Characterizing Real-world Patterns of Early Childhood Vaccination

Anne M. Butler[1], Jason G. Newland[1], John M. Sahrmann[1], Caroline A. O'Neil[1], Sena Sayood[1], Leah J. McGrath[2]

[1] Washington University School of Medicine, St. Louis, Missouri, USA; [2] NoviSci, Durham, North Carolina, USA.

BACKGROUND

- Vaccine hesitancy – defined as delaying or skipping vaccines - is increasingly common.
- Knowledge is limited on the effects of delayed vaccine schedules.
- Prior to performing studies that compare the effects of recommended versus delayed vaccine schedules, more information is needed on patterns of childhood vaccination.

OBJECTIVE

- To characterize patterns of vaccine delay among commercially-insured children in the United States.

METHODS

- **Data Source**: IBM® MarketScan® Commercial Database (2009-2017)
- **Study Population**: Infants who received a timely first dose of diphtheria-tetanus-acellular pertussis (DTaP) vaccine at 38-92 days of age between October 1, 2009 and June 30, 2017. Infants with contraindications to vaccination during the baseline period (0-37 days of age) were excluded.
- **Study Design:** Cohort study where the index date was anchored on the earliest timely dose of a 2-month vaccine (Table 1); follow-up occurred from the index date and the earliest of: 580 days of age, health plan disenrollment, or December 31, 2017.
- **Vaccine Ascertainment:**
  - CPT codes were used to collect vaccine administration history, including antigen, formulation, dose, and date of administration.
  - The following injectable and oral vaccine antigens were ascertained: DTaP, polio, pneumococcal conjugate, rotavirus, *Haemophilus Influenza* type b (Hib), measles, mumps, rubella, and varicella.
  - Timely receipt was defined as concomitant administration of the CDC-recommended number of antigens (Table 1) during four time windows (2, 4, 6, and 12-15 months of age), allowing a grace period of -7, +21 days (Figure 1).
- **Statistical Analysis**:
  - 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 using inverse probability of censoring weights.

Table 1: CDC-Recommended Vaccine Antigens by Age.

Age	2 Months	4 Months	6 Months	12-15 Months
No. of Antigens	5	5	4	6
Recommended Antigens	DTap, PCV, IPV, RV, Hib	DTap, PCV, IPV, RV, Hib	DTap, PCV, RV, Hib	M, M, R, VAR, PCV, Hib

Figure 1. Time windows for determination of timely vaccination receipt

RESULTS

- **Study Population:**
- Among 1,081,799 eligible infants, the median person-time of follow-up was 15.8 months; IQR, 6.6-17.3].
- The majority of vaccinations were administered by a pediatrician (77.9%).
- The majority of infants in the cohort lived in an urban area (89.5%).
- During the baseline period, 2.9% of infants in the cohort had an emergency department visit and 1.3% had an overnight hospitalization.
- **Patterns of Vaccine Utilization:**
- Most infants (84%) received all 5 CDC-recommended antigens concomitantly at 2 months of age; others only received 1 (1%), 2 (2%), 3 (4%), or 4 (9%) antigens on the same date.
- The proportion of infants receiving all recommended antigens on the same day was suboptimal, and worsened with increasing age, from 82% at 2 months to 71% at 4 months to 61% at 6 months (Figure 2).
- The distribution of number of antigens was most variable at 12-15 months.
  - This may, in part, reflect provider choice about antigens administered at 12 vs. 15 months because CDC allows a wider time frame for vaccine administration.
  - During the 12-15 month window, 36% of infants received 4 antigens concomitantly and 23% received 5 antigens concomitantly.
- Some of the cumulative incidence plots showed little variation in the timing of vaccine administration, while others showed a lot of variation (Figure 3).
  - This pattern was generally consistent for antigens administered at 2 and 4 months.
  - Variation in timing increased with advancing age.
- When cumulative incidence plots were stratified by timeliness of previous dose of the same antigen, a gap in timely receipt of subsequent doses were observed for infants who did vs. did not receive a timely previous dose (Figure 4).
  - This gap then widened for the next dose in the series.

