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Missed opportunities for simultaneous administration of the fourth dose of DTaP among children in the United States

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Abstract

Background: Simultaneous administration of all age-appropriate doses of vaccines is an effective strategy for raising vaccination coverage. Vaccination coverage for 4 dose of DTaP (diphtheria, tetanus toxoids, and acellular pertussis vaccine) among children 19–35 months in the United States has not reached the *Healthy People 2020* target of 90%. Risk factors for missed opportunities for simultaneous administration of the fourth dose of DTaP have not been investigated.

Methods: A missed opportunity for simultaneous administration of the fourth dose of DTaP is defined as the failure to administer an age-eligible fourth dose of DTaP, and during the same age-eligible period for the fourth dose of DTaP other recommended and age-appropriate doses of vaccines are given to children. This study used 2001–2014 National Immunization Survey data to describe the trend in missed opportunities for simultaneous administration of the fourth dose of DTaP from 2001 through 2014, assess the prevalence of children who missed opportunities for simultaneous administration of the fourth dose of DTaP by selected factors, and recognize significant risk factors for missed opportunities for simultaneous administration of the fourth dose of DTaP.

Results: From 2001 to 2014, the prevalence of missed opportunities for simultaneous administration of the fourth dose of DTaP among children 19–35 months in the United States ranged from 5.7% to 9.0%; across 13 factors considered, the prevalence of missed opportunities varied from 3.3% to 22.9%. Children who were late in receiving the first to third dose of DTaP had significantly higher prevalence of missed opportunities for simultaneous administration of the fourth dose of DTaP than children who received these doses on-time, with adjusted prevalence ratios for late vs. on-time of 1.7, 1.6, and 3.2, and all P-value < 0.01.

Conclusions: Improving on-time vaccination of the third dose of DTaP could substantially reduce missed opportunities for simultaneous administration of the fourth dose of DTaP.

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Conflict of interest statement

The authors declare that there is no conflicts of interest.

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Keywords

The fourth dose of DTaP; Pertussis; Missed opportunities; Risk factors; Simultaneous administration; *Healthy People 2020* Objectives

1. Introduction

Simultaneous administration of all age-appropriate doses of vaccines has been recommended by Advisory Committee on Immunization Practices (ACIP) since 1986, and this recommendation is an effective strategy for raising vaccination levels, acquiring and sustaining the national objectives of immunization rates among children 19–35 months in the United States for all recommended vaccines [1–4]. Simultaneous administration of childhood vaccines is defined as administering more than one vaccine on the same visit day, at different anatomic sites, and not combined in the same syringe [2]. Vaccination coverage studies have demonstrated that one-in-five children falling behind during the interval from age 7 months to age 16 months - mostly as a result of missed opportunities for simultaneous administration of age-appropriate vaccines [3,5].

Pertussis is a highly contagious respiratory tract bacteria infection. Pertussis incidence has been gradually increasing since the early 1980s. A total of 25,827 cases were reported in 2004, the largest number since 1959, then a total of 27,550 pertussis cases and 27 pertussis-related deaths were reported in 2010. Case counts of 48,277 from 2012 surpassed 2010 and 2011. Compared with 2012, the reported cases decreased to 28,639 in 2013, but in 2014 the reported cases increased to 32,971 [6]. Large percentage of infected children during recent pertussis outbreaks was not vaccinated by choice by their parents, although pertussis resurgence has been attributed to waning immunity and other factors, vaccine refusal was the primary reason for recent pertussis incidence increasing [7]. The reported pertussis incidence (per 100,000 persons) by age group in the United States from 1990 to 2014 has shown that infants aged <1 year continue to have the highest reported rate of pertussis, and school-aged children 7–10 years continue to contribute a significant proportion of reported pertussis cases [8]. Pertussis is a vaccine preventable disease. In order to protect children against pertussis, ACIP routinely recommended 4 doses of DTaP (diphtheria, tetanus toxoids, and acellular pertussis vaccine) for children in United States [9]. The fourth dose of DTaP, recommended at 15–18 months of age, is critical in boosting antibody titers and insuring continuous protection [2]. Only small portion of children missed the first, second, third dose of DTaP, however many children missed the fourth dose of DTaP [10–17]. About 15.8% (approximately 1 million) of children in the United States had not received their fourth dose of DTaP vaccination in 2014 [18].

