1382. Varicella Burden Disease in Argentina: 4 Years after National Vaccination Strategy

Silvina Neyro, MD[1]; Maria del Valle Juarez, n/a[2]; Marina Pasinovich, MD[1]; Carolina Rancaño, MD[1]; Nathalia Katz, MD[3]; Gabriela Elbert, MD[1]; Marcela López Yunes, n/a[4]; Daniel Stecher, MD[1]; Verónica Lucconi, MD[1]; Martín Saralegui, n/a[5]; Analía Mykietiuk, Director[6]; Carla Vizzotti, n/a[7]; [1]Ministerio de Salud y Desarrollo Social de la Nación, Capital Federal, Ciudad Autonoma de Buenos Aires, Argentina; [2]Ministry of Heath (Argentina), Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina; [3]Mininsterio de Salud y Desarrollo Social de la Nación, Capital Federal, Ciudad Autonoma de Buenos Aires, Argentina; [4]Ministry of Health (Argentina), Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina; [5]Ministry of Health, Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina; [6]Director of Control for Immunopreventable Diseases, Ministry of Heath (Argentina), Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina; [7]Secretary of Access to Health, Ministry of Halth (Argentina), Ciudad Autonoma de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina

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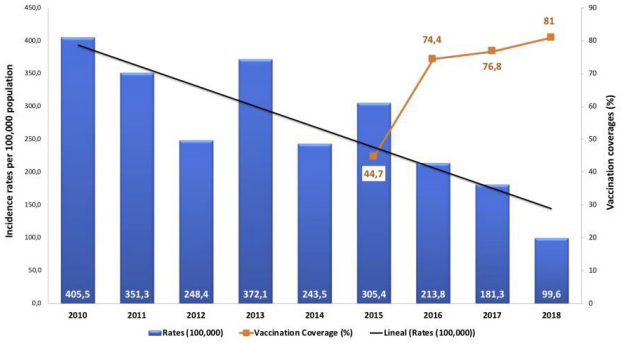
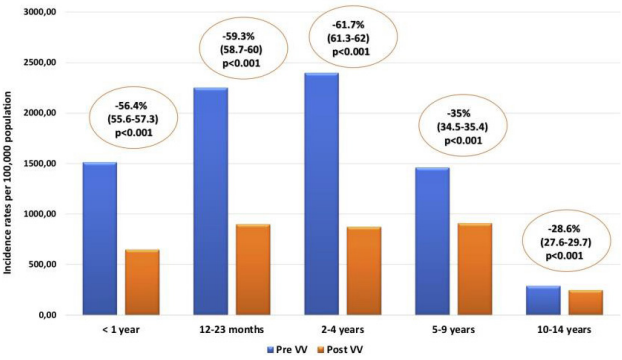
Background. In Argentina, around 150,000-180,000 total Varicella (VZV) cases per year (c/y) are registered; however, underreport exists and some 400,000 cases are estimated to occur annually. Varicella vaccine (VV) was included in the National Immunization Schedule (NIS) in 2015, with a 1-dose schedule administered at 15 months-of-age. We aimed to describe and to compare the epidemiological situation of VZV infections in Argentina in two periods: pre (2010-2014) and post (2016-2018) vaccine introduction in NIS.

Global Incidence rates and vaccine coverages



Incidence rates (age groups)



Methods: Before-and-after study comparing cases and incidence rates (100,000) of varicella reported to the National Health Surveillance System between pre-vaccination period (Pre-VV) and post-vaccination (Post-VV), excluding year of intervention (2015) since it was considered a transition year. Epi Info 7 was used for data analysis.

Results. Vaccination coverage (VC) for 2015 was 44.7%; 74.4% in 2016; 76.8% in 2017 and 81% in 2018 (Figure 1). 728,392 cases of VZV were notified (R=363.1) in Pre-VV period and 222,305 cases in Post-VV (R=180.7), with a global incidence rate reduction of 49% (95%CI= 40.9-56.2; p< 0.001). Both 12-24 months of age and 2-4 years old groups (Pre-VV R=2,253 and Post-VV R=900; Pre-VV R=2,399 and Post-VV R=875, respectively) showed the greatest reductions in incidence rates (-59.3% [95%CI 58.7-60] p< 0.001 and -61.7% [95%CI 61.3-62] p< 0.001). Age groups not affected by vaccination (< 1 year, 5-9 years and 10-14 years) presented minor but significant reductions (-56.4% [95%CI 55.6-57.3] p< 0.001; -35% [95%CI 34.5-35.4] p< 0.001; and -28.6% [95%IC 27.6-29.7] p< 0.001 respectively) (Figure 2).

