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RESEARCH ARTICLE

Hepatitis B Birth Dose: First Shot at Timely Early Childhood Vaccination

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Introduction: Current U.S. recommendations state that newborns weighing ≥2,000 grams should receive a birth dose of hepatitis B vaccine, yet approximately one quarter do not receive this first dose as scheduled. The relationship between timely receipt of the first hepatitis B vaccine and other early childhood vaccines remains unclear.

Methods: Washington State newborns (birth weight ≥2,000 grams) who received birth hospitalization care at an urban academic medical center between 2008 and 2013 were included. Multivariable logistic regression was used to assess whether hepatitis B vaccine receipt during the birth hospitalization was associated with completing the seven-vaccine series by 19 months, adjusting for select sociodemographic, clinical, and birth hospitalization characteristics. Analyses were conducted in 2017−2018.

Results: Of the 9,080 study participants, 75.5% received hepatitis B vaccine during the birth hospitalization, and 53.6% completed the seven-vaccine series by 19 months. Overall, 60.0% of infants vaccinated against hepatitis B during the birth hospitalization completed the seven-vaccine series by 19 months compared with 33.8% of those who were unvaccinated at discharge (p<0.001). The odds of series completion were nearly 3 times higher among infants who received versus did not receive hepatitis B vaccine during the birth hospitalization (AOR=2.92, 95% CI=2.61, 3.26).

Conclusions: Infants who received hepatitis B vaccine during their birth hospitalization had higher odds of receiving all recommended vaccines by 19 months independent of other factors associated with vaccine receipt. Understanding the factors that influence this first parental vaccine decision and how hepatitis B vaccine delay or declination may affect subsequent vaccination requires further research.

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INTRODUCTION

The Advisory Committee on Immunization Practices recommends a seven-vaccine series for all children by age 19 months,[1] yet nearly 30% of those aged 19−35 months nationally have not received the full complement of recommended vaccines.[2] Understanding the factors that influence vaccine uptake is key to ensuring that children are protected against vaccine-preventable diseases and herd immunity remains high enough to protect those too young or ill to be vaccinated. Investigation of a parent's first vaccine decision and its relationship with subsequent vaccine uptake could be valuable but has been underexamined.

Limited studies have assessed the relationship between receipt of the first hepatitis B (HepB) vaccine, which is

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recommended within 24 hours of birth for all medically stable newborns weighing ≥2,000 grams,[3] and completion of other childhood vaccinations recommended between ages 2 and 19 months. Studies conducted in the 1990s identified delayed receipt of the first HepB vaccine as a risk factor for lower uptake of *Haemophilus influenzae* type b, diphtheria−tetanus−(whole-cell or acellular) pertussis, poliovirus, and measles vaccines by age 35 months.[4,5] More recent studies using state registries[6,7] and national survey data[8] showed that infants whose parents delay the HepB birth dose have lower uptake of routinely recommended vaccines between ages 19 and 35 months. However, these previous studies were based on parental report,[4] vaccine records available at the child's home, or mailed surveys to the child's vaccine provider,[4,5] and did not assess all currently recommended vaccines,[4,5,8] or lacked relevant demographic data[6,7] that are strongly associated with vaccination coverage.[9,10]

The current study, therefore, aims to assess whether HepB vaccination during the birth hospitalization (as recommended during the study period) is associated with completing all recommended vaccines by age 19 months using electronic medical record (EMR) and immunization registry vaccine data, as well as including more comprehensive sociodemographic data than previous studies. It is hypothesized that infants who receive timely HepB vaccine will have higher vaccine completion by 19 months than those who do not.

METHODS

Study Sample

This retrospective cohort study included all Washington State infants born at ≥2,000 grams who received birth hospitalization care at the University of Washington Medical Center, a large academic medical center in Seattle, WA, between January 1, 2008 and December 31, 2013. The sample was limited by birth weight because of distinct recommendations by the Advisory Committee on Immunization Practices for HepB vaccination of infants born at <2,000 grams.[3] Infants without complete admission and discharge data, and those who transferred to University of Washington Medical Center after birth were excluded. The analyses were conducted in 2017 and 2018. The study was approved by the Seattle Children's Hospital and Washington State IRBs.

