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Sociodemographic, clinical and birth hospitalization characteristics and infant Hepatitis B vaccination in Washington State

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ABSTRACT

Objective: Hepatitis B (HepB) vaccine is recommended at birth; however, national coverage estimates fall far below target levels. Studies describing the factors associated with infant HepB vaccination are lacking. This study aimed to identify the sociodemographic, clinical and birth hospitalization factors associated with timely receipt of the first HepB vaccine dose.

Study Design: This retrospective cohort study included Washington State infants born weighing ≥2000 g who received birth hospitalization care at an urban academic medical center between January 2008–December 2013. Multivariable logistic regression was used to estimate adjusted odds ratios (AOR) and 95% confidence intervals (CI) for associations between maternal and infant characteristics and HepB vaccine receipt during the birth hospitalization.

Results: Of the 9080 study infants, 75.5% received HepB vaccine during the birth hospitalization. Infants had higher odds of being vaccinated during the birth hospitalization if they were Hispanic (AOR 2.08; CI: 1.63, 2.65), non-Hispanic black (AOR 2.34; CI: 1.93, 2.84) or Asian (AOR 2.70; CI: 2.22, 3.28) compared to non-Hispanic white. Infants with a Spanish- *vs.* English-speaking mother (AOR 1.97; CI: 1.46, 2.68), public *vs.* private insurance (AOR 2.01; CI: 1.78, 2.29), and those hospitalized ≥96 h *vs.* 24 to <48 h (AOR 1.67; CI: 1.34, 2.09) also had higher odds of vaccination.

Conclusions: Populations that are typically underserved (e.g., publicly insured, racial/ethnic minorities) had higher odds of receiving HepB vaccine during the birth hospitalization. These findings may aid in identifying high-risk infants who could benefit from targeted interventions to increase initial HepB vaccination.

1. Introduction

In 2005, the U.S. Advisory Committee on Immunization Practices (ACIP) recommended that all medically stable infants born weighing ≥2000 g receive the first dose of Hepatitis B (HepB) vaccine during their birth hospitalization. In 2016, the ACIP updated their guidance, recommending HepB vaccination of these infants within 24 h of birth [1]. HepB vaccine is 75% efficacious in preventing perinatal Hepatitis B virus (HBV) transmission when given within this recommended timeframe (94% efficacious if combined with HepB immune globulin) [1–3]. Receipt of HepB vaccine shortly after delivery also increases the likelihood of completing the 3-dose series [4,5], thus achieving optimal long-term protection against HBV.

Nearly 1000 infants are perinatally infected in the U.S. annually [6,7]. This is related to multiple factors, including failure to identify

Abbreviations: **ACIP**, Advisory Committee on Immunization Practices; **AOR**, Adjusted Odds Ratio; **EMR**, electronic medical record; **HBsAg**, Hepatitis B surface antigen; **HBV**, Hepatitis B virus; **HepB**, Hepatitis B vaccine; **RUCA**, Rural Urban Commuting Area; **WAIIS**, Washington State Immunization Information System.

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HBV-infected mothers due to lack of testing for HBV surface antigen (HBsAg) and errors in testing or reporting of maternal HBsAg results [8]. In some cases, HBV-infected mothers are properly identified, but prophylaxis is not administered to the infant [8]. These findings underlie the national recommendation to administer a birth dose of HepB vaccine to all infants as a safety net against exposures during the perinatal period and later in life [1,9].

National data show that approximately 71% of U.S. newborns receive the first HepB vaccine by 3 days of age [10] (i.e., a proxy measure for HepB vaccine administration during the birth hospitalization due to lack of hospital-level data). Little is known about maternal, infant or birth hospitalization factors affecting receipt of the first HepB vaccine. One previous study used hospital-level data to evaluate maternal and infant characteristics and receipt of the HepB birth dose [11]. However, this study was small (n = 259), and the variables were limited to maternal race and language and infant sex. Another study assessed HepB birth dose receipt among a primarily Caucasian population in Iowa [12]. The purpose of the current study was to identify sociodemographic, clinical and birth hospitalization factors associated with the timing and receipt of the first HepB dose with the goal of identifying risk factors for under-vaccination that may be targeted in future interventions.

