Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013

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Summary

Background **The quantification of the burden of disease attributable to hepatitis B virus (HBV) infection and the adaptation of prevention and control measures requires knowledge on its prevalence in the general population. For most countries such data are not routinely available. We estimated the national, regional, and global prevalence of chronic HBV infection.**

Methods **For this systematic review and pooled analysis, we searched for data on prevalence of chronic HBV infection published between Jan 1, 1965, and Oct 23, 2013, in the databases Medline, Embase, CAB Abstracts (Global health), Popline, and Web of Science. We included studies reporting the hepatitis B surface antigen (HBsAg) serological marker of chronic HBV infection in non-high-risk groups and extracted data into a customised database. For each country, we calculated HBsAg prevalence estimates and 95% CIs weighted by study size. We extrapolated prevalence estimates to population sizes in 2010 to obtain the number of individuals with chronic HBV infection.**

Findings **Of the 17 029 records screened, 1800 report on the prevalence of HBsAg covering 161 countries were included. HBsAg seroprevalence was 3·61% (95% CI 3·61–3·61) worldwide with highest endemicity in countries of the African region (total 8·83%, 8·82–8·83) and Western Pacific region (total 5·26%, 5·26–5·26). Within WHO regions, prevalence ranged from 0·20% (0·19–0·21; Mexico) to 13·55% (9·00–19·89; Haiti) in the Americas, to 0·48% (0·12–1·90; the Seychelles) to 22·38% (20·10–24·83; South Sudan) in the African region. We estimated that in 2010, globally, about 248 million individuals were HBsAg positive.**

Interpretation **This first global assessment of country-level population prevalence of chronic HBV infection found a wide variation between countries and highlights the need for continued prevention and control strategies and the collection of reliable epidemiologic data using standardised methodology.**

Funding **World Health Organization.**

Introduction

Chronic hepatitis B virus (HBV) infection continues to be a major public health issue worldwide[1–4] despite the availability of an effective vaccine and potent antiviral treatments. The risk of developing chronic HBV infection decreases with age at infection, from about 90% when infected perinatally up to 6 months of age to 20–60% between the ages of 6 months and 5 years.[1,5] 25% of people who acquire HBV as children will develop primary liver cancer or cirrhosis as adults.[6] Recent Global Burden of Disease estimates indicate a high morbidity and mortality attributable to chronic HBV, despite decreases over the past decades.[7,8]

In sub-Saharan Africa and east Asia, transmission predominantly occurs in infants and children by perinatal and horizontal routes (ie, resulting from close contact which is not parenteral, perinatal, or sexual in nature) whereas in more industrialised countries, rates of new infection and acute disease are highest among young adults and transmission predominantly occurs via injection drug use and high-risk sexual behaviours.[9–13]

In 2014, the 67th World Health Assembly of the WHO reaffirmed the resolution on viral hepatitis prevention and control highlighting the need to monitor viral hepatitis prevention, diagnosis and treatment progress.[14] Accurate, national-level epidemiological information is imperative to inform prevention and control priorities, to assess the impact of implemented strategies and for updating burden of disease estimates. However, there are no up-to-date global systematic reviews reporting country-level chronic HBV prevalence. Previous systematic reviews on HBV prevalence were limited in scope (eg, they focused on specific regions or populations).[15–20]

We report national-level prevalence estimates of chronic HBV derived by a systematic review of peer-reviewed literature reporting HBV prevalence (hepatitis B surface antigen [HBsAg]) in the general population for all countries for which sero-epidemiologic data were available. We also estimate the number of people living with chronic HBV infection on a national, regional, and global level and address changes over time.

Methods

Search strategy and study selection

We undertook and report our systematic review in line with the criteria outlined in the PRISMA guidelines.[21] We did a systematic search on articles published between Jan 1, 1965, and Oct 23, 2013, in the databases Medline,

Embase, CAB Abstracts (Global health), Popline, and Web of Science. We developed a search strategy and adapted it for each database using a combination of Medical Subject Headings (MeSH) and free text including terms related to HBV and to prevalence (appendix). We supplemented database searches by inspecting publications referenced in studies identified in the systematic search. These searches were developed in consultation with an expert generalist librarian.

Publications were catalogued using Endnote X6. Figure 1 shows the flowchart of the study selection process. Two authors (AS and JJO) systematically screened search results and independently reviewed retrieved records applying the eligibility criteria (panel). In brief, observational studies on chronic HBV infection seroprevalence (HBsAg prevalence), done in the general population, among blood donors, health-care workers (HCWs), and pregnant women were considered for inclusion in this systematic review. Studies were excluded if they were systematic reviews or meta-analyses, surveillance reports, case studies, letters or correspondence, or did not contain HBsAg seroprevalence data. Studies were also excluded if they exclusively reported prevalence estimates for high-risk population groups (eg, migrants and refugees). Eligible literature, identified in title or abstracts screening, was obtained for full text screening and grouped by country and WHO region. We translated non-English language papers using google translator or by asking colleagues proficient in the language in question.

During full text screening, we excluded articles reporting data without specifying the serological marker. For the USA, we considered the National Health and Nutrition Examination Survey (NHANES) as a nationally representative source for prevalence of chronic HBV.[22] Nevertheless, we followed the same full text screening approach for all studies found for the USA but only included reports on original NHANES data.

