



Published in final edited form as:

*Vaccine*. 2015 March 10; 33(11): 1393–1399. doi:10.1016/j.vaccine.2015.01.010.

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

Amelia Jazwa, MSPH<sup>1</sup>, Margaret S. Coleman, PhD, MA<sup>1</sup>, Julie Gazmararian, PhD, MPH<sup>2</sup>, La'Marcus T. Wingate, PharmD, PhD<sup>1</sup>, Brian Maskery, PhD<sup>1</sup>, Tarissa Mitchell, MD<sup>1</sup>, and Michelle Weinberg, MD, MPH<sup>1</sup>

<sup>1</sup>U.S. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases, Division of Global Migration and Quarantine

<sup>2</sup>Emory University, Rollins School of Public Health

### Abstract

**Background**—Refugees are at an increased risk of chronic Hepatitis B Virus (HBV) infection because many of their countries of origin, as well as host countries, have intermediate-to-high prevalence rates. Refugees arriving to the US are also at risk of serious sequelae from chronic HBV infection because they are not routinely screened for the virus overseas or in domestic post-arrival exams, and may live in the US for years without awareness of their infection status.

**Methods**—A cohort of 26,548 refugees who arrived in Minnesota and Georgia during 2005–2010 was evaluated to determine the prevalence of chronic HBV infection. This prevalence information was then used in a cost-benefit analysis comparing two variations of a proposed overseas program to prevent or ameliorate the effects of HBV infection, titled ‘Screen, then vaccinate or initiate management’ (SVIM) and ‘Vaccinate only’ (VO). The analyses were performed in 2013. All values were converted to US 2012 dollars.

**Results**—The estimated six year period-prevalence of chronic HBV infection was 6.8% in the overall refugee population arriving to Minnesota and Georgia and 7.1% in those 6 years of age. The SVIM program variation was more cost beneficial than VO. While the up-front costs of SVIM were higher than VO (\$154,084 vs. \$73,758; n=58,538 refugees), the SVIM proposal displayed a positive net benefit, ranging from \$24 million to \$130 million after only 5 years since program initiation, depending on domestic post-arrival screening rates in the VO proposal.

**Conclusions**—Chronic HBV infection remains an important health problem in refugees resettling to the United States. An overseas screening policy for chronic HBV infection is more cost-beneficial than a ‘Vaccination only’ policy. The major benefit drivers for the screening policy are earlier medical management of chronic HBV infection and averted lost societal contributions from premature death.

Corresponding Author: Brian Maskery, 1600 Clifton Road, MS E-03, Atlanta, GA 30333, wqm7@cdc.gov.

**Disclaimer:** The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Centers for Disease Control and Prevention or the institutions with which the authors are affiliated.

We declare no conflicts of interest.

## Keywords

Vaccine; Screening; Hepatitis B Virus; Refugee; Cost-Benefit

---

## Background

Worldwide, Hepatitis B virus (HBV) infections pose a serious public health threat. More than 350 million people worldwide carry chronic HBV infection, placing them at risk for developing serious sequelae and leading to 600,000 premature deaths annually. The rates of HBV infection vary between countries and regions [1, 2]. Some Asian and African countries, many of which are origins for US-bound refugees, have disease rates exceeding 10% [3]. This leads to concern for possible importation of chronic HBV infection to the United States. In 2010, 73,000 refugees resettled to the United States, with more than half arriving from countries with intermediate (2% to 7% of the population) to high (> 8% of the population) prevalence of chronic HBV infection [4–6]. Domestic estimates of chronic HBV infection prevalence in refugees after US arrival range from 7% to 11% [1, 4, 7, 8].

US federal and state governments fund medical care for refugees overseas and for just under a year after refugee resettlement. Afterwards, refugees may be eligible for Medicaid, but eligibility varies by state. Further some states are changing Medicaid rules to expand or narrow eligibility definitions in response to the Affordable Care Act. However, regardless of the variable coverage, the federal government and many state governments have a direct financial interest in mitigating medical conditions arising from chronic HBV infections. The Centers for Disease Control and Prevention (CDC) requires that refugees undergo medical screening overseas to identify and treat medical conditions defined by regulation as diseases of public health significance. HBV does not fall within these regulations and therefore is not included in routine overseas refugee screening. In addition, practices with regards to HBV screening differ among state refugee agencies. Consequently, an unknown proportion of refugees remain unaware of their infection because HBV screening is not mandatory [9–11]. The variability in state practices for refugee screening may change based on updated recommendations by the United States Preventive Services Task Force to screen asymptomatic adults for HBV in certain high risk groups [12].

Further, many refugees are unvaccinated against HBV prior to US entry. As required by law, most refugees receive at least one dose of Hepatitis B vaccine to become legal permanent residents (LPR) one year or more after arrival, but an unknown number of vaccinees are already infected. These time gaps and inconsistent policies governing overseas and domestic screening and vaccination delay the identification of persons with chronic HBV infection, allowing disease progression without medical management and leading to potential risk of transmission.

