Summary and Relevant Evidence to Recommendations Framework

Sara Oliver MD, MSPH

Advisory Committee on Immunization Practices

June 26, 2019

Overview

- Review of topics under consideration
- Relevant Evidence to Recommendations framework
- Work Group interpretation

Topics Under Consideration

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be included as an option in the Vaccines for Children (VFC) Program for the infant series at 2, 4, and 6 months of age

Topics Under Consideration

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be included as an option in the Vaccines for Children (VFC) Program for the infant series at 2, 4, and 6 months of age

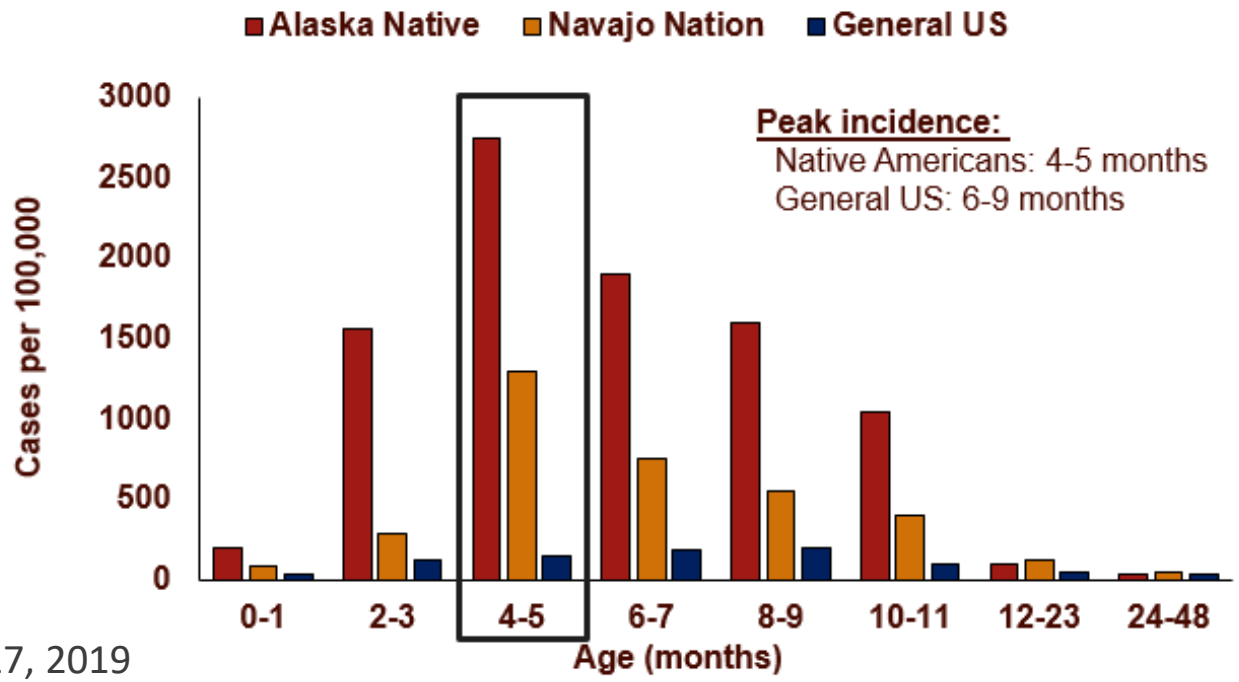
Hib Epidemiology and Hib Vaccines in AI/AN Population

- In the pre-vaccine era, Hib disease occurred at younger age among AI/AN population, compared to the general U.S. population

Hib Epidemiology and Hib Vaccines in AI/AN Population

- In the pre-vaccine era, Hib disease occurred at younger age among AI/AN population, compared to the general U.S. population

H. influenzae meningitis in children <5 years – Native Americans vs. General US, 1971-1977



From Laura Hammitt's presentation at ACIP meeting Feb 27, 2019

Hib Epidemiology and Hib Vaccines in AI/AN Population

- PRP-OMP vaccines achieve protective immunity in majority of infants after 1st dose

