

[Home](#) [Journals](#) [Specialties](#) [The Lancet Clinic](#) [Global Health](#) [Multimedia](#) [Campaigns](#) [More](#) [Information for](#) [Submit a Paper](#)

THE LANCET

Gastroenterology & Hepatology

Welcome, Maureen Kamischke

[Claim Your Subscription](#) | [Subscribe](#) | [My Account](#) | [Logout](#)

[Online First](#) [Current Issue](#) [All Issues](#) [Audio](#) [About the Journal](#) [Advisory Board](#) [Register](#)

[Advanced Search](#)

[< Previous Article](#)

Online First

[Next Article >](#)

Access this article on [ScienceDirect](#)

Articles

Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study

The Polaris Observatory Collaborators[†]

[†] Collaborators listed at the end of the Article

Published: 26 March 2018

[PlumX Metrics](#)

DOI: [https://doi.org/10.1016/S2468-1253\(18\)30056-6](https://doi.org/10.1016/S2468-1253(18)30056-6) | [CrossMark](#)

Article Info

[Summary](#) [Full Text](#) [Tables and Figures](#) [References](#) [Supplementary Material](#)

Summary

Background

The 69th World Health Assembly approved the Global Health Sector Strategy to eliminate viral hepatitis by 2030. Although no virological cure exists for hepatitis B virus (HBV) infection, existing therapies to control viral replication and prophylaxis to minimise mother-to-child transmission make elimination of HBV feasible. We aimed to estimate the national, regional, and global prevalence of HBsAg in the general population and in the population aged 5 years in 2016, as well as coverage of prophylaxis, diagnosis, and treatment.

Methods

In this modelling study, we used a Delphi process that included a literature review in PubMed and Embase, followed by interviews with experts, to quantify the historical epidemiology of HBV infection. We then used a dynamic HBV transmission and progression model to estimate the country-level and regional-level prevalence of HBsAg in 2016 and the effect of prophylaxis and treatment on disease burden.

Findings

We developed models for 120 countries, 78 of which were populated with data approved by experts. Using these models, we estimated that the global prevalence of HBsAg in 2016 was 3.9% (95% uncertainty interval [UI] 3.4–4.6), corresponding to 291 992 000 (251 513 000–341 114 000) infections. Of these infections, around 29 million (10%) were diagnosed, and only 4.8 million (5%) of 94 million individuals eligible for treatment actually received antiviral therapy. Around 1.8 (1.6–2.2) million infections were in children aged 5 years, with a prevalence of 1.4% (1.2–1.6). We estimated

Article Options

[PDF \(1 MB\)](#)

[Download Images\(.ppt\)](#)

[Email Article](#)

[Add to My Reading List](#)

[Export Citation](#)

[Create Citation Alert](#)

[Cited by in Scopus \(0\)](#)

Linked Articles

COMMENT

[Delineating the global challenges of hepatitis B virus infection](#)

that 87% of infants had received the three-dose HBV vaccination in the first year of life, 46% had received timely birth-dose vaccination, and 13% had received hepatitis B immunoglobulin along with the full vaccination regimen. Less than 1% of mothers with a high viral load had received antiviral therapy to reduce mother-to-child transmission.

Interpretation

Our estimate of HBV prevalence in 2016 differs from previous studies, potentially because we took into account the effect of infant prophylaxis and early childhood vaccination, as well as changing prevalence over time. Although some regions are well on their way to meeting prophylaxis and prevalence targets, all regions must substantially scale-up access to diagnosis and treatment to meet the global targets.

Funding

John C Martin Foundation.

Introduction

Discovery of HBsAg in 1965 led to development of an effective vaccine against hepatitis B virus (HBV), which became available in 1981 and, given that untreated HBV can lead to fibrosis, cirrhosis, and hepatocellular carcinoma, represented the world's first anticancer vaccine.^{1, 2, 3} Although introduction of the vaccine was widespread, its cost limited broad use in infants born in low-income and middle-income countries. This coverage expanded widely after Gavi, the Vaccine Alliance began to support HBV vaccination programmes in 2001. However, after the introduction of highly effective curative therapies for hepatitis C virus (HCV) in 2013, HBV became somewhat overshadowed in public health prioritisation, and its cure remains elusive. Accurate epidemiological assessments at the national level are necessary to accurately establish the current disease burden and the effect of existing interventions, and to provide insight into priority actions for the future.

In 2015, combating viral hepatitis by 2030 was included in the Sustainable Development Goals (3.3).⁴ Then, in 2016, the World Health Assembly passed the Global Health Sector Strategy on Viral Hepatitis, which aims to eliminate HBV and HCV by 2030.⁵ The targets include 90% global coverage of three-dose infant vaccination by 2020; timely birth-dose vaccination in 50% of infants by 2020, and in 90% by 2030; and prevalence in children aged 5 years of 1% by 2020, and 0·1% by 2030. Reduction of incidence among infants is important because most HBV infections in infants become chronic, which is the leading source of new chronic HBV infections. As well as the prevention targets, the 2030 targets include diagnosis of 90% of people infected with HBV and antiviral treatment of 80% of those diagnosed and eligible for treatment. In addition to the global targets, specific WHO regions have set their own objectives, which are often more aggressive than the World Health Assembly targets.

Previous reports^{6, 7, 8, 9, 10, 11} describing the country-level and regional prevalence of HBsAg have primarily consisted of meta-analyses and literature reviews. The most recent studies have reported global prevalence estimates of 248 million or 257 million individuals with HBV infection.^{6, 7} These reports were limited by their calculation of averages using a combination of robust and non-representative studies, studies done in different age groups, and studies done at different timepoints. Additionally, data in children are scarce because most studies only include adults and are not adjusted for the population by age and sex. Moreover, these estimates are historical and do not consider the effect of vaccination and other efforts to prevent mother-to-child transmission.^{6, 7, 8, 9, 10, 11}

Research in context

Evidence before this study

After the 69th World Health Assembly approved the Global Health Sector Strategy to eliminate

viral hepatitis by 2030, there was a renewed sense of urgency in combating HBV. The strategy set diagnosis, treatment, and prophylaxis targets to reduce prevalence among children aged 5 years and liver-related deaths. Previous global reports of HBsAg prevalence follow traditional systematic review and meta-analysis procedures, while including studies among blood donors, which typically report a low prevalence. However, most of these studies exclude the effect of vaccination. Other studies report the use of hepatitis B immunoglobulin and antiviral treatment of pregnant women at the country level, but none has quantified the methods of prophylaxes at a regional or global level. Additionally, any reports of cascade of care have been at the local or national level.

Added value of this study

We combined a traditional meta-analysis, national expert interviews, and modelling to estimate HBsAg prevalence, prophylaxis use, and proportion diagnosed and treated at the national, regional, and global levels in 2016. We used a dynamic transmission and disease burden model that took into account the effect of prophylaxis and treatment on HBsAg prevalence. A Delphi process was used to strengthen the traditional systematic review process, and involved consultation with 620 experts to obtain feedback on inputs and outputs for 78 national models. Another 42 models were developed on the basis of published data. Estimates for the remaining 80 countries were extrapolated from these 120 countries, which alone accounted for 93% of the world's population.

Implications of all the available evidence

The global prevalence reported here is higher than previous estimates because it excluded studies done in blood donors and other non-representative populations. The diagnosis and treatment data provide evidence of countries that have made progress. The data presented here are a marker on the road to elimination of hepatitis B and can support the creation of national strategies to meet the 2030 targets.

One previous study¹² used modelling to predict the future disease burden of HBV and propose potential strategies to address this increasing public health problem. That study found that a target of 90% reduction in new chronic infections and 65% reduction in mortality could be achieved by scaling up coverage of infant vaccination (to 90% of infants), birth-dose vaccination (to 80% of neonates), use of peripartum antivirals (to 80% of HBeAg-positive mothers), and population-wide testing and treatment (to 80% of eligible people).

The aims of this study were to quantify the national, regional, and global HBsAg prevalence in the general population and in the population aged 5 years; to estimate use of prophylaxis for mother-to-child transmission; and to model the cascade of care (number of patients diagnosed, eligible for treatment, and treated) in 2016.

Methods

Search strategy and selection criteria

In this modelling study, we included all countries with a total population of 1·0 million people or more. We also included Fiji, Kiribati, and Belize because of our collaborations with the WHO Regional Office for the Western Pacific and the Pan American Health Organization (PAHO). We obtained input data for these countries through a literature review and a Delphi process, which used experts to fill any data gaps and to confirm data when available. Full details of data collection, scoring of data sources, Delphi process, and modelling are summarised in the [appendix](#).

For the literature review, we searched PubMed and Embase between Jan 1, 1960, and March 1, 2016, without language restrictions using the search terms “[Country Name] AND [(hepatitis b) or HBV] AND [prevalence]” and “[Country Name] AND (‘prevalence’/exp OR prevalence) AND (‘hepatitis b’/exp OR ‘hepatitis b’ OR ‘hcv’/exp OR ‘hcv’)”. Titles and abstracts were reviewed for relevance, and only

studies that included HBsAg prevalence were included. We also included grey literature, ministry of health reports, conference presentations, local journals, and personal communications with local experts in the analysis. We excluded studies published before 1985 (with the exception of those done in Mauritania and Senegal because studies done before 1985 were deemed the most representative for these countries) and studies done solely in non-representative populations (eg, blood donors, people who inject drugs, haemophiliacs, and specific ethnic groups).