Conclusion. A decreasing trend in VZV number of cases and incidence rates was observed, especially in children less than 5 years old, despite suboptimal VC. The reduction of VZV cases in non-vaccinated age groups could be related to a decline in the transmission risk. Improving VC will likely reflect a greater impact on the burden of disease.

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

1383. Characterizing Real-world Patterns of Early Childhood Vaccination

Anne M. Butler, PhD[1]; Jason Newland, MD, MEd, FPIDS[2]; John Sahrmann, MS[2]; Caroline O'Neil, MA, MPH[2]; Sena Sayood, MD[3]; Leah McGrath, PhD[4]; [1]Washington University in St. Louis, St. Louis, Missouri; [2]Washington University, St. Louis, Missouri; [3]Washington University School of Medicine, St. Louis, MO; [4]NoviSci, Inc, Durham, North Carolina

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Background. Vaccine hesitancy is increasingly common, but more information is needed on patterns of childhood vaccination. We characterized patterns of vaccine delay among commercially-insured children in the U.S.

Methods. Using the IBM MarketScan Commercial Database, we identified infants who received a timely first dose of diphtheria-tetanus-acellular pertussis (DTaP) vaccine from October 2009 to June 2017. We used CPT codes to collect vaccine administration history on antigen, formulation, dose, and date. We ascertained injectable and oral vaccine antigens (DTaP, polio, pneumococcal conjugate, rotavirus, Haemophilus influenza type b (Hib), measles, mumps, rubella, varicella). Timely receipt was defined as concomitant administration of the CDC-recommended number of antigens during the following time windows: 2, 4, 6, and 12-15 months of age (grace period: -7, +21 days). We generated heat maps to illustrate age distributions at receipt of specific antigens and doses. We created Sankey diagrams to illustrate the number of antigens received concomitantly during each time window and depict transitions to different states over time (e.g., no vaccine delay to vaccine delay). For each antigen and dose, we estimated the cumulative incidence of receipt.

Results. Among 1,066,216 eligible infants, the majority (84%) concomitantly received all 5 CDC-recommended antigens at 2 months of age while others only received 1 (1%), 2 (2%), 3 (4%) or 4 (9%) antigens. Many vaccinations were delayed – 30% and 39% of children did not receive all recommended antigens concomitantly at 4 and 6 months, respectively. The heat map shows wide variation in age at vaccination. For several antigens including Hib, measles, mumps, rotavirus, rubella, and varicella, the cumulative incidence increased steeply at ≥2 time points, suggesting vaccine delay for some infants (e.g., the first dose of Hib was administered to 85% of infants by 2 months of age, with subsequent small but distinct increases at 4, 6, 12, and 15 months of age).

Conclusion. Using real-world data to study early childhood vaccination patterns, we observed evidence of substantial deviation from the CDC-recommended schedule. These results expand current knowledge on the magnitude and timing of antigen- and dose-specific vaccine delay on a population level.

Disclosures. **Jason Newland, MD, MEd, FPIDS**, **Merck** (Grant/Research Support)**Pfizer** (Other Financial or Material Support, Industry funded clinical trial) **Leah McGrath, PhD**, **NoviSci, Inc.** (Employee)

1384. Conceptual Economic Model Methodology for Infant Pneumococcal Conjugate Vaccine Program and its Impact on Antimicrobial Resistance

Raymond Farkouh, PhD[1]; Arianna Nevo, MPH[2]; Jennifer Uyei, PhD, MPH[2]; Benjamin Althouse, PhD, ScM[3]; Cassandra Hall-Murray, PharmD[1]; Joseph Lewnard, PhD[4]; Matthew Wasserman, MSc.[1]; [1]Pfizer, Inc., Collegeville, Pennsylvania; [2]IQVIA, San Francisco, California; [3]Institute for Disease Modeling, Seattle, Washington; [4]University of California Berkeley, Berkeley, California

