Immunization Update and ACIP Highlights – June 2024

July 3, 2024

The Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control (CDC) met on June 26–28, for its regular triennial vaccine meeting. For archives of minutes and slides, go to the ACIP meeting website and click on "Meeting Materials." Below are the key highlights:

SUMMARY

Respiratory Syncytial Virus (RSV) Vaccine, Adult – Vote
ACIP voted to recommend a single lifetime dose for all adults ages 75 years and older and for those ages 60–74 years who are at risk for severe RSV disease. Recommendations for younger adults at risk will be evaluated in the future. mRESVIA™ mRNA RSV vaccine by Moderna was approved by the FDA for use in adults ages 60 and older.

Hexavalent Vaccine (DTaP, Hep B, IPV, Hib) – Vote
Vaxelis® is recommended preferentially in American Indian/Alaska Native (AI/AN) infants for H. influenzae protection as an option besides PedvaxHIB®, which also has a preferential recommendation.

COVID-19 Vaccines – Vote
ACIP recommends the 2024–2025 formulation as authorized or approved by the FDA in persons ages 6 months and older. As advised by the FDA, Moderna and Pfizer vaccines will target the KP.2 lineage (a sublineage of JN.1) and Novavax vaccine will target the JN.1 lineage.

Influenza Vaccines – Vote
Influenza vaccine composition will be trivalent for the 2024–2025 influenza season due to the removal of the B/Yamagata strain. Adult solid organ transplant patients on immunosuppressive medications ages 18 through 64 years may receive a high-dose or adjuvanted influenza vaccine.

Pneumococcal Vaccines – Vote
ACIP recommends pneumococcal conjugate vaccine, 21-valent (PCV21:CAPVAXIVE™) by Merck as an option for adults ages 19 years and older who currently have a recommendation to receive a dose of PCV.

Meningococcal Vaccines
ACIP reviewed clinical trial data of a candidate GSK pentavalent meningococcal ABCWY (MenABCWY) vaccine, and continued discussion regarding a revised adolescent meningococcal schedule with a planned vote at its February 2025 meeting.

RSV Immunizations – Maternal/Pediatric

- Nirsevimab was highly effective in the 2023–2024 season.
- Maternal RSV vaccine Abrysvo™ was safe with preterm deliveries in line with expected underlying population rates. Abrysvo™ is not recommended at this time for subsequent pregnancies, and Nirsevimab should be used to protect those infants.

Other vaccines:

- The Human Papilloma Virus (HPV) vaccine work group is reconvening to evaluate fewer doses, wording around starting administration at age 9 years and shared clinical decision-

making guidance for those ages 27–45 years.

- Chikungunya vaccine is being evaluated for use in U.S. territories as either a routine vaccine or as a response to outbreak.
- Dengue vaccine Dengvaxia® is being discontinued due to low demand even though cases have recently increased dramatically world-wide.

Respiratory Syncytial Virus (RSV) Vaccines – Adults

The ACIP voted to revise last year's recommendations for adult RSV vaccination and to recommend a single lifetime dose of RSV vaccine (Abrysvo™:Pfizer, Arexvy®:GSK or mRESVIA™:Moderna) which should be administered to all adults ages 75 years and older and to those ages 60–74 years who are at risk for severe RSV disease. These ages and risk conditions result in the most cost-effective strategy with a good safety profile. Shared clinical decision making is no longer recommended. The list of chronic medical conditions or other factors that increase the risk of severe RSV disease include: lung disease, cardiovascular disease (excluding hypertension), liver disorders, severe obesity (BMI=40kg/m2 and above), moderate or severe immunocompromise, chronic kidney disease (stages 4–5), hematologic disorders, neurologic or neuromuscular disorders, diabetes mellitus with end organ damage (such as neuropathy, nephropathy or retinopathy), frailty, residence in a nursing home or other long-term care facility, or other chronic medical conditions that a licensed practitioner determines increases risk for severe RSV disease.