2. Methods

2.1. Study setting and population

This retrospective cohort study was conducted at a large academic medical center in Seattle, Washington. The study sample included infants who received birth hospitalization care in the medical center's newborn nursery, intermediate care nursery or neonatal intensive care unit (NICU) between January 1, 2008 and December 31, 2013 and were documented to be Washington State residents based on residential address. Infants who transferred to the study medical center after birth and those without complete admission or discharge data were excluded. From this larger cohort of infants (n = 11,833), only those born at ≥2000 g were included in the final study sample.

During the study period, the medical center had a written policy supporting HepB vaccination of infants prior to hospital discharge based upon existing ACIP recommendations. HepB vaccine was included in the routine newborn order set. No other vaccine-promoting strategies (e.g., standing orders or provider alerts in the electronic medical record [EMR]) were used.

2.2. Data sources

Sociodemographic, clinical (including HepB vaccine administration), and birth hospitalization data were retrospectively abstracted from study participants' EMR. To capture HepB doses given in other clinical settings after hospital discharge, EMR data were linked to the participants' vaccine records in the Washington State Immunization Information System (WAIIS) using select identifiers and a standardized matching algorithm. Previous studies have demonstrated that WAIIS is highly complete [13]. The Centers for Disease Control and Prevention (CDC) estimates that ≥95% of Washington State children aged <6 years participated in WAIIS during the study period, and a 2014 validation study in a large integrated health care organization reported that only 1% of recorded vaccinations were missing in WAIIS [13,14]. To maintain consistency with national and state reporting standards [15], the present study excluded infants with no matching WAIIS record, <2 recorded doses (of any vaccine) by 19 months, or an inactive WAIIS status (i.e., infant moved out of state). In the larger infant cohort from which the present sample was obtained, 1466 (12.4%) had incomplete or inactive WAIIS data.

2.3. Outcome measures

The primary outcome of interest was HepB vaccine receipt during the birth hospitalization. Secondary outcomes were HepB vaccine receipt within 24 h, 3 days, or 30 days after birth or by 19 months (<580 days). The secondary timepoints allowed us to assess adherence to past and current ACIP recommendations and compare our findings to previous studies, including those using national data. The 24-h and 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.

2.4. Independent variables

2.4.1. Maternal and infant sociodemographic characteristics

Sociodemographic data included infant sex (male, female), insurance status (public, private), and race/ethnicity. 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 multi-racial/other. The latter included classifications of American Indian, Alaska Native, Native Hawaiian and Pacific Islander due to small samples (n = 103 total). Maternal language was categorized as English, Spanish and other. Area-level income was measured for each patient based on the median household income in his/her ZIP code. We used U.S. Census Bureau data [17] to stratify ZIP codes into those below *vs*. at or above the Washington State median household income in 2010 ($54,888) [18]. Urban *vs*. rural residency was measured using Rural Urban Commuting Area (RUCA) codes, a 10-point classification system which categorizes geographic areas as primarily rural or urban based on census tract and commuting data. The institution's ZIP code-to-census tract crosswalk assignment and a 2-category classification (RUCA Type C) [19] were used to assign ZIP code-level RUCA designations for each study participant.

2.4.2. Clinical and birth hospitalization characteristics

Preterm birth was defined as birth <37 weeks gestation [20]. Sub-categories for gestational age included extremely preterm (23–26 weeks), very preterm (27–31 weeks), moderate to late preterm (32–36 weeks), or term to post-term (37–43 weeks). Length of the birth hospitalization was calculated as hours between admission and discharge and categorized as <24 h, ≥24 to <48 h, ≥48 to <96 h, and ≥96 h. Hospital service included the newborn nursery, intermediate care nursery and NICU.

2.5. Statistical analysis

Descriptive statistics were used to characterize the overall study sample. Bivariate chi-square tests were used to detect associations between sociodemographic, clinical and birth hospitalization characteristics and vaccine outcome measures. Multivariable logistic regression was used to assess factors associated with receiving HepB vaccine during the birth hospitalization after adjusting for sociodemographic, clinical and birth hospitalization characteristics. Included variables were determined *a priori* based on factors known or suspected to be associated with HepB birth dose receipt [11,21]. To describe absolute and relative differences, logistic regression and recycled predictions were used to estimate the adjusted prevalence of outcomes based on sociodemographic, clinical and birth hospitalization characteristics. *P*-values were based on two-tailed tests and considered significant at $P < 0.05$. Stata version 14.0 (Stata Corp. 2015, Stata Statistical Software, College Station TX) was used for all analyses.

