Timing of Monovalent Vaccine Administration in Infants Receiving DTaP-based Combination Vaccines in the United States

Gary S. Marshall, MD,* Tanaz Petigara, PhD,† Zhiwen Liu, PhD,† Lara Wolfson, PhD,‡ David Johnson, MD, MPH,† Michelle G. Goveia, MD, MPH,† and Ya-Ting Chen, PhD†

Background: The recommended US infant immunization schedule includes doses of diphtheria, tetanus, acellular pertussis (DTaP), inactivated poliovirus (IPV), *Haemophilus influenzae* type b (Hib) and hepatitis B virus (HepB) during the first 6 months of life. Little information is available about the timing of associated, complementary monovalent vaccine administration in infants receiving DTaP-based pentavalent combination vaccines.

Methods: This was a retrospective cohort study of infants born between July 1, 2010, and June 30, 2018, in the US MarketScan commercial claims and encounters database. Descriptive statistics were used to assess vaccine administration patterns. Multivariate logistic regression was performed to explore factors associated with coadministration of DTaP-IPV/Hib and HepB.

Results: Among infants who received DTaP-HepB(IPV) (n = 129,885), 93.7% had claims for at least 2 Hib doses; most (91.5%-98.3%) of these doses were administered on the same day as DTaP-IPV/HeBP doses. Among infants who received DTaP-IPV/Hib (n = 214,172), 95.3% had claims for ≥2 doses of HepB. Although coverage was high, 59.2% received the second HepB dose on the same day as the first DTaP-IPV/Hib dose, and 44.6% received the third dose of HepB on the same day as the third DTaP-IPV/Hib dose. Differences in coadministration of the second and third HepB doses with DTaP-IPV/Hib were associated with the region of residence, provider type, health plan type and coadministration of pneumococcal conjugate vaccine and rotavirus vaccine.

Conclusions: Almost all infants received the appropriate, complementary monovalent vaccine series. However, this study found variability in the timing of HepB doses in relation to DTaP-IPV/Hib doses with many infants not completing the HepB series until 9 months of age.

Key Words: infant, vaccination, combination vaccines, vaccination timeliness, vaccination coverage

(Pediatr Infect Dis J 2022;41:775–781)

Accepted for publication May 19, 2022

From the *Norton Children’s and University of Louisville School of Medicine, Louisville, Kentucky; †Merck & Co., Inc., Rahway, New Jersey; and ‡Sanofi, Swiftwater, Pennsylvania.

This paper was funded by MSP Vaccine Company, a partnership between Merck & Co., Inc., NJ, and Sanofi, Swiftwater, PA.

Y.-T.C., T.F., Z.L., L.W. and M.G.G. are employees of Merck & Co., Inc., NJ; D.J. is an employee of Sanofi, Swiftwater, PA. G.S.M. reports involvement as an investigator and consultant for GSK, Merck, Seqirus, Pfizer and Sanofi and also as a speaker for Sanofi. Address for correspondence: Tanaz Petigara, PhD, 351 N. Sunnynook Pike, North Wales, PA 19454-2505. E-mail: tanaz.petigara@merck.com.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal’s website (www.pidj.com).

Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-No Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 0891-3668/22/4109-0775 DOI: 10.1097/INF.0000000000003609

While routine childhood vaccination has greatly reduced the burden of infectious diseases in developed countries, rates of vaccine refusal or delay have increased, leading to suboptimal coverage and disease outbreaks. In addition to concerns about potential adverse events following vaccination, the number of injections or antigens administered at a single visit and fear of injections are reasons for vaccine hesitancy. Furthermore, healthcare providers themselves may be reluctant to administer multiple injections at a single visit.

