Disclosures. **C. Jones**, Rebiotix, Inc.: Employee, Salary. **K. Blount**, Rebiotix, Inc.: Employee, Salary. **T. Savidge**, Rebiotix: Grant Investigator, Research grant.

2553. Individual Patient-Level Data Meta-Analysis of Live Attenuated and Inactivated Influenza Vaccine Effectiveness Among US Children, 2013–2014 Through 2015–2016

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Background. Quadrivalent live attenuated influenza vaccine (LAIV4) was not recommended for use in the United States for the 2016–2017 and 2017–2018 influenza seasons based on US observational studies of vaccine effectiveness (VE) from 2013–2014 to 2015–2016. We pooled individual patient data on children aged 2–17 years enrolled in 5 US studies during these 3 influenza seasons to further investigate VE by vaccine type.

Methods. Analyses included 17,173 children enrolled in the US Department of Defense Global Laboratory-based Influenza Surveillance Program, US Influenza Vaccine Effectiveness Network, Influenza Incidence Surveillance Project, Influenza Clinical Investigation for Children, and a Louisiana State University study. Participants' specimens were tested for influenza by reverse transcription-polymerase chain reaction (RT-PCR), culture, or a combination of rapid antigen testing and RT-PCR. VE was calculated by comparing odds of vaccination with either inactivated influenza vaccine (IIV) or LAIV4 among influenza-positive cases to test-negative controls and calculated as 100 × (1 − odds ratio) in logistic regression models with age, calendar time, influenza season, and study site (random effect). Patients were stratified by prior season vaccination status in a subanalysis.

Results. Overall, 38% of patients (N = 6,558) were vaccinated in the current season, of whom 30% (N = 1,979) received LAIV4. Pooled VE of IIV against any influenza virus was 51% (95% CI: 47, 54) versus 26% (95% CI: 15, 36) for LAIV4. Point estimates for pooled VE against any influenza by age group ranged from 45% to 58% for IIV and 19% to 34% for LAIV4 during the 3 seasons (Figures 1 and 2). Pooled VE against influenza A(H1N1)pdm09 was 67% (95% CI: 62, 72) for IIV versus 20% (95% CI: −6, 39) for LAIV4. Pooled VE against influenza A(H3N2) was 29% (95% CI: 14, 42) for IIV versus 7% (95% CI: −11, 23) for LAIV4, and VE against influenza B was 52% (95% CI: 42, 60) for IIV and 66% (95% CI: 47, 77) for LAIV4. VE against influenza A(H1N1)pdm09 was lower for LAIV4 versus IIV across all strata of prior season vaccination (Figure 3).

Conclusion. Consistent with individual studies, our pooled analyses found that LAIV4 effectiveness was reduced for all age groups against influenza A(H1N1)pdm09 compared with IIV. This result did not vary based on prior vaccination status.

Figure 1. Adjusted VE of IIV by influenza (sub)type and age group

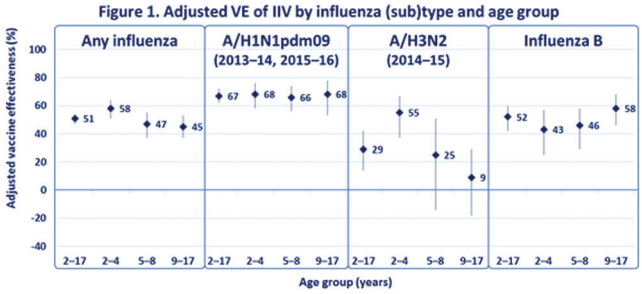


Figure 2. Adjusted VE of LAIV by influenza (sub)type and age group

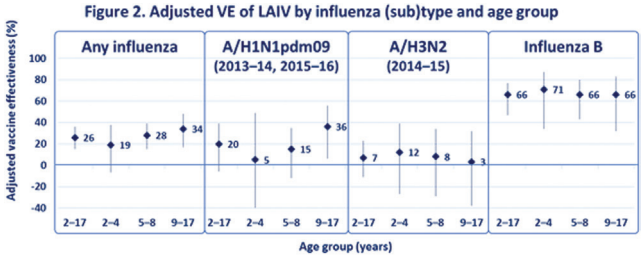
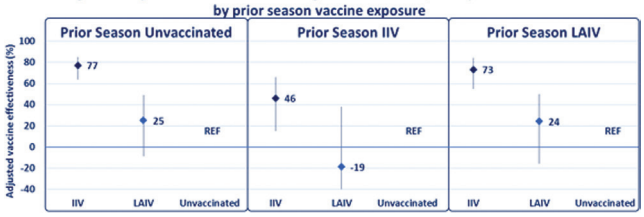


Figure 3. Adjusted VE of IIV and LAIV against influenza A/H1N1pdm09 stratified by prior season vaccine exposure



Disclosures. **H. Caspard**, AstraZeneca: Employee, Salary.

