MEETING OF THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP)

APRIL 15-16, 2025
MEETING SUMMARY

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

TUESDAY: APRIL 15, 2025

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Keipp Talbot (ACIP Chair) called the April 15, 2025, Advisory Committee on Immunization Practices (ACIP) meeting to order. Dr. Melinda Wharton (ACIP Executive Secretary) made opening announcements about the availability of presentation slides on the ACIP website, the scheduled oral public session, and the written public comment process through regulations.gov at Docket ID CDC-2025-0017. She reviewed conflict of interest (COI) policies for ACIP members. She welcomed and introduced the new committee members: Ms. Karyn Lyons and Dr. Jane Zucker. Dr. Keipp Talbot conducted a roll call to establish a quorum. A list of members, ex officio members, and liaison representatives is included in the appendices at the end of this summary document. No COIs were identified for the first day of this meeting. Dr. Chen disclosed prior involvement with VLA2001 vaccine trials, noting service on data and safety monitoring boards for Valneva vaccine trials that concluded in August 2024. She also co-authored a paper with Valneva scientists, published in September 2024, on chikungunya vaccine development, and received no compensation from industry for that work. To avoid the perception of a conflict of interest related to these past activities, she will abstain from voting on the chikungunya vaccine recommendations.

MPOX VACCINE

Dr. Faisal Minhaj (CDC/NCEZID) provided an overview of the monkeypox virus (MPXV). It is within the *Orthopoxvirus* genus and the Poxviridae family, in the same genus that contains variola virus, the causative agent of smallpox. It was discovered in 1958 following two outbreaks of a pox-like disease in a research monkey colony. Although the animal reservoir is unknown, it is likely to be small African mammals. The World Health Organization (WHO) implemented the preferred term “mpox” for the disease in November 2022. There are two clades of MPXV. Clade I is historically associated with greater disease severity in a higher proportion of people in central Africa. Clade II, which is found in West Africa, was the cause of the 2022 global outbreak.

The first human case of mpox was identified in the Democratic Republic of the Congo (DRC) in 1970. In 2003, a U.S. outbreak of 47 cases occurred when small mammals from Ghana infected pet prairie dogs. In 2017, an outbreak of 122 cases occurred in Nigeria, involving 17 states. This outbreak followed a period of very few reported cases for decades in Nigeria and West Africa. Multiple travel-associated cases followed, including 2 U.S. cases in 2021. The ongoing global Clade II mpox outbreak followed in 2022.

The first case of the global mpox outbreak was identified in May 2022 in the United Kingdom. This outbreak primarily affected gay, bisexual, and other men who have sex with men (MSM). It spreads through close skin-to-skin contact, including sex. Deaths have primarily occurred among individuals with severe immunocompromise due to advanced HIV. The U.S. case counts and deaths comprise 1/3 of cases and deaths globally, with more than 30,000 cases and more than 60 deaths in the U.S.

During the current outbreak, the peak in U.S. cases occurred in summer 2022; since that time, cases have continued to occur in the U.S. As of March 2025, cases continue to occur, with a 7-day moving average in recent months ranging from 3.3 to 1.2 cases per day.

Due to the ongoing outbreak, in February 2023, the ACIP recommended the 2-dose JYNNEOS® vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak. Dose 2 is administered one month after Dose 1. Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include the ongoing risk of mpox introduction into a community due to disease activity in another geographic area.

In October 2023 ACIP made an interim recommendation for use of JYNNEOS vaccine in the current outbreak, recommending vaccination with the 2-dose JYNNEOS vaccine series for persons aged 18 years and older at risk for mpox. Dose 2 should be administered 28 days after Dose 1, and persons at risk include the following:

Gay, bisexual, and other men who have sex with men (MSM), or a person who has sex with MSM who in the past 6 months have had one of the following:

- A new diagnosis of ≥ 1 sexually transmitted disease
- More than one sex partner
- Sex at a commercial sex venue
- Sex in association with a large public event in a geographic area where mpox transmission is occurring

Sexual partners of persons with the risks described in above

Persons who anticipate experiencing any of the above

This is an interim recommendation which should be revisited in 2-3 years.

Even as the global Clade II outbreak continues, there has also been an increasing number of cases in the DRC and surrounding central and east African countries, resulting in travel-associated Clade I cases in multiple countries.

From June 2022 through September 2024, in the U.S. overall, JYNNEOS vaccine coverage among eligible individuals was 42.2% for 1 dose and 26.2% for the 2-dose series. Modeling data suggests that *any* increase in coverage reduces the risk of outbreaks and that low coverage (<50%) could promote larger outbreaks.

The case trend for mpox cases among children and adolescents is similar to that for adults, with the peak of cases occurring in the summer and fall of 2022, and cases sporadically occurring since then.

Previously, there were no data evaluating JYNNEOS in children <18 years. An NIH-sponsored trial completed last year evaluated JYNNEOS in 12–17-year-old adolescents. With these new data, the work group is proposing to extend the current recommendations down to 12-17 year-old adolescents.

Proposed recommendation 1:

ACIP recommends the 2-dose JYNNEOS vaccine series for persons 12–17 years of age at risk of mpox during an mpox outbreak§.*

**Dose 2 administered one month after Dose 1*

§Public health authorities determine whether there is an mpox outbreak; a single case may be considered an mpox outbreak at the discretion of public health authorities. Other circumstances in which a public health response may be indicated include ongoing risk of introduction of mpox into a community due to disease activity in another geographic area.

Proposed recommendation 2:

ACIP recommends vaccination with the 2-dose† JYNNEOS vaccine series for persons aged 12–17 years at risk for mpox §*

** Interim recommendation to be revisited in 2-3 years*

† Dose 2 administered 28 days after Dose 1

§ Persons at risk:

1. Gay, bisexual, and other men who have sex with men (MSM), or a person who has sex with MSM who in the past 6 months have had one of the following:

- *A new diagnosis of ≥ 1 sexually transmitted disease*
- *More than one sex partner*
- *Sex at a commercial sex venue*
- *Sex in association with a large public event in a geographic area where mpox transmission is occurring*

2. Sexual partners of persons with the risks described in above

3. Persons who anticipate experiencing any of the above

The Evidence to Recommendation (EtR) frameworks on these two proposed recommendations will be presented at this meeting, with the expectation of voting at the June 2025 ACIP meeting.

Dr. Buddy Creech (Vanderbilt) presented findings on the safety and immunogenicity of mpox vaccination in adolescents. He described the study as a Phase 2, randomized, open-label, multisite trial (DoSES) designed to inform public health strategies for using the Modified Vaccinia Ankara (MVA) [Bavarian Nordic (BN), JYNNEOS] vaccine against mpox. Stage 1 evaluated the FDA-approved 2-dose subcutaneous (SC) regimen compared to two separate intradermal dose-sparing regimens in adults aged 18–50 years. Stage 2 assessed the noninferiority of the 2-dose SC regimen in adolescents aged 12–17 years compared to adults aged 18–50 years.

MVA-BN was administered subcutaneously on Days 1 and 29 to healthy, vaccinia-naïve adolescents aged 12–17 years, compared to adults aged 18–50. The study aimed to support licensure of JYNNEOS for use in adolescents. Enrollment targeted a cohort representative of the U.S. population based on 2020 Census data, intending to include at least 25% of participants aged 12–14 years.

The study population included 315 adolescents aged 12–17 years, of whom 161 were 12-14 years of age and 211 were adults. All participants received Dose 1, and nearly all received Dose 2. Almost all participants completed their primary endpoint evaluation at Day 43. Solicited systemic and local reactions were similar between adolescents and adults. Erythema, induration, and pruritus were more common in both groups after Dose 2. The most common systemic reactions were fatigue, headache, and myalgia, occurring at similar frequencies after both doses.

The severity of solicited adverse events within 7 days of Dose 1 was 55% mild, 36% moderate, and 2% severe among adolescents, and 50% mild, 31% moderate, and 3% severe among adults. Following Dose 2, adolescents reported 36% mild, 42% moderate, and 6% severe events, while adults reported 35% mild, 37% moderate, and 19% severe events. Erythema and induration were the most common severe reactions.

The most frequent local reactions were pain at the injection site, erythema, and injection site nodules. Injection site nodules were reported by 117 adolescents (37%), typically appearing at the beginning of the second week, and by 78 adults (59%). Nodule rates were similar between younger and older adolescents (40% vs. 34%). Discoloration was reported by 53 adolescents (17%) and 38 adults (28%).

Dizziness was reported more frequently in adolescents than in adults. No event resulted in syncope or medical attention; 7 of 8 occurred within 1 day of vaccination. Rates were similar to those reported with other adolescent vaccines. Three adolescents and 4 adults received only the first dose of the vaccine. Two adolescent participants became pregnant during the study. Children were born without complications or congenital anomalies.

Immunogenicity was assessed using a vaccinia virus (Western Reserve strain) plaque-reduction neutralization titer (PRNT) assay. Peak humoral responses (Day 43) after a 2-dose regimen in adolescents were noninferior to those in adults. Geometric mean titers at Day 43 were higher in adolescents than in adults, and seroconversion at Day 43 (defined as the proportion of participants with at least a 2-fold rise in antibody titer compared to pre-Dose 1) was very high and similar in the two groups.

MPXV-specific PRNT assays are still underway. Neutralization in the presence of complement appears more representative of *in vivo* neutralization; testing of various complement sources has led to the identification of critical reagents needed for neutralization across both Clade I and Clade II MPXV. One hundred paired samples are being tested against Clade I and Clade II MPXV in the presence of complement.

Limitations included the study population being different compared to the global pediatric population at risk of mpox. Efforts were made to ensure that the population was representative of the U.S. population and that the ages of volunteers were distributed across the adolescent age group.

Dr. Creech concluded that the interim data from this Phase 2 clinical trial demonstrate that the MVA-BN vaccine is safe and well-tolerated in adolescents aged 12–17 years. The peak geometric mean titer (GMT) met prespecified noninferiority criteria for adolescents aged 12–17 years compared to adults aged 18–50 years. These findings are relevant to U.S. adolescents and areas where mpox is endemic, such as the DRC. Evaluations in younger children are needed to protect those most vulnerable, particularly given ongoing transmission among children in the DRC and neighboring African countries.

Dr. Shaw inquired whether there was a difference in complement-mediated enhancement between adolescents and adults, and if so, whether it was due to the early or late components of complement.

Dr. Creech responded that, in general, there is no difference between adolescent and adult neutralization. However, differences are observed with MPXV and other viruses when conducting plaque reduction neutralization assays. For MPXV, complement is required to neutralize both mature virions and extracellular enveloped virions.

Dr. Beigel added that the answer remains a work in progress. Assays using complement have been conducted, and increasing titers were observed. However, investigation into the underlying mechanisms has not yet begun. That work remains ongoing.

Dr. Schechter asked how soon after the immunization did dizziness occur, compared to dizziness and syncope with other adolescent vaccines.

Dr. Creech shared that all events occurred within one day of vaccination, with minimal variation. The characteristics were consistent with those typically seen in adolescents receiving Tdap, HPV, or influenza vaccines. These included transient, mild, and self-limited reports of lightheadedness that resolved quickly, reflecting patterns commonly observed in vaccinated adolescents.

Dr. Schechter raised the question regarding reports of more severe erythema and whether these correlated with discoloration or nodule formation, specifically, whether multiple manifestations of local reactions tended to occur together.

Dr. Creech shared that severe erythema was defined as greater than 10 cm, and severe induration or swelling, distinct from nodule formation, was defined as greater than 10 cm. While some correlation existed between erythema and nodule formation, the association was inconsistent; not all individuals with erythema developed nodules, and not all individuals with nodules had a history of preceding erythema. Generally, local reactions appeared around one week post-vaccination. Nodules in adolescents tend to be smaller than those in adults. The largest in adults measured up to 7 or 8 cm, while the largest in adolescents was 6 cm. Most adolescent nodules were under 2 cm, approximately a finger's width. These reactions typically resolved over time, were not usually painful or distressing, and in some cases, severe erythema was accompanied by pruritus at the injection site. While local reactions often clustered, they did not consistently present together. However, erythema was frequently accompanied by pruritus and occasionally by nodule formation.

Dr. Faisal Minhaj (CDC/NCEZID) presented the EtR for vaccination with JYNNEOS for adolescents at risk of mpox during outbreaks, focused on the question of ACIP recommending the 2-dose JYNNEOS vaccine series for persons 12–17 years of age at risk of mpox during an mpox outbreak.

Regarding the public health problem, Dr. Minhaj stated that two distinct outbreaks are occurring: Clade I and global Clade II. The DRC is the most affected by Clade I, and other countries have identified travel-associated cases. The U.S. ranks among the countries with the highest burden of disease due to Clade II. No week has passed without ≥1 reported case in the U.S. from May 2022 to March 2025. Cases have been identified in both adolescent and adult populations. Clinical manifestations of mpox can be severe, especially in severely immunocompromised persons in whom the infection can result in death. The work group determined that outbreaks of mpox are of public health importance.

For benefits and harms, Dr. Minhaj restated earlier findings on the immunogenicity and safety of JYNNEOS, confirming that the vaccine is safe and well tolerated in adolescents. The adolescent arm of the study met the pre-specified criteria for noninferiority. Unsolicited related adverse effects were primarily injection site reactions. Dizziness, commonly observed in this age group, is unlikely to represent a safety concern after vaccine administration. CDC vaccine safety data sources for JYNNEOS include the Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), V-safe, and single-patient Emergency Investigational New Drug (EIND) procedures. From 2022 to 2023, at least 1,245 persons <18 years of age received one or more doses of JYNNEOS. No serious adverse events were identified from any of these data sources. The work group determined that the desirable anticipated effects were large, the undesirable

anticipated effects were small, and that the desirable effects outweighed the undesirable ones, favoring intervention.

Dr. Minhaj noted that the NIH rapidly completed trial recruitment for the values domain, with participants expressing support for joining the trial to help friends. During outbreaks, pediatric close contacts were vaccinated. The Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) surveyed youth advisors, with 12 out of 13 respondents expressing support for vaccination. It remains uncertain what type of outbreak may occur in the future or how adolescents would perceive their risk and the acceptability of vaccination. The work group concluded that the target population would "probably" perceive the desirable effects as large relative to the undesirable effects. The work group was torn on whether there was “possibly important uncertainty or variability” and “probably no important uncertainty or variability” in how much people value the primary outcome. The nature of the outbreak may impact how adolescents view their risk and their likelihood of accepting vaccination.

Dr. Minhaj described two surveys for the acceptability domain: one administered to Adolescent Medicine Trials Network (ATN) providers and another to mothers of adolescents and younger children. Of the 21 surveyed ATN providers who care for at-risk adolescents, over half already offered the mpox vaccine. 95% reported they would recommend the vaccine for eligible patients and expressed no concerns. The majority noted challenges the financial cost to the clinic being the most frequently cited concern. The survey of mothers of children aged ≤18 years resulted in indications that most mothers do not perceive their children as being at risk for mpox; however, the intent to vaccinate was higher than expected. The work group felt that the intervention would “probably” be acceptable to key stakeholders.

For the health equity domain, Dr. Minhaj noted that Black adolescents represent a significant proportion of mpox cases but a smaller proportion of vaccine uptake, reflecting known racial inequities. No specific groups or settings would be disadvantaged by a recommendation for JYNNEOS use during mpox outbreaks. Immunogenicity is consistent among immunocompetent individuals aged 12 to 17 years. Vaccine implementation should ensure equitable access. Endorsement by ACIP could support broad acceptance of the recommendation through mechanisms such as insurance coverage, support from health departments, and availability in pharmacies. The work group concluded that the impact on health equity would probably increase.

For the feasibility domain, Dr. Minhaj explained that a wide range of vaccinators are authorized to administer the vaccine. Facility sites include public health departments, sexually transmitted infection (STI) clinics, adolescent health clinics, and pediatric offices. The vaccine uses the same immunization information systems (IIS) and reporting infrastructure as other vaccines. Limitations to access include poor availability in rural communities, high vaccine cost, and the possibility that pediatricians may defer vaccination to STI or adolescent clinics. The 2-dose schedule, administered 28 days apart, requires follow-up and reminders. Once thawed and refrigerated, JYNNEOS remains viable for either 4 or 8 weeks, allowing time to schedule the second dose. Frozen storage is approximately 18 months. The work group concluded that the intervention is “probably” feasible to implement.

For the resource domain, Dr. Minhaj stated that JYNNEOS is commercially available and supported by similar mechanisms for billing and reimbursement, including Medicaid, Medicare, and 317 funding. Vaccines are generally considered a good use of resources during an outbreak. However, the cost-effectiveness of vaccination during a future outbreak in adolescents remains uncertain. The work group concluded that the intervention would “probably” be a reasonable and efficient allocation of resources.

Overall, the work group felt that the desirable consequences clearly outweigh the undesirable consequences in most settings, concluding the EtR presentation.

Ms. Moser asked whether the proposed recommendation is to change the starting age from 18 to 12, or whether the recommendations would be separate.

Dr. Minhaj responded that the recommendations would be separated, but the adolescent recommendation would be aligned with the language in the adult recommendation.

Ms. Moser inquired whether mpox data collection has been impacted due to funding and staffing changes.

Mr. Duffy shared that VAERS is still collecting reports.

Dr. Shaw requested comments on the ongoing Clade I outbreak in the DRC. Two distinct outbreaks were noted: Clade IA, which is more rural and primarily affects children, with about 60–70% of cases linked to household transmission, and Clade IB, which is more urban and occurs mainly among adults. Dr. Shaw asked whether this is still the case, whether there are any known biological reasons for the differences in transmission, and which Clade I subtypes have been observed in the U.S.

Dr. Minhaj commented that clade IA is predominantly seen endemically in the DRC and other endemic countries. In the DRC, about 50% of the population is under 15 years of age; given this, it is not surprising that many cases occur among children. Population dynamics also differ, with more crowded housing and other factors that do not directly translate to the U.S. There is nothing specific about the virus that determines which populations are affected; rather, it depends on the communities it enters. Clade IB is predominantly found in the eastern part of the DRC and has spread to other countries. It has primarily affected heterosexual sex networks and older populations, including adults. Again, the networks through which the virus enters, not a biological difference in the virus, influence transmission patterns. In terms of cases in the U.S., I. Four cases of Clade I have been reported so far, all of which were travel-associated and identified as Clade IB. Most travel-associated cases have been of Clade IB, although a few Clade IA cases have also been reported, including some in other countries.

Dr. Schechter inquired whether data on adolescent vaccination or vaccination in younger children would likely become available in the coming months, based on its use in Africa, and asked Dr. Creech whether any participants had been evaluated for symptoms of myocarditis, given the inclusion and exclusion criteria related to the condition. He inquired if myocarditis was assessed during the trial or if it was noted as a pertinent negative or absence.

Dr. Minhaj noted that trials are underway to evaluate children younger than 12 years of age, and once the data are available, they will hopefully be presented.

Dr. Creech followed up and shared that there were no symptoms that would have triggered an evaluation for myocarditis or pericarditis. This is consistent with existing data, which shows that the vaccine does not appear to cause these conditions in teenagers. The eligibility criterion was included out of an abundance of caution.

Mr. Duffy added that, based on CDC surveillance data, no cases of myocarditis have been reported or identified in individuals under 18 years of age from any listed surveillance systems.

Dr. Fryhofer pointed out that the website and the presentation contained differing statements regarding the balance of consequences.

Dr. Minhaj clarified that there are two EtR responses, and the next.

Dr. Kurilla asked how many children aged 12 to 17 would be considered high risk under the recommendation. Concerns were raised about how healthcare providers with low caseloads of

these individuals and pharmacies in areas with low population density would manage administration. Challenges may still exist in ensuring access for at-risk individuals.

Dr. Minhaj clarified that the proposed recommendation applies to the use of JYNNEOS during an mpox outbreak. This is not limited to the 2022 outbreak; it could also apply to future outbreaks, like the 2003 incident involving infected pet prairie dogs. The recommendation allows public health authorities to advise the use of JYNNEOS for adolescents deemed to be at risk. This allows the CDC or public health authorities to issue guidance identifying at-risk populations and recommending vaccination for adolescents, if appropriate. It was noted that the proposed question appears to be related to the following item for discussion.

Dr. Minhaj then presented the evidence to support the recommendation framework for the routine use of JYNNEOS vaccine for adolescents at risk of mpox during the current outbreak (proposed ACIP recommendation 2). It was noted that globally, Clade I and Clade II outbreaks are currently ongoing. In the United States, most vaccine doses were administered during the summer and fall of 2022. Overall vaccine coverage among the adult population at risk is approximately 42% for 1-dose and 26% for 2-dose, which remains low and has not significantly changed over the past year. This is important because once population immunity exceeds 50% for at least 1-dose, the likelihood of large outbreaks decreases significantly. Regardless of reaching the 50% threshold, any increase in vaccine coverage is correlated with a decrease in cases. The work group determined that mpox outbreaks are of public health importance.

Dr. Minhaj highlighted new safety and immunogenicity data for the benefits and harms domain for JYNNEOS in adolescents. The adolescent arm met the prespecified criteria for non-inferiority and was well-tolerated in this population. Vaccine administration data show that over 1,200 adolescents received the vaccine nationwide, with no serious adverse events reported from any data sources. Based on these findings, the work group determined that the desirable anticipated effects are “large”, while the undesirable effects are “small”. The work group favored the intervention.

Dr. Minhaj noted that the NIH rapidly completed trial recruitment for the values domain, with participants expressing support for joining the trial to help friends. During outbreaks, pediatric close contacts were vaccinated. The Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) surveyed youth advisors, with 12 out of 13 respondents expressing support for vaccination. The work group felt that the target population “probably” felt that the desirable effects are large relative to the undesirable effects. The work group was uncertain on whether there was “possibly important uncertainty or variability” and “probably no important uncertainty or variability” in how much people value the main outcome, primarily due to the limited data on this population.

For acceptability, Dr. Minhaj re-emphasized that most mothers do not perceive their children as at risk for mpox; however, the intent to vaccinate was higher than expected. During the current outbreak, vaccines were primarily administered to adolescents through public health and STI clinics. Of the 21 surveyed ATN providers who care for at-risk adolescents, over half already offered the mpox vaccine. 95% reported they would recommend the vaccine for eligible patients and expressed no concerns. The majority noted challenges with providing the vaccine, with financial cost to the clinic being the most cited concern. The work group felt that the intervention would “probably” be acceptable to key stakeholders.

For the health equity domain, Dr. Minhaj reinforced that Black adolescents represent a significant proportion of mpox cases but a smaller proportion of vaccine uptake, reflecting known racial inequities. No specific groups or settings would be disadvantaged by a recommendation for JYNNEOS use during mpox outbreaks. Immunogenicity is consistent among immunocompetent individuals aged 12 to 17 years. Vaccine implementation should

ensure equitable access. Endorsement by ACIP could support broad acceptance of the recommendation through mechanisms such as insurance coverage, support from health departments, and availability in pharmacies. The work group felt the impact on health equity would be “probably increased.”

For the feasibility domain, Dr. Minhaj reminded the committee that a wide range of vaccinators are authorized to administer the vaccine for the feasibility domain. Facility sites include public health departments, STI clinics, adolescent health clinics, and pediatric offices. The vaccine uses the same IIS and reporting infrastructure as other vaccines. Limitations to access include poor availability in rural communities, high vaccine cost, and the possibility that pediatricians may defer vaccination to STI or adolescent clinics. The 2-dose schedule, administered 28 days apart, requires follow-up and reminders. Once thawed and refrigerated, JYNNEOS remains viable for either 4 or 8 weeks, allowing time to schedule the second dose. Frozen storage is approximately 18 months. The work group felt that the intervention “probably” would be feasible to implement.

For the resource domain, Dr. Minhaj reiterated that JYNNEOS is commercially available and supported by similar mechanisms for billing and reimbursement, including Medicaid, Medicare, 317 funding, and the Vaccines for Children (VFC) program. Vaccines are generally considered a good use of resources during an outbreak. However, the cost-effectiveness of vaccination during a future outbreak in adolescents remains uncertain. The work group concluded that the intervention would “probably” be a reasonable and efficient allocation of resources.

The work group felt that overall, the desirable consequences probably outweigh the undesirable consequences in most settings due to uncertainty within the population.

Proposed Recommendation 2:

ACIP recommends vaccination with the 2-dose† JYNNEOS vaccine series for persons aged 12–17 years at risk for mpox §*

** Interim recommendation to be revisited in 2-3 years*

† Dose 2 administered 28 days after Dose 1

§ Persons at risk:

1. Gay, bisexual, and other men who have sex with men (MSM), or a person who has sex with MSM who in the past 6 months have had one of the following:

- *A new diagnosis of ≥ 1 sexually transmitted disease*
- *More than one sex partner*
- *Sex at a commercial sex venue*
- *Sex in association with a large public event in a geographic area where mpox transmission is occurring*

2. Sexual partners of persons with the risks described in above
3. Persons who anticipate experiencing any of the above

Dr. Loehr asked about background data on cost-effectiveness for resource use. He expressed hesitance in making a recommendation without any sense of resource use.

Dr. Minhaj shared that, unfortunately, the work group did not have data on the cost-effectiveness of vaccination in the adolescent population.

Dr. Loehr noted that approximately 150 adolescents were diagnosed with Mpox during the outbreak, but only 10 cases have been reported over the past two years. How many adolescents would fall into that category if this recommendation were intended for those at risk is unclear. For adults, the estimated annual prevalence among MSM is about 3%, which

translates to several hundred thousand individuals potentially at risk. However, that number is likely much lower for adolescents. As a result, this recommendation could lead to vaccinating tens to hundreds of thousands of individuals to prevent a very small number of cases. Additionally, the cost of the vaccine, estimated between $200 and $300 per dose, raises concerns about the scale of resource use. This was described as a potentially extraordinary expenditure for a relatively small public health impact. Dr. Loehr stated that he would like much more information about resource use before voting on this recommendation.

Dr. Brewer encouraged the work group to align the dosing intervals, noting that Recommendation 1 includes a one-month interval between doses, while Recommendation 2 specifies a 28-day interval. The current adult recommendation also uses a 28-day interval; alignment would help ensure consistency. He proposed striking the phrase 'vaccination with' from the current wording, noting that Recommendation 1 simply states 'recommend the vaccine.' This change would help to align the two recommendations and improve clarity for the committee.

Dr. Brooks requested raw numbers and population-at-risk estimates. Additionally, clarification was sought on whether the goal of a routine recommendation in the U.S. is to prevent potential outbreaks or to protect at-risk individuals regardless of outbreak status. Given the low number of cases and the rarity of severe complications, questions were raised about the justification for vaccinating a large population to prevent a relatively uncommon infection. While the rationale for vaccination during outbreaks is evident, further insight was requested into the work group’s reasoning for recommending routine vaccination now when infection is uncommon.

Dr. Minhaj noted that the recommendation to lower the age group was based on evidence that adolescents were at risk during the 2022 outbreak. Although current case numbers are low, a significant proportion of cases during the outbreak occurred in this population. While the number of individuals covered by the recommendation would be small, it could still help prevent mpox cases in this population, particularly with the increasing number of Clade I cases and the potential for importation.

Dr. Laura Bachman noted that estimating the exact number is challenging and requires extrapolation from available data, such as HIV pre-exposure prophylaxis (PrEP) use. For example, IQVIA data from 2021 show that approximately 6,500 adolescents were prescribed PrEP. However, this dataset has limitations, as not all prescriptions are captured. Additionally, it is estimated that only 15–20% of eligible adolescents are on PrEP. As a result, determining a precise number remains difficult.

Dr. Tracy Beth Høeg (FDA) thanked the presenters and highlighted concerns regarding the risk-benefit balance of proposed Recommendation 2. It was noted that adolescents are at very low risk for mpox, with fewer than 20 cases reported in the past year. Given the limited safety data, including the relatively small number of vaccinated adolescents and the 315 participants in the clinical trial, it is difficult to determine whether the benefits clearly outweigh the potential harms. Additionally, it was pointed out that the clinical trial excluded adolescents with significant heart or medical conditions, which providers should consider when evaluating the safety data's applicability to broader populations.

Dr. Agam Rao responded that a cost-effectiveness analysis was not conducted when the recommendation was made for adults. The intent was for the vote to be revisited in a few years, with the understanding that a cost-effectiveness analysis could be performed at that time. Although fewer cases are occurring, the associated morbidity and mortality remain significant. This recommendation was intended as an age extension of the existing adult recommendation. It was emphasized that if these adolescent data had been available during the adult vote, the

recommendation would likely have included this population, as the perceived risk was comparable. This clarification was provided to address questions related to the adult vote.

LYME DISEASE VACCINE

Dr. Grace Marx (CDC/NCEZID) introduced the new Lyme Disease Vaccines Work Group. Lyme disease is the most common vector-borne disease in the U.S., with an estimated 476,000 cases diagnosed and treated annually. Estimated healthcare costs for Lyme disease range from $345 million (M) to $968M each year.

Lyme disease vaccines were developed in the 1990s using outer surface protein A antigens from the *Borrelia burgdorferi* spirochete to prevent transmission during tick bites. LYMErix™, licensed by the FDA, was available from 1998 to 2002 but was discontinued due to low demand. Since then, Lyme disease has steadily increased in the U.S., with expansion outward from high-incidence areas in the Northeast, mid-Atlantic, and Midwest. New vaccines are in development, including the protein subunit vaccine candidate VLA15, which is now in Phase 3 trials. Several mRNA candidates are also in early clinical trials.

The work group's objectives are to review Lyme disease epidemiology, risk of Lyme disease, and vaccine candidate data; assess safety, immunogenicity, efficacy, and economic analyses; develop vaccination policy options for ACIP consideration; and identify data gaps.

Dr. Marx will serve as the work group lead. The work group chair and other members will be announced in the coming months. The first work group meeting is scheduled for May 2025. Epidemiology, burden, and clinical manifestations of Lyme disease will be presented at the June 2025 ACIP meeting.

INFLUENZA VACCINES

Dr. Jamie Loehr, chair of the Influenza Work Group, introduced the session. Dr. Loehr shared information on the 2025–2026 influenza vaccine composition and highlighted the importance of the update to the A(H3N2) component. Dr. Loehr shared that the group’s presentation will include interim vaccine effectiveness estimates for the 2024-2025 season and an update on self- or caregiver administration of FluMist® (available for the 2025–2026 influenza season). Votes on the recommendations for the 2025-2026 season will take place at the June 2025 ACIP meeting.

Dr. Aaron Frutos (CDC/NCIRD) provided interim estimates of 2024–2025 seasonal influenza vaccine effectiveness (VE). Four networks contributed to VE estimates against laboratory-confirmed influenza in children, adolescents, and adults across outpatient and inpatient settings: IVY (Investigating Respiratory Viruses in the Acutely Ill), NVSN (New Vaccine Surveillance Network), US Flu VE Network, and VISION (Virtual SARS-CoV-2, Influenza, and Other Respiratory Viruses Network).

For pediatrics, NVSN includes patients from outpatient clinics, emergency departments, urgent care centers, and hospitals. The US Flu VE Network includes patients from outpatient clinics, emergency departments, and urgent care. VISION includes patients from emergency departments, urgent care, and hospitals. For adults, IVY includes patients admitted to the hospital. The networks include all ages across inpatient and outpatient settings and are geographically diverse, including patients from 23 states.

All network enrollees sought medical care for acute respiratory illness between fall 2024 and early 2025. Each network uses a test-negative design, comparing the odds of vaccination

among influenza-positive cases (confirmed by molecular assay) to those testing negative for both influenza and SARS-CoV-2. Vaccination status was determined based on receipt of any 2024-2025 seasonal flu vaccine, using medical records, immunization registries, claims data, and/or self-report.

VE was calculated as (1-adjusted OR) × 100%. All networks adjusted for region, age, and calendar time of illness; IVY, US Flu VE, and VISION also adjusted for sex and race/ethnicity. VE was estimated for A(H1N1)pdm09 and A(H3N2) when data allowed. VISION did not report subtype-specific VE due to limited data. Some estimates were excluded due to small sample sizes or non-converging models. VE for influenza B was not estimated, as it accounted for less than 3% of surveillance specimens.

Pediatric VE against any final influenza estimate ranged from 32% to 60% in outpatient settings and 63% to 78% in inpatient settings. Pediatric VE against influenza A(H1N1)pdm09 estimates ranged from 53% to 72% in outpatient settings and was 63% in the inpatient setting. In the NVSN pediatric VE against influenza A(H3N2) is estimated to be 42% in the outpatient setting and 55% in the inpatient setting. VE against H3N2 was not significant for outpatients in the US Flu VE network, with a point estimate of 16%.

Among adults, the estimate for VE against any influenza ranged from 36% to 54% in the outpatient setting and 41% to 55% in the inpatient setting. The estimated VE against influenza A(H1N1)pdm09 among adults was 42% in the outpatient setting and not significant with a point estimate of 39% in the inpatient setting. The estimated VE against influenza A(H3N2) among adults was not significant in the outpatient setting, with a point estimate of 25% and was 51% in the inpatient setting. For adults aged ≥65 years, estimated effectiveness against any influenza was 51% in outpatient settings in the VISION network and not significant with a point estimate of 18% in the US Flu VE network, and 38% to 57% in inpatient settings.

Estimates show that the 2024–25 influenza vaccine reduced the risk of medically attended outpatient visits and hospitalizations for influenza among children, adolescents, and adults across 23 U.S. states. VE was effective against influenza A, with variation by subtype and network. These results were published in MMWR in February 2025.

Dr. Joshua Quint (California DPH) presented on the study of interim influenza vaccine effectiveness estimates against laboratory-confirmed influenza in California, October 2024–January 2025.

Recent changes in California's reporting have expanded public health data sources, allowing VE analyses across various age groups and settings using electronically reported vaccination and testing records. Since June 2023, negative influenza test results have been reportable to the state's electronic communicable disease reporting; positive results have been reportable since October 2019. These data are submitted electronically by laboratories across the state. All influenza vaccination records are now reportable to CAIR, the state's immunization registry.

At the end of the 2023-24 season, the California team compared their interim VE estimates to those from CDC's other VE platforms. Despite differences in populations and systems, the estimates were remarkably similar. For children ages 6 months to 18 years, VE was 56%, falling within the confidence intervals for nearly all the CDC platforms.

A case-control (test-negative) design was used, classifying those who tested positive for influenza as case patients. The analysis covered October 1, 2024, to January 31, 2025, and included California residents aged ≥6 months with a molecular or culture influenza test reported to the state's electronic lab system. Participants were considered vaccinated if they had at least one documented dose of seasonal flu vaccine in the immunization registry ≥14 days before testing. The earliest positive or negative test (if no positives) was used for individuals with

multiple test results. Labs with weekly positivity rates >50% were excluded due to data quality concerns, accounting for <5% of total tests. VE was calculated as (1 − adjusted OR) × 100%, using a mixed-effects logistic regression model adjusted for continuous age, race/ethnicity, testing week, and county as a random effect.

Weekly flu activity in California peaked in late December with approximately 17,000 positive test results and remained high through January. In total, 85% of positive specimens were influenza A, and 7% were type B.

Among samples tested by public health laboratories, the predominant subtypes were H3 (53%) and H1 (43%). Only 300 influenza B samples were lineage typed, so those results are limited. Only about 5% of all tests are subtyped by public health labs, and these may overrepresent severe cases.

Of 591,000 samples meeting eligibility criteria, 23% were positive for influenza and 77% were negative. Vaccination rates were 17.6% among positive cases and 25.9% among negative controls.

The median age of cases was 30 years compared to 43 years for controls. Race distribution was similar, though cases were 5 percentage points more likely to be Hispanic and 7 percentage points less likely to be white.

Adjusted VE against lab-confirmed influenza was 44.7% overall (95% CI: 43.7 to 45.6). By age group, the following estimates were calculated: 0-18 years, 50%; ages 19 to 49 years, 46%; ages 50 to 64 years, 39%; and ≥65 years, 39%. VE against influenza A was 42% overall, while VE against type B was higher at 71%. Among subtyped cases, VE was 47.9% for H3N2 and 49.5% for H1N1.

For children ages 2 to 17 years, the estimated VE for live attenuated influenza vaccine (LAIV) was 61% compared to 48% for those who received another vaccine type. These rates were 45% and 52% in the previous season. Median ages were similar across groups.

Cumulative VE estimates showed early-season variability with wide confidence intervals. VE peaked at 55% in early December before declining to about 45% by the end of the study period. Monthly analysis showed the highest VE in November at 56%, followed by a decrease in December and January, when confidence intervals were narrowest.

Type-specific monthly VE remained high for influenza B at approximately 75% in December and 70% in January, in contrast to the decreasing pattern observed for influenza A.

Limitations included incomplete documentation and reporting of vaccination and testing; inability to assess partial versus full vaccination status for children under 9 years; lack of information on symptoms, test setting, and outcomes such as illness, hospitalization, or death; incomplete and potentially biased reporting of influenza subtypes; and lack of control for confounding factors such as health-seeking behavior and pre-existing conditions.

Dr. Quint summarized that the data indicate that current influenza vaccines protect against laboratory-confirmed influenza in individuals aged ≥6 months. VE was higher for influenza B and among younger age groups, but vaccination offered protection across all ages. This study also highlights how expanded and improved public health data systems can be used to generate timely, in-season VE estimates.

Dr. Shaw inquired whether there is any information on VE against H3N2 in older adults.

Dr. Quint responded that this season's CDC’s VE estimates do not yet include H3N2-specific data for older adults. However, this information is routinely estimated each year, and final

estimates from networks that include older adult populations will be available at the end of the season.

Dr. Asturias requested data on the timing of immunization and illness to help determine whether the observed decline in VE for influenza A types is related to waning immunity over time or specific strain effects.

Dr. Quint shared that the group did not include vaccination timing in the model. Still, it could be inferred that the decline in VE toward the end of the season is likely related to earlier vaccination timing.

Dr. Zhu added that the group has a manuscript under peer review that examines explicitly waning immunity and overall VE estimates. While the group has not closely analyzed waning for this season yet, the trends are expected to be like those observed in previous seasons.

Ms. Moser requested clarification on whether the comparison group consisted solely of unvaccinated children or included those who received the inactivated influenza vaccine.

Dr. Zhu shared that for the pediatric LAIV analysis, approximately 455 children were vaccinated with LAIV. The control group for this comparison consisted of unvaccinated children. A similar control group was used for children who received non-LAIV vaccines, meaning unvaccinated children served as the comparison group for both analyses. While the population was stratified by vaccine type, a similar unvaccinated group was used as the reference for each VE calculation.

Ms. Moser inquired whether all four VE networks were still funded to collect data throughout this season and next.

Dr. Ellington confirmed that three of the four networks will continue active data collection during the 2025–2026 season. However, the IVY Network is planned to sunset and will not contribute data for the next flu season.

Dr. Cineas asked whether there was a data breakdown for VE estimates by vaccine type (for example, high dose) and age group, specifically for patients ≥65 years of age.

Dr. Frutos shared that there is no data at this time, and Dr. Zhu also shared that the group does not have those estimates available yet. However, product-specific VE was calculated for the previous season, and those estimates will be available soon.

Dr. Høeg asked whether potential bias was accounted for in the test-negative design studies presented, for example, based on the likelihood of seeking testing.

Dr. Frutos stated that one of the key strengths of the platforms and networks used to estimate vaccine effectiveness each year is that both influenza-positive and influenza-negative individuals have acute respiratory illness. Since estimates are based on medically attended influenza rather than all infections, the potential bias from differences in testing behavior is considered minimal. The estimates are believed to be accurate.