This study was approved by the Seattle Children's Hospital and Washington State Institutional Review Boards.

3. Results

A total of 9080 infants with a birth weight of ≥2000 g received birth hospitalization care at the study medical center. Most were non-white, had an English-speaking mother, were publicly insured, and lived in ZIP codes classified as urban or above-median household income (Table 1). Most infants were discharged from the hospital within 48 h, received care in the newborn nursery and were born at term/post-term gestation. The lowest gestational age at birth was 28 weeks.

3.1. HepB vaccination during birth hospitalization

Overall, 75.5% of infants received HepB vaccine during their birth hospitalization (Table 1). HepB vaccine rates fell slightly during the study period from 78.4% in 2008 to 74.6% in 2013, with the lowest rate in 2012 (73.3%) (**Supplemental Figure 1**).

The odds of receiving HepB vaccine during the birth hospitalization were higher among infants who were Hispanic, non-Hispanic black or Asian (*vs.* non-Hispanic white), had a mother who spoke Spanish or another language (*vs.* English), were publicly (*vs.* privately) insured, remained hospitalized for ≥96 (*vs.* 24 to <48) hours, or were on newborn service (*vs.* intermediate care or NICU) (Table 2). Infant sex, multi-racial/other race/ethnicity, rural-urban residence, median household income, and preterm status were not associated with HepB vaccination during the birth hospitalization. Table 2 shows the adjusted prevalence and absolute differences for HepB vaccination during the birth hospitalization, which suggest a range in magnitude from 72% to 87% for race/ethnicity and 77% to 87% for maternal language. The adjusted prevalence for HepB vaccine among infants discharged from their birth hospitalization in <24 h was 64% *vs.* 86% among those discharged ≥96 h.

3.2. HepB birth dose timing

In a subset of infants born on or after October 19, 2010 (n = 4666, see Methods), 29.1% received their first HepB dose

Table 1
Demographic, clinic and birth hospitalization characteristics in total sample and by HepB vaccination status during the birth hospitalization.

Patient characteristic	Total study sample[a] N = 9080	Received HepB[b] n = 6858	Did not receive HepB[b] n = 2222
Sex			
Male	4649 (51.2)	3493 (50.9)	1156 (52.0)
Female	4431 (48.8)	3365 (49.1)	1066 (48.0)
Race/ethnicity[c]			
Hispanic	1170 (14.6)	1029 (16.8)	141 (7.5)
Non-Hispanic white	3901 (48.7)	2525 (41.2)	1376 (73.2)
Non-Hispanic black	1759 (21.9)	1567 (25.6)	192 (10.2)
Asian	1081 (13.5)	933 (15.2)	148 (7.9)
Multiracial/other	103 (1.3)	80 (1.3)	23 (1.2)
Maternal language			
English	6486 (76.0)	4652 (71.6)	1834 (90.4)
Spanish	853 (10.0)	766 (11.8)	87 (4.3)
Other	1190 (14.0)	1083 (16.7)	107 (5.3)
Insurance status			
Private	3747 (44.2)	2412 (37.6)	1335 (64.3)
Public	4737 (55.8)	3996 (62.4)	741 (35.7)
Rural-urban residence			
Rural	237 (2.6)	161 (2.4)	76 (3.4)
Urban	8840 (97.4)	6696 (97.7)	2144 (96.6)
Income estimate			
<$54,888	2801 (31.0)	2227 (32.7)	574 (26.0)
≥$54,888	6227 (69.0)	4591 (67.3)	1636 (74.0)
Clinical and birth hospitalization characteristics			
Gestational age, weeks			
27–31	16 (0.2)	9 (0.1)	7 (0.3)
32–36	968 (10.7)	681 (9.9)	287 (12.9)
37–43	8093 (89.1)	6166 (89.9)	1927 (86.8)
Length of stay, hours			
<24	820 (9.1)	412 (6.0)	408 (18.4)
≥24 to < 48	3956 (43.6)	3114 (45.4)	842 (37.9)
≥48 to < 96	3296 (36.3)	2580 (37.6)	716 (32.2)
≥96	1008 (11.0)	752 (11.0)	256 (11.5)
Medical service			
Newborn nursery	7266 (80.0)	5707 (83.2)	1559 (70.2)
Intermediate care nursery	1330 (14.7)	1011 (14.7)	319 (14.4)
NICU	484 (5.3)	140 (2.0)	344 (15.5)