Immunogenicity of 2 or 3 Hib conjugate vaccine doses in Alaska Native infants

Age (mos) of serum collection	HbOC (2, 4, 6 months)				PRP-D (2, 4, 6 months)				PRP-OMP (2, 4 months)			
	n	GMC (µg/ml)	≥0.15 µg/ml (%)	≥1.0 µg/ml (%)	n	GMC (µg/ml)	≥0.15 µg/ml (%)	≥1.0 µg/ml (%)	n	GMC (µg/ml)	≥0.15 µg/ml (%)	≥1.0 µg/ml (%)
2	55	0.15	30 (55)	3 (5)	56	0.06	14 (25)	2 (4)	44	0.16	20 (45)	6 (14)
4	54	0.07	13 (24)	0 (0)	55	0.04	6 (11)	1 (2)	44	1.37	40 (91)	25 (57)
6	56	0.59	44 (79)	24 (43)	55	0.06	15 (27)	6 (11)	43	2.71	43 (100)	34 (79)
7	53	13.72	53 (100)	50 (94)	40	0.55	31 (78)	18 (45)	--	--	--	--
9-12	52	3.7	50 (96)	42 (81)	42	0.19	27 (64)	9 (21)	39	0.53	34 (87)	13 (33)
15-18	35	1.53	32 (91)	24 (69)	32	0.08	14 (44)	1 (3)	28	0.23	20 (71)	4 (14)

GMC: geometric mean concentration. Results for PRP-T not shown.

From Laura Hammitt's presentation at ACIP meeting Feb 27, 2019

Hib Epidemiology and Hib Vaccines in AI/AN Population

- In the pre-vaccine era, Hib disease occurred at younger age among AI/AN population

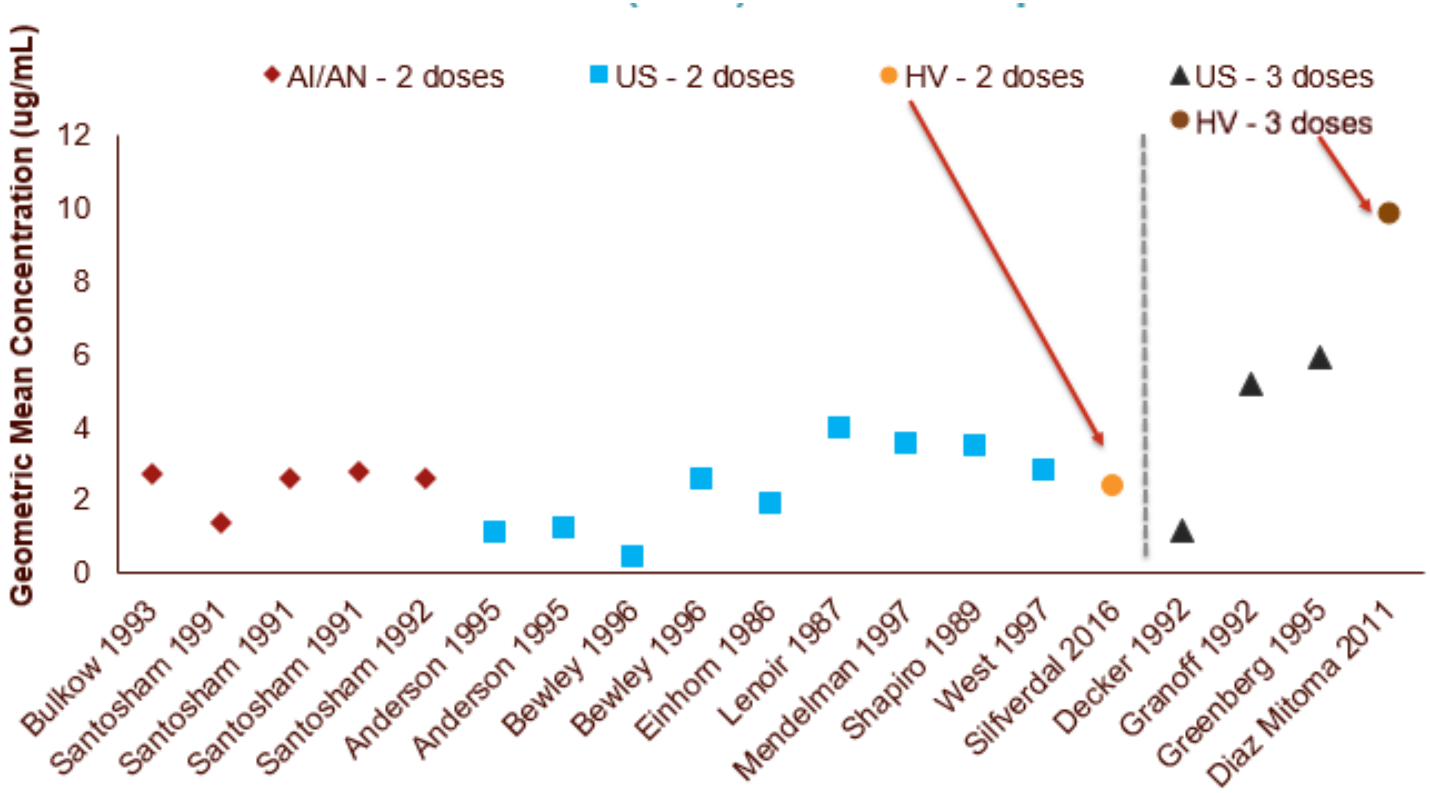
- PRP-OMP vaccines achieve protective immunity in majority of infants after 1st dose

