Improving Childhood Vaccination Coverage: Understanding Maternal and Infant Characteristics Associated with Receipt of Hepatitis B and Other Recommended Vaccinations

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Dissertation Abstract

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Vaccines are one of the most successful public health measures in modern medicine. Each year, thousands of illnesses, hospitalizations and deaths are directly prevented through immunization and indirectly through herd immunity. Paradoxically, vaccines have been so effective at preventing childhood diseases that a growing number of U.S. parents now question whether vaccination is necessary and whether perceived vaccine risks outweigh the benefits. In an era when few parents have firsthand experience with many of the diseases that vaccines prevent, new approaches are needed to maintain and increase vaccination coverage. Despite the rapid decline of vaccine preventable diseases (VPDs) in the U.S. these diseases are still common worldwide and will quickly resurface if vaccination rates are not maintained, as evidenced by recent outbreaks of pertussis and measles.

Hepatitis B (HepB) is the first vaccine on the U.S. Childhood Immunization Schedule, which recommends seven shots (known as the 7-vaccine series) by 19 months of age. A HepB vaccine birth dose is recommended within 24 hours of birth for all medically stable infants born weighing at least 2000 grams and is the only vaccine recommended before the second month of age. We hypothesized that a missed HepB birth dose, accompanied by specific maternal and

infant characteristics, could serve as a “red flag” to identify newborns who may be at high risk for missing subsequent childhood vaccines and could benefit from early, targeted interventions.

Using a sample of infants born in Washington state between 2008 and 2013, this dissertation investigates predictors of the HepB birth dose (Aim 1), whether receipt of the HepB birth dose is associated with completing other recommended vaccines by 19 months (Aim 2) and whether timely HepB vaccine receipt, in conjunction with select maternal and infant characteristics, can be used to predict the risk of missing future childhood vaccinations (Aim 3). In Aim 1, we found that populations which are typically underserved (e.g., publicly insured, racial/ethnic minorities) were the most likely to receive the HepB birth dose, while infants who were non-Hispanic white, privately insured, and/or had an English-speaking mother were less likely to be vaccinated. Aim 2 showed that receiving the HepB birth dose was strongly associated with completing the 7-vaccine series by 19 months. In Aim 3, we developed and validated a risk prediction model which reliably identified newborns at risk for low completion of the 7-vaccine series by age 19 months.

The results of our research suggest that the risk for low vaccination coverage is not evenly distributed in the population and that specific sociodemographic, clinical and birth hospitalization characteristics may indeed be associated with, and potentially predict, individual vaccine uptake. Further, receiving HepB during the birth hospitalization emerged as a key indicator of parental vaccine acceptance. The combined study findings highlight areas for future interventional research in healthcare settings aimed at increasing childhood vaccination coverage and serve as an important foundation for research focused on barriers to vaccine receipt in key subpopulations.

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Chapter 1. INTRODUCTION

1.1 Vaccines Provide a Major Public Health Benefit

Infectious diseases took an enormous toll on the U.S. population in the early 20th century. More than 15,000 Americans died from diphtheria in 1921, the year before the diphtheria vaccine was licensed.[1] That same year 469,924 measles cases were reported, and 7,575 patients died. In 1922, 107,473 pertussis cases were reported, of which 5,099 died.[2] More recently, in 1965, a rubella epidemic infected 12.5 million people and resulted in the deaths of over 2,000 babies and 11,000 miscarriages.[1]

In the pre-vaccine era, vaccine preventable diseases (VPDs) were common and most people had seen or had first-hand experience with their effects. Polio was particularly visible, and historians note that polio exemplified the public's fears of contagious diseases.[3] Whereas people died or recovered from most VPDs, polio often disabled healthy, active children and those who were permanently disabled remained in the community.[4] In the 1950s, polio outbreaks caused more than 15,000 cases of paralysis each year in the United States.[5] During polio epidemics, schools and camps were closed, theaters were shut, draft inductions were suspended, nonessential meetings were cancelled, and public drinking fountains were turned off.[3,6] The benefits of vaccines were clear in this environment and parents were understandably eager to vaccinate.

Since 1900, vaccines against 21 major diseases (including those described above) have been developed[7,8] and are currently on the U.S. Immunization Schedule for Infants and Children.[9] Seven shots – known as the 7-vaccine series – are recommended by 19 months of age (4 doses of diphtheria-tetanus-pertussis, 3 poliovirus, 1 measles-mumps-rubella (MMR), 3

Haemophilus influenza Type b, 3 hepatitis B (HepB), 1 varicella, 4 pneumococcal). Rotavirus, Hepatitis A and influenza vaccinations are also recommended in early childhood (see **Table 5.1**).

Childhood vaccination rates in the U.S. are high overall. Most children are routinely vaccinated with three or more doses of poliovirus vaccine (93%), one or more doses of MMR (92%) and one or more doses of varicella vaccine (91%).[10] However, fewer than 70% complete the 7-vaccine series on time, and a small but increasing proportion of children receive no vaccines by age 24 months.[10] Furthermore, geographic clustering of under- and un-vaccinated children create pockets of children at increased risk of disease transmission, which may be masked by high overall vaccination coverage rates.[11-13]

Despite these gaps, the Centers for Disease Control & Prevention (CDC) estimate that vaccinations have prevented more than 322 million illnesses, 21 million hospitalizations and 732,000 deaths among U.S. children born between 1994 and 2014, saving $295 billion in direct costs and $1.38 trillion in total societal costs.[1,14] Smallpox has been eradicated; no cases of polio have originated in the United States since 1979 (although internationally imported cases have occurred as recently as 1993); since 2000, only four cases of diphtheria and 16 cases of congenital rubella syndrome have been reported to the CDC.[15,16] Yet, VPDs continue to circulate worldwide. For example, the World Health Organization estimates that each year more than 100,000 infants are born with congenital rubella syndrome, 90,000 children die from measles and 199,000 die from meningitis and pneumonia as a result of Haemophilus influenzae type B (Hib).[17-20]

Recent VPD outbreaks in the United States[20,21] highlight the continued importance of maintaining high herd immunity to protect individual health, those too young or ill to be vaccinated and the wider community. Individual vaccination coverage has implications beyond personal vaccine decision making and uptake. Importantly, although high-income families are the most likely to delay or defer vaccinations,[22,23] the societal benefits of herd immunity may be particularly vital for low-income families who experience disparities in health care and outcomes and may be disproportionately affected by lost wages and expenses when caring for a sick child.[24] For example, to contain a recent measles outbreak, a 21-day quarantine was required for exposed children at an average family cost of $775 per child.[25] While these costs can be reasonably absorbed by high-income families, lower income families are the least likely to have sick leave or savings to draw from, making financial recovery after childhood illnesses more difficult.[26]

1.2 Vaccine Safety Concerns Have Replaced Fear of VPDs

Paradoxically, the success of vaccines and the subsequent decrease of many childhood diseases has led a growing number of parents to question whether vaccines are still necessary and whether vaccine risks outweigh their benefits.[22,23,27,28] Parents may be concerned about too many vaccines, too soon, vaccine ingredients, and discredited research claiming a link between autism and vaccines.[29,30] Research is clear, however, that vaccines are safe, effective and that delaying or refusing vaccination has led to VPD outbreaks that may jeopardize public health.[20,21] Furthermore, technological advances have reduced the number of antigens in vaccines, most vaccine side effects are minor (for example, a sore arm or low-grade fever) and before the Advisory Committee on Immunization Practices (ACIP) recommends adding a new vaccine to the immunization schedule, it reviews comprehensive safety and efficacy data from clinical trials.[31,32]

Today, only 1-2% of U.S. parents refuse all recommended vaccines.[33,34] However, many more have concerns about vaccines. An estimated 25-35% of parents cautiously accept vaccines, while 20-30% are considered vaccine hesitant (defined as a delay in acceptance or refusal of vaccination despite the availability of vaccination services).[34,35]

National surveys show that over half (54%) of parents have concerns about adverse effects, while 11% report that children do not need vaccines for diseases that are no longer common.[36] The 'fence sitters', that is the 25-50% of parents with concerns about vaccines, may particularly benefit from early interventions.[37] Parents consistently cite their child's provider as the most influential factor in their vaccine decision-making,[33,38-44] suggesting that there may be an opportunity to identify and intervene through early and consistent parent-provider communication. It is often unclear how to identify parents who may be vaccine hesitant, however, instruments such as the Parent Attitudes About Childhood Vaccines survey (PACV), which uses a 0-100 scoring system (100 indicates higher vaccine hesitancy) may help identify future child immunization status.[45]

1.3 Socio-demographic Differences in Vaccine Decision Making: Description of Conceptual Model

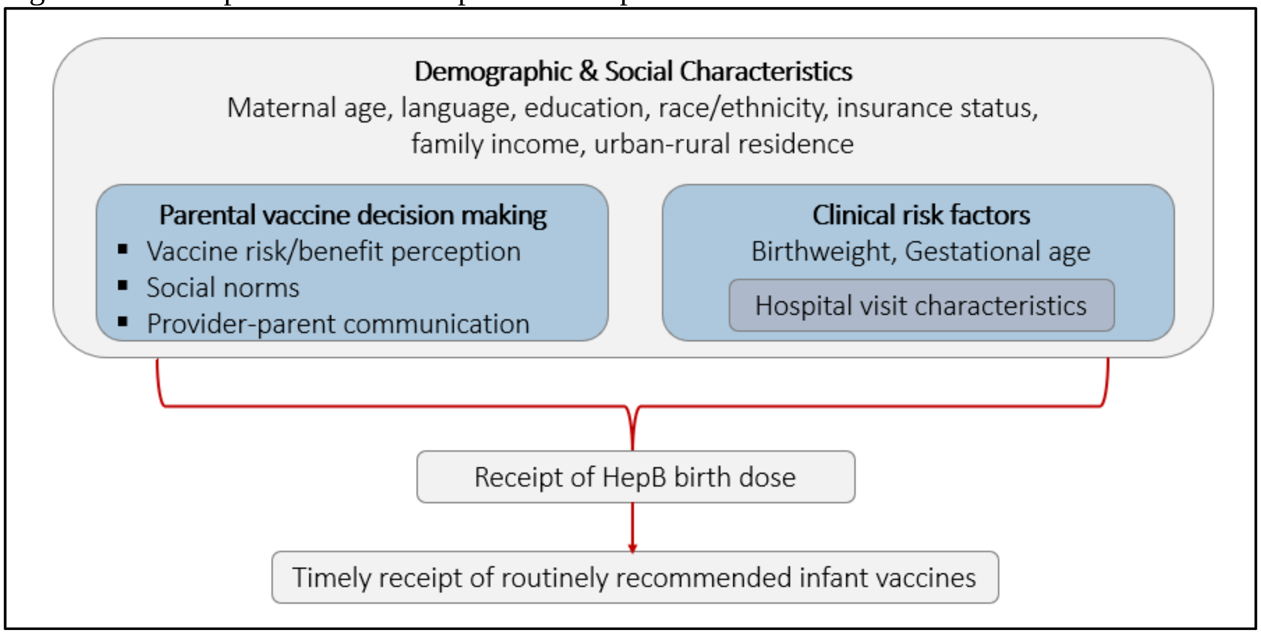
Vaccine acceptance varies by sociodemographic characteristics and socially patterned differences in health behaviors, beliefs and access to health care. Two distinct groups of children – children on the high end[22,27,33] and the low end[22,46-50] of the socioeconomic (SES) spectrum - have lower vaccination rates compared to the general population, albeit through different risk factors and mechanisms.

Children living in poverty have historically had the lowest vaccination coverage and are disproportionately affected by vaccine preventable diseases.[22,49,50] Poor vaccination coverage among low SES families is associated with inadequate insurance,[51-53] minority race/ethnicity,[22,47,48,54-56] poverty,[46-48] rural residence[46,48,57,58] and low maternal educational level.[47] Between 1989 and 1991, a measles outbreak in the U.S. resulted in 55,000 cases, 11,000 hospitalizations and 123 deaths, and almost exclusively affected unvaccinated racial and ethnic minority children living in low-income communities.[59,60] Largely because of this measles outbreak, a federal program called Vaccines for Children has provided free vaccines to under- and uninsured children since 1994 and has been credited with narrowing disparities and increasing overall vaccination coverage rates.[60-63]

Although disadvantaged populations have a long history of low vaccination coverage in the United States, the socioeconomic and racial divisions in vaccine uptake have shifted in recent years. In the mid-1990s, a new phenomenon developed in which well-educated, high-income parents began refraining from vaccinating their children, thereby joining the ranks of impoverished families with respect to low vaccination coverage.[22] Vaccine refusal and delay is seen in all sociodemographic groups, but is most common among non-Hispanic white, English-speaking, upper income, privately insured and college-educated parents.[22,27-29] In contrast to the financial and logistical barriers faced by low-SES parents, high-income, well-educated parents who opt out of vaccinations often make deliberate risk-benefit decisions based on the perceived advantages of their child experiencing the natural disease, perceived risks of vaccines and beliefs regarding vaccine effectiveness.[23,29,64] Parents may believe that vaccines are no longer necessary and that vaccine-preventable diseases have decreased due to improvements in water, sanitation and hygiene, rather than through vaccinations.[65]

Social norms and peer influence based on one's sociodemographic characteristics are significant determinants of vaccine uptake. Analysis suggests that the most significant predictor of vaccine decision making is the proportion of people in a subject's social setting who promote vaccine refusal or delay.[66,67] Because neighborhoods in the U.S. are often segregated by income, education level and race,[68,69] vaccine refusal and delay tends to cluster geographically by the resulting social networks, creating pockets of children susceptible to VPDs, which then take root and spread within the community and to other surrounding communities.[13,70,71] A disproportionate number of index cases for recent VPD outbreaks have been among intentionally unvaccinated children, which eventually spread to the larger community.[21,25,72]

Figure 1.1 Conceptual model: Acceptance and uptake of recommended infant vaccines



The conceptual model (Figure 1.1) depicts the above-described contextual factors and demographic, social and clinical characteristics, which influence parental vaccine decision making for the first recommended infant vaccine – the HepB birth dose – and ultimately the timely receipt of other routinely recommended childhood vaccines.

1.4 HepB Birth Dose Receipt and Receipt of Future Childhood Vaccines

HepB vaccination serves as a vital safety net against exposure to hepatitis B virus (HBV) in infancy and later in life. HBV is a leading cause of chronic liver disease in the United States, and an estimated 2.2 million U.S. residents are infected with HBV.[73] Importantly, infants are more susceptible to HBV compared to older age groups. Without post-exposure prophylaxis, including HepB vaccination, up to 90% of infants infected at birth or in the first months of life develop chronic HBV compared to 1-5% of infected adults and 30% of children under five years of age.[74-77] For these reasons, the ACIP recommends that all medically stable infants born weighing ≥2000 grams receive the first dose of HepB vaccine within 24 hours of birth.[78] Nationally, 74% of infants complete the HepB birth dose within three days of birth.[10]

A key component of this dissertation is evaluating whether a missed HepB birth dose, in conjunction with select maternal and infant characteristics, can serve as an early 'red flag' to identify newborns at high risk for lower vaccine uptake. Although vaccine communication in the outpatient setting often does not start until the 2-month pediatrician visit when multiple vaccines are due, early identification of high-risk infants may prompt providers to initiate targeted interventions, such as more intensive screening or earlier vaccine communication, before they would otherwise do so. Given that parents consistently cite parent-provider communication as the most influential aspect of their vaccine decision making[33,38,40] it is reasonable to hypothesize that effective vaccine communication during the 2-month window between a missing HepB birth dose and when other recommended vaccines are due may help improve early childhood vaccine uptake.

Finding new ways to identify the subset of parents at high risk for delaying or refusing the HepB birth dose as well as subsequent vaccines is essential to individual and public health and is particularly timely given the growing levels of vaccine hesitancy and resulting vaccine preventable outbreaks.

1.5 Chapter 1 Summary

Childhood immunization provides important societal benefits by protecting both individuals who are vaccinated and the wider community. This dissertation addresses important gaps in the literature by evaluating infant and maternal characteristics associated with the first vaccine on the U.S. Childhood Immunization schedule, the Hep B birth dose, and identifying children at risk of subsequent under-receipt of recommended childhood vaccinations. Specifically, we examined the sociodemographic, clinical and birth hospitalization characteristics of infants who have received the HepB birth dose during their birth hospitalization (Chapter 2), whether a timely HepB birth dose was associated with completing the 7-vaccine series by 19 months of age (Chapter 3), and whether a statistical risk prediction tool using timely HepB vaccine receipt, in conjunction with select maternal and infant characteristics, can consistently identify infants at greater risk of missing recommended childhood vaccinations (Chapter 4).

Our study results serve as a basis for identifying sub-populations of infants who may benefit from targeted interventions to increase childhood vaccinations and could inform future studies examining the underlying reasons for low vaccine uptake, research on potentially modifiable factors, and interventions to maximize vaccine receipt.

1.6 NOTES FOR CHAPTER 1

1. Centers for Disease Control and Prevention. What would happen if we stopped vaccinations? Available at: http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm. Accessed November 18, 2015.

2. U.S. Department of Health, Education and Welfare. Vital statistics -- special report, national summaries: Reported incidence of selected notifiable diseases, United States, each division and state, 1950. Available at: https://www.cdc.gov/nchs/data/vsus/vsus_1950_1.pdf. Accessed March 2019.

3. Allen A. *Vaccine: The controversial story of medicine's greatest lifesaver*. New York: Norton & company; 2007.

4. Groce NE, Banks LM, Stein MA. Surviving polio in a post-polio world. *Soc Sci Med*. 2014;107:171-8.

5. Centers for Disease Control and Prevention. Polio for Health Care Professionals. Available at: https://wwwcdcgov/polio/us/hcphtml. Accessed April 2019.

6. Smith J. *Patenting the Sun: Polio and the Salk Vaccine*. New York: William Morrow and Company;1990.

7. Plotkin SA. History of vaccination. *Vaccines.* 1999; 111(34): 12283–12287.

8. Centers for Disease Control and Prevention. Ten great public health achievements--United States, 1900-1999. *MMWR Morb Mortal Wkly Rep*. 1999;48:243-8.