Data collection and processing

We extracted data such as HBsAg prevalence, sex and age distributions of the infected study population (if available), time period(s) of the estimate, population studied (general population, pregnant women, students), setting of the study (urban, rural), scope of the study (single centre, multicentre, city, multicity, region, national), type of analysis (surveillance, meta-analysis, review article, modelling, other, unknown), and sample size from the studies. Data were then scored using a multiobjective decision-analysis approach, resulting in a score of 1–3 for each study. For published studies, the overall score was based on the weighting of the scores for generalisability, sample size, and year of the study (appendix). Each study was scored independently by two epidemiologists. To assess generalisability, clear classification guidelines were used (appendix). When the estimate was based on expert opinion, the study received a score of 1 as a default, a score of 2 if it was based on published or unpublished data, and a score of 3 if it was based on a well designed national study, unpublished or ahead of print, or a large national database (appendix). The highest-scoring study was chosen to provide the representative estimate for each country, with the exception of countries in which lower scoring studies were recommended by local experts. Although studies in blood donors were excluded from use as base estimates, they were used to provide estimates of the lower bound of the uncertainty interval (UI).

Countries were divided into three categories: approved, estimated, and extrapolated. For approved countries, we used a Delphi interview process with 620 national and regional experts to build consensus regarding the inputs and key findings (appendix). These experts were identified through our previous work on HCV,¹³ and by referral and recommendations from leaders in the field. At a minimum, we received feedback regarding the inputs for this category. In 53 of the 78 countries, at least one face-to-face meeting was held to review both inputs and outputs with the experts. The experts either approved the inputs, rejected them and provided a better source of data (sometimes unpublished data), or recommended data from analogous countries with a similar health-care system.

For estimated countries, inputs were based on published studies, which were reviewed and scored by two epidemiologists and the primary investigator (HR). When age and sex distributions were unavailable for a country, we estimated the distributions using those from another country with a similar vaccination history by calibrating the prevalence to match that of the country with unavailable age and sex data. For extrapolated countries, in which no prevalence data were available, the weighted average of countries within the same region, as defined by the Global Burden of Diseases (GBD), was used (appendix).¹⁴

To estimate the population diagnosed with HBsAg, we reviewed (in order of priority) national notification or registry data, peer-reviewed literature, and expert opinion. The number of individuals treated annually was estimated with (in order of priority) national databases, audit sales data, government reports, estimates from major treatment centres, and drug suppliers.

Country-level estimates from WHO and UNICEF¹⁵ were used as a baseline for estimates of the proportion of infants receiving the first dose of vaccination within the first 24 h of life (timely birth dose) and those receiving a complete schedule of vaccination (at least three doses at age 1 year). In countries with a consistently high historical coverage that reported a single year as 0% coverage, we assumed that this result was a reflection of non-reporting and not a change in strategy. The PAHO did a robust review of the vaccination schedule in the region, and this review supplemented the report

from WHO and UNICEF.^{15, 16} Estimates of the proportion of infants born to HBsAg-positive mothers who received both timely birth dose and hepatitis B immunoglobulin were based on country interviews, national immunisation guidelines, and WHO reports, as described in the [appendix](#). WHO data were used for countries with missing interviews or national data.¹⁷ However, a comparison of the reported prophylaxis data in the WHO report with countries we interviewed indicated that use of hepatitis B immunoglobulin was overestimated in the WHO report. For countries in which data were only available from the WHO report, we assumed that if a country reported that all pregnant women are screened for HBsAg and that all infants born to HBsAg-positive mothers receive hepatitis B immunoglobulin then, in reality, only 50% of all infants born to HBsAg-positive mothers who receive timely birth dose also receive hepatitis B immunoglobulin. If no national screening of pregnant women was reported, but hepatitis B immunoglobulin was reported to be administered, then the estimate decreased to 20%. These estimates were then adjusted on the basis of feedback from experts or regional leads and, unless specified, we assumed that 96% of pregnant women are screened in countries with robust health-care systems.¹⁸ Estimates of antiviral treatment in mothers with high viral loads, as a method to prevent perinatal transmission, were based mostly on expert opinion ([appendix](#)). Prophylaxis coverage was not extrapolated to countries that did not report data.

Modelling

The PRoGReSs model is a compartmental, deterministic, dynamic Markov disease progression model developed in Microsoft Excel to quantify the annual prevalence of HBsAg by disease stage, sex, and age in each country. A full description of the model is provided in the [appendix](#). The model was populated with reported country-specific demographic data (population, mortality, births, and sex ratios at birth), epidemiological data (HBsAg prevalence, age and sex distributions, and prevalence of HBeAg in HBsAg-positive women of childbearing age), and data on intervention coverage (diagnosis, antiviral treatment of general population, peripartum antiviral treatment of mothers, infant vaccination, and catch-up vaccination; [appendix](#)).

Disease progression and mother-to-child transmission rates were determined as a function of viral load to allow analysis across countries with different genotypes and were assumed to be constant across countries. We established disease progression rates using data from the REVEAL study¹⁹ and the Stanford cohort (university and community clinics; Nguyen MH, unpublished) in the USA ([appendix](#)). We developed a function ([appendix](#)) to estimate the risk of developing chronic HBV infection using data from countries that reported HBsAg and core-antibody prevalence before vaccination.^{20, 21}

Each country model was independently fitted to the reported prevalence of HBsAg by sex and age group in a given year, and to the reported number of diagnosed cases of HBV infection in a given year ([appendix](#)). We calculated the incidence of infections due to mother-to-child transmission using reported data on births, prophylaxes coverage (timely birth dose, three-dose vaccination, hepatitis B immunoglobulin, and peripartum antiviral treatment of mothers), and the forecasted HBsAg prevalence in women of childbearing age ([appendix](#)). The incidence of horizontally acquired infections was back-calculated with the force of infection (a function determining the rate of infection with HBV among the susceptible population) and mortality, after accounting for clearance of HBsAg in all years up to and including the year of reported HBsAg prevalence ([appendix](#)).

Disease stages considered in the model were HBsAg-positive, cirrhosis (compensated or decompensated), hepatocellular carcinoma, and liver transplantation. The population in each disease stage was further divided into low viral load (HBV DNA <20 000 IU/mL), high viral load (HBV DNA ≥20 000 IU/mL), and treatment-responder subpopulations, with separate progression rates for each ([appendix](#)). HBsAg-positive people with a high viral load, or compensated cirrhosis, decompensated cirrhosis, or hepatocellular carcinoma independent of viral load, were considered eligible for antiviral treatment, in line with WHO treatment guidelines.²² Discontinuation of treatment was incorporated in the model, but was only used in the models for Iran, Pakistan, and Qatar after request by the expert panels.

To validate the model, we chose countries that had prevalence estimates at two or more timepoints ([appendix](#)). The model was calibrated to the first reported HBsAg prevalence by age, and the forecasts were compared with the second reported HBsAg prevalence by age.

Statistical analysis

We calculated UIs and did sensitivity analyses using Crystal Ball release 11.1.2.3.500. β -PERT distributions were used for all uncertain inputs.²³ We used Monte Carlo simulation to estimate 95% UIs, with 1000 simulations run per country. We assumed that UIs for prevalence estimates in all countries were independent. The UI for each country was calculated on the basis of range inputs for prevalence, transmission rates, transition rates, and mortality rates ([appendix](#)). These country UIs were used to calculate regional and global UIs. For these estimates, two sources of uncertainty were considered: country-level uncertainty in prevalence and its effect on the regional and global prevalence. The 2016 prevalence estimates and 95% UIs for each country were consolidated and defined as assumption variables. We also did a sensitivity analysis to identify countries that accounted for the greatest variation in the global prevalence because of their estimated prevalence uncertainties.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or preparation of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

We identified 42 691 studies in the literature review, of which 435 were used in this analysis. Validation of all inputs and outputs with national experts is ongoing, but, as of publication, 78 countries had provided feedback.

The literature review provided prevalence estimates for 128 countries, with a mean global HBsAg prevalence of 4.9%, or around 364 million infections after exclusion of estimates from studies done in blood donors or other non-representative populations. Using 120 country-specific models, representing 93% of the global population and 90% of all estimated HBsAg-positive infections, we estimated that 291 992 000 (95% UI 251 513 000–341 114 000) individuals were HBsAg positive in 2016, corresponding to a global prevalence of 3.9% (95% UI 3.4–4.6; [Table 1](#), [Table 2](#)). For eight countries (Afghanistan, North Korea, Eritrea, Lithuania, Nepal, Palestine, Somalia, and Ukraine), data were insufficient to establish age and sex distributions or HBsAg prevalence, or the identified studies did not pass the quality threshold and no model was developed. Estimates of HBsAg prevalence were not available for all countries, and the quality of the available studies varied across countries ([figure 1](#)). 2016 estimates of HBsAg prevalence in the general population and in children aged 5 years across countries are shown in [figure 1](#).

Table 1

2016 estimates of HBsAg prevalence, treatment, and prophylaxis, by country

Click to view table

Only countries that were modelled are shown. HBIG=hepatitis B immunoglobulin.

* Data are estimate (95% uncertainty interval).

† Treatment eligible reflects the estimated number of HBsAg-positive individuals (diagnosed and

undiagnosed) with a high viral load ($\geq 20\ 000$ IU/mL), with cirrhosis or hepatocellular carcinoma, or who have undergone liver transplantation.

† The denominator in this column is the estimated HBsAg-positive population.

§ Proportion of all infants.

¶ Proportion of infants of HBsAg-positive mothers who received HBIG, first dose of hepatitis B vaccination ≤ 24 h after birth, and two or more doses of vaccine in the first year of life.

|| Proportion of mothers with high viral loads who received antiviral therapy to reduce mother-to-child transmission.

Table 2

2016 estimates of HBsAg infection prevalence, treatment, and prophylaxis, by region



HBIG=hepatitis B immunoglobulin.

