstrating that it is safe and generated an antibody response equivalent to that seen in adults. Adolescents are among the population groups affected by mpox in the current outbreak in the DRC. Bavarian Nordic received EMA approval to extend the MVA-BN authorization to include adolescents.

As part of the U.S. government's response to the current mpox outbreak, NIAID has updated its priorities for mpox research. The NIAID mpox research agenda includes objectives to respond to the mpox outbreak including trials to evaluate ways to stretch the vaccine supply, and to develop novel vaccines and therapeutics.

For malaria, two NIH-supported trials of a novel malaria vaccine in healthy adults in Mali found that all regimens were safe and generated a robust immune response. The vaccine candidates conferred a significant degree of protection from parasite infection and clinical malaria that was sustained over two years without the need for any booster dosing.

For RSV, NIAID is conducting a randomized, open-label Phase 4 study of maternal RSV vaccination compared to infant nirsevimab or both products combined. The trial opened to enrollment in September 2024 and evaluates antibody titers for one year, which is expected to inform clinical use of these products.

NIAID has named Sarah W. Read, MD, MHS, as the Principal Deputy Director for the institute following Dr. Hugh Auchincloss's retirement in September 2024.

NIH has established the Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness network—called ReVAMPP— to focus on "prototype pathogens" to develop vaccine candidates and monoclonal antibodies to better protect against emerging pathogens. By studying specific prototype pathogens, scientists will build a knowledge base that could be applied to future emerging viruses.

MENINGOCOCCAL VACCINES

Dr. Jamie Loehr, chair of the ACIP Meningococcal Vaccines Work Group, introduced the meningococcal vaccines session. The work group is working on three main topics. The work group is reviewing GSK's pentavalent MenABCWY vaccine, with a regulatory decision expected by February 14, 2025, and anticipating a vote on this topic in February 2025. The work group also has discussed the newly approved interval and dosing change for MenB-4C (BEXSERO), with a vote planned for this meeting. The work group also is continuing its review of the adolescent meningococcal vaccine schedule and expects a vote in 2025.

From 1996-2023, meningococcal disease cases dropped by 90%. There are 0.13 cases per 100,000 population (1 in a million cases). This drop is primarily attributed to serotypes B, C, and Y. There was an increase in cased due to serogroup Y in 2023. During 2012-2021, many of the cases were seen in the elderly and age group <1 year, but current policy discussions are focused on the age groups 11-15, 16-20, and 21-25 years of age.

Dr. Xiaoyu Dong (CDC/NCIRD) presented the results of the economic analyses of GSK (MenABCWY) vaccine among adolescents in the U.S. The goal for the economic analysis was to evaluate the effectiveness of vaccinating adolescents with the GSK pentavalent vaccine (MenABCWY) compared to the current recommendation of the MenACWY/MenB vaccine. The current recommendation is MenACWY vaccine (Q): 1st dose at 11–12 years; 2nd dose at 16 years. In addition, ACIP recommends MenB vaccine (B): 1st and 2nd dose at 16–23 years (preferred 16–18 years), based on shared clinical decision-making.

Three policy questions (PICOs) are under consideration.

1. PICO 1: Should the pentavalent vaccine (P, MenABCWY) be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines at the same visit? (Q-P-B)
2. PICO 2: Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only? (P-P)
3. PICO 3: Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only? (Q-P-P)

The intervention was the use of pentavalent in adolescents compared to current recommendations or related strategies. For reference, each strategy was compared to no vaccination. The economic model included the entire cohort of current 11-year-olds in the U.S. Vaccination costs and meningococcal cases were assessed for 19 years. Costs and health outcomes of meningococcal cases were evaluated from age 11 years through the participant's entire lifetime. The analysis was from the societal perspective and a 3% discount rate was applied.

Invasive meningococcal disease (IMD) rates among unvaccinated individuals were based on observed rates from 2003-2005 for serogroups ACWY and from 2012-2014 for serogroup B. Case fatality rates were estimated at 15.4% for serogroups ACWY and 9.4% for serogroup B. Some of the sequelae of IMD include hearing loss, skin scarring, neurologic disability, and single and multiple amputations. Vaccine efficacy was estimated at 79% for the first Q dose and 99% for the subsequent doses and 64% for the first dose of B and 79% for the second, with waning over time for all doses. In PICO 1, the intervention P is introduced as an alternative to QB. In PICO 2, P doses were introduced to replace current Q doses.

In PICO 3, P replaced the B dose. The vaccine cost per dose (including administration) $177 for Q, $224 for B, and $245 for P.

The model estimated that without vaccination, there would be an estimated 233 IMD cases and 33 deaths. The two vaccination strategies in PICO 1 yielded identical outcomes, with 142 IMD cases and 19 deaths. In PICO 2, the main difference between the compared strategies was the protection that P doses offer against serogroup B, which prevented an additional 12 IMD cases and one death. In PICO 3, the difference in health outcomes comes from the last dose in each strategy. The final dose of P in the Q-P-P will prevent one additional IMD case compared to using B as the last dose. Both Q-P-B and Q-P-P were cost-saving compared to Q-QB-B. However, compared to no vaccination, the cost per QALY gained was high for all vaccination strategies (>$2M per QALY).

Dr. Dong provided a summary comparison of GSK's model to the CDC model. GSK's model used a higher incidence and coverage rate than was used in CDC's. The initial VE for 1st dose MenB was 64% in the CDC model compared to 33.5% in GSK's model. In CDC's model, VE declined to 0% in 5-10 years compared to 0% after more than 20 years in GSK's model. CDC's model included five sequelae outcomes with an aggregate probability of 22%, while GSK's model included 16 sequelae outcomes with an aggregate probability of 55%. Both models showed cost-saving for PICO 1. The GSK model showed a higher ICER than CDC's models for PICO 2. Both models showed cost-saving in PICO 3 when the intervention was compared to Q-QB-B.

The study had limited VE data, assumptions on the third dose effectiveness of MenACWY, unknown pre-vaccination incidence rates, and estimated costs for GSK's pentavalent vaccine. The study also did not account for additional protection against gonorrhea, the potential increase in vaccine uptake, or benefits from fewer adverse events from reduced injections. The CDC model used vaccine coverage data based on the current shared clinical decision-making practices and did not model any changes to the routine use of MenB vaccines.

Dr. Dong summarized that Q-P-B was cost-saving relative to the current recommendation (vs. Q-QB-B). P-P could improve health outcomes but costs $11.3 million per QALY saved (vs. Q-Q). Q-P-P could improve health outcomes, but estimated economic value varied depending on the comparator. Q-P-P is cost-saving compared to Q-QB-B, but compared to Q-P-B, it costs $4.5 million per QALY gained.

Dr. Maldonado was surprised that the work group would choose to give a vaccine at three different times rather than a pentavalent vaccine, which we would only have to give twice, especially in a population like adolescents, who are very hard to bring back. She was curious how retaining an adolescent three different times would not impact efficacy. She questioned how 2 doses of a broader vaccine (i.e., pentavalent vaccine) would be least cost-effective and whether the vaccine cost drives this decrease. She also inquired whether P-P can be compared to Q-QB-B.

Dr. Dong clarified that Dr. Maldonado is speaking on PICO2, in which P-P is compared to Q-Q. Within this comparison, the travel trips would be the same: one trip for the first dose and another for the second. When the incremental cost-effectiveness ratio is calculated, the advantage of having fewer trips would be canceled. The study is limited when comparing P-P trips to other strategies. She also clarified that P-P was not compared to Q-QB-B because it was not one of the PICO questions, but there would be a reduced trip in this comparison.

Dr. Leidner stated that if there is an additional request to compare P-P to Q-QB-B, the economics team would gladly do so.

Dr. Schechter questioned whether the comparison of Q-P-P vs. Q-QB-B in PICO 3 would be comparable with other pentavalent formulations already available.

Dr. Dong shared that PICO 1 is cost-saving because the net health outcome is the same. Overall, cost-saving occurs because P is less than the cost of QB. In Q-P-P vs. Q-QB-B, Q-P-P is cost-saving because the last dose of P protects against serogroup ACWY. The difference between P and QB makes the price lower.

Dr. Leidner added that if Dr. Schechter was referring to the pentavalent vaccine that is already in use, the results from this analysis, which was done presented June 2023, were similar, and it was also cost-saving.

Dr. Schechter inquired if the baseline risk was lower than before the availability of vaccines and whether this would be associated with increased cost estimates. He also asked about the vaccine coverage inputs in the model; for the Q-P-B model, was their overlap between the 27.3% receiving Q and the 32.4% receiving P? He also asked what impact a coverage lower than 59% would have on cost-effectiveness.

Dr. Leidner confirmed that if the disease risk is lower, the disease burden would be lower, and there would be less disease to prevent with the use of vaccines. Therefore, the cost-effectiveness ratios could increase. In this scenario, if a person was using shared clinical decision-making after they got their second Q, they went on to get their B series. Those who did not choose to get the B vaccine still got the Q vaccine to finish their Q series. He also stated that a lower coverage simulation was not run, but this is also something the team could investigate in the future.

Dr. Shaw requested confirmation that the P-P intervention would prevent the need for a second B vaccine. In this case, comparing P-P to Q-QB-B would be relevant.

Dr. Dong responded that this simulation was not included in the model, and Dr. Leidner added that it would be brought back to the team to develop this comparison.

Dr. Loehr requested that the committee consider that we are only looking at hundreds of cases vs other diseases that result in thousands of cases. Regarding the cost analysis, PICO 1 is cost-saving because the manufacturer has priced it so that MenACWY might be $180 and Men B would be $180, but combined, they are only $220. The pentavalent vaccine is much less expensive than the two vaccines combined, resulting cost-saving compared to separate administration. He reminded the group that the ACIP has decided on shared clinical decision-making for MenB vaccine at the current time, so many people get Q-Q without B-B. He emphasized that the ICER is in millions, not thousands, of dollars per QALY. Many other ACIP-like organizations will not consider ICERs over $100,000 to $150,000 per QALY gained. He wants the group to know that we are contemplating spending a lot of money on very few cases. He recognizes this is a dramatic, devasting disease for those who get it but would like to consider fiscal prudence. He suggested that the manufacturers heed the concern that vaccine prices are becoming too expensive for him as an ACIP member to contemplate.

Ms. Moser added that cost is only one part of the work group's consideration. This disease kills 1 to 2 of 10 people that it infects and permanently disables half of those who survive; the committee has to take into account the costs beyond the economic costs. The models are sensitive to changes in inputs and so there is uncertainty about what will actually happen, if a recommendation is made. She also shared that there are a variety of points of view within the committee.

Dr. Middleman called for action regarding pharmaceutical companies' high vaccine costs. She also added that the vaccine recommendation is confusing and should be simpler and more concise.

Dr. Sarah Schillie (CDC/NCIRD) discussed the Evidence to Recommendations Framework (EtR), which includes GRADE for the GSK Pentavalent (MenABCWY) vaccine. As a review, the current routine schedule includes one MenACWY dose at age 11-12 years and a booster at 16 years. Two MenB doses at age 16-23 years (shared clinical decision-making [SCDM]). The MenACWY vaccine is also recommended for persons at increased risk, including some microbiologists, those exposed during an outbreak, those traveling to hyperendemic areas, first-year college students (if not already vaccinated), and those with some health conditions such as asplenia, complement deficiency, complement inhibitor use, or HIV infection. MenB is also recommended for persons at increased risk, including some microbiologists, those exposed during an outbreak, and those with some medical conditions, including asplenia, complement deficiency, and complement inhibitor use. MenACWY vaccines are interchangeable, but MenB vaccines are not.

There are two new MenABCWY vaccines. Pfizer manufactured Penbraya, which ACIP voted on in October 2023. GSK manufactures the other and is anticipating an ACIP vote in February 2025. Each vaccine is a combination of an existing MenACWY and an existing MenB vaccines. Both vaccines are intended to be administered as two doses separated by six months and indicated for persons 10-25 years of age. The ACWY component in the Pfizer vaccine is Nimenrix, while in the GSK, the component is Menveo. The B component in the Pfizer vaccine is TRUMENBA®, and BEXSERO in the GSK.

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

- Should the GSK pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines at the same visit?
- Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?
- Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenB only?

The critical outcomes included meningococcal disease caused by serogroups A, B, C, W, and Y, short-term immunity, and serious adverse events. PICO 1 translates to the schedule option Q-P-B, PICO 2 to the schedule option P-P-B, and PICO 3 to the schedule option Q-P-P.

Dr. Schillie began the discussion of the EtR domains with the public health problem. Invasive meningococcal disease (IMD), which often presents as meningitis or bacteremia, progresses rapidly. It affects previously healthy young people, and 10-15% of cases are fatal even with antibiotic therapy. About 20% of survivors experience long-term sequelae. The work group felt that IMD is an important public health problem for all three PICOs.

Seven trials were included for evidence review for benefits and harms. Included studies were randomized trials; all except one were blind to the observer. Four studies contributed to assessing short-term immunity one month after one MenACWY vaccine dose in healthy persons. The seroresponse risk ratio ranged from 0.94 to 1.03 for serogroups A, C, W, and Y. The certainty was deemed moderate. For persons at increased risk, the certainty estimate was further downgraded for indirectness and the certainty was low. The certainty of evidence for short-term immunity after series completion was similar to that found following one dose.

No studies informed long-term immunity for the MenACWY vaccine. One study informed long-term immunity assessed at two years for MenB vaccine. The overall certainty level was low for healthy people and very low for people at increased risk.

Seven studies informed adverse events. Serious adverse events related to vaccination occurred among three subjects who received the pentavalent vaccine compared to one who received the MenACWY vaccine and two who received the MenB vaccine. The certainty was rated moderate for healthy people and low for people at increased risk. For non-serious adverse events for healthy people, the certainty level ranged from moderate to high, with low to moderate certainty levels for people at increased risk.

In summary, for PICO 1, evidence for meningococcal disease caused by serogroups A, B, C, W, and Y and interference with other vaccines administered concurrently is lacking. Evidence for short-term immunity for ACWY and B serogroups is moderate and low for healthy persons and persons at increased risk, respectively. Evidence for serious adverse events is moderate and low for healthy people and people at increased risk, respectively. Similarly, evidence for nonserious adverse events is moderate and low for healthy people and people at increased risk, respectively. Evidence for persistent immunity is only available for MenB serogroups and is low and very low for healthy persons and persons at increased risk, respectively. The summary is similar for PICO 2 and 3, but the evidence lacks informing persistent immunity for MenACWY serogroups, affecting PICO 2.

The work group felt that the desirable anticipated effects are small for all three PICOs. The undesirable anticipated effects are minimal for PICOs 1 and 3 and small for PICO2. For PICO 1, the work group felt the intervention was favored but varied for PICO 2 and 3. The overall certainty of evidence for short-term immunity was moderate or low for the three questions, and the overall certainty of evidence for serious adverse events was moderate or low for the three questions.

For the values domain, in 2023 about 85% of 13-year-olds received at least one MenACWY vaccine dose, and approximately 60% of 17-year-olds had at least two doses, and about 32% and 13% of 17-year-olds received at least one or two doses of MenB vaccine, respectively. Additionally, almost 90% of 16- to 23-year-olds and 69% of their parents indicated they would prefer a simplified vaccine schedule, with fewer injections and fewer visits. The work group felt that the target population would feel that the desirable effects were large relative to the undesirable effects for PICO 1, were probably large for PICO 2, and were large or probably large for PICO 3. This is similar to the work group's rating for the Pfizer pentavalent vaccine. The work group felt that there was probably not or was not important uncertainty or variability in how much people value the primary outcome for PICO 1. There was more uncertainty for PICO 2 and 3, similar to the ratings for the Pfizer pentavalent vaccine.

For acceptability, the CDC's General Best Practice Guidance for Immunization and the American Academy of Pediatrics Red Book both state a general preference for combination vaccines over separate injections of equivalent component vaccines. Adolescents prefer fewer injections due to injection site discomfort, and parents/caregivers prefer fewer injections to reduce the number of physician visits. The work group felt that the intervention is or probably is acceptable to key stakeholders with more confidence and acceptability for PICO 1.

