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The Current Burden of Hepatitis B in the United States: A State, Territorial, and County Modelling Analysis

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ABSTRACT

Accurate estimates of the prevalence of chronic hepatitis B virus (HBV) in the United States (US) are necessary for policy makers and community-based organisations to make informed decisions regarding the allocation of resources to work towards the elimination of HBV as a public health threat. The primary aim of this study was to quantify the current HBV prevalence in the US at the state, county, and territorial level. The secondary aim was to quantify which countries of birth lead HBV infections. Using previously validated and published population-based country level Markov models, the prevalence of HBV among immigrants in the US by country of birth was estimated in 2021. These estimates were then applied to county level population estimates from the 2018–2022 American Community Survey. This resulted in new county, state, territorial (Puerto Rico and Washington, D.C.), and national level HBV prevalence estimates. The total number of HBV infections in the US was estimated to be 1.7 million (UI: 795,000–4.1 million) corresponding to a prevalence of 0.50% (UI: 0.24%–1.23%). The state with the highest prevalence was Hawai'i, 1.3% (UI: 0.5%–40%), while Wyoming was estimated to have the lowest prevalence, 0.2% (UI: 0.1%–1.1%). The largest number of total infections was found in California, 347,100 (UI: 193,700–729,200). The Aleutians West Census Area was the county with the highest prevalence, 2.9% (UI: 0.8%–9.7%), while Los Angeles County had the highest number of infections, 96,700 (UI: 54,800–190,600). These data can aid planners at all levels to better understand the complexities of HBV in the US. Thus, providing evidence for targeted public health interventions that will reduce the burden of HBV and improve the lives of those living with the disease.

1 | Introduction

Since the 69th World Health Assembly in 2016 endorsed the Global Health Sector Strategy to eliminate viral hepatitis infection as a public health threat by 2030 [1], countries have been attempting to better understand the burden of viral hepatitis in order to work towards the World Health Organization's (WHO) global targets [2]. In the United States (US), the Viral Hepatitis National Strategic Plan paid heed to this call, setting a roadmap towards elimination [3]. To work towards elimination, an accurate estimate of hepatitis B virus (HBV) prevalence, as defined as hepatitis B surface antigen positivity, is the necessary starting point. This task can prove difficult in countries where the prevalence of HBV is quite low [4]. Many Western countries have identified migrants as key communities impacted by HBV that significantly contributes to the national burden [5–10]. Unfortunately, national serosurveys often under-sample high-risk populations, including migrants, thus potentially underestimating the total infections present in the country [4].

The prevalence of HBV infection in the US is an example of the difficulties in understanding the disease burden in a low prevalence setting. The results of the most recent National Health and Nutrition Examination Survey (NHANES) estimated a national HBV prevalence of 0.32% (95% confidence interval (CI), 0.24%–0.41%), representing 817,000 (95% CI, 613,000–1,100,000) infected individuals ≥15 years in the period of 2013–2018 [11, 12]. Others have estimated a much higher prevalence of HBV infections in the US (1.04–2.49 million) [13–15]. Migrants are a major contributor to the HBV infected population and under-sampling this population in the NHANES study could explain a lower prevalence [11, 16]. NHANES utilises surveys or door knocks, which can make response challenging for migrant communities, with limited English proficiency, to participate. There may also be hesitation to acknowledge foreign-born status and country of birth.

Previous studies have attempted to quantify the impact of immigration in the US. However, these studies were limited by using HBV prevalence estimates that were non-representative of the migrant population, combining prevalence estimates from different age groups across countries, and then applying these estimates to the countries' migrant population [13–16]. By not considering HBV prevalence by age, the age of the migrant population, nor the temporal effect, these previous estimates may have overestimated the burden by not considering the large decline in prevalence among younger age groups as a result of global vaccination efforts.

To address these shortcomings, our country-specific disease burden and transmission models were integrated with an immigration module, which considered the age, sex and annual number of individuals gaining lawful permanent resident (LPR) status from 1900 to 2020. These positive cases were added to the United States model, thus creating a new estimate for the HBV prevalence in the country. This analysis culminated in a publication, which estimated that there were 1.8 million HBV infections in the US, representing a prevalence of 0.55% (UI: 0.41%–0.77%) [17]. This study also provided estimates regarding the prevalence of HBV among immigrants in the United States by country of birth.

While these data have been useful, there is a strong need for more localised estimates so that national, state, and local governments can better understand the current burden of HBV in their area. Based on these data, stakeholders will be better positioned to respond to a burden which falls disproportionately upon foreign-born communities. These data can aid state and local health departments in their allocation of resources, while allowing for more precise targeted interventions of the areas and communities most impacted. While this will positively impact the ability of local, state, and national agencies to meet screening, treatment, and vaccination targets, the real impact is the lives saved and infections averted.

The primary aim of this study was to quantify the current HBV prevalence in the US at the state, county, and territorial level. The secondary aim was to quantify which countries of birth have the largest share of HBV infections in the US by state, county, and territory in 2021.

