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Factors Associated with Missed Opportunities for Simultaneous Administration of the Fourth Dose of Pneumococcal Conjugate Vaccine for Children in the United States

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Abstract

An important standard for childhood immunization is simultaneous administration of all age-eligible doses of vaccines. Vaccination coverage for 4 doses of pneumococcal conjugate vaccine (PCV) for children 19–35 months has not achieved the *Healthy People 2020* objective of 90% in the United States, and the fourth dose of PCV is commonly missed in the series. Research has not been conducted on the factors associated with missed opportunities for simultaneous administration of the fourth dose of PCV. A missed opportunity for simultaneous administration of the fourth dose of PCV is characterized as failing to administer an age-appropriate fourth dose of PCV to children when in the same provider visit the children did receive other age-eligible vaccines. During the period of 2008–2015, 4.5% to 7.8% of young children in the United States experienced missed opportunities for simultaneous administration of the fourth dose of PCV; across all selected factors, the proportion of missed opportunities varied from 4.1% to 11.3%. The timeliness of the first through the third doses of PCV vaccination, and age group of mothers were factors significantly related to missed opportunities for simultaneous administration of the fourth dose of PCV; the adjusted prevalence ratios ranged from 1.2 to 2.0. Missed opportunities could be reduced by provider implementation of systems to ensure that all recommended vaccines are offered at each visit. Systems tools providers could use to reduce missed opportunities include patient recall, provider reminders, standing orders, extended office hours, and use of immunization information systems (IIS).

Keywords

pneumococcal conjugate vaccine; simultaneous administration; childhood vaccination; missed opportunities; National Immunization Survey-Child

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Disclaimer

The findings and conclusions in this article are solely the responsibility of the authors and do not necessarily represent the official view of the Centers for Disease Control and Prevention.

INTRODUCTION

Simultaneous administration of all age-eligible vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) is a powerful strategy for raising vaccination coverage, acquiring and sustaining the national objective of vaccination coverage levels for children 19–35 months in the United States (CDC, 2011; USDHHS 1992; King et al., 1994). Simultaneous administration of childhood vaccines is characterized as administering more than one vaccine at the same healthcare visit, at different anatomic sites, and not combined in the same syringe (CDC, 2011). One significant reason related to low vaccination coverage is the failure to simultaneously administer all age-eligible vaccines to children (King et al., 1994; Luman et al., 2009).

Streptococcus pneumoniae is a leading cause of serious illness, including bacteremia, meningitis, and pneumonia among children and adults worldwide (Nuorti et al., 2010; Thigpen et al., 2011). Approximately 10% of all patients with invasive pneumococcal disease die of their illness (Pilishvili et al., 2012; Robinson et al., 2001). Following the introduction of the pneumococcal conjugate vaccines (PCV) in the United States, the overall invasive pneumococcal disease rate decreased from 100 cases per 100,000 people in 1998 to 9 cases per 100,000 in 2015 (CDC, 2017). However, *Streptococcus pneumoniae* continues to cause a variety of common clinical syndromes, despite vaccination programs for children and some adults (Huang et al., 2011).

Invasive pneumococcal disease caused by serotypes included in currently available vaccines is preventable. In 2000, the ACIP recommended routine use of 7-valent pneumococcal conjugate vaccine (PCV7) for all infants and young children (CDC, 2008). In February 2010, a new 13-valent pneumococcal conjugate vaccine (PCV13) was approved by the FDA and has since replaced PCV7 (CDC, 2010). The ACIP recommends that the 13-valent pneumococcal conjugate vaccine (PCV13) be used for all children aged <5 years (Mung et al., 2010). For routine immunization of infants, PCV13 is recommended as a 4-dose series at age 2, 4, 6, and 12–15 months (CDC, February 2016). The fourth dose of PCV is critical in boosting antibody titers and optimizing population level protection (CDC, 2011). Vaccination coverage from the National Immunization Survey-Child (NIS-Child) indicated that the fourth dose of PCV is among the most commonly missed vaccines for children (NIS, 2015). In 2015, an estimated 15.9% (approximately 1 million) of children aged 19–35 months in the United States were at risk because they had not received their fourth dose of PCV (Hill et al., Vaccination coverage for 4 PCV for children 19–35 months has never gained the 90% objective of *Healthy People 2020* (Hill et al., 2016; USDHHS, 2017). To increase vaccination of children with the fourth dose of PCV, one of the immunization strategies for healthcare practices and providers is to reduce missed opportunities for simultaneous administration of the fourth dose of PCV vaccine (CDC, 2011; USDHHS 1992; King et al., 1994). Risk factors for missed opportunities for simultaneous administration of the fourth dose of PCV have not been previously examined. This study analyzes 2008–2015 NIS-Child data, depicts the trend in missed opportunities, measures the prevalence of missed opportunities by selected factors, and determines significant risk factors for missed opportunities for simultaneous administration of the fourth dose of PCV.

