# Centers for Disease Control and Prevention Immunization Safety Office Update

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Advisory Commission on Childhood Vaccines (ACCV)
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# Disclaimer

- The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the CDC

# Topics

- Presentations at February 2019 ACIP meeting*
- Selected publications

*https://www.cdc.gov/vaccines/acip/meetings/downloads/agenda-archive/agenda-2019-02-508.pdf

# ACIP Update – Influenza

- Influenza activity for 2018-19*
  - Remains elevated
  - Influenza A(H1N1)pdm09 viruses have predominated overall
  - H3N2 viruses were detected more commonly than H1N1 viruses in the Southeast and have increased in other regions in recent weeks
  - WHO's recommendation for the H3N2 component for the 2019-20 Northern Hemisphere vaccine has been delayed until March 21 to allow for the collection of more data and testing

Data through week 7, ending 2/16/19

*

# ACIP Update – Influenza Vaccine Effectiveness*

- Interim pooled results for the 2018-19 season indicate protection against influenza
  - 47% (95% CI 34-57) vaccine effectiveness against **any** influenza virus
  - 46% (95% CI 30-58) against H1N1pdm09, 44% (95% CI 13-64) against H3N2
- Age stratified effectiveness estimates
  - Children aged 6 months -17 years: 61% (95% CI 44-73) against **any** flu, 62% (95% CI 40-75) against H1N1pdm09
  - Adults aged 18-49 years: 37% (95% CI 9-56) against **any** flu; 45% (95% CI 14-64) against H1N1pdm09
  - Adults ≥50 years: neither estimate was statistically significant

*Study period 11/23/18—2/2/19. Source: US Flu VE Network – KWA, MFC, U Mich, U Pitt, and Baylor. Enrolment: Outpatients aged ≥6 mos with ARI with cough ≤7 days duration. Test-negative design

# ACIP Update – Influenza

- Seqirus presentation on Afluria QIV Phase 3, randomized, observer blinded, comparator-controlled study 2016-17
  - Demonstrated noninferior immunogenicity to a US-licensed comparator QIV
  - Safety and tolerability of Afluria QIV is similar to comparator QIV in children 6-59 months
    - Overall any fever (≥99.5˚F) rate for Afluria QIV was 7.2% and 11.9% for comparator QIV
    - No febrile convulsion during the first 7 days
    - Severe related fever are similar between the 2 groups in both age groups (6-35 months and 36-59 months)
- Afluria QIV was FDA approved in Oct. 2018 for children 6-59 months of age based on Phase 3 study

QIV - Quadrivalent inactivated influenza vaccine

# ACIP Update – Influenza

- Case-control study of inactivated influenza vaccine and spontaneous abortion (SAB) in the Vaccine Safety Datalink (VSD), 2012-13, 2013-14 and 2014-15 findings*
  - No significant association between influenza vaccine receipt and SAB, regardless of prior season vaccination status
  - Odds ratios were less than or close to 1.0 in all risk windows
  - No significant associations in season-specific analysis
  - Findings support safety of influenza vaccine in early pregnancy

*Study PI: Donahue J. MFC

# ACIP Update – Influenza Vaccines for Young Children

- Licensure changes
  - Afluria (IIV3) and Afluria Quadrivalent (IIV4)
    - Age indication expanded from ≥5 years to ≥6 months in Oct. 2018
    - Children aged 6-35 months receive smaller dose volume
      - 0.25 mL vs. 0.5 mL for those aged ≥3 years
  - Fluzone Quadrivalent (IIV4)
    - 6-35 months previously received 0.25 mL/dose
    - January 2019: Licensed 0.5 mL/dose for all ages
      - Randomized non-inferiority trial of immunogenicity and safety of the 0.25 mL vs. 0.5mL in children aged 6-35 months presented to ACIP Oct. 2018
      - Per labeling 0.25 mL or 0.5 mL acceptable for 6-35 months

IIV3 – Trivalent inactivated influenza vaccine
IIV4 – Quadrivalent inactivated influenza vaccine

