Summary and Relevant Evidence to Recommendations Framework

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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
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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
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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 1\textsuperscript{st} dose**

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

<table>
<thead>
<tr>
<th>Age (mos) of serum collection</th>
<th>HbOC, (2, 4, 6 months)</th>
<th>PRP-D, (2, 4, 6 months)</th>
<th>PRP-OMP, (2, 4 months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>GMC (µg/ml)</td>
<td>≥0.15 µg/ml (%)</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>0.15</td>
<td>30 (55)</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>0.07</td>
<td>13 (24)</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>0.59</td>
<td>44 (79)</td>
</tr>
<tr>
<td>7</td>
<td>53</td>
<td>13.72</td>
<td>53 (100)</td>
</tr>
<tr>
<td>9-12</td>
<td>52</td>
<td>3.7</td>
<td>50 (96)</td>
</tr>
<tr>
<td>15-18</td>
<td>35</td>
<td>1.53</td>
<td>32 (91)</td>
</tr>
</tbody>
</table>

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

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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 1\textsuperscript{st} 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 1\textsuperscript{st} dose

Available data after 2\textsuperscript{nd} and 3\textsuperscript{rd} 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 1\textsuperscript{st} dose

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
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- 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

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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
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:\n  
  - 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

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

- “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.”

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

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\(^1\)

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
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