



Centers for Disease Control and Prevention (CDC) Immunization Safety Office (ISO) Update

Advisory Commission on Childhood Vaccines (ACCV) meeting
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Recent Publications

Adverse Events Following Quadrivalent Meningococcal Diphtheria Toxoid Conjugate Vaccine (Menactra®) Reported to the Vaccine Adverse Event Reporting System (VAERS), 2005-2016

- Myers T, et al. Vaccine. 2020 Sep 11;38(40):6291-6298.
- Summary: Licensed in January 2005, Menactra was the first quadrivalent meningococcal conjugate vaccine approved to provide protection against invasive meningococcal disease. It is licensed for use in individuals aged 9 months through 55 years. Researchers reviewed reports of adverse events (AEs) after Menactra to the Vaccine Adverse Event Reporting System (VAERS) from 2005-2016, including serious reports, selected pre-specified outcomes, and use during pregnancy. During the study period, VAERS received 13,075 reports of AEs following Menactra vaccination. Most reports (94%) were classified as non-serious; commonly reported AEs included injection site redness and swelling, fever, headache, and dizziness. There were 36 reports of death following Menactra; researchers did not find any evidence to suggest the vaccine caused the deaths. This review did not reveal any new safety concerns and provides further reassurance regarding the safety of Menactra.

Available at: <https://pubmed.ncbi.nlm.nih.gov/32747215/>

Guillain-Barré syndrome following high-dose influenza vaccine administration in the United States, 2018–2019 season

- Perez-Vilar S, et al. J Infect Dis. 2020 Nov 2;jiaa543.
- Summary: While an association between influenza vaccination and Guillain-Barré syndrome (GBS) was first noticed in 1976, studies in subsequent flu seasons have assessed the risk and found either no or small risk of GBS following influenza vaccination. Early during the 2018-2019 flu season, the Vaccine Safety Datalink (VSD) identified a statistical signal for an increased risk of GBS in days 1–42 following high-dose influenza vaccine (IIV3-HD) administration. The signal was rapidly evaluated using Medicare data by conducting early- and end-of-season analyses. The Medicare analyses, which included more than 7 million IIV3-HD vaccinations, did not detect a statistically significant increased GBS risk. The VSD end-of-season analysis also did not find an increased GBS risk among more than 600,000 IIV3-HD vaccinations. These analyses determined that if a GBS risk existed, it was similar to that from prior seasons.

Available at: <https://pubmed.ncbi.nlm.nih.gov/33137184/>

Evaluating the Association of Stillbirths After Maternal Vaccination in the Vaccine Safety Datalink

- Panagiotakopoulos L, et al. *Obstet Gynecol.* 2020 Nov 5.
- Summary: ACIP recommends women receive vaccinations against flu and tetanus, diphtheria, and acellular pertussis (Tdap) during each pregnancy. Despite reassuring safety data, pregnant women often have concerns about the safety of vaccines for them and their babies. Researchers used the Vaccine Safety Datalink to evaluate whether vaccinations given during pregnancy were associated with stillbirth (fetal death occurring on or after 20 weeks gestation). The study compared 795 stillbirths (confirmed with medical record review) and 3,180 live birth controls between Sept. 30, 2015 and Jan. 1, 2020. Researchers found 51.7% of stillbirth cases and 52.9% live birth controls were exposed to vaccines during pregnancy, including flu and Tdap vaccines. The findings show that vaccination during pregnancy did not increase the risk of stillbirth, including recommended, non-recommended, and contraindicated vaccines. Overall, the study results support the safety of ACIP recommendations during pregnancy.

Available at: <https://pubmed.ncbi.nlm.nih.gov/33156197/>

The Reporting Sensitivity of the Vaccine Adverse Event Reporting System (VAERS) for Anaphylaxis and for Guillain-Barré Syndrome

- Miller ER, et al. Vaccine. 2020. Nov 3;38(47):7458-7463.
- Summary: Underreporting is an important limitation that is common to passive surveillance systems. The number of adverse events (AEs) that occur after vaccination and the percentage of those that get reported to the Vaccine Adverse Event Reporting System (VAERS) is unknown. To determine the sensitivity of VAERS in capturing AE reports, researchers analyzed pre-specified outcomes - anaphylaxis and Guillain-Barré syndrome (GBS) - reported to VAERS and determined if they are similar to previous estimates for other severe AEs. These estimates used were obtained from published studies of the Vaccine Safety Datalink of anaphylaxis and GBS following vaccination. VAERS sensitivity for capturing anaphylaxis after seven different vaccines ranged from 13-76%; sensitivity for capturing GBS after three different vaccines ranged from 12-64%. For anaphylaxis and GBS, VAERS sensitivity is comparable to previous estimates for detecting important AEs following vaccination.

