



# Economic Analyses to Inform and Support Health Policy for Chronic Hepatitis B Treatment

Mehlika Toy<sup>1</sup> · David W. Hutton<sup>2</sup> · Samuel So<sup>1</sup>

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## Abstract

**Purpose of Review** Summarize insights into the economic impact of global hepatitis B treatment policies.

**Recent Findings** With the highly effective antiviral treatment, entecavir and recently tenofovir, coming off patent, hepatitis B treatment is now very inexpensive and may save costs in the long run. In the USA alone, dramatic increases in screening and treatment would prevent between 80 and 100 thousand cases of cirrhosis, 50 and 60 thousand cases of liver cancer, and 80 to 100 thousand HBV-related deaths over the next 50 years.

**Summary** Cost-effectiveness analyses can provide information in the form of what a proper course of action will cost, and what the benefits will be in terms of health impact. Since the sharp reduction in antiviral drug pricing, the focus should be on treating patients with generic antivirals to ensure that the chronic hepatitis B care and treatment efforts are highly cost-effective and even cost-saving.

**Keywords** Hepatitis B treatment · Cost-effectiveness · Health policy · Economic analyses

## Introduction

The World Health Organization (WHO) estimates that 257 million people are currently living with chronic hepatitis B virus (HBV) infection, resulting in approximately 887,000 deaths per year [1••]. Often those who have the infection are diagnosed later in life, when liver cirrhosis or cancer has developed. In response to the United Nations' 2030 Sustainable Development Goal of combating viral hepatitis, in 2016 the WHO issued the first global health sector strategy on viral hepatitis to eliminate the disease as a public health problem by 2030 [2]. Endorsed by all WHO member states, the strategy set important prevention and vaccination targets to reduce HBV transmission by 90% by 2030 and increase chronic hepatitis B (CHB) diagnosis and treatment from an estimated 9%

and 8%, respectively, in 2015 to 90% and 80%, respectively—with the overall goal of reducing CHB-related deaths by 65% by 2030.

Economic analyses have informed health policy and helped secure investment for the elimination of viral hepatitis [3]. Economic analysis has facilitated a better understanding of the relationship between economic growth and health, but has also helped to make the case that investments in health produce excellent returns not just in terms of reduction in morbidity and mortality but also through their impact on economic wellbeing [4]. The purpose of this review is to summarize insights into the economic impact of global hepatitis B treatment policies.

## Treatment of Chronic Hepatitis B

Treatment with the highly effective and low resistance first line antiviral medication is as simple as taking a pill a day. Although not curative, continued suppressive therapy when indicated would prevent disease progression and reduce the risk of costly liver disease complications.

Treatment decisions are based on several formal guidelines issued by medical societies such as the American Association for the Study of Liver Diseases (AASLD) [5], the European Association for the Study of the Liver (EASL) [6], and the

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✉ Mehlika Toy  
mttoy@stanford.edu

<sup>1</sup> Asian Liver Centre, Department of Surgery, Stanford University School of Medicine, Palo Alto, CA, USA

<sup>2</sup> Department of Health Management and Policy, School of Public Health, Michigan University, Ann Arbor, MI, USA

WHO [7]. Indication for treatment is based on evidence of liver damage (cirrhosis or elevation in ALT levels) and viral load (HBV DNA level). The WHO guideline also makes provision for the management of patients when access to HBV DNA testing is not possible. The goal of therapy for CHB is to improve quality of life and survival by preventing progression of the disease to cirrhosis, decompensated cirrhosis, end-stage liver disease, hepatocellular carcinoma (HCC), and death. With the highly effective treatment, entecavir and recently tenofovir, coming off patent, hepatitis B treatment is now very inexpensive and may save costs in the long run. Yet, few countries are investing in hepatitis B elimination. A recent study [8•] looking at access to treatment of hepatitis B virus infection worldwide concludes that low price and generic medicines effective against HBV are underutilized in low- and middle-income countries. The study also suggests that development and adaptation of national viral hepatitis control strategy and the development and use of the global HBV care cascade can open the way to public sector procurement of medicines and diagnostics at lower prices. Figure 1 shows the tenofovir and entecavir price drops in the last 5 years.

