

# Prevalence of Chronic Hepatitis B Among Foreign-Born Persons Living in the United States by Country of Origin

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Estimates of the prevalence of chronic hepatitis B (CHB) in the United States differ significantly, and the contribution of foreign-born (FB) persons has not been adequately described. The aim of this study was to estimate the number of FB persons in the United States living with CHB by their country of origin. We performed a systematic review for reports of HBsAg seroprevalence rates in 102 countries (covering PubMed from 1980 to July 2010). Data from 1,373 articles meeting inclusion criteria were extracted into country-specific databases. We identified 256 seroprevalence surveys in emigrants from 52 countries (including 689,078 persons) and 1,797 surveys in the general populations of 98 countries (including 17,861,035 persons). Surveys including individuals with lower or higher risk of CHB than the general population were excluded. Data were combined using meta-analytic methods to determine country-specific pooled CHB prevalence rates. Rates were multiplied by the number of FB living in the United States in 2009 by country of birth from the U.S. Census Bureau to yield the number of FB with CHB from each country. We estimate a total of 1.32 million (95% confidence interval: 1.04-1.61) FB in the United States living with CHB in 2009; 58% migrated from Asia and 11% migrated from Africa, where hepatitis B is highly endemic. Approximately 7% migrated from Central America, a region with lower CHB rates, but many more emigrants to the United States. This analysis suggests that the number of FB persons living with CHB in the United States may be significantly greater than previously reported. Assuming 300,000-600,000 U.S.-born persons with CHB, the total prevalence of CHB in the United States may be as high as 2.2 million. (HEPATOLOGY 2012;00:000-000)

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Abbreviations: ACS, American Community Survey; CHB, chronic hepatitis B; CDC, Centers for Disease Control and Prevention; CI, confidence interval; FB, foreign-born; FE, fixed effect; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; NHANES, National Health and Nutrition Examination Surveys; RE, random effects.

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Additional Supporting Information may be found in the online version of this article.

Chronic hepatitis B (CHB) is a major global health problem, with an estimated 350-400 million persons affected worldwide.<sup>1,2</sup> The prevalence of CHB varies greatly among countries, with the highest rates in Asia, Africa, and the Pacific Islands.<sup>1</sup> Approximately 15%-25% of persons with CHB are at risk for premature death from CHB-related complications, primarily hepatocellular carcinoma and end-stage liver disease.<sup>3,4</sup>

The true burden of CHB in the United States is unknown, because screening for CHB is not part of routine care and CHB surveillance activities are underfunded, underdeveloped, and poorly integrated.<sup>3</sup> Published estimates of the total number of persons living with CHB in the United States range from 550,000 to 2 million,<sup>5-8</sup> of whom 40%-70% may be foreign-born (FB) persons.<sup>5</sup> Approximately 2.8% of the refugees entering the United States from 2006 to 2008 who were tested through screening programs were hepatitis B

surface antigen (HBsAg) positive<sup>9</sup>; even higher rates were reported in refugees arriving between 1979 and 1991.<sup>10</sup> In contrast, only 0.1%-0.2% of U.S.-born persons are chronically infected with hepatitis B virus (HBV).<sup>5-8</sup>

The Institute of Medicine concluded that estimates of CHB prevalence rates based on National Health and Nutrition Examination Surveys (NHANES) are underestimates, because the persons at greatest risk for CHB in the United States (e.g., institutionalized, homeless, and FB) are underrepresented.<sup>3</sup> In this study, we present an alternative approach to estimating the burden of CHB that uses U.S. Census data for the number of FB from 102 different countries of origin and estimates of the CHB rates in these persons derived from systematic review and meta-analysis of HBsAg seroprevalence reported in immigrants and in-country populations of these countries.

Better estimates of the true burden of CHB and the ethnic and cultural characteristics of the affected population will help develop programs for prevention, earlier diagnosis, and linkage to care. The extensive database of country-specific HBsAg survey data created for this study may also be a resource for additional studies of CHB epidemiology.

## Materials and Methods

Results are reported using applicable components of the Meta-Analysis of Observational Studies in Epidemiology recommendations.<sup>11</sup> Because 102 meta-analyses were done, some components are shown as aggregate tables, rather than schematics. Data for individual countries are available at the Hepatology and Plan A websites ([www.plan-a.com](http://www.plan-a.com)).

**Source for FB Populations.** All countries in the 2009 American Community Survey (ACS) for which FB populations were reported were included in the analysis.<sup>12</sup> The ACS reports FB living in the United States by country of birth and decade of entry to the United States and includes persons living in housing units and group quarters without regard to immigration status; undocumented persons are assumed to participate.<sup>13</sup>

**Search Strategy.** PubMed searches were conducted from June 29 to July 4, 2010, and combined a country or region name and a demonym (e.g., "Korean") with the free-text search terms "hepatitis b, hbsag," and either "epidemiologic studies, prevalence, and seroprevalence" (search A), or "migrant, immigrant, and foreign" (search B). Search C combined a country name and the free-text term "hbsag." Duplicate articles were removed at the country and regional level. Additional studies were identified by manual searches of selected reference lists.

**Study Selection and Data Extraction.** Titles and abstracts of articles identified in searches were scanned, and data from relevant articles were extracted into standardized country-specific Excel databases. The following were extracted as available: country; geographic location; year of survey; sample population; age and sex of sample; sampling method; sample number (i.e., total, males and females); HBsAg seroprevalence rates (i.e., total and sex specific); assay; bibliographic information; comments; and source of article. The most conservative HBsAg seroprevalence rate reported in each survey was used for the meta-analyses. Data were segmented to yield sex-specific rates, where possible, and male- and female-specific data from the same study were entered separately. Age-specific rates were grouped into children and adults, where possible. Although no language restrictions were applied to searches, resources precluded retrieval and translation of all potentially relevant articles in languages other than English. The percentage of non-English articles identified in searches varied by country from 0% (e.g., for most Southeast and South Central Asian countries) to 100% (i.e., 9 of 9 for Kazakhstan). Because of the scarcity of data from Central America and the large number of migrants to the United States, all accessible non-English articles for this region were partially translated. For other regions, non-English articles with sufficient data in the abstract were included and we attempted to access articles if title or abstract indicated they reported serosurveys. Because articles in Chinese, Korean, Russian, and other Eastern European languages were difficult to access and translate, only a few full-text articles in these languages were evaluated.

