Appendix

The current and future burden of hepatitis B in Switzerland: a modelling study

Francesco Negro, Beat Müllhaupt, David Semela, Sarah Blach, Philip Bruggmann, Andrea De Gottardi, Jean-Francois Dufour, Montserrat Fraga, Antonio Galante, Homie Razavi, Joana Vieira Barbosa, Devin Razavi-Shearer

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Section 1. Description of the PRoGReSs Model (adapted from [1])

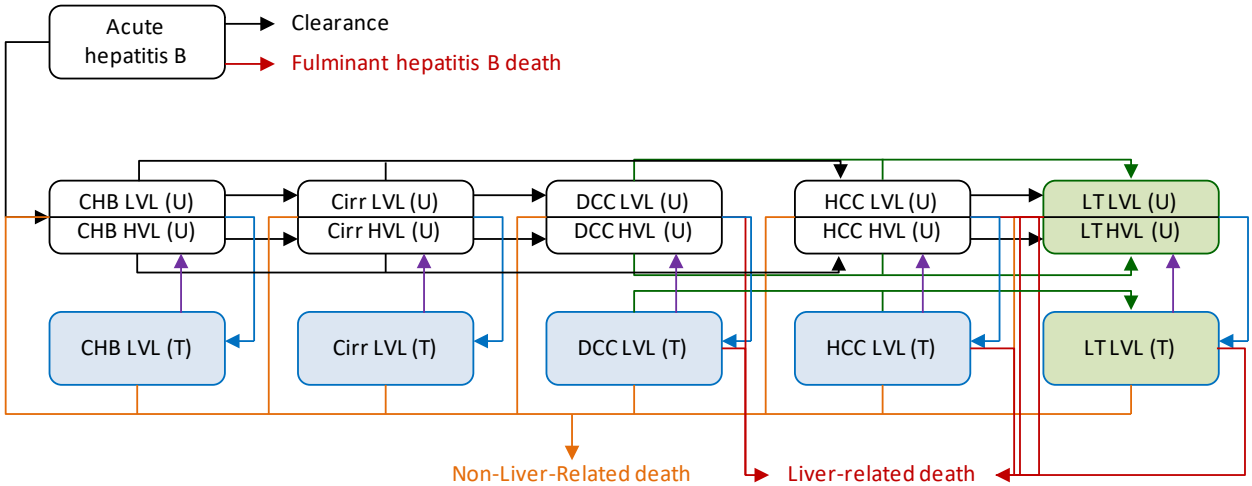
The PRoGReSs model was named after the modelers who developed it – Ken **P**asini, Homie **R**azavi, Ivane **G**amkrelidze, and Devin **R**azavi-**S**hearer. It is a compartmental, deterministic, dynamic Markov disease progression model developed in Microsoft Excel and Microsoft Visual Basic (Microsoft Corporation, Redmond, WA, United States) to quantify the annual HBV-infected population by disease stage, sex, and age in a country. Excel was selected due to its transparency, flexibility, and widespread availability.

The disease stages considered in the PRoGReSs model were chronic hepatitis B, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and liver transplant. Populations with decompensated cirrhosis and hepatocellular carcinoma were considered liver transplant-eligible.

HBV-infected population in each disease stage was further divided into high-viral load (HBsAg-positive with HBV DNA of 20,000 IU/mL or more), low-viral load (HBsAg-positive with HBV DNA of less than 20,000 IU/mL), and treatment responder subpopulations. The population susceptible to HBV was also tracked by age and sex, consisting of uninfected individuals who had never been exposed to HBV and had not been successfully immunized. The scheme of the modeled disease progression of HBV is presented in Figure 1.

Newly infected cases entered the model through the incidence calculation described below. Those developing a chronic hepatitis B infection were split into low- and high-viral load cases using reported data on respective proportions of high-viral load cases among HBeAg-negative and HBeAg-positive populations. Since the risk for chronic hepatitis B infection largely depends on the age of acquisition of infection, the model began in 1900 to allow for full flexibility of age of infection of the currently infected population and to estimate the current susceptible population.

Figure 1. Flow of disease progression of HBV



Legend: CHB — chronic hepatitis B; Cirr — compensated cirrhosis; DCC — decompensated cirrhosis; HCC — hepatocellular carcinoma; LT — liver transplant; LVL — low-viral load; HVL — high-viral load; U — untreated/non-responder; T — treatment responder; black arrows — disease progression; orange arrows — non-liver-related death; red arrows — liver-related death; blue arrows — treatment response; purple arrows — treatment discontinuation; green arrows — liver transplantation

Disease progression, aging, and mortality

The number of cases transitioning annually from one disease stage in a given year, sex, and age to (1) death, (2) another disease stage, (3) treatment responder stage, (4) liver transplant stage, or (5) back to untreated stage to the following year and following age was calculated by multiplying the annual (1) mortality, (2) disease progression, (3) treatment response, (4) liver transplant, and (5) treatment discontinuation rates, respectively, by the prevalent

population in the given disease stage, year, sex, and age (Equation 1). The remaining population moved to the next year and age, while staying in the same disease stage, to simulate aging. Population aged 85 and above was considered a single cohort.

The annual background (all-cause) mortality rate by sex and age group was applied to all populations. An additional liver-related mortality rate was applied to populations with decompensated cirrhosis, hepatocellular carcinoma, and liver transplant recipients (Tables 1–2).

Different progression rates by sex and age group were used for low- and high-viral load cases (Table 1). The original progression rates were deduced from published data. A discontinuation variable was used to estimate the duration of treatment. The default input was indefinite. At the population level, the annual number of treated patients was estimated where discontinuation by one patient and start up by another patient had the same effect as one patient continuing treatment. It was also assumed that those on treatment would stay at the same liver disease stage, with the exception of CHB and cirrhosis individuals progressing to HCC. Clinical trials have shown regression of fibrosis and cirrhosis with time but the model does not allow regression as to remain conservative in regard to the effect of current treatment.[2]

Equation 1. Prevalent cases in stage $\boldsymbol{x}$, at time $\boldsymbol{t}$, of sex $\boldsymbol{s}$, and age $\boldsymbol{a}$

$$\textbf{Prevalent cases}_{\boldsymbol{x,t,s,a}} = \text{Prevalent cases}_{x,t-1,s,a-1,} \times \left(1 - d_{t-1,s,a-1}\right) \times \left(1 - l_{x,t-1,s,a-1}\right) \times \left(1 - p_{x\to y_1,s,a-1}\right) \times \left(1 - p_{x\to y_2,s,a-1}\right) \times \cdots \times \left(1 - p_{x\to y_n,s,a-1}\right) \times \left(1 - r_{x,t-1}\right) \times \left(1 - s_{x,t-1}\right) \times (1 - c_t) + \text{New cases}_{x,t,s,a}$$

where:

$\boldsymbol{d_{t,s,a}}$ is annual background mortality rate at time t, for sex s, at age a

$\boldsymbol{l_{x,t,s,a}}$ is annual liver-related mortality rate for stage x, at time t, for sex s, at age a

$\boldsymbol{p_{x\to y_1,s,a}}$, $\boldsymbol{p_{x\to y_2,s,a}}$, …, $\boldsymbol{p_{x\to y_n,s,a}}$ are annual progression rates from stage x to y_1, stage x to y_2, …, stage x to y_n, respectively, for sex s, at age a

$\boldsymbol{r_{x,t}}$ is annual treatment response rate for stage x, at time t, defined as

$$r_{x,t} = \frac{\text{Total initiating treatment}_{x,t} \times \text{Treatment response rate}_t}{\text{Total treatment-eligible cases}_{x,t-1}}$$

$\boldsymbol{s_{x,t}}$ is annual liver transplantation rate for stage x, at time t, defined as

$$s_{x,t} = \frac{\text{Total liver transplantations}_{x,t}}{\text{Total liver transplant-eligible cases}_{x,t-1}}$$

