Public health impact of a population based approach to HBV and HCV prevention and treatment in Armenia

This is a summary of the key outcomes of a hepatitis C disease burden and a hepatitis B transmission and disease burden analysis undertaken by the Center for Disease Analysis Foundation, in collaboration with WHO-EURO, the WHO Country Office in Armenia, and the Ministry of Health of Armenia.

Key points

- If no change is made to HBV or HCV treatment and prevention in Armenia then:
    - The total number of HCV and HBV infections will decline, but morbidity and mortality are projected to increase as the infected population ages
- We modelled different strategies for each disease:
    - HCV
        - Stepwise – This scenario incrementally increased the number of individuals diagnosed and treated, reaching a maximum of 3,000 in 2026 and beyond
        - WHO 2030 - The treatment, diagnosis, and prevention paradigm required to meet the Global Health Sector Strategy on viral hepatitis (GHSS) targets for elimination of viral hepatitis by 2030
    - HBV
        - Prevention
            - HBIG Only – This scenario increased the screening of pregnant women and the linkage of infants born to HBsAg+ mothers to hepatitis B immunoglobulin (HBIG) to 100% by 2025
            - EMTCT+ 2030 – This scenario builds on the above scenario by linking all eligible pregnant women to peripartum anti-viral treatment by 2025
        - Stepwise – This scenario combines the HBIG Only scenario with a stepwise increase in diagnosis and treatment with a maximum treated of 3,000
        - WHO 2030 – This scenario combines the HBIG Only scenario with the diagnosis and treatment paradigm required to meet the GHSS 2030 targets, treating a maximum of 7,500

Results of these strategies:

- The Stepwise scenario for HCV is expected to result in
    - A 50% reduction in total viremic infection and >660 lives saved
- While HCV screening and treatment must be increased in order to reach 2030 WHO targets, a reduction in the number of new infections must also take place through active prevention measures
- Utilizing the WHO 2030 scenario for HCV in Armenia would result in:
    - An 72% decline in total viremic HCV infections, and liver related deaths will decline by 74%, saving >1 900 lives
- Both the Stepwise and WHO 2030 scenarios were found to be highly cost effective, but if lower prices were negotiated they would both become immediately cost-saving
- The prevalence of HBV among 5-year-olds is expected to decrease as result of current timely birth dose and three dose coverage, if the EMTCT+ 2030 scenario was implemented it would avert 130 chronic cases of HBV through 2050 and would eliminate HBV among infants in 2025 and beyond
- When examining just the impact of increasing prophylaxes measures, if all mothers were screened for HBsAg, then both the HBIG Only and EMTCT+ 2030 scenarios would be immediately cost saving
- When the HBIG Only scenario is combined with a large-scale diagnosis and treatment strategy over 3,300 lives could be saved through 2050

Hepatitis C related disease burden

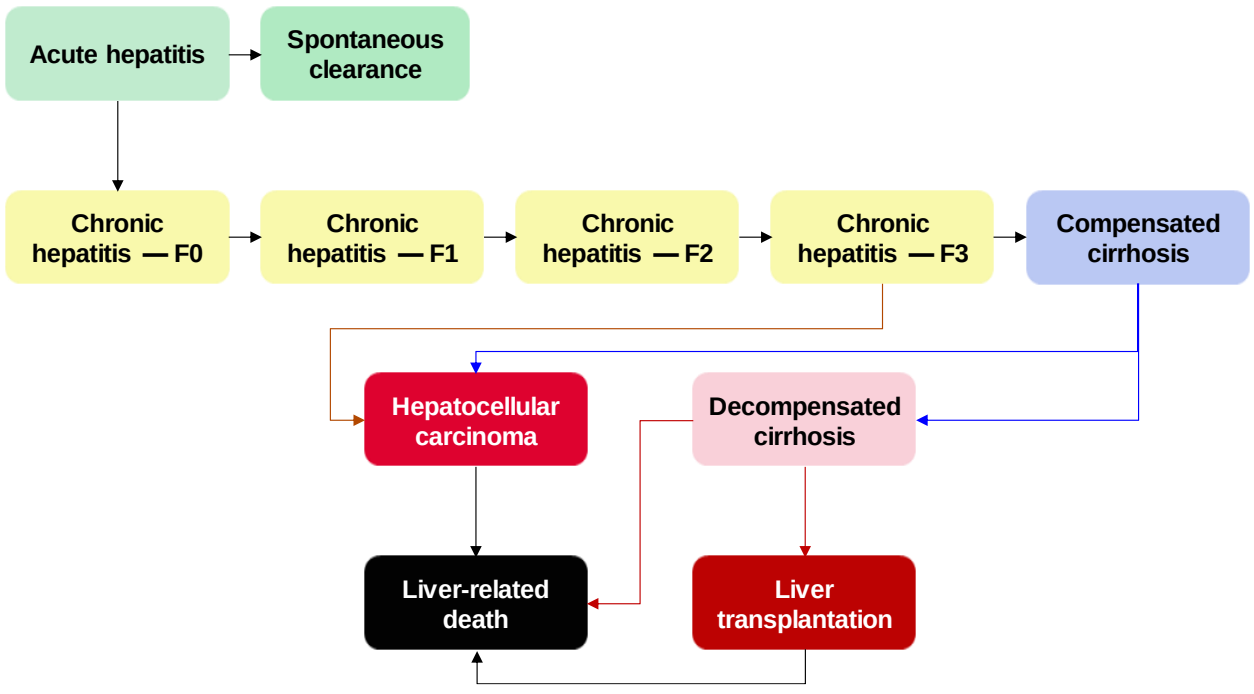
Based on a combination of published studies and expert consensus in 2018, it was estimated that 4.0% (2.9-6%) of the adult population of Armenia were anti-HCV positive [1]. After applying a viremic rate of 70% (65-72%), and adjusting for younger ages; it was estimated that in 2018 there were 68,000 Armenians viremically infected, correlating to a prevalence of 2.8% among all ages[2]. There are three risk groups that are routinely tested for HCV, active PWID, urban and rural migrant workers. The anti-HCV prevalence in these groups was most recently estimated to be 66.1%, 3.3%, and 2.1% respectively [3-5]. When these groups were weighted by population and utilized the 70% viremic rate, they account for over 9% of all viremic infections in Armenia.

Hepatitis C sustained viral response (SVR) can reverse the effects of early stage fibrosis and slow the progression of cirrhosis into decompensation or hepatocellular carcinoma (HCC)[6, 7]. This reduces liver-related mortality 20-fold and all-cause mortality 4-fold[8].

New HCV medicines (direct acting antivirals, DAAs) can achieve SVR in >95% of HCV cases. In Armenia, the plurality of individuals infected have genotype 1, 45.2%; but there is a large portion that have genotype 3, 36.6% [9]. For the purposes of the analyses, a SVR rate of 92% for all genotypes on DAA treatment regimens was utilized.

The model

The mathematical model is an Excel based disease progression model which was calibrated using reported, Armenian specific, epidemiologic data. The progression is as follows [10]:



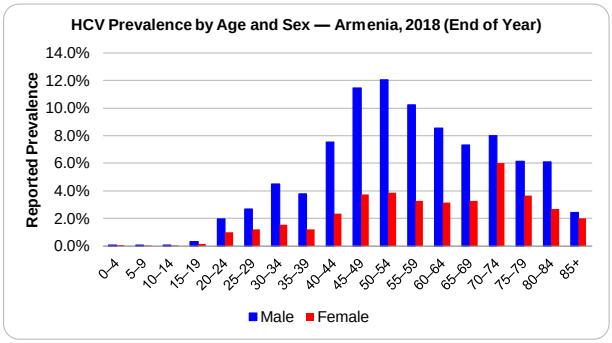
Input data

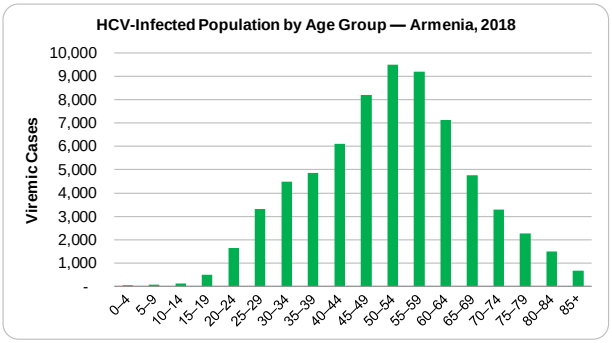
The following epidemiologic data were inputs into the model:

Historical Input	Estimate	Estimate Year
RNA+ HCV Infections	68,000	2018
Total Diagnosed (anti-HCV+)	9,000	2018
Annual Newly Diagnosed (anti-HCV+)	2,350	2018
Annual Number Treated	1,000	2018

The base case: If there is no change through 2030

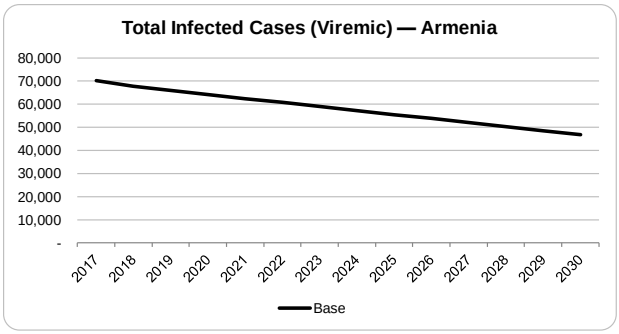
We calculated the impact on HCV infections and mortality if there is no change to HCV treatment policies as follows:

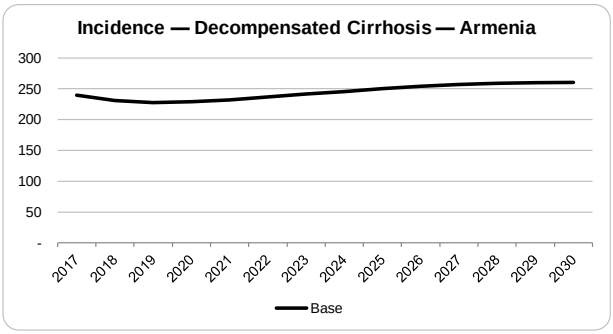


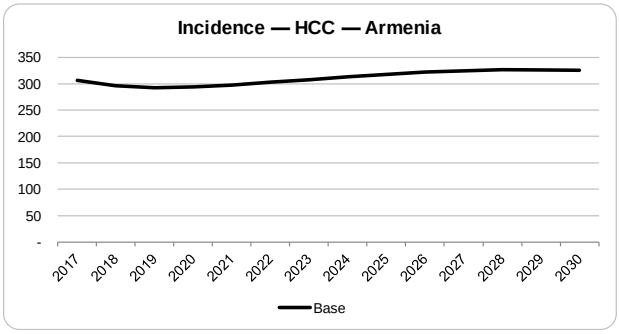


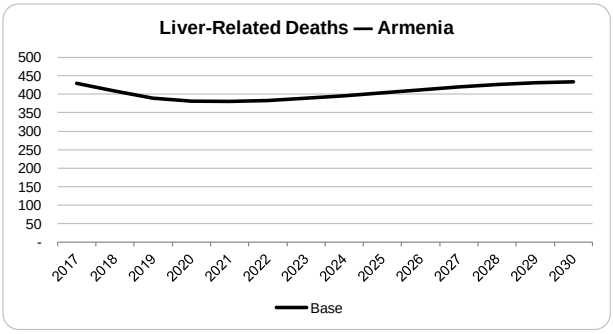
	2018	2019	2020	2022	2024	≥2026
Treated	1,000	1,000	1,000	1,000	1,000	1,000
Newly Diagnosed	1,640	1,640	1,640	1,640	1,640	1,640
Fibrosis Stage	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0
New Infections	750	680	660	630	590	560
Treated Age	0-85+	0-85+	0-85+	0-85+	0-85+	0-85+
SVR	92%	92%	92%	92%	92%	92%

Under the current treatment paradigm, the number of viremic cases peaked in 2008 and will continue to decline by 34% between 2017 and 2030, resulting in 46,700 cases by the end of 2030. Liver related deaths, HCC, and decompensated cirrhosis will increase by 1-8%. New cases of hepatocellular carcinoma will increase by 6% to 330 in 2030. New cases of decompensated cirrhosis cases will increase by 8% to 260 cases in 2030. Given the screening and treatment paradigm in Armenia, there are estimated to be 430 liver related deaths in 2030.









Two Strategies

There were two different policy strategies modeled:

1. Stepwise
    a. This scenario aimed to gradually increase diagnosis and treatment in a manner that is compatible with the current healthcare system
2. WHO 2030
    a. This scenario was developed to meet the following WHO 2030 Targets:
        i. 90% of patients diagnosed by 2030
        ii. 80% reduction in new infections by 2030
        iii. 80% of the treatment eligible population treated by 2030
        iv. 65% reduction in liver related mortality by 2030

Stepwise

This strategy requires the following numbers of people to be diagnosed and treated for HCV:

	2018	2019	2020	2022	2024	≥2026
Treated	1,000	1,000	1,250	1,500	2,000	3,000
Newly Diagnosed	1,640	2,000	2,250	2,500	2,750	3,000
Fibrosis Stage	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0
New Infections	750	680	660	620	580	530
Treated Age	0-85+	0-85+	0-85+	0-85+	0-85+	0-85+
SVR	92%	92%	92%	92%	92%	92%

WHO 2030

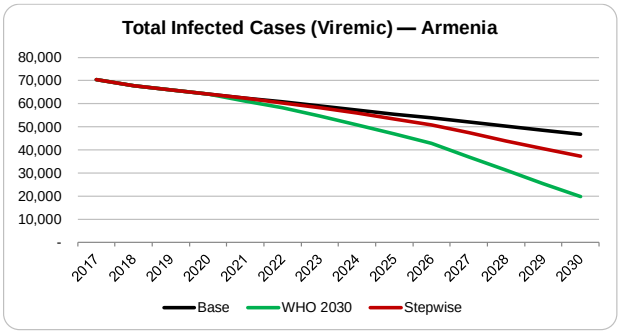
This strategy requires the following numbers of people to be diagnosed and treated for HCV:

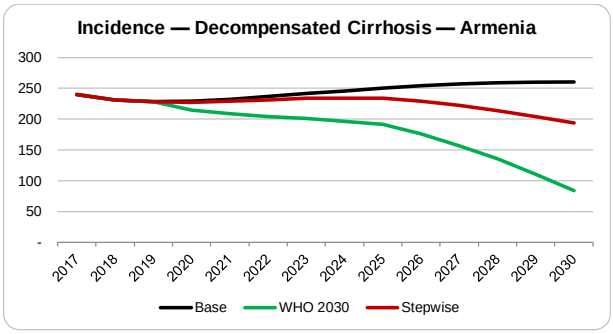
	2018	2019	2020	2022	2024	≥2026
Treated	1,000	1,000	2,500	3,250	3,750	5,750
Newly Diagnosed	1,640	2,000	2,500	3,000	5,000	6,000
Fibrosis Stage	≥F0	≥F0	≥F0	≥F0	≥F0	≥F0
New Infections	750	680	660	540	430	330
Treated Age	0-85+	0-85+	0-85+	0-85+	0-85+	0-85+
SVR	92%	92%	92%	92%	92%	92%

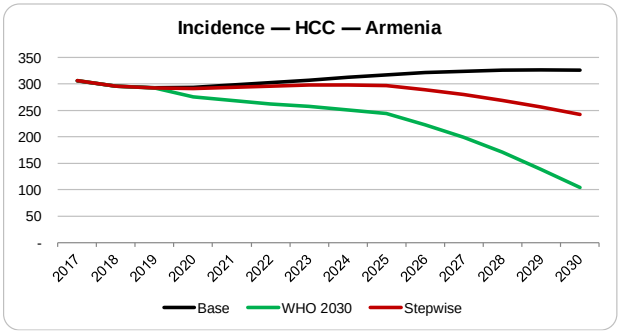
Outputs

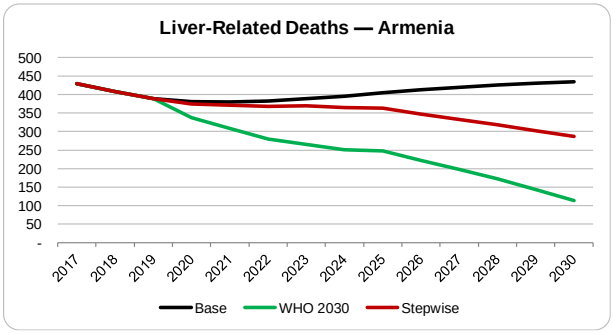
Stepwise - Total infections will decline by 53% and liver related deaths, new cases of HCC and decompensated cirrhosis will decline by 19-33%, saving over 660 lives

WHO 2030 - Total infections will decline by 72% and liver related deaths, new cases of HCC and decompensated cirrhosis will decline by 65-74%, saving over 1,900 lives