Sociodemographic, clinical, and birth hospitalization data were retrospectively abstracted from study subjects' EMR. Vaccine administration data, including doses given during the birth hospitalization and after hospital discharge at affiliated practices, were obtained from the EMR. To capture doses given in other clinical settings after hospital discharge, select identifiers and a standardized matching algorithm linked EMR data to the subjects' vaccine records in the Washington State Immunization Information System (WAIIS). Although providers are not mandated to report to WAIIS, the Centers for Disease Control and Prevention estimates that at least 95% of Washington children aged <6 years participated in WAIIS during the study period.[11] A 2014 validation study in a large integrated healthcare organization in Washington State reported that only 1% of recorded pediatric vaccinations were missing in WAIIS.[12] WAIIS completeness may be enhanced by automated EMR data transfers, which comprise most (>95%) of WAIIS data (MP DeHart, Washington State Department of Health, personal communication, 2019) and have higher accuracy than manual submissions.[13] Additionally, WAIIS records are inactivated when children die or move out of state. Infants with incomplete or inactive WAIIS records or fewer than 2 recorded doses (of any vaccine) by 19 months were not included in the present study, consistent with national and state reporting standards.[14]

Measures

The primary outcome was completion of the seven-vaccine series (4 doses of diphtheria−tetanus−[whole-cell or acellular] pertussis, 3 poliovirus, 1 measles−mumps−rubella, 3 *H. influenzae* type b, 3 HepB, 1 varicella, 4 pneumococcal) by age 19 months. Secondary outcomes included receipt of individual vaccines within the seven-vaccine series, rotavirus (2 doses), and influenza (2 doses) vaccines by 19 months. The 19-month cut off (i.e., age <580 days) has been used previously to define timely vaccine receipt.[15]

The main independent variable was HepB vaccine receipt during the birth hospitalization. Subgroup analysis further evaluated HepB vaccine receipt within 3 or 30 days of birth. The 3-day outcomes were assessed only in a subset of infants born on or after October 19, 2010, which corresponded to the date when time stamp data for vaccine administration became available in the medical center's EMR. The 3-day cut point was selected because it is used as a proxy measure in national data for HepB vaccine administration during the birth hospitalization. The 30-day cut point was selected to capture infants medically ineligible to receive HepB vaccine until age 1 month.[3]

Sociodemographic data included infant sex (male, female), insurance status (public, private), race/ethnicity, maternal language, area-level income, and urban/rural residency status. Race/ethnicity and maternal language were recorded at point of care by hospital staff. Race/ethnicity was categorized using U.S. Census Bureau classifications[16] and collapsed into Hispanic, non-Hispanic white, non-Hispanic black, Asian, and multiracial/other for parsimony and interpretability. Maternal language was categorized as English, Spanish, and other. Area-level income was measured for each patient based on the median household income in their zoning improvement plan (ZIP) code using 2010 Census Bureau data.[17] ZIP codes were stratified into equal quartiles with household income ranging from $20,135 to $42,799 (Q1), $42,800 to $50,844 (Q2), $50,845 to $62,239 (Q3), and $62,240 to $174,729 (Q4). Urban versus rural residency was measured using Rural−Urban Commuting Area codes, a 10-point classification system that categorizes geographic areas as primarily rural or urban based on Census tract and commuting data. Rural−Urban Community Area designations were assigned for each study participant using the institution's ZIP code to Census tract crosswalk assignment and a two-category classification (Type C).[18]

Preterm birth was defined as birth at <37 weeks gestation,[19] and term birth was defined as 37−43 weeks gestation. Length of the birth hospitalization stay was calculated as hours between admission and discharge, and categorized as <24 hours, ≥24 and <48 hours, ≥48 and <96 hours, and ≥96 hours. Hospital service during the birth hospitalization included newborn nursery, intermediate care nursery, and neonatal intensive care unit.

Statistical Analysis

Logistic regression models were used to assess the relationship between HepB vaccine receipt during the birth hospitalization (or within 3 or 30 days of birth) and receipt of vaccines recommended by 19 months. In secondary analysis, separate multivariable logistic regression models were fit to assess the relationship between HepB vaccine receipt during the birth hospitalization and receipt of individual vaccines in the seven-vaccine series, rotavirus vaccine, and influenza vaccine by 19 months. All models were first unadjusted and then adjusted for the following characteristics known or suspected to be associated with childhood vaccination: infant sex, race/ethnicity, maternal language, insurance status, rural–urban and income estimates, gestational age, birth hospitalization service, and length of stay.[9,10,20] Stata, version 14.0, was used for all analyses; *p*-values were based on two-tailed tests and considered significant at $p<0.05$.

