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Amelia Lynn Jazwa Date

Comparing Proposed Hepatitis B Screening Policies for Refugees Newly Arriving to the United States

By

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Master of Science in Public Health

Epidemiology

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By

Amelia Lynn Jazwa

B.S., The University of North Carolina at Chapel Hill, 2011

Thesis Committee Chair:
Julie Gazmararian, PhD, MPH

An abstract of
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Abstract

Comparing Proposed Hepatitis B Screening Policies for Refugees Newly Arriving to the United States

By Amelia Lynn Jazwa

Background: Chronic Hepatitis B Virus (HBV) infection is a serious and costly disease that affects over 2 million people worldwide. Refugees arriving to the United States are at an increased risk of chronic HBV infection due to high prevalence rates in their countries of origin and high-risk settings in refugee camps. In addition, refugees are at increased risk of serious sequellae from chronic HBV infection because they are not screened for the virus overseas and may reside for years in the United States without knowing their infection status.

Methods: A cohort of 26,548 refugees who arrived in Minnesota and Georgia between the years 2005-2010 was analyzed for prevalence of chronic HBV infection. Logistic modeling was used to determine differences in odds of disease by age, sex, and arrival year. This prevalence information was used to perform a cost-benefit analysis of two overseas screening policies: 'Screen and vaccinate' and 'Vaccinate only'.

Results: The estimated period prevalence of chronic HBV infection was 6.8% for the overall arriving refugee population and 7.1% in those ages 6 and older. Females had 0.66 times the odds of being HBsAg positive compared to males, controlling for age and arrival year ($p<0.001$). The odds of being HBsAg positive increased 1.01 times with each year of age, controlling for sex and arrival year ($p<0.001$). The 'Screen and vaccinate' policy was cost-beneficial compared to the 'Vaccinate only' policy. While the up-front costs of the 'Screen and vaccinate' policy are higher ($154,083.72 vs. $73,757.88, n=58,538 refugees), the 'Screen and Vaccinate' policy displays a positive net benefit, even after only 5 years from policy initiation.

Conclusions: Refugees arriving to the United States bear a moderate-to-high burden of chronic HBV infection. The main benefits of the 'Screen and vaccinate' policy come from early medical management of chronic HBV infection. An overseas screening policy to reduce the effects of long-term sequellae can reduce costs for the refugee and society as a whole. Further, while not quantified, controlling chronic HBV improves quality of life for resettled refugees.

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Table of Contents

Introduction

Chronic Hepatitis B Virus (HBV) infection places a significant burden on many populations throughout the world. Around 2 billion people are infected worldwide, with more than 350 million people carrying chronic infection with HBV, placing them at risk for developing cirrhosis, liver cancer, and other chronic liver diseases (1). Consequently, chronic HBV infection-related liver disease leads to approximately 600,000 deaths worldwide each year (2). Asian and Central and South African countries exhibit some of the highest rates of chronic HBV infection, with prevalence greater than 10% in some countries (3).

Two United States government agencies, the Department of State and Health and Human Services, fund the provision of care for refugees resettled domestically from around the world. Many of these refugees arrive stateside from Asian and African countries with high chronic HBV prevalence. The purpose of this study is to estimate the prevalence of chronic HBV infection among refugees newly arriving to the United States and to use this prevalence estimate to calculate which of two overseas policy options is most cost-beneficial at reducing the health burden of HBV infection. In the '*Vaccinate only*' policy option, refugees will receive no HBV screening overseas but instead will all be vaccinated overseas against HBV, except where medically contraindicated or history of vaccination is available. In the '*Screen and vaccinate*' option, refugees will first be screened for Hepatitis B and then those without infection or history of vaccination will be vaccinated overseas. We draw on data from a six-year cohort of refugees that arrived to the states of Minnesota and Georgia between 2005 and 2010 and who were screened for chronic HBV infection to compare the two options.

Background

Biology, Transmission, and Clinical Features

HBV is an infectious, hepatotropic virus that targets the cells of the liver. HBV is shed through a variety of bodily fluids (2), and consequently transmitted through blood, saliva, semen, and vaginal secretions, and, to a lesser extent, other bodily fluids, such as breast milk (4). HBV can survive on surfaces in the environment and be transmitted through contact for up to 7 days (4, 5). The virus enters the liver via the bloodstream and replicates only in the liver (2).

HBV infection can self-resolve or lead to either an acute infection or chronic disease. Acute infection is asymptomatic in about 50% of infected individuals. When acute infection is symptomatic, individuals can present with symptoms of anorexia (loss of appetite), nausea, vomiting, abdominal pain, and jaundice. Acute infection can lead to severe complications including fulminant hepatitis (acute liver failure) (5, 6). About 5% of acute infections in adults convert to chronic infections, and 75% of these chronic cases will remain asymptomatic until the onset of cirrhosis and/or end-stage liver disease. The other 25% of chronic HBV infected individuals progress to symptomatic illness and die prematurely from cirrhosis, liver cancer, or other liver disease (5).

Chronic HBV Infection Epidemiology among Refugees in the United States

Between 47% and 70% of current chronic HBV cases in the United States originate outside of the US (7), and a small number of these cases are found in refugees. In 2010, the US resettled over 73,000 refugees, with almost 53,000 arriving from Asian countries and another 13,000 from African countries (8). Many of the newly arriving refugees come from countries with intermediate to high prevalence of chronic HBV

infection, estimated using Hepatitis B surface antigen (HBsAg) screening test positivity as a proxy for chronic HBV infection prevalence (4, 9). In addition, Hepatitis B vaccination coverage is less than 75% on average in South-East Asian and African countries (10).

Estimates of chronic HBV infection prevalence in refugees in the US vary across regions, ranging from 7% to 11% percent (1, 9, 11, 12). Some states and cities act as hubs for refugees from specific countries. For example, California resettles a significant proportion of refugees arriving from Iraq and Iran, while Florida resettles the majority of Cuban refugees; this may account for the variation in current estimates of the prevalence of chronic HBV infection among refugees (13).

Refugees are required by public health regulations developed by the Centers for Disease Control and Prevention (CDC) to undergo medical screening before arriving in the US. This screening is aimed specifically at detection of diseases and conditions that are legally defined by regulation as diseases of public health significance, e.g. tuberculosis disease. These diseases need to be treated before the refugee can enter the US. Hepatitis B is not on this list of diseases of public health significance that must be treated prior to entry and therefore is not included in routine screening overseas. Many refugees receive screening shortly after they arrive in the US, but are not required to be vaccinated or screened for HBV until they apply to become legal permanent residents (LPRs), usually a year after arrival (14). This potential time gap can delay identification of chronic HBV infection, and consequently delay medical management to prevent disease progression, as well as hamper prevention efforts to reduce disease spread.

While US Refugee agencies in some states have high screening rates for chronic HBV infection (e.g. 85-99%), other agencies have low (e.g. 31%) or undocumented screening rates, potentially allowing chronically infected individuals to slip through the cracks and continue living without knowledge of their infection (15-18). Not knowing one's infection status can worsen health outcomes for the chronically infected individuals and lead to these individuals unknowingly spreading the disease to others.

Cost Burden of Chronic Hepatitis B Virus Infection

Chronic HBV infection is a serious and potentially costly disease. Currently, there is no cure for chronic HBV infection; infected individuals need ongoing medical management to monitor for the development and slow progression of liver disease and liver cancer. Such management can be costly, with estimated per-case drug costs ranging from $1,500 to $16,000 or more annually, depending on the severity of liver degradation (19, 20). If the liver becomes completely compromised, a liver transplant is necessary and can cost more than $140,000 for the surgery, and many thousands of dollars more for post-surgical care (19, 20).

Prevention of infection through vaccination, or diagnosis of infection at an earlier stage when prevention of serious late-stage sequellae is more feasible, has been shown to be cost-effective (20-22). While these cost-analyses provide useful knowledge for screening high risk individuals in developed countries, it is important to determine whether screening for chronic HBV infection in refugees overseas provides a cost-beneficial procedure to detect cases of chronic HBV infection and to vaccinate only those who need it.

Screening and Vaccination Processes

Screening for chronic HBV infection in refugees is a mechanism to detect HBV infection in the early acute stage or to initiate vaccination in the uninfected to prevent chronic HBV infection. Screening has become less costly with the development of new tools for assays, in particular a rapid screening test. The rapid screening test is quick, inexpensive, and only requires the collection of a small blood spot, rather than a venous blood draw (23). Currently the Advisory Committee on Immunization Practices (ACIP) recommends that all foreign-born persons including immigrants, refugees, and internationally adopted children born in Asia, the Pacific Islands, Africa, and other regions in which chronic HBV infection is highly endemic, should be tested for HBsAg, regardless of their vaccination status (6).