**Inclusion Criteria.** Studies included in the meta-analyses reported original data on HBsAg seroprevalence. Because no seroprevalence data were available for immigrants from many countries, we included data for general in-country populations of the countries of origin. Population-based surveys and studies of groups, such as pregnant women, school children, military recruits, and healthy controls from cohort studies were included. Surveys including persons with lower or higher risk of CHB than the general population were excluded. Prevalence data from blood donors were not used, except as noted, for countries for which little or no other data were available. Surveys of populations at increased risk for HBV infection (e.g., health care workers, sex workers, and persons with immunodeficiency) were excluded. Studies in indigenous populations (e.g., Inuit and Amazonian tribes) with HBsAg seroprevalence much higher than nonindigenous populations were also excluded. An exception was made for

the Hmong, who comprise a large proportion of immigrants from Laos.<sup>10</sup> Other criteria were samples of at least 50 persons and publication in 1980 or later in a peer-reviewed journal, except as noted (i.e., three meeting abstracts were included in the analysis for China and two in the analysis for Mexico). Seroprevalence using any type of HBsAg assay was allowed (complete criteria are described in Supporting Table 1).

**Statistical Analysis: Calculation of Pooled Prevalence Rates.** Fixed effect (FE) and random effects (RE) meta-analyses of HBsAg seroprevalence rates from studies that met the inclusion criteria were conducted to calculate country-specific pooled CHB prevalence rates. RE analysis, which assumes heterogeneity among surveys, was considered more appropriate based on the nature of the data: HBV was unevenly distributed and we expected different rates from different surveys carried out in different populations in different locations at different times. FE analysis was conducted for comparison. Between-study heterogeneity was assessed for each country dataset using Cochran's Q test and the I<sup>2</sup> statistic.<sup>14,15</sup> For most countries, data were insufficient for exploration of heterogeneity. Separate pooled rates were calculated for emigrants and for in-country populations for countries for which data were available, and results were compared using a Z test.<sup>15</sup> Subgroup analyses were also done by decade of survey and by sex. For the 17 countries with at least 25 surveys, meta-regression analyses, based on the RE models using survey date as the covariate, were done using Comprehensive Meta-Analysis software (Biostat, Englewood, NJ). For a few countries with low HBsAg seroprevalence rates (e.g., Japan, Australia, New Zealand, Canada, and northern and western European countries), rates from large, population-based studies were used instead of meta-analysis.

**Assessment of Study Quality.** Study-quality assessment was done for only a subset of the data (i.e., Bangladesh, China, India, Iran, Korea, Pakistan, Philippines, Thailand, and Vietnam) to determine whether weighting based on study quality made a difference in the pooled prevalence rates. We developed a three-category scale (Supporting Table 2), scored each study, and calculated the pooled prevalence rates with and without the additional weighting factor, as described by Sutton et al.<sup>16</sup>

**Results**

**Search Results.** Flow of the systematic review is summarized by world region in Table 1. Results for individual countries are in Supporting Table 3. More than 17,500 articles were identified in PubMed

**Table 1. Results of Systematic Review: HBsAg Seroprevalence Articles Identified in PubMed (1980-2010) by World Region**

World Region	Citations Identified in Country Searches (A+B+C)	Articles After Removal of Country Duplicates	Articles After Removal of Region Duplicates	Full-Text Articles Reviewed		Articles Entered in Databases		Total Articles in Databases	Articles Used in Meta-Analyses	Full-Text Articles Reviewed for Meta-Analyses
				From Country Searches	From Other Sources	From Country Searches	From Other Sources			
Asia	12,670	9,622	8,703	1,430	1,311	232	1,541	716	674	
Central America	461	339	271	110	99	44	143	35	31	
Caribbean	557	417	251	68	66	43	109	30	29	
South America	2,187	1,531	883	233	277	24	301	91	89	
Northern America	—	—	—	—	—	—	—	—	—	
Oceania	718	504	364	28	31	1	32	20	20	
Africa	5,386	3,642	2,239	414	438	73	511	222	213	
Europe	7,041	5,403	4,981	576	561	78	639	259	236	
All regions	29,020	21,458	17,692	2,859	2,783	495	3,276	1,373	1,292	

NB: Duplicate papers identified in more than one world region are not accounted for.

Northern America = FB from Canada and Bermuda living in the United States.

For northern America, Japan, Australia, New Zealand, and northern and western Europe, which have low CHB rates and relatively modest numbers of emigrants to the United States, rates from a few large population studies were used instead of rates from systematic review and meta-analysis.

Search results for individual countries are available in Supporting Table 3.

