**Appendix**: Cost-Benefit Comparison of Two Proposed Overseas Programs for Reducing Chronic Hepatitis B Infection among Refugees: Is Screening Essential?

Amelia Jazwa, MSPH; Margaret S. Coleman, PhD, MA; Julie Gazmararian, PhD, MPH; La’Marcus T. Wingate, PharmD, PhD; Brian Maskery, PhD; Tarissa Mitchell, MD; Michelle Weinberg, MD, MPH

Corresponding Author: Brian Maskery

 1600 Clifton Road, MS E-03

 Atlanta, GA 30333

 wqm7@cdc.gov

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# Decision tree and Markov models

Supplemental Figure 1. Decision-Tree Model from TreeAge Pro for Cost-Benefit Analysis of ‘Screen, Then Vaccinate or Initiate Management’ and ‘Vaccinate Only’ Proposals

Overview of Decision-Tree Comparing ‘Screen, Then Vaccinate or Initiate Management’ to ‘Vaccinate Only’ Proposals



Hepatitis B Markov Nodes: Subset of Decision-Tree Model for Cost-Benefit Analysis with Expanded Markov Nodes



Hepatitis B Diseases Progression: Expanded Markov Nodes











# Chronic HBV Infection Disease State Descriptions

Note: In the Markov model, refugees with chronic HBV infection progress annually through disease states depending on immune response and treatment status. No refugee began in decompensated cirrhosis or hepatocellular carcinoma states during the screening process overseas because these individuals would be too sick to undergo travel for resettlement. Refugees in ‘Chronic HBV Infection’ state and ‘Compensated cirrhosis’ state can move to a less or more severe state. Refugees in ‘Decompensated cirrhosis’ state or ‘Hepatocellular carcinoma’ state can only move to more severe states. ‘Death from background causes’, ‘Recovery’, and ‘HBV-related death’ are end states in the model.

|  |  |
| --- | --- |
| **Disease State** | **Description** |
| Delayed clearance  | The HBV is cleared out of the body and the patient no longer considered to have chronic HBV infection or to be a carrier of infection [[1](#_ENREF_1), [2](#_ENREF_2)]. |
| Inactive carrier  | Asymptomatic infection in which the HBV is not actively replicating and limited damage is occurring to the liver [[1-3](#_ENREF_1)]. |
| Chronic HBV infection | HBV is actively replicating in the liver, but serious sequelae have not occurred [[1](#_ENREF_1), [2](#_ENREF_2)]. If aware of their disease status, a patient may undergo yearly treatment to keep the infection under control and prevent further sequelae. |
| Compensated cirrhosis | Scarring of the liver is occurring, but the patient has no clinical symptoms [[1](#_ENREF_1), [2](#_ENREF_2)]. If aware of their disease status, a patient may undergo yearly treatment to keep the infection under control and prevent further sequelae. |
| Decompensated cirrhosis | Significant scarring of the liver has occurred and the patient has severe and possibly life-threatening symptoms, such as variceal bleeding (hemorrhage from varices) and hepatic encephalopathy (reduction in brain function because the liver cannot remove toxins from the body) [[1](#_ENREF_1), [2](#_ENREF_2)]. This state requires yearly treatment and often becomes so severe that a patient will undergo a liver transplant. |
| Hepatocellular carcinoma | Cancer of the liver [[1-3](#_ENREF_1)]. This state requires yearly treatment and often becomes so severe that a patient will undergo a liver transplant.  |
| Liver transplant | An intensive surgery where the liver of the patient with chronic HBV infection is replaced with a donor liver [[1](#_ENREF_1), [2](#_ENREF_2)]. |
| Recovery | A successful liver transplant that leads to the clearance of the chronic HBV infection from the patient.  |
| HBV-related death | Death from any cause related to chronic HBV infection and sequelae. |
| Death from background causes | Death from any cause not related to chronic HBV infection and sequelae. |

# Chronic HBV Infection: Treatment Costs

Note: Treatment regimens for chronic HBV infection, compensated cirrhosis, and decompensated cirrhosis were collected from the *Red Book: Pharmacy's Fundamental Reference*. Multiple drug regimens exist for each disease state. An average annual cost of the possible drug regimens was used in the economic model, assuming an equal proportion of patients would be prescribed each regimen for a disease state.

|  |  |  |
| --- | --- | --- |
| **Disease State** | **Drug Regimen Options** | **Average Annual Cost** |
| Chronic HBV infection | 1. Peginterferon alfa-2a
2. Tenofovir Disoproxil Fumarate
3. Entecavir
 | $13,267  |
| Compensated cirrhosis | 1. Tenofovir Disoproxil Fumarate
2. Entecavir
 | $13,904  |
| Decompensated cirrhosis | 1. Adefovir Dipivoxil/Lamivudine
2. Tenofovir Disoproxil Fumarate /Lamivudine
3. Adefovir Dipivoxil /Telbivudine
4. Tenofovir Disoproxil Fumarate / Telbivudine
 | $25,108  |

# Prevalence calculations

We took five years of refugee entrance data using DHS data to estimate the fraction of the total refugee population that arrived from each of seven regions. The prevalence rate in each region was estimated from our Minnesota and Georgia data sets. Then, we applied the region-specific prevalence rates from our study to the DHS populations. This resulted in a slightly lower HBsAg+ prevalence rate (6.2% vs. 7.1%) relative to what would be estimated from just using the Georgia and Minnesota datasets. Since this rate was lower, we used it as our main result. We included a model with the unadjusted (7.1%) rate in the appendix because our sample size for some regions was too small to get accurate prevalence rates (e.g., 15 refugees from W. Asia and 57 refugees from E. Asia).