Chronic HBV infection is costly, and sequelae to unmanaged infection incur high medical expenses. The clinical spectrum of HBV infection ranges from the inactive hepatitis B surface antigen (HBsAg) carrier state to the chronic phase with complications from chronic hepatitis and cirrhosis [13]. Approximately 15 to 40% of people who develop chronic HBV infection are expected to progress to cirrhosis and end-stage liver disease whereas

reactivation is a rare occurrence in inactive carriers [14]. It is estimated that in 2011, per-case drug costs ranged from \$1,500 to \$16,000 or more annually, while a liver transplant costs >\$150,000 [15, 16]. Preventing infection through vaccination or screening and diagnosis at an earlier stage, when medical management can prevent or delay serious late-stage sequelae, makes both public health and financial sense and has been demonstrated to be cost-effective in general populations [16–20].

While data are available about the costs and benefits of HBV screening in other populations, no published reports have addressed whether costs of screening and vaccinating refugees overseas will be offset by costs avoided by delaying serious sequelae through early medical management. Some studies indicate that HBV screening and treatment is cost-effective in US immigrants. Two studies found it cost-effective to screen immigrants from countries with HBV seroprevalence in the range of >2–3% [17, 19]. HBV seroprevalence in U.S.-resettled refugees falls within or above the range of these studies, indicating that a refugee-focused screening and vaccination program may prove economically beneficial compared to vaccination-only programs.

The analysis reported here first estimates chronic HBV infection prevalence among newly-arrived US refugees in Minnesota and Georgia during 2005–2010, and then uses prevalence estimates in a cost-benefit analysis [21]. Two proposed overseas program variations are analyzed: ‘Vaccinate only’ (VO), in which refugees are vaccinated for Hepatitis B without HBV screening, versus ‘Screen, then vaccinate or initiate management’ (SVIM), in which refugees are screened for HBV prior to vaccination and HBV-positive refugees arrive with a referral to follow up with a liver specialist.

## Methods

### Epidemiologic Methods

This study used original datasets of refugee populations from the Minnesota Department of Health and Georgia Department of Public Health for the years 2005–2010. Refugees from Georgia and Minnesota were included based on availability of data from these two states. We treated the 26,548 refugees who arrived to both states from 82 countries of origin as a single cohort. The original data were provided in the form of de-identified refugee records that included: Hepatitis B surface antigen (HBsAg) screening test results, a proxy for chronic HBV infection; self-reported and documented vaccination status (including anti-HBs and anti-HBc testing); and demographics (age, sex, and country of origin). The study population was restricted to those 6 years of age and older because transition probabilities from acute to chronic HBV infection stabilize around age 6 and the treatment for children with chronic HBV infection is different than that for adults [22, 23]. The datasets were reviewed for completeness of the HBsAg screening test variable. Any patient record missing HBsAg screening test results was excluded from the analysis (14.6% of data), leaving a final cohort of 22,675 observations for analysis. No imputation methods were used to replace missing data. Refugees with missing test data were more likely to be older, arrive in Georgia, and originate from Southeast Asia or sub-Saharan Africa.

Univariate analyses were performed to determine population-wide distributions of demographic variables. The normality of the continuous variables was assessed, and bivariate analyses were run to examine HBsAg positivity by region, country, arrival year, sex, and age.

Descriptive statistics were used to determine prevalence, calculated as the number of chronic HBV cases per 100 refugees. The estimated number of chronic cases entering the United States annually and over the 6-year study period was determined by multiplying the prevalence estimate with total US refugee population over that same period, estimated by the Department of Homeland Security [6].

All epidemiologic analyses were performed by using SAS version 9.3 (Cary, NC).

### Economic Analysis Methods

A decision tree, incorporating a Markov model to represent changing states of chronic HBV infection (Figure 1), was developed using TreeAge Pro Suite 2009 (Williamstown, MA) to compare the costs and benefits of the two program variations, SVIM and VO. For SVIM, all refugees are screened for HBV prior to vaccination and HBV-positive refugees arrive in the United States with guidance for initiating disease management. For VO, all refugees are vaccinated with Hepatitis B vaccine without prior HBV screening, although a proportion undergo screening after US arrival. In the Markov model, refugees with chronic HBV infection progress annually through the following disease states depending on immune response and treatment status: inactive carrier, chronic HBV infection, compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma (Appendix) [24–26]. No refugee began in decompensated cirrhosis or hepatocellular carcinoma states during the screening process overseas because these individuals may be too sick to undergo travel for resettlement [24, 26]. Death from chronic HBV infection and sequelae was an end state in the model. In addition, an age-specific background mortality rate was added to the decision tree to account for refugees who die from other causes [27]. The analysis takes a generic health care payer perspective and adds mortality risk reduction benefits using VSL.

Multiple secondary sources were used to determine the economic model rate and cost inputs. Two sets of transition rates were used to differentiate disease progression patterns: one for patients undergoing treatment and one for patients who experience natural disease progression (Table 1). The annual transition rates for chronic HBV infection were extracted from published reports [‘7–‘9, 25, 28, 29]. Background mortality for causes of death other than HBV sequelae were calculated using the CDC WONDER database [24].