Economic Impact Analysis

Direct costs

Direct costs included all costs associated with managing chronic HCV infection, cirrhosis and liver cancer. They included:

- Healthcare costs
  - Costs of hospitalization for HCV sequelae
  - Inpatient and outpatient costs
  - Treatment costs for cirrhosis and liver cancer
- Diagnostic and other blood tests (anti-HCV, confirmatory & RNA)
- Genotyping, viral load & liver disease staging
- Antiviral therapy (DAA) costs

The healthcare costs were estimated utilizing expert consensus:

Annual Cost per diagnosed patient*	**Price (Dram)**
Fibrosis (F0-F2)	40,000
Fibrosis (F3)	46,000
Compensated Cirrhosis	72,000
Decompensated Cirrhosis	1,512,000
Hepatocellular Carcinoma	3,682,000

***These does not include the cost of anti-viral treatment or HCV specific diagnostics (anti-HCV, HCV, RNA, genotyping, and viral load), since those are considered separately**

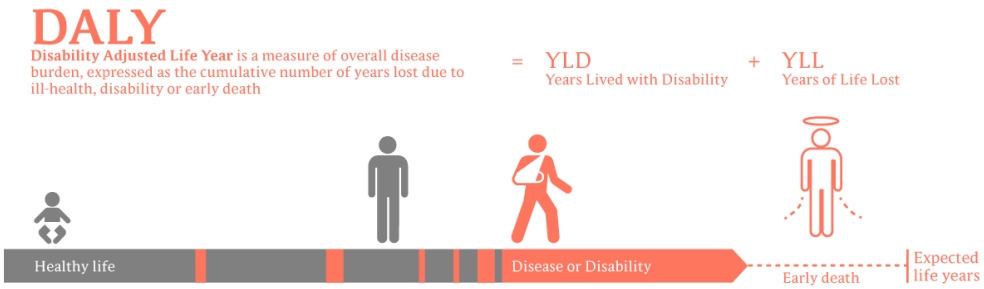
Currently, 90% of the costs are incurred by the patient for F0-decompensated cirrhosis and 100% of the cost of HCC. Due to the costs being incurred by patients as well as the relatively low number of individuals diagnosed, the annual health care costs were applied to the diagnosed population. All of the following diagnostic and follow-up costs are incurred by the patient with the exception of the anti-HCV rapid test.

Intervention	**Price (Dram)**	**Screening**	**Tests for viremic confirmation (current)**	**Tests for viremic confirmation (scenario)**	**Tests for treatment assessment (current)**	**Tests for treatment assessment (scenario)**
Anti-HCV test	270	1				
HCV-RNA test/PCR	10,000		1	1	3	1
Genotyping	50,000				1	
Staging/Liver Biopsy/Fibroscan	40,000				1	
ELISA	5,000		1			
APRI	5,000					1
Post-SVR monitoring (per cirrhotic patient per year)	38,000					

Currently everyone pays out of pocket for treatment; the cost of a cure is by genotype, and stage was estimated utilizing expert consensus:

Genotype/Stage	Cost/cure (Dram)
G1/4/5/6	370,000
G2	300,000
G3 (F0-F3)	300,000
G3 (≥F4)	650,000

Indirect economic losses



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Health effects are denominated in disability-adjusted life years (DALYs)

- DALY = Years of Life Lost (YLL) + Years Lost due to Disability (YLD)
  Years of Life Lost (YLL)
  Number of deaths —HCV-related deaths calculated in model
  Life expectancy at age of death — available from national census data or extrapolated based on estimates from UN World Population Prospects
  Discount rate — depends on analysis
  Years Lost due to Disability (YLD)
  Number of incident cases by stage of liver disease — calculated in model
  Disability weight — published estimates
  Duration of disability — calculated in model

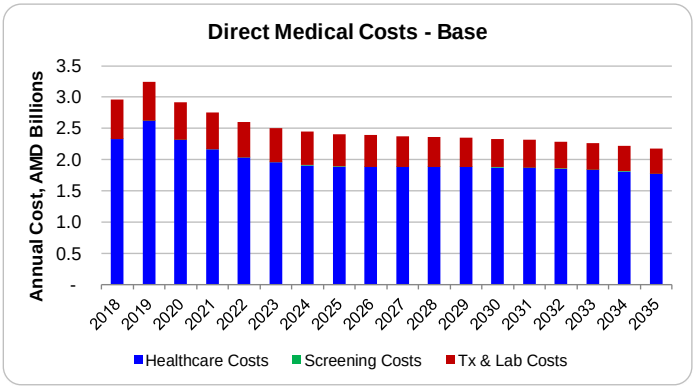
The following parameters were utilized for the calculation of DALYs:

Parameter	Value	Source
Disability weights F0-F4 Decompensated cirrhosis Hepatocellular carcinoma Liver transplant	 0 0.178 0.466[†] 0.024[‡]	[11]
Discount rate	0-3%	[12]
Age-weighting modulation constant	0 (none)	
GNI per capita in Armenia	1 837 007	[13]

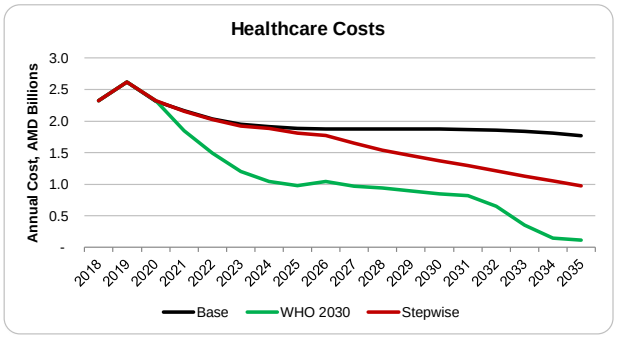
Economic losses associated with HCV infection are calculated in the economic impact analysis and assume the value of one DALY averted equals the GNI per capita of a country [14]. The economic losses are calculated for DALYs incurred at ages 20-69.

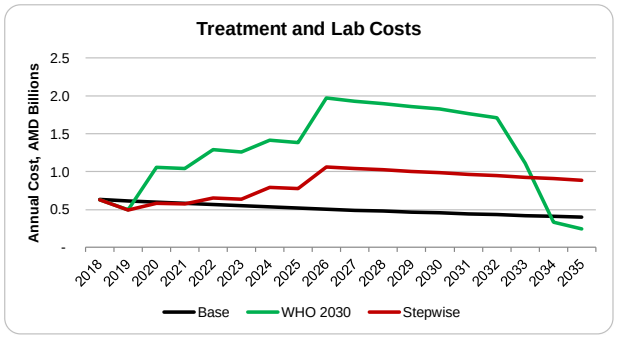
Costs to Armenian society

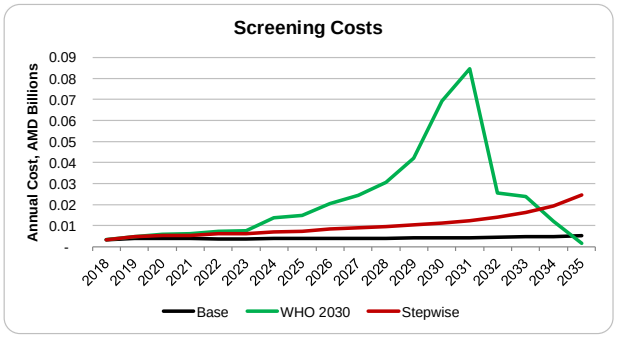
Under the current treatment and screening paradigm, there is estimated to be over 2.5 billion Dram spent annually on the direct medical costs of HCV in Armenia. The vast majority of costs are healthcare costs, but there are significant amounts being spent on treatment and lab costs as well. Although the costs are expected to slightly decrease, they are not expected to drop below 2 billion Dram through 2035.

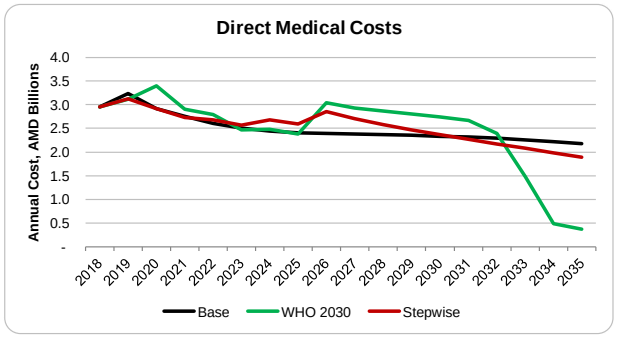


The Stepwise scenario saves less on healthcare costs, however the upfront costs of screening and treatment are lower making the annual direct medical costs lower than the base starting in 2031. While the WHO 2030 scenario requires a much larger upfront cost, the annual direct medical costs begin to decrease at a much faster rate after becoming lower than the base in 2033.

