

|                      | IFN- $\gamma$ autoantibody (n=18) |            | healthy adult (n=18) |           | p-value <sup>b</sup> |
|----------------------|-----------------------------------|------------|----------------------|-----------|----------------------|
|                      | Pre                               | Post       | Pre                  | Post      |                      |
| Tetanus IgG          |                                   |            |                      |           |                      |
| <0.1                 | 7 (38.9%)                         | 2 (11.1%)  | 1 (5.6%)             | 0 (0%)    | 0.151                |
| $\geq 0.1$           | 11 (61.1%)                        | 16 (88.9%) | 17 (94.4%)           | 18 (100%) |                      |
| p-value <sup>w</sup> | 0.025*                            |            | 0.317                |           |                      |
| Diphtheria IgG       |                                   |            |                      |           |                      |
| <0.1                 | 4 (22.2%)                         | 1 (5.6%)   | 13 (72.2%)           | 0 (0%)    | 0.317                |
| $\geq 0.1$           | 14 (77.8%)                        | 17 (94.4%) | 5 (27.8%)            | 18 (100%) |                      |
| p-value <sup>w</sup> | 0.083                             |            | <0.001*              |           |                      |

<sup>b</sup>Mann-Whitney Test (compared between group)

<sup>w</sup>Wilcoxon Signed Ranks Test (compared within group)

**Table 2 Study population with positive serology for tetanus and diphtheria prior and after vaccination**

| History of boosted TT (tetanus IgG; IU/mL) | IFN- $\gamma$ autoantibody (n=6) |           | healthy adult (n=7) |           | p-value <sup>b</sup> |
|--|----------------------------------|-----------|---------------------|-----------|----------------------|
|  | Pre                              | Post      | Pre                 | Post      |                      |
| Unboosted                                  |                                  |           |                     |           |                      |
| <0.1                                       | 4 (66.7%)                        | 2 (33.3%) | 0 (0%)              | 0 (0%)    | 0.027*               |
| 0.1-0.5                                    | 0 (0%)                           | 1 (16.7%) | 3 (42.9%)           | 0 (0%)    |                      |
| 0.5-1                                      | 2 (33.3%)                        | 0 (0%)    | 3 (42.9%)           | 0 (0%)    |                      |
| 1.01-5                                     | 0 (0%)                           | 3 (50%)   | 1 (14.3%)           | 5 (71.4%) |                      |
| >5   | 0 (0%)                           | 0 (0%)    | 0 (0%)              | 2 (28.6%) |                      |
| p-value <sup>w</sup>                       | 0.059                            |           | 0.026*              |           |                      |
| $\geq 0.1$ (Immunized)                     | 2 (33.3%)                        | 4 (66.7%) | 7 (100%)            | 7 (100%)  | 0.111                |
| p-value <sup>w</sup>                       | 0.157                            |           | 1                   |           |                      |
| Boosted 1-5 yr                             |                                  |           |                     |           |                      |
| <0.1                                       | 0 (0%)                           | 0 (0%)    | 0 (0%)              | 0 (0%)    | 0.172                |
| 0.1-0.5                                    | 0 (0%)                           | 0 (0%)    | 0 (0%)              | 0 (0%)    |                      |
| 0.5-1                                      | 2 (40%)                          | 1 (20%)   | 0 (0%)              | 0 (0%)    |                      |
| 1.01-5                                     | 2 (40%)                          | 4 (80%)   | 3 (100%)            | 2 (66.7%) |                      |
| >5   | 1 (20%)                          | 0 (20%)   | 0 (0%)              | 1 (33.3%) |                      |
| p-value <sup>w</sup>                       | 1                                |           | 0.317               |           |                      |
| $\geq 0.1$ (Immunized)                     | 5 (100%)                         | 5 (100%)  | 5 (100%)            | 5 (100%)  | 1                    |
| p-value <sup>w</sup>                       | 1                                |           | 1                   |           |                      |
| Boosted >10 yr                             |                                  |           |                     |           |                      |
| <0.1                                       | 3 (42.9%)                        | 0 (0%)    | 1 (12.5%)           | 0 (0%)    | 1                    |
| 0.1-0.5                                    | 1 (14.3%)                        | 0 (0%)    | 2 (25%)             | 1 (12.5%) |                      |
| 0.5-1                                      | 1 (14.3%)                        | 0 (0%)    | 2 (25%)             | 0 (0%)    |                      |
| 1.01-5                                     | 2 (28.6%)                        | 4 (57.1%) | 3 (37.5%)           | 3 (37.5%) |                      |
| >5   | 0 (0%)                           | 3 (42.9%) | 0 (0%)              | 4 (50%)   |                      |
| p-value <sup>w</sup>                       | 0.015*                           |           | 0.026*              |           |                      |
| $\geq 0.1$ (Immunized)                     | 4 (57.1%)                        | 7 (100%)  | 7 (87.5%)           | 8 (100%)  | 1                    |
| p-value <sup>w</sup>                       | 0.083                            |           | 0.317               |           |                      |

