



# Adherence to chronic hepatitis B screening guidelines for persons from intermediate to high prevalence Countries

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## Abstract

The adherence to the CDC guideline on screening non-U.S. born persons for hepatitis B virus infection was assessed. A retrospective cohort study was conducted at University of Washington primary care clinics using the electronic medical records. Persons from hepatitis B virus prevalent countries were identified using country of origin and language. Of 2329 eligible for screening, only 617 (26.5%) were screened. The prevalence of HBsAg was 35 (5.7%). Among women of reproductive age (18–44 years, n=906), 238 (26.3%) were screened, and 7 (2.9%) were HBsAg positive. Low screening practice for chronic hepatitis B infection, and high infection prevalence among those screened was noted. The findings indicate that potentially three out of every one detected case may be missed. Urgent efforts are needed to scale up and consistently implement HBV screening at primary care clinics.

**Keywords** Hepatitis B virus · Screening · Non-U.S. born

## Introduction

In 2015, an estimated 257 million people were living with chronic hepatitis B (HBV) infection, the majority of whom reside in low-and-middle-income countries (LMICs), particularly in Africa and Asia [1–4]. Because most individuals with chronic HBV infection are asymptomatic, many remain undiagnosed, and the World Health Organization (WHO) estimates that only 9% of persons living with chronic HBV have received a diagnosis [1]. Due to an ongoing lack of timely diagnosis among many individuals with chronic HBV, HBV-related hepatocellular carcinoma (HCC), as well as cirrhosis and its complications remain significant causes of morbidity and mortality worldwide [1, 5].

In the United States (U.S.), the majority of persons living with chronic HBV are foreign-born. Despite guidance, issued in 2008, from the U.S. Centers for Disease Control and Prevention (CDC) recommending one-time HBV screening for persons born in countries with an HBV prevalence  $\geq 2\%$  [6], data indicate that adherence to screening guidelines for non-U.S. born individuals remains low, particularly in primary care [7–10].

In Seattle and King County, Washington, more than 22% of residents are non-U.S. born, many of whom immigrated from countries in Southeast Asia and Eastern African, where hepatitis B surface antigen (HBsAg) seroprevalence often exceeds 8% [2, 9–11]. The proportion of individuals from HBV-endemic countries who have been screened for chronic HBV is not known. In this study, we estimated the proportion of individuals from intermediate ( $\geq 2\%$ ) and high ( $\geq 8\%$ ) HBV prevalence countries who were screened for chronic HBV at University of Washington (UW) affiliated primary care clinics between 2016 and 2019, and evaluated factors associated with HBV screening in this population.

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## Methods

### Study design and population

We completed a retrospective cohort analysis of HBV screening among patients receiving care at all UW affiliated primary care clinics. The study population included individuals  $\geq 18$  years of age, originating from intermediate or high HBV-endemic countries, defined by the WHO and CDC as those with an HBsAg seroprevalence  $\geq 2\%$  [12]. Individuals were included in the analysis if they established care at one of the UW primary care clinics in the year 2016, and if they had at least one additional follow-up visit by the end of 2019. Birthplace and preferred spoken language, as documented in the electronic medical record system (EMR), were used to determine eligibility criteria by country of origin. Individuals with documented HBV screening results (HBsAg or HBV DNA testing) prior to 2016 were excluded from our cohort.

### Data collection, variables, and analysis

Demographic information and laboratory values were extracted from the EMR for all patients who met the inclusion criteria. Key variables of interest included: HBsAg, HBV DNA, age, sex, race, ethnicity, clinic site (grouped into categories based on hospital and network), number of clinic encounters and health insurance status.

Our main outcome of interest was screening for chronic HBV infection, defined as receipt of a HBsAg test anytime during the study period (2016 and 2019). For patients who were found to be HBsAg-positive, we evaluated the

proportion who underwent liver function testing or liver imaging (Ultrasound or CT scan), as well as the proportion linked to HBV specialty care, defined as completion of a hepatology clinic visit. HBV screening and linkage to care was similarly evaluated among women of reproductive age within our cohort, defined as women between the ages of 18 and 44 years.