**Table 2. Surveys in Emigrants and in General In-Country Populations Included in the Meta-Analyses by World Region**

World Region	FB Living in United States, 2009	Total Number of Surveys	Surveys by Date			Total Sample Number	Survey Sample Composition by Sex		
			Before 1990	1990-1999	2000 and After		Males	Females	Sex Not Specified
All surveys									
Asia	10,639,219	1,066	309	386	371	13,879,228	5,696,391	6,944,496	1,238,341
Central America	14,381,701	58	9	33	16	908,475	7,446	34,501	866,528
Caribbean	3,444,258	36	16	12	8	81,159	661	20,393	60,105
South America	2,600,687	142	28	83	31	1,540,104	20,482	92,435	1,427,187
Northern America	833,943	—	—	—	—	—	—	—	—
Oceania	187,587	50	28	14	8	45,007	4,219	5,971	34,817
Africa	1,475,642	341	165	115	61	271,341	135,138	95,400	40,803
Europe	4,870,823	360	141	140	79	1,824,799	101,086	944,097	779,616
All regions	38,433,860	2,053	696	783	574	18,550,113	5,965,423	8,137,293	4,447,397
Surveys in emigrants from country of origin to United States and elsewhere									
Asia	10,639,219	173	58	44	71	590,856	170,795	91,602	328,459
Central America	14,381,701	4	2	1	1	2,218	0	105	2,113
Caribbean	3,444,258	13	9	2	2	21,459	278	2,140	19,041
South America	2,600,687	2	0	0	2	476	0	0	476
Northern America	833,943	—	—	—	—	—	—	—	—
Oceania	187,587	4	1	3	0	30,941	0	0	30,941
Africa	1,475,642	27	9	8	10	25,504	4,756	8,284	12,464
Europe	4,870,823	33	4	20	9	17,624	2,065	7,484	8,075
All regions	38,433,860	256	83	78	95	689,078	177,894	109,615	401,569
Surveys in general populations living in country of origin									
Asia	10,639,219	893	251	342	300	13,288,372	5,525,596	6,852,894	909,882
Central America	14,381,701	54	7	32	15	906,257	7,446	34,396	864,415
Caribbean	3,444,258	23	7	10	6	59,700	383	18,253	41,064
South America	2,600,687	140	28	83	29	1,539,628	20,482	92,435	1,426,711
Northern America	833,943	—	—	—	—	—	—	—	—
Oceania	187,587	46	27	11	8	14,066	4,219	5,971	3,876
Africa	1,475,642	314	156	107	51	245,837	130,382	87,116	28,339
Europe	4,870,823	327	137	120	70	1,807,175	99,021	936,613	771,541
All regions	38,433,860	1,797	613	705	479	17,861,035	5,787,529	8,027,678	4,045,828

Northern America = FB from Canada and Bermuda living in the United States.

For northern America, Japan, Australia, New Zealand, and northern and western Europe, which have low CHB rates and relatively modest numbers of emigrants to the U.S., rates from a few large population studies were used instead of rates from systematic review and meta-analysis.

Results for individual countries are available in Supporting Table 4.

searches; full text of 2,859 articles was assessed and data from 3,276 articles were entered into country-specific databases. In all, we found 1,373 articles reporting data meeting criteria for use in the meta-analyses. Many articles report data for more than one survey (e.g., pregnant women and military recruits) and these were entered separately. A total of 2,053 HBsAg seroprevalence surveys involving 18.6 million subjects were used in the meta-analyses (Table 2; Supporting Table 4). Of these, 256 were surveys of emigrants (involving 689,078 subjects from 52 countries); 1,797 were surveys done in the general populations still living in the country (involving 17,861,035 subjects in 98 countries). Approximately 34% of the surveys were conducted before 1990; approximately 38% were between 1990 and 1999, and 28% were in 2000 or later. Overall, approximately 32% of the survey population was male and 44% was female; sex was not reported for 24% of the total sample.

The results of this systematic review reveal the limited availability of HBsAg seroprevalence data around the globe. Although at least one usable survey was found for all countries except Guyana and Macedonia, five or fewer surveys meeting inclusion criteria were found for one third of the countries. The median number of surveys was nine per country (range, 0-376), and more than half of the total surveys were from 11 countries. For 50 countries, no surveys in emigrants were found. Availability of data differed substantially by region; 1,066 usable surveys were found for Asia, but only 58 for Central America.

**Seroprevalence Rates by Country.** Surveys used in each country-specific meta-analysis are available at <http://www.plan-a.com>. HBsAg seroprevalence rates reported for most countries varied significantly from survey to survey. This variation was observed in surveys among emigrants and among in-country



populations and was expected, given that surveys were carried out in different populations at different times. For example, rates in India ranged from 0.25% among pregnant women attending antenatal clinics in Calcutta during 2002-2004 to 11.4% among rural adults in Western Maharashtra in 1992.<sup>17,18</sup> Rates in China ranged from 0.7% in a 1999 survey of young children in Taipei City to 39% in adult males in Massago, Taiwan, in 1996.<sup>19,20</sup>

**Pooled Seroprevalence Rates.** Country-specific RE pooled prevalence rates calculated by combining all available studies for each of the 102 countries are shown in Table 3 (no weighting by study quality was included). Countries with the highest pooled HBsAg rates were Sudan (18.6%), Liberia (16.5%), Guinea (16.3%), Eritrea (15.5%), and Zimbabwe (13.9%). Weighted average CHB rates for the FB in the United States by world region of origin were calculated by using the country-specific RE pooled prevalence rates and the number of FB in the United States from each country in the region. FB persons who migrated from Africa had the highest average CHB rate (10.3%), followed by FB from Asia (7.27%), Oceania (4.78%), and the Caribbean (4.52%). The weighted average CHB prevalence rate from the RE meta-analyses for all FB living in the United States was 3.45% (95% confidence interval [CI]: 2.72-4.19).

CI for the country-specific RE pooled CHB rates were broad (Table 3). Cochran's Q test and I<sup>2</sup> statistic performed for each country-specific meta-analysis supported heterogeneity among the surveys for the majority of countries (Supporting Table 5). The I<sup>2</sup> statistic was 55% or higher (indicating significant heterogeneity) for all except three meta-analyses.<sup>14,15</sup> Q tests were significant ( $P < 0.10$ ) in the meta-analyses for all countries except six, although this test lacks statistical power in meta-analyses involving small numbers of studies.<sup>14,15</sup> Using FE meta-analyses, the weighted average CHB pooled prevalence rate for all FB living in the United States was 2.52% (95% CI: 2.35-2.69). The FE pooled prevalence rate was slightly higher than the RE pooled prevalence rate (13.3%, compared to 12.3%) for China, the country contributing the largest number of FB with CHB. For most other countries, the FE rate was similar to or lower than the RE rate (data not shown).

**Seroprevalence Rates in Emigrants and In-Country Populations.** To assess whether CHB rates in these groups would differ, we calculated separate RE pooled prevalence rates for emigrants and for in-country populations (Supporting Table 6). No data for emigrants were available for 50 countries and none for in-country

populations were available for four countries. In 35 (71%) of the 49 countries for which comparison was possible, the pooled seroprevalence rate in emigrants did not differ from the rate in in-country populations (i.e.,  $P > 0.05$  in a Z test<sup>15</sup>); in 10 countries (i.e., Philippines, Thailand, India, Iran, Pakistan, Fiji, Somalia, Zimbabwe, Egypt, and Morocco), the pooled rate in the in-country populations was higher, and in four countries (i.e., Cambodia, Afghanistan, Ethiopia, and Senegal), the pooled rate in emigrants was higher.

