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Disparities in hepatitis A virus (HAV) vaccination coverage among adult travelers to intermediate or high-risk countries: The role of birthplace and race/ethnicity

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ABSTRACT

Background: While the hepatitis A virus (HAV) vaccine is recommended for United States (US) travelers to endemic regions, vaccination rates are lower among non-US-born adults and some racial minority groups.
Purpose: We aimed to examine the relationship between birthplace, race and their interaction as predictors of self-reported HAV vaccination among adult travelers to high-risk countries (HRCs) through analysis of the National Health Interview Survey (NHIS), 2012–2015.
Methods: The study included 36,872 US adult participants in the 2012–2015 NHIS who traveled to countries where HAV is endemic. The main outcome was self-reported HAV vaccination (≥2 doses). Complex survey methods were applied to all models to provide statistical estimates that were representative of US adults. Multivariable logistic regression models adjusting for demographic, socioeconomic, medical, and access-to-care characteristics were fitted to examine the association between birthplace, race, race-by-birthplace (for interaction) and vaccination status.
Results: For adult travelers to HRCs, the adjusted odds ratio (AOR) of HAV vaccination was lower for non-US-born compared to US-born adults, AOR 0.86 (95% CI; 0.76, 0.98). For Hispanics, the AOR of HAV vaccination was 0.80 (95% CI; 0.70, 0.91) as compared to non-Hispanic-Whites. Furthermore, a significant qualitative interaction between birthplace and race was found (P-value 0.0005). Among non-Hispanic Blacks, the adjusted odds of HAV vaccination for non-US-born adults were 1.35 (95% CI; 1.06, 1.72) times the odds for US-born adults. In contrast, the AORs of HAV vaccination of non-US-born versus US-born adults were 36% (95% CI; 17%, 51%) and 30% (95% CI; 12%, 44%), lower for Asians and Hispanics, respectively.
Conclusions: The association between birthplace and HAV vaccination status differs by race among travelers to HRCs, with US-born non-Hispanic Black and non-US-born Asian and Hispanic adults having lower odds of vaccination. Health care resources should be focused on these target populations to improve travel vaccination compliance.

1. Background

Hepatitis A is a viral liver infection caused by exposure to the hepatitis A virus (HAV) and can cause acute inflammation of the liver. The risk of developing hepatitis A, and in turn, being hospitalized or dying due to hepatitis A, increases with age [1]. Additionally, HAV co-infection with either hepatitis B or hepatitis C can result in severe morbidity [2]. HAV is primarily transmitted through the fecal-oral route but may also be spread *via* person-to-person contact or from ingestion of HAV-contaminated food or water [3]. The risk of hepatitis A is associated with conditions such as lack of clean water, poor sanitation and inadequate personal hygiene [4]. Global regions with an elevated risk of HAV infections

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include low- and middle-income countries (LMICs) where running water and proper waste disposal are lacking.

Groups considered at risk for HAV infection include international travelers to or in close contact with an international adoptee from areas of high or intermediate HAV endemicity, men who have sex with men (MSM), users of injection and non-injection drugs, persons with chronic liver disease (e.g. hepatitis B or hepatitis C), clotting factor disorders, or those who work with HAV in the laboratory setting [5]. Most recently, widespread person-to-person HAV outbreaks have occurred in persons experiencing homelessness [6].

While the overall prevalence of hepatitis A in the United States (US) has decreased in the last two decades, between 2014 and 2015, the total number of confirmed cases has increased by 12.2% [4]. Aside from the potential medical complications, hepatitis A infection can be a source of healthcare and economic burdens to infected patients, since 35% of individuals with acute HAV infection get hospitalized [7]. Adults hospitalized with HAV can lose an average of 33 work-days, while those with outpatient visits miss sixteen work-days on average [7].

About 13% of the population in the US was born outside of its borders [8]. Immigrants and their families frequently travel back to their home country to visit friends and relatives (VFRs) [9,10]. As a result, non-US-born individuals are at higher risk of travel-related infections and their associated morbidity and mortality risks. With that in mind, the majority of non-US-born do not readily seek recommended pre-travel medical care such as vaccinations against hepatitis infections [9]. Vaccination against HAV is recommended as preexposure prophylaxis for all travelers from the age of 6 months and older when traveling internationally to an area of high or intermediate HAV endemicity [11].

