1458. Effectiveness of Influenza Vaccine in Preventing Death among Ontario Residents Aged ≥65 Years during 20 Seasons

David Shay, MD, MPH[1]; Benjamin Ridenhour, PhD[2]; Michael Campitelli, MSc[3] and Jeffrey C. Kwong, MD[3]; [1]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, [2]Dept of Biological Sciences, University of Idaho, Moscow, Idaho, [3]Institute for Clinical Evaluative Sciences, Toronto, ON, Canada

Session: 161. Influenza and Influenza Vaccines
Friday, October 6, 2017: 12:30 PM

Background. Estimation of influenza vaccine effectiveness (VE) among older adults at high risk of serious complications of influenza infection is challenging. These challenges include identifying and adjusting for potential confounders. The rarity of documented influenza deaths, even among individuals at greatest risk, makes VE assessment for this outcome particularly difficult. Thus, population-level linkages of public health system records are helpful in estimating VE for preventing death.

Methods. We conducted a retrospective cohort study from 1993 through 2013 among community-dwelling residents of Ontario aged ≥65 years. Eligible subjects were registered with Ontario's publicly funded health insurance program, which provided universal, free access to physician services, hospital care, and vaccines; we excluded those with no contact with the health system during the prior 3 years. We assessed influenza VE for preventing death from any cause and death for which the primary cause was a respiratory or circulatory condition. Influenza vaccination was determined using physician and pharmacist billing claims. Temperature and influenza virus detection data were collected from provincial sources. Ratio-of-ratios models were used to estimate VE, by comparing marginal changes in outcome rates among vaccinated and unvaccinated groups at various levels of influenza circulation. We evaluated several methods of characterizing temporal variation in influenza circulation and several geographic scales for using influenza and temperature data in VE estimation models.

Results. During the 20-year study period, we estimated VE among a mean of 1.39 million subjects each season, of whom a mean of 51.9% were vaccinated. During weeks of high influenza A circulation, we estimated that VE for the prevention of any death was 16% (95% CI -6% to 38%) and for the prevention of a respiratory or circulatory death was 21% (95% CI 2% to 40%). The precision of VE estimates improved when regional-level rather than Ontario-wide temperature data were used.

Conclusion. During weeks of influenza A circulation over 20 seasons, we found that modest but significant reductions in deaths with an underlying respiratory or circulatory cause occurred among Ontario residents aged ≥65 who received an influenza vaccine.

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

1459. The Pregnancy Vaccine Effectiveness Network (PREVENT): Establishing a Multi-Country Cohort to Estimate Vaccine Effectiveness (VE) against Hospitalized Influenza During Pregnancy

Sarah Ball, MPH, ScD[1]; Allison Naleway, PhD[2]; Jeffrey C. Kwong, MD[3]; Annette K. Reagan, PhD, MPH, MinfDis[4]; Kimberley Simmonds, PhD[5]; Becca Feldman, ScD, MS[6]; Eduardo Azziz-Baumgartner, MD, MPH[7]; Brandy Wyant, MPH[1]; Nicola P. Klein, MD, PhD[8]; Deshayne Fell, PhD[9]; Paul Effler, MD, MPH[10]; Stephanie Booth, MPH[5]; Mark Katz, MD[6]; Fatimah S. Dawood, MD[7]; Patricia Shifflett, RN, MS[1]; Michael L. Jackson, PhD, MPH[11]; Sarah Buchan, ScH, MSc[3]; Avram Levy, PhD[6]; Steven Drews, PhD[5]; Shikha Garg, MD, MPH[7]; Stephanie Irving, MHS[2]; Margaret L. Russell, MD PhD[12]; Edwin Lewis, MPH[8]; Bradley Crane, MS[2]; Sharareh Modaressi, MD, MPH[8]; Matthew Slaughter, MSBA[2]; Kristin Goddard, MPH[8] and Mark G. Thompson, PhD[7]; [1]Abt Associates, Cambridge, Massachusetts, [2]Kaiser Permanente Center for Health Research, Portland, Oregon, [3]Institute for Clinical Evaluative Sciences, Toronto, ON, Canada, [4]Curtin University, Perth, Australia, [5]University of Calgary, Calgary, AB, Canada, [6]Clalit Research Institute, Tel Aviv, Israel, [7]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, [8]Kaiser Permanente Vaccine Study Center, Oakland, California, [9]Ottawa Hospital Research Institute, Ottawa, ON, Canada, [10]Communicable Disease Control Directorate, Perth, Australia, [11]Kaiser Permanente Washington Health Research Institute, Seattle, Washington, [12]Community Health Sciences, University of Calgary, Calgary, AB, Canada

Session: 161. Influenza and Influenza Vaccines
Friday, October 6, 2017: 12:30 PM

Background. Pregnant women are at greater risk of complications from influenza (flu) infection than the general population. Although vaccination is an effective method to prevent influenza, the vaccine is underutilized during pregnancy. A challenge to maternal flu vaccination is the paucity of data about the effectiveness of inactivated influenza vaccines (IIV) in preventing severe outcomes in pregnant women. To inform policy and address this knowledge gap, CDC developed a multi-country collaboration to investigate the preventive value of IIV during pregnancy during multiple flu seasons. We present the progress to date of this Network.