**Seroprevalence Rates by Survey Date.** To assess whether CHB seroprevalence had changed over time (e.g., as a result of immunization), subgroup analyses were conducted for surveys carried out during three different decades (i.e., before 1990, 1990-1999, and 2000 and later). RE pooled prevalence rates by decade of survey for each country are shown in Supporting Table 7. For 63 countries, the pooled rates in surveys done in 2000 and after were not significantly different from pooled rates in surveys done before 1990. For 36 countries, rates were lower in the later decade, and for three countries, rates were higher. Because of the small numbers of surveys in each subgroup (median, 2-3; mean, 6-8; range, 0-142), the pooled rates from these subgroup analyses must be interpreted with caution. I<sup>2</sup> estimates indicated that substantial between-survey heterogeneity was still evident in most subgroups. Results of 15 of the 17 country-specific metaregression analyses agreed with the subgroup analyses.

**HBsAg Rates by Sex.** Because higher HBsAg seroprevalence has been reported in males than in females for some populations,<sup>21</sup> RE pooled prevalence rates were calculated for males and for females using sex-specific data, which were available for 60 countries (Supporting Table 8). Although rates were generally higher in males than in females, the data were not sufficient to use for prevalence calculations.

**Study Quality.** Pooled prevalence rates were not appreciably affected by weighting for study quality in the nine countries we tested. Pooled prevalence rates weighted for study quality fell within the CIs of the pooled rates not weighted for quality (data not shown). We did not assess study quality for the remaining 93 countries and did not use quality weighting in the calculation of pooled prevalence rates used for estimating the number of FB living with CHB.

**Number of FB With CHB Living in the United States.** Based on census data and pooled CHB prevalence rates from the RE meta-analyses using all surveys for a given country combined, we estimated that the number of FB in the United States living with CHB

**Table 3. CHB Rates From Random Effects Meta-Analyses and Prevalence of FB with CHB Living in the United States by Country of Origin**

Country/Region	FB Living in the United States, 2009	CHB Prevalence Rate (%)			Prevalence of FB With CHB in the United States		
		RE Pooled Prevalence Rate	Lower 95% CI	Upper 95% CI	Midrange Prevalence	Lower 95% CI	Upper 95% CI
<b>Rates and prevalence summarized by world region of origin</b>							
Asia	10,639,219	7.27	6.48	8.07	773,397	689,367	858,194
Central America	14,381,701	0.67	0.39	0.97	96,489	56,471	140,062
Caribbean	3,444,258	4.52	2.47	6.57	155,852	85,173	226,412
South America	2,600,687	1.31	0.72	1.91	34,135	18,750	49,561
Northern America	833,943	0.70	0.59	0.90	5,798	4,905	7,466
Oceania	187,587	4.78	3.05	6.51	8,974	5,725	12,218
Africa	1,475,642	10.30	7.72	12.89	152,054	113,869	190,256
Europe	4,870,823	2.01	1.44	2.56	97,995	70,029	124,747
All regions	38,433,860	3.45	2.72	4.19	1,324,693	1,044,288	1,608,916
<b>Rates and prevalence by country</b>							
Asia	10,639,219	7.27	6.48	8.07	773,397	689,367	858,194
Eastern Asia	3,344,739	8.97	8.47	9.48	300,082	283,207	317,088
China	1,987,625	12.25	11.70	12.80	243,484	232,552	254,416
Korea	1,012,911	5.26	4.69	5.83	53,279	47,506	59,053
Japan	330,418	0.63	0.60	0.70	2,082	1,983	2,313
Eastern Asia, other/NS*	13,785	8.97	8.47	9.48	1,237	1,167	1,307
South Eastern Asia	3,662,673	9.32	8.15	10.48	341,225	298,464	383,800
Philippines	1,733,864	7.36	6.32	8.39	127,612	109,580	145,471
Vietnam	1,149,355	12.48	11.46	13.50	143,440	131,716	155,163
Thailand	205,280	5.97	5.42	6.52	12,255	11,126	13,384
Laos	195,988	13.61	11.58	15.64	26,674	22,695	30,653
Cambodia	144,379	10.27	7.01	13.53	14,828	10,121	19,534
Indonesia	81,708	3.93	3.08	4.77	3,211	2,517	3,897
Myanmar	75,825	11.63	9.53	13.73	8,818	7,226	10,411
Malaysia	46,608	5.58	4.27	6.88	2,601	1,990	3,207
Singapore	29,666	6.02	5.03	7.01	1,786	1,492	2,080
South Central Asia	2,696,931	3.61	3.05	4.19	97,311	82,165	112,891
India	1,665,055	3.23	2.92	3.55	53,781	48,620	59,109
Iran	360,050	3.10	2.69	3.50	11,162	9,685	12,602
Pakistan	282,507	4.17	3.59	4.75	11,781	10,142	13,419
Bangladesh	139,773	4.83	4.02	5.64	6,751	5,619	7,883
Afghanistan	59,699	10.46	5.85	15.07	6,245	3,492	8,997
Uzbekistan	54,875	6.34	4.22	8.46	3,479	2,316	4,642
Nepal	45,648	2.32	1.71	2.93	1,059	781	1,337
Sri Lanka	42,152	2.41	-0.72	5.53	1,016	0	2,331
Kazakhstan‡	25,076	4.95	3.34	6.56	1,241	838	1,645
South Central Asia, other/NS*	22,096	3.61	3.05	4.19	797	673	925
Western Asia	859,497	3.41	2.40	4.46	29,300	20,646	38,334
Iraq	150,012	1.31	-0.25	2.87	1,965	0	4,305
Israel	138,262	1.26	0.97	1.55	1,742	1,341	2,143
Lebanon	121,337	1.66	0.86	2.46	2,014	1,043	2,985
Turkey	110,212	5.32	4.86	5.79	5,863	5,356	6,381
Armenia	84,870	0.57	0.19	0.94	484	161	798
Syria†	62,802	5.62	4.82	6.42	3,529	3,027	4,032
Jordan	59,703	6.36	3.72	9.00	3,797	2,221	5,373
Saudi Arabia	44,915	7.24	6.54	7.94	3,252	2,937	3,566
Yemen	36,251	13.23	10.35	16.11	4,796	3,752	5,840
Kuwait	19,645	3.85	1.99	5.71	756	391	1,122
Azerbaijan	15,919	3.11	1.39	4.84	495	221	770
Georgia	15,569	3.89	1.25	6.54	606	195	1,018
Asia, not specified*	75,379	7.27	6.48	8.07	5,480	4,884	6,080
Central America	14,381,701	0.67	0.39	0.97	96,489	56,471	140,062
Mexico	11,478,234	0.49	0.34	0.65	56,243	39,026	74,609
El Salvador	1,157,217	0.39	0.33	0.55	4,513	3,819	6,365
Guatemala	790,508	3.72	1.38	6.07	29,407	10,909	47,984
Honduras	459,393	0.56	0.41	0.72	2,573	1,884	3,308
Nicaragua	256,496	0.68	-0.41	1.78	1,744	0	4,566
Panama	104,426	0.87	0.48	1.26	909	501	1,316
Costa Rica‡	89,232	0.57	-0.07	1.20	509	0	1,071