Vaccination coverage for 4 doses of DTaP among children 19–35 months has not reached the 90% target of *Healthy People 2020*. Missed opportunities for simultaneous vaccinations were recognized as one main cause for under vaccination of children, and reducing missed opportunities may increase vaccination coverage significantly [5,19]. A recent study indicated that if missed opportunities for simultaneous administration of the fourth dose of DTaP had been eliminated, the vaccination coverage for 4 dose of DTaP could have

reached the 90% target of *Healthy People 2020* [20]. Missed opportunities for simultaneous administration of the fourth dose of DTaP is an important issue on raising immunization rate for 4 dose of DTaP and protecting children against pertussis, however risk factors for missed opportunities for simultaneous administration of the fourth dose of DTaP have not been examined.

The immunization information for a large sample of 260,660 children aged 19–35 months in the United States has been collected from the 2001–2014 National Immunization Survey (NIS) and been applied to this research. This study described the trend in missed opportunities for simultaneous administration of the fourth dose of DTaP from 2001 through 2014, assessed the prevalence of children who missed opportunities for simultaneous administration of the fourth dose of DTaP by selected factors, recognized significant risk factors for missed opportunities for simultaneous administration of the fourth dose of DTaP among 13 selected factors, and determined the adjusted prevalence ratios for missed opportunities for simultaneous administration of the fourth dose of DTaP by significant risk factors distinguished.

2. Material and methods

2.1. Data resources

CDC started the National Immunization Survey (NIS) in 1994. NIS has been used to evaluate vaccination coverage among children 19–35 months in the United States according to the immunization schedule recommended by ACIP [9]. The NIS collects immunization information through telephone survey of households and mail survey of immunization providers. The NIS data collected from 2001 through 2014 were analyzed in this study. Detailed descriptions of the 2001–2014 NIS and corresponding response rates have been published elsewhere [21].

2.2. Vaccination definition and selected factors

Four doses of DTaP vaccine are recommended by ACIP for children during the first 2 years of their life in the United States [9]. By ACIP recommended immunization schedule, the children were defined as on-time in receiving the first, second, third dose of DTaP, if providers administered the first, second, third dose by 2, 4, 6 months of age to children, respectively (i.e., before turning 3, 5, 7 months of age, respectively); or else, the children were defined as late in receiving the first, second, third dose of DTaP [17].

In this study, among children who received the first 3 doses of DTaP but missed the fourth dose of DTaP, a missed opportunity for simultaneous administration of the fourth dose of DTaP is defined as the failure to administer an age-eligible fourth dose of DTaP, and during the same age-eligible period for the fourth dose of DTaP other recommended and age-appropriate doses of vaccines are given to children [22].

The NIS has been collecting immunization data for young children by a variety of socio-demographic characteristics, such that immunization workers can assess the vaccination coverage by those domains, identify groups at risk of low vaccination coverage, and help the people in those groups to raise vaccination coverage. Thirteen factors including timeliness of

children in receiving the first, second, third dose of DTaP, children health insurance status, and other socio-demographic factors were selected for this risk factor study to explore missed the opportunities for simultaneous administration of the fourth dose of DTaP.

2.3. Statistical methods

To implement NIS complex sample survey design into the data analysis of this study, SUDAAN 11.0.0 [23] procedures were applied throughout all of the statistical analysis process. This study combined 2001–2014 NIS data for the risk factor analysis which could reduce sampling errors and correct coverage biases [24]. The trend in missed opportunities for simultaneous administration of the fourth dose of DTaP among children in United States was assessed by weighted univariate procedure across calendar year of 2001–2014. Weighted categorical data analysis was used to assess the prevalence rates of missed opportunities for simultaneous administration of the fourth dose of DTaP vaccine across selected factors with combined 2001–2014 NIS data. The NIS weights have been created based on the landline and the cell-phone samples. The weighting scheme involves the adjustment for household nonresponse, undercoverage of the eligible population, and provider non-response. Prevalence ratios were used to evaluate the association of each factor with missed opportunities for simultaneous administration of the fourth dose of DTaP. To recognize significant factors associated with missed opportunities for simultaneous administration of the fourth dose of DTaP, multivariable logistic regression was conducted [25]. The adjusted prevalence ratios and associated P-values for each of the factors in the final model were reported.