9. Centers for Disease Control and Prevention. Immunization schedules for infants and children. Available at: https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Accessed May 2019.

10. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19-35 months - United States, 2017. *MMWR Morb Mortal Wkly Rep.* 2018;67:1123-8.

11. Smith PJ, Marcuse EK, Seward JF, Zhao Z, Orenstein WA. Children and adolescents unvaccinated against measles: Geographic clustering, parents' beliefs, and missed opportunities. *Public Health Rep*. 2015;130(5):485–504.

12. Omer SB, Enger KS, Moulton LH, Halsey NA, Stokley S, Salmon DA. Geographic clustering of nonmedical exemptions to school immunization requirements and associations with geographic clustering of pertussis. *Am J Epidemiol*. 2008;168:1389-96.

13. Lieu TA, Ray GT, Klein NP, Chung C, Kulldorff M. Geographic clusters in underimmunization and vaccine refusal. *Pediatrics*. 2015;135:280-9.

14. Centers for Disease Control and Prevention. Report shows 20-year U.S. immunization program spares millions of children from diseases. Available at: http://www.cdc.gov/media/releases/2014/p0424-immunization-program.html. Accessed October 2016.

15. World Health Organization. WHO vaccine-preventable diseases: monitoring system. 2016 global summary Available at: http://apps.who.int/immunization_monitoring/globalsummary/ Accessed November 18, 2018.

16. Centers for Disease Control and Prevention. Polio elimination in the United States. Available at: https://www.cdc.gov/polio/us/index.html. Accessed January 2018.

17. Organization WH. Measles. Available at: http://www.who.int/immunization/diseases/measles/en/. Accessed February 2018.

18. Robertson SE FD, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: Global update. *Rev Panam Salud Publica* 14(5):306–15 2003;14:306-15.

19. World Health Organization. Global burden of Haemophilus influenzae type B (Hib). Available at: http://www.emro.who.int/health-topics/haemophilus-influenzae-type-b/disease-burden.html. Accessed March 2019.

20. Centers for Disease Control and Prevention. Measles Cases in 2019. Available at: https://wwwcdcgov/measles/cases-outbreakshtml. Accessed March 2019 2019.

21. Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the United States: A review of measles and pertussis. *JAMA*. 2016;315:1149-58.

22. Smith PJ, Chu SY, Barker LE. Children who have received no vaccines: Who are they and where do they live? *Pediatrics.* 2004;114(1):187-195.

23. Dube E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccin Immunother*. 2013;9:1763-73.

24. Khazan O. How a measles quarantine can lead to eviction. Available at: https://www.theatlantic.com/health/archive/2019/03/measles-outbreaks-cost-workers-without-paid-sick-leave/585178/. The Atlantic, 2019. Accessed February 2019.

25. Sugerman DE, Barskey AE, Delea MG, et al. Measles outbreak in a highly vaccinated population, San Diego, 2008: Role of the intentionally undervaccinated. *Pediatrics*. 2010;125:747-55.

26. Economic Policy Institute. The need for paid sick days. Available at: https://wwwepiorg/publication/the_need_for_paid_sick_days/ Accessed April 2019

27. Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. *Public Health Rep.* 2011;126(2):135-146.

28. Gowda C, Dempsey AF. The rise (and fall?) of parental vaccine hesitancy. *Hum Vaccin Immunother.* 2013;9:1755-62.

30. Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Parental vaccine safety concerns in 2009. *Pediatrics*. 2010;125:654-9.

31. Institute of Medicine. The Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence, and Future Studies. Summary avaiable at: https://www.ncbi.nlm.nih.gov/books/NBK206953/. Accessed June 2019.

32. Centers for Disease Control and Prevention. Possible Side-effects from Vaccines. Available at: https://www.cdc.gov/vaccines/vac-gen/side-effects.htm. Accessed June 2019.

33. Gust DA, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics* 2008;122:718-25.

34. Leask J, Kinnersley P, Jackson C, Cheater F, Bedford H, Rowles G. Communicating with parents about vaccination: a framework for health professionals. *BMC Pediatr* 2012;12:154.

35. MacDonald NE, Hesitancy SWGoV. Vaccine hesitancy: Definition, scope and determinants. *Vaccine* 2015;33:4161-4.

36. Freed GL, Clark SJ, Hibbs BF, Santoli JM. Parental vaccine safety concerns. The experiences of pediatricians and family physicians. *Am J Prev Med* 2004;26:11-4.

37. Leask J. Target the fence-sitters. *Nature* 2011;473:443-5.

38. Wheeler M, Buttenheim AM. Parental vaccine concerns, information source, and choice of alternative immunization schedules. *Hum Vacc Immunother*. 2013;9:1782-9.

39. Favin M, Steinglass R, Fields R, Banerjee K, Sawhney M. Why children are not vaccinated: A review of the grey literature. *Int Health* 2012;4:229-38.

40. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider-parent vaccine discussions at health supervision visits. *Pediatrics* 2013;132:1037-46.

41. Bigham M, Remple VP, Pielak K, McIntyre C, White R, Wu W. Uptake and behavioural and attitudinal determinants of immunization in an expanded routine infant hepatitis B vaccination program in British Columbia. *Can J Public Health* 2006;97:90-5.

42. Richards A, Sheridan J. Reasons for delayed compliance with the childhood vaccination schedule and some failings of computerised vaccination registers. *Aust N Z J Public Health* 1999;23:315-7.

43. Smith PJ, Kennedy AM, Wooten K, Gust DA, Pickering LK. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. *Pediatrics* 2006;118:e1287-92.

44. Gust DA, Woodruff R, Kennedy A, Brown C, Sheedy K, Hibbs B. Parental perceptions surrounding risks and benefits of immunization. *Semin Pediatr Infect Dis* 2003;14:207-12.

45. Opel DJ, Taylor JA, Zhou C, Catz S, Myaing M, Mangione-Smith R. The relationship between parent attitudes about childhood vaccines survey scores and future child immunization status: a validation study. *JAMA Pediatr* 2013;167:1065-71.

46. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kolasa M. National, State, and Selected Local Area Vaccination Coverage Among Children Aged 19-35 Months - United States, 2014. *MMWR Morb Mortal Wkly Rep* 2015;64:889-96.

47. Luman ET, McCauley MM, Shefer A, Chu SY. Maternal characteristics associated with vaccination of young children. *Pediatrics* 2003;111:1215-8.

48. Kim SS, Frimpong JA, Rivers PA, Kronenfeld JJ. Effects of maternal and provider characteristics on up-to-date immunization status of children aged 19 to 35 months. *Am J Public Health* 2007;97:259-66.

49. Bobo JK, Gale JL, Thapa PB, Wassilak SG. Risk factors for delayed immunization in a random sample of 1163 children from Oregon and Washington. *Pediatrics* 1993;91:308-14.

50. Klevens RM, Luman ET. U.S. children living in and near poverty: risk of vaccine-preventable diseases. *Am J Prev Med* 2001;20:41-6.

51. Santoli JM, Huet NJ, Smith PJ, et al. Insurance status and vaccination coverage among US preschool children. *Pediatrics* 2004;113:1959-64.

52. Allred NJ, Wooten KG, Kong Y. The association of health insurance and continuous primary care in the medical home on vaccination coverage for 19-to 35-month-old children. *Pediatrics* 2007;119:S4-S11.

53. Smith PJ, Stevenson J, Chu SY. Associations between childhood vaccination coverage, insurance type, and breaks in health insurance coverage. *Pediatrics* 2006;117:1972-8.

54. Daniels D, Jiles RB, Klevens RM, Herrera GA. Undervaccinated African-American preschoolers: a case of missed opportunities. *Am J Prev Med* 2001;20:61-8.

55. Herrera GA, Zhao Z, Klevens RM. Variation in vaccination coverage among children of Hispanic ancestry. *Am J Prev Med.* 2001;20:69-74.

56. Kenyon TA, Matuck MA, Stroh G. Persistent low immunization coverage among inner-city preschool children despite access to free vaccine. *Pediatrics* 1998;101:612-6.

57. National Academies of Sciences, Engineering and Medicine. Quality through collaboration: The future of rural health care. Available at: https://www.nap.edu/read/11140/chapter/10. Accessed May 2019.

58. Hart LG, Larson EH, Lishner DM. Rural definitions for health policy and research. *Am J Public Health* 2005;95:1149-55.

59. Atkinson WL, Orenstein WA, Krugman S. The resurgence of measles in the United States, 1989-1990. *Annu Rev Med* 1992;43:451-63.

60. Hinman AR, Orenstein WA, Schuchat A, Centers for Disease C, Prevention. Vaccine-preventable diseases, immunizations, and MMWR--1961-2011. *MMWR Suppl* 2011;60:49-57.

61. Zimmerman RK, Tabbarah M, Janosky JE, et al. Impact of vaccine economic programs on physician referral of children to public vaccine clinics: a pre-post comparison. *BMC Public Health* 2006;6:7.

62. Zimmerman RK, Mieczkowski TA, Mainzer HM, et al. Effect of the Vaccines for Children program on physician referral of children to public vaccine clinics: a pre-post comparison. *Pediatrics* 2001;108:297-304.

63. Szilagyi PG, Humiston SG, Pollard Shone L, Kolasa MS, Rodewald LE. Decline in physician referrals to health department clinics for immunizations: the role of vaccine financing. *Am J Prev Med* 2000;18:318-24.

64. Sobo EJ. Social Cultivation of Vaccine Refusal and Delay among Waldorf (Steiner) School Parents. *Med Anthropol Q* 2015;29:381-99.

65. Kata A. A postmodern Pandora's box: anti-vaccination misinformation on the Internet. *Vaccine* 2010;28:1709-16.

66. Sturm LA, Mays RM, Zimet GD. Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections. *J Dev Behav Pediatr* 2005;26:441-52.

67. Salathe M, Bonhoeffer S. The effect of opinion clustering on disease outbreaks. *J R Soc Interface* 2008;5:1505-8.

68. Pew Research Center. The rise of residential segregation by income. Available at: http://www.pewsocialtrends.org/2012/08/01/the-rise-of-residential-segregation-by-income/. Accessed November 2018.

69. Dressler WW OK, Gravlee CC. Race and ethnicity in public health research: Models to explain health disparities. *Annual Rev Anthropol* 2005;24:231-52.

70. Omer SB, Enger KS, Moulton LH, Halsey NA, Stokley S, Salmon DA. Geographic clustering of nonmedical exemptions to school immunization requirements and associations with geographic clustering of pertussis. *Am J Epidemiol*. 2008;168:1389-96.

71. Atwell JE, Van Otterloo J, Zipprich J, et al. Nonmedical vaccine exemptions and pertussis in California, 2010. *Pediatrics* 2013;132:624-30.

72. Zipprich J, Winter K, Hacker J, et al. Measles outbreak--California, December 2014-February 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64:153-4.

73. Kowdley KV, Wang CC, Welch S, Roberts H, Brosgart CL. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatology* 2012;56:422-33.

74. U.S. Department of Health and Human Services. Healthy People 2020. Avaialble at: https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives. Accessed August 2018.

75. McMahon BJ, Alward WL, Hall DB, et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis* 1985;151:599-603.

76. Centers for Disease Control and Prevention. Hepatitis B Information. Available at: http://www.cdc.gov/hepatitis/hbv/. Accessed June 10, 2016.

77. Seeff LB, Beebe GW, Hoofnagle JH, et al. A serologic follow-up of the 1942 epidemic of post-vaccination hepatitis in the United States Army. *N Engl J Med* 1987;316:965-70.

78. Centers for Disease Control and Prevention. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2018;67.

Chapter 2. Sociodemographic, Clinical and Birth Hospitalization Characteristics and Infant Hepatitis B Vaccination in Washington State

Chapter 2.1 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 grams 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 9,080 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 hours vs. 24 to <48 hours (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.

2. 2 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 hours of birth.[1] HepB vaccine is 75% efficacious in preventing perinatal Hepatitis B virus (HBV) transmission when given within this recommended timeframe (94% efficacy 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 1,000 infants are perinatally infected in the U.S. annually.[6,7] This is related to multiple factors, including failure to identify 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.

2.3 METHODS

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.

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, 1,466 (12.4%) had incomplete or inactive WAIIS data.

Outcome Measures

The primary outcome of interest was HepB vaccine receipt during the birth hospitalization. Secondary outcomes were HepB vaccine receipt within 24 hours, 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-hour 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.

Independent Variables

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.

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 hours, ≥24 to <48 hours, ≥48 to <96 hours, and ≥96 hours. Hospital service included the newborn nursery, intermediate care nursery and NICU.

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.

2.4 RESULTS

A total of 9,080 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 2.1**). Most infants were discharged from the hospital within 48 hours, received care in the newborn nursery and were born at term/post-term gestation. The lowest gestational age at birth was 28 weeks.

HepB Vaccination during Birth Hospitalization

Overall, 75.5% of infants received HepB vaccine during their birth hospitalization (**Table 2.1**). 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 2.1**).

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 2.2**). Infant sex, multi-racial/other race/ethnicity, rural-urban residence, median household income, and preterm delivery were not associated with HepB vaccination during the birth hospitalization. **Table 2.2** 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 hours was 64% *vs*. 86% among those discharged ≥96 hours.

HepB Birth Dose Timing

In a subset of infants born on or after October 19, 2010 (n = 4,666, see Methods), 29.1% received their first HepB dose within 24 hours (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 **Figures 2.1 and 2.2.** 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 vaccination coverage by 19 months (**Figure 2.1**).

2.5 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 the birth hospitalization, including 29% in the first 24 hours, 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 of 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 <2000g, 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 hours 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]

2.6 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.

Table 2.1. 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=9,080		Received HepB[b] n=6,858		Did not receive HepB[b] n=2,222	
Sex						
Male	4,649	(51.2)	3,493	(50.9)	1,156	(52.0)
Female	4,431	(48.8)	3,365	(49.1)	1,066	(48.0)
Race/ethnicity[c]						
Hispanic	1,170	(14.6)	1,029	(16.8)	141	(7.5)
Non-Hispanic white	3,901	(48.7)	2,525	(41.2)	1,376	(73.2)
Non-Hispanic black	1,759	(21.9)	1,567	(25.6)	192	(10.2)
Asian	1,081	(13.5)	933	(15.2)	148	(7.9)
Multiracial/other	103	(1.3)	80	(1.3)	23	(1.2)
Maternal language						
English	6,486	(76.0)	4,652	(71.6)	1,834	(90.4)
Spanish	853	(10.0)	766	(11.8)	87	(4.3)
Other	1,190	(14.0)	1,083	(16.7)	107	(5.3)
Insurance status						
Private	3,747	(44.2)	2,412	(37.6)	1,335	(64.3)
Public	4,737	(55.8)	3,996	(62.4)	741	(35.7)
Rural-urban residence						
Rural	237	(2.6)	161	(2.4)	76	(3.4)
Urban	8,840	(97.4)	6,696	(97.7)	2,144	(96.6)
Income estimate						
<$54,888	2,801	(31.0)	2,227	(32.7)	574	(26.0)
≥$54,888	6,227	(69.0)	4,591	(67.3)	1,636	(74.0)

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	8,093	(89.1)	6,166	(89.9)	1,927	(86.8)
Length of stay, hours						
<24	820	(9.1)	412	(6.0)	408	(18.4)
≥24 to <48	3,956	(43.6)	3,114	(45.4)	842	(37.9)
≥48 to <96	3,296	(36.3)	2,580	(37.6)	716	(32.2)
≥96	1,008	(11.0)	752	(11.0)	256	(11.5)
Medical service						
Newborn nursery	7,266	(80.0)	5,707	(83.2)	1,559	(70.2)
Intermediate care nursery	1,330	(14.7)	1,011	(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 = 1,066 (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 2.2. 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)
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	**0.09 (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.