2 | Materials and Methods

2.1 | Data Selections and Modelling Methods

The Polaris Observatory maintains 170 country-specific HBV disease burden models—the PRoGReSs model—that are updated annually with data from literature, databases, and in-country experts. Updates can occur more frequently when there is engagement at the national level to develop national strategic plans occurring outside of the annual update period. PRoGReSs is a compartmental, deterministic, dynamic Markov model that estimates vertical and horizontal transmission, the impact of HBV prophylaxis programs, disease progression, all-cause mortality, liver-related deaths, and the impact of HBV treatment on disease progression and transmission. It is developed in Microsoft Excel and Microsoft Visual Basic (Microsoft Corporation, Redmond, WA, United States) to quantify the annual HBV-infected population by disease stage, sex, and age in a country. The disease stages considered in the PRoGReSs model are chronic hepatitis B, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and liver transplantation. Excel was selected due to its transparency, flexibility, and widespread availability. The model has been assessed for accuracy by testing its ability to accurately predict paediatric prevalence, liver cancer incidence, and liver-related deaths in various settings [4]. Regarding reliability, since this model is developed using Microsoft Excel's nonvolatile functions only—that is, functions whose values are the same from one moment to the next, provided that none of the functions' arguments has changed—by design, it will produce the same output for a given input.

The model has been tested in settings that differ greatly by HBsAg prevalence, genotype, HBeAg prevalence, and mother to child transmission interventions to ensure it is generalizable. While the demographic and epidemiological inputs are country specific, the progression rates and transmission rates are universal with one exception. Due to the lower mean age of hepatocellular carcinoma development in Sub-Saharan Africa, different progression rates were developed based on empirical data and utilised for countries in this region (Section S1).

Details on the search strategy, study selection criteria, data collection and processing, and modelling were previously published [4]. Briefly, a literature review is combined with grey literature (ministry of health publications and databases, conference presentations, and local journals), and then entered into a quality scoring system using a multi-objective decision analysis approach resulting in scores of 1–3 for each study considered. In-country experts have been identified via prior collaborations and are primarily made up of leading gastroenterologists and hepatologists as well as public health officials. These experts partake in a Delphi interview process to validate the inputs and outputs, providing better data sources when available. The appendix outlines details of data and model updates since the most recent publication (Section S1). Each of these models estimates the annual number of infected individuals by disease stage, age, and sex from 1900 onward.

2.2 | Immigration and Data Analyses

The previous immigration analysis was rerun with the most updated data and models available (Sections S2–S4) [17]. To briefly summarise, the annual number of immigrants receiving LPR status in the US was collected from 1900 onward by country of birth, age, and sex. Country level models were available and utilised for 99.4% of all immigrants receiving lawful permanent resident status in the US since 1900. For countries in which immigration data existed but models were not available, a regional average using the Global Burden of Disease regions (Table S5) was applied. These regions were utilised as they are grouped based on similar cause of death patterns. Each country-level model compatible with immigration data was used to annually provide two inputs: (1) HBV-positive immigrants entering the US—added to the US prevalent population, and (2) immigrants susceptible to HBV infection entering the US. For the former, the annual HBV prevalence by age and sex in the country of birth was applied to the number of incoming immigrants by age and sex, distributed by the stage of liver disease. This process explicitly considered the historical and continued impact of HBV prophylaxis programs in the countries of birth. For the second set of inputs, the annual proportions of infected and recovered cases or those previously immunised in the countries of birth were applied to the incoming immigrants by age and sex. Once in the US model, the entire population was subject to the disease progression of HBV infection that may lead to HBV-related deaths, the age and sex specific US background mortality and the impact of vaccination, screening, and treatment schedules within the US. The assumptions regarding the US interventions to prevent, screen and treat HBV are detailed in the previous publication as well as the appendix [17].

This analysis provided the age-adjusted prevalence estimate among immigrant communities by country of birth. The American Community Survey (ACS) 2018–2022 5-year estimate data for place of birth for the foreign-born population in the United States and Puerto Rico were collected and combined with the modelled prevalence of immigrants by country of birth (Table S7) [18].

The ACS contains county level population estimates for 127 countries of birth as well as multiple regions. When a country of birth specific modelled immigrant estimate was not available, the regional Global Burden of Disease average was used (Table S5). When ACS data were only available by region, a regional estimate, as defined by the countries included in ACS regions, was applied (Table S6).

The ACS also estimates the non-foreign-born population by county and territory [19]. The non-foreign-born population was divided into two populations—Asian and Pacific Islanders and the remainder [20]. This split was necessary, as it has been well established that Asian and Pacific Islanders historically have the highest HBV prevalence among racial and ethnic groups in the US [11, 21]. However, NHANES does not differentiate between non-foreign-born and foreign-born Asian and Pacific Islanders. To overcome this shortcoming, we developed a US model that only considered Asian and Pacific Islanders and immigrants from these countries (Section S5). This exercise resulted in a prevalence of 0.69% among non-foreign-born Asian and Pacific Islanders, similar to the prevalence found in Asian Americans in California [22]. This was the base estimate in the analysis. For the uncertainty analysis, the non-foreign-born estimate of 0.12% was applied for the low, and the 5.20% estimate among Asians was applied for the high [11]. For the remainder of the non-foreign-born population, the most recent NHANES published estimate of 0.12% (CI: 0.07%–0.20%) was applied [11].