Methods. PREVENT was established in April 2016 to: i) estimate incidence of influenza and vaccination rates; ii) describe epidemiologic characteristics associated with illness; and iii) estimate IIV effectiveness in preventing hospitalizations during pregnancy associated with RT PCR -confirmed influenza. We selected sites that could identify the population of women known to be pregnant during flu seasons and integrate their hospitalization data, clinical laboratory testing, and vaccination records. We will assess VE using the case test-negative control design and use meta-analyses to pool VE estimates across sites and account for significant differences. Primary analyses will be completed by August 2017.

Results. Seven sites in Australia, Canada, Israel, and the US were selected; a protocol and data dictionary were finalized. We identified 1,024 pregnant women hospitalized with acute respiratory illness and RT-PCR tested, during six influenza seasons (2010–11 through 2015–16). Of the qualifying women, 550 (54%) tested positive for flu. Positivity varied by site (range 41% (US)–61.8% (Ontario, CAN)), and vaccination coverage varied across sites and seasons (range 7.3% (Ontario, CAN)–46% (US)). Analyses will examine flu season characteristics, vaccination patterns, and clinical and birth outcomes related to respiratory illness during pregnancy and flu incidence.

Conclusion. Laboratory-confirmed influenza hospitalization during pregnancy is a relatively low-frequency event. Pooling data across multiple sites offers a way to estimate VE against severe influenza outcomes in pregnant women that is informative to influenza vaccine policy.

Disclosures. **A. Naleway**, MedImmune: Investigator, Research grant; Pfizer: Investigator, Research grant; Merck: Investigator, Grant recipient; **N. P. Klein**, GSK: Investigator, Research grant; sanofi pasteur: Investigator, Grant recipient; Merck & Co: Investigator, Grant recipient; MedImmune: Investigator, Grant recipient; Protein Science: Investigator, Research grant; Pfizer: Investigator, Grant recipient; **S. Irving**, Medimmune/AstraZeneca: Investigator, Research support

1460. Are Higher Vitamin D Levels Associated with Improved Influenza Vaccine Immunogenicity and Fewer Healthcare Encounters for Respiratory Infections among Young Adults?

Rachel Lee, MD[1]; Seunghyun Won, PhD[2,3]; Christian Hansen, BS[1] and Nancy Crum-Cianflone, MD, MPH[2,4,5]; [1]Operational Infectious Diseases, Naval Health Res. Ctr., San Diego, California, [2]Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biostatistics, Uniformed Services University of the Health Sciences, Bethesda, Maryland, [3]Henry M. Jackson Foundation for the Advancement of Military Medicine, Bethesda, Maryland, [4]Scripps Mercy Hospital, San Diego, California, [5]Naval Medical Center San Diego, San Diego, California

Session: 161. Influenza and Influenza Vaccines
Friday, October 6, 2017: 12:30 PM

Background. Influenza continues to cause significant morbidity and mortality each year. Vaccination is the primary prevention; however, its effectiveness may be limited even among young, healthy adults. Vitamin D deficiency is highly prevalent and may be associated with poor vaccine immunogenicity and an increased risk for respiratory infections.

Methods. We conducted a retrospective cross-sectional study among young, healthy military personnel to evaluate the associations between 25(OH)D levels with post-influenza vaccination antibody titers (seroprotection defined as a titer of ≥1:40 post-vaccination) and healthcare encounters for respiratory infections during the 2009–2010 influenza season. 25(OH)D levels were analyzed as continuous and categorical [normal (>30 ng/mL), insufficient (20–30 ng/mL), and deficient (<20 ng/mL)] variables. Separate univariate and multivariable logistic regression models were utilized to determine the associations between 25(OH)D levels with antibody responses and respiratory conditions adjusting for possible confounders.