RESULTS

A total of 9,080 infants weighing ≥2,000 grams received birth hospitalization care at the study hospital between 2008 and 2013. Infant sociodemographic, clinical, and birth hospitalization characteristics are shown in Table 1 overall and across receipt of the seven-vaccine series by 19 months in Appendix Table 1.

Overall, 75.5% of the study population received HepB vaccine during the birth hospitalization, and 53.6% completed the seven-vaccine series by 19 months. Completion of the seven-vaccine series increased slightly during the study period, from 51.7% in 2008 to 55.7% in 2013, with the lowest rate in 2010 (51.2%). Of those who received the HepB birth dose, 60.0% completed the seven-vaccine series by 19 months versus 33.8% who did not receive HepB vaccine before hospital discharge ($p<0.001$).

The odds of seven-vaccine series completion by 19 months were higher among infants who received than among those who did not receive the HepB birth dose in both unadjusted and adjusted models (unadjusted OR=2.94, 95% CI=2.66, 3.25 [not shown]; AOR=2.92, 95% CI=2.61, 3.26; Table 2). There was a significant association between HepB birth dose receipt and receipt of individual vaccines in the seven-vaccine series, rotavirus, and influenza vaccines by 19 months (Figure 1). The strength of association varied by vaccine type, with the lowest association between HepB birth dose receipt and 4-dose diphtheria–pertussis–tetanus series completion (AOR=1.68, 95% CI=1.51, 1.88) and the highest association between HepB birth dose receipt and 3-dose HepB series completion (AOR=7.99, 95% CI=6.99, 9.16).

Table 1. Characteristics of Study Population

Characteristics[a]	*n* (%) (*n*=9,080)
Sex	
Male	4,649 (51.2)
Female	4,431 (48.8)
Race/ethnicity	
Hispanic	1,170 (14.6)
Non-Hispanic white	3,901 (48.7)
Non-Hispanic black	1,759 (21.9)
Asian	1,081 (13.5)
Multiracial/other	103 (1.3)
Maternal language	
English	6,486 (76.0)
Spanish	853 (10.0)
Other	1,190 (14.0)
Insurance status	
Private	3,747 (44.2)
Public	4,737 (55.8)
Rural–urban residence	
Rural	237 (2.6)
Urban	8,840 (97.4)
Estimated household income[b]	
$20,135–42,799	365 (4.0)
$42,800–50,844	1,109 (12.3)
$50,845–62,239	3,574 (39.6)
$62,240–174,729	3,980 (44.1)
Gestational age, weeks	
<37	984 (10.8)
37–43	8,093 (89.2)
Birth hospitalization length of stay, hours	
<24	820 (9.1)
≥24 to <48	3,956 (43.6)
≥48 to <96	3,296 (36.3)
≥96	1,008 (11.0)
Birth hospitalization service	
Newborn nursery	7,266 (80.0)
Intermediate care	1,330 (14.7)
Neonatal ICU	484 (5.3)

[a]All proportions shown in table are based on known data. Number and percentage of missing data are as follows: maternal race/ethnicity=1,066 (11.7%); maternal language=551 (6.1%); insurance status=596 (6.6%); rural–urban residence=3 (0.03%); estimated household income=52 (0.6%); gestational age=3 (0.03%).
[b]Based on 2010 U.S. Census Bureau ZIP code–level median household income.
ICU, intensive care unit; ZIP, zoning improvement plan.

In the subset of infants born on or after October 19, 2010 (*n*=4,666), infants who received HepB vaccine within 3 days of birth had nearly threefold greater odds of seven-vaccine series completion by 19 months than those unvaccinated within 3 days (63.0% vs 37.2%, $p<0.001$; AOR=2.92, 95% CI=2.51, 3.39). Most (98.0%) infants who received HepB vaccine within 3 days were

Table 2. AOR and 95% CI of Seven-Vaccine Series Completion Within 19 Months of Birth[a]

