Direct and Indirect Impact of 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Invasive Pneumococcal Disease (IPD) Among Children and Adults in the U.S.

Tamara Pilishvili, Centers for Disease Control and Prevention
Ryan Gierke, Centers for Disease Control and Prevention
Monica Farley, Emory University
William Schaffner, Emory University
Ann Thomas, Oregon Public Health Division
Arthur Reingold, University of California
Lee Harrison, University of Pittsburgh
Ruth Lynfield, Minnesota Department of Health
Shelley M. Zansky, New York State Department of Health
Susan Petit, Connecticut Emerging Infections Program

Only first 10 authors above; see publication for full author list.

Final published version: http://dx.doi.org/10.1093/ofid/ofx162.158

Copyright information:
© The Author 2017. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access work distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Accessed August 9, 2019 8:06 AM EDT
Table: Symptoms, signs, laboratory findings

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number (%) abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (temperature &gt; 100.4)</td>
<td>36/36 (100%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15/20 (75%)</td>
</tr>
<tr>
<td>Headache</td>
<td>23/32 (72%)</td>
</tr>
<tr>
<td>Rash</td>
<td>18/36 (50%)</td>
</tr>
<tr>
<td>WBC count &lt; 6,000</td>
<td>11/36 (31%)</td>
</tr>
<tr>
<td>Platelets &lt; 120,000</td>
<td>12/36 (33%)</td>
</tr>
<tr>
<td>Bilirubin ≤ 1.5</td>
<td>3/36 (8%)</td>
</tr>
<tr>
<td>AST &gt; 50</td>
<td>25/36 (69%)</td>
</tr>
</tbody>
</table>

Number (%) abnormal

<table>
<thead>
<tr>
<th>Age &lt; 18</th>
<th>Age &gt; 18</th>
<th>Total</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>36/36 (100%)</td>
<td>3/36 (8%)</td>
<td>39/90 (43%)</td>
<td></td>
</tr>
<tr>
<td>15/20 (75%)</td>
<td>12/36 (33%)</td>
<td>27/90 (30%)</td>
<td></td>
</tr>
<tr>
<td>23/32 (72%)</td>
<td>11/36 (31%)</td>
<td>34/90 (38%)</td>
<td></td>
</tr>
<tr>
<td>18/36 (50%)</td>
<td>25/36 (69%)</td>
<td>43/90 (48%)</td>
<td></td>
</tr>
</tbody>
</table>

*Comparing pediatric vs. adult cases.

2492. Direct and Indirect Impact of 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Invasive Pneumococcal Disease (IPD) Among Children and Adults in the U.S.

Tamaral Pillsvilh1, MPH1, Ryan Gierke, MPH2, Monica Farley, MD, FIDSA3; William Schaffner, MD, FIDSA, FSHEA1; Ann Thomas, MD, MPH4; Arthur Reingold, MD, FIDSA5; Lee Harrison, MD5; Ruth Lynfield, MD, FIDSA5; Shelley M. Zandek, PhD6, ScD3; Lisa Miller, MD, MSPh7; Laura Bailey, MS1, MD, MPH8; Vannesa Beall, PhD9; and Cynthia Whitney, MD, MPH, FIDSA10; National Center for Immunizations and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; 1Department of Medicine, Emory University School of Medicine and Atlanta VA Medical Center, Atlanta, Georgia; 2Vanderbilt University School of Medicine, Nashville, Tennessee; 3Oregon Public Health Division, Portland, Oregon; 4University of California - Berkeley, Berkeley, California; 5University of Pittsburgh, Pittsburgh, Pennsylvania; 6Minnesota Department of Health, St. Paul, Minnesota; 7New York State Department of Health, Albany, New York; 8Connecticut Emerging Infections Program, New Haven, Connecticut; 9Preventive Medicine Residency Program, University of Colorado School of Public Health, Aurora, Colorado; 10New Mexico Department of Health, Santa Fe, New Mexico; 11Centers for Disease Control and Prevention, Atlanta, Georgia.

