DTaP-containing combination vaccines use and adherence to the recommended infant-toddler vaccination series among privately insured children in the US

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ABSTRACT

Objective: Despite universal recommendation of the 4-dose diphtheria, tetanus, and pertussis (DTaP) vaccine series, coverage and timeliness in the US remain suboptimal. DTaP-containing combination vaccines are presumed to improve vaccine coverage rates and timeliness, but research supporting this claim is limited. We aimed to investigate the associations between DTaP-containing vaccine use and adherence to the recommended DTaP immunization schedule.

Methods: Using a national claims database in the US, we identified children born between 2009-2016 that received ≥ 1 DTaP-containing vaccine and had ≥ 24 months of enrolment from birth, excluding those with DTaP vaccinations not aligned with approved dose indications. Children were classified by DTaP-containing vaccine receipt: combination vaccines only, stand-alone vaccines only, or a mixture of both. Outcome measures included: 1) completion of the 4-dose series and 2) timeliness of doses received. Outcomes were adjusted for gender, birth year, race, and socioeconomic status.

Results: The study cohort contained 412,441 children. Of these, 167,084 (40.5%) received combination vaccines only, 61,342 (14.9%) received stand-alone vaccines only, and 184,015 (44.6%) received a mixture of both. Combination vaccine recipients were nearly 3 times as likely to complete the 4-dose series (OR 2.93 (95% CI: 2.88, 2.99)) and for all doses received, more than 4 times as likely to receive doses on time (OR 4.12 (95% CI: 4.04, 4.21), relative to stand-alone vaccine recipients.

Conclusion: Children receiving DTaP-containing combination vaccines had significantly greater adherence to the recommended vaccination series. These findings provide compelling evidence in support of the preferential use of DTaP combination vaccines.

INTRODUCTION

- Incidence of pertussis across the US has dramatically declined since the introduction of the tetanus, diphtheria toxoids, and whole-cell pertussis vaccines in the 1940s.[1]
- The Advisory Committee on Immunization Practices (ACIP) currently recommends acellular pertussis (DTaP) vaccines be administered at 2, 4, and 6 months (the primary series), with a 1st booster dose at 15-18 months and a 2nd booster dose at 4-6 years.[2]
- Despite universal recommendation of the 4-dose DTaP vaccine series in infants and toddlers, adherence (i.e. coverage and timeliness) remain suboptimal in the US.
- DTaP-containing combination vaccines are presumed to improve vaccine coverage rates and timeliness, but research supporting this claim is limited.
- The purpose of this study was to investigate the associations between DTaP-containing vaccine use and adherence to the ACIP's recommended DTaP immunization schedule among privately insured children in the US using data from a large national claims database.

METHODS

Data Source & Cohort

- Data were extracted from Optum's de-identified Clinformatics® Data Mart (CDM) to create a cohort of all privately insured children born between January 1, 2009 and December 31, 2016 with at least 24 months of continuous enrolment from birth, and records of receiving at least 1 DTaP-containing vaccination during the study period (2009-2018; **Figure 1**).

Exposure Groups & Outcomes

- Patients were classified by DTaP-containing vaccine receipt: combination vaccines only, stand-alone vaccines only, or a mixture of both (**Table 1**).
- Adherence outcomes assessed included: 1) completion, defined as receipt of 4 DTaP-containing vaccines within 20 months of life, and 2) timely receipt, where children were classified as timely if all received DTaP-containing vaccine doses were administered ≤ 2 months after the respective recommended ages.