Vaccination provides immunity against chronic HBV infection. A Hepatitis B recombinant vaccine was licensed in the United States in 1986 (5), and by 1991, a strategy for chronic HBV infection elimination through vaccination was set in motion. The vaccine is given in a three-dose series, with the highest antibody titer occurring after the third dose (5). The ACIP recommends universal vaccination of infants with the Hepatitis B vaccine and catch-up vaccination for children for whom this vaccine is not documented. In addition, it is recommended that uninfected, unvaccinated household and sexual contacts of those with a positive test result for chronic HBV infection be vaccinated (6).

Gaps in current literature in the U.S.

In currently published work, screening has been shown to be cost-effective but under varying circumstances and with limited studies specific to refugee populations (19-

22, 24-27). For example, one study of screening and subsequent treatment for chronic HBV infection in the US shows cost effectiveness with infection prevalence as low as 0.3%, yet, a study of Akha tribal children in Northern Thailand showed that screening for chronic HBV infection before vaccination was cost-effective only if the population prevalence of infection was >22% (20, 26). These varying results provide evidence that there is information missing on the costs and benefits of HBV screening and Hepatitis B vaccination in general, and especially in refugees resettling in the US. In addition, the varying estimates of chronic HBV infection prevalence among refugees resettled in the United States could affect the estimates of cost-benefit ratios that result from economic evaluations of policies to screen refugees for chronic HBV infection (1, 9, 11, 12). This analysis seeks to obtain a better estimate of the prevalence of HBV among refugees newly arriving to the United States and then use this estimate in a cost-benefit analysis to compare the effects of only vaccinating or screening and vaccinating prior to arrival.

Pilot Study and Population Focus

The CDC is currently executing a pilot project that offers voluntary testing and treatment for certain medical conditions, including for intestinal parasites, anemia, and chronic HBV infection, to U.S.-bound refugees at the time of the initial required medical assessment in Thailand (Mae Sot). A few of the major purposes of this pilot project are to determine the prevalence of chronic HBV infection in two populations of Burmese refugees resettling to the United States from Thailand and Malaysia, to provide education to and further medical evaluation of those determined to be infected, and to vaccinate those who are uninfected. To extend this pilot project, CDC is interested in determining whether screening all refugees overseas is cost-beneficial as compared with simply

vaccinating the entire population.

While not screening and only vaccinating all refugees against Hepatitis B would be a simpler policy to administer, there might be increased costs over time for undiagnosed chronic HBV cases. Although most refugees receive additional medical evaluation after domestic arrival, this initial post-arrival exam competes with many other important priorities such as learning a new language, finding a home and job, and placing children in school. Further, not all states administer refugee exams expeditiously so some might not be screened and diagnosed, or be diagnosed a year or more after arrival in the US. If, on the other hand, 100% of all refugees can be screened during the required overseas medical exams, refugees with chronic HBV infection could arrive in the United States with medical management plans and enter medical care earlier to prevent more serious and costly sequellae. Arriving with knowledge of disease would, hopefully, push the refugee to prioritize his/her own medical care. In addition, vaccinating only those who have never been exposed to the disease could reduce vaccination costs.

The overarching question is, would the cost of the 'Screen and vaccinate' policy, as compared with the 'Vaccinate only' policy, avoid enough costs of late-stage medical treatment and premature death to make the 'Screen and vaccinate' policy worthwhile?

Methods

Overview

This cohort study was conducted to determine chronic HBV infection prevalence using unique, original datasets from the Minnesota Department of Health and the Georgia Department of Public Health for the years 2005-2010 with a study population of 26,548 refugees. The policies of 'Screen and vaccinate' and 'Vaccinate only' for chronic HBV infection in this population were then compared using economic analysis.

The epidemiologic analysis of this population included calculating the 6-year prevalence estimate of chronic HBV infection for the years 2005 to 2010, the trend in yearly prevalence of chronic HBV infection between 2005 and 2010, and the estimated average number of chronic HBV cases entering the United States each year. In addition, logistic modeling was used to estimate the odds of chronic HBV infection by age, sex, and arrival year.

The economic estimates were calculated from a societal perspective that included costs for: policy implementation and administration; disease medical care; and premature death. Estimates were made using population analysis in a decision tree model that compared the 'Vaccinate only' policy with the 'Screen and vaccinate' policy. In the 'Vaccinate only' policy option, refugees will receive no HBV screening overseas but instead will all be vaccinated overseas against HBV, except where medically contraindicated or history of vaccination is available. In the 'Screen and vaccinate' option, refugees will first be screened for Hepatitis B and then those without infection or history of vaccination will be vaccinated overseas. At each node of the decision tree the population was adjusted by the likelihood of the event that the node represents, e.g. testing positive or needing vaccination. The risk-adjusted population at each node was

multiplied by the cost of screening, vaccination, or treatment, as appropriate. A final net benefit was calculated by subtracting the cost per refugee of the 'Screen and vaccinate' policy from the 'Vaccinate only' policy and multiplying this by the average number of refugees that arrived to the US each year between 2005 and 2010. All benefits and costs were discounted to present values.

Study Population

The study population consisted of a cohort of refugees that arrived to the United States and were resettled in the states of Minnesota and Georgia between the years 2005 to 2010. The cohort consisted of 26,548 refugees of all ages, male and female, from 82 different countries of origin, and who had received a screening test for Hepatitis B surface antigen (HBsAg), a proxy for chronic HBV infection.

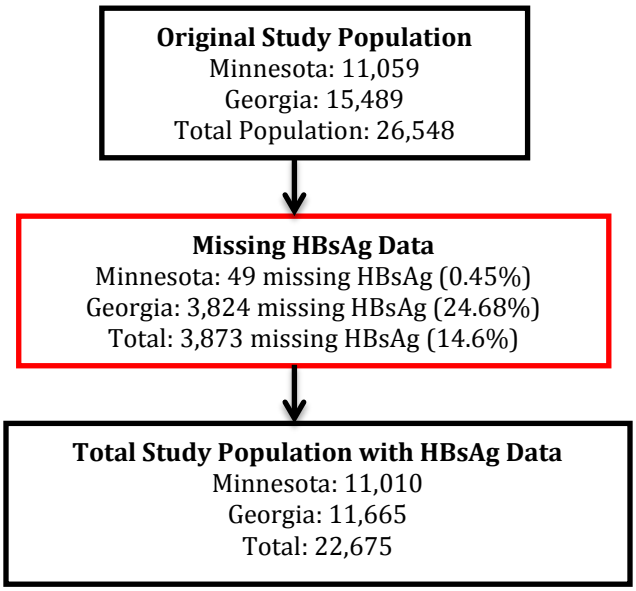
Original Data Sources

The Minnesota Department of Health and Georgia Department of Public Health provided de-identified records of refugees screened for Hepatitis B after arrival in these states during 2005 to 2011. The data included the variables of interest: Hepatitis B surface antigen (HBsAg) test result; vaccination status; and demographics such as, age, sex, and country and region of origin.

The Georgia dataset contained information for all foreigners and their I-94, or non-immigrant, status. The possible categories of the I-94 status included Refugees, Asylees, Cuban/Haitian Entrants, Special Immigrant Visa Iraqis, and Victims of Human Trafficking. All observations that were not coded as 'Refugee' were deleted (1,583 observations out of 17,072 deleted = 9.3% of the data) leaving 15,489 refugee observations. All 11,059 observations in the Minnesota dataset were refugees.

The Georgia and Minnesota datasets were then reviewed for completeness of the variable HBsAg screening test, since HBsAg positivity was used as a proxy for chronic HBV infection in this study. This process is summarized in Figure 1. Any observation that did not indicate a positive or negative test result was deleted, including 'Indeterminate', 'Not Done', 'Pending', and 'Missing' (Minnesota dataset) or 'Missing' and 'Not Tested' (Georgia Dataset). For Minnesota, 0.45% of observations were deleted. For Georgia, 24.7% of observations were deleted. Together at this stage, the datasets originally contained 26,548 observations; 14.6% of the total data were deleted, leaving 22,675 observations for descriptive statistics and analysis of chronic HBV infection prevalence. No imputation methods were used to replace missing data.

Figure 1. Refugee Study Population



The datasets for Minnesota and Georgia were both condensed to only variables that overlapped between the datasets and that were of interest for the analysis, including HBsAg test status, vaccination status, country of origin, region of origin, age, sex, arrival year, and US state of resettlement. The variables that were kept in both datasets are

described in Appendix A. The datasets were concatenated and observations kept their individuality with a unique identifier for each subject.