Arexvy® was approved for an expanded age indication by the FDA this month for use in adults ages 50–59 at risk for severe RSV disease, and the FDA is reviewing an application for Abrysvo™ for an expanded age indication for adults at risk ages 18–59 years. Pfizer presented data showing duration of protection with Abrysvo™ of at least 2 years. Recommendations for younger adults at risk and for a potential revaccination schedule will be evaluated in the future as more evidence is provided.

mRESVIA™ mRNA RSV vaccine by Moderna was approved by the FDA in May 2024 for use in adults ages 60 years and older. Vaccine efficacy (VE) against RSV lower respiratory tract disease (LRTD) with 2 or more lower respiratory signs or symptoms was 56% at 0–12 months from vaccination and 30% at 13–24 months. In comparison:

- Arexvy® VE against RSV LRTD with 2+ or 3+ lower respiratory symptoms was 79% at 0–12 months and 59% at 13–24 months post-vaccination.
- Abrysvo™ VE against RSV LRTI with 2+ respiratory symptoms was 62% at 0–12 months and 55% at 13–24 months post-vaccination.
- Abrysvo™ VE against RSV LRTI with 3+ respiratory symptoms was 86% at 0–12 months and 74% at 13–24 months post-vaccination.

mRESVIA™ had a good safety profile during clinical trials with no cases of Guillain Barré Syndrome (GBS) or acute disseminated encephalomyelitis and no imbalance in other neurologic or cardiac conditions compared to an unvaccinated reference population. Revaccination with mRESVIA™ 12 months after primary vaccination elicits a neutralizing antibody response similar to that following primary vaccination.

GSK's Arexvy® revaccination study showed higher RSV-A and RSV-B neutralizing antibody titers when a second dose was administered 24 months after primary dose compared to a 12-month interval. The lower the level of prevaccination RSV-A and RSV-B neutralizing antibody titers observed post initial vaccination, the higher the seroresponse rates which resulted after revaccination.

Under real-world conditions, RSV vaccination with Abryvo™ or Arexvy® provided protection against severe RSV disease among U.S. adults ages 60 years and older in this first season of use as demonstrated by the VISION network, IVY network, Veterans Health Administration, and end-stage renal disease Medicare patients.

These surveillance network observational studies provided more evidence than was provided during licensure efficacy trials of vaccine effectiveness in adults ages 75 and older (with similar VE for those age 75 to those ages 60–74 for ED visits and hospitalization), in those with immunocompromising conditions (VE = 73–80% hospitalization) and in those with underlying conditions, especially cardiopulmonary disease.

The Vaccine Safety Datalink found a statistical signal for immune thrombocytopenic purpura (ITP) in persons ages 60+ who received Arexvy®. It is too early to determine if this represents a true association and plans are in place for a more detailed chart review of ITP in the next season. No other statistical signals were observed.

Cases of GBS have been identified with use of Arexvy® and Abrysvo™, with 3 attributable cases of GBS per million doses of Arexvy® administered (range 0–10 cases) and 16 attributable cases of GBS per million doses of Abrysvo™ administered (range 3–19). The CDC estimated numbers of averted hospitalizations and ICU admissions are much larger than potential GBS cases for all age groups for both Abrysvo™ and Arexvy. Estimated numbers of avertable deaths are much larger than potential cases of GBS for adults ages 75 and older and for adults ages 60–74 with at least one chronic condition. The numbers of avertable deaths are larger but become more similar in magnitude to potential GBS cases for adults ages 50–59 with at least one chronic condition and ages 60–74 without chronic conditions, particularly for Abryso™. The desire to expand age indications for younger patients with chronic conditions was tempered by the concern of potentially lower benefits versus potential harms, resulting in the committee waiting to vote to recommend to persons under age 60 until more data was available.

