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

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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 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.

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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.[1–3] 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[6–11] 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

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.

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.[6–11]

See Online for appendix

One previous study[12] 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 'hbv'/exp OR 'hbv')". 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,

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
Asia Pacific, high income											
Japan	0·65%	0·6% (0·5 to 0·6)	719 (667–776)	70 000/221 000 (32%)	516 000 (72%)	<0·1% (<0·1 to <0·1)	330 (320–420)	99%	99%	97%	0%
Singapore	3·60%	2·4% (2·1 to 2·7)	134 (116–154)	710/48 100 (1%)	1500 (1%)	0·2% (0·2 to 0·3)	100 (100–160)	96%	91%	21%	0%
South Korea	2·98%	2·4% (2·3 to 3·0)	1244 (1155–1502)	230 000/708 000 (32%)	1 028 000 (83%)	0·1% (<0·1 to 0·2)	520 (340–940)	98%	93%	92%	3%
Asia, central											
Armenia	2·00%	1·9% (1·7 to 2·1)	55 (50–62)	20/14 500 (<1%)	5300 (10%)	0·2% (0·1 to 0·2)	60 (60–90)	94%	98%	46%	0%
Azerbaijan	2·70%	1·8% (1·5 to 2·1)	179 (149–201)	60/47 600 (<1%)	11 800 (7%)	0·3% (0·3 to 0·5)	490 (440–700)	94%	99%	0%	0%
Georgia	2·90%	2·5% (1·9 to 3·0)	100 (76–117)	50/26 600 (<1%)	16 000 (16%)	0·4% (0·3 to 0·5)	190 (160–250)	92%	94%	43%	0%
Kazakhstan	3·54%	2·7% (1·9 to 3·6)	479 (336–645)	130/128 000 (<1%)	58 500 (12%)	0·2% (0·1 to 0·3)	670 (480–1300)	83%	95%	0%	0%
Kyrgyzstan	4·70%	6·3% (4·1 to 8·5)	374 (245–504)	1100/100 000 (1%)	49 500 (13%)	0·4% (0·3 to 0·7)	550 (370–940)	96%	97%	0%	0%
Mongolia	10·60%	4·1% (3·1 to 4·8)	126 (95–146)	1200/47 300 (3%)	16 900 (13%)	0·2% (0·2 to 0·4)	140 (100–270)	99%	98%	0%	0%
Tajikistan	8·00%	6·7% (5·6 to 8·6)	586 (487–754)	200/157 000 (<1%)	19 200 (3%)	0·4% (0·4 to 0·8)	900 (760–1700)	97%	92%	0%	0%
Turkmenistan	15·60%	9·5% (8·7 to 11·4)	538 (492–646)	180/144 000 (<1%)	14 800 (3%)	0·7% (0·7 to 1·5)	710 (700–1600)	98%	99%	0%	0%
Uzbekistan	8·10%	8·0% (4·1 to 11·7)	2514 (1294–3664)	12 500/771 000 (2%)	253 000 (10%)	0·6% (0·3 to 0·9)	3500 (2000–5700)	99%	99%	0%	0%
Asia, east											
China	7·20%	6·1% (5·5 to 6·9)	86 007 (77 170–97 466)	3 500 000/32 315 000 (11%)	16 085 000 (19%)	0·2% (0·2 to 0·4)	37 300 (30 300–63 400)	99%	96%	84%	0%
Hong Kong	7·80%	6·4% (5·4 to 7·4)	471 (393–539)	36 600/167 000 (22%)	125 000 (27%)	0·2% (0·1 to 0·5)	140 (70–270)	99%	100%	99%	5%
Taiwan	13·70%	9·4% (9·2 to 10·7)	2185 (2149–2504)	228 000/821 000 (28%)	1 396 000 (64%)	0·3% (0·2 to 0·5)	560 (380–1000)	98%	92%	98%	0%
Asia, south											
Bangladesh	5·50%	4·8% (3·3 to 6·2)	7865 (5428–10 042)	540/2 957 000 (<1%)	2400 (<1%)	0·7% (0·5 to 0·9)	20 700 (14 000–26 300)	94%	0%	0%	0%
India	2·97%	2·5% (2·2 to 2·7)	32 703 (29 547–35 907)	4700/9 175 000 (<1%)	519 000 (2%)	1·0% (0·9 to 1·1)	246 000 (223 000–274 000)	88%	47%	2%	0%
Pakistan	2·50%	2·1% (2·0 to 3·3)	3962 (3906–6364)	26 400/1 271 000 (2%)	126 000 (3%)	0·6% (0·7 to 1·0)	30 600 (30 500–49 700)	86%	<1%	15%	0%
Asia, southeast											
Cambodia	4·60%	3·0% (2·9 to 5·1)	466 (455–797)	1500/165 000 (1%)	25 900 (6%)	0·6% (0·6 to 1·1)	2300 (2200–4000)	99%	83%	0%	0%
Indonesia	7·10%	6·8% (6·3 to 8·2)	17 695 (16 451–21 531)	21 500/6 379 000 (<1%)	414 000 (2%)	4·3% (4·1 to 5·4)	201 000 (193 000–251 000)	85%	85%	0%	0%
Laos	4·10%	3·7% (3·3 to 4·6)	251 (226–310)	170/86 600 (<1%)	4100 (2%)	1·0% (0·9 to 1·2)	1700 (1400–2000)	82%	9%	2%	0%