Cost estimates were determined for program implementation and administration, medical care, and premature death (Table 2). The cost of overseas labor was estimated from United Nations refugee camp labor costs [30]. Cost information for overseas screening and vaccination supplies and procedures was provided by CDC [31]. The *Physicians Fee and Coding Guide* and the *Red Book: Pharmacy’s Fundamental Reference* were used for domestic cost estimates for medical management and treatment protocols for chronic HBV infection [32, 33]. Treatment protocol costs included only the cost of drug therapy. All costs were converted to 2012 US dollars using the Consumer Price Index [34]. Benefits were

estimated by reduced treatment costs and mortality risk reduction, estimated with a Value of Statistical Life (VSL) of \$5,000,000 USD [35, 36]. VSL estimates the monetary benefit of reductions in premature mortality risk for a group of individuals, not the actual dollar value of a life [37].

Multiple assumptions were made to construct the economic model. These included—

1. 100% compliance with overseas screening and vaccination and 100% sensitivity and specificity of the screening test.
2. Exclusion of acute HBV infections because refugees with an acute infection would be too ill to resettle to the United States.
3. For SVIM, HBsAg-positive individuals do not undergo vaccination [38].
4. For both SVIM and VO proposals, 30% of refugees have documented vaccination and are not revaccinated. This estimate was from the documented vaccination status among the Minnesota and Georgia cohorts.
5. Assumption that 60% of individuals that test positive follow up with a specialist for treatment and the other 40% go through natural disease progression; 2% start treatment irrespective of screening program; and 10% per year drop out of treatment or monitoring [39, 40].
6. Estimations of costs for overseas screening and vaccination using online and secondary sources [41, 42]
7. Use of an average range of drug costs to account for various drug regimens prescribed to individuals because multiple treatment regimens exist for chronic HBV infection and related sequelae,

Benefits and costs were discounted to present values at an annual rate of 3%. Net benefits were calculated by subtracting the cost per person of the SVIM proposal from the VO proposal. Where the final net benefit is positive, the SVIM is more cost-beneficial than the VO proposal. For estimating net benefits of an average annual cohort of refugees, we used the average annual number of refugees entering the United States during the study period (58,538 refugees).

In addition, we performed sensitivity analyses for time since initiation of the proposals, with the cohort followed for 5 years (base estimate), 10 years, and 15 years, and the proportion screened in the United States in the VO arm estimated at 30%, 50% (base estimate), 70%, and 90%. We do not calculate costs or benefits beyond these time periods because Hepatitis B treatment regimens may change over the longer term. Currently, even though screening is recommended for refugees upon arrival, many refugees receive no domestic screening; a conservative rate of 50% domestic screening was used as the base estimate [9–11]. Analyses were also performed with and without VSL in the model.

The study was submitted for human subjects determination at CDC and institutional board reviews at Emory University, the Georgia Department of Public Health, and the Minnesota Department of Health; all four institutions deemed this study exempt from IRB review.

## Results

### Prevalence Results

The demographics for the Minnesota and Georgia combined refugee cohort for 2005–2010 were mean age of 26.1 years, 48.4% female, and 86.0% originated from Sub-Saharan African or South/Southeast Asian countries (Table 3). During the same time frame, the estimated 6-year period prevalence of chronic HBV infection was 6.8% for the overall arriving refugee population and 7.1% in refugees ≥ 6 years of age. Almost one-third (30.6%) of refugees ≥ 6 years of age had received at least one dose of the HBV vaccine before arriving in the United States. An estimated 24,937 refugees age 6 and older entered the United States during 2005–2010 with chronic HBV infection (Table 4), an average of 4,156 cases per year.

### Cost-Benefit Analysis Results

The SVIM proposal showed a positive net benefit when the Value of Statistical Life (VSL) was estimated at US \$5,000,000. While the program initiation costs for the SVIM proposal were higher than those of the VO proposal (\$154,084 vs. \$73,758, respectively; n=58,538 refugees), the SVIM program proposal showed positive net benefits after only 5 years of implementation (Table 5). The positive net benefits resulted from early treatment, which prevented or delayed serious sequelae and reduced the number of premature deaths from chronic HBV. In the base case scenario comparing SVIM to VO with 50% domestic screening, there was a positive net benefit of \$90 million and 20 HBV-associated deaths averted after 5 years of implementation.

Variations in the economic estimates were attributable to time since initiation of the screening program and proportion screened in the United States in the VO proposal. The net benefit was positive for SVIM over VO in all scenarios except when both VSL was valued at \$0 and domestic screening was 50% or below in the VO program proposal, indicating that the SVIM proposal is the preferred option (Table 5). The negative net benefit scenarios used a VSL of \$0; therefore, VO is preferred only when no monetary value is assigned to premature death.

As domestic screening rates decreased for the VO proposal, the overseas SVIM proposal became more cost-beneficial, with SVIM always the preferred option when VSL is incorporated in the model. For example, if 70% of refugees were screened in the United States in the VO proposal, the SVIM proposal would avert 12 premature deaths and provide an estimated net benefit of \$24 million over the VO proposal, after 5 years from program initiation for an annual cohort of 58,538 refugees. Yet, in the scenario with only 50% of refugees screened in the United States in the VO proposal, the SVIM proposal would avert 20 premature HBV-related deaths and provide an estimated net benefit of \$90 million over the VO proposal, after 5 years from program initiation for the same size cohort (Table 5).

