Veterans Health Administration (VHA) electronic medical records were linked with Centers for Medicare and Medicate Services administrative claims to capture the study outcomes of hospitalizations and baseline characteristics. The inverse probability of treatment weight (IPTW) method was used to adjust for potential confounding due to unmeasured factors associated with IIV3-SD, IIV3-HD, or IIV4 vaccination. The probability was estimated based on patient sociodemographic characteristics, comorbidities, pre-influenza season hospitalizations, prior season influenza vaccination, and use of immunosuppressive medication.

Results. Our study population included 782,346 VHA patients vaccinated during the 2014–2015 season. Of these, 10,543 (1%) received IIV4, while 59,536 (8%) received IIV3-HD and 712,267 (91%) received IIV3-SD. 11,626 (1.5%) were female and 588,324 (76%) were non-Hispanic white. Compared with those that received IIV3-SD vaccine, the IPTW-adjusted rVE for IIV3-HD was 7% (95% CI, 9%–21%) against all-cause, 15% (95% CI, 10%–17%) against cardiorespiratory associated, and 13% (95% CI, 8%–17%) against influenza/pneumonia-associated hospitalization. For those that received IIV4, the IPTW-adjusted rVE was 4% (95% CI, 1%–4%), 1% (95% CI, −2%–5%), and 0% (95% CI, −9%–8%), respectively.

Conclusion. IIV3-HD is more effective than, and IIV4 is as effective as, IIV3-SD vaccination in preventing influenza/pneumonia-associated, cardiorespiratory, and all-cause hospitalizations. Additional studies that employ methods to control for unmeasured confounding are warranted as the use of IIV4 expands.

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990. Impact of Influenza Vaccination Setting on Timing of Vaccination in a National Sample of Influenza-Vaccinated Adults

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Background. The CDC recommends annual influenza vaccination by the end of October if possible. Timing of vaccination is vital since people over 65 may be at risk for intraseason immunity waning. Traditionally, vaccinations occur in doctor's offices, but other settings are increasing the availability and convenience of vaccines. The objective was to assess the association between timing and setting of influenza vaccination.

Methods. The 2015 Behavioral Risk Factor Surveillance System (BRFSS) telephone survey was used to identify adults in the United States who reported a flu shot in the past year. Based on self-reported date of flu shot, the 2014–2015 flu season was included and divided into early (July–October) vs. late (November–May) vaccination. Settings of vaccination included doctor's office, clinic/hospital, store, and work. Covariates of interest were demographics, having a checkup within previous 1 year, insurance, obesity (BMI ≥ 30), alcohol use, current smoking status, and comorbidities. Comorbidities (hypertension, high cholesterol, stroke, angina, heart attack, skin cancer, other cancer, arthritis, depression, kidney disease, diabetes, asthma, and chronic obstructive pulmonary disease) were categorized as 0, 1–2, or 3+ present. Logistic regression, stratified by age ≥65, identified predictors of early vaccination.

Results. A total of 130,615 patients were included. Patients vaccinated in doctor's offices and stores tended to be older and have higher rates of comorbidities compared with those in clinics or at work. In age-stratified analyses, patients 18–64 had higher odds of early vaccination at clinics (odds ratio 1.11, 95% confidence interval 1.02–1.22), stores (OR 1.09, 95% CI 1.002–1.19), and work (OR 1.88, 95% CI 1.71–2.05) compared with doctor's offices. Patients aged ≥65 had higher odds of early vaccination at stores (OR 1.17, 95% CI 1.07–1.27) and work (OR 1.67, 95% CI 1.33–2.09). Patients with certain traits (e.g., males, smokers, and those with children) have lower odds of early vaccination.

Conclusion. Vaccination setting is associated with vaccination timing: nontraditional (store, work) settings increase the odds of receiving a flu shot before the end of October. Age plays a key role in when and where patients receive flu vaccinations. Vaccination programs in nontraditional settings should consider targeting the later flu season to increase participation.