For the sensitivity analyses, we assessed the representativeness of included study data and assigned the category "non-representative" to studies done in indigenous populations or in locations within countries known as particularly low or high endemicity areas for HBV. We assessed representativeness on the basis of information available from source manuscripts and author expert opinion.

Data extraction

Following full text review, we extracted data from each study using the following variables: study characteristics (study and sample collection dates, study locations ie, city, subnational [an area, region, state, or province in a country], or national level), participant characteristics (age range, sex, year, and population group), and prevalence of the HBV marker, type of laboratory tests, and number of participants the HBV marker prevalence was based on.

Statistical analysis

We estimated the prevalence of chronic HBV infection (HBsAg seroprevalence) based on pooled data from all eligible studies for each country. 95% confidence intervals (CIs) were obtained from logistic regression using R-package stats and converted to prevalence values using expit transformation. For regional prevalence estimates, countries were grouped into six WHO regions: Africa, the Americas, the Eastern Mediterranean, Europe, South East Asia, and the Western Pacific. Regional HBsAg prevalence estimates were produced from country-specific estimates, weighted according to the population size of each country. Similarly, regional 95% CIs were obtained from weighted country-specific variances of the prevalence estimate from the logistic regression model. We used map data from Natural Earth to graphically represent results, using previously defined HBV endemicity levels based on the prevalence of HBsAg: low (<2%), lower-intermediate (2–4·99%), higher-intermediate (5–7·99%), and high (≥8%).[15]

See Online for appendix

For the **Natural Earth website** see http://www.naturalearthdata.com/

We did a sensitivity analysis excluding studies classified as non-representative to assess the potential impact of these studies on HBsAg prevalence. For the assessment of potential changes of HBsAg prevalence

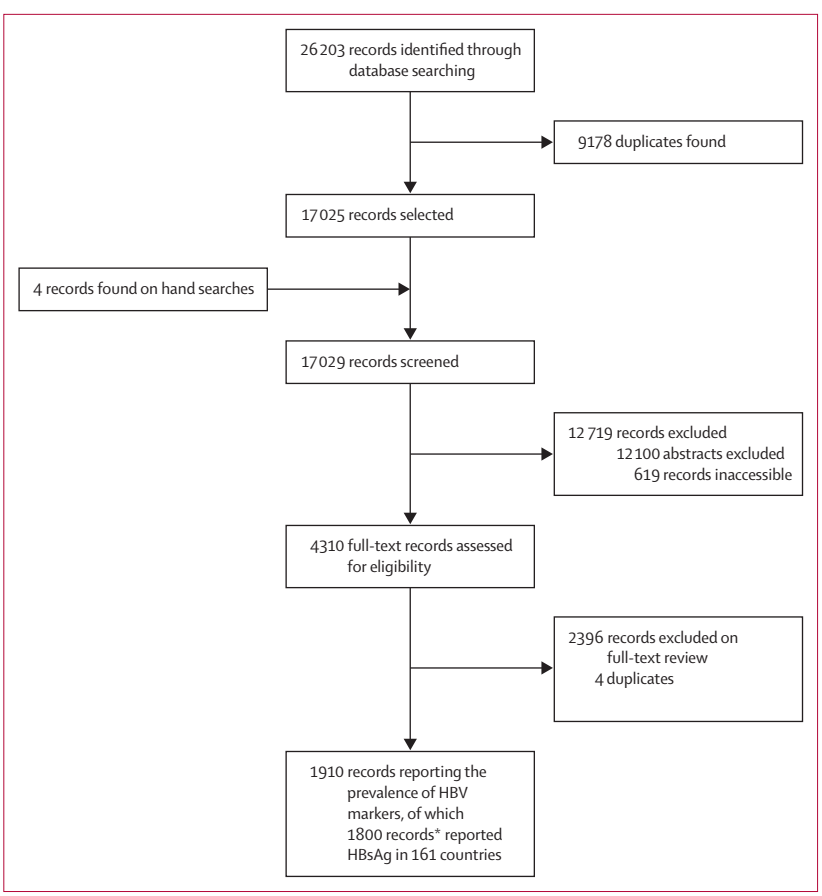

Figure 1: **Flowchart of study selection**
*In total we found 1862 reports on the prevalence of HBsAg due to multicentric, multinational studies.

Panel: Study selection criteria

Selection, grading, and clarification of hepatitis reports

- Hepatitis reports were restricted to serological test results for hepatitis B surface antigen (HBsAg)
- Hepatitis B reports that did not specify the serological marker were excluded
- Multicentre, multinational reports were extracted separately in the respective country category
- Hepatitis reports were classified as national (if so specified or if it was a multicentre study from multiple regions in countries to be considered national level), subnational (in a particular geographic region), and city level
- Hepatitis reports from one city were assumed to be from one site unless otherwise stated
- If calculation or typographical errors were detected in source documents, reports were recalculated and clarified with authors if possible

Study exclusion criteria

Publication type:

- Guidelines
- Perspectives, correspondence
- Systematic reviews or meta-analyses
- Surveillance registration or national notifiable disease reports of (acute) incident hepatitis virus cases and case studies