Dr. Kurilla inquired whether there has been any attempt or consideration to estimate VE stratified by whether individuals had a prior season flu infection and/or had received a flu vaccine.

Dr. Frutos responded that while the group did not account for this in the interim estimates, it is regularly examined and will be included in upcoming analyses.

Dr. Allyn Bandell (AstraZeneca) shared the details of FluMist for self- or caregiver administration, which was licensed by the FDA last fall and will be available for the upcoming 2025-2026 season. FluMist for self- or caregiver administration will be available for home

delivery. It expands access by allowing individuals or caregivers to administer it at home, with ordering through an online pharmacy service and using screening that aligns with that used in a traditional pharmacy setting.

FluMist builds on the growing acceptance of in-home healthcare. This flexibility can help overcome common barriers like busy schedules. A recent modeling study by the University of Pittsburgh found that increasing flu vaccination coverage in children ages 5 to 17 years of age using caregiver-administered FluMist could reduce symptomatic flu cases across all age groups. This approach helps prevent missed school and work and may reduce the spread of flu at home and in schools.

Step-by-step instructions, developed through a human-factors usability study, ensure ease of use. The online pharmacy service, FluMist Home, supports vaccine ordering, delivery, and documentation. A return shipment program is provided to guide proper disposal after use.

Several studies have evaluated the effectiveness, immunogenicity, reactogenicity, and safety of self- and caregiver-administered FluMist. A study of over 4,500 adults found no significant differences in effectiveness, immunogenicity, or adverse events between self-administered and healthcare-administered FluMist. Reactogenicity was also comparable. A Department of Defense study involving more than 1,000 adults found no variation in immunogenicity by administration method. Mean geometric titers for influenza A were comparable ($p = 0.43$), and local/systemic reactogenicity events were similar. In a study of caregiver administration to children aged 2.6 to 17 years, all doses were successfully given. Adverse events were mild, and some caregivers noted they would not have been able to vaccinate without the home option.

AstraZeneca conducted an FDA-required human factors usability study to inform the instructions for use and packaging. The goal was to ensure intended users could administer FluMist safely and correctly, avoiding common errors like underdosing or incorrect administration. Participants reflected the target population, including a mix of male and female participants, right/left handedness, a range of educational levels, and with and without experience with nasal sprays. Results showed that 100% of users successfully administered the full dose and understood the instructions.

The final packaging and instructions used in the human factors study were submitted to the FDA in the supplemental BLA. When the FluMist package is opened, patients see an instruction sheet that provides information on storage, administration, and disposal. It guides users step-by-step, from inspecting the package to administering one spray per nostril, using plain language and visuals. It also addresses common concerns like nasal dripping and includes guidance on proper disposal.

The online pharmacy service, FluMist Home, supports patients who want to administer FluMist at home. It's important to note that AstraZeneca and ASPN (the pharmacy partner) are following standard roles for vaccine manufacturers and pharmacies. AstraZeneca will manufacture and supply the vaccine, develop educational and awareness campaigns, and provide support for FluMist-related questions. ASPN will manage the FluMist Home service, including eligibility screening, dispensing, delivery, and pharmacist counseling. ASPN pharmacists will also follow state-specific regulations for determining patient eligibility, issuing prescriptions, and documenting FluMist administration in immunization information systems based on the shipping address.

Persons ordering the vaccine will receive text notifications with the delivery time; no signature is required. Inside the package is a sheet listing the contents, storage instructions, the Vaccine Information Statement, and a QR code linking to how-to videos. FluMist should be refrigerated

until use. Delivery is timed to ensure proper temperature and handling through two-day delivery services. Patients will receive texts until the vaccine administration is confirmed.

Upon receipt of confirmation of vaccination, vaccination data is entered into the state immunization system using the same process used by retail pharmacies. The pharmacy can send records to the patient's physician, and patients can also download their vaccination record from the portal to share with their provider. This mirrors standard retail pharmacy practices.

FluMist packaging includes a return shipment program for safe disposal of the used sprayer, which is considered medical waste. A prepaid, pre-labeled envelope is provided, so there is no need to visit the post office. The envelope holds multiple sprayers and can be placed in a home mailbox. A medical waste company handles tracking and proper disposal.

Dr. Asturias asked what happens if a patient experiences an adverse event at home, how it would be reported, and who would be responsible for the patient.

Dr. Bandell shared that patients can access instructions in the package and online. If they experience an adverse event, they can report it through the ASPN pharmacist by email or chat, directly to AstraZeneca, or through VAERS. This process mirrors existing practices in the retail pharmacy setting, similar to other medications used at home.

Dr. Cineas asked whether the usability studies included non-English speakers and inquired about plans to develop materials in Spanish and other languages.

Dr. Bandell explained that the usability study primarily included individuals whose first language was English. However, Spanish-language support is planned for next season. The package insert is already available in Spanish, and ASPN Pharmacy offers online and customer support for Spanish speakers this year. Additional Spanish-language resources and broader language support are planned for future rollout. Other languages are to follow.

Dr. Chen requested clarification on the recommended temperature range and the 12-hour out-of-refrigerator limit.

Dr. Bandell responded that the temperature range is the same as in clinical settings, typically between 35 and 45 degrees Fahrenheit. Most household refrigerators in the U.S. fall within this range, and this information is clearly communicated to the consumer multiple times.

Dr. Zucker requested clarification on IIS reporting, specifically whether there is a step for attestation or verification that the vaccine was administered by the patient or caregiver after it is shipped to the household and before the pharmacy reports the dose to the registry.

Dr. Ami Patel (ASPN) responded that before reporting to the IIS, the pharmacy follows up with the patient or caregiver to confirm that the vaccine was administered. The dose is not reported until confirmation is received.

Dr. Zucker sought confirmation that, given the over 50 state immunization registries, a system will be in place to report to each registry.

Dr. Patel explained that they are contracting with a widely used reporting vendor, commonly utilized by retail pharmacies, to ensure nationwide connectivity and reporting to all jurisdictions. They have already begun contracting with the company and building the connections, with plans to complete testing before September, when the first reporting is expected.

Ms. Lyons asked whether there are any anticipated issues with state laws related to linking to an IIS through an online pharmacy rather than a pharmacy with a physical location in that state.

Dr. Patel acknowledged that some states require a physical location within the jurisdiction to report to their IIS. They plan to work directly with those IIS programs to determine how best to comply with local requirements.

Ms. Lyons followed up to ask whether a mechanism was available to offer FluMist to a younger child.

Mr. Leone explained that pharmacy laws vary by state, and those differences will be integrated into the system's modeling. For example, suppose a child is under a certain age, such as under seven, and state law prohibits pharmacy administration for that age group. In that case, the system will block the request and prompt the user to seek vaccination in a traditional setting. He emphasized that FluMist will still be available in traditional healthcare settings, and individuals ineligible through the service will be encouraged to consult their pediatrician or healthcare provider.

Ms. Moser noted that compliance in the trials appeared to be strong and asked about the mechanisms in place for follow-up beyond text messaging. She also inquired about plans for handling the return or disposal of unused vaccine, whether this is expected to be a significant issue, and how it is being addressed.

Dr. Bandell explained that the returns program was designed to be as simple and convenient as possible. All materials are preprinted and pre-labeled; the package can be placed directly back in the mailbox. Multiple sprayers can be included in the return. She added that there is no expectation that compliance with the return process will be an issue.

Ms. Moser clarified that she was concerned about unused or unwanted vaccines.

Dr. Patel clarified that, for safety reasons, they cannot accept returns once the product has been dispensed. Patients would be instructed to dispose of the unused vaccine in the same manner as a used dose.

Dr. Loehr asked whether it would be possible to distinguish self-administered from provider-administered FluMist in immunization registries and whether there would be a clear indicator for that distinction.

Dr. Bandell confirmed that this distinction can be made and noted that the NDC numbers for self-administered and healthcare-administered FluMist are different. This allows immunization registries to identify the method of administration through the NDC code.

Dr. Loehr raised the issue of handling situations when a child does not receive the full vaccine dose, such as when the child moves, the spray misses the nose or is accidentally sprayed on the cheek. He sought clarification on how parents should manage obtaining another dose in these cases.

Dr. Patel explained that the patient or caregiver can contact the pharmacy to report what happened in such situations. The pharmacy would handle the appropriate reporting to VAERS, work with the patient's insurance to obtain a second dose through available overrides and ensure the replacement dose is spaced four weeks apart.

Dr. Loehr commented that many individuals must provide proof of flu vaccination, and questions often arise about whether self-administered doses at home are sufficient. It was noted that determining the acceptability of home administration is the responsibility of the hospital or organization, not the manufacturer. Suppose a hospital decides not to accept home dosing. In that case, that decision lies with the institution, and it would not be reasonable to expect the manufacturer to develop a system to meet the specific requirements of different organizations.

COVID-19 VACCINES

Dr. Robert Schechter (ACIP, Work Group Chair) introduced the COVID-19 Vaccines Work Group. In August 2024, the Food and Drug Administration authorized and approved the 2024-2025 COVID-19 vaccines:

- Moderna COVID-19 vaccine* in persons ≥6 months
- Novavax COVID-19 vaccine** in persons ≥12 years
- Pfizer-BioNTech COVID-19 vaccine* in persons ≥6 months

*Omicron JN.1 lineage, KP.2 strain
**Omicron JN.1 lineage, JN.1 strain

ACIP recommends everyone aged ≥6 months should receive 2024–2025 COVID-19 vaccination.

- Children aged 6 months–4 years may need multiple doses of COVID-19 vaccines to be up to date, including at least 1 dose of 2024–2025 COVID-19 vaccine
- People aged 5–64 years should get 1 dose[1] of 2024–2025 COVID-19 vaccine
- People who are ≥65 years[2] and people ≥6 months of age with moderate or severe immunocompromise[3] should receive a second dose of 2024–2025 COVID-19 vaccine 6 months after their first 2024–2025 dose (minimum interval of 2 months)
- People with moderate or severe immunocompromise may receive additional doses of 2024–2025 COVID-19 vaccines under shared clinical decision-making (minimum interval of 2 months)

1. People who are unvaccinated and receive Novavax COVID-19 vaccine for initial vaccination should receive 2 doses of 2024–2025 Novavax COVID-19 vaccine

2. People who are unvaccinated and receive Novavax COVID-19 vaccine for initial vaccination should receive 2 doses of 2024–2025 Novavax COVID-19 vaccine followed by a third dose of any 2024–2025 COVID-19 vaccine dose 6 months (minimum interval 2 months) after the second dose.

3. 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.

From October 2021 to March 2025, provisional weekly COVID-19 death data reported to the CDC show a consistent decline in deaths each year. In the first three years, there were typically two surges annually: a larger winter surge followed by a smaller late summer or fall surge. In 2025, the winter surge was smaller than the summer/fall surge in 2024, indicating a potential shift in the seasonal pattern. Over the past four years, similar patterns in hospitalizations have emerged, with the winter peak being larger than the late summer/fall peak, but as seen with COVID-19 deaths, the winter surge in early 2025 was smaller than the summer/fall surge in 2024.

COVID-19 illness levels have declined compared to previous years, while the 2024-2025 influenza season was more severe than the 2023–2024 season. As a result, estimates for illnesses, outpatient visits, and hospitalizations are higher for influenza than for COVID-19. Despite this, death estimates are similar for both diseases, reflecting a higher likelihood of severe outcomes from a case of COVID-19.

Vaccination coverage for the 2023–2024 and 2024–2025 formulations remained low. By spring, cumulative coverage for adults aged ≥18 years reached only about 20% in both years. This indicates that most adults, including those at higher risk for severe outcomes, remain unimmunized.

The work group has considered risk-based and universal recommendations for the 2025–2026 COVID-19 vaccines. In the spring, the FDA's Vaccines and Related Biological Products Advisory Committee is expected to meet to discuss and recommend strain selection for the 2025–2026 COVID-19 vaccines. ACIP will review and vote on the recommended use at its June meeting. Vaccine availability is anticipated in late summer or early fall.

Dr. Bishoy Rizkalla (Moderna) provided an overview of Moderna's next-generation COVID-19 vaccine, mRNA-1283, in individuals ≥12 Years of Age. COVID-19 remains a leading cause of hospitalization among respiratory viruses in the U.S. Risk factors for severe COVID-19 infection include advancing age and pre-existing chronic conditions.

The next-generation COVID-19 vaccine, mRNA-1283, is designed to offer stronger protection, especially for those most at risk. Unlike current vaccines that use the full spike protein, mRNA-1283 targets only the N-terminal and receptor-binding domains, which trigger strong immune responses. This streamlined approach shortens the mRNA sequence and allows for a lower 10-microgram dose, one-fifth of the original. It also positions mRNA-1283 as a strong candidate for future combination vaccines like Moderna's investigational flu-COVID vaccine, mRNA-1083.

Study 301 is a Phase 3 study assessing the safety, immunogenicity, and efficacy of mRNA-1283. It is a randomized, blinded Phase 3 trial with participants aged ≥12 years. They were randomly assigned to receive either mRNA-1283 or mRNA-1273 (commercially known as Spikevax®). Both of these vaccines were bivalent vaccines targeting the original SARS-CoV-2 strain and the Omicron BA.4/5 variants, in line with 2023 vaccine recommendations.

Demographics and baseline characteristics were balanced between groups. Half of the participants had a chronic condition linked to a higher risk of severe COVID-19 outcomes, as defined by the CDC. Prior SARS-CoV-2 infection and time since the last COVID-19 vaccination were also similar between groups.

Safety was monitored through a median follow-up of 8.8 months. There were no imbalances in adverse events between the vaccine groups. No cases of myocarditis or pericarditis were reported among mRNA-1283 recipients, and no safety concerns were identified.

mRNA-1283 elicited a higher antibody response at Day 29 compared to Spikevax. The highest BA.4/BA.5 neutralizing antibody geometric mean ratio (GMR) at Day 29 was observed in adults aged ≥65 years. mRNA-1283 consistently produced higher antibody responses compared to Spikevax over time in this age group. Neutralizing antibody responses against Omicron XBB.1.5, observed in a separate study, were similar between mRNA-1283 and Spikevax.

Prespecified success criteria for relative vaccine efficacy were met, with an estimated relative efficacy of 9.3% for mRNA-1283 compared to Spikevax in preventing CDC-defined COVID-19. In adults, efficacy increased with age, reaching a point estimate of 13.5% in those aged ≥65 years. Among adolescents, immune responses were comparable between the two vaccines, supporting similar protection, though estimates were less precise due to a smaller sample size and lower case numbers. Overall, efficacy findings were consistent with earlier immunogenicity results, with adults aged ≥65 years showing the highest neutralizing antibody levels and the greatest estimated efficacy. Relative vaccine efficacy was favorable for mRNA-1283 among individuals with comorbidities and in preventing severe COVID-19.

Dr. Rizkalla summarized that mRNA-1283 was generally well tolerated, and no safety concerns were identified. The study met its primary noninferiority endpoints for immunogenicity and

relative efficacy compared to Spikevax. Although the study was designed to demonstrate noninferiority, results showed higher immune responses among older adults and a trend toward greater efficacy with advancing age and among individuals with chronic conditions linked to severe COVID-19. This vaccine has the potential to reduce the COVID-19 burden, especially among those most vulnerable to severe outcomes. The anticipated Prescription Drug User Fee Act (PDUFA) date is by the end of May, with plans to offer mRNA-1283 for COVID-19 prevention this fall using an updated formulation aligned to circulating SARS-CoV-2 variants recommended by the FDA.

Dr. Asturias asked whether using one-fifth of the antigen dose in the new vaccine formulation might be a better strategy, considering the existing natural or vaccine-induced immunity in most of the population. He noted that, as seen with other vaccines, boosting with a lower dose can sometimes be more effective than using a traditional high dose.

Dr. Rizkalla responded that it has been well established that the receptor binding domain and the N-terminal domain contain key epitopes critical for generating neutralizing antibodies and cell-mediated immune responses. Clinically, mRNA-1283 has shown that, even at a fraction of the dose, it can produce higher neutralization levels compared to spike-based antigen designs. A broad range of clinical and nonclinical studies has evaluated this construct across multiple variants, including the original SARS-CoV-2 strain, Beta, and Omicron variants such as BA.1, BA.4/5, XBB.1.5, as well as more recent variants like JN.1 and KP.2. Across all studies, mRNA-1283 consistently outperformed Spikevax in inducing neutralizing antibodies. This strong correlation between neutralizing antibody response and protection is further supported by efficacy data, reinforcing mRNA-1283 as a robust vaccine design.

Dr. Shaw inquired about the single fatal event reported in the Spikevax group. He also asked whether there were any imbalances in prior COVID-19 infection or vaccination history between the groups, as both can affect immune responses.

Dr. Rizkalla explained that they conducted sensitivity analyses to assess responses based on the number of prior COVID-19 vaccine doses. These analyses looked at both immune response and efficacy. The findings showed that mRNA-1283 consistently induced higher immune responses compared to Spikevax, regardless of how many prior doses an individual had received. This translated into consistent efficacy results that aligned with the primary analysis. There were no fatal events in the mRNA-1283 investigational vaccine group. One fatal event occurred in the Spikevax group involving a 77-year-old female with a history of cardiovascular disease. The death occurred suddenly within a week of vaccination. The investigator determined the event was unrelated to the vaccine and most likely due to the individual’s underlying cardiovascular condition.

Dr. Cineas questioned whether the study population, which included individuals with multiple comorbidities, also included immunocompromised patients.

Dr. Rizkalla clarified that immunocompromised individuals were not included in the study. However, it is expected to perform at a comparable level because mRNA-1283 shares a common platform with Spikevax and shows similar immune responses.

Ms. Moser noted the encouraging potential for higher and more durable immune responses in older adults. She asked for comments on the similar rates of adverse events, despite the lower dose of the newer vaccine.

Dr. Rizkalla commented that both vaccines induce strong immune responses, so differences in systemic adverse events would not necessarily be expected. He noted a trend toward fewer local reactions with mRNA-1283, which may be explained by its lower dose and smaller injection volume: 10 micrograms in 0.2 mL for mRNA-1283 compared to 50 micrograms in 0.5 mL for Spikevax.

Dr. Kamboj asked whether there were any comparisons of T-cell responses between mRNA-1273 and mRNA-1283.

Dr. Rizkalla responded that T-cell responses were evaluated in the Phase 2 study, comparing mRNA-1283 at the Phase 3 dose to mRNA-1273 (Spikevax). The findings showed comparable CD4 and CD8 T-cell responses between the two vaccines, with responses persisting through the 366-day duration of the study.

Dr. Schechter asked whether it would be possible to get a more detailed age breakdown for myocarditis risk, specifically within the 18 to 30 or 18 to 40 years age range. Referring to slide six of the presentation, which grouped data for adolescents and then adults aged 18 to 64 years, the request was made to see sample sizes and risk data for younger adults who may have been at higher risk for myocarditis in the trial.

Dr. Rizkalla noted that no myocarditis or pericarditis were observed throughout the program and offered to return to the work group with a breakdown of demographics for the 18 years and older population.

Dr. Høeg raised a question about how the efficacy of Spikevax was determined in the context of a noninferiority study comparing it to mRNA-1283. Given the high level of underlying population immunity from prior infection, there was interest in whether the comparison relied on real-world data, which can be affected by healthy vaccine bias, or on neutralizing antibodies, which have not been clinically validated in individuals with prior infection. The question focused on how efficacy, particularly against outcomes like hospitalization, COVID-19-related death, and long COVID, was assessed for Spikevax to evaluate the relative performance of mRNA-1283.

Dr. Rizkalla responded that the Phase 3 study was comparing the relative vaccine efficacy between the two arms, based on CDC-defined COVID-19.

Dr. Høeg asked how Moderna could determine the efficacy of mRNA-1283 if we don’t know what the efficacy of what it Is being compared to.

Dr. Edwards explained that each season, as the strain composition of the Spikevax product is updated, vaccine effectiveness is measured throughout that season. This process helps establish and continuously update the vaccine effectiveness profile for each variant composition, including the one used in the current trial.

Dr. Fiona Havers (CDC/NCIRD) provided updates on COVID-19–associated hospitalizations. The trends described are based on data from COVID-NET, a population-based surveillance system that tracks laboratory-confirmed COVID-19 hospitalizations. COVID-NET covers about 10% of the U.S. population. It includes data from over 300 hospitals in 98 counties across 13 states. Hospitalizations are included if a positive SARS-CoV-2 test was reported within 14 days before or during admission, with testing based on clinical judgment and facility policy. Basic demographic data is collected for all cases, while detailed clinical data are gathered from a stratified random sample.

COVID-19 hospitalization rates have shown both winter and summer peaks, unlike RSV and influenza, which typically peak only in winter. For the 2024–2025 season, COVID-19 hospitalization rates are lower than the previous season; since the beginning of the COVID-19 pandemic, many hospitalizations have occurred outside the typical respiratory virus season. Since the 2021–2022 peak, rates have declined across all age groups. Hospitalization rates vary by age group and virus, with the highest rates observed in infants aged <6 months and in older adults. In the 2023–2024 season, adults aged ≥75 years continued to experience the highest cumulative hospitalization rates of any adult age group.

During the 2024–2025 season, children and adolescents made up about 4% of COVID-19–associated hospitalizations. Pediatric hospitalization rates were highest in infants aged <6 months. Children aged <5 years had higher influenza and COVID-19-associated hospitalization rates than school-aged children and adolescents (aged 5–17 years). For children ≤4 years, COVID-19 hospitalization rates during the 2022–2023 and 2023–2024 seasons were similar to those for influenza. Among children aged 5–17 years, COVID-19 hospitalization rates were lower than influenza during the same seasons. Between October 2022 and April 2024, older children hospitalized with COVID-19 were more likely to have underlying medical conditions than younger age groups. About 1 in 5 hospitalized children and adolescents with COVID-19 were admitted to the ICU. Fewer than 5% of eligible hospitalized children and adolescents had received the most recently recommended COVID-19 vaccination.

Dr. Havers summarized that pediatric COVID-19-associated hospitalization rates are highest among the youngest age groups. Among school-aged children, hospitalization rates are generally higher for influenza than for COVID-19. More than half of children and adolescents hospitalized with COVID-19 had multiple underlying conditions, with the proportion increasing with age. Additionally, most hospitalized children had not received the most recently recommended COVID-19 vaccine during the 2023–2024 seasons.

Adults aged ≥65 years account for more than two-thirds of all COVID-19–associated hospitalizations among adults. Hospitalization rates increase with age, and in recent years, adults aged ≥65 years have consistently had higher COVID-19 hospitalization rates than those for influenza. The risk of COVID–19–associated hospitalization is also elevated among community-dwelling adults aged ≥18 years with underlying medical conditions. About 1 in 5 adults hospitalized with COVID-19 were admitted to the ICU. Most adults hospitalized during the 2023-2024 season had not received a COVID-19 vaccine since September 2022. Furthermore, as of November 30, 2024, only 30% of nursing home residents had received the 2024–2025 COVID-19 vaccine.

Dr. Havers summarized that COVID-19 hospitalization rates are highest among the oldest age groups, with adults aged ≥75 years accounting for about half of all adult hospitalizations. While overall hospitalization rates have declined over time, adults aged ≥75 years continued to have the highest rates in the most recent season with complete data, surpassing all other adult age groups, even compared to previous seasons. The risk of COVID-19 hospitalization also persists during the summer months. Most hospitalized patients had not received the most recent COVID-19 vaccine before admission. Chronic kidney disease, diabetes, and coronary artery disease were associated with an increased risk of hospitalization across all adult age groups. The relative risk of hospitalization among adults with vs. without select medical conditions generally declined with increasing age for most, but not all, conditions examined.

Dr. Ruth Link-Gelles (CDC/NCIRD) shared interim estimates of the effectiveness of the 2024–2025 COVID-19 vaccine. These findings reflect the added benefit of vaccination in a population with widespread vaccine and infection-induced immunity. Vaccine coverage was similar in the 2023-2024 and 2024-2025 seasons for all adults but slightly higher among older adults during the 2024–2025 season. Coverage reached just under 25% for adults aged ≥18 years and approximately 41% to 47% for older age groups.

VE is measured by comparing the frequency of health outcomes in vaccinated versus unvaccinated individuals. During the monovalent COVID-19 vaccine rollout, absolute VE was used, focusing on differences between vaccinated and unvaccinated groups. During the bivalent period, relative VE was used to compare outcomes between recipients of different vaccine types. For the 2024–2025 COVID-19 vaccines, VE is measured using a combined approach, comparing disease rates in those who received the 2024–2025 vaccine to those who did not, regardless of prior vaccination or infection. This method is similar to how seasonal influenza VE is typically assessed.

The first VE platform is the VISION Network, a multi-site system that uses electronic health records from over 300 emergency departments and urgent care centers, and more than 200 hospitals. VISION uses a test-negative design and includes eligible adults with COVID-like illness and a clinical test within 10 days before and 72 hours after their healthcare visit. The analysis includes adults aged ≥18 years with COVID-like illness. Cases are defined as those with a positive nucleic acid amplification test (NAAT) or antigen test for SARS-CoV-2 and no positive test for RSV or influenza. Controls are those with a negative NAAT test for SARS-CoV-2 and no positive test for influenza or RSV, depending on age. Vaccination status is determined using electronic health records and state and city immunization registries.

The second VE platform is the IVY Network, a multi-site system in 26 hospitals across 20 U.S. states. Like VISION, it uses a test-negative design with active enrollment, including patient interviews and swab collection. Participants were adults aged ≥65 years hospitalized with COVID-like illness. Cases had a positive NAAT or antigen test for SARS-CoV-2, while controls tested negative for SARS-CoV-2, influenza, and RSV by RT-PCR. Vaccination history is determined through electronic medical records, state and local vaccine registries, and self-report. Specimens are collected for central testing and sequencing.

Among adults, the 2024–2025 COVID-19 vaccination provided additional protection against COVID-19–associated emergency department and urgent care visits, as well as hospitalizations, compared to no 2024–2025 vaccine dose. The vaccine also offered protection against COVID-19–associated hospitalizations among adults aged ≥65 years with immunocompromising conditions.

Dr. Link-Gelles reminded the committee that VE should be interpreted as the added benefit of 2024–2025 vaccination in a population with high levels of infection-induced immunity, vaccine-induced immunity, or both. While prior SARS-CoV-2 infection contributes to protection, that protection wanes over time. Increased SARS-CoV-2 circulation in late summer 2024, just before the vaccine's approval, may have raised population-level immunity against JN.1-lineage strains, potentially resulting in lower measured VE than in a population with less recent infection.

Questions and comments on Dr. Havers and Dr. Link-Gelles's presentations were taken together

Dr. Asturias commented that he was encouraged by the increased focus on children, emphasizing the need to dispel the myth that young children are not at risk for severe COVID-19 or hospitalization. He noted that the data shows that hospitalization trends in children are not decreasing. With new cohorts of unprotected infants born each year, current recommendations may need to be adjusted to highlight the importance of vaccinating young children. He pointed out that 70% of pediatric hospitalizations occur in children under four years of age, and half of these cases involve children without underlying medical conditions. He stressed the importance of recognizing children as a priority group that needs stronger protection than they currently receive.

Dr. Loehr requested clarification on how chronic kidney disease was defined in the analysis, noting its strong association with severe COVID-19. He asked whether the definition was based on creatinine clearance and whether it included class 3 or class 4 kidney disease.

Dr. Havers clarified that the relative risk of chronic kidney disease may be slightly overestimated in this analysis due to the data collection methods used in the Behavioral Risk Factor Surveillance System (BRFSS), which relies on self-reported information. This could affect the accuracy of the denominator and potentially skew the results. While there is a real increased risk associated with chronic kidney disease, comparing its magnitude to other underlying medical conditions can be challenging. Chronic kidney disease is identified through medical chart review for COVID-NET hospitalizations, without strict diagnostic criteria, whereas BRFSS relies on self-reported conditions.

Dr. Kamboj asked whether any updated data have shown an improved uptake of additional COVID-19 vaccine doses among immunocompromised patients nationwide. A second question focused on slide 13, noting the limited sample size. While it was understandable that the data were not sufficient to assess the time since vaccination, Dr. Kamboj inquired whether the number of doses was examined in any way.

Dr. Link-Gelles responded that additional doses were examined, and overall, uptake has been low within the VISION population (and nationally). Due to the timing of the analyses, few individuals were eligible for a second or subsequent dose during the study period. It was noted that they will continue to monitor this throughout the rest of the year.

Dr. Høeg commented that noting 90% of children hospitalized with COVID-19 were unvaccinated does not provide meaningful insight into vaccine effectiveness, given that nearly 90% of children in the general population are also unvaccinated, most recently 87%, and 86% the year before. The same consideration applies to adults. It's important to account for the baseline vaccination rate in the population when interpreting these findings.

Dr. Havers clarified that the slide showing the vaccination status of hospitalized children was not intended to reflect VE. For VE data, reference was made to the approach and findings presented by Dr. Link-Gelles. Children were not included in those VE analyses due to lower baseline disease rates, but monitoring will continue throughout the year. Dr. Link-Gelles added that the design of VE studies allows for adjustment based on baseline vaccination coverage, using the unvaccinated population as the reference group to compare the rate or risk of disease in vaccinated versus unvaccinated individuals.

Dr. Naima Joseph (ACOG) highlighted the high rate of COVID-19 hospitalization in young children, particularly among infants aged <6 months who are not eligible for vaccination. Previous CDC data have shown especially high rates in this group. Small studies have suggested that boosting during pregnancy may help protect these infants through maternal

immunization. Dr. Joseph expressed interest in seeing further data on the effectiveness of this approach.

Dr. Havers emphasized that the presentation primarily focused on children and infants older than six months. However, it is correct that for pediatric age groups, hospitalization rates are highest among infants aged <6 months, who rely on maternal vaccination during pregnancy for protection. Dr. Havers acknowledged this as an important point not previously highlighted in the discussion.

Dr. Lakshmi Panagiotakopoulos (CDC/NCIRD) shared the work group's considerations for the 2025–2026 COVID-19 vaccines. These include whether to maintain the current multi-dose initial series for children aged <5 years and for immunocompromised individuals, and whether to continue a universal recommendation for everyone aged ≥6 months or move to a risk-based or hybrid approach. The group is also evaluating guidance for those recommended to receive more than one dose per year, including adults aged ≥65 years and people aged ≥6 months who are immunocompromised.

The CDC's list of conditions that increase the risk of severe COVID-19 is extensive and largely based on pre-Omicron data. Researchers used multiple data sources and regression modeling to estimate how many U.S. adults have the conditions on this list. The analysis found that risk of having any condition increases with age, and about 74% of adults aged ≥18 years or older have at least one high-risk condition. Of note, some conditions from the list, such as Parkinson's disease, physical inactivity, and steroid use, were not included in the analysis, so the actual percentage is likely higher.

As of the 2024–2025 season, JN.1-lineage strains remain the predominant circulating variants of SARS-CoV-2. COVID-19 hospitalization and death rates have declined overall, though rates remain highest among adults aged ≥65 years. Pediatric COVID-19 hospitalizations were lower than those for influenza and RSV during the 2024–2025 season and lower than the previous year. COVID-19 also dropped in rank as a leading cause of death, from 8th to 12th in children between 2021 and 2023 and from 3rd to 10th in adults between 2021 and 2023. During the period September 2023 through August 2024, almost 90% of the deaths due to COVID-19 in the U.S. were among adults aged 65 years and older. Among children under 1 year, COVID-19 caused more deaths than influenza, while for those aged 1–17 years, influenza led to more deaths. Vaccine coverage remained stable, with a slight increase among adults aged ≥65 years, and vaccine effectiveness in adults held steady between 2023–2024 and 2024–2025. Cumulative hospitalization rates continue to decline since 2021. By the end of 2022, approximately 90% of children aged ≥2 years, 82% of children aged 1-2 years, and 64% of infants under 1 year of age had been infected with SARS-CoV-2. Looking at U.S. blood donors, higher exposure through infection and vaccination led to increased SARS-CoV-2 antibody levels, though gains diminished after 4 or more exposures. In 2023, an estimated 9.2 million adults and 0.3 million children in the U.S. reported having had long COVID. Vaccination reduced the risk of long COVID by up to 72% in children and up to 63% in adults, depending on symptom type. The incidence of multisystem inflammatory syndrome in children (MIS-C) fell significantly, from 6.8 to 0.08 cases per 1 million person-years between the pre-Delta period and 2024. Although most children with MIS-C in 2023 and 2024 were vaccine-eligible, few were vaccinated, and most had received their last dose more than 12 months before illness onset.

An increased risk of myocarditis was observed following COVID-19 vaccines during 2020–2022, particularly after the primary series and first booster doses. No increased risk has been detected in the VSD or in VAERS during the 2022–2023, 2023–2024, or 2024–2025 seasons to date. Myocarditis following COVID-19 vaccination typically resolves quickly, and cases are associated

with less severe cardiovascular outcomes compared to myocarditis following COVID-19 infection or conventional myocarditis.

The work group discussed concerns that shifting from a universal to a risk-based COVID-19 vaccine recommendation could reduce coverage among people with high-risk conditions. Influenza vaccination coverage among adults with high-risk conditions increased slightly after the universal recommendation in the 2010–2011 season, though the trend was already rising and plateaued shortly afterward. Hepatitis B vaccination coverage among adults with risk factors remained below pre-pandemic levels following the universal recommendation in 2022. By 2023, coverage for adults universally recommended for zoster vaccination was approaching that of pneumococcal vaccination among high-risk adults, despite longstanding recommendations for pneumococcal vaccination. It remains unclear how shifting from a universal to a risk-based recommendation would impact COVID-19 vaccine coverage.

The work group reviewed parental vaccine confidence data to better understand barriers to COVID-19 vaccine uptake among children, given that vaccination rates for children aged 6 months to 17 years remain low, at around 12%, similar to last year. Only 22% of parents said they were very likely to vaccinate their child against COVID-19 to prevent respiratory illness, which was lower than other prevention options offered in the survey. Among parents whose children had previously received one dose of the COVID-19 vaccine, most maintained the same confidence level in the vaccine's safety and effectiveness, though 15% reported less confidence. In contrast, about 45% of parents whose children had never received a COVID-19 vaccine reported decreased confidence in vaccine safety and effectiveness compared to when the vaccines first became available. Parents of children who received at least one COVID-19 vaccine dose were more likely to have already received or plan to receive the 2024–2025 vaccine for their child than those whose children had never been vaccinated. When asked why they did not vaccinate their child, parents of never vaccinated children were more likely to cite concerns about safety, effectiveness, and potential side effects. Additionally, 15% of parents whose children had received a prior dose believed their child had already received enough COVID-19 vaccine doses.

The work group reviewed COVID-19 booster recommendations from other countries for individuals who have completed an initial vaccine series. Most countries recommend boosters for older adults every 6 to 12 months, with age cutoffs ranging from 50 to 80 years. For otherwise healthy adults, the U.S. is the only country with a routine recommendation; other countries either have no recommendation, discretionary recommendations, or recommendations based on pregnancy status. Most countries recommend yearly vaccination for high-risk adults. For immunocompromised adults, most countries recommend vaccination every 6 to 12 months, with the U.S. being the only country that permits additional doses beyond two per year. Routine vaccination of healthy children is not widely recommended outside the U.S. and Canada (Canada has a discretionary recommendation in this group). The UK, Canada, and the U.S. recommend annual vaccination for high-risk children, while Australia and the WHO do not. For immunocompromised children, most countries recommend vaccination every six months, with the U.S. being the only country that permits additional doses beyond two per year.

As of February 13, 2025, after reviewing updated data on hospitalization risks, mortality trends, vaccine coverage, hesitancy, and myocarditis, the majority of the work group supported a risk-based recommendation for 2025–2026 COVID-19 vaccination. Most members who favored a non-universal policy supported a risk-based approach by conditions and exposures, a universal recommendation for certain age groups, and permissive language to allow anyone seeking protection to receive the vaccine. Additional data on vaccine effectiveness, seroprevalence, long

COVID, vaccine coverage, and MIS-C were presented, and the group received feedback from liaison organizations. These organizations raised concerns about implementation, communication, confidence, and equitable access under a risk-based recommendation. After a follow-up poll on April 3, the majority still supported a risk-based approach. Most members selecting a non-universal policy again supported risk-based recommendations by condition or exposure, universal recommendations for certain age groups, and permissive access for those seeking vaccination.

Dr. Jamieson expressed concern about moving to a risk-based COVID-19 vaccine recommendation, noting that 74% of adults have risk factors and that COVID-19 remains a leading cause of death among both adults and children. There was skepticism about the effectiveness of risk-based strategies in the US, and hepatitis B was viewed as an unsuitable comparison. Instead, influenza was seen as a more relevant example, with concern that decoupling flu and COVID-19 vaccinations could create confusion as people are just beginning to understand the importance of receiving both annually. Additional concerns included challenges with implementing a permissive recommendation, particularly regarding healthcare financing and access. Based on the information presented, support was expressed for maintaining a universal recommendation.

Dr. Loehr expressed support for considering a risk-based COVID-19 vaccine recommendation and appreciated that it is being taken seriously. Concerns were raised about the data showing that over 70% of adults aged 18 to 50 years are considered at risk, which did not align with clinical experience. The estimate seemed reasonable for older adults but appeared too high for those under 50 years of age. While in favor of the risk-based approach, there was concern about its feasibility and the message it may send, especially given that COVID-19 remains a significant public health issue with thousands of hospitalizations and deaths.

Dr. Asturias emphasized the importance of identifying data that could help protect young infants and children from COVID-19, noting that this group has not received adequate attention. Updated information on the transfer of maternal antibodies was highlighted as particularly useful, as most existing data come from earlier in the pandemic when protection was less certain. With many women now vaccinated or previously infected, current data on maternal antibody transfer would be valuable. Additional details on hospitalizations among children in their first year of life were requested, particularly the causes. Based on influenza data showing that young children are often hospitalized for fever and irritability, it would be interesting to see the causes of these hospitalizations.

Dr. Brooks emphasized the need for additional data, specifically requesting modeling on long COVID. While COVID-19 rates may be low among healthy individuals in their 30s, the potential for developing long COVID remains a concern. Even with a lower risk of long COVID, the absolute number of cases could still be significant. The primary concern was the long-term impact of long COVID, especially in younger age groups that may not receive a vaccination recommendation. Modeling the absolute number of long COVID cases in these groups was identified as an important data need.

Dr. Brewer addressed concerns about implementing a risk-based COVID-19 vaccine approach, noting that while it's commonly believed that such strategies are less effective, there is no clear evidence to support that conclusion. Although the idea has been discussed for years and shared by various groups, the data does not definitively show that risk-based approaches are less effective than universal ones. Based on the information reviewed, there was a shift in

perspective, with the view that the belief in the limitations of risk-based strategies is not currently supported by strong evidence.

Ms. Moser expressed support for exploring a risk-based COVID-19 vaccine recommendation and emphasized the importance of including the youngest children in those considerations. Echoing a previous point, it was noted that young children represent a newly susceptible group each year. Vaccinating them could help reduce hospitalization rates for those under one year old and potentially protect them from long COVID on their first exposure. While evidence on long COVID in this age group is still developing, early vaccination may also help avoid concerns previously associated with vaccinating adolescents, such as myocarditis. In a separate comment, appreciation was expressed for the public comments submitted for the meeting, particularly regarding the change in licensure status for Novavax that was anticipated to happen a few weeks ago. While acknowledging that this issue falls under FDA jurisdiction and not the committee's, a request was made for an update from the FDA ex officio to address public interest, given that the topic was not listed on the current agenda.