There was one state, Alaska, and the corresponding counties where this rule was not applied. Due to the historically high prevalence among Alaskan Natives, the non-foreign-born population in Alaska was further divided into Alaskan Native and non-Alaskan Native utilising the Alaskan Department of Labor and Workforce Development Population Estimates [23]. For the former an age weighted prevalence of 0.80% (UI: 0.5%–3.0%) was applied while for the latter the aforementioned 0.12% was applied (Section S5). Alaskan Natives have had one of the, if not the, strongest responses to HBV via vaccination, screening and treatment than any group globally. Based on personal communications with Dr. Brian McMahon, who has led these efforts from its inception, there are approximately 1200 Alaskan Natives living with HBV out of a population of 150,000 thus the 0.80% estimate. The lows and highs for the uncertainty analysis were derived from Dr. McMahon's published work that found the lowest prevalence in these communities was 0.5% and the average was 3.0% in the 1980s [24].

The estimated number of foreign-born and non-foreign-born HBV cases was combined to give county level estimates of the HBV prevalence in 2021. These data were then summed by state to estimate the state prevalence and summed again to result in the national burden.

2.3 | Uncertainty Analysis

Traditionally, confidence intervals assume normal distributions. We assume the potential for asymmetric uncertainty in all key inputs and thus utilised a Bayesian uncertainty analysis approach. For each country of birth model, the 95% uncertainty intervals of HBV transmission and disease burden in the home country were considered (Tables S2–S4, Section S7). Low prevalence was defined by low prevalence in the country of birth, low transmission probabilities, and high progression rates in the country model. As the model is dynamic, utilising a low prevalence estimate will result in lower transmission when compared to the base. By using the low transmission probabilities, this is another lever to lower transmission and thus long-term prevalence. Finally, high progression rates result in faster mortality, once again reducing the modelled prevalence and thus transmission. By combining all three factors, the result is the lowest prevalence to be expected based on the published literature. The high prevalence analysis used the high prevalence estimate in the country of birth, high transmission probabilities, and low progression rates. These rates were then applied to the low and high population estimates of the foreign-born population by country of birth in each county. While these calculations provide what would be more often considered minimum and maximum outputs, we recognise that there is additional uncertainty regarding all of the assumptions that may not be fully accounted for by this approach. The data quality of the base prevalence estimates was lowest in Eastern Europe and Central America and country level models were not available for the country of birth of 0.4% of foreign-born individuals.

While we have included the sources for all of the data inputs and assumptions in the models, we realise the entire process is quite complex and are open for communications with those interested to ensure transparency and replicability.

2.4 | Role of Funding

This analysis was funded by a research grant from GSK and made possible by grants from the John C Martin Foundation who supported country level analyses. The funders had no role in study design, data collection, data analysis, data interpretation, or preparation of the manuscript.

3 | Results

Utilising this bottom up approach to estimate the prevalence of HBV in the United States, we estimate there are 1.7 million (UI: 795,000–4.1 million) people living with HBV in the United States and Puerto Rico, corresponding to a prevalence of 0.50% (UI: 0.24%–1.23%; Table 1). Of these cases, 76% are estimated to be among the foreign-born population (1.3 million, UI: 589,000–3.1 million), with 396,000 (UI: 206,000–1,007,000) cases being among the non-foreign-born population (Table 1). Of people living with HBV who were born in the US, only 15%, or 59,000 (UI: 10,000–440,000), were among non-foreign-born Asian and Pacific Islanders.

3.1 | HBV Prevalence in US States & Territories

The highest HBV prevalence was found in Hawaiʻi, 1.3% (UI: 0.5%–4.0%); California, 0.9% (UI: 0.5%–1.9%); New York, 0.8% (UI: 0.4%–1.7%); Maryland, 0.8% (UI: 0.4%–1.7%); and New Jersey, 0.8% (UI: 0.4%–1.5%; Figure 1). The lowest HBV prevalence was found in Wyoming, 0.2% (UI: 0.1%–1.1%); West Virginia, 0.2% (UI: 0.1%–1.0%); Montana, 0.2% (UI: 0.1%–1.0%); Mississippi, 0.2% (UI: 0.1%–1.0%); and Puerto Rico, 0.2% (UI: 0.1%–0.5%; Figure 1).

When the absolute number of HBV cases in the US is examined by state, there are five states that account for over 50% of the total HBV infections: California, 347,100 (UI: 193,700–729,200); New York, 169,400 (UI: 84,500–349,800); Texas, 135,600 (UI: 66,700–342,300); Florida, 108,500 (UI: 42,500–264,100); and New Jersey, 70,700 (UI: 32,500–157,000; Figure 1).

State and territorial level prevalence estimates, including the number of people living with HBV by country of birth, for the top 30 countries of birth, can be found in Section S7. Populations of less than 50 were excluded. The full data sets are available on The Polaris Observatory at https://cdafound.org/polaris/migration/.