Results. A total of 437 subjects were evaluated. Most participants were young adults (91% were 18–39 years of age), 50% were male, and 56% resided in the southern U.S. Overall, 152 (35%) were vitamin D deficient, 167 (38%) insufficient, and 118 (27%) had normal 25(OH)D levels. There were no demographic differences by 25(OH)3 category. Only 224 (51%) demonstrated a seroprotective anti-influenza post-vaccination titer, which did not vary by categorical 25(OH)D levels [vitamin D deficient vs. normal: OR 1.10 (0.68–1.78) and insufficient vs. normal: OR 1.25 (0.78–2.01)] or continuous vitamin D levels [OR 0.98 (0.84–1.15)]. There were no associations with respiratory diagnoses between the vitamin D groups.

Conclusion. Vitamin D insufficiency and deficiency were highly prevalent despite evaluating a young, healthy adult population. There were no significant associations between 25(OH)D levels and post-vaccination antibody titers or respiratory infections. Strategies for improving influenza vaccine responses are needed since only one-half of vaccinees demonstrated seroprotective anti-influenza titers.

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

1461. The Influence of Mandatory Vs. Non-Mandatory Influenza Vaccination Policies on Workplace Absenteeism During Respiratory Virus Season

Michael S. Simberkoff, MD, FIDSA[1]; John Frederick, BA[2]; Alexandria Brown, PhD[3]; Derek Cummings, PhD[4]; Charlotte Gaydos, DrPH, FIDSA[5]; Cynthia Gibert, MD, MSc, FIDSA[6]; Geoffrey Gorse, MD, FIDSA[7]; Ann-Christine Nyquist, MD, MSPH, FPIDS[8]; Trish Perl, MD, FIDSA[9]; Connie Price, MD[10]; Lewis J. Radonovich, MD, FIDSA[11]; Nicholas Reich, PhD[12]; Maria Rodriguez-Barradas, MD, FIDSA[13] and Mary Bessesen, MD[14]; [1]VA New York Harbor Healthcare System, New York, New York, [2]Research, VA New York Harbor Healthcare System, New York, New York, [3]University of Masssachusetts, School of Public Health, Amherst, Massachusetts, [4]Department of Biology and Emerging Pathogens Institute;, University of Florida, Gainesville, Florida, [5]Division of Infectious Diseases, Department of Medicine, Johns Hopkins University, Baltimore, MD, [6]Washington, DC, VAMC, Washington, DC, [7]VA St. Louis Healthcare System, St. Louis, Missouri, [8]University of Colorado School of Medicine/Children's Hospital Colorado, Aurora, Colorado, [9]Division of Infectious Diseases; Department of Medicine, University of Texas, Southwestern, Dallas, Texas, [10]Infectious Diseases, University of Colorado School of Medicine/ Denver Health and Hospital, Denver, Colorado, [11]National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Pittsburgh, Pennsylvania, [12]Department of Biostatistics and Epidemiology, School of Public Health, University of Massachusetts Amherst, Amherst, Massachusetts, [13]Infectious Diseases Section, Department of Medicine, Michael E. DeBakey VA Medical Center, Houston, Texas, [14]Medicine, University of Colorado Denver, Aurora, Colorado

Session: 161. Influenza and Influenza Vaccines
Friday, October 6, 2017: 12:30 PM

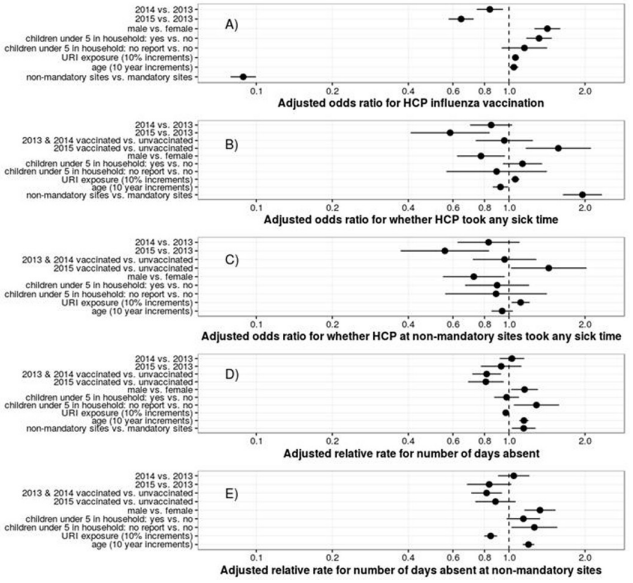
Background. We analyzed data from health care personnel (HCP) participating in the multicenter, cluster randomized Respiratory Protection Effectiveness Clinical Trial (ResPECT) obtained over three viral respiratory (influenza) illness seasons (2012–2015) at three university health systems where influenza vaccination was mandated, and four Veterans Affairs (VA) health systems where it was encouraged but not mandated, to determine the incidence and duration of symptomatic influenza like illness (SILI) associated absenteeism.