For the resource use domain, Q-P-B was cost-saving relative to the current recommendation (vs. Q-Q-B-B). P-P-N could improve health outcomes but costs $11.3 million per QALY saved (vs. Q-Q-N). Q-P-P is cost-saving compared to Q-Q-B-B. Q-P-P is $4.5 million per QALY saved more than Q-P-B. The work group felt PICO 1 would efficiently allocate resources, but this varied for PICO 2 and 3.

For equity, an increase in IMD has been observed among Black or African American individuals. Among 11- to 20-year-olds, case counts were too small to examine by year, but the average annual incidence across 2015-2023 was highest among Black or African American individuals. IMD data by ethnicity showed a higher incidence among Hispanics starting in 2019. Among 11- to 20-year-olds, the average yearly IMD rate was higher among those who were not Hispanic or Latino. Counties with lower socioeconomic status (SES) had fewer MenB doses stocked compared to higher SES counties. The provider's or patient's awareness of an SCDM recommendation is a prerequisite for patient discussions and could lead to health inequities. The pentavalent vaccine could potentially reduce disparities among those interested in MenB vaccination but not receive clinical care, including a discussion of the MenB vaccine. The lack of MenB vaccine interchangeability currently restricts existing MenABCWY vaccine use to patients and providers stocking Pfizer MenB vaccine products. The work group felt that health equity would probably be increased or be increased with the GSK pentavalent vaccine. This is different from responses previously noted for the Pfizer vaccine.

Dr. Schillie shared that challenges with insurance or financial burdens related to the pentavalent vaccine are not expected for the feasibility domain. GSK pentavalent vaccine would provide an additional option and may reduce the number of doses for some people. The lack of MenB vaccine interchangeability complicates stocking considerations. Overall, the work group felt the intervention would be feasible to implement.

In summary, the determinations are generally favorable for PICO 1 and somewhat less favorable for PICO 2 and 3. For PICO 1, the work group felt that the desirable consequences outweighed the undesirable ones. For PICO 2 and 3, the work group was divided. They did feel that there was sufficient information to move forward with the recommendation. The work group does recommend the intervention for PICO 1. It does not recommend the intervention for PICO 2 and was evenly divided in recommending PICO 3. Several Work Group members noted that it would be important to harmonize recommendations between the GSK and Pfizer pentavalent vaccines unless there is a vaccine-specific reason for having a different recommendation. An interim recommendation for the GSK vaccine could mirror the recommendation made for the Pfizer vaccine last year. Recommendations for use of both pentavalent vaccines could then be revisited as part of future adolescent schedule deliberations.

Dr. Loehr invited the ACIP members' comments on PICO 3 since the work group differed in opinion on that option but may favor it. He stated that accepting this would cause a lack of harmony between the two pentavalent vaccines. He does not feel it is acceptable because it would not be harmonized among the vaccines.

Dr. Chu agreed that harmonizing is essential. She felt the most logical thing would be to accept PICO 1 and then wait for subsequent data showing whether the P-P strategy is comparable to a three-dose strategy.

Dr. Shaw requested confirmation that the P-P-B vs the current recommendation has not been modeled.

Dr. Schillie stated that the work group is considering revisions to the adolescent schedule in the coming months but would first like to address the use of the GSK pentavalent vaccine. Currently, the work group only considers the pentavalent vaccine in the context of different options for existing recommendations.

Dr. Asturias emphasized that before integrating any pentavalent vaccine into the immunization schedule, we should transition from using a combination of vaccines with both a recommended schedule and a shared clinical decision-making schedule to including the MenB vaccine as part of the recommended schedule. If MenB is to be added, it should be fully endorsed as a recommendation rather than leaving it as a shared decision option, which could create confusion among parents and providers. This approach raises the question of whether we should prefer a three-dose series or maintain a two-dose regimen. Dr. Asturias expressed his concern about any changes that might diminish the first recommendation, which he noted that parents have consistently valued.

Dr. Loehr clarified that the Q-P-B schedule (PICO 1), which the work group is considering recommending, is still a shared clinical decision-making. The P and B are only offered if, after shared clinical decision-making, the family or the child decides that they want B.

Dr. Maldonado, as a pediatrician, expressed concerns regarding the complexities of shared clinical decision-making, particularly for primary care providers dealing with devastating diseases with low incidence rates. She highlighted the challenges faced by providers in addressing this issue, especially considering the notably low uptake of the MenB vaccine attributed to shared clinical decision-making. Dr. Maldonado suggested the importance of streamlining recommendations to align them with the routine vaccination schedule, advocating for a swift transition into a non-shared clinical decision-making approach to enhance vaccination uptake and ensure patients receive timely and effective care.

Ms. Moser clarified that the Pfizer vaccine is already approved for what we show at PICO 1. The impending schedule review made this discussion very complex for the work group. It was determined that it was best to address the GSK vaccine in comparison to the Pfizer vaccine. The work group will revisit this when we return to looking at the routine schedule.

Dr. Brooks addressed Dr. Loehr's point regarding the importance of focusing on ICERs that amount to millions of dollars. He noted that issues would likely arise if we do not achieve harmonization, and therefore, he would not support going out of harmony. He expressed his preference for PICO 1. If the family wishes to pursue option B, it would be a cost-saving choice. Seeing the absolute numbers in some of the outcome data would be beneficial since they are very, very low.

Dr. Chen agreed with the need to harmonize to reduce complexity. She also requested confirmation that the two pentavalent vaccines are not interchangeable because they contain different MenB components. If so, it would be difficult for clinics to stock all three vaccines. She raised the issue of the duration of immunity for MenACWY.

Dr. Schillie confirmed that Dr. Chen’s assumption was correct.

Dr. Talbot noted that while the QPB may appear simple, the reality is more complex. When stocking three vaccines with "Meningitis" on their labels, there is a significant risk of administering the wrong vaccine. This is an important consideration. She pointed out that when the conjugate pneumococcal vaccine was introduced, there were frequent errors in vaccine administration. Dr. Talbot appreciates the debate surrounding the appropriateness of ICERs. She is open to accepting higher ICERs, suggesting that other areas in medicine may be more suitable for cost savings. Additionally, she emphasized the importance of the working group returning to find a simplified standard vaccine that does not rely on shared clinical decision-making, as it has proven ineffective.

Dr. Schechter inquired whether there were enough data to do a sensitivity analysis on the potential protection of gonococcal disease in young adults.

Dr. Schillie responded that the vaccine is anticipated to be licensed to prevent meningococcal disease; however, it is known that these vaccines have about 30-40% efficacy against gonorrhea infections. This, however, was not factored into the cost-effectiveness analysis, but theoretically, this will make it more cost-effective when considering the benefits of gonorrhea prevention.

Dr. Sarah Schillie (CDC/NCIRD) introduced the MenB-4C (BEXSERO) interval and dosing label change. The FDA licensed BEXSERO under an accelerated approval process. New immunogenicity data support changes to the dosing schedule, which are not due to safety concerns. The new schedule was approved by FDA on August 19, 2024, and aligns with the existing schedule for MenB-FHbp (TRUMENBA).

BEXSERO was previously recommended as a two-dose series with doses administered at 0 and ≥1 month. The recommendation was for vaccinating healthy adolescents based on shared clinical decision-making as well as for persons at increased risk of MenB (persistent complement component deficiencies, those with complement inhibitor use, functional or anatomic asplenia, microbiologists routinely exposed to *Neisseria meningitidis*, or persons affected by an outbreak of serogroup B meningococcal disease).

TRUMENBA is recommended for healthy adolescents as a two-dose series with doses administered at 0 and 6 months. Persons at increased risk of MenB are recommended a three-dose series at 0, 1-2, 6 months.

The new BEXSERO label includes a two and three-dose schedule. The two-dose schedule consists of a dose at 0 and 6 months. If the second dose is administered earlier than 6 months after the first dose, a third dose should be administered at least 4 months after the second dose. For the three-dose schedule, a dose (0.5 mL) is administered at 0, 1-2, and 6 months. The choice of dosing schedule may depend on the risk of exposure and the individual's susceptibility to meningococcal serogroup B disease.

The proposed ACIP recommendations will achieve alignment with the updated schedule for BEXSERO and ACIP's TRUMENBA recommendations.

Dr. Sarah Schillie (CDC/NCIRD) presented the EtR Framework for MenB-4C (BEXSERO) interval and dosing change.

The work group developed the following PICO questions:

- Among persons aged 16 –23 years recommended for MenB vaccination based on shared clinical decision-making, should MenB-4C be administered on a 0, 6-month dosing interval, vs. a 0, ≥ 1-month dosing interval, for the prevention of invasive meningococcal disease?
- Among persons with persistent complement component deficiencies, those with complement inhibitor use, functional or anatomic asplenia, microbiologists routinely exposed to *Neisseria meningitidis*, or persons affected by an outbreak of serogroup B meningococcal disease, should MenB-4C be administered on a 0, 1–2, 6-month schedule, vs. a 0, ≥ 1-month schedule, for the prevention of invasive meningococcal disease?

A “yes” to both PICO questions aligns with existing TRUMENBA recommendations.

In the public health domain, Dr. Schillie shared that the overall incidence of meningococcal disease has declined from 2006 to 2023. People who are at increased risk for serogroup B disease include those with persistent complement component deficiency, complement inhibitor use, anatomic or functional asplenia, some microbiologists, and persons exposed during an outbreak. Depending on the condition, the estimated risk increase may be up to thousands of folds higher than the general population. From 2022 to the present, there have been nine outbreaks, including two serogroup B outbreaks (one in a college and surrounding community and one in an Amish community). For PICOs 1 and 2, the work group felt that IMD is an important public health problem.

For benefits and harm, in PICO 1, dose two of the 0, 6-month schedule was compared with dose two of the 0, 2, 6-month schedule. For PICO 2, dose three of the 0, 2, 6-month schedule was compared to dose two of the 0, 2, 6-month schedule. The most common local adverse event was injection site pain and the most common systemic adverse event was fatigue. Most events were mild or moderate, with an average duration of 1-4 days. Rates of adverse events did not substantially increase with subsequent doses of BEXSERO.

Seroresponse was assessed after dose two on a 0,6-month schedule and after doses two and three on a 0, 2, 6-month schedule. Seroresponse for the strains fHbp, NHBA, and OMV were higher following dose two with the 0, 6-month schedule compared to dose two of the 0, 2, 6-month schedule with overlapping confidence intervals for the OMV strain. This corresponds to PICO 1. Seroresponse to all four strains increased with a third dose on a 0, 2, 6-month schedule compared to dose two on the same schedule with some overlapping confidence intervals. This corresponds to PICO 2.

The work group felt that the desirable anticipated effects were small for PICO 1 and small to moderate for PICO 2. The undesirable anticipated effects were minimal to small for PICOs 1 and 2. The work group favored the new dosing schedule and both schedules for PICO 1. For PICO 2, the work group favored the new dosing schedule.

For the values domain, Dr. Schillie shared that 32% and 13% of 17-year-olds received one and two doses, respectively, in 2023. The work group did not know whether the targeted population felt the desirable effects were large relative to the undesirable effects for PICO 1. For PICO 2, the work group was divided; some thought the desirable effects were probably large relative to undesirable effects, and others did not know. The work group felt that there was probably not important uncertainty or variability in how much people valued the main outcome for PICO 1 and 2.

For the acceptability domain, harmonized dosing schedules for BEXSERO and TRUMENBA would likely be viewed favorably by providers. Doses administered at shorter-than-recommended intervals can result in a sub-optimal immune response; however, extended intervals prolong the time until one achieves protection. The new schedule may be challenging for patients needing to complete a vaccine series before complement inhibitory therapy initiation, as persons using complement inhibitors should complete or update vaccination at least 2 weeks before complement inhibitor initiation unless the risks for delaying treatment outweigh the risks of developing meningococcal disease. Among unvaccinated persons for whom complement inhibitor therapy cannot be delayed, antimicrobial prophylaxis should be administered alongside meningococcal vaccination and continued for 2 weeks after vaccine administration. Persons taking complement inhibitors likely remain at substantially increased risk for meningococcal disease, even if vaccinated and/or taking prophylaxis.

Providers could consider continued antimicrobial prophylaxis for the duration of complement inhibitor treatment based on clinical judgment. For PICO 1 and 2, the work group felt the new dosing schedule was probably acceptable to key stakeholders.

For the resource use domain, the number of doses remains the same for most healthy adolescents except for situations where spacing is invalid. An additional dose is needed for those at increased risk. The price per dose for BEXSERO is higher than that of TRUMENBA. It is possible that harmonizing the two could increase pricing competition. The work group felt that the new dosing schedule was probably a reasonable and efficient allocation of resources for PICO 1 and 2.

For the equity domain, schedules that require extended intervals or additional visits could disproportionately affect populations with lower access to health care. Among adolescents initiating MenB vaccination and not eligible for the Vaccines for Children (VFC) program, 49.6% and 35.5% completed their BEXSERO and TRUMENBA series, respectively, by age 17 years. Among those eligible for the program, 51.4% and 16.2% completed their BEXSERO and TRUMENBA series, respectively, showing that series completion was disproportionately delayed among the VFC-eligible population with an extended dosing interval. Among commercially insured adolescents, 67% and 60% of those initiating vaccination completed their BEXSERO and TRUMENBA series, respectively, by age 19. Series completion improved but still lagged for TRUMENBA compared to BEXSERO. The work group felt that health equity would probably be reduced or not impacted for PICO 1. The work group felt that there would probably not be an impact on health equity for PICO 2.

For the feasibility domain, providers may need to adjust their practices, including their reminder/recall systems, especially for providers who administer the MenB vaccine just before college enrollment. Despite the alignment of TRUMENBA and BEXSERO, different manufacturers' MenB vaccine products remain not interchangeable. The work group felt the new dosing schedule would be feasible for PICO 1 and 2.

In summary, for PICO 1, the work group landed on a spectrum of desirable and undesirable consequences that are closely balanced with the desirable ones, to desirable consequences probably or clearly outweighing the undesirable ones. For PICO 2, the spectrum was that desirable consequences probably outweighed or clearly outweighed undesirable consequences. The work group felt there was sufficient information to proceed with the PICO 1 and 2 recommendations. The work group recommended the interventions for PICO 1 and 2.

Dr. Schillie summarized the work group’s considerations regarding the BEXSERO interval and dosing change. The proposed recommendations will align with the updated FDA label for BEXSERO and harmonize with existing recommendations for TRUMENBA. The proposed recommendation would have the advantage of new dosing schedules associated with increased immunogenicity compared to previous ones, and harmonization between BEXSERO and TRUMENBA dosing intervals and schedules will likely be viewed favorably by providers. The disadvantages are that the longer interval between doses increases the time to achieve vaccine-induced protection and delays series completion and that persons receiving complement inhibitor therapy may need prolonged antimicrobial prophylaxis due to extended time for vaccine series completion.

The work group proposes the following language:

- ACIP recommends MenB-4C (BEXSERO) be administered as a 2-dose series at 0 and 6 months when given to healthy adolescents and young adults aged 16–23 years based on shared clinical decision-making for the prevention of serogroup B meningococcal disease

- ACIP recommends MenB-4C (BEXSERO) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *N. meningitidis* isolates; and persons at increased risk during an outbreak)

Proposed CDC clinical considerations include no recommendation to recall persons previously vaccinated at 0, ≥1 month (healthy adolescents or persons at increased risk). Persons should continue with booster vaccination as previously recommended. When immediate protection is desired for a healthy adolescent or young adult, based on shared clinical decision-making, providers may administer the 3-dose series at 0, 1-2, 6 months. This would apply to BEXSERO and TRUMENBA.