* Data are estimate (95% uncertainty interval).

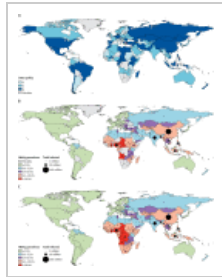
† Treatment eligible reflects the estimated number of HBsAg-positive individuals (diagnosed and undiagnosed) with a high viral load ($\geq 20\ 000$ IU/mL) or with cirrhosis, hepatocellular carcinoma, or liver transplantation, independent of viral load.

† The denominator in this column is the estimated HBsAg-positive population.

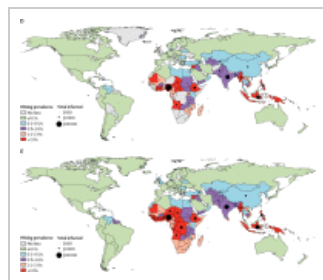
§ Proportion of all infants.

¶ Proportion of infants of HBsAg-positive mothers who received HBIG, first dose of hepatitis B vaccination ≤ 24 h after birth, and two or more doses of vaccine in the first year of life.

|| Proportion of mothers with a high viral load who received antiviral therapy to reduce mother-to-child transmission.



[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)



[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)

Figure 1

HBsAg prevalence estimates for 2016

(A) Data quality in countries with available data. 1=estimate was based on expert opinion.

2=estimate was based on published or unpublished data. 3=estimate based on a well designed national study, unpublished or ahead of print, or a large national database. (B) Estimates for

countries with available data and a model (all ages). (C) Estimates for countries with data and a

model, or for which data were extrapolated from countries in the same GBD region with available data (all ages). (D) Estimates for countries with data and a model (children aged 5 years only). (E) Estimates for countries with data and a model, or for which data were extrapolated from countries in the same GBD region with available data (children aged 5 years only). GBD=Global Burden of Diseases.

Although diagnostic testing for HBsAg has been available since the early 1970s, we estimated that only about 29 million (10%) of 292 million HBsAg-positive individuals were diagnosed in 2016 (figure 2, Table 1, Table 2). Around 94 million individuals (around 32% of the infected population) were eligible for treatment in 2016, of whom only 4·8 million received antiviral treatment (figure 2, Table 1, Table 2). The estimate of treatment-eligible patients included individuals with a high viral load (>20 000 IU/mL) and those with cirrhosis.²⁴

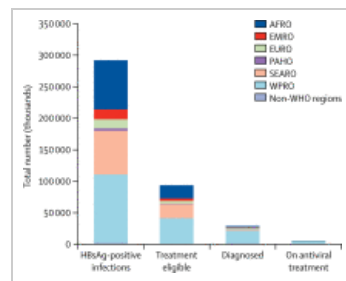


Figure 2

Global and regional hepatitis B virus cascade of care in 2016

AFRO=Regional Office for Africa. EMRO=Eastern Mediterranean Regional Office. EURO=Regional Office for Europe. PAHO=Pan American Health Organization. SEARO=South-East Asia Regional Office. WPRO=Western Pacific Regional Office.

[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)

Globally, after weighting by the number of births in each country, we estimated that 46% of infants received timely birth-dose vaccination and that 87% of those younger than 1 year received the full vaccination schedule (figure 3, Table 1, Table 2). After weighting by the estimated number of births to HBsAg-positive women, we estimated that 13% of infants born to HBsAg-positive mothers received hepatitis B immunoglobulin along with timely birth-dose and follow-up vaccination (figure 3, Table 1, Table 2). After weighting by births to mothers with high viral loads, we estimated that less than 1% of mothers with a high viral load received antiviral treatment in 2016 (figure 3, Table 1, Table 2). As a result of historical and current interventions, the prevalence in children aged 5 years was estimated to be 1·4% (95% UI 1·2–1·6), corresponding to 1·8 million (1·6–2·2) infections globally in 2016 (Table 1, Table 2).

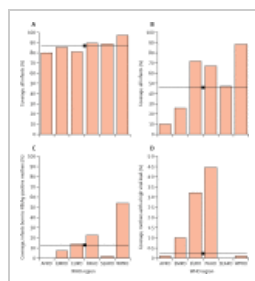


Figure 3

Global and regional perinatal prophylaxis coverage in 2016

The black horizontal lines indicate global averages. (A) Proportion of all infants who received three

or more doses of HBV vaccine. (B) Proportion of all infants who received timely birth dose (within 24 h after birth). (C) Proportion of infants born to HBsAg-positive mothers who received hepatitis B immunoglobulin, timely birth dose, and two or more doses of HBV vaccine. (D) Proportion of mothers with a high viral load who received peripartum treatment with antivirals to prevent mother-to-child transmission. AFRO=Regional Office for Africa. EMRO=Eastern Mediterranean Regional Office. EURO=Regional Office for Europe. PAHO=Pan American Health Organization. SEARO=South-East Asia Regional Office. WPRO=Western Pacific Regional Office. HBV=hepatitis B virus.

[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)

Globally, 21 countries accounted for more than 80% of the total number of HBsAg-positive infections in the general population ([figure 4A, table 1](#)), with China, India, Nigeria, Indonesia, and the Philippines accounting for more than 57% of all HBsAg-positive infections. Only 16 countries accounted for more than 80% of the estimated number of infections in children aged 5 years ([figure 4B, table 1](#)), with Nigeria, India, Indonesia, and the Democratic Republic of the Congo accounting for almost 57% of all infections.

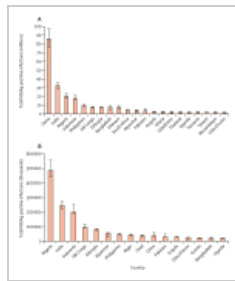


Figure 4

Countries accounting for 80% or more of the total HBsAg-positive infections in 2016

(A) General population. (B) Population aged 5 years.

[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)

Prevalence in children aged 5 years in 2016 was estimated to be highest in the WHO African Region, which had the lowest timely birth-dose coverage of all the WHO regions globally ([table 3](#)). The lowest prevalence among children aged 5 years (<0.1%) was in the PAHO region ([table 3](#)). PAHO generally has a lower prevalence before vaccination than many other regions, and vaccination has been implemented widely in the region for sufficient time that some mothers were vaccinated as infants or children. Only the Western Pacific Region had reached the recommended threshold of 90% or higher three-dose vaccination coverage in infants. However, China had a three-dose vaccination coverage in infants of 99% and a large effect on the regional average ([figure 3, table 1](#)). The global average of 46% of infants receiving a timely birth dose was also largely affected by the coverage in China, because China represented 24% of all timely birth doses administered globally ([table 1](#)). This global average was most affected by birth dose in high-income and upper-middle-income countries (coverage was estimated to be only 3% in low-income countries; [table 3](#)).

Table 3

2016 estimates of HBsAg infection prevalence, treatment, and prophylaxis, by WHO or World Bank region

Click to view table

HBIG=hepatitis B immunoglobulin. AFRO=Regional Office for Africa. EMRO=Eastern Mediterranean Regional Office. EURO=Regional Office for Europe. PAHO=Pan American Health Organization. SEARO=South-East Asia Regional Office. WPRO=Western Pacific Regional Office.

* Data are estimate (95% uncertainty interval).

† Treatment eligible reflects the estimated number of HBsAg-positive individuals (diagnosed and undiagnosed) with a high viral load ($\geq 20\,000$ IU/mL) or with cirrhosis, hepatocellular carcinoma, or liver transplantation, independent of viral load.

‡ The denominator in this column is the estimated HBsAg-positive population.

§ Proportion of all infants.

¶ Proportion of infants of HBsAg-positive mothers who received HBIG, first dose of hepatitis B vaccination ≤ 24 h after birth, and two or more doses of vaccine in the first year of life.

|| Proportion of mothers with a high viral load who received antiviral therapy to reduce mother-to-child transmission.

Of the 120 modelled countries, 22 were estimated to have already reached the 2020 target of diagnosing 30% of the infected population ([table 1](#)). Because of China, the 2020 treatment target of 5 million is achievable. China alone was estimated to treat at least 3.5 million HBsAg-positive individuals, while the remaining countries combined were estimated to treat about 1.3 million people with HBV infections, giving a total of 4.8 million people treated globally ([table 1](#)). In most countries, a large increase in screening and treatment will be needed to meet the targets of 90% diagnosed and 80% of those eligible treated by 2030, in part due to the current lack of national screening programmes for people other than pregnant women.

We validated the model in three countries (China, Iran, and the USA) that reported HBsAg prevalence by age at two timepoints ([appendix](#)). These validations showed that the model could accurately predict the future prevalence of HBsAg by age and sex under different circumstances. The quality of the forecast declined when HBeAg was used in place of viral load, showing that differentiation by viral load provides more accurate estimates of future prevalence than does HBeAg alone.²⁵

The sensitivity analysis ([figure 5A](#)) showed which countries had the largest effect on the estimated total number of HBsAg-positive individuals in 2016. Angola was the greatest source of uncertainty at the general population level, followed by Zimbabwe, Nigeria, and Russia. Six of the ten countries responsible for most of the uncertainty in the global estimate were African nations, probably due to the absence of high-quality data in the region, leading to the extrapolation by GBD region. This effect was also seen in the sensitivity analysis run for the total number of HBsAg-positive infections in the population aged 5 years ([figure 5B](#)). Eight of the top ten sources of uncertainty were African nations, probably due to the scarcity of data on children aged 5 years in Africa, along with the low use of timely birth-dose vaccination or other prophylaxis for mother-to-child transmission. This finding reiterates the need for high-quality serosurveys among the general population, particularly in sub-Saharan Africa.