Hexavalent Vaccine

AI/AN infants contract Hib infection at an earlier age and at a higher rate than other populations. PedvaxHIB® (PRP-OMP) is preferentially recommended in AI/AN infants to provide early protection because this vaccine produces a protective antibody response after the first dose, and other Hib vaccines containing PRP-T do not until later doses. In addition to the preferential recommendation for PedvaxHIB®, the committee voted to include hexavalent DTaP-IPV-Hib-HepB vaccine (Vaxelis®:Merck) as a preferred product for use in American Indian/Alaska Native (AI/AN) infants to protect against *Haemophilus influenzae* Type B (Hib) for the primary series doses. Vaxelis® includes Hib PRP-OMP conjugate, but at a lower concentration than in PedvaxHIB®, less than half the concentration of PRP and OMP.

Post-dose 1 anti-Hib IgG geometric mean concentration (GMC) ratio of Vaxelis® compared to PedvaxHIB® 30 days after vaccination met pre-specified non-inferiority criterion. Also, the proportion of infants with anti-Hib concentration above the correlate of short-term protection 30 days post-dose 1 was similar between Vaxelis® (75.7%) and PedvaxHIB® (71.2%). The proportion of infants with anti-Hib concentration above the correlate of long-term protection 150 days post-dose 1 was higher in the Vaxelis® group (83.6%) than in the PedvaxHIB® group (71.7%, $p<0.05$).

Vaxelis® is not approved for the 12–15 month booster dose. Any other Hib vaccine including PRP-OMP or PRP-T vaccines may be administered for the booster dose.

COVID-19 Vaccines

ACIP voted to recommend the administration of the 2024–2025 monovalent formulation of the COVID-19 vaccine as authorized or approved by the FDA to persons ages 6 months and older. Pfizer and Moderna are producing mRNA vaccines using the KP.2 strain of the JN.1 lineage, and Novavax is producing a JN.1 vaccine.

COVID-19 burden is currently lower than at previous points in the pandemic; however, there continue to be thousands of hospitalizations and hundreds of deaths each week. Hospitalizations this past season for those ages 75 years and older have been ten times higher than those in the next age group of 65 to 74 years and are highest in black and AI/AN populations. From October 2023 through May 2024, 46% of all COVID-19 hospitalizations were in those ages 75 years and older and 4% were in those ages 17 years and younger, with the highest rate of children in those less than 6 months of age. These infants cannot receive vaccine and depend on maternal vaccination for protection. Severe outcomes occur in the youngest age population. Fifty percent of hospitalized children ages 17 years and younger have no underlying medical conditions, but 18% of those children were still admitted to an ICU. Fifty percent of deaths in persons hospitalized due to COVID-19 were in persons ages 75 years and older.

Effectiveness—The U.S. population has underlying immunity from prior vaccination and infection. The incremental benefit of adults receiving a 2023–2024 monovalent COVID vaccine was a Vaccine Effectiveness (VE) of around 50% against emergency department/urgent care (ED/UC) encounters and hospital admissions with waning of protection seen at 3 to 4 months after vaccination, determined by surveillance network observational studies.

Safety—Statistical safety signals have been identified during the 2023–2024 seasons by the Vaccine Safety Datalink for Guillain-Barre Syndrome (GBS) in recipients of Pfizer vaccine ages 65 years and older and for ischemic stroke with both Moderna vaccine (ages 65 and older) and Pfizer vaccine (ages 50–64 years). The increased rate ratio observed for GBS may not represent a true risk. If there is a true risk, it is estimated at 4.1 attributable cases per million doses, similar to what is considered acceptable for other adult vaccines. The VSD statistical signals for ischemic stroke do not provide sufficient evidence to conclude there is a safety concern. A follow-up VSD study is in progress.

COVID-19 vaccination continues to be a cost-effective strategy, especially in those ages 65 years and older and for those with underlying medical conditions. The Bridge Access Program, which supported

uninsured adults, will sunset in August 2024. Vaccine remains free of cost to insured persons and to children through the VFC program.

Vaccines.gov provides an access tool to search for pharmacy locations. Although there is no longer an inventory function, patients can contact the pharmacies identified to make an appointment for vaccination. For the latest CDC COVID vaccine recommendations, visit the CDC's Clinical Considerations website.