## Discussion

Our results indicate that, when mortality reduction benefits are included in the analysis, higher overseas spending for adding chronic HBV infection screening to vaccination

protocols (\$154,084 for screening and vaccination compared with \$73,758 for vaccination only, n=58,538) yields net benefits ranging from \$24 million to \$130 million after only 5 years since program initiation, depending on domestic screening rates in the VO proposal. Net benefits are attributable to reduced costs from prevented sequelae and mortality through earlier diagnosis and medical management of chronic HBV infection among refugees screened. These benefits continue to accrue over time because of the reduction in the number of cases and deaths that would accumulate annual costs for treating serious sequelae. The only situation in which the VO proposal is more cost beneficial than the SVIM proposal is when premature loss of life is not assigned a monetary value and domestic follow-up rates are assumed to be less than 70%. The analysis also indicates that HBV infection remains a substantial problem among refugees in the United States, with rates at intermediate prevalence according to WHO guidelines [22].

The main economic benefits from the SVIM proposal come from early medical management of chronic HBV infection to reduce morbidity and mortality. Knowledge of infection can help refugees receive early domestic treatment and reduce the probability of costly serious sequelae. Presently, not all refugees are screened in the United States with estimates ranging from 31% to 98% of refugees screened [9–11]. We accounted for different domestic screening probabilities. With high percentages of individuals screened domestically after being vaccinated overseas through the VO proposal, the SVIM proposal was less costly due to the lower costs of screening overseas. With lower percentages of individuals screened domestically, net benefits without consideration of VSL are likely to be negative, but more deaths would be averted via SVIM relative to VO. Although screening and early treatment is likely to be cost-effective, it is not likely to be cost-saving. In addition, it is important to note that the government would be unlikely to recoup its investment in early treatment of HBV if refugee insurance or health care payment is transferred from the government to other payers after refugees first few years in the country.

The U.S. Preventive Health Services recommends HBV screening for all persons [12]. Overseas screening programs may be preferable to improving domestic screening programs for two reasons: 1) prevention of unnecessary vaccination for persons already infected and 2) CDC supervises all overseas refugee health programs, but the responsibilities for domestic program are split up among the states.

VSL was an important contributing factor to the cost-savings of the SVIM proposal. Since the monetary value of mortality risk reduction cannot be measured directly, we evaluated net benefits across a conservative range of estimates.

This study provides novel insights into refugee health screening and vaccination protocols. Previous studies have examined the cost-effectiveness of screening and vaccinating for chronic HBV infection, yet there were few studies specific to refugee populations and no studies of overseas screening and vaccination protocols in this population [15–20, 43–46]. In addition, previous cost-analyses for chronic HBV screening used published estimates for chronic HBV prevalence; our study estimated prevalence information from observed, original data sources, which gives greater reliability to the results [15, 17, 19].

This study has several limitations. First, it analyzes data from only two states, and the refugee populations from Georgia and Minnesota may not be representative of the refugee population entering the entire United States. However, prevalence estimates were corrected to be representative of all refugees entering the United States. Second, the analysis omitted young children (<5 years old) because the pediatric treatment for HBV is different from that of adults and would need a separate analysis [23]. Third, the challenge of accurately assessing costs of different outcomes of chronic HBV infection was difficult because only limited data are available for the costs of health sequelae of chronic HBV infection, and domestic costs vary by state and screening facility. Our analysis included only drug therapy costs for treatment costs, which may underestimate the true cost of treatment for HBV infection. In addition, data are limited and variable for the costs of overseas HBV screening and vaccination. Finally, the results included in the analysis represent six years of entry data for refugees; however, the origin for U.S.-bound refugees may change in the future. It is likely that a substantial portion of future U.S.-bound refugees will also depart from countries with high HBV prevalence rates; however, widespread adoption of vaccines against HBV may reduce the prevalence rate in future refugees.

The final limitation affects our fundamental assumption that, one way or another, refugees would have access to public or private insurance to pay for their health care subsequent to their initial resettlement time period of 8 months to a year. This may not be true in some states, so implementation of any proposed HBV screening program would be predicated on refugees being covered for HBV disease care in the states where they are resettled.

CDC is implementing a pilot project that offers voluntary testing and treatment for certain medical conditions, including chronic HBV infection, to US-bound refugees at the time of the initial required medical assessment in Mae Sot refugee camp in Thailand [47]. The results of our analysis indicate that expanding HBV screening along with the existing HBV vaccination protocol would be cost-beneficial.