Previous studies have recorded disparities for certain vaccinations among non-US-born individuals in the US. Analysis of two US national health surveys found disparities in vaccination levels of non-US-born children and children of non-US-born mothers for certain vaccines such as hepatitis B [10]; this may be due to many factors including different childhood vaccination practices in non-US countries, lack of vaccination awareness for travelers, and language barriers. A detailed analysis of the National Health Interview Survey (NHIS) data from 2012 found that the unadjusted vaccination coverage was higher among US-born respondents than non-US-born respondents. The adjusted results still showed that compared to US-born adults, non-US-born adults were less likely to receive a pneumococcal or tetanus-containing vaccine [10].

Multiple studies have shown racial and ethnic disparities in hepatitis A vaccination coverage in the US. Even after adjusting for socioeconomic characteristics, those racial and ethnic disparities persisted [12]. As such, vaccination coverage was generally lower for non-Hispanic blacks, Hispanics, and Asians when compared to non-Hispanic whites [12]. At the same time, non-US-born individuals face many disparities in access and awareness to vaccinations, including those related to hepatitis A. There is evidence of vaccination disparities when assessing birthplace and race/ethnicity independently but there is a lack of data on their combined impacts [10,13]. Meanwhile, no study to date has investigated the combined effects of birthplace and race/ethnicity on HAV vaccination coverage in the US. Given the differences in race/ethnicity distributions in US- and non-US-born individuals, the combined effect of these demographic variables on vaccination status is of public health interest. Detailed analysis of the role of birthplace and race/ethnicity in relation to HAV vaccination coverage can guide public health officials to tailor vaccine education and outreach efforts to specific at-risk populations. While the ultimate clinical endpoint is HAV immunity as measured by anti-HAV seropositivity, self-reported HAV vaccination has been observed to be a relatively accurate indicator of serological status for HAV protection [14].

In this study, we intended to use nationally representative data to evaluate the relationship between birthplace, race/ethnicity and hepatitis A vaccination for US adult travelers to LMICs with high or intermediate HAV endemicity. Our study aimed to examine whether birthplace (*i.e.*, US-born versus non-US-born), is associated with hepatitis A vaccination status amongst adult travelers to LMICs. Furthermore, we examined whether birthplace modified the relationship between race/ethnicity and reported HAV vaccination status for adult travelers to LMICs.

2. Methods

2.1. Study design and data source

This study was a cross-sectional analysis of US adults using publicly available data from the 2012–2015 NHIS. The NHIS is a nationally representative health survey of the civilian, non-institutionalized US population using a complex multistage sampling design. This in-person survey is conducted annually by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). The survey is administrated by both computer-assisted personal interviewing techniques and in-person interviews. Additional phone calls to participants were allowed in case of any missing survey information. The unconditional response rates for adult participants in NHIS are 61.20%, 61.20%, 58.90% and 55.20% for 2012, 2013, 2014 and 2015, respectively [15]. For this analysis, we merged sample adult and person datasets to construct the study's analytic sample.

2.2. Study population

The initial study population included all adult participants in the 2012–2015 NHIS who traveled to high or intermediate HAV endemic countries. Travel status was determined *via* responses to the following NHIS question, "Have you ever traveled outside of the United States to countries other than Europe, Japan, Australia, New Zealand or Canada, since 1995?" Aside from those with missing values, we excluded adults whose answer was either (a) refuse, (b) not ascertained, or (c) do not know.

2.3. Measures

The primary outcome was self-reported HAV vaccination status. This status was determined by two survey questions drawn from the sample adult core (original form): "The hepatitis A vaccine is given as a two-dose series routinely to some children stating at 1 year of age, and to some adults and people who travel outside the United States. Although it can be given as a combination vaccine with hepatitis B, it is different from the hepatitis B shot, and has only been available since 1995. Have you ever received the hepatitis A vaccine?" Those who answered yes on the first question were then asked about the number of hepatitis A shots received. After applying exclusion criteria, the final form of the outcome variable included two responses, yes, for those who reported receiving two or more doses of the HAV vaccine, or, no, for participants with less than two doses.

The exposure variables for this study were race/ethnicity and birthplace. The final classification of race/ethnicity included the following five groups (1) White non-Hispanic, (2) Black non-Hispanic, (3) Hispanic, (4) Asian and (5) Other. All adult participants were also asked to report their birthplace. The original form survey question asked is "[was person] born in the United States?" The responses were recorded as either US-born or non-US-born.