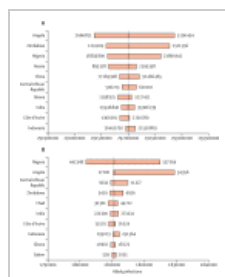


Figure 5

Sensitivity analysis of global HBsAg-positive infection



Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study - The Lancet Gastroenterology & ...

years.

[View Large Image](#) | [View Hi-Res Image](#) | [Download PowerPoint Slide](#)
Discussion

Jump to Section

Go

After excluding estimates from studies done in blood donors and other non-representative populations, on the basis of the literature alone, we estimated that the global prevalence of HBsAg was 4·9%, or roughly 364 million people. This estimate did not take into account the year of the study, ageing of the infected population, the effects of prevention strategies, or mortality since the study was published. This global prevalence decreased to around 292 million in our model when these factors were taken into account. This finding shows both the progress that has been made in controlling HBV infection globally and the importance of detailed modelling studies in addition to more routine prevalence-based estimates. The difference between our global estimate and previously published estimates^{6, 7, 8, 9, 10, 11} is largely due to the exclusion of older studies and studies done in blood donors and the inclusion of mortality and prophylaxis in our analysis.

The total population living with HBsAg is indicative of the historical prevalence of HBV, whereas the prevalence among children aged 5 years also reflects access to preventive strategies, particularly infant vaccination. When taken together, these figures show the importance of robust prophylaxis schedules. For example, China had the greatest number of HBsAg-positive people, but ranked tenth in terms of HBsAg infections in children aged 5 years. Of the 16 countries with the greatest number of infected children aged 5 years, China was the only country with timely birth-dose coverage of 90% or higher. Ten of these countries have not yet introduced timely birth dose, and Pakistan has very low timely birth dose, which is only available in the private sector. In Pakistan and other countries, the availability of birth dose as well as hepatitis B immunoglobulin is restricted to the private sector and consumers must pay out of pocket to access these measures for their infants.

The largest strides towards the elimination of HBV disease globally have been in infant vaccination. Of the modelled countries, 94 were estimated to have already met the 2020 target of 1% prevalence among children aged 5 years, and 46 have already met the 2030 target of 0·1% prevalence. However, many other countries have yet to meet these targets and have yet to introduce timely birth-dose vaccination. The peripartum antiviral treatment of mothers is another option for prophylaxes programmes and can go hand-in-hand with expansion or creation of screening programmes. Peripartum treatment of mothers might be a more viable option than administration of hepatitis B immunoglobulin because antivirals are more readily available and do not require refrigeration, and a short course of oral antiviral therapy for HBV perinatal prophylaxis could be less costly than hepatitis B immunoglobulin. Although the high prevalence among children aged 5 years in many of the African countries that do not have timely birth-dose vaccination shows the importance of this intervention, maintaining high coverage of the three-dose vaccination is also imperative for reducing the prevalence and disease burden. Syria has maintained high coverage of three-dose and timely birth-dose vaccination since early on in its HBV vaccination programme, which was initiated in 1992. However, coverage of both began to decrease in 2011, causing the prevalence among children aged 5 years to increase by 2016. Political conflicts could stall the progress made towards HBV elimination unless public health systems are supported.

The use of hepatitis B immunoglobulin, antiviral treatment, or both, will require that antenatal screening for HBsAg be put in place. In 2016, PAHO Member States expanded their commitment to the elimination of mother-to-child transmission of HIV and syphilis.²⁶ This triple elimination strategy was also endorsed by WHO Western Pacific Regional Office and South-East Asia Regional Office in

ADVERTISEMENT

Previous

Comment

[Delineating the global challenges of hepatitis B virus infection](#)

Next

Comment

[Is autofluorescence inferior to chromoendoscopy for dysplasia detection in ulcerative colitis?](#)

2017. These programmes will expand on existing programmes for HIV and syphilis to target other diseases, including HBV infection, with hepatitis B immunoglobulin and antiviral treatment. This focus on the complete elimination of mother-to-child transmission is an integral part of a comprehensive elimination strategy.

This study has several limitations. First, although data were available for 90% of the estimated number of infections globally, some of the countries for which data were extrapolated had large populations and some regions only had a few countries with data. Second, because of the absence of recent data, we used studies from before 1985 in Mauritania and Senegal. However, 97% of all included studies were done after 1990 and 83% after 2000. Third, although these estimates are currently the most accurate at the national level, they might obscure regional variations and do not account for certain populations (eg, immigrants, indigenous peoples and nations, people who inject drugs, and sex workers) that might have a higher prevalence than the general population. Fourth, we did not examine differences between rural and urban areas, which could have different access to prophylaxis. These limitations stress the need for national strategies or plans that target regions and populations most affected by HBV.

Taking into account the effect of immigration and emigration was beyond the scope of this study, but could have resulted in underestimation of the prevalence in countries with a substantial movement of people into or out of the country. Additionally, the model did not take into account HBV co-infections with HIV or hepatitis D virus (HDV), which cause faster disease progression than infections with HBV alone. HDV has a large effect on morbidity and mortality, but the effect of HDV co-infection on HBsAg prevalence should be within the uncertainty intervals of our estimates. Although we used the highest-quality disease progression rates that were available at the time, the base estimates might not have been representative of all populations. Moreover, the model did not take into account the effect of clearance of HBsAg among chronic carriers. Rates of HBsAg clearance have been shown to be low, and clearance is most likely to occur in older individuals with inactive infection.^{19, 27, 28, 29} HBsAg clearance would only affect overall prevalence in long-term forecasts because incidence is dependent on high viral load, and it has been shown that individuals who clear HBsAg can still go on to develop hepatocellular carcinoma.^{30, 31}

Extrapolation of HBsAg prevalence in children aged 5 years might underestimate or overestimate the actual prevalence in countries without data. Treatment and diagnosis estimates are probably underestimates. We found that diagnosis and treatment estimates were often higher than what was reflected in the available literature. In many countries, almost all individuals diagnosed with HIV are treated with antivirals that are also active against HBV, and thus a large proportion of those co-infected with HBV are under treatment.

Norway and the UK have recently added routine HBV vaccination to their immunisation schedules, and these changes were not considered in the analysis.³² Although antiviral treatment of mothers remains low, it has been increasing, particularly in higher-income countries where screening of pregnant women is a mainstay of their viral hepatitis programme. However, these countries tend to have a low prevalence, and thus their effect on the global estimate is small.

We now have all of the tools necessary to eliminate hepatitis B in children. In spite of this, 1.8 million children aged 5 years were infected with HBV in 2016, with a similar number of new infections occurring annually. This analysis provides a marker on the road to elimination by quantifying the use of prophylaxis and treatment at the national, regional, and global levels. This work can support national strategies to eliminate HBV and decrease the number of new infections by 90% by 2030. We have provided a situational analysis that shows how countries with a high HBV prevalence, such as China, can reduce the number of new infections through proactive national programmes.

Correspondence to: Dr Homie Razavi, Center for Disease Analysis Foundation, Lafayette, CO

80026, USA hrazavi@cdafound.org

Contributors

Devin Razavi-Shearer, Homie Razavi, and Ivane Gamkrelidze prepared the first draft and finalised the draft on the basis of comments from the other authors.