## Conclusion

This study informs the screening protocol of refugees for chronic HBV infection by comparing the costs and benefits of two overseas screening proposals; it also advances the understanding of the epidemiology of chronic HBV infection prevalence in US-bound refugees. While the SVIM proposal would increase up-front expenditures, net benefits can be observed even after just 5 years since implementation because of reduced serious sequelae from chronic HBV infection through preventing disease or identifying infection early. Implementation of an overseas screening protocol could reduce HBV screening and treatment costs in the United States and improve health outcomes for refugees with chronic HBV infection.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

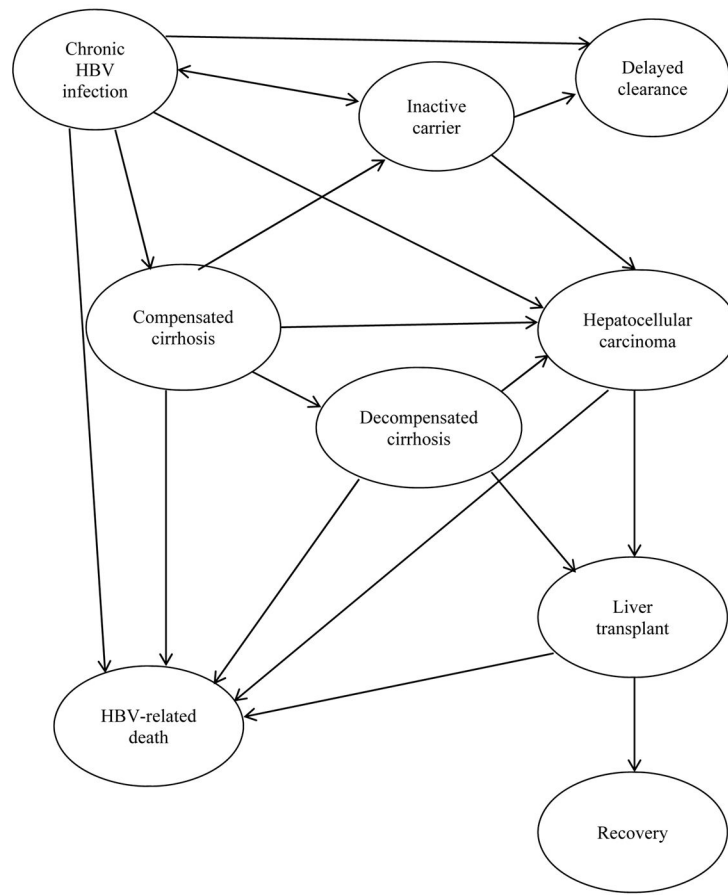
We acknowledge the comments of Kathy Byrd, MD, MPH, Division of Viral Hepatitis, NCHHSTP, and Dr. Fangjun Zhou, Senior Economist, Immunization Services Division, NCIRD, at the Centers for Disease Control and Prevention. We also acknowledge the assistance of Blain Mamo of the Minnesota Department of Health and Monica Vargas of the Georgia Department of Public Health. We also acknowledge the input of two reviewers at *Vaccine*.

## References

1. Ugwu C, Varkey P, Bagniewski S, Lesnick T. Sero-epidemiology of hepatitis B among new refugees to Minnesota. *Journal of immigrant and minority health / Center for Minority Public Health*. 2008; 10:469–74. [PubMed: 18066661]
2. Shepard CW, Simard EP, Finelli L, Fiore AE, Bell BP. Hepatitis B virus infection: epidemiology and vaccination. *Epidemiologic reviews*. 2006; 28:112–25. [PubMed: 16754644]
3. Custer B, Sullivan SD, Hazlet TK, Iloeje U, Veenstra DL, Kowdley KV. Global epidemiology of hepatitis B virus. *Journal of clinical gastroenterology*. 2004; 38:S158–68. [PubMed: 15602165]
4. Kowdley KV, Wang CC, Welch S, Roberts H, Brosgart CL. Prevalence of chronic hepatitis B among foreign-born persons living in the United States by country of origin. *Hepatology*. 2012; 56:422–33. [PubMed: 22105832]
5. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *Journal of viral hepatitis*. 2004; 11:97–107. [PubMed: 14996343]
6. United States Department of Homeland Security Office of Immigration Statistics. 2010 Yearbook of Immigration Statistics. Washington, D.C: 2011.
7. Lifson AR, Thai D, O'Fallon A, Mills WA, Hang K. Prevalence of tuberculosis, hepatitis B virus, and intestinal parasitic infections among refugees to Minnesota. *Public health reports*. 2002; 117:69–77. [PubMed: 12297684]
8. Museru OI, Vargas M, Kinyua M, Alexander KT, Franco-Paredes C, Oladele A. Hepatitis B virus infection among refugees resettled in the U.S.: high prevalence and challenges in access to health care. *Journal of immigrant and minority health / Center for Minority Public Health*. 2010; 12:823–7. [PubMed: 20204515]
9. Arizona Department of Health Services. [Accessed on 12/21/2014] Refugee Health Coordinator Annual Report. 2012. <http://www.azdhs.gov/phs/edc/odis/refugee/documents/rhc-annual-report11-12.pdf>
10. Maryland Office for Refugees and Asylees. Statistics: MORA Abstract. Baltimore: 2011. [http://www.dhr.state.md.us/blog/?page\\_id=3506](http://www.dhr.state.md.us/blog/?page_id=3506) [Accessed on 12/21/2014]
11. Minnesota Department of Public Health. [Accessed on 12/21/2014] Refugee Health Statistics: Arrival Data. <http://www.health.state.mn.us/divs/idepc/refugee/stats/index.html>
12. U.S. Preventive Services Task Force. [Accessed on 12/21/2014] Screening for Hepatitis B Virus Infection in Nonpregnant Adolescents and Adults: Final Recommendation Statement. 2014. <http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/hepatitis-b-virus-infection-screening-2014>
13. Sharma SK, Saini N, Chwla Y. Hepatitis B Virus: Inactive carriers. *Virology Journal*. 2005; 2:82. [PubMed: 16191199]
14. Villa E. Natural history of chronic HBV infection: special emphasis on the prognostic implications of the inactive carrier state versus chronic hepatitis. *Digestive and Liver Disease*. 2011; 43:S8–S14. [PubMed: 21195374]
15. Post SE, Sodhi NK, Peng CH, Wan K, Pollack HJ. A simulation shows that early treatment of chronic hepatitis B infection can cut deaths and be cost-effective. *Health affairs*. 2011; 30:340–8. [PubMed: 21289356]
16. Eckman MH, Kaiser TE, Sherman KE. The cost-effectiveness of screening for chronic hepatitis B infection in the United States. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2011; 52:1294–306. [PubMed: 21540206]