Combination vaccines, in which several antigens are administered as a single injection, increase vaccination coverage and timeliness. Since 1999, the Advisory Committee on Immunization Practices (ACIP), American Academy of Pediatrics (AAP), and American Academy of Family Physicians (AAFP) have preferred the use of combination vaccines as compared with the administration of separate component vaccines. The ACIP-recommended infant immunization schedule in the United States includes multiple doses of diphtheria, tetanus, acellular pertussis (DTaP); inactivated poliovirus (IPV); hepatitis B virus (HepB) and *Haemophilus influenzae* type b (Hib) vaccine during the first 6 months of life. Most infants in the United States receive DTaP as one of 2 pentavalent combination vaccines: Pentacel [diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus and *Haemophilus* b conjugate (tetanus toxoid conjugate) vaccine (DTaP-IPV/Hib); Sanofi, Ontario, Canada], or Pediarix [diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (Recombiant) and inactivated poliovirus vaccine (DTaP-HeBP-IPV); GSK, Rixensart, Belgium]. Following the birth dose, monovalent HepB should be administered at 1–2 and 6–18 months of age if DTaP-IPV/Hib is used; if DTaP-HeBP-IPV is used, monovalent Hib should be administered at either 2 and 4 months of age [PedvaxHIB, haemophilus b conjugate vaccine (meningococcal protein conjugate), Merck & Co., Inc., Rahway, NJ] or at 2, 4, and 6 months of age [ActHIB, haemophilus b conjugate vaccine (tetanus toxoid conjugate), Sanofi, Murcy l’Etiele, France] or [Hiberix, haemophilus b conjugate vaccine (tetanus toxoid conjugate), GSK, Rixensart, Belgium].

Little information is available about the timing of associated, complementary monovalent vaccine administration in infants receiving DTaP-based pentavalent combination vaccines. Examining monovalent vaccine administration in relation to DTaP-IPV/Hib and DTaP-HeBP-IPV could provide insights into the potential benefits of a hexavalent DTaP-based vaccine. Pediatric hexavalent vaccines have been licensed and recommended for routine use in Europe for >20 years. A hexavalent vaccine (Vaxelis, DTaP-IPV-Hib-HeBP; Sanofi, Toronto, Ontario Canada for MSP Vaccine Company, Swiftwater, PA) was approved in the United States with a recommended schedule of 2, 4 and 6 months.

METHODS

Study Design

This was a retrospective, observational cohort study using de-identified administrative claims records. Infants who received DTaP-IPV/Hib were assessed for receipt and timing of
the HepB vaccine (“HepB”) relative to doses of DTaP-IPV/Hib. Infants who received DTaP-HepB-IPV were assessed for receipt and timing of the Hib vaccine (“Hib”) relative to DTaP-HepB-IPV. As an analysis of de-identified data, this study was not considered human subjects research and was exempt from human subjects committee review and the need for informed consent, per 45 CFR 46.102. All infants were also assessed for receipt and timing of pneumococcal conjugate vaccine (PCV), which is recommended at the same ages (2, 4 and 6 months) as each pentavalent vaccine.

Study Population

The IBM MarketScan Commercial Database and Encounters database contains medical and pharmacy claims data for several million individuals who are employees, spouses and dependents covered under employer-sponsored private health insurance plans.

We included infants born between July 1, 2010, and June 30, 2018, who were continuously enrolled ≥1 year after birth, and who received either ≥3 doses of DTaP-IPV/Hib (the DTaP-IPV/Hib cohort) or ≥3 doses of DTaP-HepB-IPV (the DTaP-HepB-IPV cohort) during the first year of life. Infants were excluded if they received both DTaP-IPV/Hib and DTaP-HepB-IPV or received <3 doses of a DTaP-based pentavalent vaccine. We also excluded premature infants from the DTaP-IPV/Hib cohort since the first dose HepB is often given at 1 month and may impact the timing of subsequent doses.

Variables

In compliance with the Health Insurance Portability and Accountability Act, the study database contains the year, but not date of birth. Infants’ date of birth were determined using an approach similar to that used by Panozzo et al. Newborns were identified by the International Classification of Disease, 9th and 10th Revisions, Clinical Modification (ICD-9-CM/ICD-10-CM) codes for live births (ICD-9-CM codes V30-V39, ICD-10-CM code Z38). For infants with >1 ICD-9-CM/ICD-10-CM code on multiple dates, the date of the first code was assumed to be the birth date. Premature infants (DTaP-HepB-IPV cohort only) were identified by ICD-9-CM code 765.29 and ICD-10-CM code P07.30.