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Region | Total N (Data) | Total HBsAg+ | % by region of MN and GA data sets | HBsAg Prevalence per 100 persons (from data) | Refugee population (Total from DHS data 2005-2010) | % of popu-lation total | HBsAg prevalance (DHS data x prevalence) |
| East Asia/Pacific  | 57 | 6 | 0.3% | 10.53 | 101 | 0.0% | 10.64 |
| Europe  | 1,155 | 47 | 5.4% | 4.10 | 30,913 | 8.9% | 1268.92 |
| Latin America/ Caribbean  | 342 | 6 | 1.6% | 1.75 | 27,012 | 7.7% | 472.71 |
| North Africa/ Middle East | 1,453 | 47 | 6.8% | 3.25 | 53,595 | 15.4% | 1741.84 |
| South/ Southeast Asia  | 8,942 | 655 | 41.8% | 7.32 | 149,053 | 42.7% | 10910.68 |
| Sub-Saharan Africa | 9,444 | 762 | 44.1% | 8.07 | 88,142 | 25.3% | 7113.06 |
| West Asia | 15 | 0 | 0.1% | 0 | 237 | 0.1% | 0.00 |
| Total  |  21,408  |  1,523  | 100.0% | 7.1% | 349,053 | 100% |  21,518 (6.2%)  |

# Value of statistical life (VSL) calculations

A recent article in Vaccine summarized the reasons researchers may use the value of statistical life in economic evaluations of vaccination programs [[4](#_ENREF_4)]. One advantage of using VSL is the monetization of health benefits. By keeping benefits in dollar term instead of using other health utility units (e.g., QALYs or DALYs), both benefits and costs can be directly compared in a cost-benefit analysis. VSL has been used by other disciplines in the economic evaluation of government programs (e.g., Department of Transportation and Environmental Protection Agency). In our analysis, we used a conservative estimate of VSL compared to the $9 million estimate recommended by the Department of Transportation [[5](#_ENREF_5)].

VSL benefits were calculated on an annual basis by comparing the number of deaths in the SVIM versus VO scenarios each year. The number of deaths for each scenario in each year was multiplied by the VSL estimate to calculate mortality costs each year. Mortality costs were added to treatment costs to estimate the total cost of disease for each cohort each year. All costs were discounted at a 3% annual rate.

# Net benefit calculations with raw prevalence rate (7.1%)

We recalculated net benefits with the raw prevalence rates because of the limited sample sizes for some of the regions. This prevalence rate (7.1%) is somewhat larger than that calculated using the region-specific prevalence rates and DHS arrival rates. This estimate is probably more accurate for Georgia and Minnesota, but may be less accurate for the United States as a whole.

Net Benefits of ‘Screen, then vaccinate or initiate management’ (SVIM) compared with ‘Vaccinate Only’ (VO) program proposal for HBV infection, with varying domestic screening rates in VO proposal (2012 US$), prevalence rate= 7.1%

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Domestic Screening rate (%) | Years since implementation | VO cost/refugee  | SVIM cost/refugee | Net Benefit per refugee, no mortality valuationa | Total Net Benefit, no mortality valuationb | Number of HBV-associated deaths averted c | Total net benefit, with mortality valuationd |
| 30 | 5 | $264  | $386  | ($122) | ($7,100,000) | 33 | $140,000,000  |
|  | 10 | $607  | $712  | ($105) | ($6,100,000) | 82 | $350,000,000  |
|  | 15 | $958  | $1,002  | ($44)  | ($2,580,000)  | 128 | $510,000,000  |
| 50 (base case) | 5 | $331 | $386  | ($55) | ($3,200,000) | 23 | $110,000,000  |
|  | 10 | $712  | $712  | ($43) | ($2.500,000) | 59 | $250,000,000  |
|  | 15 | $1,003  | $1,002  | $1  | $60,000  | 91 | $370,000,000  |
| 70 | 5 | $398  | $386  | $12  | $700 ,000  | 14 | $66,000,000  |
|  | 10 | $731  | $712  | $19  | $1,100,000  | 35 | $150,000,000  |
|  | 15 | $1,047  | $1,002  | $45  | $2,630,000  | 55 | $220,000,000  |
| 90 | 5 | $465  | $386  | $79  | $4,600,000  | 4.7 | $26,000,000  |
|  | 10 | $793  | $712  | $81  | $4,700,000  | 12 | $55,000,000  |
|  | 15 | $1,092 | $1,002  | $90  | $5,270,000  | 19 | $79,000,000  |

a Net benefit = VO cost/person – SVIM cost/person

b Total net benefit = Net benefit per refugee\*size of the refugee cohort (N=58,538)

c Estimated from decision tree number of HBV-associated deaths averted = VO # deaths – SVIM # deaths without discounting

d Mortality Valuation: Value of Statistical Life = $5 million

[1] Fattovich G. Natural history of hepatitis B. Journal of hepatology 2003;39 Suppl 1:S50-8.

[2] Fattovich G, Bortolotti F, Donato F. Natural history of chronic hepatitis B: special emphasis on disease progression and prognostic factors. Journal of hepatology 2008 Feb;48(2):335-52.

[3] Schuppan D, Afdhal NH. Liver cirrhosis. Lancet 2008 Mar 8;371(9615):838-51.

[4] Laxminarayan R, Jamison DT, Krupnick AJ, Norheim OF. Valuing vaccines using value of statistical life measures. Vaccine 2014;32:5065-70.

[5] U.S. Department of Transportation. Economic Values Used in Analyses. 2013 March 1, 2013 [cited March 2013]; Available from: <http://www.dot.gov/regulations/economic-values-used-in-analysis>