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Effects of a nationwide Hib vaccine shortage on vaccination coverage in the United States

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ABSTRACT

Background: A shortage of *Haemophilus influenzae* type b (Hib) vaccine that occurred in the United States during December 2007 to September 2009 resulted in an interim recommendation to defer the booster dose, but to continue to vaccinate as recommended with the primary series during the first year of life.
Objectives: To quantify effects of the Hib shortage on vaccination coverage and to determine if any demographic subgroups were disproportionately affected.
Methods: Data from the 2009 National Immunization Survey (NIS) were divided based on child's age at the onset of the shortage. Comparisons were made in primary series coverage by 9 months between children <7 months versus ≥7 months at the start of the shortage. Comparisons in primary series plus booster dose completion by 19 months were made between children who were <12 months versus ≥12 months at the start of the shortage.
Results: Nationally, there was a difference in Hib primary series completion by 9 months among children age <7 months versus ≥7 months at the start of the shortage (73.9% versus 81.2%, $P < 0.001$). There was a large difference in the percentage of children fully vaccinated with the primary series plus booster dose by 19 months among children age <12 months versus ≥12 months at the start of the shortage (39.5% versus 66.0%, $P<0.001$). There were differential effects of the shortage on primary series coverage among states and for some demographic characteristics.
Conclusions: As expected booster dose coverage was reduced consistent with interim recommendations, but primary series coverage was also reduced by 7 percentage points nationally.
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On December 13, 2007 a shortage of *Haemophilus influenzae* type b (Hib) conjugate vaccines began due to the voluntary recall by one manufacturer of several lots of two types of Hib conjugate vaccines: PedvaxHIB®, a monovalent Hib vaccine, and Comvax®, a Hib-hepatitis B combination vaccine, both produced by Merck & Co., Inc. (West Point, Pennsylvania). At the time of the voluntary recall, there were two manufacturers with licensed Hib vaccine in the United States, Merck & Co., Inc. and Sanofi Pasteur (Swiftwater, Pennsylvania).

Due of the shortage of Hib vaccine, CDC recommended temporary suspension of the booster dose for children with no risk factors for Hib disease [1]. Because of the increased risk for Hib disease among American Indian/Alaska Native (AI/AN) children, providers who serve predominantly AI/AN children in AI/AN communities were recommended to continue to use PedvaxHIB (non-recalled lots) because it induced immunity earlier than the other Hib vaccines; these children were also recommended to continue to receive the booster dose [2]. The Pediatric Vaccine Stockpile was used to supply the shortage Hib vaccine (PedvaxHIB) to AI/AN children for the duration of the shortage [2].

The Hib vaccines of both manufacturers are recommended with dosing schedules that include a primary series followed by a booster dose in the second year of life; however, they differ on the number of doses recommended for completion of the primary series. Merck's PedvaxHIB is recommended as a 3-dose complete series, with primary series doses at 2 and 4 months and a booster at 12–15 months. Sanofi Pasteur's Hib vaccine is recommended at a 4-dose complete series, with primary doses at 2, 4, and 6 months, and a booster at 12–15 months. In June 2008 additional vaccine became available for the primary series when a combination product, DTaP-IPV-Hib (Pentacel, produced by Sanofi Pasteur), was licensed [3]. By July 2009, the Hib vaccine supply was sufficiently improved to allow the booster dose to be resumed and to begin a gradual catch-up effort to reach the children for whom the booster dose had been deferred [4]. The licensing in the United States of Hiberix® produced

Abbreviations: NIS, National Immunization Survey; Hib, Haemophilus influenzae type b; AI/AN, American Indian/Alaska Native; IHQ, Immunization History Questionnaire; VFC, Vaccines for Children; CASRO, Council of American Survey Research Organizations.

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by GlaxoSmithKline Biologicals (Rixensart, Belgium) on August 19, 2009 additionally helped to improve supply.[5] In September 2009, vaccination providers were recommended to begin active recall of children needing the booster dose. Overall, the Hib shortage lasted for approximately 18 months during 2008–2009.

The effects of the shortage were seen in the published estimates from the 2008 National Immunization Survey (NIS), where both national and state level estimates showed a reduction in Hib vaccination coverage levels. [6] There were also indications that the Hib shortage led to lower completion of the primary series [7,8]. In the current study, data from the 2009 NIS, which incorporated an improved method for measuring Hib vaccination, are analyzed to quantify the effects of the vaccine shortage on Hib vaccination coverage overall and by state, and to determine if any demographic subgroups were disproportionately affected by the shortage.