Study type:

- Vaccine efficacy trials
- Economic analyses
- Modelling, time series, or transmission studies; mortality or survival analyses; diagnostic assay or test performance studies; animal studies
- KAP (knowledge, attitude, practice) studies; qualitative studies; questionnaire-based studies
- Genotype and mutation analysis studies

Study population:

- Study populations selected based on a risk factor for viral hepatitis or on a condition associated with hepatitis infection or risk of hepatitis transmission (persons with liver disease, individuals living with HIV/AIDS, injecting and non-injecting drug users, sex-workers, men who have sex with men, hospitalised patients, institutionalised individuals (eg, people with intellectual disabilities)
- High-risk population groups (migrants, refugees, prisoners, individuals [groups] classified as low socio-economic status, homeless people, adoptees)
- Populations of pre-defined hepatitis B virus (HBV) carrier status (eg, re-activation of HBV, occult HBV, therapeutic responses)

Disease outcomes:

- Hepatitis A virus, hepatitis C virus, hepatitis D virus, hepatitis E virus, hepatitis G virus

Viral testing:

- HBV diagnosis based on non-serum testing (eg, saliva testing)
- Studies not explicitly reporting the serological marker(s) tested and the results of those measurements
- Self-reported hepatitis status without serological confirmation
- Studies not reporting the number of individuals on which the prevalence estimate was based

over time, we stratified prevalence estimates into two time periods (1957–89 and 1990–2013), based on the timepoint when serological samples were obtained. The cutoff was chosen to balance the time covered and the numbers of studies and people tested in the two time periods.

To obtain the number of people living with chronic HBV, we extrapolated our prevalence estimates to the total population living in countries and regions as per the UN Population Division for the year 2010.[23] All analyses were done with the statistical software R (version 3.0.1).[24]

Role of the funding source

This project was funded by the WHO. WHO experts were involved in scientific and technical discussions of project proceedings and content, specifically during the initial phases of the project. Data collection, analysis, interpretation, and writing of the report were done independently by the authors. All authors had full access to the study data and had the final responsibility for the decision to submit the paper for publication.

Results

After removal of duplicates and initial screening, we reviewed 4310 papers in full, of which 1800 eligible reports on the prevalence of HBsAg covering 161 countries were included in the systematic review (figure 1). Included studies on HBsAg entailed 109 415 627 individuals. The highest numbers of reports were available for China (n=167), India (n=129), Brazil (n=108), and Nigeria (n=85).

On a global level, HBsAg prevalence was 3·61% (95% CI 3·61–3·61). HBsAg seroprevalence and the number of people living with chronic HBV in the general population in six WHO world regions are reported in tables 1–6. Except for Algeria, Eritrea, and the Seychelles, most countries in Africa were of higher-intermediate endemicity (HBsAg prevalence 5–7·99%), or highly endemic for HBV (HBsAg prevalence ≥8%; table 1, figure 2). Countries in the Americas, such as Mexico, Guatemala, and the USA had mostly low endemicity levels (HBsAg prevalence <2%), but high HBsAg prevalence was observed in Haiti (table 2). The Eastern Mediterranean region was of lower-intermediate endemicity (2·00–4·99%), but Djibouti, Somalia, and Sudan showed a higher prevalence of HBsAg than other

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Algeria	4	6338	2·89% (2·50–3·33)	37 062 820	1 070 132
Angola	4	2142	12·42% (11·09–13·88)	19 549 124	2 427 669
Benin	1	424	15·57% (12·42–19·34)	9 509 798	1 480 299
Burkina Faso	7	39 082	12·05% (11·73–12·38)	15 540 284	1 872 850
Burundi	2	219	9·13% (5·97–13·73)	9 232 753	843 174
Cameroon	17	14 391	12·24% (11·71–12·78)	20 624 343	2 523 763
Cape Verde	1	179	7·26% (4·26–12·10)	487 601	35 412
Central African Republic	6	2100	13·86% (12·44–15·40)	4 349 921	602 775
Congo	4	2328	10·95% (9·75–12·29)	4 111 715	450 381
Côte d'Ivoire	8	6268	9·40% (8·70–10·14)	18 976 588	1 783 218
DR Congo	7	21 559	5·99% (5·68–6·31)	62 191 161	3 724 143
Equatorial Guinea	1	2042	8·81% (7·66–10·12)	696 167	61 366
Eritrea	2	29 594	2·49% (2·32–2·67)	5 741 159	142 976
Ethiopia	18	29 941	6·03% (5·77–6·31)	87 095 281	5 253 468
Gabon	9	6270	11·48% (10·72–12·30)	1 556 222	178 705
Gambia	7	6574	12·28% (11·50–13·09)	1 680 640	206 309
Ghana	12	18 255	12·92% (12·44–13·42)	24 262 901	3 135 370
Guinea	3	5736	15·06% (14·16–16·01)	10 876 033	1 638 231
Kenya	8	19 249	5·16% (4·86–5·48)	40 909 194	2 110 386
Liberia	4	1499	17·55% (15·70–19·55)	3 957 990	694 431
Madagascar	7	52 375	4·60% (4·42–4·78)	21 079 532	968 753
Malawi	3	581	12·22% (9·80–15·14)	15 013 694	1 834 720
Mali	8	28 657	13·07% (12·69–13·47)	13 985 961	1 828 224
Mauritania	4	3149	16·16% (14·92–17·49)	3 609 420	583 422
Mozambique	5	4303	8·34% (7·55–9·21)	23 967 265	1 999 593
Namibia	6	10 890	8·61% (8·10–9·16)	2 178 967	187 683
Niger	3	3915	15·48% (14·38–16·65)	15 893 746	2 460 181
Nigeria	85	111 637	9·76% (9·59–9·93)	159 707 780	15 586 376
Rwanda	2	180	6·67% (3·82–11·37)	10 836 732	722 449
Senegal	10	33 063	11·06% (10·72–11·40)	12 950 564	1 432 032
Seychelles	1	417	0·48% (0·12–1·90)	91 208	437
Sierra Leone	2	368	8·42% (5·99–11·73)	5 751 976	484 541
South Africa	18	136 356	6·70% (6·56–6·83)	51 452 352	3 445 477
South Sudan	3	1193	22·38% (20·10–24·83)	9 940 929	2 224 835
Swaziland	1	3047	19·00% (17·65–20·43)	1 193 148	226 726
Togo	1	230	10·87% (7·45–15·59)	6 306 014	685 436
Uganda	12	10 227	9·19% (8·65–9·77)	33 987 213	3 123 886
Tanzania	14	7185	7·17% (6·59–7·79)	44 973 330	3 223 558
Zambia	3	4239	6·06% (5·38–6·82)	13 216 985	801 313
Zimbabwe	5	5310	14·35% (13·43–15·32)	13 076 978	1 876 583
Total	318	631 512	8·83% (8·82–8·83)	857 003 124	75 641 609