MATERIALS AND METHODS

Study population

Vaccination coverage for 4 PCV had been increasing from 2001 through 2007, and PCV coverage was relatively stable during 2008–2015. Therefore, NIS-Child data collected from 2008 through 2015 were analyzed in this study. The NIS-Child is conducted by the National Center for Immunization and Respiratory Diseases (NCIRD), Centers for Disease Control and Prevention (CDC) to generate national, state, and selected local area estimates of immunization rates annually for children 19–35 months in the United States. The NIS-Child has two phases of data collection. First, independent surveys of households with cellular and landline telephones are conducted. During the telephone call, children's sociodemographic characteristics are collected, and consent to contact children's immunization providers is obtained. Second, mailed surveys are sent to children's immunization providers to acquire the children's immunization history. Specific explanation of the sample design, immunization history questionnaire, data preparation, quality control, and weighting process of the NIS-Child have been published elsewhere (CDC, September 2016).

Vaccination and socio-demographic factors

In agreement with ACIP recommendations, four doses of PCV should be administered to children during their first two years of life in the United States (CDC, February 2016). In this study, if the first, second, and third dose of PCV are given to children by age 2, 4, and 6 months (i.e. before reaching 3, 5, and 7 months), the children are defined as on-time for the first, second, and third doses of PCV, respectively. For the remaining children, those with missing values of age in months at vaccination are defined as late in receiving the first through the third dose of PCV. The fourth dose of PCV is recommended for children at age 12–15 months.

For children who are administered the first 3 doses of PCV vaccines but the fourth dose of PCV vaccine is not administered, a missed opportunity for simultaneous administration of the fourth dose of PCV is defined as failing to administer an age-appropriate fourth dose of PCV to children, during the same provider visit where the children received other age-eligible vaccines. The age eligible period is eight weeks or more after receipt of the 3rd dose of PCV. The fourth dose of PCV is only necessary for children who received the first three doses of PCV before age 12 months, or for children at high risk who received the first three doses at any age (CDC, February 2016; Dietz et al., 1994).

This study included a group of sociodemographic factors which have been found to be correlated with child vaccination status (Luman et al., 2001; Luman et al., 2005; Zhao et al., 2010). A total of 13 variables, including timeliness of child's receipt of the first, second, and third dose of PCV, mother's age group, education level and marital status, first born and health insurance status of the child, number of children in family, child's race/ethnicity, family poverty level, and number and type of vaccination providers, were included in this study to examine the risk factors associated with missed opportunities for simultaneous administration of the fourth dose of PCV. Research protocols for the evaluation

were reviewed by the CDC's National Center for Health Statistics (NCHS) Research Ethics Review Board (ERB).

Analysis methods

This study was analyzed NIS-Child data from 2008 through 2015 to estimate the trends in the percentage of children with missed opportunities for simultaneous administration of the fourth dose of PCV vaccine; the combined 2008–2015 data were used in prevalence analysis for the factors selected (Li et al., 2009). All of the data analyses in this study were performed with SUDAAN 11.0.0 (RTI, 2012). One way and two way weighted categorical data analysis were applied to trend and univariate factor analysis. Unadjusted prevalence ratios between categories for each factor was used to assess the association of that factor with missed opportunities. A multivariable logistic regression model (Hosmer et al., 2000) was implemented with all of the 13 variables to identify the statistically significant factors associated with missed opportunities in the model. The model adjusted prevalence ratios (APR) were calculated for each of all 13 factors to assess the association of each factor with missed opportunities, the final model retains all factors regardless of significance.

