A high-dose influenza vaccine for individuals age 65 or older, the high-dose trivalent vaccine (HD-3V), has in some seasons been more effective than standard-dose trivalent vaccine (SD-3V).2-7 Pooled data from seven randomized controlled trials support a general conclusion of efficacy for prevention of laboratory-confirmed influenza.2 Economic evaluations have predicted that HD-3V would also be cost-effective in older populations.2,14 Standard-dose quadrivalent (SD-4V) is now available. Currently, the Centers for Disease Control and Prevention does not have a recommendation regarding high-dose vaccines.2 Factors other than vaccine type that might affect vaccine effectiveness are not well-understood.

**Objective**

To assess the differential impact in the elderly of the currently available influenza vaccines and to evaluate other drivers of vaccine failure.

**Methods**

**Study Design:** Retrospective cohort study

**Data Sources:** Claims and enrollment databases of Humana Inc.

**Inclusion Criteria:**
- Continuous enrollment in Medicare for both calendar years of at least one of these three influenza seasons: 2013-2014, 2014-2015, or 2015-2016
- Age ≥ 65 years
- Vaccination with HD-3V, SD-3V, or standard-dose quadrivalent SD-4V vaccine during August-November in at least one of the three influenza seasons

**Exclusion Criteria:**
- Influenza diagnosis before December 15 (of year 1) of a given season
- 1 vaccine type
- Enrollment during the interval January of year (1) through May (of year 2) or death during that interval without concurrent influenza diagnosis

**Outcomes:** Measured December 15 (of year 1) through July 31 (of year 2)

**Risk of vaccine failure (influenza diagnosis occurring ≥ 2 weeks after vaccination)**
- *Likelihood of serious influenza (inpatient admission or death with concurrent influenza diagnosis occurring ≥ 2 weeks after vaccination)*

**Statistical Analyses:** Multivariate robust Poisson regression models used to estimate relative risk. Covariates included gender, race, Health and Human Services (HHS) region, vaccine type, season, vaccination month, and Charlson Comorbidity Index (CCI) based on first calendar year of the season. Reference values were selected on the basis of which level or category was most frequent.

**Results**

**Results may not be generalizable to 2015-16**

**Vaccination**

- **September**
- **November**

**Risk**

- > 1 vaccine type

**2014**

- The odds ratios approaching 2 for Gender, race, flu season, and morbidity

**Izurieta HS et al.**

- 2014;371(7):635-641

**Conclusion**

- Results suggest that HD-3V vaccine is an appropriate choice for adults age 65 and older.
- Gender, race, flu season, and morbidity were the key determinants of vaccine failure.
- Results show the importance of a good match of vaccine to prevalent strains, represented by flu season.
- The odds ratio approaching 2 for association of high CCI scores with vaccine failure showed that high morbidity makes older adults particularly vulnerable to influenza infection. This may have implications for preventing exposure in this subpopulation.

**Limitations**

- Lack of random assignment to vaccine type might preclude definitive conclusions about relative effectiveness.
- This study was subject to limitations inherent to claims analyses such as missing data, incorrect coding, and lack of data on potentially confounding clinical or behavioral factors.
- Results may not be generalizable to populations not participating in Medicare Advantage or to populations with different geographic distribution. The South was overrepresented in this study population.

**Conclusions**

**References**