PRP-OMP vaccines are preferentially recommended for AI/AN population

Pediatric Hexavalent Vaccine and AI/AN population

- Preferential recommendation based on immunogenicity data after 1st dose

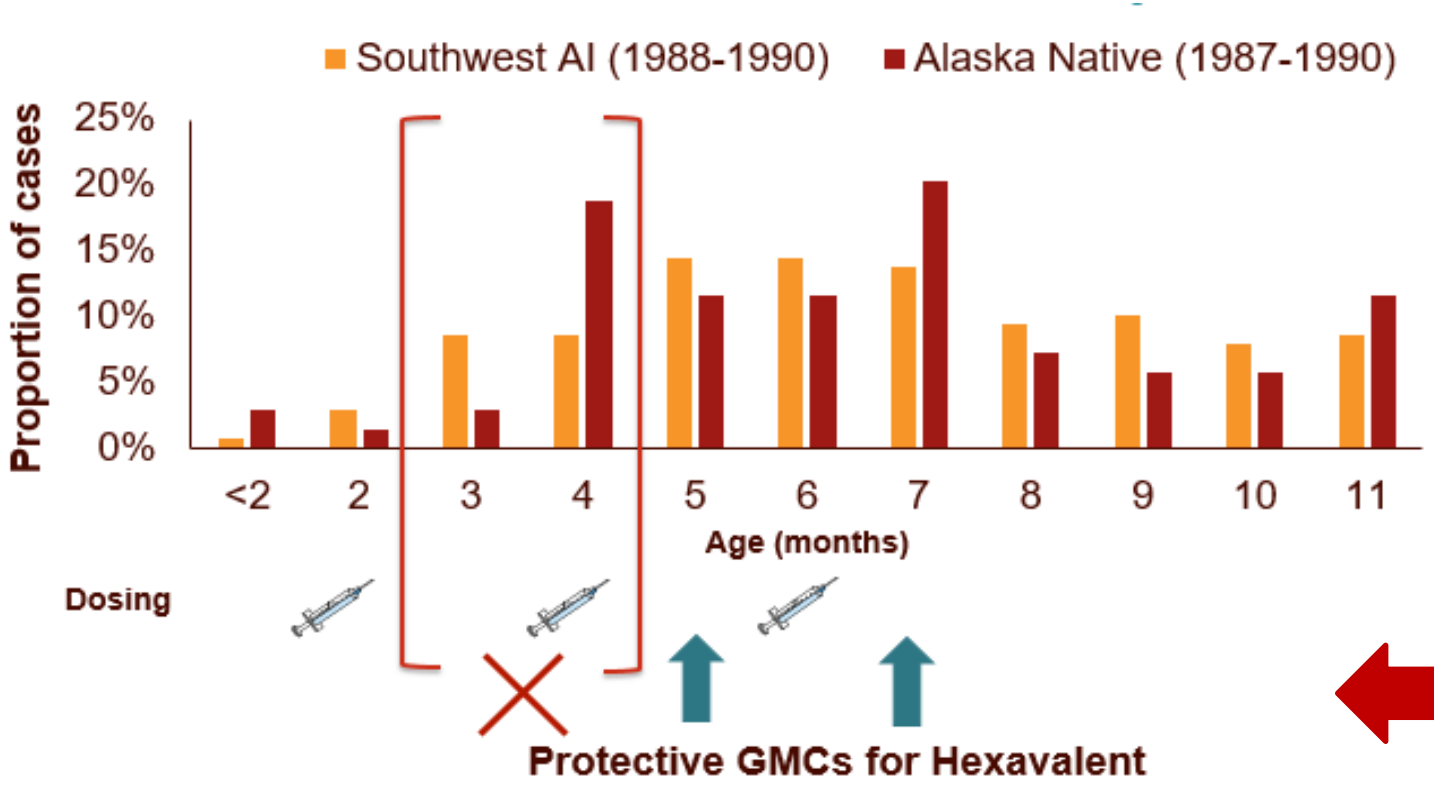
Available data after 2nd and 3rd dose show robust response