$\boldsymbol{c_t}$ is treatment discontinuation rate at time t

New cases$_{\boldsymbol{x,t,s,a}}$ is the number of cases incident or progressing to stage x, at time t, for sex s, at age

Table 1. Annual disease progression rates of HBV infection, by males and females, %

Progression rates, males																		
Age group	**0–4**	**5–9**	**10–14**	**15–19**	**20–24**	**25–29**	**30–34**	**35–39**	**40–44**	**45–49**	**50–54**	**55–59**	**60–64**	**65–69**	**70–74**	**75–79**	**80–84**	**85+**
CHB to Cirr, LVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.6	0.8	0.8	0.9	1.0	1.6	2.0	2.4	2.8
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.5	0.5	0.6	0.6	0.6	0.9	1.7	1.8	1.9
High [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.5	0.8	0.9	0.9	0.9	1.4	2.1	2.4	2.7	3.0
CHB to Cirr, HVL [1,3]	0.0	0.1	0.1	0.2	0.3	0.4	0.7	1.4	1.7	2.4	4.1	4.5	4.9	6.1	7.8	8.5	9.1	9.8
Low [1,3]	0.0	0.0	0.0	0.1	0.1	0.1	0.2	0.8	1.2	1.4	2.2	2.4	2.7	3.3	4.5	4.9	5.3	5.7
High [1,3]	0.1	0.1	0.1	0.2	0.4	0.7	1.1	1.5	2.0	3.2	4.4	5.7	6.8	10.3	14.5	17.5	20.4	23.4
CHB to HCC, LVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.3	0.3	0.3	0.3	0.3	0.4	0.4
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.3	0.3	0.3	0.3	0.3
High [1,3]	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.3	0.5	0.5	0.6	0.6	0.7	0.7	0.8
CHB to HCC, HVL [1,3]	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.2	0.4	0.6	0.7	0.8	0.8	0.8	0.9	0.9	1.0
Low [1,3]	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.3	0.2	0.7	0.5	0.5	0.5	0.5	0.5
High [1,3]	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.5	0.8	1.0	1.3	1.6	1.7	1.9	2.1	2.3	2.5
CHB to HCC, Tx Resp [4]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.3
Low [2,4-6]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
High h[2,4-6]	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.5	0.8	1.0	1.3	1.5	1.7	1.9	2.0	2.2	2.5
Cirr to HCC, LVL [1,3]	0.0	0.0	0.0	0.0	0.1	0.2	0.4	0.8	1.3	1.8	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8
Low [1,3]	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	1.2	1.2	1.1	2.1	1.7	1.7	1.7	1.7	1.7	1.7
High [1,3]	1.0	1.0	1.0	1.0	1.0	1.0	1.9	2.5	3.1	3.7	4.3	4.7	5.2	5.7	6.3	6.9	7.6	8.4
Cirr to HCC, HVL [1,3]	0.1	0.1	0.2	0.3	0.4	0.6	0.8	1.5	2.2	3.8	6.9	9.6	10.7	11.1	11.4	11.8	12.1	12.5
Low [1,3]	0.0	0.0	0.0	0.0	0.4	0.4	0.4	1.0	1.5	1.1	1.0	9.5	8.9	8.9	8.9	1.0	1.0	1.0
High [1,3]	1.4	1.4	1.4	1.4	1.4	1.5	2.0	3.0	4.0	4.8	6.9	12.7	13.2	14.5	15.9	17.5	19.3	21.2
Cirr to HCC, Tx Resp [4]	0.0	0.0	0.0	0.1	0.1	0.1	0.2	0.3	0.5	0.9	1.6	2.2	2.5	2.5	2.6	2.7	2.8	2.9
Low [2,4-6]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.6	0.5	0.5	0.5	0.1	0.1	0.1
High [2,4-6]	1.3	1.3	1.3	1.3	1.3	1.4	1.8	2.8	3.7	4.4	6.3	11.7	12.1	13.3	14.7	16.1	17.8	19.5
DCC to LR Death [7-10]	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0
Low [7]	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4
High [8]	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1
HCC to LR Death, subseq-yr [11,12]	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0
Low [13,14]	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
High [15]	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4

Progression rates, females																		
Age group	**0–4**	**5–9**	**10–14**	**15–19**	**20–24**	**25–29**	**30–34**	**35–39**	**40–44**	**45–49**	**50–54**	**55–59**	**60–64**	**65–69**	**70–74**	**75–79**	**80–84**	**85+**
CHB to Cirr, LVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.3	0.3	0.3	0.3	0.4	0.6	0.8	1.0	1.1
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.2	0.2	0.2	0.2	0.4	0.7	0.7	0.8
High [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.3	0.3	0.4	0.4	0.5	0.8	1.0	1.1	1.2
CHB to Cirr, HVL [1,3]	0.0	0.0	0.0	0.1	0.1	0.2	0.3	0.5	0.7	1.0	1.6	1.8	2.0	2.4	3.1	3.4	3.7	3.9
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.3	0.5	0.5	0.9	1.0	1.1	1.3	1.8	2.0	2.1	2.3
High [1,3]	0.0	0.0	0.1	0.1	0.2	0.3	0.5	0.6	0.8	1.3	1.8	2.3	2.7	4.1	5.8	7.0	8.2	9.4
CHB to HCC, LVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1
High [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2
CHB to HCC, HVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.4	0.5	0.6	0.6	0.6	0.7	0.7	0.7	0.7
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.2	0.6	0.5	0.5	0.5	0.5	0.5
High [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.5	0.8	1.0	1.3	1.5	1.6	1.8	2.0	2.2	2.4
CHB to HCC, Tx Resp [4]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Low [2,4-6]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
High [2,4-6]	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.5	0.7	1.0	1.2	1.5	1.6	1.8	1.9	2.1	2.4
Cirr to HCC, LVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.6	1.2	1.5	1.6	1.7	1.7	1.8	1.8
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	1.0	1.5	1.5	1.6	1.6	1.6	1.6
High [1,3]	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.4	0.8	1.7	3.4	3.7	4.1	4.5	4.9	5.4	5.9
Cirr to HCC, HVL [1,3]	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.2	0.5	0.9	2.5	5.0	6.4	6.8	7.0	7.2	7.4	7.7
Low [1,3]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.2	4.5	4.5	4.5	4.5	1.0	1.0	1.0
High [1,3]	0.8	0.8	0.8	0.8	0.8	0.9	1.2	1.7	2.3	2.8	4.0	10.0	11.0	12.1	13.3	14.6	16.1	17.7
Cirr to HCC, Tx Resp [4]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.6	1.2	1.5	1.6	1.6	1.7	1.7	1.8
Low [2,4-6]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.3	0.3	0.3	0.3	0.1	0.1	0.1
High [2,4-6]	0.8	0.8	0.8	0.8	0.8	0.8	1.1	1.6	2.1	2.6	3.7	9.2	10.1	11.1	12.2	13.5	14.8	16.3
DCC to LR Death [7-10]	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0	24.0
Low [7]	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4	7.4
High [8]	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1	63.1
HCC to LR Death, subseq-yr [11,12]	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0	21.0
Low [13,14]	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0	17.0
High [15]	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4	50.4

HBV — hepatitis B surface antigen; CHB — chronic hepatitis B; Cirr — compensated cirrhosis; DCC — decompensated cirrhosis; HCC — hepatocellular carcinoma; LR Death — liver-related death; LVL — low-viral load; HVL — high-viral load; Tx Resp — treatment responder; subseq-yr — subsequent-year