(Continued)

TABLE 3. (Continued)

Country/Region	FB Living in the United States, 2009	CHB Prevalence Rate (%)			Prevalence of FB With CHB in the United States		
		RE Pooled Prevalence Rate	Lower 95% CI	Upper 95% CI	Midrange Prevalence	Lower 95% CI	Upper 95% CI
Belize	46,195	1.28	0.72	1.83	591	333	845
Caribbean	3,444,258	4.52	2.47	6.57	155,852	85,173	226,412
Cuba	982,862	0.86	0.58	1.14	8,453	5,701	11,205
Dominican Republic	791,593	10.68	5.89	15.46	84,542	46,625	122,380
Jamaica	644,958	3.94	0.81	7.07	25,411	5,224	45,599
Haiti	535,966	4.81	3.93	5.68	25,780	21,063	30,443
Trinidad and Tobago	218,281	0.71	0.49	0.94	1,550	1,070	2,052
Barbados	51,730	0.41	0.15	0.67	212	78	347
Caribbean, other/NS*	218,868	4.52	2.47	6.57	9,904	5,412	14,388
South America	2,600,687	1.31	0.72	1.91	34,135	18,750	49,561
Colombia	617,738	1.20	0.27	2.13	7,413	1,668	13,158
Ecuador	418,907	0.47	0.42	0.51	1,969	1,759	2,136
Peru	395,185	1.85	1.29	2.42	7,311	5,098	9,563
Brazil	356,531	1.78	1.54	2.02	6,346	5,491	7,202
Guyana*	247,801	1.31	0.72	1.91	3,246	1,784	4,733
Argentina	172,877	1.00	0.39	1.62	1,729	674	2,801
Venezuela	159,655	1.93	1.13	2.73	3,081	1,804	4,359
Chile‡	84,510	0.40	0.11	0.69	338	93	583
Bolivia	73,196	3.03	0.08	5.98	2,218	59	4,377
Uruguay	43,828	0.38	0.30	0.46	167	131	202
Paraguay	15,565	0.78	0.52	1.05	121	81	163
South America, other/NS*	14,894	1.31	0.72	1.91	195	107	284
Northern America	833,943	0.70	0.59	0.90	5,798	4,905	7,466
Canada	814,122	0.70	0.60	0.90	5,699	4,885	7,327
Northern America, other/NS	19,821	0.50	0.10	0.70	99	20	139
Oceania	187,587	4.78	3.05	6.51	8,974	5,725	12,218
Australia	73,281	0.87	0.39	1.35	638	286	989
New Zealand	25,373	0.50	0.42	0.56	127	107	142
Fiji	37,412	5.78	3.68	7.87	2,162	1,377	2,944
Tonga	22,111	12.99	7.61	18.38	2,872	1,683	4,064
Micronesia	17,695	15.11	11.22	19.01	2,674	1,985	3,364
Samoa	11,715	4.28	2.46	6.10	501	288	715
Africa	1,475,642	10.30	7.72	12.89	152,054	113,869	190,256
Eastern Africa	416,205	9.66	7.06	12.26	40,185	29,372	51,008
Ethiopia	151,879	9.59	8.11	11.07	14,565	12,317	16,813
Kenya	80,657	5.70	4.21	7.20	4,597	3,396	5,807
Somalia	69,333	12.40	8.89	15.92	8,597	6,164	11,038
Uganda	21,393	10.27	8.54	11.99	2,197	1,827	2,565
Eritrea	21,001	15.52	2.02	29.02	3,259	424	6,094
Tanzania	18,429	5.65	4.43	6.86	1,041	816	1,264
Zimbabwe	17,869	13.91	10.70	17.11	2,486	1,912	3,057
Eastern Africa, other/NS*	35,644	9.66	7.06	12.26	3,441	2,515	4,368
Middle Africa	31,842	11.44	8.46	14.43	3,643	2,694	4,595
Cameroon	31,842	11.44	8.46	14.43	3,643	2,694	4,595
Northern Africa	262,346	6.62	4.60	8.64	17,365	12,057	22,661
Egypt	136,159	4.61	3.81	5.40	6,277	5,188	7,353
Morocco	55,060	3.70	1.51	5.89	2,037	831	3,243
Sudan	37,046	18.59	14.22	22.96	6,887	5,268	8,506
Algeria	17,331	6.09	0.00	12.19	1,055	0	2,113
Northern Africa, other/NS*	16,750	6.62	4.60	8.64	1,109	770	1,447
Southern Africa	80,797	6.20	4.68	7.71	5,009	3,781	6,229
South Africa	80,797	6.20	4.68	7.71	5,009	3,781	6,229
Western Africa	534,058	13.17	10.18	16.17	70,355	54,360	86,373
Nigeria	207,031	13.31	11.57	15.06	27,556	23,953	31,179
Ghana	109,091	13.44	10.50	16.38	14,662	11,455	17,869
Liberia	63,520	16.54	11.55	21.53	10,506	7,337	13,676
Cape Verde	35,350	5.65	0.16	11.14	1,997	57	3,938
Sierra Leone	32,419	11.89	6.50	17.28	3,855	2,107	5,602
Senegal	17,618	12.66	10.14	15.18	2,230	1,786	2,674