[a] All proportions shown in table are based on known data. Number and percentage of missing cases from overall totals are as follows: Maternal race/ethnicity = 1066 (11.7%); Maternal language = 551 (6.1%); Insurance status = 596 (6.6%); Rural-urban residence = 3 (0.03%); Income estimate = 52 (0.6%); Gestational age = 3 (0.03%).
[b] HepB vaccine receipt during the birth hospitalization.
[c] Race/ethnicity categorized using U.S. Census Bureau race/ethnicity classifications (www.census.gov/prod/cen2010/briefs/c2010br-02pdf).

Table 2
Adjusted odds ratios (OR), adjusted prevalence and 95% confidence intervals (CI) of HepB vaccination during the birth hospitalization.[a]

Patient characteristic	Adjusted OR (95% CI)[b]	Adjusted prevalence[c] % (95% CI)
Sex		
Male	0.96 (0.86, 1.07)	79 (78, 80)
Female	Ref	80 (78, 81)
Race/ethnicity		
Hispanic	**2.08 (1.63, 2.65)**	84 (81, 87)
Non-Hispanic white	Ref	72 (70, 74)
Non-Hispanic black	**2.34 (1.93, 2.84)**	86 (84, 88)
Asian	**2.70 (2.22, 3.28)**	87 (85, 89)
Multi-racial/other	1.56 (0.93, 2.61)	80 (72, 88)
Maternal language		
English	Ref	77 (76, 78)
Spanish	**1.97 (1.46, 2.68)**	87 (84, 90)
Other	**1.80 (1.42, 2.27)**	86 (83, 88)
Insurance status		
Private	Ref	72 (70, 74)
Public	**2.01 (1.78, 2.29)**	84 (83, 85)
Rural-urban residence		
Urban	Ref	79 (78, 80)
Rural	1.28 (0.91, 1.80)	83 (78, 88)
Income estimate		
<$54,888	1.13 (0.99, 1.28)	81 (79, 82)
≥$54,888	Ref	78 (77, 80)
Clinical and birth hospitalization characteristics		
Gestational age, weeks		
27–31	1.60 (0.51, 5.02)	86 (71, 99)
32–36	1.30 (1.05, 1.62)	83 (80, 86)
37–43	Ref	79 (78, 80)
Length of stay, hours		
<24	**0.48 (0.40, 0.58)**	64 (60, 68)
≥24 to <48	Ref	79 (77, 80)
≥48 to < 96	1.09 (0.96, 1.23)	80 (79, 82)
≥96	**1.67 (1.34, 2.09)**	86 (84, 88)
Medical service		
Newborn nursery	Ref	82 (81, 83)
Intermediate care nursery	**0.61 (0.51, 0.73)**	74 (71, 77)
NICU	**(0.07, 0.13)**	31 (25, 36)

[a] Models adjusted for all sociodemographic, clinical and birth hospitalization characteristics parameterized as listed in Table 1, including missing cases.
[b] Bold denotes significance at $p < 0.05$.
[c] All p-values for adjusted prevalence are <0.001.

within 24 h (corresponding to 39.4% of those vaccinated during the birth hospitalization), and 70.0% received the first dose within 3 days. Among all infants, 82.8% received the first HepB vaccine dose within 30 days and 94.5% by 19 months. The proportion of infants who received HepB vaccine at these time points is presented by sociodemographic, clinical and birth hospitalization characteristics in Figs. 1 and 2**.** In general, infants who were non-Hispanic white, privately insured or had an English-speaking mother received HepB vaccine later than infants in their respective referent groups. For example, within 30 days of birth, three-quarters of non-Hispanic white infants were vaccinated, while the proportions were much higher (>90%) among non-Hispanic black, Hispanic or Asian infants. Similarly, 80.0% of infants born to English-speaking mothers were vaccinated within 30 days *vs.* 94.5% of infants born to Spanish-speaking mothers, while 90.2% of publicly insured infants were vaccinated within 30 days *vs.* 73.2% of privately insured infants.

