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US Pediatric Multicenter Pneumococcal Surveillance Study Group

Session: O-34. Pediatric Vaccines

Background: The 2011 IDSA/PIDS Clinical Practice Guidelines for the Management of Community-acquired Pneumonia (CAP) in Children Older than 3 months recommended empiric treatment with either ampicillin/penicillin or ceftriaxone based on PCV13 vaccine status and the local antibiotic susceptibilities of IPD isolates. No study has addressed differences in antibiotic susceptibilities for isolates from children with pneumococcal pneumonia (PP) based on PCV13 status.

Methods: Investigators from 8 US children's hospitals identified infants and children with IPD between 1/1/2014 and 12/31/2019. IPD was documented by positive cultures from a normally sterile site. PP diagnosis required an abnormal chest radiograph. Clinical data were recorded and isolates analyzed for serotype (ST) by the capsular swelling method and antimicrobial susceptibilities by standard methods. Administration of PCV7/13 was documented through the patient's medical records, health care provider or a vaccine registry. Fisher Exact was performed; p< 0.05 was significant.

Results: 690 IPD patients with isolates were available (0–18 y); 24% (166/690) of the isolates were PCV13 STs (ST3-75, ST19F-45, ST19A-36, ST7F-5, other STs-5). The most common non-PCV13 ST isolates were ST35B-60, ST23B-59, ST33F-47, ST22F-43, ST15C-35, ST23A-27, ST15B-26, ST10A-26, ST15A-23. Of non-PCV13 isolates, 41% (217/524) were among the 7 additional STs in PCV20. For children with PP (n=157), the distributions of penicillin (Table) (p=0.8) and ceftriaxone MICs were no different for isolates obtained from children regardless of prior PCV13 doses. Less than 7% of PP isolates were resistant to penicillin (MIC >2 µg/mL).

Table. Minimal inhibitory concentrations (MIC) of pneumococcal isolates related to the number of PCV13 doses each patient received prior to pneumococcal pneumonia (PP).

	Number of PCV13 doses				
Penicillin MIC (µg/mL)					
	0	**1**	**2**	**3**	**4**
≤ 0.125	26*	12	8	17	43
0.25–0.5	4	2	1	1	5
1	1	0	0	3	1
2	4	0	0	2	5
≥4	1	2	1	2	4

*Number of pneumococcal pneumonia patients/isolates. 145/157 patients had immunization and isolate susceptibility data available for analysis.

Conclusion: PCV13 status should not modify empiric antibiotics for children with suspected pneumococcal CAP. 41% of non-PCV13 IPD isolates were among the 7 additional PCV20 STs.

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177. Safety of Measles and Pertussis-containing Vaccines in School-age Children Previously Diagnosed with Autism Spectrum Disorders

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Background: Some parents, especially those of children with autism spectrum disorders (ASD), are uncertain about the safety of childhood immunization. We compared rates of fever, febrile seizure and emergency room (ER) visits following measles and pertussis-containing vaccines recommended between ages 4–6 years among children with and without ASD.

Risk of Fever, Febrile Seizure and ER Visits following Measles and Pertussis-containing Vaccine Among Children with and without Autism Spectrum Disorders Diagnosis.				
		Difference-in-difference analysis comparing children with vs. without ASD	Risk interval analysis among children with ASD (N = 14,947)	Risk interval analysis among children without ASD (N=1,650,041)
Outcomes after immunization	Risk/control intervals (days)	Ratio of rate ratio (95% CI)	Rate ratio (95% CI)	Rate ratio (95% CI)
Risk following Measles-containing vaccines				
Fever[1]	7 - 10/14 - 28	1.07 (0.58 – 1.96)	1.22 (0.67 – 2.23)	1.14 (1.06 – 1.22)
Febrile seizure[2]	7 - 10/14 - 28	NE	NE	1.64 (1.05 – 2.55)
ER visits	4 - 10/14 - 28	1.11 (0.80 – 1.54)	1.13 (0.82 – 1.56)	1.02 (0.98 – 1.06)
Risk following Pertussis-containing vaccines				
Fever[1]	1 -3/14 - 28	1.16 (0.63 – 2.15)	1.38 (0.75 – 2.55)	1.19 (1.10 – 1.29)
Febrile seizure[2]	0 - 3/14 - 28	NE	NE	2.40 (1.58 – 3.52)
ER visits	0 – 3/14 - 28	0.87 (0.59 – 1.28)	1.11 (0.76 – 1.62)	1.27 (1.22 – 1.33)

[1] Fever diagnosed in outpatient settings
[2] Febrile seizure diagnosed in ER or inpatient settings
NE: Not estimated because cells counts were zero "0"

Methods: The study included children who were born between 1995–2012, aged 4–7 years at vaccination, and members of six integrated healthcare delivery systems within the Vaccine Safety Datalink. Children with ASD were defined based on receipt of two separate International Classification of Diseases (ICD)-9 or 10 codes. Outcomes (fever, febrile seizures, and ER visits) were identified in electronic health records. To minimize confounding by unmeasured factors related both to avoidance of vaccination and to outcomes of interest, we compared rates of each outcome between children with and without ASD, in risk and control intervals, by estimating the difference-in-differences on a log scale (i.e. the ratio of rate ratios) using logistic regressions. We also conducted risk interval analyses comparing rates of outcomes in risk intervals and control intervals within each group.