Descriptive statistics were used to compare patients who had and had not received HBV screening. Wald Chi-square test was used to identify correlates and calculate relative risk ratios (RR) of HBV screening along with 95% confidence intervals for all study participants and among the subgroup of reproductive age women. Analyses were performed using R (version 4.0.3, Vienna, Austria).

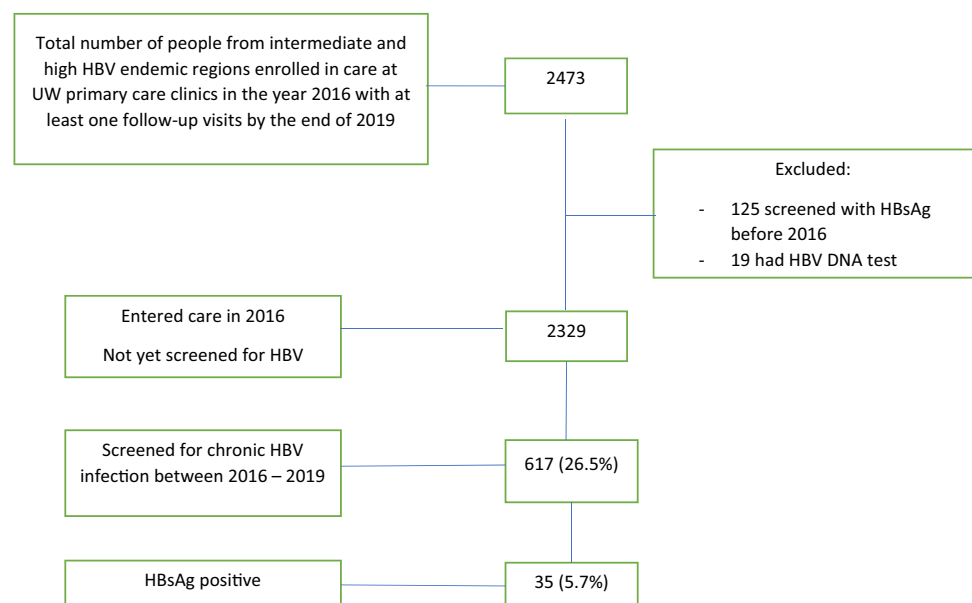
This study was approved by the human subjects division at the University of Washington.

## Results

We identified 2473 patients from intermediate to high HBV prevalence countries who established care across 42 UW primary care clinics in 2016 and had at least one additional clinic visit by the end of 2019. Of these, 144 were excluded due to prior HBsAg or HBV DNA testing, resulting in an analytic cohort of 2329 (Fig. 1).

Demographic characteristics are outlined in Table 1. The median age of the study population was 36 years (interquartile range [IQR]: 25–57); 62% ( $n = 1446$ ) were female, 63% ( $n = 1455$ ) Asian/Pacific Islanders and 15% ( $n = 354$ ) Black persons. HBsAg screening was performed in 617 (26.5%) individuals during the timeframe of interest, and 35 (5.7%) were found to be HBsAg positive. Most of the

**Fig. 1** Diagram of study population recruitment, screening and prevalence of HBV infection, 2016. UW University of Washington, HBV hepatitis B virus, HBsAg hepatitis B virus surface antigen



**Table 1** Characteristics of patients from intermediate and high HBV prevalence countries, by HBV screening status at UW primary care clinics, 2016