Table 2. Mother-to-child transmission rates of HBV, %

Vaccination status of infant	Serologic status of mother		
	HBsAg-positive with high viral load, untreated peripartum	HBsAg-positive with low viral load, untreated peripartum	HBsAg-positive with high viral load, treated peripartum
No vaccination	100.0 (90.3–100.0)[16-24]	0.0 (0.0–0.0) [19,25]	5.6 (4.5–5.6)†
Birth dose of HBV vaccine only	90.0 (81.3–100.0)[16,17,26]	0.0 (0.0–0.0) [19,25]	5.1 (4.1–5.6)†
Complete HBV vaccine series with birth dose without HBIG	13.8 (9.6–41.3)[26-28]	0.0 (0.0–0.0) [19,25]	0.7 (0.5–2.1)†
Complete HBV vaccine series with birth dose with HBIG	7.7 (2.5–20.7)[25,26,29]	0.0 (0.0–0.0) [19,25]	0.4 (0.1–1.0)†
Complete HBV vaccine series without birth dose	32.7 (29.0–35.0)[22]	0.0 (0.0–0.0) [19,25]	1.6 (1.5–1.8)†

HBV — hepatitis B virus; HBsAg — hepatitis B surface antigen; HBIG — hepatitis B immune globulin; † Assumed a 95% (response rate to treatment with tenofovir[2]) reduction relative to transmission rates for HBsAg-positive with high viral load, untreated peripartum mothers

Incidence

Annual incident cases of HBsAg infections by sex and age were calculated separately for perinatally and horizontally acquired infection (Figure 2). Incident cases developing a chronic HBsAg infection were added to the disease progression model annually, and the resulting prevalence of HBsAg was used to calculate incident cases in the following year, generating a dynamic model (Figure 3). Among those not developing a chronic infection, risk for fulminant hepatitis B was 0.5% (0.1%–1.0%).[30]

Figure 2. Incidence determination scheme in the model

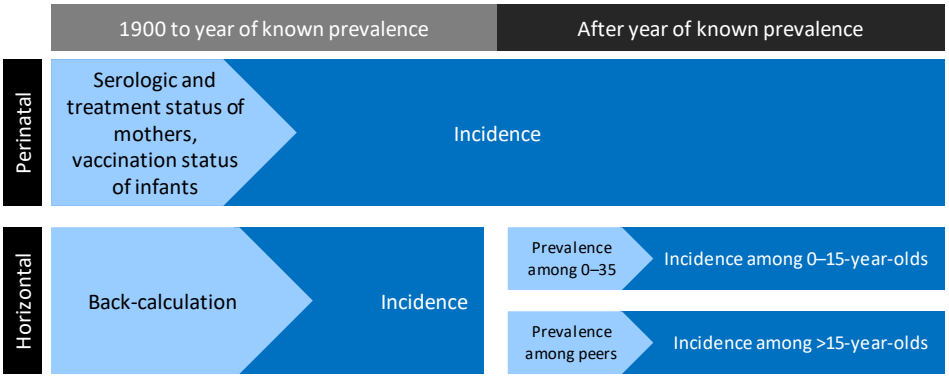
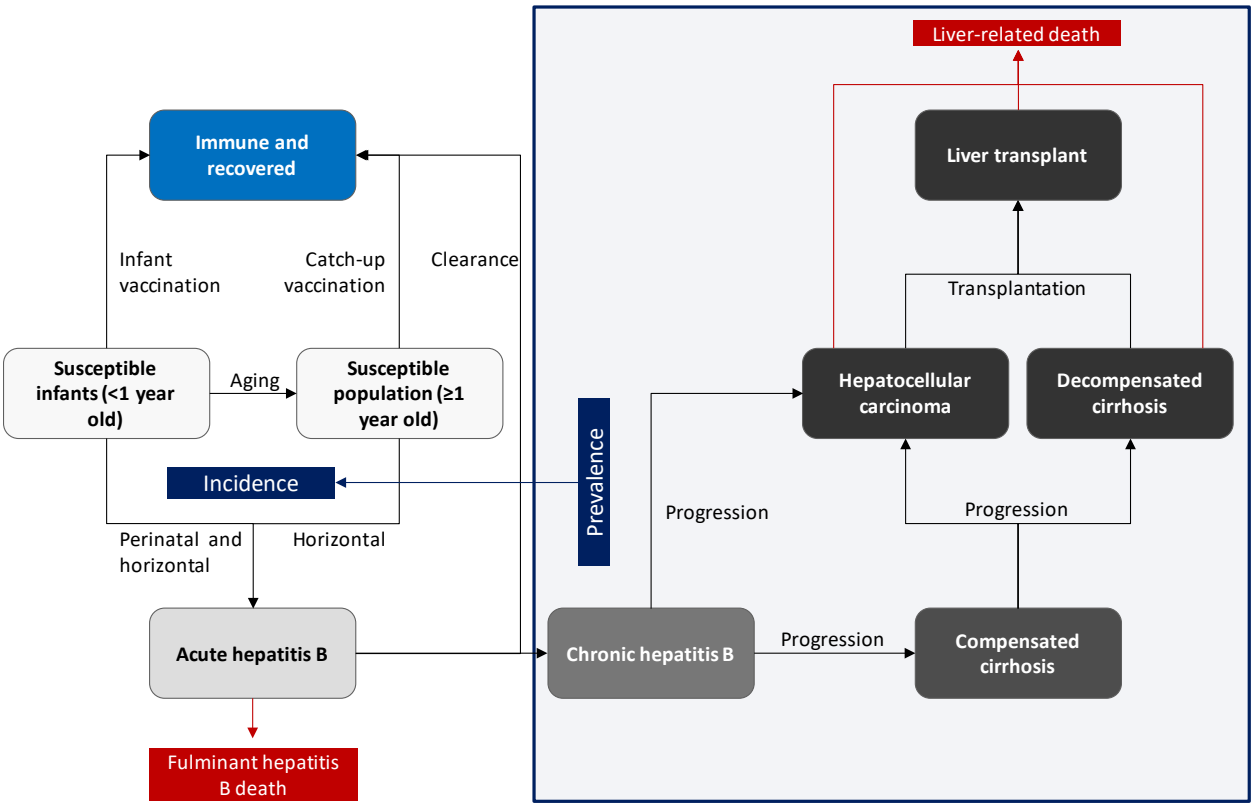


Figure 3. Flow between populations in the model



Perinatal incidence

To calculate incident cases of perinatally acquired HBsAg, the annual modeled prevalence of HBsAg among women of childbearing age is subdivided into those that are estimated to be HBeAg+ and HBeAg. The proportion among these two groups that have a high viral load and low viral load are then combined into low viral and high viral load groupings.[19,31] The high viral load group, in conjunction with the reported proportion of high viral load women receiving peripartum antiviral treatment, was used to segment the HBsAg-infected women of childbearing age into the following serologic and treatment statuses: (1) HBsAg-positive with high viral load untreated, (2) HBsAg-positive with low viral load untreated, (3) HBsAg-positive with high viral load treated, and (4) HBsAg-negative.

The reported number of annual births by mother's age group was then re-indexed to annual births by serologic and treatment status of mothers, estimated by Equation 2.

Equation 2. Total births in year $\boldsymbol{t}$ to mothers of serologic and treatment status $\boldsymbol{i}$

$$\text{Total births}_{t,i} = \sum_{A} \text{Total births}_{t,A} \times g_{t,i,A}$$

where:

A is the age group of mother (15–19, 20–24, …, 45–49)

$g_{t,i,A}$ is the proportion of A-year old women of childbearing age at time t with serologic and treatment status i

Afterwards, the births were segmented by vaccination status: (1) no vaccination, (2) birth dose of HBsAg vaccine only, (3) complete HBsAg vaccine series with birth dose without HBIG, (4) complete HBsAg vaccine series with birth dose with HBIG, and (5) complete vaccine series without birth dose.

Finally, using the transmission rates by the mothers' serologic and treatment status and the infants' vaccination status (Table 3), the number of perinatally acquired cases of HBsAg infection was calculated (Equation 3).