Dr. Høeg responded that while it is unclear to what extent an update can be provided at this time, a public update on the matter will be released very soon.

Dr. Fryhofer shared a perspective as a practicing internal medicine physician who sees many older and medically fragile patients and expressed concern for very young children as a new grandparent. Reflecting on the data showing that 74% of individuals have at least one risk factor, the point was made that, in practice, simplicity is key. The "keep it simple" approach was emphasized, particularly given that most adult vaccinations are administered in pharmacies. Risk-based recommendations can be challenging in these settings as they often require patients to self-report medical conditions or pharmacists to review medication histories, which some patients may be uncomfortable with. As a member of the COVID-19 vaccine work group and one of the 19% who supported a universal recommendation, Dr. Fryhofer explained that these concerns contributed to that position.

Dr. Loehr responded to a previous comment by referencing data from the pneumococcal vaccine work group, noting that uptake for the risk-based recommendation in adults aged 50 to 65 years was around 20%, compared to approximately 65% for the age-based recommendation in those aged 65 years and older. This was presented as evidence that risk-based recommendations may result in lower vaccine uptake. While still supportive of a risk-based approach, it was emphasized that this difference in coverage should be considered.

PNEUMOCOCCAL VACCINES

Dr. Miwako Kobayashi (CDC/NCIRD) shared the proposed plan on behalf of the Pneumococcal Vaccines Work Group. The group's term of reference is to review evidence to inform the use of new pneumococcal conjugate vaccines in U.S. adults and children.

Over the past 40 years, the U.S. pneumococcal vaccine program has undergone multiple updates, with several occurring in the last five years. During this period, three new pneumococcal conjugate vaccines were licensed for use. The most recent was the 21-valent pneumococcal conjugate vaccine (PCV21) for adults, which was licensed last year.

The work group acknowledges gaps in current pneumococcal vaccine recommendations for pregnant women. This gap is highlighted in the adult immunization schedule, which shows there

is currently no guidance for using pneumococcal vaccines in pregnant women with underlying conditions or risk factors that increase the risk of pneumococcal disease.

Additionally, ACIP has never specifically voted on pneumococcal vaccine use among hematopoietic stem cell transplant recipients. Clinical guidance for pneumococcal vaccine use was last updated in 2023 following the licensure of 15-valent pneumococcal conjugate vaccine (PCV15) and 20-valent pneumococcal conjugate vaccine (PCV20). Currently, there is no guidance on using PCV21 for this group.

Since a formal literature review on pneumococcal vaccine use in pregnant women and hematopoietic stem cell transplant recipients has not been presented to ACIP, the work group has been conducting such a review. A summary of the findings and proposed language for updated clinical guidance will be presented for the committee's review and feedback at the June 2025 ACIP meeting.

HUMAN PAPILLOMAVIRUS (HPV) VACCINES

Dr. Oliver Brooks (ACIP, Work Group Chair) introduced the Human Papillomavirus (HPV) Vaccines Work Group. HPV causes cancers of the cervix, vagina, vulva, penis, anus, and oropharynx. The HPV vaccine offers long-lasting protection against the types most likely to cause cancer. In the 19 years since its introduction, the vaccine has shown high efficacy in clinical trials, high population impact in real-world settings, and strong herd effects of vaccination programs.

The HPV Vaccines Work Group, previously active for many years, had been inactive since 2019. It was reconstituted and began meeting monthly in July 2024. The group gave its returning presentation to ACIP at the October 2024 meeting.

In the U.S., HPV vaccination recommendations include routine, catch-up, and shared clinical decision-making.

- Routine vaccination is recommended at ages 11–12 years and can start at age 9 years.
- Catch-up vaccination is recommended through age 26 years for those not adequately vaccinated earlier.
- Shared clinical decision-making is recommended for adults aged 27–45 years who are not vaccinated.

The number of HPV vaccine doses depends on the age at which the series is started:

- 2 doses are recommended if the series begins before the 15th birthday.
- 3 doses are recommended if the series begins at age 15 years or older, or for individuals with immunocompromising conditions.

The work group is reviewing two policy issues. The first is the wording of the recommended age for routine HPV vaccination. Some stakeholders support starting at age 9 years, which aligns with current ACIP recommendations. The work group is also reviewing the recommended number of HPV vaccine doses in light of growing evidence supporting fewer doses. It is evaluating data on 2 doses for individuals aged ≥15 years and 1 dose for individuals aged ≥9 years.

In 2022, the World Health Organization recommended a 2-dose HPV vaccination schedule for individuals aged ≥9 years, with a 1-dose option for those aged 9–20 years. Although low- and middle-income countries were expected to adopt the 1-dose schedule first, early adopters included the UK and Australia. Some countries did not move to a 1-dose schedule but shifted

from 3 to 2 doses for individuals aged >14 years. Regional advisory groups including those in PAHO and the WHO African Region support the 1-dose recommendation. As of April 2025, 67 countries have adopted a 1-dose schedule for some age groups, and 77 countries have adopted a 2-dose schedule.

Dr. Carla DeSisto (CDC/NCIRD) began with an overview of the work group's policy questions:

- Should 1 dose of HPV vaccine be used for prevention of HPV infection and HPV attributable disease, instead of the currently recommended vaccination schedule?*
- Should 2 doses of HPV vaccine be used for prevention of HPV infection and HPV attributable disease, instead of the currently recommended vaccination schedule?†

*There are two populations under review for this question. For individuals aged 9–14 years, the comparison is 1 dose versus the currently recommended 2 doses. For those aged ≥15 years, the comparison is 1 dose versus the currently recommended 3 doses.

†The population for with question is persons aged ≥15 years, and the comparison is 2 doses versus the currently recommended 3 doses.

There is no plan to change the recommendation of shared clinical decision-making for persons aged 27-45 years, although the number of recommended doses in this age group may change.

The four critical outcomes are HPV-associated cancers, precancers, serious adverse events related to vaccination, and incident persistent HPV infection. The six important outcomes are prevalent HPV infection, incident HPV infection, immunogenicity, anogenital warts, low-grade histological abnormalities, and recurrent respiratory papillomatosis.

For the systematic literature review, Cochrane reviewed global literature on reduced-dose HPV vaccination schedules in 2022. This review was adapted to the U.S. context, and the literature search was updated to include publications from 2022 to 2024. The literature review included 37 publications, which represent 16 studies. These publications include recently published updates from the Costa Rica Vaccine Trial (CVT), the IARC-India trial, and the Dose Reduction Immunobridging & Safety Study (DoRIS).

In the Costa Rica Vaccine Trial (CVT), women aged 18–25 years were randomly assigned to receive 3 doses of either the bivalent HPV vaccine or a control vaccine. Some received fewer doses due to factors like pregnancy or missed visits, with reasons balanced across groups. The data are being evaluated as a cohort study by the number of doses received. At the October ACIP meeting, data on protection against prevalent infection and immunogenicity through year 11 were reviewed. Sixteen years after vaccination, HPV 16/18 seropositivity remained very high at >98% in both the 1-dose and the 3-dose groups; as expected the geometric mean antibody concentration was lower in the 1-dose group. During years 11–16 post-vaccination, small but statistically significant declines in antibody levels were observed in women who received either 1 or 3 doses.

In the IARC-India trial, unmarried girls aged 10–18 were randomly assigned to receive either 2 or 3 doses of the quadrivalent HPV vaccine. A ministerial decree halting vaccination in trials resulted in cohorts receiving 1, 2, or 3 doses. Cervical screening with an HPV test began at age 25 for married participants, and age- and site-matched unvaccinated married women were recruited as controls. At the October ACIP meeting, data on protection against persistent infection through 10 years were reviewed. In their November 2024 publication, the authors reported a median follow-up time of 12 years and a total study duration of 15 years, with participants aged 25 to 33 years. VE against persistent HPV 16/18 infection was 92% with 1 dose, 94.8% with 2 doses, and 95.3% with 3 doses. Confidence intervals for these estimates overlapped. No CIN2+ cases associated with HPV 16/18 were detected among vaccinated

participants, compared to eight cases among unvaccinated women. No cases of invasive cervical cancer related to HPV 16/18 were reported in the study.

In the DoRIS trial from Tanzania, girls aged 9–14 were randomly assigned to receive 1, 2, or 3 doses of either the bivalent or 9-valent HPV vaccine. All participants were followed for 36 months, and those in the 1- and 2-dose groups were invited to join a long-term extension. The primary outcome was to assess noninferiority of HPV 16/18-specific seropositivity after 1 dose compared with 2 or 3 doses of the same vaccine. The trial also included a co-primary immunobridging objective to demonstrate noninferiority of HPV 16/18 antibody geometric mean concentrations (GMCs) after 1 dose, compared with that seen following 1 dose in efficacy studies. At the October ACIP meeting, data on immunogenicity and immunobridging to KEN SHE through two years were reviewed. The update focused on the 9-valent HPV vaccine, which is the vaccine currently used in the United States. For HPV 16, 100% of girls in both the 1-dose and 2-dose groups were seropositive five years after vaccination. For HPV 18, 93% were seropositive in the 1-dose group and 98% in the 2-dose group. Although seropositivity was high, noninferiority for HPV 18 was not met. Regarding GMCs, the 1-dose titers were lower than the 2-dose titers, as expected. In the 1-dose group, titers plateaued at month 12 and remained relatively stable through month 60. In the 2-dose group, titers declined after peaking at month 7.

Of the 59 studies identified by the Cochrane literature review, 49 were excluded due to a serious risk of bias. All excluded studies were observational. Key biases included differences in infection risk at vaccination, differences in HPV exposure during follow-up, and dose timing. These biases likely result in lower effectiveness with fewer doses. To address bias, researchers used buffer periods, stratifying results by age at vaccination or restricting the population to younger ages, adjustments for sexual activity and sociodemographic factors, and stratifying results for 2 doses by the interval between first and second doses.

Only one observational study with less than serious risk of bias, which provided data on a critical outcome, was identified in the updated systematic review. The Wu-Sweden study followed 2.2 million females aged 10–35 years from 2006 to 2022. Using linked registries, CIN2+ outcomes were assessed by the number of 4-valent HPV vaccine doses received. Adjusted Poisson models with a 12-month buffer were used, with median follow-up times of 8.4 years (unvaccinated) and 12.4 years (vaccinated). Among girls who initiated vaccination before age 15, the authors observed incidence rate ratios (IRRs) of 0.42 after 1 dose, 0.54 after 2 doses, and 0.50 after 3 doses. The overlapping confidence intervals suggest no significant difference in CIN2+ risk by number of doses. In women who initiated vaccination after age 21 years, only those who received 3 doses had a statistically significant IRR. While the comparison was to unvaccinated females and does not directly align with the work group’s policy questions, the study provides a useful example of observational data on effectiveness by number of doses.

There are several outstanding questions for reduced number of HPV vaccine doses. The longest efficacy data came from the IARC-India study (15 years post-vaccination), and the longest immunogenicity data came from the Costa Rica trial (16 years). No data exist on protection at sites other than the cervix. Of the 16 studies, 13 included only females. There are no efficacy data on males for reduced-dose schedules, and some evidence suggests lower antibody titers in adolescent males compared with females after one dose. Data are also very limited for immunocompromised individuals, and limited data exist on efficacy and immunogenicity in older age groups.

Dr. Ruanne Barnabas (Harvard University) shared the results for the KEN SHE trial. The study found that the single-dose HPV vaccination is highly efficacious, with 98% vaccine efficacy for HPV 16/18. Results are broken into 36-month and 54-month periods.

The 36-month results come from the randomized phase of the study, which included a control group. Women aged 15–20 years were recruited from three clinical trial sites in Kenya and randomly assigned to one of three groups: immediate 9-valent HPV vaccination; immediate bivalent HPV vaccination; or a control group receiving meningococcal vaccination. The study endpoint was incident persistent vaccine type-specific infection among HPV-naïve participants at vaccination. This is important, as HPV vaccines have no therapeutic effect.

Participants were followed for 36 months. For the per-protocol analysis, those with evidence of infection at enrollment or month 3 were excluded to allow for a buffer period. Cervical swabs for HPV DNA were collected every six months to assess persistent infection. Participants with prevalent HPV infection at enrollment were excluded from the per-protocol/modified intention-to-treat analysis, because the vaccine is prophylactic only.

After three years, single-dose HPV vaccine efficacy remained high and durable (VE 98% for HPV 16/18 and VE 96% for HPV 16/18/31/33/45/52/58). Based on sustained antibody levels over 16 years, the group hypothesized that single-dose vaccination would be effective and durable over 54 months.

At month 36, participants in the KEN SHE study were crossed over while maintaining the study blind to assess the durability of HPV vaccination. Those who had initially received the HPV vaccine were given meningococcal vaccination, while those who had received meningococcal vaccine were crossed over to receive the 9-valent HPV vaccine.

To evaluate the effectiveness of single-dose HPV vaccination among individuals aged 18–23 years, researchers compared the cumulative incidence of persistent HPV infection using Kaplan-Meier curves and incidence rate estimates for the immediate and delayed vaccine groups. Vaccine efficacy was analyzed as a function of time since vaccination using a Cox regression model that accounted for time and time-varying covariates to assess durability. The primary endpoint was incident persistent vaccine-type specific HPV infection, measured at two time points six months apart.

There were no differences in baseline characteristics between study groups. At cross-over vaccination, participants were 18–23 years old. Retention was 90% for three or more swabs, and the median time between endpoint swab collection was 6.00 months. HPV exposure to non-vaccine types was consistent across the study and all groups. Therefore, the only difference between the three groups was the vaccine received at randomization.

Participants vaccinated with the bivalent vaccine at age 18–23 years had similarly low rates of incident persistent HPV 16/18 infection compared to vaccination at age 15–20 years. HPV 16/18 vaccine efficacy, VE 99.2% (95% CI 96.1-99.9%), was sustained over time without evidence for waning immunity. Participants vaccinated with the 9-valent vaccine at age 18–23 years had similar rates of incident persistent HPV 16/18/31/33/45/52/58 infection compared to vaccination at age 15–20 years. HPV 16/18/31/33/45/52/58 vaccine efficacy, VE 98.9% (95% CI 94.9-99.8%), was sustained over time without evidence for waning immunity.

Dr. Barnabas summarized that single-dose HPV vaccination effectively protected adolescent girls and young women from incident persistent HPV infection over the first 54 months post-vaccination. The study’s rigorous design, high protocol adherence, high retention, and clear outcome ascertainment provide strong evidence of single-dose vaccine efficacy for individuals up to age 23 years. Efficacy against HPV types 16/18 and the seven high-risk types showed a lower confidence interval bound above 94%, consistent with licensure trials for 3 doses, with no evidence of waning protection. Exploratory analyses from the intention-to-treat population found high protection once prevalent infections at vaccination had cleared.

Ms. Cassandra Pingali (CDC/NCIRD) shared the data summary for the 2023 National Immunization Survey-Teen (NIS-Teen). NIS-Teen includes a two-phase process: a random digit dialed phone survey of parents of teens aged 13 to 17 years and a follow-up mailed survey to vaccination providers (e.g., clinics, pharmacies, health departments) if permission is granted. The provider data includes vaccination dates, types, and doses. Coverage estimates are based on provider-reported data. In 2023, the survey included 16,568 teens born between January 2005 and December 2010.

Coverage with ≥1 Tdap and ≥1 MenACWY has been high and stable since 2018. However, coverage with ≥1 HPV vaccine and proportion of HPV up to date is lower compared to most other routine vaccines.

In 2023, 89.0% of adolescents aged 13 to 17 years had received a Tdap vaccine, 88.4% had received a MenACWY vaccine, 76.8% had received an HPV vaccine, and 61.4% were up to date on HPV vaccination. This marks the second consecutive year HPV vaccination coverage has not increased among adolescents aged 13 to 17 years.

In 2023, about 77% of adolescents received an HPV vaccine. The HPV vaccine is commonly given with other recommended adolescent vaccines, with 69.5% receiving it with one or more additional vaccines in one visit. Among those who received an HPV vaccine, 47.8% received it with both the Tdap and MenACWY vaccines in one visit.

The percentage of adolescents who were HPV up to date was lower in mostly suburban and mostly rural areas compared to mostly urban areas. There were no differences in MSA status between the Tdap and MenACWY vaccinations.

Overall, vaccination coverage was lower among uninsured adolescents compared to those with private insurance across all vaccines. Adolescents with "other" insurance also had lower up-to-date HPV rates than those with private insurance. Coverage was similar between adolescents with private insurance and those with Medicaid, including for the HPV vaccine.

HPV vaccination has historically been higher among Medicaid-insured adolescents compared to those with private insurance, as observed from 2015 to 2021. However, in 2022, coverage with one or more doses declined by three percentage points among Medicaid-insured adolescents. As a result, in 2022 and 2023, HPV vaccine coverage was similar between Medicaid-insured and privately insured adolescents.

Historically, Black and Hispanic adolescents have had higher coverage with ≥1 HPV vaccine than White adolescents. In 2023, only Hispanic adolescents had higher coverage. In 2023, coverage with ≥1 MenACWY was higher among Asian adolescents compared to White adolescents.

In 2023, coverage with ≥1 dose of the HPV vaccine was 77% in the United States. Mississippi had the lowest coverage (60%), and Rhode Island had the highest coverage with ≥1 HPV vaccine (93%). HPV vaccine initiation at ages 9–10 and 11–12 has increased from 2018 to 2023, while initiation at age 13–17 has decreased from 2018 to 2023.

Dr. Pingali summarized that in 2023, 76.8% of adolescents had initiated the HPV vaccine, and 61.4% were up to date. This was the second consecutive year without increased coverage, which remains lower than for Tdap and MenACWY vaccines. Most adolescents began the HPV vaccine series at ages 11 to 12, and 47.8% received the HPV, Tdap, and MenACWY vaccines in a single visit. HPV vaccination coverage continues to vary by sociodemographic factors, health care access, and state.

Ms. Moser acknowledged the value of the NIS-Teen and NIS-Child data in showing national vaccination progress. A question was raised about whether data collection will continue or if any recent changes have impacted the ability to gather this information.

Dr. Pingali confirmed that, as far as is known, data collection for both the NIS-Teen and NIS-Child surveys is continuing.

Dr. Asturias asked whether there are differences in age at HPV vaccine initiation by geographic region in the U.S.

Dr. Pingali noted that the sample size is likely too small to analyze HPV vaccine initiation among the youngest age group, ages 9 to 10 years, as less than 5% of the national sample initiated at those ages. However, it may be possible to examine state-level data to see if stable estimates and differences can be identified. It was also shared that the group can look at initiation rates among adolescents aged 13 to 15 years to identify patterns or differences.

Dr. Brooks requested clarification on the “up to date” definition in the slide showing data over time from 2015 onward. Specifically, the question was whether "up to date" included individuals aged 9 to 14 years who only needed two doses, as the slide also referenced those with greater than or equal to three doses.

Dr. Pingali clarified that in NIS-Teen, HPV up to date is defined as receiving three or more doses, or two doses if the first dose was given before age 15 years, with at least 5 months minus 4 days between the first and second dose.

Dr. Schechter asked whether there was any evidence of disruptions or delays in vaccine administration among adolescents aged 13 to 17 years during the pandemic, similar to effects seen with other vaccines or age groups. There was also a question about the recent equalization of HPV vaccination rates between Medicaid-insured and privately insured adolescents, whether this trend reflects catch-up among privately insured adolescents, a decline among those with Medicaid, or a combination of both.

Dr. Pingali explained that vaccination coverage dropped notably among children born in 2008, who would have been 12 years of age during the pandemic. This group appeared to be the most affected. The 2009 birth cohort, who were 11 years of age in 2020, showed fewer disruptions, and the 2010 cohort, the youngest in the 2023 data, had coverage levels similar to pre-pandemic levels, except for a drop in HPV up-to-date coverage. Regarding the equalization in coverage between Medicaid-insured and privately insured adolescents, there was a 3 percentage point drop in HPV coverage from 2021 to 2022 among Medicaid-insured teens. While the cause is not entirely clear, there is speculation that changes in access to the VFC program or other pandemic-related factors may have contributed.

Dr. Jane Kim (Harvard University) shared estimates of the expected impact of single-dose HPV vaccination on the health of the U.S. population. Two independently developed mathematical models were adapted to the U.S. population to project the long-term health impact of single-dose HPV vaccination (Harvard and HPV-ADVISE). The models accounted for historical HPV vaccination coverage. They were used to explore key uncertainties related to the efficacy and duration of protection from a single dose at the population level.

The Harvard and HPV-ADVISE models are individual-based HPV transmission models that account for herd immunity and reflect multiple birth cohorts by age and sex. They share similar structures but differ in key areas. Both models include the seven high-risk HPV types in the 9-valent vaccine, but Harvard groups other types, while HPV- ADVISE models them separately. Harvard models transmission by monthly partnership duration, while HPV- ADVISE uses

transmission per sexual act. HPV- ADVISE also includes an additional CIN1 health state not captured in the Harvard model.

Both models overestimate the number of lifetime partners compared to U.S. data, suggesting higher assumed HPV exposure, especially in older age groups. This assumption is important when evaluating the potential waning of protection from a single-dose HPV vaccine.

Vaccine assumptions were based on existing clinical trial data, including the KEN SHE trial. The base case assumed 98% efficacy for one dose, indicating noninferiority to two doses. A worst-case scenario used 90% efficacy, reflecting the lower bound of published KEN SHE data. For the duration, the base case assumed lifelong protection, matching that of two doses. The worst-case scenario assumed an average duration of 25 years (normally distributed with standard deviation of 5 years), with waning starting at 15 years post-vaccination for some individuals and no protection for most by 40 years post-vaccination. Both efficacy and duration were assumed to be the same across all vaccine-targeted HPV types.

Results showed that with 2-dose or noninferior 1-dose 9-valent HPV vaccination, the models project near elimination of HPV-16 infections and an approximately 90% reduction in cervical cancer by the year 2070. Under the worst-case assumption of vaccine efficacy (90%), 1-dose vaccination is projected to produce similar population-level impacts as 2-dose or noninferior 1-dose. Even with waning 1-dose protection (average of 25 years), 1-dose vaccination is projected to produce similar population-level impacts as 2-dose or noninferior 1-dose. Assuming both lower VE (90%) and waning 1-dose protection (average 25 years), 1-dose vaccination is projected to produce a slight rise in HPV incidence (~2045) and cervical cancer incidence (~2060). All scenarios result in similar reductions in HPV 16 and cervical cancer incidence over time.

Compared to previously published results, the average vaccination age in the current analysis is at least five years later. With a 25-year duration, waning occurs when individuals are less sexually active. This means a higher percentage remains directly protected at older ages, leading to stronger indirect effects even as protection from one dose declines.

Dr. Kim concluded that the models suggest switching to a 1-dose HPV vaccination in the U.S. would result in similar reductions in HPV and cervical cancer incidence as continuing with two doses in the U.S. Even under pessimistic assumptions about vaccine efficacy and duration, the models project only limited increases in HPV infections and cervical cancer cases. This is because the switch would occur when HPV prevalence is already low, and most individuals would remain protected during peak sexual activity, providing both direct and indirect protection. Continued monitoring of 1-dose protection is important to detect any signs of waning and apply mitigation strategies if needed. Under pessimistic assumptions, switching back to a 2-dose vaccination could help recover potential losses in cancer prevention; mitigation strategies would not require revaccinating those who received one dose to be successful. The consistent results from two independent models add strength to these conclusions.

Dr. Asturias noted that while immunogenicity and efficacy of the HPV vaccine have consistently been strong, regardless of the number of doses, the key driver of the model's population-level impact appears to be the indirect effects, such as herd immunity. He asked for confirmation that the broader impact is less about the individual immune response and more about how many people are protected overall, which ultimately drives the population-level outcomes.

Dr. Kim confirmed that this is correct, emphasizing that strong indirect or herd effects from HPV vaccination are already being observed in the U.S. population. While direct protection is important, it also contributes to broader population resilience by protecting unvaccinated individuals through indirect effects.

Dr. Brooks asked whether the modeling accounted for a potential delay in detecting a rebound in HPV infections or cervical cancer cases, leading to delay in initiating mitigation efforts.

Dr. Kim responded that any potential rebound in HPV prevalence would likely be identified through clinical trial data before it becomes evident in epidemiologic trends. Ongoing trials monitor long-term vaccine efficacy, which helps detect early signs of waning. As shown in previous modeling published in the *Journal of the National Cancer Institute*, any rebound in HPV infections would occur several years later, with cervical cancer cases appearing even further down the line. If needed, mitigation strategies such as reverting to a 2-dose schedule could be implemented in time to offset potential losses in health outcomes.

Dr. Ruth Stefanos (CDC/NCIRD) reviewed the modified EtR framework. Given interpretation issues on the HPV vaccination schedule, the policy question is:

Should the ACIP recommendations state:

HPV vaccination is routinely recommended at age 9–12 years

instead of:

HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years

For the public health problem, Dr. Stefanos shared that HPV is the most common sexually transmitted infection in the U.S. Persistent infection can lead to precancers and cancers. An estimated 37,800 HPV-attributable cancers are diagnosed each year in the US.

HPV vaccination coverage has increased since its introduction, but it still lags behind other adolescent vaccines. NHANES data show that quadrivalent HPV type prevalence among sexually experienced females aged 14 to 24 years in the U.S. dropped from 18.5% in 2003 to 2006, the pre-vaccine era, to 2.8% in 2015 to 2018. This represents an 85% reduction. Similar declines were observed among sexually experienced females across different racial and ethnic groups. Declines in cervical precancers have been seen in women aged 20-24 years since 2008 and in women aged 25-29 years since 2016. Cervical cancer has been declining for several decades in the U.S., due to cervical cancer screening which allows for detection and treatment of precancers before progression to cancer. Continued declines in cervical cancer in women aged 21-24 years are likely a combination of both changes in screening recommendations and vaccination impact.

The CDC estimated the annual direct medical costs of HPV-attributable disease in 2020 U.S. dollars, published in 2023. The total yearly cost is $9.01 billion, with $4.05 billion attributed to treatment expenses.

The work group felt that HPV-related disease is of public health importance.

For the benefits, Dr. Stefanos explained that changing the wording for the routine HPV vaccination age to 9–12 years could offer greater clarity and flexibility. However, potential harms include the risk of separating the HPV vaccine from the broader adolescent platform, or at least creating the perception of doing so, and possible pushback from providers who prefer to vaccinate at age 11 years, as well as from some parents for various reasons.

Although ACIP currently allows vaccination starting at age 9 years, the wording has confused some partners. Changing the recommendation to state ages 9–12 years clearly would improve clarity. Some providers want to begin vaccination at age 9, but electronic health records often do not prompt vaccination at age 9 due to the current wording. Updating the language could help address this issue and support those aiming to start vaccination earlier.

In Clinical Decision Support for Immunization (CDSi) resources, the minimum age for HPV vaccination is 9 years, and the earliest recommended age is currently 11 years. Additionally, there is administrative guidance included in the CDSi resources that state the vaccination can be given starting at age 9 years.

While some systems reflect this in their prompts, most clinical decision support tools use the earliest recommended age to trigger alerts. As a result, prompts for HPV vaccination typically begin at age 11. Changing the wording of the routine vaccination recommendation to ages 9–12 years would update the earliest recommended age to 9 in CDSI tools, prompting HPV vaccination starting at age 9.

The policy under consideration is to change the recommended age wording to 9–12 years, not to set a new recommendation specifically for ages 9–10 years. A review was presented to ACIP in October. It found that starting HPV vaccination at ages 9–10 years was associated with higher series completion by age 13 compared to starting at 11–12 years. However, limitations in the studies prevent conclusions about cause and effect. Few children began vaccination at 9–10 years, and there may have been differences in families or providers vaccinating at ages 9–10 years. Additionally, multi-component interventions make it difficult to isolate the impact of initiation at ages 9–10 years.

For the harms, Dr. Stefanos shared that some have raised concerns that changing the wording may negatively affect the adolescent vaccination platform. While there are no data on what the potential harm might be, it is known that the HPV vaccine is often given alongside other vaccines. Among adolescents who had received the HPV vaccine, 69.5% received it at the same visit with at least one other vaccine. An additional concern is that changing the wording could lead to system prompts at age 9 years, and vaccination at that age may not be acceptable to some providers.

A majority of work group members felt that the anticipated desirable effects were moderate, while the undesirable effects were considered minimal or small. A majority of work group members felt that the desirable effects outweigh the undesirable effects and favor a change in wording.

For the acceptability and values domains, Dr. Stefanos shared that one study interviewed providers and nurses involved in an intervention including vaccination at age 9, and they generally had a positive experience. A small qualitative study in a rural setting found mixed opinions. Three clinician surveys were also conducted, with one showing that 61% of providers not currently recommending vaccination at age 9 were willing to do so. The surveys found that provider recommendations varied by provider specialty, patient age group, and framing of the recommendation. Only two studies in the systematic review examined parents' perceptions of vaccination at ages 9–10 years. While few parents reported receiving recommendations to vaccinate before age 11 years, most were willing to do so.

Dr. Stefanos summarized that the AAP recommends starting the HPV vaccination series between the ages of 9 and 12 years, and some stakeholders and advocacy groups support starting at age 9. Changing the wording would clarify that vaccination at age 9 aligns with ACIP recommendations. However, other stakeholders are concerned that this change could weaken the adolescent vaccination platform. In a limited number of studies, vaccination at ages 9–10 was acceptable to providers and parents.

Work group members felt that changing the wording of the routine vaccination age to 9–12 years was acceptable to stakeholders, with most responding "probably yes" or "yes." For parent values, limited data were available for review, and a plurality of work group members responded "don't know" to the question about whether parents feel that desirable effects of changing the

wording are large relative to the undesirable effects. Regarding uncertainty or variability in how much parents value changing the wording of the recommendation, a plurality indicated it was "probably not important," while a minority felt it was "probably important."

The remaining domains in the EtR framework and the summary work group interpretation will be presented at a future ACIP meeting.

Dr. Loehr commented that he has not found the adolescent platform to be useful, noting that in New York State, sixth graders require Tdap, and seventh graders need MenACWY, while HPV is often mixed in. He observed that most parents do not want multiple vaccines given at once. He expressed openness to hearing a defense of the adolescent platform to better understand the rationale behind recommending it.

Dr. Asturias shared that strong evidence supports the efficiency of a 1-dose approach, which would nearly halve program costs and reduce the number of doses needed to provide the same level of protection. He agreed with Dr. Loehr in discouraging the term "platform," emphasizing that the role of ACIP members is to base recommendations on evidence, prioritizing effectiveness, fewer doses, and safety.

Ms. Moser noted that data show the HPV vaccine is often given with other vaccines, even if not in every practice. She expressed concern that the undesirable effects may be underappreciated, pointing out that provider surveys indicate many parents are not ready to discuss vaccination at age 9. She also emphasized that the data on parental support for earlier vaccination were limited. Additionally, she suggested that some potential benefits, such as improving how the vaccine fits into the schedule, could be addressed without this change and CDSi tools could be enhanced to allow more flexibility for institutions that prefer to recommend HPV vaccine beginning at age 9 years. She questioned whether some of the stated benefits were as clear-cut as presented.

Ms. Lyons commented that the adolescent platform will likely be reviewed in connection with meningococcal vaccines, suggesting that changes to the platform may be forthcoming regardless. It was noted that this potential review should be considered and may reduce concerns about harm from altering the HPV vaccination schedule.

Dr. Lauri Markowitz (CDC/NCIRD) shared the work group’s next steps and considerations. The two policy questions under review are the wording of the recommendation for routine vaccination age and the number of doses in the recommended HPV vaccination series.

In October, the topic was introduced to ACIP along with a review of data on vaccination at ages 9 to 10. The work group found no strong evidence that starting at age 9 years improves coverage compared to starting at 11 to 12 years. The plan is to clarify the recommendation by changing the routine vaccination age wording to 9 through 12 years, making it clear that age 9 years is included. Dr. Stefanos presented part of the modified EtR today; because this is a minor wording change rather than a change to the recommended age, GRADE is not being used. The remainer of the EtR will be presented in June.

In October, the work group also introduced the topic of the number of doses in the HPV vaccination series and reviewed key studies supporting reduction in the number of doses, along with global updates on one-dose recommendations. Today’s presentations included updated data from major studies, a randomized trial (KEN SHE), U.S. coverage, and modeling. The work group will continue focusing on this policy question through June. At the June meeting, data from the ESCUDDO trial comparing one versus two doses will be presented, along with any additional data requested by ACIP, a full EtR framework with GRADE, and, if ready, votes on both policy questions.

Dr. Markowitz explained that ESCUDDO, the randomized trial in Costa Rica sponsored by the U.S. National Cancer Institute, is evaluating whether one dose of the bivalent or 9-valent HPV vaccine is noninferior to two doses in preventing HPV 16/18 infections in girls aged 12 to 16 years. It will also compare vaccinated participants with unvaccinated women using survey data. Results are expected before the June meeting and will be presented to ACIP.

Outstanding questions remain regarding the number of doses, especially in three key areas. First, on the duration of efficacy and immunogenicity of one dose, current data show protection through 15 to 16 years with no evidence of waning, and more data are expected. Second, there are no data on the protection at sites other than the cervix. Third, for males, 13 of the 16 studies reviewed included only females, and one-dose efficacy in males is not yet available. Some studies have found that antibody levels after one HPV vaccine dose are lower in adolescent males than in females; however, the clinical relevance is unclear.

In March 2024, Merck announced plans for clinical trials for 1-dose HPV vaccination. Two international, randomized, double-blind, efficacy clinical trials are planned, one in males 16-26 years of age, and one in females 16-26 years of age. The planned trials include elements regulators have deemed necessary, including endpoints other than persistent cervical infection and a comparison of 1-dose and 3-dose efficacy. Merck has been in discussions with FDA and EMA regarding trial design; regulatory feedback is anticipated in Q2 2025.

It would be considered off-label if ACIP recommends one dose at any age or a two-dose schedule for individuals aged 15 or older. Off-label use refers to anything not included in, or differing from, the FDA package insert. Manufacturers can only promote and provide education on FDA-licensed indications. It is important to note that ACIP has made many off-label recommendations in the past, and at least 46 licensed vaccines in the U.S. have some off-label recommendations, most of which apply to specific situations or subgroups.

The HPV Vaccines Work Group is considering potential modifications to current recommendations as data are reviewed. One option is expanding the 2-dose recommendation from ages 9 through 14 years to ages 9 through 26 years or through an older age. Another option under discussion is recommending 1 dose for certain age groups, such as 9 through 14 years, 9 through 20 years, or through an older age.

Dr. Markowitz concluded that all work group members support modifying the HPV vaccination schedule. However, there are differing views on expanding the 2-dose schedule or recommending 1 dose for certain age groups. The work group continues to review data and discuss the appropriate upper age range for these potential changes. She closed with questions for the committee on any questions or comments regarding the policy questions to be addressed, and what additional information ACIP would like to see before potentially voting at the next meeting.

Dr. Middleman commented on the importance of vaccination platforms for adolescents, drawing a parallel to the well-established platforms for infants and young children, which are deeply integrated into anticipatory guidance and comprehensive care. It was noted that adolescent platforms serve a similar purpose and contribute to consistent healthcare delivery. Data from the 2007 NCQA State of Health Care Quality report showed that adolescent immunization rates among commercial payers rose from 10.5% in 1998 to 57.7% by 2006, following the introduction of new adolescent vaccines and the VFC program. This suggests that the formation of the adolescent platform significantly improved vaccination rates. Additionally, upcoming data from Dr. Zimet is expected to show that many parents value the structure and expectations provided by vaccination platforms. Using existing data was encouraged when evaluating the role of platforms in adolescent immunization.

Ms. Arthur noted that the company is pursuing an FDA indication for a 1-dose HPV vaccine, similar to the previous change from a 3-dose to a 2-dose schedule. She emphasized the importance of alignment between agencies like the FDA and the CDC/ACIP process. She also highlighted that the company would address key data gaps discussed during the meeting, including the efficacy of 1 dose in males. Ms. Arthur stressed the importance of maintaining consistency and high evidentiary standards and encouraged consideration of all available evidence in the decision-making process.

Ms. Lyons encouraged the work group to review the small number of states requiring the HPV vaccine to ensure that moving to a 1-dose schedule or making other changes does not impact existing school entry requirements.

Dr. Loehr responded that he is comfortable with the idea that earlier dosing provides better protection, referencing a slide from the first presentation. He acknowledged that a 1-dose schedule has a lower seropositivity rate but noted uncertainty about the clinical relevance of that difference. He referenced Dr. Kim's point that indirect effects may be more impactful than seropositivity. Dr. Loehr stated he would be more comfortable supporting fewer doses if there were evidence that lower seropositivity is not clinically significant. He expressed interest in seeing more data on that issue.

Dr. Markowitz clarified that Dr. Kim was referring to vaccine efficacy, noting that strong herd protection could offset a small decline in individual efficacy. She explained that while antibody titers are lower with one dose compared to two or three, no established minimum antibody level is required for protection. Therefore, the clinical relevance of lower titers is uncertain. Dr. Markowitz emphasized that efficacy data from studies such as KEN SHE, the Costa Rica vaccine trial, and the IARC India study show high protection with one, two, or three doses.

Dr. O'Leary noted that the American Academy of Pediatrics recommends HPV vaccination at ages 9–12 years. He expressed that he has not seen compelling evidence supporting the concept of the adolescent platform. He acknowledged that observational data suggest that allowing vaccination at ages 9–10 may be beneficial. Ultimately, he emphasized that this may be the only case where the wording of an ACIP recommendation itself serves as a barrier to vaccination, by not clearly emphasizing the flexibility to begin at age 9.

Dr. Middleman expressed that the primary concern of the Society for Adolescent Health and Medicine is to follow the evidence. While a change in recommendation would make sense if the evidence strongly supported it, there is concern that current evidence may not be sufficient and that potential harms are also hard to conclusively identify. The goal is to increase HPV vaccination without unintentionally weakening the broader adolescent vaccination platform. It was emphasized that any changes should be grounded in evidence and that the current wording does not appear to discourage vaccination.

Ms. Moser emphasized that this is a communication issue, not a change in recommendation. Since HPV vaccination is already allowed at age 9 years, she cautioned that changing the wording could raise concerns among parents and providers, especially given sensitivities around the vaccine. The impact of the wording change on overall uptake should be carefully considered.

CYTOMEGALOVIRUS (CMV) VACCINES

Dr. Denise Jamieson (ACIP, Work Group Chair) introduced the launch of the Cytomegalovirus (CMV) Vaccines Work Group. The work group will review CMV and congenital CMV (cCMV)

epidemiology and disease burden, CMV vaccine safety and immunogenicity data, and initial work group considerations for CMV vaccine policy.

Dr. Tatiana Lanzieri (CDC/NCIRD) reviewed the epidemiology and disease burden of CMV and cCMV. cCMV is the most common infectious cause of congenital birth defects in the U.S., affecting over 16,000 newborns annually and is the leading non-genetic cause of childhood hearing loss. It causes an estimated 80 neonatal deaths and nearly 3,000 cases of cCMV disease each year, with long-term outcomes including hearing loss, cognitive, or motor impairments.

Congenital CMV may present at birth with signs like rash, enlarged liver or spleen, or a small head. Diagnosis is typically by PCR or culture of urine, blood, or cerebrospinal fluid within 21 days of life. Most newborns with cCMV infection have no clinical signs at birth and go undiagnosed. To improve detection, some U.S. states have implemented targeted or universal screening for cCMV.