Currently recommended for TRUMENBA (applicable to BEXSERO) when administering the 2-dose series (e.g., for healthy adolescents): If the second dose is administered <6 months after the first dose, a third dose should be administered ≥4 months after the second dose. A second dose administered ≥6 months following the first dose is valid and does not need to be repeated. When administering the 3-dose series (e.g., for people at increased risk), a third dose is not required if the second dose was administered ≥6 months after the first dose. If the third dose is administered <4 months after the second and <6 months after the first, the dose should be repeated ≥4 months after the last dose.

Unchanged clinical considerations note that MenB vaccines from different manufacturers are not interchangeable. BEXSERO may be administered simultaneously with other vaccines. Contraindications include severe allergy to a prior dose or component of the vaccine. Precautions include pregnancy and moderate or severe acute illness.

Dr. Cineas requested clarification regarding clinical considerations for patients receiving two vaccine doses. Clients will not be recalled for a third dose. If someone has already received their first dose and is coming in for their second, they will be instructed to defer their next dose for six months.

Dr. Schillie confirmed that Dr. Cineas is correct. CDC does not recommend recalling people who were previously vaccinated.

Dr. Asturias acknowledged that the proposal aligns with the new label. However, he pointed out some drawbacks, including low completion rates. He questioned whether CDC was seeing the same effects on the second dose of quadrivalent vaccine due to the shared clinical decision-making recommendation for MenB vaccine.

Dr. Schillie said that there has been no comparison to quadrivalent. Still, the vaccine coverage data shows that the VFC population has a more delayed series than the non-VFC population with an extended interval comparing TRUMENBA vs. BEXSERO.

Dr. Schechter asked about the immunogenicity difference between (0,1) and (0, 6) and how important the second dose is in the at-risk population.

Dr. Schillie reviewed the data, showing that the difference overall is small but it varies by strain for both high-risk patients and healthy adolescents.

Dr. Kamboj requested clarity on who is considered at high risk.

Dr. Schillie clarified that high-risk persons are those taking complement inhibitors, those with an inherited complement component deficiency, those with functional or anatomic asplenia, microbiologists routinely exposed to *Neisseria meningitidis*, or persons affected by an outbreak.

Dr. Chu asked whether people going to college are at high risk. She also expressed concern that people may age out of VFC before they receive their second dose. She appreciates that the clinical considerations include a caveat to address this.

Dr. Schillie responded that college students are not included in the high-risk recommendations. The work group is proposing that these students could receive the three-dose vaccination series, allowing them to receive at least two doses before moving on to college. This option is intended for those not starting their vaccination series at least six months before college enrollment.

Dr. Talbot added to Dr. Chu's point that the issue of aging out of VFC could be explicitly spelled out in clinical considerations.

Ms. Arthur commented on a letter emphasizing the importance of clinicians advising patients receiving complement inhibitors to consider starting treatment earlier. She pointed out that many patients are currently waiting six months to begin their therapy, which can lead to issues and deterioration of their condition. Additionally, she noted that the prices for these products do not align with the market prices reflected in the cost-effectiveness modeling conducted by GSK. She requested that the work group re-evaluate the pricing to ensure appropriate market prices are utilized. Finally, she expressed the need to address equity considerations regarding using MenABCWY.

Dr. Asturias motioned that ACIP recommends MenB-4C (BEXSERO) be administered as a 2-dose series at 0 and 6 months to healthy adolescents and young adults aged 16–23 based on shared clinical decision-making for the prevention of serogroup B meningococcal disease.

Dr. Loehr seconded the motion.

Dr. Cineas motioned that ACIP recommends MenB-4C (BEXSERO) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *N. meningitidis* isolates; and persons at increased risk during an outbreak).

Dr. Jamieson seconded the motion.

Dr. Jeanne Santoli (CDC/NCIRD) shared the updated VFC resolution for meningococcal vaccines. The updated resolution includes revisions of the recommended vaccination schedule and intervals sections within meningococcal B component of the resolution and updates linked documents as needed throughout the resolution.

The eligibility groups for the MenACWY component have remained the same. The table of recommended vaccination schedules and intervals has also remained the same, and the link to the recommended schedules and intervals has been updated. There have been no changes to the recommended dosage or contraindications and precautions.

The eligibility groups for the MenB component have not changed. In the vaccination schedule and intervals, BEXSERO moves into the section with TRUMENBA, with the same dosing schedule as TRUMENBA. There are no changes to the table notes, recommended dosage, contraindications, and precautions.

The eligibility groups for the combined pentavalent serogroup A, C, W, Y, and B vaccines have not changed. However, the table has been altered to remove the word “monovalent” and add “(Trumenba) (1).” The table notes, recommended dosage, contraindications, and precautions have not been changed.

Dr. Cineas motioned to approve the Vaccines for Children (VFC) resolution for vaccines to prevent meningococcal disease.

Dr. Maldonado seconded the motion.

Vote: Meningococcal Vaccines-Vote #1
Although public comment was presented before all of the votes during this meeting, they were incorporated in summary with their respective sessions for continuity.

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for Meningococcal vaccines into the record:

> *ACIP recommends MenB-4C (Bexsero) be administered as a 2-dose series at 0 and 6 months when given to healthy adolescents and young adults aged 16-23 years based on shared clinical decision-making for the prevention of serogroup B meningococcal disease*

Motion/Vote: Meningococcal Vaccines

Dr. Asturias made a motion to approve the proposed vote recommendation for meningococcal vaccines vote #1, stating, “ACIP recommends MenB-4C (Bexsero) be administered as a 2-dose series at 0 and 6 months when given to healthy adolescents and young adults aged 16-23 years based on shared clinical decision-making for the prevention of serogroup B meningococcal disease” Dr. Loehr seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored:	Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw, and Talbot
0 Opposed:	
0 Abstained:	

Vote: Meningococcal Vaccines-Vote #2

Dr. Melinda Wharton (ACIP Executive Secretary, CDC) read the following proposed ACIP voting language for Meningococcal vaccines into the record:

> *ACIP recommends MenB-4C (Bexsero) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to N. meningitidis isolates; and persons at increased risk during an outbreak).*

Motion/Vote: Meningococcal Vaccines

Dr. Cineas made a motion to approve the proposed vote recommendation for meningococcal vaccines vote #2, stating, "ACIP recommends MenB-4C (Bexsero) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *N. meningitidis* isolates; and persons at increased risk during an outbreak)." Dr. Jamieson seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored: Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw, and Talbot
0 Opposed:
0 Abstained:

Vote: Meningococcal Vaccines-Vote #3

Dr. Melinda Wharton (ACIP Executive Secretary, CDC) read the following proposed ACIP resolution for Meningococcal Vaccines for Children (VFC) into the record:

> *Approve the Vaccines for Children (VFC) resolution for vaccines to prevent meningococcal disease.*

Motion/Vote: Meningococcal Vaccines

Dr. Cineas motioned to approve the Vaccines for Children (VFC) resolution for vaccines to prevent meningococcal disease. Dr. Maldonado seconded the motion. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored: Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw, and Talbot
0 Opposed:
0 Abstained:

RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES- ADULT

Dr. Albert Shaw, ACIP Adult Respiratory Syncytial Virus Work Group Chair, introduced the respiratory syncytial virus (RSV) session. He reminded the group that in June 2023, ACIP recommended that all adults aged ≥75 and adults 60-74 years who are at increased risk of severe RSV disease receive a single dose of RSV vaccine.

Currently there are three FDA-approved RSV vaccines, two protein subunit vaccines based on the prefusion conformation of the RSV F protein – GSK's AREXVY, based on RSV-A, with $AS01_E$ adjuvant, and Pfizer's ABRYSVO, with both RSV-A and RSV-B, without adjuvant – and a messenger RNA (mRNA) vaccine, encoding the RSV F protein in prefusion conformation, Moderna's mRESVIA®, which is a monovalent RSV-A Vaccine without adjuvant. All three of these vaccines are approved for prevention of lower respiratory tract disease (LRTD) caused by RSV in adults aged ≥60 years.

GSK's AREXVY is also approved for the prevention of LRTD caused by RSV in adults aged 50–59 years who are at increased risk for LRTD caused by RSV. Pfizer's ABRYSVO is also approved and recommended for the active immunization of pregnant women of any age at 32–36 weeks gestational age for the prevention of LRTD and severe LRTD caused by RSV in infants from birth through 6 months of age. As of October 22, 2024, the FDA approved Pfizer's ABRYSVO for the prevention of LRTD caused by RSV in adults aged 18–59 years who are at increased risk for LRTD caused by RSV.

Since June, the work group has been reviewing updated data relevant to current recommendations and discussing potential policy options for an RSV vaccination recommendation in adults aged <60 years. Today's FDA and manufacturer presentations will provide updates on co-administration, duration of protection, and immunogenicity in adults with immunocompromise. The work group will share interpretations regarding these updates and considerations for future policy.

Dr. Rituparna Das (Moderna) presented data on the RSV vaccine (mRESVIA, mRNA-1345) concomitantly administered with other vaccines. Older adults face a significant burden from seasonal respiratory viruses, leading to high hospitalization rates for COVID-19, influenza, and RSV. The vaccine coverage for influenza in this group is 70%, lower for COVID-19 at 39%, and lower for RSV at 23%. Concomitant administration of vaccines is an important tool to increase vaccine coverage.

Moderna's pivotal study, Study 301, demonstrated high and durable efficacy against RSV disease, including severe disease in older adults. Efficacy and immunogenicity data from the pivotal 301 study were used to develop a correlate of protection model based on neutralizing antibody titers which was used to contextualize immunogenicity results from other studies.

Study 302, parts A and B, presented at an earlier ACIP meeting, supports the coadministration of mRNA-1345 and standard-dose influenza vaccine. It also supported the coadministration of mRNA-1345 and a periodically updated COVID-19 vaccine.

Study 304 enrolled about 1,900 adults ≥65 years in a randomized, observer-blind trial. The first group received mRNA-1345 and high-dose influenza vaccine (Fluzone High-Dose) simultaneously, while the second group received them sequentially, with Fluzone High-Dose administered first.

Both groups generated robust immune responses, measured through neutralizing antibody titers against RSV-A and RSV-B and hemagglutinin inhibition titers for four influenza strains. The geometric mean titer ratio (GMR) for all influenza strains was close to 1, but RSV GMRs were lower, indicating a reduced immune response with coadministration. However, applying the immunologic correlate of protection model, despite the difference in neutralizing antibody titers, predicted vaccine efficacy was similar with and without coadministration with high-dose influenza vaccine. The concomitant administration was well tolerated. There were predominantly mild adverse events, with the most common reactions being injection site pain, fatigue, and myalgia, with a duration of 1-3 days. The safety profile was consistent with Study 301 clinical data.

In summary, the 302 studies showed that coadministration of mRNA 1345 with standard dose influenza and COVID-19 vaccines is well tolerated, and there are no safety concerns. Additionally, robust immunogenicity was observed for all influenza strains, COVID-19, and RSV, supporting their coadministration.

Study 304 showed data that coadministration of mRNA-1345 with high-dose influenza vaccine is well tolerated, with a safety profile consistent with what was observed in the large pivotal efficacy 301 study. There were no events of GBS, acute disseminated encephalomyelitis (ADEM), or myocarditis/pericarditis. Robust immunogenicity was observed for all influenza strains and RSV. RSV titers are lower with coadministration, but using a correlate of protection model developed from study 301, the manufacturer believes that clinical efficacy against RSV disease, including severe disease, will be maintained. Overall, the coadministration of mRNA-1345 with standard and high-dose influenza vaccines and the COVID-19 vaccine is beneficial.

Dr. Chu asked whether the analysis used to correlate the risk curve could be done for subtype B neutralizing and preF binding antibodies. She also requested comment on why Moderna thinks the non-inferiority threshold for standard dose flu vaccine was met but not the non-inferiority threshold for high-dose influenza vaccine.

Dr. Das responded that the analysis was done for RSV-A and B neutralization and preF binding. RSV-A and preF correlated with RSV overall. B correlated the best with RSV-B and had a slightly lower correlation with RSV overall, but the general relationships were very similar. The group's manuscript is almost ready to share, which details this. She shared that in Study 304 the criteria were met for flu, but the titers were lower for RSV and under the .67 inferiority threshold. While the .67 threshold has been used for many vaccines, the clinical significance of this threshold is unclear. Sometimes, lower thresholds are proposed; If a lower threshold were used, the group would have met it. She believes that coadministration often leads to lower titers for influenza or RSV. Dr. Das stated that Moderna was confident that based on the correlate of protection work that has been done, the reduction would not impact clinical efficacy.

Dr. Wharton followed up on whether the age of the study population differed between the two studies.

Dr. Das confirmed that the ages did differ. In the correlate of protection (pivotal study), the age was ≥60. In the Fluzone High-Dose coadministration study, the age was ≥65. The predictive modeling is adjusted for ages ≥65. The group also subdivided the coadministration study to look at ≥75 to ensure the differences were not magnified in this group. There were fewer differences between coadministration and sequential administration that that age group.

Dr. Shaw requested data on T-cell responses as a correlate for efficacy. There is data on very high neutralizing antibody titers for RSV that are safe from challenge experiments. Infection is still possible, and the T-cell response could be preventing people from getting sick.

Dr. Das shared that the T-cell immunity piece is important. In smaller studies, Moderna has evaluated T-cell responses and has found robust CD4 and CD8 responses, with the CD4 responses having a Th1 bias. A correlation has been seen between neutralizing antibody responses and CD4 responses, which gives them confidence that neutralizing antibody does correlate with protection, although this is likely multifactorial. The group did not look at T-cell responses for coadministration. Correlates work is very tough with cellular immunity because of the requirement to collect and restore samples from all study participants.

Dr. Brooks inquired whether there was data on the simultaneous administration of all three vaccines (RSV, influenza, and COVID-19).

Dr. Das shared that the data available are only for two vaccines at a time.

Dr. Iona Munjal (Pfizer) presented on the RSVpreF vaccine in adults. ABRYSVO is Pfizer's bivalent RSV prefusion F protein vaccine, approved for adult and maternal indications. This includes a new expanded indication for adults 18- to 59 years of age who are at an increased risk for LRTD caused by RSV.

In a co-administration study of COVID-19, influenza, and RSV vaccines in adults ≥60 years of age, the study demonstrated non-inferiority, providing affirming evidence for the ACIP recommendation to allow the administration of RSV with other adult vaccinations during the same visit. In a study of adults ≥18 years of age with immunocompromising and high-risk conditions, data suggested that a single dose of RSVpreF may protect the most vulnerable adults from RSV disease.

The incidence rate and risk for severe complications from RSV infection (hospitalization, mortality, etc.) are higher among immunocompromised adults and those with other risk conditions and this difference is more pronounced in younger adults. The MONET study was a single-arm open-label multicenter study of RSVpreF in immunocompromised at-risk adults ≥18 years of age. The study enrolled 200 participants from 11 sites in the U.S. from May 2023 to March 2024. The study assessed safety, tolerability, and immunogenicity. Participants received two doses of RSVpreF one month apart. Immunogenicity assessments occurred before and one month following each dose. Safety assessments were obtained throughout seven months post-dose one, including self-reported diaries following each dose. Qualifying immunocompromising conditions included non-small cell lung cancer undergoing therapy, solid organ transplant recipients, participants with autoimmune inflammatory disorders on active immune-modulator therapy, and participants on hemodialysis due to end-stage renal disease (ESRD).

For RSV A and B, this group had high neutralizing geometric mean titers (GMT) one month after dose one, with no additional Increase after the second dose. There were robust neutralizing GMTs and geometric mean fold-rise (GMFR) against RSV-A across subgroups. The subgroups' sample sizes were smaller and should be interpreted cautiously due to wide confidence intervals. The response was similar for RSV-B across subgroups. The immune response of the immunocompromised population is similar to that seen in the pivotal efficacy RENOIR study in adults 60 and older, which followed participants for up to 2 years after one dose. The results suggest that a robust neutralizing titer response is achievable in the immunocompromised population after a single dose, and fold rises are likely high enough to confer protection. Local reactions within seven days after vaccination were mild to moderate in immunocompromised adults. Systemic events within seven days after vaccination were mostly mild to moderate in immunocompromised adults. Reports of adverse events were higher in the older age group. Two events deemed related to the vaccine were in the older group.