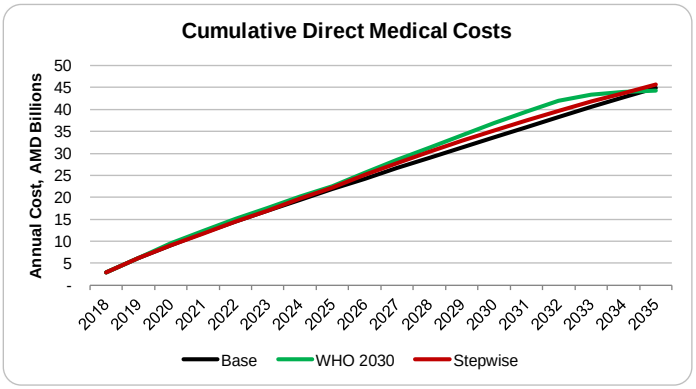




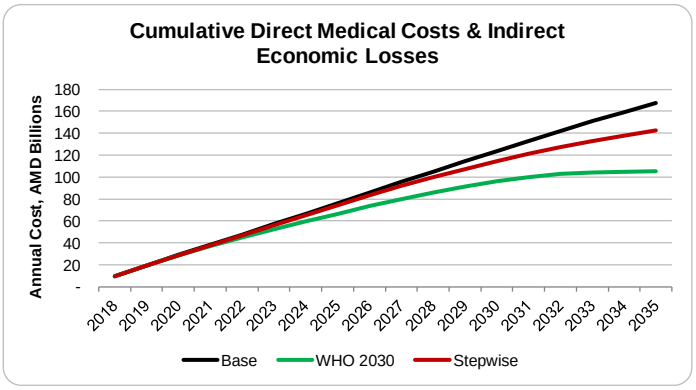




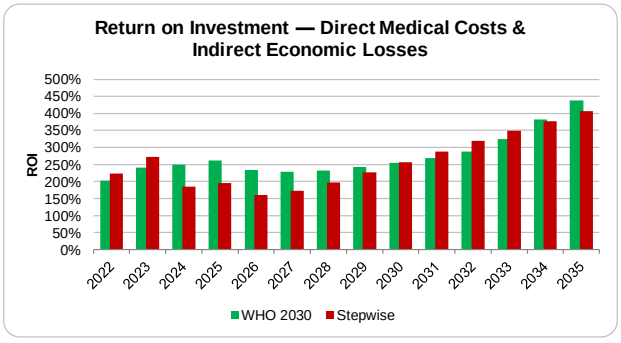
While both scenarios are highly cost-effective, cumulatively the direct medical costs of the Stepwise scenario are higher than the base. The WHO 2030 scenario reaches a cumulative direct medical cost that is lower than the base in 2035.

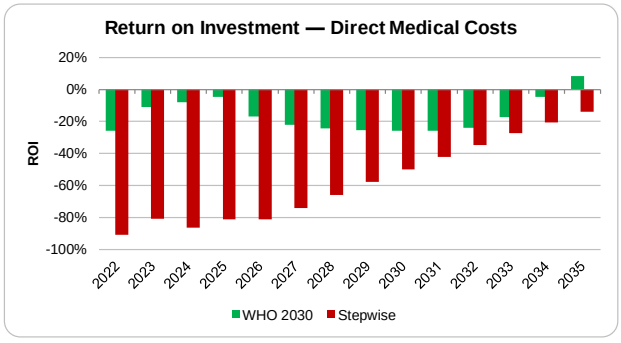


When both direct medical costs and indirect economic losses are taken into account, the cumulative costs are lower for the Stepwise and WHO 2030 scenarios in 2019.



Another way to view this data is to show that there is an immediate positive return on investment when taking both direct medical costs and indirect economic losses into account, but through 2035 there is no positive return on investment in the Stepwise scenario when only based on direct medical costs. However, starting in 2035 there is a positive return on investment for the WHO 2030 scenario when only examining direct medical costs.

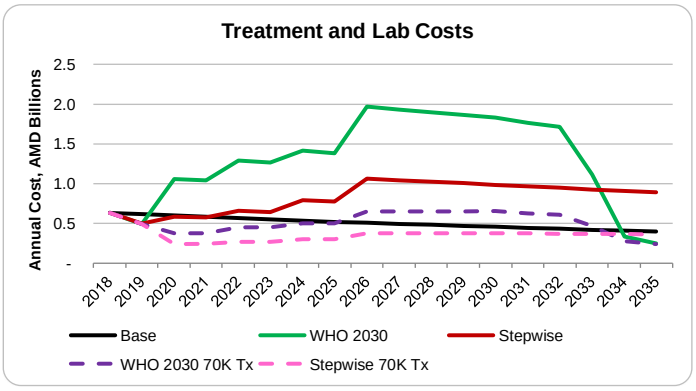




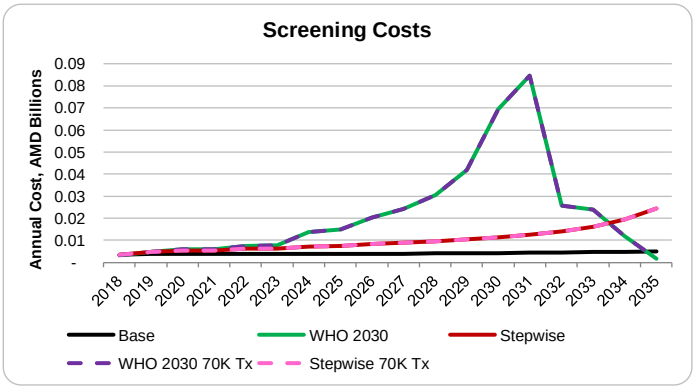
Impact of treatment cost reduction

The two previous scenarios were run again, but with a lower treatment cost. GPRO is able to procure treatment at 70,000 Dram per cure; these scenarios assumed that this cost was utilized starting in 2020.

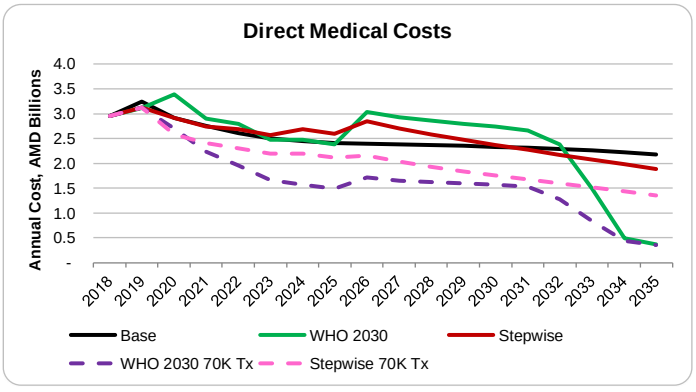
Due to the simplified testing and diagnostic strategy combined with the lower cost of treatment, the treatment and lab costs for the WHO 2030 scenario is only slightly higher than the base, and the Stepwise scenario is cheaper than the base.



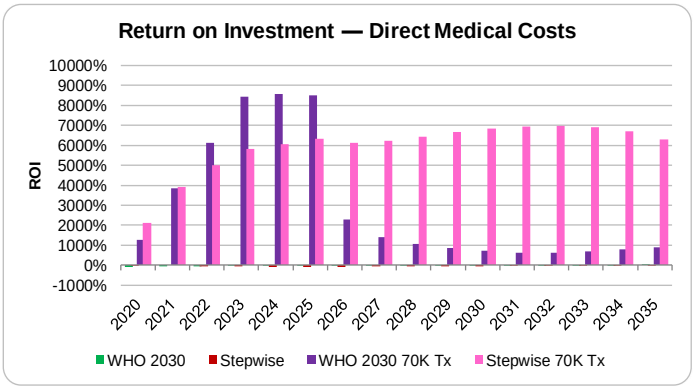
As the cost of diagnostics was not altered in this analysis, testing costs remained the same.



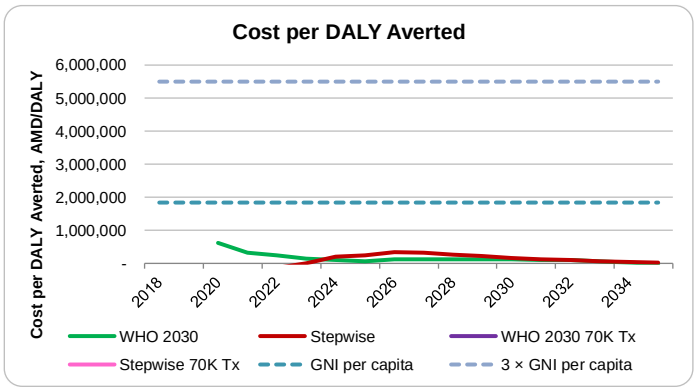
When the testing, treatment, lab, and healthcare costs are combined, the direct medical costs for both are lower than the base.



