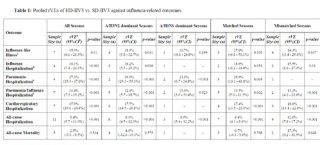
Across all influenza seasons, HD-IIV3 demonstrated improved protection against ILI compared with SD-IIV3 (rVE = 15.9%, 95% CI: 4.1–26.3%). HD-IIV3 was also more effective at preventing hospital admissions from all-causes (rVE = 8.4%, 95% CI: 5.7–11.0%), as well as influenza (rVE = 16.1%, 95% CI: 7.4–24.1%), pneumonia (rVE = 27.3%, 95% CI: 15.3–37.6%), pneumonia/influenza (rVE = 13.4%, 95% CI: 7.3–19.2%) and cardiorespiratory events (rVE = 17.9%, 95% CI: 15.0–20.8%). Some numerical differences were observed in the pooled rVE of outcomes in matched and mismatched seasons and in seasons where A/H3N2 or A/H1N1 strains were predominantly circulating (Table 1).

Conclusion: Evidence over 9 influenza seasons suggest that HD-IIV3 is consistently more effective than SD-IIV3 at reducing the clinical outcomes associated with influenza infection irrespective of circulating strain and antigenic match.

This study was funded by sanofi pasteur



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

2746. Effectiveness of Influenza Vaccine for Prevention of Influenza-associated Hospitalizations Among Immunocompromised Adults—2017–2018

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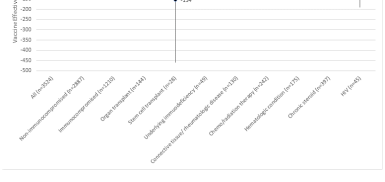
Background: Immunocompromised (IC) individuals are at higher risk for severe complications of influenza. Little literature describes vaccine effectiveness (VE) in this population. We evaluated VE for prevention of influenza-associated hospitalization among IC adults.

Methods: We analyzed data from adults hospitalized with acute respiratory illness (ARI) during the 2017–2018 FLU season at 9 hospitals participating in the US Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN) study. Details of disease severity, underlying health status, and vaccination status were obtained through enrollment interviews and medical records. Prior year clinical encounter diagnoses and enrollment interviews were used to define IC groups. IC groups were mutually exclusive. VE was evaluated with a test-negative case–control design using multivariate logistic regression with PCR-confirmed influenza as the outcome and vaccination status as the exposure, adjusting for age, race, and other factors, and stratifying by immunocompromising conditions.

Results: Of 3524 adults hospitalized with ARI, 1210 (34%) had an immunocompromising condition. Chronic steroid (n = 397), chemo/radiation therapy (n = 242), hematologic condition (n = 175), and organ transplant (n = 144) were most common. HIV (n = 45) and stem cell transplant (SCT) (n = 28) were least common. IC patients were more likely to be vaccinated than non-IC (60% vs. 55%, P = 0.002). Overall, vaccination reduced risk of influenza hospitalization by 36% (95% CI: 24,46). Among IC adults, VE was 9% (95% CI: −25,34). VE was 32% (95% CI: 5,51) for chemo/radiation therapy, 29% (95% CI: 6,47) for chronic steroids, 29% (95% CI: -6,52) for hematologic conditions, −1% (95% CI: −50,32) for organ transplant, −48% (95% CI: −190,25) for HIV, and −154% (95% CI = −458,−15) for SCT (Figure 1).

Conclusion: Vaccination reduced risk of influenza hospitalization among adults with the most prevalent immunocompromising conditions in our cohort; however, it had little to no effect in other groups, such as in HIV and organ and stem cell transplant recipients. Results support using other preventative strategies in addition to vaccinating adults with immunocompromising conditions, such as vaccination of close contacts.



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

2747. Relative Vaccine Efficacy of High-Dose vs. Standard Dose Influenza Vaccines in Preventing Probable Influenza in a US Medicare Fee-for-Service Population

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Session: 278. Vaccines: Influenza

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Background: High dose (HD) influenza vaccine has been shown to be more efficacious than standard dose (SD) vaccine in multiple randomized trials. HD is currently the most commonly used vaccine in US seniors (≥65 years of age). In this study, we evaluated the real-world relative vaccine effectiveness (rVE) of HD vs SD over 3 influenza seasons.