Equation 3. New perinatally acquired cases of HBsAg $\boldsymbol{t}$

$$\text{New perinatally acquired cases of HBsAg}_{t} = \sum_{i} \left[\text{Total births}_{t,i} \times \sum_{j} \left(f_{i,j} \times r_{i,j} \right) \right]$$

where:

i ranges over the serologic and treatment status of mothers

j ranges over the vaccination status of infants

$f_{i,j}$ is the proportion of infants with vaccination status j born to mothers with serologic and treatment status i

$r_{i,j}$ is the transmission rate from a mother with serologic and treatment status i to an infant with vaccination status j

Uninfected infants that did not receive complete HBsAg vaccine series entered the susceptible population. Chronically infected infants were added to the disease progression model.

Table 2. Mother-to-child transmission rates of HBsAg (%)

Vaccination status of infant	Serologic status of mother		
	HBsAg-positive with high viral load, untreated peripartum	HBsAg-positive with low viral load, untreated peripartum	HBsAg-positive with high viral load, treated peripartum
No vaccination	100.0 (90.3–100.0) [16-24]	0.0 (0.0–0.0) [19,25]	5.6 (4.5–5.6)†
Birth dose of HBV vaccine only	90.0 (81.3–100.0) [16,17,26]	0.0 (0.0–0.0) [19,25]	5.1 (4.1–5.6)†
Complete HBV vaccine series with birth dose without HBIG	13.8 (9.6–41.3) [26-28]	0.0 (0.0–0.0) [19,25]	0.7 (0.5–2.1)†
Complete HBV vaccine series with birth dose with HBIG	7.7 (2.5–20.7) [25,26,29]	0.0 (0.0–0.0) [19,25]	0.4 (0.1–1.0)†
Complete HBV vaccine series without birth dose	32.7 (29.0–35.0) [22]	0.0 (0.0–0.0) [19,25]	1.6 (1.5–1.8)†

HBV — hepatitis B virus; HBsAg — hepatitis B surface antigen; HBIG — hepatitis B immune globulin; † Assumed a 95% (response rate to treatment with tenofovir[2]) reduction relative to transmission rates for HBsAg-positive with high viral load, untreated peripartum mothers

Horizontal incidence

Horizontally acquired incident cases of HBsAg infection were calculated separately (1) up to the year of known prevalence by sex and age group in a country/region ("year of known prevalence"), and (2) after the year of known prevalence (Figure 2). Cases incident up to the year of known prevalence are referred to as "historical," while cases incident afterwards are referred to as "forward."

Horizontal incidence — historical

Total annual historical horizontally acquired incident cases of HBsAg were calculated by first defining a curve describing relative sizes of these incident cases ("relative incidence"). Then, a calibration procedure matching modeled prevalence to reported prevalence was used to transform relative incidence to annual incident cases by sex and age.

Relative incidence

Relative incidence was built by back-calculating arrays of quinquennial estimated incident cases for both sexes (Table 4) that satisfied the conditions in Equations 4–5. These were then converted to annual estimated incident cases, linearly interpolated over 1900–year of known prevalence, and passed through a 5-year-average filter. The resulting annual incident cases were divided by peak incident cases to generate the relative incidence curve with a peak of one.

Table 3. Array of incident (horizontal) cases $\boldsymbol{I_{t,s,A_n}}$ at time t, of sex $\boldsymbol{s}$, of age group $\boldsymbol{A_n}$

Age group / Year	⋯	**YKP − 5**	**YKP**	**YKP**
$\boldsymbol{A_0}$	⋯	$I_{\mathrm{YKP}-5,s,A_0}$	I_{YKP,s,A_0}	P_{YKP,s,A_0}
$\boldsymbol{A_1}$	⋯	$I_{\mathrm{YKP}-5,s,A_1}$	I_{YKP,s,A_1}	P_{YKP,s,A_1}
$\boldsymbol{A_2}$	⋯	$I_{\mathrm{YKP}-5,s,A_2}$	I_{YKP,s,A_2}	P_{YKP,s,A_2}
⋮	⋱	⋮	⋮	⋮

YKP — year of known prevalence; P_{YKP,s,A_n} — total prevalent population in YKP of sex s in age group A_n; A_0 is age group 0, A_1 is age group 1–4, A_2 is age group 5–9, …, A_{18} is age group 85+

Equation 4. Condition 1 for back-calculated array of incident (horizontal) cases

For each sex s and age group A_n,

$$\sum_{i=0}^{n} I_{\text{YKP}-5n+5i,s,A_i} \times \bar{c}_{A_i} \times S(d)_{\text{YKP}-5n+5i,s,A_i} \times \left(\text{HVL} \times S(l_{\text{HVL}})_{\text{YKP}-5n+5i,s,A_i} + (1-\text{HVL}) \times S(l_{\text{LVL}})_{\text{YKP}-5n+5i,s,A_i}\right) = P_{\text{YKP},s,A_n}$$

where:

YKP is year of known prevalence

I_{t,s,A_n} is incident (horizontal) cases at time t, of sex s, at age group A_n

A_0 is age group 0, A_1 is age group 1–4, A_2 is age group 5–9, …, A_{18} is age group 85+

$\bar{c}_{A_n}$ is average risk for chronic infection for age group A_n

$S(d)_{t,s,A_n}, S(l_{\text{HVL}})_{t,s,A_n}, S(l_{\text{LVL}})_{t,s,A_n}$ are survival functions from background death, liver-related death among high-viral load population, and liver-related death among low-viral load population, respectively, from time t to year of known prevalence for sex s, and age group A_n

HVL is proportion of high-viral load cases among incident cases of HBsAg

P_{YKP,s,A_n} is prevalent cases of HBsAg, of sex s and age group A_n in year of known prevalence

Equation 5. Condition 2 for back-calculated array of incident (horizontal) cases

For each time point t, sex s, and age group A_n,

$$\frac{I_{t,s,A_n}}{I_{t-5,s,A_{n-1}}} = \frac{\bar{k}_{A_n}}{\bar{k}_{A_{n-1}}} \times \frac{\text{Unvaccinated population}_{t,s,A_n}}{\text{Unvaccinated population}_{t-5,s,A_{n-1}}}$$

where:

YKP is year of known prevalence

I_{t,s,A_n} is incident (horizontal) cases at time $t \in \{\text{YKP}-85, \text{YKP}-80, \ldots, \text{YKP}\}$, sex s, and age group $A_n \in \{A_1, \ldots, A_{18}\}$

$\bar{k}_{A_n}$ is average shape parameter for age group A_n

$\text{Unvaccinated population}_{t,s,A_n}$ at time t, of sex s, at age group A_n was estimated using reported history of vaccinations in the country

Incidence calibration

A (1) scalar multiplier of relative incidence and (2) quinquennial sex and age group distributions of historical horizontal incident cases were calculated using the secant method[32] to match (1) modeled total prevalent cases (Equation 6) and (2) modeled prevalence of HBsAg by sex and age group in the year of the known prevalence to reported prevalence.

Equation 6. Total HBsAg-infected population in year of known prevalence

$$\text{Prevalent cases of HBsAg}_{\text{YKP}} = \sum_{t=1900}^{\text{YKP}} \left(\text{Incident cases of chronic HBsAg}_t - \text{Deaths among HBsAg-infected population}_t\right)$$

where:

YKP is year of known prevalence

Horizontal incidence — forward

Susceptible population

To calculate the number of new horizontally acquired HBsAg infections after the year of known prevalence, we first estimated the susceptible population in the year of known prevalence (Equation 7). Susceptible infants were calculated as described above.

Equation 7. Susceptible population S in year of known prevalence, of sex s, at age $a \geq 1$

$$S_{\text{YKP},s,a} = \left(P_{\text{YKP},s,a} - \sum_{i=0}^{a}\left[\text{Incident HBsAg cases}_{\text{YKP}-a+i,s,i}\prod_{j=i}^{a-1}\left(1 - d_{\text{YKP}-a+i,s,i}\right)\right]\right) \times \left(1 - \text{Imm}_{\text{YKP},a}\right)$$

where:

YKP is year of known prevalence

$d_{t,s,a}$ is background mortality rate at time t, of sex s, at age a

$P_{t,s,a}$ is population at time t, of sex s, at age a

$\text{Imm}_{t,a}$ is an estimate of immunization coverage of population at time t at age a

In all years following the year of known prevalence, we calculated the annual susceptible population by sex and age by (1) adding infants susceptible to infection to the existing 0-year old susceptible population, as described above, and (2) subtracting deaths due to background mortality, new infections, and new catch-up immunizations from the existing susceptible population (Equation 8).

