# MAJOR ARTICLE







# Tuberculosis and Chronic Hepatitis B Virus Infection Screening Among Non-US-Born Persons in an Integrated Health System in California

Jenna M. Wick, <sup>1,a,®</sup> Yuching Ni,<sup>2</sup> Nicole Halmer,<sup>2</sup> Robert J. Wong, <sup>3,4,®</sup> Amit S. Chitnis,<sup>5</sup> Devan Jaganath,<sup>6</sup> Amy L. Krueger, <sup>7,b</sup> and Jacek Skarbinski<sup>2,8,9,a</sup>; for the Tuberculosis Epidemiologic Studies Consortium

<sup>1</sup>Internal Medicine Residency Program, Oakland Medical Center, Kaiser Permanente Northern California, Oakland, California, USA, <sup>2</sup>Division of Research, Kaiser Permanente Northern California, Oakland, California, USA, <sup>3</sup>Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, California, USA, <sup>4</sup>Gastroenterology and Hepatology Section, Veterans Affairs Palo Alto Healthcare System, Palo Alto, California USA, <sup>5</sup>Tuberculosis Section, Division of Communicable Disease Control and Prevention, Alameda County Public Health Department, San Leandro, California, USA, <sup>6</sup>Division of Pediatric Infectious Disease, University of California San Francisco, San Francisco, California, USA, <sup>7</sup>Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, <sup>8</sup>Department of Infectious Diseases, Oakland Medical Center, Kaiser Permanente Northern California, Oakland, California, USA, and <sup>9</sup>Physician Researcher Program, Kaiser Permanente Northern California, Oakland, California, USA

*Background.* Tuberculosis infection (TBI) and chronic hepatitis B virus (HBV) infection disproportionately affect non–US-born persons. Early identification and treatment are critical to reduce transmission, morbidity, and mortality, but little is known about screening in the United States.

*Methods.* We conducted a cross-sectional study in a large integrated California health system in September 2022 assessing TBI and HBV screening among persons aged  $\geq$ 18 years who were born in countries with high TB burden (TB disease incidence rates  $\geq$ 20/100 000 population) and/or HBV burden (hepatitis B surface antigen seroprevalence >2%).

**Results.** Of 510 361 non–US-born persons born in countries with high TB burden, 322 027 (63.1%) were born in countries with high HBV burden and 188 334 (36.9%) in countries with only high TB burden. Among persons born in countries with high TB and HBV burden, 29.6% were screened for TBI, 64.5% for HBV, and 23.4% for TBI and HBV; 9.9% had TBI and 3.1% had HBV infection. Among persons born in countries with high TB burden only, 27.9% were screened for TBI and 7.5% had TBI.

**Conclusions.** Among non-US-born persons from countries with high TB and HBV burden, we found low screening rates and elevated prevalence of TBI and chronic HBV infection. Cotesting for TBI and HBV infection in non-US-born persons from countries with high TB and HBV burden might improve outcomes by identifying persons who warrant TBI treatment, HBV treatment, or HBV vaccination. Increased screening is the first step in reducing health inequities and overall disease burden.

**Keywords.** health disparities; hepatitis B; screening; tuberculosis.

In the United States, an estimated 13 million persons have tuberculosis infection (TBI) and are at risk of progression to tuberculosis (TB) disease if infection remains untreated [1–3].

Received 09 May 2024; editorial decision 19 August 2024; accepted 31 August 2024; published online 3 September 2024

Correspondence: Jenna M. Wick, MD, Internal Medicine Residency Program, Kaiser Permanente Oakland, 3600 Broadway, Oakland, CA 94611 (jenna.m.wick@gmail.com); Jacek Skarbinski, MD, Department of Infectious Diseases, 3600 Broadway, Oakland, CA 94611 (jacek.skarbinski@kp.org).

# Open Forum Infectious Diseases®

© The Author(s) 2024. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (https://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com. https://doi.org/10.1093/ofid/ofae484

Nearly 75% of TB cases reported in the United States during 2022 were among non–US-born persons [4]. The US Preventive Services Task Force recommends testing and treatment among populations at higher TBI risk, including non–US-born persons [3]. Despite the efficacy of TBI treatment for preventing morbidity and mortality, prior research has found significant gaps in TBI management, with 72% of persons receiving appropriate screening, 44% receiving a medical evaluation and TBI diagnosis, 31% starting treatment, and only 19% completing treatment [5].

In the United States, up to 2.4 million persons are living with chronic hepatitis B virus (HBV) infection, and of these individuals, 1.47 million are non–US born; approximately 59% emigrated from Asia, 19% from the Americas, and 15% from Africa [6]. The majority of adults who are immunocompetent and infected with HBV have spontaneous clearance of the virus, predominately via the adaptive immune system, but the remainder develop chronic HBV, which, if left undiagnosed and untreated, can progress from asymptomatic infection to cirrhosis and hepatocellular carcinoma [7]. Globally, most chronic

<sup>&</sup>lt;sup>a</sup>J. M. W. and J. S. contributed equally to this article.