Category	Groups	Non-screened n (%) (N = 1712)	Screened n (%) (N = 617)	Overall n (%) (N = 2329)
Age	Median (IQR)	35 (24, 57)	39 (29, 57)	36 (25, 57)
Sex	Female	1060 (61.9)	386 (62.6)	1446 (62.1)
Race	Asian or Pacific Islander	1118 (65.3)	337 (54.6)	1455 (62.5)
	White	278 (16.2)	78 (12.6)	356 (15.3)
	Black or African American	187 (10.9)	167 (27.1)	354 (15.2)
	Multiple races	12 (0.7)	5 (0.8)	17 (0.7)
	American Indian or Alaska Native	4 (0.2)	1 (0.2)	5 (0.2)
	Missing	113 (6.6)	29 (4.7)	142 (6.1)
Ethnicity	Not Hispanic or Latino	1591 (92.9)	583 (94.5)	2174 (93.3)
	Hispanic or Latino	11 (0.6)	3 (0.5)	14 (0.6)
	Missing	110 (6.4)	31 (5)	141 (6.1)
Language	English	700 (40.9)	225 (36.5)	925 (39.7)
	Mandarin	303 (17.7)	64 (10.4)	367 (15.8)
	Amharic	75 (4.4)	62 (10)	137 (5.9)
	Vietnamese	63 (3.7)	40 (6.5)	103 (4.4)
	Arabic	59 (3.4)	21 (3.4)	80 (3.4)
	Others	512 (29.9)	205 (33.2)	717 (30.8)
	Missing	619 (36.2)	127 (20.6)	746 (32)
	Insurance	Commercial	757 (44.2)	196 (31.8)
Insurance	Self-pay/Charity	573 (33.5)	272 (44.1)	845 (36.3)
	Medicaid	185 (10.8)	93 (15.1)	278 (11.9)
	Medicare	137 (8)	32 (5.2)	169 (7.3)
	Other	36 (2.1)	17 (2.8)	53 (2.3)
	Missing	24 (1.4)	7 (1.1)	31 (1.3)
Clinic	UW Neighborhood Clinics	865 (50.5)	195 (31.6)	1060 (45.5)
	HMC	266 (15.5)	306 (49.6)	572 (24.6)
	UWMC-ML	475(27.7)	76 (12.3)	551 (23.7)
	Other	106(6.2)	40 (6.5)	146 (6.3)
Number of clinic visits	Median (IQR)	4 (2, 8)	8 (4, 17)	5 (2, 10)

HBV hepatitis B virus, IQR interquartile range, UW University of Washington, HMC Harborview Medical center, UWMC-ML University of Washington Medical Center-Mount Lake

patients were screened in their first year (2016) of establishing care, 414/617 (67.1%). Among women of reproductive age (n = 906), 26.3% (n = 238) were screened for HBsAg, and 2.9% (n = 7) were HBsAg positive (Supplementary table 1).

In a univariate analysis, individuals who were Black (RR 2.07, 95% confidence interval [CI] 1.81–2.37,  $p < 0.001$ ), without health insurance, or identified as self-paying or receiving charity assistance (RR 1.38, 95% CI 1.21–1.58,  $p < 0.001$ ), and those seen at one of the clinics affiliated

with the county hospital (Harborview) (RR 3.02, 95% CI 2.66–3.43,  $p < 0.001$ ) were more likely to have undergone screening for HBV. Additionally, patients with a higher number of clinic visits during the study period were more likely to have been screened for HBV when compared with those with fewer clinic visits (median of 8 vs. 4 clinic visits,  $p < 0.001$ ). (Table 2 and Supplementary Table 2).

Of the 35 patients found to have chronic HBV infection, 31 (88.6%) had follow up liver aminotransferase testing and 26 (74.3%) had liver imaging studies. Twenty (57.1%) were

**Table 2** Univariate risk ratio for HBV screening at UW primary care clinics, by key indicators, 2016

Category	Groups	Proportion screened: non-screened	p-value *	Relative risk ratio (95% CI)
Race	Black/African American	167/187	<0.001	2.12 (1.72–2.70)
	White	78/278		
	Black/African American	167/187	<0.001	2.07 (1.81–2.37)
	All other race	450/1525		
Insurance	Self-pay/charity	272/573	<0.001	1.38 (1.21–1.58)
	All other insurance	345/957		
	Self-pay/charity	272/573	<0.001	1.57 (1.34, 1.83)
	Commercial	196/757		
Clinic	Harborview clinics	306/266	<0.001	3.02 (2.66–3.43)
	All other clinics	311/1446		
	Harborview clinics	306/266	<0.001	2.91 (2.51–3.37)
	UW Neighborhood Clinics	195/865		
Median number of clinic visits	Tested (8) vs Non-tested (4)		<0.001	

