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1401. Real-World Effectiveness of Inactivated and Live Attenuated Influenza Vaccines in Children During Three Recent Seasons: 2016–2019

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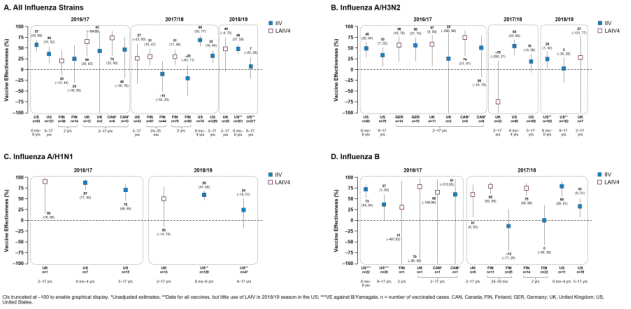
Session: P-63. Pediatric Vaccines

Background. Given the substantial burden of influenza in the pediatric population, influenza vaccination with live attenuated influenza vaccines (LAIVs) and/or inactivated influenza vaccines (IIVs) is now recommended for children in an increasing number of countries. In recent seasons, the real-world effectiveness of influenza vaccines has varied substantially. In the 2013/14 and 2015/16 influenza seasons, LAIV demonstrated reduced vaccine effectiveness (VE) against A/H1N1 strains. LAIV and IIVs have also demonstrated variable effectiveness against A/H3N2 strains in recent seasons. This study evaluated LAIV and IIV effectiveness in children between the 2016/17 and 2018/19 seasons.

Methods. Quadrivalent LAIV (LAIV4) and IIV effectiveness studies conducted in the pediatric population from 2016/17 through 2018/19 were identified from published literature, congress presentations, public health websites and personal communication with national investigators. Studies were excluded if they were from countries where Ann Arbor-backbone LAIV was not available for at least one season during the study period, were from randomized, interventional studies, or contained duplicate data from other publications.

Results. For the three seasons, point estimates of all-strain VE for children ranged from 20% to 74% for LAIV4 and from –20% to 68% for IIV (Fig 1A). During the same period, VE against A/H3N2 for children ranged from –76% to 74% for LAIV4 and from 3% to 56% for IIV (Fig 1B). Point estimates of VE against A/H1N1 for children were 50% and 90% for LAIV4 and ranged from 24% to 87% for IIV (Fig 1C). For influenza B, VE for children ranged from 31% to 80% for LAIV4 and from –12% to 80% for IIV (Fig 1D). Statistical comparison of LAIV4 and IIV VE across each season was not feasible due to the multivariate nature of each study cohort.

Figure 1. 2016–2019 Effectiveness of Inactivated and Live Attenuated Influenza Vaccines by Influenza Strain in Children



CIs truncated at –100 to enable graphical display. *Unadjusted estimates. **Data for all vaccines, but little use of LAIV in 2018/19 season in the US. ***VE against B/Yamagata. n = number of vaccinated cases. CAN, Canada; FIN, Finland; GER, Germany; UK, United Kingdom; US, United States.

Conclusion. During three recent seasons, LAIV4 and IIV showed similar moderate effectiveness against all influenza strains, A/H1N1 strains, and B strains. VE against A/H3N2 for LAIV4 and IIV was good in 2016/17, but decreased in the 2017/18 and 2018/19 seasons. VE estimates for LAIV4 and IIV overlapped for all strains and each subtype, demonstrating the general comparability of LAIV4 and IIV VE in the seasons between 2016 and 2019.

Disclosures. Allyn Bandell, PharmD, AstraZeneca (Employee, Shareholder) Raburn Mallory, MD, AstraZeneca (Employee, Shareholder) Christopher S. Ambrose, MD, MBA, AstraZeneca (Employee, Shareholder)

1402. Smart Technology and Education for Smart Protection against the Flu: Impact of a Multifaceted Quality Improvement (QI) Intervention on Influenza Vaccination Rates in Children

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Session: P-63. Pediatric Vaccines

Background. Low pediatric influenza vaccination rates are a public health challenge. It is imperative that innovative measures to promote influenza immunization are studied.