3. Results

3.1. Trend in missed opportunities for simultaneous administration of the fourth dose of DTaP from 2001 to 2014

From 2001 to 2014, the prevalence rate of missed opportunities for simultaneous administration of the fourth dose of DTaP among children 19–35 months in the United States fluctuated from 5.7% to 9.0% with both median and mean of 7.4% (Fig. 1). The number of children with missed opportunities for simultaneous administration of the fourth dose of DTaP ranged from approximately 340,000–529,000 with median and mean about 440,000. Prevalence of missed opportunities varied from 5.7% to 9.0% during 2001–2005; with less variation, from 7.0% to 8.1%, during the most recent nine years.

3.2. Prevalence of missed opportunities for simultaneous administration of the fourth dose of DTaP across selected factors, gained from weighted categorical data analysis, with combined 2001–2014 National Immunization Survey data

Weighted prevalence rates with 95% confidence interval (CI) and weighted prevalence ratios (95%CI) for missed opportunities for simultaneous administration of the fourth dose of DTaP by selected factors are shown in Table 1. Across all of the factors listed, the prevalence rates for missed opportunities for simultaneous administration of the fourth dose of DTaP varied from 3.3% to 22.9%. Among the 13 selected factors, the timeliness of the first, second, and third dose of DTaP were the factors most strongly associated with prevalence of missed opportunities for simultaneous administration of the fourth dose of DTaP. Through

the remaining factors, Black non-Hispanic children had the highest prevalence of missed opportunities of 9.6%. For children who did not have health insurance, 9.2% experienced missed opportunities. Children whose mother was married had significantly lower prevalence of missed opportunities, 6.6%, compared to the prevalence rate of 9.0% among children whose mother was not married. For children who lived in families below the poverty level, approximate 9.3% experienced missed opportunities for simultaneous administration of the fourth dose of DTaP. Weighted prevalence ratios for missed opportunities for simultaneous administration of the fourth dose of DTaP among categories of each factor were statistically significant at P-value < 0.01 level and ranged from 1.2 to 5.6. Among the 13 factors selected, prevalence ratios were highest for late vs. on-time receipt of the first, second, and third dose of DTaP (4.0, 4.8 and 5.6, respectively).

3.3. Factors significantly associated with missed opportunities for simultaneous administration of the fourth dose of DTaP, achieved through multivariable analysis, among children 19–35 months with combined 2001–2014 National Immunization Survey data

Risk factors significantly associated with missed opportunities for simultaneous administration of the fourth dose of DTaP among children 19–35 months in United States are shown in Table 2. These independent and significant risk factors are produced through multivariable analysis and presented in the final logistic model. In summary, these 7 factors could be divided into two risk groups. High risk group is consisted of timeliness of the first, second, third dose of DTaP with Adjusted Prevalence Ratio between 1.64 and 3.23. Among this high risk group, the timeliness of the third dose of DTaP is the most significantly associated with missed opportunities for simultaneous administration of the fourth dose of DTaP. Risk of missed opportunities for simultaneous administration of the fourth dose of DTaP is about 223% higher among children where the third dose of DTaP is late than in children where the third dose of DTaP vaccine is on-time. The low risk group is composed of four socio-demographic factors: Family mobility, First born child, Age group of mother, and Number of vaccination provider. In this low risk group, the Adjusted Prevalence Ratios varied from 1.07 to 1.13.

4. Discussion

Estimates with NIS data from 2001–2014 demonstrated that the published immunization rates for 4 doses of DTaP in the United States varied from 81.6% to 85.7% which are still below the Healthy People 2020 target of 90% level [18,21]. The important meaning for reaching that objective has been emphasized in the documents of US Department of Health and Human Service (DHHS) and ACIP [4,9]. If providers fully practice simultaneous administration of the fourth dose of DTaP, the vaccine uptake for the fourth dose of DTaP and further the 4 dose of DTaP could be increased significantly [5,19,20]. Our research applied this critical policy to 2001–2014 NIS data, the results of our study shown that the fourth dose DTaP uptake might be boosted about 5.7–9.0% which account for about 50% of the distance to full vaccination (100%) of 4 DTaP, and well enough to catch up the healthy people 2020 target; therefore the immunization rate for 4 DTaP will acquire the 90% level from 2005 through 2014. Results from our study indicated that the major risk factors associated with the missed opportunities for simultaneous administration of the fourth dose

of DTaP are late receipt of the first, second, and third dose of DTaP, these three timeliness factors are modifiable and it is essential for targeting intervention to these demanding components.

