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Uptake of rotavirus vaccine among US infants at Immunization Information System Sentinel Sites

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ABSTRACT

Objective: Coverage with rotavirus vaccine among US children has been lower compared to that with other routine childhood vaccines. Our objectives were to examine rotavirus vaccine (RV) uptake over time compared to other routine vaccinations, ages at administration, and quantitate potential missed opportunities for RV receipt.

Methods: We analyzed data from 6 Immunization Information System (IIS) Sentinel Sites, which represent approximately 10% of the United States (US) pediatric population. Among infants aged 5 months, we compared uptake of ⩾1 dose of RV, to that of Diphtheria, Tetanus, and acellular Pertussis (DTaP) and pneumococcal conjugate vaccine (PCV), for each quarter during 2006–2013. We used data from infants in the 2012 birth cohort to examine RV receipt in more detail.

Results: Among infants aged 5 months, the average site coverage with ⩾1 dose of RV reached 78% in 2010 and subsequently stayed steady at 79–81% through 2013. The average difference between ⩾1 dose DTaP coverage and RV coverage remained between about 6 and 8 percentage points during mid-2012 through 2013. Infants born in 2012 received RV doses closely in line with the timing recommended by the ACIP. Approximately one-third of the difference in coverage between ⩾1 dose of DTaP and ⩾1 dose of RV among infants could be due to the maximum age restriction of the first RV dose. The other two-thirds of the difference appears to have been a result of potential missed opportunities for starting the RV series--these infants received another routine immunization when age eligible to receive RV dose 1, but did not receive RV.

Conclusion: Uptake with RV during infancy remains below that of other routine vaccines. Understanding the barriers to administration of RV among age-eligible infants could help improve vaccine coverage.

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1. Introduction

Before rotavirus vaccines became available, rotavirus was the leading cause of severe gastroenteritis in children in the United States (US), resulting in approximately 55,000–70,000 hospitalizations, 250,000 emergency department (ED) visits, and 400,000 physician visits annually in children aged <5 years and total annual direct and indirect costs of approximately $1 billion [1]. In 2006, the Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination of US infants with RotaTeq (RV5) (Merck, Whitehouse Station, NJ), a 3-dose series with doses recommended at ages 2, 4, and 6 months [2]. The recommendations were updated in 2008 to include Rotarix (RV1), (GlaxoSmithKline Biologics, Rixensart, Belgium), a 2-dose series with doses recommended at ages 2 and 4 months [1]. Unlike other routine childhood vaccines, rotavirus vaccines in the US were introduced with and still have upper age-limit restrictions during infancy, with no catch-up vaccination if an infant presents beyond those ages. Specifically, the maximum age at which the first dose is to be given is 14 weeks 6 days and the maximum age of the last dose is 8 months 0 days. These age restrictions (harmonized for both rotavirus vaccines) were implemented because these were the

Abbreviations: US, United States; ED, emergency department; DTaP, Diphtheria, Tetanus, and acellular Pertussis; RV, Rotavirus Vaccine; RV5, RotaTeq; PCV, Pneumococcal Conjugate Vaccine; RV1, Rotarix; ACIP, Advisory Committee on Immunization Practices; NIS, National Immunization Survey; IIS, Immunization Information System.

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maximum ages used in the pre-licensure clinical trials [1]. Further, because the background rate of intussusception increases during the first few months of life, administering the first dose at a younger age would optimize the benefit vs risk assessment if a risk of intussusception from the first dose was identified after licensure. A risk of intussusception was subsequently identified for both RV1 and RV5, estimated in the US to be approximately 1–5 excess cases of intussusception per 100,000 vaccinated infants [3]. The overall benefit-risk assessment of rotavirus vaccination remains highly favorable, with data indicating ~44,000 rotavirus hospitalizations and 61,000 ED visits in young children were averted annually in the US following vaccine introduction [4].

Rotavirus vaccination coverage in the US has not been as high as other routine childhood vaccinations; this was not unexpected given the maximum age restrictions. Published results from Immunization Information System (IIS) Sentinel Sites demonstrated that, by 2009, coverage with ⩾1 dose of RV among infants aged 5 months had reached an average of 72% at the 8 IIS sites, but this was on average 13 percentage points lower than coverage with ⩾1 dose of Diphtheria, Tetanus, and acellular Pertussis (DTaP) Vaccine, and Pneumococcal Conjugate Vaccine (PCV) [5]. Most recently, data from the 2014 National Immunization Survey (NIS), which measures receipt of vaccines among children aged 19–35 months, determined coverage with a full series of RV (3 doses of RV5 or 2 doses of RV1) to be 72%, compared to coverage with ⩾3 doses of DTaP and PCV of 95% and 93%, respectively; children in the 2014 NIS were born January 2011 through May 2013 [6].

We used IIS Sentinel Site data to examine RV uptake over time compared to other routine vaccinations, adherence to ACIP recommendations on ages at administration, and quantitate potential missed opportunities for RV receipt.