In the U.S., two states have implemented universal newborn screening for cCMV, while 11 conduct targeted hearing screening. Three of those states also perform symptom-based screening. Additionally, 13 states are conducting cCMV surveillance. Data from all states are unavailable; cCMV prevalence likely varies by state due to differences in maternal age, demographics, and population-specific CMV rates. Data from CDC's National Health and Nutrition Examination Survey (NHANES) has shown that CMV IgG seroprevalence increases with age. From the 1988-1994 NHANES cycle to the 1999-2004 cycle, age-specific rates among those aged 6–49 years remained stable. However, from 2011-2012 to 2017-2020, seroprevalence among children aged 1–5 years rose from 21% to 29%. Updated testing for ages 6–59 years from the 2017–2020 NHANES cycle is ongoing.

CMV seroprevalence is higher among non-Hispanic Black and Hispanic women compared to non-Hispanic White women. Among women aged 20–29, rates are 36% for non-Hispanic White and 77–81% for non-Hispanic Black and Hispanic women.

Seronegative women are at risk for primary CMV infection during pregnancy, while seropositive women may experience reinfection. The risk of vertical transmission is highest with primary infection and increases by trimester, but severe outcomes like hearing loss are more likely with first-trimester infections. Non-primary infections have lower vertical transmission rates but can still cause cCMV disease if transmission occurs early in pregnancy. These findings suggest that a CMV vaccine should be given before pregnancy to protect against vertical transmission following primary infection.

The incidence of CMV primary infection and reinfection varies across populations. Proportions of cCMV infections due to non-primary maternal infection (NPI) vary with maternal seroprevalence. Still, the risk of cCMV infection is higher when the mother is CMV seronegative before pregnancy. About 12,000 (75%) cCMV infections in the U.S. every year may be attributable to primary maternal infections.

Young children play a key role in CMV transmission, shedding high virus levels in saliva and urine for months after infection. Shedding peaks at 1 to 2 years of age, which is also when many first-time mothers in the U.S. have a second pregnancy.

Modeling suggests that a vaccine given to infants, even if the duration of protection was short, could impact transmission to pregnant mothers and decrease cCMV infections. Models predict a

varying impact depending on the population to be vaccinated, vaccine efficacy, duration of protection, and coverage.

Dr. Lanzieri summarized that CMV and cCMV epidemiology are complex and have many unknowns. In the U.S., most cCMV cases are linked to primary maternal infection, while globally, non-primary infections are more common. A CMV vaccine could reduce disease burden by providing long-lasting protection before and during pregnancy or indirectly protecting pregnant women if given to toddlers.

Dr. Robert Paris (Moderna) presented an overview of the investigational CMV vaccine, mRNA-1647. Globally, cCMV affects 1 in 70 to 1 in 208 births. It occurs in about 1 in 200 births in the US, with annual healthcare costs of $6 to $7 billion. Approximately 1 in 5 infants with cCMV (symptomatic or asymptomatic at birth) develop long-term disability. Limited options for prevention, screening, and treatment make cCMV a major unmet medical need and a high priority for vaccine development, as recognized by the WHO and the U.S. National Academy of Medicine.

The clinical program aims to prevent CMV infection in seronegative women by vaccinating women of childbearing age before pregnancy, when the risk of transmission and complications is highest. Due to the low incidence of cCMV and long-term outcomes, a large, lengthy Phase 3 trial would be impractical. Instead, the initial indication will target CMV prevention in females aged 16 to 40 years of age, regardless of CMV serostatus.

Moderna's investigational CMV vaccine (mRNA-1647) contains six mRNAs designed to elicit both humoral and cellular immunity. Antigens were selected to prevent CMV infection and fetal transmission. Five mRNAs encode the pentamer subunits, required for CMV entry into most cell types; the other mRNA encodes glycoprotein B which mediates fusion of virus and host membranes during cell entry, which is necessary for viral infectivity. Prior gB-based vaccines showed 43–50% efficacy; adding the pentamer glycoprotein in mRNA-1647 is expected to improve efficacy.

The Phase 1 trial was a randomized, placebo-controlled study of mRNA-1647 in healthy adults aged 18 to 49 years of age, assessing doses from 30 to 300 micrograms. Among 154 participants, over half were CMV negative, and the vaccine was well tolerated with no safety concerns. CMV-negative and -positive participants showed neutralizing antibodies, binding antibodies, and cell-mediated responses. These results supported continued development and informed dose selection within a narrower range.

In the Phase 2 study, 315 adults aged 18 to 40 were randomized 3:1 to receive mRNA-1647 or placebo on a 0-, 2-, and 6-month schedule. About 70% were CMV negative and followed for approximately 12 months post-vaccination. Dose levels of 50, 100, and 150 micrograms were evaluated in Part 1, while Part 2 focused on additional safety and immunogenicity data for the 100 microgram dose which was the dose selected for the Phase 3 efficacy trial. The primary objectives were safety and neutralizing antibody responses.

Solicited local reactions were self-reported by participants within 7 days for each injection. Pain was the most frequent local reaction, reported by about 80% of participants; local reactions were mostly grade 1 or 2 and generally 1-3 days in duration. For systemic reactogenicity, headache, fatigue, myalgia, and chills were most common. There was some increase in systemic reactions with second and third doses. Systemic reactions were generally grade 1 or 2 and of 1-2 days duration. Related medically-attended adverse events (primarily local injection site reactions) occurred more frequently in vaccine recipients than placebo recipients. No significant safety concerns were identified during the study.

Neutralizing antibody response to mRNA-1647 was based on both epithelial cell and fibroblast cell assays to assess responses to both the pentamer and the gB antigen. Among CMV seronegative participants, as assessed by epithelial cell infection, GMTs increased after each dose and remained above the GMT seen in natural infection through 18 months; as assessed by fibroblast infection, GMTs reached the natural infection GMT at months 3 and 7, and then declined at months 12 and 18. Among seropositive participants, after the first dose antibodies against epithelial cell infection increased approximately 17-fold over baseline, and antibodies against fibroblast infection increased about 2.4-fold over baseline; the second and third doses did not appear to substantially increase antibody titers. GMTs for both assays remained above the natural infection GMT through month 18.

Demonstrating durable immune responses is key for vaccine implementation. Long-term follow-up is underway in Phase 2 and 3 trials to assess immunogenicity and efficacy. Phase 2 participants were offered enrollment in an extension study with three additional years of follow-up. An interim analysis was recently conducted on data up to 36 months post-vaccination. Durable immune response was observed through three years after the first vaccination among seronegative participants, with GMTs remaining stable from 18 to 36 months for both assays; Dr. Paris stated that results were similar for the seropositive cohort.

Dr. Paris summarized that mRNA-1647 was generally well tolerated with no safety concerns identified. The 3-dose 100 microgram regimen was highly immunogenic. Neutralizing antibody GMTs against epithelial infection remained above natural infection GMT through 12 months after the last vaccination in SMV-seronegative participants; a boosting effect was observed in CMV-seronegative participants. The vaccine induced durable epithelial and fibroblast neutralizing antibody responses lasting up to three years.

The Phase 3 pivotal efficacy trial is a randomized, observer-blind, placebo-controlled study enrolling females aged 16 to 40 years of age. CMV-positive participants help assess safety and immunogenicity, while CMV-negative participants aged 20 and older had to have regular contact with a child under five years of age. Pregnancy was an exclusion criterion. Participants were randomized 1:1 to receive 100 micrograms of mRNA-1647 or placebo on a 0-, 2-, and 6-month schedule, with two years of follow-up after the third dose to assess efficacy.

The trial's primary objective is to evaluate vaccine efficacy against primary CMV infection in the seronegative cohort, measured by seroconversion to CMV IgG positivity. Participants undergo serology testing every three months starting 28 days after the last dose. Immunogenicity is a key secondary objective, using endpoints and assays consistent with prior studies. CMV shedding is also being assessed through PCR detection of CMV DNA in urine samples after seroconversion and in CMV-positive participants throughout the study.

The study is being conducted in 290 sites in 13 countries. Enrollment was completed in October 2023, with 7,484 participants enrolled; 80% were CMV-seronegative and 20% were CMV-seropositive. The mRNA-1647 Phase 3 efficacy trial includes two planned analyses. An independent Data Safety Monitoring Board (DSMB) conducted an interim efficacy analysis in December 2024. The DSMB found no safety concerns and recommended that the study continue as planned in a blinded manner. The final efficacy analysis is anticipated in late 2025.

Dr. Paris concluded that mRNA-1647 has been generally well tolerated in adults aged 18 to 40, regardless of CMV serostatus, in Phase 1 and 2 trials. The DSMB identified no safety concerns during its review of unblinded Phase 3 data. In seronegative participants, the vaccine elicited antibody responses that exceeded those seen in natural infection, with immune persistence observed through three years. In seropositive participants, vaccination boosted immune responses above baseline after the first dose. The Phase 3 efficacy trial is ongoing in

seronegative and seropositive females aged 16 to 40 years, with the final efficacy analysis expected by the end of this year.

Dr. Shaw asked about previous studies using subunit vaccines, specifically those containing the pentamer complex and glycoprotein B ectodomain in nonhuman primate model, that found that high neutralizing antibody levels did not prevent substantial horizontal transmission. He inquired if the expectation is that the mRNA platform or use in humans will produce better outcomes. He also asked which specific antibody responses are believed to be necessary to prevent vertical transmission to the infant.

Dr. Paris responded that there is still limited understanding of the specific or dominant antibody response required to prevent vertical transmission. Regarding the nonhuman primate study, he acknowledged familiarity with it, stating it was likely conducted by Pfizer and involved a recombinant pentamer vaccine with glycoprotein B. He noted limitations in the study design, particularly related to the transmission model.

Dr. Wu (Moderna) noted that the study used rhesus CMV (RhCMV), which, while part of the same beta herpesvirus family, may have a different pathogenesis than human CMV. A key challenge in the CMV research community is the inability to use human CMV to infect animal models. As a result, studies must rely on species-specific CMV, which limits how well animal data can be translated to humans.

Dr. Zucker asked whether there is a known correlate of protection for CMV, noting that, based on the discussion, there may not be one currently identified. She also asked about expectations for individuals who are already seropositive, questioning whether vaccination is expected to prevent reinfection or if those individuals would remain at risk upon re-exposure.

Dr. Paris responded that there is no known correlate of protection for CMV. Seropositive individuals were deliberately included in the clinical development program because they still face a significant risk of vertical transmission due to reinfection or reactivation, with most cases now believed to result from reinfection. Demonstrating impact on reinfection is challenging, as current research tools are limited and unsuited for Phase 3 trials. Post-licensure, the plan will expand the clinical program to assess real-world effectiveness, including the impact on congenital infection in both CMV-negative and CMV-positive populations. While the biological significance is not fully understood, a reduction in viral shedding could indicate the vaccine's potential to limit viral replication and reduce transmission in seropositive individuals during pregnancy.

Dr. Zucker followed up by noting that approximately 1,800 participants in the study were seropositive and asked about the expected incidence of CMV shedding over the course of the study.

Dr. Paris responded that the point prevalence of CMV shedding in seropositive individuals likely ranges from 5% to 20%, depending on how recently they were infected. He noted that the study monitors this continuously and collects specimens frequently enough to expect detection of a significant frequency of viral shedding in this population.

Dr. Asturias inquired whether the antibodies have been tested for their ability to neutralize various strains of CMV and how many strains they can neutralize. He also acknowledged that cellular immunity data from the Phase 2 trial won't be presented, but wondered if there were any insights on cellular immunity development from the Phase 1 study.

Dr. Paris referenced a paper published in the *Journal of Virology* that assessed wild-type clinical strains of CMV using Phase 1 trial data. The study found no significant impact on neutralization across different viral strains. Regarding T-cell immunity, Dr. Paris confirmed that Phase 1 data

showed the induction of T-cell immunity using an ELISPOT assay. The team is now evaluating these data with a more recent ex vivo intracellular cytokine assay which they hope to present data at an upcoming meeting, showing evidence of T-cell responses immediately after vaccination and up to 12 months later. He also noted that, similar to other mRNA-based vaccines, they expect robust T-cell immunity.

Dr. Tatiana Lanzieri (CDC/NCIRD) followed up with the work group's initial considerations for CMV vaccine policy. The burden of congenital CMV is substantial, yet awareness is low. Vaccine acceptability among the public and providers, as well as the feasibility of implementation, needs assessment. Primary maternal infections, which vary by population susceptibility, cause most cCMV infections in the U.S. and lead to more severe disease in the first trimester. Vaccination before pregnancy and long-lasting protection throughout childbearing years are necessary. CMV seroprevalence increases with age, but certain populations have high prevalence by adolescence.

The Moderna CMV mRNA vaccine candidate encodes the CMV gB and pentamer complex with a three-dose schedule over six months. The ongoing Phase 3 trial includes 7,500 non-pregnant females aged 16 to 40 years of age, with about 5,000 CMV seronegative at enrollment. The seronegative group will be evaluated for the primary endpoint of vaccine efficacy, while safety and reactogenicity will be assessed in all participants. Participants will be followed for 24 months after the third dose, with a subset followed for 48 months.

The work group reviewed data from Moderna's mRNA-1647 Phase 1 and Phase 2 trials, with initial findings indicating no safety concerns and promising immunogenicity. There is a need to better understand differences in neutralizing antibody levels against epithelial cell and fibroblast entry and the cell-mediated immune response, including antibody-dependent cellular cytotoxicity and phagocytosis. Regarding long-term protection, the Phase 2 extension data show antibody persistence for at least three years after the first dose. Still, it remains important to determine if protection lasts throughout childbearing years.

Moderna's planned vaccine indication is for non-pregnant females aged 16–40 years, with a 3-dose series over 6 months. Efficacy will be assessed for primary infection in initially CMV-seronegative subjects. Data on immunity duration will be limited; protection is needed before pregnancy and throughout childbearing years. Efficacy against vertical transmission and cCMV infection or disease is yet to be determined. A better understanding of the correlates of protection against vertical transmission is needed. The benefit for CMV-seropositive individuals remains unclear, and serological testing prior to vaccination presents implementation challenges. Vaccine recommendations may evolve as future clinical trial data becomes available for other groups, such as adolescents and transplant patients. Over the next several months, the CMV work group will continue to review data as it becomes available and address additional domains within the EtR framework.

Dr. Lanzieri concluded by emphasizing that an effective CMV vaccine could reduce disease burden, with over 16,000 children born with cCMV infection in the U.S. each year, nearly 3,000 with cCMV disease. The mRNA-1647 CMV vaccine has shown safety and immunogenic in Phase 1 and 2 trials, with efficacy data from the ongoing Phase 3 trial expected next year. The vaccine should be given before pregnancy to prevent infection and reduce vertical transmission, especially in the first trimester. Protection against non-primary infections is also important. Challenges may include low awareness of cCMV and the need for serological screening before vaccination. The CMV ACIP work group will regularly review data and develop vaccine policy options.

Dr. Shaw inquired about potential plans to test the vaccine in transplantation settings, where reactivated CMV disease remains a significant issue. He noted that CMV reactivation in aging

immune systems can skew the CD8 cell repertoire and asked if there are any ongoing studies or plans related to this context.

Dr. Paris confirmed that testing the vaccine in transplant settings is an active part of their program. Moderna is currently conducting a study on hematopoietic stem cell transplant recipients, with ongoing enrollment. He acknowledged the significant unmet medical need in both stem cell and solid organ transplant populations due to CMV. Regarding the impact of CMV on aging and immune response, Dr. Paris noted ongoing discussions and welcomed input from the work group on how to address this issue as it relates to an aging population.

U.S. MEASLES UPDATE

Dr. Talbot began her introduction of the session with a statement that she finds it devastating that this update was needed; the measles vaccine is very effective with a long duration of protection, and children in the U.S. should not be dying of measles.

CAPT David Sugerman (CDC/NCIRD) shared an update on measles. Before the measles vaccine, there were 3 to 4 million cases annually in the US, with 500,000 reported. Cases dropped significantly after the vaccine was introduced in 1963. In 1989, the ACIP recommended a second dose at school entry due to school outbreaks. By 2000, the U.S. achieved measles elimination, defined as the absence of continuous spread of the disease for 12 months.

Since measles elimination, there have been 11 large outbreaks in the U.S. with more than 50 cases. Seven outbreaks occurred in the last 5 years, and nine were among close-knit communities with low vaccine coverage. Coverage in these communities was far below the 95% threshold needed for herd immunity. The most recent outbreak, concentrated in Gaines County, Texas, involved a 2-dose MMR coverage rate of 82% in public schools, with true coverage likely lower due to homeschooling or private schools without reported coverage. The outbreak spread to 21 additional counties in Texas and three counties in eastern New Mexico.

From elimination until the COVID-19 pandemic, MMR coverage remained above the 95% threshold needed for herd immunity. However, coverage has decreased since the pandemic. During the 2023–2024 school year, approximately 280,000 (7%) kindergarteners lacked documentation of two MMR doses, potentially putting them at risk for measles. MMR coverage also varies across states, with several reporting coverage below 90%. Coverage is also quite heterogeneous at the county level, potentially hiding true outbreak risk.

Following the COVID-19 pandemic, measles has resurged due to increased transmission abroad, a surge in international travel, and declines in vaccination, especially in close-knit communities with already low coverage. Cases rose from 59 in 2023 to 285 in 2024, and by April 10, 2025, had more than doubled to 712.

From 2023 to 2025, the number of outbreaks fluctuated between 4 and 16 per year, while the proportion of total cases linked to outbreaks increased from half to 93% this year, with five outbreaks ongoing. Efforts will focus on tracking the duration of these outbreaks and working closely with state and local partners to ensure the 12-month threshold is not exceeded, preserving elimination status, especially with ongoing spring and summer travel and congregate events.

As of April 10, 2025, 712 cases have been reported by 25 states in 2025; most states are reporting no or limited spread from importations. Over 90% of current national cases are linked to the southwest outbreak, driven by transmission in close-knit, under-vaccinated communities with low vaccine coverage. There are currently large outbreaks in the same close-knit community as the southwest outbreak in Ontario, Canada, and Chihuahua, Mexico.

There are two circulating measles genotypes in the US: B3 and D8, with D8 being the predominant genotype. Four distinct sequence identifiers (DSIDs) have been identified for B3 and six for D8 this year. In this outbreak, most sequences are D8 DSID 9171, found in Texas, Oklahoma, New Mexico, Kansas, and Chihuahua, Mexico, and Ontario, Canada, within the same under-vaccinated community. Four other D8 DSIDs, differing by one to two nucleotides, are also linked to the Texas outbreak. Most B3 sequences are from Vietnam, which is experiencing a large outbreak.

CDC's 2025 measles outbreak response efforts include a variety of initiatives across different areas. From March 4 through April 1, 15 CDC deployers provided on-site technical assistance in Texas, with additional teams deploying this week. Remote technical assistance was provided to state health departments. Biweekly national measles calls with public health partners and trilateral calls with Canada and Mexico were held to share updates and lessons learned. Additional MMR vaccine doses were made available to health departments. Provider outreach included releasing a Health Alert Network (HAN) advisory on the expanding measles outbreak in Texas and New Mexico and guidance for the upcoming travel season. Clinician Outreach and Communication Activity (COCA) and Epi-X alerts were issued, and a provider letter was shared summarizing routine and outbreak-related MMR vaccination recommendations. Laboratory support efforts included coordination with the Association of Public Health Laboratories Vaccine-Preventable Disease Reference Centers for genotyping and sequencing; expanded testing for wastewater surveillance with the National Wastewater Surveillance System and the Center of Excellence in Texas; and ongoing modeling to assess risk.

Dr. Asturias noted that in the Texas outbreak, with two deaths of school-age children and 41 reported cases in Lubbock, there's a case fatality rate of about 4.8%, much higher than the typical measles case fatality rate of 1–2 per thousand in outbreak situations. He questioned whether this higher mortality might reflect the underreporting of measles cases in the jurisdiction.

CAPT Sugerman confirmed that there are likely many underreported measles cases. In discussions with families in Texas, some have mentioned prior cases that recovered without testing, while others had cases but never sought treatment. He highlighted under-testing, under-diagnosis, and under-reporting as contributing factors resulting in a smaller denominator. This is particularly common in close-knit communities with lower healthcare-seeking behavior.

Dr. Zucker asked about resource mobilization during the Texas outbreak, drawing on experience managing the largest measles outbreak in New York City since 1992. The response required significant resources, with costs around $8.4 million and 7% of the health department involved. Dr. Zucker inquired about the scale of the response in Texas and other areas with ongoing outbreaks, specifically regarding resource mobilization to end transmission.

CAPT Sugerman shared that Texas has requested significant resources. With COVID-19 funding diminishing, Texas is reallocating staff and resources from other domains and regions to support the measles response. Additional financial and personnel support is needed, estimated at $30,000 to $50,000 per measles case for public health response. While efforts are being

made to support Texas and other jurisdictions, securing sufficient resources and personnel remains challenging.

Dr. Zucker emphasized that it's not just about money, but also the need for adequate staff. It was noted that contact investigations, follow-up communications, and other tasks require significant personnel, especially for an outbreak of this scale.

Ms. Moser asked when the U.S. could lose its measles elimination status, noting that elimination is defined by the absence of continued spread for 12 months.

CAPT Sugerman confirmed that the U.S. would lose its measles elimination status after 12 months of ongoing circulation of the same sequence. With four months in, this would occur around January 20th of the following year.

Dr. Kevin Ault (ACOG) inquired about the number of stillbirths, miscarriages, and pre-term deliveries during the current outbreak in Texas, noting the considerable morbidity among pregnant women in the 2019 New York City outbreak.

CAPT Sugerman confirmed that there have been no reports of stillbirths or miscarriages but noted that measles cases in pregnant women, including one case of congenital measles, have been tracked. He emphasized that pregnant women with measles face significant risks, including preterm labor, complicated deliveries, and negative infant outcomes. Additionally, there have been exposures in hospitals, where pregnant women may not initially show symptoms or a rash, leading to exposures of others.

As a family physician, Dr. Loehr mentioned seeing adults born between 1963 and 1968 who are unsure whether they received the killed virus vaccine and need a booster or titer. He noted that research indicates only a minority from those years received the killed virus vaccine. He asked for suggestions for primary care doctors when facing this question from patients.

CAPT Sugerman confirmed that less than 5% of vaccines administered between 1963 and 1967 were the inactivated version, which had lower efficacy. He emphasized that most people are likely protected. He stresses the importance of primary care doctors having direct communication with patients. Some may request a titer, while others may prefer an additional vaccine. Overall, the risk at the population level is very low due to the small number of individuals who received the inactivated vaccine.

Dr. Talbot highlighted the importance of the work done by CDC colleagues and of available vaccines, thanking everyone involved.

Dr. Wharton announced that a new webcast link for the following day’s meeting would be posted later in the evening and reminded attendees that it would not be the same link used that day. She thanked all ACIP members for their flexibility in attending the rescheduled meeting, as well as the ex officio members, liaisons, and work group leads for their excellent work. She also expressed appreciation to the ACIP Secretariat for their preparation, CDC’s Office of Communications and NCIRD’s communications team for their excellent support, and the engineers at the CDC’s Global Communications Center for helping the meeting run smoothly. She noted that while many challenges had been anticipated, most were avoided thanks to the collective efforts of everyone involved.

With no additional business posed for the day, the ACIP meeting stood in recess until 8:00 AM on April 16, 2025.

WEDNESDAY: APRIL 16, 2025

WELCOME AND INTRODUCTIONS

Call to Order/Roll Call

Dr. Keipp Talbot (ACIP Chair) called to order and presided over the April 16, 2025, 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 officio members, and liaison representatives is included in the appendices at the end of this summary document. No COIs were identified for the second day of this meeting. Dr. Chen noted that there was no conflict of interest but stated a decision to abstain from voting on chikungunya vaccine items due to prior involvement in data and safety monitoring board activities. Dr. Kuchel stated there were no current conflicts of interest but would abstain from voting on the RSV recommendations due to having served as a consultant for approximately six months about a decade ago.

MENINGOCOCCAL VACCINES

Dr. Jamie Loehr (ACIP, Work Group Chair) introduced the meningococcal vaccines session. The Meningococcal Vaccines Work Group has been developing recommendation options for GSK's pentavalent MenABCWY vaccine, which was licensed on February 14, 2025. A vote on this product and a VFC vote is scheduled for this meeting. The work group is also discussing Sanofi's MenACWY (MenQuadfi®) for use in infants. An extension of licensure of this product to age 6 weeks is anticipated in May 2025, to be followed by an ACIP vote in June 2025. Additionally, the work group continues to discuss possible changes to the meningococcal vaccine schedule for adolescents.

In October 2024, the work group presented an EtR for the GSK pentavalent vaccine and made a recommendation to the ACIP. At that meeting, the work group also recommended changing the BEXSERO schedule from 0, 1 month to 0, 6 months based on evidence that longer spacing improved immunogenicity. As a result, some calculations and evaluations had to be redone. The GSK pentavalent vaccine, when compared to BEXSERO with updated data, showed comparatively lower immunogenicity. Some analyses revealed that MenB alone performed better than the pentavalent vaccine, with non-overlapping confidence intervals. However, there is no established clinical correlate of protection, and the clinical significance of these findings remains uncertain. The work group reviewed the changes and updated the EtR accordingly, but the overall recommendation to ACIP did not change.

Dr. Sarah Schillie (CDC/NCIRD) reviewed the updated EtR and work group considerations for the GSK pentavalent MenABCWY vaccine. Currently, ACIP recommends one MenACWY dose at age 11–12 years and a booster dose at age 16 years. Two MenB doses are recommended at age 16–23 years based on shared clinical decision-making, with a preferred age range of 16–18 years.

For persons ≥2 months of age at increased risk, MenACWY vaccines are recommended for specific medical conditions, some microbiologists, exposure during an outbreak, travel to

hyperendemic areas, and first-year college students. MenB vaccines are recommended for persons ≥10 years of age with certain medical conditions, some microbiologists, and those with exposure during an outbreak.

MenACWY vaccine products are interchangeable; while using the same brand is preferred, it is not required for all doses in a series. In contrast, MenB vaccine products are not interchangeable. MenB vaccines from the same manufacturer must be used for all doses in the series, including booster doses.

Two MenABCWY vaccines are available in the U.S., one made by Pfizer (PENBRAYA™) and the other by GSK (PENMENVY). Both vaccines combine an existing MenACWY and MenB vaccine. They are both licensed as a two-dose series, with doses separated by six months for persons aged 10–25 years. The Pfizer vaccine was licensed in October 2023, and the ACIP voted on recommendations at its October 2023 meeting. The GSK vaccine was licensed on February 14, 2025, and the ACIP will vote on recommendations for this vaccine today.

ACIP recommended that the Pfizer pentavalent vaccine may be used when both MenACWY and MenB vaccines are indicated at the same visit for healthy persons aged 16–23 years when shared clinical decision-making favors MenB vaccination, and for persons aged ≥10 years who are at increased risk for meningococcal disease.

Due to a lack of direct comparison data, the meningococcal vaccines work group assessed the Pfizer and GSK pentavalent vaccines separately. The MenACWY and MenB vaccine indications have not changed with the availability of the pentavalent vaccines. ACIP previously expressed a preference to harmonize recommendations for the Pfizer and GSK pentavalent vaccines unless a vaccine-specific reason for differences exists.

Immunogenicity of meningococcal vaccines is measured using various assays. Traditional human serum bactericidal antibody (hSBA) assays use exogenous complement to assess seroprotection, seroresponse, or GMTs. For MenB strains, endogenous complement can be used to measure immune response against diverse serogroup B strains. However, a serologic correlate of protection exists only for serogroup C.

GSK's pentavalent vaccine was assessed using three policy questions.

Policy question 1

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?

– For example, 16 year-olds who decide to receive MenB vaccine based on shared clinical decision-making

Policy question 2

Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only?

–For example, 11–12 year-olds

Policy question 3

Should the GSK pentavalent vaccine be included as an option for people currently recommended to receive MenB only?

– For example, during a serogroup B outbreak

For ease of communication, the quadrivalent MenACWY vaccine is referred to as "Q," the MenB vaccine as "B," and the pentavalent vaccine as "P." Using this nomenclature, the current ACIP recommendation can be summarized as Q-QB-B (if MenB vaccine is included) or Q-Q (if it is

not). The work group supported the use of GSK's pentavalent vaccine as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines at the same visit (Q-P-B), but not for those currently recommended to receive only MenACWY (P-P) or Men B (Q-P-P).

Dr. Schillie then reviewed the updated EtR. For public health problem, Dr. Schillie shared that meningococcal disease incidence in the U.S. declined dramatically from 1996 to 2019, with further decreases in 2020 and 2021. This decline began before vaccine introduction. Since 2022, however, cases have increased. Preliminary 2024 data show 503 cases, the highest incidence since 2013, at 0.15 per 100,000 population. The work group felt that invasive meningococcal disease is of public health importance for all three policy questions for the GSK pentavalent vaccine.

The work group previously assessed the GSK pentavalent vaccine using BEXSERO administered on a 0-, 2-month schedule as the comparator for the MenB antigens. BEXSERO was initially licensed as a two-dose series given at 0 and ≥1 month. The dosing schedule was recently changed to 0, 6 months, and because longer intervals improve immunogenicity, this raises the bar for comparison.

The clinical significance of the comparatively lower immunogenicity is uncertain, as no serologic correlate of protection exists for serogroup B disease. The work group's recommendations for use of the GSK pentavalent vaccine remain unchanged, but the work group believes ACIP should consider the changes in comparative immunogenicity during its deliberations.

The work group's previous synthesis presented to ACIP found the GSK pentavalent vaccine noninferior based on hSBA titers to MenB on a 0, 2 month schedule for three strains and on a 0, 6 month schedule for two strains. Noninferiority was not demonstrated for the PorA indicator strain at either the 0–2 month or 0–6 month comparison. This strain is important as it represents the vaccine's full outer membrane vesicle component and may impact cross-protection. Success criteria for MenB protection using an endogenous complement hSBA assay were met against a broad range of strains, despite lower point estimates compared to MenB on a 0, 6 month schedule. Findings regarding serogroups A, C, W, and Y immunogenicity and safety remain unchanged. The pentavalent vaccine had a similar safety profile to MenB, with slightly more unsolicited adverse events than MenB; there were more adverse events with the pentavalent vaccine than were seen with MenACWY.

Final analyses of immunogenicity, as reflected in the package insert, were slightly different than what had been previously shared with ACIP; Dr. Schillie reviewed a number of these differences for the committee. Most differences were small and they did not change the work group's overall interpretation.

The work group previously determined that the desirable anticipated effects of the GSK pentavalent vaccine were small for all three policy questions. This assessment remains unchanged. The work group previously determined the undesirable effects to be minimal for policy question 1 and small or minimal for the other policy questions. This assessment remains unchanged. For policy question 1, based on new immunogenicity data, a minority of the work group now favors "favors comparison." The overall certainty of evidence for short-term immunity was rated as moderate or low for the three policy questions. This determination remains unchanged from the work group's previous assessment. The overall certainty of evidence for serious adverse events was rated as moderate or low for the three policy questions. This determination also remains unchanged from the work group's previous assessment.

For resource use, Dr. Schillie shared that the expected price of the GSK pentavalent vaccine remains lower than the combined prices of the component vaccines. For policy question 1, the

health outcomes are identical for the pentavalent vaccine and comparator, each preventing 91 cases of invasive meningococcal disease and 14 deaths compared to no vaccination. Regarding incremental cost-effectiveness ratios, as previously shared, QPB is cost-saving compared to the current strategy of Q-QB-B, saving $175 million with no difference in quality-adjusted life years. In the sensitivity analysis with updated price assumptions, QPB remained cost-saving. The work group concluded that policy question 1 would be an efficient allocation of resources, but this varied for policy questions 2 and 3. The work group's assessment remains unchanged.

The work group continues to believe there is sufficient information to support a recommendation. The work group recommends the pentavalent vaccine for policy question 1, does not recommend it for policy question 2, and is divided on policy question 3. Recommending for policy question 1 aligns with the existing recommendation for the Pfizer pentavalent vaccine.

Policy question 1 typically involves one dose of the pentavalent vaccine and one dose of MenB to complete the MenB series. However, the studies evaluated two doses of the pentavalent vaccine. Recommendations for both pentavalent vaccines may be revisited in future adolescent schedule discussions.

The proposed vote language is:

*ACIP recommends GSK's MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit**

*1) healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine and 2) persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia)

Dr. Talbot asked whether these products can be mixed and matched with the availability of the new QPB, the existing version, and the potential for another in the future.

Dr. Schillie responded that the manufacturer's MenB vaccine products remain non-interchangeable. Only Pfizer products can be used if a Pfizer product was used to initiate the series, and the same applies to the GSK product.

Dr. Schechter noted that he was under the impression there was more support for policy question 3 regarding the GSK product compared to past deliberations for the Pfizer product. He asked if that is the case and whether there is clarity on why that might be.

Dr. Schillie stated that there was more support for the GSK product under policy question 3 compared to policy question 2. However, the work group ultimately favored policy question 1. This position is primarily based on ACIP's desire to harmonize recommendations between the Pfizer and GSK pentavalent vaccines. She noted that policy question 3 would involve administering additional ACWY antigens.

Dr. Schechter asked whether, in the coming years, it is likely or unlikely that real-world effectiveness data will become available, either from post-immunization infections or outbreak settings.

Dr. Schillie responded that she was unsure, noting that the rarity of the disease makes it challenging to calculate real-world effectiveness. While some effectiveness data exist, they are limited by small sample sizes.

Dr. Barnett asked whether the work group considered a different recommendation for travelers to the meningitis belt of sub-Saharan Africa, given the reduced response to serogroup A, which is more common in that region.

Dr. Schillie explained that MenABCWY vaccines are typically not indicated for travel, as MenB alone is not recommended based on travel. Travel would not meet that criterion since the pentavalent vaccine is intended for use when both MenB and MenACWY are indicated. However, she acknowledged that reduced immunogenicity to serogroup A may be more relevant for travelers. Still, the pentavalent vaccine would generally not be expected for travel-related use.

Dr. Brewer asked how many vaccine types a pediatrician would need to stock to meet the new recommendations under policy question 1, which includes the Q, P, and B components. He questioned whether it would require stocking five different vaccines.

Dr. Schillie clarified that the pentavalent vaccine is optional. Providers could continue stocking one MenACWY product and one MenB product. If they wish to reduce the number of injections, they could add the pentavalent product corresponding to the MenB manufacturer they already use.

Dr. Brewer asked whether providers should stock both MenB vaccines because the products are not interchangeable.

Dr. Schillie responded that that would not be necessary, as providers could refer out the likely relatively few patients in their practice needing the other brand.

Dr. Zucker stated that, from a programmatic perspective, she supports harmonizing the schedule whenever possible, given its complexity. Unless there is a compelling reason to differentiate recommendations, she favored using the pentavalent vaccine when both components are indicated and not allowing for alternative options.

Dr. Asturias asked how the work group reconciled maintaining shared clinical decision-making with the potential cost savings of using a pentavalent vaccine. He noted that, given the complexity of the recommendations, practices may limit which vaccines they stock. He questioned whether limiting a potentially cost-saving pentavalent vaccine to a small subset of adolescents was appropriate or if he had misunderstood the approach.

Dr. Schillie explained that the pentavalent vaccine is priced significantly lower than the combined cost of the two-component vaccines. However, since it includes the MenB component, its use remains subject to shared clinical decision-making. She noted that this approach may be revisited in the future as part of adolescent schedule discussions, but for now, the MenB recommendation remains unchanged.

Dr. Shaw asked about the consideration of noninferiority for the PorA antigen, noting that PorA exhibits substantial phase variation in expression and sequence variation within and across strains. He wondered whether this is accurate and how much strain matching should be expected for a highly polymorphic protein.

Dr. Schillie explained that the PorA strain is important because it represents the vaccine's full outer membrane vesicle component. This strain did not show noninferiority in the exogenous assay. However, she emphasized that the post hoc analysis shown in the presentation suggested similar coverage for pentavalent and BEXSERO for PorA in U.S. strains, while the data shown for the exogenous assay may better represent New Zealand strains and be less relevant to the U.S. context.

Dr. Kurilla, referencing the risk-based meningococcal vaccine recommendation slides, noted that MenB is currently used on a limited, risk-based basis. He asked about a scenario in which a college student who previously received a pentavalent vaccine experiences an outbreak at their college. He questioned whether a MenB vaccination would be recommended in that setting and how likely it would be for the booster to match the original pentavalent brand.

Dr. Schillie explained that the recommendation is one dose of the pentavalent vaccine followed by a MenB dose six months later. If someone received one or two doses of a MenB-containing vaccine and then is in an outbreak setting, they should complete the series. A booster dose is typically recommended after one year if the series has already been completed. That interval can be shortened to six months if advised by public health authorities. In such cases, the booster must be from the same manufacturer as the original MenB series.

Dr. Schechter asked for clarification regarding cost savings and cost-effectiveness. He stated that his understanding was that MenB protection itself is not cost-saving, but if, through shared clinical decision-making, the patient and family choose to proceed, using the pentavalent vaccine would be more cost-saving compared to administering the individual components. He asked if this interpretation was correct.

Dr. Schillie confirmed this interpretation was correct.

Given the different booster intervals in the current recommendations, Dr. Chen asked whether the work group had considered a booster recommendation for MenACWY versus MenB, particularly for asplenic patients.

Dr. Schillie explained that current booster dose recommendations for persons with asplenia, for both MenB and MenACWY, remain unchanged. The pentavalent vaccine deliberations do not affect existing booster dose recommendations.

Dr. Loehr motioned to approve the recommended voting language.

Ms. Moser seconded the motion.

Dr. Diana Clements (GSK Medical Affairs) thanked the Meningococcal Work group for the detailed review of PENMENVY's immunogenicity and safety data. PENMENVY was FDA-licensed in February 2025 for active immunization against invasive disease caused by *Neisseria meningitidis* serogroups A, B, C, W, and Y in individuals aged 10 through 25. Dr. Clements acknowledged the work group's opinions regarding the serogroup B endpoints. In Phase 3 clinical trials, statistical significance criteria were met for all endpoints except two indicator strains, and success criteria and noninferiority were met for endpoints evaluating responses against a diverse panel of clinically relevant serogroup B strains. Additional post hoc analyses followed GSK and the FDA discussions before PENMENVY's approval. These analyses reflected the FDA's evaluation of small numeric differences between PENMENVY and BEXSERO and were neither predefined nor powered for formal testing. FDA's summary basis of approval stated, "Overall, the results support that PENMENVY induces an effective immune response against the range of clonal complexes and strain types tested, mitigating the clinical significance of two failed secondary endpoints." The comment concluded by emphasizing that the totality of the immunogenicity data supports PENMENVY's effectiveness in preventing invasive serogroup B disease.

Dr. Middleman supported using QPB for harmonization but emphasized monitoring for wasted doses and administration errors. She also recommended keeping the option of QPP under consideration in future adolescent schedule discussions to simplify immunization tracking for providers.

Dr. Talbot agreed with the recommendation but expressed concern about the logistical challenges of storing three meningitis vaccines; asking for "the meningitis vaccine" could lead to confusion about which product is administered. As Dr. Middleman also noted, it was emphasized that careful review will be needed to monitor how the program operates.