Figure 2.1. Cumulative proportion of first HepB vaccine receipt within 3, 30 or 580 days of birth, by demographic characteristics

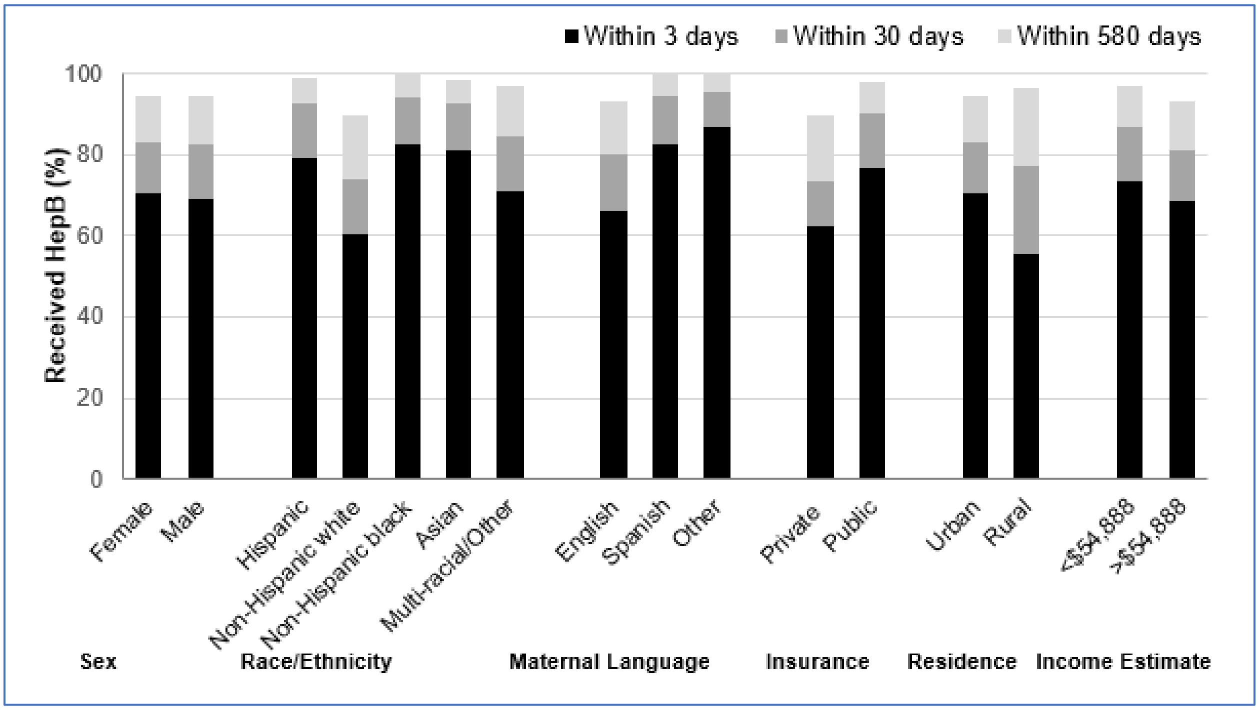
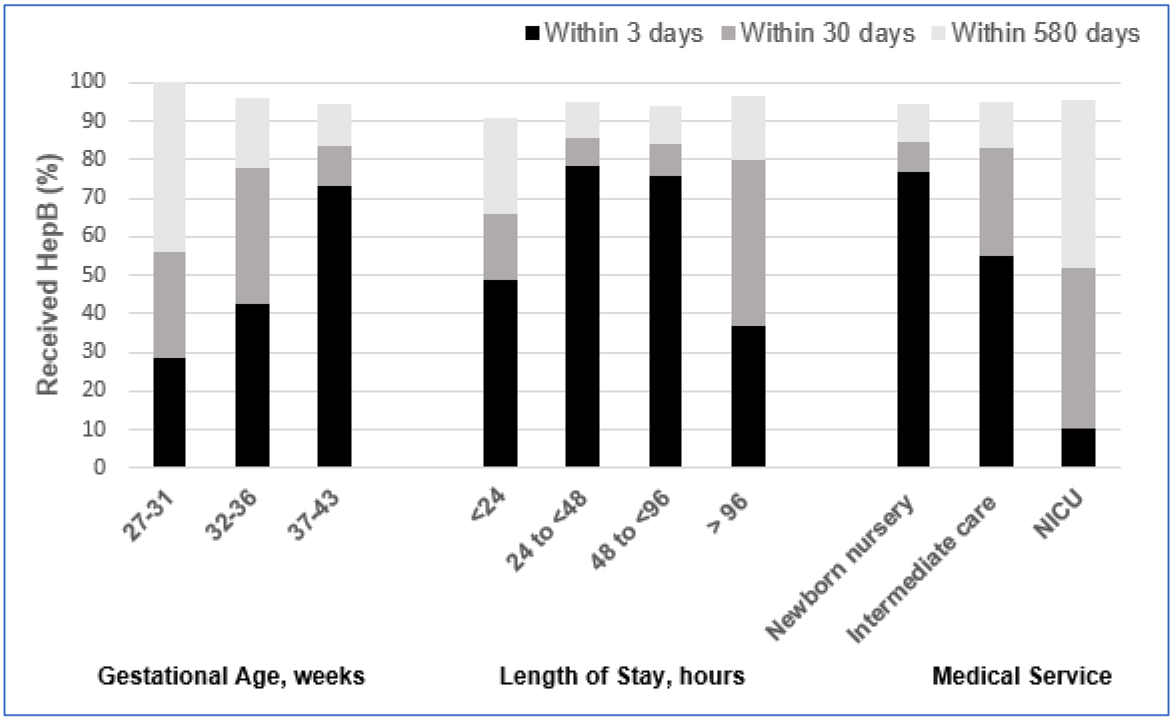
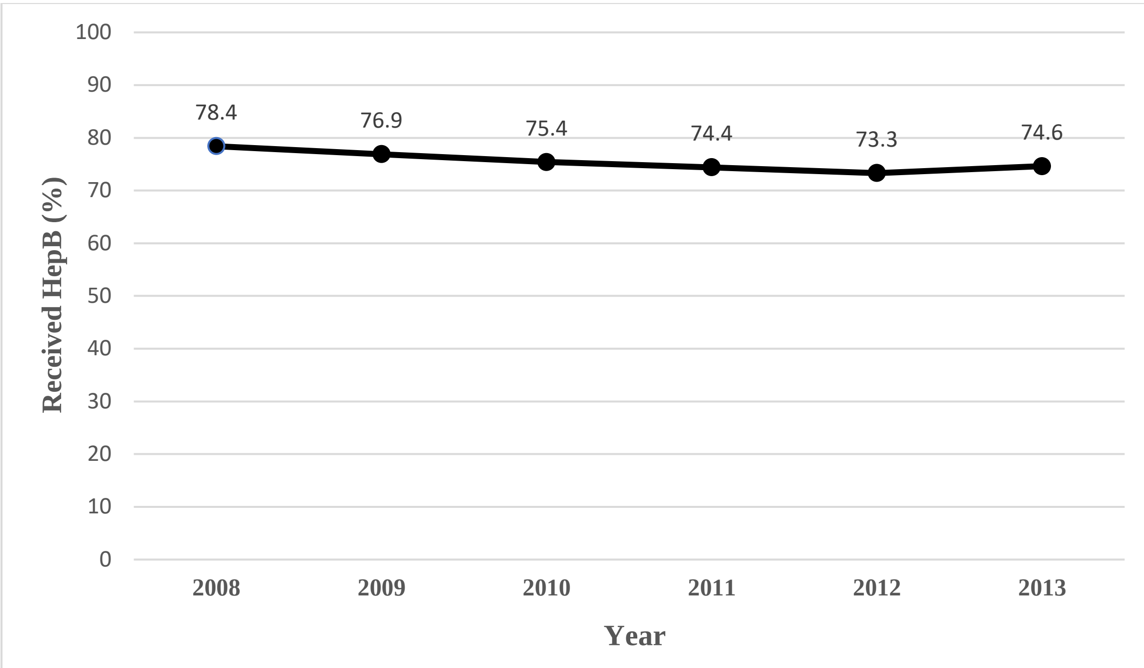


Figure 2.2. Cumulative proportion of first HepB vaccine receipt within 3, 30 or 580 days of birth, by clinical and birth hospitalization factors



Supplemental Figure 2.1. Trends in HepB vaccine receipt during the birth hospitalization, 2008-2013



2.6 NOTES FOR CHAPTER 2

1. Centers for Disease Control and Prevention. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2018;67(1).

2. Beasley RP, Hwang LY, Lee GC, et al. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet.* 1983;2(8359):1099-1102.

3. Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: Systematic review and meta-analysis. *BMJ.* 2006;332(7537):328-336.

4. Yusuf HR, Daniels D, Smith P, Coronado V, Rodewald L. Association between administration of hepatitis B vaccine at birth and completion of the hepatitis B and 4:3:1:3 vaccine series. *JAMA.* 2000;284(8):978-983.

5. Lauderdale DS OR, Goldstein KP, Daum S. Hepatitis B vaccination among children in inner-city public housing, 1991-1997. *JAMA.* 1999;282:1725-1730.

6. Ko SC, Fan L, Smith EA, Fenlon N, Koneru AK, Murphy TV. Estimated annual periantal Hepatitis B virus infections in the United States, 200-2009. *J Pediatric Infect Dis Soc*. 2016;5(2):114-121.

7. Smith EA, Jacques-Carroll L, Walker TY, Sirotkin B, Murphy TV. The national Perinatal Hepatitis B Prevention Program, 1994-1008. *Pediatrics.* 2012:129(4):609-616.

8. Anderson TA, Wexler DL. States report hundreds of medical errors in perinatal Hepatitis B prevention: Avoid tragic mistakes—Vaccinate newborns against HBV in the hospital. Immunization Action Coalition, 2003. Available at: http://immunize.org/catg.d/p2062.pdf. Accessed July 2018.

9. American Academy of Pediatrics, Committee on Infectious Diseases. Elimination of perinatal hepatitis B: Providing the first vaccine dose within 24 hours of birth. *Pediatrics.* 2017;140(3).

10. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19-35 months - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2017;66(43):1171-1177.

11. Vasireddy D, Yusi D, Berrak SG, Lichtenberger J. Factors affecting refusal rates of the birth dose of hepatitis B vaccine: A single center study. *J Pediatr Inf.* 2014;8:159-164.

12. Myers HI, Spracklen CN, Ryckman KK, Murray JC. Retrospective study of administration of vaccination for Hepatitis B among newborn infants prior to hospital discharge at a Midwestern tertiary care center. *Vaccine*. 2015 May 11; 33(20): 2316–2321.

13. Jackson ML, Henrikson NB, Grossman DC. Evaluating Washington State's immunization information system as a research tool. *Acad Pediatr*. 2014;14(1):71-76.

14. Centers for Disease Control and Prevention. Percentage of children aged < 6 years participating in an immunization information system -- United States, five cities and D.C., 2013. https://www.cdc.gov/vaccines/programs/iis/annual-report-iisar/downloads/2013-data-child-map.pdf. Accessed July 2018.

15. Murthy N, Rodgers L, Pabst L, Fiebelkorn AP, Ng T. Progress in childhood vaccination data in immunization information systems – United States, 2013-2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(43):1178-1181.

16. United States Census Bureau, Department of Commerce. Overview of race and Hispanic origin: 2010. https://www.census.gov/prod/cen2010/briefs/. Accessed April 2018

17. University of Michigan, Institute for Social Research. Median Household Income, 2006-2010. Available at: https://www.psc.isr.umich.edu/dis/census/Features/tract2zip/index.html. Accessed May 2018.

18. Washington State Office of Financial Management. Washington State and county median household income estimates: 1989 to 2015 and projection for 2016. Available at: http://www.ofm.wa.gov/economy/hhinc/medinc.pdf. Accessed July 2018.

19. Rural Health Research Center. Rural Urban Commuting Areas. Available at: http://depts.washington.edu/uwruca/ruca-approx.php. Accessed July 2018.

20. Quinn JA, Munoz FM, Gonik B, et al. Preterm birth: Case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. *Vaccine.* 2016;34(49):6047-6056.

21. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2005;54(RR-16):1-31.

22. United States Department of Health and Human Services. Healthy People 2020. https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives. Accessed August 2018.

23. Smith PJ, Chu SY, Barker LE. Children who have received no vaccines: Who are they and where do they live? *Pediatrics.* 2004;114(1):187-195.

24. Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. *Public Health Rep.* 2011;126(2):135-146.

25. New York State Department of Health. Perinatal Hepatitis B prevention program manual. https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_b/perinatal/docs/program_manual.pdf. Accessed May 2018.

26. Walker TY, Smith EA, Fenlon N, et al. Characteristics of pregnant women with hepatitis B virus infection in five U.S. public health jurisdictions, 2008-2012. *Public Health Rep.* 2016;131(5):685-694.

27. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics.* 2015;135(5):e1141-1147.

28. Centers for Disease Control and Prevention. Viral Hepatitis Surveillance – United States, 2010. https://www.cdc.gov/hepatitis/statistics/2010surveillance/commentary.htm Accessed August 2018.

29. Ocama P, Opio CK, Lee WM. Hepatitis B virus infection: current status. *Am J Med.* 2005;118(12):1413.

30. Berdahl TA, Friedman BS, McCormick MC, Simpson L. Annual report on health care for children and youth in the United States: Trends in racial/ethnic, income, and insurance disparities over time, 2002-2009. *Acad Pediatr.* 2013;13(3):191-203.

31. Leininger L, Levy H. Child health and access to medical care. *Future Child.* 2015;25(1):65-90.

32. O'Leary ST, Nelson C, Duran J. Maternal characteristics and hospital policies as risk factors for nonreceipt of hepatitis B vaccine in the newborn nursery. *Pediatr Infect Dis J.* 2012;31(1):1-4.

33. Yang S, Zarr RL, Kass-Hout TA, Kourosh A, Kelly NR. Transportation barriers to accessing health care for urban children. *J Health Care Poor Underserved.* 2006;17(4):928-943.

34. Newacheck PW, Hughes DC, Stoddard JJ. Children's access to primary care: differences by race, income, and insurance status. *Pediatrics.* 1996;97(1):26-32.

35. Washington State Department of Health. Evaluation of birthing hospitals on perinatal hepatitis B prevention practices. https://www.doh.wa.gov/Portals/1/Documents/Pubs/348-432-HospitalTechRpt.pdf. Accessed August 2018.

36. Wheeler M, Buttenheim AM. Parental vaccine concerns, information source, and choice of alternative immunization schedules. *Hum Vacc Immunother.* 2013;9(8):1782-1789.

37. Opel DJ, Heritage J, Taylor JA, et al. The Architecture of Provider-Parent Vaccine Discussions at Health Supervision Visits. *Pediatrics.* 2013;132(6):1037-1046.

38. Smith PJ, Kennedy AM, Wooten K, Gust DA, Pickering LK. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. *Pediatrics.* 2006;118(5):e1287-1292.

39. Gust DA, Woodruff R, Kennedy A, Brown C, Sheedy K, Hibbs B. Parental perceptions surrounding risks and benefits of immunization. *Semin Pediatr Infect Dis.* 2003;14(3):207-212.

40. McClure CC, Cataldi JR, O'Leary ST. Vaccine hesitancy: Where we are and where we are going. Clinical Therapeutics. 2017;39(8):1550-1562.

41. Centers for Disease Control and Prevention. Vaccination coverage among children in kindergarten - United States, 2012-13 school year. *MMWR Morb Mortal Wkly Rep.* 2013;62(30):607-612.

42. Kogan MD, Alexander GR, Jack BW, Allen MC. The association between adequacy of prenatal care utilization and subsequent pediatric care utilization in the United States. *Pediatrics.* 1998; 102(1):25-30.

Chapter 3. Hepatitis B Birth Dose: First Shot at Timely Early Childhood Vaccination

Chapter 3.1 ABSTRACT

Introduction: Current U.S. recommendations state that newborns weighing ≥2,000 grams should receive a birth dose of hepatitis B (HepB) vaccine, yet approximately one quarter do not receive this first dose as scheduled. The relationship between timely receipt of the first HepB 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 HepB 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 HepB vaccine during the birth hospitalization, and 53.6% completed the seven-vaccine series by 19 months. Overall, 60.0% of infants vaccinated against HepB 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 three times higher among infants who received versus did not receive HepB vaccine during the birth hospitalization (AOR=2.92, 95% CI=2.61, 3.26).

Conclusions: Infants who received HepB 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 HepB vaccine delay or declination may impact subsequent vaccination requires further research.

3.2 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 series.[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 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] demonstrated 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] 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 more-comprehensive sociodemographic data than included in 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.

3.3 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, Washington, between January 1, 2008 and December 31, 2013. The sample was limited by birth weight given distinct Advisory Committee on Immunization Practices recommendations 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 (PM 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 two 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 (four doses of diphtheria–tetanus–(whole-cell or acellular) pertussis, three poliovirus, one measles–mumps–rubella, three *Haemophilus influenzae* type b, three HepB, one varicella, four pneumococcal) by age 19 months. Secondary outcomes included receipt of individual vaccines within the seven-vaccine series, rotavirus (two doses), and influenza (two 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 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 $p<0.05$.

3.4 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 3.1** overall and across receipt of the seven-vaccine series by 19 months in **Appendix Table 3.3.**

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 prior to hospital discharge (*p*<0.001).

The odds of seven-vaccine series completion by 19 months were higher among infants who received versus 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 3.2**). There was a significant association between HepB birth dose receipt and receipt of individual vaccines in the seven-vaccine series and rotavirus and influenza vaccines by 19 months (**Figure 3.1**). The strength of association varied by vaccine type, with the lowest association between HepB birth dose receipt and four-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 three-dose HepB series completion (AOR=7.99, 95% CI=6.99, 9.16).

In the subset of infants born on or after October 19, 2010 (*n*=4,666; Methods section) infants who received HepB vaccine within 3 days of birth had nearly threefold greater odds of seven-vaccine series completion by 19 months versus 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 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 versus those unvaccinated within 30 days (59.4% vs 25.8%, *p*<0.001; AOR=4.40, 95% CI=3.85, 5.02).

3.5 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 much 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 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 three-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 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 demonstrated 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 hepatitis B 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 as a result 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, 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, which limits patient-level specificity regarding the influence of socioeconomic determinants on vaccine receipt.

Importantly, geographic clustering of under-vaccinated 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 non-differential. 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 is also worth noting that Washington State is one of 17 states that allows personal, philosophical, and religious exemptions and has one of the highest non-medical 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 impacts 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, and 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. Data were also 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.

3.6 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.

Table 3.1. 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[c]	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.
[c]ICU, intensive care unit.

Table 3.2. 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[d]	**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.
[d]ICU, intensive care unit.