There is a positive return on investment on the direct medical costs almost immediately for both the WHO 2030 and Stepwise scenario at the lower cost.



All of the scenarios were found to be highly cost effective, with the scenarios that utilize the lower cost of treatment being cost saving immediately.



Hepatitis B transmission and related disease burden

The percent of adults in Armenia that were HBsAg+ in 2007 was estimated to be 2% [1]. The National Registry data in combination with vaccination data was used to determine the age and sex distribution in 2017. The estimated prevalence of HBsAg+ in the general population of Armenia was 1.6% correlating to 46,500 infected individuals in 2017.

The presence of HBeAg was estimated to be 13.3% among women of child bearing age (WoCBA) that were also positive for HBsAg. This estimate was based on a regional average from CDAF's other work as well as expert opinion. It was estimated that 90% of those that were HBeAg+ had a high viral load (defined as ≥20,000 IU) and 13% of those that were HBeAg- had a high viral load [15]. Approximately 23% of the infected population were estimated to have a high viral load.

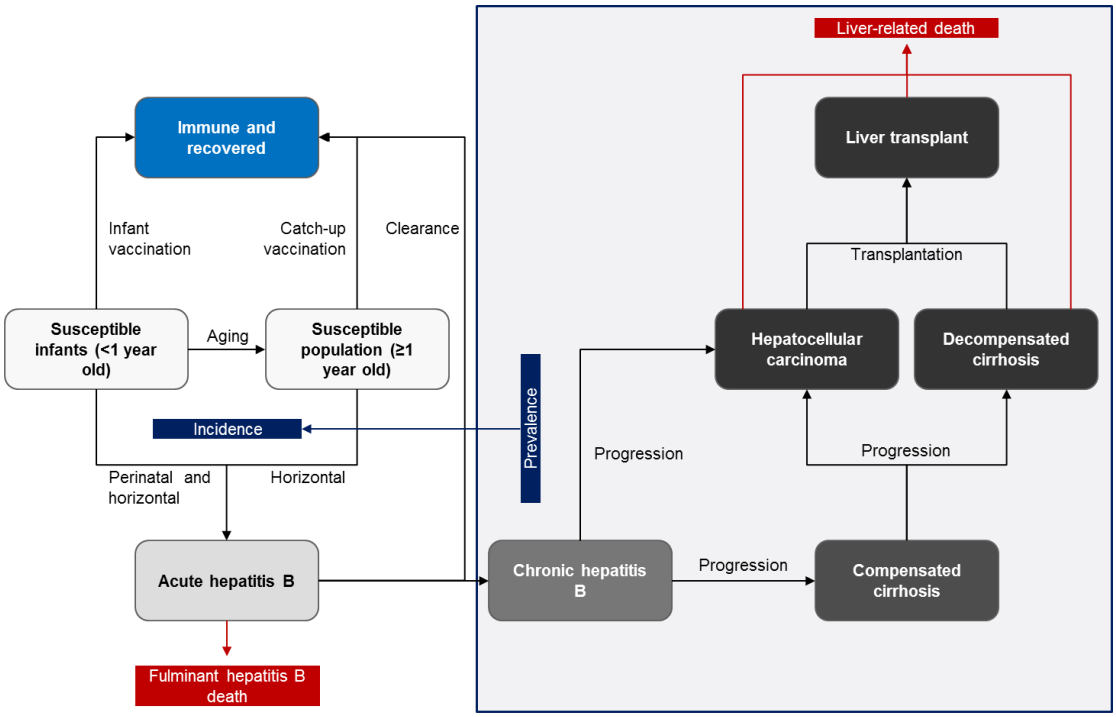
Armenia started universal three-dose and timely birth dose vaccination for hepatitis B in 1999, reaching coverage rates of over 90% for both by 2002 [16]. From the fall of 2009-2011, the Rostropovich Vishnevskaya Foundation screened all pregnant women and provided HBIG for all infants born to HBsAg+ mothers in Yerevan. They estimated that 19,000 women were screened annually as part of this program which would represent approximately 44% of all pregnant women in Armenia during those

years [17]. Currently, mothers found to be HBsAg+ must acquire HBIG in Georgia. While quantification of the percentage of infants born to HBsAg+ mothers that receive HBIG and the percentage of eligible mothers that receive peripartum anti-viral treatment is difficult, 1% was utilized in the model at this time.

While there is no cure for chronic hepatitis B, treatment results in a reduction of viral load which in turn slows the progression of the disease. Currently the WHO recommends treatment of any individuals over the age of 30 with a high viral load, as well as any individuals that are cirrhotic regardless of their viral load status [18].

The model

The mathematical model is a previously published Excel based transmission and disease progression model which was calibrated using reported, Armenian specific, epidemiologic data [19]. The transmission and progression are as follows:

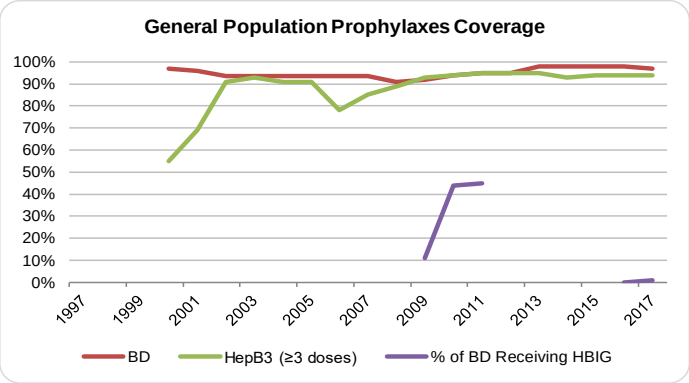


Input data

The following epidemiologic data were inputs in the model:

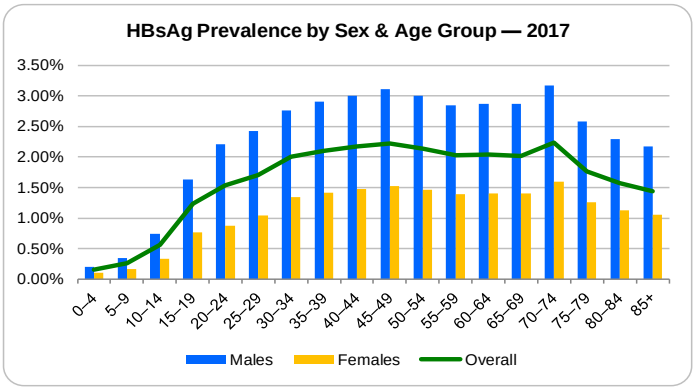
Historical Input	Estimate	Estimate Year
HBsAg+ Infections (ages 18-75)	44,100	2007
HBeAg+ prevalence among HBsAg+ WoCBA	13.3%	2015
Total Diagnosed	5,330	2015
Annual Newly Diagnosed	500	2018
Annual Number Treated	100	2018

For the scenario analysis, the base vaccination rates were assumed to remain constant at the 2017 coverage rates - 97% timely birth dose, 94% three-dose, 1% of infants born to HBsAg+ mothers receive a timely birth dose also receive HBIG, and 1% of eligible women receive peripartum anti-viral treatment. The historical vaccination coverage can be seen below:

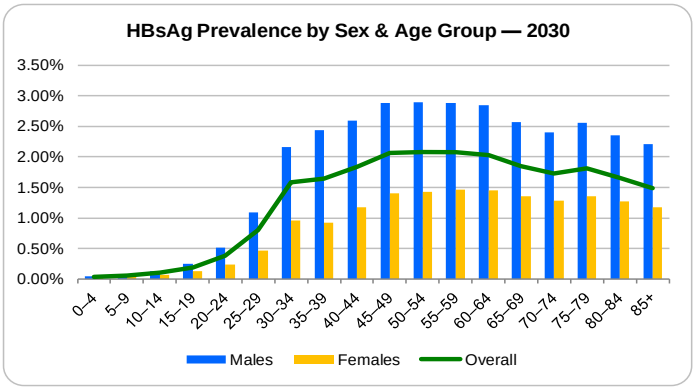


The base case: If there is no change in policy through 2030

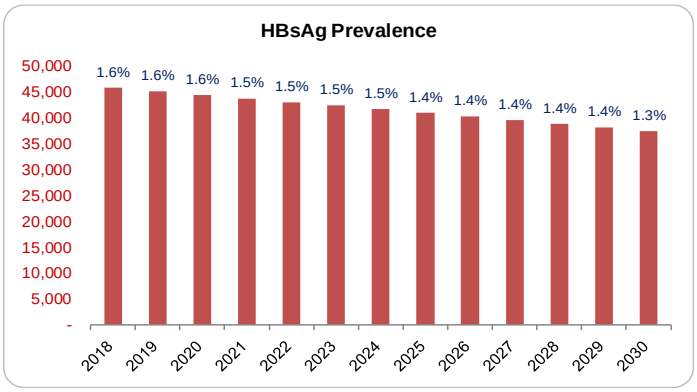
We calculated the impact on the HBV infections, morbidity and mortality if there is no change to HBV treatment and prevention policies. The starting age and sex distribution is estimated to be the following:



If no change in prevention or treatment policy, then in 2030 the age and sex distribution is estimated to be:

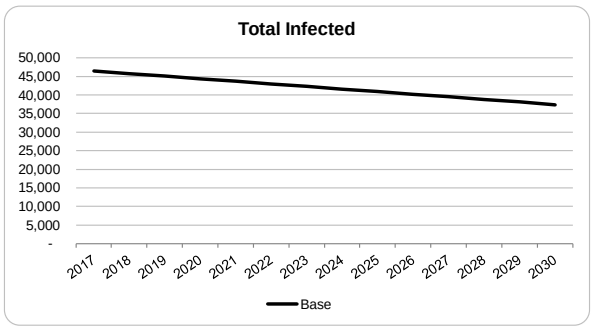


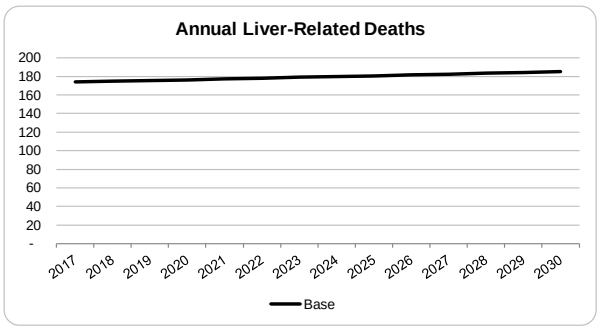
Prevalence is expected to decrease from 45,800 infections (1.6% prevalence) in 2018, to 37,400 infections, a prevalence of 1.3% by 2030:

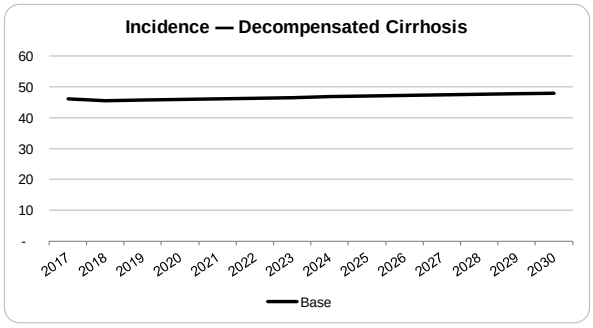


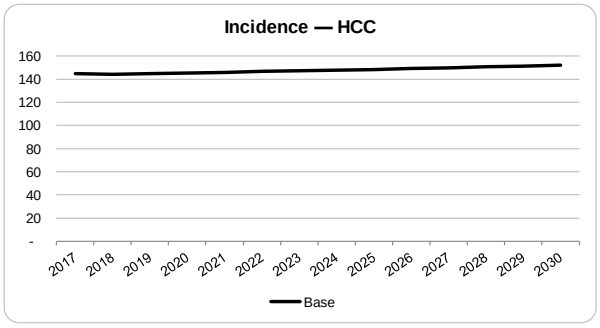
	2016	2017	≥2018
Treated	319	485	500
Newly Diagnosed	100	100	100
Treated Age	15+	15+	15+
Viral Suppression	90%	90%	90%

Under the base scenario, the number of chronic cases decrease by 19% between 2017 and 2030, resulting in 37,400 cases by the end of 2030. HBV liver-related deaths, decompensated cirrhosis and HCC will increase by 4-6% through 2030. Given the number of individuals treated in Armenia, there would be almost 190 liver-related deaths in 2030.

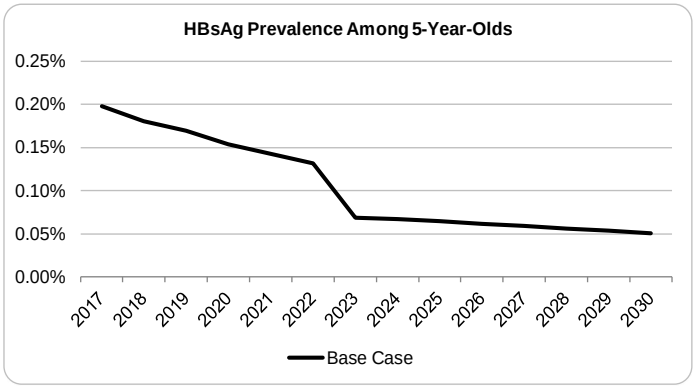








By 2030, HBsAg+ prevalence would reach <0.1% among 5-year-olds



Mother-to-Child Transmission Reduction Strategies

We created two mother-to-child transmission (MTCT) scenarios. The government has committed to screening all pregnant women; currently, approximately 25% are being screened. The HBIG Only scenario examines the impact of linking infants born to HBsAg+ mothers to HBIG with HBIG coverage increasing as screening coverage increases. The second scenario, EMTCT 2030, was designed to follow the EMTCT+ guidelines, introducing anti-viral treatment of high viral load mothers in order to eliminate MTCT of HBV in Armenia. These strategies require the following prophylaxes schedules:

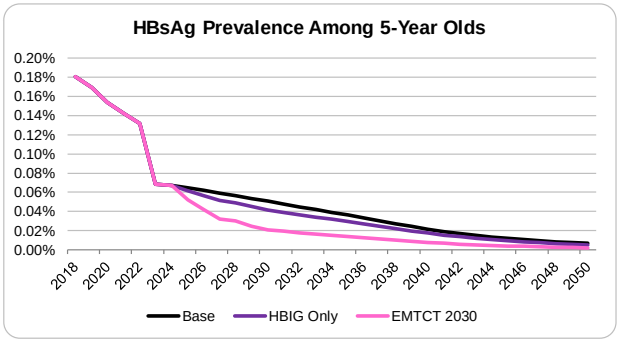
Scenario	Prophylaxis	2017	2020	2021	2022	2024	≥2025
Base	Timely birth dose	97%	97%	97%	97%	97%	97%
	3 dose	94%	94%	94%	94%	94%	94%

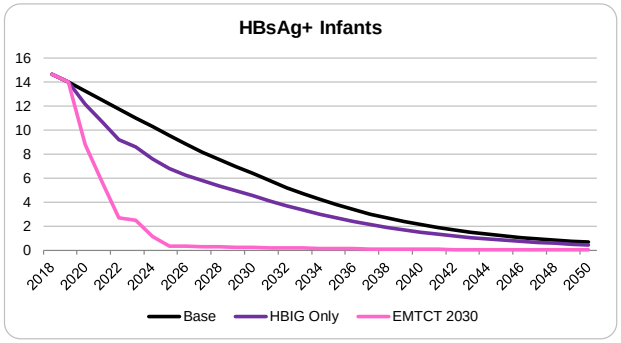
	HBIG	1%	1%	1%	1%	1%	1%
	Anti-viral Tx	1%	1%	1%	1%	1%	1%
HBIG Only	Timely birth dose	97%	97%	97%	97%	97%	97%
	3 dose	94%	94%	94%	94%	94%	94%
	HBIG	1%	30%	50%	75%	90%	100%
	Anti-viral Tx	1%	1%	1%	1%	1%	1%
EMTCT 2030	Timely birth dose	97%	97%	97%	97%	97%	97%
	3 dose	94%	94%	94%	94%	94%	94%
	HBIG	1%	30%	50%	75%	90%	100%
	Anti-viral Tx	1%	30%	50%	75%	90%	100%

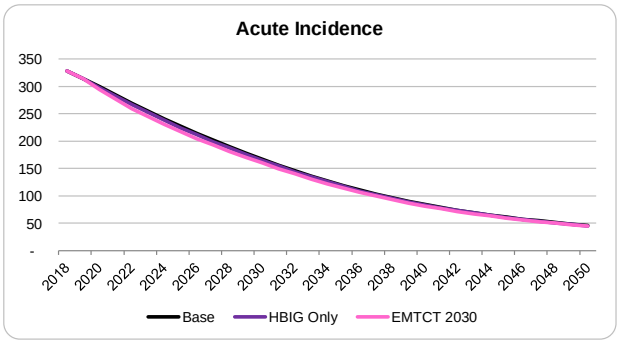
Outputs

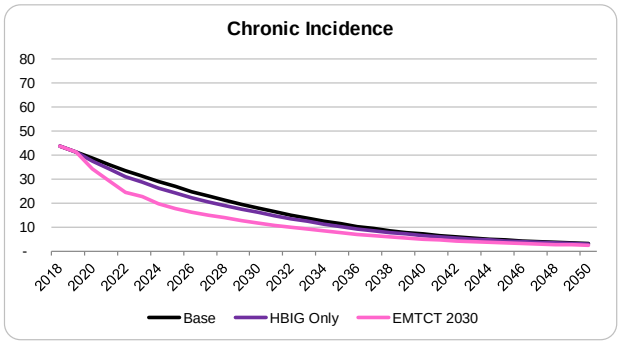
HBIG Only – Through 2050, 50 acute and 40 chronic cases of HBV will be averted.