The Polaris Observatory Collaborators

Devin Razavi-Shearer, Ivane Gamkrelidze, Mindie H Nguyen, Ding-Shinn Chen, Pierre Van Damme, Zaigham Abbas, Maheeba Abdulla, Antoine Abou Rached, Danjuma Adda, Inka Aho, Ulus Akarca, Fuad Hasan Al Ali, Faryal A I Lawati, Khalid A I Naamani, Hamad Ibrahim Alashgar, Seyed M Alavian, Sameer Alawadhi, Agustin Albillos, Said A Al-Busafi, Soo Aleman, Faleh Z Alfaleh, Abdulrahman A Aljumah, Anil C Anand, Nguyen Thu Anh, Joop E Arends, Perttu Arkkila, Kostas Athanasakis, Abate Bane, Ziv Ben-Ari, Thomas Berg, Abdul R Bizri, Sarah Blach, Carlos E Brandão Mello, Samantha M Brandon, Bisi Bright, Philip Bruggmann, Maurizia Brunetto, Maria Buti, Henry L Y Chan, Asad Chaudhry, Rong-Nan Chien, Moon S Choi, Peer B Christensen, Wan-Long Chuang, Vladimir Chulanov, Mette R Clausen, Massimo Colombo, Markus Cornberg, Benjamin Cowie, Antonio Craxi, Esther A Croes, Diego Alberto Cuellar, Chris Cunningham, Hailemichael Desalegn, Sylvia Drazilova, Ann-Sofi Duberg, Steve S Egeonu, Manal H El-Sayed, Chris Estes, Karolin Falconer, Maria L G Ferraz, Paulo R Ferreira, Robert Flisiak, Sona Frankova, Giovanni B Gaeta, Javier García-Samaniego, Jordan Genov, Jan Gerstoft, Adrian Goldis, Ilias Gountas, Richard Gray, Mário Guimarães Pessôa, Behzad Hajarizadeh, Angelos Hatzakis, Christophe Hézode, Sayed M Himatt, Andy Hoepelman, Irena Hrstic, Yee-Tak T Hui, Petr Husa, Rohani Jahis, Naveed Z Janjua, Peter Jarčuška, Jerzy Jaroszewicz, Sabahattin Kaymakoglu, David Kershenobich, Loreta A Kondili, Aliya Konysbekova, Mel Krajden, Pavol Kristian, Wim Laleman, Wai-cheung C Lao, Jen Layden, Jeffrey V Lazarus, Mei-Hsuan Lee, Valentina Liakina, Young-Suk S Lim, Ching-kong K Loo, Boris Lukšič, Reza Malekzadeh, Abraham O Malu, Adkhamjon Mamatkulov, Michael Manns, Rui T Marinho, Mojca Maticic, Stefan Mauss, Muhammad S Memon, Maria C Mendes Correa, Nahum Mendez-Sanchez, Shahin Merat, Ammal M Metwally, Rosmawati Mohamed, Jacques E Mokhbat, Christophe Moreno, Joel Mossong, Fadi H Mourad, Beat Müllhaupt, Kimberly Murphy, Erkin Musabaev, Arif Nawaz, Helen M Nde, Francesco Negro, Alexander Nersesov, Van Thi Thuy Nguyen, Richard Njougoum, Renovat Ntagirabiri, Zuridin Nurmatov, Solomon Obekpa, Ponsiano Ocama, Stephen Oguce, Ogu Omede, Casimir Omuemu, Ohene Opore-Sem, Christopher K Opio, Necati Örmeci, George Papatheodoridis, Ken Pasini, Nikolay Pimenov, Hossein Poustchi, Trần D Quang, Huma Qureshi, Alnoor Ramji, Kathryn Razavi-Shearer, Berhane Redae, Henk W Reesink, Cielo Yaneth Rios, Gabriela Rjaskova, Sarah Robbins, Lewis R Roberts, Stuart K Roberts, Stephen D Ryder, Rifaat Safadi, Olga Sagalova, Riina Salupere, Faisal M Sanai, Juan F Sanchez-Avila, Vivek Saraswat, Christoph Sarrazin, Jonathan D Schmelzer, Ivan Schréter, Julia Scott, Carole Seguin-Devaux, Samir R Shah, Ala I Sharara, Manik Sharma, Gamal E Shiha, Tesia Shin, William Sievert, Jan Sperl, Peter Stärkel, Catherine Stedman, Vana Sypsa, Frank Tacke, Soek S Tan, Junko Tanaka, Krzysztof Tomasiewicz, Petr Urbanek, Adriaan J van der Meer, Hans Van Vlierberghe, Stefano Vella, Adriana Vince, Yasir Waheed, Imam Waked, Nicholas Walsh, Nina Weis, Vincent W Wong, Joseph Woodring, Cesar Yaghi, Hwai-I Yang, Chung-Lin Yang, Kakharman Yesmambetov, Ayman Yosry, Man-Fung Yuen, Muhammed Aasim M Yusuf, Stefan Zeuzem, Homie Razavi.

Affiliations

CDA Foundation, Lafayette, CO, USA (D Razavi-Shearer BSc, I Gamkrelidze BA, S Blach MHS, S M Brandon MSE, C Estes MPH, K Murphy MSCS, H M Nde MPH, K Pasini MBA, K Razavi-Shearer BA, S Robbins MSPH, J D Schmelzer MPH, H Razavi PhD); Stanford University Medical Center, Palo Alto, CA, USA (M H Nguyen MD); Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan (Prof D S Chen MD); Department of Internal Medicine, National Taiwan University College of Medicine, Taipei, Taiwan (Prof D S Chen); Universiteit Antwerpen, Antwerp, Belgium (Prof P Van Damme PhD);

Ziauddin University, Karachi, Pakistan (Z Abbas FCPS); Salmaniya Medical Complex, Manama, Bahrain (M Abdulla MRCP); National Hepatitis Program, Ministry of Public Health, Beirut, Lebanon (A Abou Rached MD); Civil Society Network on Hepatitis, Abuja, Nigeria (D Adda MPH); Chagro-Care Trust, Jalingo, Nigeria (D Adda); Health Sciences Centre, Kuwait University, Kuwait (F H Al Ali MD); Makerere University, Kampala, Uganda (P Ocama PhD, C K Opio MD); Department of Infectious Diseases (I Aho MD) and Department of Gastroenterology (P Arkkila MD), Helsinki University Central Hospital, Helsinki, Finland; Gastroenterology, Ege University, Izmir, Turkey (Prof U Akarca MD); Royal Hospital, Ministry of Health, Muscat, Oman (F A I Lawati MD); Division of Gastroenterology and Hepatology, Department of Medicine, Armed Forces Hospital, Muscat, Oman (K A I Naamani FRCPC); Department of Medicine, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia (H I Alashgar MD); Baqiatallah Research Center for Gastroenterology and Liver Diseases, Baqiatallah University of Medical Sciences, Tehran, Iran (S M Alavian MD); Middle East Liver Diseases Centre, Tehran, Iran (S M Alavian); Rashid Hospital, Dubai Health Authority, United Arab Emirates (S Alawadhi FRCPC); University of Alcalá, Centro de Investigación Biomédica en Red Enfermedades Hepáticas y Digestivas (CIBERehd), Instituto Ramón y Cajal de Investigación Sanitaria, Madrid, Spain (Prof A Albillos PhD); Department of Gastroenterology and Hepatology, Hospital Ramón y Cajal, Madrid, Spain (Prof A Albillos); Division of Gastroenterology, Department of Medicine, Sultan Qaboos University Hospital, Muscat, Oman (S A Al-Busafi MD); Unit of Infectious Diseases (K Falconer MD), Department of Medicine Huddinge (S Aleman MD), Karolinska Institutet, Stockholm, Sweden; Department of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden (S Aleman); Liver Disease Research Center, King Saud University, Riyadh, Saudi Arabia (F Z Alfaleh MD, F M Sanai SBG); King Abdulaziz Medical City and King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia (A A Aljumah FRCPI); HCV Task Force, Indian National Association for the Study of Liver, Indraprastha Apollo Hospital, Sarita Vihar, New Delhi, India (A C Anand MD); University of Sydney, Sydney, Australia (N T Anh PhD); Department of Internal Medicine and Infectious Diseases (A Hoepelman MD), University Medical Center Utrecht, Utrecht University (J E Arends MD), Utrecht, Netherlands; Department of Health Economics, National School of Public Health, Athens, Greece (K Athanasakis PhD); Gastroenterology and Hepatology, Addis Ababa University Medical School, Addis Ababa, Ethiopia (A Bane MD); Ethiopian Gastroenterological Association, Addis Ababa, Ethiopia (A Bane MD, B Redae MD); Liver Disease Center, Sheba Medical Center, Tel Hashomer, Israel (Prof Z Ben-Ari MD); University of Leipzig, Leipzig, Germany (T Berg MD); Faculty of Medicine, Division of Infectious Diseases (A R Bizri MD), and Division of Gastroenterology (Prof F H Mourad MD, Prof A I Sharara MD), American University of Beirut Medical Center, Beirut, Lebanon; Department of Gastroenterology, Federal University of the State of Rio de Janeiro, Rio de Janeiro, Brazil (C E Brandão Mello MD); LiveWell Initiative, Lagos, Nigeria (B Bright FPCPharm); Arud Centres for Addiction Medicine, Zurich, Switzerland (P Bruggmann MD); Clinical and Experimental Medicine Department, University of Pisa, Pisa, Italy (Prof M Brunetto MD); Hospital Vall d'Hebron, CIBERehd, Barcelona, Spain (M Buti PhD); Department of Medicine and Therapeutics (Prof H L Y Chan MD, V W S Wong MD), Institute of Digestive Disease (Prof H L Y Chan), and State Key Laboratory of Digestive Disease (V W S Wong), The Chinese University of Hong Kong, Hong Kong Special Administrative Region, China; Gujranwala Liver Foundation, Siddiq Sadiq Hospital, Gujranwala, Pakistan (A Chaudhry FRCPC); Liver Research Unit, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan (Prof R N Chien MD); Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea (Prof M S Choi MD); Department of Infectious Diseases, Odense University Hospital, Odense, Denmark (Prof P B Christensen PhD); Hepatobiliary Division, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan (Prof W-L Chuang MD); Reference Center for Viral Hepatitis, Central Research Institute of Epidemiology, Moscow, Russia (V Chulanov MD, N Pimenov MD); I M Sechenov First State Moscow Medical University, Moscow, Russia (V Chulanov); Department of Hepatology (M R Clausen DSc), Centre of Excellence for Health, Immunity and Infections (Prof J V Lazarus PhD), and Department of Infectious Diseases (N Weis MD), Rigshospitalet, Copenhagen, Denmark; Department of Clinical Medicine (N Weis) and Department of Infectious Diseases (J Gerstoft MD), University of Copenhagen, Copenhagen, Denmark; Clinical and Research Center Humanitas, Rozzano, Italy (Prof M Colombo MD); Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical

School, Hannover, Germany (M Cornberg MD, Prof M Manns MD); German Liver Foundation, Hannover, Germany (M Cornberg); WHO Collaborating Centre for Viral Hepatitis, Doherty Institute, Melbourne, VIC, Australia (B Cowie PhD); Department of Internal Medicine and Medical Specialities, University of Palermo, Palermo, Italy (Prof A Craxi MD); Gastroenterologia & Epatologia,