(Continued)

TABLE 3. (Continued)

Country/Region	FB Living in the United States, 2009	CHB Prevalence Rate (%)			Prevalence of FB With CHB in the United States		
		RE Pooled Prevalence Rate	Lower 95% CI	Upper 95% CI	Midrange Prevalence	Lower 95% CI	Upper 95% CI
Guinea	14,420	16.33	14.61	18.05	2,355	2,107	2,603
Western Africa, other/NS*	54,609	13.17	10.18	16.17	7,194	5,558	8,832
Africa, NS*	150,394	10.30	7.72	12.89	15,497	11,605	19,390
Europe	4,870,823	2.01	1.44	2.56	97,995	70,029	124,747
Eastern Europe	2,119,696	3.29	2.33	4.24	69,687	49,376	89,927
Poland	437,519	1.44	1.16	1.72	6,300	5,075	7,525
Russia	405,731	2.89	2.16	3.62	11,726	8,764	14,687
Ukraine	322,538	2.20	1.15	3.24	7,096	3,709	10,450
Romania	177,035	7.19	6.56	7.81	12,729	11,613	13,826
Yugoslavia	113,702	3.98	1.32	6.64	4,525	1,501	7,550
Bosnia and Herzegovina†	102,587	3.63	2.26	5.00	3,724	2,318	5,129
Hungary	80,695	1.08	0.04	2.11	872	32	1,703
Albania	79,562	12.39	9.75	15.03	9,858	7,757	11,958
Czech Republic and Slovakia	67,212	0.70	0.43	0.98	470	289	659
Belarus	61,410	3.19	1.72	4.65	1,959	1,056	2,856
Bulgaria	50,528	4.25	2.80	5.70	2,147	1,415	2,880
Moldova	43,970	9.61	6.92	12.29	4,226	3,043	5,404
Croatia	42,986	1.47	0.84	2.10	632	361	903
Former USSR	39,742	3.83	2.74	4.91	1,522	1,089	1,951
Lithuania	34,619	2.03	1.37	2.69	703	474	931
Latvia	24,532	1.39	1.10	1.67	341	270	410
Macedonia*	24,084	3.29	2.33	4.24	792	561	1,021
Estonia†	11,244	0.58	0.42	0.74	65	47	83
Southern Europe	806,372	2.13	1.71	2.54	17,143	13,813	20,511
Italy	372,842	2.39	2.11	2.68	8,911	7,867	9,992
Portugal	207,205	1.35	0.66	2.04	2,797	1,368	4,227
Greece	144,792	3.14	2.65	3.63	4,546	3,837	5,256
Spain	81,533	1.09	0.91	1.27	889	742	1,035
Northern/western Europe	1,918,743	0.55	0.34	0.71	10,641	6,465	13,643
United Kingdom	688,262	0.54	0.30	0.60	3,717	2,065	4,130
Germany	614,841	0.60	0.40	0.80	3,689	2,459	4,919
France	158,481	0.68	0.44	1.05	1,078	697	1,664
Ireland	121,092	0.35	0.26	0.44	424	315	533
Netherlands	89,617	0.41	0.11	0.72	367	99	645
Northern/western Europe, other/NS*	246,450	0.55	0.34	0.71	1,367	830	1,752
Europe, other/not specified*	26,012	2.01	1.44	2.56	523	374	666

Abbreviations: NS, not specified.

Rates have been rounded to two decimal places.

Northern America = FB from Canada and Bermuda living in the United States.

For northern America, Japan, Australia, New Zealand, and northern and western Europe, which have low CHB rates and relatively modest numbers of emigrants to the United States, rates from a few large population studies were used instead of rates from a systematic review and meta-analysis.

\*Rate shown is weighted average for subregion or region.

†Only one study available; 95% CIs from standard error.

‡Random effects rate cannot be calculated because  $\tau^2 < 0$ ; FE rate is shown.

in 2009 (Table 3) was 1.32 million persons (95% CI: 1.04-1.61). Approximately 58% of the FB persons living with CHB migrated from Asia and approximately 11% migrated from Africa, where CHB is hyperendemic (Fig. 1). Approximately 7% of the FB with CHB in the United States were from Central America, a region with lower CHB rates, but many more emigrants to the United States. The five countries from which the largest numbers of FB with CHB originate were China (243,484; 12.3% of 1.99 million Chinese immigrants), Vietnam (143,440; 12.5% of 1.15

million Vietnamese immigrants), Philippines (127,612; 7.4% of 1.73 million Filipino immigrants), Dominican Republic (84,542; 10.7% of 791,593 Dominican immigrants), and Mexico (56,243; 0.49% of 11.5 million Mexican immigrants). Using the pooled CHB prevalence rates from the FE meta-analyses (all surveys combined), the number of FB in the United States living with CHB in 2009 was 967,281 persons (95% CI: 902,328-1.03 million).