Confounder selection was based on both *a priori* knowledge, from the literature, and theoretical rationale. We excluded all participants with missing values on exposure, outcomes or any of the covariates included in the study.

2.4. Statistical analysis

To yield results that are representative of the non-institutionalized US population, we applied complex survey methods in all statistical analyses. The use of complex survey methods allowed for the correction of NHIS selection probabilities due to oversampling of some racial minority groups [9]. All sample weights were provided by the NCHS. Taylor series linearization method was used for variance estimation. Missing values for all variance computation were assumed to be not missing completely at random. Two-tailed tests were performed, and P-values less than 0.05 were considered indicative of statistical significance. We also reported 95th percentile confidence intervals (95% CI) for all point estimates. All complex survey procedures were performed using the SAS software, version 9.4 (SAS Institute).

We estimated the overall prevalence of self-reported HAV vaccination within all categories of US travelers' demographics and characteristics. We also calculated the Relative Standard Error (RSE) for all prevalence estimates. As per the NCHS recommendations, all HAV prevalence results with RSE values between 20% and 30% were reported with a warning while those greater than 30% were not reported. In a bivariate analysis, we stratified the overall prevalence estimates by birthplace for all travelers' demographics and characteristics. Rao-Scott Chi-square tests were used to examine the difference in vaccination prevalence within each category of participants' demographics and characteristics. In the case of bivariate analysis, Rao-Scott Chi-square tests were used to evaluate the null hypothesis of no association between each demographic/characteristic level and birthplace status.

Both unadjusted and adjusted logistic regression models were used to examine the association between birthplace and self-reported HAV vaccination status. Multivariable logistic regression models adjusting for age, gender, education, region of residence, survey year, health insurance access, Chronic Liver Disease (CLD), influenza vaccination, marital status, employment status and self-reported health status were fitted to examine the associations between birthplace, race/ethnicity, race/ethnicity-by-birthplace (*i.e.*, for interaction) and self-reported HAV vaccination status.

3. Results

After excluding those with any missing values, the study's analytic sample included 36,872 adult participants in the NHIS 2012–2015 who traveled to an intermediate or high HAV endemic country. Overall, 27.90% of all travelers were non-US-born, 62.62% White non-Hispanics, 19.24% Hispanics, 7.68% Black non-Hispanics, 9.77% Asians and 0.69% identified as Other. The mean and median ages for our sample were 47.75 and 47.07 years, respectively. All but 9.07% of all participants had a high school diploma, and 73.87% had some college education or above. The majority of the study sample were married (68.63%), employed (75.75%) and insured (87.97%). An estimated 7.53% of all travelers reported having fair or poor overall health status. We found the prevalence of CLD to be 1.07%, while influenza vaccination coverage was 42.32%.

All study sample characteristics, except gender and CLD status, were significantly different (*i.e.*, P-value < 0.05) for US-born versus non-US-born travelers (Table 1). Notably, White non-Hispanics made 80.32% of US-born adults and only 16.86% of non-US-born travelers. In contrast, the prevalence of Hispanics was 44.54% and 9.45% for non-US-born and US-born travelers, respectively. Of all US-born and non-US-born travelers, 30.29% and 26.67%, respectively were in the 18–34 year age range. Compared to US-born participants, higher proportions of non-US-born travelers identified as Asians (2.25% vs. 29.21%), had high school education or less (19.76% vs. 42.59%), reported fair or poor health status (6.25% vs. 10.85%) or lived in the Western region of the US (26.15% vs. 35.66%). The weighted prevalence of HAV vaccination (≥2 doses) in the total population of adults who traveled to an intermediate or high HAV endemic country was estimated to be 16.20% (95% CI; 15.68%, 16.72%). Amongst non-US-born travelers, the highest HAV vaccination coverage of 23.33% was observed for travelers in the 18–34 years of age range. Compared to those 18–34 years of age, a decrease in HAV vaccination prevalence was associated with being 35 years of age or older. When compared to White non-Hispanics, Hispanics had significantly lower HAV vaccination prevalence (17.03% vs. 12.02%; P-value <0.0001), while a larger proportion of Asians reported receiving the HAV vaccination (17.03% vs. 19.00% P-value 0.04). Overall, HAV vaccination rates were highest amongst residents of the Western region of the US (Table 2).

