Relative vaccine effectiveness and economic assessment of quadrivalent cell-based and egg-based influenza vaccines against influenza-related hospitalizations and respiratory events in U.S. children and adults during the 2019–2020 influenza season

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BACKGROUND

Traditional egg-based manufacturing of influenza vaccines may contribute to reduced vaccine effectiveness. During viral propagation within embryonic eggs, mutations in the viral hemagglutinin protein accumulate due to selection pressures, and these changes may alter antigenicity.[1,2,3]

The possibility of egg-adapted mutations is eliminated when vaccine viruses are propagated in cell culture, producing vaccine strains more antigenically faithful to the original virus.[4,5,6] In clinical trials, a cell culture–based, inactivated quadrivalent influenza vaccine (QIVc) (Flucelvax® Quadrivalent, Seqirus USA Inc., Summit, NJ, USA), which was approved in the US in May 2016, has demonstrated comparable immunogenicity to egg-based vaccines.[7] Findings from observational studies have further suggested that such cell culture–based vaccines may have greater effectiveness than traditional egg-derived vaccines, including recent studies of QIVc.[8-12] These findings also suggest potential for a favorable cost-benefit of cell culture-based vaccines.

Given the seasonal nature of influenza, annual estimation of vaccine effectiveness in real world conditions informs vaccine regulation, policy, and product development.

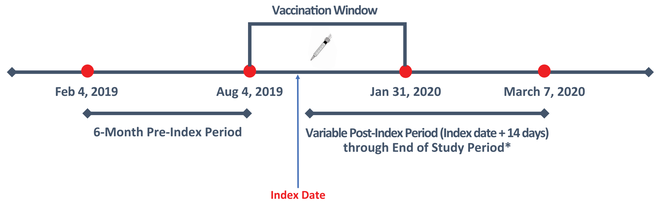
STUDY OBJECTIVE

To evaluate improved relative vaccine effectiveness (rVE) and health economic outcomes of QIVc compared to egg-derived inactivated quadrivalent influenza vaccine QIVe-SD in the reduction of influenza-related and respiratory-related hospitalizations/emergency room (ER) visits.

METHODS

- A retrospective cohort analysis was conducted among subjects 4-64 years old vaccinated with QIVc or QIVe-SD using administrative claims data in the United States of America (U.S.) for the 2019-20 influenza season (IQVIA PharMetrics® Plus). To avoid any influenza outcome misclassification with covid-19 infection, the study period concluded March 7, 2020. **Figure 1**.

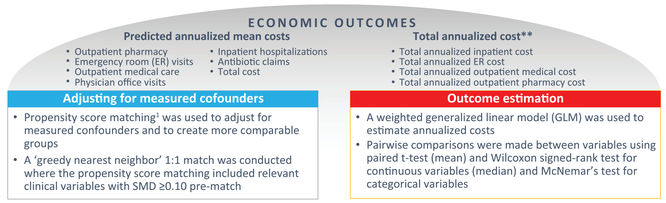
FIGURE 1. STUDY DESIGN – RETROSPECTIVE COHORT



- Baseline characteristics included age, gender, payer type, geographic region, Charlson Comorbidity Index, comorbidities, month of flu vaccination and pre-index hospitalization.
- The number of events and rates (per 1,000 vaccinated subject-seasons) of influenza-related hospitalizations/ER visits, respiratory-related hospitalizations/ER visits (e.g., any respiratory event, pneumonia, asthma/chronic obstructive pulmonary disease [COPD]/bronchial and other respiratory events) and all-cause hospitalizations were assessed using inverse probability of treatment weighting (IPTW) to adjust for baseline confounders.
- Poisson regression was used to estimate adjusted rVE. A sub-analysis for a high-risk subgroup (defined based on clinical risk groups considered at higher risk for influenza complications) was conducted. Urinary tract infection (UTI) hospitalization/ER visit was assessed as a control negative endpoint.
- Economic analyses were conducted to compare healthcare costs of the two vaccine cohorts. Outcomes were reported over the variable follow-up period, 14 days after the index date; therefore, the vaccine cost was not included. Unlike analysis of clinical outcomes, all occurring events of the same type contributed to the total cost for a subject. Following adjustment for outliers, a weighted generalized linear model was used to calculate annualized costs, which included inpatient, ER, outpatient medical and outpatient pharmacy costs. **Figure 2**.

METHODS (CONT'D)

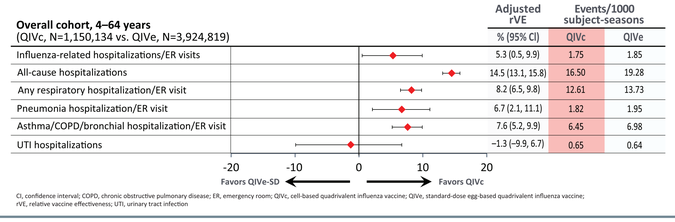
FIGURE 2. METHODOLOGY – DETERMINATION OF HEALTHCARE COSTS



RESULTS

- During the 2019–2020 influenza season, 1,150,134 recipients of QIVc and 3,924,819 of QIVe-SD were identified post-IPTW. Adjusted analysis overall (4-64 years old) found that QIVc was associated with a significantly higher rVE compared to QIVe-SD against influenza-related hospitalizations/ER visits (5.3% [95% CI: 0.5%-9.9%]). **Figure 3**.
- Similarly, in the overall population, QIVc was 14.5% (95% CI: 13.1%-15.8%), 8.2% (95% CI: 6.5%-9.8%), 7.6% (95% CI: 5.2%-9.9%) and 6.7% (95% CI: 2.1%-11.1%) more effective than QIVe-SD for the prevention of all-cause hospitalizations and hospitalization/ER visits related to any respiratory event, asthma/COPD/bronchial and pneumonia events, respectively. **Figure 3**.