<sup>b</sup>Mann-Whitney Test (compared between group)

<sup>w</sup>Wilcoxon Signed Ranks Test (compared within group)

**Table 3 Subgroup analysis in previous tetanus booster and immune response after dT**

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

## 2710. Novel Analytical Models for Pneumococcal Multiplex Opsonophagocytosis Assay Results from a Healthy Older Adult Population Vaccinated with PCV13

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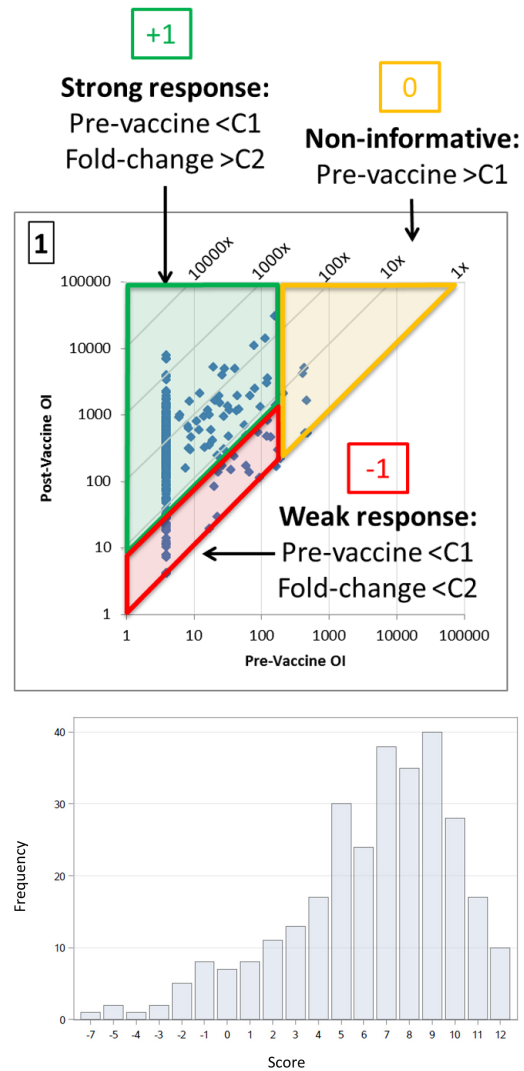
**Background:** The multiplexed opsonophagocytosis assay (MOPA) measures killing of pneumococci by serum antibodies, and is the primary method for measuring pneumococcal antibodies in adults. However, pre-vaccine opsonic activity and vaccine response are highly variable among serotypes and individuals, and there are currently no criteria to define normal MOPA results.

**Methods:** We performed post-hoc analysis of data from  $n = 311$  healthy, pneumococcal-vaccine naïve adults aged 55–74 who received 0.5 mL PCV13, and had MOPA performed for PCV13 serotypes (except serotype 3) at baseline, then on days 29 and 181 post-vaccine (Jackson et al. 2018, Vaccine). MOPA results (reported as opsonic index, or OI) were standardized using pneumococcal reference serum 007sp. Pairwise comparisons of proportions of undetectable baseline OI ( $\leq 4$ ) between serotypes were performed using Pearson's Chi-square. Immunogenicity (mean change in OI at day 29 post-PCV among samples with undetectable baseline OI) was compared between serotypes using one-way ANOVA. We then assigned a score based on cutoffs for pre-vaccine OI (cutoff 1, or C1) and fold-rise in OI at day 29 (cutoff 2, or C2) for each serotype, as shown in Figure 1. The sum of the scores for 12 serotypes was determined for each participant. We plotted the frequency distribution of total scores using different combinations of values for C1 and C2 to visually identify the optimal fit for the left-skewed distribution expected in a healthy population.

**Results:** Serotype 1 had the highest prevalence of undetectable OI at baseline (77.0%,  $P < 0.001$ ), and serotype 19A had the lowest (8.8%,  $P < 0.001$ ). Immunogenicity was highest for serotype 7F (mean change of 18354,  $P < 0.001$  for all comparisons). For vaccine response analysis, C1 = 300 and C2 = 8 produced a left-skewed distribution (Figure 2). Using these cutoffs, the median total score was 7 and the 5th percentile score was -1.

**Conclusion:** Criteria for normal MOPA results can be developed for single-time-point data, or using a scoring system for vaccine response data that integrates pre-vaccine OI and fold-rise in OI. Additional studies in healthy and disease populations are

needed to further optimize diagnostic criteria for discriminating normal vs. abnormal results.