In summary, RSVpreF was well-tolerated with no safety concerns among immunocompromised adults ≥18 years of age. One dose of RSVpreF elicited high GMTs and GMFRs in the immunocompromised study populations with no additional increase after a second dose one month apart.

To date, ABRYSVO has been most commonly co-administered with influenza and/or COVID-19 vaccine. The group conducted a randomized parallel group observer-blinded study to assess the safety, tolerability, and immunogenicity of RSVpreF with COVID and Influenza vaccine. Approximately 750 participants enrolled in the study were healthy and aged 65 or older. Groups received combinations of a COVID-19 vaccine and placebo, RSV vaccine and placebo, RSV plus COVID-19 and placebo, or all three vaccines simultaneously. There was an immunogenicity assessment before and one month following vaccination. Safety assessments were obtained throughout six months post-dose, including self-reported diaries following vaccination. The COVID-19 vaccine was Pfizer/BioNTech's bivalent COVID-19 vaccine, BNT162b2 (COMIRNATY®) and the flu vaccine was quadrivalent Fluzone High-Dose.

Co-administered Bivalent BNT162b2 COVID-19 and RSVpreF met 1.5-fold non-inferiority criteria for all four COVID and RSV antigens. Co-administered Bivalent RSVpreF, BNT162b2 COVID, and high-dose influenza vaccine met protocol-specified non-inferiority criteria. Local reactions in co-administration groups were mostly mild or moderate and similar to single-vaccine groups. The most common reaction was injection site pain. Higher proportions were found in groups that received a COVID vaccine alone or in combination with another vaccine. Severe reactions were rare and similar to those observed with a single administration. Systemic events in co-administration groups within 7 days after vaccination were primarily mild to moderate, similar to single-vaccination groups, and usually resolved within one to two days. The most frequent systemic event in all vaccine groups was fatigue, with the highest proportion of participants reporting it in the triple co-administration group. The proportion of participants reporting serious adverse events was similar across all study groups. There were no reports of GBS or deaths throughout the study.

Co-administration is common; safety and immunogenicity data support ACIP co-administration guidelines regarding RSVpreF with COVID and/or influenza vaccines. A single dose of RSVpreF was safe and immunogenic in immunocompromised and high-risk adults. Ongoing clinical trials and post-licensure studies provide meaningful data to assess the product's safety, effectiveness, and benefit/risk. No new safety concerns have been identified in the post-licensure period to date.

Dr. Talbot asked why the vaccines were spaced so closely (one month apart) for the immunocompromised. It is known that a better immune response occurs when vaccines are spaced further apart.

Dr. Munjal stated that at the time, the group was unsure whether they could achieve robust immune responses on the first dose. Prior studies have shown no boost in healthy, immune-competent adults after one year. Pfizer was trying to obtain data on whether immunocompromised persons could be protected before one RSV season, so it was critical that protection be provided early on. With robust responses and no increase with the second dose, the group is looking at more extended vaccine schedules in an ongoing revaccination study.

Dr. Shaw applauded the study of immunocompromised people because it is a group at risk for RSV disease. As the work group has expressed, the range of immunocompromise in this study is mild, particularly with the inclusion of people with end-stage renal disease who have altered immune responses but not in the range of solid organ transplant recipients, for example. He and his work group colleagues encouraged evaluation in much more immune-compromised groups.

He also requested additional details on what the serious adverse events within the immunocompromised groups were and if there were any episodes of transplant rejection.

Dr. Munjal concurred that there is a wide range of immunocompromised populations. Pfizer is doing a more extensive post-licensure safety and effectiveness study which will be analyzed by immunocompromised state to gain more information. The group has also done studies with and without the hemodialysis population, and the results are similar. Regarding the severe adverse events identified, there were two participants with severe adverse events in the younger group and four in the older group. Kidney transplant rejection was among those, as well as an episode not deemed severe, but there was an episode of lung transplant rejection. The investigator considered them unrelated to vaccination.

Dr. Chu echoed Dr. Shaw, saying that the degree of immunocompromise in this study is not necessarily that for which the data are needed. Data are needed for those who recently are post-transplant, particularly lung and stem cell transplants. She encourages the group to study this population because clinicians are more challenging to convince for a single dose in this group.

Dr. Munjal stressed that enrolling this population is challenging, especially achieving the enrollment of a sizable group within this population. However, they are included in the post-licensure studies, and Pfizer will generate data in those populations and continue to explore moving forward.

Dr. Susan Gerber (GSK) presented updates on AREXVY. As a reminder, AREXVY is indicated for active immunization to prevent lower respiratory tract disease (LRTD) caused by RSV in individuals ≥60 years of age and individuals 50-59 years of age at increased risk for LRTD caused by RSV. To date, around nine million doses have been administered in the U.S.

In the RSV-OA=ADJ-023 study, the group focused on solid organ transplant recipients as the first step in understanding AREXVY's role in protecting immunocompromised individuals. The study evaluated immunogenicity and safety after one dose versus two doses one month apart in lung and transplant recipients ≥18 years of age, compared to a single dose in immunocompetent adults ≥50 years of age. The analysis shared today is from visit four, one month post-dose two for adults with solid organ transplant, and 3 months after the single dose in adults ≥50 years of age. The study will extend to six and twelve months for further immunogenicity and safety evaluations. To be included, solid organ transplant recipient adults needed to be >12 months out from kidney or lung transplant on immunosuppressive therapy and medically stable. Adults ≥50 years of age needed to be medically stable but could have chronic, stable underlying conditions or comorbidities.

Demographics were generally balanced. Most solid organ transplant patients were 50 year of age and older. Approximately 70% had received kidney transplants. Transplant patients were a median of 5-6 years post-transplant. This was a worldwide study that included eight different countries.

The immunogenicity results showed that neutralizing antibodies for RSV-A and RSV-B were higher after the second dose than the first dose. Two doses of RSVPreF3 + $AS01_E$ elicit robust humoral immune responses in kidney and lung transplant recipients, similar in magnitude to that following one dose in immunocompetent adults ≥50 years of age. Solid organ transplant recipients not receiving mycophenolate had a similar humoral immune response after dose 1, compared with immunocompetent adults ≥50 years of age. RSVPreF3 + $AS01_E$ induced similar RSV-A and RSV-B neutralizing antibody responses in kidney and lung transplant recipients. RSVPreF3 + $AS01_E$ induced robust CD4+ T-cell responses in kidney and lung transplant recipients.

For safety, results showed solicited adverse events were broadly similar between solid organ transplant groups and adults ≥50 groups within seven days post-vaccination. Related unsolicited adverse events were similar between groups within 30 days post-vaccination. Serious adverse events were similar between dose one and dose two solid organ transplant groups. No safety concerns were identified.

Study AReSVi-006 (pivotal efficacy study) is a Phase 3 randomized placebo-controlled observer-blind multi-country efficacy study investigating the efficacy of AREXVY in preventing RSV LRTD over three seasons. The study includes around 25,000 participants in 17 countries. All RSV cases were PCR-confirmed.

A single dose of RSVPreF3 + $AS01_E$ demonstrated clinically meaningful vaccine efficacy against RSV-LRTD over three RSV seasons. The cumulative vaccine efficacy of a single dose of RSVPreF3 + $AS01_E$ against severe RSV-LRTD over three seasons was 72.3% without season as a covariant. A single dose of RSVPreF3 + $AS01_E$ shows consistent vaccine efficacy for subgroups over three RSV seasons. The safety profile remains consistent and acceptable over three seasons. There were no reports of GBS or ADEM.

In conclusion, one dose of RSVPreF3 + $AS01_E$ provides robust RSV-A and RSV-B neutralizing antibody responses and high CD4+ T-cell responses: acceptable safety profile in kidney and lung transplant recipients ≥18. RSVPreF3 + $AS01_E$ provides clinically meaningful efficacy over three seasons (median follow-up time 30.6 months) in adults ≥60, with a continued acceptable safety profile. The estimated public health benefits of RSVPreF3 + $AS01_E$ are increased, given its efficacy over three seasons compared to previous efficacy estimates. Ahead of this year's RSV season, it is important to protect vulnerable individuals ≥50 years of age who are at high risk for severe RSV disease.

Dr. Chu expressed interest in the third-season data. She asked if there were data for season three against hospitalization.

Dr. Gerber responded that there were eight hospitalizations in total. The study, however, was not designed to conclude that vaccines were effective against hospitalizations. Of the eight hospitalizations, two were from the vaccine arm and six in the placebo arm.

Dr. Shaw asked if there were any episodes of transplant rejection in the serious adverse events.

Dr. Bryant reported that there was one report of renal transplant rejection in a 72-year-old male. It occurred 147 days after the second dose of RSV. The patient was also found to have a BK infection on biopsy, which could increase the risk of rejection. Based on the case details, the investigator and GSK determined this to be unrelated. Regarding the grade three events, most grade three unsolicited events were related to isolated types of infection and reflected background morbidity in the transplant groups. One related unsolicited grade three event was a case of diarrhea considered unrelated by GSK.

Dr. Talbot inquired whether GSK was investigating extending the interval between immunizations to see if improving the response within this population was possible. She believes there may be benefits because it will last multiple RSV seasons.

Dr. Gerber shared that this is the first step, and six- and twelve-month results are expected from this study. The group is looking into discussing other high-risk immunocompromised populations in hopes of performing more immunogenicity studies on different types of immunocompromised populations.

Dr. Schechter questioned how the group approached additional doses in the non-immunocompromised groups and what level of waning and effectiveness would merit consideration for further doses.

Dr. Gerber stated that GSK has demonstrated clinically meaningful efficacy over three RSV seasons. The 012 study will extend the 006 study and include another two RSV seasons, and that coupled with the immunogenicity 004 study (planned for 60 months) will provide data on different immunization schedules and the persistence of a single dose. There is also discussion about performing real-world effectiveness studies that will look at persistence of a single dose. Combined, these will help inform revaccination strategy and future guidance.

Dr. Patricia Lloyd (FDA) shared results on the evaluation of Guillain-Barré syndrome (GBS) following RSV vaccination among adults ≥65 years of age.

Three RSV vaccines are approved for use in the U.S. in adults ≥60 years of age: RSVPreF3+AS01 (GSK, AREXVY), RSVPreF (Pfizer, ABRYSVO), and mRNA-1345 (Moderna, mRESVIA). Pre-licensure clinical trials identified a small number of GBS cases in RSVPreF3+AS01 and RSVPreF vaccines. Reports submitted to the Vaccine Adverse Event Reporting System (VAERS) identified higher GBS rates post-RSVPreF3+AS01 and RSVPreF vaccination than expected background rates.

FDA and their collaborators conducted a self-controlled case series study to assess the safety of RSV vaccines among adults ≥65 years of age. There were early-season analyses with data through April 6, 2024, and included vaccines administered through October 22, 2023. There was also an end-of-season analysis with data through July 13, 2024, and vaccines through January 28, 2024. This presentation focuses on the end-of-season analysis. In the SCCS design, the rate of incident GBS in the risk interval (1-42 days after RSV vaccination) is compared with the rate in the control interval (43-90 days following RSV vaccination).

In the end of season analysis, 3.2M doses of RSV vaccine were included, compared with 1.3M doses in the early season analysis. The group observed 95 GBS cases in the end-of-season analysis, with 56 vaccinated with AREXVY and 39 with ABRYSVO. Of the 95 cases observed, 75 medical records were reviewed. Fifty-one of the cases were confirmed GBS cases. Twenty-four were classified as having insufficient evidence or not a case. Overall, the positive predictive value (PPV) of diagnostic codes in the identifying chart confirmed GBS was 68%.

For GSK's AREXVY, the study estimated an adjusted GBS incidence rate ratio (IRR) of 2.46 (95% confidence interval [CI]: 1.19–5.08) in the risk interval, compared with the control interval. This corresponds to an attributable risk of 0.65 (95% CI: 0.18–1.12) GBS cases per 100,000 doses of AREXVY administered. For Pfizer's ABRYSVO, the study estimated an adjusted GBS incidence rate ratio (IRR) of 2.02 (95% CI: 0.93–4.40) in the risk interval, compared with the control interval. This corresponds to an attributable risk of 0.90 (95% CI: -0.02–1.81) GBS cases per 100,000 doses of ABRYSVO administered. There was no evidence of difference in GBS risk among persons with and without same day concomitant vaccination with RSV vaccines.

The studies' strengths include an adjustment for potential time-invariant confounding, more precise estimates of GBS due to use of a large database, findings generalizable to ≥65 year old adult U.S. population, and medical record review to improve the classification of GBS. The limitations include potential misclassification of GBS in administrative claims data, the study was not intended to compare GBS risk between the two vaccine products, IRR estimates may be sensitive to the number of records returned and adjudicated through medical record review, potential misspecification of post-RSV vaccination risk and control intervals for GBS, potential for residual confounding, and attributable risk calculations based on a small number of cases may be difficult to interpret.

To summarize the results, the group observed an elevated risk of GBS following both RSV vaccines. In the end-of-season data analysis through July 2024, the group observed a statistically substantial elevated IRR for GBS following vaccination with RSVPreF3+AS01; GBS risk was elevated yet not statistically significant following RSVPreF vaccination. Results remained the same when restricting confirmed GBS cases through medical record review. There was no evidence of a difference in GBS risk among persons with and without same-day concomitant vaccination with RSV vaccines.

In conclusion, our findings suggested an increased GBS risk following RSVPreF3+AS01 and RSVPreF among adults aged ≥65 years of age. These results are consistent with pre-licensure clinical trials and surveillance systems such as VAERS. End-of-season SCCS analysis results are largely chart-confirmed from medical record review and include approximately three times more vaccine doses and GBS cases than the early-season SCCS results. GBS risk following vaccination with RSVPreF3+AS01 and RSVPreF is rare, with less than 10 cases per 1 million vaccinations. There is no difference in GBS risk among persons with and without same-day concomitant vaccination with RSV vaccines.

Dr. Asturias inquired about the effect of age on the incidence of GBS.

Dr. Lloyd answered that they were unable to look at smaller age groups due to the small sample size.

Dr. Maldonado requested clarity on the significance of a PPV and how it was adjudicated and inquired why she thought the PPV was different among the two groups.

Dr. Lloyd responded that the PPV or positive predictive value gives the group an idea of how likely a diagnostic code is to reflect true GBS. Of the 95 cases, the FDA team requested records, and two neurologists reviewed the records and determined, based on the Brighton Collaboration case definition, whether the case represented a true case of GBS. Of the 75 cases for whom records were reviewed, 68% were deemed to be true cases. This was done stratified by risk and control intervals. These estimates were used to apply to the analysis. The group created multiple data sets where the status of the claims identified cases was imputed by assigning them the status of a chart confirmed status based on the probability equal to the PPV. The PPV was used to adjust for the records not returned following the request. The FDA team is still considering the reason for the difference in PPV by risk and control intervals. One reason could be that if a physician knows that an individual was recently vaccinated, they might be more likely to classify them as GBS even without an association with a vaccine.

Dr. Talbot thanked Dr. Lloyd and the rest of the FDA team for sharing these data with the committee.

Representatives of GSK shared a letter, which was submitted to the Federal Register. When discussing RSV adult vaccine recommendations, GSK thanks the ACIP for the opportunity to comment and requested the following to maximize the public health benefit: First, bring to a vote that the RSV vaccine AREXVY consistent with the FDA-labeled indication be recommended for the 13 million U.S. adults from 50-59 years of age with recognized medical conditions that increase their risk for severe RSV outcomes. The recommendation for people aged 50-59 years at risk will help ensure equitable access to vaccines. While RSV is now FDA-approved for individuals aged 50-59 at increased risk, insurers are not covering the cost of vaccinations without an ACIP recommendation, which is a burden on patients and a barrier to receiving the vaccine in the pharmacy. This should be a priority, and a lack of a vote at today's meeting would be a missed opportunity to provide access to the vaccine for this age group before the upcoming respiratory season. Secondly, the group requested to amend the policy from a high-risk recommendation for individuals 60- to 74 years of age to a routine recommendation for adults ≥60 years of age. This would help close the RSV vaccination equity gap and ensure all those eligible can gain access to this vaccine to help protect against RSV.