### Cost-Effectiveness Analysis

Cost-effectiveness analysis (CEA) is a method used to evaluate the outcomes and costs of interventions designed to improve health [9]. The purpose of a CEA in healthcare is to help decision-makers determine how to allocate resources across a defined number of competing needs in order to maximize health outcomes from a limited budget [10]. An intervention is considered cost-saving if it is both more effective and less costly than the status quo. The quality-adjusted life year (QALY) is a measure of effectiveness—more time spent in good health [11]. The incremental cost-effectiveness ratio (ICER) is a measure of value and can be thought of the price

to gain one QALY. The ICER is the incremental costs of implementing an intervention over another intervention (or no intervention), divided by the incremental effectiveness (QALYs) from another intervention (or no intervention). For CEAs in medical decision-making, Markov models [12] are often used to determine the long-term impacts of interventions. In these models, simulated patients enter the model in a particular health state, e.g., chronic hepatitis B e-antigen positive, and can transition between states, in each cycle (i.e., day, week, month, and year) according to transition probabilities estimated from cohort studies and/or randomized control trials. These types of models are particularly useful for evaluating hepatitis B policies since liver damage caused by chronic viral hepatitis infection can take years or decades to manifest itself as cirrhosis, HCC, or death.

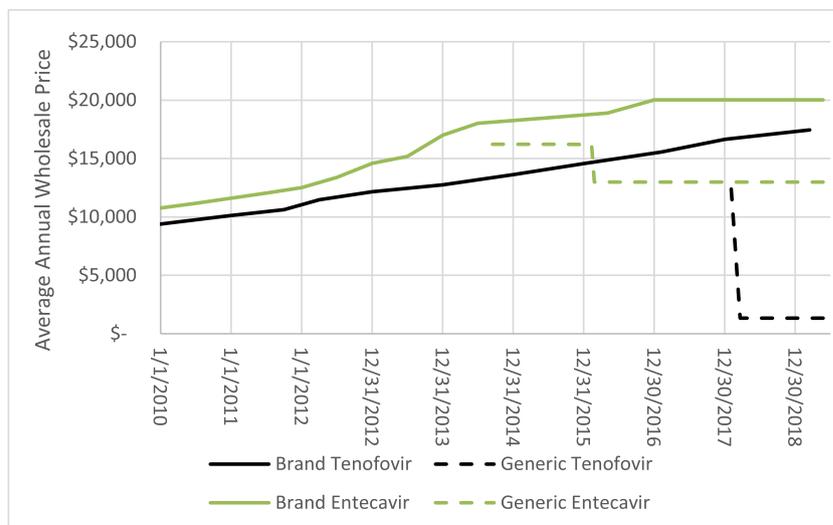
### Economic Impact of Hepatitis B Treatment Policies

A recent review by Sicuri et al. [4] suggests that national governments, global health policymakers, and donors always need to know how much a health intervention will cost, and what the benefits will be in terms of health and economic wellbeing. Cost-effectiveness analyses can provide that type of information.

Many recent cost-effectiveness analyses have shown that hepatitis B treatment with highly-effective antiviral therapies is cost-effective. Table 1 shows the summary of cost-effectiveness of hepatitis B treatment. A recent review found hepatitis B screening and treatment is cost-effective [13]. Studies in China [14–16], UK [17], USA [18, 19•], Gambia [20], and Turkey [21] have all found treatment to be highly cost-effective. Treatment has become even more cost-effective with tenofovir coming off patent in December 2017.

Looking at the example of China, the annual treatment for HBV with branded tenofovir cost US\$2,920 per year when

**Fig. 1** Tenofovir/Entecavir (first-line treatment) price drops in the last 5 years. Source: Redbook. Actual prices paid (average sales price) is often less than average wholesale price



**Table 1** Summary of cost-effectiveness of hepatitis B treatment

Study	Country	Intervention	Populations	ICER*
Hahne, 2013 [13]	Multiple	Screening and treatment	General population, antenatal, migrants	\$3,095–\$39,879/QALY **
Goyal, 2016 [14]	China	Antiviral treatment vs. no treatment	Chronic hepatitis B and/or D	Cost-saving
Toy, 2015 [15]	China	Antiviral treatment vs. no treatment	Chronic hepatitis B	Cost-saving
Toy, 2014 [16]	China	Monitor and treat vs. no monitoring	Inactive chronic hepatitis B	\$3,431/QALY
Birmingham, 2015 [17]	UK	Interferon and antiviral treatment vs. no treatment	Chronic hepatitis B	\$13,133/QALY
Chahal, 2019 [18]	USA	Screening, Vaccination, and treatment	High-Risk	\$17,645–\$25,551/QALY
Toy, 2018 [19•]	USA	Screening and treatment	High-Risk	\$103/QALY
Nayagam, 2016 [20]	The Gambia	Screening and treatment	Adults	\$553/QALY
Kockaya, 2015 [21]	Turkey	Tenofovir vs. other treatments	Chronic hepatitis B	Cost-saving

