SIMULATION MODELING OF HEPATITIS B VIRUS DISEASE PROGRESSION, HEPATITIS FLARES, AND FUNCTIONAL CURE

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Amir M. Mohareb[1,2], Virginia Talbot[1], Arthur Kim[2], Maya Hajny Fernandez[1], Anders Boyd[3], Kenneth Freedberg[1,2], Emily Hyle[1,2]

[1]Medical Practice Evaluation Center, Massachusetts General Hospital, Boston, MA, USA, [2]Division of Infectious Diseases, Massachusetts General Hospital, Boston, MA, USA, [3]Amsterdam University Medical Center, Amsterdam, Netherlands

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BACKGROUND

>300 million people live with chronic hepatitis B virus (HBV), which includes 3- 4 million people with HIV coinfection.

We developed and validated a computer simulation model of HBV infection, which can be used to investigate disease progression, response to treatment, and HBV cure.

METHODS

Nine health states in the HBV simulation model (Figure 1):

(1) HBV-uninfected
(2) No fibrosis
(3) Moderate or severe fibrosis
(4) Cirrhosis
(5) Hepatocellular carcinoma (HCC)
(6) End-stage liver disease (ESLD)
(7) Hepatitis flare (ALT >2x upper limit of normal)
(8) HBV surface antigen (HBsAg) loss (HBV cure)
(9) Death

We incorporated antiviral effects of nucleoside/ nucleotide analogue therapy with input parameters derived from published studies. We projected clinical outcomes, including the cumulative incidence of HCC and the risk of hepatitis flares and HBsAg loss following treatment cessation.

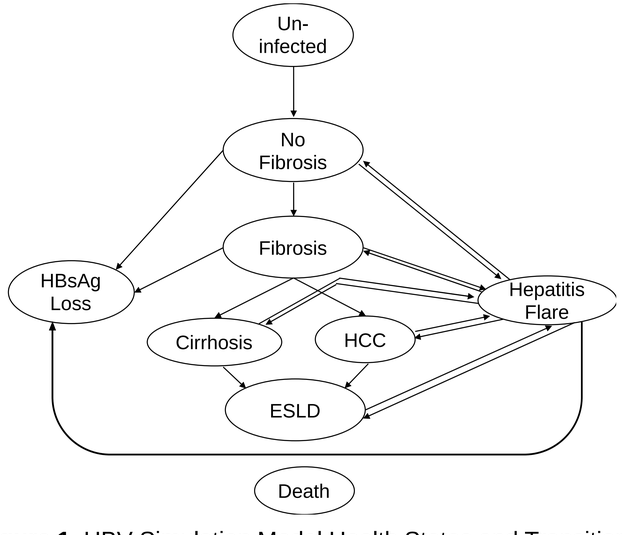


Figure 1. HBV Simulation Model Health States and Transitions

Note: all health states can lead to Death (arrows removed for simplicity)

We designed and validated an **HBV simulation model** to investigate questions in **HBV disease progression** and **functional cure.**

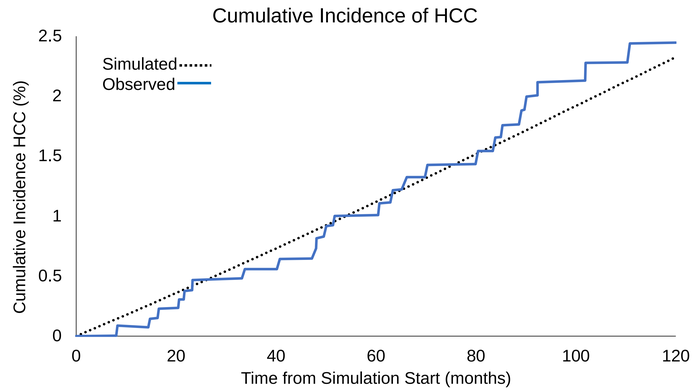
Table 1. Select model input parameters

Simulated Cohort Characteristics	**Mean (standard deviation) starting age:** 40 (3) years **Male/female ratio:** 0.6/0.4 **Setting:** Western Pacific (HBV genotype B/C)		
Population	**Natural History (per 100 PYs)**	**Tenofovir Risk Reduction (%)**	**Reference**
Fibrosis/ Cirrhosis Incidence			
20 to <30y	0.3	63	Iloeje, Gastroenterol 2010 Lin, Dig Dis Sci 2022 Shimakawa, Gut 2018 Lok, Hepatol 2016
30 to <40y	0.8		
40 to <50y	1.9		
≥50y	2.5		
HCC Incidence			
20 to <30y	0.05	41	Wong, J Gastro Hepatol 2011 Li, J Gastro Hepatol 2016 Chen, JAMA 2006 Lok, Hepatol 2016
30 to <40y	0.09		
40 to <50y	0.25		
≥50y	0.42		
Hepatitis Flares Incidence			
No Fibrosis	2.0	85	Ghany, Lancet Gastro Hep 2020 Brahmania, Clin Gastro Hep 2019
Fibrosis or HCC	4.5		
Cirrhosis	10.0		
HBsAg Loss Incidence	1.0	N/A	Yeo, Gastroenterol 2019 Zhou, Lancet Gastro Hep 2019

RESULTS

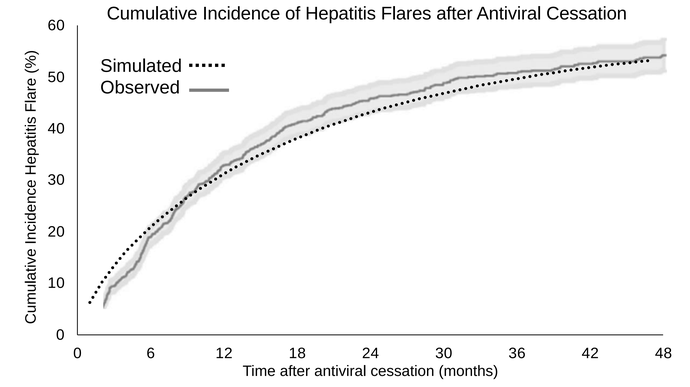
Table 2. Model-simulated 10-year cumulative incidence of health states

Treatment Scenario	Fibrosis (%)	Cirrhosis (%)	HCC (%)	HBsAg loss (%)	Survival (%)
Off tenofovir	27.5	7.3	1.0	11.2	95.1
On continuous tenofovir	12.7	2.0	0.1	8.7	97.7
Following tenofovir cessation	26.1	6.6	0.9	13.8	95.3



Observational HCC data derived from Patmore, *J Hepatol.* 2023.

Figure 2. Validation of HCC : simulated and observed cumulative incidence of HCC for people with chronic HBV



Observational data on hepatitis flares derived from Hirode, *Gastroenterol.* 2022.

Figure 3. Validation of hepatitis flares: simulated and observed hepatitis flares incidence after antiviral cessation

CONCLUSIONS

- We developed and validated an HBV simulation model that incorporates the impact of treatment and its cessation on clinical outcomes.
- When used in conjunction with established HIV models, it can be used to simulate HIV-HBV coinfection.
- This model will help to address clinical questions such as HBV cure, the risks and benefits of tenofovir cessation, and tenofovir-based HIV pre-exposure prophylaxis in people with HBV.