RESULTS

Trend in proportion of missed opportunities for simultaneous administration of the fourth dose of PCV in years 2008–2015.

The prevalence of children with at least one missed opportunity for simultaneous administration of the fourth dose of PCV for children 19–35 months in the United States from 2008–2015 varied between 4.5% and 7.8% (Figure 1), with median of 5.7% and mean of 5.9%. The number of children with missed opportunities for simultaneous administration of the fourth dose of PCV decreased from approximately 479,000 in 2008 to 256,000 in 2015, with median of 331,000 and mean of 351,000. During this 8 years period, the prevalence of missed opportunities dropped significantly; the average decrease is about 0.4% per year and the linear trend is significant with P-value < 0.001.

Prevalence in missed opportunities for simultaneous administration of the fourth dose of PCV by vaccination and socio-demographic components using combined 2008–2015 National Immunization Survey-Child data.

This study showed the weighted prevalence (%) and 95% confidence intervals (CI), and the unadjusted prevalence ratios with 95% CI in missed opportunities for simultaneous administration of the fourth dose of PCV by timeliness of the first three doses of PCV vaccination, and 10 other selected socio-demographic factors in Table 1. Overall of the 13 factors considered, the prevalence of missed opportunities for the fourth dose of PCV ranged from 4.1% to 11.3%, with mean of 6.5% and median of 6.2%. The delay in administering the first, second, and third dose of PCV vaccine was associated with the largest missed opportunity prevalence of 10.1%, 11.3%, and 11.3%. Among the remaining 10 factors, non-Hispanic black children had the next highest prevalence rate (7.5%) in missed opportunities. Prevalence of missed opportunities was 7.4% for children living in families below poverty level, or children receiving all vaccination from public providers. Children who received

the 3rd dose of PCV on-time had the lowest percentage of missed opportunities (4.1%) for simultaneous administration of the 4th dose of PCV among all categories of all 13 factors.

Multivariable logistic regression analysis of the association between all factors and missed opportunities for simultaneous administration of the fourth dose of PCV with combined 2008–2015 National Immunization Survey-Child data.

All adjusted prevalence ratios (APR) of missed opportunities for simultaneous administration of the fourth dose of PCV were demonstrated in Table 2. The presence of underlying late vaccination of the first 3 doses of PCV were significantly correlated to the risk for missed opportunities, after controlling for all other factors. Children late in receiving the first, second, and third dose of PCV vaccination were 1.2, 1.4, and 2.0 times more likely (95% confidence interval [CI]: 1.02–1.34, 1.20–1.58, 1.77–2.23) to miss the opportunity for simultaneous administering the fourth dose of PCV compared with children with on-time in receiving the first 3 doses of PCV. Delay in receiving the third dose of PCV was related to the highest APR of missed opportunities among all of the 13 factors analyzed in this study. Mother's age ≥ 29 years was positively associated with missed opportunities for the fourth dose of PCV, compared to mother's age ≤ 30 years, (APR= 1.16; 95% CI= 1.06, 1.27). The remaining socio-demographic factors were not significantly associated with missed opportunities in the multivariable analyses.

DISCUSSIONS

This study showed that prevalence of missed opportunities for simultaneous administration of the fourth dose of PCV decreased significantly from 7.8% to 4.5% from 2008 to 2015. This current research determined that delays in receipt of the first, second, and third dose of PCV are the most significant risk factors related to missed opportunities for simultaneous administration of the fourth dose of PCV. To reduce missed opportunities for simultaneous administration of the fourth dose of PCV, immunization providers should be encouraged to adhere to the National Vaccine Program Office's Standards for Pediatric Immunization Practice (USDHHS, 1992). Among the 17 recommended practices, three are most relevant to reduce missed opportunities: (1). Administering vaccines simultaneously (at the same visit), in accordance with recommendations from the ACIP, the American Academy of Pediatrics, and the American Academy of Family Physicians is safe, effective and indicated. Although the immunization schedule provides age flexibility for administering certain vaccine doses, simultaneous administration decreases the number of visits needed and the potential for missed doses and enables earlier protection. When indicated vaccines are not simultaneously administered, arrangements should be made for the patient's earliest next return to receive the needed vaccination(s). (2). Healthcare professionals should review the vaccination status of all patients at all health care visits to minimize the number of missed opportunities to vaccinate. This review should determine whether the patient has received any vaccinations elsewhere or is at high risk for disease or undervaccination. This information should be documented in the patient's chart and preventive health summary. (3). Healthcare professionals or others who administer vaccinations should be knowledgeable and receive continuing education in vaccine storage and handling; the recommended vaccine schedule, contraindications, and administration techniques; treatment

