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Session: 278. Vaccines: Influenza
Saturday, October 5, 2019: 12:15 PM

Background: Despite greater than 90% of US active duty (AD) military personnel receiving influenza vaccination annually, vaccine effectiveness (VE) among AD members has been substantially lower than in groups with less vaccine uptake. The substrate used in vaccine production may impact immunogenicity and thus VE. The PAIVED study is investigating VE of 3 different influenza vaccine formulations; a sub-study assesses immunogenicity. This analysis compares demographic characteristics and influenza-like illness (ILI) experience among main and sub-study participants for the first year of PAIVED.

Methods: During the 2018–2019 influenza season, PAIVED enrolled participants at 5 military medical centers, recruiting sub-study subjects from the main cohort excluding marine recruits. All participants were randomized (1:1:1) to receive either egg-based, cell-culture based or recombinant influenza vaccine. At enrollment, participants provided key demographic and behavioral data. Weekly surveillance for ILI symptoms was performed electronically. Sub-study volunteers underwent an additional blood draw prior to and at 21–35 days post vaccination ± an optional buccal swab.

Results: 200 (23.5%) of 852 non-recruit PAIVED participants enrolled in the immunogenicity sub-study. Similar to the main cohort, 46% of sub-study volunteers were female, 85% were physically active, and 6% smoked tobacco. Sub-study participants were younger (47 ± 16 years vs. 51 ± 17 years, $P = 0.004$) and more likely to be AD (34% vs. 22%, $P = 0.001$). Although 70% of both groups identified as White, the percent African American (20% sub-study; 13% main), Asian (3%; 7%), multi-racial (2%; 5%), and unknown (6%; 4%) differed ($P = 0.02$). More sub-study participants developed an ILI (19% vs. 12%, $P = 0.02$).

Conclusion: The convenience sampling method used for recruitment into the sub-study was effective. The younger age and higher AD status in the sub-study group may be informative for evaluation of military readiness issues. The greater incidence of ILI in the sub-study increases the chance differences in immune response by vaccine type may be interpretable in the context of circulating influenza strains. Targeted efforts to enhance recruitment of a racially diverse sub-study cohort may be warranted.

Disclaimer
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2758. Identifying Populations at High-Risk for Influenza-Related Hospitalization: A Real-World Analysis of Commercially Insured Population in the United States

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Session: 278. Vaccines: Influenza
Saturday, October 5, 2019: 12:15 PM

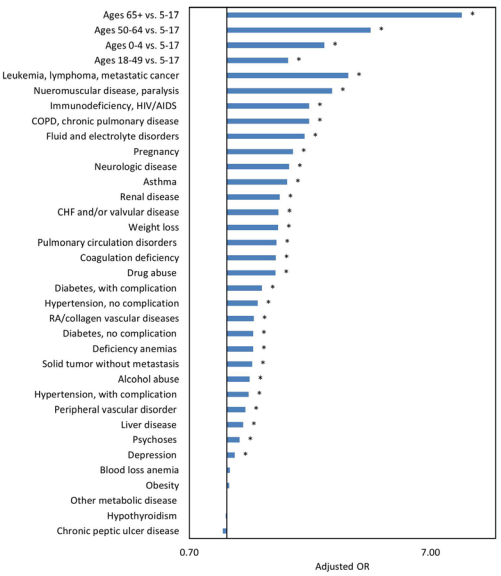
Background: The disease burden of seasonal influenza (flu) is high and contributes to morbidity, mortality and healthcare utilization. While only 1–2% of flu cases are hospitalized, these events are costly. The objective of this study was to describe and quantify risk factors for flu hospitalization.

Methods: Patients with 1 flu diagnosis (Dx) over 4 seasons (October 1, 2014–May 31, 2018) in IQVIA's Real-World Data Adjudicated Claims – US database were selected into the study; the earliest flu Dx was the index date. Patients were required to have ≥12 months continuous enrollment in their health plan before index (baseline), ≥30 days after index, and either a record of a flu test ± 14 days of index or a flu Dx in the primary position. Comorbidities during a fixed 12-month baseline period were categorized by AHRQ and CDC definitions. The study outcome of interest, flu-related hospitalization during the 30-day follow-up period, was defined as hospitalization with Dx of flu or a pre-defined flu-related complication in any position. A logistic regression model assessed the odds of flu-related hospitalization, adjusting for age, sex, region, payer, season of index Dx, evidence of flu vaccination, and comorbidities.