Azienda Ospedaliera Universitaria Policlinico, Palermo, Italy (Prof A Craxi); Trimbos Institute, Utrecht, Netherlands (E A Croes MD); Department of Epidemiology and Demography (D A Cuellar MSc) and Department of Health Promotion and Disease Prevention (C Y Rios MPH), Ministry of Health and Social Protection, Bogota, Colombia; Te Pūmanawa Hauora, Massey University, Wellington, New Zealand (C Cunningham PhD); Gastroenterology Unit, St Paul's Hospital Millenium Medical College, Addis Ababa, Ethiopia (H Desalegn MD, B Redae); Department of Internal Medicine, Hospital Poprad, Slovakia (S Drazilova MD); Department of Infectious Diseases, Faculty of Medicine and Health, Örebro University, Örebro, Sweden (A-S Duberg PhD); Federal Medical Centre, Jalingo, Nigeria (S S Egeonu PhD); Ain Shams University, Cairo, Egypt (Prof M H El-Sayed MD); Division of Gastroenterology (Prof M L G Ferraz MD) and Division of Infectious Disease (Prof P R Ferreira MD) Federal University of São Paulo, São Paulo, Brazil; Department of Infectious Diseases and Hepatology, Medical University of Bialystok, Bialystok, Poland (Prof R Flisiak MD); Department of Hepatogastroenterology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic (S Frankova MD, J Sperl PhD); Department of Infectology and Travel Medicine (P Kristian MD, G Rjaskova MD, Prof I Schréter MD) and First Department of Internal Medicine (Prof P Jarčuška MD), Medical Faculty, PJ Safárik University, Kosice, Slovakia; Infectious Diseases, Università della Campania, Naples, Italy (Prof G B Gaeta MD); Hospital Universitario La Paz, CIBERehd, Instituto de Investigación Hospital Universitario La Paz, Madrid, Spain (J García-Samaniego MD); University Hospital Queen Joanna, Sofia, Bulgaria (J Genov MD); Clinic of Gastroenterology, University of Medicine Victor Babes, Timisoara, Romania (A Goldis MD); Center for Disease Analysis, Louisville, CO, USA (I Gountas MSc); Kirby Institute, University of New South Wales, Sydney, NSW, Australia (R Gray PhD, B Hajarizadeh PhD); Division of Gastroenterology and Hepatology, University of São Paulo School of Medicine, São Paulo, Brazil (M Guimarães Pessôa MD, Prof M C Mendes Correa PhD); Department of Hygiene, Epidemiology and Medical Statistics, Athens University Medical School, Athens, Greece (Prof A Hatzakis MD); Hellenic Scientific Society for the Study of AIDS and Sexually Transmitted Diseases, Athens, Greece (Prof A Hatzakis); Service d' Hépatologie-Gastroentérologie, Hôpital Henri Mondor, Créteil, France (C Hézode PhD); Ministry of Public Health Qatar, Doha, Qatar (S M Himatt MD); General Hospital Pula, Pula, Croatia (I Hrstic PhD); Department of Medicine, Queen Elizabeth Hospital, Hong Kong Special Administrative Region, China (Y-T T Hui FRCP); Department of Infectious Diseases of the University Hospital Brno, Masaryk University Brno, Czech Republic (P Husa MD); Disease Control Division, Ministry of Health, Putrajaya, Malaysia (R Jahis MPH); British Columbia Centre for Disease Control, Vancouver, BC, Canada (N Z Janjua, M Krajdén MD); School of Population and Public Health (N Z Janjua), Department of Pathology and Laboratory Medicine (M Krajdén), and Department of Gastroenterology (A Ramji MD), University of British Columbia, Vancouver, BC, Canada; Department of Infectious Diseases and Hepatology, Medical University of Silesia, Katowice, Poland (J Jaroszewicz MD); Gastroenterology, Istanbul University, Istanbul, Turkey (Prof S Kaymakoglu MD); Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Tlalpan, Mexico (Prof D Kershenobich MD); Center for Global Health, Istituto Superiore di Sanità, Rome, Italy (L A Kondili PhD, S Vella PhD); Republican Diagnostic Center, Astana, Kazakhstan (A Konysbekova MD); University Medical Center, Astana, Kazakhstan (A Konysbekova); University Hospitals Leuven, KU Leuven, Leuven, Belgium (Prof W Laleman MD); Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong Special Administrative Region, China (W C Lao MBBS); Department of Public Health Sciences, Loyola University Chicago, Chicago, IL, USA (J Layden MD); Barcelona Institute for Global Health, Hospital Clínic de Barcelona, Barcelona, Spain (Prof J V Lazarus); Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan (Prof M-H Lee PhD); Centre of Hepatology, Gastroenterology, and Dietetics, Faculty of Medicine, Vilnius University, Vilnius, Lithuania (V Liakina PhD); Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea (Prof Y-S S Lim MD); Department of Medicine and Geriatrics, Kwong Wah Hospital, Hong Kong Special Administrative Region, China (C K Loo MBBS); Clinical Department of Infectious Diseases, Split

University Hospital and Split University Medical School, Split, Croatia (Prof B Lukšić MD); Liver and Pancreatobiliary Diseases Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran (R Malekzadeh, Prof S Merat MD, H Poustchi MD); Benue State University Teaching Hospital, Makurdi, Nigeria (A O Malu FMCP, S Obekpa MBBS); Research Institute of Virology, Tashkent, Uzbekistan (A Mamatkulov, E Musabaev MD); German Center for Infection Research, Partner Site Hannover-Braunschweig, Hannover, Germany (Prof M Manns); Gastroenterology and Hepatology Department, Hospital Santa Maria, Faculty of Medicine, University of Lisbon, Lisbon, Portugal (R T Marinho MD); Clinic for Infectious Diseases and Febrile Illnesses, University Medical Centre, Ljubljana, Slovenia (Prof M Maticic MD); Center for HIV and Hepatogastroenterology, Düsseldorf, Germany (S Mauss MD); Asian Institute of Medical Science, Hyderabad, Sindh, Pakistan (M S Memon FCPS); Liver Research Unit, Medica Sur Clinic Foundation, Mexico City, Mexico (Prof N Mendez-Sanchez MD); Community Medicine Research Department, National Research Center, Giza, Egypt (Prof A M Metwally PhD); University of Malaya Medical Centre, Kuala Lumpur, Malaysia (Prof R Mohamed MD); Division of Infectious Diseases and Division of Clinical Microbiology, Lebanese American University Medical Center—Rizk Hospital, Beirut, Lebanon (J E Mokhbat MD); CUB Hôpital, Erasme, Université Libre de Bruxelles, Brussels, Belgium (Prof C Moreno MD); Laboratoire National de Santé, Dudelange, Luxembourg (J Mossong PhD); Swiss Hepato-Pancreato-Biliary Center and Department of Gastroenterology and Hepatology, University Hospital Zürich, Zürich, Switzerland (Prof B Müllhaupt MD); Department of Gastroenterology, Fatima Memorial Hospital College of Medicine and Dentistry, Shadman, Lahore, Pakistan (A Nawaz MD); Divisions of Gastroenterology and Hepatology and of Clinical Pathology, Geneva University Hospital, Geneva, Switzerland (Prof F Negro MD); National Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan (A Nersesov MD); WHO, Vietnam Country Office, Hanoi, Vietnam (V V T Nguyen PhD); Virology Department, Centre Pasteur of Cameroon, Yaounde, Cameroon (Prof R Njououm PhD); Kamenge University Hospital, Bujumbura, Burundi (R Ntagirabiri MD); Department of Epidemiological Surveillance, Ministry of Health of the Kyrgyz Republic, Bishkek, Kyrgyzstan (Z Nurmatov MD); Advocacy for the Prevention of Hepatitis in Nigeria, Jos, Nigeria (S Obekpa); Department of Pediatrics, University of Jos, Jos, Nigeria (Prof S Oguche FMCPaed); Federal Ministry of Health, Abuja, Nigeria (O Omede MPH); University of Benin, Benin City, Nigeria (C Omuemu FWACP); Kwame Nkrumah University of Science and Technology, Kumasi, Ghana (Prof O Opare-Sem MD); Gastroenterology, Ankara University, Ankara, Turkey (N Örmeci MD); Department of Gastroenterology (Prof G Papatheodoridis PhD) and Department of Hygiene, Epidemiology and Medical Statistics (V Sypsa PhD), Medical School of National and Kapodistrian University of Athens, Laiko General Hospital, Athens, Greece; Communicable Disease Control Division, General Department of Preventive Medicine, Vietnam Ministry of Health, Hanoi, Vietnam (T D Quang PhD); Pakistan Medical Research Council, Islamabad, Pakistan (H Qureshi MD); Department of Hepatology, Academic Medical Center, Amsterdam, Netherlands (H W Reesink MD); Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA (L R Roberts MD); The Alfred Hospital, Melbourne, VIC, Australia (Prof S K Roberts MD); Monash University, Melbourne, VIC, Australia (Prof S K Roberts, Prof W Sievert MD); Monash Health, Melbourne, VIC, Australia (Prof W Sievert); Nottingham Digestive Diseases Centre and NIHR Nottingham Biomedical Research Centre, Nottingham University Hospitals NHS Trust, University of Nottingham, Nottingham, UK (S D Ryder DM); Liver Unit, Hadassah Medical Center, Jerusalem, Israel (Prof R Safadi MD); University of Tartu, Tartu University Hospital, Tartu, Estonia (Prof R Salupere MD); Division of Gastroenterology, Department of Medicine, King Abdulaziz Medical City, Jeddah, Saudi Arabia (F M Sanai); Instituto Tecnológico y de Estudios Superiores de Monterrey, Nuevo Leon, Mexico (J F Sanchez-Avila MD); Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India (V Saraswat DM); Department of Medicine, JW Goethe University Hospital, Frankfurt, Germany (Prof S Zeuzem MD); Viral Hepatitis and Resistance Group, University Hospital of Frankfurt, Frankfurt, Germany (Prof C Sarrazin MD); Medical Department II, Department of Gastroenterology, Hepatology, and Infectiology, St Josefs-Hospital Wiesbaden GmbH Wirtelsäulenzentrum, Wiesbaden, Germany (Prof C Sarrazin); WHO Western Pacific Regional Office, Manila, Philippines (J Scott MPH, J Woodring DO); Department of Infection and Immunity, Luxembourg Institute of Health, Esch sur Alzette, Luxembourg (C Seguin-Devaux PhD); Department of Hepatology, Institute of Liver Diseases, Hepato-Pancreato-Biliary Surgery and Liver Transplant,