<sup>&</sup>lt;sup>b</sup>Previously worked with the Division of Tuberculosis Elimination for this activity; National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

HBV infection results from mother-to-child transmission during birth and early childhood [8]. Children with perinatally acquired HBV usually remain hepatitis B e-antigen positive and have high levels of viral replication for prolonged periods [9]; thus, they are at high risk of progression to chronic infection and serious complications. Monitoring, antiviral therapy, and cancer surveillance can decrease morbidity and mortality for persons with chronic HBV. Therefore, early HBV diagnoses among asymptomatic persons can facilitate specific clinical interventions and guidance or behavioral counseling to reduce morbidity and transmission. However, in the United States, only 50% of persons with chronic HBV infection have been diagnosed [10]. Among persons with chronic HBV infection who developed cirrhosis, <40% have received antiviral therapy [11]. Updated 2023 Centers for Disease Control and Prevention (CDC) guidelines recommend onetime universal screening of all adults aged >18 with hepatitis B surface antigen (HbsAg), antibody to hepatitis B surface antigen (HbsAb), and total antibody to hepatitis B core antigen (HbcAb) [12]. Onetime HbsAg screening of adults was estimated to be highly cost-effective and predicted to prevent, for every 100 000 adults screened, an additional 7.4 cases of compensated cirrhosis, 3.3 cases of decompensated cirrhosis, 5.5 cases of hepatocellular carcinoma, 1.9 liver transplants, and 10.3 HBV-related deaths when compared with current screening practices [12]. In addition, HBV infection can be prevented with highly effective and well-tolerated vaccines. In 2022, the CDC Advisory Committee on Immunization Practices switched from a risk-based approach to a universal recommendation for all adults aged 19 to 59 years to receive HBV vaccination [13]. Moreover, previous studies in the US adult population have shown a high prevalence of TBI-HBV coinfection, and a study from California noted that 4% of persons with TB disease were coinfected with HBV [14-16].

Non-US-born persons are disproportionately at risk for TB and HBV; thus, cotesting non-US-born persons for TBI and HBV might present an opportunity to improve screening for both infections. Improved screening is the prerequisite for providing vaccination and treatment, with the ultimate goal to reduce morbidity and mortality of both infections. However, little is known about screening for TBI and HBV among non-US-born persons in the United States. To better understand screening practices, we conducted a cross-sectional study of non-US-born adults in a large integrated health system in California and assessed TBI and HBV screening practices as well as prevalence of diagnosed TBI and HBV infection.

# **METHODS**

Kaiser Permanente Northern California (KPNC) is an integrated health system that provides comprehensive care to 4.6 million members in northern and central California. Most care,

including laboratory testing, is conducted in KPNC facilities, including 266 medical offices and 21 hospitals [17].

We conducted a cross-sectional study of non–US-born adult KPNC members from countries that we categorized as having a high TB burden as defined by the CDC (TB disease incidence rates ≥20/100 000 population) [18] with or without high HBV burden (HBsAg seroprevalence >2%) [19]. Individual countries with high TB or HBV burden are shown in Figure 1. We assessed TBI and HBV screening using data obtained from the KPNC electronic health record database (Epic Systems Corporation) on 30 September 2022. The study was approved by the KPNC Institutional Review Board (1838887) with a waiver of the requirement for informed consent as a data-only study based on information collected as a part of routine care.

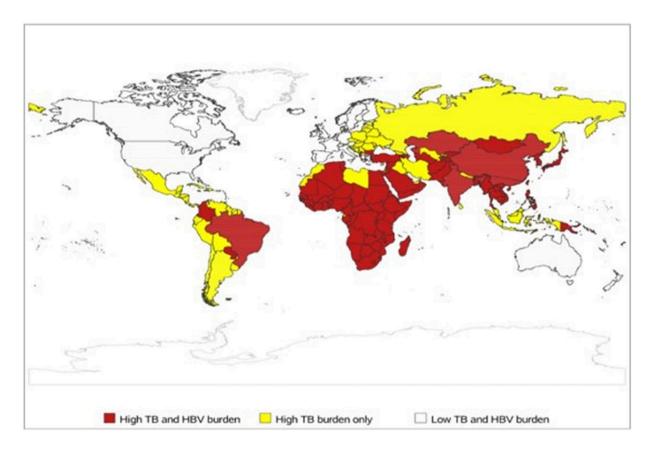
We included all persons aged  $\geq$ 18 years who had at least 1 year of continuous membership prior to the index date of 30 September 2022 and were born in a country with high TB burden, with and without high HBV burden (documented location of birth in electronic medical records). Persons born in countries with only a high HBV burden were excluded due to small sample sizes. We excluded persons with a history of TB disease prior to 30 September 2022 (based on *ICD-9* and *ICD-10* codes; Supplemental Table 1), as persons with prior TB disease were ineligible for TBI screening.

