The Potential Impact of a Cure for Chronic Hepatitis B Infection

A population Health and Economic Analysis in Australia

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Stanford University

Previous Modelling for Chronic Hepatitis B Infection

CHRONIC CARE

By Mehlika Toy, David W. Hutton, and Samuel So

Population Health And Economic Impacts Of Reaching Chronic Hepatitis B Diagnosis And Treatment Targets In The US

ABSTRACT The National Academies of Sciences, Engineering, and Medicine have concluded that eliminating the public health problem of chronic hepatitis B is feasible. We examined the economic and public health impact of reaching the World Health Organization targets of having 90 percent of chronic hepatitis B cases diagnosed and 80 percent being treated by 2030 in the United States with an annual incremental increase in screening and treatment rates. To reach the targets by 2030 would require screening approximately 14.5 million adults in at-risk populations to diagnose an estimated 870,000 undiagnosed cases and would result in substantial health gains: an increase of 16.5 million quality-adjusted life-years (QALYs), and reductions in liver-related deaths of 37 percent and in cases of compensated cirrhosis of 24 percent, decompensated liver cirrhosis of 51 percent, and liver cancer of 35 percent. Achieving the targets by 2030 would be highly cost-effective at $103 per QALY and would be cost-saving if the antiviral drug price were no more than $114 per month. Achieving them by 2025 would be cost-saving and would reduce liver-related deaths by 47 percent.

PLOS ONE

HEPATOLOGY

VIRAL HEPATITIS

Population Health Impact and Cost-Effectiveness of Monitoring Inactive Chronic Hepatitis B and Treating Eligible Patients in Shanghai, China

Screening and Early Treatment of Migrants for Chronic Hepatitis B Virus Infection Is Cost-Effective

RESEARCH ARTICLE

Cost-Effectiveness and Cost Thresholds of Generic and Brand Drugs in a National Chronic Hepatitis B Treatment Program in China

Abstract

HEPATOLOGY

AASLD

Potential Impact of Long-Term Nucleoside Therapy on the Mortality and Morbidity of Active Chronic Hepatitis B

EDITORIAL

Preventing hepatocellular carcinoma: the crucial role of chronic hepatitis B monitoring and antiviral treatment

Hepatic Oncology

Cost-Effectiveness Analysis

- CEA is a method to evaluate the outcomes and costs of interventions designed to improve health
- Help decision maker determine how to allocate resources
- Who is the target audience for the study?

Influence an opinion on a subject or add the weight of information on an intervention

Practice guidelines that may be influenced by a CEA, but eventually physicians and patients who make the decision

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Cost-Effective or Cost-Saving

Cost-effective ≠ cost savings

Cost-effective ≠ affordable

"**Cost-effective**" implies that we are willing to spend additional money to gain additional health benefits

"**Cost-saving**" implies that we will gain health benefits by implementing the intervention, and we will save money as well

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WHO Definition of Cost-Effectiveness

Intervention/treatment is considered Highly Cost-Effective:

Cost is less than 1x GDP per capita for 1 QALY

In Australia< 49,927 USD (67,259 AUD)/QALY

In the US, < 57,466 USD/QALY

In China, < 8,123 USD (55,421 RMB)/QALY

WHO-CHOICE. Choosing interventions that are cost effective
World Bank 2012 GDP per capita, http://data.worldbank.org/indicator/NY.GDP.PCAP.PP.CD

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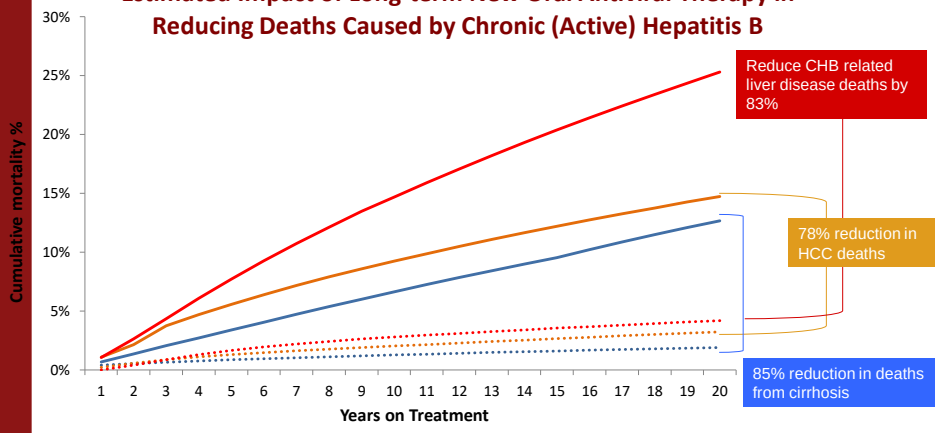
Estimated Impact of Long-term New Oral Antiviral Therapy in Reducing Deaths Caused by Chronic (Active) Hepatitis B



Toy, M et al. Hepatology 2014;60(1):46-55

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Aim

Model the potential population health impact and cost of a potential cure for chronic hepatitis B in Australia.