Equation 8. Susceptible population S after year of known prevalence, of sex s, at age $a \geq 1$

$$S_{t,s,a} = S_{t-1,s,a-1} \times \left(1 - d_{t-1,s,a-1}\right) - \text{New HBsAg Cases}_{t,s,a} - \text{Catch-up immunizations}_{t,s,a}$$

where:

$d_{t,s,a}$ is background mortality rate at time t, of sex s, at age a

Incidence function

Incidence of horizontally acquired HBsAg infection was assumed to be a linear function of HBsAg prevalence with high viral load (Equation 9). For those younger than 15, incidence was determined by prevalence of HBsAg with high viral load among 0–35-year-olds to simulate household infection from siblings, peers, parents, and other adults. For those 15 or older, incidence was a function of prevalence with high viral load among peers of the same age.

Equation 9. Incident (horizontal) cases I in year $t >$ YKP, of sex s, and age a

$$I_{t,s,a} = \begin{cases} S_{t-1,s,a-1} \times \left(1 - d_{t-1,s,a-1}\right) \times p_{t-1,0\text{–}35} \times (k_a \times C_s) & \text{if } 0 \leq a < 15 \\ S_{t-1,s,a-1} \times \left(1 - d_{t-1,s,a-1}\right) \times p_{t-1,a} \times (k_a \times C_s) & \text{if } a \geq 15 \end{cases}$$

where:

$p_{t,a}$ is prevalence of HBsAg with high viral load at time t, at age (group) a

$S_{t,s,a}$ is the susceptible population at time t, of sex s, at age a

$d_{t,s,a}$ is background mortality rate at time t, of sex s, at age a

k_a is the shape parameter for age a

C_s is scale parameter for sex s (see below)

Scale parameter C_s for both sexes s was inferred through a calibration procedure that matched the number of cases incident in the year of known prevalence to those incident in the following year, thereby tying the forward incident cases to historical incident cases.

Section 2. Delphi Process (adapted from[1])

		Activities
Phase 1 – Data Gathering	1a	**Identify country experts who are willing to collaborate** • Experts were identified through HBV-related scientific contributions, or through referrals and recommendations from leading researchers. • The panel consisted of gastroenterology and hepatology professors and clinicians from across Switzerland as well as an infectious disease and addiction medicine specialist. • The final panel included representatives from the following cities/regions: Geneva, Laussane, Lugano, Pully, St. Gallen, and Zurich
	1b	**Literature Search** • Review the CDAF internal database for previously identified sources • Review online sources (FOPH, WHO, etc.) to capture non-indexed sources • Run a literature search to identify recent publications • Summarize input data available through the literature • Gather empirical data for new HCC cases, liver transplants (LT), percent of HCC and LT due to HBV, annual newly diagnosed, annual treated, and annual prophylaxes coverage • Build draft model based on published data • Schedule meeting with experts
Phase 2 – Country Meetings and Modeling	2a	**Expert Meeting 1 (2-3 hours)** • Provide a background on the project, model and methodology • Review data identified in Phase 1b and highlight gaps in data • Request data in local non-indexed journals, unpublished data and any other available data (e.g., hospital-level data) that can be used to fill the gaps
	2b	**Follow up with Experts Post Meeting 1** • Send minutes of the meeting and list of remaining action items to experts • Follow up with experts to collect missing data and get copies of publications in the local journals, unpublished data, and government reports • Analyze data and send to experts for approval
	2c	**Disease Burden Modeling** • Populate disease burden model with inputs and calibrate model to empirical data • Develop preliminary what-if scenarios to prepare for meeting 2 • Develop a slide deck summarizing all inputs and associated data sources • Perform a final check of the model and slide deck and approve internally
	2d	**Expert Meeting 2 (2-3 hours)** • Review all inputs as well as data provided by experts since meeting 1 and results of analyses of any raw data provided • Gain agreement on all inputs to be used in the model • Update the model using any updated inputs • Run scenarios requested by experts and review results and insights • Agree on final strategies that would be considered as part of a national strategy
Phase 3 – Follow-up Analyses	3a	**Follow-up Analyses** • Update model as necessary and send results to experts • Address follow-up questions with the expert panel by email or teleconference • Lock down inputs and outputs as approved • Generate follow-up analyses including immigration analyses • Review assumptions and results of follow-up analyses by email and teleconference

Section 3. Uncertainty Analysis

Since the 95% CI in the Swiss situation analysis (FOPH) provided a broader range than was identified in our immigration analysis, a second scenario was developed where we populated the PRoGReSs model with a base prevalence of 0.72% and range of 0.32% to 0.89%. In 2020, this corresponded to 62,700 (UI: 27,700-77,000) HBsAg+ cases (Figure 4). Due to the impacts of mortality and the efforts of prophylaxis measures, this number was expected to decrease to 56,890 (UI: 20,300-71,700), 0.62% (0.22%-0.78%), by 2030 (Figure 5). Among the total infected population, we estimated that 61% of cases were between the ages of 35 and 59. In 2020, there were an estimated 48 (UI: 9-66) incident cases of decompensated cirrhosis, 173 (UI: 58-238) incident cases of HCC and 198 (UI: 60-270) liver-related deaths. HBsAg+ prevalence was estimated to be <0.1% among both infants and 5-year-olds in 2020. Applying the EASL treatment guidelines to the Swiss infected population, the model estimates that 21.0% (n=13,400) of all infected individuals would be eligible for treatment.

- **The Base Case** – If the current treatment and diagnostic levels were continued in the future, the incidence of decompensated cirrhosis would decrease by 8% [from 48 (9-66) in 2020 to 43 (1-64) in 2030], while HCC and liver-related deaths would increase by 21% [from 173 (58-238) in 2020 to 209 (64-319) in 2030] and 22% [from 198 (60-270) in 2020 to 238 (63-349) in 2030], respectively as the infected population advances in disease state and age between 2020 and 2030.
- **Stop Tx –** If all treatments were stopped in 2022 there would be an estimated 38% increase in the incidence of decompensated cirrhosis [from 48 (9-66) in 2020 to 66 (16-89) in 2030], a 35% increase in the incidence of HCC [from 173 (58-238) in 2020 to 234 (65-308) in 2030] and a 37% increase in liver-related deaths [from 198 (60-270) in 2020 to 271 (72-358) in 2030] by 2030. Compared to the Base Case, this scenario would result in an additional 110 cases of decompensated cirrhosis, 120 cases of HCC and an additional 140 lives lost.
- **Tx All – Curr Guide –** By increasing diagnosis and linkage to care so that all individuals eligible for treatment receive treatment there would be an estimated 65% reduction in the incidence of decompensated cirrhosis [from 48 (9-66) in 2020 to 17 (1-34) in 2030], a 4% increase in the incidence of HCC [from 173 (58-238) in 2020 to 180 (58-365) in 2030] and a 3% increase in liver-related deaths [from 198 (60-270) in 2020 to 203 (57-365) in 2030] by 2030. Compared to the Base Case, this scenario would avert 100 cases of decompensated cirrhosis, 120 cases of HCC and save 120 lives.