Session: 278. Pneumococcal and Pertussis Vaccines
Saturday, October 7, 2017: 2:00 PM

Background. In February 2010, PCV13 was introduced for routine use among children aged ≤ 5 years. In June 2012, PCV13 was recommended for use in series with 23-valent polysaccharide vaccine (PPSV23) for adults ≥ 19 years with select medical conditions, and in August 2014, for all adults ≥ 65 years. We evaluated the direct and indirect effects of PCV13 6 years post-introduction on invasive pneumococcal disease (IPD).

Methods. IPD cases (isolation of pneumococcus from sterile sites) were identified among residents of Active Bacterial Core surveillance (ABCs) sites during July 2007–June 2016. Isolates were serotyped by Quelling, PCR, or whole genome sequencing and classified as PCV13 or non-vaccine type (NVT). Incidence changes were estimated as percent changes (one minus rate ratio) and 95% confidence intervals (95% CI) between pre-PCV13 (2007–2009) and two post-PCV13 periods (July 2014–June 2015 and July 2015–June 2016).

Results. ABCs identified 31,190 IPD cases between 2007 and 2015, with 2,750 cases among children <5 years and 10,930 among those ≥65 years. During the two post-PCV13 periods, overall IPD rates were 35%–62% lower relative to 2007–2009 among all age groups, including <5 years and ≥65 years (Figure). Significant reductions in PCV13-type IPD incidence were observed for all age groups during both post-PCV13 periods, with incidence 84% (95% CI 78, 88%) and 68% (95% CI 63, 73%) lower in 2015–2016 among children <5 years and adults ≥65 years, respectively.

PCV13-type IPD reductions were driven by serotypes 19A and 7E IPD due to non-vaccine types also declined significantly among children <5 years (<27%, 95% CI –42, –9%) and adults ≥65 years (>24%, 95% CI –34, –14%). PCV13-type IPD incidence did not differ significantly between the two post-PCV13 periods.

Conclusion. IPD incidence declined among children and adults in the U.S. following PCV13 introduction among children. The lack of difference in PCV13 rates between 2014–2015 and 2015–2016 suggests no measurable early impact of PCV13 introduction among adults ≥65 years. To date, we found no evidence of significant replacement disease with non-PCV13 types. Further work is needed to explain reductions in non-vaccine type disease observed in the post-PCV13 era.
2493. Invasive Pneumococcal Disease in Massachusetts Children 6 Years Following Introduction of PCV13

Inci Yildirim, MD MSc1; Brent Little, PhD2; Stephen I. Pelton, MD3; Pediatric Infectious Diseases, Emory University, Atlanta, Georgia; Pediatric Infectious Diseases, Boston University, Boston, Massachusetts and, 1Boston University Schools of Medicine and Public Health, Boston, Massachusetts

Session: 278. Pneumococcal and Pertussis Vaccines
Saturday, October 7, 2017: 2:00 PM

Background. A second generation 13-valent-pneumococcal conjugate vaccine (PCV13) replaced PCV7 in the childhood immunization schedule in Massachusetts (MA) beginning in April 2010

Methods. Cases of invasive pneumococcal disease (IPD) in children <18 years of age were detected through an enhanced surveillance system in MA since 2001. All cases in children and Streptococcus pneumoniae (SP) isolates, when available, are submitted to Department of Public Health (MDPH) and parents/physicians are interviewed for confirmation of demographic and clinical data. All available isolates are confirmed as SP, serotyped by Quellung reaction

Results. Three-hundred-thirty-seven IPD cases have been identified in MA children between 4 January 2010 and 31.31.2017(Figure). Thirty-five (10.4%) were in toddlers 12 to 24 months; 100 (29.7%) in children between 2 and 5 years of age and infants <6 months; 41(12.2%) in children between 6 and 12 months; 60 (17.8%) in children between 4.January 4, 2010 and 03.31.2017(Figure). Thirty-five(10.4%) were in children with at least one comorbidity (Table). The proportion of VST disease declined to 24.1% from 59.2% over 6 years after PCV13 (21 cases), 3(18 cases), 19F (7cases), 6A(3 cases), serotypes 14, 18C and 5(1 case each) the proportion of VST disease declined to 24.1% from 59.2% over 6 years after PCV13 (p < 0.001). Serotypes 15B (13.5%), 3F (12.5%) and 22F (12.5%) were the most common nonvaccine serotypes (NVST).