2554. Safety and Immunogenicity of NasoVAX, a Novel Intranasal Influenza Vaccine

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Background. NasoVAX is a replication-deficient adenovirus-based vaccine designed to express influenza hemagglutinin in nasal epithelial cells when given as a nasal spray. In preclinical studies, NasoVAX was associated with divergent strain protection. Prior preclinical and clinical studies with the vector demonstrated lack of impact from baseline adenovirus immunity.

Methods. Sixty healthy adults were randomized to an A/California 2009-based monovalent NasoVAX formulation at doses of 10^9, 10^{10}, or 10^{11} viral particles or saline placebo, all given as a 0.25 mL nasal spray in each nostril. Subjects were followed for safety, including solicited local and systemic side effects. Immune measures included hemagglutination inhibition (HAI) and neutralizing antibody (MN) at days 1, 15, 29, 90, and 180, and γ-interferon ELISpot at day 1 and 8. A parallel cohort of 20 similar subjects were dosed with Fluzone® injectable influenza vaccine containing an A/California 2009 component and had assessments at the same timepoints. The laboratory was blind to treatment assignment for these comparator samples.

Results. NasoVAX was well tolerated with no serious adverse events and no fever. Solicited symptoms such as nasal congestion, sore throat, and headache did not increase with dose and were not statistically different than placebo. Available immune response data are shown below.

Group	NasoVAX (10^9 vp)	NasoVAX (10^{10} vp)	NasoVAX (10^{11} vp)	Fluzone®	Placebo
Seroprotection Rate at Day 29 (≥1:40 HAI)	80%	100%	100%	95%	53%
(95% CIs)	(51.9%, 95.7%)	(78.2%, 100.0%)	(78.2%, 100.0%)	(75.1%, 99.9%)	(26.6%, 78.7%)
MN Responder Rate at Day 29 (2-fold rise)	40%	47%	73%	70%	0%
(95% CIs)	(16.3%, 67.7%)	(21.3%, 73.4%)	(44.9%, 92.2%)	(45.7%, 88.1%)	(0.0%, 21.8%)
Median ELISpot Day 8 SFC/10^6 PBMC	58.0	12.0	307.5	55.5	0.0
(95% CIs)	(5.31, 110.69)	(0.0, 60.36)	(2.15, 612.78)	(4.12, 106.87)	(0.0, 38.49)

Conclusion. NasoVAX intranasal influenza vaccine was well tolerated and elicited comparable antibody responses and nearly 6-fold higher cellular immune responses than a licensed injectable vaccine.

Disclosures. **S. Tasker**, Altimmune, Inc: Employee and Shareholder, Salary. **V. Krishnan**, Altimmune, Inc.: Employee and Shareholder, Salary. **S. Bart**, Altimmune, Inc.: Research Contractor, fee for research services. **A. Suyundikov**, Altimmune, Inc.: Employee, Salary. **P. G. Booth**, Altimmune, Inc.: Research Contractor, fee for research services. **A. Wight O'Rourke**, Altimmune, Inc.: Employee and Shareholder, Salary. **J. Zhang**, Altimmune, Inc.: Employee and Shareholder, Salary. **B. Georges**, Altimmune, Inc.: Employee and Shareholder, Salary. **S. Roberts**, Altimmune, Inc.: Employee and Shareholder, Salary.

2555. Predicting Risk of Breakthrough Invasive Pneumococcal Disease in Children After 13-Valent Pneumococcal Conjugate Vaccination