Vaccine administration was identified using Current Procedural Terminology (CPT) codes (Supplemental Digital Content 1, http://links.lww.com/INF/E758). The database does not reliably capture birth doses of HepB; therefore, any HepB claim recorded in the first 28 days of life was assumed to be the first (birth) dose, and infants without HepB codes in the first 28 days of life were assumed to have received HepB at the hospital of birth. This assumption was based on relatively high uptake of the HepB birth dose; estimated vaccine coverage for the birth dose among children born during 2016–2017 was 76%. Any HepB claim from 29 to 169 days following birth was counted as the second HepB dose and assigned to the first dose of DTaP-IPV/Hib; 24 weeks (168 days) is the minimum age to give the last dose of HepB, according to ACIP recommendations. Any HepB claim from 170 days to 30 days following birth was counted as the third HepB dose and assigned to the third dose of DTaP-IPV/Hib. If there was more than one HepB claim identified within 30 days (before or after) of the second DTaP-HepB-IPV dose was assigned to the second DTaP-HepB-IPV dose. Any Hib claim identified 30 days before or any number of days after, up to 12 months from birth, was assigned to the third DTaP-HepB-IPV dose.

A PCV claim was assigned to the first or second DTaP-based pentavalent dose if it was identified before or up to 30 days after the pentavalent dose. A third PCV claim identified before or any number of days after, up to 12 months from birth, was assigned to the third pentavalent dose.

Data Analysis

Analyses were conducted separately for the DTaP-IPV/Hib and DTaP-HepB-IPV cohorts. Demographic characteristics and vaccine administration patterns are presented as frequencies and percentages for categorical variables and as means and standard deviation (SD) values for continuous variables. Univariate and multivariate logistic regression were performed to explore factors associated with coadministration of DTaP-IPV/Hib and Hib on the same day. The dependent variable was receipt of monovalent HepB on the same day as DTaP-IPV/Hib. Independent variables were sex, region of residence, provider type, health plan type, and receipt of PCV or rotavirus vaccine (RV) on the same day as the pentavalent vaccine. Since prior experience with older siblings can either increase parental acceptance of multiple co-administered injections or motivate requests to delay vaccination, we also included the number of children <10 years of age in the family as an independent variable. Multicollinearity was assessed using variance inflation factors. All analyses were performed using SAS version 9.3.

RESULTS

Sample Characteristics

A total of 344,057 infants met the inclusion criteria, 214,172 in the DTaP-IPV/Hib cohort and 129,885 in the DTaP-HepB-IPV cohort (Supplemental Digital Content 3, http://links.lww.com/INF/E758). The demographic characteristics of the 2 cohorts were similar (Table 1).

Timing of HepB in Relation to DTaP-IPV/Hib

The mean (SD) of the number of days between birth and the first dose of DTaP-IPV/Hib was 64.5 (8.8) days (Table 1). The mean number of days separating the first and second and third DTaP-IPV/Hib doses was 65.3 (11.1) and 66.6 (15.6) days, respectively, demonstrating that doses were administered according to the recommended schedule of 2, 4 and 6 months.

Among infants who received DTaP-IPV/Hib, 95.3% had claims for at least 2 doses of HepB. A total of 95.0% of infants who received the first DTaP-IPV/Hib dose also received a HepB dose between 2 and 6 months of age (29–169 days), and 93.0% of infants who received the third DTaP-IPV/Hib dose also received a HepB dose between 7 and 12 months from birth (170–365 days).