Available at: <https://pubmed.ncbi.nlm.nih.gov/33039207/>

Advisory Committee on Immunization Practices (ACIP)

October 2020 meeting topics

Immunization Schedule

- ACIP approved changes to the recommended immunization schedules for 2021
- The changes reflect ACIP votes taken during 2020
- CDC will release the new immunization schedules in February 2021

Seasonal Influenza Vaccine

- Efficacy of FLUCELVAX Quadrivalent (cclIV4) in subjects aged 2-17 years presented by Seqirus
 - cclIV4 was licensed for people aged ≥ 4 years in 2016
 - Phase III trial: overall vaccine efficacy was 54.6% (95% CI 45.7, 62.1)
 - cclIV4 was well tolerated, with similar rates of AEs between the two vaccination groups (cclIV4 compared to Menveo)
- Influenza disease burden estimates for the 2019-20 Season
 - 38 million illnesses and 22,000 deaths
- Influenza vaccine impact estimates for the 2019-20 Season
 - Vaccine prevented:
 - 7.5 million illnesses
 - 105,000 hospitalizations
 - 6,300 deaths

Orthopoxvirus Vaccine

- Monkeypox is a global threat
 - Increase in cases in Nigeria and Democratic Republic of the Congo
 - Secondary transmissions are a threat to health care workers
- Jynneos vaccine
 - A live attenuated non-replicating vaccine
 - Approved in 2019 to prevent smallpox and monkeypox disease in adults 18 years or older
 - Policy question: Should JYNNEOS[®] be recommended for persons who are at risk for occupational exposure to orthopoxviruses?
 - Next steps: review data and conduct GRADE
 - ACIP vote scheduled for June 2021 meeting

Dengue Vaccine

- Dengvaxia (CYD-TDV) vaccine poses novel challenges and the ACIP workgroup has been discussing stakeholder acceptability, logistics, and feasibility for a potential phased approach to vaccination in Puerto Rico where dengue is endemic
- Evidence to recommendations (EtR) judgements are dependent upon the performance of pre-vaccination screening test for prior dengue infection
- ACIP plans to review more information and vote on vaccine recommendations in 2021

Pneumococcal Vaccine

- Current vaccines are:
 - PPSV23
 - PCV13
- New PCV products on the horizon:
 - Merck PCV15 (PCV13 serotypes +22F and 33F)
 - Licensure anticipated Q3-4, 2021
 - Pfizer PCV20 (PCV13 serotypes +8, 10A, 11A, 12F, 15B, 22F and 33F)
 - Licensure anticipated in June 2021
- ACIP will review considerations and evidence supporting the use of new vaccines in adults
- Licensure for children anticipated in 2022 or 2023

Cholera Vaccine

- In 2017, ACIP recommended the cholera vaccine for adult travelers (aged 18–64 years) to an area of active cholera transmission
- This workgroup will review more recent pediatric data to inform whether ACIP should recommend cholera vaccine for travelers aged 2–17 years

Zoster Vaccine

- ACIP has recommended Shingrix (RZV) since Oct 2017
- Zostavax (ZVL) no longer sold in the United States effective July 1, 2020
- Updates provided on post-licensure safety monitoring of RZV in VAERS and VSD
- Potential risk of Guillain-Barré syndrome (GBS) observed for RZV
- An increased risk of GBS was observed following herpes zoster infection
- Risk-benefit analysis to be presented at a future ACIP meeting

Tick-borne Encephalitis (TBE) Vaccine

- Pfizer plans to submit a Biologics License Application (BLA) to the Food and Drug Administration (FDA) for a TBE vaccine
- Licensure possible in 2021
- TBE is endemic in parts of Europe and Asia
- ACIP to consider use of TBE vaccine in:
 - U.S. adults and children visiting or living in TBE endemic areas
 - Laboratory workers

Rabies Vaccine

- ACIP is considering updates to:
 - The rabies pre-exposure prophylaxis vaccine dosing schedule
 - Clinical guidance on risk groups

COVID-19 vaccines

Information from ACIP's September and October meetings

Vaccine Update

- Four vaccines in active Phase III clinical trials in the United States
 - AZD1222 vaccine (AstraZeneca)
 - Ad26.COV2.S vaccine (Janssen)
 - BNT162b2 vaccine (Pfizer/BioNtech)
 - mRNA-1273 vaccine (Moderna)