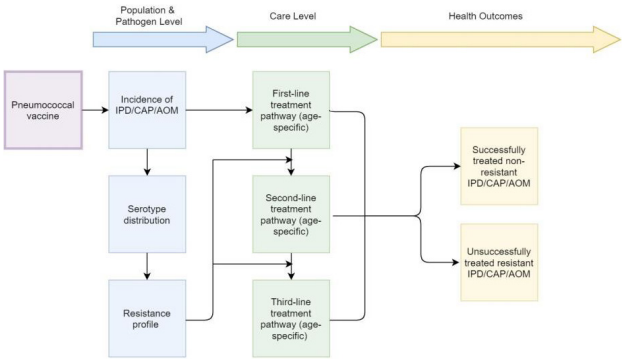
Session: P-63. Pediatric Vaccines

Background. Antimicrobial resistance (AMR) is a global threat to effective prevention and treatment of an ever-increasing range of infections. Pneumococcal conjugate vaccines (PCV) used in infant national immunization programs have been shown to decrease AMR pneumococci. Cost-effectiveness models evaluating the value for money of PCV programs have not considered the economic impact of reducing antimicrobial prescribing or prolonged infections due to treatment failures. Standardized frameworks are needed for models to address outcomes and impact on health resource utilization related to AMR.

Methods. We developed a conceptual modeling methodology suitable for a health economic evaluation of an infant PCV program. We considered impact of PCVs on pneumococcal disease (PD) specifically related to clinical management of AMR-PD, including AMR epidemiology, antibiotic prescribing patterns, and healthcare resource utilization. Model inputs were evaluated regarding optimal and available data sources considering the complex nature of AMR at the national, regional, and global level.

Results. The proposed framework considers impact of PCVs on antimicrobial prescribing due to invasive pneumococcal disease (IPD), community acquired pneumonia (CAP), and acute otitis media (AOM) across 3 pathways (Figure 1). The population and pathogen-level pathway describe epidemiology and vaccine impact. The care level pathway describes clinical disease management. The health outcomes pathway characterizes resistant or successfully treated PD costs and quality of life.

Conceptual Economic Model Methodology



Conclusion: We present a generalizable methodology to quantify impact of PCVs on cases and outcomes of PD related to AMR. Modelling vaccine-preventable burden of AMR-PD requires data extrapolations and assumptions due to the myriad of interconnected pathways (i.e. microbiology, epidemiology, environment, health systems). Further work is needed to validate assumptions and linkages across incomplete data sources.

Disclosures. **Raymond Farkouh, PhD**, **Pfizer** (Employee) **Arianna Nevo, MPH**, **Pfizer, Inc.** (Other Financial or Material Support, I am an employee of IQVIA. IQVIA received funding from Pfizer to carry out the project.) **Jennifer Uyei, PhD, MPH**, **Pfizer, Inc.** (Other Financial or Material Support, I am an employee of IQVIA. IQVIA received funding from Pfizer to carry out the project.) **Cassandra Hall-Murray, PharmD**, **Pfizer, Inc.** (Employee) **Joseph Lewnard, PhD**, **Pfizer, Inc.** (Consultant, Grant/Research Support, Advisor or Review Panel member) **Matthew Wasserman, MSc.**, **Pfizer Inc.** (Employee)

1385. Concomitant Administration of Liquid Porcine Circovirus-free Human Rotavirus Vaccine with Routine Pediatric Vaccines Does Not Impact Immune Responses in Infants: Results from a Phase 3, Randomized Trial in the United States

Remon Abu-Elyazeed, MD, PhD[1]; Nicola P. Klein, MD, PhD[2]; Leentje Moerman, PhD[3]; Michael Povey, MSc[3]; Anthony Pruitt, MD[4]; Shelly Senders, MD[5]; Peter Silas, MD[6]; Dan Bi, MD, MPH[3]; [1]GSK, Philadelphia, Pennsylvania, United States, Philadelphia, Pennsylvania; [2]Kaiser Permanente Vaccine Study Center, Oakland, California, United States, Oakland, California; [3]GSK, Wavre, Belgium, Wavre, Brabant Wallon, Belgium; [4]Wee Care Pediatrics, Roy, Utah, United States, Roy, Utah; [5]Senders Pediatrics, Cleveland, Ohio, United States, Euclid, Ohio; [6]Wee Care Pediatrics, Syracuse, UT