Countries in the African Region where no eligible reports on HBV reporting HBsAg were available were: Botswana, Chad, Comoros, Guinea-Bissau, Lesotho, Mauritius, and São Tomé and Príncipe.

Table 1: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO African Region**

countries in the region such as Iran (table 3). The European region was a lower-intermediate endemicity region; however, HBsAg prevalence increased eastwards, ranging from 0·01% (95% CI 0·01–0·01) in the UK to 10·32% (8·56–12·38) in Kyrgyzstan (table 4). Overall, the South East Asian region had low endemicity levels but on a country-level, a HBsAg prevalence below 2% was only noted in India, Indonesia, and Nepal (table 5). Other countries in this region had low-intermediate to high-intermediate endemicity levels. The Western Pacific region was a high-intermediate endemicity region (5–7·99%), with a higher HBsAg prevalence in Pacific Island States such as the Solomon Islands than in larger countries such as China and Australia (table 6).

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Argentina	11	3549199	0·77% (0·77–0·78)	40374224	312806
Barbados	1	500	1·40% (0·67–2·91)	280396	3926
Belize	5	2231	4·71% (3·90–5·67)	308595	14524
Bolivia	4	1357	0·44% (0·20–0·98)	10156601	44908
Brazil	108	3898502	0·65% (0·65–0·66)	195210154	1275813
Canada	25	498814	0·76% (0·74–0·79)	34126240	260865
Chile	2	1179	0·68% (0·34–1·35)	17150760	116375
Colombia	5	3794	2·29% (1·86–2·82)	46444798	1065023
Costa Rica	2	7262	0·62% (0·46–0·83)	4669685	28936
Cuba	1	538	1·30% (0·62–2·70)	11281768	146789
Dominican Republic	1	489	4·09% (2·65–6·25)	10016797	409685
Ecuador	1	500	2·00% (1·08–3·68)	15001072	300021
Guatemala	1	12668	0·22% (0·15–0·32)	14341576	31699
Haiti	2	155	13·55% (9·00–19·89)	9896400	1340803
Jamaica	3	825	3·76% (2·65–5·29)	2741485	103013
Mexico	32	787039	0·20% (0·19–0·21)	117886404	237858
Nicaragua	2	1452	0·55% (0·28–1·10)	5822209	32078
Panama	3	6493	1·68% (1·39–2·02)	3678128	61746
Peru	18	18213	2·10% (1·90–2·32)	29262830	615366
Suriname	2	1253	3·91% (2·97–5·14)	524960	20529
USA*	4	112505	0·27% (0·24–0·30)	312247116	843724
Venezuela	15	138249	0·48% (0·44–0·52)	29043283	139283
Total	248	9043217	0·81% (0·81–0·81)	937089925	7622334

Countries in Region of the Americas where no eligible reports on HBV reporting HBsAg were available were: Antigua and Barbuda, The Bahamas, Dominica, El Salvador, Grenada, Guyana, Honduras, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Trinidad and Tobago, and Uruguay. *Of the 420 articles for the USA that were full text reviewed, four entailed original NHANES data for HBsAg and fulfilled the eligibility criteria of this systematic review and were hence included.

Table 2: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO Region of the Americas**

Overall, country-specific HBsAg prevalence estimates did not change after exclusion of studies that were deemed non-representative—ie, those that were conducted in highly endemic areas in a country (eg, the country estimate for Brazil did not change when studies done in a high endemicity area were excluded).