Dr. Jeanne Santoli (CDC/NCIRD) shared an update on the VFC resolution for meningococcal vaccines. The purpose of the resolution is to incorporate the new combination pentavalent

vaccine. There are no changes to the eligible groups, recommended schedules, intervals, table notes, dosage, or contraindications for the resolution's meningococcal conjugate or serogroup B components.

One table note was updated to reference the new pentavalent vaccine and clarify that MenB vaccines remain non-interchangeable. No other changes were made to this component of the resolution. In the combination pentavalent section, language was revised to be more general, referring to a "dose of the combination vaccine" instead of naming a specific product. The dosing schedule, booster guidance, and notes for children not at increased risk were updated to reflect this broader wording and to reinforce the lack of interchangeability for MenB vaccines. There were no changes to dosage, contraindications, or precautions.

Dr. Loehr motioned to approve the updated VFC resolution for vaccines to prevent meningococcal disease.

Dr. Brooks seconded the motion.

Dr. Sarah Schillie (CDC/NCIRD) introduced the proposed age extension for MenQuadfi use in infants. With the discontinuation of Menactra® in 2023, two MenACWY vaccines remain available in the United States: MenQuadfi and MENVEO. MenQuadfi is licensed for individuals aged two years and older, while MENVEO is licensed for use starting at two months of age. The same vaccine product is preferred but not required for all doses in the series.

The MenACWY vaccine is routinely recommended for individuals aged 11–12 years and 16 years and individuals ≥2 months old with medical or other risk factors. The dosing schedule for those with risk factors varies by age: for individuals <2 years, 2, 3, or 4 doses may be recommended; for those ≥2 years, 2 doses are recommended ≥8 weeks apart. Depending on the condition, booster doses are recommended for those who remain at risk, at 3- or 5-year intervals.

With the discontinuation of Menactra, MENVEO has been the only MenACWY vaccine available in the U.S. for individuals under 2 years of age. Sanofi is seeking infant licensure for MenQuadfi, anticipated in May 2025. The proposed schedule includes a four-dose series for those initiating at 6 weeks through 5 months of age, with doses at 2, 4, 6, and 12–18 months, and the first dose eligible as early as 6 weeks. For those initiating at 6 through 23 months, a two-dose series is proposed, with the second dose given in the second year of life and at least 3 months after the first. For individuals aged 2 years and older, a single dose is recommended.

Dr. Rachel Dawson (Sanofi) presented on the safety and immunogenicity of MenQuadfi in infants. The public health burden of meningococcal disease remains a significant global challenge. The disease can strike rapidly, sometimes taking a life in less than 24 hours, and has a high case fatality rate of 10–15%. Among survivors, one in five experienced permanent sequelae. Since introducing the first MenACWY conjugate vaccine in 2005, invasive meningococcal disease caused by serogroups C, W, and Y has declined by over 90%. However, infants continue to experience the highest incidence of invasive meningococcal disease.

MenQuadfi is a quadrivalent meningococcal conjugate vaccine designed to help prevent disease caused by serogroups A, C, W, and Y. It was approved by the FDA in April 2020 for use in individuals aged ≥2 years. Studies supporting the expansion of age indication to include infants as young as 6 weeks have been completed and will be presented. The vaccine is conjugated to tetanus toxoid and contains 10 micrograms of each of the four meningococcal polysaccharides. It is fully liquid, does not require reconstitution, and is supplied in a single-dose vial.

MET42 evaluated the immunogenicity and safety of MenQuadfi when co-administered with routine pediatric vaccines in healthy infants and toddlers in the U.S. and Puerto Rico. The study enrolled over 2,600 meningococcal vaccine-naive infants aged ≥42 to ≤89 days. Participants received either MenQuadfi or MENVEO, along with routine pediatric vaccines, at 2, 4, 6, and 12 months. Safety follow-up included immediate adverse events within 30 minutes of each vaccination, solicited adverse events days 0-7 after each vaccination, and unsolicited adverse events through 30 days after each vaccination, and serious adverse events from the day of the first vaccination through six months after the last vaccination. Baseline characteristics, including sex, age, race, and ethnicity, were balanced between groups.

For safety results, serious adverse events were reported in 5.7% of the MenQuadfi group and 4.4% of the MENVEO group. Two serious adverse events were considered related to the vaccine: one febrile seizure in the MenQuadfi group, occurring 13 days after the 15-month dose in a participant with a prior history of seizures, and one case of fever in the MENVEO group eight hours after the 2-month dose. A total of 18 adverse events of special interest (AESIs) were reported, in 0.8% of the MenQuadfi group and 0.6% of the MENVEO group. All were considered unrelated to the vaccine except for the febrile seizure. Two participants in the MenQuadfi group discontinued due to serious adverse events: one due to infantile spasms and one due to cardiac arrest. The death was deemed unrelated to the study vaccine or procedures by both the investigator and the sponsor.

For immunogenicity results, MenQuadfi was noninferior to MENVEO based on seroresponse after the fourth dose when vaccines were administered at 2, 4, 6, and 12 months of age, and noninferior based on seroprotection after the third dose when vaccines were administered at 2, 4, 6, and 12 months of age. Noninferiority of immune responses to routine pediatric vaccines co-administered with MenQuadfi, compared to MENVEO, was also demonstrated. Geometric mean titers against serogroups A, C, W, and Y after the third dose were comparable or higher in the MenQuadfi group. No new safety concerns were identified, and the safety profile and tolerability of MenQuadfi were comparable to MENVEO.

MET41 had a similar design to MET42. It included almost 2,800 meningococcal vaccine-naive participants aged ≥42 to ≤89 days, following a comparable vaccination schedule for both groups. Safety follow-up was the same as in the earlier study. Baseline characteristics, including sex, age, race, and ethnicity, were balanced between groups.

In this study, 4.6% of subjects reported serious adverse events, with none deemed related to the study vaccines. Serious adverse events were reported in 5.2% of the MenQuadfi group and 3% of the MENVEO group. AESIs related to febrile and non-febrile seizures were reported by 0.7% of participants, with 0.9% in the MenQuadfi group and 0.1% in the MENVEO group. None of these AESIs were considered vaccine-related. Confounding factors, such as personal or family history of seizures, infections, or receipt of other vaccines like MMR, were identified in 87.5% of cases. Additionally, 92% of seizure events did not meet the Brighton Collaboration case definition criteria. There were 12 discontinuations due to adverse events, mainly in the MenQuadfi group, and three deaths occurred (due to non-accidental head injury, sudden unexplained death in infancy, and an infant found unresponsive). None of the deaths were considered related to the study vaccine or procedures.

MET61 evaluated the safety and immunogenicity of MenQuadfi in infants aged 6 through 23 months in the United States using a two-dose schedule. The study population included 950 participants, with infants aged 6 to 7 months and toddlers aged 17 to 19 months. Group 1 received MenQuadfi plus routine pediatric vaccines at 6 to 7 months and 12 to 13 months. Group 2 received MENVEO on a similar schedule. Group 3 received MenQuadfi at 17 to 19 months and again at 20 to 23 months, while Group 4 received Menactra at the same intervals.

Safety follow-up was similar to previous studies. Baseline characteristics, including sex, age, race, and ethnicity, were balanced across all groups.

For safety, serious adverse events were reported by 1.6% of participants in Group 1 (MenQuadfi), 3.3% in Group 2 (MENVEO), 1% in Group 3 (MenQuadfi), and 3.9% in Group 4 (Menactra). One participant in the MENVEO group experienced an immediate unsolicited adverse event (head injury), and one case of acute myeloid leukemia, unrelated to the vaccine, led to study discontinuation in the MENVEO group. In the Menactra group, one febrile convulsion was reported as an AESI and considered related to vaccination. AESIs were reported by 0.3% in Group 1, 0.6% in Group 2, and 1.9% in Group 4, with none related to the study vaccines. Investigators and the sponsor deemed all other serious adverse events unrelated to vaccination. No deaths were reported.

For immunogenicity, Immune responses following the first dose of MenQuadfi co-administered with routine pediatric vaccines in infants aged 6 to 7 months were noninferior to MENVEO. Six to seven months later, responses to serogroup A were comparable, and responses to serogroups C, W, and Y were higher than those of the comparator group. Thirty days after the second dose, given at 20 to 23 months of age, GMTs were higher for all serogroups in the MenQuadfi group than the Menactra group.

Dr. Dawson concluded that MenQuadfi demonstrated robust immunogenicity and a reassuring safety profile when administered to infants and toddlers starting vaccination as early as 6 weeks of age.

Dr. Cineas asked whether the immunogenicity studies included infants already indicated for meningitis vaccination.

Dr. Dawson responded that the studies were conducted in healthy infants and did not include immunocompromised infants or those at higher risk for invasive pneumococcal disease.

Dr. Asturias inquired whether there has been any calculation of the total amount of tetanus toxoid that infants receive, considering that, in addition to meningococcal vaccines, many pentavalent combination vaccines (DTaP, Hib, Hepatitis B, with or without IPV) are administered. He also wanted to know if any analysis had been done to assess this exposure.

Dr. Dawson stated that an integrated safety analysis of over 6,000 infants across six clinical trials, including three pivotal U.S. trials, found no material safety impact from co-administration of MenQuadfi with DTaP-containing vaccines. Safety outcomes were comparable to those observed with MENVEO and Menactra, which do not contain tetanus toxoid. Co-administration of MenQuadfi with DTaP-containing vaccines was not associated with additional safety concerns.

Dr. Loehr noted that the work group was particularly concerned about the difference in febrile seizures, with 19 cases reported compared to one. All 19 febrile seizures were concluded to be unrelated to the study vaccine, while the febrile seizures in MET61 and MET42 were considered related. Dr. Loehr commented that this was an unusual pattern and asked for clarification.

Dr. Dawson explained that a comprehensive safety evaluation focused on febrile and non-febrile seizures. Most cases occurred outside the immediate post-vaccination period. Two instances occurred within seven days and had confounding factors such as a personal or family history of seizures, concomitant infections, or administration of other vaccines. Only three cases lacked identifiable confounding factors. Based on cumulative evidence, there was no support for a causal link between MenQuadfi and seizures.

Dr. Loehr sought clarification on who determined whether the seizure events were related to the study vaccines, specifically whether the study group, the sponsor, or an independent investigator made the assessment.

Dr. Dawson stated that the investigators and sponsors made these determinations independently. The investigators were blinded to treatment allocations and independently evaluated serious adverse events, which were then reported to regulatory authorities within 24 hours in accordance with the study protocol.

Dr. Loehr followed up with a question about how a determination would be adjudicated if the investigator considered an event related to the study vaccine, but the sponsor did not.

Sanofi provided clarity and stated that it was noted that in one case involving the comparator Menactra, the principal investigator assessed the event as related, and the sponsor agreed, acknowledging that febrile convulsions are a known and accepted risk associated with Menactra in the pediatric population. Regarding a case in MET42, the principal investigator assessed a febrile seizure related to the study vaccine. However, the sponsor respectfully disagreed. This was described as a rare occurrence among over 6,060 assessments. The event occurred 13 days after the fourth dose, alongside routine pediatric vaccines, and during an active otitis media infection. Due to these confounding factors, the sponsor did not consider the seizure related to the study vaccine.

Dr. Sarah Schillie (CDC/NCIRD) shared the work group's considerations regarding MenQuadfi in infants. The work group reviewed three Phase 3 studies conducted in U.S. infants aged 6 weeks through 19 months. 4,321 infants received at least one dose of the MenACWY vaccine co-administered with other pediatric vaccines. Two studies followed a 3+1 schedule with doses at 2, 4, 6, and 12–18 months, and one study used a 1+1 schedule with the first dose given at ≥6 months of age. Additionally, 1,717 infants received a comparator vaccine, either MENVEO or Menactra, co-administered with other pediatric vaccines across six arms.

In study MET42, seroresponse after the fourth dose was similar between the intervention and comparison groups for serogroups A, Y, and W, and was higher among intervention recipients for serogroup C. In study MET61, seroresponse after the fourth dose was similar between intervention and comparison recipients for all four serogroups. Solicited local and systemic adverse reactions were similar across study groups in MET42. In MET61, local reactions were slightly more frequent among MenQuadfi recipients, with a minor difference observed for systemic reactions.

In MET41, febrile or non-febrile seizures were more frequent among MenQuadfi recipients, with 19 subjects (0.9%) in the intervention group and 1 subject (0.1%) in the comparison group experiencing a seizure. The primary investigator and the sponsor deemed all events unrelated to the study vaccine. In MET42, one febrile seizure occurred in a participant who received the study vaccine and had a prior history of seizures; this event was deemed related to the study vaccine.

There were four total deaths across two studies, all among MenQuadfi recipients. The primary investigator and sponsor deemed all deaths unrelated to the vaccine. Causes of death included non-accidental head injury 30 days after vaccination, sudden unexplained death in infancy 24 days after vaccination, an infant found unresponsive in bed 4 days after vaccination, and cardiac arrest 6 days after vaccination.

The pooled safety analysis from MET41 and MET42 showed a higher rate of serious adverse events in the MenQuadfi group (5.2% compared with 3.7% for the MENVEO group for the entire study period).

Dr. Schillie concluded that post-dose 4 immune responses were similar between MenQuadfi and comparison recipients, with higher GMTs for serogroup C among MenQuadfi recipients. Rates of solicited local and systemic reactions were similar between groups, although local reactions were slightly more frequent in MenQuadfi recipients in MET61. A greater proportion of febrile and non-febrile seizures, serious adverse events, and deaths occurred in the MenQuadfi group.

The studies included healthy infants, and as such, results may not be representative of infants recommended for vaccination based on risk factors. Because risk factors for infant meningococcal vaccination are rare, clinical studies typically enroll predominantly healthy infants. The work group also noted high attrition rates across the studies. Overall, the work group felt that the benefits of having an additional vaccine option may outweigh the potential risks.

Dr. Talbot asked whether the work group felt the reported deaths were unrelated to the study vaccine.

Dr. Schillie stated that the work group still had some unresolved questions regarding the deaths and the febrile and non-febrile seizures.

Vote: Meningococcal Vote

Dr. Sarah Schillie read the following proposed ACIP voting language for the meningococcal vaccine into the record:

*ACIP recommends GSK's MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit**

**1) healthy persons aged 16–23 years (routine schedule) when shared clinical decision-making favors administration of MenB vaccine, and 2) persons aged ≥10 years who are at increased risk for meningococcal disease (e.g., because of persistent complement deficiencies, complement inhibitor use, or functional or anatomic asplenia).*

Motion/Vote: Meningococcal Vaccines

Dr. Loehr motioned to approve the recommended voting language, stating," ACIP recommends GSK's MenABCWY vaccine may be used when both MenACWY and MenB are indicated at the same visit." Ms. Moser seconded the motion. No COIs were declared. The motion carried with 15 in favor and 0 opposed. The disposition of the vote was as follows:

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

Vote: Meningococcal-VFC Vote

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP VFC vote for Meningococcal into the record:

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

Motion/Vote: Meningococcal Vaccines

Dr. Loehr motioned to approve the updated VFC resolution for vaccines to prevent meningococcal disease. Dr. Brooks seconded the motion. No COIs were declared. The motion carried with 15 in favor and 0 opposed. The disposition of the vote was as follows:

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

RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINES - ADULT

Dr. Albert Shaw (ACIP, Work Group Chair) introduced the Adult Respiratory Syncytial Virus Work Group. In June 2024 ACIP recommended that all adults aged ≥75 years and adults aged 60–74 years who are at increased risk of severe RSV disease receive a single dose of RSV vaccine.[1,2]

1. Recommendation is for any Food and Drug Administration–approved RSV vaccine (AREXVY [GSK]; ABRYSVO™ [Pfizer]; or mRESVIA® [Moderna]). There is no product preference.

2. Eligible adults are currently recommended to receive a single dose of RSV vaccine; adults who have already received RSV vaccination should not receive another dose.

Chronic medical conditions and other risk factors that increase the risk of severe RSV disease include chronic cardiovascular disease, chronic lung or respiratory disease, diabetes mellitus, severe obesity, end-stage renal disease or dialysis dependence, chronic hematologic disorders, chronic liver disease, neurological or neuromuscular conditions, residence in a nursing home, moderate to severe immunocompromise and other chronic medical conditions or risk factors that a provider determines would increase risk of severe disease due to viral respiratory infection (e.g., frailty).

There are currently three FDA-approved RSV vaccines. Two are protein subunit vaccines, based on the RSV F protein in a stabilized prefusion conformation – AREXVY (GSK), monovalent RSV-A, with $AS01_E$ adjuvant; and ABRYSVO™ (Pfizer), bivalent RSV-A/RSV-B, without adjuvant. The third vaccine is an mRNA encoding the RSV F protein in the prefusion conformation, mRESVIA® (Moderna), monovalent RSV-A, without adjuvant.

All three of these vaccines are approved for preventing lower respiratory tract disease (LRTD) caused by RSV in adults aged ≥60 years. GSK's AREXVY is 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 approved for the prevention of LRTD caused by RSV in adults aged 18–59 years who are at increased risk of LRTD caused by RSV. It is also approved and recommended for active immunization in pregnancy 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. Moderna has applied for licensure for adults aged 18–59 years who are at increased risk of LRTD caused by RSV with regulatory action anticipated by June 12, 2025. There is no current ACIP recommendation for RSV vaccination in adults aged <60 years, except for the maternal vaccination recommendation.

The Adult RSV Work Group is proposing a policy recommendation for age expansion of the use of RSV vaccines to include adults aged 50-59 years at increased risk of severe RSV disease. Dr. Shaw acknowledged that there is also one FDA-approved vaccine for RSV prevention in adults aged <50 years. The work group continues to evaluate recommendations for RSV vaccination in this age group. Policy for the use of RSV vaccines in adults aged <50 years will be revisited at the June 2025 meeting.

Dr. Frances Priddy (Moderna) presented an update on the safety and immunogenicity of mRNA-1345 in 18–59 year-olds at increased risk for RSV disease and the revaccination of adults at 12 or 24 months.

Up to one-third of U.S. adults <60 years may be considered at high risk for RSV-associated hospitalization. The most common conditions in this age group that increase the risk of severe RSV disease include asthma, morbid obesity, and diabetes. RSV-associated hospitalization rates were at least two to three times higher in younger adults with selected high-risk conditions compared to those without. Recent RSV-NET data indicated that over 60% of adult RSV hospitalizations occurred in individuals <65 years of age. Among adults aged 50–64 years, clinical outcomes were severe, with 22% requiring ICU admission and an in-hospital mortality rate of approximately 3%.

To support expanded use, an ongoing Phase 3 study evaluates the safety and immunogenicity of mRNA-1345 in adults aged 18–59 years with risk factors for severe RSV, including heart disease, chronic respiratory conditions, or diabetes. The study assesses outcomes after a single dose, with success defined as noninferior immunogenicity compared to the pivotal efficacy trial.

The primary objectives of the study are to assess the safety and tolerability of the vaccine in high-risk adults aged 18–59 years, and to compare RSV-A and RSV-B GMTs at Day 29 after a single 50 µg dose in this population versus adults aged 60 years and older from the pivotal Phase 2/3 efficacy trial. The secondary objective is to compare seroresponse rates (SRRs) between high-risk adults aged 18–59 years and adults aged ≥60 years who received the same 50 µg dose in the pivotal study.

Over 500 adults were enrolled to receive a 50 µg dose of mRNA-1345, including 306 participants aged 50–59 years. The median age was 53 years, and 54% of participants were female. The study included a racially and ethnically diverse population. Medical conditions associated with increased risk for severe RSV disease were well-represented among participants. Thirty percent of participants had two or more pre-existing comorbidities. The most common were coronary artery disease, asthma, type 1 or type 2 diabetes, and obesity. Notably, 18% of participants were classified as morbidly obese.

The vaccine was generally well tolerated in adults aged 18–59 years at increased risk for RSV disease, with respect to local reactions; injection site pain was more common among the younger adults. The vaccine was generally well tolerated in adults aged 18–59 years at increased risk for RSV disease, with respect to systemic reactions. Unsolicited adverse events were evaluated in 502 adults who received 50 µg and 497 who received 30 µg. Within 28 days, there were no related serious adverse events, deaths, discontinuations, or cases of anaphylaxis, thrombocytopenia, Guillain-Barré syndrome, acute disseminated encephalomyelitis, or acute myocarditis/pericarditis.

mRNA-1345 vaccination (50 µg) in adults,18-59 years at increased risk of RSV disease, met the pre-specified noninferiority criteria for RSV-A and RSV-B neutralizing antibody geometric mean ratios. These results confirm that the vaccine is immunogenic in younger adults with medical conditions that increase their risk for severe RSV disease and is likely to provide protection consistent with the efficacy observed in the pivotal study. Immune responses in the 50–59-year-

old subgroup were similar to those observed in the 18–49-year-old group. Individuals with medical risk factors for RSV showed consistent neutralizing antibody responses compared to the entire study population; there was no impact of body mass index (BMI) on antibody response. mRNA-1345 is anticipated to be effective in this population, regardless of underlying risk conditions or obesity category.

Dr. Priddy summarized that the vaccine demonstrated a favorable safety and tolerability profile, with immune responses in at-risk adults aged 18–59 years comparable to those in adults ≥60 years of age. She noted that the data are under FDA review, with a PDUFA date of June 12, 2025. Given the significant burden of RSV-related hospitalizations in adults <60 with underlying conditions, mRNA-1345 offers a promising solution with a favorable benefit-risk profile.

Efficacy against LRTD with two or more symptoms and against severe RSV disease persists for up to three seasons. However, efficacy point estimates decline over time, as with all licensed RSV vaccines. These findings and the known waning of natural RSV immunity support the need to evaluate revaccination strategies to sustain protection.

Revaccination with mRNA-1345 was evaluated in two studies at 12 and 24 months. In Study 302, adults ≥ 50 who received a primary dose on Day 1 were revaccinated at 12 months. In Study 301, a subset of adults aged ≥60 from the pivotal trial who received the primary dose on Day 1 were randomized at 24 months to receive either mRNA-1345 or placebo in a 2:1 ratio. Both studies used the licensed 50 µg dose of mRNA-1345.

Revaccination at 12 months with mRNA-1345 met the pre-specified noninferiority criteria for RSV-A, with similar results observed for RSV-B. These results were presented to ACIP at a previous meeting.

The 24-month revaccination study included approximately 1,000 adults. The median age was 68 years, over half were female, and participants represented diverse racial and ethnic backgrounds. About one-third had at least one comorbidity, and approximately one-third were classified as obese. Notably, 30% of participants were over the age of 70 years.

Dr. Priddy summarized that 24-month revaccination with mRNA-1345 was well tolerated, with mostly mild to moderate local and systemic reactions that were short in duration. Reactogenicity was similar to that observed after the primary dose, and no safety concerns were identified during the six-month follow-up. There were no reports of Guillain-Barré syndrome, acute disseminated encephalomyelitis, myocarditis, or pericarditis.

Revaccination at 24 months with mRNA-1345 met the pre-specified noninferiority criteria for RSV-A, with similar results for RSV-B. Based on the RSV-A and RSV-B titers achieved, using the correlates of protection model Moderna presented to ACIP in October 2024, the predicted vaccine efficacy against lower respiratory tract disease for both strains and endpoints (LRTD with 2 or 3 symptoms) ranged from approximately 60% to 70% following revaccination. This is consistent with the efficacy observed one year after primary vaccination. Based on the correlates of protection model, these results suggest that revaccination, if recommended, restores vaccine efficacy.

Dr. Priddy summarized that mRNA-1345 effectively restores immune titers in older adults at 12- and 24-month revaccination intervals, reaching levels comparable to those observed after the primary vaccination. Revaccination was well tolerated, with no safety concerns identified. Immune response durability was observed for up to 24 months following the primary dose, and neutralizing antibody responses for RSV-A and RSV-B after revaccination were noninferior to those seen after initial vaccination. The correlates of the protection model indicate that revaccination restores vaccine efficacy, offering protection comparable to that of the primary

dose. Revaccination has the potential to offer sustained protection, particularly for individuals at increased risk of severe RSV disease, for whom periodic revaccination could be beneficial.

Dr. Shaw commented that while revaccination boosts neutralizing antibody titers, the magnitude of the increase appears substantially lower compared to the primary vaccination. He noted that the initial rise in titers following primary vaccination was approximately eight- to nine-fold, whereas the increase after revaccination was about half that or less. He asked whether there are any speculations about the underlying mechanism driving this difference.

Dr. Priddy responded that the titers at 12 and 24 months were measured in two studies with different study populations and age cutoffs, so direct comparisons should be made cautiously. However, she emphasized that the studies met noninferiority criteria commonly accepted for regulatory review of booster vaccines at both time points. She acknowledged no clear biological explanation for why titers at 24 months appeared lower than those at 12 months. One possible reason is that participants in the 12-month study had slightly higher baseline titers before revaccination, and prior data suggest individuals with higher starting titers tend to have higher post-boost responses. Nonetheless, she emphasized that meeting noninferiority criteria and applying the correlates of protection model to the 24-month titers support that these levels are still predictive of substantial efficacy.

Dr. Brooks noted that while RSV is a seasonal virus, the current approach does not involve offering the vaccine on a strictly seasonal schedule. He then asked for thoughts on the potential for co-administration of the RSV vaccine with other vaccines, such as COVID-19 or influenza.

Dr. Priddy shared that co-administration of the RSV vaccine has been studied with both standard-dose and high-dose influenza vaccines and the COVID-19 vaccine in adults aged 50 and older. The findings showed no safety concerns, and immunogenicity was acceptable. Based on these results, she concluded that co-administration is reasonable from safety, immunogenicity, and efficacy perspectives.

Dr. Zucker requested clarification on the term "correlate of protection," specifically whether it refers to a threshold inferred from trial results or if objective data shows that antibody titers must exceed a certain level to protect against RSV infection.

Dr. Priddy explained that the correlate of protection model she referenced was developed using data from the pivotal efficacy trial of mRESVIA. Although based on a single trial, the model is robust, drawing on nearly 400 cases across various endpoints and linking closely to the efficacy observed in the first 12 months. She emphasized that while it is a strong model for interpreting results with mRESVIA, it is not currently applied to other RSV vaccines.

Dr. Zucker raised concerns about the lower antibody titers observed after revaccination compared to the initial vaccination. The question was whether this could be attributed to the older age of the study population and potential immune senescence, resulting in a weaker immune response. There was also concern that this pattern could extend to younger populations. If revaccination produces a less robust response, individuals may receive their strongest protection only after the initial dose, potentially leaving them less protected as they age into higher-risk groups for severe RSV disease. Dr. Zucker asked for thoughts on this issue.

Dr. Priddy responded that, in general, robust immune responses are observed in younger populations. She noted that concerns about having only one opportunity to generate a strong immune response in adults aged 18-59 years may not be merited, as primary vaccination in that group has consistently produced strong responses. Regarding the lower titers seen after 24-month revaccination, Dr. Priddy acknowledged that this study was conducted in adults aged 60 and older. However, the titers observed were not viewed as significantly different from those seen after 12-month revaccination. She explained that, according to the correlates of protection

model, higher titers are associated with higher efficacy, but the relationship flattens at the upper end. Once titers reach a certain threshold, further increases provide only modest gains in efficacy. For example, a titer of approximately 12,000 corresponds to a predicted vaccine efficacy of 60% to 70%, which is immunologically similar to the response seen at 12 months.

Dr. Susan Gerber (GSK) presented an update on AREXVY. AREXVY is approved for adults ≥60 years of age and adults 50–59 years of age at increased risk for RSV-related lower respiratory tract disease. As of March 2025, approximately 11 million doses have been administered in the U.S.

Study 004 assesses immunogenicity across revaccination schedules and the persistence of immune response following a single dose over five years. Initial results from Study 012, an extension of the pivotal efficacy Study 006, also evaluate immunogenicity and persistence of immune response.

Study 012 includes a one-dose group that was re-randomized at 36 months. One group was revaccinated 36 months after receiving dose one in Study 006, one group will be revaccinated at 48 months, and one group will not be revaccinated. The study will continue for two more years. The placebo group from Study 006 was offered a vaccine dose at 36 months.

Study 004 includes a one-dose arm re-randomized at 36 months, with one group revaccinated. It also includes arms that have been revaccinated at various intervals. The M12, M24 group was revaccinated at 12 and 24 months and the M24 group at 24 months and is scheduled for another dose at 48 months. The focus in today's presentation is on 36-month revaccination results from both studies, beginning with Study 004.

In Study 004, neutralizing antibody levels to RSV-A and RSV-B increased after each vaccine dose. The single-dose group showed an initial rise followed by a gradual decline that remained above baseline through 37 months. Revaccination at 12 and 24 months led to antibody increases after each dose, though not as high as after the first. The group revaccinated at 24 months showed higher titers than the M12, M24 group. Revaccination at 36 months resulted in a robust antibody response at 37 months, comparable to the 24-month group. Peak responses after revaccination were about 60% of the peak after the initial dose. $CD4^+$ T-cell levels consistently increased after each dose, including in the 36-month revaccination group, indicating strong cellular immunity.

In Study 012, the extension of the pivotal Study 006, approximately 10 times more individuals were revaccinated at 36 months compared to Study 004. Among those re-randomized, about 40% had at least one comorbidity associated with severe RSV disease. Data from the immunogenicity subset of Study 006 shows a similar priming response after dose one compared to the overall population. A robust peak in antibody response to RSV-A and RSV-B was observed one month after revaccination at 36 months. This consistent pattern was also seen across frailty statuses, including among frail and pre-frail individuals, compared to the fit group and the overall population.

Higher fold increases following revaccination at 36 months were seen in those with lower pre-revaccination titers compared to those with higher pre-revaccination titers, although the post-revaccination titers were lower among those with lower pre-revaccination titers. Lower pre-revaccination titers were associated with higher seroresponse rates (≥4-fold increase) following revaccination.

In Study 004, the safety and reactogenicity profile following revaccination at 36 months was similar to that observed after the first dose. In Study 012, unsolicited adverse events within 30 days of revaccination at 36 months were comparable to those reported after the first dose in the

crossover group. Serious adverse events reported up to six months were also similar between groups.

Dr. Gerber summarized that revaccination with AREXVY elicited robust humoral and cellular immune responses, including in individuals with certain comorbidities. While no established correlate of protection exists for adults, cellular immunity and mucosal IgA may contribute to protection, particularly across age groups. RSV neutralizing antibody responses after revaccination at 36 months were similar to those observed at 24 months. Lower pre-revaccination RSV-A and RSV-B titers were associated with higher seroresponse rates. Safety and reactogenicity profiles at 36 months were comparable to those following the initial dose.

Evidence supporting revaccination with AREXVY includes robust humoral and cellular immune responses following revaccination, including for individuals with certain co-morbidities. RSV neutralizing antibody responses were similar following revaccination at 24-month and 36-month intervals. Lower pre-revaccination titers were associated with higher seroresponse rates. The safety and reactogenicity profile following revaccination was similar to that seen following the first dose. Real-world vaccine effectiveness data and ongoing immunogenicity studies will help inform optimal revaccination timing. Importantly, an estimated 13 million U.S. adults aged 50–59 years of age are at risk for severe RSV disease, and over three years, AREXVY may help prevent thousands of hospitalizations among individuals with heart failure, chronic obstructive pulmonary disease (COPD), and diabetes.

Dr. Loehr questioned whether the neutralizing titers referenced in the studies differ from those used in other brands, such as Moderna.

Dr. Gerber responded that in GSK's studies, neutralizing titers are expressed in ED60, but that she could not comment on studies by other companies.

Dr. Brewer asked for clarification on the results shared that were stratified by pre-vaccination neutralizing antibody titers by quartile, noting that one interpretation is that only some individuals may need a second or additional dose, while another interpretation is that all four groups experience a clinically meaningful benefit.

Dr. Gerber explained that, while there is not a complete understanding of correlates of protection, the quartile data shows no systematic trends related to demographic characteristics or comorbidities. Similar humoral immune responses were observed across comorbidity and frailty groups. However, lower pre-revaccination neutralizing antibody titers were associated with higher seroresponse rates.

Dr. Brewer asked whether individuals in the fourth quartile appear to benefit from vaccination in a clinically meaningful way.

Dr. Gerber noted that determining the clinical benefit of revaccination requires considering both immunogenicity and vaccine effectiveness data. While immunogenicity data provide important insights, vaccine effectiveness, particularly protection against hospitalization, will be key to understanding the clinical significance of revaccination across different schedules. These data must be evaluated together to inform a meaningful revaccination strategy.

Dr. Talbot asked whether vaccine efficacy studies are being conducted.

Dr. Gerber stated that vaccine effectiveness studies are underway, with results expected soon. Appreciation was expressed for CDC's vaccine effectiveness data, and it was noted that, together with ongoing immunogenicity studies, these findings will help inform the approach to revaccination.

Dr. Talbot noted that no additional vaccine efficacy studies were being done by GSK.

Dr. Schechter asked whether data from individuals infected during the study or in separate infection studies show similar patterns in neutralizing antibody responses, and if the diminished response observed after multiple vaccine doses is also seen following infection or reinfection.

Dr. Gerber clarified that Studies 004 and 012 were immunogenicity trials and did not monitor or assess for acute RSV infection. All enrolled participants were RSV seropositive, and no data on infection or reinfection responses were collected. Regarding efficacy, Dr. Gerber noted that maintaining a placebo arm was not feasible due to widespread vaccine approval. As a result, the focus has shifted to vaccine effectiveness studies, with results expected soon.

Dr. Shaw inquired how the model presented in the final data slide, which showed RSV infections or deaths by comorbidity, was developed.

Dr. David Singer (GSK Health Economics and Outcomes Research Team) stated that the model is based on a similar framework used for the cost-effectiveness analysis. The slide shows expected outcomes averted per one million AREXVY vaccinations over a three-year time horizon, with more detailed information to be presented later.

Dr. Ismael Ortega-Sanchez (CDC/NCIRD) presented the economic analysis of adult RSV vaccination. Dr. Ortega-Sanchez presented on behalf of the study team, which was led by Dr. David Hutton from the University of Michigan. The study aims to evaluate the cost-effectiveness of RSV vaccination by comparing vaccination to no vaccination using an incremental cost-effectiveness ratio. The analysis includes three groups. Today's focus is on the policy-relevant group: adults aged 50–59 years with at least one medical condition. The cost-effectiveness analysis evaluates three vaccines under two separate base case scenarios. One scenario is for the prefusion F protein subunit RSV vaccines from Pfizer and GSK, and the other is for the mRNA RSV vaccine from Moderna. Each vaccine is compared to no vaccination, but not directly compared to one another.

The analysis defines "at least one chronic medical condition" as including chronic pulmonary disease, asthma, coronary artery disease, diabetes, chronic kidney disease, or severe obesity (BMI ≥40). Due to data limitations, heart failure and immunocompromise, including lung and hematopoietic cell transplant recipients, were analyzed separately.

The three-year projected effectiveness of the protein subunit vaccines against emergency department visits and hospitalizations was based on clinical trial data, real-world vaccine effectiveness studies from season one, and a meta-analysis. Effectiveness was modeled to decline stepwise to lower levels in seasons two and three, with a linear decrease assumed to reach zero efficacy by 36 months.

Unlike the prefusion F protein subunit RSV vaccines, there are no published vaccine effectiveness results for Moderna's mRNA RSV vaccine. All effectiveness assumptions in the model are based on clinical trial efficacy against symptomatic disease, with a median follow-up of less than two years per participant.

The vaccine effectiveness assumption for Moderna’s RSV vaccine is based on data from the randomized controlled trial. While protection may extend beyond 24 months, the base case assumes effectiveness declines to 0% by month 24. Due to greater uncertainty around long-term efficacy, a scenario analysis also includes a linear regression model developed by Moderna. This model incorporates multiple data points and extends protection to approximately three years.

Medical cost inputs were updated by individual condition and adjusted using a multiplier approach based on the relative length of stay by chronic medical condition from the CDC’s RSV-NET surveillance system. Base costs were sourced from a 2024 study by Averin and

colleagues, published in *Open Forum Infectious Diseases* in 2024, sponsored by Pfizer. Unlike earlier sources that focused only on adults 60 and older, this analysis includes adults under 60 years of age. Post-hospitalization costs also account for skilled nursing facility care. Additionally, a previous calculation error in inputting productivity values for adults aged 50 to 64 years has been corrected. Among the adverse events, the likelihood of Guillain-Barré syndrome for the GSK and Pfizer vaccines was included using results from an FDA analysis based on a 42-day risk window among Medicare beneficiaries aged ≥65 years.

The principal scenario analyses presented today include three key assumptions that differ from the base case: a longer three-year duration of protection for the Moderna vaccine, vaccination targeted to specific chronic medical conditions rather than grouping under "at least one," and the use of alternative public sector vaccine prices instead of manufacturer list prices.

In the base case analysis presented in June 2024, assuming two years of vaccine protection for all products, the estimated societal cost was approximately $150,000 per quality-adjusted life year (QALY) gained from vaccinating adults aged 50–59 years with at least one chronic condition using the GSK vaccine, which was the only licensed product for this indication at that time.

Updated estimates show that for adults aged 50–59 years with at least one medical condition, the prefusion protein subunit vaccine with a three-year duration of protection is associated with a societal cost of approximately $43,000 per QALY gained. For the mRNA vaccine, the estimated cost is about $150,000 per QALY with two-year protection and about $95,000 per QALY with three-year protection.

The number needed to vaccinate (NNV) to prevent an RSV outcome varies by vaccine type and assumed duration of protection, with different values shown for each specific disease outcome. A lower NNV indicates a greater estimated public health impact per dose administered. For example, vaccinating 510 adults aged 50–59 years with at least one chronic condition using a protein subunit vaccine with assumed protection lasting three years would prevent one RSV-related hospitalization. For the mRNA vaccine, between 681 and 932 individuals would need to be vaccinated to prevent one hospitalization, depending on the assumed duration of protection.

The incremental cost-effectiveness ratio was estimated using vaccine prices from the Federal Supply Schedule used by the Department of Veterans Affairs, with prices set at $263 for the GSK vaccine, $258 for the Pfizer vaccine, and $204 for the Moderna vaccine. Holding all other factors constant, the cost per QALY gained for adults aged 50–59 with one chronic medical condition decreased by over 40% for the subunit vaccines, from $42,000 to $26,000. For the mRNA vaccine, the cost decreased by approximately 48% for the two-year protection scenario and 62% for the three-year scenario. These reductions occurred despite only a 10% decrease in vaccine prices.

This analysis has several limitations. It does not account for transmission or indirect effects of vaccination, and not all RSV risk factors were included. Some high-risk conditions, like interstitial lung disease, were excluded due to limited data. Key inputs, such as disease burden, costs, and caregiver productivity losses, are uncertain. The duration and waning of vaccine protection, particularly for the mRNA vaccine, also remains unclear.

Dr. Ortega-Sanchez concluded that vaccinating adults aged 50–59 years with at least one chronic medical condition may be cost-effective, with a cost of $43,070 per QALY for the subunit vaccine, $152,293 per QALY for the mRNA vaccine assuming two-year protection, and $95,182 per QALY assuming three-year protection. Vaccination appears to be cost-saving for individuals with immune compromise (hematopoietic cell or lung transplant), heart failure, COPD, chronic

kidney disease, or severe obesity (BMI ≥40). In scenarios using lower vaccine prices, the vaccines were found to be more cost-effective.

Dr. Ismael Ortega-Sanchez (CDC/NCIRD) presented a comparison of economic models of RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease. The policy question is whether a single dose of any licensed RSV vaccine should be recommended for adults aged 50–59 years who are at increased risk of severe RSV disease.

