Factors Associated With Coadministration of Pentavalent DTaP-IPV/Hib and Monovalent Hepatitis B Vaccine in the United States

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Background

- The recommended US vaccination schedule includes doses of DTaP, IPV, Hib, and HepB during the first 6 months of life (in addition to PCV13 and RV)
- Most infants receive DTaP as one of two pentavalent combination vaccines (DTaP-IPV/Hib or DTaP-HepB-IPV); stand-alone HepB or Hib are used to complement these combinations to comply with the recommendations
- Previous research has indicated that providers and parents have reservations about administering too many vaccines at one time; this can lead to delayed schedule adherence[1,2]
- Preliminary data from a previous presentation found variability in the timing of the HepB doses in infants receiving DTaP-IPV/Hib.[3] Reasons for the observed variability in the timing of HepB administration have not been investigated

Objectives

- To explore factors associated with coadministration of DTaP-IPV/Hib and HepB on the same day among children <1 year of age

Methods

Study Design

This was a retrospective observational cohort study using administrative claims records of infants in the MarketScan® Commercial Claims and Encounters databases from July 1, 2010, to June 30, 2016

Variables

- Three HepB doses are recommended at birth, 1-2 and 6-18 months, with the last dose valid after 24 weeks from birth and at least 16 weeks between the 2nd and 3rd dose
- HepB birth doses are not registered in the database but were presumed to have been received
- Infants were assessed for HepB claims relative to the first and third DTaP-IPV/Hib doses (**Figure 1**)
  - Any HepB claim from 29 to 169 days following birth was counted as HepB Dose 2 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 Advisory Committee on Immunization Practices (ACIP) recommendations)
  - Any HepB claim from 170 days to 12 months following birth was counted as HepB Dose 3 and assigned to the third dose of DTaP-IPV/Hib
- Vaccine administration was identified using Current Procedural Terminology (CPT) codes

Statistical Analysis

Associations between demographic, provider, and insurance characteristics; receipt of other pediatric vaccines; and coadministration of DTaP-IPV/Hib and HepB were analyzed using multivariate logistic regression in infants who had HepB assigned to DTaP-IPV/Hib

- Dependent variable: received HepB on the same day as DTaP-IPV/Hib
- Independent variables: gender, region, provider type, health plan type, coadministration of PCV13 or RV, having children under 10 years in the same family, and premature birth

Results

Table 1. Baseline Characteristics of Study Cohort That Received DTaP-IPV/Hib and HepB Doses[a]

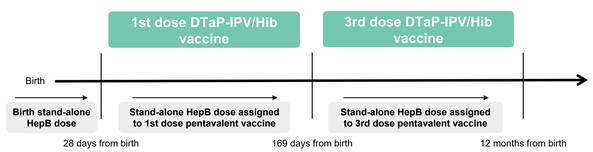
Variable	1st DTaP-IPV/Hib and 2nd HepB (N=165,553)	3rd DTaP-IPV/Hib and 3rd HepB (N=162,217)
Gender		
Male	85,055 (51.4%)	83,468 (51.5%)
Female	80,478 (48.6%)	78,749 (48.5%)
Region in US		
North Central	43,577 (26.3%)	42,224 (26.0%)
Northeast	27,789 (16.8%)	27,171 (16.7%)
West	19,114 (11.5%)	19,003 (11.7%)
South	59,957 (36.2%)	59,215 (36.5%)
Provider type		
Pediatrician	133,263 (80.5%)	130,864 (80.7%)
Family practitioner	7,648 (4.6%)	7,359 (4.5%)
Other	19,607 (11.8%)	19,236 (11.9%)
Health plan type		
HMO/POS	27,519 (16.6%)	26,335 (16.2%)
PPO/EPO	111,649 (67.4%)	108,802 (67.1%)
CDHP/HDHP	20,565 (12.4%)	21,459 (13.2%)
Fee for service/unknown	5,800 (3.5%)	5,621 (3.5%)
Received PCV[b]		
Yes	162,160 (98.0%)	158,855 (97.9%)
No	3,373 (2.0%)	3,362 (2.1%)
Received RV[b]		
Yes	158,252 (95.6%)	154,822 (95.4%)
No	7,281 (4.4%)	7,395 (4.6%)
Number of children <10 years old in the same family		
0	78,128 (47.2%)	75,356 (46.5%)
≥1	87,405 (52.8%)	86,861 (53.5%)
Premature birth		
Yes	9,923 (6.0%)	9,733 (6.0%)
No	155,610 (94.0%)	152,484 (94.0%)

CDHP, consumer-directed health plan; EPO, exclusive provider organization; HDHP, high-deductible health plan; HMO, health maintenance organization; N, number of patients; POS, point of service; PPO, preferred provider organization.