2. Materials and methods

Data were analyzed from the six IIS Sentinel Sites. IIS are confidential, population-based systems that record and consolidate vaccination doses administered by participating providers to persons residing in a given geopolitical area. IIS Sentinel Sites are sites that have high data quality and have received competitive supplemental funds to collaborate with the Centers for Disease Control and Prevention (CDC) for program evaluation and vaccine use assessments. IIS Sentinel Site data analyzed for the period of interest (2006–2013) included the entire states of Michigan, Minnesota, North Dakota, and Wisconsin, all of New York City, and six counties encompassing the Portland metropolitan area in Oregon (56% of the state population). These IIS Sentinel Sites represent approximately 10% of the U.S. pediatric population. De-identified individual record-level data were received from IIS Sentinel Sites and processed in accordance with IIS best practice [7]. Children known to be deceased or children who moved from the jurisdiction were excluded from the analysis.

For each IIS Sentinel Site, vaccination coverage with ⩾1 dose of RV, DTaP, or PCV (PCV 7-valent or 13-valent) was assessed among infants aged 5 months (5 months 0 days through 5 months 30 days) on the last day of each quarter (i.e., March 31, June 30, September 30, December 31), for the years 2006–2013. Coverage was calculated by dividing the number of infants aged 5 months who had received the vaccine by the total number of infants aged 5 months in the Sentinel Site population in the IIS database. Unweighted averages were then calculated by summing the site-specific coverages and dividing by the number of sites. For each quarter 2011 through 2013, differences in RV and DTaP coverage among infants aged 5 months were calculated for each site separately, and averaged across sites.

For each site, data from infants born during January 1, 2012 through December 31, 2012 were used to examine age in completed weeks (0–51 weeks) at receipt of RV doses 1, 2 and 3. Data from infants of the 2012 birth cohort (site-specific and all sites combined) were also used to examine the frequency of potential missed opportunities for starting the RV series within the ACIP-specified age window. Among all infants who received ⩾1 dose of a non-influenza vaccine (RV, DTaP, PCV, hepatitis B vaccine, *H. influenzae* type b vaccine, or inactivated polio vaccine) before age 1 year, those with a "potential missed opportunity" to receive the first dose of RV were defined as infants who never received RV, but who had received ⩾1 non-rotavirus infant vaccination when aged 6 weeks 0 days through 14 weeks 6 days. This study was exempt from IRB review since it involved examination of secondary, de-identified data.

3. Results

The average proportion of infants in IIS Sentinel Sites aged 5 months who had received ⩾1 RV dose reached 60% in the last quarter of 2007, approximately 1.5 years after the ACIP first voted to recommend routine use among US infants of the available newer generation RV (Fig. 1). The average site coverage with ⩾1 dose of RV continued to increase and reached 78% in later 2010, and has subsequently has stayed steady at 79–81% through the end of 2013. This compares to an average site coverage with ⩾1 dose of DTaP of 87–90% for almost every quarter since third quarter of 2007 (2 quarters in 2013 had average site coverage of 85%) and, for that same period, 84–88% coverage with ⩾1 dose of PCV (1 quarter in 2013 had average site coverage of 83%).[1] Among the sites, the average difference between ⩾1 dose DTaP coverage and RV coverage remained between about 6 and 8 percentage points during second quarter of 2012 through fourth quarter of 2013 (Fig. 2), although there appeared to be a gradual reduction in the difference at 4 of the 6 sites during this period. At the last time point in this evaluation, fourth quarter of 2013, the mean and median site coverage with ⩾1 RV dose was 79% and 82%, respectively, with range of 71–85%. The mean (which was the same as the median) of the differences between sites' DTaP and PCV coverage, versus RV coverage, was 6% and 4%, respectively (Table 1).

Doses of RV recorded in the IIS indicated that infants born in 2012 were receiving the vaccines closely in line with the timing of doses recommended by the ACIP (Fig. 3). Of all the first doses given during the first year of life, on average at the sites, <1% of first doses were administered before age 6 weeks 0 days, and 4% (site range, 3–5%) were administered after age 14 weeks 6 days. Of all the second and third RV doses, on average, only <1% and 1% of the doses, respectively, were administered after the recommended maximum age of 8 months 0 days (35 weeks in our analysis). On average across the sites, 78% of first doses were administered during the 3-week period of ages 8 through 10 weeks, 71% of second doses were administered during ages 17 through 19 weeks, and 72% of third doses during ages 26 through 28 weeks.

Overall, among the 410,336 infants in the 2012 birth cohort at the sites combined who had received at least one non-influenza vaccination during infancy, 62,324 (15%) did not receive RV (Fig. 4). Of that group who did not receive RV, 27,876 (45%) had received another routine immunization during ages 6 weeks 0 days through

[1] From March 22, 2010 through May 14, 2010, RV1 was temporarily suspended by the Food and Drug Administration following the detection of the adventitious agent porcine circovirus type 1 in RV1. Fragments of porcine circovirus type 2 DNA were identified in RV5. The FDA ultimately concluded that these were not a safety risk (http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm205547.htm). IIS Sentinel Site data show a small decrease in RV coverage in first half of 2010, which might have resulted from this issue.