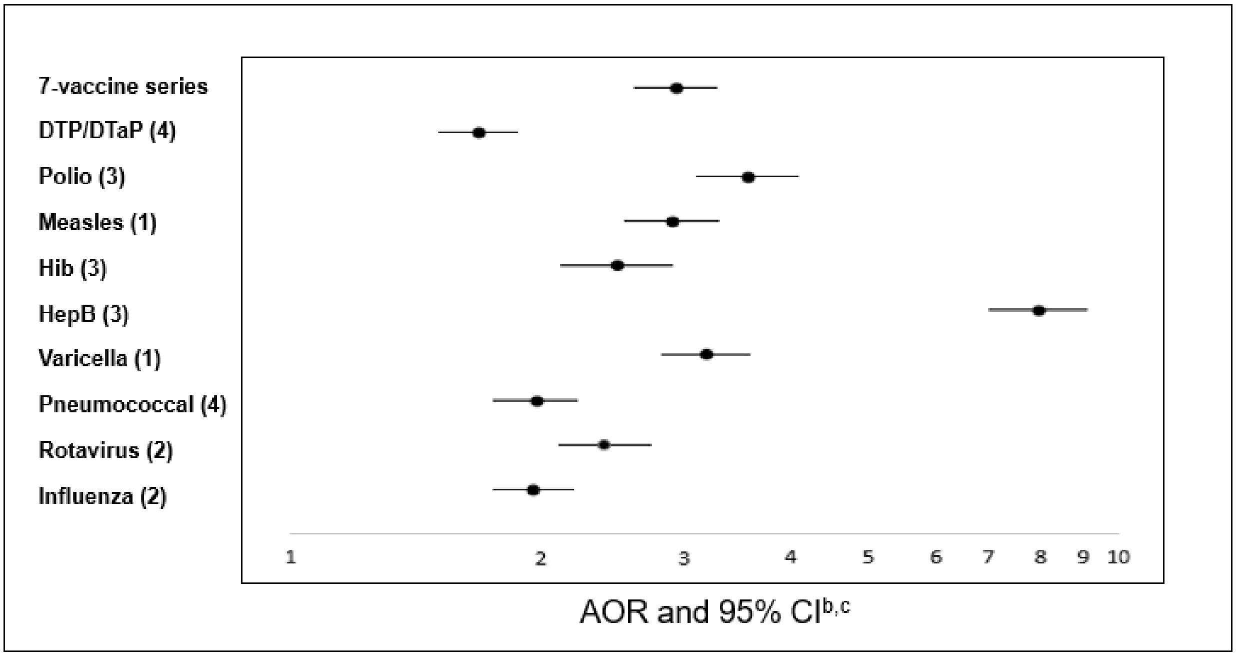
Appendix Table 3.3 Study Participant Characteristics by Seven-Vaccine Series Completion Within 19 Months of Birth[a,b]

Patient characteristics	Received seven-vaccine series, n=4,867, n (%)	Did not receive seven-vaccine series, n=4,213, n (%)
Sex		
Male	2,501 (51.4)	2,148 (51.0)
Female	2,366 (48.6)	2,065 (49.0)
Race/ethnicity		
Hispanic	693 (15.8)	477 (13.2)
Non-Hispanic white	2,039 (46.5)	1,862 (51.3)
Non-Hispanic black	879 (20.0)	880 (24.3)
Asian	729 (16.6)	352 (9.7)
Multiracial/other	47 (1.1)	56 (1.5)
Maternal language		
English	3,476 (74.8)	3,010 (77.5)
Spanish	538 (11.6)	315 (8.1)
Other	630 (13.6)	560 (14.4)
Insurance status		
Private	2,163 (47.3)	1,584 (40.5)
Public	2,410 (52.7)	2,327 (59.5)
Rural–urban residence		
Rural	107 (2.2)	130 (3.1)
Urban	4,759 (97.8)	4,081 (96.9)
Estimated household income[c]		
$20,135–42,799	166 (3.4)	199 (4.8)
$42,800–50,844	581 (12.0)	528 (12.6)
$50,845–62,239	1,900 (39.2)	1,674 (40.0)
$62,240–174,729	2,195 (45.3)	1,785 (42.6)
Birth hospitalization length of stay, hours		
<24	315 (6.5)	505 (12.0)
≥24 to <48	2,232 (45.9)	1,724 (40.9)
≥48 to <96	1,793 (36.8)	1,503 (35.7)
≥96	527 (10.8)	481 (11.4)
Birth hospitalization service		
Newborn nursery	4,045 (83.1)	3,221 (76.4)
Intermediate care nursery	699 (14.4)	631 (15.0)
Neonatal ICU[d]	123 (2.5)	361 (8.6)

[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%); income estimate=52 (0.6%).
[b]Gestational age removed due to exclusion of infants <2,000 grams.

[c]Based on 2010 U.S. Census Bureau ZIP code-level median household income.
[d]ICU, intensive care unit.

Figure 3.1. 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.

3.7 NOTES FOR CHAPTER 3

1. Centers for Disease Control and Prevention. Recommended Child and Adolescent Immunization Schedule for ages 18 or younger, United States, 2019. www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Updated February 5, 2019. Accessed January 2019.

2. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months—United States, 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(40):1123–1128. https://doi.org/10.15585/mmwr.mm6740a4.

3. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 2018;67(1):1–31. https://doi.org/10.15585/mmwr.rr6701a1.

4. Yusuf HR, Daniels D, Smith P, Coronado V, Rodewald L. Association between administration of hepatitis B vaccine at birth and completion of the hepatitis B and 4:3:1:3 vaccine series. *JAMA*. 2000;284(8):978–983. https://doi.org/10.1001/jama.284.8.978.

5. Lauderdale DS, Oram RJ, Goldstein KP, Daum RS. Hepatitis B vaccination among children in inner-city public housing, 1991–1997. *JAMA*. 1999;282(18):1725–1730. https://doi.org/10.1001/jama.282.18.1725.

6. Wagner AL, Eccleston AM, Potter RC, Swanson RG, Boulton ML. Vaccination timeliness at age 24 months in Michigan children born 2006–2010. *Am J Prev Med*. 2018;54(1):96–102. https://doi.org/10.1016/j.amepre.2017.09.014.

7. Wilson P, Taylor G, Knowles J, et al. Missed hepatitis B birth dose vaccine is a risk factor for incomplete vaccination at 18 and 24 months. *J Infect*. 2018;78(2):134–139. https://doi.org/10.1016/j.jinf.2018.09.014.

8. Mennito SH, Darden PM. Impact of practice policies on pediatric immunization rates. *J Pediatr*. 2010;156(4):618–622. https://doi.org/10.1016/j.jpeds.2009.10.046.

9. Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. *Public Health Rep*. 2011;126(Suppl 2):135–146. https://doi.org/10.1177/00333549111260S215.

10. Smith PJ, Chu SY, Barker LE. Children who have received no vaccines: who are they and where do they live? *Pediatrics*. 2004;114(1):187–195. https://doi.org/10.1542/peds.114.1.187.

11. CDC. Percentage of children aged <6 years participating in an immunization information system—United States, five cities and D.C., 2013. www.cdc.gov/vaccines/programs/iis/annual-report-iisar/downloads/2013-data-child-map.pdf. Accessed April 2019.

12. Jackson ML, Henrikson NB, Grossman DC. Evaluating Washington State's immunization information system as a research tool. *Acad Pediatr*. 2014;14(1):71–76. https://doi.org/10.1016/j.acap.2013.10.002.

13. Stockwell MS, Natarajan K, Ramakrishnan R, et al. Immunization data exchange with electronic health records. *Pediatrics*. 2016;137(6):e20154335. https://doi.org/10.1542/peds.2015-4335.

14. Murthy N, Rodgers L, Pabst L, Fiebelkorn AP, Ng T. Progress in childhood vaccination data in immunization information systems—United States, 2013–2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(43):1178–1181. https://doi.org/10.15585/mmwr.mm6643a4.

15. Luman ET, Barker LE, McCauley MM, Drews-Botsch C. Timeliness of childhood immunizations: a state-specific analysis. *Am J Public Health*. 2005;95:1367–1374. https://doi.org/10.2105/AJPH.2004.046284.

16. U.S. Department of Commerce. Overview of Race and Hispanic Origin: 2010. www.census.gov/prod/cen2010/briefs/c2010br-02.pdf. Published March 2011. Accessed March 2019.

17. University of Michigan Population Studies Center. Median Household Income. www.psc.isr.umich.edu/dis/census/Features/tract2zip/index.html. Accessed March 2019.

18. Rural Health Research Center. Rural–Urban Commuting Codes. http://depts.washington.edu/uwruca/index.php. Accessed March 2019.

19. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: final data for 2017. *Natl Vital Stat Rep*. 2018;67:1–50.

20. Oster NV, Williams EC, Unger JM, et al. Sociodemographic, clinical and birth hospitalization characteristics and infant hepatitis B vaccination in Washington State. *Vaccine*. In press. Online March 28, 2019. https://doi.org/10.1016/j.vaccine.2019.03.050.

21. Jiles RB, Daniels D, Yusuf HR, McCauley MM, Chu SY. Undervaccination with hepatitis B vaccine: missed opportunities or choice? *Am J Prev Med*. 2001;20(4 Suppl 1):75–83. https://doi.org/10.1016/S0749-3797(01)00276-8.

22. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics*. 2015;135(5):e1141–e1147. https://doi.org/10.1542/peds.2014-3213.

23. Suri G, Sheppes G, Schwartz C, Gross JJ. Patient inertia and the status quo bias: when an inferior option is preferred. *Psychol Sci*. 2013;24(9):1763–1769. https://doi.org/10.1177/0956797613479976.

24. Gal D. A psychological law of inertia and the illusion of loss aversion. *Judgm Decis Mak*. 2006;1(1):23–32. https://doi.org/10.1037/e683162011-083.

25. Halpern SD, Ubel PA, Asch DA. Harnessing the power of default options to improve health care. *N Engl J Med*. 2007;357:1340–1344. https://doi.org/10.1056/NEJMsb071595.

26. Henrikson NB, Anderson ML, Opel DJ, Dunn J, Marcuse EK, Grossman DC. Longitudinal trends in vaccine hesitancy in a cohort of mothers surveyed in Washington State, 2013–2015. *Public Health Rep*. 2017;132(4):451–454. https://doi.org/10.1177/0033354917711175.

27. Wheeler M, Buttenheim AM. Parental vaccine concerns, information source, and choice of alternative immunization schedules. *Hum Vacc Immunother*. 2013;9(8):1782–1789. https://doi.org/10.4161/hv.25959.

28. Gust DA, Woodruff R, Kennedy A, Brown C, Sheedy K, Hibbs B. Parental perceptions surrounding risks and benefits of immunization. *Semin Pediatr Infect Dis*. 2003;14(3):207–212. https://doi.org/10.1016/S1045-1870(03)00035-9.

29. Hofstetter AM, Lappetito L, Stockwell MS, Rosenthal SL. Human papillomavirus vaccination of adolescents with chronic medical conditions: a national survey of pediatric subspecialists. *J Pediatr Adolesc Gynecol*. 2017;30(1):88–95. https://doi.org/10.1016/j.jpag.2016.08.005.

30. Rosenthal SL, Weiss TW, Zimet GD, Ma L, Good MB, Vichnin MD. Predictors of HPV vaccine uptake among women aged 19–26: importance of a physician's recommendation. *Vaccine*. 2011;29(5):890–895. https://doi.org/10.1016/j.vaccine.2009.12.063.

31. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider–parent vaccine discussions at health supervision visits. *Pediatrics*. 2013;132(6):1037–1346. https://doi.org/10.1542/peds.2013-2037.

32. New York State Department of Health. Perinatal Hepatitis B Prevention Program Manual. www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_b/perinatal/docs/program_manual.pdf. Updated May 2011. Accessed March 2019.

33. Shelby A, Ernst K. Story and science: how providers and parents can utilize storytelling to combat anti-vaccine misinformation. *Hum Vaccin Immunother*. 2013;9(8):1795–1801. https://doi.org/10.4161/hv.24828.

34. Ritov I BJ. Reluctance to vaccinate: omission bias and ambiguity. *J Behav Dec Mak*. 1990;3:263–277. https://doi.org/10.1002/bdm.3960030404.

35. Ritov I BJ. Status-quo and omission bias. *J Risk and Uncertainty*. 1992;5(1):49–61. https://doi.org/10.1007/BF00208786.

36. Burton T, Saini S, Maldonado L, Carver JD. Parental refusal for treatments, procedures, and vaccines in the newborn nursery. *Adv Pediatr*. 2018;65(1):89–104. https://doi.org/10.1016/j.yapd.2018.04.006.

37. Block SL. Playing newborn intracranial roulette: parental refusal of vitamin K injection. *Pediatr Ann*. 2014;43(2):53–59. https://doi.org/10.3928/00904481-20131223-04.

38. Hamrick HJ, Gable EK, Freeman EH, et al. Reasons for refusal of newborn vitamin K prophylaxis: implications for management and education. *Hosp Pediatr*. 2016;6(1):15–21. https://doi.org/10.1542/hpeds.2015-0095.

39. Centers for Disease Control and Prevention. Measles Cases in 2019. www.cdc.gov/measles/cases-outbreaks.html. Updated April 29, 2019. Accessed March 2019.

40. Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the United States: a review of measles and pertussis. *JAMA*. 2016;315(11):1149–1158. https://doi.org/10.1001/jama.2016.1353.

41. Glanz JM, Wagner NM, Narwaney KJ, et al. Web-based social media intervention to increase vaccine acceptance: a randomized controlled trial. *Pediatrics*. 2017;140(6): https://doi.org/10.1542/peds.2017-1117.

42. Kressin NR, Chang BH, Hendricks A, Kazis LE. Agreement between administrative data and patients' self-reports of race/ethnicity. *Am J Public Health*. 2003;93:1734–1739. https://doi.org/10.2105/AJPH.93.10.1734.

43. Smith PJ, Marcuse EK, Seward JF, Zhao Z, Orenstein WA. Children and adolescents unvaccinated against measles: geographic clustering, parents' beliefs, and missed opportunities. *Public Health Rep*. 2015;130(5):485–504. https://doi.org/10.1177/003335491513000512.

44. Lieu TA, Ray GT, Klein NP, Chung C, Kulldorff M. Geographic clusters in underimmunization and vaccine refusal. *Pediatrics*. 2015;135(2):280–289. https://doi.org/10.1542/peds.2014-2715.

45. Klevens RM, Luman ET. U.S. children living in and near poverty: risk of vaccine-preventable diseases. *Am J Prev Med*. 2001;20(4 Suppl 1):41–46. https://doi.org/10.1016/S0749-3797(01)00281-1.

46. Yang YT, Delamater PL, Leslie TF, Mello MM. Sociodemographic predictors of vaccination exemptions on the basis of personal belief in California. *Am J Public Health*. 2016;106:172–177. https://doi.org/10.2105/AJPH.2015.302926.

47. Allred NJ, Wooten KG, Kong Y. The association of health insurance and continuous primary care in the medical home on vaccination coverage for 19- to 35-month-old children. *Pediatrics*. 2007;119(Suppl 1):S4–S11. https://doi.org/10.1542/peds.2006-2089C.

48. Adorador A, McNulty R, Hart D, Fitzpatrick JJ. Perceived barriers to immunizations as identified by Latino mothers. *J Am Acad Nurse Pract*. 2011;23(9):501–508. https://doi.org/10.1111/j.1745-7599.2011.00632.x.

49. Syed ST, Gerber BS, Sharp LK. Traveling towards disease: transportation barriers to health care access. *J Community Health*. 2013;38(5):976–993. https://doi.org/10.1007/s10900-013-9681-1.

50. Yang S, Zarr RL, Kass-Hout TA, Kourosh A, Kelly NR. Transportation barriers to accessing health care for urban children. *J Health Care Poor Underserved*. 2006;17(4):928–943. https://doi.org/10.1353/hpu.2006.0137.

51. Sobo EJ. Social Cultivation of Vaccine Refusal and Delay among Waldorf (Steiner) School Parents. *Med Anthropol Q*. 2015;29(3):381–399. https://doi.org/10.1111/maq.12214.

52. Kata A. A postmodern Pandora's box: anti-vaccination misinformation on the Internet. *Vaccine*. 2010;28(7):1709–1716. https://doi.org/10.1016/j.vaccine.2009.12.022.

53. Dube E, Gagnon D, MacDonald N, Bocquier A, Peretti-Watel P, Verger P. Underlying factors impacting vaccine hesitancy in high income countries: a review of qualitative studies. *Expert Rev Vac*. 2018;17(11):989–1004. https://doi.org/10.1080/14760584.2018.1541406.

54. Seither R, Calhoun K, Street EJ, et al. Vaccination coverage for selected vaccines, exemption rates, and provisional enrollment among children in kindergarten—United States, 2016–17 school year. *MMWR Morb Mortal Wkly Rep*. 2017;66(40):1073–1080. https://doi.org/10.15585/mmwr.mm6640a3.

55. Centers for Disease Control and Prevention. 2017–18 school year vaccination exemption reports. www.cdc.gov/vaccines/imz-managers/coverage/schoolvaxview/data-reports/exemptions-reports/2017-18.html. Updated October 11, 2018. Accessed March 2019.

56. National Conference of State Legislatures. States with religious and philosophical exemptions from school immunization requirements. www.ncsl.org/research/health/school-immunization-exemption-state-laws.aspx. Published January 30, 2019. Accessed March 2019.

57. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Dietz V. Vaccination coverage among children aged 19-35 months—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2016;65(39):1065–1071. https://doi.org/10.15585/mmwr.mm6539a4.

Chapter 4: A Risk Prediction Tool to Identify Newborns at High Risk for Missing Early Childhood Vaccination

4.1 ABSTRACT

Background: Over one-quarter of children aged 19-35 months have not received recommended vaccinations. We aimed to develop and validate a prediction tool to identify newborns at high risk for missing early childhood vaccines.

Methods: A retrospective cohort of 9,080 infants born weighing ≥2000g at an urban academic medical center between 2008-2013 were included. Risk models were constructed using derivation and validation samples. K-fold cross-validation was used to identify adverse risk factors for model inclusion based on alpha=0.01. Adverse risk factors were summed, creating a score, and categorized as low (0-2 risk score), medium (3-4 risk score), and high (5-7 risk score) risk. Logistic regression was used to evaluate the likelihood of not completing the 7-vaccine series by age 19 months. The final model was tested using the validation sample.

Results: Overall, 53.6% of study infants failed to complete the 7-vaccine series by 19 months. Missed hepatitis B vaccination during the birth hospitalization was the strongest predictor of 7-vaccine series non-completion. The likelihood of 7-vaccine series non-completion was much higher among infants in the high (77.1%; adjusted odds ratio [AOR] 5.6; 95% CI: 4.5, 6.9) and medium (52.7%; AOR 1.9; 95% CI: 1.7, 2.1) *vs.* low-risk category (38.7%) in the derivation sample. Similar results were observed in the validation sample.

Conclusions: Our prediction model using information readily available in birth hospitalization electronic medical records consistently identified newborns at high risk for under-vaccination. Early identification of high-risk families could be useful to providers as timely and targeted vaccine interventions are initiated.