After extrapolation to population estimates as per the UN Population Division for the year 2010 we estimated that over 248 million individuals were HBsAg posititve worldwide. The largest number of people living with chronic HBV live in the Western Pacific region (over 95 million individuals, table 6) followed by the African region (over 75 million individuals, table 1). The region of the Americas had the smallest number of infected individuals (over 7 million individuals, table 2). The three countries with the highest population of HBsAg-positive individuals were: China (74 million, table 6), India (17 million, table 5) and Nigeria (15 million; table 1).

Over two time periods considered (1957–89 and 1990–2013), we noted decreases in prevalence in countries of the South East Asian, Western Pacific, and the Eastern Mediterranean regions (appendix). In South East Asia decreases in prevalence were primarily recorded in Thailand, India, and to a lesser extent in Bangladesh. In the Western Pacific region, decreases in prevalence were obvious in China, South Korea, Malaysia, and Singapore. In the Eastern Mediterranean region, decreases in prevalence were primarily noted in Saudi Arabia, Iran, and Turkey. Consistently low HBsAg prevalence was noted in most countries in the Americas, western Europe, Japan, and Australia. Throughout the two time periods considered, the African region continued to be of upper intermediate to high endemicity. We also noted a tendency towards an increasing prevalence in a few countries in eastern Europe, and an increasing trend in some African countries, namely Nigeria, where a HBsAg prevalence of 8·52% (95% CI 7·70–9·42) was recorded in 1957–89 and a prevalence of 9·81% (9·63–9·99) in 1990–2013 (appendix).

Discussion

This global systematic review showed that in 2010, about 248 million individuals in the general population, worldwide were chronically infected with HBV. We noted a wide variation in the estimates of HBsAg prevalence between countries, which might be partly explained by varying risk factors and transmission routes across countries. Prevalence estimates at the country level indicate a high burden of infection in sub-Saharan Africa and some countries in the Western Pacific region in

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Afghanistan	2	4511	1·62% (1·29–2·03)	28 397 812	459 552
Bahrain	1	4859	1·19% (0·92–1·54)	1 251 513	14 939
Djibouti	1	9006	10·40% (9·79–11·05)	834 036	86 775
Egypt	29	353 431	1·71% (1·67–1·76)	78 075 705	1 338 923
Iran	45	17 965 990	0·96% (0·95–0·96)	74 462 314	713 547
Iraq	2	495 998	0·67% (0·65–0·70)	30 962 380	208 310
Jordan	2	19 000	1·86% (1·68–2·06)	6 454 554	119 919
Kuwait	2	12 642	0·80% (0·66–0·97)	2 991 580	23 900
Lebanon	9	31 538	1·21% (1·10–1·34)	4 341 092	52 719
Libya	2	68 761	2·16% (2·05–2·27)	6 040 612	130 193
Morocco	8	232 765	1·09% (1·05–1·14)	31 642 360	345 699
Oman	3	1477	5·55% (4·49–6·84)	2 802 768	155 604
Pakistan	67	1 221 014	2·76% (2·73–2·79)	173 149 306	4 772 683
Palestine*	1	778	1·80% (1·07–3·02)	..	..
Qatar	2	1275	1·73% (1·14–2·61)	1 749 713	30 191
Saudi Arabia	36	312 787	3·18% (3·12–3·24)	27 258 387	866 675
Somalia	9	4535	14·77% (13·77–15·84)	9 636 173	1 423 646
Sudan	9	5965	9·76% (9·03–10·54)	35 652 002	3 478 536
Syria	2	4039	2·62% (2·17–3·17)	21 532 647	565 105
Tunisia	4	43 984	6·17% (5·95–6·40)	10 631 830	655 787
United Arab Emirates	2	1859	0·70% (0·41–1·20)	8 441 537	59 032
Yemen	15	15 641	8·38% (7·96–8·83)	22 763 008	1 907 954
Total	253	20 811 855	3·01% (3·01–3·01)	579 071 329	17 409 688

*We restricted estimation of HBsAg carriers to both WHO Member States and countries with available population data as provided by the UN Population Division; therefore Palestine was not included in the calculation of the total number of people living with chronic HBV.

Table 3: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO Eastern Mediterranean Region**

particular. These results highlight a continuous need for ongoing prevention of HBV transmission. Temporal trends over two time periods indicate a decrease in HBsAg prevalence in most countries. However, despite improvements, chronic HBV infection remains highly prevalent, particularly in some countries in Africa with trends signalling a further increase. Decreases in HBsAg prevalence, particularly in more industrialised nations are probably due to efforts in hepatitis B vaccination, screening of blood products, screening and post-exposure prophylaxis of health-care workers, and increased availability of safe injection materials.[25]

Since the universal HBV immunisation recommendation was passed in 1992,[26] the number of countries including hepatitis B vaccinations in their national vaccination schedules has constantly increased.[27] Despite existing recommendations for implementing a hepatitis B vaccine birth dose within 24 h after birth to prevent transmission and the risk of chronic infection in exposed newborn babies, its implementation has been missing in countries where this global epidemic is concentrated because of economic and logistic constraints.[14,28–30] Additionally, unsafe blood products and medical procedures particularly in resource-poor settings persist being important routes of transmission to individuals and in turn their susceptible contacts.[30,31] Furthermore, poor health outcomes among those who are infected and could be treated in resource-poor settings are affected by issues around antiviral treatments such as the indefinite duration of therapy necessitating strict compliance, coupled with the restricted access to available treatments.[30,31]