Table 1 continues on next page

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
(Continued from previous page)											
Malaysia	0·62%	0·9% (0·5 to 1·0)	291 (159–310)	5300/101 000 (5%)	25 900 (9%)	<0·1% (<0·1 to 0·1)	310 (190–480)	98%	88%	42%	0%
Myanmar	9·70%	8·3% (4·6 to 9·4)	4376 (2427–4950)	180/1 514 000 (<1%)	5900 (<1%)	5·8% (3·1 to 6·3)	54 300 (29 500–59 400)	90%	0%	0%	0%
Philippines	16·70%	9·8% (8·8 to 10·9)	10 143 (9068–11 303)	60/2 832 000 (<1%)	342 000 (3%)	2·2% (2·0 to 2·5)	47 600 (43 900–55 900)	91%	59%	0%	0%
Thailand	4·00%	3·5% (1·6 to 4·0)	2412 (1126–2784)	11 900/898 000 (1%)	117 000 (5%)	0·2% (<0·1 to 0·3)	1300 (680–2200)	99%	99%	49%	0%
Vietnam	10·00%	8·2% (7·3 to 10·3)	7764 (6863–9745)	45 000/3 232 000 (1%)	1 352 000 (17%)	1·2% (1·1 to 1·5)	18 700 (16 900–23 400)	96%	68%	0%	0%
Australasia											
Australia	0·98%	1·0% (0·9 to 1·0)	234 (222–252)	15 100/98 900 (15%)	144 000 (62%)	<0·1% (<0·1 to 0·1)	290 (200–410)	94%	91%	86%	0%
New Zealand	2·60%	2·0% (1·4 to 3·4)	95 (66–158)	10 000/35 200 (28%)	67 000 (71%)	<0·1% (<0·1 to <0·1)	30 (20–50)	92%	2%	96%	96%
Caribbean											
Belize	4·00%	1·4% (0·6 to 1·7)	5 (2–6)	5/1200 (<1%)	420 (8%)	0·1% (<0·1 to 0·1)	8 (4–11)	95%	0%	0%	0%
Cuba	1·05%	0·6% (0·5 to 0·7)	71 (59–80)	180/18 000 (1%)	36 600 (52%)	<0·1% (<0·1 to <0·1)	1 (0–1)	100%	99%	99%	100%
Dominican Republic	3·20%	1·7% (1·1 to 2·0)	179 (112–209)	600/43 300 (1%)	15 500 (9%)	0·2% (0·1 to 0·3)	480 (310–620)	80%	79%	0%	0%
Haiti	2·50%	2·9% (2·7 to 4·1)	313 (290–446)	120/73 600 (<1%)	10 200 (3%)	1·2% (1·1 to 1·7)	2900 (2700–4200)	70%	0%	0%	0%
Jamaica	5·30%	5·0% (2·4 to 5·7)	143 (69–164)	90/34 100 (<1%)	320 (<1%)	0·7% (0·4 to 0·9)	300 (150–360)	98%	0%	0%	0%
Europe, central											
Albania	7·11%	6·9% (4·7 to 9·3)	202 (137–272)	190/45 200 (<1%)	7100 (4%)	0·2% (0·2 to 0·5)	80 (50–150)	99%	99%	19%	0%
Bulgaria	3·86%	3·2% (1·9 to 5·6)	227 (136–402)	1600/56 500 (3%)	29 200 (13%)	<0·1% (<0·1 to <0·1)	30 (20–70)	91%	96%	0%	90%
Croatia	0·70%	0·6% (0·5 to 1·0)	24 (21–44)	400/5800 (7%)	9000 (38%)	<0·1% (<0·1 to 0·1)	30 (20–50)	93%	98%	93%	90%
Czech Republic	0·56%	0·4% (0·2 to 0·5)	45 (19–58)	1500/10 500 (14%)	9500 (21%)	<0·1% (<0·1 to <0·1)	2 (1–3)	96%	99%	98%	99%
Hungary	0·60%	0·4% (0·4 to 0·5)	40 (36–44)	240/9700 (2%)	1600 (4%)	<0·1% (<0·1 to <0·1)	80 (70–90)	<1%	<1%	13%	0%
Poland	1·00%	0·9% (0·7 to 1·1)	359 (269–438)	7500/147 000 (5%)	200 000 (56%)	<0·1% (<0·1 to <0·1)	200 (150–290)	96%	93%	98%	0%
Romania	4·40%	3·4% (3·2 to 3·7)	679 (625–734)	7/169 000 (<1%)	66 300 (10%)	0·2% (0·1 to 0·2)	320 (290–490)	90%	93%	0%	0%
Slovakia	1·74%	1·6% (0·7 to 1·8)	86 (36–99)	660/20 400 (3%)	6000 (7%)	<0·1% (<0·1 to 0·1)	40 (19–60)	96%	99%	77%	0%
Slovenia	1·00%	1·0% (0·4 to 1·1)	21 (9–23)	880/5200 (17%)	1100 (5%)	0·3% (0·1 to 0·3)	70 (30–80)	88%	<1%	100%	0%

Table 1 continues on next page

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
(Continued from previous page)											
Europe, eastern											
Belarus	4·80%	4·3% (3·9 to 4·8)	404 (374–458)	5/79 000 (<1%)	19 000 (5%)	0·1% (0·1 to 0·2)	130 (110–210)	96%	99%	48%	0%
Estonia	2·60%	0·5% (0·5 to 0·6)	7 (6–7)	50/2500 (2%)	320 (5%)	<0·1% (<0·1 to <0·1)	5 (4–7)	93%	90%	93%	0%
Russia	2·0%	1·4% (0·6 to 1·7)	1947 (893–2393)	3000/347 000 (1%)	537 000 (28%)	<0·1% (<0·1 to 0·2)	1600 (800–2700)	97%	96%	0%	0%
Europe, western											
Belgium	0·66%	0·6% (0·5 to 0·7)	64 (54–77)	480/18 800 (3%)	29 300 (46%)	<0·1% (<0·1 to <0·1)	50 (40–60)	97%	<1%	63%	0%
Denmark	0·24%	0·3% (0·2 to 0·3)	15 (14–19)	750/3600 (21%)	8200 (55%)	0·1% (0·1 to 0·2)	100 (90–130)	<1%	<1%	36%	96%
Finland	0·23%	0·2% (0·2 to 0·2)	11 (10–12)	2700/2900 (94%)	7000 (66%)	<0·1% (<0·1 to <0·1)	17 (15–20)	<1%	<1%	98%	80%
France	0·65%	0·5% (0·4 to 0·7)	353 (291–443)	19 000/100 000 (19%)	70 000 (20%)	<0·1% (<0·1 to <0·1)	200 (160–280)	88%	91%	86%	0%
Germany	0·30%	0·3% (0·2 to 0·6)	241 (167–454)	20 000/69 800 (29%)	67 000 (28%)	<0·1% (<0·1 to <0·1)	80 (50–190)	88%	<1%	96%	8%
Greece	2·30%	1·8% (1·5 to 2·0)	200 (168–222)	23 200/45 600 (51%)	83 600 (42%)	<0·1% (<0·1 to <0·1)	40 (40–50)	96%	98%	92%	96%
Ireland	0·10%	0·1% (0·1 to 0·1)	4 (4–5)	60/1100 (5%)	2400 (54%)	<0·1% (<0·1 to <0·1)	2 (1–5)	95%	<1%	86%	0%
Israel	1·75%	1·7% (1·2 to 2·4)	142 (97–195)	1600/34 800 (5%)	20 100 (14%)	0·4% (0·3 to 0·6)	640 (440–900)	95%	95%	19%	0%
Italy	0·60%	0·6% (0·3 to 0·7)	332 (202–430)	35 000/75 800 (46%)	97 100 (29%)	<0·1% (<0·1 to <0·1)	30 (16–50)	94%	96%	90%	10%
Netherlands	0·20%	0·3% (0·1 to 0·4)	47 (25–68)	5500/12 000 (42%)	22 500 (51%)	<0·1% (<0·1 to <0·1)	60 (30–110)	93%	99%	89%	50%
Norway	0·50%	0·3% (0·3 to 0·4)	17 (15–20)	220/4200 (5%)	3200 (19%)	<0·1% (<0·1 to 0·1)	50 (50–80)	<1%	<1%	90%	0%
Portugal	1·45%	1·2% (0·9 to 1·5)	125 (91–160)	1800/35 500 (5%)	7900 (6%)	<0·1% (<0·1 to <0·1)	30 (18–50)	98%	97%	0%	0%
Spain	0·70%	0·6% (0·4 to 0·9)	287 (208–401)	12 500/67 100 (19%)	43 000 (15%)	<0·1% (<0·1 to <0·1)	50 (40–90)	97%	98%	90%	0%
Sweden	0·20%	0·2% (0·1 to 0·2)	19 (10–24)	1700/5700 (30%)	16 800 (86%)	<0·1% (<0·1 to <0·1)	40 (20–50)	67%	<1%	90%	96%
Switzerland	0·44%	0·5% (0·3 to 0·9)	44 (22–76)	2200/11 200 (20%)	28 700 (65%)	<0·1% (<0·1 to <0·1)	20 (12–50)	<1%	<1%	90%	0%
UK	0·69%	0·7% (0·5 to 0·9)	441 (307–620)	27 900/111 000 (25%)	83 400 (19%)	0·2% (0·1 to 0·3)	1600 (1100–2200)	<1%	<1%	12%	75%
Latin America, Andean											
Peru	0·42%	0·3% (0·3 to 0·4)	92 (81–127)	310/21 600 (1%)	12 400 (13%)	<0·1% (<0·1 to <0·1)	290 (260–420)	89%	79%	0%	0%
Latin America, central											
Colombia	0·47%	0·3% (0·1 to 2·2)	130 (69–1056)	290/31 200 (1%)	57 100 (44%)	<0·1% (<0·1 to 0·4)	380 (210–3200)	91%	87%	23%	0%
Costa Rica	0·20%	0·2% (0·1 to 0·2)	9 (7–11)	20/2300 (1%)	1300 (14%)	<0·1% (<0·1 to <0·1)	19 (15–20)	97%	91%	40%	0%
El Salvador	1·06%	1·0% (0·5 to 1·2)	65 (30–76)	140/15 700 (1%)	3200 (5%)	0·2% (<0·1 to 0·2)	160 (90–220)	93%	81%	0%	0%