4.2 INTRODUCTION

Childhood vaccination is the most effective way to prevent many infectious diseases at individual and population levels.[1] Although overall vaccination rates remain high nationally,[2] the rise of vaccine hesitancy[3,4] coupled with recent outbreaks of vaccine preventable diseases[5,6] highlights the continued importance of promoting and increasing childhood vaccination coverage.

Given wide variation in vaccine uptake by sociodemographic and clinical characteristics,[7-9] it can be difficult for clinicians to easily and accurately identify individual infants at risk for missing future childhood vaccinations whose parents may benefit from targeted interventions. Risk prediction models using patient characteristics to identify those at highest risk for adverse outcomes and behaviors are increasingly used to complement clinical decision-making.[10-16] Two previous risk prediction models for childhood vaccinations have been reported, one to predict vaccination coverage among preschool-age emergency department (ED) patients,[17] and another to predict receipt of select childhood vaccines among patients at urban, safety net community health centers.[18] The target populations and vaccinations assessed in these previous studies were limited. To our knowledge, no population-based risk prediction models have been developed to identify newborns at risk of future under-vaccination. A risk prediction tool based on readily available variables could be integrated into clinical decision support to encourage the initiation of interventions such as more intensive screening or earlier vaccine communication with parents of infants identified as high risk for delaying or declining recommended childhood vaccinations.

Our objective was to develop a clinically relevant statistical model using sociodemographic, clinical and birth hospitalization characteristics to predict the risk of an infant failing to complete the recommended 7-vaccine series[19] by 19 months of age.

4.3 METHODS

Study Sample and Setting

The study sample and setting has been described previously.[20,21] In brief, all infants with a birthweight ≥2000 grams who received birth hospitalization care between January 1, 2008 and December 31, 2013 at the University of Washington Medical Center (UWMC), a large academic medical center in Seattle, Washington, were included. All study participants were documented to be Washington State residents based on residential address. Infants without complete admission and discharge data and those who transferred to UWMC after birth were excluded. The study was approved by the Seattle Children's Hospital and Washington State Institutional Review Boards.

Data Sources

Sociodemographic, birth hospitalization, and clinical data, including vaccine doses given during the birth hospitalization, were retrospectively collected from electronic medical records (EMR). Select identifiers and a standardized matching algorithm were used to link EMR data to vaccine records in the Washington State Immunization Information System (WAIIS) in order to capture vaccinations administered in other clinical settings after hospital discharge. Infants with <2 recorded doses of any vaccine or incomplete or inactive WAIIS records were excluded from the present study, consistent with national and state reporting standards.[22]

Measures

The primary outcome for the prediction model was failure to receive the recommended number of doses of seven pediatric vaccines. This 7-vaccine series includes 4 doses of diphtheria-tetanus-[whole-cell or acellular] pertussis (DTP/DTaP), 3 poliovirus, 1 measles-mumps-rubella, 3 Haemophilus influenza Type b, 3 Hepatitis B (HepB), 1 varicella, 4 pneumococcal conjugate vaccines by age 19 months.[19] The 19-month cut off (i.e., <580 days of age) has been used previously to define timely vaccine receipt.[23]

Independent Variables

Maternal and Infant Sociodemographic Characteristics

Sociodemographic data included infant sex (male, female), maternal language (English, Spanish, other), insurance status (public, private) and race/ethnicity. Race/ethnicity was categorized using U.S. Census Bureau classifications[24] 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). 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 data and commuting information.[25] Area-level income was measured for each patient based on the median household income in his/her ZIP code using 2010 Census Bureau data.[26] ZIP-level median household income was stratified into equal income quartiles.

Clinical and Birth Hospitalization Visit Characteristics

HepB vaccine receipt during the birth hospitalization, as recommended by ACIP during the study period, was assessed. Preterm birth was defined as birth at <37 weeks gestation[27] and term/post-term birth was defined as birth between 37-43 weeks gestation. Birth hospitalization length of stay was calculated as the number of hours between admission and discharge and categorized as <24 hours, ≥24 and <48 hours, ≥48 and <96 hours and ≥96 hours. Medical service during the birth hospitalization included newborn nursery, intermediate care nursery and neonatal intensive care unit (NICU).

Statistical Analysis

An adverse risk model was derived based on a random sample of two-thirds of the study population. Within the derivation sample, we used a k-fold cross-validation approach with k=5 folds, repeated 5 times, to iteratively create test and validation samples. Among each set of k-1 folds, backward regression was used to identify candidate variables for the adverse risk model. All available variables (described above) were included. No assumptions were made as to the magnitude or direction of the associations with non-completion of the 7-vaccine series; as such, a two-sided alpha=.01 level was used given the large sample size. The predictive capacity of the candidate variables from each regression were tested in the k^{th} fold using area under the ROC curve (AUC), a common metric to evaluate model performance in this setting. This process was repeated 5 times, creating 25 models and their associated error values. A *best* set of predictor variables was defined as those comprising the top five models with the highest AUC. For each variable from this set, the adverse category (that is, the category associated with higher likelihood of not completing the 7-vaccine series) was identified. Weighting was assigned by comparing the average regression coefficients for each retained variable.

For each patient in the entire derivation set, the number of adverse risk factors was calculated, creating an adverse risk score. Risk groups were established based on the observed distribution and average regression coefficients to ascertain a best set of prediction variables.

We recognize that the initial (baseline) HepB vaccination was a component of the combined 7-vaccine series outcome. Thus, we performed a sensitivity analysis in which we removed the 3-dose hepatitis B series from the combined 7-vaccine series outcome and re-evaluated the defined risk model.[28]

All risk models were evaluated using logistic regression. Low risk was used as the reference category for non-completion of the 7-vaccine series in the derivation set and then validated in the independent validation sample of the remaining one-third of patients. Models were first unadjusted and then adjusted to include unretained predictors, as the retained variables were embedded in the risk score. P-values for the risk models were based on two-tailed tests and considered significant at $p<0.05$ unless otherwise noted. Stata version 14.0 (Stata Corp. 2015, Stata Statistical Software, College Station TX) was used for all analyses.

4.4 RESULTS

Cohort Characteristics

A total of 9,080 infants weighing ≥2000 grams received birth hospitalization care at the study hospital between 2008-2013 and were included in the study. Two-thirds of the study population (n=6,053, 66.7%) was randomly assigned to the derivation sample and the remaining one-third (n=3,027, 33.3%) to the validation sample. Sociodemographic, clinical and birth hospitalization characteristics for infants in the derivation and validation samples are shown in **Table 4.1**. A lower proportion of infants in the validation *vs.* derivation sample were born at <37 *vs*. 37-43 weeks gestation (p=0.01). The other characteristics were similar between the two samples. Non-completion of the 7-vaccine series by age 19 months was 46.8% in the derivation sample and 45.7% in the validation sample (p=0.85).

Predictors of 7-Vaccine Series Non-Completion

Based on selection techniques, four candidate predictors (infant sex, income estimate, urban-rural residence, gestational age) were removed from the final trimmed models, and six variables were included in the final prediction model: race/ethnicity, maternal language, insurance status, birth hospitalization length of stay, birth hospitalization medical service, and receipt of the HepB vaccine during the birth hospitalization. The composite AUC for the top five models was 0.67.

Within the derivation sample, the strongest predictor for failing to complete the 7-vaccine series by age 19 months was not receiving the HepB vaccine during the birth hospitalization (adjusted odds ratio [AOR] 2.9; 95% CI: 2.5, 3.3) (data not shown). Other risk factors associated with failure to complete the series included non-Hispanic white race/ethnicity, maternal language of English, public insurance, birth hospitalization stay of < 24 hours, and NICU or progressive care nursery medical service during the birth hospitalization. In contrast, predictors of 7-vaccine series completion by age 19 months were Hispanic, Asian, Non-Hispanic black or multi-racial race/ethnicity, maternal language of Spanish or other language, private insurance, birth hospitalization stay of ≥24 hours, and newborn nursery service during the birth hospitalization. Using the six retained variables in the model, each infant's predictors were summed and a risk score assigned to each participant. HepB birth dose receipt contributed approximately twice the predictive value of 7-vaccine series completion when compared to the average regression coefficients of the other retained variables and, thus, was assigned twice the weight of all other variables in the model. Results of the risk scores, based on the observed distributions, were used to define three risk groups: low (0-2 risk score), medium (3-4 risk score), and high (5-7 risk score). Most infants were in the low or medium-risk groups (58.5% and 32.2%, respectively) with the remainder (9.3%) in the high-risk group (**Table 4.1**). Higher scores indicated an increased risk of failing to complete the 7-vaccine series by age 19 months. For example, a privately insured, Hispanic infant with a Spanish-speaking mother who received a timely HepB birth dose and was discharged from the newborn nursery service ≥ 24 hours would be considered low risk (see scoring scheme in **Table 4.2**). In contrast, a non-Hispanic white infant with an English-speaking mother, a missed HepB birth dose, and a birth hospitalization stay of < 24 hours would be considered at high risk for not completing the 7-vaccine series by age 19 months.

Table 4.3 shows the relationship between non-completion of the 7-vaccine series and risk group. Within the derivation cohort, 38.7% of infants in the low-risk category failed to complete the series by age 19 months compared to 52.7% and 77.1% of those in the medium- and high-risk categories, respectively. Similar results were seen in the validation sample.

Likelihood of 7-Vaccine Series Non-Completion

The adjusted odds of 7-vaccine series non-completion were much higher among infants in the high (odds ratio [OR] 5.6; 95% CI: 4.5, 6.9) and medium (OR 1.9; 95% CI: 1.7, 2.1) *vs.* low-risk category **(Table 4.4)**. The sensitivity analysis, which assessed completion of the 6-vaccine series (i.e., excluding HepB from the 7-vaccine series) showed similar results when comparing infants categorized as high (AOR 4.3; 95% CI: 3.6, 5.3) and medium (AOR 1.6; 95% CI: 1.4, 1.8) *vs.* low-risk.

4.5 DISCUSSION

In this study, a risk prediction model was developed and validated to estimate failure to complete the recommended 7-vaccine series by age 19 months using sociodemographic, clinical, and birth hospitalization information in a large, diverse infant population from Washington State. The risk model was restricted to a small number of explicitly defined variables, which can be reliably measured and easily obtained from the EMR during an infant's birth hospitalization. Considering that the 7-vaccine series is universally recommended, yet nearly 30% of children aged 19-35 months have not received the full series,[2] a risk model that identifies a subset of infants with a five-fold greater odds of non-completion may be highly beneficial for early intervention.

Many studies report that infant and maternal characteristics and parental beliefs impact childhood vaccine uptake.[7,8,29-31] Formal identification of infants at high risk for missing future vaccines could be achieved through use of a risk prediction score based upon key factors. However, prior risk models developed to predict individual-level vaccine uptake have reported difficulty in ascertaining a usable model in their respective study populations. One study of

Latino infants who received primary care services at safety net community health centers found that the developed model could not reliably predict which infants would be under-immunized at age 12 months.[18] Another study, restricted to preschool age ED patients, reported that the information readily available during an ED visit was not sufficient for accurate prediction of under-vaccination.[17]

Importantly, our risk prediction model is the first to include timely receipt of the HepB birth dose, which was the strongest predictor for completion of future vaccines in the current study, and has been shown to be strongly associated with uptake of future childhood vaccinations in previous research.[21,32-36] This first parental vaccine decision may reflect a variety of factors. For example, parental declination could reflect a preference to receive the HepB vaccine in the pediatrician's office, perception of low infant risk for HepB infection, limited understanding of HepB disease severity, vaccine safety concerns in the newborn period, or general vaccine hesitancy.[37-39] Qualitative research suggests that some pediatric practices already informally screen for vaccine hesitancy based on acceptance or declination of the HepB vaccine during the birth hospitalization.[39] This information is then used to alert practice staff of potential vaccine hesitancy, allowing the practices to be prepared for the visit and tailor their vaccine counseling strategies or schedule extra time for the first vaccination visit at age two months.[39]

Formal screening through use of a validated risk prediction tool could more accurately and efficiently identify newborns early in the vaccination process who may benefit from targeted interventions, serving as a critical "red flag" for practices and providers. For example, it could prompt providers to initiate a vaccine conversation with these families before they might otherwise do so. Parents consistently report that vaccine decisions and acceptance are strongly influenced by their child's healthcare provider.[40-42] Research also suggests that there is a spectrum of parental vaccine hesitancy and that communication approaches should be tailored for each group depending on readiness to vaccinate.[43] For instance, strategies such as eliciting the parents' motivations to vaccinate while avoiding excessive persuasion and adversarial debates are suggested for more hesitant parents, while offering decision aids may be helpful for parents who selectively vaccinate.[43] Thus, early knowledge of a newborn's risk for future under-vaccination may also help providers anticipate and tailor their communication approach with individual families.

Limitations

This study has several limitations. First, external validation is considered the most stringent test of a prediction model.[44-46] Our model was internally validated, which may limit generalizability.[47-49] This limitation may be partially compensated for by our use of a large patient sample, an iterative cross-validation technique, and inclusion of a limited number of predictors, all of which may enhance the quality of prediction models.[50] Second, the moderate predictive power of the current model suggests that major determinants of missed vaccinations remain to be studied. Ideally, other important predictors of infant vaccination such as maternal education, parental attitudes about childhood vaccination, and provider communication behaviors[9,31,51,52] would be included. Although these and other factors are important indicators of vaccine uptake, it may be impractical to routinely measure or obtain these data for all patients. It is worth noting that Washington State has one of the highest non-medical exemption rates in the U.S..[53] Thus, our results may not be generalizable to settings with a less vaccine hesitant population. Third, the medical center in our study is a tertiary care referral center that sees a high-risk patient population, and the model does not adjust for disease severity. As such, high-risk infants may be over-represented. This limitation may be mitigated by statistically adjusting for birth hospitalization length of stay and medical service and by our exclusion of infants born weighing <2000 grams. In addition, although HepB vaccine receipt—a key predictor in the risk model—is not recommended for medically unstable infants,[54] nearly all infants would have been eligible for HepB vaccine before their birth hospitalization discharge. Fourth, infants born at <2000 grams were excluded due to distinct ACIP recommendations for HepB vaccination of these infants.[54] Thus, the model is not applicable to low birth weight infants. However, fewer than 3% of U.S. infants are born weighing <2000 grams,[55] potentially minimizing the impact of this limitation. Finally, vaccine data may have been misclassified or misreported within the data collection systems. Previous work suggests that WAIIS is a nearly-complete reporting system with a high degree of internal validity,[56,57] and the Centers for Disease Control and Prevention estimates that at least 95% of Washington children aged <6 years were recorded in WAIIS during the study period.[57]

4.6 CONCLUSION

This study demonstrates that a prediction model using infant sociodemographic, clinical and birth hospitalization data consistently identifies newborns at risk for under-vaccination by 19 months of age. Using a prediction tool for early identification of infants at high risk for missing childhood vaccination could be useful to providers, prompting them to initiate targeted interventions, including early vaccine communication with families. Risk prediction tools, such as the Kaiser sepsis calculator,[58] and BiliTool, designed to assess risk for newborn hyperbilirubinemia,[59,60] have been successfully implemented in newborn settings. Future studies are needed to demonstrate how to best utilize this or a similar childhood vaccination prediction tool in a clinical practice setting. Enhanced methods of identifying and counseling parents of high-risk infants may be particularly timely given growing levels of vaccine hesitancy and resulting vaccine preventable disease outbreaks.

Table 4.1: Demographic, clinical and birth hospitalization characteristics of patients in the derivation and validation cohorts, 2008-2013

Characteristic[a]	Derivation cohort N=6,053 (%)	Validation cohort N=3,027 (%)	p-value
Infant sex			0.85
Male	3,095 (51.1)	1,554 (51.3)	
Female	2,958 (48.9)	1,474 (48.7)	
Race/ethnicity			0.95
Hispanic	767 (14.4)	403 (15.0)	
Non-Hispanic white	2,604 (48.8)	1,297 (48.4)	
Non-Hispanic black	1,165 (21.8)	594 (22.2)	
Asian	723 (13.6)	358 (13.4)	
Multiracial/other	75 (1.4)	28 (1.0)	
Maternal language			0.42
English	4,307 (75.9)	2,179 (76.3)	
Spanish	557 (9.8)	296 (10.4)	
Other	809 (14.3)	381 (13.3)	
Insurance status			0.37
Private	2,477 (43.8)	1,270 (44.8)	
Public	3,175 (56.2)	1,562 (55.2)	
Rural-urban residence			0.89
Rural	157 (2.6)	80 (2.6)	
Urban	5,894 (97.4)	2,946 (97.4)	
Estimated household income[b]			0.16
$20,135 – 42,799	262 (4.4)	103 (3.4)	
$42,800 – 50,844	734 (12.2)	375 (12.5)	
$50,845 – 62,239	2,392 (39.7)	1,182 (39.3)	
$62,240 – 174,729	2,630 (43.7)	1,350 (44.9)	
Gestational age, weeks			0.01
<37	692 (11.4)	292 (9.7)	
37-43	5,359 (88.6)	2,734 (90.4)	
Birth hospitalization length of stay, hours			0.81
<24	546 (9.0)	274 (9.0)	
≥24 to <48	2,635 (43.5)	1,321 (43.6)	
≥48 to <96	2,192 (36.2)	1,104 (36.5)	
≥96	680 (11.2)	328 (10.8)	
Medical service			0.07
Newborn nursery	4,802 (79.3)	2,464 (81.4)	
Intermediate care	919 (15.2)	411 (13.6)	
Neonatal ICU	332 (5.5)	152 (5.0)	
Received HepB vaccine[c]	4,584 (75.7)	2,274 (75.1)	0.53
Risk category[d]			0.82
Low	3,543 (58.5)	1,792 (59.2)	
Medium	1,948 (32.2)	955 (31.6)	
High	562 (9.3)	280 (9.3)	

a. All proportions shown in table are based on known data in total study sample (n=9,080). Number and percentage of total 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%); Income estimate = 52 (0.6%); Gestational age = 3 (0.03%).

b. Based on 2010 U.S. Census Bureau ZIP-code level median household income.
c. Received the HepB vaccine before birth hospitalization discharge.
d. Low risk category (0-2 risk score), medium (3-4 risk score), high (5-7 risk score)

Table 4.2: Risk calculator for failure to complete the 7-vaccine series[a] by age 19 months

Infant Characteristic		Points
HepB vaccination[b]	No	2
	Yes	0
Race/ethnicity	Non-Hispanic (NH) white	1
	Hispanic, Asian, NH black, multi-racial	0
Maternal language	English	1
	Spanish or other language	0
Insurance type	Public	1
	Private	0
Hospital service[b]	NICU	1
	Newborn/intermediate care	0
Length of stay[b]	< 24 hours	1
	≥ 24 hours	0

a. 4 doses of diphtheria-tetanus-[whole-cell or acellular] pertussis (DTP/DTaP), 3 poliovirus, 1 measles-mumps-rubella, 3 Haemophilus influenza Type b, 3 HepB, 1 varicella, 4 pneumococcal conjugate vaccines
b. During birth hospitalization

Table 4.3: Proportion of derivation and validation cohorts who did not complete 7-vaccine series by age 19 months by risk category

	Derivation cohort (N=6,053)		Validation cohort (N=3,027)	
Risk category[a]				
	n	**%**	**n**	**%**
Low	1,371/3,543	38.7	664/1,792	37.1
Medium	1,027/1,948	52.7	504/955	52.8
High	433/562	77.1	214/280	76.4

a. Low (0-2 risk score), medium (3-4 risk score), and high (5-7 risk score)

Table 4.4: Odds ratios (OR) and 95% confidence intervals (CI) of 7-vaccine series non-completion by age 19 months in the derivation and validation samples

	Derivation sample (n=6,053) OR (95% CI)		Validation sample (n=3,027) OR (95% CI)	
Risk Level[a]				
	Unadjusted	**Adjusted**	**Unadjusted**	**Adjusted**
Low	Ref	Ref	Ref	Ref
Medium	1.8 (1.6, 2.0)	1.9 (1.7, 2.1)	1.9 (1.6, 2.2)	1.9 (1.6, 2.2)
High	5.3 (4.3, 6.5)	5.6 (4.5, 6.9)	5.5 (4.1, 7.4)	5.5 (4.1, 7.5)

a. Low (0-2 risk score), medium (3-4 risk score), and high (5-7 risk score).