Table 1. DTaP-containing vaccines available from 2009-2018 (study period)

Manufacturer	Brand Name	Formulation	Stand-Alone / Combination	Approved Doses	CPT® Code[a]
Sanofi Pasteur	*Daptacel*	DTaP	Stand-Alone	1-5	90700
GlaxoSmithKline	*Infanrix*	DTaP	Stand-Alone	1-5	90700
Sanofi Pasteur	*Tripedia*[b]	DTaP	Stand-Alone	1-5	90700
Sanofi Pasteur	*Pentacel*	DTaP-IPV/Hib	Pentavalent	1-4	90698
Sanofi Pasteur	*TriHiBit*[b]	DTaP/Hib	Quadrivalent	4	90721
GlaxoSmithKline	*Pediarix*	DTaP-IPV-HepB	Pentavalent	1-3	90723

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[b] *Tripedia* and *TriHiBit* were discontinued in 2011.

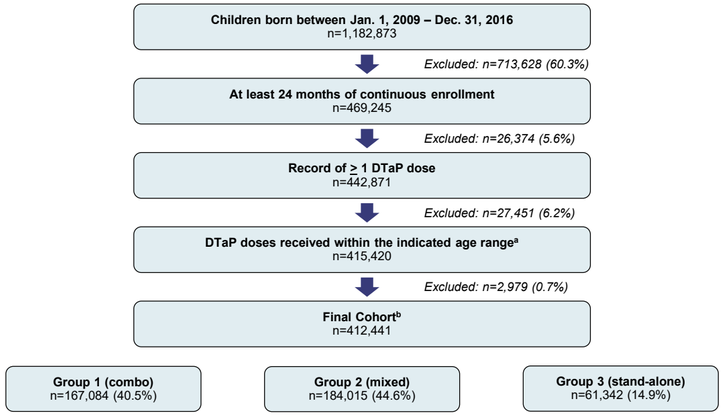
Statistical Analyses

- Outcomes were adjusted for gender, birth year, race, and socioeconomic status via a logistic regression model; odds ratios (ORs) with 95% confidence intervals (CI) were calculated using robust standard errors.
- Additional sensitivity analyses were conducted to assess the stability of the estimated associations while varying specifications of the outcome definitions.

RESULTS

Study Cohort

Figure 1. Flowchart of cohort selection and exposure group designation



[a] Indicated age range for DTaP vaccines is between 6 weeks to 7 years of age (i.e. up to the 7th birthday) for all DTaP-vaccines in this study, with the exception of DTaP-IPV/Hib (Pentacel), where the upper-bound of the indication is 5 years of age (i.e. up to the 5th birthday).
[b] Patients with missing gender data, records of DTaP doses administered prior to their birthdate, and/or ≥ 6 recorded DTaP doses were excluded.

Adherence Outcomes

- Completion of the 4-dose series was highest among combination vaccine recipients (group 1) (75.6%), followed by mixed (group 2) (72.7%) and stand-alone vaccine recipients (group 3) (51.4%) (**Table 2**).
- Completion of the 4-dose series was ~3 times higher among combination vaccine recipients (OR, 2.93 [95% CI: 2.88, 2.99)], relative to stand-alone recipients
- Timely receipt of the age appropriate doses was highest among combination vaccine recipients (81.1%), followed by mixed (70.3%) and stand-alone vaccine recipients (51.0%).
- Children who received combination vaccines only were more than 4 times as likely to have received their respective doses on time (OR, 4.12 (95% CI: 4.04, 4.21), relative to stand-alone recipients.
- Sensitivity analyses demonstrated that the estimated associations remain relatively constant, even when varying the specifications of the outcome definitions.

Table 2. Percentage of children classified as complete versus incomplete and delayed receipt versus timely receipt, stratified by exposure group

Exposure Group	Total (n=)	Outcome 1: Complete			Outcome 2: Timely Receipt		
		Incomplete n= (%)	Complete n= (%)	OR[a] (95% CI)	Delayed Receipt n= (%)	Timely Receipt[b] n= (%)	OR[c] (95% CI)
Group 1 (combo)	167084	40830 (24.4)	126254 (75.6)	2.93 (2.88, 2.99)	31626 (18.9)	135458 (81.1)	4.12 (4.04, 4.21)
Group 2 (mixed)	184015	50212 (27.3)	133803 (72.7)	2.54 (2.49, 2.59)	54733 (29.7)	129282 (70.3)	2.28 (2.24, 2.32)
Group 3 (stand-alone)	61342	29784 (48.6)	31558 (51.4)	Ref.	30045 (49)	31297 (51)	Ref.