In view of restrictions in health care in some countries and population groups in which this epidemic is primarily centred and given prevailing demographic, and global migration trends, we expect the HBV attributable disease burden and the reservoir of people living with chronic HBV to not only remain high in countries with high HBV endemicity but also possibly increase in highly industrialised, low-endemicity countries receiving migrants from high-endemicity countries. This reservoir of infection and ongoing transmission warrants effective prevention, screening, and monitoring strategies to identify infected individuals and their susceptible contacts, and to provide antiviral therapy, which constitutes an essential part of HBV infection control.[28–31]

Blood donors, pregnant women, and health-care workers included in our systematic review have been used to assess prevalence of chronic HBV infection in the general population.[17,32] Blood donations in many countries are voluntary and donors are subjected to rigorous

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Albania	8	48758	7·79% (7·56–8·03)	3150143	245509
Austria	3	1786	1·23% (0·81–1·86)	8401924	103495
Azerbaijan	1	576	2·78% (1·71–4·49)	9094718	252631
Belarus	1	10156	4·60% (4·21–5·02)	9491070	436425
Belgium	2	3984	0·68% (0·47–0·99)	10941288	74150
Bosnia and Herzegovina	2	8942	1·11% (0·91–1·35)	3845929	42580
Bulgaria	1	2221	3·92% (3·19–4·81)	7389175	289445
Croatia	4	13531	1·11% (0·95–1·30)	4338027	48090
Cyprus	2	9364	2·69% (2·38–3·04)	1103685	29702
Czech Republic	4	5582	1·24% (0·98–1·56)	10553701	130456
Denmark	12	198941	0·91% (0·87–0·95)	5550959	50336
France	33	1412054	0·26% (0·25–0·27)	63230866	165728
Georgia	5	4807	2·64% (2·22–3·14)	4388674	115948
Germany	20	105027	0·70% (0·65–0·76)	83017404	584134
Greece	35	680364	0·97% (0·95–1·00)	11109999	108150
Hungary	4	35511	0·53% (0·46–0·61)	10014633	53301
Iceland	1	1420	0·14% (0·04–0·56)	318042	448
Ireland	1	16222	0·03% (0·01–0·07)	4467561	1377
Israel	20	445427	0·96% (0·93–0·99)	7420368	71184
Italy	70	1980899	2·52% (2·49–2·54)	60508978	1522546
Kazakhstan	2	430	6·05% (4·15–8·73)	15921127	962673
Kosovo*	2	71540	4·17% (4·03–4·32)	NA	NA
Kyrgyzstan	1	979	10·32% (8·56–12·38)	5334223	550313
Lithuania	2	26710	1·70% (1·55–1·86)	3068457	52156
Netherlands	10	1717081	0·40% (0·39–0·41)	16615243	67009
Norway	4	33085	0·01% (0·00–0·03)	4891251	444
Poland	9	5145391	0·42% (0·42–0·43)	38198754	161016
Portugal	3	5610	1·02% (0·78–1·31)	10589792	107597
Moldova	3	4976	7·38% (6·68–8·14)	3573024	263525
Romania	21	152651	5·61% (5·50–5·73)	21861476	1226898
Russia	19	104353	2·73% (2·64–2·83)	143617913	3926499
Serbia	2	52755	0·48% (0·43–0·55)	9647109	46631
Slovakia	1	59279	1·74% (1·64–1·85)	5433437	94500
Slovenia	1	207697	0·28% (0·25–0·30)	2054232	5657
Spain	49	260251	0·34% (0·32–0·37)	46182038	158287
Sweden	6	15523	0·59% (0·48–0·73)	9382297	55606
Switzerland	3	5999	0·18% (0·10–0·33)	7830534	14358
Tajikistan	1	708	7·20% (5·52–9·36)	7627326	549426
Turkey	73	7527924	4·00% (3·99–4·02)	72137546	2887888
Ukraine	1	3594	1·45% (1·10–1·89)	46050220	666280
UK	22	31762297	0·01% (0·01–0·01)	62066350	3300
Uzbekistan	3	9903	6·99% (6·50–7·51)	27769270	1940456
Total	467	52154308	2·06% (2·06–2·06)	898605916	18486179

Countries in European Region where no eligible reports on HBV reporting HBsAg were available were: Andorra, Armenia, Finland, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, San Marino, Macedonia, and Turkmenistan. *We restricted estimation of HBsAg carriers to both WHO Member States and countries with available population data as provided by the UN Population Division; therefore Kosovo was not included in the calculation of the total number of people living with chronic HBV.