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								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
(Continued from previous page)											
Guatemala	1·80%	0·6% (0·4 to 0·7)	100 (66–111)	1300/24 100 (5%)	9200 (9%)	<0·1% (<0·1 to <0·1)	330 (210–360)	80%	38%	3%	0%
Mexico	0·21%	0·1% (0·1 to 0·2)	137 (115–250)	320/33 300 (1%)	12 500 (9%)	<0·1% (<0·1 to <0·1)	280 (240–550)	93%	98%	0%	20%
Nicaragua	1·50%	0·8% (0·4 to 0·9)	51 (27–56)	190/12 400 (2%)	3200 (6%)	<0·1% (<0·1 to <0·1)	60 (30–60)	99%	0%	0%	0%
Venezuela	1·80%	1·2% (1·1 to 1·8)	364 (340–576)	260/87 300 (<1%)	29 000 (8%)	0·2% (0·2 to 0·3)	1000 (970–1700)	84%	56%	0%	0%
Latin America, southern											
Argentina	0·26%	0·2% (0·1 to 0·3)	79 (47–117)	80/18 900 (<1%)	16 300 (21%)	<0·1% (<0·1 to <0·1)	170 (100–260)	92%	81%	8%	0%
Chile	0·15%	0·1% (<0·1 to 0·2)	26 (9–43)	50/6100 (1%)	22 700 (89%)	<0·1% (<0·1 to <0·1)	8 (3–14)	95%	<1%	0%	0%
Latin America, tropical											
Brazil	0·60%	0·4% (0·2 to 0·6)	760 (415–1249)	22 500/184 000 (12%)	212 000 (28%)	<0·1% (<0·1 to <0·1)	580 (330–1100)	86%	76%	41%	0%
North Africa or Middle East											
Algeria	2·15%	1·5% (1·4 to 1·7)	607 (578–703)	900/150 000 (1%)	39 100 (6%)	<0·1% (<0·1 to 0·1)	790 (720–1300)	95%	99%	0%	0%
Bahrain	1·00%	1·0% (0·6 to 1·1)	14 (9–15)	0/3300 (0%)	450 (3%)	<0·1% (<0·1 to <0·1)	5 (2–9)	99%	99%	99%	25%
Egypt	1·00%	1·0% (0·9 to 1·2)	996 (884–1116)	2300/244 000 (1%)	25 000 (3%)	0·2% (0·1 to 0·2)	3500 (3200–4000)	95%	13%	0%	0%
Iran	1·79%	1·7% (1·6 to 1·9)	1400 (1313–1498)	18 000/359 000 (5%)	339 000 (24%)	<0·1% (<0·1 to <0·1)	320 (270–550)	99%	95%	48%	10%
Iraq	3·50%	3·5% (3·2 to 3·9)	1302 (1189–1460)	8/313 000 (<1%)	6400 (<1%)	0·6% (0·6 to 0·7)	6700 (6100–7700)	73%	47%	0%	0%
Jordan	3·00%	2·4% (1·3 to 2·8)	230 (124–261)	680/45 400 (1%)	2100 (<1%)	<0·1% (<0·1 to 0·1)	130 (90–260)	98%	95%	88%	0%
Kuwait	4·80%	1·8% (1·1 to 2·4)	73 (45–99)	1/19 000 (<1%)	5500 (8%)	<0·1% (<0·1 to <0·1)	30 (16–50)	95%	99%	0%	0%
Lebanon	1·69%	1·2% (1·1 to 1·3)	70 (66–77)	940/16 000 (6%)	2600 (4%)	<0·1% (<0·1 to <0·1)	30 (30–50)	90%	99%	0%	0%
Libya	2·20%	1·5% (1·4 to 1·8)	94 (88–113)	580/30 200 (2%)	15 000 (16%)	0·2% (0·2 to 0·3)	250 (210–350)	97%	99%	0%	0%
Morocco	1·81%	1·1% (0·8 to 1·2)	388 (276–439)	14 400/88 000 (16%)	150 000 (39%)	<0·1% (<0·1 to <0·1)	150 (110–180)	98%	17%	0%	90%
Oman	2·50%	2·5% (2·1 to 2·9)	111 (95–127)	700/24 100 (3%)	6700 (6%)	0·2% (0·2 to 0·2)	150 (120–160)	99%	99%	0%	0%
Qatar	1·20%	1·2% (1·1 to 1·4)	31 (28–35)	850/7500 (11%)	5500 (18%)	0·2% (0·2 to 0·2)	40 (40–50)	98%	96%	100%	57%
Saudi Arabia	1·76%	1·6% (1·1 to 1·9)	532 (353–600)	2/121 000 (<1%)	30 000 (6%)	<0·1% (<0·1 to 0·1)	640 (390–730)	98%	98%	63%	0%
Syria	5·60%	5·7% (3·2 to 6·5)	1054 (598–1194)	5/253 000 (<1%)	49 300 (5%)	2·3% (1·4 to 2·8)	10 400 (6400–12 500)	65%	71%	0%	0%
Tunisia	5·30%	3·9% (3·6 to 4·2)	444 (414–477)	1900/95 700 (2%)	55 400 (12%)	0·2% (0·2 to 0·3)	370 (340–570)	98%	85%	0%	0%
Turkey	4·00%	2·6% (1·9 to 3·5)	2091 (1536–2786)	76 000/551 000 (14%)	113 000 (5%)	0·1% (<0·1 to 0·2)	1400 (1100–2300)	98%	99%	48%	0%