ACIP: Path to COVID-19 Vaccine Recommendations

- Currently
 - Work Group meeting weekly; reviewing Phase I/II data from manufacturers as data are available
 - Designing structure for independent data review that will occur once Phase III data are available
- Once data are available from Phase III Clinical Trials
 - ACIP Work Group will conduct independent review of safety and efficacy data
 - Evidence to Recommendation (EtR) Framework and GRADE
 - Based on this data review, Work Group will present policy options to full ACIP
- If/when an FDA decision is announced
 - ACIP will have ‘emergency’ meeting with public comment session
 - Review safety and efficacy data using GRADE/EtR
 - ACIP will vote on recommendations for vaccine, populations for use
 - ACIP recommendations could be more targeted or detailed than FDA “Conditions of Use”
- After an ACIP vote
 - ACIP submits recommendations to CDC Director
 - If recommendations are accepted, they are published in the MMWR and become official CDC Policy

Topics covered at the October ACIP meeting

Vaccine Development & Regulatory

- Update from VRBPAC meeting:
 - Dr. Doran Fink (FDA)
- NVX-CoV2373 Vaccine Candidate:
 - Dr. Filip Dubovsky (Novavax)
- Janssen's SARS-CoV-2 Vaccine Program:
 - Dr. Jerry Sadoff (Janssen)

Implementation

- Update on vaccine implementation planning:
 - Dr. Janell Routh (CDC)
- Vaccinate with Confidence:
 - Dr. Amanda Cohn (CDC)

Safety

- FDA safety surveillance systems:
 - Dr. Steven Anderson (FDA)
- Post-authorization safety monitoring plans:
 - Dr. Tom Shimabukuro (CDC)

Allocation and Epidemiology

- Modeling strategies for the initial allocation of COVID-19 vaccines: Dr. Matthew Biggerstaff (CDC)
- Updates to immunity and epidemiology to inform COVID-19 vaccine policy: Dr. Megan Wallace (CDC)
- Ethical principles for early vaccine allocation:
 - Dr. Mary Chamberland (CDC)

Work Group Interpretation

- Work Group interpretation of data: Dr. Sara Oliver (CDC)
- Policy questions, Evidence to Recommendation Framework,
 - and outcomes: Dr. Kathleen Dooling (CDC)

Summary of CDC post-authorization/post-licensure safety monitoring of COVID-19 vaccines

- The Vaccine Safety Datalink (VSD), Clinical Immunization Safety Assessment (CISA) Project, and other planned projects are key components of COVID-19 vaccine safety monitoring and adverse event assessment
- VAERS is the U.S. frontline vaccine safety monitoring system
 - VAERS traditionally has provided the initial data on the safety profile of new vaccines when they are introduced for use in the population
 - Healthcare providers (HCPs) can play an important role in identifying and reporting potential AEs to VAERS: **HCPs are partners in safety monitoring**
- Vaccine safety assessment for essential workers (v-safe)
 - v-safe is a new smart-phone based active surveillance program
 - HCPs can play an important role in helping CDC enroll patients in v-safe at the time of vaccination: **HCPs are partners in safety monitoring**



- **v-safe** is a new smart-phone based active surveillance program for COVID-19 vaccine safety
 - Uses text messaging to initiate web-based survey monitoring
 - Conducts electronic health checks on vaccine recipients
 - Daily for first week post-vaccination; weekly thereafter until 6 weeks post-vaccination
 - Additional health checks at 3, 6, and 12 months post-vaccination
 - Includes active telephone follow-up through the VAERS program with vaccine recipients reporting a clinically important event during any **v-safe** health check
 - A VAERS report will be taken during telephone follow-up, if appropriate
 - Captures information on pregnancy status and enables follow-up on pregnant women

ACIP COVID-19 Vaccine Safety Technical Sub-Group (VaST)

- Transition of VaST to a smaller data review group
 - Built off lessons learned from H1N1 vaccine safety monitoring
 - Consensus that FACA would ensure transparency, independence, and public accountability
 - Composition
 - ACIP and NVAC representation
 - 7 independent expert consultants
 - ACIP ex officio members (NIH, FDA, OIDP, CMS, HRSA, IHS)
 - VA and DoD liaison

ACIP COVID-19 Vaccine Safety Technical Sub-Group (VaST)

- Post-implementation Objectives
 - Review, evaluate, and interpret post-authorization/approval COVID-19 vaccine safety data
 - Serve as the central hub for technical SMEs from federal agencies conducting post-authorization/approval safety monitoring to share vaccine safety surveillance data
 - Advise on analyses, interpretation, and data presentation
 - Liaise with the ACIP COVID-19 Vaccines WG on issues of safety data presentation to the ACIP and application of safety data to policy decisions

ACIP COVID-19 Vaccine Safety Technical Sub-Group (VaST)

- Deliverables
 - Frequent COVID-19 vaccine safety technical reports for internal ACIP and CDC and federal partner use
 - Frequent COVID-19 vaccine safety data summaries for public release

Thank You

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

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