# ACIP Update – Human Papillomavirus Vaccine

- Considerations for mid-adult HPV vaccination
  - Rapid acquisition of HPV in late teens and early 20's
  - Progression from incident infection to cervical precancer can be within a few years
  - Over 90% of infections clear and 30-40% of cervical precancers clear
  - Time from progression of precancer to cervical cancer is >20 years – estimate from statistical analysis
  - Age at cervical precancer detection depends on screening; difficult to estimate age at causal infection from epidemiologic/surveillance data
  - Less is known about natural history of HPV at non-cervical sites & about progression from infection to cancer in males
  - Challenges estimating burden of disease due to incident infections in mid-adults from empiric data

# ACIP Update – Human Papillomavirus Vaccine

- HPV vaccine consideration for adults
  - Current HPV vaccination program predicted to reduce HPV-burden of disease substantially (e.g. 82% reduction in anogenital wart diagnosis and 59% of cervical cancers over 100 years)
  - Extending vaccination to 45-year-old males and females is predicted to produce small reductions in this burden of disease
  - Cost effectiveness of mid-adult vaccination is highly sensitive to
    - Level of natural immunity after infection & rate of progression to cervical lesions
    - Historical vaccination coverage
  - Overall value and acceptability was moderate
    - ≥50% in all studies except one
    - Willingness to receive vaccine high in both studies among MSM
    - Not valued by respondents with low perceived risk (e.g. marriage, monogamous relationship, few sex partners)
- ACIP workgroup will continue to review economic modeling results, complete Evidence to Recommendation Framework and prepare for a vote in June 2019

# ACIP Update – Combination Vaccines

- Pediatric hexavalent vaccine-Vaxelis
  - Contains DTaP, IPV, Hep B and Hib (PRP-OMP)
  - Given in 3 doses at 2, 4, 6 months
  - Licensed by FDA on 12/21/18
  - Consider if will be included in the Vaccine for Children (VFC) Program
  - Consider preferential recommendation for American Indian/Alaska Native population
  - VFC vote tentatively planned for June 2019
  - MMWR publication planned for Fall 2019
  - Supply not available until at least 2020
  - Evaluated in 6 Phase 3 clinical studies
    - Demonstrated robust immunogenicity and acceptable safety profile consistent with its component vaccines
  - Already used in the EU with over 1.5 million doses distributed since May 2017 and no unexpected safety signals

# ACIP Update - *Haemophilus influenza* type b in Native American Children

- Hib disease rates are higher among native American children than others
- Two Hib conjugate vaccines are available in the United States
  - PRP-T: PRP-tetanus toxoid (ActHib)
  - PRP-OMP: PRP *N. meningitidis* outer membrane protein (OMP) (PEDVAX-HIB)
- The American Academy of Pediatrics made a preferential recommendation for PRP-OMP over PRP-T
  - Because of the risk of invasive Hib disease at younger ages, the Indian Health Service has recommended a preference for PRP-OMP (PEDVAX-HIB) Hib conjugate vaccine based on seroconversion rates of 60% after the first dose compared with only 20% for other Hib conjugate vaccines
- Post-dose 1 immunogenicity for Hexavalent vaccine is unknown
- Establishing immunogenicity post-dose 1 in high-burden Native American populations is important and could inform policy regarding whether a preferential recommendation should be made for the American Indian/Alaska Native populations

# ACIP Update – Pneumococcal Vaccines

- Evaluation of 2014 recommendation for PCV13 in adults aged ≥65 years based on invasive pneumococcal disease (IPD), pneumonia, mortality and safety
- Two new products in Phase 3 trials (PCV15 and PCV20)
- Serotype 3 (ST3) causes most of the remaining PCV13-type disease burden in the US and countries using PCV13
  - PCV13 may provide some level of direct protection against IPD and pneumonia caused by ST3
  - Given VE and PCV13 coverage to date (~40%), population-level impact is expected
  - No evidence of population-level impact on ST3 disease to date
  - High-level of uncertainty remains on the expected benefits of PCV13 against ST3 disease