A representative from Moderna shared that the co-administration of vaccines represents an urgent public priority to address the public health need to improve vaccine coverage for RSV and other respiratory infections such as SARS-CoV-2 and influenza. mRESVIA has demonstrated robust efficacy and safety with up to 86.7% protection against severe RSV-related respiratory illness. Importantly, this protection has proved durable through three RSV seasons, including during periods of heightened viral activity. Co-administration simplifies the vaccination process, reducing barriers for healthcare providers and patients. Coadministration data substantiated by correlates of protection demonstrate that clinical efficacy is maintained. Moderna is committed to contributing strong evidence to the ongoing discussion of the RSV vaccination strategy and the company looks forward to working with the ACIP and public health to expand access and protection for all individuals at risk of RSV exposure.

Dr. Michael Melgar (CDC/NCIRD) presented the work group's interpretations of the updated data on RSV vaccination in adults.

Dr. Melgar recapped what was known about GBS as of June 2024. A small number of GBS cases were observed in clinical trials within 42 days after protein subunit RSV vaccination (GSK's AREXVY and Pfizer's ABRYSVO). Due to the small number of cases, it was unclear whether they represented a genuine association between RSV vaccination and GBS. Post-licensure data from 2023–2024 from the VAERS, VSD, and the partnership between the FDA and the Centers for Medicare and Medicaid Services (CMS) suggested, but could not confirm, an elevated risk of GBS after protein subunit RSV vaccination. The current older adult RSV vaccine recommendation is intended to focus the vaccination program on older adults in whom the benefits of vaccination most clearly outweigh the potential risks. There have been no cases of GBS within 42 days after Moderna mRESVIA vaccination in clinical trials; post-licensure safety surveillance for this vaccine began in June 2024 after licensure, and data are not yet available.

As Dr. Lloyd just presented, the FDA/CMS analysis now includes ~3.2 million protein subunit RSV vaccine doses and 95 GBS cases identified through diagnostic codes. The incidence rate ratio of GBS following both vaccines was elevated; results reached statistical significance for GSK's AREXVY but not for Pfizer's ABRYSVO, which had fewer doses administered. Attributable GBS risk was similar for both products. 30–50% of doses were concomitantly administered with another vaccine; there is no evidence that concomitant vaccination explains the increase in GBS rate after protein subunit RSV vaccination.

The work group also reviewed examples from other licensed and recommended vaccines of benefit-risk considerations, including seasonal influenza and recombinant zoster vaccine. The work group concluded that available data support the existence of an increased risk of GBS after protein subunit RSV vaccination. Available data suggest that risk is comparable to and potentially greater than, other currently licensed and recommended adult vaccines and that there is no evidence of a differential risk between the two protein subunit vaccines. The work group emphasized that the risk of GBS associated with protein subunit RSV vaccines should be considered in the context of the public health benefits of RSV vaccination.

The work group also reviewed an updated mathematical model analysis comparing the numbers of RSV-associated hospitalizations, ICU admissions, and deaths avertable per one million vaccinations vs. the potential vaccine-attributable GBS cases. This analysis has been updated to include updated risk estimates for GBS, updated VE assumptions, and the base case evaluation of protein subunit RSV vaccination generally rather than the GSK and Pfizer vaccines individually. The results showed preventable RSV outcomes continued to exceed potential cases of GBS for adults ≥75 years of age (general population) and adults 60- to 74 years of age at increased risk of severe RSV disease.

The work group also reviewed updated safety data from the VSD on protein subunit RSV vaccines, and there is no statistical signal for GBS in rapid cycle analysis to date. As was seen in June 2024, there is a numerical imbalance in the number of GBS cases after GSK AREXVY vaccination in adults aged ≥60 years, but the number of cases is small. The system is currently underpowered to determine whether there is an association with GBS. A review of the charts reveals a numerical imbalance in the small number of immune thrombocytopenia (ITP) cases following GSK AREXVY vaccination in adults aged 60 years and older without administering another simultaneous vaccine. However, the current system lacks sufficient power to establish whether there is a connection between vaccination and ITP. Additionally, fewer doses of Pfizer ABRYSVO were administered in the VSD; therefore, no conclusions can be made regarding the safety of this vaccine at this time.

Co-administration of RSV and other recommended adult vaccines, particularly seasonal influenza and COVID-19, is common. The work group was reassured to see these first-ever data from Pfizer demonstrating that three-way co-administration of protein subunit RSV vaccine, mRNA COVID-19 vaccine, and high-dose influenza vaccine was safe and generated a non-inferior immune response. The work group acknowledges the findings of inferior RSV-neutralizing antibody response with co-administration of the Moderna RSV vaccine and high-dose influenza vaccine but feels the clinical significance of this finding is currently unknown. These data should also be put in the context of a lack of a consistent pattern in combinations of RSV vaccine and other concomitant vaccinations that resulted in inferior immune responses.

Overall, the work group noted a limited understanding of the clinical significance of decreased antibody titers with RSV vaccine co-administration. Given the considerable benefits of co-administration and evidence of its safety, the Work Group continues to feel co-administration is acceptable. In addition, the Work Group looks forward to learning more about Moderna's analysis of immunologic correlates of protection for RSV as additional peer-reviewed methods become available.

GSK and Pfizer presented clinical trial data on using RSV vaccines in adults aged ≥18 years with immune compromise. These are the first clinical trial results in these populations at high risk of severe RSV disease. Notably, these trials studied the safety and the immune response to RSV vaccination but did not estimate efficacy against clinical endpoints. The work group was encouraged to see clinical trial data in this population but would have preferred to see data among adults with the most severe forms of immune compromise, who are at highest risk of severe RSV disease (e.g., hematopoietic stem cell transplant, recent lung transplant). The work group also felt that Pfizer's inclusion of adults with end-stage renal disease on dialysis used too broad a definition of immune compromise. The work group expressed uncertainty about whether neutralizing antibody titers will correspond to similar clinical efficacy observed in immunocompetent older adults. Absent clinical efficacy data, the work group expressed uncertainty in whether two doses of GSK's AREXVY would be required to ensure adequate protection against severe RSV disease in solid organ transplant recipients.

Dr. Melgar closed with policy considerations. The work group affirms that the current older adult RSV vaccine recommendations are appropriate. The work group believed that the benefits of RSV vaccination outweigh the risks of GBS among the populations for whom RSV vaccination is currently recommended. The work group continues to evaluate recommendations for the use of RSV vaccines in adults aged <60 years. Developing an RSV vaccine policy in adults <60 years of age will require careful consideration of this population's balance of public health benefits and risks. The updated results presented at this meeting increase certainty that protein subunit RSV vaccination is associated with GBS risk, though uncertainty remains regarding the magnitude of risk. The working group will use these data to evaluate risks and benefits, including identifying which groups under 60 years of age may have benefits that outweigh the associated risks.

Regarding immunocompromised adults, the work group recognizes this is a heterogeneous group that is not all at the same risk of severe RSV. While the data presented at this meeting covered a subset of those with immune compromise, the work group does not feel it substantially increases certainty that those with the most severe forms of immune compromise will benefit from vaccination (e.g., hematopoietic stem cell transplant recipients). Therefore, the work group did not feel that today's data motivated an immediate policy expansion for this group in younger adults, mainly while the FDA-CMS analysis on GBS risk is ongoing.

The work group continues to feel additional data are necessary before voting on an RSV vaccine recommendation in younger adults -- specifically, final results from the FDA-CMS analysis of the first season of RSV vaccination in Medicare beneficiaries; pending certainty in safety findings, data demonstrating vaccine efficacy or effectiveness against clinical endpoints in the most severely immunocompromised adults; and immunogenicity data after revaccination with more extended time intervals following initial vaccination. When data are available, the work group will propose a policy question to the ACIP committee.

Dr. Asturias encouraged the work group to use age as an important way to categorize the risk of GBS. Evidence shows that rates are higher in older adults, and it is counterproductive to assume the same risk of GBS in younger ages when the baseline risk is known to be higher in older adults.

Dr. Kamboj highlighted that there are still critical gaps in immunogenicity data from immunocompromised patients. For example, the clearest is excluding patients with hematologic malignancy and hematopoietic cell transplant. Hematologic malignancies account for about 10% of all cancers, and if you look at RSV-related hospitalizations, more than half happen in this population. The other gap is redosing and the interval between redosing. Also, the durability of response and possible immunologic interference between co-administered vaccines should be examined in immunocompromised patients.

Dr. Brewer shared his appreciation of the work group's data showing the lives saved through vaccination in contrast to the current data on GBS. He also highlighted that Pfizer presented a slide showing that co-administration is now the norm. He felt it would be beneficial to elaborate on this data to determine whether co-administration benefits some specific groups more than others.

Dr. Brooks summarized several points from the presentations and expressed his confidence in the vaccination process against RSV. He recalled that only three years ago, there was no vaccine to protect against RSV. He found the data presented helpful and very reassuring.

Dr. Schechter inquired whether any data supported an association between GBS and RSV infection, which would further enhance the risk-benefit calculation.

Dr. Melgar stated that there have been reports of individual cases of GBS that were preceded by documented lab-confirmed RSV infection; however, this has not been an epidemiological study that has calculated an elevated risk of GBS after RSV vaccination. A respiratory prodrome often precedes GBS, and RSV may be responsible for some portion of GBS that happens in the community. This has not been included in the risk-benefit calculations because of lack of direct evidence to quantify. The group continues to monitor the literature for new findings on this topic

IMMUNIZATION SCHEDULES

Dr. Sybil Cineas (ACIP, Work Group Chair) introduced the immunization schedules session on behalf of the Combined Immunization Schedules Work Group. The work group updates the schedules each year for individuals 18 years and younger (child/adolescent schedule) and those aged 19 and older (adult schedule). The work group harmonizes the content between the child/adolescent and adult schedules. The immunization schedules are primarily designed to be a tool for healthcare providers to ensure individuals get all the vaccines they need when they need them. Dr. Cineas emphasized that the working group does not create new vaccine policies. The schedule changes reflect existing ACIP recommendations approved by the CDC director. ACIP's annual approval is necessary before publication.

Dr. Nanda Issa (CDC/NCIRD) presented the 2025 Child and Adolescent Schedule revisions for children ≤18 years of age. On the cover page, edits have been made to show that the influenza vaccines have been changed from quadrivalent to trivalent, reflecting the vaccine formulations for this season. In addition, there is a new row for the cell culture-based inactivated influenza vaccine.

Table 1 (immunization schedule by age group) added an abbreviation for the cell culture-based inactivated influenza vaccine. To harmonize with the adult schedule, the overlaying text for the yellow influenza vaccine bars now states one dose annually or one to two doses annually. In the COVID-19 vaccine row, the overlaying text was changed to one or more 2024–2025 vaccine doses to reflect the current vaccines approved or authorized by the FDA. The “<18 years” “notation was removed from the vaccine column for the inactivated Poliovirus row. The gray “no guidance/not applicable” bar on the IPV row and 18 years column was changed to green, indicating that catch-up vaccination is recommended to align with recommendations made at the ACIP June 2023 meeting. For the Dengue row, the yellow bar was changed to purple to reflect that it is only recommended for specific populations in the age group. To harmonize with Table 3, the legend for the gray bar was changed to “No Guidance/Not Applicable.”

There were no proposed updates to Table 2 (catch-up schedule)

In Table 3 (immunization schedule by medical indication), in the COVID-19 row the columns for immunocompromised patients and HIV infection with severe immunosuppression have been changed to brown bars to reflect that additional doses are recommended. For the inactivated influenza row, an overlaying text of “solid organ transplant 18 years” has been added to reflect the ACIP recommendation allowing the use of high-dose and adjuvanted influenza vaccine in specific solid organ transplant recipients aged 18 years.

In the notes, COVID-19 has been revised to align with the 2024–2025 COVID-19 vaccine recommendation. The “Routine vaccination” section outlines recommendations for those not immunocompromised, and the “Special situations” section is for those moderately or severely immunocompromised. Each section outlines the recommended vaccination series by age group and COVID-19 vaccination history. It was also added that all vaccine doses should be from the same manufacturer for healthy children ages 6 months through 4 years, and everyone age 6 months and older who is moderately or severely immunocompromised and receiving their initial vaccination series. A link was also provided to the guidance on the interchangeability of COVID-19 vaccines. Helpful information, including links, was added at this section's end. DTaP has a new bullet in “Special situations,” which summarizes the guidance use of Td in children <7 years of age with a contradiction specific to the pertussis component of DTaP. *Haemophilus influenzae* type b (Hib) vaccination has been updated with the preferential recommendation to use VAXELIS or PedvaxHIB® as the primary series for American Indian and Alaska Native infants. Guidance for using Hib in children receiving early component complement inhibitors was added. The influenza vaccination notes were updated with the 2024–2025 influenza vaccine recommendations, including information for using adjuvanted and high-dose inactivated influenza vaccines in solid organ transplant recipients aged 18 years receiving immunosuppressive medications. The MMR note was revised to clarify the recommendations for international travel. In MenB, the routine and special situation vaccination sections were updated to reflect the new ACIP recommendation for a two-dose series for healthy adolescents and a three-dose series for those at increased risk for the disease. It was also indicated that the three-dose series may be used to optimize rapid protection. The pneumococcal note was revised to include information clarifying that, due to limited data, there is no current ACIP recommendation for using PCV or PPSV23 vaccines during pregnancy. A link to information on existing data was also added. For RSV immunization with nirsevimab, updated CDC guidance was added for infants born October through March, which states that administration should ideally occur during the birth hospitalization. Additionally, information was added clarifying that infants whose mothers received the RSV vaccine in a previous pregnancy should receive nirsevimab. Information was also included regarding the best time of year to administer nirsevimab. Lastly, for maternal RSV vaccination, there is clarification regarding using the RSV vaccine during a subsequent pregnancy, that additional doses are not recommended.

In the Appendix, the work group clarified that the use of MMRV is contraindicated in persons with HIV infection of any severity. A note was also included in Varicella and MMR rows that if MMRV is being administered, both rows should be reviewed for contraindication and precautions.

Dr. Jamieson commented on the importance of vaccination during pregnancy to protect the pregnant person and the newborn. She stated that sometimes, messages about pregnancy get lost in a complex array of footnotes. It is always essential to look for opportunities to promote vaccines during pregnancy. The revision of the immunization schedule may be such an opportunity. Currently, it is included as a medical condition, but given the complexity of the schedule, it may be helpful to separate it into a separate section.

Dr. Issa agreed to consider this.

Ms. Moser discussed using a lowered interval for special circumstances for MenB vaccines, like someone going to college who does not have the full six months. Notes related to this should be considered to clarify.

Dr. Loehr suggested that the college statement should be generalized and apply to anyone seeking optimized protection, not just college students.

Dr. Wodi stated that the work group must adhere to the recommendations made by the specific work group. In the clinical consideration, the only example was the college students. The work group is not allowed to make new recommendations.

Dr. Schillie agreed with Ms. Moser and Dr. Loehr that the statement could be broader. While college students are the most apparent example, it should not be limited to just that group. The clinical consideration of language will include broader language than just specifying college students.

Dr. Wharton suggested that the work group post the considerations online in time for them to be cited by the schedule.

Dr. Brewer commented that RSV is referred to as immunization while all the others are referred to as vaccination. He inquired whether there was a reason for the switch in language.

Dr. Wharton clarified that on the pediatric side, the RSV product is a long-acting monoclonal antibody that provides passive immunization, not a traditional vaccine.

Dr. Schechter noted that some pediatricians have discussed the implications of scheduling a six-month check-up during the fall or winter. This visit requires five or six injections in order to administer all of the recommended vaccines. A reaffirmation of the safety and efficacy of this practice or further guidance on the matter would be beneficial.