3.2 | HBV Prevalence in US Counties

The highest prevalence was found in Aleutians West Census Area, Alaska, 2.9% (UI: 0.8%–9.7%); Aleutians East Borough, Alaska, 2.0% (UI: 0.4%–9.0%); Santa Clara County, California, 2.0% (UI: 1.3%–3.7%); Queens County, New York, 1.8% (UI: 1.0%–3.4%); and San Francisco County, California, 1.8% (UI: 1.1%–3.5%; Figure 2).

Twenty-five percent of people living with HBV in the US and Puerto Rico reside in 11 counties (Table 2). The counties with the largest number of people living with HBV were Los Angeles County, California, 96,700 (UI: 54,800–190,600); Queens County, New York, 42,600 (UI: 24,100–81,300); Orange County, California, 38,600 (UI: 24,600–73,500); Santa Clara County, California, 37,800 (UI: 25,600–70,400); and Kings County, New York, 34,500 (UI: 19,000–65,900; Figure 3).

County level prevalence estimates, including the number of people living with HBV by country of birth, can be found online at https://cdafound.org/polaris/migration/.

3.3 | HBV Infection Among the US Foreign-Born Population

At the national level, there are 12 countries of birth that represent 47% of all infections and 62% of infections among the foreign-born population (Figure S2). First generation migrants from four of these countries—Mainland China, the Philippines, Vietnam, and India—make up 31% of all people living with HBV in the US and Puerto Rico. However, there is great heterogeneity at the state level. In California, the top foreign-born population is from the Philippines; in New York, Mainland China; in Texas, Vietnam; in New Jersey, India; and in Florida, Jamaica (Section S7).

The portion of people living with HBV that are first generation migrants, out of the total infections, varies greatly by state, with West Virginia representing the lowest share, 30%, and New York the highest, 87% (Table 1).

4 | Discussion

This study estimates that the prevalence of HBV in the US and Puerto Rico was 0.50% (UI: 0.24%–1.23%), or 1.7 million (UI: 795,000–4.1 million) infections among all ages, which is significantly higher than the nationally reported estimate of 0.32% (CI: 0.24%–0.41%), representing 817,000 (CI: 613,000–1,100,000) in ages ≥15 years, or 0.28% (CI: 0.22%–0.35%), representing 862,000 (CI: 668,000–105,600) infections among those ≥6 years old [11, 12]. These findings provide additional evidence that the HBV prevalence in the US has been underestimated in national serosurveys. This situation is likely to be the case in other Western countries that have a low baseline prevalence but where immigration accounts for the majority of HBV infections [5, 9, 10, 25].

The states which led with the absolute number of HBV cases were in many ways unremarkable. California, New York, Texas,

TABLE 1 | The prevalence of hepatitis B in the US localities in descending order of total infections, 2021.

Locality	HBV prevalence (UI)	Total HBV infections (UI)	Infections among foreign-born (UI)	Infections among non-foreign-born (UI)	Share of foreign-born out of total infections
California	0.9% (0.5%–1.9%)	347,100 (193,700–729,200)	298,430 (172,350–548,430)	48,620 (21,360–180,810)	86%
New York	0.8% (0.4%–1.7%)	169,400 (84,500–349,800)	147,040 (73,430–285,300)	22,360 (11,110–64,490)	87%
Texas	0.5% (0.2%–1.2%)	135,600 (66,700–342,300)	103,080 (49,520–263,640)	32,480 (17,150–78,620)	76%
Florida	0.5% (0.2%–1.2%)	108,500 (42,500–264,100)	86,810 (30,500–219,400)	21,650 (11,960–44,750)	80%
New Jersey	0.8% (0.4%–1.7%)	70,700 (32,500–157,000)	60,550 (27,400–128,080)	10,170 (5080–28,890)	86%
Illinois	0.5% (0.2%–1.1%)	57,900 (28,200–143,100)	42,860 (20,390–104,650)	15,010 (7800–38,410)	74%
Massachusetts	0.7% (0.4%–1.4%)	50,700 (26,700–99,800)	42,890 (22,570–80,120)	7820 (4090–19,640)	85%
Virginia	0.6% (0.2%–1.6%)	50,000 (21,200–139,700)	39,100 (15,820–108,480)	10,860 (5390–31,270)	78%
Washington	0.6% (0.3%–1.4%)	49,600 (26,900–109,100)	39,930 (22,140–80,190)	9640 (4710–28,910)	81%
Georgia	0.5% (0.2%–1.3%)	48,800 (20,700–140,800)	36,090 (13,950–110,540)	12,750 (6780–30,220)	74%
Pennsylvania	0.4% (0.2%–0.9%)	48,300 (22,500–113,300)	32,640 (14,030–78,800)	15,630 (8500–34,490)	68%
Maryland	0.8% (0.4%–1.7%)	47,600 (21,600–103,800)	40,530 (17,900–85,990)	7070 (3690–17,790)	85%
Ohio	0.3% (0.1%–0.8%)	36,000 (16,300–92,300)	21,860 (8380–63,780)	14,120 (7880–28,480)	61%
Michigan	0.4% (0.2%–0.9%)	35,900 (16,100–87,900)	23,800 (9490–61,670)	12,080 (6600–26,250)	66%
North Carolina	0.3% (0.1%–0.9%)	34,700 (14,500–98,600)	22,350 (7780–72,040)	12,350 (6760–26,580)	64%
Hawai'i	1.3% (0.5%–4.0%)	19,100 (7500–57,500)	14,980 (6400–31,420)	4100 (1060–26,040)	79%
Minnesota	0.5% (0.2%–1.3%)	28,900 (13,800–73,200)	21,480 (10,060–52,830)	7370 (3730–20,340)	74%
Arizona	0.3% (0.2%–0.7%)	24,400 (12,200–52,800)	16,330 (7830–35,390)	8040 (4400–17,450)	67%
Indiana	0.3% (0.1%–0.9%)	19,800 (8100–62,900)	11,630 (3630–45,840)	8160 (4500–17,080)	59%
Nevada	0.6% (0.3%–1.5%)	20,000 (8900–48,100)	16,240 (7040–36,770)	3730 (1810–11,370)	81%
Colorado	0.3% (0.1%–0.9%)	19,600 (8600–52,400)	12,770 (4950–37,380)	6780 (3680–15,040)	65%