Results: The study included 14,947 children with ASD and 1,650,041 children without ASD. After measles or pertussis-containing vaccination, there were no differences in association between the two groups for fever or ER visits (Table). There were no febrile seizures identified among children with ASD. Within the ASD group, rates of fever, seizure or ER visits did not differ significantly between the risk and control intervals after vaccination. However, among the non-ASD group, measles and pertussis-containing vaccines were associated with higher rates of fever and seizure in risk intervals compared to controls intervals. Pertussis-containing vaccines were associated with increased risk of ER visits in risk interval compared to control interval (Table).

Conclusion: We found no difference in the risk of fever, and ER visits comparing children with autism to children without autism after measles or pertussis-containing vaccines. The study provides some reassurance that these vaccines are not less safe in children with ASD.

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178. Vaccine Effectiveness Against Influenza-associated Hospitalizations and Emergency Department (ED) Visits Among Children in the United States in the 2019–2020 Season

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Background: The 2019–20 influenza season was predominated by early onset B/Victoria viruses followed by A(H1N1)pdm09 virus circulation. Over 95% of circulating B/Victoria viruses were subclade V1A.3, different from the Northern Hemisphere

vaccine strain. Annual estimates of influenza vaccine effectiveness (VE) are important because of frequent changes in circulating and vaccine viruses.

Methods: We assessed VE among children 6 months–17 years old with acute respiratory illness and <10 days of symptoms enrolled during the 2019–20 influenza season at 7 pediatric hospitals (ED patients < 5 years at 3 sites) in the New Vaccine Surveillance Network. Combined mid-turbinate/throat swabs were tested for influenza virus using molecular assays. We estimated age-stratified VE from a test-negative design using logistic regression to compare odds of vaccination among children testing positive versus negative for influenza, adjusting for age in years, enrollment month, and site. For these preliminary analyses, vaccination status was by parental report.

Results: Among 2022 inpatients, 324 (16%) were influenza positive: 38% with influenza B/Victoria alone and 44% with influenza A(H1N1)pdm09 alone (Table). Among 2066 ED children, 653 (32%) were influenza positive: 45% with influenza B/Victoria alone and 43% with influenza A(H1N1)pdm09 alone. VE was 62% (95% confidence interval [CI], 51%–70%) against any influenza-related hospitalizations, 68% (95% CI, 55%–78%) for A(H1N1)pdm09 and 55% (95% CI, 35%–69%) for B/Victoria. VE by age group for any influenza-related hospitalizations was 57% (95% CI, 40%–69%) among children 6 months to < 5 years and 66% (95% CI, 49%–77%) among children 5–17 years. VE was 53% (95% CI, 42%–62%) against any influenza-related ED visits, 46% (95% CI, 28%–60%) for A(H1N1)pdm09 and 54% (95% CI, 39%–66%) for B/Victoria. VE by age group was 52% (95% CI, 37%–63%) among children 6 months to < 5 years and 42% (95% CI, 16%–60%) among children 5–17 years.

Table. Influenza viruses detected from children in VE analysis dataset for NVSN, 2019-2020

Virus Detected	Inpatient (N=319)	ED (N=652)
	n	n
B/Victoria alone	124	292
A(H1N1)pdm09 alone	141	278
A(H3N2) alone	2	3
A(H1N1)pdm09 and B/Victoria	1	3
A(H1N1)pdm09 and B, lineage unknown	2	0
A, not subtyped and B/Victoria	1	3
A, not subtyped and B, lineage unknown	1	0
A, not subtyped alone	17	17
B/Yamagata alone	3	2
B/Victoria and B/Yamagata	0	1
B, lineage unknown alone	32	54

Conclusion: Influenza vaccination in the 2019–20 season provided substantial protection against laboratory-confirmed influenza-associated hospitalizations and ED visits associated with the two predominantly circulating influenza viruses among children, including against the emerging B/Victoria virus V1A.3 subclade.

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179. Individual and State-level Factors Associated with Receipt of Multiple Recommended Adolescent Vaccines in the United States

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Session: O-34. Pediatric Vaccines

Background: The Advisory Committee on Immunization Practices (ACIP) routinely recommends several adolescent vaccines, including human papillomavirus (HPV); quadrivalent meningococcal conjugate (MenACWY); and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccines. Limited data are available on the percentage of adolescents receiving this complement of ACIP-recommended vaccines and factors that may increase likelihood of completion.

Methods: This study used 2015–18 pooled National Immunization Survey-Teen (NIS-Teen) data to estimate national and state-level completion rates by age 17 of a two-dose MenACWY series, two- or three- dose HPV series (depending on age at first vaccination), and a Tdap vaccine, using multivariable logistic regression modeling to adjust for individual characteristics. NIS-Teen data were then combined with public state-level data to construct a multilevel model evaluating effects of both individual- and state-level factors on completion.