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

## 2711. Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine Against Invasive Pneumococcal Disease in Older Adults

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**Background:** Routine use of 13-valent pneumococcal conjugate vaccine (PCV13) has been recommended for infants since early 2010 and for adults  $\geq 65$  years since 2014 when KPNC began routine use of PCV13 in adults. PCV13 vaccine effectiveness (VE) against vaccine-type invasive pneumococcal disease (IPD) has been demonstrated; however, recent surveillance data have been interpreted as showing limited population-level impact of PCV13 on serotype 3 IPD. We estimated PCV13 VE against IPD due to vaccine serotypes at Kaiser Permanente Northern California (KPNC).

**Methods:** The study period spanned September 2014 through September 2018. The cohort included KPNC members who were aged  $\geq 65$  years with no record of pneumococcal polysaccharide vaccine (PPV23) receipt before age 65 years. We compared IPD cases with KPNC members who were the same age on the date of the positive pneumococcal culture using conditional logistic regression, conditioned on age and date, and controlled for sex, race, KPNC service area and membership history, prior season influenza vaccine receipt, PPV23 receipt after age 65 years, risk factors for IPD, and healthcare utilization.

**Results:** From September 2014 to September 2018, PCV13 vaccine coverage among persons  $\geq 65$  years old increased from  $< 1\%$  to 77%. During the same period, there was a total of 245 IPD cases. For a variety of reasons, we did not have serotype results for 57 (23%) IPD cases, which were excluded from the analysis. There were 61 (25%) PCV13-type IPD cases included in the analysis, of which 33 (14%) were serotype 3. PCV13 VE against PCV13-type serotypes was 68.0% (95% CI: 37.7%, 83.6%;  $P$ -value  $< 0.01$ ), and 53.4% (95% CI: -10.0%, 80.3%;  $P = 0.08$ ) against serotype 3.

**Conclusion:** During the first 4 years of PCV13 vaccination implementation in adults  $\geq 65$  years of age at KPNC, PCV13 provided significant protection against PCV13-type IPD. Further surveillance will allow for more precise estimation of PCV13 VE on overall and serotype 3 IPD over time.

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

**2712. Safety and Immunogenicity of two Doses of ExPEC4V Vaccine Against Extraintestinal Pathogenic *Escherichia coli* Disease in Healthy Adult Participants**

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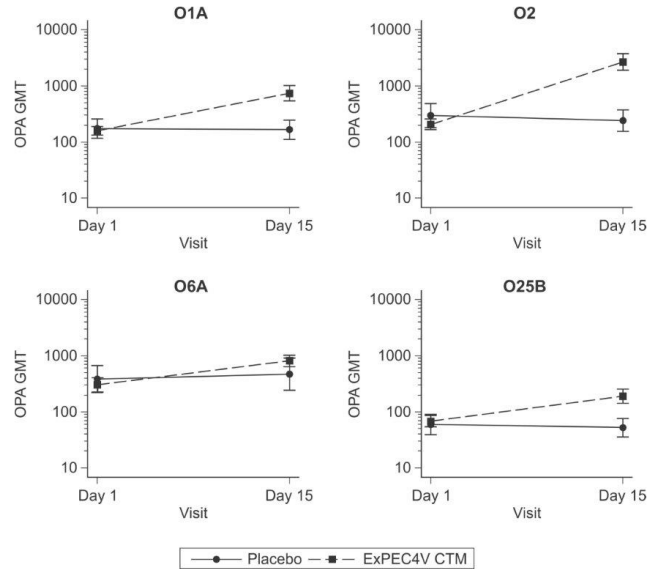
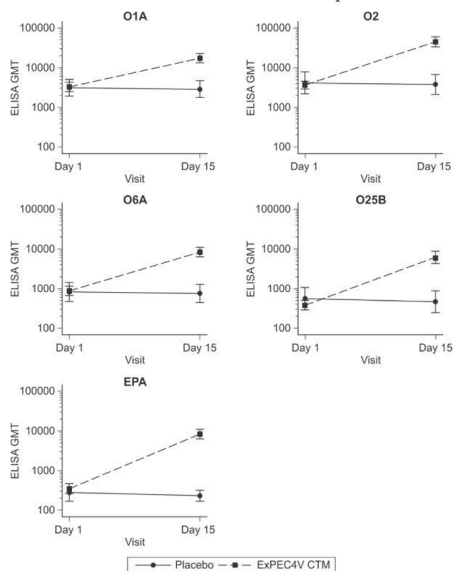
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**Background:** The ExPEC4V vaccine contains 4 *Escherichia coli* O-antigens (O1A, O2, O6A, O25B) conjugated to exotoxin protein A and is being studied for prevention of Invasive Extraintestinal pathogenic *E. coli* (ExPEC) Disease (IED). This phase-2 double-blind study assessed safety and immunogenicity of ExPEC4V Clinical Trial Material (CTM), manufactured via a redesigned process (optimized O1A strain).