Figure 4: HBV Cascade of Care in Switzerland using the FOPH Range, 2020

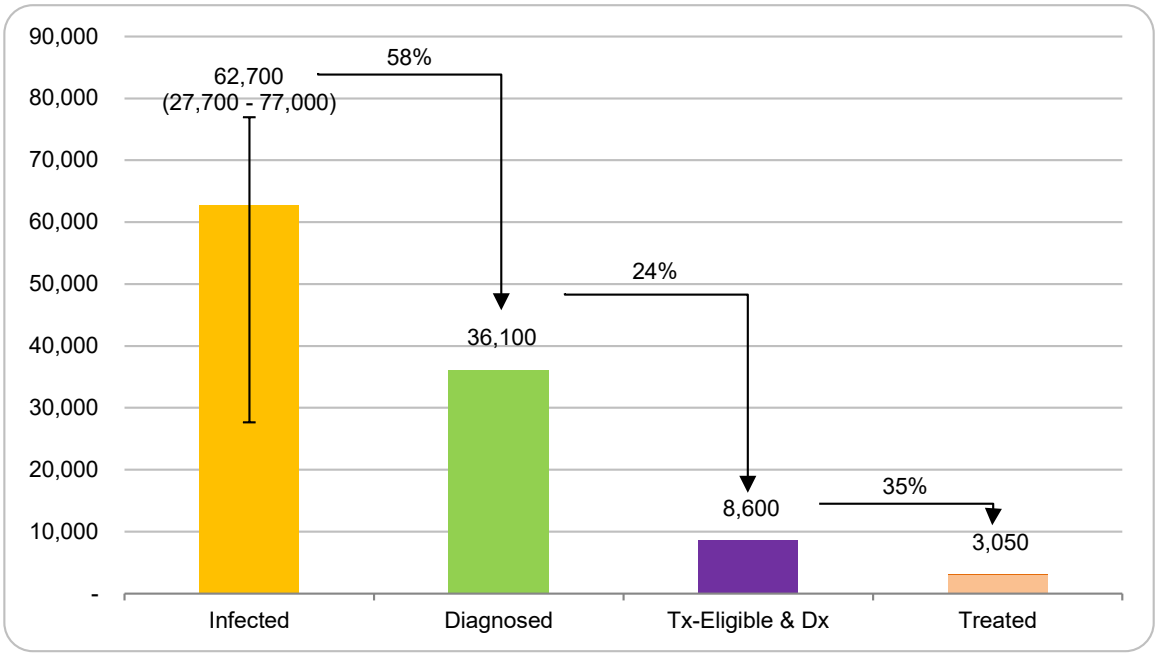


Figure 5. HBV morbidity and mortality in Switzerland using the FOPH range, 2020-2030

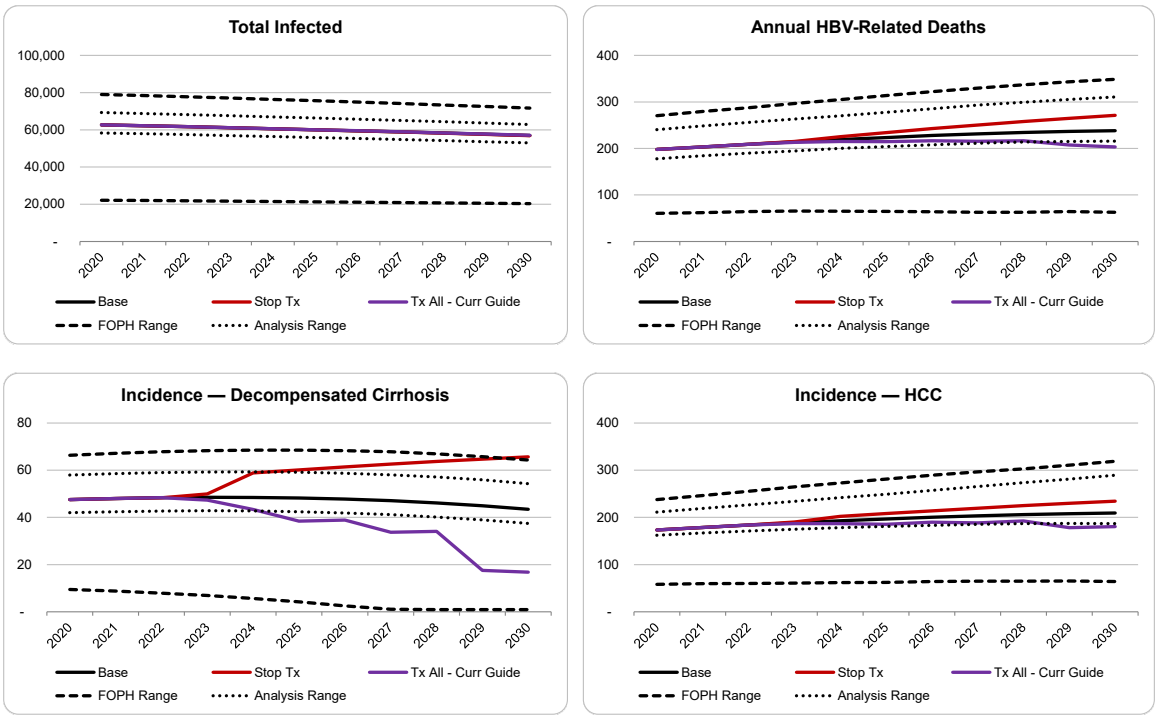


Table S1. Published HBV prevalence data, by country, with source

Country/Territory	Prev. Est. Status	HBV Prevalence Base	Study Year	HBV Prevalence Low	HBV Prevalence High	HBV Prevalence Source	HBV Age Source
Afghanistan	E	EX	--	EX	EX	EX	EX
Albania	I	7.20%	2005-2013	4.56%	11.80%	EC, [33-35]	[36]
Algeria	E	2.15%	1998	1.40%	3.23%	[37]	EX[1]
Angola	E	13.00%	2002	9.30%	15.10%	[38-40]	EX[2]
Argentina	I	0.26%	2013-2014	0.10%	0.42%	[41]	[42]
Armenia	I	2.00%	2007	1.81%	2.38%	[43], EC	[44]
Australia	I	0.98%	2016	0.80%	1.19%	[45]	[45]
Austria	E	EX	--	EX	EX	EX	EX
Azerbaijan	E	2.70%	2010*	2.00%	3.14%	[46]	EX[3]
Bahrain	I	1.00%	2015	0.58%	1.16%	EC,[47], EX	[48]
Bangladesh	I	5.50%	2008*	3.14%	7.7%	[49-51]	[51]
Belarus	E	4.80%	2006*	4.22%	5.57%	[52], EX	EX[4]
Belgium	I	0.66%	2003	0.51%	0.84%	[53]	[53]
Belize	I	4.00%	1992	0.47%	5.08%	[54,55], EX	EX[5]
Bhutan	I	1.60%	2017	0.80%	3.20%	[56]	[56]
Bolivia	E	EX	--	EX	EX	EX	EX
Bosnia and Herzegovina	E	EX	--	EX	EX	EX	EX
Brazil	I	0.75%	2017	0.21%	0.80%	[54,57-59]	[60]
Bulgaria	I	3.86%	1999-2000	1.70%	7.70%	[61-63]	[64]
Burkina Faso	I	8.80%	2010	7.74%	10.20%	[65], EX	[66]
Burundi	I	4.60%	2002	4.30%	5.90%	[67]	[67]
Cambodia	I	3.30%	2010-2012	2.70%	6.40%	[68], EX	[68]
Cameroon	I	11.90%	2011	10.90%	12.80%	[69,70]	[69]
Canada	I	0.65%	2015	0.40%	1.30%	EC, [71,72]	[73]
Central African Republic	E	11.60%	2010	10.20%	13.50%	[74], EX	[74]
Chad	E	12.20%	2012	10.1%	14.20%	[75,76], EX	[75]
Chile	I	0.15%	2009-2010	0.01%	0.30%	[77-79]	[80]
China, Mainland	I	7.20%	2006	6.70%	7.70%	[81]	[81]
Colombia	I	1.5%	1990	0.13%	4.85%	EC, [82,83]	[84]
Comoros	E	EX	--	EX	EX	EX	EX
Congo	E	EX	--	EX	EX	EX	EX
Costa Rica	I	0.20%	1994	0.12%	0.23%	[54,85], EX	EX[5], EC
Côte d'Ivoire	I	12.81%	2009	5.10%	15.10%	[76,86], EX	[86]
Croatia	I	0.70%	2010-2011	0.5%	1.5%	[87-89]	EX[6]
Cuba	I	1.05%	1995	0.58%	1.22%	[54,90], EX	[91]
Czechia	I	0.56%	2001	0.05%	0.66%	[92], EC, [93]	EX[6], EC
Democratic People's Republic of Korea	I	7.00%	2016	EX	EX	[94]	EX
Democratic Republic of the Congo	E	3.30%	2013-2014	1.80%	4.70%	[95]	[95]
Denmark	I	0.24%	2007	0.23%	0.37%	[96]	[96]
Dominican Republic	E	3.20%	1993	0.95%	3.40%	[54,97], EX	[97]
Ecuador	E	EX	--	EX	EX	EX	EX
Egypt	I	1.00%	2015	0.81%	1.31%	[98,99], EX	[98]
El Salvador	I	1.06%	2014	0.12%	2.64%	EC[54], EX	EX[5], EC