Table 1 continues on next page

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
(Continued from previous page)											
United Arab Emirates	3·70%	1·0% (0·5 to 1·2)	95 (47–108)	1/23 800 (<1%)	2700 (3%)	<0·1% (<0·1 to <0·1)	60 (30–70)	99%	99%	0%	0%
Yemen	4·20%	3·2% (1·5 to 6·7)	882 (405–1860)	6/215 000 (<1%)	3500 (<1%)	0·8% (0·4 to 1·7)	6000 (2900–12 800)	86%	0%	0%	0%
North America, high income											
Canada	0·67%	0·6% (0·4 to 1·1)	230 (145–383)	18 000/76 000 (24%)	134 000 (58%)	<0·1% (<0·1 to 0·1)	320 (190–590)	73%	<1%	68%	0%
USA	0·30%	0·3% (0·2 to 0·3)	875 (654–1033)	90 000/294 000 (31%)	305 000 (35%)	<0·1% (<0·1 to <0·1)	710 (530–960)	93%	64%	54%	20%
Oceania											
Fiji	2·00%	2·0% (1·8 to 2·3)	18 (16–21)	3/11 600 (<1%)	380 (2%)	0·3% (0·2 to 0·4)	50 (40–80)	93%	95%	0%	0%
Kiribati	15·00%	9·1% (6·2 to 10·5)	10 (7–12)	0/5300 (0%)	70 (<1%)	1·8% (1·2 to 2·0)	50 (40–60)	81%	79%	0%	0%
Papua New Guinea	11·90%	6·6% (6·0 to 7·7)	535 (482–621)	3/293 000 (<1%)	429 000 (80%)	2·6% (2·5 to 3·2)	5200 (4800–6200)	61%	35%	0%	0%
Sub-Saharan Africa, central											
Angola	13·00%	10·2% (9·3 to 11·4)	2931 (2667–3290)	830/1 296 000 (<1%)	1100 (<1%)	3·1% (3·2 to 4·0)	27 200 (27 100–34 400)	80%	0%	0%	0%
Central African Republic	11·60%	12·1% (11·0 to 13·5)	556 (507–620)	150/245 000 (<1%)	210 (<1%)	7·4% (7·1 to 8·7)	9700 (9300–11 400)	54%	0%	0%	0%
Gabon	9·20%	5·1% (3·2 to 6·0)	101 (63–118)	150/23 900 (1%)	2000 (2%)	1·8% (1·2 to 2·3)	800 (560–1000)	75%	0%	0%	0%
Sub-Saharan Africa, east											
Burundi	4·60%	2·8% (2·6 to 3·3)	294 (272–342)	3700/93 800 (4%)	8200 (3%)	0·4% (0·4 to 0·5)	1700 (1400–1800)	94%	0%	0%	0%
Ethiopia	9·40%	7·7% (7·0 to 8·1)	7882 (7171–8302)	840/1 572 000 (<1%)	778 000 (10%)	2·9% (2·7 to 3·1)	81 900 (75 700–87 500)	96%	0%	0%	0%
Kenya	2·10%	1·2% (0·9 to 1·5)	559 (421–749)	60/129 000 (<1%)	360 (<1%)	0·1% (0·1 to 0·2)	1900 (1400–2500)	78%	0%	0%	0%
Madagascar	6·90%	5·5% (4·7 to 6·4)	1357 (1177–1595)	140/272 000 (<1%)	2700 (<1%)	1·9% (1·6 to 2·2)	13 400 (11 700–15 800)	93%	0%	0%	0%
Malawi	8·20%	3·2% (2·7 to 3·9)	585 (488–711)	60/170 000 (<1%)	380 (<1%)	0·4% (0·3 to 0·4)	2000 (1700–2500)	84%	0%	0%	0%
Mozambique	11·60%	7·5% (5·6 to 8·7)	2161 (1610–2517)	230/524 000 (<1%)	1400 (<1%)	2·0% (1·5 to 2·3)	17 900 (13 400–21 000)	96%	0%	0%	0%
Rwanda	5·70%	3·4% (2·2 to 4·3)	400 (268–514)	40/98 000 (<1%)	780 (<1%)	0·3% (0·2 to 0·4)	980 (650–1300)	98%	0%	0%	0%
Sudan	6·93%	5·3% (4·2 to 6·2)	2084 (1665–2472)	13/505 000 (<1%)	113 000 (5%)	0·8% (0·6 to 0·9)	8800 (6900–10 500)	93%	0%	0%	0%
Tanzania	6·00%	4·1% (3·2 to 5·4)	2261 (1755–3022)	240/379 000 (<1%)	1500 (<1%)	0·7% (0·5 to 0·9)	11 600 (9200–16 100)	97%	0%	0%	0%

Table 1 continues on next page

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
(Continued from previous page)											
Uganda	10·30%	5·5% (4·5 to 6·0)	2291 (1856–2473)	3000/647 000 (<1%)	148 000 (6%)	1·5% (1·2 to 1·7)	20 100 (16 800–22 800)	93%	0%	0%	3%
Zambia	5·90%	3·3% (3·0 to 3·6)	540 (492–604)	60/150 000 (<1%)	350 (<1%)	0·9% (0·8 to 1·0)	4800 (4200–5300)	99%	0%	0%	0%
Sub-Saharan Africa, southern											
Zimbabwe	15·40%	8·5% (7·9 to 9·7)	1377 (1274–1571)	1500/424 000 (<1%)	7400 (<1%)	1·2% (1·2 to 1·5)	5900 (5400–6900)	90%	0%	0%	0%
Sub-Saharan Africa, west											
Burkina Faso	8·80%	6·1% (5·4 to 6·6)	1130 (1014–1231)	640/329 000 (<1%)	4400 (<1%)	1·0% (0·9 to 1·1)	5700 (5100–6400)	91%	0%	0%	0%
Cameroon	11·90%	6·8% (6·5 to 7·4)	1605 (1523–1740)	960/579 000 (<1%)	23 400 (1%)	1·7% (1·6 to 1·9)	12 200 (11 600–13 500)	85%	0%	0%	0%
Chad	12·20%	10·5% (8·2 to 12·3)	1516 (1189–1771)	540/668 000 (<1%)	4000 (<1%)	8·0% (6·3 to 9·2)	38 800 (30 300–44 700)	78%	0%	0%	0%
Côte d'Ivoire	13·00%	8·9% (5·5 to 9·4)	2099 (1305–2230)	1200/533 000 (<1%)	73 900 (4%)	3·5% (2·3 to 3·9)	23 800 (15 500–26 300)	96%	0%	0%	0%
Ghana	12·30%	10·3% (6·9 to 11·4)	2897 (1938–3227)	800/847 000 (<1%)	14 500 (<1%)	2·1% (1·4 to 2·4)	16 200 (10 900–18 200)	93%	0%	0%	0%
Mali	8·70%	5·2% (4·9 to 5·9)	936 (879–1068)	350/206 000 (<1%)	122 000 (13%)	1·3% (1·2 to 1·5)	7800 (7400–400)	73%	0%	0%	0%
Mauritania	15·70%	9·3% (8·7 to 10·2)	400 (376–439)	140/96 000 (<1%)	2300 (<1%)	2·0% (2·0 to 2·5)	2400 (2300–2900)	86%	64%	0%	0%
Nigeria	12·20%	11·2% (10·1 to 12·8)	20 767 (18 836–23 870)	5100/4 298 000 (<1%)	43 500 (<1%)	8·4% (7·6 to 9·6)	486 000 (442 000–557 000)	45%	36%	0%	0%
Senegal	11·00%	8·1% (7·5 to 9·0)	1249 (1154–1385)	960/360 000 (<1%)	50 500 (4%)	1·6% (1·5 to 1·8)	7900 (7000–8800)	93%	0%	0%	0%
The Gambia	5·97%	4·8% (4·4 to 5·2)	98 (90–107)	20/25 400 (<1%)	320 (<1%)	1·2% (1·1 to 1·4)	830 (760–960)	95%	98%	0%	0%
Global	4·9%	3·9% (3·4–4·6)	291 992 (251 513–341 114)	4 762 000/94 043 000 (5%)	28 813 000 (10%)	1·4% (1·2 to 1·6)	1 811 000 (1 607 000–2 162 000)	87%	46%	13%	<1%

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 (≥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.