[a]Values presented as N (%) of patients.

[b]Administration on the same day as DTaP-IPV/Hib or not.

Figure 1. Assignment of HepB Doses Up to 12 Months From Birth



A HepB claim from 29 to 169 days following birth was counted as HepB Dose 2 and was assigned to the first dose of DTaP-IPV/Hib. A HepB claim from 170 days to 12 months following birth was counted as HepB Dose 3 and was assigned to the third dose of DTaP-IPV/Hib.

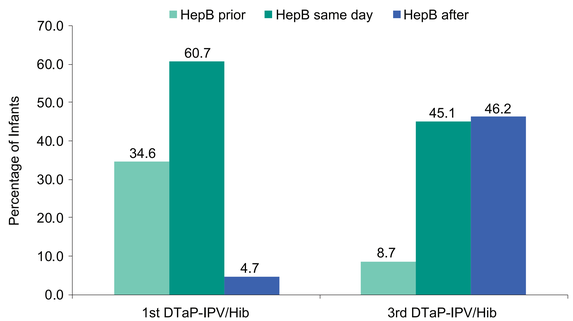
Table 2. Multivariate Analysis of Factors Associated With Administering HepB on the Same Day As DTaP-IPV/Hib

Variables	Comparator	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* value	Odds ratio (95% CI)	*P* value
Gender (referent: female)	Male	1.01 (0.99-1.03)	0.3007	0.997 (0.977-1.018)	0.7884
Region in US (referent: South)	North Central	0.68 (0.66-0.69)	**<0.0001**	0.630 (0.613-0.647)	**<0.0001**
	Northeast	0.38 (0.36-0.39)	**<0.0001**	0.462 (0.448-0.477)	**<0.0001**
	West	1.41 (1.36-1.46)	**<0.0001**	1.332 (1.288-1.379)	**<0.0001**
Provider type (referent: family practitioner and other)	Pediatrician	0.54 (0.52-0.55)	**<0.0001**	0.581 (0.565-0.598)	**<0.0001**
Health plan type (referent: HMO/POS)	PPO/EPO	0.88 (0.86-0.91)	**<0.0001**	0.921 (0.895-0.947)	**<0.0001**
	CDHP/HDHP	0.84 (0.81-0.87)	**<0.0001**	0.937 (0.903-0.973)	**0.0007**
	Fee for service/ unknown	1.11 (1.04-1.18)	0.0012	1.451 (1.366-1.542)	**<0.0001**
Received PCV on the same day as DTaP-IPV/ Hib (referent: no)	Yes	6.96 (6.30-7.70)	**<0.0001**	4.140 (3.740-4.584)	**<0.0001**
Received RV on the same day as DTaP-IPV/ Hib (referent: no)	Yes	1.06 (1.00-1.12)	0.0456	0.971 (0.921-1.023)	0.2672
Number of children <10 years old in the same family (referent: 0)	≥1	1.00 (0.98-1.02)	0.8117	1.009 (0.988-1.030)	0.4049
Premature birth (referent: no)	Yes	0.88 (0.85-0.92)	**<0.0001**	0.960 (0.919-1.003)	0.0680

Bold indicates statistically significant at *P*<0.001.

Interpretation: 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.