17. Hutton DW, Tan D, So SK, Brandeau ML. Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. *Annals of internal medicine*. 2007; 147:460–9. [PubMed: 17909207]
18. Veldhuijzen IK, Toy M, Hahne SJ, De Wit GA, Schalm SW, de Man RA, et al. Screening and early treatment of migrants for chronic hepatitis B virus infection is cost-effective. *Gastroenterology*. 2010; 138:522–30. [PubMed: 19879275]
19. Wong WW, Woo G, Jenny Heathcote E, Krahn M. Cost effectiveness of screening immigrants for hepatitis B. *Liver international : official journal of the International Association for the Study of the Liver*. 2011; 31:1179–90. [PubMed: 21745300]
20. Rossi C, Schwartzman K, Oxlade O, Klein MB, Greenaway C. Hepatitis B screening and vaccination strategies for newly arrived adult Canadian immigrants and refugees: a cost-effectiveness analysis. *PLoS One*. 2013; 8:e78548. [PubMed: 24205255]
21. Drummond, MF., et al. *Methods for the Economic Evaluation of Health Care Programmes*. 2. Oxford University Press; 1997.
22. Centers for Disease Control and Prevention. Hepatitis B. In: Atkinson, W.; Hamborsky, J.; Stanton, A.; Wolfe, C., editors. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. 12. Washington DC: Public Health Foundation; 2012.
23. Jonas MM, Block JM, Haber BA, Karpen SJ, London WT, Murray KF, et al. Treatment of children with chronic hepatitis B virus infection in the United States: patient selection and therapeutic options. *Hepatology*. 2010; 52:2192–205. [PubMed: 20890947]
24. Fattovich G. Natural history of hepatitis B. *Journal of hepatology*. 2003; 39(Suppl 1):S50–8. [PubMed: 14708678]
25. Fattovich G, Bortolotti F, Donato F. Natural history of chronic hepatitis B: special emphasis on disease progression and prognostic factors. *Journal of hepatology*. 2008; 48:335–52. [PubMed: 18096267]
26. Schuppan D, Afdhal NH. Liver cirrhosis. *Lancet*. 2008; 371:838–51. [PubMed: 18328931]
27. Centers for Disease Control and Prevention National Center for Health Statistics. Underlying Cause of Death 1999–2010 on CDC WONDER Online Database. 2012.
28. Kanwal F, Farid M, Martin P, Chen G, Gralnek IM, Dulai GS, et al. Treatment alternatives for hepatitis B cirrhosis: a cost-effectiveness analysis. *The American journal of gastroenterology*. 2006; 101:2076–89. [PubMed: 16968510]
29. Wilkins T, Zimmerman D, Schade RR. Hepatitis B: diagnosis and treatment. *American family physician*. 2010; 81:965–72. [PubMed: 20387772]
30. United Nations Office of Human Resources Management. *United Nations Salaries, Allowances, Benefits, and Job Classification*. 2007.
31. Personal communication, Margaret S. Coleman. Senior health economist, Division of Global Migration and Quarantine, Centers for Disease Control and Prevention. Jan 10. 2013
32. Red Book. 2010: Pharmacy's Fundamental Reference. U.S.A: Physicians Desk Reference Incorporated; 2010.
33. HealthCare Consultants of America Inc. *Physicians Fee & Coding Guide*. U.S.A: HealthCare Consultants of America; 2011.
34. U.S. Department of Labor Bureau of Labor Statistics. *Consumer Price Index*. 2013.
35. U.S. Department of Transportation. *Economic Values Used in Analyses*. 2013.
36. U.S. Environmental Protection Agency. *Guidelines for Preparing Economic Analyses*. 2010.
37. Laxminarayan R, Jamison DT, Krupnick AJ, Norheim OF. Valuing Vaccines Using Value of Statistical Life Measures. *Vaccine*. 2014; 39:5065–70. [PubMed: 25045822]
38. Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control*. 2006; 55:1–33. quiz CE1-4. [PubMed: 17159833]