# ACIP Update – Pneumococcal Vaccines

- What is the direct effect of new adult PCV13 recommendation on pneumonia and hospitalizations among adults ≥65 years of age?
  - PCV13 is effective against community-acquired pneumonia (CAP), non-healthcare associated CAP (non-HA CAP), and lobar pneumonia
    - Vaccine effectiveness (VE) for all-cause CAP: 6–11%
    - Similar to Gessner et al (clinical trial)*: PCV13 VE of 8% (CI 1-15) against all-cause CAP
  - PCV13 VE higher among low risk adults
    - Lowest CAP incidence
  - ~28,000 CAP hospitalizations averted within 40 months after implementation of new adult PCV13 recommendation

*Gessner et al (Pfizer funded). *Vaccine* 2018

# ACIP Update – Pneumococcal Vaccines

- Policy Question: Should PCV13 be administered routinely to all immunocompetent adults aged ≥65 years in the context of indirect effects from pediatric PCV use experienced to date? Evidence to recommendations and GRADE presented

**Summary of Key Issues**

| Reasons Raised in Favor of Continuing Routine PCV13 Use | Reasons Raised in Favor of Discontinuing Routine PCV13 Use |
|---|---|
| • PCV13 effective in preventing PCV13-type pneumococcal disease<br>• Vaccine preventable disease reduced through indirect effects, but not eliminated<br>• Easier to adhere to universal prevention strategies than to risk-based ones<br>• Frequent changes to recommendations may negatively impact the perceived importance of future vaccines<br>• A more comprehensive approach to adult pneumococcal vaccine recommendations maybe needed (combine changes in a single recommendation) | • Overall impact from vaccinating older adults PCV13 disease is minimal in the context of indirect effects from pediatric PCV use<br>• Low remaining burden of vaccine preventable disease limits the potential benefit from direct effects<br>• Lack of clear population-level impact on disease since 2014<br>• Conservation of resources<br>• Simplification of the recommendations |

# ACIP Update – Meningococcal B Vaccines

- Discussion on meningococcal B vaccine booster doses for those fully vaccinated
  - GSK presented on Bexsero
    - Vaccine-induced antibody persist to varying degrees up to 8 years after 2-dose primary series of Bexsero
  - Pfizer presented on Trumenba (both 2 dose and 3 dose series)
    - For high risk groups, the data suggest that a 3-dose series followed by a booster dose will enhance persistence of breath of coverage. (Timing of booster dose to be established)

# ACIP Update – Meningococcal B Vaccines

- Workgroup recommends Men B booster for
  - Persons at high risk due to medical issues (persistent complement component deficiencies, complement inhibitor use, functional or anatomic asplenia, and microbiologists)
    - first booster one year after the primary series and every 2-3 years thereafter
  - Persons at risk during an outbreak
    - a booster dose if 6 months or more have passed since completion of the primary series
- ACIP will vote on this issue at upcoming meeting

# Selected publications

# Recent Publication

- DeStefano F, Bodenstab HM, Offit PA. **Principal controversies in vaccine safety in the United States.** *Clin Infect Dis*. 2019 Feb 12.
  - Key points: Concerns about vaccine safety can lead to decreased acceptance of vaccines and resurgence of vaccine-preventable diseases. The main current controversies about the safety of vaccines are not supported by the available biological and epidemiologic evidence.
  - Available at https://www.ncbi.nlm.nih.gov/pubmed/?term=destefano%2C+offit