Methods. Aim: To study impact of a multifaceted QI intervention on influenza vaccination rates in children evaluated at outpatient clinics, urgent care (UC) and emergency departments (ED) at UnityPoint Health tertiary care centers (UPH) across Northwestern (NW) and Northcentral (NC) Iowa (IA). Patients aged 6 months-18 years evaluated at UPH in NW and NC IA (encompassing 5 outpatient clinics, 2 UC, 2 ED) were included. A multifaceted QI intervention was implemented on 9/1/2018 consisting of all of the following concomitantly: 1. Patient/family education: Posters about flu vaccination displayed at entrance, in waiting rooms and patient rooms throughout the clinics, UC, ED as well as patient/family handouts emphasizing importance of influenza immunization. 2. Information Technology: "Health maintenance" reminder in outpatient electronic medical record (EMR- EPIC) that appears as soon as a patient's chart is accessed to remind nurses/providers that influenza vaccine is due. 3. Provider Education flyers at study sites about debunking flu myths. We compared pre-intervention period (P1, 09/01/2017– 05/31/2018) with intervention period (P2, 09/01/2018 – 05/31/2019) for influenza vaccination rates.

Results. A total of 10050 and 9889 patients were evaluated during P1 and P2 respectively. Influenza vaccination rate increased significantly from 56.1% (5642) in P1 to 73.3% (7252) in P2 (p< 0.0001). Patients were 1.43 times more likely to get vaccinated during P2 than P1 (95% CI= 1.32-1.46). Regionally during P2, influenza vaccination rate was higher than the national (62.6%; p< 0.0001) and Iowa state averages (65.8%; p< 0.0001) respectively. Proportion of children aged < 9 years receiving second dose of influenza vaccine increased from 43% to 69% (p< 0.001). Influenza vaccination rates among children aged 6-36 months increased significantly [40% (1078/2671) in P1 to 47.2% (1287/2723) in P2; p< 0.01].

Conclusion. With the combined educational and technologic intervention, pediatric influenza vaccination rates increased significantly across NW and NC IA, including proportion of patients receiving second dose of the vaccine.

Disclosures. Richard Malley, MD, Merck (Consultant)

1403. The Pediatric Emergency Room as a Promising Setting for Receiving the Flu Shot

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Session: P-63. Pediatric Vaccines

Background. Children are the most likely population to get influenza, and are two times more likely compared to adults aged 65 and greater (attack rate by age group: 0-17 yo 9.3%, 18-74 yo 8.8%, 65 + 3.9%). Additionally, children are at high risk of suffering complications from influenza. According to the CDC, the overall effectiveness of the 2018-2019 flu vaccine for both strains A and B was 48% in children aged 6m-8 years and 7% in children aged 9- 17 years. Currently our Pediatric Emergency Department (PED) does not routinely offer influenza vaccine to unvaccinated patients. Our project goals are to identify barriers to the administration of influenza vaccine in the PED and to offer and administer influenza vaccine to eligible patients.

Methods. After performing root cause analysis with key stakeholders, the first countermeasure implemented in a Plan-Do-Study Act (PDSA) cycle was the development of a screening form including eligibility criteria, history of influenza vaccine, consent for vaccine or reason for declining vaccine. The screening form was administered by resident physicians in our PED from October to November who then went on to order the vaccine for eligible patients who consented. Primary outcome measures included number of patients screened per month, percent of patients who desired the vaccine, and the percent of patients who received the vaccine in the ED during their visit. Secondary outcome measures included length of PED stay.