Methods: This study includes a cohort of Medicare fee-for-service enrollees during influenza seasons 2011–2012 to 2013–2014 who received either HD or SD at a pharmacy or an outpatient clinic. HD recipients were matched 1:1 to SD recipients based on location, date of vaccination, age, and gender. Fine-Gray subdistribution hazard models with competing risk of death were used to adjust for residual confounding. The study outcome of probable influenza was defined as any inpatient stay with an influenza diagnosis on the claim, or an outpatient medical encounter with a rapid influenza test/culture followed by an antiviral prescription. Analyses were stratified based on vaccination location (clinic vs pharmacy) as it is expected that physicians carrying both vaccines may prioritize HD to frailer patients, while pharmacists may not exercise clinical judgment.

Results: Over the influenza seasons 2011–2012, 2012/–2013, and 2013–2014, 1.6–2.2 million seniors were immunized at a pharmacy; and 3.3–3.5 million at a clinic. After matching, there were 535,598; 1,017,552; and 1,548,164 in the pharmacy cohort, and 821,662; 1,151,080; and 1,559,488 in the clinic cohort, across study years. The rVE over 2011/12, 2012/13, and 2013/14 during peak influenza circulation was 21.8% (95% CI: −5.9%, 42.3%), 14.8% (9.3%,19.9%), and 16.9% (9.2%, 23.9%), respectively, in the pharmacy cohort; and 16.5% (−5.9%, 34.2%), 15.1% (10.9%, 19.1%), 10.0% (2.9%, 16.6%), respectively, in the clinic cohort.

Conclusion: HD was consistently associated with better protection against probable influenza events requiring outpatient or inpatient care. The slightly lower treatment effects observed in the outpatient clinic cohort could be a result of confounding by indication due to physicians triaging HD to frailer patients.

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

2748. Single Intranasal (IN) Dose of M2SR (M2-Deficient Single Replication) Live Influenza Vaccine Protects Adults Against Subsequent Challenge with a Substantially Drifted H3N2 Strain

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Background: Demonstration of protection by a M2SR (M2 deficient Single Replication) monovalent H3N2 vaccine was assessed in a phase 2a clinical trial in which the challenge virus was substantially drifted from the vaccine. M2SR is an investigational, live virus vaccine containing hemagglutinin (HA) and neuraminidase (NA) selected from targeted Type A influenza strains. M2SR undergoes only a single round of infection in the respiratory epithelium but evokes an immune response profile similar to wild-type influenza virus and protects ferrets against both homologous and heterologous influenza variants.

Methods: A blinded, randomized, placebo-controlled human challenge study (EudraCT #: 2017-004971-30) was conducted with M2SR containing HA and NA from A/Brisbane/10/2007 (H3N2). 18–55-year-old subjects received 1 IN dose of saline or 10^8 $TCID_{50}$ of vaccine. 4 weeks later, 99 subjects were challenged IN with 10^6 $TCID_{50}$ H3N2 A/Belgium/4217/2015 (Figures 1 and 2).

Results: Adverse events (AE) were similar between placebo (N = 51) and M2SR recipients (N = 48) during the 28 days after immunization. After challenge with A/Belgium/4217/2015, 35% of M2SR recipients experienced influenza infection and illness, compared with 49% of placebo subjects (Figure 3). An 18% reduction in viral load was noted after challenge for M2SR subjects. Serum microneutralization response to vaccine was detected in 54% of M2SR subjects (vs. 0/51 placebo subjects), and among these subjects a 34% reduction in viral load and 51% reduction in symptom scores was noted after challenge vs placebo. Among the 29% of subjects with post-vaccine response to both vaccine and challenge strains, a 62% reduction in viral load and 56% reduction in symptom scores was noted after challenge with highly drifted H3N2 (Figure 4).

Conclusion: One dose of M2SR protected healthy adults against influenza infection and illness with a highly drifted challenge strain. This is believed to be the first study to demonstrate protection against challenge with an influenza strain substantially different