

A Comprehensive Real-World Analysis to Compare Adjuvanted Trivalent Influenza Vaccine and Trivalent High Dose Influenza Vaccine by Age and Period of High Influenza Activity for the 2018-19 Season among U.S. Elderly

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BACKGROUND

- Influenza vaccine effectiveness decreases with increasing age due to the senescence of immune function and a reduced immune response to antigens.¹
- There is also considerable vaccine effectiveness heterogeneity depending on the influenza activity time period, especially during seasons where two different circulating strains predominated, such as the 2018-19 flu season.²

OBJECTIVE

The objective of this study was to assess the effect of age and high influenza activity period (HIAP) on the relative vaccine effectiveness (rVE) of adjuvanted trivalent influenza vaccine (aTIV) vs. trivalent high-dose influenza vaccine (HD-TIV) among elderly (≥65y) recipients in the U.S.

METHODS

STUDY DESIGN AND DATA SOURCES

- A retrospective cohort analysis using IQVIA's professional fee claims (Dx), prescription claims (Rx) and hospital charge master data (CDM) in the U.S.
- Representative of all payers in the U.S. Data cover ~82% of all physicians activities, ~90% of all pharmacy claims and data for over 400 hospitals across all regions.

SAMPLE SELECTION

- Subjects ≥65 years were included in the study if they met the following criteria:
 - At least 1 claim for aTIV or TIV-HD between 8/1/2018 and 1/31/2019; date of vaccination termed the index date.
 - The flu season was defined from 8/1/2018 – 7/31/2019.³
 - HIAP was defined from 12/23/2018– 3/30/2019.
 - With a 6-month pre-index period (baseline) and variable follow-up through end of flu season.
 - Without any other flu vaccine during the flu season or influenza-related hospitalizations/ER visits or office visits from 8/1/2018 up to 13 days post-index.

STUDY MEASURES

- Baseline characteristics were assessed in the 6-month baseline period (Table 1).
- Following study outcomes were assessed from (index date + 14) through end of flu season for different age groups (65-74yrs, 75-84yrs, and ≥85 years) as well as during HIAP:
 - Influenza-related hospitalization/ER visit
 - Influenza-related office visit
 - Any cardio-respiratory hospitalization/ER visit composite (CRD)

STATISTICAL ANALYSIS

- Inverse Probability of Treatment Weighting (IPTW) was used to adjust for imbalances between measured confounders, following the same approach used by CMS/FDA.^{3,4}
- Variable with absolute SMD ≥0.1 and clinically relevant variables were adjusted with IPTW.
- Regression analysis: IPTW-weighted multivariate Poisson regression.

RESULTS

- Prior to IPTW, the study sample comprised 561,243 aTIV and 1,672,797 TIV-HD subjects.
- After IPTW adjustments, study cohorts were balanced with SMD<0.10 for all study covariates (aTIV = 561,315; TIV-HD = 1,672,779). Almost half of the subjects were between 65-74 years age (Table 2).
- Following Poisson regression, aTIV was more effective in reducing influenza-related office visits and any CRD-related hospitalizations compared to TIV-HD during HIAP (Figure 1).
- When analyzed across age groups, the rVE for aTIV compared to TIV-HD against influenza-related office visits was not significantly different for age group 65-74 years but was significantly higher for age groups 75-84 years and ≥85 years (Figure 1).
- rVE against any CRD-related events was significantly higher for aTIV vs. TIV-HD for age groups 65-74 years and 75-84 years but not for ≥85 years. (Figure 1).
- aTIV was statistically comparable to TIV-HD for preventing influenza-related hospitalizations/ER visits across different age groups (Figure 1).

TABLE 1. BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS (UNADJUSTED)

CHARACTERISTIC	aTIV N=561,243	TIV-HD N=1,672,797	SMD	CHARACTERISTIC	aTIV N=561,243	TIV-HD N=1,672,797	SMD
Mean (SD) age (years)	75.1 [6.3]	75.0 [6.3]	-0.01	Pre-index comorbid conditions of interest (%)			
Female (%)	59.5%	59.6%	0.00	Asthma	3.6%	3.7%	0.01
Payer type (%)				Blood disorders	0.3%	0.3%	0.00
Cash	0.3%	0.3%	0.01	Chronic lung disease	8.3%	8.7%	0.01
Medicaid	0.0%	0.1%	0.01	Diabetes	21.0%	22.6%	0.04
Medicare Part D	30.1%	26.0%	-0.09	Heart disease	12.4%	12.7%	0.01
Medicare	48.5%	51.3%	0.05	Kidney disorders	8.8%	9.2%	0.01
Third party	20.9%	22.3%	0.03	Liver disorders	2.2%	2.3%	0.00
Other/Unknown	0.1%	0.1%	-0.02	Neurological or neurodevelopmental conditions	4.8%	5.0%	0.01
Geographic region (%)				Weakened immune system	10.1%	10.2%	0.00
Northeast	17.4%	16.3%	-0.03	IBD	0.6%	0.6%	0.00
Midwest	15.7%	18.3%	0.07	Composite of the above	47.4%	49.1%	0.03
South	49.8%	44.2%	-0.11	Indicators of frail health status (%)			
West	17.1%	21.2%	0.10	Home oxygen use	4.4%	4.8%	0.02
Month of flu vaccine (%)				Wheelchair use	2.3%	2.6%	0.02
August	3.4%	4.2%	0.04	Walker use	3.3%	3.4%	0.01
September	28.6%	30.7%	0.04	Dementia	1.2%	1.3%	0.00
October	49.8%	47.4%	-0.05	Urinary catheter use	0.3%	0.3%	0.00
November	11.8%	12.6%	0.02	Falls	0.9%	0.8%	0.00
December	4.1%	3.3%	-0.04	Fractures	0.5%	0.5%	0.00
January	2.3%	1.7%	-0.04	Composite of the above	10.5%	11.0%	0.02
Mean (SD) CCI score	0.9 (1.3)	0.9 (1.4)	0.04				
Pre-index hospitalization [%]	8.0%	8.2%	0.01				