Secondary Data Sources

Inputs were estimated using a variety of secondary sources. These inputs included:

- Average number of all refugees resettling in the United States
- Calculated costs of overseas labor
- Cost information for overseas screening and vaccination supplies and procedures
- Domestic costs for medical management of chronic HBV infection
- Chronic HBV infection annual transition probabilities
- Background mortality for causes of death other than HBV sequellae

The inputs of interest, their purposes, and the data sources where the information was obtained are summarized in Table 1.

Table 1. Summary of Data Sources Used for Analysis of Overseas Screening Programs for Chronic HBV Infection Among Refugees Arriving to the United States

Input Variable	**Purpose**	**Data Source**
Average number of refugees entering the US annually	Calculate yearly and overall estimated number of chronic HBV cases entering the US in the newly arriving refugee populations	Department of Homeland Security (8)
Overseas Refugee Camp Labor Costs	Economic model input	United Nations (28)
Overseas screening and	Economic model input	CDC (Dr. Margaret

vaccination supplies costs		Coleman, personal communication)
Domestic costs for medical management of chronic HBV infection (allowable charge data)	Economic model input	Physician's Fee and Coding Guide (29)
Domestic costs of medical protocols for chronic HBV infection	Economic model input	Red Book: Pharmacy's Fundamental Reference (30)
Chronic HBV transition probabilities for natural and treatment-related disease progression	Economic model input	Literature Sources (21, 22, 31-34)
Background mortality in the US for 2005-2010	Economic model input	CDC WONDER database (35)

Epidemiologic Analysis

First, initial univariate analyses were run to determine distributions of variables of interest (region, country, arrival year, sex, age, HBsAg positivity, and % Vaccinated) for the total population and then restricted to those 6 years of age and older, with no upper age restriction. The literature indicates that there are varying transition probabilities to chronic HBV disease for those 5 years and younger, but after 5 years of age, the transition probabilities even out (5). We included only those 6 years of age and older in analyses because the economic model would be more stable and provide a more accurate

analysis. Second, the normality of the continuous variables was assessed; the age predictor was slightly right skewed but did not warrant transformation for logistic modeling. Third, bivariate analyses were run to examine HBsAg positivity by region, country, arrival year, sex, and age. Age was grouped into 5 relevant categories for easier interpretation (Appendix A).

These descriptive statistics were used to determine prevalence statistics. First, Hepatitis B prevalence was calculated as follows:

$$Chronic\ HBV\ prevalence\ (\%) = \frac{Number\ of\ refugees\ tested\ positive}{Number\ of\ refugees\ tested} * 100$$

Second, percent change in chronic HBV infection positivity from year to year was calculated with the following equation:

$$Percent\ change = \frac{(Current\ year\ prevalence - Previous\ year\ prevalence)}{Previous\ year\ prevalence} * 100$$

The significance of the chronic HBV infection positivity variation from year to year was determined with chi-square analysis. Third, the yearly and overall estimated number of chronic cases entering the US in the newly arriving refugee populations was determined by standardizing Minnesota and Georgia state estimates to the United States refugee population using the following equation:

$$Estimated\ \#\ Chronic\ HBV\ Cases = HBV\ Prevalence \times Total\ \#\ arriving\ refugees$$

Fourth, logistic regression was run with the predictors age, sex, arrival year, region of origin or country of origin, and the outcome of HBsAg positivity. Age was entered in the model as a continuous variable and also as a 5-group categorical variable; centering of the continuous age variable at 6 years or at the median age was also considered for regression analysis of this cohort, but centering did not affect regression results. Sex was entered as a categorical (1/0) variable. Arrival year was entered into the model as an

ordinal categorical variable because it was assumed that arrival year has a linear impact across each one-year increment. Region of origin was used in the model to determine if there was variation in the estimates of the other predictors by region. Country of origin was considered as well, but bivariate analysis of cell count sizes for the HBsAg variable by country were less than 5 for many countries so estimates would be unstable and interpretation difficult.

All epidemiologic analyses were performed using SAS version 9.3 (Cary, NC). An alpha of 0.05 was used for all statistical tests performed, including chi-square, t-test, and logistic modeling.

Economic Analysis

The procedure for the economic analysis is described below in detail. Important assumptions made for performing the cost-benefit analysis are outlined first. Subsequently, the decision tree and Markov model used for analysis will be illustrated. Finally the procedure for the cost-benefit analysis of the 'Screen and vaccinate' and 'Vaccinate only' policies is explained.

Assumptions

1. Only patients age 6 and older were included because acute to chronic infection transition probabilities for HBV levels out around age 6 (5).
2. In the 'Vaccinate only' policy, refugees may undergo screening in the United States; the probability of being screened is the same for those who are HBsAg positive and HBsAg negative. In the 'Screen and vaccinate' policy, no individual will be screened upon arrival to the US, with the assumption that they will arrive with documentation of previous screening.

3. In the ‘Vaccinate only’ policy, those who were vaccinated but who have disease and are not screened in the United States undergo a natural history of disease progression, which leads to higher probabilities of serious sequellae, while those who are screened in the United States undergo a treatment-related annual progression with lower probabilities of serious sequellae. In the ‘Screen and vaccinate’ policy, all refugees who are HBsAg positive undergo a treatment-related annual progression with lower probabilities of serious sequellae.
4. There is 100% compliance with initial screening and vaccination, regardless of screening protocol.
5. There is 100% sensitivity and specificity of the screening test. There is also 100% effectiveness of the vaccine for those uninfected with HBV.
6. There is a homogenous population in regards to chronic HBV transition probabilities. From logistic modeling of the population ages 6 and above, it was determined that there were no statistically significant differences of prevalence by region in the odds of chronic HBV infection stratified on sex, age, and arrival year.
7. For the ‘Screen and Vaccinate’ Policy, individuals who are HBsAg positive should not be vaccinated (7.1%), as recommended by the Advisory Committee for Immunization Practices (36).
8. For both the ‘Screen and Vaccinate’ and ‘Vaccinate only’ policies, 30% of individuals are assumed to have a history of vaccination and will not be vaccinated for Hepatitis B. The 30% estimate comes directly from the Georgia

Department of Public Health and Minnesota Department of Health datasets; this is only an estimate and can vary by state and by year.

9. Since screening is occurring along an unknown time point in an infected individual's disease progression, we assumed that some individuals would already have compensated cirrhosis; we assumed no one would have decompensated cirrhosis or Hepatocellular Carcinoma during the screening process in the refugee camps because these individuals would most likely be too sick to undergo the travel and medical screening at the camp and would thus be excluded from the screening group (37, 38).
10. In regards to overseas costs, when there is a wide range of variety in how medical services are delivered in different locations, the pricing or cost in one or a couple of locations is no more likely to be an accurate reflection of other locations than an average would be (Dr. Margaret Coleman, CDC, "personal communication", 2013). For this reason, the costs for overseas screening were estimated from UNICEF and the International Drug Price Indicator Guide rather than attempting to calculate costs for multiple specific locations.
11. A 100% overhead cost was added to each overseas screening test and vaccination cost to account for overseas medical staff costs, transportation, security, vaccine administration, maintenance of vaccine cold chain, and other costs related to performing the screening test and/or vaccination.
12. The age-adjusted background mortality rate, calculated from United States age-specific mortality rates, reflects the background mortality rate in refugees.

13. The chronic HBV mortality estimated by the decision tree model reflects the chronic HBV mortality rate in refugees in general. From the literature, it was estimated that about 1.1% of the 2000 global birth cohort would be expected to die prematurely from HBV-related causes, with specific estimates of 1.2% in Africa, 1.1% in Southeast Asia, and 2.2% in the Western Pacific, and including countries of low, intermediate, and high endemicity (39). While our study population represented a cohort with an intermediate/high chronic HBV endemicity, the cohort represented 80 different countries, which indicates that our chronic HBV mortality of slightly more than 2.2% of deaths in the cohort aligns with previous global estimates.

Decision Tree

The economic analysis is based on a decision tree model that compares the two overseas screening policies of 'Screen and Vaccinate' and 'Vaccinate only'. Figure 2a and 2b are a simplified reproduction of the decision tree sequencing for the two screening policies. At each node, the entering population is reduced by the associated risk. For example, in Figure 2a at node 1, 92.9% of refugees test negative and proceed to vaccination node, while 7.1% will test positive and proceed to different disease progression states. At each node the cost of each step (e.g., screening test, vaccination, illness, and death) is multiplied by the relevant risk-adjusted population. In addition, individuals that have chronic HBV infection can transition through multiple disease states, which are represented with a Markov model.