We analyzed outcomes for 2 categories based on country of birth: high TB and HBV or high TB burden only. The primary outcomes were as follows:

- Percentage of persons screened for TBI: at least 1 interferon gamma release assay (IGRA) or tuberculin skin test (TST) with a valid result before 30 September 2022
- Percentage of persons diagnosed with TBI: at least 1 positive IGRA result or TST with induration ≥10 mm before 30 September 2022 (persons with a positive TST result but negative IGRA result were classified as not having TBI)
- Percentage of persons screened for HBV: at least 1 HBsAg test completed before 30 September 2022
- Percentage of persons with chronic HBV infection: at least 1 HBsAg positive result before 30 September 2022
- Percentage of persons with past HBV infection: total HBcAb positive result and HBsAg negative result before 30 September 2022
- Percentage of persons with receipt of at least 1 dose of hepatitis B vaccine or evidence of prior immunity based on HbsAb positivity (this excludes persons with HBcAb positivity)

Testing performed outside the KPNC system was not included. Select conditions that increase risk for progression to TB disease were as follows:

 HIV infection based on ICD-9 codes 079.53, 042, V08, and 795.71 and ICD-10 codes B20, B97.71, Z21, and O98.7



**Figure 1.** Countries categorized as high TB burden with and without high HBV burden. High-burden countries are categorized as a TB disease incidence rate ≥20 per 100 000 population and a hepatitis B surface antigen seroprevalence >2%. Abbreviations: HBV, hepatitis B virus; TB, tuberculosis.

- Solid organ transplantation based on *ICD-9* codes V42.0, V42.1, V42.6, V42.7, V42.83, and V42.84 and *ICD-10* codes Z94.0 to Z94.4
- Leukemia or lymphoma based on ICD-9 codes 200 to 208 and ICD-10 codes C81-C96
- Receipt of tumor necrosis α inhibitors based on pharmacy records: adalimumab, certolizumab, etanercept, golimumab, infliximab
- Receipt of high-dose corticosteroids defined as ≥20-mg prednisone equivalents of oral or systemic corticosteroids daily for ≥30 days based on pharmacy records
- Receipt of other immunosuppressants based on pharmacy records: abatacept, anakinra, auranofin, azathioprine, baricitinib, canakinumab, cyclosporine, fingolimod, guselkumab, leflunomide, mycophenolate mofetil, risankizumab, rituximab, secukinumab, sirolimus, tacrolimus, thalidomide, tofacitinib, tocilizumab, and ustekinumab
- Diabetes mellitus based on *ICD-9* codes 249 and 250 and *ICD-10* codes E08 to E11 and E13
- End-stage renal disease based on ICD-9 585.6 code and ICD-10 code N18.6

Other covariates included demographic characteristics (age, sex, race/ethnicity) and Charlson Comorbidity Index score [20].

#### **RESULTS**

We identified 510 361 non-US-born persons from countries with a high TB burden, of whom 322 027 (63.1%) were born in countries with high TB and HBV burden and 188334 (36.9%) were born in countries with high TB burden only (Table 1). Within the medical record, 58.8% of patients had a country of birth listed. Among persons born in countries with high TB and HBV burden, 60.0% were female, as compared with 55.0% female in persons born in countries with a high TB burden only, and the majority of persons were aged >50 years in both groups. Among persons born in countries with high TB and HBV burden, 8726 (2.7%) were of Hispanic ethnicity, as compared with 149 345 (79.3%) persons born in countries with high TB burden only. However, 266 969 (82.9%) persons born in countries with high TB and HBV burden were of Asian race, as compared with 5615 (3.0%) persons born in countries with only a high TB burden. The majority had

Table 1. Characteristics of Persons Born Outside the United States in Countries With High TB Burden, With and Without High HBV Burden: September 2022