39. McHugh JA, Cullison S, Apuzzio J, Block JM, Cohen C, Leong SL, et al. Chronic hepatitis B infection: a workshop consensus statement and algorithm. *J Fam Pract.* 2011; 60:E1–8. [PubMed: 21901174]
40. Cohen C, Holmberg SD, McMahon BJ, Block JM, Brosgart CL, Gish RG, et al. Is chronic hepatitis B being undertreated in the United States? *J Viral Hepat.* 2011; 18:377–83. [PubMed: 21143343]
41. Management Sciences for Health. International Drug Price Indicator Guide. 2012.
42. UNICEF. Vaccine Price Data: Hep B. 2012.
43. Centers for Disease Control and Prevention. Cost of vaccinating refugees overseas versus after arrival in the United States, 2005. *MMWR.* 2008; 57:229–32. [PubMed: 18322445]
44. Aggarwal R, Ghoshal UC, Naik SR. Assessment of cost-effectiveness of universal hepatitis B immunization in a low-income country with intermediate endemicity using a Markov model. *Journal of hepatology.* 2003; 38:215–22. [PubMed: 12547411]
45. Custodio H, Mirza A, Salahuddin A, Ferguson K, Rathore M. Cost-effectiveness of hepatitis B serology testing before hepatitis B vaccination in the Akha tribal children in northeastern Thailand. *The Pediatric infectious disease journal.* 2011; 30:725. [PubMed: 21750450]
46. Lee TA, Veenstra DL, Iloeje UH, Sullivan SD. Cost of chronic hepatitis B infection in the United States. *Journal of clinical gastroenterology.* 2004; 38:S144–7. [PubMed: 15602162]
47. Personal communication, Michelle Weinberg. Medical Officer, Division of Global Migration and Quarantine, Centers for Disease Control and Prevention. Dec 1. 2012



**Figure 1.**

Markov Model for chronic HBV infection

Note: Individuals begin in one of the following states: chronic HBV infection, delayed clearance, inactive carrier, or compensated cirrhosis. Individuals may transition among states or remain in the same state annually throughout the duration of the analysis (5 years, 10 years, or 15 years). Individuals may also transition to a 'death from background causes' state from any Markov state except 'HBV-related death,' starting in the second year (not shown).

**Table 1**

Parameter Estimates for Chronic HBV Prevalence and Annual Disease Transition Rates for Early Treatment-related Progression and Natural Progression of Disease for Cost-Benefit Model

Parameter	Value	Sources
<b>HBsAg positivity</b> ( 6 years of age)	0.071	GDPH, MDH <sup>a</sup>
<b>Follow-up with liver specialist given chronic HBV diagnosis</b>	0.60	[17]
<b>Initial states for Markov Model among persons HBsAg-positive test results</b>	<b>Value</b>	<b>Sources</b>
Inactive carrier	0.75	Assumed
Chronic HBV	0.212	Assumed
Compensated cirrhosis	0.038	Assumed
<b>Treatment Probabilities</b>	<b>Annual Rate</b>	<b>Sources</b>
Inactive carrier →Delayed clearance	0.00425	[19, 25]
Inactive carrier →Chronic HBV	0.02	[17, 19]
Inactive carrier → Hepatocellular carcinoma	0.003	[17, 19]
Chronic HBV→Inactive carrier	0.3	[17, 19, 25, 29]
Chronic HBV→Delayed clearance	0.008	[25]
Chronic HBV→Compensated cirrhosis	0.0045	[18]
Chronic HBV→Hepatocellular carcinoma	0.002	[18]
Chronic HBV→HBV Death	0.00002	Assumed
Compensated cirrhosis →Inactive Carrier	0.165	[18]
Compensated cirrhosis →Decompensated cirrhosis	0.02	[18, 28]
Compensated cirrhosis →Hepatocellular carcinoma	0.016	[18, 28]
Compensated cirrhosis →HBV Death	0.024	[18]
Decompensated cirrhosis→ Liver transplantation	0.06	[17,19]
Decompensated cirrhosis→Hepatocellular carcinoma	0.2	[17, 19, 28]
Decompensated cirrhosis→ HBV death	0.173	[17, 19, 28]
Hepatocellular carcinoma→Liver transplantation	0.15	[17, 19, 28]
Hepatocellular carcinoma→HBV death	0.35	[17, 19, 28]
Liver transplantation→ HBV death	0.066	[17, 19, 28]
Default treatment <sup>b</sup>	0.10	Assumed
<b>Natural Progression Probabilities</b>	<b>Annual Rate</b>	<b>Sources</b>
Inactive Carrier→Delayed Clearance	0.00425	[19, 25]
Inactive Carrier→Chronic HBV	0.02	[17, 19]
Inactive Carrier→Hepatocellular carcinoma	0.003	[17, 19]
Chronic HBV→Inactive carrier	0	Assumed
Chronic HBV→Compensated cirrhosis	0.038	[17, 19, 25]
Chronic HBV→Hepatocellular carcinoma	0.01	[17, 19, 25]