Figure 2a. Simplified Decision Sequence for 'Screen and Vaccinate' Policy of Decision Tree Comparing Hepatitis B Screening Policies for Refugees Newly Arriving to the US

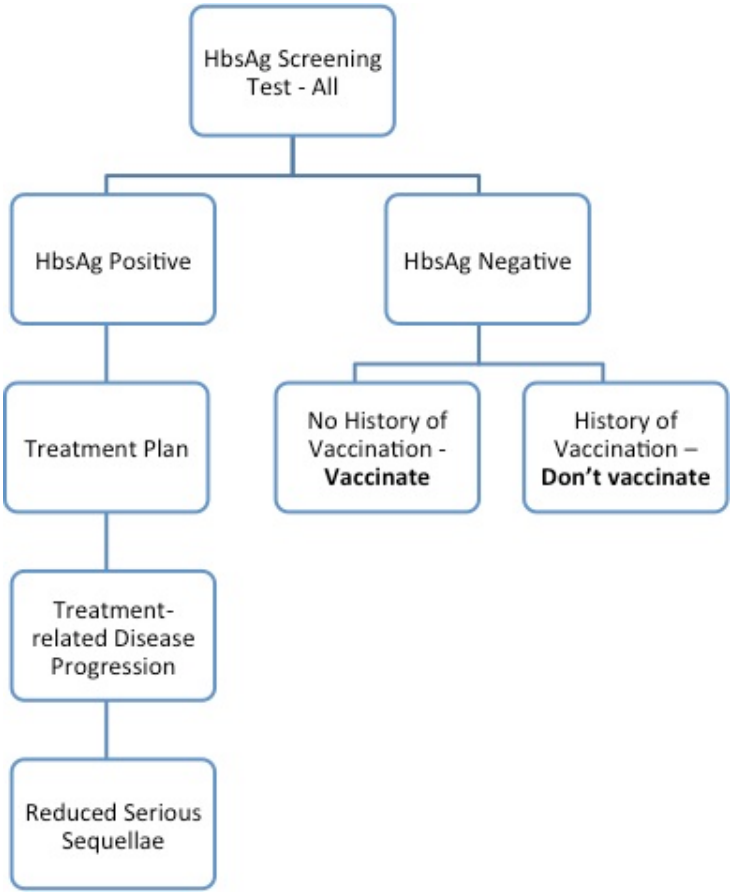
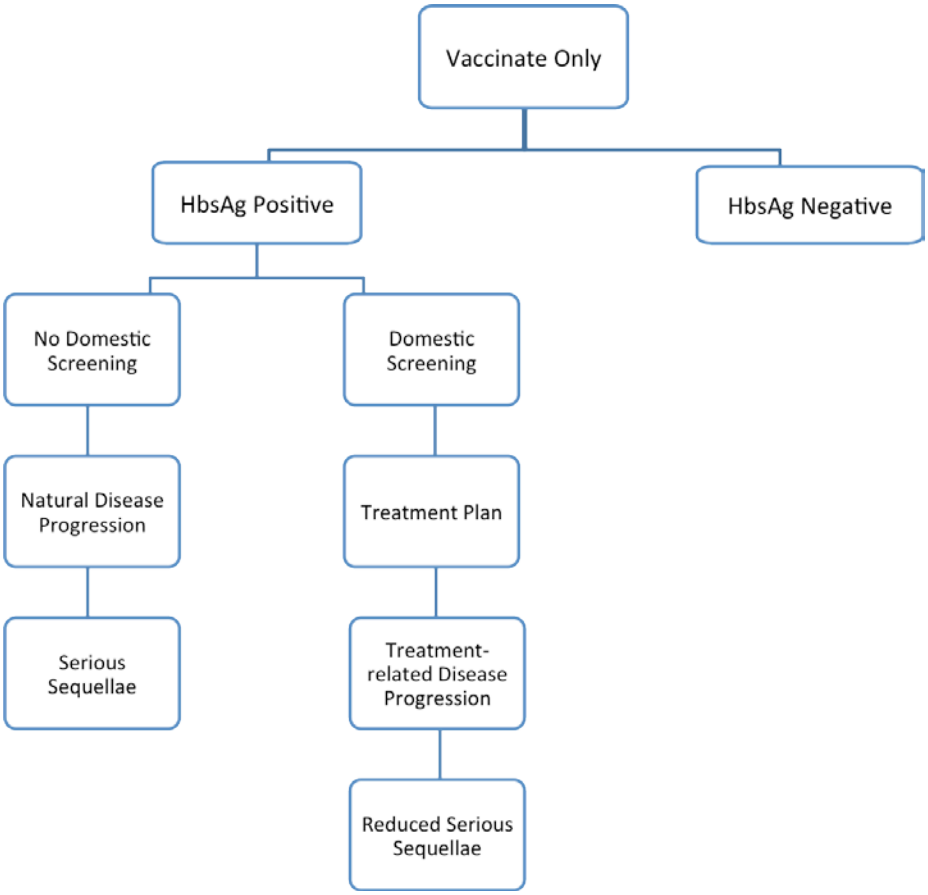


Figure 2b. Simplified Decision Sequence for 'Vaccinate only' Policy of Decision Tree Comparing Hepatitis B Screening Policies for Refugees Newly Arriving to the US



Markov Model

Chronic HBV infection is not a static disease. Individuals can transition from asymptomatic states to symptomatic states and back again in some cases, depending on individual immune response and treatment status (32, 37, 38). For this reason, a Markov model was used to create a more realistic representation of chronic HBV infection transition states. Disease states considered in this model include the inactive carrier state, chronic HBV infection, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and death. The inactive carrier state is asymptomatic infection where the HBV is not actively replicating and limited damage is occurring to the liver (32, 38).

Chronic HBV infection is a disease state where the virus is actively replicating in the liver but serious sequellae have not occurred (32, 38). Compensated cirrhosis is a disease state where scarring of the liver is occurring but a patient does not present with clinical symptoms (38). Decompensated cirrhosis is a disease state where there is significant scarring of the liver and a patient presents with severe and possibly life-threatening symptoms, such as variceal bleeding (hemorrhage from varices) and hepatic encephalopathy (reduction in brain function because the liver can not remove toxins from the body) (39). Hepatocellular carcinoma is cancer of the liver, a rapidly advancing disease state (32, 38).

In the initial Markov stage, an infected individual started in either the 'Inactive Carrier' state, the 'Chronic HBV Infection' state, or the 'Compensated Cirrhosis' state (Appendix B). From the initial disease states, individuals could transition to an array of states. Transition probabilities for disease states are described in Appendix C. A background mortality rate was used to account for individuals who may die from other competing causes besides chronic HBV infection. Background mortality was calculated by multiplying the age-specific study population by age-specific rates from CDC WONDER for 2005-2010, summing age-specific estimated study population cohort deaths, and dividing by the total study population to obtain a background mortality rate of 2.4 per 100,000 population.

Cost-Benefit Analysis

Economic analyses were performed using the TreeAge Pro Suite 2009 (Williamstown, MA). The decision tree model was entered into TreeAge Pro with associated probability parameters and costs (Appendix B). Appendices C and D describe

the parameter and cost estimates used in the economic model. After these probabilities and costs were entered into the model, benefits and costs were discounted to present values at a discount rate of 3%. A final net benefit was calculated by subtracting the cost per person of the 'Screen and vaccinate' policy from the 'Vaccinate only' policy. A cohort of 58,538 refugees was used to estimate total policy net benefits because this was the average number of refugees entering the United States over the 6-year period of data utilized for analysis. The Value of Statistical Life (VSL) represented death monetarily at a value of $5,000,000. Analyses were performed with and without the VSL in the model. In addition, sensitivity analyses were performed for time since policy initiation (5 years, 10 years, and 15 years) and the proportion screened in the US in the 'Vaccinate only' arm (30%, 50%, 70%, and 90%).

Ethical Considerations

The study was submitted to CDC IRB, Emory University IRB, Georgia Department of Public Health IRB, and the Minnesota Department of Health IRB for review; all four institutions deemed this study exempt from review because it uses previously collected de-identified data and does not involve contact with human subjects.

Results

Epidemiology of HBsAg Positivity in Refugees Arriving to the US

Of the total sample refugee population from 2005-2010, the mean age was 26.1 and 48.4% were female. Of the population greater than 6 years old, the mean age was 27.4, 48.3% were female, and 85.9% of individuals arrived from countries in Sub-Saharan Africa and South/Southeast Asia (Table 2). The estimated period prevalence of chronic HBV infection for the period 2005-2010 was 6.8% for the overall arriving refugee population and 7.1% in those ages 6 and older. Almost one-third (30.6%) of refugees age 6 and older had received at least one dose of the HBV vaccine before arriving in the US.