Rota-090 Study Group

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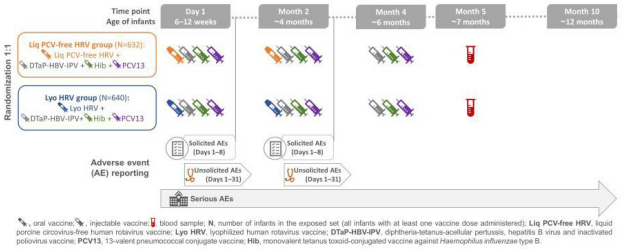
Background. Porcine circovirus type 1 (PCV-1) material was detected in the human rotavirus vaccine (HRV) in 2010. Although no safety risk was identified for infants vaccinated with HRV, a PCV-free HRV (no detection of PCV-1 and PCV-2 according to the limit of the tests used) was developed, which showed comparable immunogenicity and safety profile to the initial HRV. We assessed the non-inferiority of immune responses elicited by routine vaccines (co-)administered with either liquid (Liq) PCV-free HRV or lyophilized (Lyo) HRV, and the immunogenicity and safety of HRVs in infants.

Methods. In this phase 3, randomized, single-blind study (NCT03207750) in the United States, healthy infants aged 6–12 weeks received 2 doses of Liq PCV-free HRV or Lyo HRV at study month (M)0, M2 and routine vaccines at M0, M2, M4 (**Figure 1**). Co-primary objectives were to hierarchically demonstrate non-inferiority of immune responses to routine vaccine antigens when (co-)administered with Liq PCV-free HRV compared to Lyo HRV, 1 month post-dose 3 of the routine vaccines and to rule out a 10% decrease in seroresponse to pertussis antigens. Immunogenicity and safety of HRVs were also evaluated (**Figure 1**).

Figure 1. Study design



, oral vaccine; , injectable vaccine; blood sample; **N**, number of infants in the exposed set (all infants with at least one vaccine dose administered); **Liq PCV-free HRV**, liquid porcine circovirus-free human rotavirus vaccine; **Lyo HRV**, lyophilized human rotavirus vaccine; **DTaP-HBV-IPV**, diphtheria-tetanus-acellular pertussis, hepatitis B virus and inactivated poliovirus vaccine; **PCV13**, 13-valent pneumococcal conjugate vaccine; **Hib**, monovalent tetanus toxoid-conjugated vaccine against *Haemophilus influenzae* type B.

Results. 1272 infants were vaccinated and 990 (Liq PCV-free HRV: 489; Lyo HRV: 501) were included in the per-protocol set. All statistical criteria were met for the 2 co-primary objectives (**Table 1**). Seroprotection/seropositivity rates were ≥ 99.3% for all DTaP-HBV-IPV antigens, ≥ 97.4% for Hib and ≥ 90.8% for most PCV13 serotypes. Geometric mean concentrations/titers for the routine vaccine antigens were comparable between groups (**Table 2**). 76.3% of infants in Liq PCV-free HRV and 78.9% in Lyo HRV had anti-RV antibody concentration ≥ 20 U/mL. The incidence of solicited (**Figure 2**) and unsolicited adverse events (AEs) were similar in both groups. Of 75 serious AEs (SAEs), 2 (Lyo HRV: abdominal distension; intussusception) were considered vaccine-related by investigator; 1 fatal SAE (Liq PCV-free HRV: sudden infant death syndrome) was considered non-vaccine related by investigator.

Table 1. Non-inferiority of the immune responses to routine vaccine antigens when (co-)administered with HRV (Liq PCV-free HRV vs Lyo HRV) and exclusion of 10% decrease in seroresponse to pertussis antigens, 1 month post-dose 3 (per-protocol set)