Methods. Participants reported SILI daily, vaccination status, and days absent from work due to SILI weekly throughout a 12 week period during the peak viral respiratory illness season each year. Adjusted effects of vaccination and other modulating factors on absenteeism rates were estimated using multivariable regression models.

Results. Overall 97.1%, 96.3%, and 92.1% of participants reported being vaccinated during each of the three study years where the vaccine was mandated, while 67.9%, 63.3%, and 60.4% reported vaccination at sites where it was encouraged but not mandated. The percent of HCP claiming any sick days at mandatory sites was estimated to be 5.9% lower than at non-mandatory sites (95% CI, -12.5, -1.4; $P = 0.02$). Among HCP who reported at least one sick day, the mean number of symptomatic sick days at mandatory sites was 0.74 lower than at non-mandatory sites (95% CI, -1.37, -0.37, $P < 0.01$). After adjusting for possible confounding factors (e.g., season, vaccination statues, mandatory or non-mandatory vaccination site, age, children at home) the relative rate of sick days taken by vaccinated compared with unvaccinated subjects was reduced in the entire cohort of HCP and in the vaccinated compared with unvaccinated subset of HCP from non-mandatory sites (see Figure).

Conclusion. We conclude that influenza vaccination rates are increased and SILI-related absenteeism is decreased at sites where influenza vaccination is mandated and that this should be one of the factors taken into consideration when healthcare facilities make decisions about influenza vaccination policies.

Figure: Adjusted Odds Ratio for Vaccination Status and Taking Any Sick Time, Adjusted Relative Rate of Sick Days Taken.



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

1462. Transcriptome Analysis in Human Breast Milk and Blood after Inactivated or Attenuated Influenza Immunization

Elizabeth P. Schlaudecker, MD, MPH[1]; Johannes Goll, MS[2]; Travis Jensen, BS[2]; Carey Petrie, PhD[2]; Casey Gelber, MS[2]; Phillip Dexheimer, MS[3]; Mark Steinhoff, MD, FIDSA[1] and David I. Bernstein, MD, MA, FIDSA[3]; [1]Division of Infectious Diseases, Global Health Center, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, [2]The EMMES Corporation, Rockville, Maryland, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Session: 161. Influenza and Influenza Vaccines
Friday, October 6, 2017: 12:30 PM

Background. The goal of this study was to identify transcriptomic signatures (RNA-Seq) in human peripheral blood mononuclear cells (PBMCs) and breast milk lymphocyte cells (BMLCs) in response to trivalent inactivated influenza vaccine (TIV) or live attenuated influenza vaccine (LAIV).

Methods. We performed a randomized, double-blind study in breastfeeding women who received either LAIV and intramuscular placebo, or TIV and intranasal placebo. A subset of subjects with available samples (LAIV, $n = 10$ and TIV, $n = 6$) was used for this study. Human milk was collected on days 0, 2, 8, and 28, and blood samples were collected on days 0 and 28. PBMC and BMLC RNA was extracted for RNA-Seq and differentially expressed (DE) gene analysis.

Results. We identified a total of 382 DE BMLC genes in the LAIV group, most of which were up-regulated at day 28. DE genes were preferentially involved in innate immune signaling pathways including cytokine-cytokine receptor interaction, TNF signaling, and NF-kappa B signaling. For TIV, 3 DE genes were identified of which 2 (*IL1A* and *IL1B*) overlapped with LAIV. Response time trends for co-expressed gene clusters by vaccine group showed that LAIV generally induced an early (day 2) up-regulation of innate immune signaling pathway genes, while TIV induced peak innate immune signaling gene responses ahead of LAIV (day 8 vs. day 28). A group of known interferon-alpha/β-inducible genes (*IFIT3*, *OAS3*, *IFI44L*, *MX1*, *OAS2*, *IFIT1*, *IFI6*) showed higher responses at day 2 for TIV but stronger peak levels by day 28 for the LAIV group (Fig 1). While no such innate immune signaling responses were observed in PBMCs at day 28, we identified an up-regulation of IgG gene *(IGHG1* and *IGHG3*) expression in the TIV group (Fig 2).

Conclusion. We observed increased innate immune signaling responses in BMLC but not in PBMC at day 28 for the LAIV group. We hypothesize that breastfeeding extends the innate response to LAIV via mucosal immunity. Gene cluster time trends indicated an earlier innate immune signaling response for TIV. The day 28 increase in *IGHG3* gene expression levels in TIV group PBMCs was correlated with corresponding increases in serum ELISA IgG titers for the influenza B antigen (Fig 3). Additional studies are required to investigate the differences in innate response signaling seen for BMLC and PBMC in this study.