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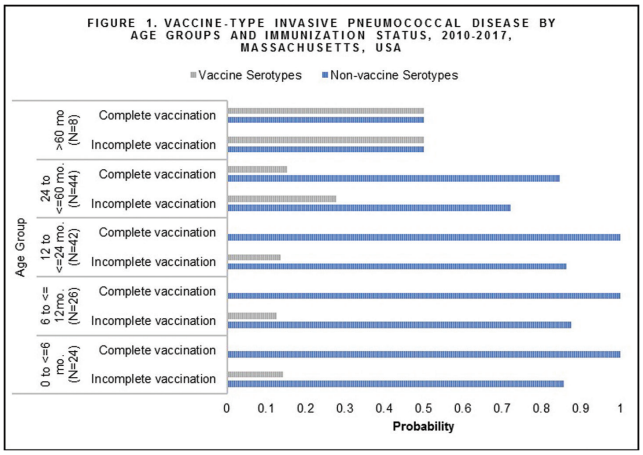
Background. Thirteen-valent-pneumococcal conjugate vaccine (PCV13) replaced PCV7 in the childhood immunization schedule in Massachusetts beginning in April 2010. We evaluated the predictors of vaccine-type (VT) invasive pneumococcal infection (IPD) occurrence despite vaccination.

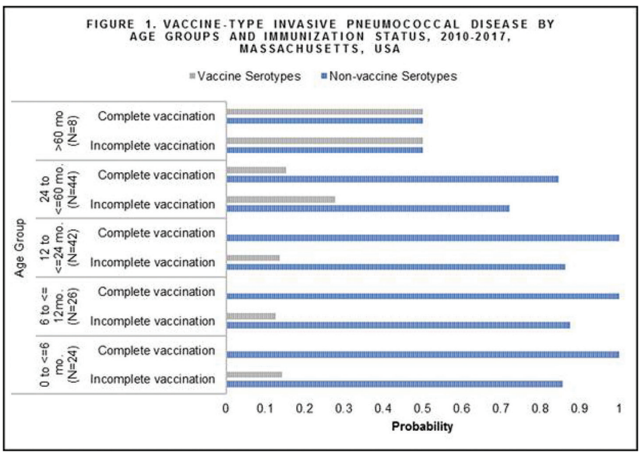
Methods. Cases of IPD in children <18 years of age were detected through an enhanced surveillance system in MA since 2001. All cases and *Streptococcus pneumoniae* (SP) isolates are submitted to Department of Public Health (MDPH) and parents/physicians are interviewed for confirmation of demographic and clinical data. All available isolates are serotyped by Quellung reaction. Children who received any dose of PCV7 were excluded from this study. We used 4-layer, feed-forward, neural network with back-propagation learning algorithm, random forest algorithm with 150 classification trees, and extreme gradient boosting (XGBoost) algorithm based on boosted trees with over than 200 iterations to make prediction about risk of nonvaccine serotype (NVST) causing IPD.

Results. Overall, 144 IPD cases have been identified between April 1, 2010, and March 31, 2017, and 27 (19%) were VT IPD. Compared with children with complete PCV13 vaccination, IPD among those with incomplete immunization was more likely

to be due to VT (9%, 95% CI 4–18% vs. 19%, 95% CI 10–31%, respectively). Despite complete immunization, 80 of 144 (55.6%) of all IPD in >60 months was breakthrough IPD (Figure 1). Among children with ≥1 comorbid condition and incomplete PCV13, 4 of 18 (22%) IPD were due to VT. Children with incomplete vaccination and pneumonia were most likely (11/17, 65%) to have VT; however, bacteremia without focus cases with incomplete vaccination were most likely (44/45, 3%) to have NVST (Figure 2). Our algorithm performs with 85% accuracy and 92% precision scores.

Conclusion. IPD due to VT after PCV13 vaccination mostly occurs in older children with incomplete PCV13 immunization, among those with underlying comorbidity, and among those who present with pneumococcal pneumonia. Evaluating the immune response following PCV13 vaccination in children with comorbidity could increase our understanding of breakthrough pneumococcal infections despite vaccination with PCV13.





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

2556. Retrospective Evaluation of Mismatch From Egg-Based Isolation of Influenza Strains Compared With Cell-Based Isolation and the Possible Implications for Vaccine Effectiveness