Only 59.2% of infants received the second HepB dose on the same day as their first dose of DTaP-IPV/Hib. Fewer than half (44.6%) of infants received the third HepB dose on the same day as the third DTaP-IPV/Hib dose (Fig. 1A). Administration of the third HepB dose was clustered around both 6 and 9 months of age (Fig. 2). The proportion of infants who received the third dose at 9 months increased over time (Supplemental Digital Content 4, http://links.lww.com/INF/E758). Among infants who did not receive DTaP-IPV/Hib and HepB on the same day, the mean time interval between the DTaP-IPV/Hib and HepB doses was 33.1 (10.9) days
Timing of Vaccine Administration

for the first DTaP-IPV/Hib dose and 86.3 (22.4) days for the third DTaP-IPV/Hib dose.

Timing of Hib in Relation to DTaP-HepB-IPV

The mean (SD) number of days between birth and the first dose of DTaP-HepB-IPV was 64.3 (8.8) days (Table 1). The mean number of days between the first and second and second and third DTaP-HepB-IPV doses was 66.0 (11.1) and 67.7 (16.1) days, respectively, again indicating that doses were administered according to schedule.

Among infants who received DTaP-HepB-IPV, 93.7% had claims for at least 2 Hib doses, and 85.9% had claims for at least 3 (Table 1). Almost all (98.3%) infants received Hib on the same day as their first (98.3%), second (97.6%), or third (91.5%) doses of DTaP-HepB-IPV (Fig. 1B).

Timing of PCV in Relation to DTaP-IPV/Hib and DTaP-HepB-IPV

Almost all infants received a PCV dose on the same day as each of their doses of DTaP-IPV/Hib (97.8% for first dose, 97.1% for second and 94.4% for the third dose; Fig. 3A) or DTaP-HepB-IPV (98.1% for first dose, 97.4% for second and 95.4% for the third dose; Fig. 3B).

Factors Associated with Coadministration of HepB and DTaP-IPV/Hib Vaccines

Unadjusted associations between patient demographic, insurance and providers characteristics, and coadministration of HepB and DTaP-IPV/Hib are presented in Supplemental Digital Content 5, http://links.lww.com/INF/E758. All covariates, except for sex, were significant at $P < 0.25$ and included in the multivariate analysis. Variance inflation factor values did not exceed 2, indicating low correlation among covariates.

Differences in coadministration of the second dose of HepB with the first dose of DTaP-IPV/Hib were associated with region of residence, provider type, health plan type, coadministration of PCV and coadministration of RV (Table 2). Infants in the Midwest [odds ratio (OR): 0.70 (95% confidence interval [CI]: 0.69–0.72)] and Northeast [OR: 0.39 (95% CI: 0.38–0.40)] were less likely than infants in the south to receive the second dose of HepB on the same day.
day as the first dose of DTaP-IPV/Hib; those in the west were more likely [OR: 1.30 (95% CI: 1.26–1.34)]. Infants vaccinated by pediatricians [OR: 0.57 (95% CI: 0.56–0.59)] were less likely to receive the second dose of HepB on the same day as the first dose of DTaP-IPV/Hib compared with infants vaccinated by family physicians. Infants enrolled in preferred provider organization (PPO)/exclusive

FIGURE 1. Vaccine administration up to 12 months from birth for (A) DTaP-IPV/Hib and HepB (B) DTaP-HepB-IPV and Hib. A: The percentage of infants receiving HepB before, the same day or after DTaP-IPV/Hib administration. B: The percentage of infants receiving Hib before, the same day or after DTaP-HepB-IPV administration.

FIGURE 2. Timing of HepB administration in relation to DTaP-IPV/Hib administration.
Timing of Vaccine Administration

and consumer-directed health plans (CDHP)/high-deductible health plan (HDHP) [OR: 0.84 (95% CI: 0.81–0.86)] were less likely to receive the second dose of HepB on the same day as the first dose of DTaP-IPV/Hib compared with infants covered under a health maintenance organization (HMO)/point of service. Infants

CDHP indicates consumer deductible health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; POS, point of service; PPO, preferred provider organization; PCV, pneumococcal conjugate vaccine; RV, rotavirus vaccine.

An odds ratio <1 indicates that an infant was less likely to receive HepB and DTaP-IPV/Hib on the same day. An odds ratio >1 indicates that an infant was more likely to receive HepB and DTaP-IPV/Hib on the same day.