From Laura Hammitt's presentation at ACIP meeting Feb 27, 2019

Pediatric Hexavalent Vaccine and AI/AN population

- Preferential recommendation based on immunogenicity data after 1st dose



No data post-dose 1

From Laura Hammitt's presentation at ACIP meeting Feb 27, 2019

Current Work Group Thoughts

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population

Current Work Group Thoughts

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population

The Work Group and ACIP members felt that immunogenicity data post-dose 1 is needed before ACIP could consider a preferential recommendation for the AI/AN population

Topics Under Consideration

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be included as an option in the Vaccines for Children (VFC) Program for the infant series at 2, 4, and 6 months of age

Relevant Evidence to Recommendations Framework

- **Benefits and Harms**: Desirable/undesirable effects
- **Values**: Target population values and preference
- **Acceptability**: Is the intervention acceptable to key stakeholders
- **Feasibility**: Anticipated implementation issues

Benefits and Harms

Evidence to Recommendations Framework
Potential Benefits: DTaP-IPV-Hib-HepB vaccine

- Immunogenicity: Non-inferiority criteria met
  - Exceptions:
    - GMC for one of five pertussis antigens (FHA) post-dose 3
      - However, achieved with % vaccine response
    - GMC for one of thirteen pneumococcal antigens (PN6B) post-dose 3
      - However, met non-inferiority endpoints set in PCV13 studies

Evidence to Recommendations Framework
Potential Benefits: Combination vaccines

- Increased number of vaccine doses due is associated with deferring doses, leading to missed opportunities and decreased coverage[1]

- Receipt of at least 1 combination vaccine independently associated with improved coverage rates[2]
  - Individual vaccines as well as vaccine series (e.g. infant series)

[1]Meyerhoff et al. Preventative Medicine 2005; 540-544
[2]Marshall et al. Pediatr Infect Dis J 2007; 496-500

Evidence to Recommendations Framework
Potential Harms: DTaP-IPV-Hib-HepB vaccine

- Safety: Profile consistent with component vaccines
- Higher rate of fever, particularly compared to pentavalent regimens
  - No increase in fever-related medical events

Evidence to Recommendations Framework
Potential Harms: Combination vaccines

- Potential disadvantages of combination vaccines include[1]:
  - Adverse events that might occur more frequently after administration of a combination vaccine compared with administration of separate antigens
  - Confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses
  - Reduced pathogen coverage if the combination product covers fewer types of one particular vaccine-preventable disease-causing agent
  - Extra doses of certain antigens in the combination product
  - Shorter shelf-life than in individual component vaccines

[1]General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html

Values and Preferences

Evidence to Recommendations Framework

Values

- "Use of combination vaccines can reduce the number of injections patients receive and alleviate concern associated with the number of injections… The use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines. Considerations should include provider assessment, patient preference, and the potential for adverse events."[1]

- "Combination vaccines represent one solution to the issue of increased numbers of injections during single clinic visits and generally are preferred over separate injections of equivalent component vaccines." [2]

[1]General Best Practice Guidelines for Immunization. Best Practice Guidance of the ACIP. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
[2]American Academy of Pediatrics. Red Book 2018 Report of the Committee on Infectious Diseases. 31st Edition.