\*Wald Chi-square

HBV hepatitis B virus, UW University of Washington

**Table 3** Linkage to further care for patients identified with chronic HBV infection at UW primary care clinics, 2016

Linkage to care	n (%) (N = 35)
Listed as problem in medical record	33 (94.3)
Follow up liver enzyme studies	31 (88.6)
Liver/abdominal imaging	26 (74.3)
Hepatology clinic evaluation	20 (57.1)
Treatment offered	9 (25.7)

HBV hepatitis B virus

subsequently evaluated in hepatology clinic, and 9 (25.7%) received treatment during the study period (Table 3).

## Discussion

Despite guidelines from the CDC recommending one-time screening for all persons born in countries with a  $\geq 2\%$  prevalence for HBV, we found that only a quarter of the 2329 eligible patients were screened for chronic HBV in this contemporary primary care cohort.

Our findings are in keeping with other published studies, which have shown that provider adherence to accepted national guidelines for health screening and vaccination recommendations among immigrant and refugee populations is generally low within the U.S. [13]. Specifically, screening rates for chronic hepatitis B infection among non-U.S. born persons have been reported as low as 7–36% in the literature, including in an academic primary care setting [14–16]. A

study from Mayo Clinic Rochester indicated that only 31% of Asian Americans were screened for chronic HBV infection at their health center, with screening mostly occurring during pregnancy, pre-employment evaluations, and rarely in the setting of routine primary care [15]. In a similar study from the Mayo Clinic, authors found a baseline HBV screening rate of 7.2% within primary care, which increased to 31.4% after providers were sent reminder emails regarding HBV screening a week prior to scheduled visits with eligible patients [14]. Collectively, the findings, paired with our current study, suggest that HBV screening is not consistently implemented in most primary care practices, and many cases of chronic infection are likely going undiagnosed. Majority of the screening occurred on initial visit when the patients established care. This might be because of relatively longer time allotted for initial patient visits allowing more patient-physician contact than subsequent follow up visits.

The prevalence of HBV among screened individuals in our study was 5.7%. This is consistent with the prevalence of chronic HBV in intermediate and high prevalence countries, including countries with a large immigrant population in King County such as Vietnam, China, Philippines, and Ethiopia [1]. Comparably high rates of HBV infection have also been described among foreign-born individuals in studies from other high-income countries such as Canada (5.4%) [3], Germany (3.6%) [4], Italy (9.6%) [16], as well as in other cities/states within the US such as Baltimore (3.7%–6.1%) [17] and Minnesota (8.5%) [15]. If this HBV prevalence held true for our clinic population as a whole, there were potentially as many as 133 (5.7% of 2329) individuals with chronic HBV that could have been identified.

Current screening practices may have resulted in as many as 98 missed chronic HBV diagnoses.

Perinatal transmission is the main route of HBV transmission in endemic areas, and as such, screening women of reproductive age for HBV infection is a crucial step in HBV prevention and linkage to care [18]. In this study, the proportion of reproductive age women who were screened for chronic HBV was similarly low (26.3%). Nevertheless, the prevalence of the infection among reproductive aged women was lower, 2.9%, when compared to the total population. While the reasons for this are not addressed in this study, owing to their younger age, it is possible that women of reproductive age were more likely than older women to have been vaccinated against HBV at birth or in early childhood.