# Recent Publication

- McClure DL, Jacobsen SJ, Klein NP, Naleway AL, Kharbanda EO, Glanz JM, Jackson LA, Weintraub ES, McLean HQ. **Similar relative risks of seizures following measles containing vaccination in children born preterm compared to full-term without previous seizures or seizure-related disorders.** *Vaccine*. 2019 Jan 3;37(1):76-79.
  - Conclusion: Vaccination with a measles-containing vaccine in the second year of life is associated with a similar relative risk of a first seizure in children born preterm as in those who were born full-term.
  - Available at https://www.ncbi.nlm.nih.gov/pubmed/?term=%22Similar+Relative+Risks+of+Seizures+following+Measles+Containing+Vaccination+in+Children+Born+Preterm+Compared+to+Full-term+without+Previous+Seizures+or+Seizure-related+Disorders%22

# Recent Publication

- Kochhar S, Excler JL, Bok K, Gurwith M, McNeil MM, Seligman SJ, Khuri-Bulos N, Klug B, Laderoute M, Robertson JS, Singh V, Chen RT; Brighton Collaboration Viral Vector Vaccines Safety Working Group (V3SWG). **Defining the interval for monitoring potential adverse events following immunization (AEFIs) after receipt of live viral vectored vaccines.** *Vaccine*. 2018 Nov 26.
  - Key points: Challenges and available options for choosing an appropriate risk window for AEFI are reviewed. Depending on the infrastructure, human resources and databases available in different countries, the appropriate option or combination of options can be determined by regulatory agencies and investigators.
  - Available at https://www.ncbi.nlm.nih.gov/pubmed/?term=Defining+the+interval+for+monitoring+potential+adverse+events+following+immunization+(AEFIs)+after+receipt+of+live+viral+vectored+vaccine

# Recent Publication

- McNeil MM, Duderstadt SK, Sabatier JF, Ma GG, Duffy J. **Vaccination and risk of lone atrial fibrillation in the active component United States military.** *Hum Vaccin Immunother*. 2018 Nov 16.
  - Results: We did not find an increased risk of lone atrial fibrillation after AVA, influenza or smallpox vaccine. These findings may be helpful in planning future vaccine safety research.
  - Available at https://www.ncbi.nlm.nih.gov/pubmed/?term=Vaccination+and+Risk+of+Lone+Atrial+Fibrillation+in+the+Active+Component+United+States+Military

# Recent Publication

- Landazabal CS, Moro P, Lewis P, Omer SB. **Safety of 9-valent human papillomavirus vaccine administration among pregnant women: adverse event reports in the Vaccine Adverse Event Reporting System (VAERS), 2014-2017**. *Vaccine*. 2019 Feb 21;37(9):1229-1234.
  - Results: No unexpected adverse events were observed among these pregnancy reports.
  - Available at https://www.sciencedirect.com/science/article/pii/S0264410X18316414

# Recent Publication

- Su JR, Duffy J, Shimabukuro TT (2019). Chapter 1: **Essentials of Vaccine Safety**. In Poland GA and Whitaker JA (Eds.), ***Vaccinations***. St. Louis, MO: Elsevier.
  - Available at https://www.elsevier.com/books/vaccinations/9780323554350

# Recent Publication

- Su J, Moro PL, Ng CS, Lewis PW, Said MA, Cano MV. **Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016.** *J Allergy Clin Immunol*. 2019 Jan 14.
  - Conclusion; Anaphylaxis after vaccination is rare in the United States and can occur among persons with no history of hypersensitivity. Most persons recover fully with treatment, but serious complications, including death, can occur.
  - Available at https://www.ncbi.nlm.nih.gov/pubmed/30654049

# Recent Publication

- Hesse EM, Shimabukuro TT, Su JR, Hibbs BF, Dooling KL, Goud R, Lewis P, Ng CS, Cano MV. **Postlicensure safety surveillance of recombinant zoster vaccine (Shingrix) –United States, October 2017--June 2018**. *MMWR* Feb. 1, 2019: 68 (4); 91-94.
  - Results: Although VAERS data are subject to the limitations inherent in passive surveillance, the initial safety data from VAERS monitoring during the first 8 months of RZV use are consistent with the safety profile observed in prelicensure clinical trials. No adverse events reported for RZV were disproportionate to adverse event reporting patterns observed for other vaccines in the VAERS database.
  - Available at https://www.cdc.gov/mmwr/volumes/68/wr/mm6804a4.htm