Acceptability

Evidence to Recommendations Framework
Acceptability

- Prior evaluation of combination vaccines in 2003 among Medicaid patients in Georgia showed that **85%** of children received at least 1 combination vaccine in the first year of life[1]

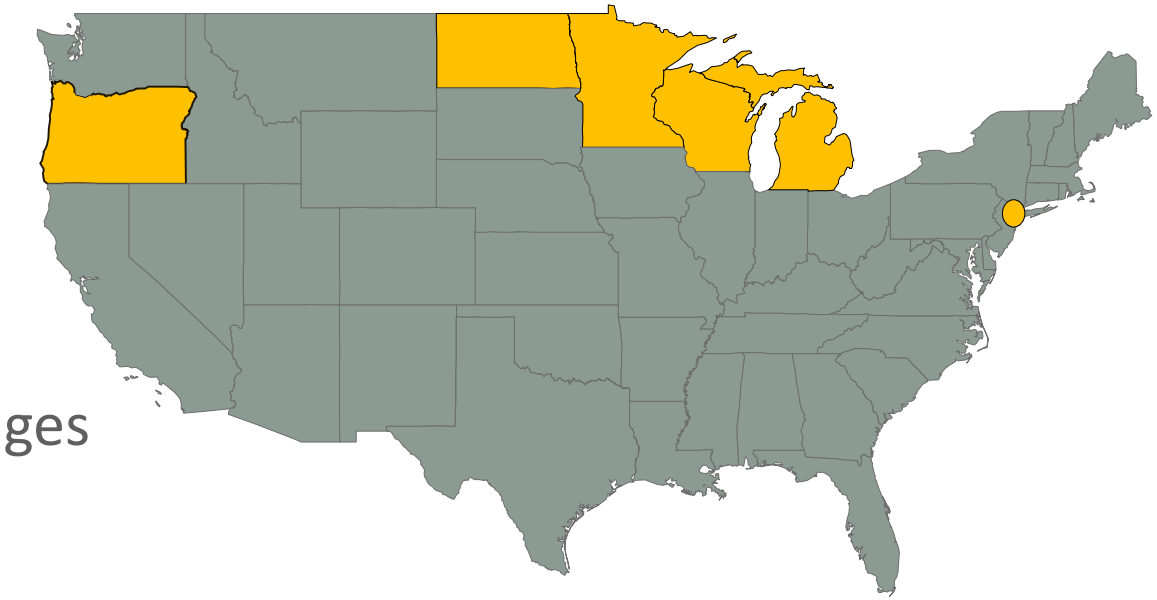
[1]Marshall et al. Pediatr Infect Dis J 2007; 496-500

Evidence to Recommendations Framework
Acceptability

- Frequency of combination vaccines and single vaccines for the infant series in multiple birth cohorts from 2014–2018
  - Using Immunization Information Systems (IIS)
  - Evaluation assessed 2 different antigens
    - DTaP and Hib