TABLE 2. Multivariate Analysis of Factors Associated with Co-administering HepB and DTaP-IPV/Hib

| Variable | HepB Dose 2 on the Same Day as DTaP-IPV/Hib Dose 1 | HepB Dose 3 on the Same Day as DTaP-IPV/Hib Dose 3 |
|----------|-----------------------------------------------|-----------------------------------------------|
|          | Odds Ratio (95% CI) | P       | Odds Ratio (95% CI) | P       |
| Male (referent: female) | 1.00 (0.99, 1.02) | 0.6244 | 1.00 (0.99, 1.02) | 0.6641 |
| Region (referent: south) | Midwest 0.70 (0.69, 0.72) | <0.0001 | 0.67 (0.65, 0.69) | <0.0001 |
|                  | Northeast 0.39 (0.38, 0.40) | <0.0001 | 0.48 (0.47, 0.50) | <0.0001 |
|                  | West 1.30 (1.26, 1.34) | <0.0001 | 1.40 (1.36, 1.44) | <0.0001 |
| Provider type (referent: family practitioner and other) | Pediatrician 0.57 (0.56, 0.59) | <0.0001 | 0.57 (0.55, 0.58) | <0.0001 |
| Health plan type (referent: HMO/POS) | PPO/EPO 0.87 (0.85, 0.89) | <0.0001 | 0.88 (0.85, 0.90) | <0.0001 |
|                  | CHDP/HDHP 0.84 (0.81, 0.86) | <0.0001 | 0.93 (0.90, 0.96) | <0.0001 |
|                  | FFS/unknown 0.95 (0.91, 1.01) | 0.0772 | 1.22 (1.16, 1.29) | <0.0001 |
| Received PCV on the same day as DTaP-IPV/Hib (referent: no) | Received RV on the same day as DTaP-IPV/Hib (referent: no) | 1.40 (1.34, 1.47) | <0.0001 | 1.54 (1.47, 1.61) | <0.0001 |
| Number of children <10 years old in the same family (referent: 0) | 0.99 (0.97, 1.01) | 0.4113 | 0.95 (0.93, 0.97) | <0.0001 |

FIGURE 3. Percentage of infants receiving PCV before, the same day or after administration of (A) DTaP-IPV/Hib and (B) DTaP-HepB-IPV. A: The percentage of infants receiving PCV before, the same day or after DTaP-IPV/Hib administration. B: The percentage of infants receiving PCV before, the same day or after DTaP-HepB-IPV administration.
who received PCV on the same day as the first dose of DTaP-IPV/Hib were more likely to receive the second dose of HepB [OR: 9.79 (95% CI: 8.95–10.72)] on the same day. Infants who received RV on the same day as the first dose of DTaP-IPV/Hib were also more likely to receive the second dose of HepB [OR: 1.40 (95% CI: 1.34–1.47)]. The same factors were associated with coadministration of the third dose of HepB and the third dose of DTaP-IPV/Hib. In addition, infants living in households with one or more siblings under 10 years were less likely to receive the third dose of HepB on the same day as the third dose of DTaP-IPV/Hib [OR: 0.95 (95% CI: 0.93–0.97)].

DISCUSSION

Examining monovalent vaccine administration in relation to DTaP-IPV/Hib and DTaP-HepB-IPV could provide insights into the potential benefits of a hexavalent DTaP-based vaccine. Almost all infants in this study received the appropriate monovalent vaccine series that was complementary to the pentavalent DTaP-based vaccine they received. In addition, almost all infants received the PCV series. For infants receiving DTaP-HepB-IPV, Hib and PCV doses were almost always given on the same day as the pentavalent vaccine, at approximately 2, 4 and 6 months of age. In contrast, only 60% of infants received a HepB dose on the same day as the first DTaP-IPV/Hib dose (around 2 months of age), and fewer than half received a HepB dose on the same day as the third dose of DTaP-IPV/Hib (around 6 months of age).