Determine the threshold where the drug cost becomes cost-saving for the population.

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Vision of ICE-HBV

ICE-HBV aims to fast-track the discovery of a safe, effective, affordable and scalable cure to benefit all people living with CHB, including children and people living with HCV, HDV and HIV co-infection. ICE-HBV intends to contribute to the elimination of CHB as a global public health challenge

- **Goal 1** – Generate knowledge, foster collaborations, and perform research to accelerate scientific innovation, in collaboration with key stakeholders.
- **Goal 2** – Disseminate knowledge and engage key stakeholders to ensure the timely translation of discoveries into positive health outcomes and quality of life.
- **Goal 3** - Support a sustainable international multidisciplinary scientific coalition to find a cure for HBV and HDV infection.

Source: Dr. Peter Revill, Doherty Institute, ICE-HBV

ICE-HBV International Coalition to Eliminate HBV
PROMOTING GLOBAL COLLABORATION IN HBV CURE RESEARCH

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Poll Question

Having a potential cure for chronic hepatitis B we could?

a) Increase quality of life and prevent unnecessary premature deaths

b) Decrease costs

c) Both a and b

d) We already have indefinite antiviral treatment, we don't need a cure

Markov Model and Disease Progression Estimates

- Adapted from a Markov Model for the United States
- Probabilities for age and disease specific rates were taken from recent meta-analysis and systematic review

  Thiele et al. PLoS One 2014

  Rafetti et al. Liver International 2016
- Background mortality Australia
- Liver Transplantation Rates Australia
- Costs Chronic Hepatitis B management and treatment

Study Cohort

- 2018 population from previous modeling study (Doherty Institute)
- Age-specific HBsAg prevalence
- Prevalence of inactive hepatitis, HBeAg +/- active hepatitis and cirrhosis (from US data and Doherty Institute)
- Assumptions: Start with eligibility from current treatment guidelines

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When is Conventional Antiviral Treatment Needed?

✓ **Antiviral treatment is needed if the person has evidence of active liver damage or cirrhosis.**

✓ **First line antivirals:**

- Entecavir (0.5 mg/day)
- Tenofovir (TDF 300 mg/day, or TAF 25 mg/day)

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Cost and Utilities

Variable	Base Case	Range
Cost (AUD dollars) $		
Antiviral drug	$ 3,124	3124-5036
Total Annual monitoring	$ 594	476-712
Chronic Hepatitis B	$ 152	122-182
Cirrhosis	$ 1,760	1408-2112
Decompensated cirrhosis	$ 31,707	25366-38048
Hepatocellular carcinoma	$ 20,633	16507-24759
Hepatocellular carcinoma surveillance	$ 1,760	1408-2112
Liver Transplantation 1st year	$ 285,083	228067-342099
Liver Transplantation 2nd year	$ 45,726	36581-54871
Health State Utilities		
uActive CHB	0.89	(0.80-0.92)
uCirrhosis	0.87	(0.78-0.88)
uInactive CHB	0.95	(0.90-0.99)
uDecompensated cirrhosis	0.82	(0.49-0.82)
uHepatocellular carcinoma	0.84	(0.77-0.85)
uLiver Transplantation	0.86	(0.72-0.84)
uSeroclearance	0.99	(0.95-1.00)
uPartial cure	0.99	(0.95-1.00)
uFunctional cure	1.00	(0.95-1.00)
uViral suppression	1.00	(0.95-1.00)

Medicare (MBS) & the Pharmaceutical Benefits Scheme (PBS) data
Chinnaratha et al. 2016, journal of gastroenterology & hepatology
Subramaniam et al. 2012, Internal Medicine Journal