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

991. Randomized Trial of High Dose, Adjuvanted, and Standard Inactivated Influenza Vaccine Immune Response Against Egg- and Cell-Propagated Vaccine Strains in Older Adults, 2016–2017 Season

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Background. High dose (HD-IIV), standard dose (SD-IIV), and MF-59 adjuvanted (aIIV) influenza vaccines are licensed for adults ≥65 years old, but there is no preferential recommendation for a specific product. These vaccines are manufactured using egg-adapted high growth reassortant viruses. Recent data suggest that antibodies generated by egg-adapted A(H3N2) viruses may contribute to reduced vaccine effectiveness. We report results from the first year of a 2-year randomized trial of vaccine immunogenicity, including response to A(H3N2) vaccine strains propagated in egg (H3N2-egg) and cell culture (H3N2-cell).

Methods. Adults 65–74 years old were randomized to receive 2016–2017 trivalent inactivated influenza vaccines: SD-IIV (n = 60), HD-IIV (n = 59), and aIIV (n = 60). Pre- and post-vaccination sera were analyzed by microneutralization assays (MN) to egg- and cell-propagated A(H3N2) vaccine virus, A/Hong Kong/4801/2014 and tested by hemagglutination inhibition (HI) assays to A/California/7/2009 A(H1N1)pdm09-like and B/Brisbane/60/2008-like viruses. Endpoints were postvaccination geometric mean titer (GMT), mean fold rise (MFR), and seroconversion. Respiratory swabs from adults with acute respiratory illness during the season were tested by RT-PCR to identify vaccine failures.

Results. Prevaccination MN and HI titers were similar across study arms. There were no differences across study arms in postvaccination MN GMT, seroconversion, and MFR against H3N2-egg and H3N2-cell (figure). However, response was lower against H3N2-cell than H3N2-egg. HI MFR for H1N1pdm09 and B/Brisbane were significantly higher in HD-IIV than SD-IIV and aIIV recipients (figure). Eight participants had PCR-confirmed A(H3N2) infection: 1/60 (2%) SD-IIV, 4/57 (7%) HD-IIV, and 3/60 (5%) aIIV recipients. Postvaccination H3N2-cell MN GMT was 15 and 63, respectively for A(H3N2) cases and noncases. Among the eight A(H3N2) cases, postvaccination MN titers were ≥1:40 against H3N2-egg for 6 cases vs. 0 cases against H3N2-cell.

Conclusion. Postvaccination MN titers against H3N2 egg- and cell-propagated vaccine viruses were similar across study arms, although antibody response was lower to H3N2-cell. HD-IIV generated greater antibody response against A(H1N1)pdm09 and B compared with SD-IIV or aIIV.

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992. 2016–2017 Influenza Burden of Disease and End-of-Season Influenza Vaccine Effectiveness (VE) Estimates for Preventing Influenza-Related Hospitalization Among Canadian Adults: An Analysis From the Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network

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Background. To inform public health decision making around influenza prevention and treatment, ongoing surveillance of the influenza burden of disease and assessment of influenza vaccine effectiveness (VE) is critical. The Canadian Immunization Research Network (CIRN) Serious Outcomes Surveillance (SOS) Network conducts active surveillance each influenza season to characterize the burden of influenza disease and to provide estimates of influenza VE to prevent influenza-related hospitalization in Canadian adults (≥16 years of age).

Methods. Active surveillance for influenza was conducted at 13 hospitals in four provinces beginning on November 15, 2016 and ending April 30, 2017. Patients admitted with any respiratory diagnosis or symptom were eligible for enrolment. Eligible patients had a nasopharyngeal swab collected and tested for influenza using polymerase chain reaction (PCR). Patients who tested positive for influenza were considered cases; patients who tested negative for influenza were eligible to become matched controls. Detailed demographic and medical information were obtained from the medical record. Influenza VE was estimated as 1 – odds ratio (OR) of influenza in vaccinated vs. unvaccinated patients × 100% using conditional logistic regression, with corresponding 95% confidence intervals (CIs).