Global Hospitals, Mumbai, India (S R Shah DM); Division of Gastroenterology, Department of Medicine, Hamad Medical Corporation, Doha, Qatar (M Sharma DM); Egyptian Liver Research Institute And Hospital, Dakahliah, Egypt (Prof G E Shiha PhD); Georgetown University, Washington, DC, USA (T Shin MS); Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium (Prof P Stärkel MD); Christchurch Hospital and University of Otago, Christchurch, New Zealand (C Stedman PhD); University Hospital Aachen, Aachen, Germany (F Tacke MD); Department of Hepatology, Selayang Hospital, Selangor, Malaysia (S S Tan MRCP); Department of Epidemiology, Infectious Disease Control and Prevention, Institute of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan (Prof J Tanaka PhD); Department of Infectious Diseases, Medical University of Lublin, Lublin, Poland (K Tomaszewicz PhD); Department of Internal Medicine, First Faculty of Medicine, Charles University in Prague and Central Military Hospital, Prague, Czech Republic (P Urbanek MD); Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, Netherlands (A J van der Meer MD); Department of Gastroenterology and Hepatology, Ghent University Hospital, Ghent, Belgium (Prof H Van Vlierberghe MD); Medical School University of Zagreb, University Hospital of Infectious Diseases Zagreb, Zagreb, Croatia (Prof A Vince MD); Foundation University Islamabad, Islamabad, Pakistan (Y Waheed PhD); National Liver Institute, Menoufiya, Egypt (Prof I Waked MD); PAHO, Washington, DC, USA (N Walsh MD); Department of Hepatology and Gastroenterology, School of Medical Science, Saint Joseph University, Beirut, Lebanon (C Yaghi MD); Academia Sinica, Taipei, Taiwan (H-I Yang PhD); Division of Health Technology Assessment, Center for Drug Evaluation, Taipei, Taiwan (C-L Yang MS); Clinic of Hepatology, Gastroenterology and Nutrition, Astana, Kazakhstan (K Yesmembetov MD); Cairo University, Cairo, Egypt (Prof A Yosry PhD); Department of Medicine, Queen Mary Hospital, The University of Hong Kong, Hong Kong, Special Administrative Region China (Prof M-F Yuen MD); and Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan (M A M Yusuf FRCP)

Declaration of interests


DR-S, IGa, SB, SMB, CE, KM, HMN, KP, KR-S, SR, JDS, and HR report grants from John C Martin Foundation, during the conduct of the study, and grants from Gilead Sciences, AbbVie, WHO, National Academy of Sciences, Intercept Pharmaceuticals, and Boehringer Ingelheim, outside the submitted work. MHN reports grants and personal fees from Bristol-Myers Squibb (BMS), Gilead Sciences, and Janssen, and personal fees from Novartis, Anylam, and Dynavax, outside the submitted work. PVD acts as chief and principal investigator for vaccine trials done on behalf of the University of Antwerp, Belgium, for which the University obtains research grants from vaccine manufacturers; speaker's fees for presentations on vaccines are paid directly to an educational fund held by the University of Antwerp, and PVD receives no personal remuneration for this work. ACA reports personal fees from Mylan Pharmaceuticals, outside the submitted work. JEA reports fees paid to his hospital for participation on the advisory boards of Gilead Sciences, ViiV Healthcare, BMS, Janssen, and AbbVie, and grants from BMS, Merck Sharp & Dohme (MSD), AbbVie, and ViiV Healthcare, outside the submitted work. TB reports grants, personal fees, and non-financial support from AbbVie and Gilead Sciences; grants and personal fees from BMS, Janssen, Roche, MSD, and Sequana Medical; and personal fees from Bayer, Vertex, Tibotec, Intercept, Sirtex, and Alexion, outside the submitted work. PB reports grants and personal fees from AbbVie, Gilead Sciences, and MSD, outside the submitted work. MBr reports personal fees from BMS, Gilead Sciences, and Janssen, and grants from BMS, outside the submitted work. HLYC reports personal fees from Gilead Sciences, BMS, AbbVie, Roche, MedImmune, and Intellia, outside the submitted work. PBC reports grants from AbbVie, Gilead Sciences, and MSD, outside the submitted work. VC reports personal fees from AbbVie, BMS, Gilead Sciences, and MSD, and grants from BMS, outside the submitted work. MCor reports personal fees from AbbVie, BMS, Boehringer Ingelheim, Biogen Idec, Falk Foundation, Gilead Sciences, Janssen, MSD, Roche Diagnostics, Roche Pharma, and Siemens, outside the submitted work. SD and PJ report personal fees and non-financial support from AbbVie and Gilead Sciences, and personal fees from MSD, outside the submitted work. MHE-S is an advisory board member for Perspectum Diagnostics, and reports grants and non-financial support from Gilead Sciences, and non-financial support from AbbVie and Quadri Pharma, outside the submitted work.

RF reports grants, personal fees, and non-financial support from Roche and Gilead Sciences, and personal fees and non-financial support from BMS, outside the submitted work. GBG reports grants and personal fees from Gilead Sciences, outside the submitted work. JG-S reports grants and personal fees from Gilead Sciences, and personal fees from MSD, Abbvie, Janssen, and BMS, outside the submitted work. JGer reports grants and personal fees from AbbVie, Gilead Sciences, Janssen, MSD, BMS, and ViiV Healthcare, outside the submitted work. RG reports grants from New South Wales Ministry of Health and provided project advice regarding viral hepatitis treatment to Gilead Sciences, outside the submitted work. AHa reports unrestricted grants from AbbVie, MSD, Gilead Sciences, BMS, and Novartis, and non-financial support from Gilead Sciences, outside the submitted work; he was also on advisory boards for AbbVie, Gilead Sciences, and BMS. CH reports personal fees from AbbVie, BMS, Gilead Sciences, Janssen, and MSD, outside the submitted work. JJ reports personal fees and non-financial support from Gilead Sciences and AbbVie, and personal fees from Roche and BMS, outside the submitted work. MK reports grants from Roche, Siemens, Hologic, and Boehringer Ingelheim, outside the submitted work. JVL reports grants and personal fees from Gilead Sciences and personal fees from Cepheid, outside the submitted work. MMan reports personal fees from Roche, BMS, GlaxoSmithKline, Aevi Genomic Medicine, ENYO Pharma, and CureVac, and grants and personal fees from Gilead Sciences and Novartis, outside the submitted work. SMAu reports personal fees and non-financial support from Gilead Sciences and BMS, outside the submitted work. CM reports grants and personal fees from AbbVie, Gilead Sciences, and BMS; personal fees from MSD; and grants from Roche, outside the submitted work. BM reports grants and personal fees from Gilead Sciences and personal fees from AbbVie, MSD, BMS, Bayer, Intercept, and Sigma-Tau, during the conduct of the study. FN reports personal fees and non-financial support from Gilead Sciences, during the conduct of the study. AR reports grants and personal fees from AbbVie, Gilead, and MSD, and personal fees from BMS, Celgene, Janssen, Intercept, and Lupin, outside the submitted work. HWR reports grants and personal fees from AbbVie, BMS, Boehringer Ingelheim, ENYO Pharma, Gilead Sciences, Janssen, MSD, PRA Health Sciences, Regulus, and Roche; personal fees from Alnylam and R-Pharm; and grants from Replicor, outside the submitted work. LRR reports grants from the Center for Clinical and Translational Science and the Swedish Research Council (Ghana), during the conduct of the study. LRR also reports grants from Gilead Sciences, BTG, Ariad, and Wako, outside the submitted work, and was a consultant and advisory board member for Wako, Medscape, Axis, OncLive, Bayer, Tavec, and Grail. SDR has served as an advisory board member and speaker for Gilead Sciences, AbbVie, and MSD. OS has served as a consultant and on advisory boards for MSD; received research grants from AbbVie, BMS, MSD, Boehringer Ingelheim, R-Pharm, and Hepatera; and served as a speaker for Abbott, AbbVie, BMS, Gilead Sciences, Janssen, MSD, and R-Pharm. JFS-A reports personal fees from AbbVie and grants from Gilead Sciences and Janssen, outside the submitted work. CSa reports personal fees from Gilead Sciences and BMS, outside the submitted work. PS reports grants and personal fees from Gilead Sciences, AbbVie, and BMS, and personal fees from Intercept, outside the submitted work. CSt has consulted with and served on advisory boards for Gilead Sciences, AbbVie, and MSD. VSy reports grants and personal fees from Gilead Sciences, personal fees and non-financial support from AbbVie, and personal fees from Janssen, outside the submitted work. KT reports grants and personal fees from AbbVie, Gilead Sciences, and BMS; personal fees from MSD and Alfa Wasserman; and grants from Janssen, outside the submitted work. AJvdM reports grants and personal fees from Gilead Sciences and personal fees from AbbVie, outside the submitted work. IW reports personal fees from AbbVie, Gilead Sciences, Janssen, Marcyrl, Mylan, Onxio, and Pharco, outside the submitted work. NW reports personal fees paid to her department from AbbVie, BMS, Gilead Sciences, and MSD, outside the submitted work. VWW reports personal fees from Gilead Sciences, BMS, and MSD, outside the submitted work. M-FY was a speaker or advisory board member for AbbVie, BMS, Gilead Sciences, Roche, GlaxoSmithKline, Fujirebio, Biocartis, and MSD, outside the submitted work. SZ reports consultancy and lecture fees from AbbVie, Gilead Sciences, and MSD, and consultancy fees from Intercept, outside the submitted work. All other authors declare no competing interests.