Results: More than 1.6 million medically-attended flu cases were identified, of which 18,509 (1%) had a hospitalization. 40% of patients were < 18 years of age, 47% were male, and 28%, 15%, 24%, and 33% were identified in the 2014–2017 flu seasons, respectively. More hospitalized patients were ages 50+ compared with non-hospitalized patients (57% vs. 20%) and 44% of hospitalized patients had 4 or more AHRQ/CDC comorbidities vs. 8% of non-hospitalized patients. In adjusted analyses, older age (65+ vs. 5–17; OR = 9.4, 95% CI 8.8–10.1) and leukemia/lymphoma/metastatic cancer (OR = 3.2, 95% CI = 2.9–3.5) were key drivers of hospitalization (Figure 1).

Conclusion: The risk of flu-related hospitalization is high for elderly populations and those with certain underlying co-morbidities among all age groups. While these findings reflect the burden of medically-attended flu in a younger, commercially insured population, additional research is needed to address the flu burden in high-risk populations.

Figure 1. Odds ratios for flu-related hospitalization from logistic regression model, adjusting for baseline characteristics and comorbid conditions



*p<.05

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2759. Immunogenicity of Inactivated Influenza Vaccines Given Early vs. Late After Pediatric Allogeneic Hematopoietic Cell Transplantation

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Session: 278. Vaccines: Influenza
Saturday, October 5, 2019: 12:15 PM

Background: Pediatric hematopoietic cell transplant (HCT) recipients often fail to have robust responses to influenza (flu) vaccine. We conducted a blinded phase II trial comparing high-dose (HD) trivalent inactivated vaccine (TIV) vs. standard dose (SD) quadrivalent inactivated vaccine (QIV).

Methods: Children 3–17 years old and 3–35 months post-allogeneic HCT were enrolled at 9 centers and randomized to either 2 doses of HD-TIV or SD-QIV during the 2016–2017 flu season. We compared immune responses by hemagglutination inhibition (HAI) from children 3–11 (early) vs. 12–35 (late) months (m) post-HCT to 3 common flu vaccine antigens, irrespective of vaccine type. HAI responses were evaluated at baseline (visit 1), 1 m post dose 1 (visit 2) and dose 2 (visit 3), and 7 m post dose 2 (visit 4). Geometric mean titers (GMT) were adjusted for baseline log-titer values.

Results: Thirty-one children, median age 11 (7–15) years, were enrolled; 17 (55%) were immunized early and 14 (45%) late. Over 50% of patients had a potentially seroprotective (≥1:40) HAI titer at baseline, with no significant difference post-vaccination between early and late subjects. Table 1 compares early vs late subjects with HAI seroconversion (4-fold HAI titer rise). Post dose 1, late subjects, compared with early, had higher rates of seroconversion to all influenza strains. Post dose 2, early subjects, compared with late, had increased seroconversion. Late subjects had higher GMTs for H1N1 post dose 1 and 2, H3N2 after dose 1, and strain B/VIC post dose 1 and 2 (Figure 1). Although immunogenicity waned throughout flu season, higher seroconversion rates and GMT to H3N2 and strain B/VIC were retained in late subjects.

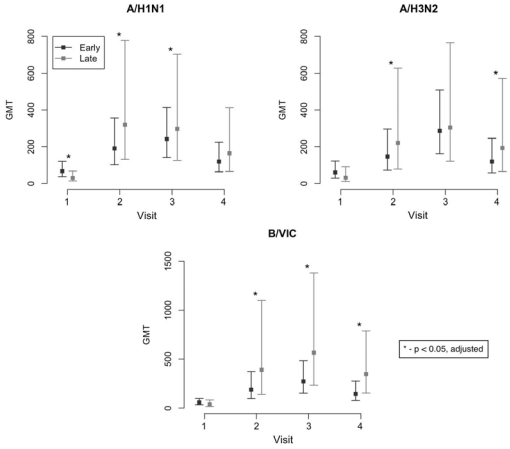
Conclusion: Compared with subjects in early post-HCT group, late post-HCT subjects had better flu vaccine immune responses as noted by higher GMT and HAI seroconversion. However, 2 doses seemed more beneficial in the early post-HCT group. Future analyses are underway, including comparing immunogenicity of HD vs. SD flu vaccine.