EMTCT 2030 - With the introduction of anti-viral treatment of high viral load mothers, 160 acute and 130 cases of chronic HBV would be averted by 2050. By 2026, there would be no infants infected with HBV in Armenia. Some of these 130 individuals that averted infection due to the interventions would have gone on to develop later stages of the disease and would eventually die as the result of HBV related complications after 2050.









Treatment Scenarios

In addition to the two prevention strategies, two treatment strategies were also modeled:

1. Stepwise

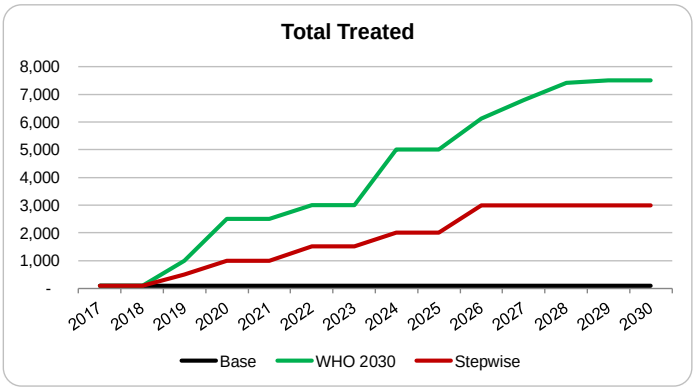
a. Building upon the HBIG Only prevention strategy, this scenario was developed in order to stepwise increase the diagnosis and treatment of HBV in a manner that would be compatible with the current healthcare system capacities

2. WHO 2030
    a. Building upon the HBIG Only prevention strategy, this scenario was developed to meet the following 2030 targets:
        i. 90% of patients diagnosed by 2030
        ii. 80% of eligible patients on treatment by 2030
        iii. Approaching a 65% reduction in liver related mortality by 2030

Scenario Inputs

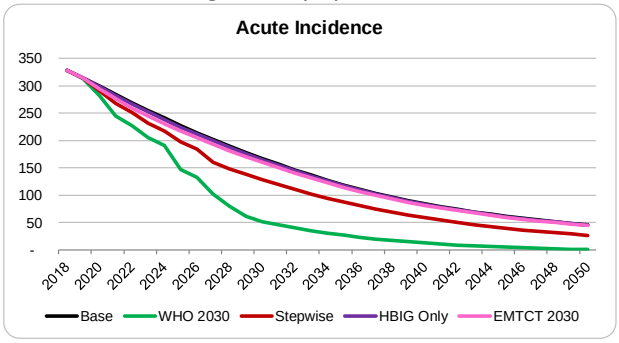
In addition to the HBIG Only prophylaxis schedule, these strategies required the following numbers of individuals to be diagnosed and treated for HBV:

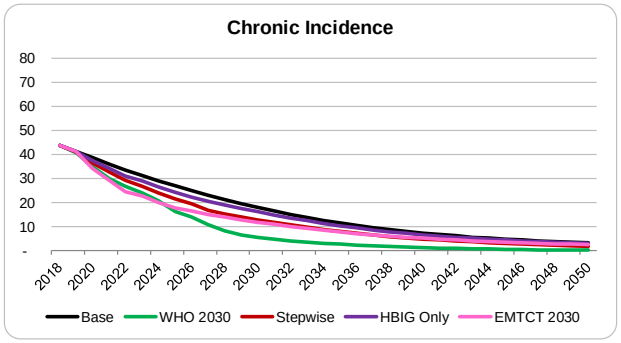
Diagnosed by Scenario	2019	2020	2022	2024	≥2026
Base	500	500	500	500	500
Stepwise	750	1,000	1,250	500	2,000
WHO 2030	1,000	2,000	2,250	2,750	3,500



Outputs

The number of new cases of HBV will drop due to the combination of perinatal prophylaxes and treatment in the general population:



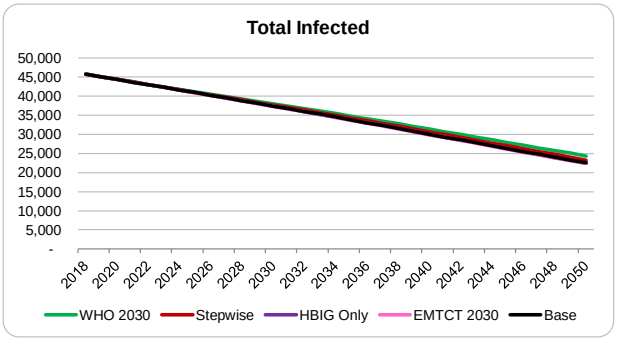


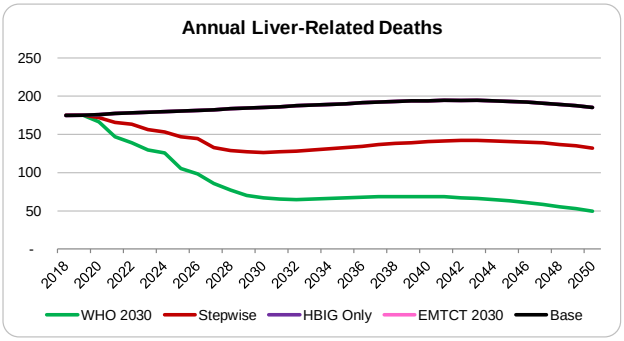
Stepwise - The number of new cases of HBV will decrease due to the combination of perinatal prophylaxes and treatment in the general population. By 2050, 800 acute and 100 chronic cases of HBV

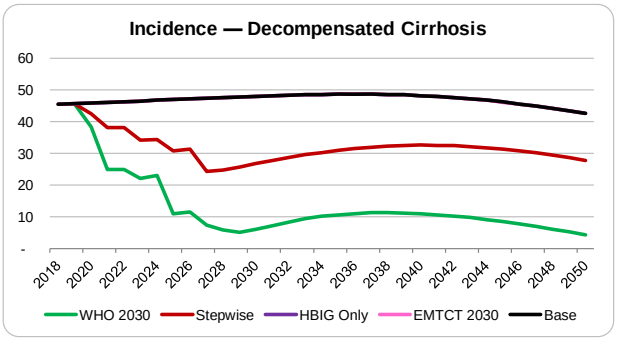
can be avoided, saving almost 1,500 lives. An estimated 500 new cases of decompensated cirrhosis and 1,200 new cases of HCC could be averted by 2050.

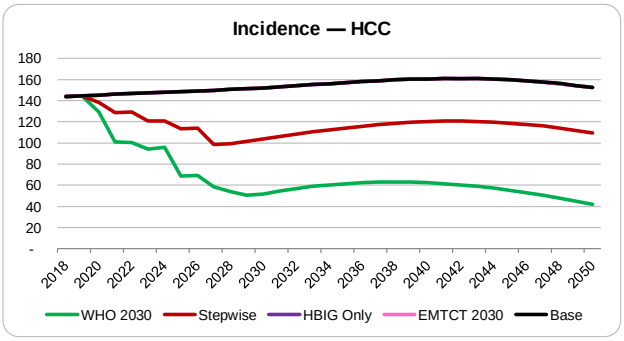
WHO 2030 - By 2050 there will be an estimated 1,100 new cases of decompensated cirrhosis and 2,800 new cases of HCC averted. By 2050, just over 3,300 lives could be saved. In addition, 2,300 acute and 200 chronic cases of HBV could be avoided.