\*all values converted to 2018 dollars using the US GDP deflator

\*\*Hahne is converted from Euros to USD

purchased by patients before it went off patent in 2017. In February 2017, China announced that entecavir and tenofovir were included in the updated national list of reimbursable medicines. Even before going off patent, according to the findings from a recent study [16] where we assessed the health impact and cost-effectiveness of a strategy of monitoring patients with inactive CHB and treating patients who developed active disease with highly potent oral antiviral drugs, such as entecavir or tenofovir, an estimated 73% of HCC cases are preventable when this strategy of monitoring inactive and treating active hepatitis patients is implemented.

### Broad Population Impact

In the USA, reaching the WHO diagnosis and treatment targets by 2030 would require screening around 14.5 million at-risk adults to diagnose an estimated 870,000 undiagnosed cases. Achieving the WHO targets by 2030 would also result in substantial health gains: an increase of 16.5 million QALYs, a 37% reduction in liver-related deaths, and a 35% reduction in liver-related cancer cases [19•]. We also found that if the WHO diagnosis and treatment targets are reached 5 years earlier by 2025, liver-related death will decrease by 47% and liver cancer cases by 43%, and will be cost-saving. Generic tenofovir became available for the first time in the USA in January 2018, with an acquisition cost as low as \$1380 per year, which is a 90% reduction in price compared with brand tenofovir. The drug cost has dropped even further since then. The sharp reduction in antiviral drug costs, coupled with the elimination strategies proposed by the National Academies [22••], represents an excellent opportunity to eliminate the public health problem of CHB in the USA.

In a recent study [23•], we calculated what it would cost to eliminate hepatitis B and C in 67 high prevalence countries if treatment were included as part of Universal Health Coverage (UHC), a package of essential services that everyone has