and reporting of adverse events; vaccine benefit and risk communication; and vaccination record maintenance and accessibility. CDC sponsors distance-based training opportunities (eg, satellite broadcasts, web-based training, videotapes, self-administered print materials) for healthcare professionals.

Timing of the third dose of PCV is important in finding age eligible missed opportunities for the fourth dose of PCV. The age eligible period is eight weeks or more after receipt of the 3rd dose of PCV, however this interval requirement does not have significant impact on the missed opportunities since only 2.1% children in our analysis had less than an 8 week interval between their third dose of PCV and the visit where a missed opportunity to vaccinate was observed. For children who start late or fall behind on recommended vaccinations of PCV, ACIP's recommended childhood immunization schedule also includes a catch-up schedule for PCV (CDC, February 2016).

Education of parents/guardians about the benefits and risks of vaccination in a culturally appropriate manner and in easy-to-understand language might be another possible strategy for reducing missed opportunities (USDHHS, 1992; Seeber et al., 2017; Awadh et al., 2014). Health care professionals should allow sufficient time with parents/guardians to discuss the benefits of vaccines, the diseases that they prevent, any known risks from vaccines, the immunization schedule and the need to receive vaccines at the recommended ages and to answer any questions parents may have

Use of systems to remind parents/guardians, patients, and healthcare professionals when vaccinations are due and to recall those who are overdue is an evidence-based strategy in reducing missed opportunities for simultaneous administration of the fourth dose of PCV. This is also one of the best practices in the Standards for Pediatric Immunization Practice. Patient reminder/recall interventions inform individuals that they are due (reminder) or overdue (recall) for specific vaccinations. Patient reminders/recalls can be mailed or communicated by telephone; an autodialer system can be used to expedite telephone reminders. Patients who might be at high risk for not complying with medical recommendations, for example, those who have missed previous appointments, should receive more intensive follow-up. Providers' client reminder and recall system have been verified to be a critical strategy to catch every missed opportunity for simultaneous administration of the fourth dose of PCV, and this system must be continued (The Guide to Community Preventive Services, 2015). Similarly, provider reminder systems alert healthcare professionals when vaccines are due or overdue for their patients. Notices should be placed in paper or electronic patient charts or communicated to healthcare professionals by computer or other means. Immunization information systems (IIS) can facilitate automatic generation of reminder/recall notices.

The results of this study had several limitations. The NIS-Child RDD (Random Digital Dialed) sample may not represent the whole target population of 19–35 month children in the US. Some of the providers do not respond to the Immunization History Questionnaire, and measurement errors occur in reporting childhood vaccination status by parents/providers. Even if a weighting technique has been adopted to control sampling and non-sampling error, all of those factors could still cause certain bias in the estimation of

missed opportunities (Kirk et al., 2017). Further, missed opportunities for simultaneous administration of the fourth dose of PCV are counted for provider visit where a child received other age-eligible vaccines but not the fourth dose of PCV. However, there might be other opportunities such as children who visited a medical provider for reasons other than vaccination and did not receive any vaccines at that visit. Thus, this research could under-estimate missed opportunities for simultaneous administration of the fourth dose of PCV (Nuorti et al., 2010; Luman et al., 2005). Also, this is an observational study with survey data, which can't demonstrate a causal inference between factors and missed opportunities. Finally, this study evaluated the prevalence of missed opportunities for simultaneous administration of the fourth dose of PCV for the children who received the first three doses of PCV before 12 months of age. Since we don't identify children at high risk in NIS, we may have excluded some high risk children with three doses, at least one received at or after 12 months, who still should get the 4th dose of PCV.