One potential explanation for this finding is that the recommended timing of Hib doses (2, 4 and, if Hib-tetanus toxoid conjugate is used, 6 months of age) is the same as DTaP-HepB-IPV. The same is true for PCV, the schedule for which matches both pentavalent DTaP-based vaccines. On the other hand, the recommended HepB schedule calls for doses at birth, 1–2 months and 6–18 months of age. While the second and third doses of HepB can potentially align with the DTaP-IPV/Hib schedule, in that HepB (dose 2) at 2 and 6 months (dose 3) would be appropriate, these data suggest that HepB doses for a large number of infants are being separated from doses of DTaP-IPV/Hib. Administration of the third HepB dose was clustered around both 6 and 9 months of age and the proportion of children who received the third dose at 9 months increased over time. To our knowledge, this pattern has not been previously documented and merits further investigation. Infants on a DTaP-IPV/Hib schedule are eligible to receive HepB, PCV and RV at the 6-month visit. Perceived pain and crying due to multiple injections are a common reason for parental requests to delay vaccination.28 As the maximum age for the third RV dose is 8 months, as recommended by the ACIP, it is plausible that the third HepB dose is delayed to the 9-month visit to alleviate parental concerns, and this practice has grown over time. ACIP recommends administering all vaccines for which a person is eligible at the same visit to increase the likelihood of series completion by the appropriate age.28 Nearly 25% of infants in the United States follow an alternative vaccine schedule.29 The use of a hexavalent vaccine in the United States would result in 1–4 fewer injections in the childhood vaccination schedule (depending on the current schedule in use), potentially mitigating a key driver of requests for delays.

Completion of the HepB series by 9 months of age is within the timeframe recommended by the ACIP may have few serious health consequences. However, any delay in vaccination potentially places infants at risk for not completing the series by the appropriate age and vulnerable to disease.21 A hexavalent vaccine, which would ensure completion of the HepB series by 6 months of age, may be most beneficial for infants at high risk for Hep B infection such as infants born to HBsAg+ mothers. However, the COVID-19 pandemic has demonstrated that routine immunization practices can be disrupted on an unprecedented scale. Vaccination rates declined significantly across all recommended pediatric vaccines in the United States in 2020 due to stay-at-home orders and social distancing.22 Despite catch-up efforts, vaccination coverage in the United States has not yet rebounded to pre-pandemic levels and many infants remain vulnerable to vaccine-preventable diseases.23 In this context, the benefits of a hexavalent vaccine, which would eliminate the need for separate HepB or Hib vaccinations before 12 months of age, are more far reaching.

We did not include Medicaid data in our analysis given the potential for under reporting of vaccines for children doses and the variability in state policies and coding practices for Medicaid claims.30 Vaccine coverage among children covered by private insurance is higher than children insured by Medicaid and uninsured children.25 It is possible that the proportion of infants who received the appropriate number of monovalent doses would be lower if this analysis was conducted in a Medicaid or uninsured population. Compliance with well child visits is lower among infants who are publicly insured or uninsured.31 In a retrospective study of mainly publicly insured and uninsured children, the 2-, 4- and 6-month visits were most frequently attended; compliance subsequently declined and rebounded at 5 years.32 Within a commercially insured population, we found differences in coadministration of HepB and DTaP-IPV/Hib were associated with region of residence, provider type, health plan type, and coadministration of PCV and RV. Regional differences could reflect parental requests to “spread out” vaccinations, since vaccine hesitancy, defined as being conflicted about or opposed to getting vaccinated, tends to cluster geographically.33,34 Furthermore, pediatricians may be more willing to comply with parental requests to delay vaccines. A previous survey found that pediatricians were more likely to often or always agree with requests to spread out vaccines compared to family physicians.34 The association between health plan type—for example, PPO/EPO-insured infants were less likely than HMO/POS-insured infants to receive HepB and DTaP-IPV/Hib on the same day—could reflect provider incentives in place for the latter plan type.35 Qualitative studies with parents and providers could be undertaken to further explore these associations. A hexavalent vaccine, by administering all relevant antigens at the same time, would assure timely completion of the HepB series by 6 months of age and reduce disparities by insurance status or other factors.