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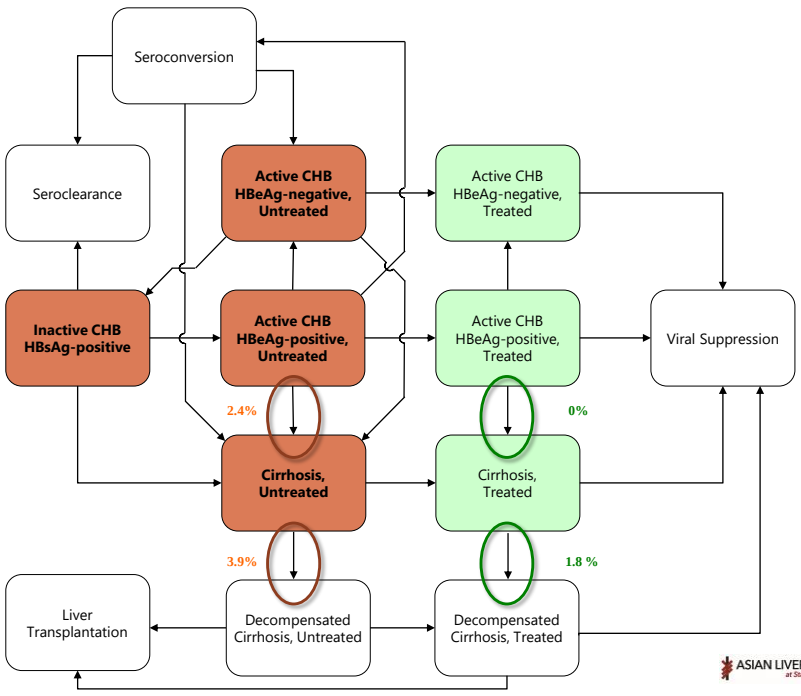

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Functional Cure

Sustained undetectable HBsAg and HBV DNA in serum with or without seroconversion after completing a 24 week of treatment and decrease risk of HCC.

Where HBV is reduced to permanently harmless levels after stopping treatment, but some residual virus may still be present in the body.

Partial Cure

Detectable HBsAg but persistently undetectable HBV DNA in serum after completion of a finite 24 week course of treatment

Lok et al. Hepatitis B cure: from discovery to regulatory approval, 2017 Journal of Hepatology
www.who.int/hepatitis/news-events/hbv-cure-overview/en/

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Scenario Analysis

Scenario	Rx	Rx duration	Effectiveness	Monitoring	Costs	Starting eligibility
Current Practice	Conventional first line therapy, ETV or TDF	Indefinite	Viral Supression Seroclearance	Monitoring 2x year, HCC surveillance	ETV generic: AUD$ 3,124 TDF: AUD$ 5,036 Monitoring: AUD$ 594, HCC surveillnce: AUD $1760	• Active e-positive. • Active e-negative • Cirrhosis
Partial Cure	Cure, new hypothetical drug	24 weeks	Viral Supression Seroclearance Tested success rate: 50/70/90, no cure: follow conventional therapy indefinitely	Moderate monitoring after stopping treatment Cirrhosis continue surveillance indefinitely	Range AUD$ 13,000-59,000 Monitoring: AUD$ 297	• Active e-positive. • Active e-negative • Cirrhosis
Functional Cure	Cure, new hypothetical drug	24 weeks	Seroclearance Tested success rate: 50/70/90 no cure: follow conventional therapy indefinitely	No further ongoing care, Cirrhosis surveillance continue	Range AUD$ 13,000-75,000 Monitoring: AUD$ 297 only during cure treatment	• Active e-positive. • Active e-negative • Cirrhosis

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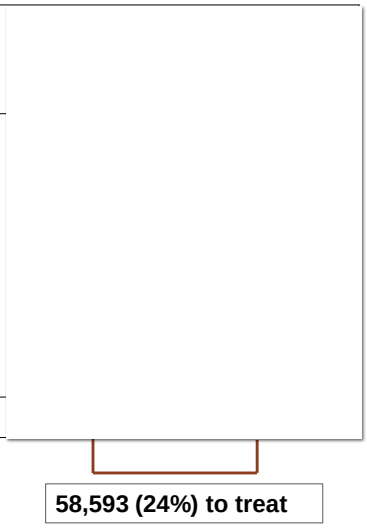
Population Level Prevalence of CHB in Australia by Age and Disease Status among Adults

Age Group (Years)	HBsAg positive
20-29	43,194 (1.51%)
30-39	63,727 (1.51%)
40-49	52,796 (1.42%)
50-59	37,255 (1.42%)
60-69	23,287 (0.87%)
70-79	13,454 (0.87%)
80+	6,026 (0.69%)
Total	239,739 (1.03%)



58,593 (24%) to treat

Surveillance for hepatitis B indicators 2016, WHO Collaborating Center for Viral Hepatitis, The Peter Doherty Institute for Infection & Immunity

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Poll Question

How much do you think the potential cure drug needs to cost in order to be cost-saving (more effective and less costly compared to the current practice)?

a) Between AUD$ 13,000- $35,000

b) Between AUD$ 45,000- $90,000

c) More than AUD$100,000

Sub-Group Specific Cost Outcomes

Cost-Saving

	Drug success rate	50%	70%	90%
Cirrhosis	Functional Cure	< AUD$ 21,000	< AUD$ 30,000	< AUD$ 35,000
	Partial Cure	< AUD$ 13,000	< AUD$ 18,000	< AUD$ 23,000
CHB only	FC and PC	< AUD$ 13,000	< AUD$ 18,000	< AUD$ 23,000