Decreases in HAV vaccination prevalence were significantly associated with being 35 years of age or older, identifying as Hispanic, attaining high school education or less, being widowed, separated or divorced, not being employed in the past twelve months, reporting poor or fair health status, and not receiving the influenza vaccination when compared to their respective reference levels amongst all, US-born and non-US-born travelers (Table 2). Compared to White non-Hispanics, Asians reported significantly higher HAV vaccination rates only amongst US-born travelers, while Hispanics had lower HAV vaccination for non-US-Born adults. Not having access to health insurance was a significant predictor of lower HAV vaccination amongst only non-US-born.

US-born participants had significantly higher unadjusted HAV vaccination rates when compared to non-US-born adults (17.40% vs. 13.11%; p-value <0.0001). Non-US-born male and female adults had significantly lower HAV vaccination rates when compared to their US-born counterparts. US-born Asians and Hispanics had a significantly higher vaccination rate compared to non-US-born Asians and Hispanics (30.18% vs. 16.78%; $p < 0.0001$ and 18.18% vs. 8.64%; $p < 0.0001$), respectively. Non-US-born participants had significantly lower HAV vaccination rates when compared to US-born travelers in all age groups, amongst those with less than high school education, and adults with a college degree or above. US-born adults had higher HAV vaccination rates for all categories of marital status, employment status, self-reported health status, access to health insurance and influenza vaccination status. Non-US-born travelers without CLD, and residents of the Midwest, Southern or Western regions of the US reported significantly lower HAV vaccination rates compared to US-born travelers (Table 2).

The association between race/ethnicity and HAV vaccination was statistically significant in all adjusted models (P-value <0.05). The adjusted Odds Ratio (AOR) of HAV vaccination was lower for non-US-born adults compared to US-born, AOR 0.86 (95% CI; 0.76, 0.98) (data not shown). We found a significant qualitative interaction between birthplace and race/ethnicity (P-value 0.0005). In the interaction model assessing the effect of birthplace on the association between HAV vaccination and race/ethnicity, US-born Asians had a higher AOR of vaccination 1.38 (95% CI; 1.07, 1.76) while non-US-born Hispanics had a lower AOR 0.63 (95% CI; 0.50, 0.81), both in comparison to their non-Hispanic White counterparts (Table 3). Additionally, there were significant findings in the interaction model assessing the effect of race/ethnicity on the association between HAV vaccination and birthplace (Table 4). Among non-Hispanic Blacks, the adjusted odds of HAV vaccination for non-US-born adults were 1.35 (95% CI; 1.06, 1.72) times the odds for US-born adults. In contrast, the AORs of vaccination of non-US-born versus US-born adults were 36% (95% CI; 17%,

Table 1
Characteristics of study sample by birthplace for US adults who traveled[†] to intermediate or high hepatitis A virus endemicity country, National Health Interview Survey, 2012–2015 (n = 36,872).