(Continues)

Locality	HBV prevalence (UI)	Total HBV infections (UI)	Infections among foreign-born (UI)	Infections among non-foreign-born (UI)	Share of foreign-born out of total infections
Connecticut	0.5% (0.2%–1.2%)	18,900 (7400–42,400)	14,870 (5230–33,310)	4010 (2160–9100)	79%
Tennessee	0.3% (0.1%–0.9%)	18,500 (7500–61,100)	10,250 (2900–44,330)	8270 (4600–16,790)	55%
Missouri	0.3% (0.1%–0.9%)	16,600 (7200–55,100)	9170 (3070–39,770)	7470 (4140–15,340)	55%
Oregon	0.4% (0.2%–1.0%)	16,100 (7600–41,900)	10,950 (4860–29,050)	5160 (2710–12,800)	68%
Wisconsin	0.3% (0.1%–0.7%)	14,900 (6400–44,100)	7630 (2500–27,740)	7290 (3950–16,360)	51%
South Carolina	0.2% (0.1%–0.7%)	12,200 (4800–37,300)	6100 (1410–25,580)	6060 (3410–11,680)	50%
Louisiana	0.2% (0.1%–0.8%)	11,300 (4800–38,900)	5630 (1680–27,430)	5620 (3120–11,480)	50%
Kentucky	0.2% (0.1%–1.0%)	11,100 (4500–45,600)	5690 (1440–34,610)	5440 (3030–10,960)	51%
Oklahoma	0.3% (0.1%–0.9%)	10,800 (4800–34,300)	6000 (2160–23,990)	4790 (2620–10,290)	56%
Alabama	0.2% (0.1%–0.7%)	10,500 (4600–36,000)	4470 (1190–24,630)	6010 (3400–11,390)	43%
Iowa	0.3% (0.1%–1.1%)	10,100 (3900–36,200)	6210 (1740–27,940)	3870 (2120–8300)	62%
Utah	0.3% (0.1%–0.8%)	9500 (4300–26,100)	5600 (2140–17,330)	3920 (2120–8780)	59%
Kansas	0.3% (0.1%–1.2%)	9100 (4000–34,000)	5560 (2030–26,100)	3550 (1920–7930)	61%
Puerto Rico	0.2% (0.1%–0.5%)	6500 (3000–15,900)	2660 (810–9320)	3840 (2220–6600)	41%
Arkansas	0.2% (0.1%–1.0%)	6700 (2700–29,300)	3040 (730–21,340)	3690 (2020–7990)	45%
Nebraska	0.3% (0.1%–1.3%)	6500 (2600–24,800)	4200 (1370–20,050)	2300 (1270–4730)	65%
Rhode Island	0.6% (0.3%–1.3%)	6300 (2900–14,200)	5090 (2250–11,450)	1220 (660–2720)	81%
Mississippi	0.2% (0.1%–1.0%)	5500 (2300–29,200)	1920 (310–22,030)	3620 (2030–7140)	35%
New Mexico	0.2% (0.1%–0.8%)	4900 (2100–17,100)	2490 (720–12,320)	2410 (1340–4810)	51%
Delaware	0.4% (0.2%–1.0%)	4400 (1900–10,400)	3300 (1270–7980)	1140 (630–2400)	74%
New Hampshire	0.3% (0.1%–0.8%)	4100 (1600–10,800)	2470 (660–7540)	1630 (910–3220)	60%
District of Columbia	0.6% (0.3%–1.2%)	4000 (1800–8200)	3180 (1400–6410)	770 (410–1780)	81%
Idaho	0.2% (0.1%–0.9%)	3800 (1600–15,900)	1590 (330–11,510)	2190 (1220–4340)	42%
Alaska	0.6% (0.2%–2.1%)	4300 (1600–15,700)	2570 (650–9780)	1740 (980–5880)	60%
Maine	0.2% (0.1%–0.7%)	3400 (1400–9800)	1750 (430–6700)	1630 (920–3060)	52%
West Virginia	0.2% (0.1%–1.0%)	3200 (1300–17,600)	950 (110–12,930)	2250 (1240–4680)	30%

(Continues)

TABLE 1 | (Continued)