Influenza Vaccines

The ACIP voted to approve routine annual administration of the 2024–2025 formulation of influenza vaccines for persons ages 6 months and older. All influenza vaccines in the U.S. will be trivalent rather than quadrivalent formulations. Due to a lack of cases caused by B/Yamagata lineage viruses over several season, the WHO and the FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) recommended excluding B/Yamagata strain from influenza vaccines. Vaccine manufacturers have shifted production for the U.S. market from quadrivalent to trivalent influenza vaccines.

There are approximately 430,000 persons in the U.S. who are solid organ transplant (SOT) recipients, which comprises 0.1% of the U.S. population. The majority (96%) of SOTs are in adults. Adult solid organ transplant patients on immunosuppressive therapy are at high risk for complications from infection with influenza virus (69% of a 5-year cohort of SOT recipients with influenza required hospitalization). Their immunosuppressed status can contribute to a reduced response to influenza vaccination. Currently, use of high-dose and adjuvanted influenza vaccines are only FDA approved for persons ages 65 years and older. Studies comparing high-dose and adjuvanted influenza vaccines compared to standard dose in immunosuppressed solid organ transplant recipients show higher seroconversion rates with rate ratios ranging from 1.17 to 1.64 for adjuvanted compared to standard dose vaccine and from 1.13 to 2.46 for high-dose compared to standard dose vaccine. Although no direct evidence exists of improved protection against influenza, relying on indirect immunogenicity data, the ACIP has voted to recommend high-dose inactivated (HD-IIV3) or adjuvanted inactivated (aIIV3) influenza vaccines as acceptable options for influenza vaccination of solid organ transplant recipients ages 18 through 64 years who are receiving immunosuppressive medication regimens, without preference over other age appropriate IIV3s or RIV3. High-dose and adjuvanted influenza vaccines were deemed safe, with no increase in transplant rejection or graft failure. Due to lack of studies comparing RIV to standard dose IIVs, there is not a preference for RIV in SOT recipients although it is a higher dose vaccine approved for persons ages 18 and older.

The U.S. Department of Agriculture (USDA) has confirmed cases of highly pathogenic avian influenza A(H5N1) in dairy herds in over 100 farms across the U.S. with high levels of virus in raw milk. There have been 3 confirmed human cases in dairy farm workers, 1 in Texas and 2 in Michigan. There have been no human-to-human transmissions. The CDC is continuing surveillance efforts and has candidate vaccine virus that could be submitted to manufacturers for vaccine production that would protect against this clade of A(H1N1), but no need is anticipated at this time.

Safety information concerning milk and beef supplies is located on USDA websites. Pasteurized milk is safe, but raw, unpasteurized milk should be avoided.

Pneumococcal Vaccines

The FDA approved Merck's 21-valent pneumococcal conjugate vaccine (PCV21:CAPVAXIVE™) on June 17, 2024. ACIP voted to recommend PCV21 as an option for adults ages 19 years and older who currently have a recommendation to receive a dose of PCV. Those recommended to receive a dose of PCV include:

- Adults ages 65 and older who have never received a dose of PCV
- Adults ages 19 through 64 years with a risk condition, who have never received a dose of PCV
- Adults ages 19 years and older who have received a PCV (i.e., PCV7 or PCV13), but have not completed the recommended series
- Those recommended for a dose of PCV20 based on shared clinical decision-making for adults ages 65 years and older who have completed the recommended series with PCV13

PCV20 was previously approved for these indications. PCV21 is not just PCV20 with one additional serotype. It has 11 added serotypes compared to PCV20 and has removed 10 serotypes that are contained in PCV20 in order to better match the serotypes more commonly circulating in the adult population.