Characteristics	US adult travelers			P-value[*]
	All n (%)	US-born n (%)	Non-US-born n (%)	
Total	36,872	25,895 (72.10)	10,977 (27.90)	
Gender				0.5142
Male	17,396 (50.43)	12,188 (50.56)	5208 (50.07)	
Female	19,476 (49.58)	13,707 (49.44)	5769 (49.93)	
Age group, years				<0.0001
18–34	10,611 (29.28)	7544 (30.29)	3067 (26.67)	
35–49	10,438 (29.55)	6637 (26.98)	3801 (36.21)	
50–64	9327 (26.35)	6804 (26.94)	2523 (24.81)	
65+	6496 (14.82)	4910 (15.79)	1586 (12.30)	
Race/ethnicity				<0.0001
White non-Hispanic	21,494 (62.62)	20,072 (80.32)	1422 (16.86)	
Black non-Hispanic	3255 (7.68)	2266 (7.22)	989 (8.88)	
Asian	3907 (9.77)	671 (2.25)	3236 (29.21)	
Hispanic	7903 (19.24)	2626 (9.45)	5277 (44.54)	
Other	313 (0.69)	260 (0.76)	53 (0.50)	
Education				<0.0001
<High school	3812 (9.07)	949 (3.52)	2863 (23.39)	
High school	6125 (17.07)	4113 (16.24)	2012 (19.20)	
Some college	10,731 (29.23)	8513 (32.75)	2218 (20.13)	
College or above	16,204 (44.64)	12,320 (47.48)	3884 (37.28)	
Marital status				<0.0001
Married[‡]	21,516 (68.63)	14,680 (67.17)	6836 (72.40)	
Widowed, separated or divorced	7441 (12.95)	5358 (13.09)	2083 (12.58)	
Single	7915 (18.42)	5857 (19.74)	2058 (15.02)	
Employment status in the past 12 months				<0.0001
Employed	27,346 (75.75)	19,558 (77.06)	7788 (72.37)	
Not employed[§]	9526 (24.25)	6337 (22.94)	3189 (27.63)	
Self reported health status				<0.0001
Poor/fair	3076 (7.53)	1780 (6.25)	1296 (10.85)	
Good, very good or excellent	33,796 (92.47)	24,115 (93.75)	9681 (89.15)	
Health insurance				<0.0001
Yes	31,989 (87.97)	23,757 (92.26)	8232 (76.88)	
No	4883 (12.03)	2138 (7.74)	2745 (23.12)	
Influenza vaccination				<0.0001
Yes	15,716 (42.32)	11,757 (44.60)	3959 (36.45)	
No	21,156 (57.68)	14,138 (55.40)	7018 (63.55)	
Chronic liver disease				0.9649
Yes	422 (1.07)	288 (1.07)	134 (1.08)	
No	36,450 (98.93)	25,607 (98.93)	10,843 (98.92)	
Survey year				0.0060
2012	8990 (23.99)	6298 (24.55)	2692 (22.55)	
2013	9162 (24.79)	6299 (24.52)	2863 (25.49)	
2014	9694 (25.18)	6865 (24.85)	2829 (26.02)	
2015	9026 (26.04)	6433 (26.08)	2593 (25.93)	
Region of residence				<0.0001
Northeast	5832 (16.71)	4000 (16.05)	1832 (18.42)	
Midwest	6827 (19.92)	5543 (23.16)	1284 (11.56)	
South	12,075 (34.56)	8442 (34.64)	3633 (34.35)	
West	12,138 (28.81)	7910 (26.15)	4228 (35.66)	

n = number of adults in the sample, % = weighted sample proportion, totals might not add up to 100% due to rounding, US = United States, CI = confidence interval.
[†] Adults who ever traveled outside of the United States to countries other than Europe, Japan, Australia, New Zealand or Canada, since 1995.
[‡] Including those living with a partner.
[§] Including those who never had a job.
[*] Rao-Scott Chi Square P-value for the difference between non-US-born and US-born adults.

51%) and 30% (95% CI; 12%, 44%), lower for Asians and Hispanics, respectively.

4. Discussion

HAV vaccination is highly effective and can reduce the burden of disease for at-risk US residents traveling to endemic countries, but disparities in vaccination coverage continue to exist in the general population. We sought to assess the association of being non-US-born and HAV vaccination coverage among adult travelers to HAV endemic countries with a particular interest in the interaction between birthplace and race/ethnicity. We observed significant differences by birthplace in the distribution of education (surrogate for health literacy), age (routine vaccination for children in high incidence states during the late 1990s), health insurance

Table 2
Reported HAV vaccination prevalence by birthplace among US adults who traveled[†] to intermediate or high hepatitis A virus endemicity country, National Health Interview Survey (NHIS), 2012–2015.