	Non-US-Born Persons From Countries With								
		/ith or Without ' Burden	High TB and	d HBV Burden	High TB Burden Only				
	No.	%	No.	%	No.	%			
Total	510 361	100	322 027	63.1	188 334	36.9			
Sex									
Male	213 500	41.8	128 751	40.0	84 749	45.0			
Female	296 861	58.2	193 276	60.0	103 585	55.0			
Age, y									
18–29	21 571	4.2	12 616	3.9	8955	4.8			
30–39	70 765	13.9	44 463	13.8	26 302	14.0			
40–49	103 674	20.3	62 315	19.4	41 359	22.0			
50–59	114 700	22.5	69 220	21.5	45 480	24.1			
60–69	98 074	19.2	64 172	19.9	33 902	18.0			
70–79	65 837	12.9	45 690	14.2	20 147	10.7			
≥80	35 740	7.0	23 551	7.3	12 189	6.5			
Race and ethnicity									
White	39 401	7.7	12 382	3.8	27 019	14.3			
Black	9171	1.8	8091	2.5	1080	0.6			
Hispanic	158 071	31.0	8726	2.7	149 345	79.3			
Asian	272 584	53.4	266 969	82.9	5615	3.0			
American Indian/Alaska Native	1246	0.2	1092	0.3	154	0.1			
Hawaiian/Pacific Islander	8113	1.6	7979	2.5	134	0.1			
Other/multiple/unknown	21 775	4.3	16 788	5.2	4987	2.6			
CCI score at index date									
0	283 819	55.6	180 842	56.2	102 977	54.7			
1	80 016	15.7	49 151	15.3	30 865	16.4			
2	45 495	8.9	28 230	8.8	17 265	9.2			
≥3	69 377	13.6	45 463	14.1	23 914	12.7			
No visits prior year	31 654	6.2	18 341	5.7	13 313	7.1			
mmune compromised									
HIV infection	1251	0.2	568	0.2	683	0.4			
Solid organ transplantation	1872	0.4	1177	0.4	695	0.4			
Diabetes mellitus	113 098	22.2	72 254	22.4	40 844	21.7			
End stage renal disease	4128	0.8	2697	0.8	1431	0.8			
Leukemia and lymphoma	4296	0.8	2561	0.8	1735	0.9			
Receipt of TNF-α inhibitors	1077	0.2	588	0.2	489	0.3			
Receipt of chronic, high-dose steroids	11 044	2.2	6990	2.2	4054	2.2			
Receipt of other immunosuppressants	8267	1.6	4854	1.5	3413	1.8			
Fime as member pre-index date, y, median (IQR)	7.8	4.6-11.4	7.8	4.6-11.4	7.8	4.6-11			
Any prior HBV vaccination	121 837	23.9	79 662	24.7	42 175	22.4			

High-burden countries for TB and HBV are categorized as TB disease incidence rates  $\geq$ 20 per 100 000 population and hepatitis B surface antigen seroprevalence >2%, respectively. Abbreviations: CCI, Charlson Comorbidity Index; HBV, hepatitis B virus; TB, tuberculosis; TNF- $\alpha$ , tumor necrosis factor  $\alpha$ .

a Charlson Comorbidity Index score of 0 in persons born in countries with high TB and HBV burden (56.2%) and persons born in countries with only a high TB burden (54.7%). The most prevalent immune compromising condition was diabetes mellitus in persons born in countries with high TB and HBV burden (22.4%) and persons born in countries with only a high TB burden (21.7%). The median time as a Kaiser Permanente member prior to the index date was 7.8 years (IQR, 4.6–11.4).

Of persons born in countries with high TB and HBV burden, 95 410 (29.6%) were screened for TBI, 207 570 (64.5%) for HBV, and just 75 419 (23.4%) for TBI and HBV (Table 2). Among all persons born in countries with high TB and HBV burden, 31 918 (9.9%) tested positive for TBI (Table 3) and 9949 (3.1%) tested positive for chronic HBV (Table 4). Among persons born in countries with high TB and HBV burden who were tested, 33.5% tested positive for TB and 5.1% tested positive for chronic HBV. Of persons born in countries with only high TB burden, 52 472 (27.9%) were screened for

Table 2. Screening for TBI or HBV Infection Among Persons Born Outside the United States From Countries With High TB, With and Without High HBV Burden: September 2022

Region/Country	TB ± HBV	Total No.	Any TBI Screening		Any HBV Screening		Screened for TBI and HBV		No Testing Done	
			No.	%	No.	%	No.	%	No.	%
Born in country with										
High TB or HBV burden	TB or HBV	510 361	147 882	29.0	307 035	60.2	113 607	22.3	169 051	33.1
High TB and HBV burden	TB + HBV	322 027	95 410	29.6	207 570	64.5	75 419	23.4	94 466	29.3
High TB burden only	TB only	188 334	52 472	27.9	99 465	52.8	38 188	20.3	74 585	39.6
By region										
Africa	TB + HBV	11 204	4457	39.8	7162	63.9	3542	31.6	3127	27.9
	TB only	612	184	30.1	342	55.9	141	23.0	227	37.1
Caribbean	TB + HBV	572	206	36.0	341	59.6	162	28.3	187	32.7
	TB only	3633	1221	33.6	1982	54.6	850	23.4	1280	35.2
South America	TB + HBV	4177	1481	35.5	2378	56.9	1076	25.8	1394	33.4
	TB only	8862	2989	33.7	5294	59.7	2266	25.6	2845	32.1
Central America	TB only	141 162	39 155	27.7	74 675	52.9	28 622	20.3	55 954	39.6
Asia	TB + HBV	294 005	85 311	29.0	190 570	64.8	67 578	23.0	85 702	29.1
	TB only	22 082	5909	26.8	11 041	50.0	4124	18.7	9256	41.9
Europe	TB + HBV	1605	456	28.4	820	51.1	317	19.8	646	40.2
	TB only	11 921	2993	25.1	6083	51.0	2167	18.2	5012	42.0
Oceania	TB + HBV	10 464	3499	33.4	6299	60.2	2744	26.2	3410	32.6
	TB only	62	21	33.9	48	77.4	18	29.0	11	17.7
By country										
Mexico	TB only	111 567	30 104	27.0	57 425	51.5	21 738	19.5	45 776	41.0
Philippines	TB + HBV	80 850	29 322	36.3	53 720	66.4	23 544	29.1	21 352	26.4
China <sup>a</sup>	TB + HBV	82 870	18 977	22.9	56 670	68.4	15 231	18.4	22 454	27.1
India	TB + HBV	49 757	16 240	32.6	27 516	55.3	12 118	24.4	18 119	36.4
Vietnam	TB + HBV	33 745	7641	22.6	24 425	72.4	6505	19.3	8184	24.3
El Salvador	TB only	15 591	4698	30.1	9115	58.5	3584	23.0	5362	34.4
Korea	TB + HBV	10 705	2568	24.0	6271	58.6	1949	18.2	3815	35.6