Parameter	Value	Sources
Chronic HBV→HBV Death	0.00002	Assumed
Compensated cirrhosis→Decompensated cirrhosis	0.073	[17, 19, 25, 28]
Compensated cirrhosis→Hepatocellular carcinoma	0.034	[17, 19, 25, 28]
Compensated cirrhosis→HBV death	0.049	[17, 28]
Decompensated cirrhosis→Hepatocellular carcinoma	0.06	[17, 19]
Decompensated cirrhosis→Liver transplantation	0.2	[17, 19, 28]
Decompensated cirrhosis→ HBV death	0.173	[17, 19, 28]
Hepatocellular carcinoma→Liver transplantation	0.15	[17, 19, 28]
Hepatocellular carcinoma→HBV death	0.35	[17, 19, 28]
Liver transplantation transition→HBV death	0.066	[17, 19, 28]
Enter treatment <sup>c</sup>	0.02	[20]

<sup>a</sup> GDPH: Georgia Department of Public Health; MDH: Minnesota Department of Health. This rate accounts for the difference in composition between refugees arriving in Georgia and Minnesota relative to refugees arriving in the entire United States. See online appendix for details.

<sup>b</sup> Rossi et al. assumed an annual rate of 10% and considered a range of 0–20% in their sensitivity analysis.

<sup>c</sup> This annual rate of patients entering treatment assumes that patients enter treatment for reasons unrelated to overseas screening or screening during comprehensive exams shortly after arrival.

**Table 2**

Cost Estimates for Overseas Screening and Domestic Treatment of Chronic HBV Infection for Cost-Benefit Model

Program Costs	Material Cost (2012 US\$)	Cost (2012 US\$, plus 100% Overhead) *	Source
Rapid Screening Test Kit	\$0.74	\$1.49	[41]
Vaccine (3 doses)	\$0.90	\$1.80	[42]
Annual Chronic HBV Treatment Costs	Unadjusted Cost	Adjusted Cost (2012 US\$)	Source
Initial US Medical Visit **	\$113	\$119	[Unpublished data]
Inactive Carrier	\$750	\$790	[17]
Chronic Hepatitis	\$12,591	\$13,267	[32]
Compensated Cirrhosis	\$13,196	\$13,904	[32]
Decompensated Cirrhosis	\$23,829	\$25,108	[32]
Hepatocellular Carcinoma	\$38,715	\$44,048	[28]
Liver Transplant	\$156,758	\$167,143	[17, 28]
Transplant Recovery	\$24,065	\$27,218	[17, 28]

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

\*\* One time cost; includes domestic screening test cost

**Table 3**

Descriptive Statistics for Study Cohort of Refugees Newly Arriving to Minnesota and Georgia during 2005–2010

Variable	All Ages (N=22,675)	Ages 6+ (N=21,409)
<b>AGE, Mean (SD)</b>	26.1 (16.5)	27.4 (16.0)
<b>Age Category (years), n(%) *</b>		
<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 (65.4)
<b>Female, n (%)</b>	10,966 (48.4)	10,334 (48.3)
<b>REGION, n (%) *, **</b>		
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 (0.0)	11 (0.1)
West Asia	16 (0.1)	15 (0.1)
<b>HBsAg, n (%)</b>		
Positive	1,546 (6.8)	1,515 (7.1)
Negative	21,129 (93.2)	19,894 (92.9)
<b>Vaccinated ( 1 dose), n (%)</b>	7,226 (31.9)	6,557 (30.6)

\* Numbers may not add up to 100% due to rounding

\*\* Missing = 1

**Table 4**

Estimated Annual Number of Refugees 6 years of age entering the United States who are infected with HBV, by arrival year

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

**Table 5**

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\$)

Domestic Screening rate (%)	Years since implementation	VO cost/refugee	SVIM cost/refugee	Net Benefit per refugee, no mortality valuation <sup>a</sup>	Total Net Benefit, no mortality valuation <sup>b</sup>	Number of HBV-associated deaths averted <sup>c</sup>	Total net benefit, with mortality valuation <sup>d</sup>
<b>30</b>	5	\$235	\$337	(\$102)	(\$6,000,000)	28	\$130,000,000
	10	\$535	\$622	(\$87)	(\$5,100,000)	72	\$300,000,000
	15	\$841	\$875	(\$34)	(\$1,990,000)	112	\$450,000,000
<b>50 (base case)</b>	5	\$297	\$337	(\$40)	(\$2,300,000)	20	\$90,000,000
	10	\$592	\$622	(\$30)	(\$1,800,000)	51	\$220,000,000
	15	\$883	\$875	\$8	\$470,000	80	\$320,000,000
<b>70</b>	5	\$358	\$337	\$21	\$1,200,000	12	\$24,000,000
	10	\$649	\$622	\$27	\$1,600,000	31	\$130,000,000
	15	\$925	\$875	\$50	\$2,930,000	48	\$200,000,000
<b>90</b>	5	\$420	\$337	\$83	\$4,900,000	4.1	\$24,000,000
	10	\$706	\$622	\$84	\$4,900,000	10	\$49,000,000
	15	\$968	\$875	\$93	\$5,440,000	16	\$70,000,000

<sup>a</sup> Net benefit = VO cost/person – SVIM cost/person

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

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

<sup>d</sup> Mortality Valuation: Value of Statistical Life = \$5 million