Characteristics	AOR (95% CI)
Patient characteristics	
HepB vaccine receipt[b]	**2.92 (2.61, 3.26)**
Sex	—
Male	1.02 (0.93, 1.11)
Female	ref
Race/ethnicity	—
Hispanic	1.00 (0.83, 1.21)
Non-Hispanic white	ref
Non-Hispanic black	0.95 (0.82, 1.09)
Asian	**1.66 (1.43, 1.94)**
Multiracial/other	0.81 (0.54, 1.22)
Maternal language	—
English	ref
Spanish	**1.74 (1.42, 2.14)**
Other	0.94 (0.81, 1.09)
Insurance status	—
Private	**1.78 (1.60, 1.99)**
Public	ref
Rural–urban residence	—
Rural	1.00 (0.74, 1.35)
Urban	ref
Estimated household income[c]	—
$20,135–42,799	0.88 (0.69, 1.12)
$42,800–50,844	0.96 (0.83, 1.11)
$50,845–62,239	0.98 (0.89, 1.08)
$62,240–174,729	ref
Clinical and birth hospitalization characteristics	
Gestational age, weeks	—
<37	0.97 (0.81, 1.17)
37–43	ref
Birth hospitalization length of stay, hours	—
<24	**0.75 (0.63, 0.89)**
≥24 to <48	ref
≥48 to <96	0.94 (0.85, 1.04)
≥96	1.13 (0.94, 1.34)
Birth hospitalization service	—
Newborn nursery	ref
Intermediate care	0.89 (0.76, 1.04)
Neonatal ICU	**0.46 (0.36, 0.60)**

Note: Boldface indicates statistical significance ($p<0.05$).
[a]Models adjusted for all sociodemographic, clinical, and birth hospitalization characteristics listed in Table 1, including missing cases.
[b]HepB vaccine receipt during the birth hospitalization.
[c]Based on 2010 U.S. Census Bureau ZIP code–level median household income.
ICU, intensive care unit; ZIP, zoning improvement plan.

vaccinated during their birth hospitalization; the remaining infants were vaccinated at other healthcare facilities after discharge. Infants who received HepB within 30 days of birth had fourfold greater odds of timely series completion than those unvaccinated within 30 days (59.4% vs 25.8%, $p<0.001$; AOR=4.40, 95% CI=3.85, 5.02).

DISCUSSION

In this large statewide sample, a strong association was found between HepB birth dose receipt and timely uptake of other recommended early childhood vaccines. Slightly more than half (53.6%) of the study population completed the seven-vaccine series by 19 months, and a much higher proportion of those who received a timely HepB birth dose completed the series by 19 months (60.0%) compared with those who did not (33.8%). Infants who received HepB vaccine during their birth hospitalization had higher odds of completing the seven-vaccine series by 19 months compared with infants who remained unvaccinated at their birth hospitalization discharge. This effect remained after adjusting for infant characteristics known or hypothesized to be associated with vaccine receipt.[20] These results indicate that failure to receive a timely HepB birth dose could serve as a critical "red flag" to outpatient providers, identifying infants early in the immunization process who are at a high risk for low vaccine uptake and may benefit from targeted interventions.

A major study strength was the ability to evaluate EMR vaccine administration data and link these to state immunization registry data to assess vaccination coverage through 19 months. Moreover, key sociodemographic, clinical, and birth hospitalization characteristics were captured that could have confounded the association between timely receipt of HepB and subsequent vaccine receipt. Previous studies have assessed HepB vaccine receipt within 3 days of birth[6] (i.e., as a proxy measure for HepB vaccine administration during the birth hospitalization owing to a lack of hospital-level data), 7 days of birth,[4,7] and 3 months of birth.[5] Despite the methodologic differences, the current findings mirror previous studies to consistently show that timely receipt of the first HepB dose is associated with higher uptake of routinely recommended childhood vaccines. In the current study, the markedly increased odds of HepB series completion may simply reflect the fact that initiating HepB vaccination during the birth hospitalization provides a head start for 3-dose HepB series completion, which was similarly shown using National Immunization Survey data.[21]

The strong association between receiving the HepB birth dose and uptake of future childhood vaccines identified in the present study suggests a need for targeted interventions encouraging parental acceptance of the first HepB vaccine dose. However, potential barriers to