Several limitations inherent to administrative claims database studies apply to this study. Vaccine administration was derived from CPT codes, which may be recorded inaccurately. Results are limited to vaccine utilization patterns among privately insured infants and may not be generalizable to all infants in the United States. It is possible that there is greater use of interventions to improve vaccination rates, such as patient/parent reminder and recall systems, among privately insured infants. The MarketScan is a US claims dataset that is widely used to examine vaccination coverage and utilization patterns. However, as with all claims databases, there are limitations around the number of variables available for analysis. Finally, in the present analysis, assumptions were made to assign coadministration status of HepB and DTaP-IPV/Hib, which may have resulted in misclassification. We assumed that all infants received a birth dose of HepB; for infants who did not receive a birth dose, labeling the first dose received after 28 days of life as dose 2 may have been inaccurate. Some of these may have been Dose 1. However, claims on the same day for HepB and DTaP-IPV/Hib are likely to truly indicate vaccines given on the same day.

CONCLUSIONS

Almost all privately insured infants received the appropriate, complementary monovalent vaccine series. However, this study
found variability in the timing of HepB doses in relation to DTaP-IPV/Hib doses with many infants not completing the HepB series until 9 months of age. Any vaccination delay potentially places infants at risk for not completing the series by the appropriate age.

ACKNOWLEDGMENTS
The authors thank the ScribCo for medical writing assistance.