PCV21 has increased coverage of the serotypes causing invasive pneumococcal disease IPD in adults compared to PCV20. Serotypes included in PCV20 cover 54–58% of adult IPD cases, and PCV21 serotypes cover 81–84% of adult IPD cases. Among adults hospitalized with community acquired pneumonia, 4.1% are infected with *S. Pneumoniae* serotypes included in PCV21 that are not included in PCV15 or PCV20. In head-to-head analysis, PCV21 was shown to have non-inferior immunogenicity to serotypes shared with PCV20. When PCV21 was co-administered with quadrivalent inactivated influenza vaccine (IIV4), the influenza A:H3N2 subtype did not meet non-inferiority criteria.

PCV21 is not recommended if vaccination has been completed with a PCV20.

ACIP discussed whether to lower the age for universal adult pneumococcal vaccination from 65 years and older to 50 through 64 years or to include a recommendation for ages 19 through 49 years. Due to lower incidence of risk and poor cost effectiveness, the committee did not consider the age 19 through 49 years universal recommendation. The workgroup will bring more data to the October 2024 meeting to consider a universal recommendation for either PCV21 or PCV20 in ages 50–59 years to increase equity. There is a concern that PCV duration of protection may only last 15 years, and more data is needed to understand if another PCV dose would be needed after age 65 years if one were given in the 50–59-year age cohort. Currently, only 22.2% of adults ages 19 through 64 with a high-risk indication for PCV have been vaccinated, and committee members stressed the need to focus attention on improving vaccination rates of that population even without an expanded age indication.

PCV21 does not include serotype 4 which occurs at higher rates in AI/AN populations and has been seen in homeless populations. ACIP may recommend that PCV20 or PCV15 be used in communities where there are high proportions (i.e., ≥30%) of disease due to serotype 4 rather than PCV21.

Meningococcal Vaccines

There has been a dramatic uptick in the numbers of cases of Meningococcal serogroup Y cases in 2023 and 2024. In many jurisdictions, the increase is primarily due to NmY sequence type (ST) 1466 (clonal complex CC174). Predominant populations with this strain are black (64%) or HIV positive (18%), ages 30 through 60 years. This strain is susceptible to all treatment and prophylaxis antibiotics. Ciprofloxacin resistance is increasing in other subtypes. Subtype ST-3587 is seen predominantly in Hispanic or Latino individuals and is resistant to penicillin and ciprofloxacin.

The greatest number of cases of serogroup B are in infants ages one year and younger and in ages 16 through 20 years. Cases of ACWY are predominantly in infants ages 1 year and younger and in adults ages 26 years and older.

In October 2023, the ACIP recommended Pfizer's pentavalent meningococcal AVCWY vaccine as an option when both MenACWY and MenB are indicated at the same visit. At this June 2024 meeting, it evaluated GSK's candidate pentavalent meningococcal vaccine with plans to recommend in February 2025. The candidate vaccine MenABCWY has a favorable safety profile similar to Meningococcal B vaccine although there are more adverse events for MenABCWY than MenACWY. One dose of MenABCWY was non-inferior to MenACWY in MenACWY primed recipients. Immunogenicity against serogroup B strains was non-inferior compared to MenB given at 0 and 2 months for 3 of 4 strains and for 2 of 4 strains when compared to MenB given at 0 and 6 months.

After 24 months, titers from pentavalent MenABCWY waned substantially for serogroup A and for 3 of the B strains. There was a robust booster response. This waning was concerning to committee members.

ACIP is reevaluating the meningococcal vaccine schedule. It may remove the age 11–12 years dose, and it is trying to move away from shared clinical decision making to risk-based recommendations for MenB. Potential language for a risk-based recommendation was presented:

"Risk groups including adolescents planning to attend college, and adolescents in a congregate living setting (e.g., congregate foster care, boarding school, correctional facility, etc.) who are anticipated to remain in this setting long enough to complete the MenB vaccine series.

Any adolescent who desires protection may receive MenB vaccine, even if they are unsure of their future plans which may inform congregate living risk."

Cost effectiveness of MenB vaccine is in the millions of dollars per quality adjusted live year, and members do not want to make the recommendation too permissive.