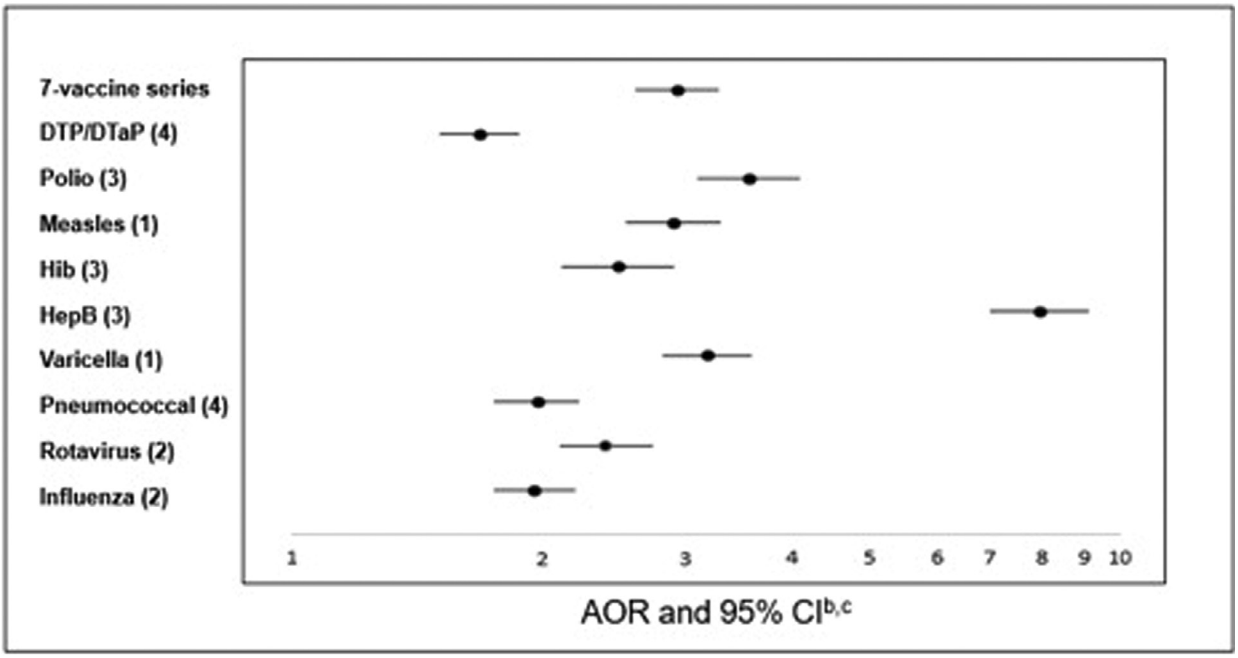

Figure 1. Association between hepatitis B birth hospitalization dose receipt and completion of recommended childhood vaccines[a] by age 19 months.

[a]Number of doses recommended for each vaccine listed in parentheses. The seven-vaccine series is comprised of the following: diphtheria–tetanus–(whole-cell or acellular) pertussis (DTP/DTaP), polio, measles-containing vaccine (measles), *Haemophilus influenzae* type b (Hib), hepatitis B (HepB), varicella, pneumococcal.

[b]Estimates adjusted for infant sex, race/ethnicity, maternal language, insurance status, rural–urban and income estimates, gestational age, birth hospitalization service, and length of stay.

[c]X-axis is shown in logarithmic scale.

timely receipt of the first HepB vaccination exist. Previous research suggests that HepB vaccine receipt during the birth hospitalization is lower among infants who are privately versus publicly insured, have an English- versus Spanish-speaking mother, or are non-Hispanic white versus other races/ethnicities.[20] Patients who are less likely to receive a timely HepB vaccination also fall into the demographic group at lowest risk for maternal HepB virus infection,[22] potentially influencing parental decision making and provider vaccine communication. Yet, a timely HepB birth dose may be the first step in establishing vaccination as the reference point and increasing future vaccine compliance. Research suggests that completing an activity for the first time (e.g., vaccination) increases its acceptance and establishes the new activity as the default option.[23–25] Consistent with this, a longitudinal study showed significant decreases in maternal vaccine hesitancy between a child's birth and age 24 months[26] and hypothesized that mothers' confidence in vaccine safety and efficacy grew as their experience with vaccines accumulated.

Given that parents consistently cite their child's provider as influential in vaccine decision making,[27,28] provider-guided interventions including engagement in vaccine discussions during (or potentially before) pregnancy, or during the 2-month window between a missing HepB birth dose and when other recommended vaccines are due, could help improve early childhood vaccine uptake. Research suggests that the most effective vaccine communication strategies are a strong provider recommendation using a presumptive, rather than participatory approach, pursing initial recommendations if a parent resists, and tailoring messages to address the unique needs and concerns of each patient and family.[29–31] These communications should address previously identified barriers to HepB birth dose receipt, including a preference to be vaccinated in the provider's office after birth hospitalization discharge, perceptions that an individual baby is not at risk based on maternal health behaviors and history, and a lack of understanding of the seriousness of HepB virus infection.[32] Providers could also consider utilizing evidence-based narratives of vaccine-preventable disease cases or describe why, as parents, they chose to vaccinate their own children, which some parents may find more compelling.[33]