Results. Preliminary results show that 75% (42/56,CI: 62%-86%) of children screened in the PED between October and November were eligible for the influenza vaccine. Of those eligible, 59% (29/42, CI: 43%-74%) received the vaccine. The average length of stay was comparable between those that received influenza vaccine and those that did not (p value 0.4756).

Conclusion. A subset of eligible patients are now being offered and receiving the flu shot in our PED. Over half of eligible patients received the influenza vaccine, demonstrating that a resident administered screening form has been a successful countermeasure for increasing vaccine rates. Future PDSA cycles will focus on further increasing the number of patients screened and capturing patients who consented but did not receive vaccine.

Disclosures. **All Authors**: No reported disclosures

1404. Twenty-year impact of Pneumococcal Conjugate Vaccines (PCV) on the burden of invasive pneumococcal disease in US children less than 5 years of age

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Session: P-63. Pediatric Vaccines

Background. Clinical trials of PCV7 demonstrate significant reductions in vaccine-type (VT) invasive pneumococcal disease (IPD), clinically diagnosed pneumonia in children less than 5 years of age and VT acute otitis media in children < 2 years of age. Observational, population-based studies demonstrate a reduction in overall IPD in US children following the introduction of PCV7 and PCV13. The cumulative impact of PCV on IPD syndromes over the 20 years following introduction into the US national immunization program has not been detailed.

Methods. Published and unpublished data from the Active Bacterial Core (ABC) surveillance network were used to calculate annual incidence rates of IPD and the proportional distribution by syndrome in children < 5 years of age. Cases averted were calculated from published incidence for each IPD syndrome

and population data, for the pre-PCV, PCV7, and PCV13 eras. Cases averted over 2000-2009 were assumed due to PCV7 only, and those averted from 2010-2019 were assumed due to PCV13 only. It was assumed that in the absence of PCVs, disease incidence would have remained constant.

Results. Annual cases of overall IPD, pneumococcal meningitis, and bacteremic pneumonia each declined more than 85% between the pre PCV7 incidence and the estimated incidence for 2019 (table 1). Overall, we estimated 282,600 cases of IPD, including 30,500 cases of meningitis and 78,400 cases of bacteremic pneumonia were averted. We calculated a reduction of ~ 287,600 VT cases of IPD minimally offset by an increase of ~5,000 non-VT cases. Deaths per 100,000 children < 5 years of age attributable to IPD declined by 67% in 2009 and by 64% in 2019 compared to 1997-1999. In total, 1,628 deaths in children < 5 years were averted between 2000 and 2019.

Table 1. Annual Cases of IPD by syndrome in US Children Less than 5 years of age

		Deaths attributable to Pneumococcal Disease		Invasive Pneumococcal Disease		Meningitis		Bacteremic Pneumonia	
Era	**Year**	**Rate/100,000**	**Decline from baseline**	**No.**	**Decline from baseline**	**No.**	**Decline from baseline**	**No.**	**Decline from Baseline**
Pre-PCV 7	1997-1999	0.8	baseline	17,209	baseline	1,098	baseline	3,766	baseline
PCV7	2009	0.26	67.1%	4,449	74.1%	244	77.8%	1,644	56.3%
PCV13	2019	0.29	64.3%	1,382	92.0%	168	84.7%	421	88.8%

Conclusion: The substantial public health impact of PCVs over the last two decades, as measured in cases and deaths averted in children less than 5 years, re-enforces the important role vaccines play in reducing the burden of serious disease in children.