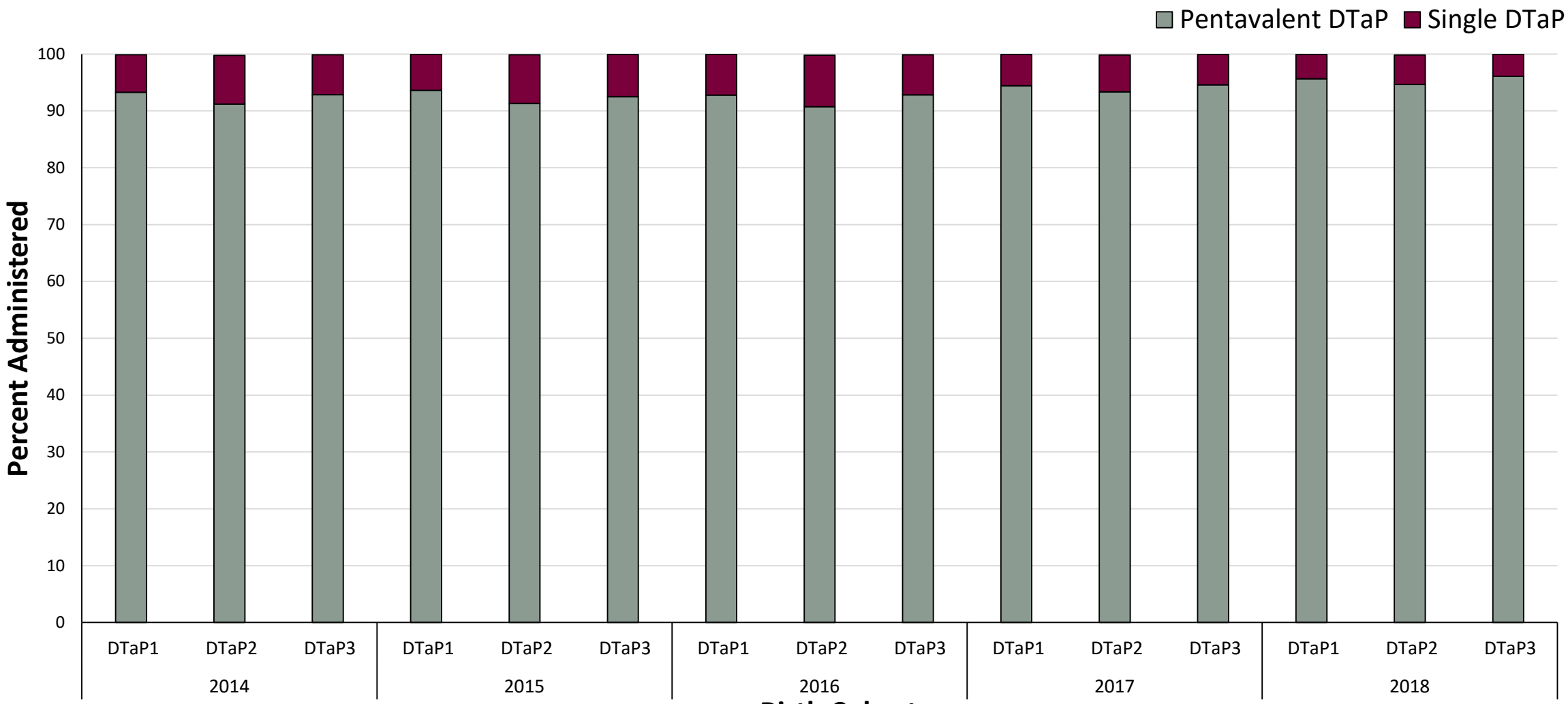
IIS Sentinel Sites

- **Six Sites (2014-2018): MI, MN, ND, NYC, OR, WI**
- **IIS Sentinel Site data**
  - Strengths
    - Provider-submitted
    - Population-based
    - Timely
    - Containing data for all pediatric ages
  - Limitation
    - May not be generalizable