Figure 2. Timing of HepB Vaccination Relative to DTaP-IPV/Hib



- Baseline characteristics of infants with claims indicating DTaP-IPV/Hib and HepB doses are shown in **Table 1**; 165,553 had first DTaP-IPV/Hib and second HepB, and 162,217 had 3rd DTaP-IPV/Hib and third HepB
- Among 165,553 infants who received a first DTaP-IPV/Hib dose, 60.7% received **HepB Dose 2** on the same day (**Figure 2**)
- Among 162,217 infants who received a third DTaP-IPV/Hib dose, 45.1% received **HepB Dose 3** on the same day (**Figure 2**)
- Differences in coadministration of DTaP-IPV/Hib and **HepB Dose 2** were associated with region of residence, provider type, health plan type, coadministration of PCV, and premature birth (**Table 2**)
  - Infants in the North Central (OR: 0.68 [95% CI: 0.66-0.69]) and Northeast (OR: 0.38 [95% CI: 0.36-0.39]) regions were less likely than infants in the South to receive the first dose of DTaP-IPV/Hib and HepB on the same day; those in the West were more likely (OR: 1.41 [95% CI: 1.36-1.46])
  - Infants vaccinated by pediatricians (OR: 0.54 [95% CI: 0.53-0.55]) were less likely to receive the first dose of DTaP-IPV/Hib and HepB on the same day compared with infants vaccinated by family physicians
  - Infants enrolled in preferred provider organization (PPO)/exclusive provider organization (EPO) plans (OR: 0.88 [95% CI: 0.86-0.91]) and a consumer-directed health plan (CDHP)/high-deductible health plan (HDHP) (OR: 0.84 [95% CI: 0.81-0.87]) were less likely to receive HepB on the same day as DTaP-IPV/Hib than infants covered under a health maintenance organization (HMO)/point of service (POS)
  - Infants who received PCV on the same day as the first dose of DTaP-IPV/Hib were more likely to receive HepB (OR: 6.96 [95% CI: 6.30-7.70]) that day
- Differences in coadministration of DTaP-IPV/Hib and **HepB Dose 3** were associated with region of residence, provider type, health plan, and coadministration of PCV
  - Infants in the North Central (OR: 0.63 [95% CI: 0.61-0.65]) and Northeast (OR: 0.46 [95% CI: 0.45-0.48]) regions were less likely than infants in the South to receive the third dose of DTaP-IPV/Hib and HepB on the same day; those in the West were more likely (OR: 1.33 [95% CI: 1.29-1.38])
  - Infants vaccinated by pediatricians (OR: 0.58 [95% CI: 0.57-0.60]) were less likely to receive the third dose of DTaP-IPV/Hib and HepB on the same day compared with infants vaccinated by family physicians
  - Infants enrolled in PPO/EPO plans (OR: 0.92 [95% CI: 0.90-0.95]) and CDHP/HDHPs (OR: 0.94 [95% CI: 0.90-0.97]) were less likely to receive the third dose of HepB on the same day as DTaP-IPV/Hib than infants covered under an HMO/POS
  - Infants who received PCV on the same day as the third dose of DTaP-IPV/Hib were more likely to receive HepB Dose 3 (OR: 4.14 [95% CI: 3.74-4.58]) that day

Limitations

- Several limitations inherent to administrative claims database studies apply to this study
  - Vaccine administration was derived from CPT codes, which may have been recorded inaccurately
  - A claim for a vaccine does not guarantee the vaccine was administered
- Assumptions were made to assign coadministration status of HepB and DTaP-IPV/Hib, which may result in misclassification. We assumed that all infants received a birth dose of HepB as the first dose. In reality, some of the second HepB doses per our definition may have been the infant's first dose. However, claims on the same day for HepB and DTaP-IPV/Hib are likely to be accurate and indicate vaccines given on the same day
- The results of this study show trends in vaccination among privately insured infants and may not be generalizable to all infants

Conclusions

- Differences in coadministration of DTaP-IPV/Hib and HepB were associated with region of residence, provider type, health plan type, and coadministration of PCV
- The reasons underlying these differences in coadministration merit exploration
- By assuring coadministration of all relevant antigens at the same time, a hexavalent vaccine containing DTaP, IPV, Hib, and HepB could reduce variability in coadministration

References

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3. Alemayehu B, et al. *Open Forum Infect Dis.* 2019;6(suppl 2):S948-S949.

Disclosures

TP, Y-TC, ZL, and MG are employees of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA; DJ is an employee of Sanofi Pasteur, Swiftwater, PA, USA. GSM reports involvement as an investigator and consultant for GSK, Merck, Seqirus, Pfizer, and Sanofi Pasteur and also as a speaker for Sanofi Pasteur.

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