Abbreviations: HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; TB, tuberculosis; TBI, tuberculosis infection; IGRA, interferon gamma release assay; TST, tuberculin skin test.

In total, 911 persons with indeterminate HBV testing results are not included. Any TBI screening is defined as at least 1 IGRA or TST with a valid result before 30 September 2022. Screened for HBV is defined as at least 1 HBsAg test completed before 30 September 2022. Mexico, Philippines, China, India, Vietnam, El Salvador, and Korea are the 7 countries with largest non–US-born patient populations in Kaiser Permanente Northern California.

TBI, 14 147 (7.5%) were diagnosed with TBI, 99 465 (52.8%) were screened for HBV, and 340 (0.2%) had been diagnosed with chronic HBV. Among persons born in countries with only high TB burden who were tested, 27% tested positive for TB. In all, 362 479 persons (71.0%) born in countries with high TB burden had not been screened for TBI, and 127 958 persons (39.7%) born in countries with high TB and HBV burden had not been screened for HBV. Among 277 903 persons from countries with high TB and HBV burden who did not have chronic or past HBV infection (ie, currently eligible for HBV vaccination), just 74 241 (26.7%) had prior HBV vaccination (defined as at least 1 dose of the HBV vaccine), and 39.7% had any evidence of HBV immunity (HBsAb positive or received at least 1 dose of HBV vaccine). Among persons born in high TB and HBV countries, only 79 662 (24.7%) had prior HBV vaccination.

## **DISCUSSION**

Undiagnosed TBI and HBV infection is often asymptomatic but can lead to TB disease or hepatic fibrosis, cirrhosis, and hepatocellular carcinoma, respectively; screening is the first necessary step to guide appropriate management to reduce morbidity and mortality. In a large health care system in California, less than one-third of non-US-born adults from countries with high TB and high HBV burden were screened for TBI (29.6%), and approximately two-thirds were screened for HBV (64.5%), highlighting the need for increased screening for both infections. These low screening rates may be due to many factors, including inadequate knowledge of guidelines, insufficient time of outpatient visits, and concern for stigma associated with these infections. Despite these low screening rates, a high percentage of non-US-born adults from countries with high TB and HBV burden were diagnosed with TBI (9.9%) or HBV (3.1%), and prevalence rates would be even higher if

<sup>&</sup>lt;sup>a</sup>China includes Hong Kong, Macau, and Taiwan.

Table 3. TBI Screening Test Results Among Persons Born Outside the United States in Countries With High TB Burden, With and Without High HBV Burden: September 2022

Region/Country	TB ± HBV	Total No.	Screened for TBI		IGRA or TST Positive (TBI Diagnosis)		All IGRA or TST Negative		No TBI Testing Done	
			No.	%	No.	%	No.	%	No.	%
Born in country with										
High TB or HBV burden	TB or HBV	510 361	147 882	29.0	46 065	9.0	101 817	19.9	362 479	71.0
High TB and HBV burden	TB + HBV	322 027	95 410	29.6	31 918	9.9	63 492	19.7	226 617	70.4
High TB burden only	TB only	188 334	52 472	27.9	14 147	7.5	38 325	20.3	135 862	72.1
By region										
Africa	TB + HBV	11 204	4457	39.8	1861	16.6	2596	23.2	6747	60.2
	TB only	612	184	30.1	52	8.5	132	21.6	428	69.9
Caribbean	TB + HBV	572	206	36.0	68	11.9	138	24.1	366	64.0
	TB only	3633	1221	33.6	232	6.4	989	27.2	2412	66.4
South America	TB + HBV	4177	1481	35.5	272	6.5	1209	28.9	2696	64.5
	TB only	8862	2989	33.7	966	10.9	2023	22.8	5873	66.3
Central America	TB only	141 162	39 155	27.7	10318	7.3	28 837	20.4	102 007	72.3
Asia	TB + HBV	294 005	85 311	29.0	28 137	9.6	57 174	19.4	208 694	71.0
	TB only	22 082	5909	26.8	1575	7.1	4334	19.6	16 173	73.2
Europe	TB + HBV	1605	456	28.4	117	7.3	339	21.1	1149	71.6
	TB only	11 921	2993	25.1	1002	8.4	1991	16.7	8928	74.9
Oceania	TB + HBV	10 464	3499	33.4	1463	14.0	2036	19.5	6965	66.6
	TB only	62	21	33.9	2	3.2	19	30.6	41	66.1
By country										
Mexico	TB only	111 567	30 104	27.0	7441	6.7	22 663	20.3	81 463	73.0
Philippines	TB + HBV	80 850	29322	36.3	11 308	14.0	18014	22.3	51 528	63.7
China <sup>a</sup>	TB + HBV	82 870	18 977	22.9	5687	6.9	13 290	16.0	63 893	77.1
India	TB + HBV	49 757	16 240	32.6	4776	9.6	11 464	23.0	33 517	67.4
Vietnam	TB + HBV	33 745	7641	22.6	2657	7.9	4984	14.8	26 104	77.4
El Salvador	TB only	15 591	4698	30.1	1570	10.1	3128	20.1	10 893	69.9
Korea	TB + HBV	10 705	2568	24.0	900	8.4	1668	15.6	8137	76.0