**Methods:** Participants ( $\geq 18$  years) in stable health were randomized (3:1) to receive ExPEC4V dose 4:4:4:8  $\mu\text{g}$  PS/serotype or placebo on Day 1 and second vaccination on Day 181 (6 months after first vaccination). Participants will be followed for safety until end of study at Day 360. Reactogenicity and immunogenicity (by ELISA, opsonophagocytic killing [OPA] assays) were evaluated pre-vaccination, and 15 days after first and second vaccinations (Day 195).

**Results:** Of 100 participants randomized (mean age 56, 48% males) and vaccinated (ExPEC4V,  $n = 75$ ; placebo,  $n = 25$ ), 97 completed Day 30. Solicited local AEs were higher for ExPEC4V (38.7%) than placebo (20%); most frequent was pain/tenderness (38.7% vs 20%). Solicited systemic AEs were higher in ExPEC4V (49.3%) than placebo (20%); most frequent was fatigue (32% vs. 12%). No serious or grade 3 solicited local AEs were reported. One participant in ExPEC4V experienced a grade 3 solicited systemic fatigue considered vaccine-related by investigator. ExPEC4V demonstrated immune responses against all serotypes at Day 15. Geometric mean titer effective concentration rank by serotypes was O2 > O1A > O6 > O25B (Figures 1 and 2). At Day 15,  $\geq 82\%$  of participants in ExPEC4V and none in placebo had  $\geq 2$ -fold increase from baseline of ELISA titer for all serotypes. In ExPEC4V,  $\geq 47\%$  had  $\geq 2$ -fold increase from baseline of OPA titer for all serotypes, while 8% in placebo had  $\geq 2$ -fold increase only for O6A. Good correlation was observed between ELISA and OPA across serotypes ( $r \geq 0.76$ ).

**Conclusion:** ExPEC4V elicited robust and functional immune responses across all serotypes and was well tolerated with no vaccine safety findings. This study supports the development of future multivalent ExPEC vaccine to prevent IED.



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**2713. Effectiveness of 23-Valent Pneumococcal Polysaccharide Vaccine in Korean National Population Cohort over 65 Years Old**

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**Background:** Twenty-three valent pneumococcal polysaccharide vaccine (PPSV) has been introduced to the National Immunization Program (NIP) for adults aged 65 years and older in Korea since 2013. We describe the effectiveness evaluation of PPSV among adults against pneumococcal infections including all-cause pneumonia (ACP), pneumococcal pneumonia (PP), and invasive pneumococcal diseases (IPD) using national population cohort.

**Methods:** Vaccination records of the national population, aged 65 years and older, from NIP registry by Korea Centers for Disease Control and Prevention (KCDC) were matched to their corresponding medical records by National Health Insurance Service (NHIS) for retrospective cohort analysis. Adults vaccinated with 1-dose PPSV between 2013 and 2016 were compared with those non-vaccinated. Primary outcomes were hospitalization due to ACP, PP, and IPD. Vaccine effectiveness (VE) adjusted for high risk and underlying conditions was calculated as one minus hazard ratio (HR) using Cox regression.

**Results:** Records of 6,743,002 cohort members were included. Forty-three percent were male, and median age was 75-years. Among the cohort, 3,425,949 (51%) were vaccinated during the study period. Incidence (per 100,000 person-years) of each disease in vaccinated and unvaccinated, respectively, was 2,184 and 1,584 for ACP, 8.9 and 5.4 for PP, and 1.6 and 1.9 for IPD. VE against IPD was 41.7% (95% CI 28.8–52.3) and against IPD sepsis was 53.5% (95% CI 39.8–64.0). PPSV was also protective against ACP with VE 7.2% (95% CI 6.6–7.8). When stratified by age-group, adults aged 65–74 years were better protected from ACP (VE 16.5% [95% CI 15.6–17.3]) compared with older adults aged 75 years or older (VE -0.4% [95% CI -1.2 to 0.4]), while VE was higher in older adults against IPD (VE 47.6% [95% CI 32.4–59.4]) and IPD sepsis (VE 54.9 [95% CI 38.4–66.9]) than in 65–74 years group (IPD VE 30.4% [95% CI 3.4–49.9]; sepsis VE 49.0% [95% CI 19.7–67.6]).

**Conclusion:** Single-dose PPSV strategy for adults in general population is protective against PCV, IPD, and IPD sepsis.

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**2714. *Streptococcus pneumoniae* Nasopharyngeal Carriage in Canadian Adults Hospitalized with Community-Acquired Pneumonia from 2010 to 2017**

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