Results: After adjusting for individual-level factors, the national completion rate for these ACIP-recommended vaccines by age 17 was 30.6% (95% confidence interval [CI]: 30.1–31.0%). However, rates for individual states varied substantially, from 11.3% in Idaho (CI: 6.9–18.0%) to 56.4% in Rhode Island (CI: 49.8–62.8%) (Figure 1).

In the multilevel model, individual characteristics associated with increased likelihood of receiving the recommended vaccines by age 17 included female gender, black or Hispanic race, Medicaid coverage (vs. private/other), last provider visit at age 16 or 17, generally having ≥1 provider visit in last year, and receiving a provider recommendation for HPV vaccination. Residing in a state with a MenACWY vaccination mandate for elementary and secondary schools was the only state-level variable that significantly increased the likelihood of completion (odds ratio: 1.6; CI: 1.2–2.3) (Figure 2).

Figure 1: Model-Adjusted Completion Rates of ACIP-Recommended HPV, MenACWY, and Tdap Vaccines by Age 17 Years in the United States, 2015–18. ACIP, Advisory Committee on Immunization Practices; HPV, human papillomavirus; MenACWY, quadrivalent meningococcal conjugate; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis. Note: Vaccination completion is based on completion of the HPV series (i.e., receipt of 2 doses for individuals aged 9–14 years at first vaccination or receipt of 3 doses for individuals aged 15 years or older at first vaccination), completion of the MenACWY series (i.e., receipt of 2 doses), and receipt of a Tdap vaccine. Note: Model-adjusted composite vaccination completion is adjusted for sex, race/ethnicity, mother's educational attainment, health insurance status, continuity of health insurance coverage since age 11, whether the individual was 16 or 17 years old at their last checkup, number of physician or other healthcare professional visits in past 12 months, whether a doctor or other healthcare professional ever recommended that the individual receive HPV vaccination, and state. The model-adjusted estimate is generated by taking the average of the predicted probability of vaccination for each individual as if they were all from the same state (while retaining all other characteristics).

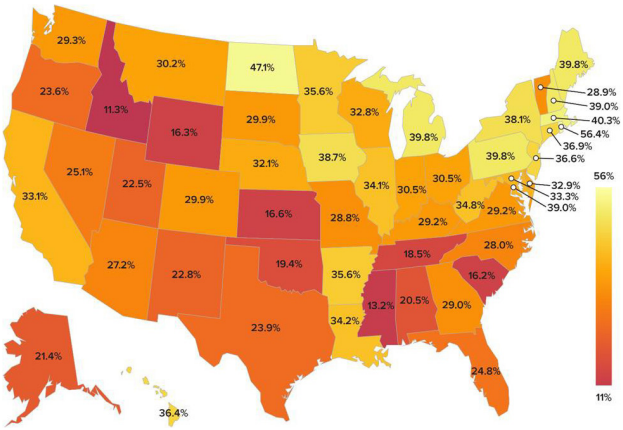
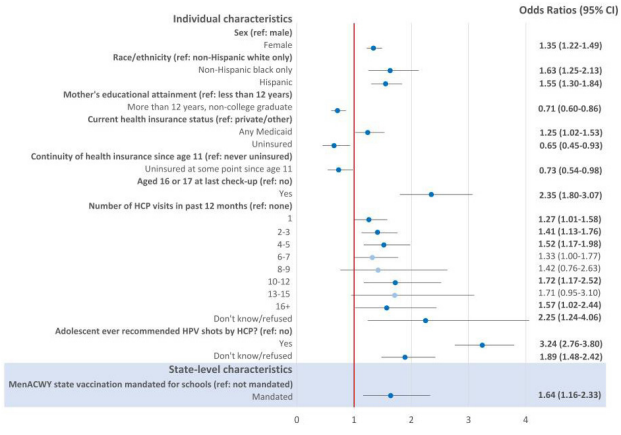


Figure 2: Individual-Level and State-Level Characteristics Associated with an Individual's Completion of ACIP-Recommended HPV, MenACWY, and Tdap Vaccines by Age 17 Years in the United States, 2015–18. ACIP, Advisory Committee on Immunization Practices; CI, confidence interval; HCP, healthcare professional; HPV, human papillomavirus; MenACWY, quadrivalent meningococcal conjugate; ref, referent category; Tdap, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis. Note: Bold characters and darker circles indicate significant results. Note: Vaccination completion is based on completion of the HPV series (i.e., receipt of 2 doses for individuals aged 9–14 years at first vaccination or receipt of 3 doses for individuals aged 15 years or older at first vaccination), completion of the MenACWY series (i.e., receipt of 2 doses), and receipt of a Tdap vaccine.



Conclusion: Recommended adolescent vaccine completion rates are suboptimal and highly variable across states. Provider recommendations, visits at 16–17 years of age, and state mandates for MenACWY are implementable strategies associated with completion of recommended adolescent vaccines.

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