Any TBI screening is defined as at least 1 IGRA or TST with a valid result before 30 September 2022. TBI diagnosis is defined as at least 1 positive IGRA result or TST with induration ≥10 mm before 30 September 2022 (persons with a positive TST result but a negative IGRA result were classified as not having TBI). Mexico, Philippines, China, India, Vietnam, El Salvador, and Korea are the 7 countries with largest non–US-born patient populations in Kaiser Permanente Northern California.

Abbreviations: HBV, hepatitis B virus; IGRA, interferon gamma release assay; TB, tuberculosis; TBI, tuberculosis infection; TST, tuberculin skin test

estimated only among persons who received screening tests (33.5% tested positive for TBI and 5.1% for chronic HBV). Moreover, approximately 1 in 4 persons from countries with high TB and HBV burden who did not have HBV infection had received HBV vaccination. Greater awareness from providers and health systems of the often-unrecognized burden of both diseases in the United States is needed to improve screening and vaccination rates. There were no electronic medical record TB or HBV screening prompts during this study period; thus, ordering these tests depended entirely on providers' knowledge of current guidelines. Creating a standard electronical medical record prompt may be one solution to increase testing and vaccination.

The CDC 2025 National TB Program Objectives and Performance target to reduce TB disease incidence among non–US-born persons to 8.8 cases per 100 000 will partially rely on increased screening and treatment of TBI in this population [21]. In our large integrated health system, only 29% of

all non–US-born persons were ever screened for TBI, which is comparable to screening rates that have been found in other US health care settings [22, 23]; as such, significant improvement in screening is needed to support TB disease elimination in the United States.

Similarly, the US Department of Health and Human Services' Viral Hepatitis National Strategic Plan set a goal to eliminate the public health threat of viral hepatitis A, B, and C infections in the United States by 2030 [24]. This strategic plan involves the components of prevention, increased surveillance and data usage, improvement in health outcomes, reduction in viral hepatitis—related disparities and health inequities, and coordinated efforts among all partners and stakeholders. In our large health care system, non—US-born persons from countries with high TB and HBV burden had a relatively high prevalence of chronic HBV infection (3.2%), but overall rates of HBV screening and HBV vaccination could be improved substantially. Although there are now expanded recommendations

<sup>&</sup>lt;sup>a</sup>China includes Hong Kong, Macau, and Taiwan.

Table 4. HBV Screening Among Persons Born Outside the United States in Countries With High TB Burden, With and Without High HBV Burden: September 2022

Region/Country	TB ± HBV	Total No.	Not Screened		Screened for HBV and HBV Negative		Screened and Chronic HBV Infection		Screened and Past HBV Infection	
			No.	%	No.	%	No.	%	No.	%
Born in country with										
High TB or HBV burden	TB or HBV	510 361	224 242	43.9	239 014	46.8	10 289	2.0	36 451	7.1
High TB and HBV burden	TB + HBV	322 027	127 958	39.7	149 945	46.6	9949	3.1	33 826	10.5
High TB burden only	TB only	188 334	96 284	51.1	89 069	47.3	340	0.2	2625	1.4
By region										
Africa	TB + HBV	11 204	4682	41.8	5262	47.0	204	1.8	1049	9.4
	TB only	612	304	49.7	287	46.9	1	0.2	20	3.3
Caribbean	TB + HBV	572	275	48.1	279	48.8	0	0.0	18	3.1
	TB only	3633	1846	50.8	1633	44.9	15	0.4	137	3.8
South America	TB + HBV	4177	2004	48.0	2087	50.0	6	0.1	80	1.9
	TB only	8862	3977	44.9	4680	52.8	24	0.3	181	2.0
Central America	TB only	141 162	71 829	50.9	67 875	48.1	125	0.1	1327	0.9
Asia	TB + HBV	294 005	115 371	39.2	136 453	46.4	9630	3.3	32 210	11.0
	TB only	22 082	11 993	54.3	9381	42.5	117	0.5	587	2.7
Europe	TB + HBV	1605	850	53.0	693	43.2	16	1.0	46	2.9
	TB only	11 921	6319	53.0	5177	43.4	55	0.5	366	3.1
Oceania	TB + HBV	10 464	4776	45.6	5171	49.4	93	0.9	423	4.0
	TB only	62	16	25.8	36	58.1	3	4.8	7	11.3
By country										
Mexico	TB only	111 567	58 068	52.0	52 563	47.1	83	0.1	848	0.8
Philippines	TB + HBV	80 850	31 718	39.2	39 656	49.0	1555	1.9	7861	9.7
China <sup>a</sup>	TB + HBV	82 870	28 394	34.3	36 600	44.2	4364	5.3	13 359	16.1
India	TB + HBV	49 757	24 691	49.6	24 050	48.3	177	0.4	835	1.7
Vietnam	TB + HBV	33 745	10 263	30.4	15 094	44.7	2317	6.9	5987	17.7
El Salvador	TB only	15 591	7242	46.4	8064	51.7	28	0.2	257	1.6
Korea	TB + HBV	10 705	4830	45.1	4300	40.2	247	2.3	1322	12.3