4.7 NOTES FOR CHAPTER 4

1. Orenstein WA, Ahmed R. Simply put: Vaccination saves lives. *Proc Natl Acad Sci.* 2017;114:4031-3.

2. Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination Coverage Among Children Aged 19-35 Months - United States, 2017. *Morb Mortal Wkly Rep.* 2018;67:1123-8.

3. Olive JK, Hotez PJ, Damania A, Nolan MS. The state of the antivaccine movement in the United States: A focused examination of nonmedical exemptions in states and counties. *PLoS Med.* 2018;15:e1002578.

4. Omer SB, Richards JL, Ward M, Bednarczyk RA. Vaccination policies and rates of exemption from immunization, 2005-2011. *N Engl J Med.* 2012;367:1170-1.

5. Centers for Disease Control and Prevention. Measles Cases in 2019. Available at: https://wwwcdcgov/measles/cases-outbreakshtml Accessed March 2019.

6. Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association Between Vaccine Refusal and Vaccine-Preventable Diseases in the United States: A review of measles and pertussis. *JAMA.* 2016;315:1149-58.

7. Smith PJ, Chu SY, Barker LE. Children who have received no vaccines: who are they and where do they live? *Pediatrics.* 2004;114:187-95.

8. Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. *Public Health Rep.* 2011;126 Suppl 2:135-46.

9. Dube E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccin Immunother.* 2013;9:1763-73.

10. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997;336:243-50.

11. Nigrovic LE, Kuppermann N, Macias CG, et al. Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *JAMA.* 2007;297:52-60.

12. Cohn KA, Thompson AD, Shah SS, et al. Validation of a clinical prediction rule to distinguish Lyme meningitis from aseptic meningitis. *Pediatrics.* 2012;129:e46-53.

13. Boyle TP, Kimia AA, Nigrovic LE. Validating a clinical prediction rule for ventricular shunt malfunction. *Pediatr Emerg Care*. 2018;34(11):751-756.

14. Wang L, Porter B, Maynard C, et al. Predicting risk of hospitalization or death among patients with heart failure in the veterans health administration. *Am J Cardiol.* 2012;110:1342-9.

15. Sultan AA, West J, Grainge MJ, et al. Development and validation of risk prediction model for venous thromboembolism in postpartum women: multinational cohort study. *BMJ.* 2016;355:i6253.

16. Kessler RC, Hwang I, Hoffmire CA, et al. Developing a practical suicide risk prediction model for targeting high-risk patients in the Veterans health Administration. *Int J Methods Psychiatr Res.* 2017;26(3); doi: 10.1002/mpr.1575

17. Humiston SG, Rodewald LE, Szilagyi PG, et al. Decision rules for predicting vaccination status of preschool-age emergency department patients. *J Pediatr.* 1993;123:887-92.

18. Hambidge SJ, Phibbs SL, Davidson AJ, et al. Individually significant risk factors do not provide an accurate clinical prediction rule for infant underimmunization in one disadvantaged urban area. *Ambul Pediatr* 2006;6:165-72.

19. Centers for Disease Control and Prevention. Recommended Immunization Schedule for Persons Aged 0 Through 18 Years. Available at: http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Accessed June 2019.

20. Oster NV, Williams E, Unger JM, Newcomb PA, Jacobson EN, deHart MP, Englund JA, Hofstetter AM Sociodemographic, Clinical and Birth Hospitalization Characteristics and Infant Hepatitis B Vaccination in Washington State Vaccine, *Vaccine* 2019;37(38):5738-5744.

21. Oster NV, Williams E, Unger JM, Newcomb PA, Jacobson EN, deHart MP, Englund JA, Hofstetter AM. Hepatitis B Birth Dose: First Shot at Timely Early Childhood Vaccination. In press, *Am J Prev Med*.

22. Murthy N, Rodgers L, Pabst L, Fiebelkorn AP, Ng T. Progress in Childhood Vaccination Data in Immunization Information Systems - United States, 2013-2016. *Morb Mortal Wkly Rep* 2017;66:1178-81.

23. Luman ET, Barker LE, McCauley MM, Drews-Botsch C. Timeliness of childhood immunizations: a state-specific analysis. *Am J Public Health*, 2005;95:1367-74.

24. United State Census Bureau Department of Commerce. Overview of race and Hispanic origin, 2010. Available at: https://www.census.gov/prod/cen2010/briefs/. Accessed June 2019.

25. Rural Health Research Center. Rural Urban Commuting Areas. Available at: http://depts.washington.edu/uwruca/ruca-approx.php. Accessed April 2019.

26. University of Michigan Population Studies Center. Median Household Income 2006-2010. Available at: https://www.psc.isr.umich.edu/dis/census/Features/tract2zip/index.html. Accessed August, 2019.

27. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final Data for 2017. *Natl Vital Stat Rep.* 2018;67:1-50.

28. Jiles RB, Daniels D, Yusuf HR, McCauley MM, Chu SY. Undervaccination with hepatitis B vaccine: missed opportunities or choice? *Am J Prev Med.* 2001;20:75-83.

29. Klevens RM, Luman ET. U.S. children living in and near poverty: risk of vaccine-preventable diseases. *Am J Prev Med.* 2001;20:41-6.

30. Yang YT, Delamater PL, Leslie TF, Mello MM. Sociodemographic Predictors of Vaccination Exemptions on the Basis of Personal Belief in California. *Am J Public Health.* 2016;106:172-7.

31. Sobo EJ. Social Cultivation of Vaccine Refusal and Delay among Waldorf (Steiner) School Parents. *Med Anthropol Q.* 2015;29:381-99.

32. Lauderdale DS, Oram RJ, Goldstein KP, Daum RS. Hepatitis B vaccination among children in inner-city public housing, 1991-1997. *JAMA.* 1999;282:1725-30.

33. Yusuf HR, Daniels D, Smith P, Coronado V, Rodewald L. Association between administration of hepatitis B vaccine at birth and completion of the hepatitis B and 4:3:1:3 vaccine series. *JAMA.* 2000;284:978-83.

34. Wagner Al, Eccleston AM, Potter RC, Swanson RG, Boulton ML. Vaccination timeliness at age 24 months in Michigan children born 2006-2010. *Am J Prev Med.* 2018;54:96-102.

35. Wilson P, Taylor G, Knowles J, et al. Missed Hepatitis B Birth Dose Vaccine Is a Risk Factor for Incomplete Vaccination at 18 and 24 Months. *J Infect.* 2019;78(2):134-139.

36. Mennito SH, Darden PM. Impact of practice policies on pediatric immunization rates. *J Pediatr* 2010;156:618-22.

37. Burton T, Saini S, Maldonado L, Carver JD. Parental Refusal for Treatments, Procedures, and Vaccines in the Newborn Nursery. *Adv Pediatr.* 2018;65:89-104.

38. New York State Department of Health. Hepatitis B Prevention Program. Available at: https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_b/perinatal/docs/program_manual.pdf. Accessed May 2018. 2011.

39. Mohanty S, Carroll-Scott A, Wheeler M, et al. Vaccine Hesitancy in Pediatric Primary Care Practices. *Qual Health Res.* 2018;28(13):2071-2080.

40. Wheeler M, Buttenheim AM. Parental vaccine concerns, information source, and choice of alternative immunization schedules. *Hum Vacc Immunother*. 2013;9:1782-9.

41. Kennedy A, Basket M, Sheedy K. Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey. *Pediatrics*. 2011;127 Suppl 1:S92-9.

42. Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Sources and perceived credibility of vaccine-safety information for parents. *Pediatrics*. 2011;127 Suppl 1:S107-12.

43. Leask J, Kinnersley P, Jackson C, Cheater F, Bedford H, Rowles G. Communicating with parents about vaccination: a framework for health professionals. *BMC Pediatr*. 2012;12:154.

44. Laupacis A, Sekar N, Stiell IG. Clinical prediction rules. A review and suggested modifications of methodological standards. *JAMA*. 1997;277:488-94.

45. Bleeker SE, Moll HA, Steyerberg EW, et al. External validation is necessary in prediction research: a clinical example. *J Clin Epidemiol.* 2003;56:826-32.

46. Moons KG, Altman DG, Reitsma JB, Collins GS, Transparent reporting of a multivariate prediction model for individual prognosis or development. New guideline for the reporting of studies developing, validating, or updating a multivariable clinical prediction model: The TRIPOD Statement. *Adv Anat Pathol.* 2015;22:303-5.

47. Justice AC, Covinsky KE, Berlin JA. Assessing the generalizability of prognostic information. *Ann Intern Med.* 1999;130:515-24.

48. Van Houwelingen JC, Le Cessie S. Predictive value of statistical models. *Stat Med.* 1990;9:1303-25.

49. Harrell FE, Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med.* 1996;15:361-87.

50. Steyerberg EW, Eijkemans MJ, Habbema JD. Stepwise selection in small data sets: a simulation study of bias in logistic regression analysis. *J Clin Epidemiol.* 1999;52:935-42.

51. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider-parent vaccine discussions at health supervision visits. *Pediatrics.* 2013;132:1037-46.

52. Opel DJ, Mangione-Smith R, Robinson JD, et al. The influence of provider communication behaviors on parental vaccine acceptance and visit experience. *Am J Public Health.* 2015;105:1998-2004.

53. Seither R, Calhoun K, Street EJ, et al. Vaccination coverage for selected vaccines, exemption rates, and provisional enrollment among children in kindergarten - United States, 2016-17 School Year. *Morb Mortal Wkly Rep.* 2017;66:1073-80.

54. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep.* 2018;67:1-31.

55. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final data for 2016. *Natl Vital Stat Rep*. 2018;67:1-55.

56. Jackson ML, Henrikson NB, Grossman DC. Evaluating Washington State's immunization information system as a research tool. *Acad Pediatr.* 2014;14:71-6.

57. Centers for Disease Control and Prevention. Percentage of children aged < 6 years participating in an immunization information system -- United States, five cities and D.C., 2013. Available at: https://www.cdc.gov/vaccines/programs/iis/annual-report-iisar/downloads/2013-data-child-map.pdf. Accessed August 2019.

58. Kuzniewicz MW, Walsh EM, Li S, Fischer A, Escobar GJ. Development and implementation of an early-onset sepsis calculator to guide antibiotic management in late preterm and term neonates. *Jt Comm J Qual Patient Saf*. 2016;42:232-9.

59. Chang PW, Kuzniewicz MW, McCulloch CE, Newman TB. A clinical prediction rule for rebound hyperbilirubinemia following inpatient phototherapy. *Pediatrics*. 2017;139(3). doi: 10.1542/peds.2016-2896.

60. BiliTool. Available at: bilitool.org. Accessed July 2019.

Chapter 5. CONCLUSION

5.1 Summary of Findings

The overarching goal of this research was to identify subgroups of newborns at greatest risk for low childhood vaccination coverage who might benefit from early and targeted vaccination interventions. We examined whether timely receipt of the first HepB vaccine dose varied by select infant and maternal characteristics (Aim 1) and, in turn, whether HepB vaccination at birth was associated with completing all recommended childhood vaccines (see **Table 5.1**) by age 19 months (Aim 2). Based on our findings, we developed and validated a risk prediction model, which consistently identified newborns at risk for low vaccination coverage by age 19 months (Aim 3). These three papers are presented in Chapters 2-4.

Taken together, the results suggest that the risk for low vaccination coverage is not evenly distributed in the population and that specific sociodemographic, clinical and birth hospitalization characteristics may indeed be associated with, and potentially predict, individual vaccine uptake. Our findings point to timely receipt of the Hep B birth dose as the strongest predictor of 7-vaccine series completion by age 19 months, in conjunction with select sociodemographic characteristics, highlighting the birth hospitalization as a key potential intervention lever. These studies generate new questions and avenues for future investigation.

5.1.1 Variation in HepB Birth Dose by Infant and Maternal Characteristics

Chapter 2 explored the infant and maternal characteristics associated with receipt of the first HepB vaccination – the "birth dose" – which (during the study period) was recommended during the birth hospitalization. We showed that populations that are typically underserved (e.g., publicly insured, racial/ethnic minorities) had a higher likelihood of receiving HepB vaccine during the birth hospitalization. Interestingly, infants who were the least likely to receive the HepB birth dose (e.g., non-Hispanic white, with an English-speaking mother) fall into the demographic group with the lowest risk for maternal hepatitis B virus (HBV) infection.[1] We hypothesized that one reason for low HepB vaccination among this demographic subset may be that parents are hesitant to vaccinate their newborn against a disease that they consider very low risk for mother-to-baby transmission and that, similarly, providers may be reluctant to strongly recommend HepB vaccination to these patients due to the low perceived risk. The socio-demographics of this subset is consistent with vaccine hesitant populations,[2-4] thus, these parents may also have vaccine safety related concerns. Further study is needed to ascertain the impact, if any, that perceptions of HBV infection risk may have on parental decision-making and provider communication.

A better understanding of the underlying mechanisms that drive variation in HepB birth dose uptake is needed in order to design optimal interventions aimed at improving timely infant HepB vaccination. Potential interventions may include provider alerts in the electronic medical record (EMR), hospital standing orders for the HepB birth dose and use of presumptive, rather than participatory, provider recommendations.[5,6]

5.1.2 Variation in 7-Vaccine Series Completion by Timely Receipt of the HepB Birth Dose

In Chapter 3, we evaluated whether HepB vaccine receipt during the birth hospitalization was associated with completing the 7-vaccine series by 19 months. We found that newborns who received HepB vaccine during their birth hospitalization were three times more likely to receive all recommended vaccines by 19 months independent of other factors associated with vaccine receipt. The results of our studies suggest that HepB vaccine receipt has the potential to serve as a “sentinel” vaccine to identify vaccine-hesitant parents early in the vaccination process. Screening systems could be studied further and potentially developed into practical methods for providers and practices to increase general vaccine uptake. The development of a risk prediction model (Aim 3, below) may be the first step in this direction.

Finally, it is not apparent from the current results whether receipt of the HepB birth dose itself influences future vaccination coverage or if acceptance of the HepB birth dose simply reflects parental decisions about all childhood vaccinations. It is reasonable to assume that receipt of one vaccine may make it easier to accept the next. Previous studies suggest that completing an activity for the first time (e.g., vaccination) increases its acceptance and establishes the new activity as the default option,[7-9] and that maternal vaccine hesitancy significantly decreases between a child’s birth and age 24 months, potentially as mothers’ confidence in vaccine safety and efficacy grows in tandem with their vaccine experiences.[10] Given suboptimal vaccination rates and the fact that vaccination decisions can occur as a result of status quo bias, in which people are hesitant to deviate from their current baseline or a previously made decision[7,11] broad campaigns aimed at promoting a culture of vaccine acceptance are indicated.

5.1.3 Risk Prediction Model for Future Childhood Vaccines

The risk prediction model, described in Chapter 4, used newborn sociodemographic, clinical and birth hospitalization data to predict individual vaccination coverage by age 19 months. Our prediction model provides a basis for evaluating an individual newborn’s likelihood of completing recommended childhood vaccines. The risk prediction model was restricted to a small number (n=6) of explicitly defined variables, which are readily available in the EMR during an infant's birth hospitalization.

We envision that a risk prediction score could be calculated during the birth hospitalization, then summarized in the hospital discharge paperwork, which is typically forwarded to the primary care provider. For example, the hospital discharge paperwork would state that the family declined HepB during the birth hospitalization and, based on other specified sociodemographic and clinical risk factors, the infant's risk of future vaccine delay or refusal is "X" as calculated by the prediction score. Given that the risk score does not require extensive calculations, it could be summed using a simple scoring scheme, or be further developed into a user-friendly online calculator or incorporated into clinical decision support tools in the EMR at the point of care (i.e., during the birth hospitalization). Future research is needed to determine how to best implement, disseminate and evaluate the tool in clinical practice.