Conclusion. In the post-PCV13 era, IPD is primarily due to NVSTs and disproportionately observed in children with comorbid conditions. In the most recent year (4.1.2016 through 3.31.2017) an increase in incidence was observed in MA children after six years of declining cases following implementation of PCV13.

2494. Analysis of Invasive Pneumococcal Infections Due to 13-Pneumococcal Conjugate Vaccine Serotypes at 8 US Children's Hospitals During 2014 to 2016

Sheldon L. Kaplan, MD, FIDSA1; William J. Barson, MD, FIDSA2; Phihana Ling Lim, MD3; Jose Romero, MD4; John S. Bradley, MD, FIDSA, RPIDS, RAAD5; Tim T. Tran, MD, FIDSA6; Laurence B. Griner, MD7; Jill Hoffman, MD8; Kristina Hulten, PhD9 and Edward O. Mason Jr, PhD, FIDSA10: Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas; 1Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, Ohio; Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; 2University of Arkansas for Medical Sciences, Little Rock, Arkansas; 3Pediatric Infectious Diseases, University of California at San Diego School of Medicine, San Diego, California; 4Northwestern University Feinberg School of Medicine, Chicago, Illinois; 5Wake Forest University School of Medicine, Winston-Salem, North Carolina; 6Children's Hospital, Los Angeles, Los Angeles, California; 7Baylor College of Medicine and Texas Children's Hospital, Houston, Texas

Session: 278. Pneumococcal and Pertussis Vaccines
Saturday, October 7, 2017: 2:00 PM

Background. The 13-Valent Pneumococcal Conjugate Vaccine (PCV13) was licensed in 2010 and is directed against serotypes (ST) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. Details of cases of invasive pneumococcal disease (IPD) due to PCV13 ST since 2010 in the US are sparse. We describe IPD cases due to PCV13 ST seen at 8 US children's hospitals over years 2014 to 2016 which may aid in understanding why some IPD cases due to these ST have persisted.

Methods. Children with IPD have been prospectively identified at 8 children's hospitals in the US since 1993. Data from 2014 through 2016 were analyzed. Demographic, clinical data and number and dates of PCV doses were collected on case report forms and isolates were sent to a central laboratory for serotyping. PCV doses are counted if IPD occurred ≥2 weeks after a dose.

Results. PCV13 ST accounted for 19.7% (271/137) and 26.8% (30/112) and 26% (33/127) of IPD cases in 2014, 2015 and 2016, respectively. ST 3, 19A and 19F accounted for 90% of the PCV13 ST IPD cases, >50% of the children had received ≥2 doses of PCV13 prior to IPD. Details of the 30 children with ≥2 doses of PCV 15 were of an age at diagnosis for which ≥2 doses of PCV was recommended. An underlying condition was noted in 18. For PCV13 ST, the types of IPD were pneumonia (n = 39), mastoiditis (n = 15), bacteremia (n = 15), meningitis (n = 12) and other sites of infection (n = 9). Whereas the numbers of yearly cases were similar for ST3 (12, 10, 13) and ST19A (8, 16, 6), the numbers for 19F increased slightly (3, 8, 10).

Conclusion. Four to 6 years after PCV13 was introduced, PCV13 ST (especially ST 3, 19A and 19F) accounted for about 25% of IPD in children. For all of the PCV13 ST, over half of these IPD cases occurred in children who had received ≥2 doses of the recommended PCV schedule; 25% of cases occurred in children who had not received any doses but were of the age at diagnosis that at least 2 PCV doses should have been received. Additional PCV13 ST IPD cases may be preventable if the PCV13 schedule is followed as recommended.

Disclosures. S. L. Kaplan, Pfizer: Grant Investigator and Speaker at PCV13 Launch Meeting in China, Research grant and Speaker honorarium; J. S. Bradley, Merck & Co., Inc.: Investigator, Research support