In total, 911 persons with indeterminate HBV testing results are not included. Chronic HBV infection is defined as at least 1 HBSAg positive result before 30 September 2022. Past HBV infection is defined as HBcAb positive result and HBSAg negative result before 30 September 2022. Mexico, Philippines, China, India, Vietnam, El Salvador, and Korea are the 7 countries with largest non–US-born patient populations in Kaiser Permanente Northern California.

Abbreviations: HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; TB, tuberculosis.

for HBV screening and vaccination, non–US-born persons from endemic regions should initially be prioritized given their high risk for HBV, which also provides an opportunity to concurrently consider TBI testing in this patient population.

Combining screening efforts for TBI and HBV infection in non–US-born persons from countries with high TB and HBV burden has numerous advantages and can broadly support both disease control efforts. First, TBI and HBV screening can be conducted via laboratory testing on blood, and both sets of tests could be offered through the same clinical encounter and conducted as part of the same laboratory visit. Moving away from TST toward IGRA testing can facilitate ease of screening to improve rates. Effectively implementing combined screening may be achieved with prompts for non–US-born patients, as well as bundling TBI and HBV screening with other recommended screening interventions. Second, a recent metanalysis suggested that persons with chronic HBV are more than twice as likely to have TBI than persons without chronic

HBV, highlighting their shared risk factors and the importance testing for both when one is considered [22]. Third, among persons with TBI, screening for HBV infection is important, as underlying chronic HBV infection significantly increases the risk of drug-induced liver injury from potentially hepatotoxic TBI treatment regimens (eg, rifamycins and isoniazid) [25]. Fourth, national strategic plans for TB and HBV control prioritize reducing health disparities. Non-US-born persons from regions with high TB and HBV burden, including Asia, Africa, and Oceania, have increased prevalence of TBI and chronic HBV infection and are thus disproportionately affected. Focused efforts in this population would support overall efforts to reduce the high burden of disease and poor outcomes, thereby reducing health disparities. Fifth, updated HBV screening and testing recommendations include screening all adults aged ≥18 years for hepatitis B at least once in their lifetime via a triple-panel test [26]; accordingly, all persons included in this analysis should be screened for HBV infection. In

<sup>&</sup>lt;sup>a</sup>China includes Hong Kong, Macau, and Taiwan.

2022 California mandated health care facilities to provide HBV screening, as well as hepatitis C screening, in an effort to improve adherence to existing HBV screening guidelines. Similarly, the HBV vaccine is recommended for all adults aged 19 through 59 years and adults aged  $\geq$ 60 years with risk factors for hepatitis B infection [16].

This study has several strengths and limitations. A key strength is that our analysis is based on a large data set containing 4.5 million members in northern and central California, who receive most of their care within our system; thus, we have robust ascertainment of demographic and clinical characteristics as well as laboratory testing and receipt of vaccinations. In addition, KPNC members have been shown to have similar demographic characteristics to the general population, thereby enabling broader interpretation of results [17]. Moreover, country of birth was available in the medical record for 58.8% of all KPNC members. Many patients are missing the data for country of birth in the medical record, highlighting the importance of collecting social determinants of health data. However, this is still a substantial number, and it is more likely that a non-US-born patient will have country of birth listed; as such, this data set can provide a better understanding of screening practices in this population. A key limitation is the cross-sectional design of this study and inability to delve further into potential drivers of low screening prevalence in our health system.

In summary, TBI and chronic HBV infection can lead to significant morbidity and mortality, and this cross-sectional study of non–US-born persons from countries with high TB and HBV burden highlights the need for increased screening for TBI and chronic HBV infection. Combining screening efforts for TBI and HBV may decrease blood draws and facilitate identification of, and specific clinical interventions to prevent, HBV- and TB-associated mortality.

### **Supplementary Data**

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Note

Potential conflicts of interest. All authors: No reported conflicts.