Table 4: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO European Region**

pre-donation screening and assessments. One must therefore consider a healthy donor effect in this population, which might have led to an underestimation of the prevalence of chronic HBV in the general population in some countries, such as Iran and India, where large-scale studies among blood donors were available. Among health-care workers, the prevalence of chronic HBV has been found to be similar to that of the general population

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Bangladesh	16	94 352	3·10% (2·99–3·21)	151 125 475	4 678 624
Bhutan	1	2106	5·84% (4·92–6·93)	716 939	41 873
India	129	3 764 669	1·46% (1·44–1·47)	1 205 624 648	17 553 389
Indonesia	14	69 639	1·86% (1·76–1·96)	240 676 485	4 468 684
Myanmar	1	65 236	3·40% (3·26–3·54)	51 931 231	1 765 643
Nepal	15	772 238	0·82% (0·80–0·84)	26 846 016	218 943
Sri Lanka	1	1913	2·51% (1·90–3·31)	20 758 779	520 868
Thailand	31	920 403	6·42% (6·37–6·47)	66 402 316	4 260 008
Total	208	5 690 556	1·90% (1·90–1·90)	1 789 987 553	34 000 099

Countries in the South East Asian Region where no eligible reports on HBV reporting HBsAg were available were: North Korea, Maldives, and Timor-Leste.

Table 5: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO South East Asian Region**

	Number of studies	Number of participants	Prevalence estimates (%, 95% CI)	Population size per country	HBsAg-positive population
Australia	27	1 167 112	0·37% (0·36–0·38)	22 404 488	83 121
Brunei Darussalam	3	4507	4·06% (3·52–4·68)	400 569	16 265
Cambodia	5	5829	4·05% (3·57–4·59)	14 364 931	581 596
China	167	9 942 577	5·49% (5·47–5·50)	1 359 821 465	74 601 204
Fiji	3	4433	4·80% (4·21–5·48)	860 559	41 349
Japan	42	5 507 701	1·02% (1·01–1·02)	127 352 833	1 294 431
Kiribati	3	987	22·70% (20·19–25·41)	97 743	22 183
Laos	1	13 897	8·74% (8·28–9·22)	6 395 713	558 710
Malaysia	8	240 943	0·74% (0·70–0·77)	28 275 835	208 540
Marshall Islands*	3	808	7·80% (6·14–9·86)	NA	NA
Federated States of Micronesia	2	1428	3·50% (2·66–4·59)	497 585	17 422
Mongolia	9	6813	9·07% (8·41–9·78)	2 712 738	246 070
Nauru	3	5939	17·55% (16·60–18·53)	NA	NA
New Zealand	15	309 130	4·11% (4·04–4·18)	4 368 136	179 357
Niue*	1	1147	11·86% (10·11–13·86)	NA	NA
Palau*	1	34	2·94% (0·41–18·14)	NA	NA
Papua New Guinea	9	8514	14·59% (13·85–15·35)	6 858 945	1 000 565
Philippines	10	160 096	4·63% (4·53–4·73)	93 444 322	4 326 212
South Korea	19	3 651 102	4·36% (4·36–4·37)	48 453 931	2 111 914
Samoa	1	398	5·53% (3·67–8·25)	186 029	10 283
Singapore	11	28 577	4·09% (3·87–4·33)	5 078 969	207 943
Solomon Islands	4	3543	18·83% (17·57–20·15)	526 447	99 108
Tahiti*	1	50	2·00% (0·28–12·88)	NA	NA
Tonga	2	1202	14·81% (12·91–16·93)	104 098	15 416
Tuvalu*	1	28	7·14% (1·79–24·48)	NA	NA
Vanuatu	4	2925	17·54% (16·20–18·96)	236 299	41 443
Vietnam	13	14 459	10·79% (10·29–11·31)	89 047 397	9 607 438
Total	368	21 084 179	5·26% (5·26–5·26)	1 811 489 032	95 270 570

The country in the Western Pacific Region where no eligible reports on HBV reporting HBsAg were available was Cook Islands. *We restricted estimation of HBsAg carriers to both WHO Member States and countries with available population 9data as provided by the UN Population Division; therefore Marshall Islands, Nauru, Niue, Palau, Tahiti, and Tuvalu were not included in the calculation of the total number of people living with chronic HBV.

Table 6: **HBsAg seroprevalence and the number of people living with chronic HBV in the general population in the WHO Western Pacific Region**

in countries with intermediate and high endemicity such as Turkey and Pakistan.[17,18] HBV vaccination policies for health-care workers have particularly been adopted in highly industrialised countries. In resource-poor settings, however, inadequate occupational safety and infection control practices prevail, hence health-care workers might