Table 2. Descriptive Statistics for Study Cohort of Refugees Newly Arriving to the US Between 2005-2010

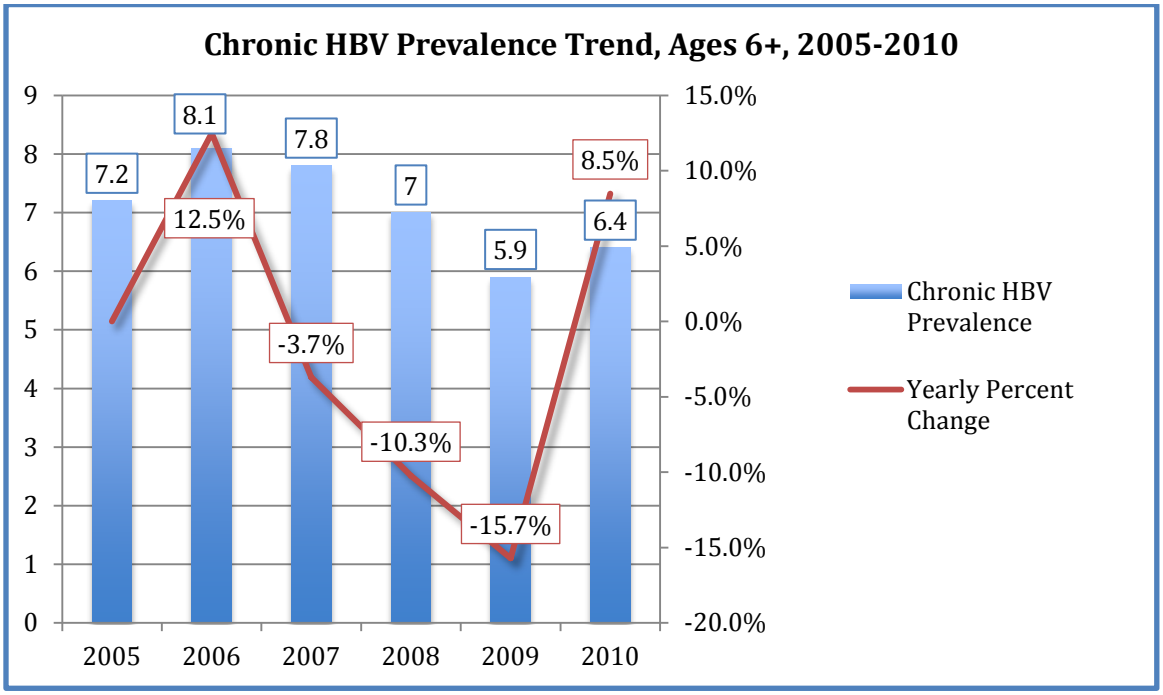
Variable	All Ages (N=22,675)	Ages 6+ (N=21,409)
AGE, Mean(SD)	26.1 (16.5)	27.4 (16.0)
IQR* (25%, 50%, 75%)	(14.7, 22.0, 35.0)	(16.0, 22.9, 36.0)
Age Category, n(%)		
<1	184 (0.8)	------
1-5	1,082 (4.8)	------
6-10	2,196 (9.7)	2.196 (10.3)
11-18	5,218 (23.0)	5,218 (24.4)
19+	13,995 (61.7)	13,995 (65.3)
Female, n(%)	10,966 (48.4)	10,334 (48.3)

REGION, n(%)		
East Asia/Pacific	59 (0.3)	57 (0.3)
Eastern Europe	1,194 (5.3)	1,144 (5.3)
Latin America/Caribbean	348 (1.5)	342 (1.6)
North Africa/Middle East	1,551 (6.8)	1,453 (6.8)
South/Southeast Asia	9,573(42.2)	8,942 (41.8)
Sub-Saharan Africa	9,922(43.8)	9,444 (44.1)
Southern Europe	11 (0.1)	11 (0.1)
West Asia	16 (0.1)	15 (0.1)
Missing	1	1
ARRIVAL Year, n(%)		
2005	1,432 (6.3)	1,395 (6.5)
2006	5,305 (23.4)	5,037 (23.5)
2007	3,740 (16.5)	3,540 (16.5)
2008	3,124 (13.8)	2,957 (13.8)
2009	3,860 (17.0)	3,647 (17.0)
2010	5,214 (23.0)	4,833 (22.6)
HBsAg, n(%)		
Positive	1,546 (6.8)	1,515 (7.1)
Negative	21,129 (93.2)	19,894 (92.9)
Vaccinated, any, n(%)	7,226 (31.9)	6,557 (30.6)

*IQR = Interquartile Range

The prevalence of chronic HBV infection significantly varied from year to year in refugees age 6 or older ($p<0.001$). Chronic HBV infection prevalence increased from 2005 to 2006, decreased each year from 2006 to 2009, and increased again in 2010 (Figure 2).

Figure 2. Chronic HBV Prevalence Trend with yearly Percent Change for Study Cohort of Refugees Newly Arriving to the US Between 2005-2010, Ages 6+



On average, each year during the 2005-2010 period there were 4,156 refugees, ages 6 years and older, entering the United States with chronic HBV infection (Table 3). There were an estimated 24,937 total cases in refugees age 6 and older entering the United States between 2005 and 2010.

Table 3. Estimated Annual Number of Refuges Entering the US Infected with HBV, by Arrival Year, Ages 6+

Arrival Year	HBsAg Prevalence (per 100 refugees)	Total refugees entering the US	Estimated HBV cases
2005	7.2	53,738	3,869
2006	8.1	41,053	3,325
2007	7.8	48,281	3,766
2008	7.0	60,193	4,214
2009	5.9	74,654	4,405
2010	6.4	73,311	4,692
6-year Average	7.1	58,538	4,156
6-year Total	7.1	351,230	24,937

Logistic modeling demonstrated that region of origin did not significantly affect odds ratio estimates for age, sex, and arrival year. The final model, Model 2, contained the predictors age, sex, and arrival year and the outcome HBsAg positivity (Appendix D). Females had 0.66 times the odds of being HBsAg positive compared to males, controlling for age and arrival year ($p<0.001$). The odds of being HBsAg positive increased 1% with each year of age, controlling for sex and arrival year ($p<0.001$). The odds of being HBsAg positive in each subsequent arrival year was 0.93 times the previous year, showing a decreased odds of HBsAg over the study period, controlling for age and sex ($p<0.001$).

Cost-Benefit Analysis

The 'Screen and vaccinate' policy was more cost-beneficial than the 'Vaccinate Only' policy at all time points analyzed (5 years, 10 years, and 15 years) when the Value of Statistical Life (VSL) was set to US $5,000,000. While the initial costs for the 'Screen and vaccinate' program were more than the 'Vaccinate only' program ($154,084 vs. $73,758, respectively; n=58,538 refugees), the 'Screen and vaccinate' program showed a positive net benefit, due to avoided serious sequellae and reduced number of chronic HBV deaths (Tables 4).

The results changed with several variables including time since initiation of the screening program and proportion screened in the United States in the 'Vaccinate only' program. We do not know how domestic health departments will change their HBsAg screening policies in reaction to either an overseas 'Screen and vaccinate' or 'Vaccinate only' program, but we do know that far from all refugees are currently screened in the US (15-18). For this reason, conservative results of domestic HBsAg screening of 50% and 70% of all refugees are presented here (Table 4). Results of a sensitivity analysis of 30% and 90% screened domestically are presented in Appendix E. Where the net benefit is negative, the 'Vaccinate only' policy is the preferred option. Where the net benefit is positive, the 'Screen and vaccinate' policy is the preferred option. Since the net benefit is positive in 6 out of 8 scenarios presented, it is the overall preferred option. The only two negative benefit scenarios utilized a VSL equal to $0, so 'Vaccinate only' is preferred only when premature death is not valued.