#### References

- Miramontes R, Hill AN, Yelk Woodruff RS, et al. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011–2012. PLoS One 2015; 10:e0140881.
- Haddad MB, Raz KM, Lash TL, et al. Simple estimates for local prevalence of latent tuberculosis infection, United States, 2011–2015. Emerg Infect Dis 2018; 24:1930–3.
- Menzies D. Screening for latent tuberculosis infection. JAMA Netw Open 2023; 6: e2312114.

- Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2022. Atlanta, GA: US Department of Health and Human Services, 2023.
- Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. Lancet Infect Dis 2016; 16:1269–78.
- Wong RJ, Kaufman HW, Niles JK, Meyer WA III, Chitnis AS. Prevalence of hepatitis B virus and latent tuberculosis coinfection in the United States. J Public Health Manag Pract 2022; 28:452–62.
- Wong RJ, Rupp L, Lu M, et al. Prevalence of hepatitis B virus (HBV) and latent tuberculosis co-infection and risk of drug-induced liver injury across two large HBV cohorts in the United States. J Viral Hepat 2023; 30:512–9.
- Bertumen JB, Pascopella L, Han E, et al. Epidemiology and treatment outcomes of tuberculosis with chronic hepatitis B infection—California, 2016–2020. Clin Infect Dis 2024; 79:223–32.
- Wong R, Brosgart C, Welch S, et al. An updated assessment of chronic hepatitis B
  prevalence among foreign-born persons living in the United States. Hepatology
  2021; 74:607–26.
- Dusheiko G, Agarwal K, Maini MK. New approaches to chronic hepatitis B. N Engl J Med 2023; 388:55–69.
- 11. World Health Organization Hepatitis Programme. Hepatitis B vaccination and prevention of mother-to-child transmission. Available at: https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hepatitis/prevention/mother-to-child-transmission-of-hepatitis-b#:~:text=Hepatitis%20B%20vaccination%20can%20be, HBV%20and%20early%20childhood%20transmission. Accessed 8 March 2024.
- Lok ASF, Lai CL. A longitudinal follow-up of asymptomatic hepatitis B surface antigen-positive Chinese children. Hepatology 1988; 8:1130-3.
- Bixler D, Barker L, Lewis K, Peretz L, Teshale E. Prevalence and awareness of hepatitis B virus infection in the United States: January 2017–March 2020. Hepatol Commun 2023: 7:e0118.
- Ogawa E, Yeo YH, Dang N, et al. Diagnosis rates of chronic hepatitis B in privately insured patients in the United States. JAMA Netw Open 2020; 3:e201844.
- Toy M, Hutton D, Harris AM, Nelson N, Salomon JA, So S. Cost-effectiveness of 1-time universal screening for chronic hepatitis B infection in adults in the United States. Clin Infect Dis 2022; 74:210–7.
- Weng MK, Doshani M, Khan MA, et al. Universal hepatitis B vaccination in adults aged 19–59 years: updated recommendations of the advisory committee on immunization practices—United States, 2022. MMWR Morb Mortal Wkly Rep 2022; 71:477–83.
- Davis AC, Voelkel JL, Remmers CL, Adams JL, McGlynn EA. Comparing Kaiser Permanente members to the general population: implications for generalizability of research. Perm J 2023; 27:87–98.
- Centers for Disease Control. Tuberculosis refugee health domestic guidance. Available at: https://www.cdc.gov/immigrant-refugee-health/hcp/domestic-guidance/tuberculosis.html. Accessed 12 June 2024.
- GBD 2019 Hepatitis B Collaborators. Global, regional, and national burden of hepatitis B, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol 2022; 7:796–829.
- Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the Charlson Comorbidity Index predicted in-hospital mortality. J Clin Epidemiol 2004; 57:1288–94.
- Division of Tuberculosis Elimination, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention. 2025 national TB program objectives and performance targets. October 2022. Available at: https://www.cdc.gov/tb/programs/evaluation/indicators/default.htm. Accessed 25 March 2023.
- Shapiro AE, Gupta A, Lan K, Kim HN. Latent tuberculosis screening cascade for non-US-born persons in a large health system. Open Forum Infect Dis 2023; 10: ofad303.
- Vonnahme LA, Raykin J, Jones M, et al. Using electronic health record data to measure the latent tuberculosis infection care cascade in safety-net primary care clinics. AJPM Focus 2023; 2:100148.
- US Department of Health and Human Services. Viral hepatitis national strategic plan: a roadmap to elimination for the United States (2021–2025). 2020. Available at: https://www.hhs.gov/sites/default/files/Viral-Hepatitis-National-Strategic-Plan-2021-2025.pdf. Accessed 23 May 2023.
- Chen J, Hubbard A, Bagley L, Shiau R, Wong RJ, Chitnis AS. Prevalence of latent tuberculosis infection among persons with chronic hepatitis B virus infection: a systematic review and meta-analysis. Dig Dis Sci 2022; 67:2646–54.
- Conners EE, Panagiotakppoulos L, Hofmeister MG, et al. Screening and testing for hepatitis B virus infection: CDC recommendations—United States, 2023. MMWR Recomm Rep 2023; 72:1–25.