Locality	HBV prevalence (UI)	Total HBV infections (UI)	Infections among foreign-born (UI)	Infections among non-foreign-born (UI)	Share of foreign-born out of total infections
North Dakota	0.3% (0.1%–1.5%)	2500 (800–11,500)	1560 (320–9670)	920 (520–1790)	63%
South Dakota	0.3% (0.1%–1.4%)	2400 (900–12,600)	1350 (310–10,700)	1050 (600–1940)	56%
Montana	0.2% (0.1%–1.0%)	2000 (800–11,400)	620 (70–8750)	1340 (750–2690)	32%
Vermont	0.2% (0.1%–0.9%)	1600 (600–5700)	810 (140–4080)	780 (430–1610)	51%
Wyoming	0.2% (0.1%–1.1%)	1000 (400–6300)	320 (40–4900)	700 (390–1410)	31%
Total	0.5% (0.2%–1.2%)	1,665,000 (795,900–4,117,000)	1,269,000 (589,000–3,110,000)	396,000 (205,900–1,007,000)	76%

Abbreviations: FB, foreign-born; HBV, Hepatitis B Virus (Hepatitis B surface antigen positive).

and Florida lead the country in terms of total population, while simultaneously having large and longstanding foreign-born communities. Similarly, Los Angeles and New York City compose the leading counties in terms of the absolute number of HBV cases.

The highest percentage prevalence was found in the Aleutians (East and West). These counties have small populations, 3407 and 5219 respectively, with a high portion of that population being foreign-born, 32% and 44% respectively. Hawaiʻi has the highest percentage prevalence of all states, due to the historical and continued high share of the population that is composed of foreign-born Asian and Pacific Islanders and their descendants.

We estimate that nationally, 76% (1.3 million out of 1.7 million total infections) of the prevalent population were among the foreign-born population. However, there is great heterogeneity in the share of foreign-born infections by state and county (Table 1). While New York could likely meet the WHO diagnosis target of 90% by exclusively screening the foreign-born population, West Virginia would diagnose just one third of the threshold. These localised estimates can aid planners in understanding what types of interventions would be most impactful. In states and counties with very high shares of all infections being among the foreign-born population, screening and vaccination can be hyper-focused on these counties and populations. Most states and counties will require mixed methods to reach the 90% diagnosis threshold. Focusing on the foreign-born population, while also screening those most at risk of living with HBV (anyone born prior to widespread vaccination efforts). This study also provides evidence that there is great heterogeneity in the foreign-born communities most impacted (Section S7). This has major impacts on local planning for elimination efforts as it can help direct community engagement and community workers to ensure that these populations are screened, vaccinated, and treated.

The recent Center for Disease Control and Prevention recommendations for the universal screening of adults for HBV will likely have a major impact on increasing the number of people living with HBV being aware of their status. While this is certainly a positive step towards the elimination of HBV as a public health threat, we must ensure that the universal approach does not obscure the need for targeted interventions. The reality is that in 44 states, the majority of HBV infections are among the foreign-born population. These diverse communities face different cultural and linguistic barriers to screening and linkage to care than the general population. While the universal approach can help reduce stigma, it is imperative that the communities most impacted by HBV are included in the planning and implementation of screening and treatment programs to increase their probability of being successful.

There were several limitations to this analysis. The data for the foreign-born population is based on ACS data, which in a recent year was shown to under count the noncitizen foreign-born population [26]. This could lead to underestimates of the foreign-born population, and thus the total number of infections in the US. The groups most likely to be excluded from this count would be non-immigrants (temporary workers, students, exchange visitors, and diplomats) and undocumented immigrants. In our previous analysis, we attempted to quantify these populations utilising national data, showing that these groups could potentially lead to an additional 89,000 and 184,000 cases respectively nationally [17]. As these data are not available at the granular level that was utilised in the current study, they were not explicitly included although some should be accounted for in the foreign-born population estimates.

The analysis also assumes that the prevalence and the modelled disease stage distribution of the foreign-born living with HBV by age and sex is the same as in the general population in the country of birth. The prevalence among the foreign-born population may be lower than the modelled estimate of the general population of the birth country as a result of the healthy migrant effect. One of the primary drivers of the healthy migrant effect is that new migrants are younger. Since we used annual age and sex specific data in our estimates, the age of the migrants has already been considered thus reducing this bias. Other explanations for the healthy migrant effect, particularly in the US, are that in some cases migrants represent higher-income individuals from urban areas that would likely have increased access to hospital births and HBV vaccination. On the other hand, the HBV prevalence may be