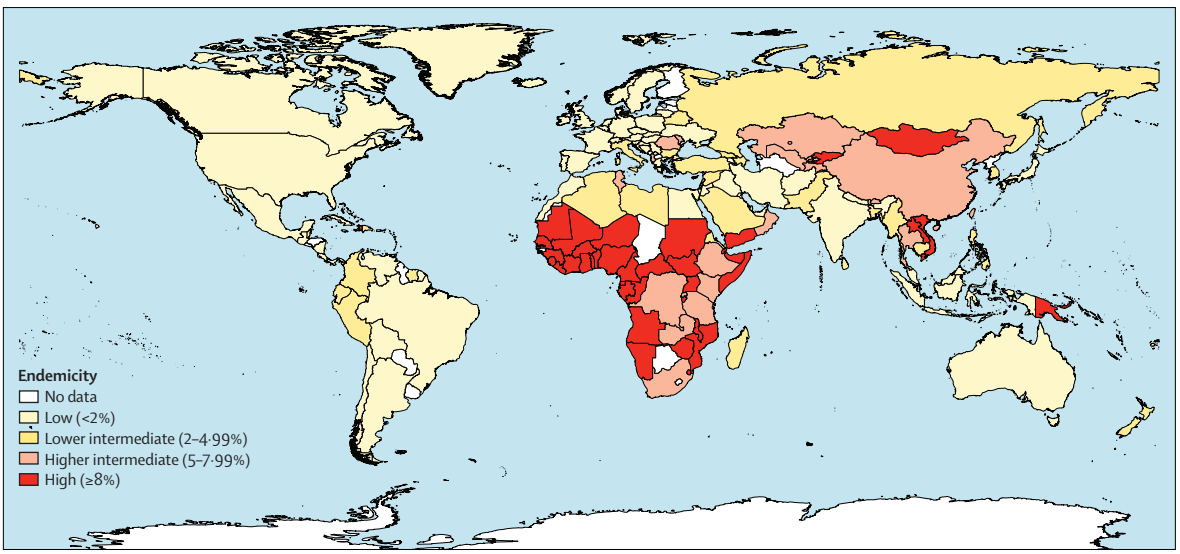

Figure 2: **Global HBsAg endemicity (1957–2013)**

be more likely to acquire infections.[33] However, since only 0·10% of all study individuals included in our analysis were health-care workers, their effect on overall HBsAg prevalence estimates is likely to have been negligible.

The main limitations of this systematic review are related to the available data. First, there is a paucity of prevalence studies, and the quality of reporting of studies varied. For instance, many available studies were focused on adults (16–50 years) or did not report age-specific and sex-specific prevalence. Data available on prevalence in infants and young children were particularly sparse. Therefore, potential vaccination effects might not be reflected or appear with a time lag. A more refined analysis, such as one that includes year of routine infant vaccination and the assessment of cohort effects, would provide more detailed and country-specific characteristics of the HBV epidemiology. However, the restricted availability of original data over years and age groups as well as the lack of recent studies would make such an analysis possible only in a very few countries (eg, China, Italy, Japan, and Turkey).

Second, prevalence data were typically collected on a subnational-level. A substantial within-country variability in prevalence reports was noted, which might be attributable to the fact that studies were done in diverse geographical areas and recruitment settings. Local estimates hence, might not be representative of national-level prevalence particularly in large countries with much geographic and ethnic variation. We also identified studies that specifically targeted high-endemicity geographical areas or indigenous populations, or both, and classified these included studies as non-representative. Although this classification involved some subjectivity, our sensitivity analysis showed no relevant effect of these studies on prevalence estimates, since they were predominantly studies with small sample sizes (eg, studies in the Andaman Islands in India).

Third, the relative dearth of recent seroepidemiological studies, particularly from hot spots of high HBV endemicity is a serious limitation. The reliance on older studies runs the risk of generating prevalence estimates that do not reflect the current epidemiological situation. Furthermore, relying on less accurate serological tests used in older studies might increase the uncertainty about the validity of estimates. Regularly conducted standardised serological surveys at the national level are imperative to best assess the epidemiological situation and the impact of interventions.

Fourth, some limitations of this review related to our methodology also bear mention. We excluded high-risk population groups (eg, migrants) from our systematic review, which would have provided a more complete picture of national-level prevalence. We could not assess representativeness in the health-care workers or blood donor population since contextual information was unavailable from most source reports. Furthermore, with the assessment of HBsAg prevalence in two time periods, we can only provide crude information about changes over time.

Finally, our pooled estimates include all reported observations. Since most studies were done in more recent years, the prevalence estimates in our main analysis are likely to reflect the current situation of chronic HBV infection prevalence. This prevalence might differ for countries, where most of the available data is from an earlier period, which might have impacted on the respective country's overall estimate.

This report provides estimates of the scale of the HBV epidemic at country, regional, and global levels to inform efforts for developing and targeting an effective response. International comparisons showed a high burden of chronic HBV infections; however, wide inequities in the prevalence of chronic HBV were found across countries.

The findings of this report indicate an unmet need for prevention and control of this infection, particularly in high-endemicity countries. Investments in comprehensive and effective strategies to interrupt the transmission of hepatitis B and reduce resultant morbidity and mortality are urgently required. Furthermore, the magnitude of this epidemic warrants investments in research and concerted efforts in developing epidemiological research capacity, particularly within resource-poor countries to accurately quantify the problem and assess the effect of interventions.

Contributors

JJO developed the study protocol, designed and coordinated the study. AS and JJO developed the search strategy. AS tailored the search strategy to each database, piloted the search and performed the literature searches. AS and JJO performed the systematic review, extracted data, and assessed the relevance and accuracy of reports for use in generation of estimates. GK provided technical expertise and advice on relevance and accuracy of reports. AS developed and maintained the Endnote citation database. JH maintained the customised data extraction Excel sheet and generated maps. JH and RM developed the analysis technique and RM supervised the data analysis for the generation of national-level, regional and global estimates. AS wrote the manuscript with contributions from JJO; GK, JH, and RM commented.

Declaration of interests

We declare no competing interests.

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