Future research is also needed to assess whether incorporating other important predictors of vaccination such as maternal education, parental attitudes about childhood vaccination and provider communication behaviors[2-6] would improve the current prediction model. The model's generalizability would further be enhanced by external validation in an independent population. It is possible that other populations would produce different results, and whether this is indeed the case should be evaluated in future work.

In conclusion, this dissertation provides an important initial study into the association between select infant and maternal characteristics, receipt of the HepB birth dose and completion of future recommended childhood vaccinations. Our findings consistently identified timely receipt of the Hep B birth dose as the strongest predictor of 7-vaccine series completion by age 19 months. Therefore, population-wide approaches to increase receipt of this critical first vaccination, with an emphasis on subgroups that may be particularly vulnerable to vaccine hesitancy, may increase childhood vaccination coverage. Given the important role of parental attitudes about vaccinations, a clearer understanding of the underlying mechanisms which influence parental vaccine decision-making is needed in order to design and implement the most effective interventions.

Table 5.1. Recommended Immunization Schedule for Children Through 23 Months of Age—United States, 2019[a]

Vaccine	Birth	1 mo	2 mos	4 mos	6 mos	9 mos	12 mos	15 mos	18 mos	19-23 mos
Hepatitis B (HepB)	1st dose	2nd dose			← 3rd dose →					
Rotavirus (RV) RV1 (2-dose series); RV5 (3-dose series)			1st dose	2nd dose	See Notes					
Diphtheria, tetanus, & acellular pertussis (DTaP: <7 yrs)			1st dose	2nd dose	3rd dose			← 4th dose →		
Haemophilus influenzae type b (Hib)			1st dose	2nd dose	See Notes		← 3rd or 4th dose, See Notes →			
Pneumococcal conjugate (PCV13)			1st dose	2nd dose	3rd dose		← 4th dose →			
Inactivated poliovirus (IPV: <18 yrs)			1st dose	2nd dose	← 3rd dose →					
Influenza (IIV)					Annual vaccination 1 or 2 doses					
or										
Influenza (LAIV)										
Measles, mumps, rubella (MMR)					See Notes		← 1st dose →			
Varicella (VAR)							← 1st dose →			
Hepatitis A (HepA)					See Notes		2-dose series, See Notes			
Meningococcal (MenACWY-D ≥9 mos; MenACWY-CRM ≥2 mos)			See Notes							
Tetanus, diphtheria, & acellular pertussis (Tdap: ≥7 yrs)										
Human papillomavirus (HPV)										
Meningococcal B										
Pneumococcal polysaccharide (PPSV23)										

Range of recommended ages for all children; Range of recommended ages for catch-up immunization; Range of recommended ages for certain high-risk groups; Range of recommended ages for non-high-risk groups that may receive vaccine, subject to individual clinical decision-making; No recommendation

a. For full schedule through 18 years of life and current notations see https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf

5.2 NOTES FOR CHAPTER 5

1. Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. Pediatrics 2015;135:e1141-7.

2. Sobo EJ. Social Cultivation of Vaccine Refusal and Delay among Waldorf (Steiner) School Parents. *Med Anthropol Q.* 2015;29:381-99.

3. Dube E, Gagnon D, MacDonald N, Bocquier A, Peretti-Watel P, Verger P. Underlying factors impacting vaccine hesitancy in high income countries: A review of qualitative studies. *Expert Rev Vaccines.* 2018;17:989-1004.

4. Dube E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccin Immunother.* 2013;9:1763-73.

5. Opel DJ, Mangione-Smith R, Robinson JD, et al. The Influence of Provider Communication Behaviors on Parental Vaccine Acceptance and Visit Experience. *Am J Public Health.* 2015;105:1998-2004.

6. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider–parent vaccine discussions at health supervision visits. *Pediatrics*. 2013;132(6):1037–1346.

7. Suri G, Sheppes G, Schwartz C, Gross JJ. Patient inertia and the status quo bias: when an inferior option is preferred. *Psychol Sci*. 2013;24(9):1763–1769.

8. Gal D. A psychological law of inertia and the illusion of loss aversion. *Judgm Decis Mak*. 2006;1(1):23–32.

9. Halpern SD, Ubel PA, Asch DA. Harnessing the power of default options to improve health care. *N Engl J Med*. 2007;357:1340–1344.

10. Henrikson NB, Anderson ML, Opel DJ, Dunn J, Marcuse EK, Grossman DC. Longitudinal trends in vaccine hesitancy in a cohort of mothers surveyed in Washington State, 2013–2015. *Public Health Rep*. 2017;132(4):451–454.

11. Ritov I BJ. Status-quo and omission bias. *J Risk and Uncertainty*. 1992;5(1):49–61.

BIBLIOGRAPHY

Adorador A, McNulty R, Hart D, Fitzpatrick JJ. Perceived barriers to immunizations as identified by Latino mothers. *J Am Acad Nurse Pract*. 2011;23(9):501–508. https://doi.org/10.1111/j.1745-7599.2011.00632.x.

Allen A. *Vaccine: The controversial story of medicine's greatest lifesaver*. New York, NY: W.W. Norton & company; 2007.

Allred NJ, Wooten KG, Kong Y. The association of health insurance and continuous primary care in the medical home on vaccination coverage for 19- to 35-month-old children. *Pediatrics*. 2007;119(Suppl 1):S4–S11.

American Academy of Pediatrics Committee on Infectious Diseases. Elimination of perinatal hepatitis B: Providing the first vaccine dose within 24 hours of birth. *Pediatrics.* 2017;140(3).

Anderson TA, Wexler DL. States report hundreds of medical errors in perinatal Hepatitis B prevention: Avoid tragic mistakes—vaccinate newborns against HBV in the hospital. Immunization Action Coalition, 2003. http://immunize.org/catg.d/p2062.pdf. Accessed July 2018.

Atkinson WL, Orenstein WA, Krugman S. The resurgence of measles in the United States, 1989-1990. *Annu Rev Med.* 1992;43:451-63.

Atwell JE, Van Otterloo J, Zipprich J, et al. Nonmedical vaccine exemptions and pertussis in California, 2010. *Pediatrics.* 2013;132:624-30.

Beasley RP, Hwang LY, Lee GC, et al. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet.* 1983;2(8359):1099-1102.

Berdahl TA, Friedman BS, McCormick MC, Simpson L. Annual report on health care for children and youth in the United States: Trends in racial/ethnic, income, and insurance disparities over time, 2002-2009. *Acad Pediatr.* 2013;13(3):191-203.

Bigham M, Remple VP, Pielak K, McIntyre C, White R, Wu W. Uptake and behavioural and attitudinal determinants of immunization in an expanded routine infant hepatitis B vaccination program in British Columbia. *Can J Public Health.* 2006;97:90-5.

Bleeker SE, Moll HA, Steyerberg EW, et al. External validation is necessary in prediction research: a clinical example. *J Clin Epidemiol.* 2003;56:826-32.

Block SL. Playing newborn intracranial roulette: Parental refusal of vitamin K injection. *Pediatr Ann*. 2014;43(2):53–59. https://doi.org/10.3928/00904481-20131223-04.

Bobo JK, Gale JL, Thapa PB, Wassilak SG. Risk factors for delayed immunization in a random sample of 1163 children from Oregon and Washington. *Pediatrics.* 1993;91:308-14.

Boyle TP, Kimia AA, Nigrovic LE. Validating a clinical prediction rule for ventricular shunt malfunction. *Pediatr Emerg Care*. 2018;34(11):751-756.

Burton T, Saini S, Maldonado L, Carver JD. Parental refusal for treatments, procedures, and vaccines in the newborn nursery. *Adv Pediatr*. 2018;65(1):89–104. https://doi.org/10.1016/j.yapd.2018.04.006.

Centers for Disease Control and Prevention. 2017–18 school year vaccination exemption reports. Available at: www.cdc.gov/vaccines/imz-managers/coverage/schoolvaxview/data-reports/exemptions-reports/2017-18.html. Accessed March 2019.

Centers for Disease Control and Prevention. Immunization schedules for infants and children. Available at: https://wwwcdcgov/vaccines/schedules/easy-to-read/childhtml. Accessed May 2019.

Centers for Disease Control and Prevention. Measles cases in 2019. Available at: https://wwwcdcgov/measles/cases-outbreakshtml Accessed March 2019 2019.

Centers for Disease Control and Prevention. Percentage of children aged < 6 years participating in an immunization information system -- United States, five cities and D.C., 2013. Available at: https://www.cdc.gov/vaccines/programs/iis/annual-report-iisar/downloads/2013-data-child-map.pdf. Accessed February 2018.

Centers for Disease Control and Prevention. Polio elimination in the United States. Available at: https://www.cdc.gov/polio/us/index.html. Accessed January 2018.

Centers for Disease Control and Prevention. Polio for Health Care Professionals. Available at: https://wwwcdcgov/polio/us/hcphtml Accessed April 2019.

Centers for Disease Control and Prevention. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 2018;67(1).

Centers for Disease Control and Prevention. Recommended child and adolescent immunization schedule for ages 18 or younger, United States, 2019. www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Accessed January 2019.

Centers for Disease Control and Prevention. Report shows 20-year U.S. immunization program spares millions of children from diseases. Available at: http://www.cdc.gov/media/releases/2014/p0424-immunization-program.html. Accessed October 2016.

Centers for Disease Control and Prevention. Ten great public health achievements--United States, 1900-1999. *MMWR Morb Mortal Wkly Rep.* 1999;48:243-8.
Centers for Disease Control and Prevention. Vaccination coverage among children in kindergarten - United States, 2012-13 school year. *MMWR Morb Mortal Wkly Rep.* 2013;62(30):607-612.

Centers for Disease Control and Prevention. Viral Hepatitis surveillance – United States, 2010. Available at: https://www.cdc.gov/hepatitis/statistics/2010surveillance/commentary.htm Accessed November 2017.

Centers for Disease Control and Prevention. What would happen if we stopped vaccinations? Available at: http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm. Accessed November 18, 2015.

Chang PW, Kuzniewicz MW, McCulloch CE, Newman TB. A clinical prediction rule for rebound hyperbilirubinemia following inpatient phototherapy. *Pediatrics.* 2017;139.

Cohn KA, Thompson AD, Shah SS, et al. Validation of a clinical prediction rule to distinguish Lyme meningitis from aseptic meningitis. *Pediatrics.* 2012;129:e46-53.

Daniels D, Jiles RB, Klevens RM, Herrera GA. Undervaccinated African-American preschoolers: a case of missed opportunities. *Am J Prev Med.* 2001;20:61-8.

Department of Health and Human Services. Healthy People 2020: Understanding and improving health. Available at: www.healthypeople.gob/document/html/uih/uih_4.htm#immuniz. Accessed June 2016.

Dressler WW, Oths KS, Gravlee CC. Race and ethnicity in public health research: Models to explain health disparities. *Annu Rev Anthropol.* 2005;34:231-52.

Dube E, Gagnon D, MacDonald N, Bocquier A, Peretti-Watel P, Verger P. Underlying factors impacting vaccine hesitancy in high income countries: A review of qualitative studies. *Expert Rev Vac*. 2018;17(11):989–1004. https://doi.org/10.1080/14760584.2018.1541406.

Dube E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. *Hum Vaccin Immunother.* 2013;9:1763-73.

Dube E, Vivion M, MacDonald NE. Vaccine hesitancy, vaccine refusal and the anti-vaccine movement: influence, impact and implications. *Expert Rev Vaccines.* 2015;14:99-117.

Economic Policy Institute. The need for paid sick days. Available at: https://wwwepiorg/publication/the_need_for_paid_sick_days/ Accessed April 2019

Favin M, Steinglass R, Fields R, Banerjee K, Sawhney M. Why children are not vaccinated: a review of the grey literature. *Int Health.* 2012;4:229-38.

Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997;336:243-50.

Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Parental vaccine safety concerns in 2009*. Pediatrics.* 2010;125:654-9.

Freed GL, Clark SJ, Butchart AT, Singer DC, Davis MM. Sources and perceived credibility of vaccine-safety information for parents. *Pediatrics.* 2011;127 Suppl 1:S107-12.

Gal D. A psychological law of inertia and the illusion of loss aversion. *Judgm Decis Mak*. 2006;1(1):23–32. https://doi.org/10.1037/e683162011-083.

Glanz JM, Wagner NM, Narwaney KJ, et al. Web-based social media intervention to increase vaccine acceptance: a randomized controlled trial. *Pediatrics*. 2017;140(6): https://doi.org/10.1542/peds.2017-1117.

Gowda C, Dempsey AF. The rise (and fall?) of parental vaccine hesitancy. *Hum Vaccin Immunother.* 2013;9:1755-62.

Groce NE, Banks LM, Stein MA. Surviving polio in a post-polio world*. Soc Sci Med.* 2014;107:171-8.

Gust DA, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. *Pediatrics.* 2008;122:718-25.

Gust DA, Woodruff R, Kennedy A, Brown C, Sheedy K, Hibbs B. Parental perceptions surrounding risks and benefits of immunization. *Semin Pediatr Infect Dis*. 2003;14(3):207–212. https://doi.org/10.1016/S1045-1870(03)00035-9.

Halpern SD, Ubel PA, Asch DA. Harnessing the power of default options to improve health care. *N Engl J Med*. 2007;357:1340–1344. https://doi.org/10.1056/NEJMsb071595.

Hambidge SJ, Phibbs SL, Davidson AJ, et al. Individually significant risk factors do not provide an accurate clinical prediction rule for infant underimmunization in one disadvantaged urban area. *Ambul Pediatr.* 2006;6:165-72.

Hamrick HJ, Gable EK, Freeman EH, et al. Reasons for refusal of newborn vitamin K prophylaxis: implications for management and education. *Hosp Pediatr*. 2016;6(1):15–21. https://doi.org/10.1542/hpeds.2015-0095.

Harmsen IA, Mollema L, Ruiter RA, Paulussen TG, de Melker HE, Kok G. Why parents refuse childhood vaccination: A qualitative study using online focus groups. *BMC Public Health.* 2013;13:1183.

Harrell FE, Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Stat Med.* 1996;15:361-87.

Hart LG, Larson EH, Lishner DM. Rural definitions for health policy and research. *Am J Public Health.* 2005;95:1149-55.

Henrikson NB, Anderson ML, Opel DJ, Dunn J, Marcuse EK, Grossman DC. Longitudinal trends in vaccine hesitancy in a cohort of mothers surveyed in Washington State, 2013–2015. *Public Health Rep*. 2017;132(4):451–454. https://doi.org/10.1177/0033354917711175.

Herrera GA, Zhao Z, Klevens RM. Variation in vaccination coverage among children of Hispanic ancestry. *Am J Prev Med.* 2001;20:69-74.

Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Dietz V. Vaccination coverage among children aged 19-35 months—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2016;65(39):1065–1071. https://doi.org/10.15585/mmwr.mm6539a4.

Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19-35 months - United States, 2016. *MMWR Morb Mortal Wkly Rep.* 2017;66(43):1171-1177.

Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months—United States, 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(40):1123–1128. https://doi.org/10.15585/mmwr.mm6740a4.

Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kolasa M. National, State, and Selected Local Area Vaccination Coverage Among Children Aged 19-35 Months - United States, 2014. *MMWR Morb Mortal Wkly Rep.* 2015;64:889-96.

Hinman AR, Orenstein WA, Schuchat A, Vaccine-preventable diseases, immunizations, and MMWR--1961-2011. *MMWR Suppl.* 2011;60:49-57.

Hofstetter AM, Lappetito L, Stockwell MS, Rosenthal SL. Human papillomavirus vaccination of adolescents with chronic medical conditions: a national survey of pediatric subspecialists. *J Pediatr Adolesc Gynecol*. 2017;30(1):88–95. https://doi.org/10.1016/j.jpag.2016.08.005.

Humiston SG, Rodewald LE, Szilagyi PG, et al. Decision rules for predicting vaccination status of preschool-age emergency department patients. *J Pediatr.* 1993;123:887-92.

Jackson ML, Henrikson NB, Grossman DC. Evaluating Washington State's immunization information system as a research tool. *Acad Pediatr*. 2014;14(1):71–76. https://doi.org/10.1016/j.acap.2013.10.002.

Jiles RB, Daniels D, Yusuf HR, McCauley MM, Chu SY. Undervaccination with hepatitis B vaccine: missed opportunities or choice? *Am J Prev Med*. 2001;20(4 Suppl 1):75–83. https://doi.org/10.1016/S0749-3797(01)00276-8.

Justice AC, Covinsky KE, Berlin JA. Assessing the generalizability of prognostic information. *Ann Intern Med.* 1999;130:515-24.

Kata A. A postmodern Pandora's box: anti-vaccination misinformation on the Internet. *Vaccine*. 2010;28(7):1709–1716. https://doi.org/10.1016/j.vaccine.2009.12.022.

Kennedy A, Basket M, Sheedy K. Vaccine attitudes, concerns, and information sources reported by parents of young children: results from the 2009 HealthStyles survey. *Pediatrics.* 2011;127 Suppl 1:S92-9.

Kenyon TA, Matuck MA, Stroh G. Persistent low immunization coverage among inner-city preschool children despite access to free vaccine. *Pediatrics.* 1998;101:612-6.

Kessler RC, Hwang I, Hoffmire CA, et al. Developing a practical suicide risk prediction model for targeting high-risk patients in the Veterans health Administration. *Int J Methods. Psychiatr Res* 2017;26.

Khazan O. How a measles quarantine can lead to eviction. Available at: https://www.theatlantic.com/health/archive/2019/03/measles-outbreaks-cost-workers-without-paid-sick-leave/585178/. The Atlantic, 2019. Accessed February 2019.

Kim SS, Frimpong JA, Rivers PA, Kronenfeld JJ. Effects of maternal and provider characteristics on up-to-date immunization status of children aged 19 to 35 months. *Am J Public Health.* 2007;97:259-66.