According to the ACIP recommendations, licensed combination vaccines can be used whenever any components of the combination are indicated [2]. The 4 doses of DTaP series may be administered with any FDA licensed single-component vaccines or combination vaccines. By the ACIP recommended vaccination schedule, the 1st through the 4th dose of DTaP should be administered at 2, 4, 6, 15–18 months age of children with single-component or combination vaccines. NIS has implemented this ACIP's policy of interchangeability of combination vaccines and single-component vaccines in NIS data collection process such as DTaP up-to-date vaccination status, age in months of DTaP vaccination, and type of DTaP vaccine. Therefore, the results of this study are applicable to any DTaP contained vaccinations for young children in the US. NIS 2001–2014 data shown that about 40% of children in the US were administered with single-component vaccine for the 4th dose of DTaP.

To improve timeliness of the first 3 doses of DTaP vaccinations, the following suggestions could be helpful. Timeliness is the immunization schedule recommended by ACIP, in any circumstances physicians and staff must read it carefully, which are the basic and practical guides for all of the immunization workers in their efforts to protect children against vaccine-preventable diseases, and those schedule should be implemented in physicians and staff daily immunization activities. Education of providers to follow the ACIP's recommended immunization schedule rather than something like 'Alternative Vaccination Schedule'. Because the percentage of late in receiving the 3rd dose of DTaP is significantly higher than those of late in receiving the 1st and 2nd dose DTaP, in practice the providers may need to pay special attention to the timeliness of the 3rd dose of DTaP, and to do everything possible to administer the 3rd dose of DTaP on-time at age of 6 months. Use client reminder and recall interventions to remind members of a target population that vaccinations are due (reminders) or late (recall), which has been established to be the effective interventions in immunization practice [26].

In this study, we analyzed missed opportunities for simultaneous administration of the fourth dose of DTaP among children who received the first 3 doses of DTaP but missed the fourth dose of DTaP. Therefore, vaccine hesitancy may be one factor associated with missed opportunities for simultaneous administration of the fourth dose of DTaP. It is rather difficult to categorize a population-group as vaccine-hesitant accurately, however immunization workers have realized that there is an increasing trend toward vaccine hesitancy [27]. Different tools and ways have been developed to counter vaccine hesitancy. Education of vaccine-hesitant parents might be one effective intervention which should pay special attention to improve parent's confidence in the value of vaccines including the following topics: "Vaccines are necessary to protect the health of children", "If I do not vaccinate my child, he/she may get a disease and cause other children or adults also to get the disease", and "Vaccine are safe" [28]. Education of parents by addressing those questions may reduce parents' vaccine hesitancy, enhance parents' vaccine acceptance. Thus parents could be willing to bring their children to receive the 4 doses of DTaP vaccination on-time, and

further to reduce the missed opportunities for simultaneous administration of the fourth dose of DTaP vaccine.

Our research possessed several restrictions. First, this study solely accounted for the vaccination visits in our hunting for missed opportunities for simultaneous administration of the fourth dose of DTaP. However, in real life, many missed opportunities may exist in the process of parents who seek child health care, for example well child visits, screening visits, annual visits etc. Consequently, in this research missed opportunities for simultaneous administration of the fourth dose of DTaP might be underestimated [22]. Second, landline telephone survey design was utilized to sample household in early years of NIS, later years of NIS adopted dual-frame strategy in data collection process. Thus survey non-coverage could have negative impact on the results of our study. Nevertheless, latest publications in peer-reviewed journals suggested that the potential bias in estimates of missed opportunities for simultaneous administration of the fourth dose of DTaP vaccine resulting from not sampling households with cell phone service might be small [18,29–31].

5. Conclusions

This study suggests that the timeliness in receiving the first, second, and third dose of DTaP vaccine are significant and potentially modifiable risk factors for missed opportunities for simultaneous administration of the fourth dose of DTaP. Encouraging providers to deliver all recommended vaccines that are due at each visit might decrease missed opportunities for simultaneous administration of the fourth dose of DTaP. Future interventions focusing on the group of late in receiving the third dose of DTaP could substantially eliminate missed opportunities for simultaneous administration of the fourth dose of DTaP, further to increase 4 DTaP vaccination coverage level, and reduce pertussis infection among children in the United States.