Table 4. Net Benefits of 'Screen and vaccinate' compared to 'Vaccinate only' Policy for HBV infection, 50% and 70% domestic screening in 'Vaccinate only' Program

	VSL[+]		5 year cost	10 year cost	15 Year cost
50% Domestic Screening	**$0**	Screen and Vaccinate cost/refugee	$701	$1,204	$1,585
		Vaccinate Only cost/refugee	$619	$1,021	$1,358
		Net Benefit*	($82)	($183)	($227)
		Total Net Benefit**	($4,800,116)	($10,712,454)	($13,288,126)
	$5,000,000	Screen and Vaccinate cost/refugee	$1,162	$2,138	$2,826
		Vaccinate Only cost/refugee	$4,401	$9,839	$14,860
		Net Benefit	$3,239	$7,701	$12,034
		Total Net Benefit	$189,604,582	$450,801,138	$704,446,292
70% Domestic Screening	$0	Screen and Vaccinate cost/refugee	$701	$1,204	$1,585
		Vaccinate Only cost/refugee	$804	$1,246	$1,601
		Net Benefit	$103	$42	$16
		Total Net Benefit	$6,029,414	$2,458,596	$936,608
	$5,000,000	Screen and Vaccinate cost/refugee	$1,162	$2,138	$2,826
		Vaccinate Only cost/refugee	$3,257	$6,910	$10,198
		Net Benefit	$2,095	$4,772	$7,372
		Total Net Benefit	$122,637,110	$279,343,336	$431,542,136

[+]Value of Statistical Life
*'Vaccinate only' cost/person – 'Screen and vaccinate' cost/person = Net Benefit
**Cohort: N=58,538

As domestic screening rates increase for the 'Vaccinate only' policy, the overseas 'Screen and vaccinate' policy becomes less cost-beneficial, although 'Screen and vaccinate' is always the preferred option when VSL is incorporated in the model. For example, after 10 years, if 50% of refugees were screened in the US in the 'Vaccinate only' policy, the 'Screen and vaccinate' policy would provide an estimated net benefit of $450,801,138 over the ten-year period for a cohort of 58,538 refugees compared to the 'Vaccinate only' policy (Table 4a). Yet, if 70% of refugees were screened in the US in the 'Vaccinate only' policy, the 'Screen and vaccinate' policy would only provide an

estimated net benefit of $279,343,336 over the ten-year period for the same size cohort compared to the ‘Vaccinate only’ policy (Table 4b).

Discussion

The results of this study indicate that spending more up front for adding HBV screening to vaccinating protocols overseas for refugees ($154,084 compared to $73,758, n=58,538), pays off in the long term. The only situation in which the 'Vaccinate only' policy is more cost beneficial than the 'Screen and vaccinate' policy is when loss of life is not valued monetarily. Where we place a value on loss of life, 'Screen and vaccinate' is always the preferred option. The analysis also finds that HBV infection remains a significant problem among refugees in the United States. The 6-year period prevalence of chronic HBV infection of 7.1% is in the intermediate to high range (5). Since chronic HBV infection can cause lasting impacts on the liver, infected individuals need to know their status as early as possible in order to manage their disease to reduce serious sequellae.

In the cost-benefit analysis, the main benefits from the 'Screen and Vaccinate' policy come from early medical management of chronic HBV infection. While upfront costs of an overseas screening policy are higher compared to simply vaccinating anyone without a record of vaccination, the knowledge of infection can help individuals receive early treatment upon arrival to the United States and thus reduce the probability of costly serious sequellae. Currently not all refugees are screened in the United States with estimates varying from 31% to 98% of refugees being screened, indicating that infected individuals do not necessarily have a high likelihood of learning their status upon arrival to the United States. We accounted for different domestic screening probabilities, and even with high percentages of individuals domestically screened, the 'Screen and vaccinate' policy was still less costly than the 'Vaccinate only' policy. This is due to the

high expense of the most serious sequellae such as decompensated cirrhosis and HCC, and the lost societal contributions from early death, represented by VSL.

The VSL was an important contributing factor to the cost-savings of the 'Screen and vaccinate' policy. While it is hard to measure the value of a life lost, the VSL aims to contribute some estimation of the burden that early death places on society. By including a value of VSL in the model, we showed that it is not only treatment for the serious sequellae of chronic HBV infection that leads to high cost burden on the health system, but also that early life lost due to these sequellae places an economic burden on society as a whole.

Strengths

This study provides novel insights on refugee health and vaccination policies related to chronic HBV infection and has at least seven strengths. First, while some previous studies have examined the cost-effectiveness of screening and vaccinating for HBV, there were few studies specific to refugee populations and no studies of overseas screening and vaccination policies in this population (19-22, 24-27). Second, this study used the most recent available data for refugee screening from Minnesota and Georgia Departments of Public Health, both of which have established refugee resettlement policies. Both states resettle refugees from a large variety of countries of origin and between 2,000 and 4,000 refugees each year, which provides a reasonably representative population of all refugees resettled in the United States when estimates are modeled with this data. In addition, previous cost-analyses for chronic HBV screening used literature estimates for chronic HBV prevalence, making our study results more reliable because the prevalence information was obtained from novel, up-to-date data sources (19, 21, 34).

Third, this study provides estimates of the prevalence of chronic HBV infection in refugees newly arriving in the United States trending over a 6-year period, which added knowledge to changes and trends in prevalence in this population. Fourth, the Department of Homeland Security keeps records on all refugees entering the United States so there is essentially no missing information related to refugee population numbers resettled in each state. Fifth, refugees are often placed with Voluntary Resettlement Agencies (VOLAGS) in their arrival state and these agencies keep track of who has received a medical screening; in both Minnesota and Georgia, estimates indicate greater than 90% of new refugees receive medical screenings in their first year in the United States, which indicates good completeness of data and provides support for the utilization of this data for prevalence estimates (17, 18). Sixth, the decision tree model with Markov states more accurately represents an infected individuals transition through different disease states of chronic HBV infection compared to a static model. Seventh, accounting for background mortality also provides a more accurate estimate of the change in the cohort because it addresses competing causes for death to some degree.

Limitations

Despite the strengths of this study, there are at least five limitations. First, this study only analyzes refugee data from two states and the refugee populations from Georgia and Minnesota may not be representative of the refugee population of the entire United States. Both datasets were large, contained information on a refugees from over 80 different countries of origin, and in the case of Minnesota, contained very few missing observations (0.45%) so it is hoped that they could be considered an accurate random sample. Second, observations with missing HBsAg data were deleted and no imputation

methods were used to replace missing data on HBsAg test status. While this could be a potential source of selection bias in the study, imputing the missing data values could lead to misclassification bias, which could further bias the prevalence estimates and estimated odds ratios. Third, calculated prevalence estimates may be an inaccurate estimate of the prevalence in the United States because data were provided from only two states; if so, the economic analysis performed with these estimates could have inaccuracies and be less applicable to all newly arriving refugees in the United States. As stated before, the datasets had potential to be nationally representative and the observed prevalence in this population is in the range of estimates found previously (1, 9, 11, 12). Fourth, the prevalence for only those ages six and above was estimated and used in the cost analysis so this study does not address cost estimates for individuals who are 5 years of age and under. The treatment of young children would be dealt with in a different manner though, and there would need to be a more thorough analysis to accompany this one for those ages 5 years and younger (40). In addition, odds of disease in females were lower than in males; the study did not address differences in probability of disease or disease transition states between sexes in the cost-benefit analysis. Yet, the ratio of males to females remained statistically similar over the study period (2005 to 2010) so it can be assumed that the cohort probabilities entered into the economic model encompassed the gender distribution of the study cohort. Fifth, the challenge of accurately assessing costs of different outcomes of chronic HBV infection was difficult because there is limited data available on actual cost data for health sequellae of chronic HBV infection. Infection can cause a variety of outcomes and some conditions may be tracked as unrelated to chronic HBV infection if infection status is unknown. Domestic treatment costs vary by state and

facility so estimated costs may not be accurate to what a refugee experiences for care; in some cases, their treatment costs may be subsidized by the government, while in other cases, treatment costs may be more than estimated by this study. There is also limited data on cost of overseas screenings and vaccinations, and costs in the United States vary by state and screening facility. We used average costs in the model to try to estimate this variation.

Areas for Further Study

There is still much to be known about the effects of screening on reducing chronic HBV infection burden in refugees arriving to the United States. There are different types of screening tests and an analysis of which one is the most cost-beneficial could help to reduce costs even further. In addition, documented annual disease transition probabilities specific to refugees in the United States are non-existent; this information would be extremely useful in understanding the severity of disease that the average HBsAg infected refugee experiences. It would also be useful to know what types of health insurance refugees usually acquire after their eight months of Refugee Medical Assistance coverage has ended in order to estimate more accurate costs paid by the government and the refugee (41).