Country/Territory	Prev. Est. Status	HBV Prevalence Base	Study Year	HBV Prevalence Low	HBV Prevalence High	HBV Prevalence Source	HBV Age Source
Eritrea	E	9.18%	1995	EX	EX	[100]	EX
Estonia	I	0.50%	2015	0.39%	0.63%	EC, EX	EX[7], EC
Eswatini	E	EX	--	EX	EX	EX	EX
Ethiopia	I	9.40%	2015	8.90%	12.00%	EC	EC
Federated States of Micronesia	E	EX	--	EX	EX	EX	EX
Fiji	I	2.00%	2016	1.80%	2.30%	[101,102], EC	[102]
Finland	I	0.23%	2005-2007	0.20%	0.27%	[103], EX	EX[8]
France	I	0.30%	2016	0.13%	0.70%	[104]	[105,106]
Gabon	E	9.20%	2007	3.1%	10.70%	[76,107], EX	[107]
Gambia, The	E	5.97%	2007-2008	5.30%	6.90%	[108], EX	[108]
Georgia	I	2.90%	2015	2.38%	3.51%	[109]	[109]
Germany	I	0.32%	2008-2011	0.20%	0.80%	[110,111]	[110,112]
Ghana	I	12.3%	1995-2015	5.1%	13.90%	[76,113,114], EX	[113]
Greece	I	2.16%	2014	1.36%	2.58%	[115,116]	[115]
Guatemala	I	1.80%	1990	0.38%	2.07%	[54,117], EX	EX[5], EC
Guinea	E	EX	--	EX	EX	EX	EX
Guinea-Bissau	E	EX	--	EX	EX	EX	EX
Guyana	E	EX	--	EX	EX	EX	EX
Haiti	I	2.5%	2012	2.8%	5.0%	[54,118-120]	[120]
Honduras	E	EX	--	EX	EX	EX	EX
Hong Kong	I	7.80%	2015	5.50%	9.05%	[121,122], EX	[121]
Hungary	E	0.60%	2015*	0.50%	0.70%	[123]	EX[6]
India	I	2.97%	2000-2001	2.59%	3.35%	[124]	[124]
Indonesia	I	7.10%	2013	6.44%	9.40%	[125] EX, [126]	[125]
Iran	I	1.79%	2016	1.67%	1.91%	[127]	[128]
Iraq	I	3.50%	2015	1.60%	4.06%	EC, [129], EX	[129]
Ireland	E	0.10%	2003	0.09%	0.20%	[130], EX	[130]
Israel	I	1.78%	2015	0.98%	2.70%	[131]	[131]
Italy	I	0.60%	2010	0.26%	0.90%	[132] EX	[133]
Jamaica	I	5.30%	1990-1991	0.64%	5.65%	[54,134,135]	EC
Japan	I	0.93%	2011	0.87%	0.99%	[136]	[137]
Jordan	I	3.00%	2006-2013	0.96%	3.48%	[138,139], EX	EX[9], EC
Kazakhstan	I	3.54%	2016*	2.00%	5.20%	[140,141]	[141]
Kenya	E	2.10%	2007	1.40%	3.10%	[142]	[142]
Kiribati	I	15.00%	2015	7.00%	17.00%	[143]	[144]
Korea, Republic of	I	2.90%	2016	2.50%	3.50%	[145,146]	[147]
Kosovo	E	2.4%	2005	1.85%	4.2%	[148-150]	[148]
Kuwait	I	4.80%	2003-2004	1.90%	5.57%	[151,152], EX	[152]
Kyrgyzstan	I	4.70%	2015	3.60%	10.30%	EC[153,154]	EC
Laos	I	4.10%	2011	2.6%	5.5%	[155]	[155]
Lebanon	I	1.69%	2011-2012	1.60%	1.89%	[156]	[157]
Lesotho	E	EX	--	EX	EX	EX	EX
Liberia	E	EX	--	EX	EX	EX	EX
Libya	E	2.20%	2005	1.90%	2.60%	[158], EX	[158]
Madagascar	E	6.90%	2011-2013	5.60%	8.60%	[159]	[159]

Country/Territory	Prev. Est. Status	HBV Prevalence Base	Study Year	HBV Prevalence Low	HBV Prevalence High	HBV Prevalence Source	HBV Age Source
Malawi	E	8.20%	1989-2008	5.60%	9.40%	[160]	[160]
Malaysia	I	3.64%	2019	2.85%	3.99%	EC	[161]
Mali	E	8.70%	2014	7.70%	10.10%	[162], EX	EX[10]
Marshall Islands	E	EX	--	EX	EX	EX	EX
Mauritania	E	15.70%	1983*	13.80%	18.20%	[163], EX	EX[10]
Mexico	I	0.21%	1999-2000	0.10%	0.40%	[164]	[165]
Moldova	E	9.44%	1994	7.27%	11.89%	[166] EX	[166] EX
Mongolia	I	11.10%	2013	10.10%	12.10%	[167]	[167]
Morocco	I	1.81%	2005-2011	0.95%	2.10%	[168], EX	[168]
Mozambique	I	10.19%	2004	8.40%	14.00%	[169,170] EC	[171]EC
Myanmar	E	6.5%	2015	2.41%	10.65%	[139,172,173], EX	EX
Nepal	I	0.9%	1990	0.63%	1.40%	[174-176]	[174]
Netherlands	I	0.20%	2007	0.10%	0.50%	[177,178]	[177]
New Zealand	I	2.60%	1999-2002	1.71%	5.70%	[179], EC	[179]
Nicaragua	E	1.50%	1990-1992	0.18%	1.73%	[54,180], EX	EX[5]
Niger	E	EX	--	EX	EX	EX	EX
Nigeria	I	12.20%	2013	10.30%	14.50%	[181]	[181]
Norway	E	0.50%	1992-2009	0.44%	0.61%	[182], EX	[182]
Oman	I	2.50%	2016	2.00%	3.00%	EC	[183]
Pakistan	I	2.17%	2018	1.10%	11.90%	[184,185]	[185]
Palestine	E	4.00%	2012	2.00%	6.00%	[186]	EX
Panama	E	EX	--	EX	EX	EX	EX
Papua New Guinea	E	11.90%	1989	10.47%	13.80%	[187], EX	EX[11]
Paraguay	E	EX	--	EX	EX	EX	EX
Peru	I	0.42%	2009*	0.33%	0.50%	[188-190]	EC
Philippines	I	16.70%	2003	14.3%	19.1%	[191]	[191]
Poland	I	1.00%	2010	0.63%	1.30%	EC, [192]	[193-199], EC
Portugal	I	1.45%	2014	0.90%	2.00%	[200]	[200]
Qatar	I	1.27%	2016	1.55%	2.50%	EC, EX	EC
Romania	I	4.40%	2006-2008	4.00%	4.80%	[201]	[201]
Russia	I	2.0%	2013	0.21%	2.78%	[139,202], EX	[203]
Rwanda	E	5.70%	2009-2011	2.90%	4.48%	[204,205]	[205]
Samoa	E	EX	--	EX	EX	EX	EX
Sao Tome and Principe	E	EX	--	EX	EX	EX	EX
Saudi Arabia	I	1.91%	2016	1.31%	2.37%	EC, [206], EX	[207-209], EC
Senegal	E	11.00%	1973*	9.70%	12.80%	[210], EX	[210]
Sierra Leone	E	EX	--	EX	EX	EX	EX
Singapore	E	3.60%	2010	2.90%	4.20%	[211]	[211]
Slovak Republic	I	1.74%	2011	2.0%	0.01%	[139,212], EX	EC
Slovenia	I	0.45%	2015	0.44%	0.59%	EC, [139,213], EX	[214]
Solomon Islands	E	EX	--	EX	EX	EX	EX
Somalia	E	18.99%	1992*	--	--	[215]	--
South Africa	I	5.00%	2019	5.08%	6.22%	EC, EX	[216]
South Sudan	E	EX	--	EX	EX	EX	EX
Spain	I	0.70%	2016	0.40%	1.00%	[217,218], EC	[218], EC