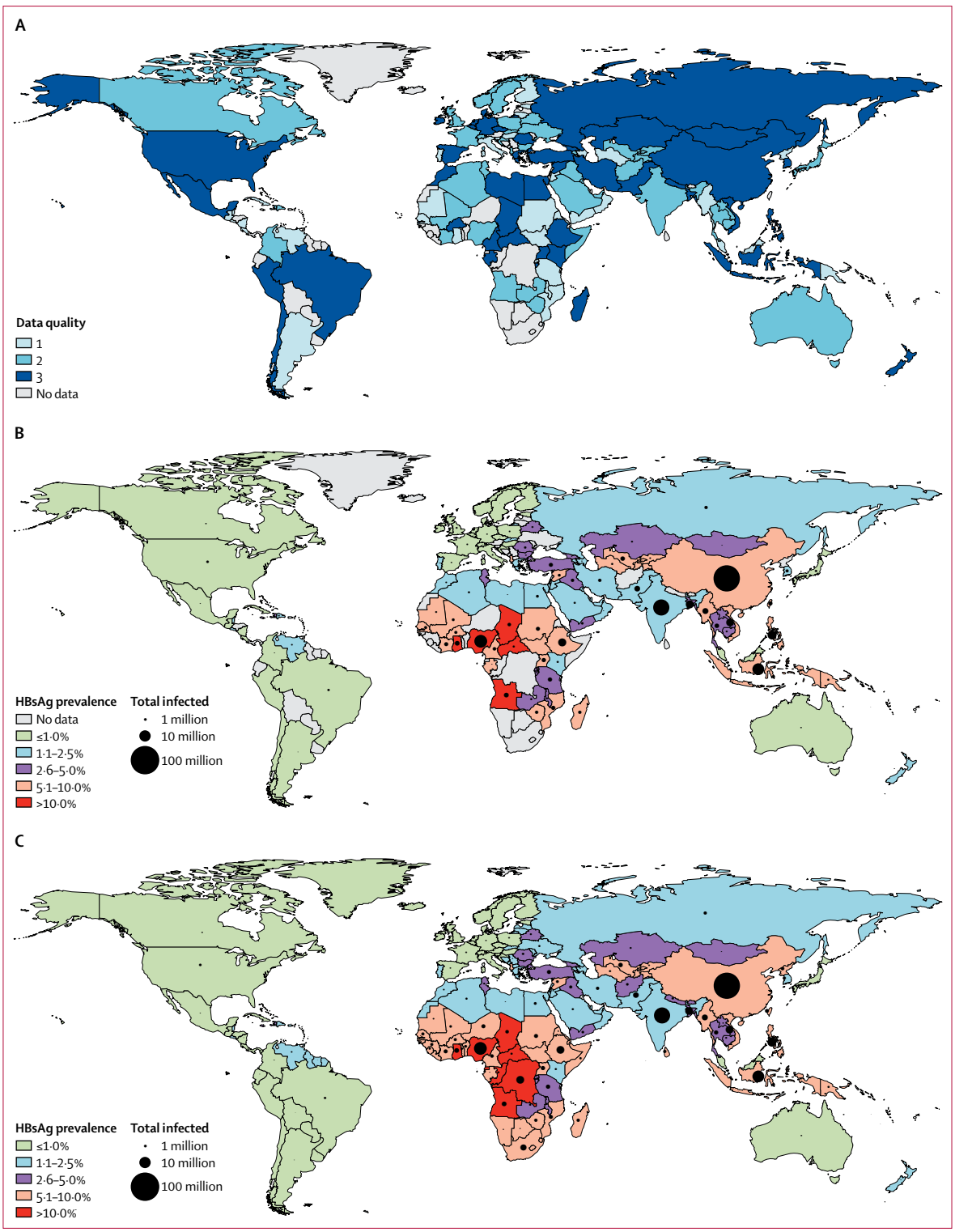
Table 1: **2016 estimates of HBsAg prevalence, treatment, and prophylaxis, by country**