The four models used for comparison were the GSK model, the Moderna model, the Pfizer model, and the UM-CDC model. The models follow similar designs, using a static analytical decision-making approach and relying on probabilistic or deterministic sensitivity analyses to address data uncertainties. Each model applies to a hypothetical population of U.S. adults aged 50–59 years who are at increased risk for severe RSV disease. However, the models differ significantly in their assumptions about the duration of vaccine protection. Notably, the CDC model includes two base case scenarios: a three-year time frame for prefusion protein subunit vaccines and a two-year time frame for the mRNA vaccine.

Although all models focus on the high-risk population aged 50–59 years, the definition of "high-risk" varies across models. For example, GSK's base-case centers on COPD and includes other conditions only in a scenario analysis. In contrast, Moderna, Pfizer, and the CDC base-case scenarios define high-risk as having at least one condition from a selected list. The specific conditions included in each model also differ, which may contribute to variations in reported outcomes.

The GSK and CDC models assumed different incidences of RSV-related hospitalization and outpatient care, as well as the associated medical costs for hospitalizations, emergency department visits, and outpatient visits. For example, the incidence of RSV hospitalization among individuals with chronic obstructive pulmonary disease is nearly twice as high in the GSK model compared to the CDC model.

The Moderna model shows higher incidence rates than the CDC model, with outpatient visits approximately 35% higher and hospitalizations more than twice as high. However, the CDC model applies higher hospitalization costs, approximately four times greater, while outpatient visit costs remain about four times higher in the Moderna model.

Pfizer assumed higher baseline incidence rates of RSV compared to the CDC model. However, the medical costs for hospitalization, emergency department visits, and outpatient care are comparable between the two models.

The inputs related to indirect costs and quality of life from RSV disease include several factors, with the assumed RSV case fatality ratio being the most impactful on results. This rate ranged from 4.3% in the Moderna model to 7% in the GSK model. The CDC model was the only one to adjust its assumed mortality rate of 6.4 deaths per 100 RSV hospitalizations to account for deaths among non-hospitalized individuals. Unlike the other three models, the Moderna model did not assign any cost value to RSV-associated premature death, which increased its estimated societal cost and made the vaccine appear relatively less cost-effective.

The GSK model assumes five years of protection from a single dose, which differs from the shorter duration of protection used in the CDC model.

The CDC model assumes three years of protection for the Pfizer vaccine, which exceeds clinical trial follow-up by about one year. In contrast, Pfizer's model assumes the initial level of protection lasts seven months, declines through months 16 to 18, and is extrapolated to 42 months, with 0% protection afterward. A separate scenario extends hospitalization protection to 72 months, not part of Pfizer's base-case. Protection beyond 24 months is considered highly uncertain.

Moderna's model uses trial data and linear regression to project that vaccine efficacy declines to 0% at 29 months for RSV-ARD, 35 months for RSV-LRTD, and 37 months for RSV-LRTD requiring hospitalization or an ED visit. Using the same trial data, the CDC takes a more conservative stepwise approach, assuming two years of protection. After this period, estimates of residual protection are based on assumptions and carry greater uncertainty.

For the five-year and three-year time frames, GSK reports cost savings for all individual conditions analyzed, including COPD, heart failure, coronary artery disease, and diabetes. In contrast, under the CDC base-case with a three-year vaccine effectiveness assumption, the estimated societal cost is approximately $44,000 per QALY for adults with at least one chronic condition vaccinated with a prefusion protein subunit RSV vaccine. CDC estimates range from cost-saving for chronic kidney disease, COPD, and severe obesity (BMI ≥40), to about $57,000 per QALY for individuals with diabetes.

Pfizer reported cost-saving estimates across all selected higher-risk conditions for the three-year base case and for extended scenarios up to 70 months. In contrast, the CDC estimated a societal cost of approximately $42,000 per QALY for the Pfizer vaccine over three years in adults with at least one chronic condition.

For the mRNA vaccine, the base case results differ in time frame assumptions. CDC assumes two years of protection in the base case, estimating a societal cost of approximately $152,000 per QALY for adults with at least one chronic medical condition. Moderna reports a lower cost of about $76,000 per QALY for the same two-year period. Moderna reports an even lower cost of about $65,000 per QALY in its three-year base case, which is about 15% lower than its two-year estimate and roughly two-thirds lower than the CDC's estimate of about $95,000 per QALY when protection is assumed to last three years.

The analysis has several limitations that may lead to underestimating the cost-effectiveness of RSV vaccination. These include the potential impact of RSV on the long-term prognosis of underlying conditions, the indirect effects of vaccination on unvaccinated individuals (e.g., prevention of RSV transmission), and the quality-of-life impact on caregivers during RSV illness. Two models do not include, and two only partially include, the productivity impact on caregivers. Manufacturer models do not account for long-term medical costs after RSV hospitalization or emergency department visits, such as those associated with rehabilitation or long-term care. Serious adverse events, such as Guillain-Barré syndrome, are only partially included or considered in scenario analyses. Vaccine efficacy beyond the median follow-up time in clinical trials remains unknown. All four models assume seasonal vaccination with optimal timing in late summer or early fall.

Dr. Ortega-Sanchez concluded that differences in key inputs and assumptions across models explain the variation in results. The most influential factors are the annual incidence of RSV hospitalization and outpatient disease, vaccine effectiveness and duration of protection, and the medical cost of RSV hospitalization. These differences affect cost-effectiveness outcomes by vaccine type, protection duration, and risk conditions. For a three-year protection period, the

protein subunit vaccines show outcomes ranging from societal cost-saving up to a societal cost of $43,000 per QALY gained. In some models, such as the CDC's, it is cost-saving under certain conditions. For the mRNA vaccine, assuming three years of protection, the cost per QALY ranges from approximately $65,000 in the Moderna model to approximately $95,000 in the CDC model. Overall, vaccinating adults aged 50–59 years at higher risk of severe RSV disease is projected to reduce disease burden significantly. Clinical trial efficacy data and conservative assumptions about the duration of protection support the potential for meaningful disease reduction.

Dr. Shaw asked whether the incorporation of a factor for premature death might help address the potential effects of RSV vaccination on pre-existing conditions, such as RSV infection precipitating congestive heart failure or COPD exacerbations.

Dr. Ortega-Sanchez responded that in the CDC model, life expectancy was adjusted by specific medical condition and included resulting mortality in model. Dr. Hutton added that productivity losses from those deaths was included. The model did not include adverse outcomes from other health conditions that might have been precipitated by RSV infection.

Drs. Michael Melgar (CDC/NCIRD) and Diya Surie (CDC/NCIRD) shared the EtR for RSV vaccination in adults aged 50–59 years. The work group is considering a risk-based recommendation, with the policy question "Should adults aged 50–59 years at increased risk of severe RSV disease be recommended to receive a single dose of RSV vaccination?" Dr. Melgar reminded the committee that one RSV vaccine is also approved by FDA for vaccination of adults aged 18-49 years at increased risk of severe RSV disease; that policy question is planned for discussion at the June 2025 meeting.

For the public health domain, Dr. Melgar shared that RSV is a concern among adults aged 50–59 years, particularly those with underlying conditions. Although overall disease rates in this group are 10–50% lower than in adults 60–64 years of age, they still account for an estimated 15,000–20,000 RSV-associated hospitalizations annually. Most hospitalized adults have at least one chronic condition.

Common conditions include cardiovascular disease, diabetes, and COPD. Asthma, immune compromise, and severe obesity are more common in adults aged 50-59 years than in older adults but remain among the top 10 conditions in both groups. Adults with COPD have hospitalization rates 4.6 times higher than those without. The strongest independent risk factor is having two or more chronic conditions, followed by age ≥75 years.

Among adults 50 years of age and older, those 50–59 years of age without chronic conditions have the lowest RSV hospitalization rates. However, those with chronic kidney disease, COPD, severe obesity, asthma, or coronary artery disease experience RSV hospitalization rates similar to adults ≥75 years without these conditions. There are other underlying conditions that were not included in this analysis that are known to be associated with an increased risk of severe RSV disease; these include heart failure and immune compromise, especially in those who are recipients of lung or hematopoietic stem cell transplants. If RSV vaccination were recommended for adults 50-59 years of age using a narrower definition of chronic medical conditions, about 30% of this age group would be eligible. The work group felt that RSV "probably is" or "is" of public health importance among adults aged 50–59 years who are at increased risk of severe RSV disease.

The GRADE evidence review focused on use of RSV vaccine [AREXVY (GSK), ABRYSVO (Pfizer), or mRESVIA (Moderna)] compared to no RSV vaccine in adults aged 50–59 years at increased risk of severe RSV with the following outcomes:

- Medically attended RSV lower respiratory tract disease (LRTD)
- Hospitalization for RSV respiratory illness
- Death due to RSV respiratory illness
- Serious adverse events after vaccination
- Inflammatory neurologic events (e.g., Guillain-Barré syndrome)

For the benefits and harms domain, the work group treated the three licensed RSV vaccines (two protein subunit vaccines from GSK and Pfizer, and Moderna's mRNA vaccine) as a single intervention in GRADE. This decision was based on the non-product-specific policy question and the fact that each vaccine has already been GRADEd individually in prior ACIP meetings.

Only GSK and Pfizer have FDA licensure for adults aged 50–59 years; any recommendation made would apply only to licensed products in this age group. If Moderna later receives licensure for this age group, it would be incorporated into the recommendation. All three vaccines target the same RSV antigen; product-specific considerations are shown where relevant.

No manufacturer has conducted an efficacy trial in adults aged 50-59 years, but all three companies have performed immunogenicity studies in high-risk immunocompetent 50-59 year olds and compared those results to those found in adults 60 years of age and older, in whom efficacy has been demonstrated; all three vaccines resulted in noninferior or superior levels of neutralizing antibody responses in the younger age group compared with that observed in older adults.

For potential harms, safety data from the GSK and Pfizer trials in adults aged 50–59 years with risk conditions were used, with no extrapolation from other age groups. Moderna's trial was excluded from the safety assessment due to the absence of a placebo group. The pooled relative risk of serious adverse events was 1.13, with concerns about imprecision and inconsistency. Inflammatory neurologic events could not be assessed, as none were reported in vaccine or placebo arms.

The certainty assessments in GRADE focused on outcomes that the work group considered critical. RSV vaccination may reduce hospitalization for RSV respiratory illness, with low certainty. It may result in little difference in serious adverse events, with low certainty. Death due to RSV respiratory illness and inflammatory neurologic events could not be GRADEd.

Available FDA data support the existence of an increased risk of Guillain-Barré syndrome after receipt of the protein subunit RSV vaccines in adults ≥65 years of age; using the same risk-benefit model previously used to look at the older population, 1M doses of protein subunit vaccines administered to adults aged 50-59 years at increased risk of severe RSV disease could prevent 2,000 hospitalizations, 430 ICU hospitalizations, and 130 deaths over three RSV seasons; if the absolute risk from adults ≥65 years of age is applied to adults aged 50-59 years, 0-18 cases of Guillain-Barré syndrome might occur per million people vaccinated.

Regarding RSV revaccination, limited efficacy data show that a second dose 12 months after the first does not improve protection against symptomatic disease. Revaccination boosts neutralizing antibody levels and, for the adjuvanted vaccine, stimulates a CD4 T-cell response. However, for GSK’s vaccine, the antibody response after revaccination does not reach the levels observed after the first dose, even when the second dose is given 3 years later. For Moderna’s vaccine, neutralizing antibody responses at 12 and 24 months met noninferiority criteria compared to dose one, though the peak response at 24 months remained lower.

Several unknowns remain. It is unclear whether longer intervals between doses, such as 5 years, would lead to stronger antibody responses. It is also unknown whether the lower antibody

responses after revaccination are sufficient to provide clinical protection. Correlates of protection for RSV are still being defined, and the relative roles of humoral and cellular immunity are not yet fully understood. Furthermore, all revaccination data currently come from immunocompetent individuals, so how immunocompromised adults might respond is not known.

For immunocompromised adults, GSK evaluated two doses of AREXVY in individuals with renal or lung transplants. After one dose, neutralizing antibody titers were lower than in immunocompetent adults aged 50 years and older. A second dose given one month later increased titers to levels similar to immunocompetent adults two months post-vaccination. Cellular immune responses were comparable, and no major safety concerns were identified, though one participant experienced renal transplant rejection after RSV vaccination.

Pfizer studied ABRYSVO in adults with conditions such as autoimmune disorders, solid organ transplants, end-stage renal disease on dialysis, or non-small cell lung cancer. One month after a single dose, neutralizing antibody titers were similar to those in immunocompetent adults ≥ 60 years. The neutralizing antibody response in participants with autoimmune disorders on immunomodulator therapy and in solid organ transplant recipients appeared lower than in adults with end-stage renal disease. A second dose did not significantly increase titers. No specific safety concerns were reported, though one renal and one lung transplant rejection occurred.

The majority of the work group felt that the desirable anticipated effects of RSV vaccination in high-risk adults aged 50–59 years of age were moderate, with a minority opinion feeling they were small. Most of the work group felt the undesirable anticipated effects were small, with a minority opinion of “don’t know.” The majority of the work group felt the desirable effects outweighed the undesirable effects and favored intervention, with a minority feeling that they were unclear.

For the values and preferences domain, Dr. Surie shared that in a CDC omnibus survey from April 2024, 19% of adults aged 18–59 reported being very or moderately concerned about RSV disease. This reflects responses from the general adult population, not specifically those with underlying conditions. In comparison, 28% of adults aged 60–74 years expressed the same concern.

Additional data from the National Immunization Survey showed that among adults aged 60–74 years with risk conditions, nearly 50% reported concern about RSV disease, and 80% believed the vaccine provides important protection. As of February 15, 2025, 47% of adults ≥75 years of age had received the RSV vaccine, compared to 37% of adults aged 60–74 years at increased risk. In both age groups, 12% reported they plan to get vaccinated.

While no data specifically assesses how patients value the estimated protection against RSV compared to the potential risk of Guillain-Barré syndrome, a few considerations are relevant. Adults are generally willing to accept some vaccine-associated adverse events in exchange for disease prevention. However, the baseline and vaccine-associated risk of Guillain-Barré syndrome may vary by age and presence of chronic conditions. Similarly, willingness to accept the risk of Guillain-Barré syndrome may differ based on a person's age, health status, and perceived risk of RSV-related illness.

Dr. Surie summarized that about 20% of adults aged 18–59 years report being very or moderately concerned about RSV, compared with approximately 30 to 35% of adults aged 60 years and older. However, there are no specific data for adults aged 50–59 years at increased risk of severe disease. As of February 2025, RSV vaccine uptake in the National Immunization Survey was 37% among adults aged 60–74 years at increased risk and 47% among adults aged 75 years and older. Finally, there are no data on how adults weigh protection against RSV compared to the potential risk of Guillain-Barré syndrome; this may vary by age or other factors.

When asked whether the desirable effects of RSV vaccination are large relative to the undesirable effects, the majority of the work group responded, "Probably yes" with a minority responding "varies" and "don't know." When asked if there is important uncertainty or variability in how much adults aged 50–59 years at increased risk value the main outcomes, most work group members felt there is probably important uncertainty or variability, with a minority opinion that there was probably not important uncertainty or variability.

For the acceptability and feasibility domain, almost 50% of adults aged 60–74 years with risk conditions had no concerns about RSV vaccination. Among those with concerns, the top reasons included lack of knowledge, concern about serious side effects, and no provider recommendation.

In a June 2024 provider survey, 58% of healthcare providers responded that they regularly check RSV vaccine eligibility, while 29% do so only sometimes or never. Common barriers to recommending the vaccine include anticipated refusal, financial concerns, and vaccine fatigue.

Additional challenges to implementation of a risk-based recommendation for RSV vaccine include high vaccine cost leading to a large-upfront investment to stock the vaccine, reliance on pharmacies where risk assessment and billing for risk-based recommendations may be challenging and added complexity of the adult immunization schedule.

Dr. Surie summarized that approximately 50% of adults aged 60–74 years with risk conditions have no concerns about the RSV vaccine. Among those concerned, the most common reasons were limited knowledge, concern about serious side effects, and lack of provider recommendation. About 60% of providers regularly check RSV vaccine eligibility. Key barriers to recommending the vaccine include concerns about patient vaccine fatigue and anticipated refusal. Additional implementation barriers include vaccine cost, challenges of a risk-based recommendation in pharmacy settings, and increased complexity of the adult vaccine schedule.

The work group felt that recommending RSV vaccines for adults aged 50–59 years at increased risk of severe disease would be or probably would be acceptable to key stakeholders. For feasibility, most members felt that it would be or probably would be feasible to implement a recommendation for RSV vaccination among adults aged 50-59 years at increased risk of severe RSV disease.

For the resource use domain, Dr. Surie shared that at current list prices, the CDC-University of Michigan model estimated societal costs of $43,000 to $152,000 per quality-adjusted life year gained from RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease. Vaccination may be cost-saving for those with certain conditions, but key uncertainties remain, including RSV illness incidence, mortality, duration of protection for a single dose of RSV vaccine, and real-world effectiveness of Moderna's vaccine. The work group felt RSV vaccination could be cost-effective for a broader adult population if vaccine prices were substantially reduced. Overall, most work group members felt that RSV vaccination for adults aged 50–59 years at increased risk is or probably is a reasonable and efficient use of resources.

For equity, the median age of RSV hospitalization is younger among Black, Hispanic, and American Indian/Alaska Native adults compared to White and Asian/Pacific Islander adults. While overall RSV rates are lower in adults aged 50–59 years than in older adults, Black adults in this age group have 2.3 times the hospitalization rate of White adults. This disparity is likely due to a higher prevalence of risk conditions among Black adults in this age group.

Dr. Surie summarized that although RSV rates are generally lower in adults <60 years of age, Black adults aged 50–59 years experience significantly higher hospitalization rates than their White peers. Chronic conditions that increase RSV risk are more common in some racial and ethnic groups, and RSV vaccine uptake has varied by race and ethnicity. The work group felt

that recommending RSV vaccination in adults aged 50–59 years at increased risk of severe RSV disease would probably increase health equity.

The work proposed the following vote language:

ACIP recommends that adults 50–59 years of age who are at increased risk of severe RSV disease[1] receive a single dose of RSV vaccine[2,3].

1. CDC will publish Clinical Considerations that describe chronic medical conditions and other risk factors for severe RSV disease for use in this risk-based recommendation.

2. RSV vaccination is recommended as a single dose only. Persons who have already received RSV vaccination are NOT recommended to receive another dose.

3. RSV vaccine can be administered with any product licensed in this age group.

Among adults aged 50–59 years at increased risk of severe RSV disease, the majority of the work group felt that desirable consequences probably outweigh undesirable consequences in most settings, with a minority view that the balance between desirable and undesirable consequences is closely balanced or uncertain.

When the work group was asked whether there was sufficient information to proceed with a recommendation, the majority said yes. Most supported recommending RSV vaccination for adults aged 50–59 years at increased risk, though a minority preferred a shared clinical decision-making approach or felt no recommendation should be made at this time.

Overall, the work group majority believed that the risk conditions used to guide RSV vaccination recommendations for adults aged 60–74 years should also apply to adults aged 50–59 years. The work group emphasized the need for additional data to determine the optimal revaccination interval and to support policy decisions related to revaccination. They also stressed the importance of continued safety surveillance monitoring.

Dr. Diya Surie (CDC/NCIRD) presented clinical considerations for the work group. Currently, only GSK's AREXVY and Pfizer's ABRYSVO vaccines are licensed for adults aged 50–59 years at increased risk of severe RSV disease. If Moderna's mRNA RSV vaccine gains FDA licensure for this group, it would be included in the existing recommendation by default. Notably, Pfizer’s ABRYSVO is also licensed and recommended for use during pregnancy to help prevent RSV-associated lower respiratory tract disease in infants. No other RSV vaccine is approved for use in pregnancy.

The work group proposed using the same risk conditions currently applied in the recommendation for adults aged 60–74 years for the new 50–59 age group. These conditions were selected based on evidence connecting them to an increased risk of severe RSV disease or a strong rationale suggesting they could worsen outcomes from a respiratory infection.

RSV vaccination offers the most benefit when given in late summer or early fall, just before the RSV season begins. Adults who have already received a dose do not require another at this time. While additional doses may be needed in the future, the optimal timing is still unknown.

Immunogenicity data show that with a small number of exceptions, co-administration of RSV vaccines with other vaccines met pre-specified noninferiority criteria compared to separate administration. However, the work group notes that the clinical significance of the observed decrease in antibody titers with co-administration is not fully understood.

GSK presented results from a co-administration study of AREXVY and the recombinant zoster vaccine (Shingrix). Immunogenicity noninferiority criteria were met and no specific safety concerns were identified. Reactogenicity was higher with simultaneous administration than AREXVY alone, but similar to Shingrix alone. Serious adverse events occurred in 4.9% of the simultaneous group versus 2.3% of the sequential group, with no clustered patterns by organ

system or event type. No cases of Guillain-Barré syndrome or acute disseminated encephalomyelitis were reported.

Overall, the work group interprets co-administration of RSV vaccines with other recommended adult vaccines as common practice. CDC considers co-administration acceptable given the clear benefits and available safety data. Notably, the RSV-specific guidance differs from the CDC's general best practices, recommending routine simultaneous administration of all indicated vaccines for individuals without contraindications. The RSV guidance states that co-administration is acceptable, reflecting uncertainty in immunogenicity results from co-administration studies. This guidance may be updated as new evidence emerges, and the work group looks forward to learning more about an analysis by Moderna on immunologic correlates of protection for RSV when a peer-reviewed publication is available.

When deciding whether to co-administer other vaccines with an RSV vaccine, providers may consider whether the patient is up to date on recommended vaccines, the likelihood of the patient returning for additional doses, the risk of acquiring vaccine-preventable diseases, the reactogenicity profiles of the vaccines, and patient preferences.

Dr. Loehr asked whether anyone from the minority opinion group would like to comment further or if they felt the shared perspective accurately represented their views.

Dr. Melgar noted that the minority opinion was driven by uncertainty, particularly about the risk of Guillain-Barré syndrome and the unknown effectiveness of a second RSV dose. Some members questioned whether it might be better to wait until age 60 years to vaccinate, given the increasing risk with age. Despite these concerns, most felt that extending the risk-based recommendation to adults aged 50–59 years would likely provide the greatest public health benefit.

Dr. Zucker expressed concern about the uncertainty and asked whether the work group discussed shared clinical decision-making. While she is not a strong supporter of that approach, she noted that using it would create a different recommendation for adults aged 50–59 years compared to those 60–74 years of age, which she would prefer to avoid. She acknowledged that some individuals in the 50–59 year age group, such as lung or stem cell transplant recipients, would clearly benefit from vaccine access. She asked whether shared clinical decision-making would be realistic or add too much complexity.

Dr. Talbot noted a significant disparity in vaccine uptake when shared clinical decision-making was used for adults over 60. One reason for considering vaccination starting at age 50 was to help reduce those disparities. She expressed concern that sharing clinical decision-making for the 50–59 year age group could worsen existing disparities.

Dr. Zucker commented that providers who care for high-risk patients, such as those in transplant settings, would likely recommend the vaccine and have better access to it. Within the 50–59 year age group, there is a clear subgroup that would benefit from vaccination. In these cases, providers would likely take a more proactive approach, rather than relying on general recommendations or decisions made in pharmacy settings.

Dr. Brooks shared being struck by data showing a subgroup with the same risk level as adults aged 75 and older. Another point was that Black, Hispanic, and American Indian or Alaska Native adults had a median age of hospitalization 7 to 10 years younger than other groups, indicating a higher risk at younger ages. Although the overall median age was 62 to 64 years, the lower end of the range supported including adults aged 50–59 years. However, uncertainty around revaccination tempered this view. While the benefit of revaccination currently seems marginal, Dr. Brooks expressed hope that future data will clarify its value. Considering all

factors, there was hesitation about leaning toward clinical decision-making, but ultimately, the overall balance of evidence supported moving forward with a recommendation.

Ms. Moser noted that the revaccination question was also central in her mind as she reviewed the data. While immune responses after revaccination were lower than after the primary dose, they were still higher than pre-vaccination levels, and T-cell responses were stronger. She emphasized the importance of considering this and expressed hope for more data in the future. She also pointed out that some individuals who have already received one dose may now face exposure to RSV through natural infection. Given this, she supports moving forward with the proposed recommendation.

Dr. Goldman offered a perspective from general internal medicine, noting experience administering the RSV vaccine in a private practice setting. He stated that he was very supportive of lowering the age and keeping the recommendation as simple as possible. He appreciated the broad risk-based approach and emphasized the importance of allowing patients to self-attest when accessing the vaccine at pharmacies. From a clinical standpoint, obtaining, storing, billing, and reimbursement for the vaccine has been manageable with appropriate systems in place, so this should not pose a barrier. The main concern is potential delays from insurance companies in implementing any recommendation. Many patients 50 years of age and older with conditions like emphysema, heart disease, or lung disease have expressed interest in receiving the vaccine. Dr. Goldman encouraged avoiding shared clinical decision-making, maintaining broad risk criteria, and ensuring access through providers and pharmacies.

Dr. Fryhofer noted that one aspect not mentioned in the discussion was the influence of having a new grandchild. In conversations with patients, especially older adults, the presence of a grandchild has often been a motivating factor for choosing to get the RSV vaccine. She asked whether this consideration had come up previously.

Dr. Melgar explained that the work group has considered the difference between the risk of exposure to RSV and the risk of severe illness. While increased exposure, such as in preschool teachers or new grandparents, has come up in discussions, the work group has generally focused its recommendations on individuals at highest risk for severe outcomes like hospitalization or ICU admission. This focus is based on clinical risk rather than exposure alone. The benefit-risk balance is clearer for those with underlying conditions, guiding the group's approach.

Dr. Loehr motioned to accept the proposed voting language.

Dr. Kamboj seconded the motion.

In additional discussion, Dr. Kamboj noted that some data presented showed individuals with lower pre-vaccination titers had better responses to revaccination. This finding is particularly relevant to the immunocompromised population, and Dr. Kamboj emphasized the importance of further exploring this in future research.

Vote: RSV-Adult Vote

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP vote for RSV-Adult into the record:

ACIP recommends that adults 50–59 years of age who are at increased risk of severe RSV disease[1] receive a single dose of RSV vaccine[2,3].

1. CDC will publish Clinical Considerations that describe chronic medical conditions and other risk factors for severe RSV disease for use in this risk-based recommendation.

2. RSV vaccination is recommended as a single dose only. Persons who have already received RSV vaccination are NOT recommended to receive another dose.

3. RSV vaccine can be administered with any product licensed in this age group.

Motion/Vote: RSV-Adult Vaccines

Dr. Loehr motioned to approve the RSV-Adult vaccine language recommendation, stating, "ACIP recommends that adults 50–59 years of age who are at increased risk of severe RSV disease receive a single dose of RSV vaccine." Dr. Kamboj seconded the motion. No COIs were declared. The motion carried with 14 in favor, 1 abstained, and 0 opposed. The disposition of the vote was as follows:

14 Favored: Asturias, Brewer, Brooks, Chen, Cineas, Jamieson, Kamboj, Loehr, Lyons, Moser, Schechter, Shaw, Zucker, and Talbot

1 Abstained: Kuchel

Following the vote, Dr. Schechter encouraged Moderna and other manufacturers to continue gathering data on the durability of protection, noting the importance of this information in light of cost-effectiveness analyses. He also emphasized the need for data on the clinical implications of lower peak titers following additional doses, stating that such information would help guide ACIP's deliberations.

Dr. Brooks echoed Dr. Schechter's comments regarding the lower titers, stating that while they may be acceptable, more data is needed to confirm this. He also noted that this was the strongest equity-focused vote and congratulated ACIP for favoring the recommendation.

Dr. Zucker echoed previous comments and emphasized that revaccination is the central area of uncertainty. There is an urgent need for additional data and clarity on how revaccination should be approached, as it will be necessary to achieve adequate antibody titers.

Dr. Kamboj emphasized the need for more studies focused on individuals with moderate to severe immunocompromise, who are at the highest risk for RSV disease, calling it a clear call to action.

Dr. Talbot agreed.

CHIKUNGUNYA VACCINES

Dr. Edwin Asturias (ACIP, Work Group Chair) introduced the Chikungunya Vaccines Work Group session. Chikungunya is a mosquito-borne viral disease that can cause severe disability, congenital anomalies, and early death. This year alone, over 80,000 cases and 46 deaths have been reported across many countries, including five in South America. The Chikungunya Vaccines Work Group, formed in May 2022, has reviewed disease risks for travelers, lab workers, and residents in U.S states and territories with reported transmission. Two chikungunya vaccines are licensed: a live attenuated vaccine (Valneva, licensed in November

2023) and a virus-like particle vaccine (Bavarian Nordic, licensed in February 2025). Both were approved based on immunogenicity and safety data, with further efficacy studies pending.

The work group will present evidence supporting recommendations for the use of the chikungunya virus-like particle vaccine among adolescent and adult travelers and among laboratory workers. The presentation also includes updated safety data on the live attenuated vaccine and proposed revised recommendations, and clinical guidance for use of the virus-like particle vaccine in pregnant and lactating women.

Dr. Susan Hills (CDC/NCEZID) shared the EtR and proposed recommendations for use of the virus-like particle chikungunya vaccine (CHIK-VLP) among adolescents and adult travelers. Bavarian Nordic manufactures CHIK-VLP under the trade name VIMKUNYA™. It was licensed on February 14, 2025, to prevent chikungunya in adolescents and adults aged ≥12 years and is administered as a single-dose primary series. Like the previously licensed live attenuated vaccine, CHIK-VLP received FDA approval through the Accelerated Approval pathway, which can be used for serious conditions with unmet medical needs.

Traditional approval through efficacy trials would have been difficult due to the unpredictable and typically short duration of chikungunya outbreaks, and no established immunologic correlate of protection exists. Effectiveness was demonstrated by using a surrogate endpoint, which was a neutralizing antibody titer that prevented viremia in non-human primates challenged with virus. Safety was evaluated in adequate and well-controlled studies. As required by the pathway, a post-marketing clinical trial will be conducted by Bavarian Nordic to confirm clinical benefit, efficacy, safety, and immunogenicity.

The policy question for consideration by ACIP is “Should CHIK-VLP be recommended for use in persons aged ≥12 years traveling to areas with risk of chikungunya virus transmission?”

For the public health problem domain, Dr. Hills shared that chikungunya is a mosquito-borne disease identified in approximately 120 countries over recent decades. While not all have ongoing transmission, many tropical and subtropical regions continue to report cases. In 2024, about 620,000 cases were reported globally, though the burden is likely underestimated due to underdiagnosis and limited testing in some areas.

A key feature of this disease is that outbreaks can be large and explosive. Attack rates are often high, with between one-third and three-quarters of the population affected. The disease can lead to significant morbidity and place enormous strain on health services.

In terms of clinical presentation, chikungunya typically causes fever and polyarthralgia. The joint pain is often severe and can be debilitating. It commonly affects multiple joints, particularly in the hands and feet, making everyday activities like typing or walking difficult. Other symptoms may include headache, myalgia, fatigue, rash, abdominal pain, and vomiting. No specific antiviral treatment exists, so management is limited to supportive care.

Serious illness is uncommon but can occur due to direct consequences of infection such as encephalitis or myocarditis, or due to worsening of underlying medical conditions. The case fatality rate is low, with deaths primarily reported in two groups: older adults, particularly those with co-morbidities, and young infants infected perinatally or through mosquito bites.

A major consequence of chikungunya is joint pain that can persist or recur after the acute illness. While most patients recover within 7 to 10 days, some experience prolonged or

relapsing arthralgia, along with symptoms such as fatigue. The risk of ongoing joint pain varies and is influenced by illness severity, age, and pre-existing joint conditions.

CDC conducted a meta-analysis to better characterize persistent arthralgia. Among patients who sought care, 100% reported joint pain during the acute phase. At 3 months post-infection, about 51% continued to experience joint pain, and at 12 months, 38% still reported symptoms.

The work group next considered whether chikungunya poses a public health concern for U.S. travelers. The risk varies as transmission can differ substantially by location and by year. For example, case counts in U.S. travelers were high during the 2014–2015 outbreak in the Americas. In contrast, from 2022 to 2024, only about 100 to 200 cases were reported annually, although the true number is likely higher due to underdiagnosis and underreporting. Except during 2014–2015, 3–18 times fewer chikungunya cases were reported annually than dengue cases.

Risk estimates for travelers were calculated based on data, with limitations, gathered during previous outbreaks in Puerto Rico and the United States Virgin Islands. Among travelers spending one week in an outbreak area, the estimated risk was 667 cases per 100,000 for clinical chikungunya, 27 per 100,000 for hospitalization, and 253 per 100,000 for chronic arthralgia of any severity at 12 months. In contrast, the risks were much lower for travelers to non-outbreak areas: approximately 6.7 cases per 100,000 for clinical disease, 0.3 per 100,000 for hospitalization, and 2.5 per 100,000 for chronic arthralgia. For travelers to non-outbreak areas for a longer period of 6 months, the risks were approximately 176 cases per 100,000 for clinical disease, 7 per 100,000 for hospitalization, and 67 per 100,000 for chronic arthralgia.

Based on all the factors reviewed, the work group felt that the public health importance of chikungunya for U.S. travelers varies. The most important factor is the level of virus transmission at the traveler's destination. Other contributing factors include travel duration, age, and underlying medical conditions.

For the benefit and harms domain, based on the GRADE assessment, the first question addressed was how substantial the anticipated desirable effects are. The work group identified short- and long-term vaccine efficacy against disease as critical outcomes. However, the assessment was based on immunogenicity data because no efficacy data were available. The surrogate marker of protection was a neutralizing antibody titer, estimated using a validated non-human primate model.

Short-term immunogenicity was assessed based on seroresponse at 21 days post-vaccination. Key data came from two randomized controlled trials: one in adolescents and adults aged 12 to 64 years (2,559 participants with results in vaccine arm), and another in adults aged ≥ 65 years (189 participants with results in vaccine arm). The overall seroresponse rate was 97%, with 98% in the < 65 years group and 87% in the ≥ 65 years group.

Seroresponse data at 12 months from the Phase 3 trial were not available for long-term immunogenicity. However, one Phase 2 study included adults aged 18 to 45 years (46 participants with results) and reported a seroresponse rate of 91% at 11 months. Due to the limited data, the work group reviewed 6-month seroresponse rates from Phase 3 studies. Among participants aged 12 to 64 years, the rate was 85%, and among those aged ≥ 65 years, it was 76%. The work group felt that the desirable anticipated effects were large.

To assess the undesirable effects of vaccination, the outcomes the work group considered critical included overall and related serious adverse events and arthralgia outcomes, including severe or persistent arthralgia and arthritis. Arthralgia was a focus given it is a prominent feature of chikungunya. For serious adverse events within six months of vaccination, two randomized trials reported rates of 0.9% among approximately 3,000 vaccinated participants and 0.6% among 671 placebo recipients. These rates were not significantly different. A site investigator considered one serious adverse event, a retinal detachment, possibly vaccine-related. However, the participant had a history of visual symptoms, and the event was ultimately considered unrelated by the chair of the safety monitoring committee. In three randomized studies, arthralgia within 7 days after vaccination was reported by 7% of vaccinated and 6% of placebo recipients and severe arthralgia by 0.2% of vaccinated and 0.2% of placebo recipients. Persistent arthralgia and arthritis were both reported by 0.03% of vaccinated and no placebo recipients. None of the differences in rates between vaccine and placebo recipients were significantly different. The work group determined that the anticipated undesirable effects were small. This conclusion was based on similar rates of serious adverse events and all arthralgia or arthritis outcomes between the vaccinated and placebo groups, along with the unclear relatedness of the one serious adverse event reported as vaccine-related by a site investigator.

The work group concluded that the desirable effects outweigh the undesirable effects, supporting vaccination and favoring the intervention. However, the overall risk varies substantially and inversely with the intensity of the chikungunya virus transmission. The risk-benefit assessment is considered favorable when the vaccine is used according to the proposed recommendations, which focus on higher-risk travelers.

Summarized results from the GRADE analysis were presented. Based on the available evidence, CHIK-VLP might result in a large increase in short-term protection against chikungunya, supported by a large effect but with low certainty. For long-term disease prevention, CHIK-VLP might also lead to a large increase in protection; however, the certainty of this evidence is very low, making the long-term benefit more uncertain.

Based on a small but important effect and low certainty in the evidence, CHIK-VLP might slightly increase serious adverse events compared with placebo. For arthralgia and arthritis outcomes, based on no demonstrated effect and moderate certainty in the evidence, CHIK-VLP probably results in little to no difference in overall arthralgia, severe arthralgia, persistent arthralgia, or arthritis after vaccination compared with placebo.

Data for the values and preference domain were gathered in an online survey conducted in 2022. Dr. Hills shared that during an outbreak period, defined as a 1 in 150 risk of chikungunya for travelers, 42% of respondents reported they were very or somewhat likely to receive a chikungunya vaccine, 32% were very or somewhat unlikely, and 26% were unsure. During a non-outbreak period, defined as a 1 in 15,000 risk of disease, 27% of respondents were very or somewhat likely to receive the vaccine, 49% were very or somewhat unlikely, and 24% were unsure. There was variability in responses, with a lower likelihood of vaccination reported among adults aged 18 to 29 years, those with lower education and household income levels, and Black respondents compared with other racial and ethnic groups. In decision-making, important factors included disease risk, vaccine side effects, avoiding long-term joint pain, and vaccine cost. The target population's responses varied in terms of whether they felt the desirable effects of vaccination were large relative to the undesirable effects. The work group felt there was important uncertainty or variability in how much people value the main outcome.

The work group identified key stakeholders for the acceptability domain as U.S. travel medicine providers, other health care professionals, and travelers. For providers, the vaccine adds a tool for disease prevention alongside mosquito bite prevention measures. For travelers, it offers protection against a potentially severe illness with long-term effects. Official recommendations may also support insurance coverage, benefiting insured travelers. The work group felt that the intervention would be acceptable to key stakeholders.

For the resource use domain, Dr. Hills shared that a cost-effectiveness analysis for chikungunya vaccination in travelers has not been published. However, past analyses of travel vaccines show that most are not cost-effective due to the high number of travelers needed to be vaccinated to prevent a single case. Still, cost-effectiveness may be less relevant for travel vaccines, as they are typically not publicly funded like routine childhood vaccines. Travelers generally decide on vaccination based on personal willingness to pay, perceived risk, and risk tolerance. The work group felt that intervention is probably a reasonable and efficient allocation of resources.

The key equity consideration is that the chikungunya vaccine will likely be paid for out of pocket, or in some cases, by insurers or employers. Some travelers will have financial means or insurance coverage to access the vaccine, while others will not. As a result, the work group felt that the impact on health equity would probably be reduced.

For feasibility, Dr. Hills shared that the vaccine is easy to administer in a healthcare setting as a single dose. CDC will provide guidance, but staying updated on areas with outbreaks and elevated risk may require frequent reference to online resources. Delays in outbreak recognition could hinder timely vaccination for travelers to these areas, but the risk-benefit analysis does not support vaccinating all travelers. The availability of two vaccines with different indications may also require clear communication. The work group felt that the option is probably feasible to implement and that the desirable consequences of vaccination probably outweigh the undesirable consequences in most settings.