Dr. Chu commented that she had received feedback on the nirsevimab administration. The use of the language during birth hospitalization is challenging because hospitals are afraid of not being reimbursed as part of the bundled payment. She also shared that in the western U.S., the later RSV season has been challenging regarding the availability of nirsevimab later in the season.

Dr. Patricia Wodi (CDC/NCIRD) presented the 2025 update to the Adult Immunization Schedule. On the cover page, the influenza rows have been updated to include abbreviations for cell culture, adjuvanted, and high-dose inactivated influenza vaccines. This is to assist providers in interpreting the recommendations in Table 1 for persons ≥65 years and solid organ transplant recipients. Additionally, the newly licensed PCV21 has been added to the pneumococcal conjugate vaccine row, and the newly licensed mRNA RSV vaccine has been added to the RSV row.

There were a number of updates to Table 1 (Immunization schedule by age group). In the COVID-19 row, the overlaying text has been updated to reflect the 2024–2025 vaccine products. For adults ≥65 years, an overlaying text has been added indicating that two more doses of the 2024–2025 vaccine are recommended. For Influenza, for adults ≥65 years, an overlaying text was added to clarify that a dose of HD-IIV3, RIV3, or allV3 is preferred. The influenza row now includes a new purple bar for ages 19–64 years with overlaying text for solid organ transplant recipients. A yellow bar has been added to the RSV row to indicate that all adults ≥75 years should be vaccinated. In the Pneumococcal row, PCV21 has been added and the yellow bar now begins at the 50-64 year old age group, indicating that everyone in this age group should be vaccinated. The risk-based recommendation for ages 19–49 years is shown with a purple bar. For the Inactivated poliovirus row, a yellow bar and overlaying text have been added stating that unvaccinated adults should complete a three-dose series. There is also clarification added that self-reporting of previous doses is acceptable. The Mpox row has added overlaying text showing the recommended doses for consistency. To harmonize with Table 2, the legend for the gray bar was changed to “No Guidance/Not Applicable.”

In Table 2 (immunization schedule by medical indication), the COVID-19 row for columns of immunocompromised patients and HIV infection with severe immunosuppression has been changed to a brown bar to reflect that additional doses are recommended. For the inactivated influenza row, an overlaying text of “solid organ transplant” has been added to the immunocompromised column reflecting the ACIP recommendation allowing the use of high-dose and adjuvanted influenza vaccine in specific solid organ transplant recipients aged 19–64 years. Purple bars have been added to the RSV row for all medical conditions to indicate that RSV vaccination is recommended for some adults at increased risk for RSV disease. A row has been added for inactivated poliovirus vaccine.

In the notes, COVID-19 has been revised to align with the 2024–2025 COVID-19 vaccine recommendation. The “Routine vaccination” section outlines recommendations for those not immunocompromised, and the “special situations” section is for those moderately or severely immunocompromised. The recommendation for a second dose for adults ≥65 years was also added. In the “Special situations” section, a statement was added stating that all vaccine doses in the initial vaccination series should be from the same manufacturer. A link was also provided to the guidance on the interchangeability of COVID-19 vaccines and a note was added with guidance for additional doses for moderately or severely immunocompromised patients. Lastly, helpful information, including links, was added at this section's end. For Hepatitis B vaccination, recommendations were added for persons ≥20 years who have immunocompromising conditions. The language that stated HEPLISAV-B® and PreHevbrio are not recommended in pregnancy due to lack of safety data in pregnant persons has been removed. This change will also be made in the child/adolescent schedule. CDC’s Division of Viral Hepatitis is working to update the guidance for HEPLISAV-B use during pregnancy based on recent updates to the FDA package insert. However, this updated guidance might not be available before the 2025 schedule is published.

Due to the timeframe for updating the guidance, this proposed deletion was not discussed with the Work Group. The influenza vaccination notes were updated with the 2024-2025 influenza vaccine recommendations, including information that adjuvanted and high-dose inactivated influenza vaccines can be used in solid organ recipients aged 19– 64 years receiving immunosuppressive medications. In meningococcal notes, the shared clinical decision-making and “Special situation” vaccination sections were updated to reflect the new ACIP recommendation for the MenB two-dose series for healthy adolescents and a three-dose series for those at increased risk for the disease. It was also indicated that the three-dose series may be used to optimize rapid protection. The guidance for the MenB vaccine during pregnancy has been updated to clarify the rationale for delayed vaccination until after pregnancy due to a lack of safety data in pregnant persons. In Mpox vaccination notes, the guidance for healthcare personnel has been revised for clarity, indicating vaccination is not recommended due to occupational risk in the workplace. The pneumococcal notes have been updated with the new recommendation for routine vaccination for those ≥50 years of age and risk-based recommendation for those 19–49 years of age. A recommendation for the use of PCV21 has also been added. New bullets have been added to clarify that adults who received PCV20 or PCV21 do not need additional doses. There is also a note that states there are no recommendations from ACIP for the use of PCV or PPSV23 during pregnancy. Lastly, a note was added stating that when PPSV23 is unavailable to complete the series, a single dose of either PCV20 or PCV21 can be administered. The RSV note has been revised to align with the updated ACIP recommendations for adults ≥60 years. The routine vaccination section now outlines guidance for pregnant persons and adults ≥75 years old. The pregnancy section was revised to clarify that additional doses of the RSV vaccine are not recommended in a subsequent pregnancy, and nirsevimab should be administered to infants born to pregnant women who received the RSV vaccine during a previous pregnancy. The “Special situations’ section outlines the new risk-based RSV vaccine recommendation for persons aged 60–74 years. A list of conditions that increase one's risk for RSV disease was also added. Guidance for the optimal timing of the year to administer to adults ≥60 years was added. In the Tdap section, recommendations have been revised for clarity. Recommendations are now listed based on previous vaccination history.

In the Appendix, PCV21 has been added in the Pneumococcal conjugate row. The language that stated HEPLISAV-B and PreHevbrio are not recommended in pregnancy due to lack of safety data in pregnant persons has been removed.

Ms. Acker stated that to her knowledge, while HEPLISAV-B was updated for pregnancy, that is not the case for PreHevbrio.

Dr. Wodi confirmed that Ms. Acker is accurate. However, the Division of Viral Hepatitis is currently working on updated guidance. This is not likely to be available until after the schedule is published. Since the group cannot use the schedule to announce a new CDC guidance or vaccination recommendation, the change has to wait for the guidance to be published.

Ms. Hayes complimented the work group on the pregnancy updates because they were more straightforward than in past years. She expressed her appreciation for the continued work by CDC on the safety of hepatitis B vaccine in pregnancy.

Dr. Ybarra commented on Table 1, RSV row, regarding the grey box for ages 50-64 years. He noted that discrepancies between FDA approvals and clinical recommendations could create confusion in medical settings, potentially affecting patient access.

Dr. Fryhofer requested clarification on whether the recommendation was to remove the note on HEPLISAV-B but not PreHevbrio. She also shared that PCV21 is unavailable in Atlanta, Georgia, and questioned whether this was a supply issue.

Dr. Wodi clarified that the team proposes removing the entire language until HEPLISAV-B use during pregnancy becomes a CDC policy. If this is done, the schedule information can differ from what is present on other CDC websites. Removing HEPLISAV-B from that language would conflict with the current published policy on other CDC websites.

Dr. Kobayashi added that according to the Merck manufacturer, PCV21 is covered by insurance companies. The manufacturer is working on ensuring the vaccines are available and can provide more clear updates.

Dr. Chen mentioned that some vaccines have pregnancy recommendations, but it would be great if they were synthesized on the CDC website on vaccination during pregnancy. A table once captured this information but is no longer available on the site. This would be helpful to clinicians.

Dr. Wodi responded that a separate vaccination schedule for pregnancy is available on the website. She is willing to share its location.

Dr. Brooks motioned to approve the *Recommended Child and Adolescent Immunization Schedule, United States, 2025*, and the *Recommended Adult Immunization Schedule, United States, 2025.*

Ms. Moser has seconded the motion.

Vote: Immunization Schedules

Dr. Melinda Wharton (ACIP Executive Secretary, CDC) read the following proposed ACIP recommendation for Immunization Schedules into the record:

Approve the Recommended Child and Adolescent Immunization Schedule, United States, 2025, and the Recommended Adult Immunization Schedule, United States, 2025.

Motion/Vote: Immunization Schedules

Dr. Brooks motioned to approve the Recommended Child and Adolescent Immunization Schedule, United States, 2025, and the Recommended Adult Immunization Schedule, United States, 2025. No COIs were declared. The motion carried with 15 favoring and 0 opposing. The disposition of the vote was as follows:

15 Favored:	Asturias, Brewer, Brooks, Chen, Chu, Cineas, Jamieson, Kamboj, Kuchel, Loehr, Maldonado, Moser, Schechter, Shaw, and Talbot
0 Opposed:	
0 Abstained:	

PUBLIC COMMENT

The floor was opened for public comment on October 24, 2024, at 2:25 PM EST. The comments made during the meeting are summarized in this document. Public members were also invited to submit written public comments to ACIP through the Federal eRulemaking Portal under Docket Number ID CDC-2024-0072. Visit regulations.gov for access to read the comments received.

Patti Wukovits
American Society for Meningitis Prevention

Patti Wukovits is a registered nurse from New York. She shared that meningococcal vaccination is very close to her heart. She lost her daughter in 2012 to meningitis b at the age of 17, three days before her high school graduation. Within hours of onset of flu-like symptoms, she was in multiorgan failure and septic shock. Despite a prompt diagnosis and appropriate medical treatment, she was declared brain dead shortly after and Ms. Wukovits was faced with the impossible decision to remove her daughter from life support. Although her daughter had received the MenACWY vaccine, the Meningitis B vaccine was unavailable. Since her daughter's death, Ms. Wukovits has dedicated herself to raising awareness by establishing the Kimberly Coffee Foundation and co-founding the American Society for Meningitis Prevention. She understands the review of the current meningococcal vaccination schedule has been postponed, and she wants to ensure it is revisited as soon as possible because of the severity of the disease, the rise in rates within the U.S., and significant gaps in vaccine coverage. She can attest to the confusion experienced among providers and parents for meningococcal vaccination. She is ecstatic about the conversation on the disease today; however, she fears that current recommendations will remain confusing and complicated without an updated review by the ACIP. Significant innovations have been made in meningitis prevention but MenB vaccines continue to be underutilized and ACIP's current recommendations for pentavalent meningococcal vaccines essentially discourage their use. She urged the ACIP to consider the extensive public health implications of postponing the review of current meningococcal vaccines and to recommend routine use of all meningococcal vaccines.

Chloe Humbert
Unaffiliated Community Member

Chloe Humbert inquired about a COVID-19 vaccine campaign, noting the lack of advertisements and billboards regarding the disease. She questioned why doctors are not held responsible for recommending the vaccine to patients with known risk factors. Chloe believes that anti-vaccination disinformation campaigns have influenced doctors in the United States. She emphasized the importance of vaccination uptake, referencing the successful U.S. polio vaccine campaign bolstered by door-to-door outreach efforts. Additionally, she feels the CDC has been inactive in its response to COVID-19. She expressed concern that the restrictions on the spring vaccine doses have allowed some affluent individuals just over 65 to get vaccinated before their vacations. At the same time, working class people with underlying conditions who are under age 65 years of age and are working in frontline jobs with contact with the public have been unable to get an additional dose due to gatekeeping, just because of the cost of the vaccine to insurance companies.

Michelle Fiscus
Association of Immunization Managers

Michelle Fiscus, a board-certified pediatrician, is the Chief Medical Officer for the Association of Immunization Managers (AIM), a member organization that supports the managers of the 64 CDC-funded immunization programs in all 50 states, eight U.S. territories and Freely Associated States, and six major cities. She expressed gratitude to ACIP for their commitment to making data-based vaccination recommendations. A significant challenge is vaccinating approximately 26 million uninsured adults. Federal funding for immunization programs, provided under Section 317 of the Public Health Service Act, has been nearly flat for the third year, falling short of the $1.6 billion estimated by the CDC to operate at full capacity. The addition of COVID-19 and RSV vaccines, combined with nine new recommended vaccine doses for adults over the past 20 years, has led to a 1,023% increase in vaccination costs, while funding has only increased by 46%. This funding gap forces organizations to prioritize certain vaccines, exacerbating disparities among vulnerable populations. AIM congratulated ACIP for expanding pneumococcal vaccine recommendations but raised concerns about the ability of programs to ensure vaccine access without additional funding. The United States needs a national Vaccines for Adults program to provide free vaccines to unvaccinated adults. The group also noted that changes to adolescent vaccination schedules are likely to impact state school vaccination requirements and may have unintended policy consequences that could negatively affect childhood vaccination rates.

Jester Jersey
Vaccination Collaborative

Jester Jersey, representing the American Society for Meningitis Prevention, emphasized the need for clear recommendations from the ACIP to protect adolescents and young adults from meningitis. Mixed messaging has caused confusion about the newly available pentavalent vaccines, complicating guidance for healthcare providers and patients. Additionally, rising antibiotic resistance challenges the healthcare system and limits our ability to address this disease effectively. Clear recommendations must be communicated to build trust among health providers and patients. While Mr. Jersey acknowledges the tools now available to help young people fight meningitis, the disease remains a significant threat, particularly to college students. He urges ACIP to clarify vaccine guidelines to reduce confusion, encourage vaccine uptake, and combat misinformation.

Pushpa Narayanaswami
Beth Israel Deaconess Med CTR/Harvard Medical School

Dr. Pushpa Narayanaswami thanked the committee for its commitment to patient safety for those receiving C5 complement inhibitors. She pointed out inconsistencies between ACIP guidelines and FDA-approved labels for meningococcal vaccinations in patients with myasthenia gravis starting C5 inhibitors, which need to be clarified for clinicians. The FDA requires meningococcal vaccines to be completed at least two weeks before therapy, while ACIP only recommends the initial doses of MenACWY and MenB be administered two weeks prior to therapy. This inconsistency has led to inconsistent patient care. Additionally, there needs to be more clarity on the duration of prophylactic antibiotic therapy. The FDA does not specify how long antibiotics should be used, whereas ACIP recommends a two-week course. She urged the ACIP to provide more explicit guidance on these issues and is willing to share additional clinical information with the committee.

Joanna Colbourne
National Foundation of Infectious Disease

Joanna Colbourne, deputy executive director of the National Foundation of Infectious Disease, emphasized the essential roles of the Advisory Committee on Immunization Practices (ACIP) and the CDC in public health. Respiratory diseases like influenza, COVID-19, RSV, and pneumococcal disease can lead to severe complications and numerous hospitalizations and deaths. Vaccination effectively reduces this impact; for instance, flu vaccinations prevented about 131,000 hospitalizations and 7,000 deaths during the 2023-2024 season, while COVID-19 vaccines avoided up to 100,000 hospitalizations in 2023. Despite vaccine availability, rates remain below recommended goals, with many at-risk individuals hesitant to get vaccinated due to concerns about side effects. The group highlighted that 75% of U.S. adults trust healthcare professionals for vaccine information. Addressing concerns through these trusted sources is vital, but a comprehensive strategy is still needed. Programs aimed at vaccinating uninsured and underinsured adults are crucial. The group is dedicated to working with the CDC to improve vaccination communication, build confidence, and enhance public health outcomes.

HUMAN PAPILLOMAVIRUS (HPV) VACCINES

Dr. Oliver Brooks (ACIP, Work Group Chair) introduced the Human Papillomavirus (HPV) Vaccine Work Group. The re-formation was announced at the June 2024 ACIP meeting. An HPV Vaccines Work Group had previously met for many years but had been inactive since 2019. The current routine vaccination age in the U.S. is 11 or 12 years; it can be started at age nine. If vaccination is started before the 15th birthday, there should be two doses (0, 6-12 months). If vaccination is started on or after the 15th birthday or if immunocompromised, there should be three doses (0, 1-2, 6 months). Catch-up vaccination can occur through the age of 26 years. There is shared clinical decision-making from age 27 to 45 years.