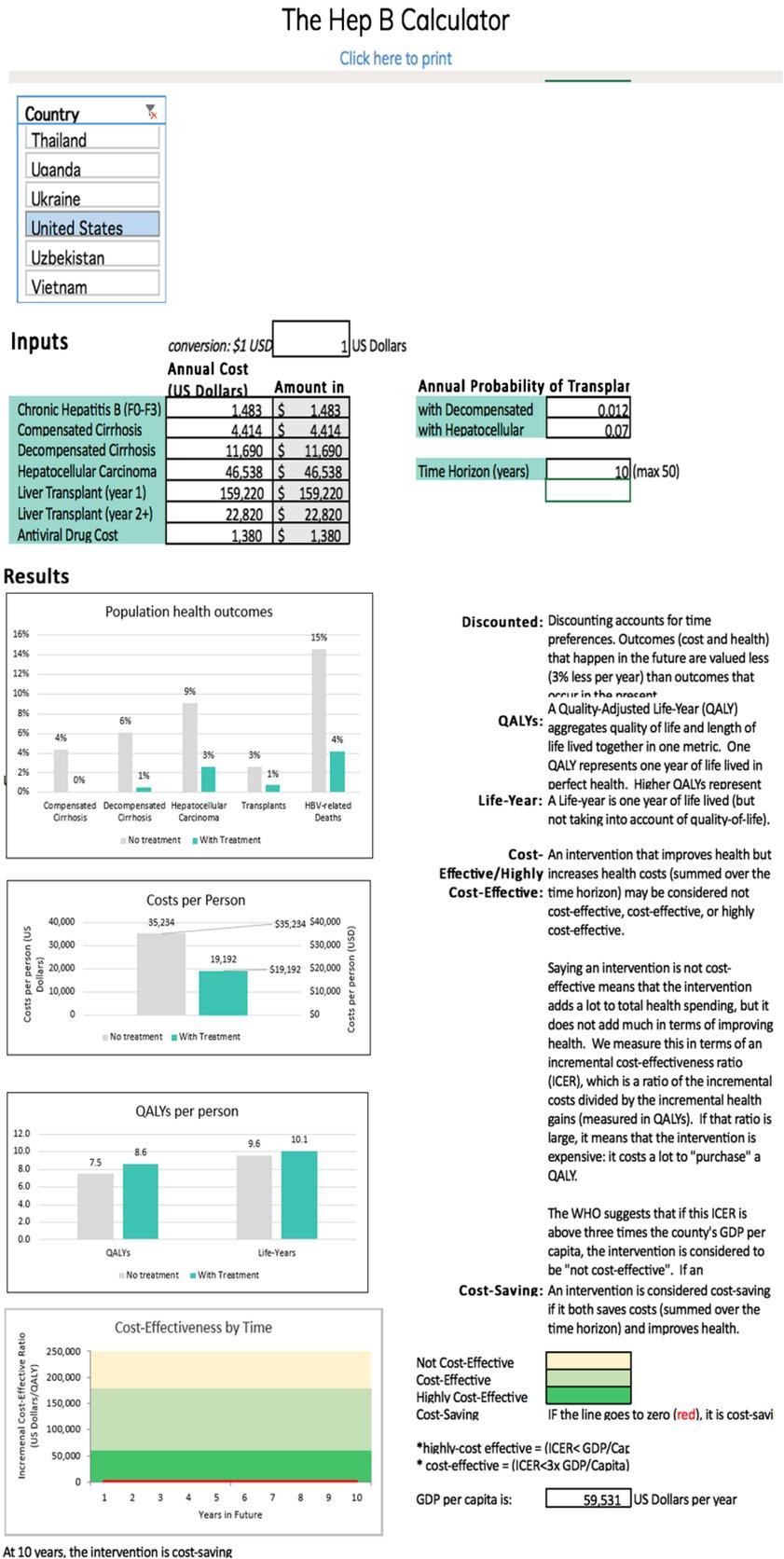
access to testing and treatment without incurring financial hardship. We assumed all the countries have access to testing and optimal drug procurement cost (US\$30 per year for tenofovir, US\$20 per year for disease monitoring, and US\$20 per year for annual HBV DNA test). We estimated that the cost of long-term hepatitis B monitoring and treatment is \$25.6 billion. HBV test accounts for a substantial portion of the costs of CHB treatment assuming there is a need for long-term HBV DNA monitoring. The World Health Organization's Western Pacific Region (WPRO) and the African regions are the regions that have the largest burden of HBV and the highest costs of HBV elimination. The cost to China is the highest with as many as 90 million people living with CHB.

### Use of Cost-Effectiveness Analyses to Inform Hepatitis B Treatment Policy Adoption

In collaboration with the WHO, we designed the Hep B Calculator ([www.hepbcalculator.org](http://www.hepbcalculator.org)), a simple, interactive, customizable online tool to evaluate the cost-effectiveness of CHB treatment for various high prevalence countries from a healthcare payer's perspective (Fig. 2).

The calculator uses a Markov model to calculate the outcomes of two strategies—treatment with antiviral therapy versus no treatment, and returns, in real-time, the following outcomes for each strategy: the cumulative lifetime incidences of compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, transplants, and HBV-related death; the total lifetime healthcare costs (including the cost of antiviral treatment and of downstream events such as liver cancer); and QALYs. In addition, it calculates the ICERs of antiviral treatment versus no-treatment for different disease stages and plots these as graphs to identify the time duration after treatment (in years) when the net cost drops below zero to reach a point where treatment is cost-saving. By putting the various

**Fig. 2** Snapshot of the HepB calculator showing the input panel



At 10 years, the intervention is cost-saving

country-specific costs-associated CHB management and treatment into the Hep B Calculator, policymakers could assess the cost-effectiveness of CHB treatment and the benefits (in terms of both health and reduced healthcare spending) of investing in hepatitis B elimination.

## Conclusions

Recent analyses have shown that with lower generic prices, treatment can be highly cost-effective in most if not all settings. Key areas for future research are to evaluate the cost-effectiveness of interventions to get people into treatment, such as screening lower-prevalence populations and linking them to care. Although hepatitis B treatment may be cost-effective, policymakers need to know the overall impact to their budgets of ramping up efforts to treat their populations. Tools to assist in these calculations may be helpful as public health officials plan for hepatitis B elimination.

## Compliance with Ethical Standards

**Conflict of Interest** Mehlika Toy, David W. Hutton, and Samuel So each declare no potential conflicts of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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