# Recent Publication

- Haber P, Moro PL, Ng C, Dores GM, Lewis P, Cano M. **Post-licensure surveillance of trivalent adjuvanted influenza vaccine (aIIV3; Fluad), Vaccine Adverse Event Reporting System (VAERS), United States, July 2016-June 2018.** *Vaccine*. 2019 Feb 7.
  - Conclusions: Although our review of aIIV3 in VAERS did not identify any unexpected health conditions of concern, we observed more than twice the expected number of reports with administration of the vaccine to persons outside of the age range for which the vaccine is approved in the U.S. Health care providers should be educated on the age groups for whom aIIV3 is recommended.
  - Available at : http://authors.elsevier.com/sd/article/S0264410X19301288

# Recent Publication

- Tartof SY, Qian L, Liu IA, Tseng HF, Sy LS, Hechter RC, Lewin BJ, Jacobsen SJ. **Safety of Influenza Vaccination Administered During Hospitalization.** *Mayo Clin Proc*. 2019 Jan 3
  - Conclusion: Our findings provide reassurance about the safety of influenza vaccination during hospitalization. Every contact with a health care professional, including during a hospitalization, is an opportunity to vaccinate.
  - Available at : https://www.ncbi.nlm.nih.gov/pubmed/30635116

# 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.

# ACIP Update – Japanese Encephalitis Vaccine

- Three votes passed
  - JE vaccine recommendations
    - JE vaccine is recommended for persons moving to a JE-endemic country to take up residence, longer-term (e.g. ≥1 month) travelers to JE-endemic areas, and frequent travelers to JE-endemic areas.
    - JE vaccine also should be considered for shorter-term (e.g. <1 month) travelers with an increased risk of JE based on planned travel duration, season, location, activities, and accommodations.
    - Vaccination also should be considered for travelers to endemic areas who are uncertain of specific duration of travel, destinations, or activities.
    - JE vaccine is not recommended for travelers with very low risk itineraries, such as shorter-term travel limited to urban areas or travel that occurs outside of a well-defined JE virus transmission season.
  - New recommendation for primary series schedule in adults aged 18-65 years
    - In adults aged 18-65 years, the primary vaccination schedule is two doses administered on days 0 and 7-28.
  - New recommendations for JE-VC booster dose
    - A booster dose (i.e. third dose) should be given at ≥1 year after completion of the primary JE-VC series if ongoing exposure or re-exposure to JE virus is expected.

# ACIP Update – Anthrax Vaccine

- AV7909 (NuThrax)
  - New anthrax vaccine available only for emergency use authorization
  - Anthrax vaccine absorbed with CPG 7909 adjuvant
  - Anticipated to be added to Strategic National Stockpile in July 2019 for post-exposure prophylaxis (PEP) for *Bacillus anthracis* exposure in combination with antimicrobial therapy
  - Has limited safety data
  - Is an option for PEP if AVA supplies are exhausted or unavailable
- Vote passed 15 to 0: Anthrax vaccine use for pre-exposure prophylaxis (PrEP) in persons not at current high risk of exposure to anthrax
  - A booster dose of AVA may be given every 3 years to persons not currently at high risk of exposure to *Bacillus anthracis* who have been previously primed with AVA

# ACIP Update – Zoster Vaccine

- Recombinant zoster vaccine (RZV) demand continues to outpace supply
- ~8.59 M doses distributed through 2018, a greater number of doses expected in 2019
- 2-dose RZV series completion >75% among Medicare beneficiaries
- A preliminary statistical signal for GBS among RZV recipients has been observed based on 4 claims in VSD data
  - ACIP work group agrees that there is insufficient evidence at this time to support a change in policy or practice
  - More investigation is required to determine whether this is, or is *not*, is a safety problem Clinical validation necessary (underway)
  - Evaluation of near real-time data in multiple systems (underway)