**FB With CHB from Subgroup Analyses.** RE pooled prevalence rates were calculated from surveys in



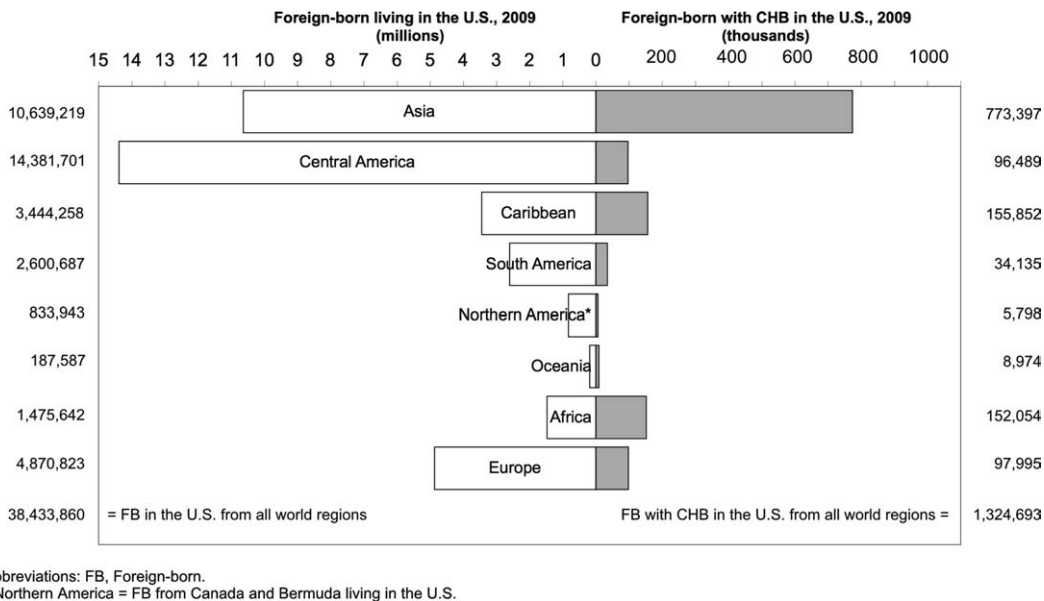


Fig. 1. FB populations living in the United States and prevalence of FB with CHB in the United States from RE meta-analysis by world region of origin, 2009.

emigrants for 52 countries for which data were available. Substituting these rates for the rates from all studies combined (for a given country) yielded an estimate of 1.23 million (95% CI: 784,175-1,833,960) FB in the United States with CHB (Fig. 2). Subgroup analysis also suggests that CHB rates in some countries declined over time. To account for this, an alternative calculation was done using the number of FB living in the United States in 2009 that arrived from each country in each of three decades (i.e., before 1990, 1990-1999, and 2000-2009), combined with the country-specific RE pooled CHB rate based on surveys done in the corresponding decade (Supporting Table 9). This calculation indicates the number of FB living with CHB in the United States in 2009 was 1.42 million (95% CI: 952,011-1,898,658). Because of the small number of surveys in the subgroups, both estimates

based on subgroup analyses had greater uncertainty than the estimate based on all surveys combined and should be interpreted with caution.

### Discussion

In this study, we used an approach to estimating the prevalence of CHB in the FB that avoided a major shortcoming of CHB studies based on sampling of FB persons living in the United States—namely, that these studies underrepresent FB persons and others at high risk for CHB.<sup>3,22</sup> Our approach focused on the FB, and we systematically reviewed, on a county-by-county basis, the majority of available data on HBsAg seroprevalence rates in emigrants and in-country populations of 102 countries from which FB in the United States originate. The results of this analysis suggest

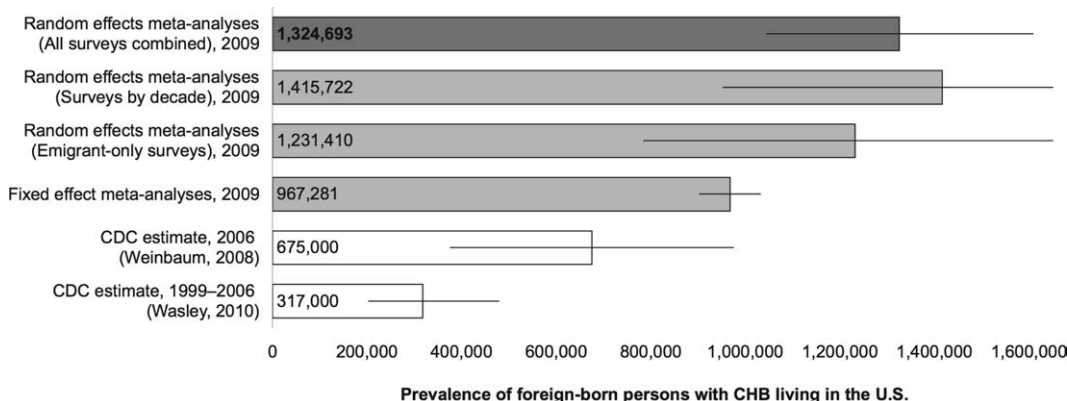


Fig. 2. Prevalence of FB persons with CHB living in the United States: comparison of estimates from CDC and these meta-analyses.

that the number of FB persons living with CHB in the United States is larger than previous estimates (Fig. 2).

A report based on data from NHANES for 1999-2006 estimated 730,000 (95% CI: 550,000-940,000) persons with CHB living in the United States, of whom 317,000 (95% CI: 202,000-479,000) were FB.<sup>6</sup> This is almost certainly an underestimate, because NHANES underrepresents populations at high risk for HBV, such as Asian-Pacific Islanders and institutionalized, incarcerated, and homeless persons.<sup>3,22</sup> A second study estimated that 800,000-1.4 million persons in the United States were living with CHB in 2006, of whom 229,000-534,000 were U.S.-born and 375,000-975,000 were FB.<sup>5</sup> These estimates are based on multiple data sources, including (1) NHANES, (2) estimates of the number and CHB prevalence of persons in institutions and group quarters, (3) country-specific CHB prevalence rates reported in the literature, and (4) estimates of the U.S. population by country of birth. Cohen et al., using census data and estimates of CHB rates by ethnicity, calculated a total CHB prevalence of 2 million persons, of whom 774,027 were FB Asians and Pacific Islanders.<sup>7</sup> Because the FB population grew by less than 3% from 2006 to 2009,<sup>12</sup> the difference between our estimate of 1.32 million FB with CHB and earlier estimates is explained by higher CHB rates derived from the meta-analyses. The RE meta-analyses based on all surveys for a given country combined yielded an average CHB prevalence rate among the FB in the United States of 3.45% (95% CI: 2.72-4.19). The average rates from the meta-analyses in which surveys and FB populations were stratified by decade are 4.45% (95% CI: 2.85-6.09), 3.40% (95% CI: 2.33-4.53), and 2.95% (95% CI: 2.13-3.82), for the decades "before 1990," "1990-1999," and "2000 and later," respectively. These rates are significantly higher than 0.89% (95% CI: 0.55-1.35) found for FB in NHANES 1999-2006<sup>6</sup> and 2.6% derived by Weinbaum et al.<sup>5</sup> The rate from this meta-analysis is also higher than the prevalence of 0.59% found in NHANES 1999-2008 for white, black, or Hispanic FB persons, but similar to the prevalence of 3.28% for FB of other race or ethnicity.<sup>8</sup>

This estimate of 1.32 million FB with CHB includes undocumented persons. The U.S. Census Bureau assumes ACS data include undocumented persons, who represented approximately 30% of the FB in the United States in 2009.<sup>12,13</sup> Adding our estimate of 1.04-1.61 million FB persons with CHB to previous estimates of 229,000-534,000 noninstitutionalized U.S.-born persons with CHB and 74,000 institu-

tionized persons with CHB,<sup>5</sup> the total prevalence of CHB in the United States may be as high as 2.2 million.