Table 1. Percent of early (E) vs late (L) subjects with HAI seroconversion[d]

Visit	Strain								
	A/H1N1			A/H3N2			B/VIC		
	E	L	P Value	E	L	P Value	E	L	P Value
2[b]	6	71	<0.001	0	57	0.002	19	71	0.01
3[c]	24	71	0.02	29	64	0.11	35	79	0.04
4[c]	8	46	0.08	15	62	0.04	15	77	0.006

[a]Early (n=17) & Late (n=14)
[b]Early (n=16) & Late (n=14)
[c]Early (n=13) & Late (n=13)
[d]From baseline

Figure 1. Geometric Mean Titers Pre- and Post-Vaccination in Subjects Receiving Early vs Late Flu Vaccine



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2760. Accounting for Vaccination History in Estimates of Current Season Vaccine Effectiveness in the US Flu VE Network, 2012–2013 Through 2017–2018

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Session: 278. Vaccines: Influenza
Saturday, October 5, 2019: 12:15 PM

Background: Current season vaccine effectiveness (VE) and influenza risk may vary in persons based on vaccination history. United States Influenza Vaccine Effectiveness (US Flu VE) Network studies have explored prior vaccination effects using a single referent group of patients unvaccinated in both the prior and current seasons. We investigated vaccine benefit among those with and without prior season vaccination.

Methods: Our analysis included data from the US Flu VE Network among patients aged ≥9 years old with acute respiratory illness during 6 influenza seasons, 2012–2013 through 2017–2018. We determined current and prior season vaccination status from documented immunizations. Current season VE against laboratory confirmed influenza was estimated using multivariate logistic regression with an interaction term for prior and current season vaccination. Models were adjusted for age, calendar time, high-risk status, and site.

Results: Of 31,819 patients included in the analysis over 6 seasons, 9188 were influenza positive by RT–PCR. Percent flu positivity was greatest among those unvaccinated (34%), followed by those vaccinated in the prior season only (29%), those vaccinated in both seasons (25%), and those vaccinated in the current season only (23%). Among patients with prior season vaccination, current season VE against any influenza was 14% (95% CL: 5, 22) and against A(H3N2), A(H1N1)pdm09, and B was 10% (95% CL: 3, 17), 36% (95%CL: 25, 46), and 40% (95% CL: 33, 46), respectively. Among patients unvaccinated in the prior season, VE was 42% (95% CL: 37, 46) against any influenza in the current season and was 31% (95%CL: 22, 39), 57% (95% CL: 47, 65), and 55% (95% CL: 48, 61) against A(H3N2), A(H1N1)pdm09, and B, respectively. We observed significant interaction of prior season vaccination on current season VE in 4 of 6 seasons ($P < 0.20$).

Conclusion: Current season vaccination was overall protective regardless of vaccination history. Among those vaccinated in the prior season, current season vaccination may provide some benefit in addition to residual protection from previous vaccination.

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2761. Interventions to Improve Influenza Vaccination Coverage in Children with Medical Comorbidities: A Meta-Analysis

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Session: 278. Vaccines: Influenza
Saturday, October 5, 2019: 12:15 PM

Background: Influenza vaccination is the most effective influenza prevention tool for children with medical comorbidities. Despite this, coverage remains inadequate. Numerous interventions to improve vaccination coverage have been assessed, yet there remains a paucity of data comparing the relative efficacy and effectiveness of different interventions.

Methods: We searched MEDLINE, PubMed, Scopus, Embase, CINAHL, CENTRAL, and Web of Science (1980 to March 2019) for studies evaluating interventions which sought to improve influenza vaccine coverage in children with medical comorbidities. Interventions were divided into those targeting parents, targeting vaccination providers, and targeting the hospital, clinic or ward. Screening and data extraction from publications meeting inclusion criteria was performed by two reviewers. Results were pooled and meta-analyses were performed using Mantel–Haenszel random-effects models in Review Manager 5.

Results: 35 articles met inclusion criteria; 14 cross-sectional, 12 randomized trials, and 9 cohort studies, 25 articles had sufficient data for pooled analysis. Of the included interventions, 17 were based within primary care or community-based settings, 17 were based in hospitals or tertiary clinics, and 1 intervention was conducted across both primary and tertiary settings. Interventions overall increased influenza vaccination likelihood by 33% (RR = 1.33: 95% CI 1.31, 1.35). Interventions targeting providers' influenza vaccine knowledge increased vaccine coverage (RR = 1.42: 95% CI