Conclusion

This study adds unique knowledge about refugees and chronic HBV infection by providing a novel comparison of costs and benefits of two overseas screening policies and advances the understanding of the epidemiology of HBV prevalence in refugees newly arriving to the US. Currently, only a proportion of refugees are screened in the United States; implementation of an overseas screening policy would reduce the costs

from screening in the United States and has the potential to lead to improved health outcomes for refugees with chronic HBV infection. While this policy would increase upfront program expenditures, net benefits can be observed even after just 5 years since implementation because of reduced serious sequellae from chronic HBV infection. Refugees resettle in the United States for the hopes of a better life, and reduction of serious seqeullae from a chronic disease is one step towards improved quality of life. It is hoped that the addition of these findings to current literature will lead to further study into affecting policy that dictates the most effective screening strategies for chronic HBV infection in refugees, with the aim of reducing infection with or serious sequeallae from chronic HBV infection

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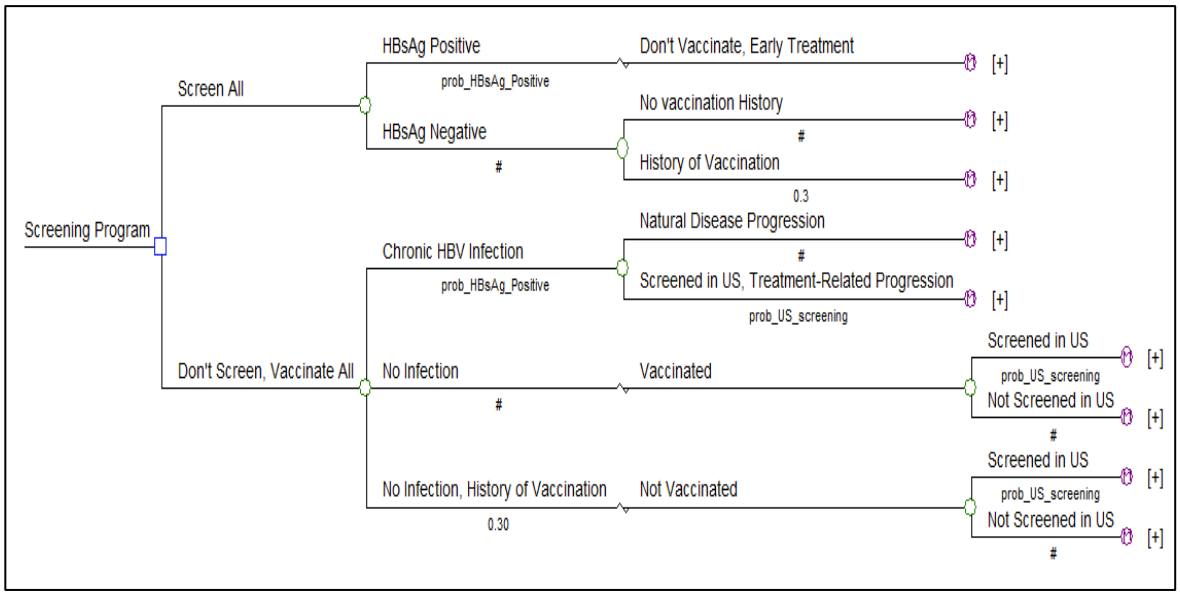
Appendix A. Variables from Minnesota and Georgia Datasets Used in Chronic Hepatitis B Virus Infection analysis

#	Variable	Type	Variable Details
1	Unique ID	Numerical	Observation ID
2	Sex	Categorical	1 = Female 2= Male
3	Age	Numerical	Continuous from 0 to 105
4	Country of Origin	Categorical	61 different country options
5	Region of Origin	Categorical	East Asia/Pacific Eastern Europe Latin America/Caribbean North Africa/Middle East South/Southeast Asia Sub-Saharan Africa Southern Europe West Asia
6	Arrival Date	Numerical	Exact date of arrival to the US
7	HBV Vaccination Status	Categorical	Combined GA and MN variables, any dose amount: 1 = Vaccinated (any dose) 0 = Not Vaccinated
8	Arrival Year	Numerical	Year of Arrival to US: 2005

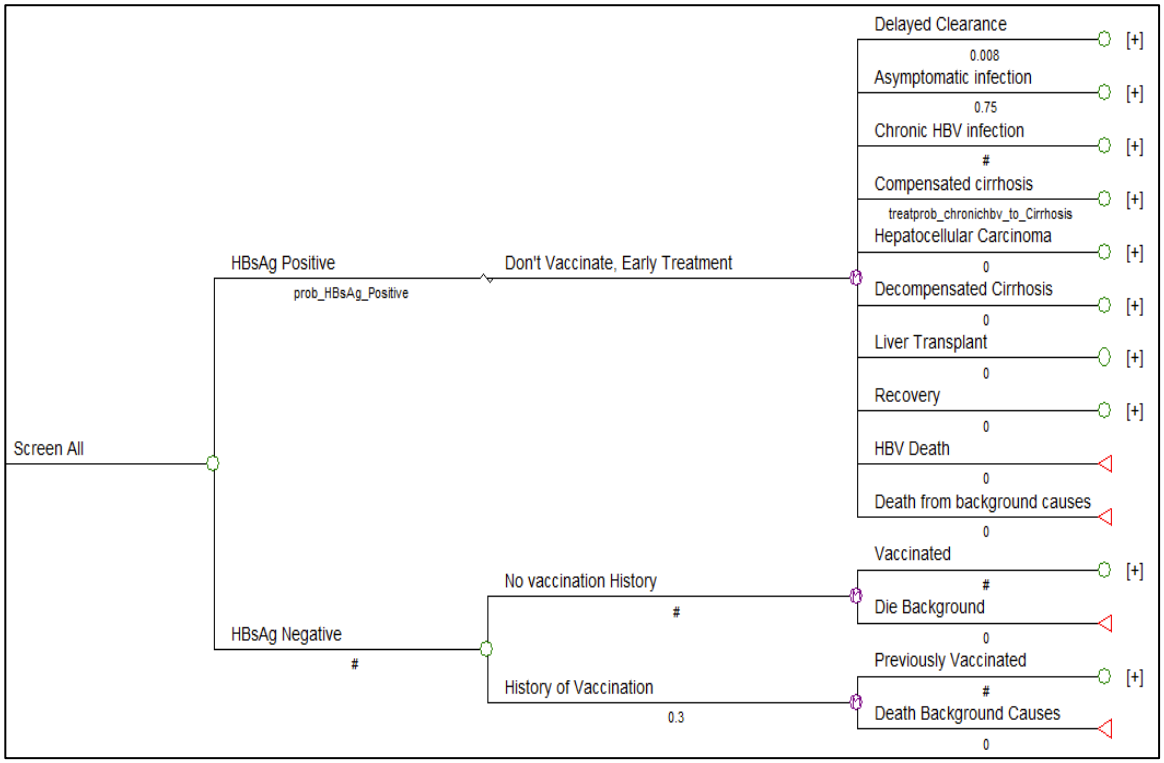
			2006 2007 2008 2009 2010
9	Age Group	Ordinal	0 = < 1 year 1 = between 1 and 5 years 2 = between 6 and 10 years 3 = between 11 and 18 years 4 = greater than 18 years
10	State	Categorical	Minnesota or Georgia

Appendix B. Decision Tree Model from TreeAge Pro Used for Cost-Benefit Analysis of 'Screen and vaccinate' and 'Vaccinate only' Policies