Between 31 and 579 days of age, higher proportions of non-Hispanic white infants were "catching up" with their first HepB vaccine dose compared to Hispanic, Non-Hispanic black, and Asian infants (16.2% *vs.* 5.5–6.0%), privately *vs.* publicly insured infants (16.6% *vs.* 7.9%), and infants of English- *vs.* Spanish-speaking mothers (13.4% *vs.* 5.4%) (data not shown). Thus, gaps by these characteristics narrowed, although infants who were non-Hispanic white, had English-speaking mothers, or were privately insured still had the lowest proportion of vaccine coverage by 19 months (Fig. 1).

4. Discussion

This study offers unique insight into infant HepB vaccination through its evaluation of detailed sociodemographic, clinical, and birth hospitalization information linked to state immunization registry data in a large, diverse infant population from Washington State. Unlike previous studies with limited ability to capture the precise timing of infant HepB vaccination, our study revealed that only three-quarters of eligible infants received HepB vaccine during

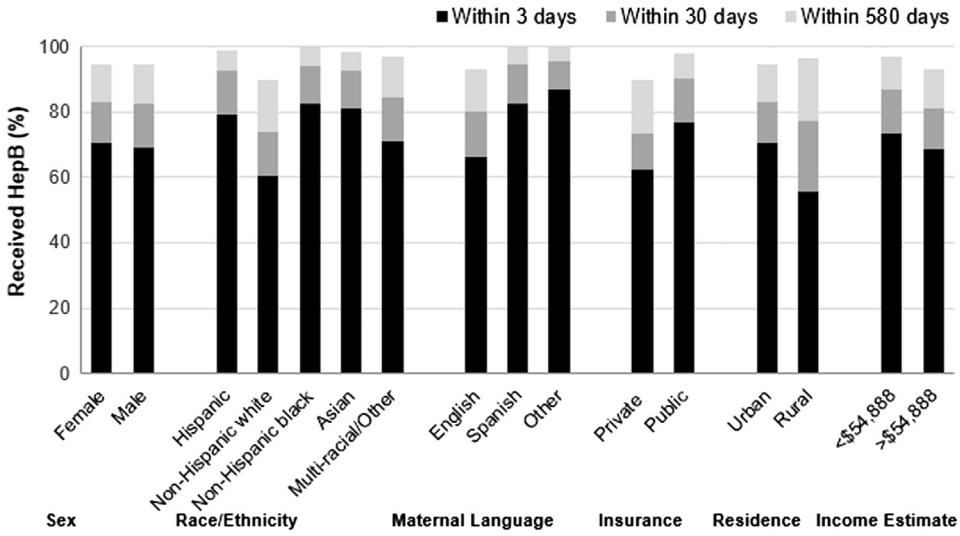

Fig. 1. Cumulative proportion of first HepB vaccine receipt within 3, 30 or 580 days of birth, by demographic characteristics.