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

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
Asia Pacific, high income	1·4%	1·1% (1·1–1·3)	2102 (1942–2438)	301 000/980 000 (31%)	1 549 000 (74%)	<0·1% (<0·1 to <0·1)	1500 (760–1500)	99%	97%	88%	2%
Asia, central	6·5%	5·5% (3·6–7·5)	4951 (3224–6739)	15 500/1 436 000 (1%)	445 000 (9%)	0·4% (0·3 to 0·7)	7200 (5000–12 500)	95%	97%	<1%	0%
Asia, east	7·3%	6·2% (5·6–7·0)	90 269 (81 157–102 331)	3 833 000/33 907 000 (11%)	17 925 000 (20%)	0·2% (0·2 to 0·4)	38 800 (31 400–66 000)	99%	96%	82%	<1%
Asia, south	3·1%	2·7% (2·3–3·1)	46 239 (40 372–54 320)	32 800/13 917 000 (<1%)	673 000 (1%)	0·9% (0·8 to 1·1)	311 000 (281 000–366 000)	88%	34%	3%	0%
Asia, southeast	8·6%	6·8% (5·8–8·2)	44 936 (38 080–53 564)	88 600/15 747 000 (1%)	2 368 000 (5%)	2·9% (2·6 to 3·6)	339 000 (298 000–412 000)	90%	68%	1%	0%
Australasia	1·2%	1·1% (1·0–1·4)	329 (288–410)	25 100/134 000 (19%)	211 000 (64%)	<0·1% (<0·1 to 0·1)	320 (220–460)	94%	76%	88%	16%
Caribbean	2·5%	2·0% (1·5–2·5)	887 (665–1129)	1200/212 000 (1%)	78 700 (9%)	0·6% (0·5 to 0·8)	4400 (3800–6200)	81%	42%	2%	2%
Europe, central	2·0%	1·7% (1·3–2·1)	1934 (1482–2431)	14 900/540 000 (3%)	379 000 (20%)	<0·1% (<0·1 to 0·1)	970 (750–1500)	86%	75%	33%	14%
Europe, eastern	2·1%	1·5% (0·8–1·8)	3171 (1731–3311)	4100/845 000 (1%) [A2]	748 000 (25%)	<0·1% (<0·1 to 0·2)	2300 (1200–3900)	83%	83%	6%	0%
Europe, western	0·6%	0·6% (0·4–0·8)	2404 (1731–3311)	159 000/616 000 (26%)	606 000 (25%)	<0·1% (<0·1 to <0·1)	3100 (2200–4400)	70%	47%	59%	26%
Latin America, Andean	0·4%	0·3% (0·3–0·4)	170 (151–237)	570/40 100 (1%)	23 000 (14%)	<0·1% (<0·1 to <0·1)	560 (500–800)	88%	53%	0%	0%
Latin America, central	0·6%	0·4% (0·3–0·9)	903 (690–2251)	2600/218 000 (1%)	122 000 (14%)	<0·1% (<0·1 to 0·1)	2400 (1900–6400)	91%	81%	6%	3%
Latin America, southern	0·2%	0·2% (0·1–0·3)	110 (58–169)	130/26 500 (<1%)	41 200 (37%)	<0·1% (<0·1 to <0·1)	190 (110–290)	93%	59%	7%	0%
Latin America, tropical	0·6%	0·4% (0·2–0·6)	785 (429–1290)	23 200/190 000 (12%)	219 000 (28%)	<0·1% (<0·1 to <0·1)	600 (350–1200)	86%	72%	39%	0%
North Africa and Middle East	2·6%	2·1% (1·6–2·6)	10 528 (8132–13 106)	118 000/2 587 000 (5%)	860 000 (8%)	0·3% (0·2 to 0·4)	31 400 (22 400–44 200)	92%	58%	15%	3%
North America, high income	0·3%	0·3% (0·2–0·4)	1106 (799–1416)	108 000/370 000 (29%)	439 000 (40%)	<0·1% (<0·1 to <0·1)	1000 (720–1500)	91%	59%	58%	14%
Oceania	11·0%	6·2% (5·5–7·2)	686 (615–797)	7/380 000 (<1%)	523 000 (76%)	2·4% (2·3 to 2·9)	6300 (5900–7600)	64%	41%	0%	0%
Sub-Saharan Africa, central	12·6%	10·1% (9·1–11·4)	12 215 (11 019–13 715)	3800/5 327 000 (<1%)	11 100 (<1%)	3·6% (3·6 to 4·5)	137 000 (136 000–169 000)	86%	0%	0%	0%
Sub-Saharan Africa, east	7·9%	5·1% (4·3–5·8)	22 244 (18 716–25 390)	9100/4 947 000 (<1%)	1 149 000 (5%)	1·4% (1·2 to 1·6)	178 000 (155 000–202 000)	88%	<1%	0%	<1%
Sub-Saharan Africa, southern	15·4%	8·5% (7·9–9·7)	6857 (6346–7827)	7300/2 112 000 (<1%)	36 900 (<1%)	1·2% (1·2 to 1·5)	22 300 (20 600–26 300)	86%	3%	0%	0%
Sub-Saharan Africa, west	11·8%	9·8% (8·5–11·1)	39 166 (33 905–44 401)	12 900/9 512 000 (<1%)	406 000 (1%)	5·8% (5·2 to 6·7)	722 000 (640 000–826 000)	66%	18%	0%	0%
Global	4·9%	3·9% (3·4–4·6)	291 992 (251 513–341 114)	4 762 000/94 043 000 (5%)	28 813 000 (10%)	1·4% (1·2 to 1·6)	1 811 000 (1 607 000–2 162 000)	87%	46%	13%	<1%

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 (≥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.

Table 2: **2016 estimates of HBsAg infection prevalence, treatment, and prophylaxis, by region**



(Figure 1 continues on the next page)

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

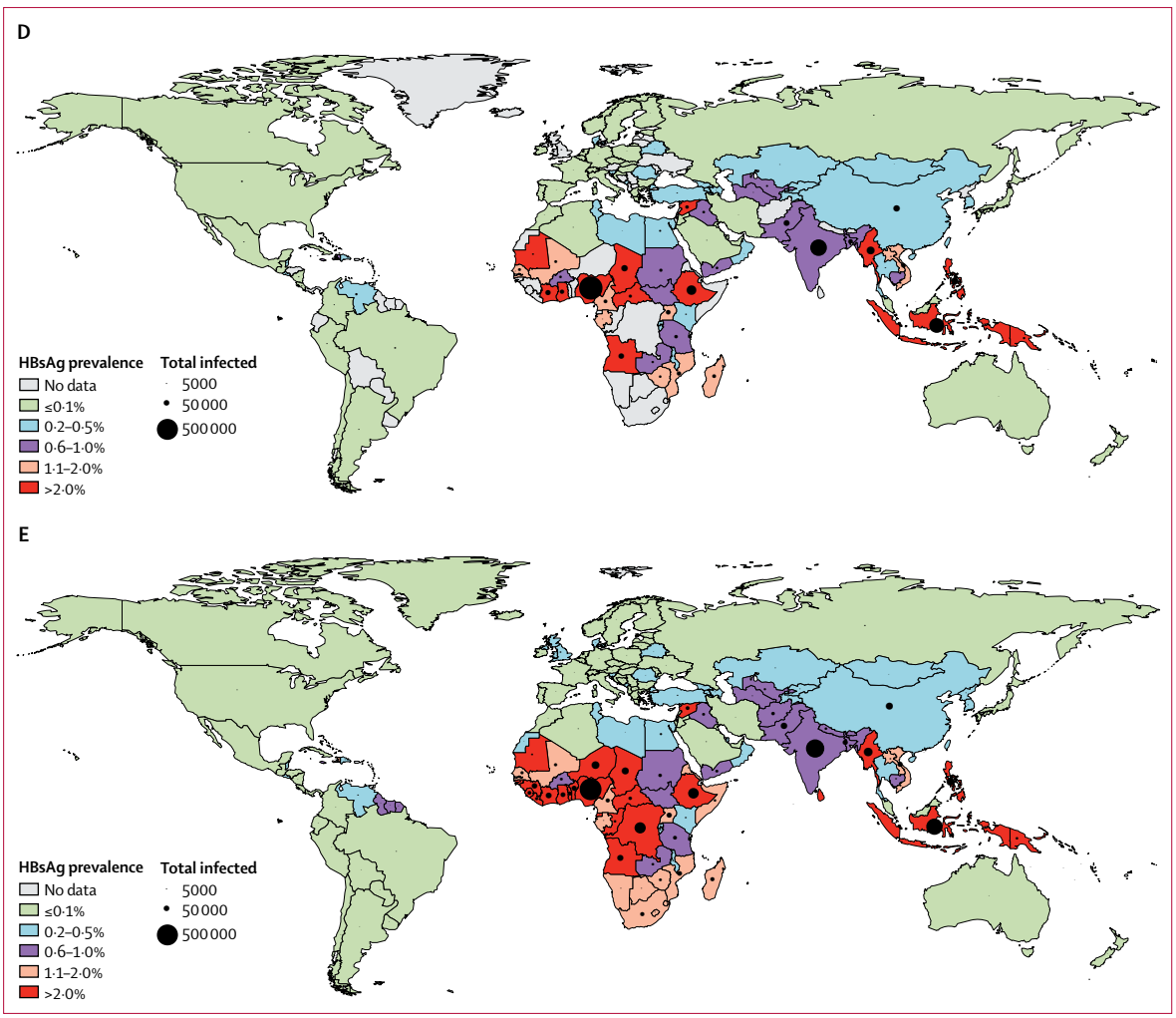


Figure 1: **HBsAg prevalence estimates for 2016**
(A) Data quality in countries with available data. 1=estimate was based on expert opinion. 2=estimate was based on published or unpublished data. 3=estimate based on a well designed national study, unpublished or ahead of print, or a large national database. (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.