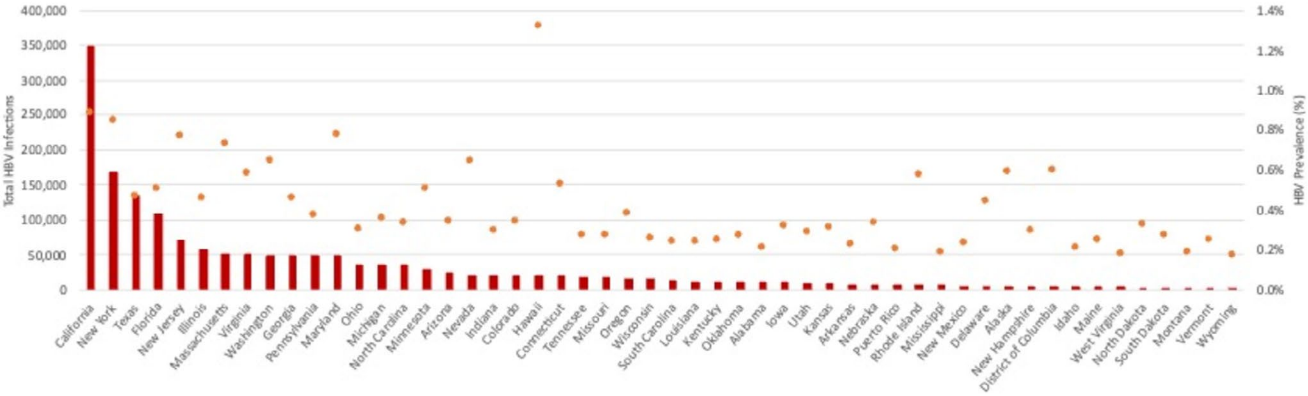

FIGURE 1 | The prevalence of HBV by US State and Territory, 2021.

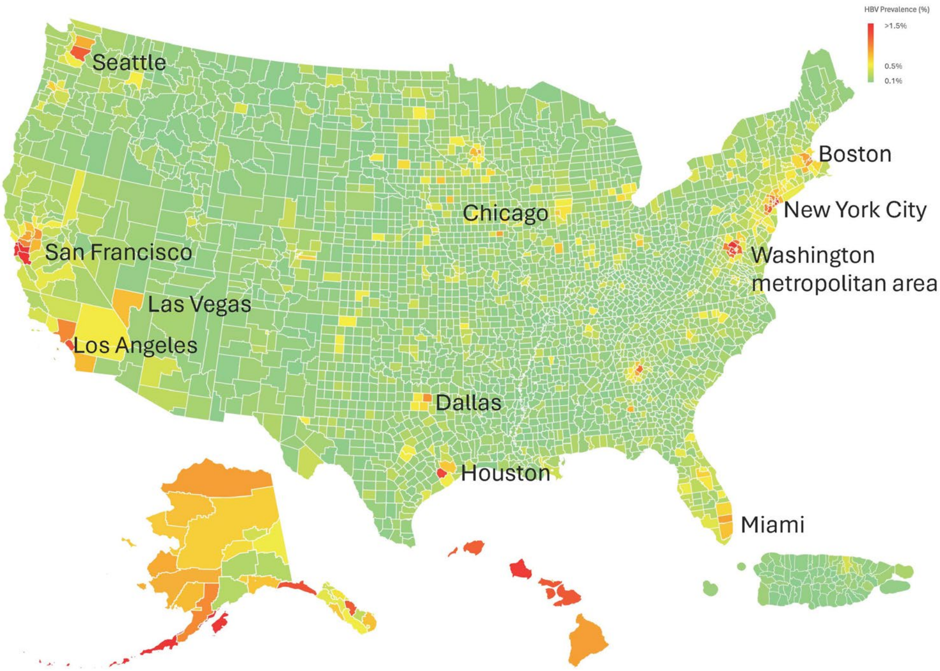

FIGURE 2 | The prevalence of HBV by US County (%), 2021.

TABLE 2 | Ten counties in the US with the highest number of hepatitis B infections, 2021.

Locality	Total HBV infections (UI)	HBV prevalence (UI)
Los Angeles County, California	96,730 (54,820–190,560)	1.0% (0.6%–1.9%)
Queens County, New York	42,560 (24,120–81,270)	1.8% (1.0%–3.4%)
Orange County, California	38,580 (24,570–73,530)	1.2% (0.8%–2.3%)
Santa Clara County, California	37,780 (25,570–70,370)	2.0% (1.3%–3.7%)
Kings County, New York	34,500 (19,000–65,880)	1.3% (0.7%–2.5%)
Harris County, Texas	33,030 (17,660–66,670)	0.7% (0.4%–1.4%)
Cook County, Illinois	30,990 (16,360–62,750)	0.6% (0.3%–1.2%)
King County, Washington	26,410 (16,610–49,890)	1.2% (0.7%–2.2%)
Alameda County, California	26,250 (15,980–53,660)	1.6% (1.0%–3.2%)
San Diego County, California	25,000 (12,420–52,810)	0.8% (0.4%–1.6%)
Miami-Dade County, Florida	19,440 (7440–48,930)	0.7% (0.3%–1.8%)

Abbreviation: HBV, Hepatitis B Virus (Hepatitis B surface antigen positive).