RSV Immunizations – Maternal/Pediatric

In the 2023–2024 RSV season, 51.2% of infants less than 8 months of age were protected against RSV virus, although there was delay in that protection until the end of the season for many infants due to insufficient supply of Nirsevimab. Nirsevimab was received by 43% of infants, and 17.8% of pregnant women with infants born from September through January received Abrsyvo™.

Safety—Post-licensure maternal RSV vaccine Abrysvo™ has reflected the same safety profile that was seen during pre-licensure trials. There have been no cases of GBS reported. The committee was concerned because there have been cases of GBS in those ages 60 and older who have received Abrysvo™. Preliminary findings in the Vaccine Safety Datalink suggest that the incidence of preterm births is 4.1% among pregnant persons who received Pfizer RSV vaccine during the 2023–2024 respiratory season, which is within the VSD's expected range of the incidence of preterm births at 32–36 weeks gestation (3.1–6.1%) before the introduction of this vaccine.

Effectiveness—Nirsevimab was highly effective in the 2023–2024 RSV season. Effectiveness against RSV-associated hospitalization was 91% in the New Vaccine Surveillance Network (NSVN) and 98% in VISION study sites. Effectiveness against any medically attended RSV associated acute respiratory infection episode in NVSN was 89% and effectiveness against RSV-associated ED visits was 77% in VISION.

Data was insufficient this season to assess effectiveness of maternal vaccination or duration of protection from maternal vaccination or infant Nirsevimab receipt.

ACIP members stated that in light of the high effectiveness of Nirsevimab, insurance companies should cover it and add the cost to their well-newborn delivery DRGs. Birthing facilities should sign up to become VFC providers.

In order for ACIP to make recommendations for use of maternal RSV vaccination during subsequent pregnancies after the first pregnancy where it is administered, additional data are needed about safety of administration, antibody response during subsequent pregnancies and duration of protection. For older adults, repeat doses did not elicit as high of an immune response as was seen with the first dose.

At this time, people who received a maternal RSV vaccine during a previous pregnancy are not recommended to receive additional doses during future pregnancies. Infants born to people who were vaccinated only during a prior pregnancy should receive Nirsevimab. It is anticipated recommendations may change in the future as more data becomes available.

Other Vaccines

HPV—ACIP announced the reconvening of a Human Papilloma Virus (HPV) vaccine work group. It will evaluate recommendations for fewer doses in response to World Health Organization recommendations, wording around the age 9 years start date and increase guidance for those having shared clinical decision-making discussions with patients ages 27 through 45 years.

Chickungunya—Chikungunya is rare in the U.S. with one case in Texas and 12 cases reported in Florida. It is more common in U.S. territories. ACIP approved recommendations for adult travelers and laboratory workers to receive the live attenuated vaccine (IXCHIQ:Valneva™) in February 2024. Recommendations for persons in U.S. territories and residents of the U.S. are in development, as well as recommendations for a virus-like particle vaccine by Bavarian Nordic which has been submitted to the FDA for BLA.

Chikungunya vaccine use in U.S. territories would avert 67–90% of cases and associated health outcomes versus no vaccination. Although a prospective routine vaccine strategy could cost $400 million, it would be more cost effective than waiting to vaccinate with an outbreak strategy.

Dengue—Dengue Tetravalent Vaccine (Dengvaxia®) was approved by the ACIP in 2021 but is being discontinued due to low demand despite a dramatic increased incidence of dengue in various parts of the world. The last dose of Dengvaxia® will expire at the end of August 2026; therefore, do not start the series later than August 31, 2025. Dengvaxia® is indicated for people with prior infection. Taketa withdrew their candidate vaccine from FDA review in July 2023. TV003/TV005 dengue vaccine is in late-stage phase 3 trials. No dengue vaccines are currently under review by the FDA and no dengue vaccines will be available in the U.S. after the discontinuation of Dengvaxia®.

Questions regarding immunization? Contact Tamara Sheffield, MD, MPA, MPH, Medical Director, Immunization Programs, Intermountain Healthcare Canyons Region, at **801-442-3946**.