Characteristics	All (n = 36,872) % (95% CI)	US-born (n = 25,895) % (95% CI)	Non-US-born (n = 10,977) % (95% CI)	P-value[**]
Total	16.20 (15.68–16.72)	17.40 (16.78–18.02)	13.11 (12.15–14.06)	<0.0001
Gender				
Male[¶]	16.59 (15.86–17.32)	18.13 (17.22–19.05)	12.57 (11.30–13.85)	<0.0001
Female	15.81 (15.07–16.54)	16.65 (15.79–17.51)*	13.64 (12.36–14.92)	0.0001
Age group, years				
18–34[¶]	23.33 (22.13–24.52)	25.39 (23.97–26.81)	17.26 (15.33–19.19)	<0.0001
35–49	15.13 (14.22–16.05)*	15.84 (14.67–17.01)*	13.77 (12.21–15.34)*	0.0462
50–64	12.62 (11.78–13.47)*	13.50 (12.48–14.52)*	10.15 (8.78–11.53)*	0.0002
65+	10.63 (9.55–11.71)*	11.40 (10.11–12.69)*	8.08 (6.19–9.97)*	0.0083
Race/ethnicity				
White non-Hispanic[¶]	17.03 (16.34–17.73)	17.09 (16.37–17.81)	16.34 (13.76–18.92)	0.5854
Black non-Hispanic	15.51 (13.58–17.45)	14.80 (12.65–16.95)	17.00 (13.93–20.07)	0.1780
Asian	19.00 (17.23–20.78)*	30.18 (25.42–34.95)*	16.78 (14.98–18.58)	<0.0001
Hispanic	12.02 (11.01–13.03)*	18.18 (16.11–20.26)	8.64 (7.51–9.77)*	<0.0001
Other	25.58 (19.02–32.14)*	27.40 (20.03–34.76)*	N/A	N/A
Education				
<High school	8.17 (6.81–9.52)*	13.44 (10.16–16.71)*	6.12 (4.83–7.40)*	<0.0001
High school	10.09 (9.06–11.11)*	10.08 (8.83–11.34)*	10.09 (8.41–11.78)*	0.9915
Some college	16.92 (15.83–18.02)*	17.31 (16.08–18.53)*	15.31 (13.07–17.56)	0.1325
College or above[¶]	19.70 (18.92–20.48)	20.26 (19.34–21.18)	17.85 (16.15–19.56)	0.0212
Marital status				
Married[‡,¶]	15.32 (14.71–15.93)	16.39 (15.63–17.16)	12.74 (11.67–13.81)	<0.0001
Widowed, separated or divorced	12.13 (11.12–13.13)*	12.97 (11.73–14.21)*	9.86 (8.13–11.60)*	0.0078
Single	22.36 (20.82–23.90)*	23.77 (21.98–25.55)*	17.59 (15.16–20.02)*	<0.0001
Employment status in the past 12 months				
Employed[¶]	17.04 (16.43–17.65)	18.17 (17.45–18.90)	13.93 (12.82–15.04)	<0.0001
Not employed[§]	13.58 (12.65–14.51)*	14.81 (13.57–16.05)*	10.94 (9.43–12.46)*	0.0004
Self reported health status				
Poor/fair	11.81 (10.38–13.25)*	13.62 (11.36–15.88)*	9.12 (6.92–11.32)*	0.0132
Good, very good or excellent[¶]	16.56 (16.01–17.11)	17.65 (17.00–18.30)	13.59 (12.56–14.62)	<0.0001
Health insurance				
Yes[¶]	16.72 (16.15–17.28)	17.52 (16.86–18.19)	14.21 (13.16–15.26)	<0.0001
No	12.45 (11.08–13.82)*	15.92 (13.62–18.23)	9.44 (7.81–11.07)*	<0.0001
Influenza vaccination				
Yes[¶]	18.78 (17.96–19.61)	19.88 (18.87–20.89)	15.31 (13.67–16.95)	<0.0001
No	14.31 (13.66–14.96)*	15.40 (14.59–16.22)*	11.84 (10.80–12.88)*	<0.0001
Chronic liver disease				
Yes[¶]	19.46 (14.51–24.42)	21.24 (14.88–27.61)	14.90 (7.54–22.26)[***]	0.1550
No	16.17 (15.65–16.69)	17.36 (16.74–17.98)	13.09 (12.13–14.04)	<0.0001
Region of residence				
Northeast[¶]	12.65 (11.86–13.43)	12.90 (11.98–13.83)	12.06 (9.94–14.19)	0.5240
Midwest	15.79 (14.66–16.93)*	16.31 (15.16–17.46)*	13.13 (10.84–15.42)	0.0098
South	15.02 (14.06–15.98)*	15.98 (14.72–17.24)*	12.52 (10.92–14.13)	0.0024
West	19.97 (18.92–21.02)*	23.01 (21.77–24.26)*	14.20 (12.47–15.93)	<0.0001

N/A: Relative Standard Error greater than 30%.
% = Weighted sample proportion, US = United States, CI = confidence interval.
[†] Adults who ever traveled outside of the United States to countries other than Europe, Japan, Australia, New Zealand or Canada, since 1995.
[‡] Including those living with a partner.
[§] Including those who never had a job.
[¶] Declared reference.
[*] Significant difference between each characteristic level within place of birth status (all, US-born or foreign-born) and declared reference (Rao-Scott Chi Square, P-value < 0.05).
[**] Rao-Scott Chi Square P-value for the difference between foreign-born and US-born adults.
[***] Warning, Relative Standard Error between 20% and 30%.