Statistical criteria	Antigen	Assessed outcome
To assess non-inferiority of the immune responses to routine vaccines antigens when (co-)administered to Liq PCV-free HRV *vs* Lyo HRV		
DTaP-HBV-IPV		
LL of 2-sided standardized asymptotic 95% CI for the difference in % of infants with anti-D and anti-T antibody concentration ≥0.1 IU/ml between groups ≥-10.00%	Anti-D Anti-T	*Liq PCV-free HRV – Lyo HRV % difference* -0.00 (95% CI: **-0.80**–0.79) -0.00 (95% CI: **-0.79**–0.77)
LL of 2-sided standardized asymptotic 95% CI for the difference in % of infants with anti-HBs antibody concentration ≥10 IU/mL between groups ≥-10.00%	Anti-HBs	*Liq PCV-free HRV – Lyo HRV % difference* -0.65 (95% CI: **-1.90**–0.16)
LL of standardized asymptotic 95% CI for the difference in % of infants with anti-polio type (1, 2, 3) antibody titers ≥8 ED_{50} between groups ≥-5.00%	Anti-polio 1 Anti-polio 2 Anti-polio 3	*Liq PCV-free HRV – Lyo HRV % difference* 0.21 (95%CI: **-0.60**–1.15) -0.01 (95%CI: **-1.02**–0.98) -0.00 (95%CI: **-0.87**–0.84)
LL of the 2-sided 95%CI of anti-PT, anti-FHA and anti-PRN antibody GMC ratio ≥0.67	Anti-PT Anti-FHA Anti-PRN	*Liq PCV-free HRV/Lyo HRV GMC ratio* 0.94 (95%CI: **0.86**–1.03) 1.00 (95%CI: **0.92**–1.08) 0.97 (95%CI: **0.86**–1.10)
PCV13		
LL of the 2-sided 95% CI of antibody GMC ratio ≥0.5, for each of the 13 pneumococcal serotypes	Anti-PnPS 1 Anti-PnPS 3 Anti-PnPS 4 Anti-PnPS 5 Anti-PnPS 6A Anti-PnPS 6B Anti-PnPS 7F Anti-PnPS 9V Anti-PnPS 14 Anti-PnPS 18C Anti-PnPS 19A Anti-PnPS 19F Anti-PnPS 23F	*Liq PCV-free HRV/Lyo HRV GMC ratio* 1.03 (95%CI: **0.93**–1.14) 1.00 (95%CI: **0.91**–1.11) 0.99 (95%CI: **0.90**–1.09) 1.05 (95%CI: **0.94**–1.17) 1.01 (95%CI: **0.92**–1.12) 0.96 (95%CI: **0.83**–1.12) 0.99 (95%CI: **0.91**–1.08) 1.03 (95%CI: **0.93**–1.14) 1.00 (95%CI: **0.89**–1.13) 1.03 (95%CI: **0.92**–1.14) 1.04 (95%CI: **0.93**–1.15) 1.03 (95%CI: **0.95**–1.12) 0.98 (95%CI: **0.87**–1.10)
Hib		
LL of 2-sided standardized asymptotic 95% CI for the difference in % of infants with anti-PRP antibody concentration ≥0.15 µg/mL between groups ≥-5.00%	Anti-PRP	*Liq PCV-free HRV – Lyo HRV % difference* 0.17 (95%CI: **-1.94**–2.28)
LL of 2-sided standardized asymptotic 95% CI for the difference in % of infants with anti-PRP antibody concentration ≥1 µg/mL between groups ≥-10.00%	Anti-PRP	*Liq PCV-free HRV – Lyo HRV % difference* -0.88 (95%CI: **-5.75**–3.99)
To rule out a 10% decrease in seroresponse to pertussis antigens when (co-)administered to Liq PCV-free HRV *vs* Lyo HRV		
p-value* <0.025 for testing H0 (seroresponse in the Liq PCV-free HRV group <85%) to anti-PT, FHA, PRN. Seroresponse was defined as the % of infants with antibody concentration above a threshold that leads to 95% seroresponse in the Lyo HRV group.	Anti-PT Anti-FHA Anti-PRN	*p-value* **<0.0001** **<0.0001** **<0.0001**

DTaP-HBV-IPV, diphtheria-tetanus-acellular pertussis, hepatitis B and inactivated poliovirus combination vaccine; **Hib**, monovalent tetanus toxoid-conjugated vaccine against *Haemophilus influenzae* type B; **PCV13**, 13-valent pneumococcal conjugate vaccine; **Liq PCV-free HRV**, liquid porcine circovirus-free human rotavirus vaccine; **Lyo HRV**, lyophilized human rotavirus vaccine; **LL**, lower limit; **CI**, confidence interval; **IU**, international units; **D**, diphtheria; **T**, tetanus; **HBs**, hepatitis B surface antibody; ED_{50}, median effective dose; **PT**, pertussis toxoid; **FHA**, filamentous hemagglutinin; **PRN**, pertactin; **GMC**, geometric mean concentration; **PRP**, polyribosyl-ribitol phosphate; **PnPS**, pneumococcal capsular polysaccharide; **H0**, null hypothesis.
* The p-value was calculated by integrating on the p-values of 1-sided tests (null hypothesis: seroresponse in the Liq PCV-free HRV group ≤85%) and the posterior probability of the threshold in the Lyo HRV group.