While the overall proportion of patients screened for HBV in our study was low, a few groups were more likely to be screened than others; although no subgroup had a screening rate higher than 50%. These included Black persons and uninsured individuals. The reasons for this cannot be ascertained by our study data; however, it is possible that some of the providers had higher awareness of HBV prevalence among African-born persons when compared to other similarly at-risk groups, or that systemic racial bias contributes to altered perceptions of patients' risk for certain infectious diseases. Unfortunately, we did not come across similar studies addressing this issue or preferential screening among persons of different races. The presence of a dedicated clinic for international communities at Harborview Medical Center, King County's public hospital, which is run by UW, may also account for higher rates of HBV screening among county hospital clinics and among uninsured individuals, as a higher proportion of patients seen within Harborview's primary care clinics are uninsured, when compared to other primary care clinics across the UW system [9].

It is perhaps not surprising that patients screened for HBV were more likely to have a greater number of clinic visits during the timeframe of interest (median of 8 versus 4). Patients with more frequent clinic visits might have been sicker and had greater opportunity to undergo screening for infections including HBV. It is probable that the increased frequency of physician–patient contacts facilitated more complete health care maintenance plans. Nevertheless, it is notable that the median number of clinic visits for patients not screened was four, i.e., a follow-up rate of approximately once a year for this cohort. This finding further accentuates that guideline-based HBV screening has been inadequately incorporated into routine primary care, as yearly follow-up over the course of four years should have provided sufficient time to complete routine infectious diseases screening.

Patients with HBV infection need regular lifelong follow up because they are at increased risk of progression to liver cirrhosis and hepatocellular cancer [19]. While most patients diagnosed with chronic HBV in this cohort were

subsequently followed in their primary clinic with liver enzymes and imaging, linkage to hepatology clinic was only completed by 20 (57%). It is important to note, however, that immediate referral to specialty care may not be necessary, as specialty care needs depend on the stage of chronic HBV, and the proportion of patients linked to care in our study is relatively consistent with that of HBV infected patients from other domestic studies, including cohorts from Denver (29% linked to care) and Philadelphia (53% linked to care) [20]. However, the importance of regular follow up, monitoring of disease activity as well as health education, which can be done at primary care level, cannot be over emphasized. Adherence to longitudinal monitoring of patients with chronic HBV at the provider level is particularly important given several studies which indicate low awareness regarding HBV transmission and care needs among immigrant communities [2, 11, 14, 21].

There are certain limitations worth noting in our study. Birthplace and primary language were not always complete in the medical record system and we may have missed certain groups of eligible patients, including English speakers originating from countries of high HBV prevalence. Additionally, patients who were screened for HBV in other healthcare settings might have been misclassified as unscreened in this study due to our inability to access outside facility records. We required that patients have a minimum of two clinic visits during the intended study period for this study. This was taking into consideration that all the routine healthcare screening tests (including the HBV screening) might not be completed on a single visit, but this might have introduced some selection bias into our sample. Finally, these data come from a single healthcare system and may not be generalizable to other clinical settings.

## Conclusions

This study found a low frequency of screening and high prevalence of chronic HBV infection among people from HBV endemic countries seen in a network of primary care clinics. For each diagnosed hepatitis B case, potentially three cases were missed within our cohort. There is an urgent need to prioritize, scale up and consistently implement HBV screening among persons from intermediate to high HBV prevalent countries to prevent the transmission and long-term complications of chronic HBV infection. Additional efforts are needed to understand how best to simplify, implement and adhere to HBV screening guidelines within primary care.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s10900-022-01102-7>.

**Author contributions** ED and HNK: Conceptualization and protocol development. AG and HNK: data collection. ED, HNK, MAC, KL: study design and data analysis. All the authors contributed to interpretation of results. ED: drafted the first manuscript. All authors contributed to reviewing, preparing and approving the final draft for publication.

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**Data availability** The author confirms that all data generated or analysed during this study are included in this article.

**Code availability** Not applicable.

## Declarations

**Conflict of interest** The authors have no competing interests to declare that are relevant to the content of this article.

**Ethical approval** This study was approved by the human subjects division at the University of Washington.

**Consent to participate** Not applicable, retrospective record analysis.

**Consent for publication** Not applicable.

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