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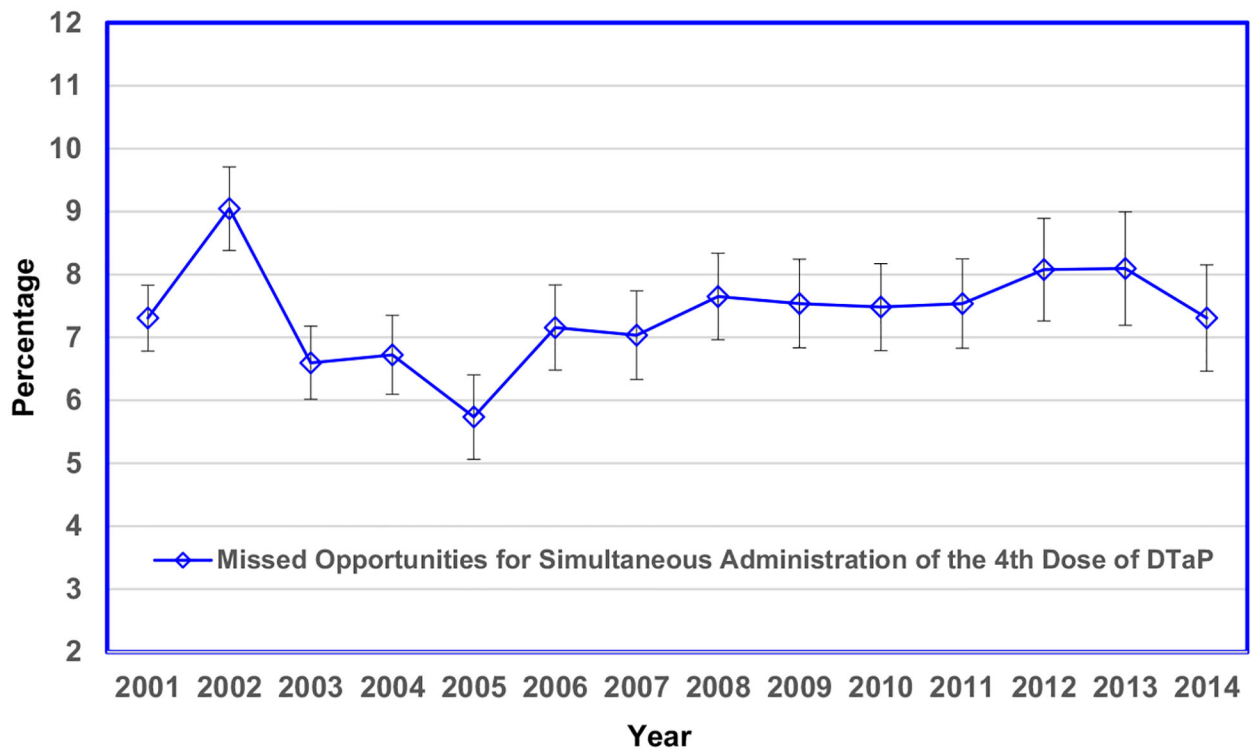


Fig. 1. Trend in missed opportunities in percentage (%) with 95% confidence interval (CI) for simultaneous administration of the fourth dose of DTaP^a among children 19–35 months in the United States, National Immunization Survey, 2001–2014. ^a Diphtheria and Tetanus toxoids and acellular Pertussis.

Table 1

Prevalence of missed opportunities for simultaneous administration of the fourth dose of DTaP^d by selected factors, obtained from weighted categorical data analysis, among children 19–35 months in the United States, with combined 2001–2014 National Immunization Survey data.