The work group proposed the following recommendations:

*ACIP recommends virus-like particle chikungunya vaccine for persons aged ≥12 years traveling to a country or territory where there is a chikungunya outbreak.**

In addition, virus-like particle chikungunya vaccine may be considered for persons aged ≥12 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time e.g., 6 months or more.

**Resources will be available on CDC website*

Dr. Kamboj requested comments on the safety of the vaccine among those who have previously been exposed.

Dr. Hills explained that approximately 85% of chikungunya virus cases are symptomatic, meaning 15% to 25% may be asymptomatic. A study in an endemic area evaluated vaccine safety in individuals with prior exposure to the virus. Those previously exposed showed a higher rate of local injection site swelling and a more rapid immune response. Although the sample size was small (~40 participants), overall safety appeared acceptable, with injection site swelling being the only notable difference compared to individuals without prior exposure.

Dr. Shaw asked whether there is any information on the rate of adverse reactions for the VLP vaccine compared to the live attenuated vaccine currently in use.

Dr. Hills explained that no head-to-head studies exist between the VLP and live attenuated vaccines, so direct comparisons are impossible. However, available data suggest that the VLP vaccine may be associated with a lower rate of systemic adverse events, while local reactions may be slightly higher. In contrast, the live attenuated vaccine appears to have a higher rate of systemic reactions. Without comparative studies, these observations remain inconclusive.

Dr. Shaw asked about the representation of older adults in the studies evaluating the VLP vaccine.

Dr. Hills confirmed that older adults were included in a dedicated study for individuals aged ≥65 years. The study enrolled approximately 400 participants, with about 200 receiving the VLP vaccine.

Dr. Brewer raised concerns about the implications of relying on website updates to declare an outbreak. Specifically, there was a question about what happens if the website cannot be updated for several weeks or months, and whether alternative language could be included to allow for more flexibility in declaring an outbreak under such circumstances.

Dr. Hills explained that defining outbreaks aims to provide accurate guidance specifically for U.S. travelers. This involves assessing the number of cases and the size of the outbreak and confirming that cases are laboratory-confirmed. In the past, some reported outbreaks were found not to be chikungunya due to a lack of lab confirmation. The team also considers whether outbreaks occur in areas commonly visited by U.S. travelers, as some are very localized and pose little to no risk to this population. While the CDC aims to post updates on its website, other sources such as ProMED, commercial groups that track outbreaks, and subscription services used by travel medicine providers may also provide relevant information. The purpose of defining outbreaks clearly in CDC recommendations is to offer consistent and reliable guidance for U.S. travelers making individual risk-benefit decisions.

Dr. Talbot suggested allowing more flexibility in defining an outbreak if the CDC cannot update its website. The proposal was to revise the guidelines to allow recognition of an outbreak based on credible evidence from other sources, rather than relying solely on CDC postings.

Dr. Hills acknowledged that travel medicine and healthcare providers can use any sources they choose to assess outbreak risk. However, the CDC aims to offer specific, reliable guidance for U.S. travelers. In the absence of CDC updates, providers can consult other sources, but the CDC is cautious about broadening its definition of an outbreak. Some widely shared outbreak reports have later proven inaccurate, and the CDC prefers to rely on confirmed, accurate information before issuing recommendations.

Dr. Zucker asked whether the recommendation involves two separate votes: one on the core recommendation and a second on the additional language related to shared clinical decision making.

Dr. Hills shared that the work group proposes this as a combined recommendation that includes both the core recommendation and a "may be considered" component. It will be presented as one vote, and the second component falls under shared clinical decision making.

Dr. Zucker also requested clarification on what qualifies as "elevated risk," noting that a single confirmed case from five years ago may not seem sufficient and requested an explanation of the rationale behind the definition.

Dr. Hills explained that "elevated risk" is based on a median of one chikungunya case among U.S. travelers over the past five years. In earlier recommendations, the definition was broader and included any area with transmission in the last five years, identifying 52 countries. However, further analysis showed that 27% of those countries had no reported U.S. traveler cases since 2018. The work group refined the definition using traveler case data to better reflect risk to U.S. travelers. Using the median of one U.S. traveler case over five years narrowed the list to eight countries: India, Brazil, Mexico, the Philippines, Thailand, Pakistan, Nigeria, and Colombia. These countries are considered to pose a more consistent risk to U.S. travelers.

Dr. Schechter inquired whether the proposed language is similar to the current language for the live vaccine, aside from the age group difference, or if there are any other notable differences.

Dr. Hills confirmed that the question will be answered in the following presentation.

Dr. Zahn posed a hypothetical scenario where a traveler is visiting a country rarely frequented by U.S. travelers. In such a case, no U.S. traveler cases may have been reported, but the traveler might still feel at risk and question the applicability of the recommendation. Dr. Zahn noted this type of question could reasonably arise.

Dr. Hills clarified that any traveler could receive the vaccine if they choose. If a travel medicine provider identifies a concern about transmission, or if the traveler has personal knowledge of risk, such as having family in the area, they may opt to be vaccinated. The recommendations reflect situations with a risk level similar to 1 in 15,000, where the risk-benefit assessment generally supports vaccine use in many circumstances. However, individual travelers can make their own decisions in consultation with a provider.

Dr. Loehr motioned to accept the proposed language for the CHIK-VLP recommendations.

Dr. Asturias seconded the motion.

Dr. Erin Staples (CDC/NCEZID) provided the EtR and proposed recommendations for the use of virus-like particle chikungunya vaccine among laboratory workers. At least 44 chikungunya virus infections were reported in lab workers globally over 50 years; of these, 43 were symptomatic, 1 was asymptomatic, and there were no deaths. Four U.S. cases have been reported since 2015, when the disease became nationally notifiable. These likely reflect underestimates due to a lack of a formal laboratory surveillance system.

Documented transmission routes for chikungunya virus in laboratory settings include aerosol and percutaneous exposure. Two cases involved needlestick injuries while handling infected mice; a third involved a forceps injury during dissection of infected mosquitoes. Mucosal exposure is also a possible route of transmission.

Cross-protection is important for vaccinating laboratory workers who may handle multiple chikungunya virus genotypes (Asian, West African, and East/Central/South African). The CHIK-VLP vaccine is based on the West African genotype, which is the most genetically distinct, though all genotypes are considered a single serotype with limited antigenic variation. Available data suggest potential cross-protection: one nonhuman primate study showed protection

against the East/Central/South African genotype, and serum from vaccinated individuals neutralized all three genotypes, with some variability in neutralizing antibody titers between lineages. While promising, cross-protection has not been definitively established.

The policy question the work group considered was “Should chikungunya virus-like particle vaccine be recommended for laboratory staff at risk for chikungunya virus infection?”

For the public health domain, the work group determined that chikungunya is not of public health importance overall in the U.S., as only occasional cases are reported among laboratory workers. However, laboratorians do work with the virus, and there is a potential risk of acute infection with severe polyarthralgia and possible chronic arthralgia.

The work group determined that the desirable anticipated effects of vaccination with CHIK-VLP were moderate. Clinical trial data showed strong short-term serologic responses. Still, data on long-term protection are limited, which is a key consideration for laboratorians who may work with the chikungunya virus over many years. While CHIK-VLP likely provides cross-protection against all genotypes, this has not been confirmed. The work group assessed the undesirable anticipated effects as small, with no significant differences between vaccine and placebo groups in serious adverse events or arthralgia outcomes.

The work group determined that the desirable effects of CHIK-VLP vaccination outweigh the undesirable effects, based on acceptable immunogenicity and safety data from clinical trials and the benefits of prevention from a potentially severe illness. The certainty of evidence was rated as low for short-term efficacy, very low for long-term efficacy, and low for potential adverse events, based on the clinical trial data and the GRADE assessment conducted by the work group.

The work group determined that laboratorians are likely to view the desirable effects of vaccination as large compared with the undesirable effects. There is unlikely to be important variability in values, as laboratorians generally understand the disease risks and the benefits of vaccination, and most scientists value vaccination.

The work group determined vaccine recommendations would likely be acceptable to key stakeholders, including occupational health directors, laboratory managers, and laboratorians, as their availability would enhance laboratory safety.

The work group determined that recommending the chikungunya vaccine represents a reasonable use of resources. Vaccination would apply to a limited number of staff involved in research or specific diagnostic work, and the cost of vaccination is small compared to the potential impact and cost of an occupational infection.

The work group determined that equity would likely be increased if employers offered chikungunya vaccination to laboratory staff, as this would enhance worker safety and address occupational health concerns.

The work group determined that vaccination is feasible to implement, as it can likely be integrated into existing occupational health programs for laboratory workers.

Considering all domains of the EtR framework, the work group determined that the desirable consequences of CHIK-VLP vaccination for laboratory workers at risk of chikungunya virus infection probably outweigh the undesirable consequences in most settings.

The draft recommendation developed by the work group is:

ACIP recommends the virus-like particle chikungunya vaccine for laboratory workers with potential for exposure to chikungunya virus.

The recommendations will be accompanied by implementation guidance stating that institutional biosafety committees should conduct a risk assessment for each laboratorian working with the chikungunya virus. This assessment should consider the type of work performed and the biosafety level at which the work is being conducted. Vaccination is unnecessary for staff handling routine clinical samples, as standard precautions are sufficient in those settings.

Dr. Talbot inquired whether the vaccine would be administered as a one-time vaccination, or would revaccination be required for worker who stayed in roles with potential for exposure to chikungunya virus.

Dr. Staples noted that the vaccine is currently administered as a single dose. As mentioned by Dr. Hills, additional long-term immunogenicity data are needed to determine whether revaccination may be necessary.

Dr. Loehr motioned to accept the recommendations for laboratory workers to receive CHIK-VLP vaccination.

Dr. Cineas seconded the motion.

Dr. Susan Hills (CDC/NCEZID) shared the surveillance for adverse events following use of the live attenuated chikungunya vaccine (CHIK-LA) among travelers. CHIK-LA (IXCHIQ®, manufactured by Valneva) was licensed in the United States in November 2023 for individuals aged ≥18 years as a single dose primary schedule. It was licensed based on immunogenicity and safety data in about 3,500 adults, including about 350 adults aged 65 years and older.

In the pivotal Phase 3 trial, there were safety data from 3,082 subjects. Solicited local reactions within 10 days after vaccination were reported by 15% of CHIK-LA recipients compared to 11% by placebo recipients. Solicited systemic adverse events within 10 days after vaccination were reported by 50% of CHIK-LA recipients and 27% of placebo recipients. The systemic events that were most common among the vaccine recipients were headache, fatigue, and myalgia, which were reported by ~25%-30% of vaccinees.

Chikungunya-like adverse reactions were defined as fever ≥100.4F (38C) and ≥1 of the following: arthralgia or arthritis, myalgia, headache, back pain, rash, lymphadenopathy, or certain neurologic, cardiac, or ocular symptoms, with symptom onset within 30 days of vaccination. Based on this definition, chikungunya-like adverse reactions were reported by 11.7% of vaccine recipients and 0.6% of placebo recipients, with severe reactions preventing daily activity or requiring medical intervention in 1.6% of vaccine recipients vs 0% of placebo recipients and prolonged reactions with duration of ≥30 days in 0.5% of vaccine recipients vs 0% of placebo recipients. These reactions prompted a warning in the package insert that IXCHIQ may cause severe or prolonged chikungunya-like adverse reactions.

Based on the available data at the time of licensure, in the EtR presented to ACIP in February 2024, the work group concluded that CHIK-LA is a reactogenic vaccine, but with adverse event rates comparable to some other reactogenic vaccines. The work group also emphasized the need to monitor for rare adverse events after licensure, since the clinical trials, which included about 3,500 vaccinated individuals, were too small to detect rare outcomes. Dr. Hills noted that at the time of licensure, FDA indicated that two post-marketing studies would be required to collect additional data on safety and vaccine effectiveness. In addition, the manufacturer will additionally be conducting a safety study among 5,000 U.S. travelers, gathering information on medically attended adverse events of special interest, and an observational registry study of pregnant women in Brazil.

Post-licensure surveillance for adverse events following this vaccine has been conducted through VAERS, a national spontaneous reporting system co-managed by CDC and FDA. VAERS is designed to detect rare or unexpected adverse events or shifts in reporting patterns that may signal a safety concern requiring further investigation. Reports can be submitted by healthcare providers, patients, family members, or vaccine manufacturers. While VAERS is effective as an early warning system, it has limitations, including under- and over-reporting, variable report quality, lack of data on vaccine doses administered, and the absence of an unvaccinated comparison group. Therefore, it is generally not possible to determine whether a reported adverse event was caused by the vaccine.

ACIP recommendations for CHIK-LA were approved in February 2024. While the exact start date for distribution and administration is unknown, the first adverse event report, a non-serious case, was submitted on May 6, 2024. In total, 28 adverse event reports were submitted in 2024, excluding one non-serious foreign report. Of these, 22 were for non-serious adverse events and 6 were for serious adverse events. Among the 22 non-serious reports, 10 described chikungunya-like reactions, 4 involved arthralgia or arthritis without fever, and 8 were for other events, including syncope, flushing, rash with headache, generalized musculoskeletal pain, low-grade fever with headache (2 reports), and respiratory tract symptoms (2 reports).

Dr. Hills then presented details on the six patients with serious adverse events.

Case 1 involved an 83-year-old male with multiple comorbidities, including coronary artery disease, chronic heart failure, chronic kidney disease, hypertension, hyperlipidemia, and chronic thrombocytopenia. No other vaccines were administered at the same time as CHIK-LA. Symptoms began three days after vaccination. He was seen in the emergency department with generalized weakness on day 7 and returned to the hospital on day 11 when he was admitted. Chikungunya virus testing was not available. The patient was discharged after two days with a diagnosis of encephalopathy and generalized weakness suspected to be due to chikungunya vaccination. His symptoms resolved completely after 3.5 weeks.

Case 2 involved a 77-year-old male with comorbidities including coronary artery disease, hypothyroidism, benign prostatic hyperplasia, hyperlipidemia, hypertension, and selective IgA deficiency. He received a co-administered inactivated Japanese encephalitis vaccine. Symptoms began four days after vaccination. He presented to urgent care on day 6 and was diagnosed with a viral illness. On day 8 he presented to the hospital with profound weakness and intermittent confusion and was admitted. He was hospitalized for 7 days and discharged with diagnoses of acute metabolic encephalopathy possibly related to vaccination and (resolved) fever of unknown origin. Chikungunya virus testing was not available. He had ongoing weakness 4 months after vaccination.

Case 3 involved an 86-year-old male with underlying conditions including diabetes mellitus, heart failure, anemia, hypertension, hypothyroidism, and hyperlipidemia. No other vaccines were co-administered. Symptoms began three days after vaccination. Confusion precipitated ICU admission on day 8, where he was diagnosed with altered mental status, acute encephalopathy secondary to hyponatremia, and shortness of breath. A serum RT-PCR test conducted on day 13 was positive. He was discharged on day 31, following a 23-day hospitalization, with a diagnosis of toxic metabolic encephalopathy and fever, possibly related to a post-vaccination inflammatory response. One month after discharge, he had mostly recovered.

Case 4 involved a 68-year-old male with a medical history of prostate cancer, hypothyroidism, hypertension, and dyslipidemia. No other vaccines were administered at the same time, although he had received multiple inactivated vaccines in the preceding weeks. Symptoms of fever, headache, fatigue, and generalized body aches began five days after vaccination. He

subsequently developed photophobia and neck stiffness. He was hospitalized on day 12 with meningitis. Chikungunya virus IgM and neutralizing antibodies were detected in cerebrospinal fluid (CSF). He was discharge after three days with a diagnosis of aseptic meningitis likely secondary to recent vaccination. His headache and fatigue resolved by about one month after discharge.

Case 5 involved a 67-year-old male with hyperlipidemia who received a co-administered oral live typhoid vaccine; 19 days earlier he had also received COVID-19 and inactivated influenza vaccines. Symptoms began four days after vaccination with myalgia followed by onset of fever the next day. On day 6 tachycardia with palpitations began and on day 8 he presented to hospital with atrial flutter with rapid ventricular response. No chikungunya test was available. He was discharged after a 2-day hospitalization with a diagnosis of atrial flutter with rapid ventricular response and a suspected small and non-ST-segment elevation myocardial infarction (NSTEMI). He was fully recovered at discharge but 3 months following hospitalization remained on medication.

Case 6 involved a 74-year-old male with ischemic cardiomyopathy, hypotension, coronary artery disease, chronic leukopenia, and chronic thrombocytopenia. He received a co-administered inactivated Japanese encephalitis vaccine. Symptoms including fatigue, weakness, and lightheadedness began three days after vaccination. On day 8 he seen by his internist and noted to have lower blood pressure than usual, which persisted when he was seen again on day 15. His final diagnosis was an episode of worsened and prolonged hypotension on the background of pre-existing cardiomyopathy and hypotension, likely related to CHIK-LA vaccination. No chikungunya test available. His symptoms resolved within about 2 weeks.

Dr. Hills summarized that the six serious adverse events occurred in temporal association with CHIK-LA during 2024. All cases were in males aged 67 to 86 years. Five of the six individuals had multiple underlying medical conditions. The presentations generally fell into two categories: four cases involved neurologic symptoms, including three with encephalopathy and one with meningitis, and two cases involved cardiovascular events, including one with atrial flutter and NSTEMI and another with severe and prolonged hypotension.

The work group consulted with the Clinical Immunization Safety Assessment (CISA) Project, a CDC-supported national network of vaccine safety experts from eight medical research centers, to obtain additional expert input on the serious adverse events. Available medical records for all six serious adverse events, including four neurologic and two cardiac reports, were reviewed with CISA subject matter experts in vaccine safety, infectious diseases, cardiology, and neurology. For each case, at least one expert considered the association between CHIK-LA and the serious adverse event was plausible. However, CISA experts noted the difficulty in distinguishing between general reactogenicity in older patients with comorbidities that may lead to a serious adverse event, and an adverse event specifically caused by the chikungunya vaccine.

Several factors support a possible causal association between CHIK-LA and the reported serious adverse events. All events began within three to five days of vaccination. Among the three patients who received co-administered vaccines such as Japanese encephalitis or typhoid vaccines, a causal association with these vaccines seems less likely, given the lack of association of these types of serious adverse events with these vaccines in long-term surveillance. Investigations did not identify clear alternate causes for any of the patients, and five discharge summaries noted a potential association with vaccination. In two cases where chikungunya laboratory testing was performed, results suggested a possible link to CHIK-LA.

Dr. Hills noted that all serious adverse events following CHIK-LA occurred in individuals aged ≥65 years. Immunosenescence may impair the ability of older individuals to control the

replication of a live attenuated vaccine virus. For example, serious adverse events are more common with the live attenuated yellow fever vaccine in older adults, and age ≥60 years is listed as a precaution for its use. Wild-type chikungunya virus infections are also more likely to cause severe disease in older adults compared with younger adults.

Understanding the incidence of serious adverse events is important but challenging due to limited data on CHIK-LA doses distributed and even less on doses administered. To estimate incidence, the work group obtained sales and administration data from IQVIA, a commercial healthcare data provider. IQVIA's weekly sales perspective data reflect actual vaccine doses sold to retailers, clinics, and universities. IQVIA considers the data capture approximately 90% of total vaccine sales in the U.S. IQVIA's administration data provides projected estimates of vaccinations administered in pharmacies. It is unknown how accurately vaccinations administered in pharmacies represent vaccinations administered in other settings, such as physician offices, but they provide some information on the administration of vaccines by age group that was not otherwise available.

In 2024, approximately 13,900 doses of CHIK-LA were distributed. Approximately 9% went to pharmacies, while 91% were distributed to physician offices. There were an estimated 928 doses administered in pharmacies in 2024; of those, 53% of doses were administered to individuals aged ≥65 years.

Based on the number of serious adverse events reported to VAERS (n=6), IQVIA data on doses distributed (n=13,891), and IQVIA data for the proportion of doses administered to persons aged 65 years and older (52.7%), the estimated rate was 82 serious adverse events per 100,000 doses administered to individuals ≥65 years. This corresponds to an estimated rate of one serious adverse event per 1,220 doses administered, with a 95% confidence interval ranging from one serious adverse event per 3,333 doses to one serious adverse event per 556 doses. Focusing specifically on the subset of five hospitalizations, the estimated rate was 68 hospitalizations per 100,000 doses administered to individuals ≥65 years. This corresponds to an estimated rate of one hospitalization per 1,471 doses administered, with a 95% confidence interval ranging from one hospitalization per 5,000 doses to one hospitalization per 625 doses.

There are several limitations to these risk estimates. The calculations may be affected by imprecision in numerator and denominator data, including unknown completeness of reports submitted to VAERS and potential inaccuracies in vaccine administration data overall and by age group. In addition, although all VAERS serious adverse event reports were included in the calculations, a causal link between vaccination and each of the reported events cannot be confirmed. In summary, the overall estimates have low to very low certainty due to these limitations.

To provide updated data, as of March 21, 2025, no serious adverse events have been reported to VAERS. Nine non-serious reports from individuals in the U.S. have been received. IQVIA data shows an additional 4,250 CHIK-LA doses were sold in 2025. In February 2025 CDC distributed an alert about hospitalizations after CHIK-LA in persons ≥65 years of age; the impact of this alert on use of CHIK-LA in this age group is unknown.

The work group considered several key factors regarding serious adverse events after CHIK-LA vaccination. First, all reported serious adverse events occurred in individuals aged 65 years and older. Second, an association between CHIK-LA and the serious adverse events is plausible, although a causal link was not established for each case. Third, the findings are preliminary, as CHIK-LA has only been administered to approximately 7,700 individuals in the 65-year and older age group across clinical trials and in post-licensure use. Fourth, VAERS is intended as an early warning system to detect potential safety signals, and a signal has been identified in this age group. However, due to data limitations, further investigation is needed to better understand

the actual risk. Finally, a risk-benefit assessment is important for individual travelers ≥65 years to weigh the risk of disease against the risk of vaccination. Use of the vaccine may be appropriate in certain higher-risk scenarios, such as during an outbreak, given the known risk for severe disease and hospitalization in this population.

Based on these factors, the work group concluded that age ≥65 years should be considered a precaution for the use of CHIK-LA. In general, vaccination should be deferred in this age group, but it may be appropriate when the benefits of protection against disease outweigh the potential risks of an adverse reaction.

The work group also proposed revising the recommendations for CHIK-LA use among travelers. This was primarily in accordance with the updated EtR framework for travelers presented for CHIK-VLP vaccine with an additional risk-benefit assessment recently conducted for chikungunya risk for travelers, and also in consideration of the safety signal following vaccine use in persons aged ≥65 years.

The work group proposed revised draft recommendations for use of CHIK-LA to prevent chikungunya among travelers:

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, live attenuated chikungunya vaccine may be considered for persons aged ≥18 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time e.g., 6 months or more.

Dr. Talbot clarified for members of the public who may be listening that two different chikungunya vaccines were being discussed: a live attenuated vaccine and a virus-like particle (VLP) vaccine. The VLP vaccine is not a live vaccine, and the adverse events just discussed were observed only with the live attenuated vaccine. She followed up with a question on the FDA's plans to evaluate and review the current licensure.

Dr. Høeg responded that she would obtain that information and share it with the group as soon as possible.

Dr. Loehr asked how common it is for individuals who receive a live attenuated vaccine to have viremia 13 days later or would have evidence of the virus in cerebrospinal fluid (CSF), and whether this is considered a common or uncommon event.

Dr. Hills noted that viremia was assessed in a small group of 30 participants in the CHIK-LA clinical trials. At 3 days post-vaccination, 90% had detectable viremia; at 7 days, 17% had viremia; and by 14 days, no participants had detectable viremia. She explained that RNA is typically detected in serum for about 5 to 8 days after symptom onset in wild-type chikungunya virus infection, with occasional longer durations. The detection of viral RNA at 13 days post-vaccination, as seen in one case after CHIK-LA, is longer than what is typically observed in natural infection. Dr. Hills also mentioned that some studies have found higher viral loads in patients with severe chikungunya disease, though findings are variable. In the CHIK-LA clinical trials, there was a suggestion that viremia was associated with increased frequency and severity of adverse events, and high-level viremia was identified in one participant who experienced a serious adverse event in the Phase 3 trial.

Dr. Loehr followed up to ask whether detection in CSF was common.

Dr. Hills stated that IgM would not typically be expected in a vaccinated person's cerebrospinal fluid (CSF). However, lumbar punctures are not routinely performed on vaccine recipients. The presence of IgM in the CSF suggested the possibility of direct viral invasion of the central nervous system (CNS).

Dr. Schechter asked whether any safety data are available from using the live attenuated vaccine in settings outside the U.S.

Dr. Hills responded that the live attenuated chikungunya vaccine was licensed in mid-2024 in Europe and Canada, but distribution didn't begin until later in the year. Approximately a dozen adverse event reports have been received from France, including mainland France and Réunion, where there is a large, explosive chikungunya outbreak with about 20,000 confirmed cases. The French government purchased around 40,000 vaccine doses of CHIK-LA and a vaccination campaign began recently. The French recommendations support use in adults aged ≥65 years, particularly those with comorbidities, and adults aged 18–64 years with underlying medical conditions. All adverse event reports from France and Réunion have been non-serious to date. Additional safety data from this setting are anticipated.

Dr. Zucker asked whether the recommendation for those aged 65 years and older should be stronger than a precaution, such as contraindication, given the reported serious adverse events. Dr. Zucker also suggested including guidance to consider the alternative VLP vaccine, since a precaution may imply the live attenuated vaccine is still generally acceptable in this age group, despite current concerns.

Dr. Hills explained that the decision to designate age 65 years and older as a precaution rather than a contraindication was based on several factors. First, the data are limited, with only about 7,700 doses used in clinical trials or post-licensure as of December 2024. The level of risk remains unclear, especially since no additional serious adverse events have been reported in 2025. Second, while the association between CHIK-LA and serious adverse events is plausible, the evidence is not definitive due to incomplete investigations being conducted in patients in some cases. Third, a risk-benefit analysis may support CHIK-LA use in certain high-risk settings, such as outbreaks, especially if no alternative vaccine is available. For example, in the ongoing outbreak in Réunion, about half of the 130 hospitalized cases and half of the 31 very severe cases were in adults aged 65 years and older. Given this elevated risk, the work group felt that a precaution, with vaccination generally deferred, was the most appropriate approach.

Dr. Zucker suggested adding a footnote to the recommendation stating that providers should consider use of the VLP vaccine in individuals aged 65 and older, if available, as an alternative when vaccination is still deemed appropriate.

Dr. Hills agreed that the suggestion could be considered, noting that including footnotes within the recommendation can be challenging. The guidance accompanying the recommendation could clearly communicate the option to consider the VLP vaccine for this age group.

Dr. Asturias added that the work group carefully debated various options and aimed to balance the available evidence. Currently, there is not enough evidence to support a preferential recommendation. Instead, providing clear guidance on the precaution is considered the appropriate initial step. It was emphasized that more data are expected in the coming months, requiring ongoing reassessment. The importance of ACIP's cautious approach to issuing preferential vaccine recommendations was also acknowledged.

Dr. Høeg followed up and shared that the FDA does not yet have a response prepared but expressed appreciation for the presentation and for bringing attention to the safety signal. FDA plans to convene a group of relevant experts to discuss the issue and will follow up once a plan is developed. Dr. Høeg made an additional comment about a previous presentation. In the MenQuadfi presentation, there was an imbalance in febrile seizures that was highly statistically significant. She stated that she had done the statistics on this and suggested that this would be a good question for Sanofi, why they determined that this was not related to the vaccine.

Dr. Loehr motioned to accept the draft recommendation for CHIK-LA among travelers.

Dr. Asturias seconded the motion.

Dr. Susan Hills (CDC/NCEZID) provided the clinical guidance for using the virus-like particle chikungunya vaccine (CHIK-VLP) in pregnant women. The spectrum of illness from chikungunya virus infection during pregnancy appears similar to that in non-pregnant individuals and does not appear to be more severe. Adverse outcomes such as fetal loss, stillbirth, or preterm birth due to vertical transmission have been documented but are rare. Mouse studies and examination of placentas from infected women suggest that the placenta is generally resistant to chikungunya virus infection. However, adverse neonatal outcomes are common when infection occurs around delivery time. Intrapartum transmission occurs in approximately 30–50% of such cases, likely through transplacental transmission caused when maternal blood enters the fetal circulation by placental barrier breaches from uterine contractions during labor.

Neonatal infection following intrapartum transmission can lead to severe and sometimes fatal illness. In one prospective study, 10 of 19 (53%) infected infants developed severe disease, often presenting with encephalopathy or a sepsis-like illness. Cardiac, dermatologic, and hemorrhagic symptoms may also occur. Poor neurocognitive outcomes are common, especially with encephalopathy. Young infants infected via mosquito-borne virus transmission are also at risk of severe illness, with similar clinical presentations. This shows the potential importance of maternal vaccination for protecting infants through transplacental antibody transfer.

No data are currently available on the immune response to CHIK-VLP vaccination during pregnancy or its potential to protect young infants. However, transplacental antibody transfer following maternal immunization has been shown to be protective with several vaccines. Documented benefits include reduced infant hospitalization rates with influenza, COVID-19, and RSV vaccines, and reduced risk of preterm birth with COVID-19 vaccination.

The data are insufficient to determine any safety risks from CHIK-VLP vaccination during pregnancy, as pregnancy was an exclusion criterion in the clinical trials. Only one woman was inadvertently vaccinated during pregnancy. She was in her first trimester and enrolled in a Phase 2 study using a lower dose, unadjuvanted formulation. She had a history of two prior ectopic pregnancies, and her last menstrual period was 11 days before vaccination. An ectopic pregnancy was detected 24 days after vaccination and was assessed as unrelated to the vaccine.

Developmental and reproductive toxicology (DART) studies provide limited data. In a rabbit study, animals received the equivalent of a human dose of the vaccine on five occasions: twice before mating, twice during gestation, and once during lactation. Postnatal survival within 28 days was lower in kits born to vaccinated mothers (42%) compared to the control group (69%), although no adverse effects were observed in other postnatal development parameters. In a similar DART study, reduced pup survival rates were not observed in rats.

The objectives of chikungunya vaccination during pregnancy are to protect the pregnant woman from disease, prevent maternal infection around the time of delivery to avoid intrapartum transmission and severe illness in the newborn, and support transplacental transfer of antibodies which might protect young infants from mosquito-borne transmission and severe disease.

The proposed clinical guidance for use of CHIK-VLP in pregnant women was developed to maximize benefits and minimize potential risks of chikungunya vaccination during pregnancy. Pregnant women should avoid exposure to the chikungunya virus when possible. Pregnancy is a precaution for vaccination with CHIK-VLP based on the lack of safety and immunogenicity data in pregnant women and potential safety concerns from the toxicology study in rabbits. In general, vaccination should be deferred until after delivery. However, if the risk of infection is

high and exposure cannot be avoided, a health care provider should discuss with a pregnant woman the potential risks of chikungunya virus infection and the potential benefits and risks of vaccination so that vaccination can be considered. If vaccination is pursued, it is recommended to avoid administration during the first trimester and, when possible, to vaccinate more than two weeks before delivery. When both vaccine options are available, the non-live CHIK-VLP vaccine is preferred over the live attenuated CHIK-LA vaccine.

Chikungunya virus RNA has been detected in breast milk on very rare occasions in women from endemic areas, but no studies have shown the presence of replicating virus. In one case report, a mother with chikungunya and detectable viral RNA in her breast milk breastfed her three-month-old infant, who showed no symptoms or laboratory evidence of infection. Although data are limited, there is no evidence of chikungunya virus transmission through breastfeeding.

There are no data on breastfeeding benefits or risks after CHIK-VLP vaccination, including whether chikungunya antibodies are present in breast milk post-vaccination. No impact on lactation was observed in toxicology studies in rabbits and rats.

The primary objective of vaccinating breastfeeding women is to protect the mother from chikungunya, with a potential added benefit of reducing the infant's risk of infection by transferring protective antibodies in breast milk.

Proposed clinical guidance for use of CHIK-VLP in breastfeeding women states that breastfeeding women and their infants should avoid the risk for chikungunya virus infection, if possible (e.g., by avoiding travel to an area with transmission particularly during an outbreak). Best practice guidelines for immunization note that non-live vaccines pose no risk for mothers who are breastfeeding or their infants. Breastfeeding is not a contraindication or a precaution for vaccination with CHIK-VLP.

Dr. Jamieson supported the proposed guidance, noting that although not part of the work group, the recommendations appear reasonable. Dr. Jamieson also emphasized that this highlights yet another instance where the lack of safety data in pregnancy is unfortunate.

Dr. Joseph echoed Dr. Jamieson's support for the thoughtful approach to developing guidance for vaccine use in pregnancy. Dr. Joseph also emphasized that there is no justification for pregnancy resulting in exclusion from vaccine trials moving forward.

Vote: Chikungunya Vote #1

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for the first chikungunya vaccine vote into the record:

ACIP recommends virus-like particle chikungunya vaccine for persons aged ≥12 years traveling to a country or territory where there is a chikungunya outbreak.

In addition, virus-like particle chikungunya vaccine may be considered for persons aged ≥12 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time, e.g., 6 months or more.

Motion/Vote: Chikungunya Vote #1

Dr. Loehr motioned to approve the recommended voting language, stating, "ACIP recommends virus-like particle chikungunya vaccine for persons aged ≥12 years traveling to a country or

territory where there is a chikungunya outbreak. In addition, virus-like particle chikungunya vaccine may be considered for persons aged ≥12 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time e.g., 6 months or more." Dr. Asturias seconded the motion. No COIs were declared. The motion carried with 14 in favor, 1 abstained, and 0 opposed. The disposition of the vote was as follows:

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

Vote: Chikungunya Vote #2

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for the second chikungunya vote into the record:

ACIP recommends virus-like particle chikungunya vaccine for laboratory workers with potential for exposure to chikungunya virus.

Motion/Vote: Chikungunya Vote #2

Dr. Loehr motioned to approve the voting language, stating, "ACIP recommends virus-like particle chikungunya vaccine for laboratory workers with potential for exposure to chikungunya virus." Dr. Cineas seconded the motion. No COIs were declared. The motion carried with 14 in favor, 1 abstained, and 0 opposed. The disposition of the vote was as follows:

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

Vote: Chikungunya Vote #3

Dr. Keipp Talbot (ACIP Chair) read the following proposed ACIP voting language for the third chikungunya vote into the record:

ACIP recommends live attenuated chikungunya vaccine for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak.

In addition, live attenuated chikungunya vaccine may be considered for persons aged ≥18 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time, e.g., 6 months or more.

**Age ≥65 years is a precaution for use of CHIK-LA*

Motion/Vote: Chikungunya Vote #3

Dr. Loehr motioned to approve the recommended voting language, “ACIP recommends live attenuated chikungunya vaccine for persons aged ≥18 years traveling to a country or territory where there is a chikungunya outbreak. In addition, live attenuated chikungunya vaccine may be considered for persons aged ≥18 years traveling or taking up residence in a country or territory without an outbreak but with elevated risk for U.S. travelers if planning travel for an extended period of time e.g., 6 months or more. Age ≥65 years is a precaution for use of CHIK-LA.” Dr. Asturias seconded the motion. No COIs were declared. The motion carried with 14 in favor, 1 abstained, and 0 opposed. The disposition of the vote was as follows:

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

Dr. Daskalakis commended the team for their work on the chikungunya vaccine safety efforts, acknowledging the situation's complexity and expressing appreciation for the thorough and dedicated work.

Dr. Schechter encouraged placing the CHIK-LA recommendations alongside the CHIK-VLP recommendations, stating that doing so would help providers and the public better understand the difference in the recommendations for individuals aged ≥65 years while the safety signal is being further investigated.

PUBLIC COMMENT

The floor was opened for public comment on April 16, 2025, at 3:10 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-2025-0017. Visit regulations.gov for access to read the comments received.

Mariana Rodrigues
American Society for Meningitis Prevention

Mariana Rodrigues, Communications Director of the American Society for Meningitis Prevention, spoke on behalf of the organization’s founders, Patty Wukovitz and Alicia Stillman, sharing the personal stories that drive their mission. Patty’s daughter, Kim, was preparing for prom and high school graduation, and she had plans to become a nurse like her mother. Alicia’s daughter Emily was a college sophomore known for her humor and ability to unite people. Both Kim and Emily died from meningitis B at a time when no vaccine was available to protect them. Ms. Rodrigues emphasized that vaccines are now available, and the responsibility to recommend them lies with the ACIP. She highlighted the resurgence of measles, rising meningococcal cases, and declining vaccination rates as a call to action. Forty-five percent of healthcare providers report that current meningitis vaccine guidance is too complex, leading to confusion and leaving children unprotected. She urged ACIP to reprioritize the 2024 meningococcal vaccine platform review and issue clear, practical recommendations that providers can follow and families can trust. Ms. Rodrigues reminded the committee of the real-life impact of these decisions, referencing families whose pediatricians never mentioned the vaccine, the UVA student who recently died from meningitis, and the many healthcare

professionals advocating for stronger guidance. She closed by thanking ACIP for making evidence-based decisions that protect the future of the nation's youth.

Angela Rasmussen, PhD
Vaccine and Infectious Disease Organization, University of Saskatchewan, and Stony Brook University

Dr. Rasmussen is a principal scientist at the Vaccine and Infectious Disease Organization at the University of Saskatchewan, who also holds faculty appointments in the Department of Biochemistry, Microbiology, and Immunology at the University of Saskatchewan and the Department of Ecology and Evolution at Stony Brook University; she also serves as Co-editor-in-chief of the journal *Vaccine*. Dr. Rasmussen offered a public comment on the future of the ACIP. She emphasized the ACIP's vital role in ensuring vaccine recommendations are grounded in scientific evidence and reviewed by qualified experts. She expressed that advisory panels across the CDC and Department of Health and Human Services have been disbanded or indefinitely postponed, and there is potential risk that the ACIP could face a similar fate. She referenced statements by Secretary Kennedy indicating plans to make advisory panels and policy development less accessible to the public and to investigate vaccines based on ideological rather than scientific motivations, including revisiting the widely discredited link between the MMR vaccine and autism spectrum disorders. She pushed back on claims that ACIP members' expertise constitutes a conflict of interest, stating that vaccine development experience should be recognized as a qualification, not a liability. Vaccine recommendations must be developed through rigorous, evidence-based review by qualified scientists in a transparent process that includes public engagement. She highlighted the global significance of ACIP's work, noting that Canada's National Advisory Committee on Immunization considers ACIP recommendations in its recommendation process and urged that the ACIP continue to convene in its current form with its current expert membership.

Katrin Werner-Perez
Alliance for Aging Research

Ms. Werner-Perez serves as the Director of Health Programs, Alliance for Aging Research. She emphasized the critical role of vaccines in preventing disease and improving quality of life, particularly for older adults. She shared five recommendations from the Alliance for ACIP's consideration for strengthening public health outcomes. First, the Alliance strongly supports lowering the risk-based age recommendation for RSV vaccination to include adults aged ≥50 years, noting that RSV leads to approximately 42,000 hospitalizations annually in adults aged 50–64 years and poses a heightened risk for those with pre-existing conditions. Earlier vaccination would provide broader protection, reduce disease burden, and lower healthcare costs. Second, the Alliance called for a vote to expand the routine age-based recommendation for RSV vaccination to adults aged 60–74 years. Citing data from the June 2023 ACIP meeting, she highlighted disparities in RSV vaccination rates. A routine age-based recommendation could help address health equity by reducing the burden of RSV among racial and ethnic minority groups and individuals with lower incomes. Third, the Alliance commended ACIP for lowering the age recommendation for pneumococcal vaccines to adults aged ≥50 years and emphasized the need for clear, accessible information to be shared with providers and the public to maximize uptake and reduce pneumonia-related complications. Fourth, the Alliance urged continued prioritization of measles vaccination, referencing >700 confirmed measles cases since January 1, 2025, including a 12% hospitalization rate and three reported deaths. Given the severity of complications, especially in older adults, the Alliance encourages maintaining high coverage across all age groups and exploring whether booster doses for older adults

should be considered. Lastly, she stressed the importance of continued transparency and public participation in ACIP meetings, noting that open engagement is essential to building and maintaining trust in vaccine policy. She concluded by thanking ACIP and CDC for their continued efforts to protect public health.