In 2022, the World Health Organization recommended a two-dose schedule for persons ≥9 years. As an off-label option, a single-dose schedule can be used for those aged 9–20 years. The work group is reviewing data to inform policy for two doses for persons ≥15 years and one dose for persons ≥9 years.

The work group has also been reviewing the wording of the age for routine HPV vaccination. To allow more flexibility, the work group is considering changing the wording to “HPV vaccination is routinely recommended at age 9 to 12 years.”

The work group plans to provide a full EtR framework with evidence review using GRADE at a future ACIP meeting for the number of doses in the recommended HPV vaccination series and a modified EtR framework without GRADE for the wording of the age for routine HPV vaccination. The work group plans for votes at a future meeting.

Dr. Lauri Markowitz (CDC/NCIRD) introduced policy considerations for reducing the number of HPV vaccine doses. The first HPV vaccine licensure was 18 years ago. The vaccine has exceeded expectations with high VE in clinical trials, high population impact in real-world settings, and strong herd effects of vaccination programs. There have been implementation challenges in many countries and a lag in vaccine introduction in low- and middle-income countries.

HPV is a double-stranded DNA virus. There are >200 types, and they are closely related. It has two capsid proteins, the major one being L1. The sequence of the L1 gene determines the virus type assignment. Twelve types have been classified as high-risk (oncogenic), and two of these, HPV 16 and 18, are responsible for most HPV-attributable cancers. Low-risk types 6 and 11 cause most anogenital warts and recurrent respiratory papillomatosis. HPV is the most common sexually transmitted infection. Around 13 million persons in the U.S. become infected with a disease-causing HPV type each year. Over 90% of infections become undetectable in two years. Persistent infection can progress to cancer. Each year, an estimated 37,800 HPV-attributable cancers occur. The most common in women is cervical cancer, and the most common in men is oropharyngeal cancer.

All available HPV vaccines are virus-like particle (VLP) vaccines made from L1 major capsid proteins of the virus. The L1 protein is expressed using recombinant technology and self-assembles into VLPs, which are structurally similar to HPV virions but without any viral DNA. The VLPs retain their dominant conformational epitopes. The vaccines have been found to have high efficacy with durable protection for as long as they have been studied, now up to 16 years. Three vaccines are licensed in the U.S.: bivalent (2vHPV), quadrivalent (4vHPV), and 9-valent (9vHPV). All vaccines target the most oncogenic types, 16 and 18. The quadrivalent and 9-valent also target 6 and 11 (which cause anogenital warts). The 9-valent targets five additional high-risk types (31, 33, 45, 52, 58). Since late 2016, only the 9-valent has been available in the United States.

Data for initial licensure of HPV vaccines were obtained in trials using 3 doses administered over 6 months. The pivotal trials were large randomized controlled efficacy trials in 15- to 26-year-old women. In per protocol analyses, efficacy was over 96%, and seroconversion was close to 100%. The anticipated age group for vaccination programs was adolescents before the onset of sexual activity; efficacy studies were not considered feasible in this age group. Licensure for the 9-15-year age group was based on immunobridging studies, which demonstrated non-inferior antibody responses compared with women in efficacy trials.

HPV vaccination recommendations have evolved. In 2006, vaccination was first recommended for adolescent females with catch-up through age 26 years. At that time, the HPV vaccine was only licensed for use in females. In 2011, after licensure in males, routine vaccination was recommended for adolescent males with catch-up through age 21 years. While HPV vaccines were first licensed and recommended as a 3-dose schedule, in 2016, a 2-dose schedule was recommended for those starting the vaccination series before age 15 years. Then, in 2019, after the FDA expanded the upper age indication from 26 to 45 years, ACIP made a shared clinical decision-making recommendation for persons aged 27 to 45. At that time, the catch-up age for males was harmonized with that for females, through age 26.

The current routine vaccination age in the U.S. is 11 or 12 years. It can be started at age nine. If vaccination is started before the 15th birthday, there should be two doses (0, 6-12 months). If vaccination is started on or after the 15th birthday or if immunocompromised, there should be three doses (0, 1-2, 6 months). Catch-up vaccination can occur through age 26. There is shared clinical decision-making from age 27 to 45 years.

The introduction of a two-dose schedule was stimulated by post hoc analyses of a 3-dose randomized trial of the bivalent vaccine compared to a control vaccine in Costa Rica led by the U.S. National Cancer Institute. Not all participants completed the 3-dose schedule and efficacy was analyzed by the number of doses received. In these post hoc analyses, the efficacy of the bivalent HPV vaccine against HPV16/18 infection was similar after 3, 2, and 1 dose.

The manufacturers then conducted immunobridging trials to evaluate two doses in 9- to 14-year-olds vs. three doses in young adult women in the age group for which efficacy had been demonstrated. Seroconversion and GMTs were non-inferior in the 2-dose group. Following these studies, manufacturers submitted supplemental applications to regulatory authorities for a 2-dose series in 9–14-year-olds. Following approval, ACIP, WHO, and advisory groups in other countries recommended a 2-dose series for persons starting vaccination at 9–14 years.

The same studies that led to 2-dose schedules stimulated interest in single-dose vaccination. However, immunobridging trials would not suffice because a single dose results in lower antibody titers than two or three doses. While the basis of protection after HPV vaccination is thought to be neutralizing antibodies, there is no established minimum antibody threshold for protection. Therefore, efficacy trials are needed to evaluate single-dose vaccination.

A randomized trial, ESCUDDO, is underway in Costa Rica to evaluate the non-inferiority of one versus two doses of 2vHPV (CERVARIX) and 9vHPV (GARDASIL® 9) for preventing new cervical HPV16/18 infections that persist for at least six months. The study is sponsored by the U.S. National Cancer Institute and enrolled girls ages 12-16 years. Surveys of unvaccinated women will be conducted to evaluate one dose compared to zero doses. The first data will be available in 2025.

After ESCUDDO was planned and initiated, there was increasing interest in single-dose HPV vaccination. This was mainly because studies that initially provided data on fewer doses continued follow-up and had further encouraging data. Increasing interest in single-dose vaccination was also stimulated by the recognition of the global HPV vaccine supply/demand imbalance that prevented some countries from introducing the HPV vaccine or expanding their programs. Additional studies were planned and conducted. Reviewing these and other data led to revised World Health Organization recommendations in 2022, including, “as an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years.”

There were four trials with data on single-dose HPV vaccination considered by the WHO in their decision.

Data from the Costa Rica Vaccine Trial (CVT) and IARC-India first raised interest in single-dose vaccination and provided the longest follow-up data. Participants were not randomized to a one-dose group; one-dose data are from post-hoc analyses. The two randomized trials of interest are KEN SHE and DoRIS. In both trials, participants were randomized to a one-dose group. These trials provide the highest quality of evidence available on one-dose vaccination.

In the CVT, females aged 18–25 were randomized to receive three doses of 2vHPV or a control. Not all completed the series; post hoc analyses were done by the number of doses received. After the blinded phase of the trial, an unvaccinated control group was recruited to allow for continued efficacy determination. VE for preventing prevalent HPV 16/18 infection was similar among women who received 1, 2, and 3 doses. Serum antibody was also measured. While the antibody levels are lower in the 1-dose group than in the 2- or 3-dose groups, HPV 16 antibody levels were relatively stable through 11 years post-vaccination with all dosing schedules, and the level in the 1-dose group was at least 10-fold above the level at enrollment among those unvaccinated. There were similar results for HPV 18.

The IARC-India trial provides data on the immunogenicity and efficacy of 1, 2, and 3 doses of 4vHPV(GARDASIL®) in 10- to 18-year-old girls. The trial started as a cluster randomized trial with a comparison of two vs. three doses, but it was stopped early due to issues unrelated to the trial. Vaccination did not occur as scheduled, and the randomized trial design was lost. The study has been analyzed as an observational cohort with different vaccination schedules, including a one-dose group. Unvaccinated females age-matched to the vaccinated participants were recruited as controls. Ten years after vaccination, VE against persistent HPV 16/18 infection was over 93% and similar in all dose groups.

KEN SHE is a double-blind, randomized controlled trial conducted in sexually active females aged 15-20 years in Kenya. The participants received a single dose of 2vHPV, 9vHPV, or meningococcal (delayed HPV vaccination) vaccine. The primary objective was to determine the efficacy of single-dose vaccination in preventing incident persistent infection with the high-risk HPV types targeted by each vaccine. At month 18, VE for 9vHPV and 2vHPV against incident persistent HPV 16/18 infection was over 97%. When WHO recommended an off-label single dose in 2022, only the 18-month data from this trial were available. The 36-month data, showing sustained efficacy of >97%, were published in 2023.

The DoRIS trial is a randomized trial in girls ages 9-14 years in Tanzania. The girls received 1, 2, or 3 doses of the 2vHPV or 9vHPV. The objectives were to demonstrate the noninferiority of HPV 16 and 18 antibody response after 1 dose vs. with 2 or 3 doses of the same vaccine and to demonstrate noninferiority of HPV 16 and 18 geometric mean concentrations comparing 1 dose in this study with 1 dose in studies that evaluated efficacy. Seropositivity was high after vaccination for all vaccine groups. Strict noninferiority criteria were met for HPV 16 but not for HPV 18; however, seropositivity was at least 97.8% in all vaccine groups 24 months after vaccination for both HPV 16 and 18. Antibody levels were similar for 2 and 3-dose groups. Antibody levels were lower after one dose than two or three doses; however, antibody kinetics were similar for all doses, with a plateau between 12 and 24 months. Avidity for each HPV type was similar for 3, 2, and 1 dose for both vaccines. For the immunobridging objective, 1-dose responses were noninferior in DoRIS (9-14 year-olds) compared with those among women in studies where 1-dose efficacy was observed, including KEN SHE

Additional studies evaluating single-dose HPV vaccination have data forthcoming. They will provide evidence for impact, effectiveness, efficacy, and immunogenicity. Additional longer-term follow-up data are also expected from three of the studies reviewed today (CVT, IARC-India, and DoRIS).

Single-dose studies also provide data on 2-dose schedules (0, 6 months) in persons aged ≥15 years. Both CVT and IARC-India include participants who received 2 doses of HPV vaccine. There is also an immunogenicity trial of 2 vs 3 doses of 9vHPV among US females aged 15–26 years. This study is ongoing, but interim results published this year with data 1 month after the last dose show similar immunogenicity in the 2 and 3-dose groups.

In December 2022, the WHO reviewed the evidence and stated that a 2-dose schedule is recommended from age 9 years and for all older age groups for which HPV vaccines are licensed. As an off-label option, a single-dose schedule can be used in girls and boys aged 9-20 years. Since this recommendation, many countries have changed policies. Some of the first countries to adjust to routine single doses were England, Ireland, and Australia.

Change from a 3-dose to a 2-dose schedule for persons ages >14 years occurred in the Netherlands and Sweden. Regional advisory groups in the PAHO region (2023) and AFRO region (2024) have also made recommendations for single-dose vaccination.

Outstanding questions for single-dose vaccination include:

- Longer-term efficacy and immunogenicity
- Protection at sites other than the cervix
- Efficacy and immunogenicity in males
- Efficacy and immunogenicity in immunocompromised persons
- Efficacy and immunogenicity in older age groups

Earlier this year, Merck announced its plans to conduct two prospective clinical trials, one in females (16-26 years of age) and one in males (16-26 years of age). These randomized, double-blind, multi-year clinical trials will examine the short- and long-term efficacy and immunogenicity of a single dose of GARDASIL 9 versus the currently approved three-dose regimen. Merck is in discussions with the FDA about the protocols and timelines.

In summary, HPV vaccines were first studied and licensed in a 3-dose schedule in persons aged 9–26 years and later in a 2-dose schedule in persons aged 9–14 years. Data on single-dose HPV vaccination, including from an RCT with 3 years of follow-up, show high efficacy against incident persistent infection. Long-term follow-up suggests protection for >10 years with a single dose. In 2022, WHO updated recommendations for 2 doses for persons aged 9 years and older, with an option for single-dose HPV vaccination for persons aged 9 through 20 years, except for those immunocompromised. Countries are considering new or updated HPV vaccination policies, and an increasing number have recommended single-dose HPV vaccination. Further data on one and two doses will be available over the next year.

Ms. Deshon expressed excitement about a single-dose recommendation for providers, which would be life-changing for young people.

Ms. Arthur reminded the ACIP that there are some things in play to capture and overcome the challenges of giving HPV vaccines to get to elimination. It is important to remind the committee that the vaccine manufacturers must follow the FDA label by law. The company is pursuing a regulatory process to change the dosing schedule. It is to be noted that the process goes from three to two doses. While there may be a recommendation on the ACIP level, the company can only discuss what is on the label when talking to clinicians. Alignment is vital between the regulatory body, where robust studies are conducted, and the policy body, which is taking place within ACIP. In addition, Merck is planning to look at many of the data points covered in the presentation. She wanted to make the ACIP aware of the difference between making a change in this body and the significant importance of making a regulatory change.

Ms. Hayes stated that the bivalent vaccine was approved in 2006, and the quadrivalent vaccine was approved years later.

Dr. Wharton and Dr. Markowitz shared that this statement was incorrect. The first vaccine approved by the FDA was quadrivalent. Because of its novel adjuvant, the bivalent vaccine had an additional review by the FDA. The initial licensure for the quadrivalent vaccine was in girls and women, then boys and men.

Dr. Kamboj requested that the work group give special consideration for childhood cancer survivors because they are at higher risk for secondary malignancies related to HPV.

Dr. Markowitz shared that the work group will review various data that have emerged since the work group last met.

Dr. Ruth Stefanos (CDC/NCIRD) reviewed the introduction to policy consideration for the wording of the age for routine vaccination. As mentioned earlier, HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years. Since 2006 (the first ACIP recommendation), the wording of age at HPV vaccination initiation has not substantially changed. HPV vaccination has been considered part of the Adolescent Platform, first introduced in 1996. This platform focused on 11-12-year-olds getting vaccinated at an established visit. Tdap and MCV4 were added to this platform in 2005. Then, in 2006, HPV vaccine was added.

The CDC's Clinical Decision Support for Immunization (CDSi) project translates clinical ACIP recommendations into technical information to support the consistent integration of recommendations into clinical decision support engines such as electronic health records. CDSi resources include logic specification, supporting data, and test cases. For HPV vaccine, the resources cite the minimum age of nine years and the earliest recommended age of 11 years. Clinical decision support tools generally use the earliest recommended age for all age-based vaccine recommendations. This prompts HPV vaccination at the earliest recommended age of 11 years. This is one of the implementation challenges some have described as a barrier for practices or jurisdictions that would like to start vaccination at 9 years. However, starting vaccination at this age is consistent with ACIP recommendations. Some jurisdictions have been able to modify their prompts in systems to meet their local needs.

Lower coverage for the HPV vaccine compared to Tdap and MenACWY has been shown in adolescents aged 13-17 years during 2006-2023. For many years, there have been efforts and implementation research to help address the lower coverage for the HPV vaccine. These include focusing on the provider's recommendation, the presumptive approach, and other strategies. Beginning in the 2018–2021 Redbook, HPV vaccination recommendation language was modified. The current recommendation states, "The AAP recommends starting the series between the ages of 9 and 12 years, at an age that the pediatric health care professional deems optimal for acceptance and completion of the vaccination series." Recommended vaccination at age 9 is a strategy that some partner groups have promoted to improve HPV vaccination coverage. A recent growing number of publications have evaluated the benefits of vaccination at age 9 years.