status (surrogate for healthcare access), and portion living in Western states (routine vaccination for children in Western states with high HAV infection incidence), which could be drivers of the association of non-US-born birthplace and lower HAV vaccination rates [16,17]. Despite these differences in clinically significant covariates, the main results of the multivariate models remained significant after controlling for all significant variables. Our main findings demonstrate lower odds of HAV vaccination among non-US-born individuals as compared to US-born individuals after adjusting for all previously described covariates that could be potential confounders. Most importantly, the association between birthplace and HAV vaccination coverage differed by race/ethnicity among travelers to endemic countries. We observed that US-born Black, non-US-born Asian, and non-US-born Hispanic adults had lower odds of HAV vaccination when compared to their counterparts of the opposite birthplace. We believe US-born Black adults have lower odds of HAV vaccination than non-US-born Black adults due to persistent healthcare racial disparities and health inequity

Table 3
Association between HAV vaccination status and race/ethnicity among US and Non-US born adults who traveled to intermediate or high hepatitis A virus endemicity country, National Health Interview Survey, 2012–2015.

Race/ethnicity[†]	US born (n = 25,895)		Non-US born (n = 10,977)	
	OR	(95% CI)	OR	(95% CI)
White non-Hispanic	Ref.	Ref.	Ref.	Ref.
Black non-Hispanic	0.88	(0.72–1.06)	1.2	(0.92–1.56)
Asian	**1.38**	**(1.07–1.76)**	0.89	(0.70–1.13)
Hispanic	0.89	(0.75–1.05)	**0.63**	**(0.50–0.81)**
Other	1.53	(1.04–2.27)	1.06	(0.41–2.70)

Bold = significant association (P < 0.05), OR = odds ratio, US = United States, CI = confidence interval, Ref. = Reference group.
[†] Model adjusted for gender, age, education, marital status, employment status, self-reported health status, insurance, chronic liver disease, influenza vaccination status, survey year and region of residence.

Table 4
Adjusted Odds Ratios for HAV Vaccination Status by Race/Ethnicity for Non-US-Born versus US-Born Adults who Traveled to Intermediate or High Hepatitis A virus endemicity country, National Health Interview Survey, 2012–2015 (n = 36,872).

Race/ethnicity	Adjusted[†]		P-value
	OR	(95% CI)	
White non-Hispanic	0.99	(0.80–1.21)	0.8823
Black non-Hispanic	**1.35**	**(1.06–1.72)**	**0.0168**
Asian	**0.64**	**(0.49–0.83)**	**0.0007**
Hispanic	**0.70**	**(0.56–0.88)**	**0.0019**
Other	0.68	(0.26–1.76)	0.4257

Bold = significant association (P < 0.05), OR = odds ratio, US = United States, CI = confidence interval.
[†] Model adjusted for gender, age, education, marital status, employment status, self-reported health status, insurance, chronic liver disease, influenza vaccination status, survey year and region of residence.

for those in the US, which include both poor healthcare literacy and lack access to healthcare, as opposed to those born outside and those immigrating into the US [18].

Our results were consistent with previous studies that evaluated similar associations. Other studies have noted the lower likelihood of vaccination coverage among non-US-born as well as racial and ethnic minorities [10,12,19,20]. Our study has shown results relating to disparities in HAV vaccination coverage that can inform public health and clinical practice. Our results add to the knowledge of public health programs and clinicians to target these high-risk groups to help improve travel vaccination compliance. We continue to find more instances where US-born Black adults have healthcare or health access disparities; in our study, we recognize this compared to non-US-born Black adults. There is also a growing non-US-born Asian population that continues to be at high risk of HAV infection if not vaccinated when traveling back to their home country. Knowledge of these observed high-risk groups can encourage proper screening and discussion initiated by the clinician to routinely assess travel plans and appropriate pretravel medical care, including vaccinations. The location where medical assessments can occur are expanding from traditional settings such as clinics or physician's offices to now include community pharmacies that are equipped and able to administer various vaccinations [21,22].