CONCLUSION

Missed opportunities could be reduced by provider implementation of systems to ensure that all recommended vaccines are offered at each visit. Strategies providers could use to reduce missed opportunities for simultaneous administration of the fourth dose of PCV include patient recall, provider reminders, standing orders, extended office hours, and use of immunization information systems (IIS).

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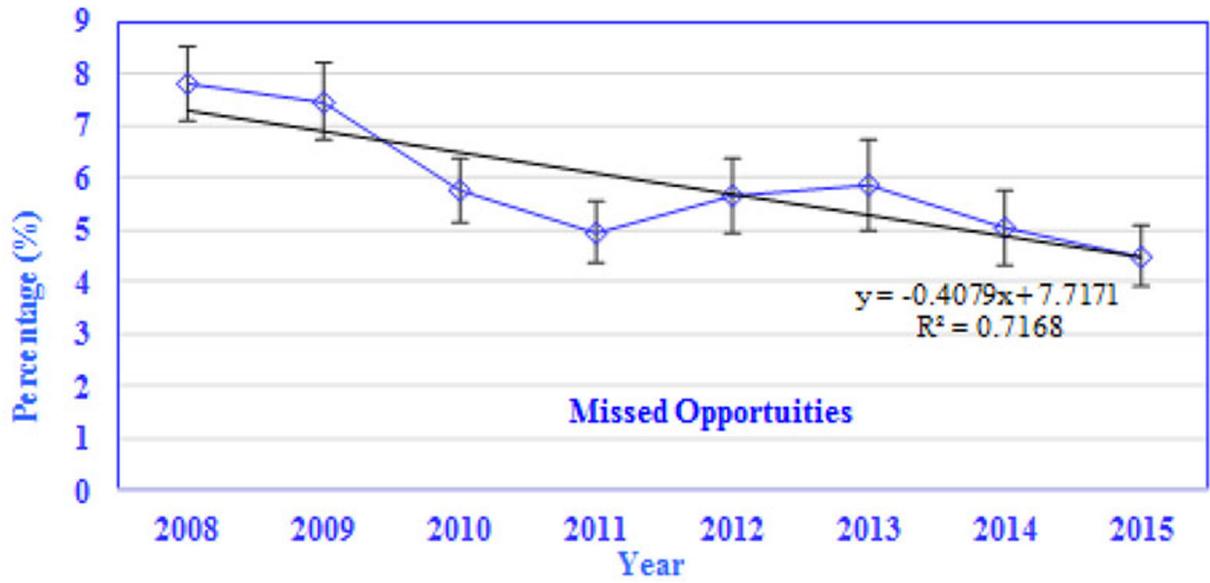


Figure 1. Trend in proportion of missed opportunities for simultaneous administration of the fourth dose of PCV^a for children 19–35 months in the United States, National Immunization Survey-Child, 2008–2015.

^a Pneumococcal conjugate vaccine.

Table 1.

Prevalence in missed opportunities for simultaneous administration of the fourth dose of PCV^d by vaccination and socio-demographic factors for children 19–35 months in the United States, using combined 2008–2015 National Immunization Survey-Child data.