Samantha Sears
National Consumers League

Ms. Sears is the Health Policy Associate with the National Consumers League (NCL). She provided public comments emphasizing NCL's long-standing commitment to increasing public access to and confidence in immunization and other preventive health measures since its founding in 1899. Citing the ongoing measles outbreaks and the recent severe respiratory illness season, she stressed the urgent need to preserve the strength and integrity of the nation's immunization infrastructure. Vaccines are extremely safe and effective at preventing disease, reducing severity, and preventing serious complications. However, declining vaccine confidence, distrust in public health systems, and barriers to access are contributing to falling vaccination rates nationwide. NCL urged ACIP to continue ensuring data availability through open meetings, which enhance transparency and allow the public and policymakers to better understand the rigorous vaccine safety and efficacy systems in place. She emphasized that transparency is essential to rebuilding trust and maintaining public confidence in vaccines and encouraged ACIP and CDC to reinforce these efforts. NCL also raised concerns about current MenB vaccine recommendations, arguing that shared clinical decision-making creates an unnecessary barrier, particularly as serogroup B has become the most common strain in individuals aged 17–23 years. She noted that this recommendation structure often results in the vaccine being perceived as optional or unnecessary and called on ACIP to strengthen and reconsider this guidance. Lastly, NCL urged ACIP to vote to recommend the RSV vaccine for high-risk adults aged 50–59 years. Without an ACIP recommendation, this vaccine remains largely inaccessible to this group, despite evidence that the burden of RSV in older adults and those with chronic conditions is underestimated. Expanding the recommendation would increase access and uptake among vulnerable populations. She closed by expressing NCL's appreciation for the opportunity to share its positions and for ACIP's continued efforts to protect the health of children and adults across the country.

Alexandra Steiner
Long COVID patient advocate

Ms. Steiner offered public comments in strong support of the committee's vital work, sharing her personal experience as a disabled young woman living with long COVID. Formerly a healthy and ambitious international affairs professional, she became severely ill and immunocompromised one and a half years ago due to a COVID infection from which she never recovered. She emphasized that timely access to safe and effective vaccines is now essential to her care, as any illness or infection seriously threatens her health. Expressing deep concern about the state of the public health system, she warned that current decisions are leading to increased infectious diseases, resulting in more deaths and disability. She highlighted the impact of limited vaccine access for people on Medicaid or underinsured people, noting that communities suffer when individuals cannot get updated vaccines. She strongly opposed political or ideological interference in vaccine science, especially as the scientific consensus continues to indicate that every COVID infection may cause lasting immune system damage. She urged the public to protect themselves through vaccination and N95 masking. She called on the committee to ensure that updated COVID vaccines of all types, including mRNA and Novavax, are made available earlier than in previous years, preferably by July before the start of

the school year. She also recommended launching print and online awareness campaigns early in the summer to promote the safety and effectiveness of the vaccines. Stressing that tens of millions of Americans with long COVID or ME/CFS are relying on vaccine access to prevent further health decline, she appealed to the committee to speak boldly in support of vaccination at every opportunity. She asked that members use their platforms to affirm that the COVID vaccine is safe, that it reduces the risk of hospitalization and death, and that COVID can cause serious and long-term illness regardless of age or background. She thanked the committee for their time and continued commitment to protecting public health through vaccination.

Stanley Plotkin, MD
University of Pennsylvania

Dr. Plotkin expressed appreciation for ACIP, describing the committee as precious to the United States, and offered detailed comments on CMV vaccine development. He emphasized that CMV is unlike measles or rubella, as protection against congenital CMV relies not just on neutralizing antibodies but on multiple components of the immune system, including antibody-dependent cellular cytotoxicity and T-cell responses. He noted that maternal CMV infection occurs more frequently than fetal transmission, which depends on several factors such as the maternal viral dose, viremia, placental infection, and subsequent transmission to the fetus. Dr. Plotkin questioned the current focus on antibodies targeting the surface pentamer in mRNA vaccines, suggesting their protective role may be limited. Citing his research, he stated that the quantity of the challenge dose influences infection, which may account for differences in CMV epidemiology between low-income and high-income countries. He urged that the success of a CMV vaccine be measured by its ability to prevent fetal transmission, not just maternal infection. He proposed that vaccinating infants in daycare could help protect mothers. He concluded by expressing hope for the return of Lyme disease vaccines in the U.S. and Europe, noting the effectiveness of the first vaccine and attributing its removal from the market to mistakes made in the 1990s, both by epidemic experts and by the CDC, which did not strongly recommend the vaccine. Given the continued spread of Lyme disease, he urged that that mistake not be repeated.

Andrew Wang, PhD, MPH
Public Health Professional

Dr. Wang shared comments on the ongoing COVID-19 pandemic. He stated he has no financial conflicts of interest or investments with vaccine manufacturers. Nearly 50% of Americans, according to a recent survey, still view the pandemic as a serious public health issue. Dr. Wang currently works at a federally qualified health center in Chicago, serving underserved communities, and conducts research focused on health equity. He emphasized that public health is under attack, with many Americans believing it is unnecessary until a crisis affects them personally. He urged the committee to remain strong in its support of science and vaccine access and stressed that updated COVID-19 vaccines are a critical part of a multi-layered prevention strategy, along with masking, testing, and ventilation. However, uptake remains low, with only 23% of adults and 12.8% of children receiving the latest vaccine. He noted that vaccine effectiveness wanes within four to six months, reinforcing the need for more frequent boosters and updated formulas that match circulating variants. Current guidelines based on age or risk status create confusion and limit access for those still facing serious risks, including long COVID. He recommended offering updated vaccines at least every six months and ensuring access to all three manufacturers: Moderna, Novavax, and Pfizer. He also called for replacing the CDC's Bridge Access Program, which ended in August 2024 and provided free vaccines to

uninsured and underinsured adults. Wang closed by thanking the committee and urging strong recommendations that ensure access to life-saving vaccines for all.

Dorit Reiss
UC Law San Francisco (formerly Hastings)

Ms. Reiss, a law professor at UC Law San Francisco, offered public comments beginning with thanks to the ACIP members and CDC staff for their long-standing service, expertise, and dedication to public health. She acknowledged the committee's careful and transparent presentation of vaccine data and noted that expert members serve as volunteers for the public good. In response to concerns raised by previous speakers, the professor clarified that ACIP is referenced in two federal statutes and cannot legally be abolished, and that under the Federal Advisory Committee Act, it must meet in public. She shared three points. First, as a parent of teenagers, she expressed gratitude for the availability of a MenABCWY vaccine that covers multiple meningococcal strains in a single dose, rather than requiring two separate shots, and having an additional option will be good. She appreciated the committee's detailed discussion of vaccine effectiveness and emphasized the importance of having experts make decisions based on complex data. Second, she reminded the committee that its recommendations directly impact access and uptake, especially through insurance coverage. Narrow recommendations and shared clinical decision-making often limit access because insurers may not cover such vaccines, and providers may not bring them up. She stressed that simple, clear recommendations lead to higher uptake and that physicians remain key decision-makers in these conversations. Third, she acknowledged the current challenges facing the CDC and public health, including staff and funding losses, and urged the committee to continue its work with clarity and scientific integrity. She emphasized the importance of maintaining an independent body like the ACIP to protect against political interference and make evidence-based decisions. In closing, she thanked the CDC staff for their continued efforts to prevent disease and protect public health, even under difficult conditions.

Paul Hennessy
Private Citizen

Mr. Hennessy urged ACIP to maintain universal COVID-19 vaccine recommendations for all age groups and to avoid shifting toward a risk-based approach that would limit access, especially for children. He argued that such limitations would increase the risk of long COVID and serious outcomes. He emphasized the need to update current guidelines to recommend vaccination every six months, given the virus's year-round circulation and multiple annual surges. The speaker stressed that preserving access for the immunocompromised and the broader public is essential. ACIP's recommendations are not requirements, so limiting access further will only create more barriers for those who choose to be vaccinated. He called for COVID-19 vaccines to be made available by July, not the fall, to prevent unnecessary increases in cases. Citing concerns with using symptom-based long COVID data, he urged improvements in how it is collected and interpreted. Mr. Hennessy criticized Moderna's mRNA-1283 vaccine for relying on bivalent data from 2022, which he argued was ineffective, and instead praised Novavax's protein-based vaccine for its broad protection, fewer side effects, and upper respiratory tract benefits. He condemned misinformation about single antigen vaccines and pointed to the FDA's delay in approving Novavax's Biologics License Application as a serious concern. While recognizing that ACIP does not advise the FDA directly, he encouraged the committee and CDC to publicly support Novavax and other alternatives and advocate for their timely approval. He also urged ACIP members to refute public misinformation, restore the Bridge Access Program, and uphold the universal recommendations that previous public commenters had supported.

Citing over 3,200 comments in favor of Novavax's approval, he warned that limiting access to this vaccine could lead to accessibility challenges and legal scrutiny. He concluded by urging ACIP and CDC to pressure the FDA, support access to all vaccine options, and stand firm in their commitment to protecting public health, stating that the public paid for these vaccines and deserves to benefit from them.

Sue Peschin, MHS
Alliance for Aging Research

Ms. Peschin, President and CEO of the Alliance for Aging Research, offered public comments in support of previous statements made by Katrin Werner-Perez, who had outlined the Alliance's recommendations to lower the risk-based recommendation for the adult RSV vaccine to ages 50–59 years and the universal recommendation to ages ≥60 years. She added several observations, starting with concern over removing flu vaccine votes from the April ACIP meeting agenda and the delay to June. She emphasized that such delays are significant, citing a recent *Journal of Infection* study showing that increasing flu vaccination rates by just 5% could prevent millions of cases and tens of thousands of hospitalizations in a moderately severe season, particularly among preschool-aged children and adults ≥65 years. If ACIP does not vote on the Vaccines for Children program resolution in June, there will be no guarantee of free flu vaccines for eligible children this fall. She also urged ACIP to issue preferential recommendations for higher-dose flu vaccines for older adults and specific high-risk groups, stating that while any flu vaccine is better than none, data show higher-dose options are more effective for these populations. She further emphasized the importance of ensuring updated COVID-19 vaccines are available before the fall, citing their significant public health impact and life-saving benefits. She called on the FDA to schedule a review of the vaccines as soon as possible so that ACIP can vote on recommendations at the June meeting or earlier. Finally, she urged ACIP to keep COVID-19 vaccine guidance simple, noting that 74% of adults aged ≥18 years have at least one condition that increases their risk of severe illness. A shift to risk-based recommendations would create widespread confusion and could lead insurers to restrict coverage. The speaker closed by thanking ACIP members and CDC staff for their dedication, acknowledging their expertise, time, and continued commitment to protecting the health of the American public.

RESPIRATORY SYNCYTIAL VIRUS (RSV) IMMUNIZATIONS- MATERNAL/PEDIATRIC

Dr. Jefferson Jones (CDC/NCIRD) introduced the Maternal/Pediatric Respiratory Syncytial Virus (RSV) Work Group for Dr. Helen Chu (ACIP, Work Group Chair) because she was unable to join this meeting. CDC and ACIP recommend that all infants be protected against severe RSV disease through either maternal RSV vaccination or infant immunization with nirsevimab. Pregnant individuals should receive a single dose of the maternal RSV vaccine between 32 and 36 weeks of gestation to provide protection to their infants through passive immunization. For infants, nirsevimab is recommended for those <8 months of age who are born during or entering their first RSV season. Additionally, nirsevimab is recommended for children aged 8–19 months who are at increased risk for severe RSV disease and are entering their second RSV season.

Dr. Jones introduced a new long-acting monoclonal antibody, clesrovimab, which could become a third option to protect infants from severe RSV disease if approved. Clesrovimab is not currently FDA-approved; however, the PDUFA target action date is June 10, 2025. The proposed indication from Merck is for use in infants <8 months of age born during or entering their first RSV season.

In September 2024, the work group reviewed and discussed safety and efficacy data on clesrovimab submitted by Merck. In October 2024, the ACIP reviewed and discussed Merck's data on clesrovimab, as well as the work group's interpretation of the findings. From November 2024 through April 2025, the work group continued its review, focusing on GRADE the evidence and evaluating the EtR framework for clesrovimab.

At the June 2025 ACIP meeting, there will be a presentation of updates to the EtR framework and clinical considerations for clesrovimab. Pending FDA regulatory action, a vote on a recommendation for clesrovimab may also occur.

Ms. Danielle Moulia (CDC/NCIRD) presented the EtR framework for clesrovimab, based on the policy question, "Should clesrovimab be recommended for all infants <8 months of age born during or entering their first RSV season?"

For the public health problem domain, Ms. Moulia shared that the CDC estimates that, in the absence of RSV prevention products, U.S. children under 5 years of age experience approximately 2 million medical encounters, 58,000 to 80,000 hospitalizations, and 100 to 300 deaths each year due to RSV. RSV is the leading cause of hospitalization among infants. Without RSV prevention products, most infants are infected within their first year of life, and nearly all are infected by age two. Among infants <6 months of age, approximately 2% to 3% are hospitalized due to RSV. The highest rate of RSV hospitalization occurs in the first months of life and declines with increasing age in early childhood. Among children hospitalized for RSV, 79% had no underlying medical conditions. Therefore, all infants are considered to be at risk for severe RSV disease. Data from the 2024–2025 RSV season indicate a return to pre-pandemic seasonality, with cases peaking from December through January. The work group felt that RSV-associated disease among infants <8 months of age is of public health importance.

The work group conducted a GRADE assessment to inform the benefits and harms of immunization with clesrovimab. Clesrovimab effectively prevented RSV-associated medically attended lower respiratory tract infections (LRTIs) and RSV-associated hospitalizations with LRTIs, with high certainty. It also effectively prevented LRTI with ICU admission, with moderate certainty. However, it was ineffective in preventing all-cause medically attended LRTI, with moderate certainty. Clesrovimab was effective in preventing all-cause hospitalization with LRTI, with high certainty. No increase in serious adverse events was observed in the clesrovimab group compared to the placebo group, with moderate certainty.

Based on the data presented, the work group concluded that clesrovimab is an efficacious long-acting monoclonal antibody for preventing severe RSV disease, including medically attended RSV and hospitalization, in young infants during their first RSV season. If approved, clesrovimab would be the second long-acting monoclonal antibody available, and having two products could help mitigate risks related to manufacturing shortages and potential loss of efficacy due to resistance mutations. Clesrovimab demonstrated a favorable safety profile, with no observed increase in serious adverse events or local or systemic solicited adverse events, including fever. However, the work group acknowledged that rare, serious adverse events are unlikely to be detected in a trial of this size. The work group felt that the desirable anticipated effects of clesrovimab were large, while the undesirable effects were small to minimal. The work group concluded that the desirable effects outweighed the undesirable effects, favoring the intervention.

For values, Ms. Moulia shared data from a study of 523 women who were either pregnant or had been pregnant in the past 12 months. Thirty-eight percent believed that their baby would have no symptoms or only mild symptoms if infected with RSV. Additionally, 24% expressed uncertainty about the severity or treatability of the disease if their baby became sick. Despite

these perceptions, respondents on average reported significant concern that their baby might require hospitalization if infected with RSV.

Several factors have been found to increase parental intent to receive an RSV immunization for their infants. In parent interviews, the two most cited factors were trust in their pediatrician's recommendation and fear of RSV infection. Additionally, education about RSV and RSV prevention options further supported parental decision-making. Factors that may decrease parental intent to receive an RSV immunization include concerns about adverse events, a desire for more time to make a decision, wanting to wait until the product has been available longer, and trust in their personal prevention measures against RSV.

As of February 2025, 50% of women aged 18-49 years who have an infant <8 months received nirsevimab for their infant. Nirsevimab uptake may be higher in settings of increased access. The work group felt that the target population probably thought the desirable effects were large relative to the undesirable effects. When asked whether there was important uncertainty or variability in how much parents and caregivers value the prevention of severe RSV disease, most of the work group felt there was probably not important uncertainty or variability.

For the acceptability domain, Ms. Moulia shared that 77% of pediatricians reported that their practice had offered nirsevimab. The majority of pediatricians agreed that nirsevimab is safe for infants and effective against severe disease in infants. RSV prevention through long-acting monoclonal antibodies has been endorsed or recommended by national providers and professional organizations, including but not limited to the American Academy of Pediatrics, the American Academy of Family Physicians, and the National Foundation for Infectious Diseases. The majority of the work group felt that immunization with clesrovimab is acceptable to key stakeholders.

For the feasibility domain, Ms. Moulia shared that clesrovimab storage, handling, and administration are anticipated to be similar to other routine vaccines. If ACIP votes to include clesrovimab, it would become the second monoclonal antibody included in the VFC program. Some factors that may impact implementation include that clesrovimab is a single-dose product regardless of weight, which may be simpler for providers than nirsevimab, which requires weight-based dosing. However, stocking clesrovimab may be challenging for providers who also need to stock nirsevimab for high-risk children aged 8 through 19 months entering their second RSV season. They may prefer to stock only one of these two long-acting monoclonal antibody products.

In a survey of pediatricians, the most commonly reported challenge after parental safety concerns was determining maternal RSV vaccination status to assess infant eligibility. This was reported less often by those currently offering nirsevimab. The next two challenges were the financial burden of purchasing nirsevimab and difficulties with reimbursement from private insurance plans, each reported by 31% of pediatricians. These challenges were more frequently reported by those currently offering nirsevimab than by those who were not.

For infants born between October and March, nirsevimab or clesrovimab will ideally be administered during the birth hospitalization. Implementing the administration of long-acting monoclonal antibodies in birthing hospitals has initially been challenging for some facilities. In a series of CDC learning collaborative calls on nirsevimab administration in birthing hospitals, common barriers included determining maternal RSV vaccination status, storage and handling, billing and cost of nirsevimab, supply shortages, determining eligibility, documenting receipt, care coordination, and VFC program requirements. The majority of the work group felt that clesrovimab was feasible to implement among all infants <8 months of age born during or entering their first RSV season.

For the resource use domain, Ms. Moulia shared data from a cost-effectiveness model created by the University of Michigan and CDC. In the base case scenario comparing an annual birth cohort in which 50% of infants are immunized with clesrovimab to a cohort without RSV immunization (other than palivizumab for eligible high-risk infants), immunization with clesrovimab is estimated to avert approximately 120,000 outpatient visits, 43,000 emergency department visits, 20,000 hospitalizations, 4,500 ICU admissions, and 20 deaths; an estimated 3,413 quality-adjusted life years (QALYs) would be gained. In this model, the estimated costs are approximately $3,000 to prevent one outpatient visit, $8,200 to prevent one emergency department visit, $17,500 to prevent one hospitalization, and $80,000 to prevent one ICU admission. The estimated cost per QALY gained is $104,500. The input to which the model was most sensitive was the disease-specific inpatient costs, with higher estimates making clesrovimab cost-saving; the estimated QALYs lost due to RSV, where lower estimates significantly increased the cost per QALY gained; and the cost of clesrovimab per dose. The majority of the work group felt that using clesrovimab among all infants <8 months of age who are born during or entering their first RSV season is, or probably is, a reasonable and efficient allocation of resources.

For the equity domain, Dr. Moulia shared that hospitalization rates among infants <6 months old differed by race and ethnicity, but this difference varies by season. ICU admission rates among infants <6 months old also differed by race and ethnicity, but again varied by season.

RSV hospitalization rates were up to 7 times higher among Alaska Native and American Indian children compared to the general population of children aged less than 1 year. National studies of death certificates found higher rates among non-Hispanic Black and Hispanic children compared to non-Hispanic White children. The majority of the work group felt that clesrovimab would probably increase health equity, while a minority responded that it would probably have no impact on health equity.

In summary, the work group felt that the Phase 2b/3 trial of clesrovimab demonstrated high efficacy in preventing severe RSV disease through 150 days. They noted that serious adverse events appeared to be balanced between the clesrovimab and placebo groups, but acknowledged that rare adverse events are unlikely to be detected in a trial of this size. The work group also discussed that, although clesrovimab has a shorter half-life than nirsevimab (42 days vs. 71 days), clinical efficacy against severe RSV disease was sustained through 150 days in the trial. They further noted that the clinical efficacies of clesrovimab and nirsevimab are not directly comparable due to differences in trial outcome definitions.

The benefits of having multiple RSV antibody products and multiple manufacturers include ensuring continued protection if RSV develops resistance to one product, maintaining supply if one product is unavailable, and the potential for reduced pricing through market competition. RSV, the leading cause of hospitalization in infants, can be prevented through immunization. However, timely administration is critical for RSV immunizations to have a meaningful public health impact. For infants born outside of the RSV season, high uptake before the start of the season is essential. For those born during the RSV season, administration should occur within the first week of life, ideally during birth hospitalization. The work group concluded that the desirable consequences of using clesrovimab clearly outweigh the undesirable consequences and recommended the intervention.

Dr. Talbot noted that there have been reports of challenges accessing RSV monoclonal antibodies in hospitals, as some hospitals are reluctant to pay for them. She asked whether there has been any progress on establishing a separate payment mechanism, explaining that hospitals receive a fixed payment for deliveries and are concerned that the cost of the antibody would need to be covered within that amount.

Dr. Jones responded that the question concerns DRG (Diagnosis-Related Group) payments. Currently, there is no available information on DRG updates. It was suggested that someone from the Centers for Medicare and Medicaid Services or the Immunization Services Division may be able to provide additional insight.

Dr. Shaw stated that, to his understanding, clesrovimab is an antibody specific to site 4 on the RSV F-protein, whereas nirsevimab targets site 0. Site 4 is present on the F-protein's pre- and post-fusion conformations. He inquired whether there is any biological difference in how this monoclonal antibody performs compared to nirsevimab.

Dr. Anushua Sinha (Merck), the lead clinical director and product development team lead for clesrovimab, responded to Dr. Shaw's question, noting that preclinical data may be of interest. In studies examining the off rates of clesrovimab on the prefusion conformation versus the post-fusion conformation of the F-protein, it was observed that clesrovimab has a very slow off rate for the prefusion conformation but a rapid off rate for the post-fusion form. This addresses the specific question regarding binding differences between the two forms. However, regarding the broader comparative question, it was noted that there is no direct head-to-head data comparing clesrovimab and nirsevimab.

Ms. Moser noted that the RSV-NET data presented only extended through February 1 and asked whether this cutoff was due to preparation for the February meeting or if it reflected broader changes to RSV-NET. She referenced potential changes related to funding and staffing that may impact data availability.

Ms. Moulia explained that some of the data were pulled initially for the February meeting, and where no updates were expected to affect interpretation, the data were left unchanged. In response to the question, Ms. Moulia is unaware of any change in funding for RSV-NET.

Dr. Talbot added that she serves as a principal investigator for RSV-NET and noted that there is always some delay in data collection and reporting, which may explain in part the data cutoff. This highlights the importance of surveillance systems in assessing the impact of diseases, vaccines, and other new interventions.

Dr. Schechter noted that seeing the lower hospitalization numbers was encouraging, though disparities remain concerning. Dr. Schechter also thanked the CDC for including language in the pediatric schedule and related communications, emphasizing that administration should ideally occur during the birth hospitalization. Dr. Schechter hoped that similar language would be considered as this policy moves forward and in any harmonized recommendations, especially considering the 70% versus 50% coverage data.

Ms. Moulia stated that the intention is to continue emphasizing the importance of administration during the birth hospitalization for both clesrovimab and nirsevimab, which is critical for infant protection.

Dr. Jefferson Jones (CDC/NCIRD) shared the proposed clinical considerations for clesrovimab. Immunity is categorized as active or passive. Active immunity occurs when a person's immune system produces antibodies in response to infection or vaccination. It takes time to develop, but it typically provides long-lasting protection. Passive immunity involves the transfer of externally produced antibodies, such as maternal antibodies across the placenta, blood transfusions, or antibody products. It offers immediate but temporary protection.

Clesrovimab is a long-acting monoclonal antibody manufactured by Merck and is a form of passive immunization. It is administered as a 105 mg dose in a 0.7 mL prefilled syringe. The same dose is recommended for all infants born during or entering their first RSV season, regardless of weight.

The recommendations for clesrovimab and nirsevimab are the same for infants <8 months old born during or entering their first RSV season, with no preference between the two products. However, only nirsevimab is recommended for children aged 8–19 months who are at increased risk of severe RSV disease and entering their second RSV season. Infants eligible for nirsevimab in their second season may have received either clesrovimab or nirsevimab in their first. There are no safety or effectiveness concerns with using clesrovimab in the first season and nirsevimab in the second.

The proposed use of RSV antibody immunizations in infants, meaning either nirsevimab or clesrovimab, remains mostly consistent with current nirsevimab recommendations. A single dose is recommended for infants under 8 months old born during or entering their first RSV season, typically October through March in most of the continental United States. This applies if the mother did not receive an RSV vaccine during pregnancy, her vaccination status is unknown, or the infant was born less than 14 days after maternal RSV vaccination.

If the mother is unlikely to mount an adequate immune response, RSV antibody may be considered for infants born to vaccinated mothers. This includes mothers with immunocompromising conditions or conditions associated with reduced transplacental antibody transfer, such as HIV infection. It may also apply to infants who undergo procedures that result in the loss of maternal antibodies, such as cardiopulmonary bypass, extracorporeal membrane oxygenation, or exchange transfusion. RSV antibody may also be considered for infants at high risk of severe RSV disease, such as those with hemodynamically significant congenital heart disease or those requiring ICU admission with oxygen needs at discharge.

RSV antibody should be administered within the first week of life for infants born from October through March, ideally during birth hospitalization. Infants with prolonged hospital stays due to prematurity or other reasons should be immunized shortly before or promptly after discharge. If not given in the hospital, the antibody should be administered in an outpatient setting. The optimal timing for infants born from April through September is shortly before the RSV season begins, typically in October or November.

In jurisdictions with different RSV seasonality, such as Alaska, southern Florida, Puerto Rico, and other tropical regions, providers should follow state, local, or territorial guidance on the timing of administration. Recommendations for the timing of infant RSV antibody administration are flexible. Healthcare providers may use clinical judgment to administer antibodies outside of October through March. Special circumstances include travel to areas with increased RSV activity or concern that the patient may not return for a timely visit.

The work group recommended that the CDC issue national guidance on RSV antibody administration with flexibility for state and local jurisdictions, while avoiding region-specific recommendations due to the complexity of implementation. The work group supported CDC’s current language on flexibility but emphasized the need for additional guidance to support decision-making. They noted that annual changes to RSV antibody timing would be challenging for jurisdictions and providers. Although RSV seasonality was relatively predictable before 2020 and appears to be returning to pre-pandemic patterns, more years of data are needed to confirm this. Because real-time RSV trends can be difficult to interpret, jurisdictions may adjust timing based on local historical patterns.

Not all RSV disease can be prevented, but in most of the U.S., administering RSV antibodies to newborns from October through March aligns protection with the highest risk period. This timing helps protect infants in their first two months of life, when they are most vulnerable to severe RSV disease. There is no evidence-based test positivity threshold at which RSV antibody is recommended. Local RSV data may be the most useful for guiding decisions.

There are potential advantages and disadvantages to starting RSV antibody administration before October. Starting earlier, such as in September, may allow more time for infants to be immunized before RSV circulation begins, which could benefit areas with earlier seasonality. However, protection is expected to be strongest shortly after administration and then decrease over time. Since the rate of decline is unknown, infants who receive an antibody in September may have reduced protection during the peak or later months of the RSV season.

Extending RSV antibody administration past March also has advantages and disadvantages. A potential advantage is that infants born in April could be immunized shortly after birth, protecting them during their highest-risk months. However, the risk of RSV exposure late in the season may be low. In addition, most infants born to unvaccinated mothers are recommended to receive only one dose. This means infants who receive a dose in April would not be recommended to receive another dose in October, even though a dose in October could protect them for the entire RSV season.

Current CDC recommendations state that the timing of RSV activity, including onset, peak, and decline, varies by location. Public health authorities may provide additional guidance for RSV antibody administration based on their jurisdictions or patient populations. In areas with clear increases in RSV transmission before October, administration before October can be considered. In areas with high transmission through the end of March, administration after March may also be considered. In regions with historical data showing consistent early or late RSV activity, the standard timing of administration may be adjusted based on expected annual patterns.

Most infants will not need both maternal vaccination and an RSV antibody. In consultation with their healthcare provider, pregnant women should choose one option. Maternal RSV vaccination provides immediate protection for the infant after birth and does not require an injection for the baby. However, protection may be reduced if the mother is immunocompromised or the infant is born soon after vaccination. There is also a potential risk of hypertensive disorders of pregnancy, including preeclampsia, associated with the maternal vaccine.

The infant RSV antibody provides direct antibody protection without relying on transplacental transfer. Its protection may wane more slowly compared to maternal vaccination. Side effects are usually mild and resolve quickly. Hypersensitivity reactions are rare but have been reported. Delayed administration of an RSV antibody may leave the infant unprotected during a period of high risk.

If clesrovimab or nirsevimab is given to an infant or child, do not give palivizumab during the same RSV season. Clesrovimab administration is expected to follow the same approach as nirsevimab. It should be given as an intramuscular injection in the vastus lateralis muscle of the anterolateral thigh. Simultaneous administration of infant RSV antibodies with routine vaccines is acceptable. Clesrovimab should be stored at refrigerated temperatures and used within 48 hours of removal from the refrigerator. It should not be frozen, shaken, or exposed to light.

The only RSV immunization recommended for infants is the RSV antibody. For pregnant women, ABRYSVO is the only approved RSV vaccine. RSV antibodies are not intended for older adults; older adults should receive RSV vaccines, not antibodies.

The proposed recommendation for reporting suspected adverse events following clesrovimab mirrors that for nirsevimab. Adverse events should be reported to MedWatch if an RSV antibody is administered alone. If it is given simultaneously with any vaccine, events should be reported to VAERS, and additional reporting to MedWatch is unnecessary.

Dr. Schechter asked whether any evidence of protection extends beyond the typical five to six months of the RSV season, given the reported half-life of up to 70 days for nirsevimab. He also

raised concerns about certain pediatric RSV antibody lots in his state that are set to expire between seasons. He noted that some of these lots were initially released with shorter expiration periods than those currently in place. He asked whether updated stability data might allow for an extension of those expiration dates, especially since these products may not qualify for return under the VFC program.

Based on real-world effectiveness studies, Dr. Jones responded that there is growing evidence of potential protection beyond 150 days for nirsevimab. However, the exact duration of protection and how quickly it may wane over time remain uncertain. A recent *MMWR* from Alaska included data suggesting extended protection, and several European studies have also reported protection beyond 150 days. That said, RSV activity tends to be minimal after this period, especially when antibodies are administered shortly before the start of the season to maximize protection during the peak. Additional data may emerge from regions with prolonged RSV seasons or tropical areas where RSV antibody is given year-round. Overall, there is building evidence of extended protection, but the level of certainty is still limited.

Dr. Santoli noted that, as with many new products, the manufacturer has worked to extend the shelf life as more data has become available for the newly released product. However, applying for a shelf-life extension for a product already in the field is a separate process. According to the manufacturer, this extension type is not currently being considered.

Dr. Shaw asked whether there is information on the extent to which monoclonal antibody products are administered during birth hospitalization. Noting that many hospitals receive bundled payments for deliveries, Dr. Shaw inquired whether the cost of the RSV antibody is being incorporated into those bundled payments and whether there are any indications of how this is being handled in practice.

Dr. Jones responded that there is limited information on whether RSV antibody administration is being incorporated into DRG payments. CMS has noted some complexities related to the drug rebate program. The Immunization Services Division is actively working with birth hospitals and immunization programs nationwide to identify key challenges, share best practices, and develop strategies to address these issues. An updated presentation on uptake and related implementation concerns is expected at a future ACIP meeting, possibly in June.

Dr. Wharton expressed deep appreciation to everyone who contributed to the successful completion of the meeting, especially given the challenges of rescheduling. She thanked the ACIP members for clearing their calendars and staying engaged through two long days of intensive evidence presentations. She also acknowledged the participation of the ex officio and liaison representatives. Dr. Wharton highlighted the exceptional leadership and dedication of the CDC work group leads, recognizing their significant efforts in organizing large volumes of information into focused and accessible presentations for the committee. She thanked the ACIP Secretariat for their extensive work behind the scenes to make the meeting possible. In addition, she acknowledged the contributions of the CDC's Office of Communications, the National Center for Immunization and Respiratory Diseases (NCIRD) communications staff, and the engineers at the CDC's Global Communications Center, noting that the meeting could not have taken place without their support.

With no additional business to be addressed at the April 2024 ACIP meeting, the meeting was officially adjourned.

hereby certify that to the best of my knowledge, the foregoing Minutes of the October 21-22, 2009 ACIP Meeting are accurate and complete.

I hereby certify that, to the best of my knowledge, the summary of the ACIP Meeting of April 15-16, 2025 are accurate and complete.

7/28/2025
Date

Dr. Keipp Talbot, Chair
Advisory Committee on Immunization Practices (ACIP)

ACIP MEMBERSHIPMEMBERSHIP ROSTER

CHAIR

TALBOT, Helen Keipp, MD
Professor of Medicine
Vanderbilt University
Nashville, TN
3/5/2024 – 6/30/2025

EXECUTIVE SECRETARY

WHARTON, Melinda, MD, MPH
Associate Director for Vaccine Policy
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Atlanta, GA

VOTING MEMBERS

ASTURIAS, Edwin Jose, MD
Professor of Pediatrics and Infectious Diseases Epidemiology
University of Colorado School of Medicine and Colorado School of Public Health
Jules Amer Chair in Community Pediatrics
Aurora, CO
Term: 7/1/2024 – 6/30/2028

BREWER, Noel T., PhD
Gillings Distinguished Professor in Public Health
Department of Health Behavior
Gillings School of Global Public Health
University of North Carolina
Chapel Hill, NC
Term: 7/1/2024 – 6/30/2028

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

CHEN, Lin H., MD, FACP, FASTMH, FISTM
Director, Mount Auburn Travel Medicine Center
Division of Infectious Diseases and Travel Medicine, Mount Auburn Hospital
Associate Professor of Medicine, Harvard Medical School
Lecturer, Massachusetts Institute of Technology
Cambridge, MA
Term: 7/1/2024 – 6/30/2028

CHU, Helen Y., MD, MPH, FIDSA
Professor of Medicine, University of Washington School of Medicine
Professor of Epidemiology, University of Washington
School of Public Health
Attending Physician, Harborview Medical Center
Seattle, WA
Term: 7/1/2024 – 6/30/2028

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

JAMIESON, Denise J., MD, MPH
Vice President for Medical Affairs
Dean, Carver College of Medicine
University of Iowa
Term: 3/4/2024 – 6/30/2027

KAMBOJ, Mini, MD, FIDSA, FSHEA
Attending Physician, Memorial Sloan Kettering Cancer Center
Professor of Medicine, Weill Cornell Medical College
New York, NY
Term: 7/1/2024 – 6/30/2028

KUCHEL, George A., MD, CM
Professor and Travelers Chair in Geriatrics and Gerontology
Director
UConn Center on Aging
Claude D. Pepper Older Americans Independence Center (OAIC)
UConn Health
Farmington, CT
Term: 7/1/2024 – 6/30/2028

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

LYONS, Karyn, MS, RN
Chief, Immunization Section
Illinois Department of Public Health
Division of Infectious Diseases
Springfield, IL
Term: 12/20/2024 – 6/30/2028

MALDONADO, Yvonne (Bonnie), MD
Senior Associate Dean for Faculty Development and Diversity
Taube Endowed Professor of Global Health and Infectious Diseases
Professor of Pediatrics and of Epidemiology and Population Health
Interim Chair, Department of Medicine
Stanford University School of Medicine
Medical Director, Infection Prevention and Control and Attending Physician
Lucile Packard Children's Hospital at Stanford
Department of Pediatrics
Palo Alto, CA
Term: 3/4/2024 – 6/30/2027

MOSER, Charlotte A., MS
ACIP Consumer Representative
Co-Director, Vaccine Education Center
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania
Term: 7/1/2024 – 6/30/2028

SCHECHTER, Robert, MD, MSc
Chief, Immunization Branch
California Department of Public Health
Richmond, CA
Term: 3/6/2024 – 6/30/2027

SHAW, Albert C., MD, PhD, FIDSA
Professor of Medicine
Section of Infectious Diseases
Yale School of Medicine
New Haven, Connecticut
Term: 3/4/2024 – 6/30/2027

ZUCKER, Jane, MD, MSc
Adjunct Professor
Department of Community Health Sciences at SUNY Downstate School of Public Health Brooklyn, NY
Term: 12/23/2024 – 6/30/2028

EX OFFICIO MEMBERS

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

Food and Drug Administration (FDA)
HØEG, Tracy Beth, MD, PHD
Special Assistant to the Commissioner
Office of the Commissioner
Silver Spring, MD

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

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

National Institutes of Health (NIH)
KURILLA, Michael, MD, PhD
Director, Division of Clinical Innovation
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Rockville, MD

Office of Infectious Disease and HIV/AIDS Policy (OIDP)
RAVI, Sanjana, PhD, MPH
Director, Division of Vaccines & Immunizations
Office of the Assistant Secretary for Health
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LIAISON REPRESENTATIVES

American Academy of Family Physicians (AAFP)
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American Academy of Physician Associates
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American College Health Association (ACHA) (alternate)
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American College of Obstetricians and Gynecologists (ACOG)
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Vice Dean for Scientific Integrity
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American Geriatrics Society (AGS)
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America's Health Insurance Plans (AHIP)
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American Medical Association (AMA)
FRYHOFER, Sandra Adamson, MD
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American Osteopathic Association (AOA)
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American Pharmacists Association (APhA)
GOODE, Jean-Venable "Kelly" R., PharmD, BCPS, FAPhA, FCCP
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Association of Immunization Managers (AIM)
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Association for Prevention Teaching and Research (APTR)
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Association of State and Territorial Health Officials (ASTHO)
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Connecticut Department of Public Health
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Biotechnology Innovation Organization (BIO)
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Council of State and Territorial Epidemiologists (CSTE)
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Canadian National Advisory Committee on Immunization (NACI)
TUNIS, Matthew, PhD
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Centre for Immunization Programs (CIP)
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Infectious Diseases Society of America (IDSA)
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International Society for Travel Medicine (ISTM)
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National Association of County and City Health Officials (NACCHO)
ZAHN, Matthew, MD
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National Association of Pediatric Nurse Practitioners (NAPNAP)
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National Foundation for Infectious Diseases (NFID)
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Pediatric Infectious Diseases Society (PIDS)
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Pharmaceutical Research and Manufacturers of America (PhRMA)
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Society for Adolescent Health and Medicine (SAHM)
MIDDLEMAN, Amy B., MD, MSEd, MPH
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Society for Healthcare Epidemiology of America (SHEA)
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DREES, Marci, MD, MS
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