The current climate related to HAV infections in the US makes the results of our study more timely to help inform public health practices. Outbreaks of HAV associated with illicit drug use and homelessness have been reported throughout the US during recent years [6,23]. As reported recently by Foster et al., cases of HAV infections increased almost 300% (approximately 15,000 reports) in 2016–2018 compared to 2013–2015 [24]. This is mostly driven by outbreaks in persons reporting illicit drug use and homelessness but also it includes outbreaks from contaminated food and MSM. The recent increase in HAV outbreaks is in vast contrast to the previous decline (approximately 95%) in rates of HAV infection during 1996–2011. This recent data combined with the longitudinal data from 1999 to 2012 noting a decreasing HAV immunity over time among US adults, exposes the high vulnerability in the US population of HAV infection [25]. Resurgence of vaccine-preventable infections such as HAV in an escalating non-immune population reaffirms the crucial need to adhere to immunization recommendations and vaccinate those groups at risk. Our study results add to this notion and help inform public health practice by analyzing the combined effect of birthplace and race/ethnicity and observing the lack of vaccination in both US-born and non-US-born racial/ethnic groups.

In addition to implications for direct clinical care and public health practice, our results can inform reporting and analysis of vaccination statistics. For example, the CDC publishes surveillance data on vaccination coverage among US adult populations annually [26]. For HAV vaccination, the vaccination coverage is stratified to assess differences in at-risk groups (e.g., travelers) and racial/ethnic groups. The data shows that HAV vaccination coverage (at least two doses) is lower for Black and Hispanic adults compared to White adults.

In contrast, Asian adults have a significantly higher prevalence of HAV vaccination compared to White adults (vaccination coverage difference of +5.1%, p < 0.05 by Rao-Scott Chi-Square for comparison to White as the reference group). While this data is useful, it might be misleading. In our sample, >80% of Asian adults who travel to HAV endemic countries were non-US-born, and as noted in our results, there was a significantly lower odds ratio of HAV vaccination among non-US-born Asian adults as compared to US-born Asian adults.

Our results note the differences in non-US-born versus US-born minority groups regarding HAV vaccination coverage. Assessment of vaccination coverage not only by birthplace and race/ethnicity independently, but also the interaction of birthplace with race/ethnicity can bring value to nationally reported vaccination coverage statistics. Modification of our vaccination report structure will help inform public health officials and clinicians throughout the country to target healthcare resources to these high-risk groups.

The results of our study need to be interpreted in the context of its limitations. First, the data utilized in our study relies on self-reported vaccination receipt, which is not validated by medical records or biological specimens measuring seropositivity. Although various measures of immunity exist, anti-HAV seropositivity is the most definitive measure; we used self-reported HAV vaccination history as a predictor marker for immunity. Denniston et al observed that self-reported vaccination status had a relatively high negative predictive value for serological results (*i.e.*, predictive of those non-immune and at risk for HAV infection) [14]. Additionally, in the multivariate logistic regression analysis, race/ethnicity and place of birth, as well as age, education, and income were sig-

nificantly associated with the categorical agreement between self-reported vaccination status and serological results. The former two covariates are of importance given their primary role as predictors of interest in our study. Secondly, given this is a cross-sectional study in which our outcome and exposure variables were obtained at the same time, temporality and therefore, causality cannot be inferred. It should be noted though that our primary exposure and primary effect modifier are both demographic data points assigned at birth, so it can be generally assumed that birthplace and race/ethnicity preceded our outcome of vaccination coverage. Lastly, this data is at risk for inaccuracies due to recall bias or the survey respondents lack knowledge about one's vaccination history or status. The potential for recall bias is also present when considering that the surveys were performed from 2012 to 2015, which may have been over a decade since the time of vaccination (travel since 1995). Further, lower education attainment within our study population may impact health literacy and understanding of vaccines received.

Despite these limitations, our study possesses strengths that inform our public health knowledge. We analyzed a large nationally representative sample of the US population who travel to HAV endemic countries with a notable representation of non-US-born and minority groups. Our study was also the first study to assess the interaction of race/ethnicity on the association of birthplace and HAV vaccination coverage among travelers. These results add to the current literature noting disparities in vaccination coverage among non-US-born adults and racial/ethnic minorities as independent groups.

In conclusion, we observed a significant interaction between birthplace and race/ethnicity on the association of HAV vaccination among travelers to endemic countries. US-born Black, non-US-born Asian, and non-US-born Hispanic adults had lower odds of HAV vaccination. We believe these results can inform public health and clinical decision-making as well as reporting statistics. Targeted outreach is needed to help educate these high-risk groups and enhance health care access to reduce the burden of HAV infection in the US and worldwide.

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