Disclosures. Rotem Lapidot, MD, MSCI, Pfizer (Consultant) Ruth Chapman, MSc, PhD, Evidera, Inc, (Evidera, Inc. received the funding to conduct this study.) (Consultant) Kelly Sutton, PhD, Evidera (Employee) Desmond Dillon-Murphy, MSc, PhD, Evidera, Inc. (Evidera, Inc. received the funding to conduct this study.) (Consultant) Shreeya Patel, PhD, Evidera, Inc, (Evidera, Inc. received the funding to conduct this study.) (Consultant) Erica Chilson, PharmD, Pfizer (Employee, Shareholder) Vincenza Snow, MD, Pfizer (Employee) Raymond Farkouh, PhD, Pfizer (Employee) Matthew Wasserman, MSc., Pfizer Inc. (Employee) Stephen I. Pelton, MD, Merck vaccine (Consultant, Grant/Research Support)Pfizer (Consultant, Grant/Research Support)Sanofi Pasteur (Consultant, Other Financial or Material Support, DSMB)Seqirus Vaccine Ltd. (Consultant)

1405. Clinical and laboratory features of fatal dengue fever in children: a case-control study

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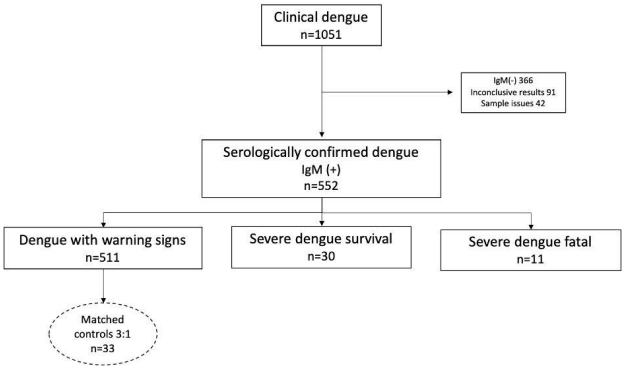
Session: P-64. Pediatric Viral Studies (natural history and therapeutic)

Background. Dengue fever (DF) is a mosquito-borne illness that causes significant morbidity and mortality in tropical climates. This study compared the clinical features of fatal DF cases to severe non-fatal, and non-severe controls in Ecuador.

Methods. Retrospective case-control study of children (1 month to 15 years) hospitalized with serologically-confirmed DF in Guayaquil, Ecuador from 2013 to 2017. Cases of severe, fatal (SF) DF were compared to two control groups: (1) severe DF survivors (SS); and (2) patients with dengue with warning signs (DWS), matched 3:1 to cases for age, sex, and admission date.

Observational trial profile



Results. 1051 patients were admitted with suspected DF and 552 were IgM-positive. Patients were classified as SF (n=11), SS (n=30), or DWS (n=511) **(Figure1)**. Among SF cases, median age was 9.6 years (IQR 5.5-11), 7 (64%) were male, and median time to death was 1.5 days (IQR 0.8-4.0). **(Table 1)** SF cases had a median of 3 (Range 0-5) encounters with healthcare providers prior to presentation, compared to 2 (Range 0-5, p=0.02) for SS and 2 (Range 0-3, p=0.02) for DWS. Physical findings more common in SF cases than controls included: higher weight, tachycardia, tachypnea, delayed capillary refill, and hepatomegaly (p< 0.05 for all comparisons). Neurological manifestations were more prevalent in the SF group: 9/11 (82%) patients compared to 15/30 (50%, p=0.09) in SS and 7/33 (21%, p< 0.01) in DWS. Total leukocyte count ($7.8x10^3$/µL versus $4.5x10^3$/µL, p=0.03) and absolute neutrophil count ($5.1x10^3$/µL versus $2.1x10^3$/µL, p=0.03) were higher in SF cases than DWS controls. Fewer SF patients received intravenous dextrose than SS controls (27% versus 70%, p=0.03) **(Table 2).**