Country/Territory	Prev. Est. Status	HBV Prevalence Base	Study Year	HBV Prevalence Low	HBV Prevalence High	HBV Prevalence Source	HBV Age Source
Sri Lanka	E	2.50%	1991*	EX	EX	[219]	EX
Sudan	E	6.93%	2000	4.89%	8.98%	[220,221], EX	[220]
Suriname	I	2.90%	2012-2013	2.20%	3.70%	[222]	[222]
Sweden	I	0.20%	2015	0.06%	0.25%	EC, [223]	[224]
Switzerland	I	0.53%	2016	0.18%	1.11%	[225]	[225]
Syria	E	5.60%	2004	1.69%	6.50%	[226,227], EX	[226]
Taiwan	I	13.20%	2012	12.90%	17.30%	[228-230]	[230]
Tajikistan	I	8.00%	2015	2.90%	5.30%	[231]	[231]
Tanzania	I	3.50%	2016-2017	3.90%	8.70%	[232,233]	[233]
Thailand	I	4.58%	2014	0.32%	4.22%	[139,234,235], EX	[235]
Timor-Leste	E	EX	--	EX	EX	EX	EX
Togo	E	EX	--	EX	EX	EX	EX
Tonga	E	EX	--	EX	EX	EX	EX
Trinidad and Tobago	E	EX	--	EX	EX	EX	EX
Tunisia	E	5.30%	1996	4.80%	5.80%	[236]	[236]
Turkey	I	4.00%	2010	3.49%	6.11%	[237-239]	[237]
Turkmenistan	E	15.60%	1995	12.44%	17.66%	[240], EX	[241]
Tuvalu	E	EX	--	EX	EX	EX	EX
Uganda	I	5.00%	2005-2019	4.56%	6.55%	[242]	[242]
Ukraine	I	1.50%	2015	0.87%	2.0%	[243], EC	[244]
United Arab Emirates	I	3.70%	1997-1998	0.23%	4.29%	[245,246], EX	EX[12]
United Kingdom	I	0.69%	2013	0.4%	1.10%	[247,248], EC	[247]
United States of America	I	0.30%	2007-2012	0.20%	0.40%	[249], EC	[249]
Uzbekistan	I	8.10%	2016	3.05%	13.30%	[241,250]	[250]
Vanuatu	E	EX	--	EX	EX	EX	EX
Venezuela	E	1.80%	1993	1.62%	4.00%	[251-253]	EX
Viet Nam	I	9.28%	2017	7.76%	12.54%	[254-256], EC	[256]
Yemen	E	4.20%	2008	1.49%	10.80%	[139,257,258]	[257]
Zambia	E	5.90%	2008*	5.19%	6.84%	[259], EX	EX[2]
Zimbabwe	E	15.40%	1989-1991	13.55%	17.86%	[260], EX	[260]

* Study year unavailable. Used publication year minus two; ** Estimate adjusted for total population; [1] Extrapolated from Libya; [2] Extrapolated from Madagascar; [3] Extrapolated from Uzbekistan; [4] Extrapolated from Poland; [5] Extrapolated from Mexico; [6] Extrapolated from Slovak Republic; [7] Extrapolated from Sweden; [8] Extrapolated from Netherlands; [9] Extrapolated from Lebanon; [10] Extrapolated from Senegal;[11] Extrapolated from Indonesia; [12] Extrapolated from Saudi Arabia; EX = Extrapolated based on GBD regional average; I = Expert Input: received feedback on inputs and model outputs from country experts; E = Estimated: prevalence modeled & estimated using published data; EC = Expert Consensus.

Table S2. Countries by GBD Region

GBD Region	Countries
Asia, Central	Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan
Asia, East	China, Democratic People's Republic of Korea, Hong Kong, Macao, Taiwan
Asia, High Income	Brunei Darussalam, Japan, Republic of Korea, Singapore
Asia, South	Afghanistan, Bangladesh, Bhutan, India, Nepal, Pakistan
Asia, Southeast	Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Maldives, Myanmar, Philippines, Sri Lanka, Thailand, Timor-Leste, Viet Nam
Australasia	Australia, New Zealand
Caribbean	*Anguilla,* Antigua and Barbuda, Aruba, Bahamas, Barbados, Belize, Bermuda, *British Virgin Islands, Cayman Islands,* Cuba, *Curacao,* Dominica, Dominican Republic, *French Guiana,* Grenada, *Guadeloupe,* Guyana, Haiti, Jamaica, Martinique, *Montserrat,* Netherlands Antilles, Puerto Rico, *Saint Barthelemy, Saint Kitts and Nevis,* Saint Lucia, *Saint Martin, Saint Maarten,* Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, *Turks and Caicos Islands, United States Virgin Islands*
Europe, Central	Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, *Kosovo,* Macedonia, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia
Europe, Eastern	Belarus, Estonia, Latvia, Lithuania, Moldova, Russian Federation, Ukraine
Europe, Western	*Aland,* Andorra, Austria, Belgium, Cyprus, Denmark, *Faroe Islands,* Finland, France, Germany, *Gibraltar,* Greece, Greenland, *Guernsey, Holy See,* Iceland, Ireland, *Isle of Man,* Israel, Italy, *Jersey, Liechtenstein,* Luxembourg, Malta, *Monaco,* Netherlands, Norway, Portugal, *San Marino,* Spain, *Svalbard,* Sweden, Switzerland, United Kingdom
Latin America, Andean	Bolivia, Ecuador, Peru
Latin America, Central	Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Venezuela
Latin America, Southern	Argentina, Chile, Uruguay
Latin America, Tropical	Brazil, Paraguay
North America, High Income	Canada, *Saint Pierre and Miquelon,* United States of America
North Africa/ Middle East	Algeria, Bahrain, Egypt, Islamic Republic of Iran, Iraq, Jordan, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen
Oceania	American Samoa, *Cook Islands* Fiji, *French Polynesia,* Guam, Kiribati, Marshall Islands, Federal States of Micronesia, *Nauru, New Caledonia, Niue, Norfolk Island, Northern Mariana Islands, Palau,* Papua New Guinea, *Pitcairn,* Samoa, Solomon Islands, *Tokelau,* Tonga, *Tuvalu,* Vanuatu, *Wallis and Futuna*
Sub-Saharan Africa, Central	Angola, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon, *Saint Helena*
Sub-Saharan Africa, East	Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mauritius, *Mayotte,* Mozambique, *Reunion,* Rwanda, Seychelles, Somalia, South Sudan, Sudan, Uganda, United Republic of Tanzania, Zambia
Sub-Saharan Africa, Southern	Botswana, Lesotho, Namibia, South Africa, Swaziland, Zimbabwe
Sub-Saharan Africa, West	Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, São Tomé and Príncipe, Senegal, Sierra Leone, Togo

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