Highly Cost-Effective (GDP per capita < $ 50,000 per QALY)

	Drug success rate	50%	70%	90%
Cirrhosis	Functional Cure	< AUD$ 43,000	< AUD$ 60,000	< AUD$ 75,000
	Partial Cure	< AUD$ 33,000	< AUD$ 45,000	< AUD$ 59,000
CHB only	Functional Cure	< AUD$ 16,500	< AUD$ 23,000	< AUD$ 31,000
	Partial Cure	< AUD$ 15,000	< AUD$ 20,500	< AUD$ 27,000

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Aggregated Population Results

Functional cure

	50%					70%					90%				
Outcome	CS	HCE	Cirrhosis	HCC	HBV-Deaths	CS	HCE	Cirrhosis	HCC	HBV-Deaths	CS	HCE	Cirrhosis	HCC	HBV-Deaths
10 years	$ 15,195	$ 22,260	38	643	916	$ 20,977	$ 31,127	23	386	589	$ 26,758	$ 39,995	8	129	263
20 years	$ 23,709	$ 39,250	138	997	1,681	$ 33,203	$ 54,399	83	598	1,131	$ 42,697	$ 69,549	28	199	580
Lifetime	$ 32,337	$ 58,747	461	1,460	2,669	$ 45,531	$ 81,415	276	876	1,890	$ 58,726	$ 104,084	92	292	1,111

Partial cure

	50%					70%					90%				
Outcome	CS	HCE	Cirrhosis	HCC	HBV-Deaths	CS	HCE	Cirrhosis	HCC	HBV-Deaths	CS	HCE	Cirrhosis	HCC	HBV-Deaths
10 years	$ 14,011	$ 19,018	38	643	956	$ 18,774	$ 26,044	23	386	646	$ 23,538	$ 33,071	8	129	336
20 years	$ 21,111	$ 32,827	138	997	1,805	$ 29,021	$ 44,863	83	598	1,304	$ 36,931	$ 56,900	28	199	803
Lifetime	$ 28,696	$ 48,458	461	1,460	2,964	$ 39,891	$ 66,467	276	876	2,302	$ 51,086	$ 84,476	92	292	1,641

Current Practice

Outcome	Cirrhosis	HCC	HBV-Deaths
10 years	92	1,377	1,900
20 years	302	2,067	3,195
Lifetime	960	2,982	4,730

HCC: (2067-199)/2067= 1868/2067= **90%**

Death: (3195-580)/3195= 2615/3195= **82%**

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Poll Question

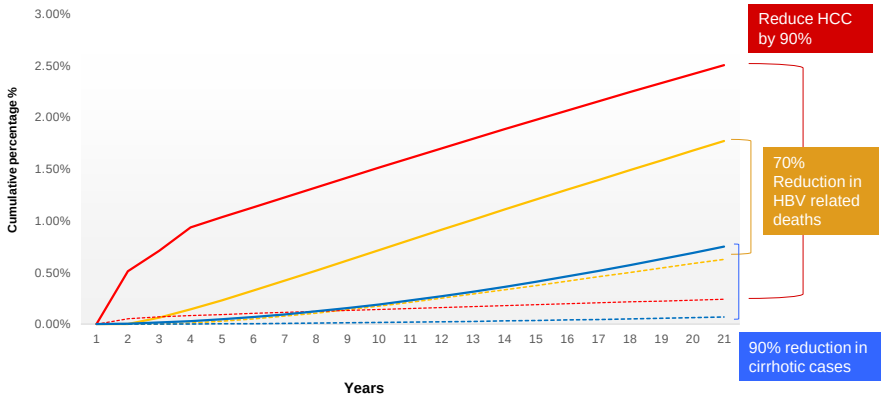
With a potential cure and access to treatment for all could we reach the World Health Organization's target of decreasing 65% of CHB deaths earlier than 2030?

a) Yes, by making sure no one is left behind

a) Maybe

b) No, I don't think so

Estimated Impact of a Functional Cure in Reducing HCC and Deaths by Chronic (active) Hepatitis B



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Conclusion

- A potential functional cure can save 90% of HCC cases and 82% of HBV related death cases compared to conservative antiviral treatment (current practice).
- In Australia, a 90% effective functional cure cost can range between $23,000-35,000 for it to be cost-saving and range between $27,000-75,000 for it to be highly cost-effective.

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Poll Question

Would finding a cure for chronic hepatitis B that is “cost-saving” make sure that “no one is left behind”?

a) Yes

b) No

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