Admission characteristics of children with dengue fever

		Severe, fatal (SF) n = 11	Severe, survived (SS) n = 30	Dengue with warning signs (DWS) n = 33
Baseline characteristics	Age (y), median (IQR)	9.6 (5.5 - 11.2)	8.1 (1.8 - 11.5)	9.7 (5.3 - 11.6)
	Female	4 (36)	13 (43)	12 (36)
	Weight (Kg)	42.0 (18.5 - 52.1)	25.5 (12 - 44)	**28 (17 - 37)***
	Previous encounters, median (IQR)	3 (2 - 4)	**2 (1 - 3)***	**2 (1 - 3)***
	Prior antibiotic use	7 (64)	20 (67)	20 (58)
History	Duration of fever (days), median (IQR)	3 (2-5)	5 (4-6)	5 (4 - 6)
	Headache/Ocular pain	3 (27)	12 (40)	14 (42)
	CNS symptoms [a]	9 (82)	15 (50)	**7 (21)****
	Muscular/joint pain	2 (18)	11 (37)	13 (39)
	Mucosal bleeding	5 (45)	14 (47)	7 (21)
	Nausea/vomiting	9 (82)	23 (77)	23 (67)
	Abdominal pain	8 (73)	23 (77)	25 (73)
	Diarrhea	4 (36)	7 (23)	13 (36)
Physical exam	Fever	4 (36)	10 (33)	10 (30)
	Altered level of consciousness [b]	9 (82)	**5 (17)****	**3 (9)****
	Tachycardia	8 (73)	**2 (7)*****	**3 (9.1)*****
	Tachypnea	5 (45)	**2 (7)****	**0*****
	Pulse pressure (mmHg), median (IQR)	36 (28 - 46)	30 (26 - 36)	30 (30 - 40)
	Rash	6 (55)	9 (30)	15 (46)
	Hepatomegaly	8 (73)	**5 (17)****	**8 (24)***
	Capillary refill (sec), median (IQR)	4 (3-4)	**3 (2-3)***	**2 (2-3)***
	Severe bleeding	2 (18)	4 (13)	1 (3)
Laboratory	WBC ($x10^3$/µl)	7.8 (5.3 - 17)	4.6 (3.7 - 8.6)	**4.5 (3.6 - 7.2)***
	ANC ($x10^3$/µl)	5.1 (3.2 - 8.5)	2.4 (1.8 – 2.9)	**2.1 (1.6 - 2.8)***
	Hematocrit (%)	37 (35 - 41)	37 (33 - 42)	38 (35 - 41)
	Platelets ($x10^3$/µL)	140 (100 - 160)	99 (71 - 160)	160 (90 - 180)
Ultrasound	Pleural effusion, n(%)	7 (64)	12 (40)	8 (24)
	Ascites, n(%)	4 (36)	8 (27)	12 (36)
	Gall bladder edema n(%)	1 (9)	5 (17)	3 (9)

WBC: White blood cells, ANC absolute neutrophil count
[a:] CNS: Lethargy, seizure, irritability, syncope.
[b:] Less than Alert on AVPU scale (A: alert V: response to verbal stimuli P: response to painful stimuli U: unresponsive)
Numbers represent n (%) unless otherwise specified
*p<0.05; ** p<0.01; ***p<0.001

Management and outcome

	Severe fatal (SF) n = 11	Severe, survived (SS) n = 30	Dengue with warning signs (DWS) n = 33
Length of stay (days), median (IQR)	1.9 (0.8 - 4.0)[§]	10 (8.7 - 14)	5 (3.7 - 5.7)
PICU admission [c]	6 (45)	17 (77)	0
Mechanical ventilation (MV)	11 (100)	9 (30)	0
Intravenous dextrose	3 (27)	**21 (70)***	14 (44)
Supplemental oxygen	5 (45)	3 (10)	**1 (3)****
Inotropes	2 (18)	0 (0)	0
Blood products	1 (9)	4 (13)	0
Antibiotics	2 (18)	4 (13)	1 (6)
Chest tube	1 (9)	3(10)	0

PICU pediatric intensive care unit
Numbers represent n (%) unless otherwise specified
*p<0.05; ** p<0.01; ***p<0.001
[§] time to death in SF group
[c] PICU admission was indicated in 11/11 (100%) of SF cases and 22/30 (73%) of SS controls; however, lack of beds limited the management in critical care area.