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 UNICEF[15] were used as a baseline for estimates of the proportion of

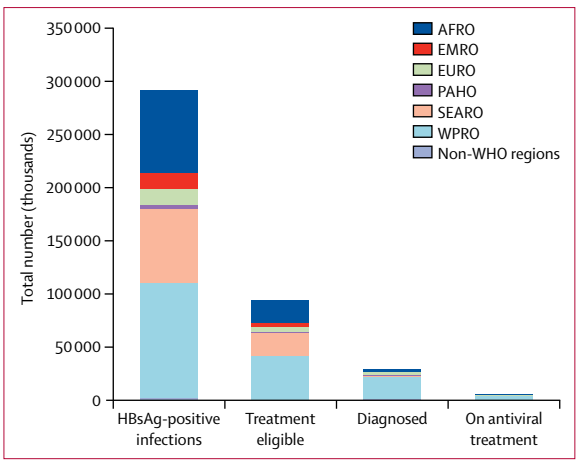


Figure 2: **Global and regional hepatitis B virus cascade of care in 2016**
AFRO=Regional Office for Africa. EMRO=Eastern Mediterranean Regional Office. EURO=Regional Office for Europe. PAHO=Pan American Health Organization. SEARO=South-East Asia Regional Office. WPRO=Western Pacific Regional Office.

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 study[19] 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; tables 1, 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.

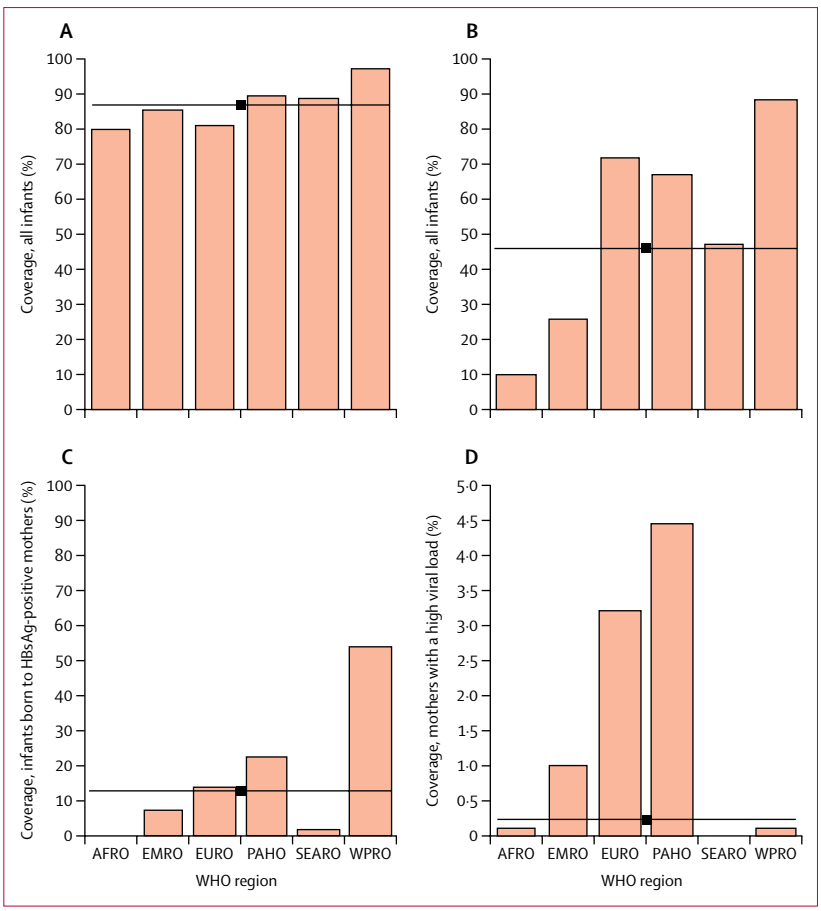


Figure 3: **Global and regional perinatal prophylaxis coverage in 2016**
The black horizontal lines indicate global averages. (A) Proportion of all infants who received three or more doses of HBV vaccine. (B) Proportion of all infants who received timely birth dose (within 24 h after birth). (C) Proportion 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.

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, tables 1, 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, tables 1, 2). The estimate of treatment-eligible patients included individuals with a high viral load (>20 000 IU/mL) and those with cirrhosis.[24]

Globally, after weighting by the number of births in each country, we estimated that 46% of infants received

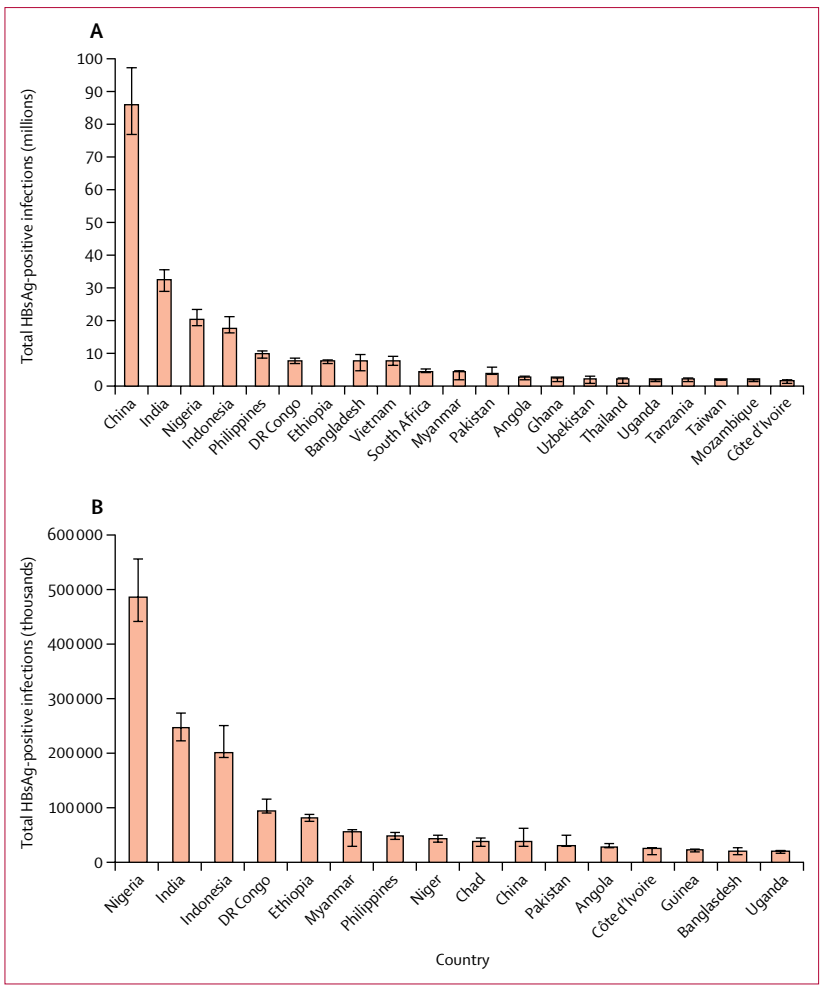


Figure 4: **Countries accounting for 80% or more of the total HBsAg-positive infections in 2016**
(A) General population. (B) Population aged 5 years.

timely birth-dose vaccination and that 87% of those younger than 1 year received the full vaccination schedule (figure 3, tables 1, 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, tables 1, 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, tables 1, 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 (tables 1, 2).