REFERENCES
1. van Panhuis WG, Grefenstette J, Jung SY, et al. Contagious diseases in the United States from 1888 to the present. N Engl J Med. 2013;369:2152–2158.
2. Omer SB, Salmon DA, Orenstein WA, et al. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. N Engl J Med. 2009;360:1981–1988.
3. Kempe A, Saville AW, Albertin C, et al. Parental hesitancy about routine childhood and influenza vaccinations: a national survey. Pediatrics. 2016;138:e2016127.
4. Hough-Telford C, Kimberlin DW, Aban I, et al. Vaccine delays, refusals, and patient dismissals: a survey of pediatricians. Pediatrics. 2016;138:e2016217.
5. McKee C, Bohannon K. Exploring the reasons behind parental refusal of vaccines. J Pediatr Pharmacol Ther. 2016;21:104–109.
6. Kennedy A, Basket M, Sheedy K. Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey. Pediatrics. 2011;127(suppl 1):S92–S99.
7. Strine TW, Luman ET, Okoro CA, et al. Predictors of age-appropriate receipt of DTaP dose 4. Am J Prev Med. 2003;25:45–49.
8. Meyerhoff AS, Jacobs RJ, Greenberg DP, et al. Variation in rotavirus vaccination timeliness in a state Medicaid population. Pediatr Infect Dis J. 2007;26:496–500.
9. Baxter AL, Cohen LL, Burton M, et al. The number of injected same-day preschool vaccines relates to preadolescent needle fear and HPV uptake. Vaccine. 2017;35:4213–4219.
10. Meyerhoff A, Jacobs RJ, Greenberg DP, et al. Clinician satisfaction with vaccination visits and the role of multiple injections, results from the COVISE Vaccine Study (Combination Vaccines Impact on Satisfaction and Epidemiology). Clin Pediatr (Phila.). 2004;43:87–93.
11. Marshall GS, Happe LE, Lunacek OE, et al. Use of combination vaccines is associated with improved coverage rates. Pediatr Infect Dis J. 2007;26:496–500.
12. Maman K, Zöllner Y, Greco D, et al. The value of childhood combination vaccines: from beliefs to evidence. Hum Vacc Immunother. 2015;11:2132–2141.
13. Kalies H, Grote V, Verstraeten T, et al. The use of combination vaccines has improved timeliness of vaccination in children. Pediatr Infect Dis J. 2006;25:507–512.
14. Marcy SM. Pediatric combination vaccines: their impact on patients, providers, managed care organizations, and manufacturers. Am J Manag Care. 2003;9:314–320.
15. Happe LE, Lunacek OE, Marshall GS, et al. Combination vaccine use and vaccination quality in a managed care population. Am J Manag Care. 2007;13:506–512.
16. Happe LE, Lunacek OE, Kruzikas DT, et al. Impact of a pentavalent combination vaccine on immunization timeliness in a state Medicaid population. Pediatr Infect Dis J. 2009;28:98–101.
17. Dodd D. Benefits of combination vaccines: effective vaccination on a simplified schedule. Am J Manag Care. 2003;9(1 suppl):S6–12.
18. Combination vaccines for childhood immunization. Recommendations of the advisory committee on immunization practices (ACIP). The American academy of pediatrics (AAP), and the American academy of family physicians (AAFP). Am Fam Physician. 1999;59:2565–74.
19. Rawson H, Crampin A, Noah N. Deaths from chickenpox in England and Wales 1995-7: analysis of routine mortality data. BMJ. 2001;323:1091–1093.
20. Sadzot-Delvaux C, Rentier B, Wutzler P, et al. Varicella vaccination in Japan, South Korea, and Europe. J Infect Dis. 2008;197(suppl 2):S185–S190.
21. Luman ET, Barker LE, Shaw KM, et al. Timeliness of childhood vaccinations in the United States: days undervaccinated and number of vaccines delayed. JAMA. 2005;293:1204–1211.
22. Patel Murthy B, Zell E, Kirtland K, et al. Impact of the COVID-19 pandemic on administration of selected routine childhood and adolescent vaccinations—10 U.S. Jurisdictions, March-September 2020. MMWR Morb Mortal Wkly Rep. 2021;70:840–845.
23. Seither R, Laury J, Mugerwa-Kasujia A, et al. Vaccination coverage with selected vaccines and exemption rates among children in kindergarten—United States, 2020-21 School Year. MMWR Morb Mortal Wkly Rep. 2022;71:561–568.
24. Panozzo CA, Becker-Depps S, Patel V, et al. Patterns of rotavirus vaccine uptake and use in privately-insured US infants, 2006-2010. PLoS One. 2013;8:e73825.
25. Hill HA, Yankey D, Elam-Evans LD, et al. Vaccination coverage by age 24 months among children born in 2016 and 2017—National Immunization Survey-Child, United States, 2017-2019. MMWR Morb Mortal Wkly Rep. 2020;69:1505–1511.
26. Robinson CL, Bernstein H, Poehling K, et al. Advisory committee on immunization practices recommended immunization schedule for children and adolescents aged 18 years or younger—United States, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:130–132.
27. Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. Public Health Rep. 2011;126(suppl 2):135–146.
28. Centers for Disease Control and Prevention. Vaccine recommendations and guidelines of the ACIP. Timing and Spacing of Immunobiologics. 2022; https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html. Accessed May 11, 2022.
29. Hargreaves AL, Nowak G, Frew P, et al. Adherence to timely vaccinations in the United States. Pediatrics. 2020;145:e20190783.
30. Layton JB, Butler AM, Brookhart MA, et al. Variation in rotavirus vaccination coding in state US Medicaid data. Vaccine. 2019;37:2892–2895.
31. Wolf ER, Donahue E, Sabo RT, et al. Barriers to attendance of prenatal and well-child visits. Acad Pediatr. 2021;21:955–960.
32. Wolf ER, Hochheimer CJ, Sabo RT, et al. Gaps in well-child care attendance among primary care clinics serving low-income families. Pediatrics. 2018;142:e20174019.
33. Olive JK, Hotez PJ, Damania A, et al. Correction: the state of the antivaccine movement in the United States: a focused examination of nonmedical exemptions in states and counties. PLoS Med. 2018;15:e1002616.
34. Kempe A, O’Leary ST, Kennedy A, et al. Physician response to parental requests to spread out the recommended vaccine schedule. Pediatrics. 2011;127(suppl 1):S92–S99.