Data provided by Michelle Lin, CDC's Immunization Services Division

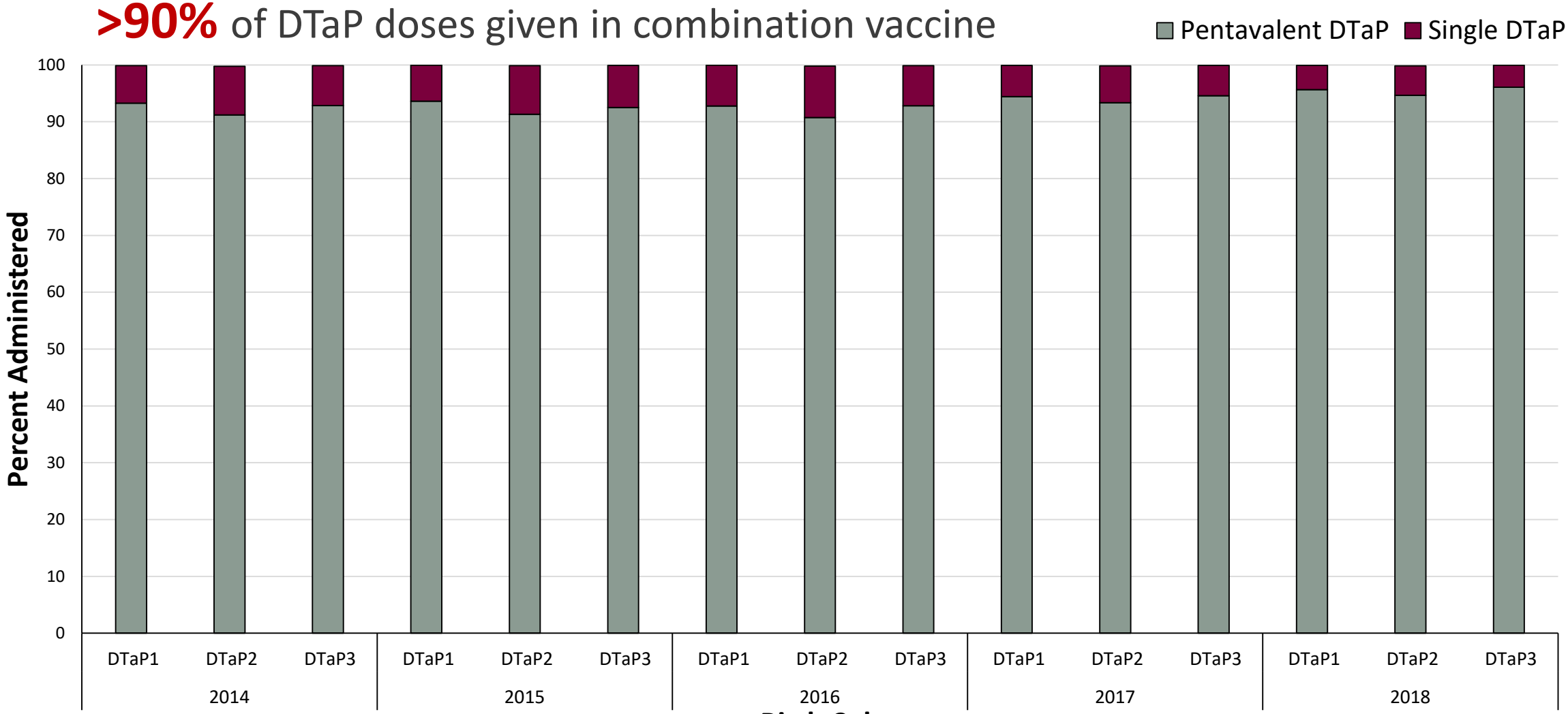
DTaP administration frequency, by vaccine type and birth cohort, IIS Sentinel Sites, 2014-2018



Data provided by Michelle Lin, CDC's Immunization Services Division

DTaP administration frequency, by vaccine type and birth cohort, IIS Sentinel Sites, 2014-2018

>90% of DTaP doses given in combination vaccine



Data provided by Michelle Lin, CDC's Immunization Services Division

Feasibility

Evidence to Recommendations Framework
Feasibility

- Additional combination vaccine (DTaP-IPV-Hib-HepB) will not alter established vaccination schedule
- Considerations for having additional product(s) available for booster doses
- DTaP-IPV-Hib-HepB vaccine not commercially available prior to 2021

Summary

Overall Work Group Interpretation

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be included as an option in the VFC Program for the infant series at 2, 4, and 6 months of age

Overall Work Group Interpretation

- Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be included as an option in the VFC Program for the infant series at 2, 4, and 6 months of age

Work Group is supportive of including this vaccine in the VFC program as one of the available options

VFC Resolutions

- 4 separate VFC resolutions
  - Diphtheria, Tetanus & Pertussis
  - *Haemophilus influenzae* type b
  - Hepatitis B
  - Polio

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