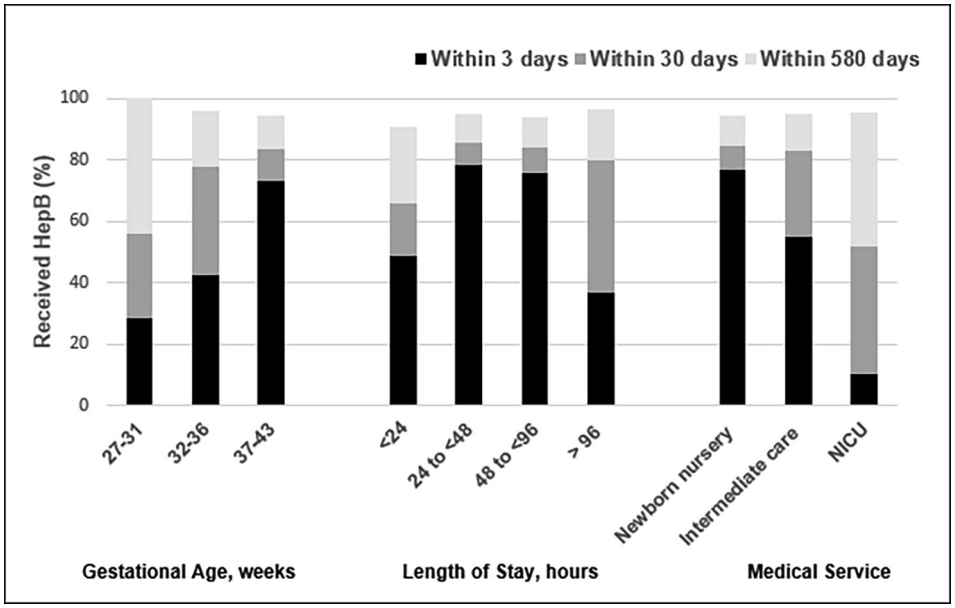

Fig. 2. Cumulative proportion of first HepB vaccine receipt within 3, 30 or 580 days of birth, by clinical and birth hospitalization factors.

the birth hospitalization; 29% received a dose in the first 24 h, and 70% within 3 days of birth. These rates, which declined slightly during the 2008–2013 study period, fall far short of the Healthy People 2020 target of 85% [22]. Importantly, this study described key patterns of HepB under-vaccination. The HepB birth dose is the first vaccine given during childhood, and its receipt has been associated with an increased likelihood of receiving other recommended vaccines by 35 months of age [4,5]. Further investigation and additional data are needed to allow us to fully understand the underlying reasons for differences in HepB vaccine uptake across subgroups. However, by identifying infant sub-populations at risk for HepB under-vaccination, this study may inform future interventions aiming to improve timely receipt of the HepB birth dose in accordance with national recommendations.

In this study, infants who were non-Hispanic white, privately insured or had an English-speaking mother were the least likely to receive HepB vaccination during the birth hospitalization. Multiple factors could explain this finding. First, these sociodemographic characteristics are consistent with those of parents who refuse or delay other early childhood vaccines [23,24]. The degree to which vaccine hesitancy impacted our results is unknown since we were unable to assess parental attitudes about HepB vaccine with the available data. However, a prior study among hospital managers reported that common reasons for HepB vaccine refusal during the birth hospitalization include a preference to receive the vaccine in the pediatrician's office, fear of vaccines in general, fear of vaccinating the newborn, and lack of understanding the seriousness of HBV infection [25].

The patients identified in our study as least likely to receive the HepB birth dose (e.g., non-Hispanic white, English-speaking) also fall into the demographic group at lowest risk for maternal HBV infection [26,27]. Differences in maternal HBV infection risk could influence parental decision-making and provider vaccine communication. Specifically, parents may be hesitant to vaccinate their newborn against a disease that they consider very low risk for mother-to-baby transmission. Similarly, providers may be reluctant to strongly recommend HepB vaccination to these patients during hospitalization due to the low perceived risk or, conversely, may target other patients based upon their sociodemographics. Future research is warranted to ascertain whether parental decision-making and provider communication are impacted by perceptions of infection risk, particularly since the universal HepB birth dose is a critical safety net regardless of individual characteristics. It is worth noting that a third of those infected with HBV have no known or acknowledged risk factors, and most are unaware of their infection [28,29]. Moreover, the HepB birth dose also protects infants with subsequent exposure such as those who unexpectedly need blood products.

In this study, infants who were publicly insured or a racial/ethnic minority – i.e., those often least likely to receive necessary health services [30,31] – were the most likely to receive the HepB birth dose within the recommended timeframe. This finding is consistent with early work assessing HepB birth dose receipt [11,32] as well as 2016 National Immunization Survey data demonstrating that, compared to children at or above the poverty level, children living in poverty have lower coverage for nearly all recommended vaccines except the HepB birth dose, for which they have higher coverage [10]. Several factors may contribute to this finding. The structural and financial barriers often faced by low-income families in obtaining vaccines are largely absent for the HepB birth dose if it is administered during the birth hospitalization rather than later in an outpatient setting. Common barriers to vaccination such as taking time off work for outpatient clinic appointments [33] or lacking a usual source of primary care [34] are obviated.