Factors		Un-weighted sample size (weighted %)	Weighted prevalence in missed opportunities % (95% CI ^b)	Unadjusted prevalence ratios (95% CI) compared to reference level
Total		131464	5.9 (5.7, 6.2)	
Timeliness of the First dose of PCV	Late	14451 (13.3)	10.1 (9.2, 11.1)	1.9(1.7,2.1)
	On-time ^c	112648(86.7)	5.5 (5.2, 5.7)	
Timeliness of the Second dose of PCV	Late	23680 (22.2)	11.3(10.5,12.0)	2.4 (2.2, 2.6)
	On-time ^c	101622 (77.8)	4.8 (4.5, 5.0)	
Timeliness of the Third dose of PCV	Late	33401 (31.2)	11.3(10.7,11.9)	2.7 (2.5, 3.0)
	On-time ^c	89224 (68.8)	4.1(3.9,4.4)	
Years of formal education of mothers	12 years	38186(46.8)	6.9 (6.5, 7.3)	1.4(1.3,1.5)
	13 years ^c	93278 (53.2)	5.1 (4.8,5.3)	
Number of children in household	1 ^d	32458 (25.7)	5.2 (4.7, 5.6)	1.2(1.1,1.3)
	2	99006 (74.3)	6.2(5.9,6.5)	
Mother's marital status	Married ^c	96970 (65.6)	5.3 (5.0, 5.6)	1.4(1.2,1.5)
	Not married	32945 (34.4)	7.2 (6.7, 7.7)	
Mother's age	29 years	45879 (42.6)	6.9 (6.5, 7.4)	1.3(1.2,1.5)
	30 years ^c	85585 (57.4)	5.2 (4.9, 5.5)	
Type of vaccination providers	Public	13968(12.3)	7.4 (6.5, 8.3)	1.3(1.1,1.4)
	Private ^c	76823 (59.0)	5.9(5.6,6.2)	
Number of vaccination providers	1 ^c	88647 (66.2)	5.8(5.5,6.1)	1.1 (1.0, 1.2)
	2	42365 (33.8)	6.2 (5.8, 6.7)	
First born child	Not	77647 (57.8)	6.3 (6.0, 6.7)	1.2(1.1, 1.3)
	Yes ^c	53817(42.2)	5.3 (5.0, 5.7)	
Children health insurance status	No	20451 (19.5)	7.3 (6.7, 7.9)	1.3(1.2,1.4)
	Yes ^c	111013(80.5)	5.6(5.3,5.9)	
Race/ethnicity of child	White, non-Hispanic ^c	79038 (48.6)	5.3(5.0, 5.6)	
	Black, non-Hispanic	12555(13.0)	7.5 (6.7, 8.3)	1.4(1.3,1.6)

Factors	Un-weighted sample size (weighted %)	Weighted prevalence in missed opportunities % (95% CI ^b)	Unadjusted prevalence ratios (95% CI) compared to reference level
Hispanic	24866 (27.4)	6.6 (6.0, 7.2)	1.2(1.1,1.4)
Family poverty status			
At or Above ^c	96200(61.6)	5.1(4.8,5.4)	1.5(1.3, 1.6)
Below	30774 (32.9)	7.4 (6.9, 7.9)	

^aPneumococcal conjugate vaccine.

^bConfidence Interval.

^cReference Level.

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Table 2.

Adjusted prevalence ratios (APR) of missed opportunities for simultaneous administration of the fourth dose of PCV^a by timeliness of the first three doses of PCV vaccination and selected socio-demographic factors for children 19–35 months in the United States with combined 2008–2015 National Immunization Survey-Child data.

Factors	Comparison	Adjusted Prevalence Ratios (APR)
		Ratio (95%CI ^b)
Timeliness of the First dose of PCV	Late vs. On-time	1.17(1.02,1.34)
Timeliness of the Second dose of PCV	Late vs. On-time	1.38(1.20, 1.58)
Timeliness of the Third dose of PCV	Late vs. On-time	1.99(1.77,2.23)
Mother's age	29 vs. 30	1.16(1.06,1.27)
Firstborn child	Not vs. Yes	1.11(0.98,1.25)
Children health insurance status	No vs. Yes	1.10(0.99,1.21)
Years of formal education of mothers	12 vs. 13	1.08(0.98, 1.19)
Number of children in household	2 vs. 1	1.01 (0.89, 1.16)
Mother's marital status	Not married vs. Married	1.03 (0.93, 1.15)
Type of vaccination providers	Public vs. Private	0.99(0.86, 1.14)
Number of vaccination providers	2 vs. 1	1.07(0.98, 1.18)
Family poverty status	Below vs. At/Above	1.08(0.97,1.20)
Race/ethnicity of child	Black vs. White, non-Hispanic	1.14(1.00,1.29)
	Hispanic vs. White, non-Hispanic	1.06(0.95,1.19)

^aPneumococcal conjugate vaccine.

^bConfidence Interval.