These combined strategies will have little impact on the total number of infected individuals as there is currently no curative therapy, however there will be a large impact on the number of lives saved as well as the number of new cases of decompensated cirrhosis and HCC.







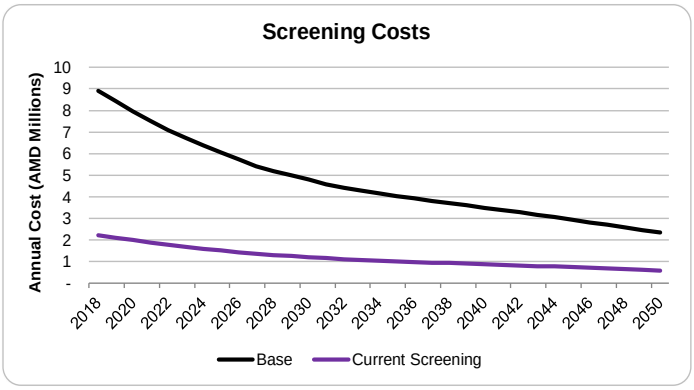


Economic Analysis of MTCT Scenarios

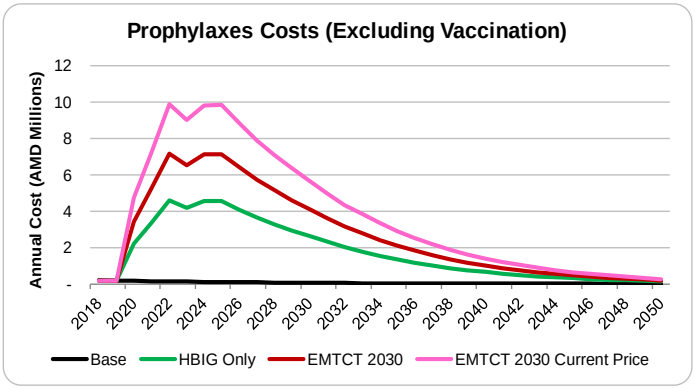
The following inputs were utilized in the economic analysis of the MTCT scenarios:

Diagnostics	Cost (Dram)	Current requirements for treatment	Scenario requirements for treatment
HBsAg rapid test	250	1	1
HBeAg test	10,000	1	
Quantitative viral load test	50,000	1	1
Interventions			
HBIG	25,000		
Current anti-viral treatment of mothers	66,000		
Future anti-viral treatment of mothers	7,000		

The cost of the current vaccination program (timely birth dose and three dose coverage) was not included in this analysis as it is currently part of the budget and the benefits of this program are already included in the base scenario. Currently, less than 25% of pregnant women are being screened for hepatitis B and this is costing approximately 2 million Dram. If screening was increased to 100% then the cost of screening every pregnant woman would be slightly less than 9 million Dram. Both of these costs would decrease in the future as the number of children being born continues to decrease.

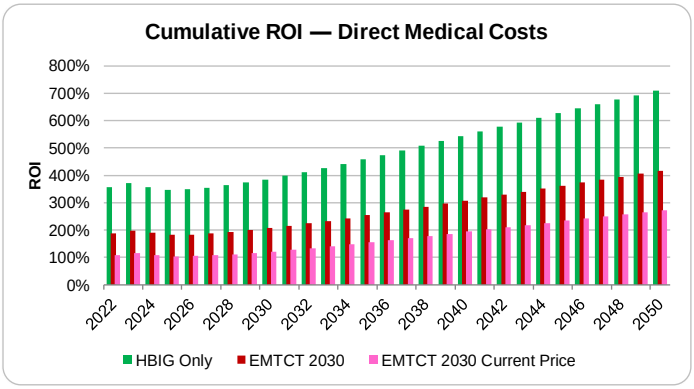


As the government has agreed to screen all pregnant women, the following analyses were run assuming 100% screening of pregnant women. The additional cost of providing HBIG to all infants born to HBsAg+ mothers would reach a maximum of 4.6 million Dram in 2022. Combining the HBIG scenario with providing all eligible pregnant women with anti-viral treatment as prophylaxis at the current pricing would reach a maximum of 9.9 million Dram in 2022. By implementing a reduced price for tenofovir in 2020 while combining the use of HBIG with anti-viral treatment of all eligible pregnant women, the maximum cost would be 7.2 million Dram in 2022. Not only does the number of births continue to drop, but the secondary impact of vaccination occurs. This is when new mothers were previously vaccinated as infants and thus their prevalence, the risk to their infants, and the costs drop dramatically.



All of the MTCT scenarios are immediately cost-saving. It must be noted that part of the cost-saving for the anti-viral treatment of pregnant women is due to the simplification of the screening strategy (1 HBsAg+ required 1 quantitative viral load test as opposed to 1 HBsAg+ test followed by 1 HBeAg+ test followed by 1 quantitative viral load test). By reducing the cost of tenofovir, the upfront costs are less with 20.4 million Dram being saved through 2030, reaching 30.1 million Dram saved by 2050. The return on investment is positive immediately as shown below and will continue to increase at a rapid rate. The benefits of these interventions will continue to increase due to the fact that those infants that had

almost universal coverage of prophylaxes in 2025 will by and large not start progressing to the later stages until 2060 and beyond. At this point the return on investment will be even greater. Furthermore, as this same cohort starts to become mothers the cost of the programs will drop dramatically for the next and all future generations.



Conclusions

Currently, although there is some screening in high risk groups, the diagnosis and treatment of hepatitis C in Armenia remains quite low. The 1,000 individuals that were treated through a special program had an impact, but there needs to be an increase in prevention, diagnosis, and treatment in order to mitigate the future disease and economic burden on the country. The Stepwise scenario showed that with even a modest increase in diagnosis and treatment, there can be hundreds of lives saved. The WHO 2030 scenario would save over 1,900 lives by 2030, and in addition to meeting the 2030 targets, would decrease the total infections in the country by 72%.

Over 2 billion Dram is being spent annually on the direct costs associated with hepatitis C with almost all of these costs being incurred by the patient. The future simplified testing and diagnostic strategy will save some costs as soon as it is implemented, but an upfront investment is necessary to greatly reduce the future direct medical costs and indirect economic losses. Both of the scenarios investigated were found to be highly cost effective, but only the WHO 2030 scenario was found to be cost saving starting in 2035. However, if a lower price for treatment was negotiated, e.g. 70,000 Dram per cure, there would be little to no upfront investment necessary as both scenarios would be immediately cost saving.

With timely birth dose and three dose coverage for infants and a starting prevalence of 1.6%, it is expected that the HBsAg prevalence in Armenia will continue to decrease. However, due to the very low number of individuals treated for hepatitis B, morbidity and mortality will continue to increase in the future. There are multiple points that can be leveraged for a larger impact, with a combination being the most effective. Currently, HIV+ individuals are already immunized as a prophylaxis measure and they are also on anti-viral treatment. Of the high-risk groups studied in Armenia, MSM and migrant workers are routinely tested for HBV. These groups report prevalence of 0.3% and 0.6% respectively in 2018 [3-5]. These groups along with PWID, FSW, health care workers, and those individuals and areas most impacted by the earthquake could benefit from a short-term catch-up vaccination program. The program would be short term, due to the fact that high coverage of HBV vaccination has been maintained for almost 20 years, and within a decade or two all individuals in high risk groups would have been previously vaccinated as infants. If screening is increased, then family clustering screening can help increase not only the number of individuals diagnosed, but also present the opportunity to vaccinate all

individuals found to be negative for HBV markers that live with HBsAg positive family members. Those found to be positive can then be more easily linked to care.

While monitoring the HBsAg status of pregnant women is an important epidemiological marker, it also presents a large opportunity for prevention. Almost 9 million Dram is estimated to be necessary to screen all pregnant women in Armenia, and the incremental costs of linking the mothers found to be positive and their infants to additional prophylactic measures would be immediately cost saving. Furthermore, Armenia would be able to build on its past achievement of being validated for eliminating mother to child transmission of HIV in 2016, and eliminating the mother to child transmission of HBV within a matter of years, thus making the burden of HBV a thing of the past for all future generations of Armenians [20].

A combination of any of these prevention measures with even small increases in diagnosis and treatment, as the Stepwise scenario has shown, would have a large impact on the number of individuals suffering and eventually dying from the later stages of HBV.

The groundwork has already been laid for many changes to the screening and prevention protocols in Armenia. Through increases in prevention, diagnosis and treatment, the elimination of hepatitis C and B could become a reality in Armenia; and in all scenarios examined would not only save money, but most importantly, would save thousands of lives.

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