Results. A total of 1,431 influenza cases were enrolled; the majority were influenza A (n = 1,299) and 100% of patients with known influenza A subtype were A/H3N2. Among all influenza cases, 144 (10.1%) patients were admitted to the intensive care unit (ICU) and 91 (6.4%) patients died within 30 days of discharge. Overall adjusted influenza VE for prevention of influenza-related hospitalization in all ages was 23.3% (95% CI: 2.9–39.4%), with slightly lower VE observed in patients ≥65 years (VE: 19.4%; 95% CI: −7.8–39.8%) and higher VE observed in patients <65 years (VE: 47.9%; 95% CI: 9.9–69.9%).

Conclusion. Overall, influenza VE was low but effective (VE: 23%) for preventing influenza-related hospitalization during the 2016–2017 season in Canada. Given the low influenza VE observed, continued assessment of influenza VE is crucial to inform immunization policy in Canada and to emphasize the importance of the development and utilization of improved influenza vaccines.

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993. Combining Key Residues of the Russian and US Live-Attenuated Influenza Viruses for a More Attenuated Virus

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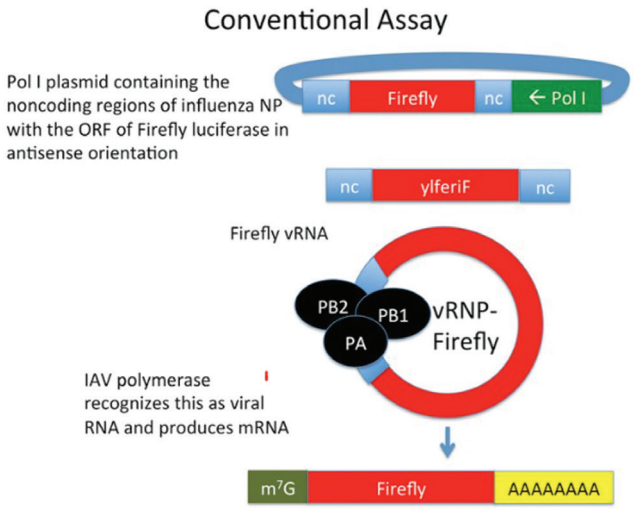
Background. The Live Attenuated Influenza Virus (LAIV) used in the United States is based on the cold-passaged A/AnnArbor/6/60 strain (AA). An alternative LAIV (Len), developed from the cold-passaged A/Leningrad/134/17/57 strain, has also been used in some countries outside the United States. Recent concerns with the efficacy and safety of the current US LAIV warrant the development of an improved LAIV.

Methods. We used *in vitro* minireplicon and multicycle viral growth assays to analyze the combined effects of polymerase mutations from LAIV (AA) and LAIV (Len) on the phenotype of PR8. Mini-replicon assays were performed in HEK-293T cells with firefly luciferase under the control of the influenza virus NP promoter; we controlled for cell density with a constitutively active Renilla luciferase. Multicycle growth curve experiments were performed at 33°C, 37°C, and 39°C in MDCK cells with an m.o.i. of 0.001. Mean values for triplicate infections at 12, 24, 48, and 72 hours were plotted as TCID50/mL.

Results. Control experiments showed replication of PR8 (AA) and PR8 (Len) in MDCK cells was significantly decreased as compared with WT PR8 at 37°C and 39°C at 24–48 hour time points, but not at 33C (the temperature of nasal passages). We found that polymerase activity was up to 3 logs more temperature-sensitive (ts) at 37°C and 39°C with the combined Len and AA mutations using the mini-replicon assay. In the growth curve experiments, the combined Len and AA mutations conferred up to a 4-log decrease in replication levels at 37°C as compared with PR8 (Len) and an even greater decrease compared with PR8 (AA).

Conclusion. Our findings suggest combining the AA and Len LAIV polymerase mutations decreases LAIV replication at body temperature (37°C), as compared with either LAIV alone. This could be useful in developing an improved LAIV that is safer in vulnerable hosts (e.g., children under the age of 2 who may be vulnerable to wheezing), while also permitting dose escalation that might result in greater efficacy.

Minireplicon assay.



Polymerase activity of combination mutants.