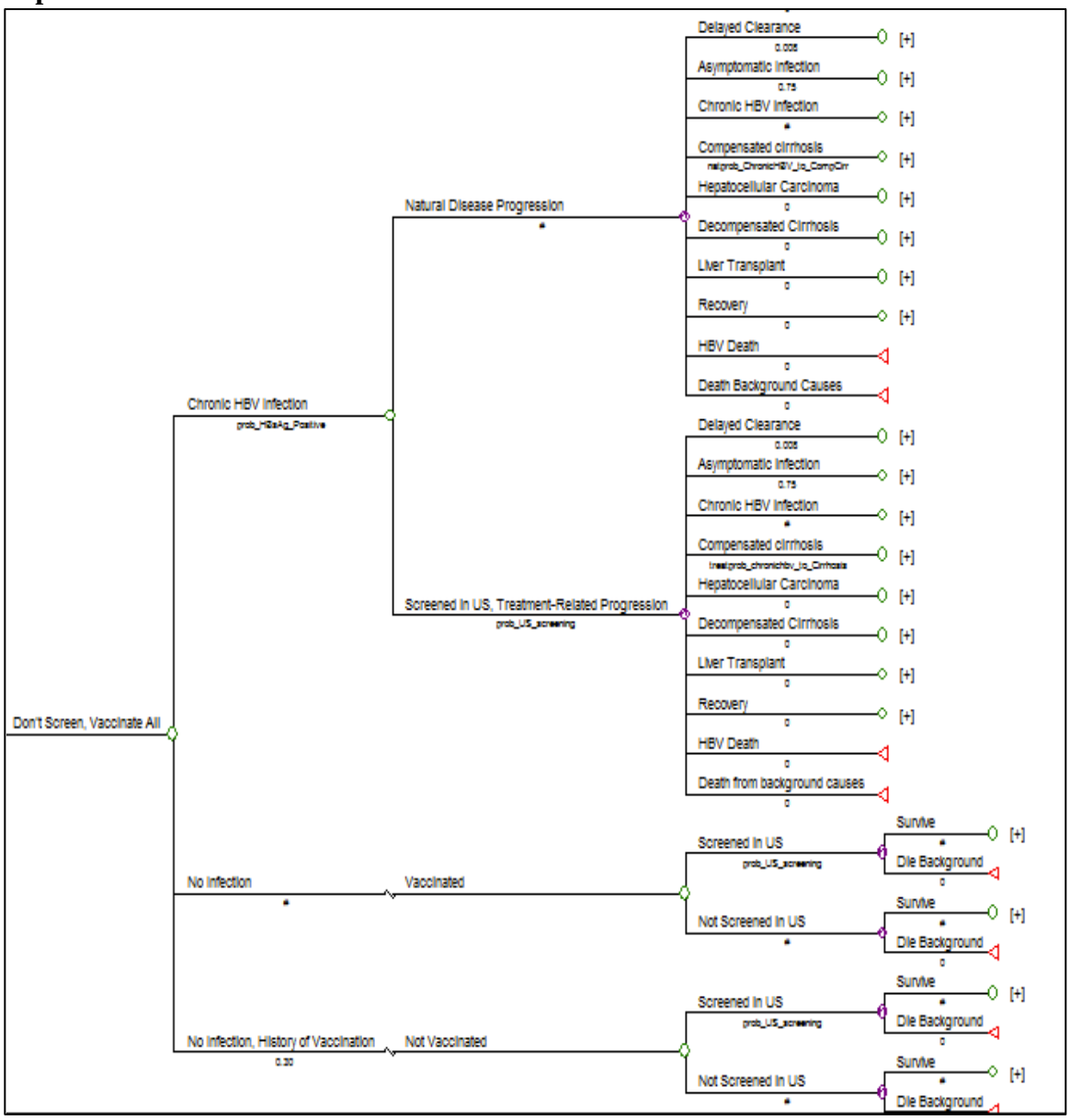
Overview of Decision Tree Comparing 'Screen and vaccinate' to 'Vaccinate only' Policies



'Screen and vaccinate' Subset of Decision Tree Model Used for Cost-Benefit Analysis with Expanded Markov Model



'Vaccinate all' Subset of Decision Tree Model Used for Cost-Benefit Analysis with Expanded Markov Model



Appendix C. Parameter Estimates for Chronic HBV Prevalence and Annual Disease Transition Probabilities for Treatment-related Progression and Natural Progression of Disease for Cost-Benefit Model

Parameter	**Value**	**References**
HBsAg Positivity (>5 years old)	0.071	GDPH, MDH*
Treatment Probabilities	**Annual Probability**	**References**
Inactive Carrier		
Delayed Clearance	0.00425	(32, 34)
Chronic HBV	0.02	(21, 34)
HCC	0.003	(21, 34)
Chronic HBV		
Inactive Carrier	0.3	(21, 22, 33)
Cirrhosis	0.0045	(22)
Hepatocellular Carcinoma	0.002	(22)
HBV Death	0.00002	
Cirrhosis		
Inactive Carrier	0.165	(22)
Decompensated Cirrhosis	0.02	(22, 31)
Hepatocellular Carcinoma	0.016	(22, 31)
HBV Death	0.024	(22)
Decompensated cirrhosis		
Liver Transplantation	0.033	(22)
Hepatocellular Carcinoma	0.047	(31)
HBV Death	0.26	(22)
HCC		
Liver Transplantation	0.012	(22)
HBV Death	0.2	(21, 22, 31)
Liver Transplantation		
HBV Death	0.066	(22)
Natural Progression Probabilities	**Annual Probability**	**Sources**
Inactive Carrier		
Delayed Clearance	0.00425	(32, 34)
Chronic HBV	0.02	(21, 34)
HCC	0.003	(21, 34)
Chronic HBV		
Compensated Cirrhosis	0.038	(21, 32, 34)
HCC	0.01	(21, 32, 34)
Compensated cirrhosis		
Decompensated Cirrhosis	0.073	(21, 31, 32, 34)
HCC	0.034	(21, 31, 32, 34)

HBV Death	0.049	(21, 31)
Decompensated cirrhosis		
HCC	0.06	(21, 34)
Liver Transplantation	0.2	(21, 31, 34)
HBV Death	0.173	(21, 31, 34)
HCC transitions		
Liver Transplantation	0.15	(21, 31, 34)
HBV Death	0.35	(21, 31, 34)
Liver transplantation transition		
HBV Death	0.066	(21, 31, 34)

*GDPH: Georgia Department of Public Health; MDH: Minnesota Department of Health

Appendix D. Cost Estimates for Chronic HBV Infection Overseas Screening and Domestic Treatment for Cost-Benefit Model

Materials Costs	**Cost US$**	**Cost US$ (plus 100% Overhead*)**	**Source**
Rapid Screening Test Kit	$0.74	$1.49	(42)
Vaccine (3 doses)	$0.90	$1.80	(43)
Treatment Costs	**Unadjusted Cost, US$**	**Adjusted 2012 Cost, US$**	**Source**
Chronic HBV infection Costs			
Initial Medical Visit	$389	$410	(Dr. Margaret Coleman, CDC, Personal Communication, 2013)
Inactive Carrier	$750	$790	(21)
Chronic Hepatitis	$12,591	$13,267	(30)
Compensated Cirrhosis	$13,196	$13,904	(30)
Decompensated Cirrhosis	$23,829	$25,108	(30)
Hepatocellular Carcinoma	$38,715	$44,048	(31)
Liver Transplant	$156,758	$167,143	(21, 31)
Transplant Recovery	$27,550	$29,375	(21, 31)

*Overhead (includes Medical staff costs, transportation, vaccine administration and other costs related to performing the screening test)

Appendix E. Logistic Modeling of HBsAg positivity by gender, age, and arrival year, ages 6+, years 2005-2010

Model	Estimate Types	Model 1: Age, Sex, Arrival Year, Region	Model 2: Age, Sex, Arrival Year
Sex (ref*: Male)	Par Est (SE), Chsq	-0.420 (0.055), <0.001	-0.420 (0.055), <0.001
	OR Estimate	0.66 (0.59, 0.73)	0.66 (0.59, 0.73)
Age	Par Est (SE), Chsq	0.010 (0.002), <0.001	0.010 (0.002), <0.001
	OR Estimate	1.010 (1.007, 1.013)	1.010 (1.007, 1.013)
Arrival year (ref: 2005)	Par Est (SE), Chsq	-0.068 (0.016), <0.001	-0.068 (0.016), <0.001
	OR Estimate	0.93 (0.91, 0.96)	0.93 (0.91, 0.96)

*Ref = reference category

Appendix F. Net Benefits of 'Screen and vaccinate' compared to 'Vaccinate only' Program, 90% and 30% domestic screening in 'Vaccinate only' Program

	VSL[+]		5 year cost	10 year cost	15 Year cost
90% Domestic Screening	**$0**	Screen and Vaccinate cost/person	$701	$1,204	$1,585
		Vaccinate Only cost/person	$989	$1,471	$1,843
		Net Benefit*	$288	$267	$258
		Total Net Benefit**	$16,858,944	$15,629,646	$15,102,804
	$5,000,000	Screen and Vaccinate cost/person	$1,162	$2,138	$2,862
		Vaccinate Only cost/person	$2,114	$3,982	$5,536
		Net Benefit	$952	$1,844	$2,674
		Total Net Benefit	$55,728,176	$107,944,072	$156,530,612
30% Domestic Screening	$0	Screen and Vaccinate cost/person	$701	$1,204	$1,585
		Vaccinate Only cost/person	$434	$797	$1,116
		Net Benefit	($267)	($407)	($469)
		Total Net Benefit	($15,629,646)	($23,824,966)	($27,454,322)
	$5,000,000	Screen and Vaccinate cost/person	$1,162	$2,138	$2,862
		Vaccinate Only cost/person	$5,544	$12,767	$19,522
		Net Benefit	$4,382	$10,629	$16,696
		Total Net Benefit	$256,513,516	$622,200,402	$977,350,448

[+]Value of Statistical Life
*'Vaccinate only' cost/person – 'Screen and vaccinate' cost/person = Net Benefit
**Cohort: N=58,538