The RE meta-analyses suggest that approximately 52% (682,622; 95% CI: 572,845-792,352) of the FB persons with CHB migrated to the United States from countries classified as having high HBV endemicity (i.e., with CHB rates 8% or higher); another 37% (495,001; 95% CI: 375,867-614,369) migrated from countries with intermediate endemicity (i.e., CHB rates 2-7.9%); the remaining 11% (147,070; 95% CI: 95,576-202,194) migrated from countries where CHB rates are less than 2%.<sup>5</sup> The contribution of persons from Central America to the FB population with CHB was larger than expected. However, because of the large number of FB in the United States from this region (i.e., 14.4 million), small differences in CHB rates result in large differences in the number with CHB. Few studies were found documenting HBsAg seroprevalence in Central America outside Mexico, and rates in blood donors were used for El Salvador, Honduras, Panama, and Belize. Additional seroprevalence data for these countries are needed.

These prevalence estimates have limitations and should be viewed as a systematic attempt to make the best use of available data. First, literature searches were limited to PubMed, and additional potentially relevant articles may have been found had we also searched EMBASE and CINAHL databases. In addition, potentially relevant surveys reported in languages other than English were omitted because not all non-English papers were acquired and translated.

Another concern is whether the country-specific CHB rates from the meta-analyses are representative of the FB who migrated to the United States and were living there in 2009. Because no seroprevalence data in emigrants were available for more than half the countries, we combined prevalence data from emigrants with data from populations still living in the countries of origin. Nationally representative surveys were included, but were available for only a few countries. Most in-country surveys were done in population subgroups at "average risk" for HBV infection (e.g., pregnant women, school children, clerical and factory workers, and military recruits). Biases introduced by using data from these subgroups likely vary from country to country and depend on factors such as dominant routes of HBV transmission, attendance rates at antenatal clinics and schools, whether military service is mandatory, and the particular array of surveys available for each country. We excluded surveys in persons at higher risk for HBV (e.g., sex workers,

injection drug users, and homeless) because these persons are less representative of emigrants.

Comparison of RE pooled prevalence rates in emigrants with those in in-country populations did not reveal a systematic bias toward higher rates in either group, although this analysis had large uncertainty. It is likely that emigrants from some countries have lower CHB rates (e.g., because they have higher socioeconomic status and resources to emigrate) or higher rates (e.g., because they lived in refugee camps) than in-country populations. If only data from surveys in emigrants are used for the 52 countries for which data are available, the estimate of the number of FB living with CHB is still significantly higher than estimates from NHANES-based studies (Fig. 2).

Furthermore, for some countries, the pooled CHB prevalence rates from the meta-analyses are higher than rates reported in immigrants recently arriving in the United States.<sup>9</sup> These studies, however, have small samples and may not be representative of FB persons arriving earlier. Supporting Table 10 compares pooled prevalence rates from the meta-analyses with data reported for refugees from 31 countries who were screened on arrival to the United States during two time periods (i.e., 1979-1991 and 2006-2008).<sup>9,10</sup> For most countries, rates from the meta-analyses are higher than rates reported for refugees arriving between 2006 and 2008; in contrast, rates from the meta-analyses are similar to rates reported for migrants arriving in 1979-1991 for most countries. Given that 40% of the FB living in the United States arrived before 1990, the earlier rates are probably more representative.<sup>12</sup>

Finally, data were not sufficient to assess other factors likely to contribute to the observed heterogeneity, such as differences by race, ethnicity, age, socioeconomic status, or geographic location within the country of origin. The FB population living in the United States in 2009 included persons of different ages who migrated to the United States in different decades through different routes (e.g., as economic migrants, family reunification participants, adoptees, or refugees). Given the limitations of the available data, we opted to pool surveys from different dates, locations, and populations within the country, and the results must be viewed with this caveat in mind.

The finding that as many as 1.6 million FB in the United States may be living with CHB—nearly twice the number previously estimated—highlights the need for HBV screening in all FB persons. As many as 60%-70% of all persons with CHB in the United States are undiagnosed, and only approximately half of those diagnosed receive appropriate care.<sup>23</sup> Numerous

personal, cultural, economic, and environmental factors create barriers that may result in a high proportion of FB persons remaining unaware of their infection.<sup>23,24</sup> Since 2008, Centers for Disease Control and Prevention (CDC) guidelines have recommended routine serologic HBsAg screening for all FB persons from countries with HBsAg prevalence rates of 2% or higher, regardless of their vaccination history, and for unvaccinated U.S.-born children of FB parents from countries with high HBsAg endemicity.<sup>5</sup> Routine screening of pregnant women is especially important, because maternal-neonatal transmission of HBV occurs in approximately 1,000 infants born to HBsAg-positive mothers in the United States each year.<sup>3</sup>

The number of FB persons in the United States increased from 19.8 million in 1990 to 38.4 million in 2009,<sup>12,25</sup> and between 1980 and 2009, more than 25 million FB persons became legal U.S. permanent residents.<sup>26</sup> The number of FB living with CHB will continue to increase with ongoing immigration from countries with intermediate and high HBV endemicity. Primary care physicians and general internists have an opportunity to identify FB persons living with CHB in the United States via screening and follow-up to ensure they benefit from monitoring and treatment.

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