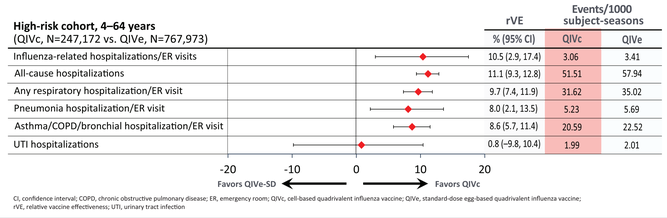
FIGURE 3. RELATIVE VACCINE EFFECTIVENESS OF QIVc VS. QIVe (ADJUSTED)



CI, confidence interval; COPD, chronic obstructive pulmonary disease; ER, emergency room; QIVc, cell-based quadrivalent influenza vaccine; QIVe, standard-dose egg-based quadrivalent influenza vaccine; rVE, relative vaccine effectiveness; UTI, urinary tract infection

- A similar trend was seen for the high-risk subgroup; for instance, rVEs for QIVc compared to QIVe-SD against influenza-related hospitalizations/ER visits resulted in 10.5% [95% CI: 2.9%-17.4%]. In addition, to the high-risk subgroup, the rVEs for QIVc compared to QIVe-SD for all-cause hospitalizations and hospitalization/ER visits related to any respiratory and pneumonia events were 11.1% (95% CI: 9.3%-12.8%), 9.7% (95% CI: 7.4%-11.9%) and 8.0% (95% CI: 2.1%-13.5%), respectively. No effect was identified for the control negative group. **Figure 4**.

FIGURE 4. RELATIVE VACCINE EFFECTIVENESS OF QIVc VS. QIVe IN HIGH-RISK SUBGROUP (ADJUSTED)

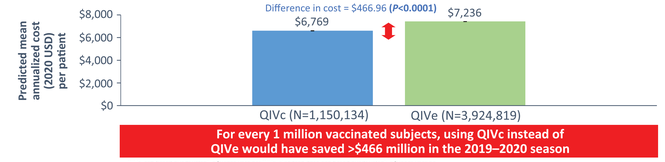


CI, confidence interval; COPD, chronic obstructive pulmonary disease; ER, emergency room; QIVc, cell-based quadrivalent influenza vaccine; QIVe, standard-dose egg-based quadrivalent influenza vaccine; rVE, relative vaccine effectiveness; UTI, urinary tract infection

RESULTS (CONT'D)

- The predicted mean annualized all-cause total cost in QIVc recipients was $6,769 and significantly lower than the $7,236 in QIVe-SD recipients, a difference of $466.96 (*P*<0.0001). **Figure 5**.

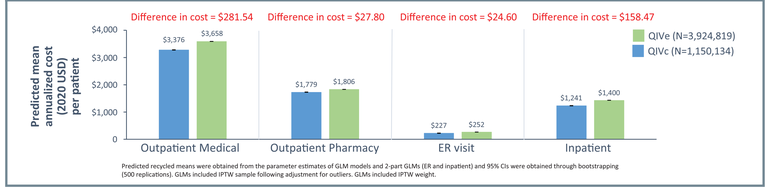
FIGURE 5. PREDICTED MEAN ANNUALIZED ALL-CAUSE TOTAL HEALTHCARE COSTS QIVc VS. QIVe



QIVc, cell-based quadrivalent influenza vaccine; QIVe, standard-dose egg-based quadrivalent influenza vaccine

- The predicted mean annualized total costs for outpatient medical, outpatient pharmacy, emergency room visit, and inpatient components were significantly lower for QIVc versus QIVe-SD (*P*<0.0001). **Figure 6**.

FIGURE 6. PREDICTED MEAN ANNUALIZED SELECT COMPONENT COSTS QIVc VS. QIVe



Predicted recycled means were obtained from the parameter estimates of GLM models and 2-part GLMs (ER and inpatient) and 95% CIs were obtained through bootstrapping (500 replications). GLMs included IPTW sample following adjustment for outliers. GLMs included IPTW weight.

CONCLUSIONS

- During the 2019–2020 influenza season, following adjustment for confounders, QIVc was significantly more effective in preventing influenza-related and respiratory-related hospitalizations/ER visits as well as all-cause hospitalizations compared to QIVe-SD among U.S. children and adults 4-64 years old.
- Healthcare costs were significantly lower for QIVc versus QIVe-SD. For every 1 million vaccinated subjects, vaccination with QIVc instead of QIVe would have saved >$466 million for the 2019–2020 influenza season; and, QIVc recipients incurred significantly lower costs than QIVe-SD recipients across four components of total healthcare costs including: outpatient medical; outpatient pharmacy; emergency room visit; and inpatient.

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