Finally, given suboptimal vaccination rates and the fact that vaccination decisions can occur because of status quo bias, in which people are hesitant to deviate from their current baseline or a previously made decision,[23,34,35] broad campaigns aimed at promoting a culture of vaccine acceptance are indicated. Social media is frequently used by the anti-vaccine community to question the necessity of newborn preventive care, such as vitamin K injections and HepB vaccination, and to downplay the potential harm of foregoing these procedures.[36−38] Scientists and public health professionals could similarly capitalize on the use of social media, especially in light of recent vaccine-preventable disease outbreaks.[39,40] In support of this, recent research suggests that providing vaccine information via social media applications is an effective way to increase vaccine knowledge during pregnancy and counteract anti-vaccine messaging.[41]

Limitations

This study has several limitations. First, the use of EMR data may result in some misclassification of race/ethnicity[42] or other sociodemographic characteristics. Specifically, the income estimates are based on area-level residential ZIP codes; this limits patient-level specificity regarding the influence of socioeconomic determinants on vaccine receipt. Importantly, geographic clustering of undervaccinated or unvaccinated children may be masked by high overall vaccination coverage rates.[43,44] Children on the low and high ends of the SES spectrum are at greatest risk for poor vaccination coverage,[45,46] albeit through different mechanisms and risk factors. Low-income families are more likely to experience vaccination barriers, including inadequate insurance coverage,[47] longer clinic wait times,[48] lack of reliable transportation, and difficulty taking time off work for clinic visits.[49,50] By contrast, privately insured, high-SES parents who opt out of vaccines often make deliberate risk−benefit decisions based on factors such as the perceived risk of experiencing the natural disease or concerns about vaccine safety.[51−53] Second, vaccine data may have been misclassified or misreported within the data collection systems, although misclassification are expected to be minimal and nondifferential. Vaccine administrations (rather than orders) were captured in the EMR using a standardized approach and routinely reported to WAIIS during the study period. Moreover, WAIIS is a nearly complete reporting system with a high degree of internal validity,[11,12] although some doses received during provider visits may have been missed given that provider reporting is not mandated in Washington State. Third, University of Washington Medical Center sees a high-risk patient population; thus, high-risk infants may be over-represented. Medically unstable infants are not eligible for HepB vaccination, and the data set did not include a disease severity measure. However, nearly all infants would have been eligible for HepB vaccine before their birth hospitalization discharge. Medical eligibility would have minimal impact on coverage estimates for future recommended vaccines given that <1% of school-aged children in Washington State have medical exemptions for vaccines.[54] It also is worth noting that Washington State is one of 17 states that allows personal, philosophical, and religious exemptions and has one of the highest nonmedical exemption rates (3.9% vs 2.0% nationally).[54−56] Thus, results may not be generalizable to settings with less vaccine-hesitant populations. However, the degree to which vaccine hesitancy affects the current findings is unclear. HepB vaccine receipt within 3 days of birth[20] was similar between the study sample and nationally reported averages during the study period (70.0% vs 71.7%), whereas completion of the seven-vaccine series was lower than national averages (53.6% vs 70.3%).[2,20,57] National data for seven-dose series completion are based on children aged 19−35 months compared with the 19-month cut off used in the current study to assess timely adherence to national recommendations; these cut off differences likely explain the observed disparity in vaccination coverage. In a sensitivity analysis, seven-vaccine series completion among children aged 19−35 months was 67.6% (data not shown), similar to national data. Finally, maternal HepB virus surface antigen screening, which could have contributed to decisions around HepB vaccination timing, was not readily available in the EMR, and thus these data are not included in the analyses. In addition, data were not collected on parental attitudes about childhood vaccination or provider communication behaviors, which are important predictors of vaccination.[31,51,53] The relationship between HepB and future vaccination, in conjunction with these attitudes, warrants further study.

CONCLUSIONS

A strong association was observed between HepB vaccination during the birth hospitalization and timely uptake of all recommended vaccines by 19 months among Washington State infants born between 2008 and 2013. Initiating early vaccine conversations, particularly with hesitant parents, may help increase both HepB birth dose receipt and other recommended vaccines. Future studies should track failed HepB birth dose receipt as a red flag for missing subsequent vaccines and develop early interventions to improve general vaccine uptake.

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SUPPLEMENTAL MATERIAL

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