Percentages were calculated as row percentages for each respective outcome (e.g. Percentage = (# of group 1 children incomplete)/(group 1 total))
[a] OR values reported are the odds of being complete (receiving 4 doses within first 20 months of life), relative to Group 3. ORs were adjusted for patient gender, birth year, race, and federal poverty status.
[b] Timely receipt was assessed regardless of completion (i.e. timeliness assessed among children who received ≥ 1 doses).
[c] OR values reported are the odds of timely receipt of the age-appropriate doses (receipt within 2 months of the recommended age), relative to Group 3. ORs were adjusted for patient gender, birth year, race, and federal poverty status.

Sociodemographic Characteristics

- We observed significant disparities in adherence (**Table 3**); black and Hispanic children were 24% (OR, 0.76 [95% CI: 0.74, 0.78]) and 30% (OR, 0.70 [95% CI: 0.68, 0.71]) less likely to complete the 4-dose series, respectively, relative to white children.
- Black and Hispanic children were 22% (OR, 0.78 [95% CI: 0.76, 0.80]) and 27% less likely (OR, 0.73 [95% CI: 0.72, 0.75]) to receive their respective doses on time, respectively, relative to white children.
- Children of higher socioeconomic status were 8% more likely (OR, 1.08 [95% CI: 1.05, 1.11]) to receive their respective doses on time, relative to children of lower socioeconomic status.

Table 3. Odds ratios (ORs) from multivariable logistic regression models

Variable	OR[a] (95% CI) *Outcome 1: Complete*	OR[a] (95% CI) *Outcome 2: Timely Receipt*
Exposure group		
Group 1 (combo)	2.93 (2.88, 2.99)*	4.12 (4.04, 4.21)
Group 2 (mixed)	2.54 (2.49, 2.59)*	2.28 (2.24, 2.32)
Group 3 (stand-alone)	Ref.	Ref.
Gender		
Female	Ref.	Ref.
Male	0.98 (0.97, 1.00)	0.98 (0.96, 0.99)*
Race		
Asian	1.00 (0.98, 1.03)	1.07 (1.04, 1.10)*
Black	0.76 (0.74, 0.78)*	0.78 (0.76, 0.80)*
Hispanic	0.70 (0.68, 0.71)*	0.73 (0.72, 0.75)*
White	Ref.	Ref.
Poverty status		
Below 400% FPL	Ref.	Ref.
Above 400% FPL	1.01 (0.98, 1.04)	1.08 (1.05, 1.11)*
Unknown	2.74 (2.52, 2.99)*	2.91 (2.67, 3.18)*

[a] Adjusted for all variables as listed in the table, as well as birth year (not listed here).
* p-value < 0.05

DISCUSSION

Strengths

- Using electronic claims data from a large national claims database enabled us to accurately assess vaccine use across a cohort of more than 400,000 children over the course of nearly a decade.

Limitations

- Our findings do not necessarily establish a causal relationship between the receipt of combination vaccines and improved adherence.
- Generalizability may be limited due to the lack of publicly insured and uninsured children in the cohort.

CONCLUSIONS

- DTaP-containing combination vaccine use was associated with significantly greater adherence to the recommended infant-toddler DTaP vaccination series.
- These findings provide compelling evidence supporting the preferential use of combination vaccines, highlighting the pivotal role that they may play in improving vaccine coverage and adherence.
- Future research is needed to further explore the associations of combination vaccine receipt and adherence to other recommended pediatric vaccines.

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DISCLOSURES

All listed authors are full-time employees of Sanofi Pasteur (US).

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