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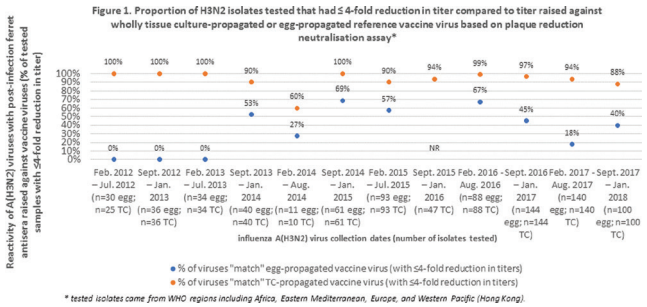
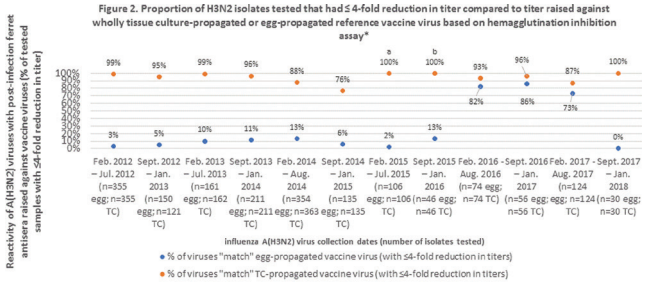
Background. Lower influenza vaccine effectiveness (VE) against circulating H3N2 strains compared with other influenza viruses is partly explained by antigenic mismatch between circulating strains and the vaccine strain (Belongia 2016). This mismatch has recently been linked to a new glycosylation site introduced in the egg-adaptation step (Zost 2017) and HA L194P substitution (Wu 2017) for H3N2. Vaccine manufactured using seed virus wholly grown in mammalian (e.g., Madin–Darby Canine Kidney—MDCK) cells, as with the NH17-18 version of Flucelvax®, avoids these mutations. Preliminary reports suggest that this cell-based vaccine showed greater VE than did similar egg-based vaccines [FDA Statement]. This study aimed to compile existing data on antigenic similarity to measure the degree of match with circulating wild-type isolates of egg- and MDCK-propagated versions of the vaccine H3N2 virus over multiple seasons.

Methods. Using publicly available reports from the Worldwide Influenza Centre, London (Crick), we compiled data on antigenic similarity, defined as H3N2 circulating wild-type virus isolates showing no more than a 4-fold reduction in titer to antisera raised against wholly MDCK- or egg-propagated versions of the vaccine H3N2 viruses. Titers were compared using hemagglutination inhibition (HI) assays and/or plaque reduction neutralization assays (PRNA).

Results. Data from Northern Hemisphere influenza seasons of 2011–2012 to 2017–2018 show a substantially higher proportion of tested circulating influenza H3N2 viruses matched the MDCK-propagated reference viruses than did corresponding egg-propagated reference vaccine viruses (Figures 1 and 2). In half of the seasons evaluated, there was little to no antigenic similarity between circulating viruses and the egg-based vaccine viral seed.

Conclusion. These data suggest higher levels of mismatch have occurred consistently with egg-propagated H3N2 reference viruses compared with MDCK-propagated reference viruses when measured against circulating wild-type isolates and may further explain the potential for lower VE observed against H3N2 historically. Furthermore, these data point to the importance of continuing to utilize cell-derived seeds in creating seasonal influenza vaccines for this strain.





Disclosures. **S. Rajaram**, Seqirus: Employee, Salary. **J. Van Boxmeer**, Seqirus: Employee, Salary. **B. Leav**, Seqirus: Employee and Shareholder, Salary. **P. Suphaphiphat**, Seqirus: Employee, Salary. **I. Iheanacho**, Seqirus: Consultant, Research support. **K. Kistler**, Seqirus: Consultant, Research support.

2557. A Model to Estimate the Potential Impact of Immunizations on Respiratory Syncytial Virus (RSV) Disease Burden Among Infants in the United States

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Background. Respiratory syncytial virus (RSV) is the leading cause of severe respiratory infections among infants worldwide. We developed a mathematical model to estimate the impact of immunizations currently under development on medically attended (MA) RSV infections (RSVi) among infants in the United States.

Methods. We created a spreadsheet-based Decision Tree model to estimate the potential impact of (1) a vaccine given to mothers in their third trimester to indirectly provide protective antibodies to infants during their first RSV season and (2) a monoclonal antibody given to infants at birth during the RSV season (November to April). We measured the annual number of MA-RSVi (hospitalizations, emergency department (ED) visits, and outpatient clinic visits) prevented by immunization before infants reach 6 months of age. Major inputs included population-based rates (from 2000 to 2009) of MA-RSVi in each healthcare setting, immunization uptake, time required to reach partial or full protection, efficacy, and duration of protection. We used 95% confidence intervals of MA-RSVi rates to generate a range of impact estimates.

Results. At baseline (without intervention), we estimated 54,523 RSV-associated hospitalizations (range 45,129–64,148), 141,646 ED visits (range 117,358–166,132) and 410,205 outpatient clinic visits (range 339,535–480,681) occur among infants