Acknowledgments

This study was funded by the John C Martin Foundation through the Polaris Observatory. We thank the Research on Hepatitis group (H28-kansei-ippan-001 and H25-kanen-ippan-010; led by JT), funded by the Ministry of Health, Labour and Welfare of Japan, for their provision of country-level data for Japan, and Örebro County Council for providing ALF grants (OLL-683801) to A-SD, which allowed collection of country-level data for Sweden.

Supplementary Material

Title	Description	Type	Size
 Supplementary appendix		pdf	1.63 MB

References

1. Blumberg, BS, Alter, HJ, and Visnich, S. A “new” antigen in leukemia sera. *JAMA*. 1965; **191**: 541–546

[View in Article](#) | [Google Scholar](#)

2. Chiron, JP, Coursaget, P, Yvonnet, B et al. Simultaneous administration of hepatitis B and diphtheria/tetanus/polio vaccines. *Lancet*. 1984; **1**: 623–624

[View in Article](#) | [Google Scholar](#)

3. Wong, VC, Ip, HM, Reesink, HW et al. Prevention of the HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis-B vaccine and hepatitis-B immunoglobulin. Double-blind randomised placebo-controlled study. *Lancet*. 1984; **1**: 921–926

[View in Article](#) | [Google Scholar](#)

4. UN. Transforming our world: the 2030 Agenda for Sustainable Development. ((accessed Dec 5, 2015).)

<https://sustainabledevelopment.un.org/post2015/transformingourworld>

Date: 2015

[View in Article](#) | [Google Scholar](#)

5. WHO. Global Health Sector Strategies for viral hepatitis 2016–21. ((accessed July 1, 2016).)

<http://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en>

Date: 2016

[View in Article](#) | [Google Scholar](#)

6. Schweitzer, A, Horn, J, Mikolajczyk, RT, Krause, G, and Ott, JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. *Lancet*. 2015; **386**: 1546–1555

[View in Article](#) | [Google Scholar](#)

7. WHO. Global hepatitis report 2017. World Health Organization, Geneva; 2017

[View in Article](#) | [Google Scholar](#)

8. Ott, JJ, Stevens, GA, Groeger, J, and Wiersma, ST. Global epidemiology of hepatitis B virus infection: new estimates of age-specific HBsAg seroprevalence and endemicity. *Vaccine*. 2012; **30**: 2212–2219

[View in Article](#) | [Google Scholar](#)

9. Kowdley, KV, Wang, CC, Welch, S, Roberts, H, and Brosgart, CL. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatology*. 2012; **56**: 422–433

[View in Article](#) | [Google Scholar](#)

10. Hope, VD, Eramova, I, Capurro, D, and Donoghoe, MC. Prevalence and estimation of hepatitis B and C infections in the WHO European Region: a review of data focusing on the countries outside the

European Union and the European Free Trade Association. *Epidemiol Infect.* 2014; **142**: 270–286

[View in Article](#) | [Google Scholar](#)

11. Ott, JJ, Horn, J, Krause, G, and Mikolajczyk, RT. Time trends of chronic HBV infection over prior decades—a global analysis. *J Hepatol.* 2017; **66**: 48–54

[View in Article](#) | [Google Scholar](#)

12. Nayagam, S, Thursz, M, Sicuri, E et al. Requirements for global elimination of hepatitis B: a modelling study. *Lancet Infect Dis.* 2016; **16**: 1399–1408

[View in Article](#) | [Google Scholar](#)

13. Blach, S, Zeuzem, S, Manns, M et al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol.* 2017; **2**: 161–176

[View in Article](#) | [Google Scholar](#)

14. Wang, H, Dwyer-Lindgren, L, Lofgren, KT et al. Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012; **380**: 2071–2094

[View in Article](#) | [Google Scholar](#)

15. WHO. WHO-UNICEF estimates of HepB_BD coverage. 2017-Jul-19. ((accessed Oct 9, 2017).)
http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tswucoveragehepb_bd.html

Date: 2017

[View in Article](#) | [Google Scholar](#)

16. PAHO. Hepatitis B and C in the spotlight. A public health response in the Americas, 2016. Pan American Health Organization, Washington, DC; 2016

[View in Article](#) | [Google Scholar](#)

17. WHO. Global policy report on the prevention and control of viral hepatitis in WHO Member States. ((accessed June 21, 2016).)

http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632_eng.pdf

Date: 2013

[View in Article](#) | [Google Scholar](#)

18. Kuo, M, Money, DM, Alvarez, M et al. Test uptake and case detection of syphilis, HIV, and hepatitis C among women undergoing prenatal screening in British Columbia, 2007 to 2011. *J Obstet Gynaecol Can.* 2014; **36**: 482–490

[View in Article](#) | [Google Scholar](#)

19. Chen, CJ and Yang, HI. Natural history of chronic hepatitis B REVEALed. *J Gastroenterol Hepatol.* 2011; **26**: 628–638

[View in Article](#) | [Google Scholar](#)

20. McMahon, BJ, Alward, WL, Hall, DB et al. Acute hepatitis B virus infection: relation of age to the clinical expression of disease and subsequent development of the carrier state. *J Infect Dis.* 1985; **151**: 599–603

[View in Article](#) | [Google Scholar](#)

21. Xia, GL, Liu, CB, Cao, HL et al. Prevalence of hepatitis B and C virus infections in the general Chinese population. Results from a nationwide cross-sectional seroepidemiologic study of hepatitis A, B, C, D, and E virus infections in China, 1992. *Hepatol Res.* 1996; **5**: 62–73

[View in Article](#) | [Google Scholar](#)

22. WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. World Health Organization, Geneva; 2015

[View in Article](#) | [Google Scholar](#)

23. Malcolm, DG, Roseboom, JH, Clark, CE, and Fazar, W. Application of a technique for research and development program evaluation. *Oper Res.* 1959; **7**: 646–669

[View in Article](#) | [Google Scholar](#)

24. CDC. Epidemiology and prevention of vaccine-preven diseases. 13th edn. Public Health Foundation, Washington, DC; 2015

[View in Article](#) | [Google Scholar](#)

25. Kramvis, A. The clinical implications of hepatitis B virus genotypes and HBeAg in pediatrics. *Rev Med Virol.* 2016; **26**: 285–303

[View in Article](#) | [Google Scholar](#)

26. PAHO. EMTCT Plus. Framework for elimination of mother-to-child transmission of HIV, syphilis, hepatitis B, and chagas. Pan American Health Organization, Washington, DC; 2017

[View in Article](#) | [Google Scholar](#)

27. Chu, CM and Liaw, YF. HBsAg seroclearance in asymptomatic carriers of high endemic areas: appreciably high rates during a long-term follow-up. *Hepatology.* 2007; **45**: 1187–1192

[View in Article](#) | [Google Scholar](#)

28. Gigi, E, Lalla, T, Orphanou, E, Sinakos, E, Vrettou, E, and Raptopoulou-Gigi, M. Long term follow-up of a large cohort of inactive HBsAg (+)/ HBeAg (-)/ anti-HBe (+) carriers in Greece. *J Gastrointestin Liver Dis.* 2007; **16**: 19–22

[View in Article](#) | [Google Scholar](#)

29. Zacharakis, GH, Koskinas, J, Kotsiou, S et al. Natural history of chronic HBV infection: a cohort study with up to 12 years follow-up in North Greece (part of the Interreg I-II/EC-project). *J Med Virol.* 2005; **77**: 173–179

[View in Article](#) | [Google Scholar](#)

30. Adachi, H, Kaneko, S, Matsushita, E, Inagaki, Y, Unoura, M, and Kobayas. Clearance of HBsAg in seven patients with chronic hepatitis B. *Hepatology.* 1992; **16**: 1334–1337

[View in Article](#) | [Google Scholar](#)

31. Ahn, SH, Park, YN, Park, JY et al. Long-term clinical and histological outcomes in patients with spontaneous hepatitis B surface antigen seroclearance. *J Hepatol.* 2005; **42**: 188–194

[View in Article](#) | [Google Scholar](#)

32. WHO EURO. World Hepatitis Day: making hepatitis elimination a reality. ((accessed Sept 26, 2017).)

<http://www.euro.who.int/en/health-topics/communicable-diseases/hepatitis/news/news/2017/07/world-hepatitis-day-making-hepatitis-elimination-a-reality>

Date: July 27, 2017

[View in Article](#) | [Google Scholar](#)

The Lancet Journals

The Lancet
The Lancet Child & Adolescent Health
The Lancet Diabetes & Endocrinology
The Lancet Gastroenterology & Hepatology
The Lancet Global Health
The Lancet Haematology
The Lancet HIV
The Lancet Infectious Diseases
The Lancet Neurology

Information & Support

About Us
Information for Authors
Information for Readers
The Lancet Careers
Customer Service
Contact Us
Privacy Policy
Terms and Conditions

Subscription

Your Account
Subscription Options
Existing Print Subscribers

The Lancet Oncology
The Lancet Planetary Health
The Lancet Psychiatry
The Lancet Public Health
The Lancet Respiratory Medicine
EBioMedicine

Copyright © 2018 Elsevier Limited except certain content provided by third parties.

The Lancet is a trade mark of Elsevier Limited.

The Lancet.com website is operated by Elsevier Inc. The content on this site is intended for health professionals.

Cookies are set by this site. To decline them or learn more, visit our Cookies page.

The Lancet demonstrates its commitment to accessibility by enabling access and optimising the experience for individuals with disabilities and impairments.