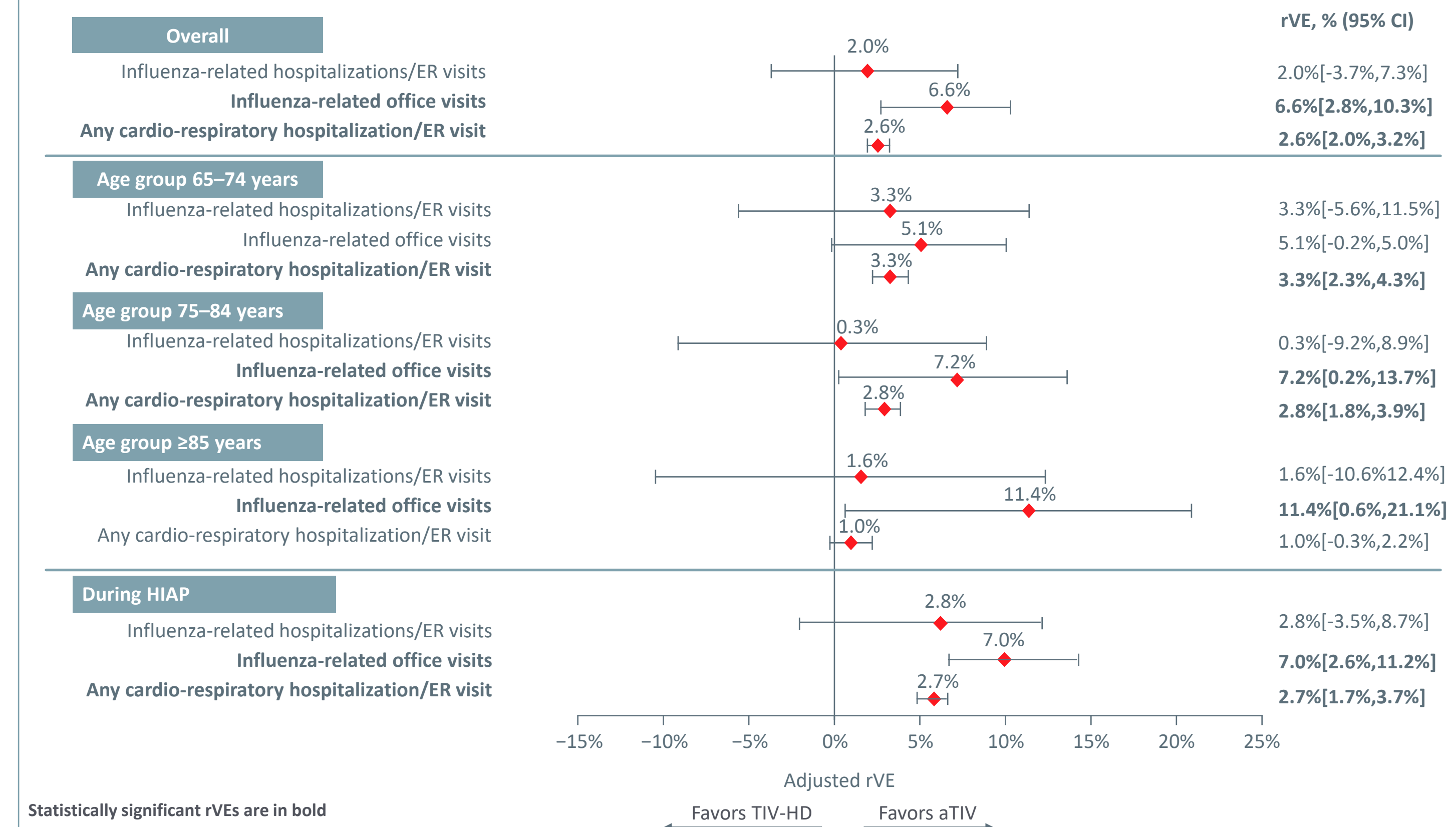
With absolute SMD ≥0.1 considered imbalanced; Significant differences are bolded.

TABLE 2. STUDY COHORTS DURING HIAP AND ACROSS DIFFERENT AGE GROUPS

	Overall/During HIAP		65-74 years		75-84 years		≥85 years	
	aTIV	TIV-HD	aTIV	TIV-HD	aTIV	TIV-HD	aTIV	TIV-HD
Number of patients (from unadjusted analysis)	561,243	1,672,797	281,613	845,762	193,084	568,924	86,546	258,111
Number of patients (after IPTW)- aTIV vs. TIV-HD	561,315	1,672,779	281,640	845,752	193,104	568,920	87,337	258,117

RESULTS

FIGURE 1. ADJUSTED rVEs OVERALL, BY AGE GROUPS, AND DURING HIAP – POST-IPTW AND POISSON REGRESSION



Statistically significant rVEs are in bold

CONCLUSIONS

- In adjusted analyses, aTIV reduced influenza-related office visits compared to TIV-HD within the two older age groups and during HIAP.
- aTIV showed higher rVE compared to TIV-HD in preventing any CRD-related benefits for subjects younger than 85 years old.
- aTIV and TIV-HD demonstrated comparable reductions in influenza-related hospitalizations/ER visits across age groups and during HIAP.
- This study confirms that the relative benefits of these two enhanced vaccines remained consistent for different age groups and during the periods of high flu activity.

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