1. Methods

Data from the 2009 National Immunization Survey (NIS) were analyzed. The data were based on interviews conducted during January 6, 2009 to February 10, 2010 for children born during January 7, 2006 through July 10, 2008. The NIS is an ongoing, national, random-digit-dial telephone survey of households with children 19–35 months at the time of interview. The household telephone survey is followed by a survey mailed to the immunization providers identified during the telephone survey and for which permission was granted. Beginning in January 2009, the NIS added a question about the type of Hib vaccine to the Immunization History Questionnaire (IHQ) mailed to vaccination providers (prior to January 2009, information on vaccine type of monovalent Hib vaccines was not requested). The IHQ has a shot grid that provides space for up to 5 doses of Hib to be entered, including the date the dose was administered, a query if the dose was administered by another practice, and a check box grid for vaccine type, including: Merck (PedvaxHib), Sanofi Pasteur (ActHib), HepB-Hib, DTaP-Hib, DTaP-IPV-Hib. All vaccination coverage results in this study are based upon provider-reported vaccinations data.

We stratified the sample of children into groups more likely versus less likely to be affected by the shortage. For the primary series analyses the two groups were children <7 versus ≥7 months on December 13, 2007, while for the primary series plus booster analyses the groups were children <12 versus ≥12 months on December 13, 2007. The age stratification for the primary series (i.e., <7 versus >7 months) allowed us to compare delayed vaccine administration taking into account that the last dose of the 3-dose series is recommended to be given at 6 months. Because the Hib shortage began December 2007 and the Hib booster dose was reinstated in July 2009, children in the 2009 NIS who were younger than 12 months at the beginning of the shortage would have become due to receive their booster dose during the shortage period. Children who were 12 months or older at the beginning of the shortage may have already received their booster dose. We also analyzed Hib primary series coverage by 19 months of age, in order to evaluate any differences in completion using broader age criteria.

1.1. Definition of up-to-date for Hib variables

Two Hib vaccination coverage variables are presented in this study, both are created using the vaccine type information from the IHQ: (1) at least primary series complete, i.e., received at least 2 or 3 doses depending on type; and (2) fully vaccinated with the primary series and booster dose. For some children and some Hib vaccines, the vaccine type was not reported. For the estimate of the percentage completing the primary series, 0.8% of children were missing vaccine type information for their first or second Hib dose. For the estimate of the percentage completing the primary series and booster dose, 4.7% of children had missing vaccine type information. The two vaccination coverage measures were computed assuming the Hib vaccines with missing type were a type requiring 3 doses for the primary series. Children who receive a mixture of vaccine types for the primary series would require 3 doses for the primary series according to Hib vaccine recommendations. More details of these new measures have previously been published [9].

In all analyses, we stratified the respondents and report results by various demographic subgroups to determine if the impact of the shortage was uniform across children in these different subgroups. Demographic characteristics of the children in the sample were obtained during the telephone interview of the parent/guardian, as part of routine NIS data collection. Poverty level was determined by using household reported income level, number of people reported living in the household and U.S. poverty thresholds. Eligibility for the Vaccines for Children (VFC) program, a federal entitlement program that provides free vaccines, includes children younger than 19 years who are: uninsured, Medicaid insured, underinsured and receive vaccines at federally qualified health or rural centers, or are American Indian/Alaska native. Characteristics of providers are provider-reported, i.e., provider type. Methodological details of the NIS have been previously published [10–13]. As a secondary analysis, to attempt to evaluate impact of type of vaccine product used by a state prior to the shortage, we classified each state by percentage Merck product used (0–25%, 26–50%, 51–75%, and 76–100%) based on public purchase vaccine distribution data collected by CDC (June 1, 2007–November 30, 2007). Data on private purchase vaccine distribution by state was not available.

We compared the percentage of children who were primary series complete by age 9 months and fully vaccinated by age 19 months among our two stratified groups of children, children more versus less likely to have been affected by the shortage. Statistical significance was tested using Wald chi-squared tests. Proportions are reported along with 95% confidence intervals (95% CI). A two-sided significance level of 0.05 was adopted for all statistical tests. Data were weighted to adjust for households having multiple telephone lines, non-assessment of households without telephones, household unit non-response, provider non-response, and to reflect population demographic totals. Analysis were conducted using SAS, release 9.2 (SAS Inc., Cary, NC) and SUDAAN, release 10.0 (Research Triangle Institute, Research Triangle Park, NC).

2. Results

For the 2009 NIS, the Council of American Survey Research Organizations (CASRO) [14] response rate was 63.7%,which is the product of the percent of telephone lines identified as residential or non-residential (82.8%), the percent of known households who completed the screening interview (92.4%), and the percent of eligible respondents who completed interviews (83.2%). Adequate provider vaccination records were obtained for 68.7% (n = 17,053).

The percentage of children who completed the primary series by 9 months was 78.2% and the percentage fully vaccinated with the primary series and booster was 47.6%. Fig. 1a and b displays (a) Hib primary series coverage and (b) primary series plus booster coverage by monthly cohort. Of the 17,053 children, 41.0% (n = 7035) were <7 months at the start of the shortage (December 13, 2007) and 59.0% (n = 10,018) were ≥7 months at that time; 69.6% (n = 11,985) were <12 months at the start of the shortage and 30.4% (n = 5068) were ≥12 months.

In Fig. 1b the trend of decreasing Hib vaccine primary series plus booster coverage can be seen among those 12 months and younger at the start of the shortage. The decrease begins to be seen