2729. mRNA Vaccines Encoding Conserved Influenza Antigens Induce Robust and Durable Immunity in Rhesus Macaques
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Background: In response to immune pressure, influenza viruses evolve, producing drifted variants capable of escaping immune recognition. One strategy for inducing a broad-spectrum immune response that can recognize multiple antigenically diverse strains is to target conserved proteins or protein domains. To that end, we assessed the immunogenicity of mRNA vaccines encoding the stem domain of hemagglutinin (HA) or nucleoprotein (NP) in nonhuman primates (NHPs).
Methods: Rhesus macaques were immunized three times intramuscularly, at 28 day intervals, with lipid nanoparticle-encapsulated mRNA encoding either HA stem (Yassine et al, 2015) or NP. Serum and PBMCs were collected up to 14 or 24 weeks, respectively, after the last vaccination. The magnitude and durability of humoral and cell-mediated immunity were evaluated. ELISA, competition ELISA, an in vitro antibody-dependent cell-mediated cytotoxicity (ADCC) reporter biosay, and microrenalization assays were used to characterize immune responses. Intracellular cytokine staining (IFN-gamma and IL-2) was used to assess antigen-specific T-cell responses.
Results: HA stem-immunized NHPs developed a robust anti-stem binding titer after a single vaccination and after two doses, antibodies recognized several antigenically distinct Group 1 HA proteins. This broad antibody response persisted for at least 14 weeks post-dose 3 (PD3). Serum antibodies showed ADCC activity and competed with a well-characterized broadly neutralizing antibody, CR9114, for binding to HA stem. However, the polyclonal primary antibodies only cross-reacted against a panel of H1N1 viruses in a microneutralization assay. HA-specific CD4+ T-cell responses that persisted for at least 24 weeks PD3. On average, 0.5% of CD4+ and 4% of CD8+ T cells produced IFN-gamma in response to NP peptide stimulation at the peak of the response, 2 weeks after the last vaccine dose was administered.
Conclusion: Lipid nanoparticle-encapsulated mRNA vaccines encoding conserved influenza antigens induce a robust and durable immune response in NHPs.
Disclosures. All authors: No reported disclosures.

2730. Estimating Deaths Attributable to Influenza Mortality Using Traditional and Novel Forecasting Methods
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Background: Seasonally-adjusted linear models (Serfling models) serve as an important surveillance measure to estimate influenza (flu) attributable deaths for resource allocation to public health programs (e.g., vaccination campaigns). We compared performance of traditional time-series and viral activity-based models to a novel open-source R package ‘Prophet’ for estimating the number of deaths attributable to influenza per season.
Methods: We evaluated models from the 122-Cities Mortality Reporting System which reports the total number of death certificates where pneumonia or flu was listed as the underlying cause of death. We computed vaccine effectiveness on an annual basis specifically in susceptible populations. The primary outcome was PCR-confirmed influenza and vaccination status was defined using electronic medical record and parental interviews. Vaccination status was defined as completely vaccinated (all doses of influenza vaccine according to child’s age); partially or not vaccinated children were defined as unvaccinated. Multivariable logistic regression models adjusted for high-risk medical condition, age, race and insurance status were used to calculate odds ratios (OR) and 95% confidence intervals. Vaccine effectiveness was calculated as (1 – OR) × 100.
Results: Of the 1224 (82.8%) children enrolled in the study with known vaccination status for both seasons, 361 (29%) tested positive for influenza. Overall, VE against influenza was 49% (95% CI, 33–61%) after adjusting for other covariates in the model. VE did not differ significantly between those vaccinated in both seasons and those vaccinated only in the current season. VE was 49% (95% CI, 41–51) (Table 1).
Conclusion: Our estimates of influenza VE for two predominantly H3N2-influenza seasons in Colorado are comparable to the CDC. VE for children 6 months to 8 years, VE against ED or UC-attended influenza illness in children did not vary significantly by prior seasons vaccination status.
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2731. Does Last Season’s Influenza Vaccination Affect Current Season's Vaccine Effectiveness in Young Children?
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Background: We evaluated influenza VE over two consecutive years vs. the current season against influenza illness during two H3N2-predominant seasons in children receiving care at emergency/urgent care (ED/UC) facilities in metropolitan Colorado.
Methods: We conducted a test-negative case-control analysis of 1478 children aged 6 months to 8 years enrolled at Children’s Hospital Colorado ED/UC with influenza like illness during the 2016–2017 and 2017–2018 influenza seasons. The primary outcome was PCR-confirmed influenza and vaccination status was confirmed using electronic medical record and parental interviews. Vaccination status was defined as completely vaccinated (all doses of influenza vaccine according to child’s age); partially or not vaccinated children were defined as unvaccinated. Multivariable logistic regression models adjusted for high-risk medical condition, age, race and insurance status were used to calculate odds ratios (OR) and 95% confidence intervals. Vaccine effectiveness was calculated as (1 – OR) × 100.
Results: Of the 1224 (82.8%) children enrolled in the study with known vaccination status for both seasons, 361 (29%) tested positive for influenza. Overall, VE against influenza was 49% (95% CI, 33–61%) after adjusting for other covariates in the model. VE did not differ significantly between those vaccinated in both seasons and those vaccinated only in the current season. VE was 49% (95% CI, 41–51) (Table 1).
Conclusion: Our estimates of influenza VE for two predominantly H3N2-influenza seasons in Colorado are comparable to the CDC. VE for children 6 months to 8 years, VE against ED or UC-attended influenza illness in children did not vary significantly by prior seasons vaccination status.

Table 1—Vaccine Effectiveness over 2016-17 and 2017-18 Influenza seasons, n=1224

| Predictor (vaccination status) | Crude Vaccine effectiveness (%) | Adjusted Vaccine effectiveness (%) | Adjusted vaccine efficiency (%) |
|-------------------------------|--------------------------------|----------------------------------|--------------------------------|
| Current season vs neither      | 0.45 (0.12, 0.65)              | 0.29 (0.10, 0.58)                | 71 (44, 116) 0.17               |
| Both seasons vs neither        | 0.39 (0.14, 0.52)              | 0.51 (0.32, 0.65)                | 49 (33, 69) <0.001              |
| Both seasons vs current season only | -0.16 (0.38, 0.28)          | 0.31 (0.15, 0.50)                | 60 (41, 115) 0.15               |
| Both seasons vs prior season only | 0.63 (0.47, 0.74)             | 0.56 (0.38, 0.70)                | 44 (30, 68) <0.001              |

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