Klevens RM, Luman ET. U.S. children living in and near poverty: risk of vaccine-preventable diseases. *Am J Prev Med*. 2001;20(4 Suppl 1):41–46. https://doi.org/10.1016/S0749-3797(01)00281-1.

Ko SC, Fan L, Smith EA, Fenlon N, Koneru AK, Murphy TV. Estimated annual periantal Hepatitis B virus infections in the United States, 200-2009. *J Pediatric Infect Dis Soc*. 2016;5(2):114-121.

Kogan MD, Alexander GR, Jack BW, Allen MC. The association between adequacy of prenatal care utilization and subsequent pediatric care utilization in the United States. *Pediatrics.* 1998; 102(1):25-30.

Kressin NR, Chang BH, Hendricks A, Kazis LE. Agreement between administrative data and patients' self-reports of race/ethnicity. *Am J Public Health*. 2003;93:1734–1739. https://doi.org/10.2105/AJPH.93.10.1734.

Kuzniewicz MW, Walsh EM, Li S, Fischer A, Escobar GJ. Development and implementation of an early-onset sepsis calculator to guide antibiotic management in late preterm and term neonates. *Jt Comm J Qual Patient Saf.* 2016;42:232-9.

Lauderdale DS, Oram RJ, Goldstein KP, Daum RS. Hepatitis B vaccination among children in inner-city public housing, 1991–1997. *JAMA.* 1999;282(18):1725–1730. https://doi.org/10.1001/jama.282.18.1725.

Laupacis A, Sekar N, Stiell IG. Clinical prediction rules. A review and suggested modifications of methodological standards. *JAMA.* 1997;277:488-94.

Leask J, Kinnersley P, Jackson C, Cheater F, Bedford H, Rowles G. Communicating with parents about vaccination: a framework for health professionals. *BMC Pediatr.* 2012;12:154.

Leask J. Target the fence-sitters. *Nature.* 2011;473:443-5.

Lee C, Gong Y, Brok J, Boxall EH, Gluud C. Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: Systematic review and meta-analysis. *BMJ.* 2006;332(7537):328-336.

Leininger L, Levy H. Child health and access to medical care. *Future Child.* 2015;25(1):65-90.

Lieu TA, Ray GT, Klein NP, Chung C, Kulldorff M. Geographic clusters in underimmunization and vaccine refusal. *Pediatrics*. 2015;135(2):280–289. https://doi.org/10.1542/peds.2014-2715.

Luman ET, Barker LE, McCauley MM, Drews-Botsch C. Timeliness of childhood immunizations: a state-specific analysis. *Am J Public Health*. 2005;95:1367–1374. https://doi.org/10.2105/AJPH.2004.046284.

Luman ET, McCauley MM, Shefer A, Chu SY. Maternal characteristics associated with vaccination of young children. *Pediatrics.* 2003;111:1215-8.

Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final data for 2017. *Natl Vital Stat Rep.* 2018;67:1–50.

Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: Final data for 2016. *Natl Vital Stat Rep.* 2018;67:1-55.

Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of Hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2005;54(RR-16):1-31.

McClure CC, Cataldi JR, O'Leary ST. Vaccine hesitancy: Where we are and where we are going. *Clin Ther.* 2017;39(8):1550-1562.

Mennito SH, Darden PM. Impact of practice policies on pediatric immunization rates. *J Pediatr*. 2010;156(4):618–622. https://doi.org/10.1016/j.jpeds.2009.10.046.

Mohanty S, Carroll-Scott A, Wheeler M, et al. Vaccine hesitancy in pediatric primary care practices. *Qual Health Res.* 2018:1049732318782164.

Moons KG, Altman DG, Reitsma JB, Collins GS, Transparent reporting of a multivariate prediction model for individual prognosis or development. *Adv Anat Pathol*. 2015;22:303-5.

Murthy N, Rodgers L, Pabst L, Fiebelkorn AP, Ng T. Progress in childhood vaccination data in immunization information systems—United States, 2013–2016. *MMWR Morb Mortal Wkly Rep*. 2017;66(43):1178–1181. https://doi.org/10.15585/mmwr.mm6643a4.

Myers HI, Spracklen CN, Ryckman KK, Murray JC. Retrospective study of administration of vaccination for Hepatitis B among newborn infants prior to hospital discharge at a midwestern tertiary care center. *Vaccine*. 2015 May 11; 33(20): 2316–2321.

National Academies of Sciences, Engineering and Medicine. Quality through collaboration: The future of rural health care. Available at: https://www.nap.edu/read/11140/chapter/10. Accessed May 2019.

National Conference of State Legislatures. States with religious and philosophical exemptions from school immunization requirements. Available at: www.ncsl.org/research/health/school-immunization-exemption-state-laws.aspx. Accessed March 2019.

New York State Department of Health. Perinatal Hepatitis B prevention program manual. Available at: https://www.health.ny.gov/diseases/communicable/hepatitis/hepatitis_b/perinatal/docs/program_manual.pdf. Accessed May 2018.

Newacheck PW, Hughes DC, Stoddard JJ. Children's access to primary care: differences by race, income, and insurance status. *Pediatrics.* 1996;97(1):26-32.

Nigrovic LE, Kuppermann N, Macias CG, et al. Clinical prediction rule for identifying children with cerebrospinal fluid pleocytosis at very low risk of bacterial meningitis. *JAMA.* 2007;297:52-60.

Ocama P, Opio CK, Lee WM. Hepatitis B virus infection: current status. *Am J Med.* 2005;118(12):1413.

O'Leary ST, Nelson C, Duran J. Maternal characteristics and hospital policies as risk factors for nonreceipt of hepatitis B vaccine in the newborn nursery. *Pediatr Infect Dis J.* 2012;31(1):1-4.

Olive JK, Hotez PJ, Damania A, Nolan MS. The state of the antivaccine movement in the United States: A focused examination of nonmedical exemptions in states and counties. *PLoS Med*. 2018;15:e1002578.

Omer SB, Enger KS, Moulton LH, Halsey NA, Stokley S, Salmon DA. Geographic clustering of nonmedical exemptions to school immunization requirements and associations with geographic clustering of pertussis. *Am J Epidemiol*. 2008;168:1389-96.

Omer SB, Richards JL, Ward M, Bednarczyk RA. Vaccination policies and rates of exemption from immunization, 2005-2011. *N Engl J Med.* 2012;367:1170-1.

Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider–parent vaccine discussions at health supervision visits. *Pediatrics*. 2013;132(6):1037–1346. https://doi.org/10.1542/peds.2013-2037.

Opel DJ, Mangione-Smith R, Robinson JD, et al. The influence of provider communication behaviors on parental vaccine acceptance and visit experience. *Am J Public Health.* 2015;105:1998-2004.

Orenstein WA, Ahmed R. Simply put: Vaccination saves lives. *Proc Natl Acad Sci.* 2017;114:4031-3.

Oster NV, Williams EC, Unger JM, et al. Hepatitis B birth dose: First shot at timely early childhood vaccination. In Press, *Am J Prev Med.*

Oster NV, Williams EC, Unger JM, et al. Sociodemographic, clinical and birth hospitalization characteristics and infant hepatitis B vaccination in Washington State. *Vaccine*. Online March 28, 2019. https://doi.org/10.1016/j.vaccine.2019.03.050.

Pew Research Center. The rise of residential segregation by income. Available at: http://www.pewsocialtrends.org/2012/08/01/the-rise-of-residential-segregation-by-income/. Accessed November 2016.

Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the United States: a review of measles and pertussis. *JAMA.* 2016;315(11):1149–1158. https://doi.org/10.1001/jama.2016.1353.

Plotkin SA. History of vaccination. *Vaccines.* 1999; 111(34): 12283–12287.

Quinn JA, Munoz FM, Gonik B, et al. Preterm birth: Case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. *Vaccine.* 2016;34(49):6047-6056.

Richards A, Sheridan J. Reasons for delayed compliance with the childhood vaccination schedule and some failings of computerised vaccination registers. *Aust N Z J Public Health.* 1999;23:315-7.

Ritov I BJ. Reluctance to vaccinate: omission bias and ambiguity. *J Behav Dec Mak.* 1990;3:263–277. https://doi.org/10.1002/bdm.3960030404.

Ritov I BJ. Status-quo and omission bias. *J Risk and Uncertainty*. 1992;5(1):49–61. https://doi.org/10.1007/BF00208786.

Robertson SE FD, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. *Rev Panam Salud Publica.* 14(5):306–15 2003;14:306-15.

Rosenthal SL, Weiss TW, Zimet GD, Ma L, Good MB, Vichnin MD. Predictors of HPV vaccine uptake among women aged 19–26: importance of a physician's recommendation. *Vaccine*. 2011;29(5):890–895. https://doi.org/10.1016/j.vaccine.2009.12.063.

Rural Health Research Center. Rural–Urban Commuting Codes. Available at: http://depts.washington.edu/uwruca/index.php. Accessed March 2019.

Salathe M, Bonhoeffer S. The effect of opinion clustering on disease outbreaks. *J R Soc Interface*. 2008;5:1505-8.

Santoli JM, Huet NJ, Smith PJ, et al. Insurance status and vaccination coverage among US preschool children. *Pediatrics*. 2004;113:1959-64.

Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 2018;67(1):1–31. https://doi.org/10.15585/mmwr.rr6701a1.

Schillie S, Walker T, Veselsky S, et al. Outcomes of infants born to women infected with hepatitis B. *Pediatrics*. 2015;135(5):e1141–e1147. https://doi.org/10.1542/peds.2014-3213.

Seeff LB, Beebe GW, Hoofnagle JH, et al. A serologic follow-up of the 1942 epidemic of post-vaccination hepatitis in the United States Army. *N Engl J Med* 1987;316:965-70.

Seither R, Calhoun K, Street EJ, et al. Vaccination coverage for selected vaccines, exemption rates, and provisional enrollment among children in kindergarten—United States, 2016–17 school year. *MMWR Morb Mortal Wkly Rep*. 2017;66(40):1073–1080. https://doi.org/10.15585/mmwr.mm6640a3.

Shelby A, Ernst K. Story and science: how providers and parents can utilize storytelling to combat anti-vaccine misinformation. *Hum Vaccin Immunother*. 2013;9(8):1795–1801. https://doi.org/10.4161/hv.24828.

Smith EA, Jacques-Carroll L, Walker TY, Sirotkin B, Murphy TV. The national Perinatal Hepatitis B Prevention Program, 1994-1008. *Pediatrics.* 2012:129(4):609-616.

Smith J. *Patenting the Sun: Polio and the Salk Vaccine.* New York: William Morrow and Company;1990.

Smith PJ, Chu SY, Barker LE. Children who have received no vaccines: who are they and where do they live? *Pediatrics*. 2004;114(1):187–195. https://doi.org/10.1542/peds.114.1.187.

Smith PJ, Humiston SG, Marcuse EK, et al. Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. *Public Health Rep*. 2011;126(Suppl 2):135–146. https://doi.org/10.1177/00333549111260S215.

Smith PJ, Kennedy AM, Wooten K, Gust DA, Pickering LK. Association between health care providers' influence on parents who have concerns about vaccine safety and vaccination coverage. *Pediatrics* 2006;118:e1287-92.

Smith PJ, Marcuse EK, Seward JF, Zhao Z, Orenstein WA. Children and adolescents unvaccinated against measles: geographic clustering, parents' beliefs, and missed opportunities. *Public Health Rep*. 2015;130(5):485–504. https://doi.org/10.1177/003335491513000512.

Smith PJ, Stevenson J, Chu SY. Associations between childhood vaccination coverage, insurance type, and breaks in health insurance coverage. *Pediatrics.* 2006;117:1972-8.

Sobo EJ. Social cultivation of vaccine refusal and delay among Waldorf (Steiner) School parents. *Med Anthropol Q*. 2015;29(3):381–399. https://doi.org/10.1111/maq.12214.

Sporton RK, Francis SA. Choosing not to immunize: are parents making informed decisions? *Fam Pract*. 2001;18:181-8.

Steyerberg EW, Eijkemans MJ, Habbema JD. Stepwise selection in small data sets: a simulation study of bias in logistic regression analysis. *J Clin Epidemiol.* 1999;52:935-42.

Stockwell MS, Natarajan K, Ramakrishnan R, et al. Immunization data exchange with electronic health records. *Pediatrics*. 2016;137(6):e20154335. https://doi.org/10.1542/peds.2015-4335.

Sturm LA, Mays RM, Zimet GD. Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections. *J Dev Behav Pediatr*. 2005;26:441-52.

Sugerman DE, Barskey AE, Delea MG, et al. Measles outbreak in a highly vaccinated population, San Diego, 2008: role of the intentionally undervaccinated. *Pediatrics*. 2010;125:747-55.

Sultan AA, West J, Grainge MJ, et al. Development and validation of risk prediction model for venous thromboembolism in postpartum women: multinational cohort study. *BMJ*. 2016;355:i6253.

Suri G, Sheppes G, Schwartz C, Gross JJ. Patient inertia and the status quo bias: When an inferior option is preferred. *Psychol Sci*. 2013;24(9):1763–1769. https://doi.org/10.1177/0956797613479976.

Syed ST, Gerber BS, Sharp LK. Traveling towards disease: Transportation barriers to health care access. *J Community Health*. 2013;38(5):976–993. https://doi.org/10.1007/s10900-013-9681-1.

Szilagyi PG, Humiston SG, Pollard Shone L, Kolasa MS, Rodewald LE. Decline in physician referrals to health department clinics for immunizations: the role of vaccine financing. *Am J Prev Med*. 2000;18:318-24.

U.S. Department of Commerce. Overview of Race and Hispanic Origin: 2010. Available at: www.census.gov/prod/cen2010/briefs/c2010br-02.pdf. Published March 2011. Accessed March 2019.

U.S. Department of Health, Education and Welfare. Vital statistics -- special report, national summaries: Reported incidence of selected notifiable diseases, United States, each division and state, 1950. Available at: https://www.cdc.gov/nchs/data/vsus/vsus_1950_1.pdf. Accessed March 2019.

U.S. Department of Health and Human Services. Healthy People 2020. Avaialble at: https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases/objectives. Accessed August 2018.

University of Michigan Population Studies Center, Institute for Social Research. Median Household Income, 2006-2010. Available at: https://www.psc.isr.umich.edu/dis/census/Features/tract2zip/index.html. Accessed May 2018.

Van Houwelingen JC, Le Cessie S. Predictive value of statistical models. *Stat Med.*1990;9:1303-25.

Vasireddy D, Yusi D, Berrak SG, Lichtenberger J. Factors affecting refusal rates of the birth dose of hepatitis B vaccine: A single center study. *J Pediatr Inf.* 2014;8:159-164.

Wagner AL, Eccleston AM, Potter RC, Swanson RG, Boulton ML. Vaccination timeliness at age 24 months in Michigan children born 2006–2010. *Am J Prev Med*. 2018;54(1):96–102. https://doi.org/10.1016/j.amepre.2017.09.014.

Wang L, Porter B, Maynard C, et al. Predicting risk of hospitalization or death among patients with heart failure in the veterans health administration. *Am J Cardiol*. 2012;110:1342-9.

Washington State Department of Health. Evaluation of birthing hospitals on perinatal hepatitis B prevention practices. Available at: https://www.doh.wa.gov/Portals/1/Documents/Pubs/348-432-HospitalTechRpt.pdf. Accessed August 2018.

Washington State Office of Financial Management. Washington State and county median household income estimates: 1989 to 2015 and projection for 2016. Available at: http://www.ofm.wa.gov/economy/hhinc/medinc.pdf. Accessed July 2018.

Wheeler M, Buttenheim AM. Parental vaccine concerns, information source, and choice of alternative immunization schedules. *Hum Vacc Immunother*. 2013;9(8):1782–1789. https://doi.org/10.4161/hv.25959.

Wilson P, Taylor G, Knowles J, et al. Missed hepatitis B birth dose vaccine is a risk factor for incomplete vaccination at 18 and 24 months. *J Infect*. 2018;78(2):134–139. https://doi.org/10.1016/j.jinf.2018.09.014.

World Health Organization. Global burden of Haemophilus influenzae type B (Hib). Available at: Available at: http://www.emro.who.int/health-topics/haemophilus-influenzae-type-b/disease-burden.html. Accessed May 2019.

World Health Organization. Measles. Available at: http://www.who.int/immunization/diseases/measles/en/. Accessed February 2018.

World Health Organization. WHO vaccine-preventable diseases: monitoring system. 2015 global summary. Available at: http://apps.who.int/immunization_monitoring/globalsummary/incidences?c=USA WHOAa.. Accessed November 18, 2015.

Yang S, Zarr RL, Kass-Hout TA, Kourosh A, Kelly NR. Transportation barriers to accessing health care for urban children. *J Health Care Poor Underserved*. 2006;17(4):928–943. https://doi.org/10.1353/hpu.2006.0137.

Yang YT, Delamater PL, Leslie TF, Mello MM. Sociodemographic predictors of vaccination exemptions on the basis of personal belief in California. *Am J Public Health*. 2016;106:172–177. https://doi.org/10.2105/AJPH.2015.302926.

Yusuf HR, Daniels D, Smith P, Coronado V, Rodewald L. Association between administration of hepatitis B vaccine at birth and completion of the hepatitis B and 4:3:1:3 vaccine series. *JAMA*. 2000;284(8):978–983. https://doi.org/10.1001/jama.284.8.978.

Zimmerman RK, Mieczkowski TA, Mainzer HM, et al. Effect of the Vaccines for Children program on physician referral of children to public vaccine clinics: a pre-post comparison. *Pediatrics*. 2001;108:297-304.

Zimmerman RK, Tabbarah M, Janosky JE, et al. Impact of vaccine economic programs on physician referral of children to public vaccine clinics: a pre-post comparison. *BMC Public Health*. 2006;6:7.

Zipprich J, Winter K, Hacker J, et al. Measles outbreak--California, December 2014-February 2015. *MMWR Morb Mortal Wkly Rep* 2015;64:153-4.