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.

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).

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

	Historical prevalence (%)	Modelled prevalence*	HBsAg-positive population, thousands*	Treated/treatment eligible† (%)	Diagnosed (%)‡	HBsAg prevalence in children aged 5 years*	HBsAg-positive population aged 5 years*	Prophylaxis coverage (%)			
								Three-dose vaccination before age 1 year§	Timely birth dose§	HBIG and full vaccination¶	Antiviral treatment of mothers‖
WHO region											
AFRO	9·5%	7·2% (6·2–8·2)	78 166 (68 191–88 606)	33 700/21 356 000 (<1%)	1 486 000 (2%)	3·4% (3·0 to 3·9)	1 046 000 (940 000–1 209 000)	80%	10%	0%	<1%
EMRO	3·0%	2·2% (1·9–3·0)	15 565 (13 041–20 412)	68 900/4 109 000 (2%)	1 000 000 (6%)	0·5% (0·4 to 0·7)	83 000 (71 100–118 000)	85%	26%	7%	1%
EURO	2·0%	1·6% (1·1–2·1)	14 426 (9590–19 965)	268 000/3 940 000 (7%)	2 274 000 (16%)	0·1% (<0·1 to 0·2)	14 800 (10 100–24 300)	82%	72%	14%	3%
PAHO	0·6%	0·4% (0·3–0·6)	3961 (2792–6492)	136 000/1 057 000 (13%)	923 000 (23%)	<0·1% (<0·1 to 0·1)	9200 (7300–16 400)	89%	67%	23%	4%
SEARO	4·0%	3·5% (2·9–4·0)	68 948 (58 382–79 753)	109 000/22 290 000 (<1%)	1 462 000 (2%)	1·5% (1·3 to 1·8)	540 000 (476 000–634 000)	89%	47%	2%	0%
WPRO	7·1%	5·7% (5·1–6·6)	108 672 (97 310–124 304)	3 918 000/40 454 000 (10%)	20 268 000 (19%)	0·5% (0·4 to 0·7)	116 000 (102 000–159 000)	97%	88%	54%	<1%
World Bank region											
High income	1·1%	0·9% (0·7–1·1)	10 307 (8469–12 646)	873 000/3 578 000 (24%)	4 691 000 (45%)	<0·1% (<0·1 to <0·1)	8700 (5800–11 900)	85%	62%	71%	9%
Upper-middle income	4·8%	4·0% (3·5–4·7)	106 829 (93 070–123 656)	3 653 000/38 250 000 (10%)	18 007 000 (17%)	0·2% (0·1 to 0·3)	74 200 (61 700–115 000)	94%	86%	61%	<1%
Lower-middle income	5·3%	4·4% (3·8–5·2)	130 891 (111 825–154 913)	151 000/39 609 000 (<1%)	4 475 000 (3%)	2·0% (1·8 to 2·4)	1 257 000 (1 117 000–1 487 000)	83%	37%	1%	<1%
Low income	8·1%	6·2% (5·3–7·0)	43 695 (38 008–49 538)	85 600/12 586 000 (<1%)	1 635 000 (6%)	1·9% (1·7 to 2·2)	470 000 (422 000–547 000)	87%	3%	0%	<1%
Global	4·9%	3·9% (3·4–4·6)	291 992 (251 513–341 114)	4 762 000/94 043 000 (5%)	28 813 000 (10%)	1·4% (1·2 to 1·6)	1 811 000 (1 607 000–2 162 000)	87%	46%	13%	<1%

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 (≥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.

***Table 3*: 2016 estimates of HBsAg infection prevalence, treatment, and prophylaxis, by WHO or World Bank region**

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.

Discussion

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[6–11] 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

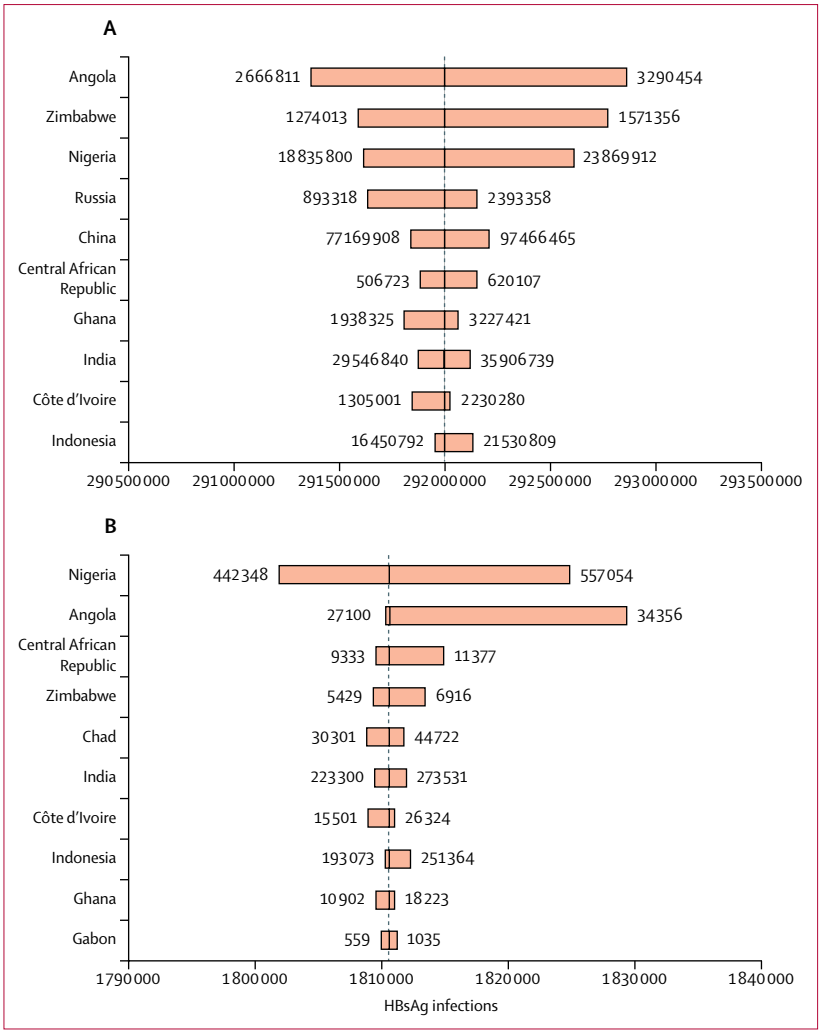


Figure 5: **Sensitivity analysis of global HBsAg-positive infection**
The black line indicates the total. (A) Top ten countries causing uncertainty at the level of the general population. (B) Top ten countries causing uncertainty at the level of the population aged 5 years.

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 limited coverage of timely birth dose, which is only available in the private sector. In Pakistan and elsewhere, the availability of birth dose as well as hepatitis B immunoglobulin is restricted to the private sector or mothers 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 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.[19,27–29] 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.

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.

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