Due to growing interest in starting vaccination at age nine and because ACIP recommendations are consistent with this, the work group plans to discuss modifying the wording of the recommendation. The proposed language change is "*HPV vaccination is routinely recommended at age 9–12 years*" rather than "*HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years.*"

Dr. Sarah Brewer (CDC/NCIRD) reviewed the literature on HPV vaccination at ages 9-10 to increase coverage. Since the HPV vaccine was first licensed and recommended in 2006 for females, the wording of the routine age recommendation has remained the same. While HPV vaccination coverage has increased since HPV vaccination was first recommended, uptake continues to be lower than other vaccines recommended in adolescence.

There have been many efforts to increase HPV vaccination in the United States. In the past few years, there has been growing enthusiasm for HPV vaccine initiation at age 9 to increase coverage.

This review aimed to critically evaluate publications investigating HPV vaccination at ages 9-10 years. Studies included were conducted in the U.S. and published between 2014 and 2024. The study population included individuals ≥9 years of age eligible to receive the HPV vaccination, their parents/caregivers, and healthcare providers administering the HPV vaccine. Outcomes include HPV vaccine initiation, series completion, acceptability among providers and caregivers, or feasibility. Thirty studies were included in the review.

Most retrospective cohort/observational studies identified vaccination completion as their primary outcome; one study's outcome was initiation. Most of these studies found that vaccination series completion was higher when initiating at ages 9–10 vs. 11–12, but study limitations preclude a cause-and-effect interpretation. A small percentage of vaccinated adolescents had initiated at 9–10 in most studies (2–8%). There was no information on reasons for initiation at age 9–10. There may have been differences between those initiating at ages 9–10 vs. 11–12, between providers vaccinating at ages 9–10 and those vaccinating at ages 11–12.

The quality improvement (QI)/intervention studies all identified initiation as an outcome, and several also included completion as an outcome. The review found that most QI/intervention studies reported increased initiation and completion. However, because these studies involved multi-pronged interventions, it is unclear whether the specific component focused on initiation at ages 9 to 10 was responsible for any increase in coverage. Within the QI/Intervention studies, vaccination at age 9 was feasible but not necessarily better than at ages 11–12.

The provider/caregiver perspectives and behavior studies included in-depth qualitative interviews from a small group of providers, more extensive online surveys of healthcare providers, and studies using both interviews and surveys focused on caregiver perspectives and experience with vaccination at ages 9-10 years. The review found that in limited settings and mostly small studies, vaccination at ages 9–10 years was acceptable by caregivers and providers.

In summary, within retrospective cohort studies, HPV vaccine initiation at ages 9–10 years was associated with higher completion by age 13; however, this was a small proportion of initiators in all studies. There could have been meaningful differences between children initiating at ages 9–10 vs. 11–12 years or providers vaccinating at ages 9–10 vs. those vaccinating at the routine age. The QI/ intervention studies' findings show vaccination at age nine was feasible but not necessarily better. Due to the multifaceted approaches, the contribution of the recommendation for initiation at age 9–10 years on increases in coverage is unclear. Vaccination at ages 9–10 years may be acceptable to caregivers and providers.

Dr. Asturias emphasized that since the beginning of this program, vaccination coverage has improved. However, we are still far from our goal and could potentially prevent another 15,000 cervical and oropharyngeal cancers. Lessons learned recently include that waning immunity has not been demonstrated, even with 10 years of follow-up data. Furthermore, early vaccination leads to better immunogenicity, a higher completion rate of the two-dose schedule, and less crowding of vaccines among teenagers. ACIP may need to revisit this issue and shift from our current "can be given" approach to a more comprehensive recommendation. This change will incur no additional costs but significantly reduce suffering and improve lives.

Dr. Schechter questioned whether completion was defined in the two-dose era or, in some studies, three doses.

Dr. Brewer responded that completion was diverse and varied from study to study. Some studies defined completion by two doses if the patient received the first dose at a certain age; it depended on the study.

Dr. Loehr recalled that there is evidence that antibody levels were significantly higher when children were immunized at a younger age. He inquired whether this information was accurate and clinically significant.

Dr. Markowitz shared that, from the initial HPV vaccine trials, it has been known that antibody response to HPV vaccination is higher with younger age at vaccination. However, there is little, if any, difference in antibody levels when vaccination is at age 9-10 years vs 11-12 years. The decline starts in older adolescents. The known higher titers in young adolescents led to the design of the immunobridging studies for 2-dose schedules, comparing 2 doses in 9–14-year-olds to 3 doses in 15–26-year-olds; noninferiority was needed for regulatory approval, and demonstration of non-inferiority was felt to be more feasible comparing these age groups. High efficacy and long duration of protection have been observed in the efficacy trials conducted among 15–26-year-olds, an age where antibody levels are lower than in younger adolescents. If there are small differences in antibody levels between ages 9–10 and 11–12 years, they are not clinically meaningful; very low levels of antibodies are protective.

Ms. Moser provided a few observations for the group. ACIP has already approved this vaccine for use as young as nine years of age. The work group is not changing the recommendation, but she felt that before it changes the wording, the work group should be aware that this has implications within itself. She requested that the work group investigate parental values related to this change and the providers' values. Parents may not want their child vaccinated at age nine. There was hesitancy around the vaccine when it first came out. She also would like the work group to consider keeping the HPV vaccine as part of the Adolescent Platform. She mentioned that completion studies should also be examined carefully. We should be aware of changing the wording to reduce pushback from parents.

Dr. Wharton questioned whether there were intervention studies in which the sole difference was the age that the vaccine was routinely offered.

Dr. Brewer responded that there was no such study. This was a limitation of the findings.

Dr. Noel Brewer shared a study by Christensen that addressed Dr. Wharton's question. In this study, age was the only difference noted, but there were likely many uncontrolled variables involved. The key takeaway is that much of excitement about vaccination at age 9 stems from studies that compare multiple variables. Interesting data emerge, including findings that discussions may be more straightforward because sex is not mentioned. Additionally, data indicates vaccination implementation challenges, such as providers being reluctant to administer more than two vaccines at a time. ACIP will need to address these issues.

Dr. Schechter followed up to ask if there was any information about durability with higher titers and if this had any implications for younger people. With changes from three to two and possibly one dose, is the best indicator initiation or completion of vaccination?

Dr. Markowitz shared that she is not aware of any data. She did share that the efficacy studies from large clinical trials were done in 15- to 26-year-olds, showing very high efficacy in young adults. This has been done through follow-up, showing no waning of protection in this age group. The work group has focused on the programmatic aspects of vaccination at ages 9-10 years rather than other aspects. Dr. Markowitz agreed that initiation of vaccination is an important indicator.

Dr. Middleman noted that annual wellness visits for children have been recommended for quite some time. While she does not believe that the Adolescent Platform originated this idea, it has undoubtedly established an expectation among healthcare providers and parents, serving as a critical touchpoint. Immunization rates for adolescents do not match those of younger children, and additional challenges regarding adolescence differ from those faced by infants. Furthermore, immunization rates are impacted by the fewer healthcare provider visits in older age groups. Requirements for routinely recommended vaccines leads to higher coverage for other vaccines recommended at the same age, indicating that grouping vaccine recommendations helps improve uptake. Dr. Middleman urged caution when considering changes to the adolescent immunization platform infrastructure and proposed expanding it to better serve young people.

Dr. Loehr offered a different perspective. As a practicing physician in a family practice, he does not see the platform as beneficial for 11-12-year-olds since children are being seen annually. He believes there is a difference from 20 years ago.

Dr. Carla DeSisto (CDC/NCIRD) reviewed the next steps for the work group's policy questions. The work group has started the GRADE process to consider the number of doses to recommend for HPV vaccination. The work group is planning a full EtR framework. In the February 2025 ACIP meeting, the work group plans to share additional data from the relevant trials and studies, modeling, and a part of the EtR.

Regarding the wording of the age for routine HPV vaccination, GRADE will not be utilized because this is a minor change to wording and not a change to the recommendation. The work group is planning a modified EtR that will only include selected domains. Part of this EtR will be shared at the February 2025 meeting.

Dr. Loehr suggested revisiting people who should receive more than one dose, like immunocompromised people. He would like a clear delineation of those who should not fall into the one-dose category.

CYTOMEGALOVIRUS (CMV) VACCINE

Dr. Denise Jamieson (ACIP, Work Group Chair) presented an introduction to the newly formed Cytomegalovirus (CMV) Vaccines Work Group. CMV is a ubiquitous betaherpesvirus and is the most common infectious cause of neurodevelopmental disabilities in children in the U.S. Around 4,000 children are diagnosed with congenital CMV disease each year. CMV causes substantial morbidity and mortality in persons with immunosuppression (solid organ and stem cell transplant recipients, cancer, or HIV). In 1999, The Institute of Medicine (currently the National Academy of Medicine) identified the CMV vaccine as the highest priority for vaccine development in the 21st century.

To date, no CMV vaccine has been licensed. Three earlier vaccine candidates were in development but did not progress to Phase 3 trials due to insufficient efficacy. One vaccine candidate did make it to Phase 3 for stem cell transplant patients but failed to achieve efficacy for primary endpoints. An mRNA vaccine candidate has made it to Phase 3; this trial in females 16-40 years of age is ongoing, and results are expected soon.

In preparation for the potential licensure of a CMV vaccine in the near future, the CMV Vaccines Work Group will review the epidemiology of CMV and congenital CMV, identify areas where additional data are needed, review safety, immunogenicity, and efficacy data for CMV vaccine candidates, and develop CMV vaccine policy options.

The first work group meeting is planned for November 2024. The work group intends to present on the burden of CMV and congenital CMV at the February 2025 ACIP meeting.

Dr. Shaw shared that an obstacle in the field is the difficulty of coming up with immunologic correlates of protection. Our traditional use of neutralizing antibodies in other circumstances for CMV has an inverse correlation with the likelihood of maternal transmission. Other antibody functions or non-neutralizing antibody functions seem to be more important. Hopefully, the manufacturer will provide antibody independence, antibody-dependent cellular phagocytosis, and other relevant immunologic factors.

Dr. Asturias expressed gratitude that ACIP is taking on this issue. AAP has been doing incredible work to raise awareness of CMV, and it is important for ACIP to take on this issue.

Dr. Chu emphasized the significance of CMV in young populations. She expressed the hope that the work group will have access to data on use in pregnancy and that the group will not have to report a lack of safety and efficacy data in this population.

MPOX VACCINE

Dr. Agam Rao (CDC/NCEZID) provided a situational update on Africa's Clade I Mpox outbreak. There are two clades or types of monkeypox virus (MPXV). The global clade II outbreak began in 2022 and continues to cause around 56 cases per week in the U.S. Similar to clade II, clade I has been known to be endemic in certain African countries for decades. Clade I is endemic in the Democratic Republic of the Congo (DRC), Central African Republic, Republic of Congo, Cameroon, and Gabon. The largest number of human cases are reported each year from the DRC.

MPXV transmission can occur by exposure to infected wildlife, person-to-person spread includes skin-to-skin contact, contact with respiratory secretions, and contact with contaminated objects.

There currently are clade I outbreaks in DRC; since 2023, many suspect and laboratory-confirmed cases have been identified in provinces previously without cases. There are at least two concurrent outbreaks, associated with clade Ia and clade Ib. Clade Ia's mortality rate was historically reported as 1.4-11%; however, the NIH trial in DRC indicates routine supportive care led to a mortality rate of ~1.7%. Clade Ib seems to cause less severe disease than clade Ia. The mortality rate is <1% in DRC. Clade Ia is believed to be spreading from animals to people (a high proportion of suspected cases in children), human-to-human spread in households, and sexual contact regardless of sexual orientation. Clade Ib is primarily being spread through sexual contact.

Clade Ia has only been detected in endemic countries, while Clade Ib has been associated with sustained spread in Burundi, Uganda, and Rwanda. There are also some travel-associated cases that do not involve sustained spread in Kenya, Thailand, Sweden, India, and Germany. In non-endemic countries, the spread is most associated with sex, while visiting countries with sustained transmission. Secondary spread has been limited in several non-endemic countries (e.g., Thailand, Sweden, India). It is uncertain at this time what the transmission mode is in some countries, but it is believed to be associated with close household contact.

In the U.S., there are currently no clade I cases. Risk is considered low for U.S. travelers. A few weeks ago, a Health Alert Network advisory recommended that clinicians provide pre-travel counseling about risk reduction strategies to patients traveling to endemic countries. Vaccination is recommended for travelers to certain countries who anticipate sex with a new partner, sex at a commercial sex venue, sex in exchange for money/goods/other trade, or sex in association with a large public event.

The risk to the general U.S. population is low. In simulations of the epidemiologic situation in the U.S., outbreaks are small and result in minimal spread between households. Modeling suggests that even with extremely high secondary attack risk, household clusters (including cases in children) would likely involve ten or fewer MPXV clade I cases, with limited spread between households. Based on what we know today and the current characteristics of viral spread, CDC does not expect children to be heavily impacted if clade I is diagnosed domestically.

Internationally, CDC and its partners have provided technical assistance and funding to DRC's Ministry of Health. CDC collaborates with public health officials in several countries bordering DRC to assess needs and support outbreak preparedness. One million doses of JYNNEOS vaccine and $500 million for support have been donated.

Domestically, the CDC has been increasing its capacity to rapidly detect, contain, and manage clade I cases should they occur domestically. It is expanding its capacity to detect clade I and clade II mpox cases through existing surveillance systems, including wastewater testing in communities across the U.S. and select airports. The CDC coordinates with state, tribal, local, and territorial public health departments to provide clinical, diagnostic, and other guidance. CDC has also been raising awareness through regular communications and updates.

In summary, there are many suspected clade I mpox cases in DRC; only ~20% are laboratory-confirmed. There has been travel-associated spread of clade Ib to some countries. These cases are milder than those associated with clade Ia. They are predominantly associated with sex (e.g., transactional sex) with subsequent spread to others (e.g., children) likely via household contact. The risk to U.S. travelers is low, but counseling and vaccination should be provided. The impact on persons in the U.S. (including children) is expected to be low.

The ACIP work group is being re-formed. The work group is charged with reviewing an NIH study about using JYNNEOS in persons 12-17 years of age. It will consider bringing to an ACIP vote the use of JYNNEOS in persons 12-17 years of age at risk for mpox during mpox outbreaks (including the global clade IIb outbreak). The group anticipates presentations (including Terms of Reference) during the February 2025 ACIP meeting and plans to publish ACIP recommendations for persons 12 years of age and older in one consolidated MMWR.

Dr. Maldonado provided an update regarding the situation in DRC, as mentioned by the Minister of Health during ID Week. Up to 70% of the reported suspected cases are in children under 15. Currently, two trials of tecovirimat are underway; one is called STOMP, which is ongoing, and the other, the PALM007 trial, has been completed. The PALM007 trial was halted due to a lack of demonstrated efficacy of tecovirimat against the clade I strain. Local healthcare providers face significant challenges, particularly the lack of infrastructure, which complicates efforts to implement effective infection control while preventing the disease's household spread. Additionally, more visual information must be disseminated to local practices to understand the disease better, as it is extensive, with an average number of lesions of almost 500. Finally, approximately 250,000 vaccines are available; however, distribution remains difficult due to infrastructure challenges.

Dr. Jamieson recommended changing the language from detailing sexual acts to summarizing the approach for those engaging in sex with new partners to avoid singling out specific groups.

Dr. Rao agreed to return this suggestion to the work group for further discussion. She also clarified that the ACIP recommendations will not include the detailed outbreak guidance, which is tailored to the specific outbreak.

Dr. Schechter asked whether the group anticipates using information from the response to the current outbreak to inform the use of vaccines in children in the U.S.

Dr. Rao believed that more information and preliminary data would be available to provide data on studies in other countries involving children as young as two years of age.

Dr. Christina Hutson (CDC/NCEZID) added to Dr. Maldonado’s comments. The PALM study showed that providing basic and essential items like food, fluids, and antibiotics went a long way to improving outcomes. The case fatality rate was much lower than what has been seen historically. It is not clear how many had underlying health conditions; some patients needed more support than others. As mentioned, Ib is consistently less than 1% mortality. In confirmed cases, children are in a very young age group. The group believes that household interactions contribute to the high numbers in this group.

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

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