Factors	Un-weighted sample size (weighted%)	Weighted prevalence % (95% CI) ^b	Weighted prevalence ratio (95% CI)
National	260,660	7.4 (7.2, 7.6)	
Timeliness ^c of the First dose of DTaP			
Late	23,004(10.4)	22.9 (22.0, 23.9)	4.0 (3.8, 4.2)
On-time	233,110(89.6)	5.7 (5.5, 5.9) ^d	
Timeliness of the Second dose of DTaP			
Late	42,295 (19.2)	21.0 (20.3, 21.7)	4.8 (4.5, 5.0)
On-time	211,200 (80.8)	4.4 (4.2, 4.6) ^d	
Timeliness of the Third dose of DTaP			
Late	63,868 (28.7)	18.5 (18.0, 19.1)	5.6 (5.3, 5.9)
On-time	187,050(71.3)	3.3 (3.2, 3.5) ^d	
Education level of mothers			
12 years	88,540 (50.0)	8.6 (8.3, 8.9)	1.4 (1.3, 1.5)
13 years	172,060 (50.0)	6.2 (6.0, 6.4) ^d	
Number of children in family			
1	66,306 (25.4)	5.8 (5.5, 6.1) ^d	1.4 (1.3, 1.5)
2	194,294 (74.6)	7.9 (7.7, 8.1)	
Marital status of mother			
Married	193,474 (67.3)	6.6 (6.4, 6.8) ^d	1.4 (1.3, 1.4)
Not married	67,126 (32.7)	9.0 (8.6, 9.4)	
Age group of mothers			
29 years	101,286 (44.9)	8.5 (8.2, 8.8)	1.3 (1.3, 1.4)
30 years	159,314 (55.1)	6.5 (6.2, 6.7) ^d	
Family mobility			
Moved	21,777 (8.4)	9.3 (8.5, 10.1)	1.3 (1.2, 1.4)
Not moved	238,646 (91.6)	7.2 (7.0, 7.4) ^d	
Number of vaccination providers ^e			
1	178,862 (67.3)	7.0 (6.8, 7.2) ^d	1.2 (1.1, 1.2)
2	81,107 (32.7)	8.2 (7.9, 8.6)	
First born child			
No	152,408 (58.0)	8.3 (8.0, 8.5)	1.4 (1.3, 1.4)
Yes	108,192 (42.0)	6.1 (5.9, 6.4) ^d	
Health insurance status of child			
No	24,531 (19.7)	9.2 (8.6, 9.8)	1.3 (1.2, 1.4)
Yes	130,146 (80.3)	7.1 (6.9, 7.4) ^d	

Factors	Un-weighted sample size (weighted%)	Weighted prevalence % (95% CI) ^b	Weighted prevalence ratio (95% CI)
Race/ethnicity			
White, non-Hispanic	154,648 (50.4)	6.6 (6.4, 6.8) ^d	
Black, non-Hispanic	28,569 (13.1)	9.6 (9.0, 10.2)	1.5 (1.4, 1.6)
Hispanic	51,418 (26.8)	7.7 (7.3, 8.2)	1.2 (1.1, 1.3)
Poverty level			
At or Above	191,344 (63.5)	6.4 (6.2, 6.6) ^d	1.5 (1.4, 1.5)
Below	54,323 (28.5)	9.3 (8.9, 9.8)	

Note: All prevalence ratios are significant at P-value < 0.01.

^aDiphtheria and Tetanus toxoids and acellular Pertussis vaccine.

^bConfidence Interval.

^cTimeliness is defined for the first, second, and third dose of DTaP vaccination as Late vs. On-time.

^dReference level.

^eProviders refer to Facilities (such as private, public, hospital, military, school, etc.) which provide immunization service to people and children who receive vaccination shot from those facilities.

Adjusted prevalence ratios of missed opportunities for simultaneous administration of the fourth dose of DTaP^a by significant risk factors, acquired from weighted multivariable analysis, among children 19–35 months in the United States, with combined 2001–2014 National Immunization Survey data.

Table 2

Factors	Comparison	Adjusted prevalence ratios	
		Ratio (95%CI) ^b	P-value
Timeliness of the First dose of DTaP	Late vs. On-time	1.71 (1.60, 1.83)	<0.01
Timeliness of the Second dose of DTaP	Late vs. On-time	1.64 (1.52, 1.77)	<0.01
Timeliness of the Third dose of DTaP	Late vs. On-time	3.23 (3.00, 3.48)	<0.01
Age group of mothers	29 vs. 30	1.08 (1.02, 1.13)	<0.01
Family mobility	Moved vs. Not-moved	1.13 (1.03, 1.23)	<0.01
Number of vaccination providers	2 vs. 1	1.07 (1.01, 1.13)	<0.02
First born child	Not vs. Yes	1.11 (1.06, 1.17)	<0.01

^aDiphtheria and Tetanus toxoids and acellular Pertussis.

^bConfidence Interval.