DISCUSSION

- Using real-world data to study early childhood vaccination patterns, we observed evidence of substantial deviation from the CDC-recommended schedule, consistent with previous reports of vaccine hesitancy.
- The proportion of children receiving all recommended antigens on the same day was suboptimal, and more likely with increasing age.
- The risk of vaccine delay was higher among children who delayed earlier doses of that antigen.
- Results can be used to design comparative studies of vaccine schedules and to inform future interventions to increase timely vaccination.

Figure 2. Sankey Diagram Illustrating Common Sequences of Vaccine Administration

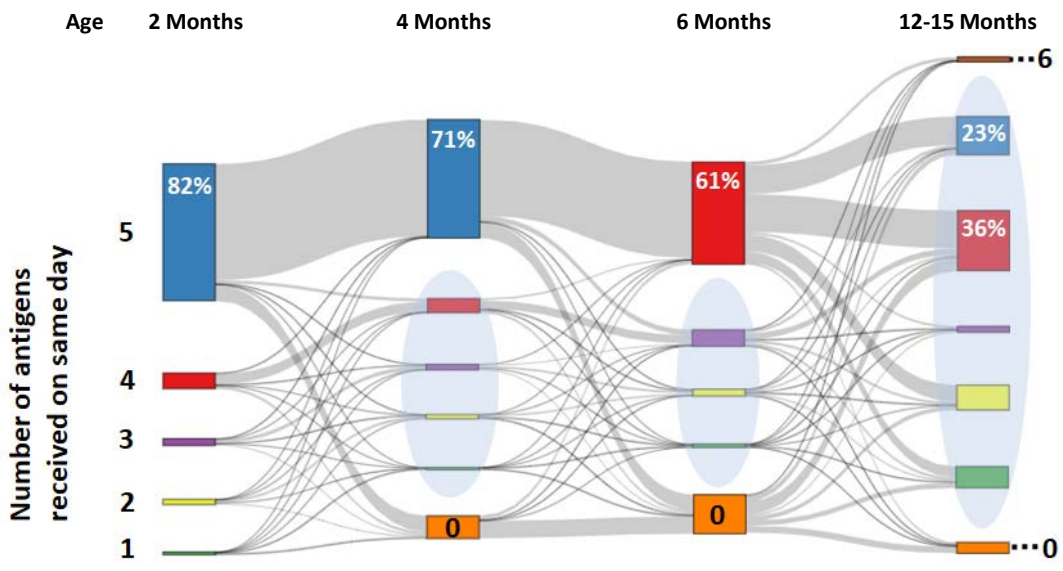


Figure 3. Spectrum of Variation in Timing of Administration

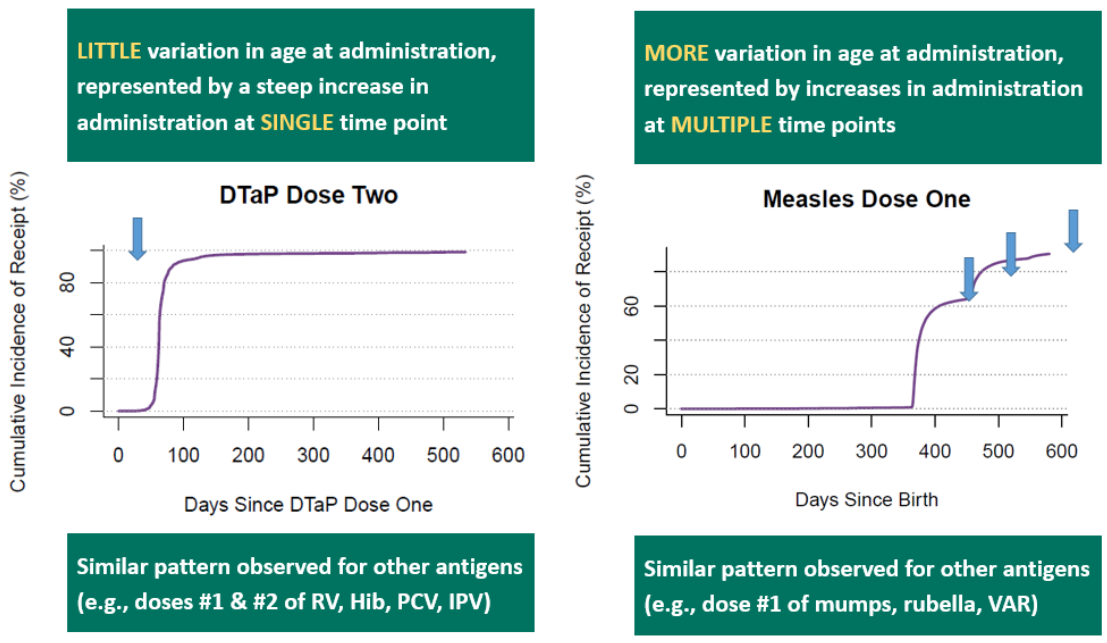
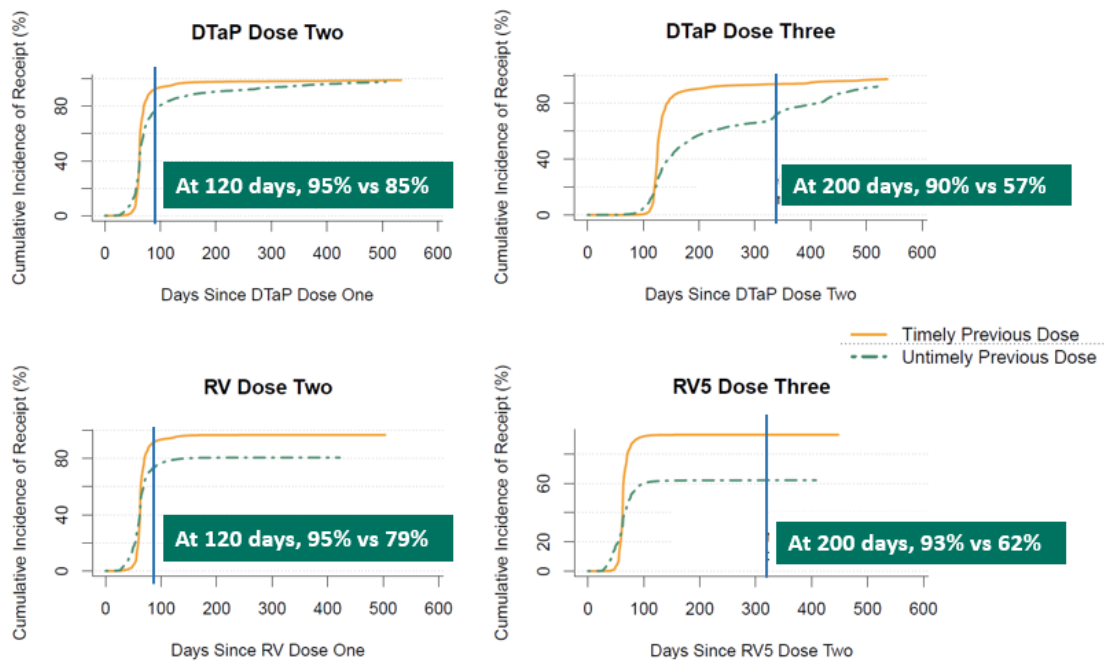


Figure 4. Cumulative Incidence of Subsequent Vaccine Dose Receipt Stratified by Timeliness of Previous Dose.



DISCLOSURES

- This project was supported by The Center for Health Economics and Policy Pilot Funding Program, Institute for Public Health at Washington University in St. Louis; The Washington University Institute of Clinical and Translational Sciences (grant UL1TR000448 from the National Center for Advancing Translational Sciences of the National Institutes of Health); National Center for Advancing Translational Sciences (NCATS), NIH under award number KL2 TR002346 (AMB: career development award scholar).
- The following personal or financial relationships relevant to this presentation existed during the conduct of the study or within the year prior to ICPE 2018: Dr. Newland has received research contracts from Merck on unrelated topics; and Dr. McGrath is an employee of and owns stock in NoviSci.

CONTACT

Anne Mobley Butler, PhD anne.butler@wustl.edu