Strategies to improve timely HepB vaccination are needed. Potential interventions may include provider alerts in the EMR and hospital standing orders for administration of HepB vaccine beginning at birth [1]. A 2012 study found that 20% of birthing hospitals in Washington State do not have both written policies and standing orders for routine HepB birth dose vaccination [35]. Importantly, parents look to their child's healthcare provider for vaccine guidance, and parental vaccine acceptance is strongly influenced by provider communication [36–39]. HepB vaccine communication could be initiated early in the vaccine decision-making process, including during pregnancy and shortly after delivery. Conversations between providers and families, particularly those who are vaccine hesitant, may be useful not only for receipt of the first HepB vaccine, but also for future vaccine uptake [40].

This study has several limitations. First, provider level data were not available, and although the medical center's policy was to administer HepB vaccine to all eligible infants before discharge, providers may have varied in their HepB vaccine-related practices, including communication with families. Second, the medical center is a tertiary care referral center that sees a high-risk patient population; thus, the study sample may over-represent higher risk infants. Medically unstable infants are not eligible for HepB vaccine, even if full-term and normal birthweight, and the dataset did not include a disease severity measure. However, we expect that nearly all infants in the study population, regardless of hospital service, would have been medically stable and thus eligible for HepB vaccination prior to discharge, with the exception of a small number of infants transferred to outside facilities for further medical management (data not available). Of note, current recommendations state that medically stable infants born weighing <2000 g to HBsAg negative mothers should receive the first HepB dose at one month of age or at hospital discharge, whichever comes first [1,9]. Further investigation of HepB birth vaccination in a larger cohort of vulnerable infants, including those <2000 g, is needed. Additionally, although we did not assess parental vaccine hesitancy, it is important to acknowledge that Washington State has one of the nation's highest non-medical vaccine exemption rates [41]. Thus, our results may not be generalizable to hospital settings with lower patient acuity or those serving a less hesitant population. Third, vaccine data may be misclassified or misreported within the current data collection systems, although we expect this to be minimal in our EMR as well as WAIIS based on documentation of high data quality [13,14]. Fourth, our area-level estimates of median income and urban-rural residence are based on dichotomized residential ZIP codes and lack patient-level specificity, limiting our assessment of socioeconomic and geographic factors as individual-level determinants of vaccine receipt. Fifth, our data were collected before the ACIP's 2016 recommendation to administer HepB vaccine within 24 h of birth. Further research is needed to examine adherence to this current recommendation. Finally, we were unable to assess other reasons for missed opportunities (e.g., provider attitudes, systems-based factors), maternal HBsAg screening, or receipt of prenatal care, which is an important predictor of infant vaccination [42].

5. Conclusion

Universal infant HepB vaccination is a key component of the national strategy to eliminate HBV transmission in the United States [1]. This study is a first step in understanding the risk factors associated with poor HepB birth dose uptake and may guide early identification of infants who could benefit from targeted interventions. Future research is needed to assess mechanisms underlying differences in HepB vaccine uptake across subpopulations, including research assessing the potential role of parent factors (e.g., risk perceptions, vaccine concerns), provider factors (e.g., recommendation strength, type), and/or systems factors (e.g., lack of standing

orders) contributing to missed vaccination opportunities. This information can then inform the design and implementation of future interventions aiming to improve timely HepB vaccination of infants.

Conflict of interest

Dr. Annika Hofstetter previously received research support from the Pfizer Independent Grants for Learning and Change. Dr. Janet Englund receives research support from Gilead, Chimerix, MedImmune, Novavax, and GlaxoSmithKline. Dr. Englund was a consultant for Pfizer and Gilead and served on a data safety monitoring board for GlaxoSmithKline. Sponsors were not involved in the study design, data collection, analysis or interpretation, the writing of the report or the decision to submit the manuscript for publication. The authors have no other conflicts of interest relevant to this article to disclose.

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Contributors' Statement

Ms. Oster conceived and designed the study, analyzed and interpreted the data, and drafted and revised the manuscript. Dr. Williams contributed substantially to the study design, analytic approach, data interpretation, and manuscript review and revision. Drs. Unger, Newcomb, Jacobson, deHart, and Englund contributed to the study conception and design, data interpretation and critical review of the manuscript. Dr. Hofstetter obtained and maintained access to the data, was substantially involved in the study design, data analyses, data interpretation, and manuscript revision and review. All authors approved of the manuscript as submitted.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.03.050.

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