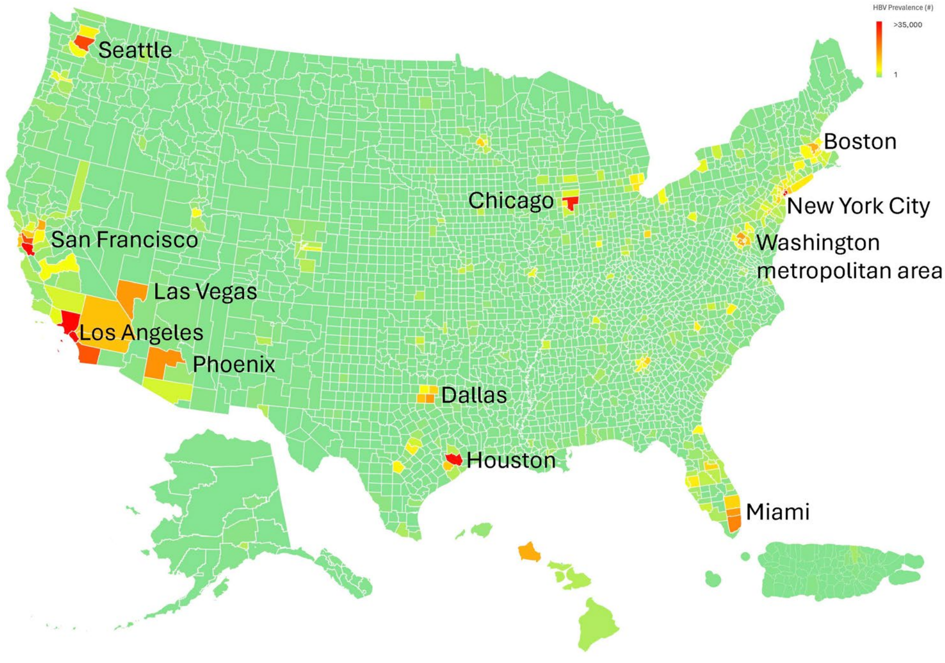

FIGURE 3 | The prevalence of HBV by US County (#), 2021.

higher among the foreign-born population than the general population in the country of birth if their path of migration included additional risks of contracting the diseases, such as some groups of refugees.

While the country of birth models utilised the best available data for the national level, this approach may obscure regional variations. This could be more impactful in an immigration analysis as once a migrant community is established it is common for others from the same region of birth to migrate to the same localised destination thus resulting in over- or under-estimates at the local level. The use of regional averages, while necessary when data are only provided by region, introduces additional limitations particularly when being applied to migrant populations from countries for which a country-specific model did not exist. This can lead to over- or under-estimates depending on how different these countries are when compared to the region as a whole. We attempted to minimalize this impact by having country models available for 99.4% of country level data; however, uncertainty remains.

While this analysis assumed that the foreign-born population in the US had the same non-hepatic mortality rate as the rest of the US population, there is the possibility that foreign-born individuals may have more limited access to healthcare which may result in higher all-cause mortality rates. This would lead to a lower total HBV prevalence among the foreign-born population. While the national US HBV vaccination programs were applied uniformly to everyone living in the US, the foreign-born population living in the US could have higher, due to targeted interventions, or lower, as a result of limited access to healthcare, vaccination coverage than the general population.

Despite these limitations, we believe that these state and county level estimates are far more accurate than previous publications, as the current modelling approach included most of the important factors associated with HBV prevalence in the US, namely age at entry and immunity status.

By providing localised prevalence estimates, local and state agencies can better understand the burden of HBV in their area, as well as have the first input for their cascades of care. The local data shows which counties, at the state and national level, have the highest prevalence of HBV and thus where efforts to screen, treat, and vaccinate should be focused. Through the reporting of the country of birth at the localised level, planners can understand which communities they need to ensure they have strong relationships with and culturally appropriate outreach materials for, thus increasing the probability of the success of these campaigns. By increasing the number of people living with HBV who are on treatment, they will live longer and healthier lives, and by vaccinating those within the community, the incidence of HBV can become a problem of the past.

Author Contributions

Devin Razavi-Shearer and Ivane Gamkrelidze conducted the immigration analysis. Devin Razavi-Shearer, Ivane Gamkrelidze, Homie Razavi, and Carolyn Wallace prepared the first draft. Samantha Hall, Devin Razavi-Shearer, Kathryn Razavi-Shearer, and Alexis Voeller populated and calibrated the underlying HBV models. Devin Razavi-Shearer, Homie Razavi, and Ivane Gamkrelidze verified all underlying data. Kathryn Razavi-Shearer created state-level figures and tables in Appendix S1. All authors had full access to all the data and accept responsibility for the publication. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Conflicts of Interest

Ivane Gamkrelidze, Samantha Hall, Homie Razavi, Devin Razavi-Shearer, Kathryn Razavi-Shearer, and Alexis Voeller: Employees—CDA Foundation. CDA Foundation has received research funding from AbbVie, Akero, Gilead, Merck, HepQuant unrelated to this work in the last 36 months. Robert Gish is a consultant for Gilead, Quest, LabCorp, and Diasorin.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Flow of disease progression of HBV. **Figure S2:** Top 20 communities of HBV-positive immigrants in the US, 2021. **Table S1:** Annual disease progression rates of HBV infection, %. **Table S2:** Annual disease progression rates of HBV infection in Sub-Saharan Africa, %. **Table S3:** Mother-to-child transmission rates of HBV, %. **Table S4:** HBV published prevalence. **Table S5:** Countries by GBD Region. **Table S6:** ACS Regions Mapped to GBD regions or Continents. **Table S7:** HBV Infection among foreign-born individuals in the US by country of birth, 2021.